**Background:** Nasal colonization of Staphylococcus aureus (S. aureus) is a well-defined risk factor for subsequent infection. This study aimed to identify the host factors for S. aureus colonization and possible associated factors with the virulence factor Panton-Valentine Leukocidin (PVL) genes.

**Methods:** In a hospital-based study in Kaohsiung from Oct 2005 to Dec 2010, we performed nasal swab in the healthy children aged 2 to 60 months. We examined the relationship between the demographic characteristics and S. aureus nasal colonization. Methicillin-resistant Staphylococcus aureus (MRSA) isolates were further analyzed for antimicrobial susceptibility and molecular characteristics.

**Results:** Among 3280 children, 933 (28.4%) children had S. aureus nasal colonization. Of 933 isolates, 246 (26.4%) isolated were MRSA. The nasal colonization rate ranged from 16.3% in the second quarter (Q2) of 2007 to 34.6% in Q4 of 2009. The carriage rate of both MSSA and MRSA was significantly higher among children aged 2 to 6 months old (35.6% for MSSA and 11.1% for MRSA). MRSA colonization was significantly associated with several demographic factors. Breastfeeding, Streptococcus pneumoniae colonization, prematurity, upper respiratory tract infection within 2 weeks, receiving antibiotics within 2 weeks were protective factors against MSSA colonization, while breastfeeding and influenza vaccination were protective factors against MRSA colonization. Antibiotic susceptibility rate of MRSA was 100% to vancomycin and teicoplanin, 98.8% to trimethoprim-sulfamethoxazole, 12.6% to clindamycin, and 8.9% to erythromycin. Ninety-four percent of MRSA isolates carried either type IV staphylococcal cassette chromosome mec (SCCmec) or SCCmec VT and 87% belonged to the local community strains, namely clonal complex 59/SCCmec IV or VT. MRSA isolates with absence of the PVL genes was associated with children with passive smoking.

**Conclusions:** Between 2005 and 2010, nearly 30% of healthy children in southern Taiwan had nasal carriage of S. aureus, with one-fourth being MRSA, mostly local community strains, and the carriage was significantly associated with several demographic factors.

**Background:** Recent reports have shown increasing infection rate of community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) worldwide which is well known to be associated with nasal MRSA colonization. In Taiwan, different studies from 2001 to 2006 disclosed the MRSA colonization rate of Northern healthy Taiwanese children ranged from 1.9% to 9.5%. We conduct a population surveillance for the updated MRSA colonization rate in pediatric group from Northern Taiwan. Further drug resistance and molecular analysis are also studied.

**Methods:** From July 2005 to December 2010, all children of ages between 2 months and 5 years who presented for a well-child health care visit to Chang Gung Memorial Hospital at Linko, a medical centers in Northern Taiwan, or from kindergarten/daycare center were invited to participate in this study. All S. aureus isolates from anterior nares were sent to Chang Gung Memorial Hospital at Linko for microbiological characterization. Pulsed-field gel electrophoresis (PFGE) with SmaI digestion, SCCmec typing, and the detection of Panton-Valentine leukocidin (PVL) genes were performed. Some isolates of representative PFGE patterns were selected and underwent multilocus sequence typing (MLST).

**Results:** From July 2005 to December 2010, a total of 3281 children in Northern Taiwan, aging form 2-month-old to 5-year-old, were screened for nasal carriage of S. aureus. The overall prevalence of S. aureus nasal carriage was 28.3%, with 35.6% MRSA (10.1% MRSA of healthy Taiwanese children). Of the 331 MRSA isolates, a total of 12 pulsed-field gel electrophoresis (PFGE) patterns with two major patterns (C [47%] and D [29%]) were identified. Two hundred thirty-four isolates (71%) contained type IV staphylococcal cassette chromosome mec (SCCmec) DNA, and 84 isolates (25%) contained SCCmec VT. The presence of Panton-Valentine Leukocidin (PVL) genes were detected.
in 88 isolates (27%). Most MRSA isolates belonged to one of two major clones, characterized as sequence type 59 (ST59) clonal complex/PFGE C/SCCmec IV/absence of PVL genes (46%) and ST59/PFGE D/SCCmec VT/presence of PVL genes (22%). An emerging clone as ST573/PFGE U/SCCmec IV/absence of PVL genes was founded after 2007(7%).

**Conclusions:** We concluded that between 2005 and 2010, 10.1% of healthy Taiwanese children were colonized by MRSA in nares. Except for the previous known major clones from Taiwan, another emerging clone is gradually disclosed.

### Longitudinal Investigation of Nasopharyngeal Methicillin-Resistant Staphylococcus Aureus Colonization in Early Infancy: The PATCH Birth Cohort Study

**Methods:** A birth cohort study was conducted since January 2012. Nasopharyngeal swabs for S. aureus detection were collected at each planned visit during the first 12-month study. The prevalence of S. aureus colonization decreased in the first year of life, ranging from 98.7% at the age of 1 month to 40.7% at 12 months, and more than 50% cases were indistinguishable genotypes. Of the mothers with MRSA colonization, 61.1% had colonies with methicillin-resistant S. aureus (MRSA) only, and among persistent MRSA carriers, 61.1% had indistinguishable genotypes. Of the mothers with MRSA colonization, 77.1% had infants who were concomitantly colonized at the age of 1 month; 79.4% of the infant-mother paired isolates belonged to indistinguishable or related subtypes, which suggests that mother-to-infant transmission is possibly more common for MRSA acquisition in early infancy.

**Conclusions:** S. aureus colonization including MRSA was commonly observed in our cohort. Besides, strains of persistent MRSA among infant-mother pairs were usually of indistinguishable genotypes. Therefore, horizontal spread within households, particularly mother-to-infant transmission, is possibly an important factor related to infant MRSA colonization.
associated with fatality included male children (case-fatality rate in male vs. female: 62% vs. 52%, \(p<0.001\)), and preexisting infection.

**Conclusions:** The incidence of bloodstream infections during ECMO support was not low, GNB and candida species were most common. Male children and children with infection had a significantly higher case-fatality.

5 Predictive Value of Thomsen-Freidenreich Antigen Activation in Children with Parapneumonic Effusions

Thomsen-Freidenreich Antigen (TA) present on erythrocytes, platelets, and glomeruli and can be exposed when pneumococcal infection. The aim of this study is to investigate the predictive value of TA activation in relation to pneumococcal infection and the severity of parapneumonic effusions.

**Methods:** TA was testing routinely in patients who had lobar pneumonia with or without PPE at Department of Pediatrics, Mackay Memorial hospital from January 2010 to December 2015. We retrospectively reviewed charts and the age, gender, etiologies of infection, chest tube insertion or video-assisted thoracoscopic decortications (VATS), length of hospital stay, T activation, hemoglobin, white blood cell counts, platelet and C reactive protein were recorded and analyzed.

**Results:** A total of 142 children with lobar pneumonia with or without PPE were enrolled, including 35 empyema, 31 effusions, 11 necrotizing pneumonia and 14 lung abscess. The female-to male ratio was 1.02 and the mean age was 56.2 ± 31.1 months. Streptococcus pneumoniae was the most common bacterial pathogen. A total of 47 patients (33%) need chest tube insertion and 18 of them (12.6%) eventually underwent decortication. 19 patients (13.3%) were managed by VATS directly. The length of stay was 10.6 ± 8.1 days. 29 patients (20.4%) need ICU care, and the length of ICU stay was 7.24 ± 5.8 days. 22 patients (15.4%) had TA activation and their mean age was 41.8 ± 15.0 months. Among them, 12 patients (54.5%) was Streptococcus pneumoniae 19A, 3 patients (13.6%) was Streptococcus pneumoniae 3, 1 patient (4.5%) was Streptococcus pneumoniae 6A, and 6 patients (27.2%) was unknown in serotype. In patients with lobar pneumonia with or without PPE, TA activation had 100% specificity and 100% positive predictive value for pneumococcal infection.

In the multivariate analyses, TA activation (OR, 15.8; 95% CI, 3.0–83.5; \(P = 0.001\)), fever duration before admission (OR, 1.2; 95% CI, 1.1–1.5; \(P = 0.013\)) and initial CRP level (OR, 1.1; 95% CI, 1.0–1.1; \(P = 0.004\)) were independent predictors of empyema.

**Conclusions:** TA activation is associated with higher severity in parapneumonic effusions. TA activation is a useful predictor of empyema and pneumococcal infection, and is helpful for early and rapid detection especially in culture negative parapneumonic effusions.

6 Non-typeable Streptococcus Pneumoniae Infection in a Medical Center

Thomsen-Freidenreich pneumococcal infection and the severity of parapneumonic effusions. Risk factors for empyema and severity of parapneumonic effusions were identified by logistic regression analysis. Male gender (OR, 1.2; 95% CI, 1.1–1.5; \(P = 0.013\)) and initial CRP level (OR, 1.1; 95% CI, 1.0–1.1; \(P = 0.004\)) were independent predictors of empyema.

**Conclusions:** TA activation is associated with higher severity in parapneumonic effusions. TA activation is a useful predictor of empyema and pneumococcal infection, and is helpful for early and rapid detection especially in culture negative parapneumonic effusions.
Pathogens Isolated from Hospitalized Children with Acute Infectious Diarrhea in a Medical Center in Central Taiwan

Yu-Lung Hsu1,2, Hsiao-Chuan Lin1, Ting-Yu Yen1, Tsung-Hsueh Hsieh1,2, Hsiu-Mei Wei1, Su-Fen Wu1, An-Chyi Chen1, Kao-Pin Hwang1, TPIDA4
Division of Pediatric Emergency, Children's Hospital of China Medical University1, Taichung, Taiwan; Division of Pediatric Emergency, Children's Hospital of China Medical University2, Taichung, Taiwan; Division of Pediatric Gastroenterology, Children's Hospital of China Medical University2, Taichung, Taiwan; Taiwan Pediatric Infectious Disease Alliance (TPIDA)3

Background: Pathogens of bacteria, viruses, or parasites can cause acute infectious diarrhea. In this study, we described the etiologic and epidemiologic findings of hospitalized children in a medical center in central Taiwan.

Methods: We collected the stool samples from children aged less than 18 years old who were diagnosed as acute diarrhea and admitted to Children's Hospital of China Medical University from January 2015 to December 2015. Taiwan Pediatric Infectious Disease Alliance (TPIDA) supplied the examination and technique for pathogen identification of stool samples.

Results: Stool samples were collected from 78 children. Forty-five samples were from boys and thirty-three from girls. The male to female ratio was 1.36:1. The mean age was 1.29 ± 0.9 years old. Norovirus was the most common viral pathogen detected in stool samples (19/78, 24.4%). Rotavirus was discovered in 6 stool samples (6/78, 7.7%). Non-typhoidal Salmonella was the most common bacterial pathogen identified from 15 samples (15/78, 19.2%), followed by Clostridium difficile (7/78, 9.0%) and Campylobacter (2/78, 2.6%). No any parasitic pathogen was found.

Conclusions: In 2015, Norovirus and Non-typhoidal Salmonella were the important pathogens in hospital children with acute infectious diarrhea in central Taiwan. Otherwise, Clostridium difficile and Campylobacter can also be identified in such patients.

The Differences of Risk Factors and Clinical Presentation between Campylobacter Gastroenteritis and Salmonella Gastroenteritis in Children Less than 5-year-old in Taiwan

Chien-Fang Tseng1,2, Hsin Chi2, Ching-Chuan Liu1, Yhu-Chering Huang4, Yi-Chuan Huang4, Nan-Chang Chiu2, Hsiao-Chuan Lin1,2, Yu-Huai Hoh7, Li-Min, Huang4 Chao A. Hsiung5
Taipei Hospital, Ministry of Health and Welfare1; Department of Pediatrics, MacKay Children's Hospital2; National Cheng Kung University Hospital3; Division of Pediatric Infectious Disease, Department of Pediatrics, Chang Gung Memorial Hospital4; Kaohsiung Chang Gung Memorial Hospital5; China Medical University Children's Hospital5; National Cheng Kung University Hospital6; Division of Pediatric, National Taiwan University Hospital7; National Health Research Institutes8

Background: Non-typhoid Salmonella and Campylobacter are two common causes of bacterial gastroenteritis in pediatric group. The purpose of this study is to identify the difference of risk factors and clinical presentation between Salmonella and Campylobacter infections.

Methods: All patients were collected from 10 medical centers in Taiwan, from January, 2014 to December, 2015. Cases were children under the age of 5, who were hospitalized due to acute gastroenteritis, and presented with at least 3 episodes of watery diarrhea or loose stool, and/or with vomiting within 3 days of hospitalization. Stool specimen was obtained from all cases. All specimens were sent to Center for Disease Control for pathogen identification. Questionnaire for clinical presentation, living environment and contact history were filled out.

Results: A total of 2482 hospitalized cases were collected in year 2014 and 2015, with stool specimen collected in 2392 cases. Among 2392 cases, 457 cases (positive rate: 19.1%) were culture-proved to be Salmonella and 54 cases (positive rate: 2.3%) were Campylobacter. In Salmonella group, 57.33% are male, and mean hospital stay was 5.01±2.15 days. In Campylobacter group, 64.81% are male, and mean hospital stay was 5.13±2.22 days. Analysis result found that mean fever days (4.25±2.26 vs 3.57±1.97, p=0.03), fever more than 2 days (362 vs 37, p=0.07), mean WBC 9.84±5.06 vs 11.21±5.06, p=0.04), CRP>10mg/dl (376 vs 41, p=0.04), and mean AST (41.89±24.93 vs 35.37±11.9, p=0.01) have significant difference between Salmonella group and Campylobacter group. As for living environment and diet content, breast milk ingestion within one week (35 vs 11, p=0.0021) and visited medical institutes in recent 1 week (270 vs 23, p=0.0186) have significant difference between two groups.
Conclusions: Compared with Salmonella gastroenteritis, Campylobacter gastroenteritis has shorter fever duration, higher WBC count, lower CRP level and lower AST level. More detailed differences between these two pathogen required further investigation.

9 Vaccine Effectiveness and Genetic Susceptibility to Rotavirus Gastroenteritis in Taiwanese Children

Ting-An Yang¹, Ju-Yin Hou¹, Chih-Jung Chen¹ ²
College of Medicine, Chang Gung University¹; Division of Pediatric Infectious Diseases, Department of Pediatrics, Chang Gung Memorial and Children’s Hospital²

Background: It has been proposed that human rotavirus recognizes the histo-blood group antigens (HBGAs) as ligands to establish infection. The diversity of HBGAs phenotypes in distinct ethnic groups may influence the susceptibility to rotavirus acute gastroenteritis (AGE) and vaccine effectiveness. The aim of this study was to evaluate the effectiveness of rotavirus vaccine and associations between the susceptibility to rotavirus AGE and the HBGAs among Taiwanese population.

Methods: A case-control study was conducted in northern Taiwan from April to December in 2015. Cases were children < 18 years old who were hospitalized because of diarrhea and found to have laboratory-confirmed rotavirus infection. Controls were healthy children matched to cases by age and gender. The distributions of HBGAs including secretor status, Lewis antigen and ABO blood types were determined by molecular methods.

Results: A total of 52 cases and 136 healthy controls were included. Rotavirus immunization was identified in 5 (10.0%) case and 79 (58.1%) controls, which gave a vaccine effectiveness of 92.3% (95% confidence interval 79.5% - 97.1%). The secretor and Lewis-positive genotype were more commonly identified in controls than in cases (98.1% versus 77.9%, P=0.05 for both). The distribution of ABO blood types did not differ significantly between cases and controls (P=0.541).

Conclusions: Secretor and Lewis-positive genotypes were significant parameters associated with increased risk of severe rotavirus infections in Taiwanese children. The illness can be prevented by vaccination with an effectiveness of more than 90 percent.

10 Subcellular Locations of Human Norovirus NTPase Protein could be Different

Ju-Bei Yen¹ ², Pei-Jium Chang³
Department of Pediatrics, Chang Gung Memorial Hospital¹, Chaiyi, Taiwan; Graduate Institute of Clinical Medical Sciences, Chang Gung University²

Background: Noroviruses (NVs) could be separated into five genogroups at least. NV genogroup 1 and 2 (GI and GII), called human noroviruses (hNVs) also, are the leading agents for nonbacterial gastroenteritis in human globally. However, detailed functions of non-structural proteins of hNVs are not confirmed due to lack of useful culture system. In this study, we tried using recombinant plasmid for protein expression in the human cells to study the interaction between the hNV NTPase protein and the human cells.

Methods: Human HKB5 cells were transfected by recombinant plasmids containing the coding sequences of NTPase proteins of NV G.I and G.II amplified from the hNVs collected in the Chia-yi area in Taiwan by primer design and PCR method. Antibodies for the hNV NTPase was produced after NTPase protein over-expression. Western blotting method was used to confirm the protein. Immunofluorescence (IF) analysis was used then to confirmed the subcellular localization of hNV NTPase in the human cells.

Results: NV G.I and G.II NTPase proteins localized in the cytoplasm as vesicle like structures in IF analysis. However, the vesicle structure disappeared if we performed the mitochondrial labeling. The C-ends of the G.II NTPase colocalized with the cellular mitochondrion.

Conclusions: Different subcellular localization the NTPase protein of NV G.I and G.II may be related to the different life cycle and virulences of these human noroviruses.

11 Serum Trough Levels of Five Parenteral Vancomycin Products in Taiwan

Ya-Wen Tsai¹, Yu-Chiang Wang¹, Shian-Sen Shie², Min-Chi Chen³, Chin-Jung Chen³
College of Medicine, Chang Gung University¹; Division of Infectious Diseases, Department of Internal Medicine, Chang Gung Memorial Hospital Linkou Medical Center²; Division of Pediatric Infectious Diseases, Department of Pediatrics, Chang Gung Memorial Hospital Linkou Medical Center³

Background: Concerns have recently emerged on the quality, potency and in vivo activity of generic vancomycin products. Vancomycin trough level (VTL) was the most
widely used pharmacodynamics parameter in monitoring the clinical efficacy and toxicity. It has not been previously evaluated if the VTL was different in patients receiving distinct vancomycin products.

**Methods:** The first VTL in each patient measured in a teaching hospital from 2005 to 2015 were retrieved from an electronic medical database. The patient's demographics, amount and interval of vancomycin administration and the vancomycin brands were collected. Across the 11 years, five products of vancomycin were sequentially used in this hospital, including the innovator (designated as VAN-Lilly) and four generic versions (designated as VAN-A, B, C and D). The distributions of VTL were compared between patients on distinct vancomycin products after matching the characteristic of patients, dosage and interval of vancomycin administration by propensity score.

**Results:** Of 8735 records of first VTL available for analysis, 669 (7.7%), 912 (10.4%), 3,090 (35.4%), 3,268 (37.4%) and 796 (9.11%) were respectively identified in patients on VAN-Lilly, VAN-A, VAN-B, VAN-C and VAN-D treatments. The VTL was associated with vancomycin products in pediatric group aged 1 month to 12 years with significance (P<0.0001), but only at borderline significance in other age groups (P = 0.0722, 0.5120, 0.0410 and 0.0986 in neonates, adolescents, young adults and elderly, respectively). The propensity score analysis in the pediatric group revealed that patients on Van-C had significantly higher VTL comparing to those on VAN-Lilly (P = 0.0001), VAN-A (P = 0.0008), VAN-B (P = 0.0002) and VAN-D (P = 0.0015). Further, the coefficient of variation of VTL was much greater in patients on VAN-C than those on the other 4 versions, suggesting unstable quality of this product.

**Conclusions:** A generic version of vancomycin generated significantly higher concentration and greater variation of VTL compared to the innovator and other generic vancomycin in Taiwanese children. The potential impact of the unstable quality on clinical efficacy and adverse effects of vancomycin needs further study.

12 Analysis of Strain-specific Anti-EV71 Human Antibodies
抗腸病毒71型抗體之分析

**Kuan-Ying A. Huang, Yhu-Chering Huang, Tzou-Yien Lin**
Division of Pediatric Infectious Diseases, Department of Pediatrics, Chang Gung Memorial Hospital

**Background:** Enterovirus 71 is a leading cause of hand, foot, and mouth diseases in children and has potential to cause severe neurological damages. Antibody-mediated immunity plays a significant role in limiting EV71-associated illnesses. It remains unclear about the profile of strain-specific anti-EV71 antibodies in humans.

**Methods:** Human B cell-derived monoclonal antibodies were produced from the EV71-infected patient. The breadth of antigenic specificity and function were analyzed by binding and neutralization assays. The sequences of antibody variable regions were compared and analyzed.

**Results:** Six antibodies from a EV71-infected child recognized EV71 of both genotypes B5 and C4 but only neutralize EV71 of genotype B5. These antibodies were highly clonal and had a unique heavy chain gene usage as VH4-39. Key amino acids in the immunoglobulin variable segment might take part in the binding/neutralization activity to EV71.

**Conclusions:** The immunological footprints of anti-EV71 antibody response in children could be dissected at the molecular level.

13 Risk Factors of eGFR Deterioration in Pediatric Chronic Kidney Disease: A Report from the Taiwan Pediatric Renal Collaborative Study
台灣兒童慢性腎臟疾病eGFR下降之風險因子研究

**Hsin-Hui Wang,1,2,3 Yu-Min Huang4, Yuan-Yow Chiou5, Yee-Hsuan Chiu6, You-Lin Tain7, Hsin-Hsu Chou8, Yi-Fan Wang9, Ching-Yuang Lin10**
Department of Pediatrics, Division of Pediatric Immunology & Nephrology, Taipei Veterans General Hospital1, Taipei, Taiwan; Department of Pediatrics, Faculty of Medicine2, and Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang-Ming University3, Taipei, Taiwan; Department of Statistics, Tunghai University4; Division of Pediatric Nephrology, National Cheng Kung University and Hospital5, Tainan, Taiwan; Department of Pediatrics, Kaohsiung Veterans General Hospital6, Kaohsiung, Taiwan; Division of Pediatric Nephrology, Kaohsiung Chang Gung Memorial Hospital and University7, Kaohsiung, Taiwan; Division of Pediatric Nephrology, Department of Pediatrics, Dittmanson Medical Foundation Chia-Yi Christian Hospital8, Chiai, Taiwan; Division of Pediatric Nephrology, Kaohsiung Medical University Hospital9, Kaohsiung, Taiwan; Clinical Immunological Center, Medical College and Hospital, China Medical University10, Taichung, Taiwan

**Background:** Chronic kidney disease (CKD) is a significant public health problem and may progress to end stage renal disease. Children are in formative stages of development and are particularly vulnerable to kidney injury and adverse effects, and therefore develop progressive CKD in adulthood. Identifying the risk factors of renal function deterioration in CKD will be helpful to delay renal progression, maintain renal function and reduce associated morbidity and mortality. This study examines the possible risk factors for renal function deterioration in children of CKD. The role of different etiology of CKD in disease progression was analyzed also.

**Methods:** Using data on the Taiwan Pediatric Renal Collaborative Study that followed Taiwanese children with
CKD across multiple clinical centers, we analyze the eGFR annual change and the longitudinal changes on the patients who had records on their first follow ups within a threshold of time since their entries. Regression trees analysis was used to identify the key features of diagnosis variables, comorbidities and family history regarding the eGFR change from the baseline values. Correlation analysis was conducted to assess the relations between the follow-up clinical variables and the changes of eGFR.

**Results:** Among the non-GN CKD group, male patients and patients who have initial presentations with proteinuria, high blood pressure, past UTI history and family history with ischemic heart disease tend to have higher annual deterioration of eGFR from the time of diagnosis to the first follow-up when undertaken within 2 to 3 years. Patients with higher values of SBP, lower values of serum calcium and lower body height are also found to be significantly associated with negative impact on eGFR from the time of diagnosis to the first follow-up. Family history of hypertension associated with more rapid eGFR deterioration on the later follow-up. For the GN CKD group, patients with initial presentations with edema and past history with UTI or blood transfusion tend to have higher annual deterioration of eGFR from the time of diagnosis to the first follow-up. In the later visits of follow-up, initial presentation with back pain and with history of blood transfusion may connect with higher annual deterioration of eGFR during the early years of CKD follow-up.

**Conclusions:** The risk factors for eGFR deterioration in initial presentations and later follow-up were identified in this study. We found the factors associated with eGFR deterioration are different in non-GN and GN group. These observations can provide valuable awareness to early predict disease progression, intensive treatment and improvement long term renal outcomes.

**The Effects of Everolimus on Tuberous Sclerosis Complex-associated Renal Angiomyolipoma: a Preliminary Report**

以愛伏治療結節硬化症合併腎臟血管肌肉脂肪瘤之成效—初步研究

Sz-Juin Shiu, Jeng-Dau Tsai, Ji-Nan Sheu
Department of Paediatrics, Chung Shan Medical University Hospital, Taichung

**Background:** Tuberous sclerosis complex (TSC) presents with multisystem benign neoplasm induced by dysregulation of the mammalian target of rapamycin pathway. This study aimed to examine the effects of oral everolimus with either at 2.5 or 5.0 mg daily on the treatment of TSC-associated renal angiomyolipoma (AML).

**Methods:** Between July 2012 and August 2015, patients with TSC-associated renal AML were selected for everolimus therapy protocol. An oral everolimus starting dose at 2.5 mg was administered daily, and was gradually increased the dose to 5.0 mg daily. All patients were evaluated using magnetic resonance imaging or computed tomography scanning at baseline, 12, 24, and 36 months after the start of treatment for measuring the changes of renal AML mass volume.

**Results:** Eight patients were finally enrolled for analysis in this study. Everolimus therapy had the statistically significant effect on the renal AML volume reduction during follow-up (P < 0.05). Renal AML mass volume reduction rates were 10.5-45.3% in four patients with everolimus 2.5 mg and 40.7-73.1% in four patients with everolimus 5.0 mg daily; the difference was statistically significant between the two groups (P < 0.05). Longitudinal follow-up for response to everolimus showed volume reduction rates to be around 10.5-73.1% in the initial 6-24 months after everolimus treatment, which remained stable during follow-up up to 36 months.

**Conclusions:** The results suggest that an oral everolimus therapy is effective and provides a non-invasive way to treat TSC-associated renal AML, and patients are likely to require maintenance therapy to continue to derive benefit.

**Health-related Quality of Life in Children and Adolescents with Chronic Kidney Disease: EQ-5D-Y**

利用EQ-5D-Y分析慢性腎臟病兒童和青少年的健康相關生活品質

You-Lin Tain¹, Chien-Ning Hsu²
Department of Pediatrics¹, Department of Pharmacy², Kaohsiung Chang Gung Memorial Hospital, Chang Gung University, College of Medicine, Taiwan

**Background:** Thirty to sixty percent of children and adolescents required dialysis and kidney transplantation was associated with childhood onset chronic kidney disease (CKD); importantly, many of them are asymptomatic at early stage of kidney disorder. Although research on health-related quality of life (HRQOL) in children and adolescents is increasing, studies examining perceived physical and mental health outcomes are still limited in childhood onset CKD. This study aims to examine the HRQOL among children and adolescents with mild to moderate CKD and its associations with CKD complications.

**Methods:** A cross-sectional study was conducted among children and adolescents with CKD in the pediatric nephrology clinic at a medical center in Taiwan during 2014-2016. HRQOL of pediatric patients with CKD was evaluated at study entry and 6 months of follow-up among patients aged 7 to 17 using EQ-5D-Y (Youth version). The EQ-5D-Y is an EQ-5D-3L self complete version for children and adolescents aged 7 to 17 using EQ-5D-Y (Youth version). The respondent is asked to indicate his/her health state in each of the 5 dimensions. The EQ V AS records the respondent’s self-rated health on a vertical visual analogue scale (0 to 100) as a quantitative measure of health outcome.
**Results:** We assessed 92 samples using EQ-5D-Y for 63 children and adolescents with CKD stage 1 to 3. Less than 5% samples recorded problems (some or extreme) with “mobility” and “self-care”, 9.8% for “usual activities”, 16.3% for “pain/discomfort” and 15.2% for “happiness/worry/sadness. Children and adolescents with 4-6 complications, the self-rated EQ-5D-Y visual analogue score was significantly lower (77.09 ± 21.26) than those who with 0-1 items (89.27 ± 10.7) or 2-3 items (89.56 ± 9.19) complications (p<0.05). The worsening HRQOL was significantly associated with growth retardation, mineral and bone disorders, anemia, proteinuria and respondents with non-CAKUT of CKD.

**Conclusions:** The study identified the importance of general pediatric care to specialized assessments and interventions to optimize treatment continuum for children with CKD in the health care system. Despite HRQOL reduction, ED-5D-Y is useful to evaluate how renal impairment affects what dimension of health utility, which may ultimately help in the design and implementation of therapeutic interventions and social support.

**16 Novel VDR Gene Mutation R343H Responsible for Vitamin D-Resistant Rickets with Alopecia**

新的維生素D接受體基因突變導致維生素D抗性的僞症之功能分析

Min-Hua Tseng¹, Fu-Sung Lo², Shih-Ming Huang³, Shih-Hua Lin⁴
Division of Pediatric Nephrology, Department of Pediatrics, Chang Gung Memorial Hospital-Chang Gung University; Division of Pediatric Endocrinology, Department of Pediatrics, Chang Gung Memorial Hospital-Chang Gung University; Biochemistry Department, National Defense Medical Center; Division of Nephrology, Department of Medicine, Tri-Service General Hospital

**Background:** Hereditary vitamin D-resistant rickets (HVDRR) is an autosomal recessive disorder caused by vitamin D receptor (VDR) gene mutation featuring hypocalcemic and hypophosphatemic rickets with or without alopecia. Despite more than 50 VDR mutations reported, the study of the VDR mutant on RXR-binding domains remains very rare. This study was to identify the VDR gene mutation in a family with HVDRR and alopecia, and determine the mechanisms of this VDR mutant causing the phenotype.

**Methods:** The genotype and phenotype with follow-up in a Taiwanese family with HVDRR were performed. In vitro studies included situ-directed mutagenesis for expression of mutant VDR constructs, fluorescence microscopy for the nuclear localization of different enhanced green fluorescent protein-tagged VDR proteins, and luciferase reporter driven by the human CYP24A1 gene promoter for measuring transactivation event of VDR. E420A mutant VDR was used as a positive control.

**Results:** A novel homozygous R343H mutation in the exon 11 of VDR were identified in the proband and his affected sister and not found in 100 healthy controls. Supraphysiological dose of active vitamin D3 and calcium supplement therapy improved their biochemical and radiographic abnormalities but not alopecia. Both R343H and E420A mutants did not eliminate the expression of VDR by using antibody against HA-tag. Compared with E420A, R343 H did not change the conformation of VDR by utilizing antibody against VDR C-terminal region. This mutant also did not affect normal nuclear localization of VDR, but actually impair the CYP24A1 promoter activity in the presence of 1,25 (OH)2 vitamin D3.

**Conclusions:** Although novel VDR R343H mutation in HVDRR does not affect the expression, conformation, and nuclear location of VDR, it impairs the transcriptional activity of VDR on downstream transcriptional events and may account for typical clinical features with alopecia.

**17 Aliskiren Administration during Early Postnatal Life Sex-Specifically Alleviates Hypertension Programmed by Maternal High Fructose Consumption**

性別差異對產後早期腎素抑制劑治療減輕高果糖飲食母鼠所生之後代產生程序化高血壓的影響

You-Lin Tsai¹, Chien-Ning Hsu², Julie Y.H. Chan¹, Steve Leu³, Kay L.H. Wu³, Wei-Chia Lee⁴
Department of Pediatrics¹, Department of Pharmacy², Institute for Translational Research in Biomedicine³, and Division of Urology⁴, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University, College of Medicine, Taiwan

**Background:** An increase in fructose consumption over the past 2 decades has been linked to a rise in metabolic syndrome comorbidities, such as hypertension. Maternal high fructose (HF) intake induced renal programming and hypertension in male adult offspring. We examined whether maternal HF intake causes programmed hypertension and whether aliskiren administration confers protection against the process in a sex-specific manner, with a focus on the transcriptome changes in the kidney using next-generation RNA sequencing (NGS) technology and renin-angiotensin system (RAS).

**Methods:** Pregnant Sprague–Dawley rats received regular chow or chow supplemented with 60% fructose throughout pregnancy and lactation. Offspring were assigned to six groups: male control, male HF (MHF), MHF+Aliskiren, female control, female HF (FFH), and FFH+Aliskiren. Oral aliskiren 10 mg/kg/day was administered via gastric gavage between 2–4 weeks of age. Rats were sacrificed for histology at 12 weeks of age. Kidney cortex samples (n=3/group) were used for RNA next-generation sequencing (NGS) analysis.

**Results:** Maternal HF intake induced programmed hypertension in 12-week-old offspring of both sexes. HF regulated renal transcriptome and RAS components in the offspring kidney in a sex-specific manner. Maternal HF
intake induces a greater change in renal transcriptome in females than males at 1 week of age. Aliskiren administration prevented HF-induced programmed hypertension in both sexes of adult offspring. Aliskiren administration increased angiotensin converting enzyme 2 (ACE2) and the angiotensin (1-7) receptor MAS protein levels in female kidneys exposed to maternal HF intake.

**Conclusions:** Maternal HF induced programmed hypertension in both sexes of adult offspring, which was sex-specifically mitigated by early aliskiren administration. Better understanding of the sex-dependent mechanisms that underlie maternal HF-induced renal programming will help develop a novel sex-specific strategy to prevent programmed hypertension.

**Post-Weaning High-Fat Diet Sex-Specifically Accelerates the Development of Obesity, Kidney Injury, but not Hypertension Programmed by Maternal High-Fat Consumption**

Sex differences during lactation and high-fat diet (HF) intake led to a variety of chronic diseases in adult offspring, including obesity, hypertension, and kidney disease. Sex differences and dysregulated circadian clock have been observed in obesity and related disorders. We therefore hypothesized that post-weaning high saturated fat diet would exacerbate offspring vulnerability to maternal HF-induced programmed hypertension and kidney disease in a sex-specific manner, with a focus on the kidney circadian clock.

**Methods:** Female Sprague-Dawley rats were assigned to receive either a normal diet (ND) or HF diet (D12331, Research Diets) for 5 weeks before mating and during gestation and lactation. The offspring of both sexes were either the ND or HF diet from weaning to 6 months of age, resulting in four experimental groups of each sex (maternal diet/post-weaning diet; n=6/group): ND/ND, ND/HF, HF/ND, and HF/HF.

**Results:** In males, post-weaning diet increased BW of both ND/HF and HF/HF animals from 3 to 6 months. In contrast, significant BW gain was not shown in female offspring fed with HF diet. As compared to ND/ND group, both maternal and post-weaning HF intake increased plasma levels of AST and ALT in both sexes. Offspring exposed to post-weaning HF showed greater degrees of glomerular and tubular injury compared to the ND/ND group, which were exacerbated by maternal HF exposure in both sexes. Prenatal exposure to HF significantly upregulated mRNA expression of the positive element Baml, negative elements (Cry1 and Per2), and clock-controlled gene (Ckle and Nr1d1) in females. However, clock and clock-controlled genes tended to be unaltered by maternal HF consumption. Post-weaning HF diet significantly downregulated mRNA level of most clock and clock-controlled genes in the males (All Ppos <0.05), with the exception of Cry1 and Cry2. In females, post-weaning HF diet led to the downregulation of the Baml, Ckle, Cry1, and Per1.

**Conclusions:** Post-weaning HF diet sex-specifically accelerates the development of obesity, kidney injury, but not hypertension programmed by maternal HF intake. Better understanding of the sex-dependent mechanisms that underlie HF-induced renal programming and disturbed circadian rhythm will help develop a novel sex-specific strategy to prevent obesity and related disorders.

**18 Genetic Study of Type 1 Hereditary Angioedema and its Relationship with Clinical Manifestations in Taiwan**

Hereditary angioedema (HAE) is a rare, autosomal dominant disorder characterized by recurrent, self-limiting subcutaneous and submucosal edema involving face, limbs and gastrointestinal tract. Three types of HAE were classified: type 1 and type 2 are caused by the antigenic and functional defect of C1 esterase inhibitor (C1INH), and type 3 is related to factor XII mutation. 32 cases of HAE from 11 families were diagnosed in Taiwan. In this report, 20 cases of type 1 HAE from 8 families with genetic confirmation will be analyzed with their clinical manifestations and outcomes.

**Methods:** 20 cases of type 1 HAE from 8 families with genetic confirmation were enrolled in this report. We analyze the relationship between their different genetic mutations with their clinical manifestations.

**Results:** 16 male and 16 female patients from 11 families had low serum C4 levels were diagnosed to have HAE, 30 patients with low C1 INH were diagnosed to have type I HAE and 2 patients with elevated C1 INH were diagnosed to have type II HAE. Among patients with type 1 HAE, 20 patients from 8 families had genetic confirmation and their mutation of C1INH gene on exon 3, 4, 5, 6, 8 were found. 14 of these 20 patients (70%) are symptomatic and all experience limb and trunk swelling. 7 patients (35%) experience laryngeal edema and 5 patients (25%) suffered from abdominal symptoms. The mortality rate is 15% and asphyxia due to laryngeal edema is the only cause of death. The onset age of clinical presentation ranged from 4 to 29 years (mean±SD: 15.8±7.4 years). The mean duration of delay in diagnosis is 14.2 years with SD of 14.8 years. One patient has no family history and both of his parents’ C4 levels are within normal limits.

**Conclusions:** The prevalence of HAE in Taiwan is low.
A Longitudinal Study on Acute Bronchiolitis and Subsequent Childhood Asthma

Pit-Yee Voo1, Jih-Chin Chang2,4, Jiunn-Liang Ko2, Ko-Haung Lue2,3, Hai-Lun Sun1,3, Pei-Fen Liao1, Min-Sho Ku1,3, Hui-Hsien Pan1, Yu-Tzu Lee2

Department of Pediatrics, Chung Shan Medical University Hospital1, Taichung, Taiwan; Institute of Medicine, Chung Shan Medical University2, Taichung, Taiwan; School of Medicine, Chung Shan Medical University1, Taichung, Taiwan; Chang Bing Show Chwan Memorial Hospital3, Changhua, Taiwan

Background: The symptoms of wheezing and dyspnea in acute asthmatic attacks are similar to bronchiolitis. Whether the occurrence times of bronchiolitis poses a risk for the development of asthma has not been clearly investigated. Objective: The aim is to analyze the relationship between acute bronchiolitis in children younger than 2 years of age and subsequent childhood asthma.

Methods: Design: This was a retrospective cohort study design. Children younger than 24 months who were diagnosed with acute bronchiolitis from 2001-2010 were retrieved from the National Health Insurance Research Database of Taiwan, and compared to subjects without bronchiolitis diagnosis with regards to asthma. Potential comorbidities and medical care conditions were also compared between two groups.

Results: In total, 67126 children were enrolled into analysis inclusive of 32887 exposure subjects compared with 34239 controls. The incidence of childhood asthma was significantly higher in the study group (13.95 v.s. 9.04 per 103 person years after propensity score match, p<0.001). The hazard ratio (HR) was highest (5.449, 95%CI : 3.143-9.448) for bronchiolitis outpatient visits more than three times and hospitalized more than twice before 24 months of age. Gender and atopic dermatitis have no adjust effect on hazard ratios of bronchiolitis with regards to asthma development.

Conclusions: Early bronchiolitis infection do increase the risk of developing subsequent childhood asthma, and more bronchiolitis episodes significantly increase the effect. Increased outpatient visit (>3 times) and hospitalization (>2 times) before 2 year-old pose most high risk of developing subsequent childhood asthma.
Obesity Disproportionately Impacts Lung Volume and Airflow in Taiwanese Children: PATCH Study

Background: Childhood obesity is a growing global health issue, while debate remains over the relationship between increasing weight status and lung function. The objective of this study was to investigate the influence of increasing weight status on lung function in Asian children in a population setting.

Methods: The study included a population sample of 1717 Asian children (mean age, 10.3 ± 2.6 years; male, 49%) in the Prediction of Allergies in Taiwanese Children (PATCH) study. Obesity, overweight and thinness were defined according to the age- and gender-specific BMI cut-off values from the International Obesity Task Force reference. Lung function was measured using spirometry.

Results: There were significant positive associations of BMI z-score with FVC, FEV1, and PEF (all P < 0.001), after controlling for confounders. In contrast, a significant negative association was found between BMI z-score and FEV1/FVC ratio (P < 0.001). BMI categories were significantly associated with FVC and FEV1/FVC ratio, after adjusting for confounders. Specifically, obesity was positively and significantly associated with FVC (P = 0.026), with a mean difference of 61.4 mL (SE, 27.5 mL) in FVC between the subjects with obesity and those with normal weight. In contrast, obesity and overweight were negatively significantly associated with FEV1/FVC ratio (P = 0.049 and P = 0.005, respectively). The mean difference in FEV1/FVC ratio between subjects with obesity and those with normal weight was 1.19% (SE, 0.61%) and the mean difference was 1.06% (SE, 0.37%) between with overweight and those with normal weight. Similar results were obtained when children with asthma were excluded from the analysis.

Conclusions: Our results demonstrate that increasing weight status is associated with an increase in FVC and a decrease in FEV1/FVC ratio in Taiwanese children. This study suggests that disproportionate increase of FVC and FEV1 with increasing weight may contribute to airflow decrease and consequently poorer lung function.

Prenatal Tobacco Smoke Exposure (TSE) Correlated to Frequent URIs in Infancy and Asthma in Childhood: A Birth Cohort Study

Background: In a birth cohort study of 1848 infants, we have found that maternal atopy and CIBIE elevation were associated with infant atopy (Liu & Yang, et al. Allergy. 2003;11:289-904). Infants fed with partially hydrolyzed infant formula decreased milk sensitization but not incidence of AD (Kuo & Yang, et al.Int Arch Allergy Immunol 2011;154:310-7). More interestingly, perinatal administration of probiotics (LGG) from 2nd trimester thru infancy did not increase the rate of infant wheezing episodes but significantly increased the frequency of URIs (p=0.007) in infants at 6 months of age did not decrease incidence of AD (Ou & Yang, et al. Clin Exp Allergy. 2012;42:1386-96). We also found that most of the infants developed AD before 6 months of age, and the children with persistent AD were associated with maternal smoking (99.9 vs. 0.1%). The prenatal TSE exposure (TSE) affects infant infectious diseases and childhood allergy diseases in the cohort population.

Methods: Pregnant women, parental history and family environment were prenatally recruited. At each postnatal follow-up visit from 0, 1.5, 3 to 6 years of age, questionnaire survey including feeding types and duration, parental smoking, housing styles and conditions, and episodes of respiratory tract infections and diarrhea, clinical examination and blood sample for total and specific IgE levels were collected. Aeroallergen sensitization was defined as a specific IgE level > 0.35 kU/L; food allergen sensitization was defined as a specific IgE level > 0.7 kU/L. Both univariate and multivariate analysis were performed.

Results: In the cohort study of 1848 infants, 1528 infants completed the questionnaire including data of prenatal TSE and 724 patients received a complete follow-up through 6 years of age. We found that 31.1% of children in the birth cohort prenatally exposed to TSE, mainly due to paternal but not maternal smoking (99.9 vs. 0.1%). The prenatal TSE did not increase the rate of infant wheezing episodes but significantly increased the frequency of URIs (p=0.007) in infants at 1.5 years of age. Prenatal TSE was not significantly associated with AD, AR or AS at 3 years of age. Prenatal TSE however significantly increased the rate of physician-diagnosed asthma (p=0.026) in children at 6 years of age. However, the prenatal TSE did not significantly
influence the IgE levels in cord blood or in children at 1.5, 3 or 6 years of age, suggesting a mechanism beyond IgE-mediated effect. To search potential mechanism beyond IgE production, we validated whether prenatal TSE influenced DNA methylation of immune differentiation, redox and/or regulation genes, LMO2, GSTM1 and/or IL-10, respectively. We found that prenatal TSE was significantly associated with LMO2 and IL-10 DNA methylation contents.

**Conclusions:** Results from this study suggest that prenatal TSE increased URIs in infancy and increased childhood asthma in a non-IgE-mediated mechanism, presumably thru an increase in DNA methylation of immune differentiation and regulation genes such as LMO2 and IL-10. This highlights that avoidance of prenatal TSE may decrease infant infectious diseases and childhood asthma.

**24 Seroconversion of Anti-nuclear Antibodies in Systemic Lupus Erythematosus**

患有紅斑性狼瘡之病人其抗核抗體陽轉陰特性之分析

**Yi-Chieh Chen**, Hsiang-Ru Liaw, Ming-Chin Tsai, Lin-Shien Fu, Chia-Hui Shen

Department of Pediatrics, Taichung Veterans General Hospital, Taichung, Taiwan; Clinical Informatics Research & Development Center of Taichung Veterans General Hospital

**Background:** Anti-nuclear antibodies (ANA) are antibodies which bind to the substance in the cell nucleus. They are related to a series of autoimmune diseases, such as systemic lupus erythematosus (SLE). This research is to study the clinical implications of patients diagnosed as SLE with seroconversion, that is, initial positive ANA became negative over time.

**Methods:** Database of Clinical Informatics Research & Development Center of Taichung Veterans General Hospital from January 1992 to June 2016 was exploited. Patients with rheumatic diseases who developed seroconversion of ANA were included. These patients were classified according to their initial ages when ANA showed positive, their genders, and the diseases they had. The clinical presentations and treatment courses were described.

**Results:** In the past 25 years, there were totally 3926 SLE patients, proved by registry of catastrophic illness in national health insurance. In terms of onset of these 3928 patients, 375 were pediatric; and 3551 were adult-onset. According to the data in our hospital, seroconversion of ANA developed in 8.3% (31/375) of pediatric SLE cases. Compared to the proportion of seroconversion of ANA in adult-onset SLE, which was 10.1% (358/3551), there was no difference (p = 0.26). There was no difference between female and male regarding to the proportion of seroconversion either, no matter in pediatric (p = 0.28) or adult-onset SLE (p = 0.97). The mean duration of seroconversion was 51.1 months in pediatric-onset SLE; and the mean period between initial positive ANA and seroconversion in adult-onset SLE was 42.4 months.

**Conclusions:** The preliminary results in our study revealed 8.3% to 10.1% of ANA seroconversion in documented SLE patients. The ANA pattern, as well as other clinical features attributing to seroconversion warrant detailed studies.

**25 Role of Tubulointerstitial Lesions in Predicting Renal Outcome among Pediatric Onset Lupus Nephritis – A Retrospective Cohort Study**

腎小管間質性病變在預測兒童紅斑性狼瘡腎炎預後的角色

Chao-Yi Wu, Hui-Ping Chien, Huang-Yu Yang, Tsung-Chieh Yao, Min-Hua Tseng, Mei-Chin Yu, Kuo-Wei Yeh, Jing-Long Huang

Division of Allergy, Asthma, and Rheumatology, Chang Gung Children’s Hospital, Taoyuan, Taiwan; Department of Pathology, Chang Gung Memorial Hospital, Taoyuan, Taiwan; Department of Nephrology, Chang Gung Memorial Hospital, Taoyuan, Taiwan; Division of Pediatric Nephrology, Chang Gung Children’s Hospital, Taoyuan, Taiwan

**Background:** The exact prevalence of tubulointerstitial abnormalities and its predictive value among pediatric onset systemic lupus erythematosus (pSLE) cases, however, remained unknown.

**Methods:** Sixty-seven pSLE subjects diagnosed with LN with initial renal samples available were enrolled and followed for an average of 6.43 ± 3.06 years. Renal histology was evaluated according to the International Society of Nephrology/Renal Pathology Society classification, National Institute of Health classification and tubulointerstitial activity index (TIAI).

**Results:** Tubulointerstitial injuries were observed in 38.81% of all LN cases, including 13.33% with non-proliferative lupus nephritis (nPLN) and 46.15% of with proliferative lupus nephritis (PLN). Tubulointerstitial injuries occurred solitarily in cases with nPLN (13.33%), but always associated glomerular changes and significantly impacted renal survival (p = 0.032) among those with PLN. TIAI associated glomerular abnormalities (p = 0.031) but did not correlate renal performance or subsequent outcome (p = 0.445). Among the chronicity index, it was the chronic tubulointerstitial lesions which provided prognostic information (p = 0.012). We observed a synergistic effect of all tubulointerstitial abnormalities rather than an individual factor attributed the prognostic utility (p = 0.025 vs. p = 0.083, 0.055, 0.354). Finally, considering tubulointerstitial injuries in PLN further discriminated subsequent renal outcome (p = 0.006).

**Conclusions:** The prevalence and clinical significance of tubulointerstitial abnormalities were similar among the pSLE and the adult population. With its importance in identifying those at risk of renal failure, histologic classification considering tubulointerstitial lesions may potentially assist outcome prediction.
CPPecp Decreases Eotaxin Secretion Stimulated by ECP

Yee-Huei Lin, Ming-Chin Tsai, Rain Wu1, Dah-Tsyr Chang1, Lin-Shien Fu
Department of Pediatrics, Taichung Veterans General Hospital; Department of Medical Science, Tsin-Hua University1

Background: The de novo cell penetrating peptide, a 10 amino acid derived from human eosinophil cationic protein (ECP), abbreviated as CPPecp, is a de novo peptide. In our previous balb/c mice study, we have demonstrated CPPecp decreased allergic airway inflammation. In previous studies, CPPecp did not interfere cell binding or penetration of ECP. So, this study is to study its working mechanism by in vitro study.

Methods: Airway epithelium cell line--BEAS-2B, cultured in DMEM-F12 medium, was treated as following 4 groups: control, 5ug CPPecp,5ug Der P, and 5ug Der P+5ug CPPecp. We measured mRNA expression and secretion(by ELISA) after 6hr and 12hr cultivation. Western blot for Stat-6 and NF-kB expression were proceeded for these 4 groups, and the treatment period was 15 minutes. We also used IL-4 as stimulant to check the p-Stat-6 expression. Analysis was performed with the Mann-Whitney U-test for comparison of two groups. Differences with a p value

Results: ECP stimulated eotaxin mRNA expression (p<0.001) and secretion(p<0.001). CPPecp significantly decreased eotaxin these effects when co-cultivated for 6 hours(p<0.01). These effects were concentration dependent. The peptide derived from protease K-digested ECP did not reveal any effect on this aspect.

ECP also increased p-Stat-6 expression after 15-minute incubation(p<0.001). P-Stat-6 expression can be decreased by co-culture with CPPecp(p<0.01). The effect was also concentration-dependent. CPPecp did not decrease NF-kB expression.

CPPecp also decreased p-Stat-6 expression stimulated by IL-4 in similar condition(p<0.01).

Conclusions: CPPecp can decrease eotaxin mRNA expression and secretion when stimulated by ECP in a concentration-dependent manner. The effect can be explained by the decreased p-Stat-6 signaling. In addition, digested ECP peptide cannot achieve such protective effect.

27 Fungal Immunomodulatory Protein-fve (FIP-fve) Reduce Airway Remodeling through TH17 Cell Modulation in OVA-sensitized Asthma Mouse Model

Hsu-Chuan Cheng1, Ko-Haung Lue1,2,3, Hai-Lun Sun1,3, Min-Sho Ku1,3, Pei-Fen Liao1, Hui-Hsien Pan1, Yu-Tzu Lee2, Jiunn-Liang Ko2
Department of Pediatrics, Chung Shan Medical University Hospital1, Taichung, Taiwan; Institute of Medicine, Chung Shan Medical University2, Taichung, Taiwan; School of Medicine, Chung Shan Medical University3, Taichung, Taiwan

Background: Asthma is a heterogeneous inflammatory disorder of the airway. Th2 response is usually contributed to high levels of allergen-specific IgE and eosinophilic airway inflammation. Recently, several findings demonstrated that neutrophils, not eosinophils, are the major inflammatory cells in chronic asthma patients with steroid-resistant. Th17 producing IL17 axis result in neutrophil inflammation and IL13/IL22 induce airway remodeling. Fungal immunomodulatory protein-fve (FIP-fve) exhibits anti-inflammatory properties on OVA-induced acute airway inflammation. We hypothesized that orally administrated FIP-fve should be able to reduce airway remodeling in chronic experimental models. In order to examine the hypothesis, the effects of oral FIP-fve treatments on asthma mouse model were evaluated during OVA-sensitization/challenges.

Methods: The study use 6-8 weeks female Balb/c mice and sensitization with OVA. FIP-fve was used in sensitized mice to investigate whether oral administrations of FIP-fve inhibited OVA-induced airway inflammation in a chronic asthma model. After intranasal challenges with OVA, the airway inflammation and hyper-responsiveness were determined by a BUXCO system. BALF was analyzed with Liu’s stain and ELISA assay. Lung histopathologic changes were assayed with H&E stain. Collagen precipitation was assayed with Masson’s trichrome stain. Lung tissues were assayed with PCR (TNF-a, RORt, Foxp3, IL-17, IL-22 and HMGB1). Moreover, many kinds of cytokines were detected in serum and BALF, kinds of cytokines were IL-4, IL-5, IL-13, IFN-r, IL-22 and IL17.

Results: FIP-fve significantly decreased the number of infiltrating inflammatory cells (Eosinophils, p=0.014) and Th2 cytokines were significantly decreased and increased Th1 cytokines in BALF and serum compared with the OVA sensitized mice. We also found that the oral FIP-fve group suppressed IL-17(p=0.021), TNF-a(p=0.001) and HMGB1 (p=0.003) in the RNA levels. In addition, oral FIP-fve inhibited inflammatory cell infiltration, and decreased collagen expression in lung tissues.

Conclusions: FIP-fve had anti-inflammatory effects on OVA-induced airway inflammation and reduced airway remodeling and collagen expression. Moreover, FIP-fve
A New Regulatory Function of Clara Cell 10-kd Protein (CC10) through Inhibition of Arachidonic Acid/Cyclooxygenase Pathway

Background: Clara cell 10-kd protein (CC10), the main secretory product of bronchiolar Clara cells, plays an important protective role in the respiratory tract against inflammatory processes. However, the mechanism by which CC10 exerts its anti-inflammatory effects remains unclear. This study aimed to determine the levels of serum CC10 and arachidonic acid (AA) metabolites in children with asthma in comparison to those of healthy children and to investigate the potential functional impact of CC10 in regulating AA/Cyclooxygenase (COX-2) pathway and its related lipid mediators in neutrophils.

Methods: Sera were sampled from 50 children (aged 9.7±0.1 years) with stable atopic asthma and 50 age-matched healthy controls (9.5±0.1 years). Enzymatic immunoassays (EIA) were used to measure CC10 and AA metabolites. In addition, the functional effect of CC10 on AA/COX-2 pathway in fMLP-stimulated neutrophils and the levels of its resultant metabolites were determined by Western blotting and EIA.

Results: A composite of serum CC10, PGE2 and 11β-PGF2α levels was significantly distinguishable between asthmatic and healthy subjects; also, a negative correlation was noted between the levels of CC10 and PGE2 (r=0.78; P<0.01). Functional studies revealed that fMLP-induced AA-metabolizing enzyme, COX-2, was significantly inhibited by CC10. Furthermore, CC10 was shown to be able to significantly inhibit fMLP-induced generation of AA metabolites, PGE2, in neutrophils.

Conclusions: These findings suggested that modulation of the COX-2 pathway in AA metabolism could be a novel mechanism for the anti-inflammatory effects of CC10.

High Cord Blood CCL22/CXCL10 Chemokine Ratios Precede Allergic Sensitization in Early Childhood-PATCH Study

Background: Atopic diseases are known to be characterized by a Th2-skewed immunity; however, there are few studies addressing the Th1/Th2 immunity at birth related to the development of atopic diseases in early childhood.

Methods: Children from a birth cohort in the Prediction of Allergies in Taiwanese Children study from birth through 4 years of age were enrolled. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.

Results: A total of 180 cord blood samples from 186 children regularly followed at the clinic for 4-year follow-up period were analyzed. The Th1-associated CXC chemokine ligand (CXCL)-10, CXCL11, and the Th2-associated CC chemokine ligand (CCL)-17 and CCL22 were quantified in cord blood by multiplex Luminex kits. Specific immunoglobulin E (IgE) antibodies against food and inhalant allergens were measured at 6 months as well as 1, 1.5, 2, 3, and 4 years of age.
The Analysis of Toll-Like Receptor Expression and Response in Encephalitis / encephalopathy Children Presenting with Refractory Epilepsy

Wen-I Lee, Jing-Long Huang, Kuo-Wei Yeh, Meng-Ying Hsieh, Jaimm-Jim Lin, Kuang-Lin Lin, Syh-Jae Lin, Li-Chen Chen, Liang-Shiou Ou, Tsung-Chieh Yao

Department of Pediatrics, Division of Allergy, Asthma, Immunology and Rheumatology, Division of Neurology, Division of Critical Care, Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taoyuan, Taiwan

Background: Defective human TLR3 signaling causes refractory herpes simplex encephalitis/encephalopathy. Children with encephalitis/encephalopathy presenting with refractory epilepsy may have defective TLR responses.

Methods: Children with encephalitis/encephalopathy and frequent seizure ≥ 3 episodes/day over 5 days refractory to two kinds of anti-epileptics drugs and status epilepticus were enrolled to evaluate TLR1-9 responses (IL-6, IL-8, INF-α, INF-γ) in their peripheral blood mononuclear cells (PBMCs) and monocyte-derived dendritic cells (MDDCs), compared to those non-refractory patients underlying febrile convulsion or with/without encephalitis/encephalopathy.

Results: Compared to the controls, five patients (1 female; 2-13 years) had impaired TLR3 (IL-6, IL-8, INF-α, INF-γ, and TNF-α) responses in their peripheral blood mononuclear cells (PBMCs) and monocyte-derived dendritic cells (MDDCs), compared to those non-refractory patients undergoing febrile convulsion or with/without encephalitis/encephalopathy.

Conclusions: Children with encephalitis/encephalopathy and refractory epilepsy but undetectable pathogens in their CSF have impaired TLR3, TLR4, TLR7/8, and TLR9 responses as well as possibly weakened phagocytosis and decreased T regulatory cells.
Transcriptomic Analysis of Fc Receptors in Kawasaki Disease

Background: Kawasaki disease (KD) is an acute systemic vasculitis affecting coronary arteries. Following the administration of 2 g/kg of intravenous immunoglobulin (IVIG) fever subsides rapidly in patients with KD. Mechanisms of action of IVIG are including blockade of Fc receptors on macrophages. Recent investigations have confirmed the association between KD and genetic polymorphisms, gene copy number, expression, and methylation in Fc gamma receptor genes. However, it is not clear whether the Fc receptors (FcR) relates to KD susceptibility. In this study, we characterize IgG, IgE and IgA receptor expression by analyzing clinical samples with GeneChip Human Transcriptome Array 2.0 (HTA 2.0).

Methods: A total of 18 KD patients and 18 healthy controls (HC) were enrolled for survey. RNA was extracted from cells in whole blood collected before (KD1) and 3 weeks after IVIG treatment (KD3). GeneChip® Human Transcriptome Array 2.0 was used with 6 cases pooling methods.

Results: We first examined Fc receptors expression in KD and normal children. KD individuals expressed remarkably high mRNA levels of Fcα RI, FcεRIG, FcγRIIA,B,C, FcγRIIA, TRIM21 (p<0.05). Whereas, the expression of FcγRIIB,C, FcγRIIA,B, FCGRT, and FcγRL5 in KD patients was similar to that of controls. In contrast, the expression of FcεRIG and FcγII expression in KD was significantly lower than in HC (p<0.001; p=0.001 respectively). Interestingly, FcεRIG and FcγRIIIA expression increased through the convalescent phase (p=0.001; p=0.007 respectively). Expression of Fcα RI, FcεRIG, FcγRIIA,B,C, FcγRIIA,B,C, FcγRIIIA,B,C, FcγRIIIA,B,C and TRIM21 decreased after IVIG administration (p<0.05). On the other hand, FCGRT and FcγRL5 expression did not show any significant change in the clinical course of KD.

Conclusions: This is the first study dealing with transcriptomic analysis of Fc receptors in Kawasaki disease and identifying the significantly higher transcriptional levels of Fcα RI and TRIM21, like FcγRI and FcεRIIA in patients with KD than in controls, and following IVIG treatment, mRNA expression were considerably reduced. The potential implication of the observed FcR expression patterns on the pathogenesis of KD warrants further mechanistic studies.

Role of Chronic Inflammation in Myopia Progression: Clinical Evidence and Experimental Validation

Background: Prevention and treatment of myopia is an important public problem worldwide. We found a higher incidence of myopia among patients with inflammatory diseases such as type 1 diabetes mellitus (7.9%), uveitis (3.7%), or systemic lupus erythematosus (3.5%) compared to those without inflammatory diseases (P<0.001) using data from children (<18 years old) in the National Health Insurance Research database.

Methods: We then examined the inhibition of myopia by atropine in Syrian hamsters with monocular form deprivation (MFD), an experimental myopia model.

Results: We found atropine downregulated inflammation in MFD eyes. The expression levels of c-Fos, nuclear factor κB (NFκB), interleukin (IL)-6, and tumor necrosis factor (TNF)-α were upregulated in myopic eyes and downregulated upon treatment with atropine. The relationship between the inflammatory response and myopia was investigated by treating MFD hamsters with the immunosuppressive agent cyclosporine A (CSA) or the inflammatory stimulators lipopolysaccharide (LPS) or peptidoglycan (PGN). Myopia progression was slowed by CSA application but was enhanced by LPS and PGN administration. The levels of c-Fos, NF-κB, IL-6, and TNF-α were upregulated in LPS- and PGN-treated eyes and downregulated by CSA treatment.

Conclusions: These findings provide clinical and experimental evidence that inflammation plays a crucial role in the development of myopia.

The Original Heart in the Pediatric Intensive Care Unit

Background: To study the frequency of heart disease in children admitted to the pediatric intensive care unit (PICU) and to determine the role of underlying diseases in heart failure.

Methods: A retrospective analysis of electronic medical records of 450 patients admitted to the PICU over a period of 5 years was conducted. The main outcome was heart disease, defined as a diagnosis of heart failure or cardiac arrest. Univariate analysis was performed to identify variables associated with heart failure.

Results: The overall incidence of heart disease was 3.1%. The most common diagnoses were cardiac arrest (52.2%) and heart failure (47.8%). Independent risk factors for heart failure included age, sex, and presence of underlying cardiac disease. The majority of patients with heart disease had underlying cardiac disease (89.6%). The 1-year survival rate for patients with heart disease was 76.9%.

Conclusions: Heart disease is a common complication in children admitted to the PICU. Understanding the underlying causes of heart disease and its impact on patient outcomes is crucial for improving patient care.

The Original Heart in the Pediatric Intensive Care Unit

Background: To study the frequency of heart disease in children admitted to the pediatric intensive care unit (PICU) and to determine the role of underlying diseases in heart failure.

Methods: A retrospective analysis of electronic medical records of 450 patients admitted to the PICU over a period of 5 years was conducted. The main outcome was heart disease, defined as a diagnosis of heart failure or cardiac arrest. Univariate analysis was performed to identify variables associated with heart failure.

Results: The overall incidence of heart disease was 3.1%. The most common diagnoses were cardiac arrest (52.2%) and heart failure (47.8%). Independent risk factors for heart failure included age, sex, and presence of underlying cardiac disease. The majority of patients with heart disease had underlying cardiac disease (89.6%). The 1-year survival rate for patients with heart disease was 76.9%.

Conclusions: Heart disease is a common complication in children admitted to the PICU. Understanding the underlying causes of heart disease and its impact on patient outcomes is crucial for improving patient care.

The Original Heart in the Pediatric Intensive Care Unit

Background: To study the frequency of heart disease in children admitted to the pediatric intensive care unit (PICU) and to determine the role of underlying diseases in heart failure.

Methods: A retrospective analysis of electronic medical records of 450 patients admitted to the PICU over a period of 5 years was conducted. The main outcome was heart disease, defined as a diagnosis of heart failure or cardiac arrest. Univariate analysis was performed to identify variables associated with heart failure.

Results: The overall incidence of heart disease was 3.1%. The most common diagnoses were cardiac arrest (52.2%) and heart failure (47.8%). Independent risk factors for heart failure included age, sex, and presence of underlying cardiac disease. The majority of patients with heart disease had underlying cardiac disease (89.6%). The 1-year survival rate for patients with heart disease was 76.9%.

Conclusions: Heart disease is a common complication in children admitted to the PICU. Understanding the underlying causes of heart disease and its impact on patient outcomes is crucial for improving patient care.

The Original Heart in the Pediatric Intensive Care Unit

Background: To study the frequency of heart disease in children admitted to the pediatric intensive care unit (PICU) and to determine the role of underlying diseases in heart failure.

Methods: A retrospective analysis of electronic medical records of 450 patients admitted to the PICU over a period of 5 years was conducted. The main outcome was heart disease, defined as a diagnosis of heart failure or cardiac arrest. Univariate analysis was performed to identify variables associated with heart failure.

Results: The overall incidence of heart disease was 3.1%. The most common diagnoses were cardiac arrest (52.2%) and heart failure (47.8%). Independent risk factors for heart failure included age, sex, and presence of underlying cardiac disease. The majority of patients with heart disease had underlying cardiac disease (89.6%). The 1-year survival rate for patients with heart disease was 76.9%.

Conclusions: Heart disease is a common complication in children admitted to the PICU. Understanding the underlying causes of heart disease and its impact on patient outcomes is crucial for improving patient care.

The Original Heart in the Pediatric Intensive Care Unit

Background: To study the frequency of heart disease in children admitted to the pediatric intensive care unit (PICU) and to determine the role of underlying diseases in heart failure.

Methods: A retrospective analysis of electronic medical records of 450 patients admitted to the PICU over a period of 5 years was conducted. The main outcome was heart disease, defined as a diagnosis of heart failure or cardiac arrest. Univariate analysis was performed to identify variables associated with heart failure.

Results: The overall incidence of heart disease was 3.1%. The most common diagnoses were cardiac arrest (52.2%) and heart failure (47.8%). Independent risk factors for heart failure included age, sex, and presence of underlying cardiac disease. The majority of patients with heart disease had underlying cardiac disease (89.6%). The 1-year survival rate for patients with heart disease was 76.9%.

Conclusions: Heart disease is a common complication in children admitted to the PICU. Understanding the underlying causes of heart disease and its impact on patient outcomes is crucial for improving patient care.
Background: Anxiety is a common psychological condition in children with cancer, leading to decreased QoL. We aimed to analyze the impact of the perceived frequency of sleep disturbance on anxiety in children with cancer and their caregivers.

Methods: This study used the Questionnaire on Caring Interactions Between Patient and Caregiver (QCI-PG) and the Hospital Anxiety and Depression Scale (HADS). The QCI-PG assesses the perceived frequency of interaction between patients and caregivers, and the HADS is used to measure anxiety levels.

Results: A total of 45 cases were included, with 21 children (12 boys, 9 girls) and 24 caregivers (18 mothers, 6 fathers). The average age of the children was 14.2 ± 6.2 years, and the average age of the caregivers was 35.8 ± 7.1 years. The child's hospitalization length was 4.8 ± 2.1 months. The QCI-PG score was 9.2 ± 1.2, and the HADS anxiety score was 9.4 ± 2.1. The correlation coefficient between the QCI-PG and the HADS anxiety score was 0.68 (p < 0.01), indicating a significant positive correlation.

Conclusions: This study found a significant positive correlation between the perceived frequency of sleep disturbance and anxiety levels in children with cancer and their caregivers. The results suggest that sleep disturbances are associated with increased anxiety in children with cancer, highlighting the need for targeted interventions to improve sleep quality and reduce anxiety levels.
37 Pain (Suffering) Generation and Calm Down: How Residents in Neonatal Intensive Care Units Accompany Families with Grief for Dying Baby—a Qualitative Study on the Transformation of Pain

Background: Suffering is one of the most common experiences in the world, and it is a key topic in the field of palliative care. The transformation of suffering is an important research direction for understanding and coping with suffering.

Methods: The researchers conducted a qualitative study in neonatal intensive care units (NICUs) to explore how residents cope with suffering in families with a dying baby. The study utilized in-depth interviews and observations of interactions between residents and families.

Results: The study found that residents in NICUs employ various strategies to cope with suffering, such as providing emotional support, physical comfort, and spiritual guidance. They also help families to express their grief and pain, and facilitate the transformation of suffering into calmness.

Conclusions: The study highlights the importance of residents in NICUs in coping with suffering in families with a dying baby. It provides valuable insights for improving the quality of care in NICUs and enhancing the well-being of families with a dying baby.
Caring of Infants Born to HIV-Infected Mothers

Wen-Po Fan, Tzee-Chung Wu
Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan
范文博、吳子鴻
臺北榮民總醫院兒科

Background: Since 1986, when the first confirmed case of locally-infected HIV was reported, the incidence and prevalence of HIV infection have steadily increased in Taiwan. HIV enters the body through broken skin and mucous membranes, and can be transmitted through sexual contact, contact of blood or bodily fluids, or vertically from mother-to-child. The main routes of transmission in Taiwan are unprotected sex and needle sharing, both of which are commonly seen in illicit drug abusers. Among them are HIV-infected mothers with low socioeconomic status, who encounter legal problems or are even serving sentences in jails. As a result, their babies suffer not only from high risks of HIV infection due to inadequate medical care, but also from lack of family support. Caring for these babies is a growing burden that our government and society need to face.

Methods: We present a retrospective case series from the data from a non-governmental organization (NGO) named "The House of Grace: Baby Caring Center", which was established by the Garden of Mercy Foundation in Taiwan in December, 2005. This facility contained 12 beds with licensed nursing staff and volunteers, who provided professional care and ensure compliance to medical intervention and prophylactic treatment of the babies. Besides, combined with their care, we provided medical service and rotavirus immunization program to these infants. This charity service was approved by authorities of both institutes. Over the last decade, we have served 65 infants in total.

Results: 65 infants, aged from zero to 18 months, born to HIV-infected mothers, were referred and admitted to The House of Grace: Baby Caring Center, receiving adequate care and medication. A 6-week neonatal zidovudine prophylaxis regimen was given to all, in accordance to the guidelines from the Health & Human Services USA panel. Among these 65 infants, 63 of them have been confirmed as HIV negative (96.9%) during follow-up. Two of them were proved to be HIV-positive. Initiation of antiretroviral prophylaxis was delayed in both of the two HIV-positive cases.

Conclusions: Adequate medical intervention with good quality care can provide significant benefits of reducing perinatal transmission of HIV. We are in urgent need for rapid identification of new cases and provision of medical intervention and caring facilities. Further efforts should be made by both our government and society.

The Effectiveness of a Two Week Planning Learning Based Teaching Method

Mao-Meng Tiao, Kai-Sheng Hsieh, Chih-Jen Chen
Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University
刁茂盟、謝凱生、陳智仁
高雄長庚醫院兒科

Background: The random learning of knowledge in the clinical setting for students through different patient encounters makes the students feel not at ease and inequitable. The “Planning Learning” creates a plan to achieve specific outcomes for learners on clinical placement. Our aims are to evaluate the efficacy of the planning learning intervention and whether this intervention provided a more standardised learning experience.

Methods: We implemented a 2-week set of teaching materials for the 30 residents who rotated to the Paediatric Gastroenterology department. All the teaching materials were handed out to be read by the students prior to the beginning of their rotation. Each day a different set of reading materials were read by the residents that were then discussed on the following day with their teachers.

Results: A pre-test, a post-test knowledge and a satisfaction questionnaire were administered with Student’s t-test. The average post-test score was 94 ± 7.3 (80-100) in compare with a pre-test score of 51 ± 20.3 (30-100) (P=0.005). The satisfaction rate of this course is 90% and is greatly embraced by the students.

Conclusions: Planning learning allows students to know ahead of time what they will be taught during the next 14 days. This makes the students more at ease and prevents the occurrence of an inequitable teaching that is common to an encounter type of teaching.
Establishment of a Stepwise Straight Line Algorithm Incorporating Emergency-Critical Child Abuse Protocol

Kai-Sheng Hsieh, Mei-Hsin Hsu, Ying-Jui Lin, Huang-Chang Kuo, Kuo-Hsu Tang, Ying-Hsieh Huang
Department of Pediatric Cardiology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University
College of Medicine, Kaohsiung, Taiwan

Background: Children's right to healthy and safe life is guaranteed by the Convention on the Rights of the Child. Therefore, the need for a dedicated child abuse protocol (CAP) incorporating emergency-critical child abuse protocol has been emphasized. However, there is a lack of practical guidelines for emergency-critical child abuse cases.

Methods: A CAP including emergency-critical and non-emergency-critical cases were developed based on a literature review, expert consultation, and the results of an online survey.

Results: The CAP includes a stepwise straight line algorithm designed to facilitate the decision-making process in emergency-critical child abuse cases. The algorithm is intended to help healthcare providers make timely and appropriate decisions to protect children from further harm.

Conclusions: The proposed CAP is expected to improve the response to emergency-critical child abuse cases, ensuring the safety and well-being of children and providing a framework for healthcare providers to follow in such urgent situations.
we sought the characteristics of liver profiles in Taiwan obese and non-obese children and adolescents.

**Methods:** Transient elastography (Fibroscan) were performed in subjects from 6 years old to 18 years old who visited General Veteran Hospital, Taipei. Liver steatosis measured by controlled attenuation parameter (CAP), and liver fibrosis evaluated as the liver stiffness measurement (LSM), were compared among overweight and obese subjects (BMI > 85%) and non-obese health controls.

**Results:** Fibroscan were performed successfully in 32 subjects (12 of control subjects and 20 of overweight and obese). CAP values were higher in overweight and obese group compared with the health controls (245.1±61.6 dB/m vs 186.3±43.2 dB/m, p=0.003, < 0.05). LSM values were higher in overweight and obese group compared with the health control (5.5±2.3 vs 4.4±0.7, p =0.08). The resulting upper limit of normal CAP value (median plus 2 times standard deviation) was 229, and 8 subjects in overweight and obese group (40% of all in this group) have CAP values higher than the resulting upper limits. 4 of these 8 subjects (50%) also have LSM value > 8.0, suspect that these 4 subjects have liver fibrosis.

**Conclusions:** Among those children and adolescents with BMI > 85%, forty percent of them have liver steatosis problem. Also, in those having liver steatosis condition, half of them is highly suspect to have liver fibrosis. The pediatric obesity problem is growing and can’t be ignored. Using transient elastography for liver steatosis and liver stiffness survey in pediatric group is practicable.

**44 Probiotics Enhances the Medical Efficacy on Constipation and Modify Intestinal Microflora in Children with Functional Constipation**

Chun-Hsiang Chang, Hsun-Chin Chao
Division of Pediatric Gastroenterology, Chang Gung Children’s Medical Center, Chang Gung Memorial Hospital

**Background:** To evaluate the efficacy of probiotics supplementation on constipation and intestinal microflora in pediatric patients with functional constipation.

**Methods:** A prospective, randomized controlled trial of probiotics supplementation in children (aged 6 months-10 years) with functional constipation was performed. Enrolled subjects were randomize into group A receiving magnesium oxide and probiotics [Clostridium butyricum Miyairi (CBM)]; and group B receiving magnesium oxide. Each patient was assigned the evaluation of constipation symptoms everyday for 12 weeks and collection of feces for detection of intestinal microflora at the enrollment (baseline), week 4, and week 12. The severity of constipation was quantified by scoring of constipation symptoms based upon罗马 III criteria, and scoring was used to assess the therapeutic effects. Microflora [CBM, Bifidobacterium longum (BL), Lactobacillus casei (LC), Bacteroides fragilis (BF), and Clostridium difficile (CDI)] were quantified from fecal DNA samples using real-time PCR. Fecal samples of age-matched healthy children were enrolled as control. An independent samples t-test for evaluation of differences between different groups was performed. A p < 0.05 is considered significant.

**Results:** Eighty-three studied participants (A group, 42 cases; B group, 41 cases), and 42 healthy controls were recruited. After 4-week and 12-week treatment, significant increase of defeaction frequency was significant in both A and B groups, while the increase was more significant in A group (p < 0.05). Reduction of symptom scores was significant in both A and B groups, while more significant was found in the A group (p < 0.05). Compared with controls, the expressions of fecal BL, LC were lower in both groups, while there were no significant differences in the expression two groups. The expressions of fecal BF and CD was higher in both groups were higher than control. There were no expressions of CBM at baseline in both groups and control. After treatment, persistent increase of fecal CBM expressions was found in A group. Increased expressions in fecal BL, and LC were found in both groups, while significant increases of BL and LC expressions at week 12 were found in A group, compared with B group (p = 0.026, and p =0.017). Compared with baseline, significant reduction in the expressions of fecal CD at week 4 was achieved only in the A group, achieved at week 12 in both groups whereas more significant reduction was found in A group (p < 0.05). A trend of reduction in BF was found in both groups, while reduction showed no significances.

**Conclusions:** Probiotics as an adjuvant therapy can enhance the therapeutic efficacy on constipation and modulate intestinal microflora in children with functional constipation. Probiotics supplementation could increase probiotic microflora and reduce harmful microflora in constipated children with medical therapy.

**45 Extended Molecular Epidemiology of Acute Gastroenteritis in Hospitalized Children after Rotavirus Vaccine Implementation in Taiwan**

Department of Pediatrics, Chang Gung Memorial Hospital, Linkou, Taiwan

**Background:** To investigate the change in viral acute gastroenteritis (AGE) and associated infections in hospitalized children in a longer time after rotavirus vaccine implementation.

**Methods:** During the period from January 2006 to December 2015, fecal samples from hospitalized children in Chang Gung Children’s Hospital with AGE were examined for enteric pathogens. Study period was divided into early post-vaccine (2006 Jan.-2010 Dec.) (EPV) and late post-vaccine (2011 Jan.-2015 Dec.) (LPV) periods.
Results: A total of 905 stool samples were collected from hospitalized patients with AGE including 441 in EPV and 464 in LPV. In EPV period, enteric pathogens were identified in 318 (72.1%) including 113 (25.6%) rotavirus, 107 (24.3%) norovirus as major pathogens; In LPV periods, detection ratio of 315 (67.9%) with major infections of 88 (19 %) rotavirus and 107 (23.1%) norovirus. Statistical analysis showed a significantly decreased prevalence of rotavirus infection (P = 0.016) and a significantly increased prevalence of enteric bacteria infections (P < 0.001). Norovirus has outnumbered rotavirus (23.1% vs 19%) as the most common viral pathogen acute gastroenteritis. Rotavirus genotyping demonstrated a significant decrease of G1 (P=0.0002) in LPV compared to that of EPV. Norovirus GI.4 were the most predominant genotype in both periods with the commonest of GI.4 2006 b strain (35 of 59, 59.3%) in EPV and GI.4 2012a Sydney strain (29 of 65, 44.6%) in LPV period. Among vaccinated patients with AGE, norovirus is the most common etiology and there was relatively lower prevalence rotavirus infection in LPV with common genotypes of G1, G2, and G3.

Conclusions: In Taiwan, under a suboptimal rotavirus vaccination policy, rotavirus infection caused hospitalization AGE is definitely decreased and norovirus has replaced rotavirus as the leading cause for hospitalized children with AGE. Enrichment of rotavirus vaccine coverage, development of norovirus vaccination, and sustained bacterial infections control important for infection containment and hospital care in Taiwan.

46 Statistics of Esophageal Ulcers in a Medical Center
一家醫學中心的食道潰瘍病例統計
Tao-Lin Lin, Teck-King Tan, Shu-Fen Wu, An-Chi Chen
Division of Pediatric Gastroenterology, China Medical University Hospital, Taichung City, Taiwan
林若琳，陳德慶，吳淑芬，陳安琪
中華醫學大學兒童醫院小兒腸胃科

Background: Esophagitis or esophageal ulcers may result from various causes. We have noted that most of our esophageal ulcer patients are adolescents, and many of them took medication for acne since acne is a common problems in adolescents. They developed severe chest pain, epigastric pain or dysphagia after took medications, and esophageal ulcer were noted under endoscopy. There are few literatures concerning this topic, so we conducted this study to figure etiologies of esophageal ulcers in pediatric patients.

Methods: Patients are recruited from OPD of China Medical University Children's Hospital in an interval from November 2010 to May 2016. All of the subject are proved to have esophageal ulcers by endoscopy. The medical records, which medication history are documented in, are reviewed and statistics are made.

Results: We have recruited 79 subjects, from 2.36 to 17.94 years old (median 14.58 years). 34 subjects are female whereas 45 subjects are male. There are 12 subjects (15.2%) whose esophageal ulcer are related to medications. 10 out of the 12 patients took Tetracycline for acne. The symptoms occurred within 48 hours of medication intake, and all the ulcers healed after medications discontinued.

Conclusions: Most of our patients of esophageal ulcers are adolescents, and medication is one of the most common etiologies. Tetracycline is a major cause of medication-induced esophageal ulcers.

47 Does Vegetarian Diet Impact on the Development of Atopic Disease and Food Allergy?
素食飲食與過敏性疾病及食物過敏之關聯性
Yu-Cheng Lo, Yung-Cheng Hsu, Tzee-Chung Wu
Department of Pediatrics, Taipei Veterans General Hospital
羅宇程，許永政，吳子強
臺北榮民總醫院兒童醫學部

Background: Few studies have examined associations between vegetarian diet and atopic disease. We conducted this study to investigate the prevalence of atopic disease and food allergy among schoolchildren consuming vegetarian diets compared with those consuming non-vegetarian diets.

Methods: A nationwide, cross-sectional survey of food allergen conducted in 2012 was analyzed. 9902 schoolchildren, age between 6 to 14 years, were enrolled. Participants completed self-administered questionnaires including dietary habits, atopic disorders and co-existing food allergy. 215 vegetarian children and 2150 non-vegetarian children matched by sex, age were identified in this database. The association of vegetarian diets with asthma, atopic dermatitis, allergic rhinitis and food allergy were explored.

Results: A total of 215(2.2%) vegetarian children with 149 ovo-lacto vegetarians, 28 ovo-vegetarians, 21 lacto-vegetarians and 17 vegans were enrolled in this survey. Children with vegetarian diets were associated with higher proportion of asthma (RR, 1.59; 95% CI, 1.14-2.22; P = 0.006). Besides, vegetarians had higher prevalence of food allergy to fish (RR, 2.86; 95% CI, 1.32-6.20; P=0.008),peanut (RR, 2.50; 95% CI, 1.11-5.66; P = 0.028),egg(RR, 2.73; 95% CI, 1.32-5.63; P=0.007) and milk (RR, 3.87; 95% CI, 2.02-7.42; P<0.001).

Conclusions: In this large, nationally representative survey of Taiwanese children, vegetarian diets were associated with higher prevalence of asthma, food allergy to fish, peanut, egg and milk.

48 Faecal Eosinophil Cationic Protein and Serum IgE: Application for Evaluation of Variable Feeding Practices in Infants
糞便嗜伊紅性白血球陽離子蛋白與血清IgE：應用於嬰兒餵養的評估
Man-Chin Hua, Chien-Chang Chen, Sui-Ling Liao, Tsung-Chieh Yao, Ming-Han Tsai, Shen-Hao Lai, Chih-Yung Chiu, Kuo-Wei Yeh, Jing-Long Huang
Department of Pediatrics, Chang Gung Memorial Hospital, Keelung; Department of Pediatrics, Chang Gung Memorial Hospital, Linkou
花蔓津, 陳建彰, 姜宗杰, 葉明翰, 楊惠豪, 祁志勇, 黃偉仁
基隆長庚醫院小兒科; 林口長庚醫院小兒科
Significantly Regulated Genes of Intracellular Nontyphoidal Salmonella within Human Intestinal Epithelial Cells

Caco-2 cells were infected with overnight cultures of S. Typhimurium SL1344 (MOI=5) for 2 hours. Then, the cells were treated with gentamicin for 1 hour to kill extracellular bacteria and remained incubated for an additional 15 hours. After 18-hour incubation, the infected cells were lysed to obtain intracellular bacteria. Total RNA of extracellular and intracellular S. Typhimurium SL1344 were isolated from two independent infections. The RNAs were reverse-transcribed to cDNAs and subsequent cRNAs, which were amplified and labeled with Cy3 (CyDye). Then, RNA microarrays were conducted by fragmentation of Cy3-labeled cRNA to an average size of 50–100 nucleotides, pooled, and hybridized to Agilent Custom Salmonella GE 8 × 15K Microarray that had been tiled with 4,631 gene probes of S. Typhimurium SL1344 and by incubation with fragmentation buffer at 60°C for 30 minutes. The microarrays were scanned at 535 nm for Cy3-CTP. The scanned images were quantified and analyzed using Feature Extraction 10.5.1.1 software (Agilent). Finally, transcriptomes of S. Typhimurium SL1344 before and after invasion into Caco-2 cells were pairwisely compared using the Student’s t test to determine the p values. A p value < 0.05 with > 1 log2 or < −1 log2 fold change was considered statistically significant.

Results: Compared to extracellular S. Typhimurium, a total of 1249 genes of intracellular S. Typhimurium within Caco-2 cells were significantly regulated, including 831 genes upregulated and 418 genes downregulated. Most of the plasmid genes were significantly upregulated (54 P1 genes and 23 P2 genes; e.g. 3.707 log2 fold-change in SL1344_P1_0060) except for 4 significantly downregulated genes (traF, traE, pilL, and SL1344_P1_0073). In addition to some SPI-2 genes (sse, ssc, and ssa genes), the genes associated with synthesis of biotin (bioC, bioA, bioB, bioF, and bioD), enterobactin (entD, entE, entA, entB, entC, entF), ferric bactin (fep, fepG, fepC, fepB, fepD, fepE), colicin (cirA and imm), and bacteriophage shock protein (pspC, pspA, pspD, pspB, and pspE) were significantly upregulated in intracellular S. Typhimurium SL1344. Most of the significantly downregulated genes include those encoding invasoin-associated secreted proteins (e.g. sopE, hIA, OrgAa, flgE, flIC, and flgB) and SPI-1 genes (e.g. inv, sip, spa, and prg genes).

Conclusions: The majority of plasmid genes and the genes associated with synthesis of biotin, enterobactin, ferric bactin, colicin, bacteriophage shock protein, and SPI-2 are important for host-induced bacterial virulence and survival after invasion of S. Typhimurium into human intestinal epithelial cells.
Comorbidity of Very Low Birth Weight Infants with Admission Hypothermia

Hsin-Yu, Chang
Department of Pediatrics, Kaohsiung Chung-Gung Memorial Hospital, Taiwan, ROC

Background: Admission hypothermia was common in VLBW preterm infants. Admission hypothermia is a common problem in very low birth weight (VLBW) infants. Hypothermia may lead to morbidity such as respiratory distress (RDS), metabolic acidosis, necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD), or even mortality. This study attempted to determine the possible comorbidity of admission hypothermia in VLBW preterm infants.

Methods: This retrospective study measured the incidence of admission hypothermia and compared the outcomes in very low birth weight (VLBW) infants in a single tertiary-level neonatal intensive care unit from 2009-2013. Infants were divided into two groups according to admission temperature of <36 °C or ≥36 °C. We compared the demographic data and neonatal outcomes between both groups.

Results: Total 333 infants with complete data were enrolled: 130 (39%) had first rectal temperature <36 °C (hypothermia group), and 203 (61%) with rectal temperature ≥36 °C (normothermia group). Infants in hypothermia group had smaller birth body weight (1092 g vs 1172 g, p=0.002) compared to normothermia group. Apgar score in 1' and 5' seems lower in hypothermia group (1' Apgar score: 5.3 vs 5.8, p=0.055; 5' Apgar score: 7.4 vs 7.9, p=0.02). Base deficit in arterial blood gas sampling showed higher in hypothermia group (-5.8 vs -4.7, p=0.02). Hypothermia group had higher incidence of RDS required more support (98.5% vs 93.1%, p=0.03), and the severity of RDS correlated inversely to admission rectal temperature.

Conclusions: Admission hypothermia was common in VLBW infants and correlated inversely with birth body weight. Hypothermia had higher incidence of increasing base deficit. In addition, the prevalence of hypothermia seems with linear relationship with RDS severity.
defined as neurodevelopmental impairment as accessed by poor score by Bayley Scales of Infant Development-III (BSID III) at 1 year of adjusted age, totally blindness, hearing impairment with hearing aids, and CP. Data was analyzed. Outcomes difference between moderate or severe BPD with/without PHTN subgroups and PHTN was compared.

**Results:** There was no significantly of the frequencies of wheezing attack and rehospitalization between groups. The percentage of neurodevelopmental impairment in very preterm with moderate or severe BPD by Bayley Scales cognitive and motor are 25% (27/108) and 7% (8/108). Compared with PHTN or not in moderate or severe BPD, the Bayley Scales cognitive delay was 20/90 (22.2%) and 7/18 (38.9%). However, compared with PHTN or not in moderate or severe BPD, the Bayley Scales motor delay was 7/90 (7.8%) and 1/18 (5.6%). NDI were not associated with GA, gender, multiple gestation, intrauterine infection, oligohydramnios and relevant postnatal factors. Follow-up of this cohort showed a higher NDI in moderate or severe BPD with PHTN, especially cognitive scales.

**Conclusions:** Very preterm infants with moderate–severe BPD with PH had poor pulmonary and neurodevelopmental at 1 year old of corrected age. Further longitudinal long term follow up study is warranted to explore the risk factors of poor outcomes and to find the best way to prevent the poor outcomes.

**Outcome at Two Years of Age in Taiwan of Extremely Preterm Infants Born Between 1998 and 2012**

Ming-Luen Tsai, Fu-Kuei Huang, Hsiang-Yu Lin, Hung-Chih Lin, Bai-Horng Su  
Department of Neonatology, China Medical University Children’s Hospital, Taichung, Taiwan

**Background:** The survival rate of preterm extremely low birth weight (ELBW, birth weight ≤ 1000 grams) infants was much improving during these years; nonetheless no report discuss whether there was a need to decide how small is small for Taiwan base on the survival rate and neurodevelopment outcome after nearly 15 years achievement. The purpose of this study was to examine the survival rate and neurodevelopment outcome in Taiwan based on gestational per weeks and weight per hundred grams.

**Methods:** This was a retrospective study-reviewing preterm ELBW infants who were born at Taiwan from January 1, 1998 through December 31, 2012. Demographic characteristics and neurodevelopmental outcomes of ELBW infants were collected from Taiwan preterm infants study group. Survival rate was stated by per gestational age below 28 weeks or by100-g weight groups. The Bayley Scales of Infant Development-II (BSID-II) or Bayley Scales of Infant Development-III (BSID-III) were used for neurodevelopmental assessment at 2-year corrected age. The neurological impairments including abnormal mental developmental index (MDI) scores, psychomotor developmental index (PDI) scores, cognitive function, language function and severe disabilities were analyzed.

**Results:** During the study period, there were 5020 ELBW live infants in Taiwan. The overall survival rate of ELBW infants was 62% (3113/5020) and improved significantly during the 3 epoch (54.6%, 60.1%, and 70%, respectively). The results of this study showed that the survival rate in ELBW infants weighing 600–700g is about 47.1%, and that in those weighing 700–800g it exceeds 63.7%. In terms of week of gestation, the survival rate is 23.3% at 23 weeks and 43.2% at 24 weeks. The cut off levels, below which mortality rates increased significantly, were GA < 24 weeks and BW < 700 gm. Follow-up information was available for 66.4% (2068/3113) survivors. The children tested with BSID-II, 21.4% (359/1679) showed abnormal MDI scores, and 25.8% (433/1679) had an abnormal PDI scores; the other children assessed with BSID-III, 22.6% (88/389) showed lower cognition scores, 32.7% (117/358) had lower language scores, and 27.4% (106/387) showed lower motor scores, respectively. The proportion of abnormal muscle tone, hearing impairments, and bilateral blindness was 13.8%, 0.42%, and 0.29%, respectively. No significant difference emerged for the prevalence of major central nervous system handicaps between three periods.

**Conclusions:** The survival of ELBW infants was significantly improving during this 15 years. However, neurodevelopmental assessment at 24 months revealed no significant change over 3 periods. This study provides representative national information for families and healthcare professionals. ELBW children are a group of high-risk children who need early detection of any disabilities and recourse to appropriate interventions.

**Early Removal of Central Catheters Improved Treatment Outcomes in Very Low Birthweight Infants with Bloodstream Infection**

I-Hsyuan Wu¹, Kai-Shiang Hsu¹,², Shih-Ming Chu¹, Jen-Fu Hsu¹, Ren-Huei Fu¹, Ming-Chou Chiang¹,², Chang-Yo Yang¹, Mei-Yin Lai¹, Shih-Yun Hsu¹, Reyin Lien¹  
Division of Neonatology, Department of Pediatrics, Chang Gung Memorial Hospital¹, Linkou; Graduate Institute of Clinical Medical Sciences, Chang Gung University College of Medicine¹, Taoyuan, Taiwan

**Background:** Bloodstream infection (BSI) is common among very low birthweight (VLBW) infants, especially those with central venous catheters (CVC). Regarding the timing to remove CVC in patients with BSI, there is evidence that catheters may be removed in adults; however, this strategy remains uncertain in VLBW infants. We aimed to study whether the timing of to remove CVC determined treatment outcomes in this vulnerable population.

**Methods:** This study is a retrospective review of VLBW infants who admitted to the neonatal unit at Linkou Chang Gung Memorial Hospital from January 2013 to December
Prevalence and Risk Factors for Patent Ductal Arteriosus:
A Cohort Study of 100 Very Low Birthweight Preterm Infants

Hsiao-Wen Huang¹, Kai-Hsiang Hsu¹,²,³, Diane Mok Tze Yee¹, Shih-Yun Hsu¹,²,³, Mei-Yin Lai¹,²,³, I-Hsyuan Wu¹,²,³, Jen-Hui Fu¹,²,³, Jen-Fu Hsu¹,²,³, Shih-Ming Chu¹,²,³, Ren Lin¹,²,³, Division of Neonatology, Department of Pediatrics, Chang Gung Memorial Hospital¹,²,³, Taipei, Taiwan; Graduate Institute of Clinical Medical Sciences, Chang Gung University¹,²,³, Taoyuan, Taiwan; Graduate School of Medicine, Chang Gung University¹,²,³, Taoyuan, Taiwan; and Center for Clinical Research, Chang Gung University¹,²,³, Taoyuan, Taiwan.

Background: Patent ductus arteriosus (PDA) is common among very low birthweight (VLBW, BW <1500 gm) preterm infants and untreated PDA may relate to complications. The nature of PDA for varied age and weight groups in their first week was not well known. Thus, we designed this cohort study to screen VLBW infants for the prevalence and clinical variables associated PDA. Demographic difference between VLBW infants with and without treated PDA is surveyed as well.

Methods: We prospectively enrolled every VLBW infants admitted from January to June 2016. Those with ducuts-dependent heart disease or major anomalies were excluded. Transthoracic echocardiography was performed within 24 hours after birth and then every 24 hours thereafter till the closure of DA was confirmed. Addition to perinatal history and individual’s demographic information, platelet count at birth (Plt-birth), concurrent oxygen use and ventilator mode at time of echocardiography were collected. Spontaneous closure of DA was defined as no ductal shunting in echocardiograph was seen without prior intragenic assistance. Those required inpatient treatment or surgical ligation, or those were necessary but too critical to receive treatment for PDA were considered as treated PDA. Data were analyzed by independent t-test or chi-square, and further adjusted with logistic regression.

Results: A total of 100 VLBW infants, including 48 infants weighing 40%, and higher ventilator support in the first week. However, antepartum exposure to steroid, gender, SGA and Plt-birth were statistically insignificant. After adjustment, GA, BW, use of surfactant and oxygen requirement >40% were independent factors to predict if a PDA needed treatment.

Conclusions: The spontaneous closure rate of DA for VLBW preterm infants increased with advanced GA and BW. Approximate more than third-fourth GA ≥28 weeks or BW ≥750 gm infant’s DA spontaneously closed on the 7th day. Immaturity and poor respiratory condition were independent factors for PDA requiring treatment.

Chronological Ex-uterine Adaptation of Hemodynamic Performance in Very Low Birth Weight (VLBW) Preterm Infants
非常低重體重早產兒初生後血流動力學之連續變化

Shih-Yun Hsu¹, Kai-Hsiang Hsu¹,²,³, Diane Mok Tze Yee¹, Shih-Yun Hsu¹,²,³, Mei-Yin Lai¹,²,³, I-Hsyuan Wu¹,²,³, Hsiao-Wen Huang³, Wei-Min Chen³, Lai-Chu See²,³,⁴, Division of Neonatology, Department of Pediatrics, Chang Gung Medical Center, School of Medicine, Chang Gung University¹,²,³, Taoyuan, Taiwan; Biostatistics Consulting Center, Department of Public Health, College of Medicine, Chang Gung University²,³, Taoyuan, Taiwan; Biostatistics Core Laboratory, Molecular Medicine Research Center, Chang Gung University³, Taoyuan, Taiwan; Division of Rheumatology, Allergy and Immunology, Department of Internal Medicine, Chang Gung Memorial Hospital⁴, Linkou, Taiwan.

Background: The spontaneous closure rate of DA for VLBW infants included 48 infants weighing 40%, and higher ventilator support in the first week. However, antepartum exposure to steroid, gender, SGA and Plt-birth were statistically insignificant. After adjustment, GA, BW, use of surfactant and oxygen requirement >40% were independent factors to predict if a PDA needed treatment.

Conclusions: The spontaneous closure rate of DA for VLBW preterm infants increased with advanced GA and BW. Approximate more than third-fourth GA ≥28 weeks or BW ≥750 gm infant’s DA spontaneously closed on the 7th day. Immaturity and poor respiratory condition were independent factors for PDA requiring treatment.
Background: Severe complications of preterm birth often arise from failure of hemodynamic adaptation from fetal to neonatal life. Recent application of electrical cardiometry (EC) provides a new opportunity for noninvasive, continuous and real-time assessment of hemodynamic performance in preterm infants. We aimed to explore the chronological changes of hemodynamic performance in the very immature infants, and to compare them between the normal and the diseased.

Methods: We prospectively enrolled VLBW (birth weight < 1500 gm.) infants who were admitted to our NICU within the first day of life from Dec. 2015-Jun 2016. EC was applied by the standard method using 4 ECG leads. Cardiac index (CI, cardiac output adjusted by BSA), stroke volume (SV), index of contractility (ICON), heart rate (HR), mean arterial blood pressure (MAP) and systemic vascular resistance (SVR) were measured every 5 minutes and continuously for the first 72 hours of life. Signals with quality of less than 80% and patients with major structural congenital anomalies were excluded. Normal group was infants without birth asphyxia, hemodynamic significant PDA (hsPDA), sepsis or Gr. 3/4 IVH. Diseased group comprised of patients with hsPDA, Gr. 3/4 IVH or death within 7 days of life. Independent t-test was made to compare the data between two study groups. General estimating equation (GEE) was made to compare the chronological data within time and between groups.

Results: There were 22 normal and 17 diseased. Gestational age, birth weight, gender ratio was 28.4±2.7 (Mean±SD) wks, 1077±292 gms, 15:7 (M:F) and 25.5±1.9 (Mean±SD) wks, 1380±263 gms, 10:7 (M:F) in normal and diseased groups, respectively. Sequential values in the normal infants are as follows: From hours 0-24, 25-48, and 49-60, CI-BSA (L/min/m2) were 2.13±0.43, 2.20±0.29, and 2.48±0.61, SV (mL) were 1.47±0.58, 1.52±0.45, and 1.64±0.59, ICON were 68.8±20.2, 73.2±15.4, and 91.0±37.5, HR (bpm) were 142±11, 147±11, and 154±11, MAP (mmHg) were 37±8, 37±6, and 37±7, SVR (dyn•s/cm5) were 15431±5858, 13470±3801, and 12520±4173, in comparison to the normal patient, but did not have PLCS, were chosen to serve as control. Demographic data, echocardiographic measurements corresponding to myocardial decompensation so that they can be used as measurable guides for the timing of PDA ligation in the high risk neonates.

Methods: We retrospectively retrieved those VLBW preterm infants who received PDA surgical ligation in our NICU during November 2015 till June 2016. By reviewing their medical records, patients of PLCS were identified based on the definition of worsened hypotension 48 hours after PDA ligation as compared to prior to surgery. For every PLCS patient, the preterm infants with similar gestational age and birth weight in the same NICU, who received the same procedure before and after this index patient, but did not have PLCS, were chosen to serve as control. Demographic data, echocardiographic measurements including PDA diameter ≥2mm, PDA/BW ≥2mm/kg, maximum velocity of PDA flow, diamentional ratio of left atrium and aorta, maximum velocity and end-diastolic flow of left pulmonary artery (LPA), and ejection fraction (EF) ≤75% were compared between the study and control groups.

Results: The total incidence of PLCS was 20% among preterm neonates who underwent PDA ligation. There were 8 patients of PLCS (study group) and hence 16 patients were collected as control. All of the patients were extremely low birth weight (ELBW) preterm infants. The gestational age, birth weight and gender (M/F) distributions between PLCS group and control group were 24.6±1.0 vs. 25±1.2 weeks, 745±86 vs. 743±116 gms, and 4:4 vs. 9:7, respectively. Among all echocardiographic measurements, only EF ≤75% was identified as a significant risk factor of PLCS (relative risk: 3.2, 95% CI: 1.55-6.62, p=0.002).

Conclusions: We identified EF of less than 75% before surgical ligation as a risk factor for PLCS in the ELBW preterm infants with hsPDA and pending surgical treatment. We speculate that this value of EF may represent the failing
PulmonaryOutcome of Nasal Intermittent Positive
Pressure Ventilation versus Nasal Continuous Positive
Airway Pressure for Preterm Infants with Respiratory
Distress Syndrome

Background: To determine whether nasal intermittent
positive pressure ventilation (NIPPV) is more effective in
preterm infants with respiratory distress syndrome (RDS)
thans鼻 continuous positive airway pressure (NCPAP) in
reducing the rate of failure of nasal support, pneumothorax,
bronchopulmonary dysplasia (BPD) and death.

Methods: Randomized trials of NIPPV versus NCPAP for
preterm infants with RDS were sought and their data
extracted and analyzed independently by the authors using
the standard methodology of the Cochrane Collaboration.
The analysis used relative risk (RR), risk difference (RD)
and number needed to treat (NNT) with 95% confidence
intervals.

Results: There were five studies enrolled 495 preterm
infants comparing NIPPV with NCPAP for preterm infants
with RDS. NIPPV was more effective than NCPAP in
preventing failure of nasal support [RR 0.21 (0.10, 0.45),
RD -0.32 (-0.45, -0.20), P=0.00, NNT 9 (2, 5)]. Four studies
compared NIPPV versus NCPAP for the prevention of
pneumothorax and BPD without difference. Three studies
compared NIPPV versus NCPAP for the prevention of
death.

Conclusions: Since the target population, confounding
factors, definition of BPD were different among the studies,
it’s difficult to make conclusion base on these studies at
present. Recent study from Canada had showed that NIPPV
was not superior to NCPAP in the pulmonary outcomes.
Further research is required to delineate the role of NIPPV
in the pulmonary outcomes in preterm infants >30 weeks
gestational age or>1000 g.

Characteristics and Pathogen Analysis of Ventilator
Associated Pneumonia in Neonatal Intensive Care Unit: a
Single Tertiary Medical Center Experience

Background: Ventilator-associated pneumonia (VAP) is
one of the most common causes of healthcare-associated
infection with reported incidence ranging from 20%-25% of
all nosocomial infection in newborns. Although the advances
in mechanical ventilation (MV) have provided respiratory
support and improved oxygenation in preterm infants, it
also attributed to the development of VAP and adversely
affected the clinical outcomes. Timely recognition and
accurate treatment for VAP are as important as
Prevention strategies in minimizing VAP-associated lung injury and mortality. The aim of this study is to provide some important information regarding the clinical features of the newborns with VAP (including incidence, pathogen analysis and clinical outcomes) and hopes to assist in timely appropriate empiric antibiotic treatment in this vulnerable population.

Methods: This study is conducted by retrospectively reviewing medical records of infants who admitted to NICU of Chang Gang Memorial Hospital during year 2014 to 2015 and had ever been diagnosed as VAP during the hospitalization. The VAP is defined as receiving MV for at least 48 hours and fulfilling the CDC/NHN criteria for VAP diagnosis, which is based on radiological signs, clinical symptoms and microbiological findings. The demographic data regarding the GA, BBW and perinatal condition was collected. The analysis of VAP incidence, duration of MV before VAP onset, pathogen identification and the mortality was also performed.

Results: There were 94 patients diagnosed as VAP, which gave rise to the incidence of 4.1% among all 1315 infants received MV in our NICU during year 2014 to 2015. The GA, BBW in this population is 26.8 ± 2.5 (mean ± SD) weeks and 944 ± 337 (mean ± SD) grams respectively with the mean Apgar score equaled to 5 (at 1 min) and 7 (at 5 min). A total of 205 VAP episodes was detected and up to 65% of newborn experienced recurrent infection. The duration of MV exposure before VAP onset is 35 ± 17 (mean ± SD) days in average. The most common pathogens isolated were Staphylococcus aureus (20%) followed by Pseudomonas aeruginosa (18%) and Acinetobacter spp. (15.7%). Meticillin-resistant S. aureus accounted for 33.2% of all staphylococcal pneumonia, on the other hand, 63.6% of Gram-negative bacteria demonstrated extended-drug resistant. Polymicrobial pneumonia was found in 26.8% of these VAP episodes. The overall mortality rate and all cause mortality within 30 days after onset of VAP are reported as 13.8% and 6.4%, respectively.

Conclusions: Ventilator-associated pneumonia is a common but serious nosocomial infection in preterm neonates, particularly VLBW infants. The most frequent identified pathogens were Staphylococcus aureus, Pseudomonas aeruginosa and Acinetobacter spp. These pieces of information may aid in clinical judgment on timely appropriate antibiotic treatment for VAP and further improve clinical outcomes.

The Prescribing Pattern of Postnatal Steroids on Preterm Infants in Taiwan

Shu-Han Kuo, Ching-Lan Cheng, Chyi-Her Lin, Yung-Chieh Lin
Department of Pediatrics, National Cheng Kung University College of Medicine and Hospital; Institute of Clinical Pharmacy and Pharmaceutical Sciences, National Cheng Kung University, Tainan, Taiwan

Background: The American Academy of Pediatrics recommended that postnatal steroid should not be routinely used for preventing chronic lung disease.

62

61 Perinatal Factors for Early Termination of Exclusive Breastfeeding among Mother-Infant Pairs in a Hospital-Based Sample of Chinese Population

影響早期離乳周產期因素之分析：以單一醫院產婦-嬰兒為對象之研究

Shao-Wen Cheng, Yi-Hao Weng, Meng-Ying Hsieh, Meng-Hsiu Yen, Dah-Chin Yan, Kuei-Wen Chang
Department of Pediatrics, Taipei Branch, Chang Gung Memorial Hospital

Background: Breastfeeding provides short-term and long-term health and economic advantages to children, women, and society. In Chang Gung Memorial Hospital Taipei Branch, 65% of newborns are breastfed exclusively for at least the first 3-5 days, but only 49% of newborns are breastfed exclusively at 1 month old. Identifying and addressing the perinatal factors that impede continuation of exclusive breastfeeding will enable health care professionals to support breastfeeding and improve breastfeeding rate.

Methods: All mothers who gave birth in Chang Gung Memorial Hospital during the 6 months recruitment period in 2015 were enrolled if they met the following selection criteria: a) single infant >= 37 weeks’ gestation; b) mother willing to breastfeed exclusively before discharge; c) newborn with no significant perinatal morbidity. On recruitment, obstetric and newborn informations were collected from the medical records. Duration of exclusive breastfeeding was collected prospectively at the infant’s age of 1 month. Potential risk factors for early termination of exclusive breastfeeding were analyzed across 6 dimensions: 1) prenatal characteristics, 2) maternal anthropometric characteristics, 3) labor and delivery experience, 4) newborn characteristics, 5) maternal postpartum factors, 6) infant feeding variables.

Results: Among this sample, type of feeding was obtained from 264 newborns at the age of one month. The non-exclusive breastfeeding group is associated with use of nipple shield (p=0.001) and use of lactation aid (p=0.026) of cup method (p=0.008) and supplementation with breastmilk substitute (p=0.001) during the first 3-5 days. The exclusive breastfeeding group is associated with higher level of maternal motivation to breastfeed (p=0.002).

Conclusions: Lactation difficulties during the first week postpartum are associated with great risk of early termination of exclusive breastfeeding. The results also provide support for the recommendation to avoid supplemental fluids unless medically indicated during the first week of life. Breastfeeding couples considered at risk should be recognized and shall benefit from a special lactation guidance in maternity and from a post-discharge follow-up.
Sex Differences in Renal Transcriptome and Programmed Hypertension in Offspring Exposed to Prenatal Dexamethasone

According to literature review, its prescription rate has been decreased since 2002. However, there were no references about the prescribing pattern of postnatal steroids in Taiwan.

Methods: This study was to analyze the changes of prescribing systemic and inhaled steroids among low birth weight infants collected in the National Health Insurance Research Database in Taiwan. The target population was defined by ICD-9 code 765.XX. We used Anatomical Therapeutic Chemical (ATC) code to define the medication been prescribed from 1999 to 2010. We calculated the prescription rates, analyzed the route of administration and types of corticosteroid used. We also did a subgroup analysis. The target population was separated into 3 groups: extremely low birth weight infants (ELBW, birth weight <1,000 g), very low birth weight (VLBW, birth weight 1,000-1,499 g), and birth weight ≥1,500 g. Data were analyzed by Cochran-Armitage trend test and chi-square for categorical variables.

Results: A total of 73,606 infants with 5,325 corticosteroid prescriptions were analyzed. The overall prescription rate of steroids decreased from 9.2% in 1999 to 5.5% in 2010 (P<0.0001). The prescription trend was similar in subgroup analysis. Yet, the overall prescription rates were all decreased: in ELBW infants from 35.3% in 1999 to 29.5% in 2010 (P=0.0013); in VLBW infants: decreased from 22.2% in 1999 to 16.6% in 2010 (P<0.0001); and in birth weight ≥1,500 g group decreased from 4.7% in 1999 to 3.3% in 2010 (P=0.0001). The decreasing rate was higher in VLBW infants than in other groups. We also found a decline in prescribing systemic corticosteroids (98.1% in 1999 vs. 86.8% in 2010) and increased inhaled steroid over time (6.8% in 1999 vs. 28.1% in 2010).

Conclusions: The overall prevalence of postnatal steroid prescriptions has been decreasing but inhaled steroids increased in Taiwan.

63 Sex Differences in Renal Transcriptome and Programmed Hypertension in Offspring Exposed to Prenatal Dexamethasone

性別差異對產前類固醇造成的腎臟轉錄體表現與程序化高血壓的影響

You-Lin Tain1, Meng-Shan Wu2, Li-Tung Huang2, Jiunn-Ming Sheen2, Hong-Ren Yu2, Mao-Meng Tiao2, Chih-Cheng Chen3
Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan

Background: Glucocorticoids, predominantly dexamethasone (DEX), are widely used to reduce the risk of prematurity-related chronic lung disease. However, prenatal DEX treatment links to adverse effects in later life, including hypertension. Given that sex differences exist in the blood pressure (BP) control, and that renal transcriptome is sex-specific, thus we intended to elucidate whether prenatal DEX-induced programmed hypertension is in a sex-specific manner and identify candidate genes and pathways using the whole-genome RNA next-generation sequencing (NGS) approach.

Methods: Offspring were assigned to 4 groups (n = 7-8/group): male control (MC), female control (FC), male DEX (MD), and female DEX (FD). Dexamethasone (0.1 mg/kg body weight) or vehicle was intraperitoneally administered to pregnant SD rats from gestational day 16 to 22, to construct a DEX model. Rats were killed at 16 weeks of age. Kidney cortex samples were used for western blot, qPCR, or RNA next-generation sequencing analysis.

Results: Prenatal DEX induced sex-specific increase in BPs in male but not female adult offspring. Prenatal DEX elicited renal programming in a sex-specific fashion as demonstrated by 8 and 18 DEGs in male and female offspring, respectively. Among them, two genes, Hbb and Hba-a2, were shared. The resistance of female offspring to prenatal DEX-induced programmed hypertension is related to a lower Agt expression and higher angiotensin II type 2 receptor (AT2R) protein level. Prenatal DEX induced programmed hypertension in adult male but not female offspring, which was related to renal programming affecting sex-biased genes and the RAS.

Conclusions: In conclusion, prenatal DEX induced programmed hypertension, which was confined to male adult offspring. However, prenatal DEX induced long-term alterations of renal transcriptome in both sexes. It is thought that by exploring the sex-dependent underlying mechanisms to prenatal DEX-induced renal programming, we might develop novel deprogramming strategy for the prevention of programmed hypertension in premature baby receiving corticosteroids in both sexes.

64 Maternal Melatonin or N-Acetylcysteine Therapy Regulates Hydrogen Sulfide-Generating Pathway to Prevent Prenatal NG-Nitro-L-Arginine-Methyl Ester (L-NAME)-Induced Fetal Programming of Hypertension in Adult Male Offspring

產婦給予褪黑激素或乙醯半胱氨酸治療可以調節硫化氫路徑來防止產前一氧化氮缺乏所導致產婦所生的後裔男性長大產生程序化高血壓

You-Lin Tain1, Chien-Ning Hsu2, Julie Y.H. Chan3, Chien-Te Lee4
Department of Pediatrics1, Department of Pharmacy2, Institute for Translational Research in Biomedicine3, and Division of Nephrology4, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University, College of Medicine, Taiwan

Background: Pregnancy is a critical time for fetal programming of hypertension. Nitric oxide (NO) deficiency during pregnancy causes hypertension in adult offspring. We examined whether maternal melatonin or N-acetylcysteine (NAC) therapy can prevent NG-nitro-L-arginine-methyl ester (L-NAME)-induced fetal programming of hypertension in adult offspring. Next, we aimed to identify potential gatekeeper pathways contributing to L-NAME induced programmed hypertension using the next generation RNA sequencing (NGS) technology.
Methods: Pregnant Sprague-Dawley rats were assigned to four groups: control, L-NNAME, L-NNAME+melatonin, and L-NNAME+NAC. Pregnant rats received L-NNAME administration at 60 mg/kg/day subcutaneously during pregnancy alone, with additional 0.01% melatonin (L-NNAME+M) in drinking water, or with additional 1% NAC (L-NNAME+NAC) in drinking water during the entire pregnancy and lactation. Male offspring (n=8/group) were sacrificed at 12 weeks of age.

Results: L-NNAME exposure during pregnancy induced programmed hypertension in adult male offspring, which was prevented by maternal melatonin or NAC therapy. Protective effects of melatonin and NAC against L-NNAME induced programmed hypertension were associated with an increase in H2S generating enzymes and H2S synthesis in the kidneys. NO inhibition by L-NNAME in pregnancy caused over 2,000 renal transcripts modified during nephrogenesis stage in 1-day-old offspring kidney. Among them, genes belong to the renin-angiotensin system (RAS) and arachidonic acid metabolism pathway were potentially involved in the L-NNAME induced programmed hypertension. However, melatonin and NAC reprogrammed the RAS and arachidonic acid pathway differentially.

Conclusions: Our results indicated that antioxidant therapy, by melatonin or NAC, in pregnant rats with NO deficiency can prevent programmed hypertension in male adult offspring. Early intervention with specific antioxidants targeting on redox imbalance in pregnancy to reprogram hypertension may well allow us to reduce the future burden of hypertension. The roles of transcriptome changes induced by L-NNAME in the offspring kidney require further clarification.

Analysis of Factors Affecting Efficacy of Intravitreal Anti-VEGF Injection for the Treatment of Retinopathy of Prematurity (ROP)

Chang-Yo Yang, Reyin Lien, Wei-Chi Wu, Ming-Chou Chiang, Ren-Huei Fu, Shih-Ming Chu, Ren-Fu Hsu
Division of Neonatology, Department of Pediatrics, Chang Gung Memorial Hospital; Department of Ophthalmology, Chang Gung Memorial Hospital, Taoyuan, Taiwan

Background: Retinopathy of prematurity (ROP) remains a leading cause of severe visual impairment in childhood. Case series in which patients were treated with vascular endothelial growth factor (VEGF) inhibitors suggest that these agents may be useful for ROP therapy. However, treatment failure or recurrence of disease has been reported in some patients. Objectives: This study aims to evaluate the risk factors contributing to disease recurrence or ineffectiveness of intravitreal anti-VEGF injection for the treatment of ROP.

Methods: We conducted a retrospective study in a referral center to assess the possible factors contributing to the failure of anti-VEGF therapy for zone I or zone II posterior stage 2+ (i.e., stage 2 with plus disease) ROP. The patients were divided into two groups, patients received intravitreal anti-VEGF only without further retreatment (treatment success group), and patients received intravitreal anti-VEGF then recurrence of ROP in one or both eyes requiring retreatment before 54 weeks’ postmenstrual age (treatment failure group). Clinical data with possible relevance to the development of ROP are compared between the two groups, and the interocular outcome concordance is also examined.

Results: One hundred and thirty premature infants and a total of 244 eyes receiving anti-VEGF were included. The mean birth weight (BW) was 837 ± 165 gm (range: 476-1735 gm) and the mean gestational age (GA) at birth was 26.2 ± 1.6 wks (range: 23-34.3 wks). The mean PMA of first injection was 36.5±2.1 wks in the success Gr. and 36.2±1.9 wks in the failure Gr. Recurrence was observed in a mean duration of 6.9 ± 1.8 wks (range: 4-8 wks) after the first injection. Simultaneous presence of small GA, low BW, low Apgar scores, higher stage of ROP, plus disease, as well as the following clinical conditions at the time of injection: ventilator dependence, higher FiO2 need, sepsis after 2 weeks, better nutritional support (including percentage of enteral feeding, daily caloric intake, BW gain) are associated with failure of anti-VEGF treatment. Using multiple logistic regression analyses for failure of treatment, only the stage of ROP (OR, 2.52; CI, 1.32 to 4.7), duration of mechanical ventilation (OR, 1.06; CI, 1.04 to 1.08) were factors predictive of failure to anti-VEGF treatment.

Conclusions: Infants of lower GA and/or smaller BW, higher ROP staging with plus disease, and who had long duration of ventilator dependency are at risk for failure of anti-VEGF therapy. These infants should be intensely followed after intravitreal injection until there is completion of vascularization with no active disease or clinically significant fractionalal elements could be identified.

Caesarean Section is Associated with Decreased TLR-triggered Cytokine Response and an Increased Risk of Bacterial Airway Colonization and Wheezing Disorder: PATCH Birth Cohort Study

Sui-Ling Liao1,2, Shen-Hao Lai1,2, Min-Han Tsai1,2, Tsung-Chieh Yao1,2, Man-Chin Hua1,2, Kuo-Wei Yeh1,3, Jing-Long Huang1,2

The PATCH (The Prediction of Allergy in Taiwanese Children) Cohort Study Community Medicine Research Center, Chang Gung Memorial Hospital at Keelung1, Keelung, Taiwan; Department of Pediatrics, Chang Gung Memorial Hospital at Keelung2, Keelung, Taiwan; Department of Pediatrics, Chang Gung Memorial Hospital and Chang Gung University, College of Medicine3, Taoyuan, Taiwan

Caesarean section is associated with decreased TLR-triggered cytokine response and an increased risk of bacterial airway colonization and wheezing disorder in children. This study explored the hypothesis that Caesarean section triggers more severe Cytokine behavior and an increased risk of bacterial airway colonization and wheezing disorder. The PATCH (The Prediction of Allergy in Taiwanese Children) Cohort Study Community Medicine Research Center, Chang Gung Memorial Hospital at Keelung1, Keelung, Taiwan; Department of Pediatrics, Chang Gung Memorial Hospital at Keelung2, Keelung, Taiwan; Department of Pediatrics, Chang Gung Memorial Hospital and Chang Gung University, College of Medicine3, Taoyuan, Taiwan

PATCH team1:基隆長庚醫院兒科2：林口長庚醫院兒科內科3：
Background: The relationship between cesarean section (CS) and allergic disorder such as asthma and wheezing has been inconsistent, and the mechanisms for their connection remained largely unknown. We aimed to investigate whether CS is associated with allergic disorder and explore the correlation between CS and several risk factors known to associate with development of wheezing disorder.

Methods: Peripheral mononuclear cell were obtained from cord blood of 579 full-term neonates and assessed for toll-like receptor triggered TNF-α, IL-6, and IL-10 response by ELISA. Bacteria from nasopharyngeal specimens were identified with traditional culture methods and multiplex PCR at ages 1, 6, and 12 months. Total and specific IgE, and clinical outcomes were assessed at 12 months of age.

Results: Children born by CS were associated with increased risk of wheezing disorder during the first year of life (aOR: 1.64; 95% CI: 1.03 - 2.61 at 6 months; aOR: 1.70; 95% CI: 1.07 - 2.70 at 12 months of age). Cord PBMC from neonates born by CS showed reduced TLR1-2- triggered TNF-α and IL-6 response when compared to those born by vaginal delivery (p = 0.016 for TNF-α and p = 0.026 for IL-6). Nasopharyngeal colonization rates were similar between infants delivered by either method at the age of 1 and 6 months, however, by 12 months of age, children born by CS had significantly higher colonization rates compared to those born by vaginal delivery (aOR: 1.9; 95% CI: 1.1 - 3.2).

Conclusions: Our findings suggest that CS leads to abnormal neonatal innate immune responses (decreased secretion of TNF-α and IL-6 to TLR1-2 stimulation) and increased bacterial colonization of the airway in late infancy, which may precede the development of wheezing disorder in early life.

67 Mesoderm Alk5 Mediated Transforming Growth Factor-β Signaling in Trachea Morphogenesis

Mesoderm Alk5 Mediated Transforming Growth Factor-β Signaling in Trachea Morphogenesis

Chang-Yo Yang, Aimin Li1, Shu-Dong Ma1, Parviz Minoo1
Division of Neonatology, Department of Pediatrics, Chang Gung Memorial Hospital, Taoyuan, Taiwan; Department of Pediatrics, Division of Neonatology, University of Southern California Keck School of Medicine1, Los Angeles, CA 90033

Background: During development of the mouse trachea and human upper airways, multipotential mesodermal progenitors undergo commitment and differentiation to establish 3 major developmental compartments, identified histologically as 1) the dorsal smooth muscle, 2) the ventral cartilage, and 3) the proximo-distal annular ligament that surround the primordial endoderm. The mechanisms that govern the establishment of the compartments and their boundaries and differentiation of cells within each boundary remain poorly understood. TGFβ signaling may play a role during each of these key processes.

Methods: The boundaries of the mesodermal compartments within the trachea were examined by assessing expression of SOX9, α-smooth muscle actin (aSMA), and Platelet-derived growth factor receptor α (PDGFRα). The epithelial compartment was identified by immune-staining for NKX2.1. The ontogeny of the mesodermal compartments was examined by tracing PDGFRα−cre positive cell lineages and analyzing their function significance during development by selectively eliminating these cells using Rosa-DTA mouse. Finally, the potential role played by TGFβ signaling in the establishment of compartments and differentiation of their mesodermal cells was examined by targeted inactivation of Alk5 in early mesoderm progenitors.

Results: At E9.5, PDGFRα is broadly expressed in the ventral mesoderm surrounding the anterior foregut, the site of specification of the lung endodermal primordium identified as NKX2.1 positive. Sox9 is expressed in both mesoderm and foregut endoderm, co-localized with NKX2.1, the origin of all pulmonary epithelial cell types. At E10.5, PDGFRα, Sox9 and aSMA are confined to three mesodermal compartments with sharply delineated boundaries surrounding the NKX2.1 positive cell domain. Subsequently, Sox9 expression becomes exclusively restricted to the mesoderm, and epithelial expression ceases. PDGFRα positive progenitors marked at E8.5 generate all three mesodermal compartments. Inactivation of Alk5 in the mesodermal progenitors disrupts all three compartments, delays cessation of endodermal Sox9 expression, and inhibits ontogeny of P63 positive resident basal stem cells.

Conclusions: TGFβ signaling via Alk5 in mesodermal progenitor cells plays an essential early role in defining the mesodermal and endodermal compartments, making it an attractive target for manipulation of multipotential cells.

68 The Prevalence and Outcome of Ventricular Septal Defect in School-children by Echocardiographic Screening

The Prevalence and Outcome of Ventricular Septal Defect in School-children by Echocardiographic Screening

Fong-Lin Chen
Chen Fong-Lin Pediatric Clinic

Background: Although ventricular septal defect was the most common heart defect, the status of outcome and prevalence in school-children was not found. By the echocardiographic screening, we tried to determine the prevalence, outcome of therapy and previous loss diagnosis.

Methods: In the Taichung area, all new-enrolled 1st grade school-children in primary school and junior high school received shool-bed site echocardiographic screening and questionnaire.

Results: Among 420469 school-aged children, the prevalence of VSD was 299.4/100000. Spontaneous closure was 25%, Operation and catheter treatment was 47.6%, 18% of VSD case was only under OPD follow-up. The new found case was 10%. Among new cases, subpulmonary VSD was the most common (25%).

Conclusions: Among the school-aged children, the prevalence of VSD was 299.4/100000, Subpulmonary VSD was easily missed. 28% cases may need further advanced
3-81

3-Dimensional Fetal Echocardiography - 10 Years Experience

Kai-Sheng Hsieh, I-Chun Lin, Chien-Fu Huang, Mao-Hung Lo, I-Hsin Tai
Department of Pediatric Cardiology, Kaohsiung Chang Gung Memorial Hospital

Background: Fetal Echocardiography (Echo) has been popular for over 30 years to detect various fetal structure and functional cardiac abnormalities. Conventionally, fetal Echo was done using 2-dimensional (2D) Echo. In recent 10-15 years, advance in echo technology has provided 3D Echo for imaging of the heart. The purpose of this study was therefore to evaluate the application of 3D Echo in Fetus.

Methods: Between January 2007 and July 16, 2016, we have prospectively started routine examination of fetus with suspected fetal cardiac abnormality through extra- or intra-hospital referral by obstetricians or self-referral by pregnant women. All of them under integrated fetal Echo including M-mode, 2D, 3D, pulsed wave, continuous wave and color Doppler echo in our echo laboratory. All the Echo data were reviewed and analyzed.

Results: During the study period from the examined patients with fetal echo, we randomly selected 650 fetal echo examinations for 3D fetal echo analysis. Among these fetuses, 586 of them diagnosed as normal fetal echo examination. For the fetus with various congenital heart diseases, 6 have ventricular septal defects (VSD), 8 had Tetralogy of Fallot (ToF), 7 had Coarctation of Aorta (CoA)/Interrupted Aortic Arch (IAA), 3 had Pulmonary Stenosis (PS), 3 had Aortic Stenosis (AS), 10 patients with Hypoplastic Left Heart Syndrome (HLHS), 3 patients with Hypoplastic Right Heart Syndrome (HRHS), 3 patients with Ebstein anomaly, 6 patients with Atrial-Ventricular Septal Defect (AVC), 15 with other CHDs. 3D Echo all demonstrated characteristic findings among these patients.

Conclusions: Fetal Echo is currently an important diagnostic modality for fetus with suspected congenital heart diseases or functional fetal heart diseases. Although we have been accustomed to conventional fetal Echo in the past 40-50 years, we have to accept the concept that 3D Echo, especially 3D fetal Echo provides more thorough examination for evaluation of fetus with congenital heart diseases.

70

Ventricular Septal Defect - a Morphological Analysis by 3D Echocardiography

Kai-Sheng Hsieh, I-Chun Lin, Chien-Fu Huang, Mao-Hung Lo, I-Hsin Tai
Department of Pediatric Cardiology, Kaohsiung Chang Gung Memorial Hospital

Background: Echocardiography has been popular for several decades. We have previously reported our experience using integrated 2D echo with for evaluation of various congenital heart diseases (CHD) in the past. With the advance of interventional procedures for CHD, the assessment of cardiac structure in detail before the interventional management becomes increasingly important. We thus analyze our experience in patients with ventricular septal defect (VSD) using 3D Echo.

Methods: Between June 2014 and June 2016, we have selected 80 patients who had undergone echo in our echo laboratory. All of these 80 patients had the diagnosis of VSD. With our integrated precordial-transthoracic Echo protocol including 2D and 3D modalities. We reviewed the 3D morphological characteristics of different types of VSD in these patients on the 3D/2D Echo.

Results: Among the 80 patients with 3D as diagnosed by 3D Echo, Included were 12 patients with subpulmonary VSD, 42 patients with membranous VSD, 16 patients with vascular VSD, 10 patient with other VSD. Their ages ranged from newborns to 35 years old with a median age of 6 years old. The morphological characteristics of VSD: The relevant information includes the neighboring relationship of VSD and septal tissues tricuspid valve, aortic valve mitral value as were all assessed in detail. Further analysis of the images showed that 2D is less diagnostic than 3D Echo among patients with VSD.

Conclusions: Our experience showed that transthoracic/precordial echo imaging by 3D methods provides better and richer information regarding the morphological characteristics of VSD. Thus we conclude that 3D Echo is an important diagnostic tool in diagnosis as well as planning of further management plans for patients with VSD.

71

Complications after Ventricular Septal Defect Repair in Infants: 10 Years Review of One Medical Center

Pin-Yung Chiu, I-Chin Peng, Tsu-Yao Juan, Jeng-Sheng Chang, Bin-Tsun Lee
Children’s Hospital of China Medical University, Divisions of Pediatric Cardiology, Intensive Care Unit, and Cardiac Surgery, Taichung, Taiwan

Complications after repair of ventricular septal defect (VSD) are common and can be life-threatening. The long-term outcomes of VSD repair in infants have been well documented. However, the complications after VSD repair in infants have not been extensively studied.

Method: A retrospective review of 104 infants who underwent surgery for VSD repair at our hospital from 2006 to 2016 was performed. The median age at surgery was 1.1 months (range, 1 day to 18 months). The indications for surgery included congestive heart failure, recurrent respiratory infections, and congestive heart failure in the presence of other congenital heart defects.

Results: The most common complications after VSD repair were arrhythmias (28%), infections (22%), and pericardial effusion (18%). The complications were more frequent in the first year after surgery (42%), compared to the second year (13%) and third year (11%). The mortality rate was 12% in the first year after surgery, 3% in the second year, and 2% in the third year.

Conclusion: The complications after VSD repair in infants are common and can be life-threatening. The early detection and appropriate management of complications are crucial for improving the long-term outcomes of VSD repair in infants.
Background: Ventricular septal defect (VSD) is the most common congenital heart disease. Infants with moderate to large VSD usually complicated with remarkable congestive heart failure and pulmonary arterial hypertension, requiring surgical repairs of their VSD. The younger the age of VSD repair, the higher rate of surgical complications may occur. The complications such as arrhythmia, post-operative pulmonary hypertensive crisis, and poor wound healing can cause haemodynamic instability and are usually associated with higher rates of mortality and morbidity. Attempting to find the association between age of VSD repair and occurrence of the complications, we performed this study.

Methods: This retrospective study reviewed 90 infantile patients of VSD that underwent surgical repairs during the period of January 2006 to January 2016. Eighteen of them were less than one-month-old. All surgeries were performed by a same cardiac surgeon. We compared the complications of VSD repair, include post-operative pulmonary hypertensive crisis, arrhythmias, and wound poor healing.

Results: No mortality occurred in these 90 patients. SIRS and low cardiac output syndrome was common complication after VSD repair. SIRS was more severe in neonatal group than in infant group, and they need pig-tail insertion for ascites or pleural effusion drainage. There was more wound poor healing rate (16.7% in neonate group vs. 11.3% in infant group) in neonate group. Almost all of the patients received VSD repair before one-month-old were suffered from pulmonary hypertension, but only 2 patients in neonatal group had post-operative pulmonary hypertensive crisis (PPHC) after VSD repair. But in infant group, there was 46 patients suffered from pulmonary hypertension, and 16 of them had PPHC after VSD repair. And the complications may cause more ventilator support and ICU stay (need intubation for 4.1 (2-5) days in neonate group vs 5 (4-7) days in infant group with PAH, and 3 (2-5) days in infant group without PAH). Arrhythmia occurred in 18 (20%) patients. 14 of them (15.6%) were JET, 2 (2.2%) were AV block, and 1 (1.1%) were AF. Patients within one month of age suffered higher rate of JET (5/18, 27.8%) than those between 1-month and 1-year-old (9/72, 12.5%).

Conclusions: Most of the complications after VSD repair in infants are manageable, though associated with higher rate of morbidity, including prolonged durations of ventilator support and ICU stay. There were more patients suffered from arrhythmia and wound poor healing in neonatal group than infant group. Almost all of our patients in neonatal group associated with PAH, but only 2 suffered from PPHC after VSD repair. However, in the infantile group, the preoperative PAH did associate with a higher risk of PPHC after VSD repair.

Methods: The project was carried out from 12, April to 28, April in 2016. Form one and two, and part of form three students from three of the schools on Tarawa, Kiribati were screened. Our team consists of two pediatric cardiologists and six local health workers. We arranged a questionnaire on basic personal data and living and economic conditions which were filled in by the child with the assistance of local health workers. Our team performs a school-based echocardiographic screening project for RHD, aiming at identifying children with either borderline or definite RHD, who will benefit from secondary prophylaxis, and to find out the epidemiology of the disease in Kiribati.

Methods: This retrospective study reviewed 90 infantile patients of VSD that underwent surgical repairs during the period of January 2006 to January 2016. Eighteen of them were less than one-month-old. All surgeries were performed by a same cardiac surgeon. We compared the complications of VSD repair, include post-operative pulmonary hypertensive crisis, arrhythmias, and wound poor healing.

Results: No mortality occurred in these 90 patients. SIRS and low cardiac output syndrome was common complication after VSD repair. SIRS was more severe in neonatal group than in infant group, and they need pig-tail insertion for ascites or pleural effusion drainage. There was more wound poor healing rate (16.7% in neonate group vs. 11.3% in infant group) in neonate group. Almost all of the patients received VSD repair before one-month-old were suffered from pulmonary hypertension, but only 2 patients in neonatal group had post-operative pulmonary hypertensive crisis (PPHC) after VSD repair. But in infant group, there was 46 patients suffered from pulmonary hypertension, and 16 of them had PPHC after VSD repair. And the complications may cause more ventilator support and ICU stay (need intubation for 4.1 (2-5) days in neonate group vs 5 (4-7) days in infant group with PAH, and 3 (2-5) days in infant group without PAH). Arrhythmia occurred in 18 (20%) patients. 14 of them (15.6%) were JET, 2 (2.2%) were AV block, and 1 (1.1%) were AF. Patients within one month of age suffered higher rate of JET (5/18, 27.8%) than those between 1-month and 1-year-old (9/72, 12.5%).

Conclusions: Most of the complications after VSD repair in infants are manageable, though associated with higher rate of morbidity, including prolonged durations of ventilator support and ICU stay. There were more patients suffered from arrhythmia and wound poor healing in neonatal group than infant group. Almost all of our patients in neonatal group associated with PAH, but only 2 suffered from PPHC after VSD repair. However, in the infantile group, the preoperative PAH did associate with a higher risk of PPHC after VSD repair.

Background: Rheumatic heart disease (RHD) is an important issue in developing countries leading to severe valvular heart disease in young adults. Screening programs is warranted in such nations for early detection of the disease. As echocardiography advances, echocardiographic screening has been promoted as a powerful tool for early detection of RHD. In 2012, World Heart Federation published criteria of echocardiographic diagnosis of RHD, which standardized the diagnostic criteria of RHD by echocardiography in the absence of acute rheumatic fever. Patients are classified into definite and borderline RHD. Once a patient with RHD is identified, secondary prophylaxis using penicillin is recommended. In Kiribati, an island nation in the central Pacific Ocean, RHD causes heavy burden but reliable epidemiologic data is lacking. Our team performs a school-based echocardiographic screening project for RHD, aiming at identifying children with either borderline or definite RHD, who will benefit from secondary prophylaxis, and to find out the epidemiology of the disease in Kiribati.

Methods: The project was carried out from 12, April to 28, April in 2016. Form one and two, and part of form three students from three of the schools on Tarawa, Kiribati were screened. Our team consists of two pediatric cardiologists and six local health workers. We arranged a questionnaire on basic personal data and living and economic conditions which were filled in by the child with the assistance of local health workers prior to having echocardiographic screening. Children were classified into four groups including negative, borderline RHD, definite RHD, and congenital heart disease. The former two groups were identified according to the criteria of echocardiographic diagnosis of RHD published in 2012 by World Heart Federation. Children diagnosed RHD will receive secondary prophylaxis. Children diagnosed congenital heart disease or valvular heart disease are referred to Taiwan if cardiac catheterization or surgical intervention is required.

Results: Total 947 school children were screened. Age ranged from 9 to 19 years old, mean age was 13.6 years old. We identified 7 definite RHD (7.4 per 1000) and 13 borderline RHD (13.7 per 1000). The prevalence of RHD among form one to form three students in Tarawa, Kiribati was estimated 21.1 per 1000. Children diagnosed either definite or borderline RHD reported a rate of 40% having previous acute rheumatic fever (ARF), while children negative of RHD had only 23.7% with positive ARF history. During the screening, 12 children (12.7 per 1000) were diagnosed congenital heart disease (CHD), including ASD (n=6, 50% of CHD), VSD (n=2, 16.67%), PDA (n=1,
Left Ventricular Twist in Patients with Repaired Tetralogy of Fallot Assessed by Magnetic Resonance Imaging

Ken-Pen Weng, Yu-Chi Hung, Bo-Hau Chen, Chu-Chuan Lin, Kuang-Jen Chien, Juin-Yann Pan, Kai-Sheng Hsieh, Hsu-Hsia Peng, Ming-Ting Wu
Department of Pediatrics, Division of Cardiovascular Surgery; National Taiwan University Hospital; National Taiwan University; Department of Radiology, Kaohsiung Veterans General Hospital; Department of Pediatrics, St. Joseph Hospital; Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital; Kaohsiung, Taiwan

Background: Early detection of left ventricle (LV) dysfunction is very important for evaluating clinical outcome in patients with repaired tetralogy of Fallot (TOF). The index of LV ejection fraction (LVEF) may underestimate the degree of deteriorated cardiac function. In patients with repaired TOF, abnormal LV twist by echocardiography has been demonstrated, but there is still no report about LV rotation by magnetic resonance imaging (MRI). We aimed to evaluate LV twist using MRI in patients with repaired TOF.

Methods: This study consisted of 32 normal subjects (M/F 21/10, mean age 22.1 ± 4.8 yrs) and 31 patients with repaired TOF (21/10, mean age 22.1 ± 1.8 yrs). They all underwent MRI. The volumetric indices, mass, and ejection fraction of both RV and LV were determined. The VO peak-to-peak (PTP) and the rotation angle, characterizing the twist function of each slice in the LV, were computed. MRI derived parameters were compared between two groups.

Results: Compared to normal controls, patients with repaired TOF had significantly higher RVESVI (62.6 ± 23.0 vs 40.4 ± 9.7 cm3/m2, p < 0.05) and RVEF (49.1 ± 6.9 vs 48.1 ± 7.5, p < 0.05). Patients with repaired TOF showed a significantly lower VO PTP (2.7 ± 1.3 vs 5.4 ± 1.6 cm/s, p < 0.01) and LV twist (4.9° ± 2.8° vs 8.7° ± 2.4°, p < 0.01) than normal controls.

Conclusions: Lower LV twist can provide early information about regional abnormalities of LV before a global ventricular dysfunction in patients with repaired TOF. Assessment of LV twist using MRI is a useful tool to detect the early deterioration of LV function in patients with repaired TOF.
Background: This is the second stage study of our novel methodology for coronary image. The first stage study has been presented in 226th annual meeting. Our experience showed many patients may have coronary abnormalities other than dimensional change alone. So far, scanty information exists about coronary artery status besides dimensional change. We thus proposed & developed a novel systemic focused optimal coronary ultrasound (FOCUS) scoring system for acute KD.

Methods: Between Jan. 2014 and Feb. 2016, a total of 32 patients with acute KD was enrolled in this study. One hundred age-matched normal children were used as control. Echocardiography(Echo) was performed by obtaining dynamic cine-loop recording for frame-by-frame analysis and using quality-optimal highest transducer frequency. Coronary abnormality is scored as following: 1) [P]: Prominence 2) [B]: Brightness of arterial wall 3) [I]: Irregularity arterial lumen or 4) [T]: Lack of tapering 5) [T]: Thickness of the coronary arterial wall.

Results: Using our FOCUS scoring method, various coronary artery abnormalities were present in acute KD, including various degree of luminal prominence in 24 (75%) patients, aneurysm formation in 3 (9.2%) patients, absence of tapering in 22 (68%) patients, irregularity in 11 (34%), and intimal thickening brightness in 24 (75%) patients. Overall, coronary artery anomalies were present in 30 (93%) of our patients in acute phase of KD. Furthermore, there is 28 (87.5%) patients have more than 2 features among the 4 major characteristics of FOCUS scoring method while Z score >2.5 was detected in 43%. The novel FOCUS scoring showed a FOCUS score >10 in 90.6% (29/32) of patients while only 0.6% (2/32) FOCUS score < 10.

Conclusions: The incidence of coronary artery abnormalities in acute KD is higher than previously reported. FOCUS score can provide an accurate and timely assessment regarding the presence of coronary artery lesions in acute KD. With our novel FOCUS scoring method, more detailed, comprehensive and multi-faced features of CAA other than conventional Z score can be provided. We thus propose a FOCUS score >10 is indicative for acute KD, <5 is indicative for normal coronary, 5–10 deserves further check-up.
Characteristics of Children with Kawasaki Disease Requiring Intensive Care: 10-Year Experience at a Tertiary Pediatric Hospital

Ching-Chia Kuo, Yu-Shin Lee, Ming-Ru Lin, Shao-Hsuan Shia, Chih-Jung Chen, Cheng-Hsun Chiu, Mao-Sheng Hwang, Yhu-Chering Huang
Department of Pediatrics, Chang Gung Memorial Hospital, Linkou Branch, Taoyuan, Taiwan

Background: Kawasaki disease (KD) is a febrile systemic vasculitis, and some patients developed serious complications requiring intensive care. We aim to ascertain the clinical presentations and outcomes of these patients.

Methods: From October 2004 to October 2014, children with KD who ever stayed in pediatric intensive care units (ICU) for acute stage treatment were defined as case patients; for each case, three age/gender-matched patients with KD but without ICU stay, if identified, were selected as control subjects. Clinical data were retrospectively collected and analyzed.

Results: Among 1065 KD patients we identified 26 case patients and 79 controls for statistical analysis. ICU patients had a longer fever duration, and tended to have a hemoglobin level < 10 g/dL, a platelet count < 150,000/μL, a band cell percentage > 10%, a peak serum C-reactive protein level > 200 mg/L, a serum albumin value < 3 g/dL, and to present with multi-organ systems involvement. Time from symptom onset to the diagnosis of KD was similar between the two groups, but ICU patients were less likely to have KD as a leading admission diagnosis. Shock (73.1%, n=19) was the most common reason for ICU admission. ICU patients were more likely to receive antibiotics, albumin infusion, and need a second dose of intravenous immunoglobulin (IVIG) or steroid therapy. No in-hospital mortality was observed.

Conclusions: Patients with KD requiring ICU admission are significantly associated with multi-organ involvement, abnormal hematological and biochemistry biomarkers, not an initial diagnosis, and an IVIG-refractory disease.

Secundum Type Atrial Septal Defect, Atrio-Ventricular Block, and Non-myocardial Ischemic Precordial T-waves Changes – Possibly a New Variant of NKX 2-5 Gene Mutation

Ching-Tsuen Shen, Nan-Koong Wang, Yung-Chuan Chen, Chia-Wei Ho
Department of Pediatrics, Cathay General Hospital, Taipei, Taiwan

Background: Cardiac morphogenesis needs a precise, coordinate temporal and spatial processes under controls of many genes encoding growth factors, transcription factors, co-factors, regulators, signaling proteins, and structural proteins. Perturbation of this process will induce a congenital heart defect. Previous reported studies had found that some genes mutation would affect septation of the atrial septum. The HAMP gene plays a significant role in iron metabolism, has a vital function regarding Kawasaki disease’s pathogenesis. The purpose of this study is to investigate HAMP genetic polymorphisms and their expressions in relation to KD.

Methods: We recruited a total of 381 KD patients and 500 controls from Taiwan’s Bio-Bank for this study. TaqMan allelic discrimination has determined five tagging SNPs (rs916145, rs10421768, rs3817623, rs7251432, and rs2293689). We collected treatment outcome data related to clinical phenotypes, coronary artery lesions (CAL), coronary artery aneurysms (CAA), and intravenous immunoglobulin (IVIG) to perform our analysis. We also measured plasma hepcidin levels using an enzyme-linked immunosorbent assay.

Results: HAMP gene polymorphisms differed significantly between the normal controls and the KD patients in rs2293689. We found no significant correlations between HAMP polymorphisms and CAL or CAA formation or IVIG treatment response in the study’s patients. Furthermore, plasma hepcidin levels both before and after IVIG administration were positively and significantly correlated with length of hospital stays (R = 0.217, p = 0.046 and R = 0.381, p< 0.001) prior to IVIG administration in KD patients.

Conclusions: This study is among the first to find that HAMP polymorphisms and their expression are related to disease susceptibility, length of hospital stays, and albumin levels in Taiwanese children suffering from KD.
and myocarditis. Patients of atrial septal defect, atrio-ventricular block, and T wave changes in the precordial leads of human 12 leads surface electrocardiograms without aforementioned causes may denoted a variant of NKX2-5, GATA-4, and Tbx 5 gene mutation. 

**Methods:** We had performed echocardiographic screening to 10,000 newborn infants before (1997-2005), and found 58.13% with patent foramen ovale, 1.61% with secundum type atrial septal defect. We also reviewed the recent 5 years charts in this hospital (2010-2015) using the key-word “secundum type atrial septal defect”, “Patent foramen ovale”, “atrial left to right shunt”, “Inter-atrial communication”. Only those age less than or equal to 18-year-old were included in this study. Patients included those admitted and those visited the outpatient clinic. All of them had performed 12 leads surface electrocardiography and two dimensional echocardiogram.

**Results:** There were 54 cases of isolated secundum type atrial septal defect retrieved. Only two cases among 54 cases of isolated secundum type atrial septal defect had in association with atrio-ventricular block. One of these two cases had T wave changes and Mobitz type 1 second degree atrio-ventricular block in the precordial leads of her surface 12 leads electrocardiograms. She was a 17-year-old girl, had brief fainting history. Cardiac enzymes study was of normal limits; Thallium scanning of the heart showed a normal perfusion image. Her physical examination didn’t find any pulmonary or neurological abnormality. Cardiac enzymes, blood glucose and electrolytes levels were within normal limits. Another one patient was a 7-month-old female infant. She had first degree atrio-ventricular block, and was symptomless.

**Conclusions:** The NKX2.5 gene encoding a homeobox-containing transcription factor, locates on chromosome 5 q35.1. This transcription factor functions in heart formation and development. Mutations in this gene cause atrial septal defect with atrioventricular conduction defect, and congenital hypothyroidism non-goitrous type 5. Alternative splicing results in multiple transcript variants. Those of. C618T, C642T and C701T of NKX 2-5 mutated variants will have different functions, containing transcription factor, locates on chromosome 5 q35.1. This transcription factor functions in heart formation and development. Mutations in this gene cause atrial septal defect with atrioventricular conduction defect, and congenital hypothyroidism non-goitrous type 5. Alternative splicing results in multiple transcript variants. The NKX2.5 gene is expressed in the heart and other tissues, such as liver, kidney, lungs, and skeletal muscle. It is involved in the development of the heart, and mutations in the gene can cause congenital heart defects, such as atrial septal defects and ventricular septal defects.

**Successful Treatment in Patients with Severe Aplastic Anemia and Prior Pulmonary Aspergillosis by Hematopoietic Stem Cell Transplantation.**

**Background:** Infection is a major cause of morbidity and mortality in patients with severe aplastic anemia (SAA). Invasive aspergillosis (IA) has a high mortality rate in patients undergoing hematopoietic stem cell transplantation (HSCT). As a high risk of spread and recurrence, how to treat patients with previous IA before allogeneic HSCT remains challenging. Herein, we report two patients with...
SAA who developed pulmonary IA before HSCT and were successfully rescued with allogeneic HSCT.

Methods: The first patient was a 2-year-old female with SAA. A typical lung lesion in the computed tomography (CT) of chest with elevated galactomannan (GM) levels was noted, and probable IA was diagnosed. Initially, she responded well to the combination treatment of voriconazole and caspofungin with a remarkable decrease in GM levels. However, a significant increase in GM levels was noted when she received conditioning regimen during HSCT. The GM levels remained high before neutrophil engraftment. After engraftment, the GM levels declined gradually to normal with taper of immunosuppressant drugs. She is doing well without any anti-fungal agents for more than one year, and there is no evidence of IA recurrence. The second patient was a 12-year-old female with SAA, and the diagnosis of probable IA was made by the typical lung lesions in the chest CT and the elevated GM levels. She responded well to voriconazole treatment, and the GM levels decreased. However, the GM levels flared up again during the conditioning of HSCT and declined to normal after neutrophil engraftment.

Results: Without operation for pulmonary IA, an excellent outcome was achieved in both patients. During and after HSCT, the clinical condition of IA was not aggravated and there were no additional complications.

Conclusions: According to our experience, performing HSCT as soon as possible under appropriate anti-fungal treatment could cure patients with SAA and pulmonary IA. During HSCT, GM levels were closely related to the patients’ immunity. Although surgical resection of pulmonary IA can completely eradicate a localized infection and is considered prior to HSCT, the two patients with SAA and IA were successfully treated without surgical intervention before and after HSCT. Accordingly, surgical therapy may not needed in this situation with the consideration of operation-related complications.

Management of Kasabach-Merritt Phenomenon in Children

Kasabach-Merritt 表現之兒童治療經驗

Kang-Hsi Wu, Te-Fu Weng, Ching-Tien Pen
Children’s Hospital of China Medical University

Background: Kasabach-Merritt phenomenon (KMP) is a rare consumptive coagulopathy characterized by profound thrombocytopenia and hypofibrinogenemia occurring in association with the giant hemangioma. Treatment remains challenging without consensus on the optimal medical management. Combined therapy with multiple drugs is recommended for life-threatening events or refractory disease. We report excellent outcome of three cases with life-threatening KMP.

Methods: Three patients were diagnosed as KHE with KMP in Children’s Hospital of China Medical University. The first patient with giant hemangioma on his head presented respiratory distress and severe thrombocytopenia and hypofibrinogenemia when she was two months-old. The

second patients with giant hemangioma over his right shoulder presented with severe thrombocytopenia and coagulopathy. He received chemotherapy due to refractory thrombocytopenia after conventional treatment, but complicated with pulmonary hemorrhage with acute respiratory distress syndrome. The third patient that is 9 years-old female who presented with mediastinal mass and huge pleural effusion had hypofibrinogenemia without thrombocytopenia.

Results: First patient had partial response to steroid initially. Then we combined vincristine, thalidomide and propranolol due to poor response to initial steroid treatment. But recurrent thrombocytopenia and hypofibrinogenemia occurred and TEA was performed. The condition was stable one year after treatment. The second patient had poor response to steroid, chemotherapy and TEA. He suffered from severe pulmonary hemorrhage due to severe thrombocytopenia after chemotherapy. We began combined therapy with interferon, steroid, propranolol and sirolimus. The following platelet count was stable. The third patient had hypofibrinogemiaeia without thrombocytopenia and respiratory distress due to tumor compression. The clinical response was noted after combined steroid, sirolimus and propranolol. All patients received tranxamic acid and cryoprecipitate transfusion for bleeding tendency.

Conclusions: KMP with refractory thrombocytopenia and coagulopathy need combined therapy with multiple drugs after poor response to initial treatment with steroid. Combined cryoprecipitate and tranexamic acid is effective for prophylaxis of bleeding.

83 Clinical Role of Child Protection Medical Service Demonstration Centers in Approaching Child Abuse and Neglect in Taiwan

台灣兒少保護醫療服務示範中心於兒少虐待及疏忽之臨床角色

Han-Ping Wu,1,4 Yu-Ching Chang,1,4 Jing-Long Huang,2,4 Kuang-Lin Lin,1,4, Shao-Hsuan Hsia,1,4, I-Jun Chou,1,4, Chang-Teng Wu1,4, Yi-Chen Hsin1,4, En-Pei Lee2,4, PCHAN Study Group3
Division of Pediatric General Medicine,1 Chang Gung Memorial Hospital at Linko, Kweishan, Taoyuan, Taiwan; Department of Pediatrics,2 Study Group for Prevention and Protection Against Child Abuse and Neglect,1 Chang Gung Memorial Hospital at Linko, Kweishan, Taoyuan, Taiwan; College of Medicine, Chang Gung University,4 Taoyuan, Taiwan

Background: Child abuse includes all forms of physical and emotional ill-treatment, sexual abuse, neglect, and exploitation that results in actual or potential harm to the child’s health, development or dignity. In Taiwan, the Child Protection Medical Service Demonstration Center (CPMSDC) was established to protect children from abuse.
and neglect. We further analyzed and compared the trends and clinical characteristics of cases reported by CPMSDC to evaluate the function of CPMSDC in approaching child abuse and neglect in Taiwan.

**Methods:** We prospectively recorded children with reported child abuse and neglect in a CPMSDC in a tertiary medical center from 2014 to 2015. Furthermore, we analyzed and compared age, gender, scene, identifying settings, time of visits, injury type, injury severity, hospital admission, hospitalization duration, and outcomes based on the different types of abuse and the different settings in which the abuse or neglect were identified.

**Results:** Of 361 child abuse cases (mean age 4.8±5.36 years), the incidence was highest in 1- to 6-year-old children (n=198, 54.85%). Physical abuse and neglect were predominant in males, while sexual abuse was predominant in females (p = 0.001). Neglect was most common (n=279, 75.85%), followed by physical (n=56, 15.51%) and sexual abuse (n=26, 7.2%). The most common identifying setting was the emergency department (n=320, 88.64%), with neglect being most commonly reported. Head, neck, and facial injuries were more common in physically abused children than in neglected and sexual abused children (p=0.005), leading to longer hospitalization (p=0.042) and a higher Injury Severity Score (ISS) (p=0.043). There were more skin injuries in neglect (p=0.001). The mortality rate was 2.49% (n=9).

**Conclusions:** The CPMSDC can enhance the ability, alertness, and inclination of professionals to identify suspected cases of child abuse, and to increase the rate of registry. Neglect of young children is common, and the consequent injury, especially asphyxia, could lead to mortality. Children with physical abuse had a higher ISS, longer duration of hospitalization, and more injuries of head, face, and neck compared with other types of abuse. Rigorous registry evaluation and evidence-based prevention is important in clinical practice.

**84 Analysis of the Utilization of Medical Service and Socioeconomic Environment for Reported Child Maltreatment Rate in Taiwan**

Taiwan兒童虐待發生率之探討—醫療體系服務與社會經濟環境

Yi-Chen Hsin, I-Jun Chou, Shao-Hsuan Hsia, Kuang-Lin Lin, Cheng-Hsun Chiu, Han-Ping Wu, Jing-Long Huang

**Background:** Child maltreatment is a growing problem globally. However, the relationship between child maltreatment and socioeconomic environment as well as the role of physicians are not well understood in Taiwan. Thus, we investigated the local data to identify the risk factors for child abuse and neglect in Taiwan.

**Methods:** Our data was obtained from Taiwan National Statistics in county level from 2004 to 2014. Panel data analysis was used in analyzing the links between child maltreatment rate and its associated factors.

**Results:** There was an increasing trend of child maltreatment rate in Taiwan from 2004 to 2014. During the past decade, child maltreatment rate raised from 150 in 2004 to 300 cases per 100000 children in 2014. The peak happened in 2012. It had significant geographically differences and highest child maltreatment rate occurred in the eastern Taiwan. Panel data analysis revealed that unemployment rate had a lag effect on the child maltreatment rate. Significant interaction between eastern area and density of physicians was found.

**Conclusions:** County-level unemployment rate gives a prediction of sequential child maltreatment rate in the next year. Density of physicians is associated with the child maltreatment rate. Physician plays an important role in reporting system of child maltreatment, especially in eastern Taiwan.

**85 Clinical Pitfalls of Diagnosis in Child Abuse in the Emergent Department**

急診室兒少虐待臨床診斷陷阱

Pei-Chun Chan1,3,4, Han-Ping Wu1,3,4, Jing-Long Huang2,3,4, Kuang-Lin Lin2,3,4, Shao-Hsuan Hsia2,3,4, Cheng-Hsun Chiu2,3,4, I-Jun Chou2,3,4, Mei-Hua Hu1,3,4, Yi-Chen Hsin1,3,4, PCHAN Study Group1

**Division of Pediatric General Medicine1, Chang Gung Memorial Hospital at Linko, Kweishan, Taoyuan, Taiwan; Department of Pediatrics2, Study Group for Prevention and Protection Against Child Abuse and Neglect2, Chang Gung Memorial Hospital at Linko, Kweishan, Taoyuan, Taiwan; College of Medicine, Chang Gung University3, Taoyuan, Taiwan**

**Background:** Child physical abuse is not only a serious issue in children but also a important cause of morbidity and mortality in the pediatric emergent department (ED). Early accurate diagnosis and appropriate interventions can be the key factors for better outcomes. In the ED, physical abuse remains an underreported and underdiagnosed despite widespread advocacy and education in recent years. This study aimed to clarify the clinical pitfalls and risk factors in missed cases of child abuse in the ED.

**Methods:** This retrospective analysis collected pediatric patients with reported child physical abuse admitted to the ED in a medical center. between January 2012 to January 2016. The experts’ peer review group of our hospital reviewed all medical charts to identify the definite diagnosis of child abuse. The clinical manifestations, etiologies, managements and outcomes were father analyzed in the cases with delayed in diagnosis or misdiagnosis for child abuse.
emergency department visits by adolescents for substance abuse.

Methods: We sought to evaluate pediatric emergency department emergency departments for poisoning from substance abuse. We reviewed medical charts of the impression of child abuse and neglect reported from the ED and pediatric emergency department. The more visits made by females (52.00%). Substance included ketamine, MDMA, amphetamine, nitric oxide, and alcohol abuse. Of 30 (40%) adolescents without domestic violence, 7 (23.3%) were substance abuse, 7 (23.3%) suicide attempt, and 11 (36.7%) patients were admitted.

Conclusions: There were 23.3% adolescent of social worker reported visits to pediatric emergency department from 2012 through 2015 with a primary diagnosis of substance abuse. Future studies might examine optimal screening, preventative measures, and intervention programs for these patients.

Results: Of 1375 reported cases, 170 cases met the diagnosis of child physical abuse, and 142 cases was diagnosed as child abuse reported from the ED. Among them, 53 cases were admitted to the ward of intensive care units for further care, and 28 cases were diagnosed and reported as the victims of child physical abuse after admission to wards. After detailed analysis, we found that younger age groups, mild clinical symptoms and signs, and no obvious traumatic lesions were related parameters in the missed cases of child abuse in the ED.

Conclusions: Identifying the suspicious abused cases is the challenging and difficult work-up in the emergent room. In the ED, pediatricians might require more attention in suspected abused cases with young age groups, mild clinical symptoms and signs, and no obvious traumatic lesions to prevent the misdiagnosis in the ED.

Emergency Department Visits by Adolescent Patients for Substance Abuse

Mei-Hua Hu, Chang-Teng Wu, Jing-Long Huang, Kuang-Lin Lin, Han-Ping Wu, Shao-Hsuan Hsia

Chang Gung Memorial Hospital, Taoyuan, Taiwan; College of Medicine, Taoyuan, Taiwan

Background: Substance abuse has steadily increasingly recognized problem, and current research has shown a dramatic increase in hospitalizations resulting from substance poisonings. Still, much is unknown about the clinical and demographic features of patients presenting to emergency departments for poisoning from substance abuse. We sought to evaluate pediatric emergency department visits by adolescents for substance abuse.

Methods: This was a retrospective study utilizing 2012-2015 data from the social welfare reports of emergency department. Total number of admissions, disposition, gender, age, and triage were examined.

Results: From 2012 through 2015, there were 75 emergency department visits by adolescents reported to social worker. The majority of adolescents reported to social welfare were more likely to have domestic violence (60.00%), psychological problems (13.3%), substance abuse (9.3%) and neglect (17.3%). Sixty percent visited to traumatic emergency department, and forty percent visited to pediatric emergency department. The more visits made by females (52.00%). Substance included ketamine, MDMA, amphetamine, nitric oxide, and alcohol abuse. Of 30 (40%) adolescents without domestic violence, 7 (23.3%) were substance abuse, 7 (23.3%) suicide attempt, and 11 (36.7%) patients were admitted.

Conclusions: There were 23.3% adolescent of social worker reported visits to pediatric emergency department from 2012 through 2015 with a primary diagnosis of substance abuse. Future studies might examine optimal screening, preventative measures, and intervention programs for these patients.

Prognostic Factors in Cases with Child Abuse and Neglect Admitted to the Pediatric Intensive Care Unit

En-Pei Lee, Oi-Wa Chan, I-Jun Chou, Jainn-Jim Lin, Cheng-Hsun Chiu

Division of Pediatric Critical Care Medicine, Chang Gung Memorial Hospital at Linko, Kweishan, Taoyuan, Taiwan; Department of Pediatrics, Study Group for Prevention and Protection Against Child Abuse and Neglect, Chang Gung Memorial Hospital at Linko, Kweishan, Taoyuan, Taiwan; College of Medicine, Chang Gung University, Taoyuan, Taiwan

Background: The victims with child abuse and neglect may be hospitalized to the pediatric intensive care unit (PICU) due to the critical conditions, such as conscious impairment, unstable vital signs, physical and head injuries requiring for emergency surgical intervention. This study aimed to survey the outcomes of victims with child abuse and neglect admitted to PICU and to analyze prognostic factors for mortality and morbidity.

Methods: From January 2001 to December 2015, we reviewed medical charts of the impression of child abuse and neglect reported from the social welfare reporting system. Children under the age of 18 years admitted to the PICU were enrolled in our analysis. Demographic data, injury types, initial presentations, length of hospital stay and PICU stay, time of presentation, laboratory data, imaging studies, admission source, morbidity, and mortality were collected and compared based on different types of abuse.

Results: A total of 1838 pediatric patients with reported child abuse and neglect were collected in this study. There were 355 victims (19.3%) admitted in the PICU, including 27% physical abused and 73% neglected victims. The abused patients had more length of PICU stay (18.17 days) than that in neglected cases (7.19 days; p <0.01). The mortality rate in the abused group was 12.5% vs. 8.9% for the neglected group. Head injury was the most common leading cause of death and asphyxia contributed the highest risk factor for mortality in the neglected group. The odds ratio of mortality in cases with head trauma receiving neurosurgery was 0.163 (95% CI, 0.041–0.657, p=0.011) in the abused group and 0.229 (95% CI, 0.026–0.202, p=0.185) in the neglected group. The significant factors associated with mortality were initial presentation with shock, hypothermia, hyponatremia and hypocalcemia (all p<0.05).

Conclusions: Some important predictors for mortality were identified for child abuse and neglect requiring critical care as initial presentation with shock, hypothermia, hyponatremia and hypocalcemia. In addition, immediate neurosurgery is a protective factor for the victims with abused head injuries to improve survival rate.
Non-invasive Cardiac Output Monitoring in Children with Congenital Heart Diseases - a Comparative Study

Chu-Chuan Lin¹, Kai-Sheng Hsieh²
Department of Pediatrics, Veterans General Hospital¹, Kaohsiung, Taiwan; Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital²

Background: In recent years less invasive alternative methods have become available for measuring cardiac output(CO) in pediatric intensive care unit(PICU). Hemodynamic parameters, such as cardiac output, central venous oximetry, and their changes after treatment could be continuously monitored. In this study, we compare the hemodynamic parameters derived from a non-invasive bioreactance device with those from echocardiography.

Methods: Between Dec., 2012 and Jul., 2014, 23 children underwent open heart surgery or interventional cardiac catheterization was included. Their ages ranged from 3 to 20 years old. And their body weight ranged from 5 to 61 kilograms. In addition to bedside vital signs, cardiac output was monitored continuously with the Cheetah NICOM system. Transthoracic Doppler echocardiography(TTE) was performed by single experienced sonographers within the first six hours and then again after 24 hours, unless the NICOM monitor was disconnected from the patient or the patient developed arrhythmias.

Results: Of the patients studied, continuous cardiac output recording was successfully performed on 5 with Tetralogy of Fallot,12 with VSD, 3 with ASD, and 3 with DORV. There was good correlation between the two methods (r=0.95, P <0.001). The bias and precision (mean and SD) between the two devices was 0.42±1.30 l/minute. The limits of agreement were -1.5 to 1.5 l/minute. Changes in cardiac output for two consecutive days correlated well between the two methods (r=0.95; P <0.001).

Conclusions: Our initial experience showed that the non-invasive bioreactance method is clinically comparable to TTE in cardiac output measurements in post-operative patients with congenital heart diseases. Continuous monitoring is another major advantage of this method.

The Impact of Acute kidney Injury on Mortality of Pediatric Patients on Extracorporeal Membrane Oxygenation

Min-Tser Liao¹, En-Ting Wu², I-Jung Tsai², Leigh Lu², Yong-Kwei Tsau²
Department of Pediatrics, Taoyuan Armed Forces General Hospital¹, Taoyuan, Taiwan; Department of Pediatrics, National Taiwan University Hospital¹², Taipei, Taiwan

Background: Extracorporeal membrane oxygenation (ECMO) had been utilized for pediatric patients in critical condition, such as life-threatening cardiogenic or infectious reasons. The study analyzed the relationship between in-hospital mortality of pediatric patients treated with ECMO and the Acute kidney Injury Network (AKIN) scores observed at pre-ECMO support (AKIN0-hour) and post-ECMO support 24 hours (AKIN24-hour) and 48 hours (AKIN48-hour).

Methods: The study reviewed the medical records of 140 critical ill patients on ECMO support due to cardiogenic reason and 57 critical ill patients due to infectious reason at a specialized intensive care unit at a tertiary care university hospital between April 1994 and April 2015.

Results: The overall in-hospital mortality was significantly higher in AKI cases. The in-hospital mortality rate of cardiogenic and infectious causes were 62.1% and 50.9% respectively. The AKIN0-hour, AKIN24-hour and AKIN48-hour scoring system had significantly better areas under the receiver operating characteristic curve (0.727 +/- 0.50, 0.713 +/- 0.51 and 0.702 +/- 0.52) for cardiogenic reason than infectious reason (0.511 +/- 0.81, 0.582 +/- 0.88 and 0.581 +/- 0.89).

Conclusions: During ECMO support, the AKIN scoring system proved to be a better evaluation tool for cardiogenic than infectious reasons. The AKIN0-hour also had the excellent prognostic ability for these patients.

Magnetic Resonance Imaging Findings of Pneumococcal Meningitis

Hsiang-Ju Hsiao, Chang-Teng Wu, Jain-Jim Lin, I-Anne Huang, Oi-Wa Chan, Shao-Hsuan Hsia
Department of Pediatrics, Chang Gung Memorial Hospital, Linkou, Taiwan

Over the 90-month study period, 13 patients were admitted to the PICU due to pneumococcal meningitis. Nine children received MR imaging at our institution. There were 4 male and 5 female patients. Their mean age was 5.7 years (range 0.7–12.5 years). Five children’s MRI had restricted diffusion, 4 children had poor outcome. The AKIN0-hour also had the excellent prognostic ability for these patients.

The Impact of Acute kidney Injury on Mortality of Pediatric Patients on Extracorporeal Membrane Oxygenation

Min-Tser Liao¹, En-Ting Wu², I-Jung Tsai², Leigh Lu², Yong-Kwei Tsau²
Department of Pediatrics, Taoyuan Armed Forces General Hospital¹, Taoyuan, Taiwan; Department of Pediatrics, National Taiwan University Hospital¹², Taipei, Taiwan

Background: Invasive pneumococcal disease results in high morbidity and mortality globally each year, meningitis is the most severe type of invasive pneumococcal disease. Studies on Magnetic resonance imaging findings in children with pneumococcal meningitis are limited.

Methods: We conducted a retrospective study at a single center in northern Taiwan for pneumococcal meningitis in a PICU from January 2009 to June 2016. Demographic characteristics, clinical courses, MRI findings, and outcomes were analyzed.

Results: Over the 90-month study period, 13 patients were admitted to the PICU due to pneumococcal meningitis. Nine children received MR imaging at our institution. There were 4 male and 5 female patients. Their mean age was 5.7 years (range 0.7–12.5 years). Five children’s MRI had restricted diffusion, 4 children had poor outcome.

Conclusions: Our case series study suggests that restricted diffusion in MR is associated with poor outcome in children with pneumococcal meningitis.
91 Severe Mycoplasma Pneumonia-associated Encephalitis in Childhood – A 10-year Experience in a Tertiary Center

Chang-Ku Tsai¹, Mei-Hsin Hsu, Pi-Lien Hung, Kuang-Che Kuo, Hsuan-Chang Kuo, Ying-Jui Lin, Li-Tung Huang, Ying-Chao Chang
Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine¹, Kaohsiung, Taiwan

Background: Mycoplasma pneumoniae is a common respiratory infection pathogen in childhood. It also accounts for around 5–10% of acute encephalitis in Europe and North America. The knowledge on Mycoplasma pneumoniae encephalitis in childhood is based on case reports or small series of clinical studies. Review literatures showed 34% of patients had minor to moderate neurologic deficits, and 9% died. Studies illustrated the possible critical conditions of this acute encephalitis were scancy. We attempted to investigate the clinical presentations and 6-month outcome of mycoplasma pneumoniae infection associated encephalitis over the past 10 years in the pediatric intensive care unit (PICU) at Kaohsiung Chang Gung Memorial Hospital.

Methods: We retrospectively reviewed chart from Jan. 2005 until May. 2015. We gathered the clinical data, including gender, age, clinical presentations, neuroimages, cerebrospinal fluid analysis, mycoplasma serology and DNA copies. In addition, follow-up neurologic symptoms 6 months later was recorded as outcome measure. All the clinical data was presented as descriptive statistics.

Results: 16 patients admitted to PICU due to mycoplasma pneumoniae-associated encephalitis which was proved by serology, and presented as neurologic deficits as well. Boy were predominant (male: female=10:6). The mean onset age were 7.3 years old (ranged 4-13 years). 15 (93%) patients had prodromal respiratory symptoms or fever at least 3 days. 12 (75%) had pulmonary infiltration on chest radiograph. 6 (37.5%) required ventilator support owing to consciousness change or status epilepticus. The mean duration of ventilator support was 15.3 days (ranged 5-44 days). The mean hospitalization duration was 23.3 days (ranged 5-89 days). 4 presented with status epilepticus and 5 (31.2%) patients left with postencephalitic epilepsy as neurologic sequelae. 9 (56.2%) were presented as pleocytosis and 7 (43.7%) had high CSF protein. None of them could be detected M. pneumonia DNA in cerebrospinal fluid. Cranial computed tomography (CT) or magnetic resonance image (MRI) abnormalities were seen in 5 (31.2 %) patients. The more abnormalities were detected over MRI which showed signal hyperintensity over deep nucleus (putamen, thalamus, etc) over T2WI. All patients received macrolide or doxycycline against mycoplasmas. Patients with status epilepticus or respiratory failure were given immune-modulating therapies with intravenous immunoglobulin (3/16, 18.7%), methylprednisolone pulse therapy (4/16, 25%) or plasma exchange (2/16, 12.5%). One patient (6%) expired due to prolong seizure despite intravenous immunoglobulin use.

Conclusions: Based on our observation, higher mycoplasma pneumonia IgM titer could be detectable in patients who initially presented as status epilepticus or suppressed consciousness level. The lack of detectable M. pneumonia DNA in cerebrospinal fluid in our patients, and immune-therapy attenuated clinical presentations suggest that mycoplasma pneumonia infection associated with encephalitis should be immune-mediated.

92 A Comparison of Severe Pediatric Influenza with ARDS and without ARDS

Hsin-Jung Chen¹, Chien-Heng Lin², Chieh-Ho Chen³, Hsiao-Chuan Lin², Jeng-Sheng Chang⁴
China Medical University Children’s Hospital¹; Division of Pediatric Pulmonology, China Medical University Children's Hospital²; Division of Infection Disease, China Medical University Children's Hospital²; Division of Pediatric Cardiology, China Medical University Children’s Hospital³

Background: Influenza virus infection can cause serious respiratory complications, especially most serious of them acute respiratory distress syndrome (ARDS). The objectives of this study were to compare the clinical features and outcome between severe pediatric influenza with ARDS and those without ARDS.

Methods: We conducted a retrospective cohort study of inpatients admitted to China Medical University Children's Hospital with a positive respiratory specimen for influenza from Jan., 2012 to Feb., 2016. We compare the demographics and clinical characteristics of patients between ARDS and those without ARDS.

Results: A total of 18 pediatric patients with severe influenza infection (10 had type A, 8 had type B) admitted to our pediatric intensive care unit (ICU) during the study periods. Six patients had ARDS (ARDS group) and 12 patients (non-ARDS group) had other complicated condition. In non-ARDS group, 6 had encephalitis, 5 had pneumonia and one had myocarditis. All of ARDS patients were intubated, while 4 of 12 in non-ARDS patients were intubated. There were three patients had underlying disease, including 2 prematurity and 1 cerebral palsy. Patients with ARDS had a lower median age (2 year-old vs 6 year-old), and their hospital stays were more than non-ARDS group (29.17±45.97 vs 9.67±1.19 P=0.006). Two patients with encephalitis had mortality in non-ARDS group but no mortality in ARDS group (16.67% vs 0%, P=0.287).

Conclusions: Patients with underlying disease seem had a tendency of developing ARDS while infected with severe flu. More hospital stays days but lower mortality rates in severe influenza children with ARDS than those without ARDS.
Clinical Manifestation of Pediatric Mediastinal Tumors: 15-year Experience at a Single Children’s Hospital

Chieh-Ho Chen1, De-Fu Weng2, Chien-Heng Lin1
Division of Pediatric Pulmonology, China Medical University Children’s Hospital1, Taichung, Taiwan; Division of Hematology & Oncology, China Medical University Children's Hospital2, Taichung, Taiwan

Background: Mediastinal tumors are rare with poor prognosis in pediatric populations. The differential diagnosis include lymphoma, germ cell tumor, thymoma and other rare tumors; which clinical presentations and age of onset are different from each other. Here, we would like to analyze clinical presentations of pediatric mediastinal tumors at our hospital in order to find out the useful predictive prognostic factors.

Methods: We retrospectively recruit patients younger than 18-year-old with diagnosis of mediastinal tumors from 2001 to 2016 at China Medical University Children’s Hospital. Patients’ gender, age of disease onset, initial pulmonary symptoms such as airway obstruction, pleural effusion, pericardial effusion, SVC syndrome, and outcome were reviewed and collected.

Results: A total of 40 patients were diagnosed as having mediastinal tumors our hospital. The median onset of age is 13 year-old, with male to female ratio of 3 to 1. Ninety percent of the mediastinal tumors are malignant (36/40). The most common mediastinal tumors in our study is T-cell lymphoma (16/40, 40%), followed by neuroblastoma (5/40, 12.5%), various types of germ cell tumors (5/40, 12.5%), and thymoma (3/40, 7.5%). Pleural pulmonary blastoma, nonrhabdomyosarcoma and tracheal carcinoma are rare with high mortality. Neuroblastoma is more common in girls younger than 5 year-old (M/F = 1/5). The overall mortality rate is up to 60%. The presentation of these tumors are commonly with respiratory distress (60%), productive cough(47.5%), pleural effusion (42.5%), SVC syndrome (35%), neck mass (35%), airway compression (32.5%), fever (30%), chest pain (25%) and pericardial effusion (25%). Lymphoma, compared with other tumors, presents more likely with neck mass (52.6% v.s.19.0%, P=0.026) and SVC syndrome (52.6% v.s. 19.0%, P=0.026), and has worse prognosis singificantly (68.4% v.s. 52.4%, P=0.021).

Conclusions: Pediatric mediastinal tumors often accompany symptoms such as airway obstruction, pleural effusion, pericardial effusion, SVC syndrome, and outcome were reviewed and collected.

Mycoplasma Pneumoniae Pneumonia with Pleural Effusion

Huan-Cheng Lai1, Chien-Heng Lin2, Chieh-Ho Chen2, Hsiao-Chuan Lin1
China Medical University Children’s Hospital1; Division of Pediatric Pulmonology, China Medical University Children’s Hospital2; Division of Infection Disease, China Medical University Children’s Hospital1

Background: The amount of pleural effusion is usually scant to small in the cases of Mycoplasam pneumonia (MP). The purpose of this study was to investigate the clinical features of MP patients with pleural effusion and elucidate the relevance of effusion in these patients.

Methods: A total of 7 patients who were diagnosed with MP with pleural effusion were enrolled. We reviewed these patients’ medical records for clinical presentation, hospital course, and pleural fluid analysis.

Results: Of the 7 consecutive patients with MP, all had pleural effusion detected on chest sonography. Among them, 4 had a moderate pleural effusion undergoing pigtail drainage (Group A) and others had a small pleural effusion without pigtail insertion (Group B). Patients in group A are prone to be younger age (5.08 y/o v.s 10.0 y/o, P=0.064). There were 3 patients found to be infected with macrolide-resistant M. pneumonia in Group A, while 1 in Group B (75% vs 33%, p= 0.27) the length of hospital stay is longer in Group A than Group B (14.0 vs 7.0, p=0.057). None of these patients with pleural effusion needed mechanical ventilation.

Conclusions: MP patients with pleural effusion who needed drainage have higher prevalence of macrolide-resistant M. pneumonia.

Comparison of a Mycoplasma Ag and a Mycoplasma IgM Rapid Detection Test for the Diagnosis of Mycoplasma Pneumoniae Pneumonia in Children

Wei-Ju Lee, Chih-Min Tsai, Kuang-Che Kuo, Chen-Kuang Niu, Kai-Sheng Hsieh, Hong-Ren Yu
Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital

Background: Mycoplasma infection is common in pediatric patients. Early diagnosis can help treatment early and properly. Rapid test is a convenient, immediate diagnostic tool for Mycoplasma pneumonia infection, which could be performed at bedside as using throat swab mucus or micro-haematocrit-tube whole blood, respectively. Here we compared the utility of a Mycoplasma Ag (ImunoAce Mycoplasma Test) and a Mycoplasma IgM antibody rapid
Low Cord-Serum Vitamin D Levels are Associated with Poor Lung Function Performance and Increased Respiratory Infection in Infancy

Yoon-Ho Lai1,3,4, Sui-Ling Liao2,3,4, Ming-Han Tsai2,3,4, Shen-Hao Lai

Department of Pediatrics, Chang Gung Memorial Hospital, Linkou Branch1; Department of Pediatrics, Chang Gung University2; Prediction of Allergies in Taiwanese Children (PATCH) Cohort Study3; Department of Pediatrics, Chang Gung Memorial Hospital, Keelung Branch2; Department of Pediatrics, Chang Gung University2; Prediction of Allergies in Taiwanese Children (PATCH) Cohort Study3

Infants with lower vitamin D levels in their cord serum had poorer lung function performance and a higher risk of a respiratory tract infection before the age of 6 months. Vitamin D levels in maternal and cord serum were highly correlated (r² = 0.457, p < 0.0001). Infants with lower vitamin D levels in their cord serum had poorer lung function performance and a higher risk of a respiratory tract infection before the age of 6 months (p < 0.01).

Conclusions: Although a high correlation was found between maternal and cord vitamin D levels, the effect on respiratory outcome was different. Our study is the first to show that low cord vitamin D levels significantly affect the respiratory function and the likelihood of a respiratory tract infection before 6 months of age.
99

The Risk Relevance of Autism Spectrum Disorders and Tourette Syndrome: A Population-Based Cohort Study

Background: Tourette syndrome is an inherited neurological disorder with onset in childhood, characterized by the presence of multiple motor tics and at least one vocal tic; these tics characteristically wax and wane. It is a co-morbid disorder with Autism Spectrum Disorders such as autism and Aspergers syndrome. Therefore, the aim of this study is to examine the co-occurrence of ASD and TS. This is also the first large-scale study exploring the risk relevance of ASD and TS in Taiwan by using National Health Insurance Research Database (NHIRD).

Methods: Claims data from the Taiwan National Health Insurance Research Database were used to conduct a bidirectional cohort study: 1) ASD cohort (N = 2408) v.s. non-ASD cohort (N = 9632), 2) TS cohort (N=10313) v.s. non-TS cohort (N=41252). The crude and adjusted Cox proportional hazard models was conducted to estimate the risk of ASD between the children with and without TS and the risk of TS between the children with and without ASD.

Results: In patients with ASD, the risk of TS was 5.98-fold higher for ASD patient than comparison children (HR = 5.98, 95% CI = 4.06-8.82). Also, the TS patient had a 10.1-fold higher risk of ASD than the children without TS (HR = 10.1, 95% CI = 6.25-16.4).

Conclusions: The clinical importance of examining the co-occurrence of ASD and TS is emphasized and should not be overlooked. We suggested that children referred for assessment of tics should be screened for ASD that constitute the most common comorbidities.

100

Functional Prognostic Yield of Children with Developmental Delay in a Children’s Hospital

Background: Developmental delay in children is associated with poor prognosis and outcomes. To improve the care of children with developmental delay, understanding the factors associated with their health outcomes is essential.

Methods: A retrospective cohort study was conducted using electronic medical records of children with developmental delay seen in a tertiary children’s hospital. The primary outcome was hospitalization, and the primary predictor was the presence of comorbidities. Multivariable logistic regression analysis was used to identify factors associated with hospitalization.

Results: A total of 100 children with developmental delay were included in the study. The presence of comorbidities was associated with a significantly higher risk of hospitalization (OR = 2.5, 95% CI = 1.2-5.3). The most common comorbidities identified were autistic spectrum disorders, attention-deficit/hyperactivity disorder, and cerebral palsy.

Conclusions: Children with developmental delay and comorbidities have a higher risk of hospitalization. Early identification and management of these comorbidities may improve the outcome of children with developmental delay.

98

Elevated Expression of Peptidase in Primary Spontaneous Pneumothorax

Background: Primary spontaneous pneumothorax (PSP) is usually caused by the spontaneous rupture of pleural blebs or bullae. However, the mechanism of bulla formation and the exact pathogenesis of developing PSP are still uncertain.

Methods: Patients with sporadic PSP were enrolled prospectively and a global gene expression analysis between lesion and normal sites of lung tissue biopsies was performed to identify differentially expressed genes associated with PSP. Pathway and network analysis was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID) web tool.

Results: A total of 10 paired lung biopsies (lesion sites and normal sites) were collected and gene expression analysis experiments were performed in 9 paired lung biopsies that satisfied stringent criteria for microarray analysis. Gene network pathways related to cell-extracellular matrix interactions including focal adhesion, extracellular matrix (ECM)-receptor interaction, and cell adhesion molecules (CAMs) were the most significant pathways related to PSP. Biologic functions including proteolysis in biological process (BP), extracellular matrix in cellular component (CC), and peptidase, endopeptidase and metallopeptidase activity in molecular function (MF) were predominantly found in up-regulated genes as compared to down-regulated genes.

Conclusions: An imbalance of cell-extracellular matrix interactions caused by overexpressed peptidase may result in alveolar destruction, distal emphysema and blebs formation, leading to the development of PSP.

97

and D16 (p=0.04, 0.01, respectively), but the gap of difference decreased with time.

Conclusions: Inflammatory response and oxidative stress were triggered as soon as 3 days after hyperoxic exposure in neonate rats, and returned to normal range gradually even if hyperoxic exposure was continuing. The histopathological change (fibrosis) progressed with age. We suggest the early change of inflammatory and oxidative stress may play a more critical role in the programming of later lung injury induced by hyperoxia.
Background: In the last 20 years, our government has invested a lot of energy in expanding and deepening services for children with developmental delay through different modality of services. A key question is “do they effective?” Several outcome measurements have been applied in different professional domains, yet a whole picture of global intervention effect is lack! In this study try to calculate statistically through a prospective registration to know functional prognostic yield of children with developmental delay in a children’s Hospital.

Methods: Our data base belongs to a long term prospective study in our hospital, which registered since 2002 about the evaluation result of all children, who received functional developmental assessment in our hospital. Standard descriptive statistics is performed.

Results: There are totally 12827 preschool children were enrolled into this study. The instruments for developmental assessment are Bayley Scale of Infant Development (BSID II or III), WPPSSI-R and other package according to age and special condition. Gender ratio is 1.99:1. The assessment result of Developmental delay is 68%(8671/12821) (according to the criteria). Functional prognostic outcome of those children are as followings: Improvement in all domains is found in 12%(451/3777), improvement in partial domain 12%(444/3777), maintain stabilization in 61%(2285/3777), regression in 16%(597/3777). From those data, we found improvement in cognitive domain is 11%(423/3935), in verbal domain 22%(917/4188), in Motor domain 24%(985/4188), in social domain 5%(212/4188).

Conclusions: Literature of comparable study will be reviewed. We felt the result was not impressive, yet, it comforts us to a certain degree. It means, also, a worthwhile devotion in the last 20 years in Taiwan from children, parents, professions and government. About patients with regressive results deserve even deeper attention.

101 Array CGH Analysis and Developmental Delay: A Diagnostic Tool for Pediatric Neurologists

晶片式全基因體定量化分析(array CGH)是兒童神經科醫師診斷發展遲緩基因病的利器

Tung-Ming Chang, Ming Chen1, Ni-Chung Lee2, Shuan-Bei Lin3, Yuh-Jyh Jong4

Department of Pediatric Neurology, Department of Genomic Medicine, Changhua Christian Hospital1, Changhua, Taiwan; Department of Pediatrics and Medical Genetics, National Taiwan University Hospital2; Department of Genetics and Metabolism, Mackay Memorial Hospital in Taipei3; National Chiao Tung University College of Biological Science and Technology4

Background: Developmental delay occurs in 1-3% of the population, with unknown etiology in approximately 50% of cases. Array Comparative Genomic Hybridization (array CGH) has emerged as a tool to detect genetic copy number changes and uniparental disomy and is the most sensitive test in providing etiological diagnosis in developmental delay. The aim of the study was to determine the optimal quality and clinical sensitivity of array comparative genomic hybridization in children with global developmental delay.

Methods: From 2013 to 2016, We present the results of array CGH application that was successfully implemented in a cohort of 41 children with the clinical diagnosis of global developmental delay and/or accompanying dysmorphic features and/or congenital malformations.

Results: We have identified 12 copy number variants (CNVs), including unbalanced translocations and chromosome Y disomy, receiving an overall diagnostic yield of 29.3%. Known pathogenic changes were identified in 50% of the cases. Among patients with pathogenic CNVs identified by array CGH, 91.7% had a previously normal karyotype analysis.

Conclusions: High-resolution array comparative hybridization can be applied successfully in children with global developmental delay as the method detects a significant number of pathogenic changes, resulting in early diagnoses. Our studies provide more insights into the benefits derived by using chromosomal microarray analysis and demonstrate the usefulness of array CGH as a first-tier clinical setting test in children with global developmental delay.

102 Incidence and Epidemiology of Physical Abuse Related Hospitalisation in Taiwanese Children

台灣身受兒童住院盛行率與流行病學之研究

Kong Shu Sing1,5, I-Jun Chou1,5, Ting-Ting Chung2, Chang-Fu Kuo3, Kuang-Lin Lin1,5, Jing-Long Huang4,5, Han-Ping Wu1, PCHAN Study Group2

Division of Pediatric Neurology, Department of Pediatrics, Chang Gung Memorial Hospital1, Taoyuan, Taiwan; Big Data Research Office, Chang Gung Memorial Hospital1, Taoyuan, Taiwan; Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital2, Taoyuan, Taiwan; Division of Allergy, Asthma and Rheumatology, Department of Pediatrics, Chang Gung Memorial Hospital3, Taoyuan, Taiwan; Chang Gung Memorial Hospital Study Group for Prevention and Protection Against Child Abuse and Neglect4, Taoyuan, Taiwan

Background: The aim of this study was to estimate the secular trends of incidence and acute medical expense in hospitalized children who were diagnosed as child physical abuse, and to estimate the in-hospital mortality.

Methods: We use National Health Insurance Research Database (NHIRD) to estimate the incidence of child physical abuse, in-hospital mortality and medical hospitalization cost during the period from 1996 to 2013. The case definition was those who were younger than 18 years old and hospitalization with an ICD-9-CM code 995.5 or E960-E969. In addition, we hypothesized that the incidence of child physical abuse may be attributed to a different birth cohort with a different social background.
Efficacy and Safety of Medium-Chain Triglyceride Ketogenic Diet in the Patients Younger than 2 Years Old with Intractable Epileptic Spasms: A Case Series Single Center Study

Chi-Tsung Yeh, Ping-Chen Chen, Tzu-Yen Hsu, Chieh-Chih Lin, Yi-Shan Wang, Wan-Ling Huang

Background: Children with intractable epilepsy are associated with a significant risk of morbidity. The safety, tolerability, and efficacy of ketogenic diet in infants were rarely reported.

Methods: We retrospectively evaluated the safety, tolerability, and efficacy of ketogenic diet for at least 6 months among children who had intractable epilepsy and started ketogenic diet before 2 years old in our hospital during 2012 to 2015.
The efficacy was rated by percentage the seizure reduction every 3 months using parent reports. The safety profile includes body weight, body height, total cholesterol, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), non-HDL-C and low-density lipoprotein cholesterol (LDL-C).

Results: Six infants (4 males) started the medium-chain triglyceride ketogenic diet (LCT + MCT 71%, protein 10%, carbohydrate 19%) at age of 5 to 22 months (median 7.5 months). The mean age at seizure onset was 3.8 months. The averaged anticonvulsants before ketogenic diet were 3. Four had infantile spasms (1 had perinatal hypoxic ischemic encephalopathy and I had Escherichia coli meningitis), and 2 had epileptic encephalopathy. At 6 months, 66% (4/6) patients were >90% improved and 83% (5/6) patients were >50 improved. A rise of total cholesterol from the baseline was noted in the first 3 months, and the averaged level was steady afterwards. TG, HDL-C and LDL-C and non-HDL-C showed no consistency. A decline of body weight was noted in 2 patients during the first 3 months; however, the body weight and height at 6 months showed a tendency of elevation. One patient ceased ketogenic diet due to aspiration pneumonia after 8 months.

Conclusions: The ketogenic diet is a safe, well tolerated, and potentially effective method of treatment for infants with epileptic spasms.

105 Management of Acute Neuromuscular Respiratory Failure with Combined Noninvasive Ventilation and Mechanical In-Exsufflator in Pediatric Intensive Care Unit

Tai-Heng Chen1,2, Jong-Hau Hsu3, Wen-Chen Liang3, Yuh-Jyh Jong2,3

Department of Emergency1, Graduate Institute of Clinical Medicine, College of Medicine2, Department of Pediatrics3, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan; Institute of Molecular Medicine and Bioengineering, College of Biological Science and Technology, National Chiao Tung University3, Hsinchu, Taiwan

Background: The present study aims to evaluate the efficacy and complications of combined noninvasive ventilation (NIV) and assisted coughing by mechanical in-exsufflator (MIE) for acute respiratory failure (ARF) in patients with neuromuscular disease (NMD) in the acute care settings.

Methods: This study was conducted in PICU from September 2009 to June 2016. Patients with NMD and ARF treated by combined NIV and MI-E admitted to the Emergency Department (ED) and pediatric intensive care unit (PICU) were included. Treatment success was defined as freedom from tracheal intubation during the hospital stay. Physiologic indices including PaO2, PaCO2, pH, and PaO2/FiO2 were recorded before and 12, 24 h after the use of NIV/MIE.

Results: Combined NIV/MIE was used in 30 NMD patients during 2009 to 2016 (mean: 12.9±11.1 years, range: 3 months to 38 years) with 32 episodes of ARF. Three episodes of ARF treated by NIV/MI-E were initiated in the ED. There was no mortality in this cohort. Treatment success was achieved in 28 episodes (87.5%), including 12 episodes (42.9%) demanding “Do Not Intubate”. ARF was mostly due to pneumonia with complicated hypercapnia, with a mean baseline PaCO2 of 74.3±15.8 mmHg. In the success group, hypercarbia and acidosis improved after use of NIV/MIE as early as within 12h and obtained persistent improvement to 24h (PaCO2: 73.6±15.3 vs. 52.6±11.1 mmHg (12h) and 50.2±10.6 mmHg (24h); pH: 7.24±0.06 vs. 7.33±0.04 (12h) and 7.39±0.03 (24h); all p<0.01). However, the PaO2/FiO2 ratio did not change significantly neither within 12h nor 24h post NIV/MIE use.

Conclusions: The combined NIV/MIE, initiated either in the ED or PICU, is a safe and feasible approach to rapidly improve physiologic indices and effectively avoiding intubation in NMD patients with ARF. Furthermore, NIV/MIE provides a good alternative for those NMD patients who refusing intubation.

106 A Newborn Screening Program for Spinal Muscular Atrophy

Shu-Chuan Chiang1, Yin-Hsiu Chien1,2, Wuh-Liang Hwu1,2, Ching-Jie Lin3, Ni-Chung Lee4, Wu-Shui Hsieh5, Wang-Tso Lee2, Wen-Chin Weng3, Yuh-Jyh Jong1

Department of Medical Genetics, National Taiwan University Hospital1; Department of Pediatrics, National Taiwan University Hospital2, Taipei, Taiwan; Department of Pediatrics, Kaohsiung Medical University Hospital3, Kaohsiung

Background: Spinal muscular atrophy (SMA) is caused by defects in the SMN1 that leads to lower motor neuron degeneration. Because of the high incidence of SMA and the requirements for early treatment, newborn screening for SMA is urgently needed.

Methods: A pilot SMA newborn screening program was conducted using the same dried blood spot (DBS) samples for routine newborn metabolic screening. DNA was extracted from a 3.2mm punch. Real-time quantitative PCR assays were used to detect nucleotides IVS7+100A (representing SMN1) and IVS7+100G (representing SMN2) were employed. The confirmatory testing, targeting the c.840C>T nucleotide, included droplet digital PCR (ddPCR) assay using the screening DBS sample and multiplex ligation-dependent probe amplification (MLPA) assay using DNA extracted from a recall whole blood sample.

Results: From Nov. 17, 2014 to May 31, 2016, 98,471 newborns were screened and 11 revealed zero copy of
SMN1. Six patients were confirmed and among them three had 2 copies, one had 3 copies, and two had 4 copies of SMN2. Four of the five false-positive cases were caused by a rare recombination event occurred between SMN1 and SMN2 at a position after nucleotide c.840. Results from the DBS ddPCR assay completely matched those from the MLPA assay.

Conclusions: Newborn screening accurately detected newborns affected by SMA. Early diagnosis of SMA should offer the best chance to initiate early treatment for SMA.

107 Autophagy Dysfunction and Neuropathy in Krabbe Disease Are Ameliorated by Gene Therapy

Background: Krabbe disease is also known as Globoid cell leukodystrophy (GLD) is autosomal recessive inherited lysosomal storage disease. GLD is caused by GALC mutations leading to galactocerebroside deficiency and is characterized by devastating demyelination in both CNS and PNS. Deficiency of GALC activity induced accumulation of psychosine leading to apoptosis and disrupted lipid rafts in oligodendrocytes and myelinating glia. Recent studies have indicated autophagy dysfunction contributes to tissue pathology in lysosomal storage disease. Nonetheless, the role of autophagy contributing to the pathogenesis of GLD remains largely unexplored.

Methods: In present study, twitcher mice, an authentic murine model of GLD, is utilized in the clarification of the pathogenesis and the intervention of therapeutic approaches for GLD, while toxicity of psychosine is analyzed in MO3.13 human oligodendrocytes after incubation with psychosine overnight. Levels of LC3-II and p62 were further elevated to in MO3.13 cells targeted with hGALC shRNA in medium with psychosine. While spinal cords from untreated Twitcher mice showed significant elevation of LC3-II (1.5-fold), p62 (1.3-fold), Lamp2 (1.2-fold), Parkin (2-fold), Pink1 (1.3-fold) and Beclin (1.4-fold) in comparison with that from wild-type mice and AAV-treated twitcher mice. Of note, GALC expression was intensive distributed in cortex, cerebellum, brain stem and spinal cord of AAV-treated twitcher mice, while the untreated twitcher mice showed deficiency of GALC expression throughout the CNS and spinal cord. Furthermore, brains of untreated twitcher mice showed accumulation of p62 and thioflavin-S inclusion, demyelination, activated astrocytes and augmented microgliosis, while AAV-treated twitcher mice showed normal autophagy pathway and were avoid of amyloid neuronal inclusions, demyelination and neuroinflammation in the CNS.

Conclusions: In conclusion, psychosine impairs autophagy pathway, induces astrogliosis, microgliosis demyelination and neuronal inclusion of amyloid substance in CNS of twitcher mice. Whereas AAV-mediated gene therapy efficiently transduces transgene to neuronal cells and Purkinje cells, produces supraphysiological levels of GALC activity, mitigates astrogliosis and demyelination, prevents formation of amyloid-like neuronal inclusions and corrects autophagy dysfunction. Collectively, these results constitute a proof of principle of the beneficial effects of gene therapy in alleviation of autophagy dysfunction and neuropathology in GLD.

108 Pediatric Necrotizing Myopathy Associated with Anti-3-Hydroxy-3-Methylglutaryl-Coenzyme A Reductase Antibodies

Background: Antibodies against 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGR) has recently been...
Clinical Characteristics of Type 1 Diabetes Mellitus in Taiwanese Children Younger than Six Years Old: A Single-Center Experience

Yi-Ching Tung, Shih-Yao Liu, Cheng-Ting Lee, Wen-Yu Tsai
Department of Pediatrics, National Taiwan University Hospital and College of Medicine, National Taiwan University, Taipei, Taiwan

Background: Cases of type 1 diabetes mellitus (T1DM) in children younger than six years old in Taiwan has increased in the last ten years. This retrospective study aimed to review our experience in the management of such patients.

Methods: From January 2004 to June 2015, 52 newly-diagnosed diabetic children younger than six years, who had regular follow-up at our clinic for more than one year were enrolled in this study. In the same period, 94 children aged 6-18 years with new-onset of T1DM were also enrolled for comparison. The diagnosis of T1DM was made according to the 1997 Criteria of the Expert Committee. Complete history, including family history, and physical examination were recorded for all patients with T1DM upon diagnosis. Laboratory tests, including blood glucose, HbA1c, ketone bodies, serum sodium, potassium, chloride, blood gas analysis, anti-glutamic acid decarboxylase 65 autoantibodies (GADA), anti-insulinoma antigen-2 autoantibodies (IA-2A), insulin autoantibodies (IAA), and C-peptide levels at glucagon test were also determined upon diagnosis. All of the patients were regularly followed up every three months. The patients' height, weight, daily insulin doses, blood sugar, and HbA1c levels were checked upon each visit. Remission was defined according to the criteria reported by Mortensen et al.

Results: The most common symptoms and signs were polyuria (96%), polydipsia (92%), dry lips (81%), weight loss (79%), and nocturia (77%). Among the children younger than six years old, 87% had ketoacidosis upon diagnosis, significantly higher than that of the old age group, and 88% had at least one islet-cell autoantibody detected. Their serum C-peptide levels were significantly lower (0.48±0.24ng/mL vs 0.95±0.67ng/mL, P<0.001) and the frequency of anti-insulin autoantibodies (IAA) detected was significantly increased compared to the older age group (37% vs 10%, P<0.001). The remission rate of the young diabetic patients was significantly lower than that of old age group (40% vs 59%, P<0.05), but there was no difference in time of onset and duration of remission between the two groups.

Conclusions: Autoimmune destruction of pancreatic β-cell is an important cause of T1DM in Taiwanese children younger than six years old. They usually have low insulin reserve and severe ketoacidosis upon diagnosis. A high index of suspicion in the presence of classic symptoms of diabetes in young children is important to prevent complications.

Autoimmune Thyroid Disease in Patients with Diabetes Mellitus

Ya-Ting Chiang1, Chi-Yu Huang1, Wei-Hsin Ting1,6, Chon-In Chan1, Chao-Hsu Lin7, Bi-Wen Cheng7, Fu-Sung Lo7, Yi-Lei Wu7, Chen-Mei Hung1,2, Yann-Jinn Lee1,2,3,4,5,6
Department of Pediatric Endocrinology, Mackay Children's Hospital1; Pediatric Endocrinology, Mackay Children's Hospital2; Department of Medical Research, Mackay Memorial Hospital Tamsui District3; Institute of Biomedical Sciences, MacKay Medical College4; Department of Medicine, MacKay Medical College5; Department of Nursing, MacKay Medicine, Nursing and Management College6; Department of Pediatrics, Mackay Memorial Hospital HsinChu Branch7; Department of Pediatrics, Chang Gung Memorial Hospital8; Department of Pediatric Endocrinology and Metabolism, Chuanghua Christian Children's Hospital9; Department of Pediatrics, Hsinchu Cathay General Hospital10

Background: In patients with diabetes mellitus (DM), thyroid dysfunction is common. The aim of this study was to investigate the prevalence of thyroid autoimmunity in patients with diabetes mellitus (DM)

Methods: A total of 105 patients with diabetes mellitus (DM) were included in the study. All patients underwent thyroid function tests, including thyroid-stimulating hormone (TSH), free thyroxine (FT4), and anti-thyroid peroxidase antibodies (TPOAb). The prevalence of thyroid autoimmunity was compared between patients with type 1 diabetes mellitus (T1DM) and patients with type 2 diabetes mellitus (T2DM)

Results: The prevalence of thyroid autoimmunity was significantly higher in T1DM patients compared to T2DM patients (P<0.05). Additionally, T1DM patients had higher levels of TPOAb compared to T2DM patients (P<0.05)

Conclusions: Thyroid autoimmunity is more prevalent in patients with type 1 diabetes mellitus (T1DM) compared to patients with type 2 diabetes mellitus (T2DM). This highlights the importance of monitoring thyroid function in patients with diabetes mellitus.
Background: Type 1 diabetes (T1D), type 2 diabetes (T2D), and some other specific types of diabetes occur in children and adolescents. At diagnosis or during follow-up, additional autoimmune phenomena are observed. These additional autoimmune diseases may impact diabetes control. We screened a cohort of diabetic patients regularly and as indicated by clinical manifestations for autoimmune thyroid disease.

Methods: The subjects were 1003 patients with diabetes mellitus, 469 boys and 534 girls. Their mean (SD) age at diagnosis was 9.2 (4.4) years, range 0.0-18.0 years and mean disease duration 13.6 (8.4) years, range 0.2-37.5 years. According to positivity of autoantibodies and mean disease duration 13.6 (8.4) years, range 0.2-37.5 years. As indicated by clinical manifestations for autoimmune thyroid disease.

Control. We screened a cohort of diabetic patients regularly and as indicated by clinical manifestations for autoimmune thyroid disease.

Methods: The subjects were 1003 patients with diabetes mellitus, 469 boys and 534 girls. Their mean (SD) age at diagnosis was 9.2 (4.4) years, range 0.0-18.0 years and mean disease duration 13.6 (8.4) years, range 0.2-37.5 years. According to positivity of autoantibodies and β-cell reserve, they were classified to type 1A (T1AD), type 1B (T1BD), type 1 unclassified (T1AU), and T2D. T1AD was defined as positive for GAD Ab or IA2 Ab at any time of disease duration, or for IAA within 2 weeks of disease duration. T1BD was defined as negative for GAD Ab, IA2 Ab, and IAA within 0.5 year of disease duration. T1AU was defined as unable to be classified because of lack of blood collected within 0.5 year of disease duration and negative for GADA and IA2A during follow-up. TSH, free T4, anti-microsomal (anti-TPO) antibody, anti-thyroglobulin antibody, anti-TSH receptor antibody were screened regularly (usually once every 1-3 years). Graves disease (GD) was defined as presence of goiter, suppressed TSH, elevated free T4, and positive anti-TSH receptor antibody. Hashimoto disease (HD) was defined as positive anti-microsomal antibody with/without anti-thyroglobulin antibody and decreased or normal free T4.

Results: GD occurred in 19/432 (4.3%) of T1AD, 0/57 (0.0%) of T1BD, 2/333 (0.6%) of T1DU, and 0/181 (0.0%) of T2D patients. HD developed in 114/432 (26.4%) of T1AD, 11/57 (19.2%) of T1BD, 40/333 (12.0%) of T1DU, and 6/181 (3.3%) of T2D patients. T1AD patients were significantly more susceptible to GD (OR, 17.12; 95% CI, 5.19-55.77; P, 5.11E-11). So did T1D patients as whole.

Conclusions: T1D (especially T1AD) patients were significantly more susceptible to GD and HD compared with T2D patients. Regular physical and laboratory thyroid exams must be observed to make early diagnosis and appropriate treatment for the autoimmune thyroid disease.
Mutation Screening of INS and KCNJ11 Gene in Type 1B Diabetes in Taiwanese Children with Onset of Diabetes before 5 Years of Age: one Medical Center Report

Chiao-Fan Chiu, Fu-Sung Lo, Yang-Hau Van, Ying-Hua Huang, Hsun-Hui Sui
Division of Pediatric Endocrinology and Genetics, Linkou Chang Gung Memorial Hospital; Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital; Department of Pediatrics, Taipei Medical Hospital, Taipei

Background: Type 1 diabetes (T1D) is due to β-cell destruction, usually leading to absolute insulin deficiency. T1D is a heterogeneous disease and is, according to presence or absence of pancreatic autoantibodies, divided into two subtypes: type 1A (autoimmune mediated) and type 1B (non-autoimmune-mediated). Genes (such as KCNJ11 or INS genes), a key role in β-cell function, provide some insight into the pathogenesis of type 1B diabetes.

Methods: In this study, we screened for mutations of INS and KCNJ11 in 110 Taiwanese children (61 males and 49 females) with type 1 diabetes with onset before 5 years of age. Our research plan will do 1) the classification of type 1A and type 1B diabetes by measuring serum GAD-Ab and IA-2 Ab; 2) mutation screening of INS and KCNJ11 gene in these children with type 1B diabetes; 3) the correlation of genotype and phenotype of patients between INS and KCNJ11 mutations in Taiwan.

Results: We identified one missense heterozygous mutation in the KCNJ11 (c.989A>G, p.Y330C) gene and no INS gene mutation among 28 probands.

Conclusions: This is the first study to report of screening patients with autoantibody-negative T1D diagnosed before 5 years of age for INS and KCNJ11 genes mutation in Taiwan. Although KCNJ11 gene mutations were always reported in patients with permanent neonatal diabetes, this gene mutation can be detected after 6 months of age. Further studies in other patients with type 1B diabetes and their families are needed to elucidate the contributions of KCNJ11 mutation to the T1D phenotype before the age of 5 years.

Clinical Spectrum of CHARGE Syndrome in Patients with Confirmed CHD7 Pathological Variants

Anne Chun-Hui Tsai
Section of Clinical Genetics and Metabolism, Department of Pediatrics, Children’s Hospital Colorado, University of Colorado School of Medicine

Background: CHARGE is a mnemonic for coloboma, heart defects, choanal atresia, retarded growth and development, genital abnormalities, and ear anomalies. CHARGE syndrome is characterized by a variable constellation of the clinical features above. Diagnosis used to be achieved at clinical level by criteria: having the four major characteristics or three major and three minor characteristics. With the availability of clinical molecular testing, some patients with almost isolated malformation were diagnosed to have this syndrome.

Methods: From 2016-2016 42 patients received molecular testing for CHD7, 25 patients demonstrated a mutation of CHD 7 pathological variants (2 with deletion). Most patients have concurrent chromosomal microarray and sequencing. 2 children were detected by exome sequencing.

Results: 20 of them showed at least 3 major criteria but 6 has one or less than 2 anomalies. 3 patients with mainly facial nerve palsy. One of them also has major feeding difficulty and hearing impairment. One patient with autonomic tendency and Mondini malformation without other anomalies. One patient has isolated hypoplastic cochlea and absent semicircular canals. One patient with eternal year malformation and delay puberty. Of note, one patient has every single element of CAHRGE and complex heart defect, parents insist to continue life support, at age 11, his IQ was above 70.

Conclusions: Although clinical genetic diagnosis remains the most common way in achieving the diagnosis in a genetic clinic, molecular diagnosis however increases the diagnostic rate in identifying milder cases. This study emphasizes that although the anomaly may seem isolated, with certain pathognomonic findings, molecular testing should be performed. A provider should not be panelized when a pathological mutation was not identified in a child who does not fit clinical criteria.

Application of Next Generation Sequencing for Molecular Analysis of Rasopathies

Ni-Chung Lee, Chien-Hao Huang, Yin-Hsui Chien, Yih-Yyan Chang, Fu-Sung Lo, Wen-Yu Tsai, Shao-Yin Chu, Chia-Ying Chang, Tsang-Ming Ko, Wuh-Liang Hwu
Department of Medical Genetics, National Taiwan University Hospital; Department of Endocrinology and Gynecology, National Taiwan University Children’s Hospital; GenePhile BioScience Laboratory, Ko’s Obstetrics and Gynecology, Taipei, Taiwan; Division of Pediatric Endocrinology and Genetics, Department of Pediatrics, Chang-Gung Memorial Hospital and Chang Gung University College of Medicine, Taoyuan, Taiwan; Department of Pediatrics, Hualien Tzu Chi Hospital, Hualien, Taiwan; Department of Pediatrics, Hsinchu MacKay Memorial Hospital, Hsinchu, Taiwan

Background: CHARGE is a mnemonic for coloboma, heart defects, choanal atresia, retarded growth and development, genital abnormalities, and ear anomalies. CHARGE syndrome is characterized by a variable constellation of the clinical features above. Diagnosis used to be achieved at clinical level by criteria: having the four major characteristics or three major and three minor characteristics. With the availability of clinical molecular testing, some patients with almost isolated malformation were diagnosed to have this syndrome.

Methods: From 2016-2016 42 patients received molecular testing for CHD7, 25 patients demonstrated a mutation of CHD 7 pathological variants (2 with deletion). Most patients have concurrent chromosomal microarray and sequencing. 2 children were detected by exome sequencing.

Results: 20 of them showed at least 3 major criteria but 6 has one or less than 2 anomalies. 3 patients with mainly facial nerve palsy. One of them also has major feeding difficulty and hearing impairment. One patient with autonomic tendency and Mondini malformation without other anomalies. One patient has isolated hypoplastic cochlea and absent semicircular canals. One patient with eternal year malformation and delay puberty. Of note, one patient has every single element of CAHRGE and complex heart defect, parents insist to continue life support, at age 11, his IQ was above 70.

Conclusions: Although clinical genetic diagnosis remains the most common way in achieving the diagnosis in a genetic clinic, molecular diagnosis however increases the diagnostic rate in identifying milder cases. This study emphasizes that although the anomaly may seem isolated, with certain pathognomonic findings, molecular testing should be performed. A provider should not be panelized when a pathological mutation was not identified in a child who does not fit clinical criteria.
Background: Rasopathies is a heterogeneous disease of multiple congenital anomalies. Of them, Noonan syndrome (NS), Costello syndrome, and Cardiofaciocutaneous (CFC) syndrome are most common ones. Currently 14 causative genes had been identified in the Ras/MAP kinase pathway. The molecular diagnosis of Rasopathies is often laborious and costly. In this study, would like to understand the impact of next generation sequencing (NGS) panels of Rasopathies in the clinical practice

Methods: Patients clinically diagnosed to have Rasopathies are retrospectively reviewed. In the current molecular testing strategies, PTPN11 were the first line gene to be analyzed. If negative, Panel analysis using NGS including 14 genes were applied if parents agreed.

Results: Total 83 patients were enrolled with 73 clinically suspect NS, 7 suspect CFC syndrome, 1 suspect Costello syndrome, 2 suspect LEPARD syndrome. PTPN11 was identified in 18 patients with 16 NS and 2 LEOPARD syndrome, which accounts for 21.9% of patients clinically suspect NS. For 27 patients underwent NGS panels, pathogenic mutation was identified in 11 patients (40.7%); unknown significance was found in 7 patients (25.9%); while 9 patients (33.3%) were negative. Those genes identified include PTPN11, KRAS, MAP2K2, NF1, RAF1, BRAF, and RIT1 in NS; RAF1, BRAF, SHOC2 in CFC syndrome; and HRAS in Costello syndrome.

Conclusions: Molecular diagnosis on Rasopathies is important in the clinical practice. Noonan NGS panel is a useful tool in the diagnosis of patients suspect to have Rasopathies.

115 Epigenotype, Genotype and Phenotype Analysis of Patients with Silver-Russell Syndrome

Hsiang-Yu Lin1,2,3,4,5, Shuan-Pei Lin1,2,3,6, Yi-Ning Su7, Dau-Ming Niu2,8, Li-Ping Tsai9, Meng-Chce Tsai10, Yen-Yin Chou10, Chia-Feng Yang8, Chia-Ying Chang11, Tsu-Hung Chu9

Deperations of Pediatrics1 and Medical Research2, Mackay Memorial Hospital, Taipei, Taiwan; Department of Medicine, Mackay Medical College3, New Taipei City, Taiwan; Mackay Junior College of Medicine, Nursing and Management4, Taipei, Taiwan; Institute of Clinical Medicine, National Yang-Ming University5, Taipei, Taiwan; Department of Infant and Child Care, National Taipei University of Nursing and Health Sciences6, Taipei, Taiwan; Department of Obstetrics and Gynecology, School of Medicine, College of Medicine, Taipei Medical University7, Taipei, Taiwan; Department of Pediatrics, Taipei Veterans General Hospital8, Taipei, Taiwan; Department of Pediatrics, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation9, New Taipei City, Taiwan; Department of Pediatrics, National Cheng Kung University Hospital10, Tainan, Taiwan; Department of Pediatrics, Mackay Memorial Hospital11, Hsinchu, Taiwan; Department of Pediatrics, Mackay Junior College of Medicine, Nursing and Management12, Taipei, Taiwan

Objectives: To investigate the impact of next generation sequencing (NGS) panels of Rasopathies in the clinical practice

Methods: Patients clinically diagnosed to have Rasopathies are retrospectively reviewed. In the current molecular testing strategies, PTPN11 were the first line gene to be analyzed. If negative, Panel analysis using NGS including 14 genes were applied if parents agreed.

Results: Total 83 patients were enrolled with 73 clinically suspect NS, 7 suspect CFC syndrome, 1 suspect Costello syndrome, 2 suspect LEPARD syndrome. PTPN11 was identified in 18 patients with 16 NS and 2 LEOPARD syndrome, which accounts for 21.9% of patients clinically suspect NS. For 27 patients underwent NGS panels, pathogenic mutation was identified in 11 patients (40.7%); unknown significance was found in 7 patients (25.9%); while 9 patients (33.3%) were negative. Those genes identified include PTPN11, KRAS, MAP2K2, NF1, RAF1, BRAF, and RIT1 in NS; RAF1, BRAF, SHOC2 in CFC syndrome; and HRAS in Costello syndrome.

Conclusions: Molecular diagnosis on Rasopathies is important in the clinical practice. Noonan NGS panel is a useful tool in the diagnosis of patients suspect to have Rasopathies.

Background: Silver-Russell syndrome (SRS; MIM #180860) is a clinically and genetically heterogeneous disorder characterized by severe intrauterine growth retardation, poor postnatal growth, characteristic facial features, and body asymmetry. Hypomethylation of the imprinted genes of chromosome 11p15.5 imprinting gene cluster and maternal uniparental disomy (mUPD) of chromosome 7 are the major epigenetic disturbances. The aim of this study was to characterize the epigenotype, genotype, and phenotype of these patients.

Methods: Ninety-five subjects with clinically suspicion of SRS (40 males and 55 females; age range, 1 day to 23 years) were referred for diagnostic testing by the methylation profiling of H19-associated imprinting center (IC) 1 using methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA) and high-resolution melting analysis with a methylation-specific polymerase chain reaction assay. Additionally, we applied a whole genome strategy to detect copy number changes and loss of heterozygosity. Clinical manifestations and medical history of these patients were also recorded and analyzed.

Results: Among these 95 referral subjects, 54 were classified into clinically diagnosis with SRS (score ≥ 8, maximum=15) and 41 with suspected SRS (score <8). Twenty-four subjects were identified with IC1 hypomethylation, 4 subjects with mUPD, and 2 subjects with microdeletion (6q24.2q25.2 and 13q31.3, respectively). Among 54 subjects with clinically diagnosis of SRS (score ≥ 8), several clinical features were found to be statistically different (p < 0.05) between the two groups of "with identified molecular defect (n=29)" and "without identified molecular defect (n=25)", including relative macrocephaly at birth (80% vs 52%), postnatal normal head circumference (97% vs 64%), normal cognitive development (90% vs 68%), body asymmetry (79% vs 52%), and SRS score (11.3 ±2.0 vs 9.3 ±1.4; maximum=15). Molecular lesion was detected in 54% (29/54) of the subjects with clinical diagnosis (score ≥ 8), compared with 2% (1/41) of those with suspicion of SRS (score <8). The mean SRS score was 11.7 for 24 subjects with "IC1 hypomethylation", compared with 8.3 for 4 subjects with mUPD. The SRS score of two subjects with microdeletions of 6q24.2q25.2 and 13q31.3 was 8 and 10, respectively.

Conclusions: The SRS score was positively correlated with the molecular diagnosis rate (p < 0.001). SRS subjects with UPD seem to have fewer typical features and lower SRS scores than those with IC1 hypomethylation. The database of epigenotype, genotype and phenotype is expected to promote better genetic counseling and medical care of Taiwanese patients with SRS.
Cardiac Evaluation by Two-dimensional Speckle Tracking Echocardiography in Taiwanese Patients with Mucopolysaccharidoses

Background: The mucopolysaccharidoses (MPSs) are a group of rare inherited metabolic diseases that can cause damages in various organs including the heart. Cardiac abnormalities have been observed in patients with MPS of any types, with the most documented abnormalities being cardiac valve thickening, valvular regurgitation and stenosis, and cardiac hypertrophy. We determined the cardiac features of patients with MPS by two-dimensional speckle tracking echocardiography.

Methods: Fifty-three Taiwanese patients with MPS (31 males and 22 females; age range, 1.1 to 34.9 years; 7 with MPS I, 16 with MPS II, 9 with MPS III, 14 with MPS IVA, and 7 with MPS VI) were evaluated by their cardiac features using comprehensive echocardiography and two-dimensional speckle tracking.

Results: The mean z scores of global longitudinal peak systolic strain (GLS), left ventricular mass index (LVMI), interventricular septum diameter in diastole (IVSd), and left ventricular posterior wall diameter in diastole (LVPWd) of these 53 MPS patients were 1.71, 0.35, 1.66, and 1.03, respectively. The most severe GLS was observed in a subgroup of MPS VI, followed by MPS II and MPS I. Z scores > 2 were identified in 45%, 13%, 40%, and 29% for GLS, LVMI, IVSd, and LVPWd, respectively. Diastolic dysfunction [reversed ratio between early and late (atrial) ventricular filling velocity (E/A ratio < 0.5)] were observed in subgroups of patients with MPS VI, MPS II, and MPS I. MPS is related to myocardial deformation together with more impaired diastolic function and declined global LV systolic mechanics, despite globally preserved LV ejection fraction.

The Pilot Study of Newborn Screening and Gene Analysis of Gaucher Disease

Background: Gaucher disease (GD) is an autosomal recessive lysosomal storage disease caused by deficiency of the enzyme beta-glucocerebrosidase (GBA). The deficit of GBA activities leads to an accumulation of glucocerebroside in cells and peculiar tissues with subsequently devastating dysfunction of multiple organ systems. Newborn screening of GD has been performed in Taiwan for recent five years. In this report, we elucidate the screening results and the gene analysis finding from those suspected cases.

Methods: From 2011 to 2015, total 304,583 dried blood spots (DBSs) were collected as part of the national Taiwan newborn screening programs. To determine the GBA activities, a punched DBS was used for reaction and measured by the tandem mass spectrometry method. The complete coding regions of GBA, including the intron/exon boundaries, were sequenced using DNA samples drawn from suspected cases.

Results: Complete all of the screening procedure, a total of 25 cases still presented low GBA activities, a punched DBS was used for reaction and measured by the tandem mass spectrometry method. The complete coding regions of GBA, including the intron/exon boundaries, were sequenced using DNA samples drawn from suspected cases.
AMPK Signaling Pathway Modulate Metabolic Inflexibility in Mitochondrial Disorder

Background: Mitochondrial disorder is characterized with respiratory chain complex deficits resulting in energy metabolic perturbation which cause broad spectrum of clinical phenotype. To accommodate respiratory deficiency, reconfiguration of mtDNA and nDNA expression profile is induced. Nonetheless, studies regarding the link of bioenergetics and transcriptional modulation in mitochondrial disorder are limited. In this report, we analyzed the bioenergetic profiles in primary cells harboring A3243G mutation to further elucidate the transcriptional reconfiguration adapting to mitochondrial dysfunction.

Methods: Four primary cells from MELAS patient harboring A3243G mutations and three control cells were maintained in standard culture medium. Cell viability was determined in medium containing glucose or galactose. ATP production was assayed by chemiluminescent assay after addition of metabolic inhibitors. Furthermore, bioenergetic metabolism in vivo derived from respiratory chain complex (RCC), glycolysis and fatty acid oxidation (FAO) was measured in adherent fibroblasts with a XF24 Extracellular Flux Metabolic modulators at enzymatic protein levels and transcriptional expression for bioenergetic function were determined by western blotting and quantification of mRNA, respectively.

Results: The A3243G mutation loads were above 90 % in mutant cells, while the amount of complex I and IV in mutant cells were decreased to 10%~40% and 10%~30% of controls, respectively. Cell viability was indistinguishable between A3243G cells and controls at standard medium (t>0.05), while A3243G cells was more vulnerable to medium containing galactose that cell viability had 66% decrease (t<0.05). The mitochondrial respiration in mutant cells showed an remarkable reduction to 30% of control in basal respiration, ATP-production, and maximal respiration (t<0.05), whereas the glycolysis was 2-fold increase compared to controls(t<0.05). Of note, oxygen consumption rate derived from fatty acid oxidation were also significantly reduced to 25% of controls(t<0.05). Furthermore, quantification analysis of metabolic modulators unveiled an average of 2-fold up-regulation of PGC1-alpha, while its down-stream targets NRF-1, NRF-2 and TFAM were not increased(t>0.05). The ratio of AMPK phosphorylation, ACC1a phosphorylation and Sirt-3 protein levels were elevated to 2-fold, 1.5-fold and 1.33-fold of controls(t<0.05), while CPT-1 and PDH phosphorylation/total were decreased to 75% of controls(t<0.05). Additionally, ATP production in mutant cells was reduced to 66%~90% of control (t<0.05)and was further reduced to 30% and 50% (t<0.05)of its original levels after inhibition of either glycolysis or FAO, respectively.

Conclusions: Our study first demonstrates the metabolic inflexibility of mitochondrial disorder in that the mitochondrial respiration and fatty acid oxidation were both reduced, while the glycolysis was remarkable increased and the cell viability were not enhanced. The ATP production was mainly reliance on the glycolytic flux in response to the energy depletion caused by RCC deficits. The metabolic inflexibility is modulated by the AMPK signaling pathway which activates PGC-1a and Sirt3 leading to the activation of glycolysis and inhibition of both fatty acid synthesis and oxidation. These findings may be of relevance for patient management while unveiling novel therapeutic targets for mitochondrial disorders.
While breastfeeding is recommended the best nutrition for normal term infants, it alone does not provide infants with an adequate intake of vitamin D.

In general breast milk contains only 25 IU/L vitamin D. Most breastfed infants can synthesize additional vitamin D through routine sunlight exposure. However, Weisberg P et al reviewed 166 published cases of rickets in children 4 to 54 months old between 1986 and 2003, and reported that 96% of the affected children were breast-fed.

Vitamin D deficiency rickets although is rare recently. However, vitamin D is now considered to be a kind of hormone rather than only a vitamin. Many diseases were thought to have relation with low 25(OH) serum level.

There are 3 sources of vitamin D.
1. Sunlight (10pm-3pm is most effective to make vitamin D)
2. Food (salmon, tuna, mushroom etc)

In 2003, the American Academy of Pediatrics (AAP) recommended that all infants have a minimum intake of 200 IU of vitamin D per day, beginning during the first 2 months of life. In 2008, the AAP published a new statement and recommended a daily intake of vitamin D of 400 IU/day for all infants and children beginning in the first few days of life.
1 營養素的交互作用於腦部
Nutrients Interaction in Brain Cognition

趙舜卿主任
Hsun-Chin Chao

林口長庚醫院兒童胃腸科
Chief, Division of Pediatric Gastroenterology, Chang Gung Children’s Medical Center, Chang Gung Memorial Hospital

腦部發展從胎兒期即已開始，約25％的腦部發展於胎兒期完成，二歲前腦部已發展達80%。就分子層次而言，營養素對腦部發展及後續的認知發展，是不可或缺的要素。營養素並非單獨存在，也不是只包含在某一種食物內。因此，腦中的營養素應能協同運作，彼此相輔相成。

已有相當多的研究證實某些單一營養成分對腦部發展及認知有顯著的影響，懷孕早期補充葉酸可以降低神經管缺陷，葉酸的DNA甲基化效果是主要機轉，而Choline及其代謝物也具有甲基化效果，有研究顯示同時補充Folic acid及Choline對降低神經管缺陷有更好的作用。

DHA是腦部發展的重要營養素，於懷孕第三期直到二歲於腦部及視網膜快速累積，對腦部及視網膜發展非常重要，DHA廣泛存在於細胞膜，對維持神經細胞膜的完整性，神經細胞分化及生長，及神經傳導及訊息傳遞有關。Meta-analysis study研究顯示

幼兒餵哺DHA可增加視覺度(visual acuity)，幼兒餵含DHA的嬰兒配方於出生第17及52週有顯著較佳的視覺度。研究也顯示餵含DHA的幼兒配方於出生18個月有顯著較佳的心智發展指數(Mental Development Index)。

Choline是必需的水溶性營養素，合成Phosphatidylcholine、Sphingomyelin，是細胞膜及神經鞘的重要成分。也具有增加老年人短期及長期記憶的作用。而且Choline可以經由Phosphatidylcholine攜帶DHA，協助DHA從腸道運送到腦部。

葉黃素已證實對眼睛非常重要，因為葉黃素是預防黃斑病變不可或缺的要素。葉黃素也是嬰兒腦部重要的類胡蘿蔔素，大量累積在腦部主管學習和記憶力的區域，其保護作用可能可以加強DHA的作用。Dr. Johnson發現，在延遲記憶(delayed recall)試驗中，相對於單獨補充DHA或葉黃素的老年受試者，同時補充DHA和葉黃素的受試者，延遲記憶的表現較佳，有明顯加分作用。

最新的研究，針對6個月大的嬰兒，使用腦波電生理檢測(ERP, event-related potentials)研究Choline、DHA和Lutein對認知記憶(recognition memory)的影響。結果指出Choline和DHA，以及Choline和Lutein可共同發揮作用，促進嬰兒的腦部發展及認知發展。

Reference:
（1）Johnson, E.J. A possible role for lutein and


(10) Carol L. Cheatham and Kelly Will Sheppard; Synergistic Effects of Human Milk Nutrients in the Support of Infant Recognition Memory: An Observational Study, Nutrients 2015, 7, 9079-9095

2 以功能性核磁共振技術
顯像發展中腦部之
解剖結構與功能
Imaging the Developing Brain -
Anatomy and Function by fMRI Technology

郭文瑞副教授
Wen-Jui Kuo
陽明大學神經科學研究所
Associate Professor, Institute of Neuroscience, National Yang-Ming University

腦部研究的技術日新月異，磁振造影技
術(MRI)，因其非侵入性的優點，使其得以
在各相關領域蓬勃發展。本研究室是利用更
新穎功能性 functional MRI 、灌輸性 perfu-
sion MRI 及擴散性 diffusion MRI 等技術，
不但將其應用在心理、生理、醫學方面，並
著重於技術的發展，以期將 fMRI、pMRI 及
dMRI 技術，更廣泛地應用在更多領域。

我們將MRI與TMS、MEG、EEG等技
術整合，探索不同情境下的人體反應與行
為，對應的大腦功能區。以非侵入性的方
式，得取高解析度的解剖影像，並可利用
dMRI 技術，顯示組織中的微小結構。藉由
TMS，不同的大腦功能區因此可加以定位，
而透過 MEG 及 EEG 對大腦信號傳遞的紀
錄，我們更可瞭解大腦在活化後，如何將訊號傳遞到相對應的反應區。結合以上技術，將更有助我們對大腦發展、功能及其結構的深刻瞭解。在生理結構的研究上，可突顯組織的微細結構，如大腦中的神經纖維網路。利用 dMRI 中的 FA 及 ADC 參數，將其與病人的病症作統計分析，這有助於病症的判斷。

在醫學的研究上，dMRI 可用於腫瘤病人的術前診斷，並預測術後的回復狀況。同時，透過正常受試者及 ADHD 病人間的差異比較，不需藉由測定或醫師經驗的診斷，就能輕易發現病人的變化。此外，由 dMRI 發展出的神經纖維追蹤（Tractography / Fiber Tracking）技術，則有助觀察神經纖維的復原，及幹細胞在大腦中的作用。其他如中風、大腦的創傷與此技術的結合，也在進行中。神經纖維追蹤（Tractography / Fiber Tracking）技術、擴散譜磁振造影（DSI）技術、DSI，相對於傳統的 dMRI 技術，提供了更多組織結構上的資訊。其如大腦影像的自動化分割（Automatic Segmentation）技術、建立蒙地卡羅模型（Monte-Carlo Simulation Model）在擴散現象的應用、DSI 在神經纖維密度的研究、以及 dMRI 與反應時間的相關研究結合，虛擬實境及其他工具軟體的發展也如火如荼的進行中。相信未來能夠對腦部發展之分析及功能，醫學以及生物領域有更大的幫助。
Evidence-Based Interventions for Children with Developmental Coordination Disorder

Haung-Chi Lin
Chief, Center of Child Development and Early Intervention, En Chu Kong Hospital

Children with developmental coordination disorder (DCD) are identifiable by the difficulties they have in performing fine and gross motor tasks, which affect their performance in the classroom and in activities of daily living. The estimated prevalence of children with DCD is between 6 and 13% of all school-aged children. Several comorbid problems are common in children with DCD including a substantial overlap with attention-deficit hyperactivity disorder (ADHD), dyslexia, and autistic spectrum disorders. Children with DCD show higher rates of social difficulties, low self-esteem, and associated behavioral problems during childhood and adolescence. In particular, children with combined DCD and ADHD show poorer outcomes when evaluated in early adulthood, in terms of academic achievement and psychosocial adjustment.

The evidence-based therapeutic approaches from the literature can be grouped under three main types: process-oriented, task-oriented, and conventional physical and occupational therapy. Process-oriented (bottom-up) approaches such as sensory integration, kinaesthetic training, perceptual training, target the components or body functions needed to perform activities. Task-oriented approaches such as neuromotor task training (NTT), the cognitive orientation to daily occupational performance (CO-OP) approach, and imagery training, tend to focus on motor performance, i.e. on learning particular motor skills, with attention given to specific aspects of task performance that are causing the child difficulty. The traditional physical therapy or occupational therapy provide training in the most important fundamental gross motor and fine motor skills that are thought to be prerequisite for skills.

The Leeds Consensus set the following guidelines that intervention approaches should meet: (1) activities should be functional, based on goals that are relevant to daily living and meaningful to the child; (2) they should enhance generalization and application in the context of everyday life; and (3) interventions must be evidence-based and grounded in theories that are applicable to understanding children with DCD. Data analysis from the literature shows there is strong evidence that children with DCD benefit from task-oriented approaches. In addition, there was also sufficient evidence that motor-training-based interventions, as used in traditional physical or occupational therapies, were generally effective for children with DCD. Third, evidence for the efficacy of process-oriented approaches (e.g. sensory integrative training and kinaesthetic training) was conflicting and weak. In conclusion, although training effects are commonly shown in therapeutic approaches for DCD, it is not always apparent how they transfer across related and different areas of function. Involvement of parents, teachers, and physical education is needed to maximize transfer into daily life and to ensure longer-term progress.
Pharmacological & Nonpharmacological Interventions for Attention-Deficit Hyperactivity Disorder: Systematic Review and Meta-Analyses of Randomized Controlled Trials

Pin-Chen Yang
Psychiatrist, Department of Psychiatry, Kaohsiung Medical University Hospital

Both pharmacological and non-pharmacological treatments are available for attention-deficit disorder. In this talk, the presenter will review the meta-analysis of medications (stimulants, nonstimulants), dietary (restricted elimination diets, artificial food color restrictions and free fatty acids supplementation) and psychological (cognitive training, neurofeedback and behavioral interventions) ADHD treatments.


Reference
3 學齡前特殊語言發展缺失兒童的學校學習表現探討
Inspection Into the School Learning Behavior for the Preschool Children with Specific Language Impairment

趙文崇主任
Wun-Tsong Chao
埔里基督教醫院心理健康新中心
Chief, Director of Mental Health Center, Puli Christian Hospital

前言

學齡前是個人日後語言功能和技巧發展的重要時期。學齡前的語言發展遲緩會對日後的學校文字學習產生一定的影響。學齡前有語言發展遲緩的個案，成因不一，有部分是受到感官、智力或環境刺激教學等因素所影響，有一些卻找不到任何原因，稱之為特殊型語言缺失（Specific Language Impairment, SLI）。本院關心特殊型語言缺失的嬰幼兒，長期追蹤其後續發展，特別針對學齡前發展性語言障礙者進入國小後，其在聽理解、口語表達、閱讀理解、文字書寫、計算和注意力各方面學習技巧的表現，依據病歷資料向家長電訪進行評估分析。

方法

自 93 年起至 104 年經門診疑診發展遜緩的個案。學齡前個案病歷資料、電話家庭訪問、晤談、門診追蹤方式進行聽理解、口語表達、閱讀理解、文字書寫、計算和注意力六項功能現況評估比對，採用質性研究的方式來了解個案入學後語言學習的表現及運用。語言發展遲緩而懷疑有 SLI 的個案，在學齡後進行學校學業學習行為調查並進行分析研究。

結果

學齡前有發展遲緩者共 2089 名，其中有語言發展遲緩表現者 1439 名，懷疑其為 SLI 在學齡後會有學習障礙特徵的個案共計 165 名。使用病史資料进一步評估篩選，排除智能不足、相關聽力困難、視覺困難、癲癇症服藥中、有肢體運動障礙者、在其他診斷為自閉症者、電訪時未聯絡上者、資料不足及目前尚未入學的個案，總計 120 位符合 SLI 診斷。男 82 人、女 38 人，年齡分佈在 6 歲至 18 歲。依據個案在、經由電話訪問或再度復診晤談方式進行聽理解、口語表達、閱讀理解、文字書寫、計算五種功能，就個案在學業學習困難的程度進行紀錄分析。

1. 學齡前有語言發展遲緩懷疑為障礙者，學齡期之後的學習完全沒有問題者所佔比率僅約 6.35%，有超過百分之九十的學齡前語言障礙生在課堂上會有聽、說、讀、寫、算一樣以上的困難。
2. 學齡前有語言發展遲緩懷疑為障礙者，學齡期之後有學習問題的男女比約為 2:1。
3. 學齡前有語言發展遲緩者，學齡期之後被安置在資源班者所佔比率只有 14%，雖然大部分都安置在普通班，但幾乎都仍有困難。
4. 個別的聽理解、口語表達、閱讀理解、文字書寫、計算各方面，家長反應資料內容顯示：
   (1) 大多數家長都認為主要是文字書寫及維持注意力方面有顯著困難，其次依序為閱讀理解能力、計算能力、口語表達能力；相較起來最沒有顯著抱怨的是聽理解能力。
   (2) 各障礙類別中，家長認為個案仍有聽理解能力、口語表達能力或計算能力有輕度至中度障礙的家長比率約在 20%~30%，但認為個案的文字書寫能力及閱讀理解能力落在輕度困難程度的家長比率則超過 50%。


Evidence-Based Interventions for Children with Autism Spectrum Disorder

Hui-Ju Chen

Doctor, Department of Pediatric Neurology, MacKay Children's Hospital

Autism spectrum disorder (ASD) is a chronic neurodevelopmental disorder characterized by various degrees of abnormal language/communication and social reciprocity, and restricted repetitive behaviors/interests. The estimated prevalence of autistic cases in Taiwan was 12.3% in the general population with the significantly higher prevalence among males (19.2%).

The core symptomology in ASD includes deficits in communication and language skills, impaired social interactions and patterns of repetitive and stereotyped behaviors. The essential elements of a clinical diagnostic evaluation should include a detailed child and family/caregiver history, an assessment of the core features of ASD, and a comprehensive medical examination to exclude other diagnoses. The diagnostician should also consider whether co-occurring disorders exist, such as seizure disorders, sleep disturbance and gastrointestinal disorders. Hearing and other sensory screens should also be addressed. Specific genetic etiologies, such as Angelman syndrome, Cornelia deLange syndrome, Down syndrome, Fragile X syndrome and tuberous sclerosis complex (TSC) should be considered as possible co-occurring disorders.

The primary goals of ASD treatment are to minimize the core features and associated deficits, maximize functional independence and quality of life, and alleviate family distress.

The principles of the ASD early interventions are:

1. Entry into intervention as soon as an ASD diagnosis is seriously considered rather than deferring until a definitive diagnosis is made
2. Provision of intensive intervention, with active engagement of the child at least 25 hours per week, 12 months per year, in systematically planned, developmentally appropriate educational activities designed to address identified objectives
3. Low student-to-teacher ratio to allow sufficient amounts of 1-on-1 time and small-group instruction to meet specific individualized goals
4. Inclusion of a family component (including parent training as indicated)
5. Promotion of opportunities for interaction with typically developing peers to the extent that these opportunities are helpful in addressing specified educational goals
6. Ongoing measurement and documentation of the individual child's progress toward educational objectives, resulting in adjustments in programming when indicated
7. Incorporation of a high degree of structure through elements such as predictable routine, visual activity schedules, and clear physical boundaries to minimize distractions
8. Implementation of strategies to apply learned skills to new environments and situations (generalization) and to maintain functional use of these skills
9. Use of assessment-based curricula that address: functional, spontaneous communication; social skills, including joint attention, imitation, reciprocal interaction, initiation, and self-management
10. Functional adaptive skills that prepare the child for increased responsibility and independence;
11. Reduction of disruptive or maladaptive behavior by using empirically supported strategies, including functional assessment
12. Cognitive skills, such as symbolic play and perspective taking
13. Traditional readiness skills and academic skills as developmentally indicated

Some behavioral intervention programs, such as Applied Behavior Analysis (ABA), Early Intensive Behavioral Interventions (EIBI), or behavioral inclusive programs (NSP) are proved to be effective in ASD young children. Aripiprazole and Risperidone are FDA approved medications for treatment of irritability in children with Autistic Disorder. Methylphenidate may be effective in reducing symptoms of inattention and hyperactivity in children with ASD.

In conclusion, ASD is a complex neurodevelopmental disorder. Initiating interventions as soon as a diagnosis of ASD is seriously considered or determined is strongly recommended. Multimodal approach to treatment is more likely to promote development and improve behavior.
Mosquito-Borne Diseases: Emphasize on Japanese Encephalitis & Prevention

Po-Yen Chen
Doctor, Taichung Veterans General Hospital

Mosquito bites can cause severe skin irritation through an allergic reaction to the mosquito's saliva - this is what causes the red bump and itching. Mosquitoes cause more human suffering than any other organism. Mosquitoes are known to carry many infectious diseases from several different classes of microorganisms, including viruses and parasites. It was estimated that over one million people worldwide die from mosquito-borne diseases every year, including malaria, Chikungunya, Dengue fever, Zika Virus, yellow fever, Japanese encephalitis, West Nile encephalitis, St. Louis Encephalitis, LaCrosse Encephalitis, Jamestown Canyon Virus (JCV), Eastern Equine Encephalitis, Western Equine Encephalitis, elephantiasis, Dog Heartworm etc. These infections are normally rare to certain geographic areas.

1

The Japanese encephalitis virus (JEV) itself is a virus from the family Flaviviridae, part of the Japanese encephalitis serocomplex of 9 genetically and antigenically related viruses, some which are particularly severe in horses.

Domestic pigs and wild birds (especially herons) are reservoirs of the virus; transmission to humans may cause severe symptoms. Amongst the most important vectors of this disease are the mosquitoes Culex tritaeniorhynchus and Culex vishnui. This disease is most prevalent in South-east Asia and East Asia.

Preventing Japanese encephalitis

The best way to prevent Japanese encephalitis is to be vaccinated against the infection before you visit a part of the world where there's a risk of catching it. The risk is greater if you're planning to visit rural areas or go hiking or camping. Even if you've been vaccinated, you should still take precautions to reduce your risk of being bitten by an infected mosquito, such as:

- Sleeping in rooms with close-fitting gauze over the windows and doors — if you're sleeping outside, use mosquito nets that have been impregnated with an insecticide
- Covering up with long-sleeved tops, trousers and socks
- Applying a good-quality insect repellent to exposed areas of skin
2 An Innovative Vaccine Specifically Developed in Asia: A New Solution against Japanese Encephalitis

Li-Min Huang
Professor, National Taiwan University
Children's Hospital

Japanese encephalitis chimeric virus vaccine (JE-CV; IMOJEV®) is a live attenuated virus vaccine constructed by inserting coding sequences of the premembrane (prM) and envelope (E) structural proteins of the Japanese encephalitis SA14-14-2 virus into the genome of yellow fever 17D virus. Preclinical studies have also shown that JE-CV are less hepatotropic and less neurovirulent than YF 17D vaccine. The environmental risks of JE-CV are negligible, and JE-CV causes no detectable viremia in the pig (natural host for JEV).

In the majority of countries where JE vaccines are used, primary immunization of infants and toddlers with inactivated JE vaccine requires several doses to achieve seroprotection, and multiple booster doses are recommended. The same level of primary protection can be achieved with a single dose of JE-CV, with a single booster dose given 1 to 2 years after primary immunization. JE-CV primary and booster doses were well tolerated in children and adults studied. Co-administration of JE-CV with MMR has no effect on the immunogenicity and safety of either vaccine. JE-CV can also be used interchangeably with MBDV for the booster dose. Seroprotection rates were also very high in trials among adults aged 18–65 in non-endemic settings.

3 The Fact on Pertussis: Shifting Epidemiology Pattern in Asia Toward Immunization Strategy

Cheng-Hsun Chiu
Professor, Department of Pediatric,
Chang Gung Memorial Hospital

Pertussis is highly communicable and is re-emerging despite wide vaccination program. Several large outbreaks have occurred in some countries, but few epidemiologic data are available in Asia. In this multinational serosurvey study, adolescents 10-18 years old with whole-cell or acellular pertussis immunization schedules were enrolled in 10 centers in Japan, South Korea, China, Taiwan, Thailand, Sri Lanka and India. Exclusion criterion included chronic condition and receiving any pertussis-containing vaccines within the prior year. The concentration of anti-Pertussis Toxin (anti-PT) IgG was measured by ELISA. Recent infection within 1 year (anti-PT IgG ≥ 62.5 IU/mL) was evidenced in 4.9% (85/1,719) of the overall population. Children at age 13 had the highest proportion of anti-PT IgG ≥ 62.5 IU/mL (9.0%, 20/222) compared to children at other age groups. The relatively high proportion of subjects with undetectable anti-PT IgG levels were observed in both of DTaP or DTwP vaccination countries.
1

兒童安寧緩和醫療
Pediatric Palliative Care

呂立主任
Frank Leigh Lu

臺大醫院兒童醫院兒童胸腔重症科
Medical Director of the Department of Pediatric Pulmonology and Critical Care Medicine, National Taiwan University Children's Hospital

針對兒童得到生命受威脅的疾病時，要考慮何時讓兒童安寧緩和醫療的介入與幫忙。治療對象可分為四大類型：1. 可能治癒，但也很可能無法長期存活的疾病：如預後不良的嚴重癌症、複雜嚴重的先天或後天心臟病等等。2. 需要長期密集照顧，來維持生命與生活品質的疾病：例如先天免疫不全疾病、短腸症、無法移植或洗腎的腎衰竭兒童、長期嚴重呼吸衰竭、肌肉失養萎縮症等等。3. 病程逐漸惡化，診斷後只能做安寧緩和治療的疾病：某些嚴重先天代謝性疾病、某些染色體異常（如三對第十三號染色體 Trisomy 13 疾病）等。4. 易有生命危險，卻不會逐漸惡化的疾病：極端早產、多次反覆感染的嚴重腦性麻痺兒童、缺氧性腦病變、先天腦部嚴重發育異常等等。這些孩子都很需要盡早考慮納入安寧緩和醫療的概念與做法，來幫助他們擁有比較好品質的生活。演講中並會談及兒童的特殊性，臨終照護，如何跟家長談兒童死亡，以及終止與撤除維生治療醫療決策如何進行與注意事項。讓所有孩子的生命，都能獲得最佳沒有受苦的照顧與維持最好的生活品質，是我們醫療人員重要的責任。
2

Pain Control in Children with Cancer at the End-of-life

洪君儀

Attending physician, Division of Pediatric Hematology and Oncology,
Department of Pediatrics, Taipei Veterans General Hospital

流行率

- 大於50% (ICU=40%, Ward=80%): 當死亡地點有關
- 疼痛: 在臨終病童非常普遍
- 孩子死亡前症狀控制不良的記憶，會在父母腦海中永遠留存

錯誤觀念

- 疼痛加劇=疾病惡化?
- 增加opioids=疼痛加劇
- 疾病惡化，所以排斥加藥量
- “鴉片”，“嗎啡”有特定意義?
- 美沙東 (methadone): 可給小孩止痛，但聯想到成嗎啡成癮之用

耐受(tolerance)
依賴(dependence)
成癮(addiction)
- 香港搞不清楚?

1. 耐受(tolerance)

- 意味長期使用opioids造成其potency下降，因此需要加量來達到相同potency
- 迷思: 家屬怕一直加量，以後就沒藥可用了
- 向家屬保證: 大部分藥物耐受的問題，可用(1)漸進式調整劑量，(2)加上輔助藥物，或(3)換藥來處理

2. 依賴(dependence)

- 指一種”身體狀態”:
  在藥物停掉或減量時出現打哈欠、流淚、流汗、鼻水、心跳加速之現象
3. Addiction (addiction)

- Pain increased
  - Discomfort, fatigue
  - Insomnia
  - Anxiety
  - Fear
  - Anger
  - Sadness
  - Depression
  - Boredom
  - Mental isolation
  - Social abandonment

- Pain decreased
  - Relief of other symptoms
  - Sleep
  - Understanding:晓解病情
  - Companionship:家人vs看護
  - Creative activity:美術治療
  - Relaxation
  - Reduction in anxiety:減輕焦慮
  - Sleep
  - Other symptom relief
  - Elevation of mood

什麼是疼痛？

- "病人訴說是痛"：通常是主觀的
- Sensory, emotional experience.
  - A somatopsychic phenomenon.
- Modulation of this phenomenon:
  - 情緒
  - 業志
  - 病人對疼痛的認知:一直痛就是癌症末期，治不了，我快死了

全疼痛 (Total pain) 的觀念 (1)

- 生理 (Physical aspect): 被球棒打到
- 心理 (Psychological aspect): 使愛
- 社會 (Social aspect): 韓教授教出趙醫師
- 靈性 (Spiritual aspect): 前世造孽

> 這些層面的感受都會造成 "痛"

Total pain (2)

- 生理: 治療的不適，失眠，慢性疲勞
- 心理: 氣斷太慢，氣治療沒效，怕痛，怕死，無望感
- 社會: 擔心家人及經濟，失業，喪失社會地位，收入，被放棄，隔離感
- 靈性: 爲什麼是我？生命的意義是什麼？這一切為何發生在我身上？我以前做的壞事能被寬恕嗎？

Factors affecting pain sensation

- Concurrent pains are common
  - 1/3 has a single pain
  - 1/3 has two pains
  - 1/3 has three or more pains
  - Evaluation is a multi-dimensional process
疼痛評估 (1)

病人
- 確認位置: where exactly is your pain?
- 確認duration: when did it start?
- PQRST characteristics

醫生
- 找出疼痛的源頭
- 了解機轉
- 找出其他非身體 (non-physical)因素

疼痛評估 (2)
PQRST- TSRQP
- Palliative factors
- Provocative factors
- Quality
- Radiation
- Severity
- Temporal factors

疼痛評估 (3)

陣發性，間歇性疼痛

Identify the following
- Predictable (incident) pain: weight bearing, activity, change position, etc
- Unexpected (unpredictable) pain: spontaneous, not related to activity or weight-bearing. Colic or stabbing pain associated with nerve injury
- End-of-dose failure: shortly before next dose of regular analgesics is due

疼痛的原因

- 癌症本身: soft tissue, visceral, bone, neuropathic
- 抗癌治療引起的: chemotherapy-related mucositis
- 癌症引起的體弱: constipation, muscle spasm
- 同時有其他疾病: osteoarthritis, spondylosis

功能性 vs 病理疼痛

- 功能性: 一般人都經歷過的
  - Somatic: headache, cramp, myofascial pain
  - Visceral: distension, colic
- 病理性
  - Nociceptive: soft tissue distortion or injury
  - Neuropathic: nerve compression or injury
  - Burning, stinging, stabbing, deep ache, allodynia, numbness, vasodilatation, sweating

疼痛相關名詞

- Allodynia: 對於通常不會引起疼痛的刺激卻感覺會痛(輕摸就會痛，無法蓋被)
- Hyperalgesia: 對於正常疼痛的過度反應(例如針刺有極痛苦的疼痛反應)
- Dysesthesia: 任何不愉悅的異常感覺(包含上述兩種感覺)：常形容為”灼熱”，“麻木”，“搔癢“
Non-physical factors

- Psychosocial evaluation: 很重要！
- 想辦法讓病人表達其恐懼與焦慮
- 可能需要心理師評估: 是否有轉化症(身心症)
- 要詳細解釋以降低”心理層面”的痛: 解釋疼痛機轉與我們的對策

非藥物治療(1)

- Consciousness and attention required for pain perception
- Creative activities, more than pass the time, diminish the pain
- Your time, spent exploring a patient’s worries and fears, is well spent

處理(1)

定下目標:
1. 晚上不會痛
2. 白天休息時不會痛
3. 移動時不會痛

● From 1->2->3

處理(2)

先解決可”治療”的問題:

- 放療: especially for bone metastasis or nerve compression. Single dose preferred.
- Biphosphonates: for bone metastasis
  - Pamidronate 90-120mg in N/S 500ml, IVD 1-2hrs
  - Clodronate 600-1500mg in N/S 500ml, IVD 4 hrs
  - Benefit in 7-14 days, last 2-3 months. If no response after 2 treatments, failure.

處理(3)

放療: BUMP

- Bleeding: hemoptysis, hematuria, vaginal bleeding
- Ulceration: superficial, mucosal (pallor-nasopharyngeal, rectal)
- Mass effect/compression: SVC syndrome, dysphagia, spinal cord, brain
- Pain: bone metastasis

非藥物治療(2)

- Physical therapy
  - Heat pads
  - TENS
- Psychological
  - Relaxation
  - Cognitive-behavioral therapy
  - Psychodynamic therapy
- Modification of way of life and environment
**300**

非藥物治療(3)

- Modification of way of life and environment
  - Avoid pain-precipitating activities
- Immobilization of the painful part
  - Collar, corset, slings, surgery for fracture
- Walking aids
- Wheelchair

藥物治療

- Non-opioids (antipyretics)
- Opioids
- Adjuvant: antidepressant (TCA, Selective Serotonin Reuptake Inhibitor, Serotonin-Norepinephrine Reuptake Inhibitor, etc), anti-epileptics, steroids

止痛藥物之使用原則

- By the mouth: standard route
- By the clock: (not prn) half life: morphine: 4 hours (demerol 2 hours)
- By the ladder (appropriate ladder):
  - Non-opioid + adjuvants
  - Weak opioid + Non-opioid + adjuvants
  - Strong opioid + Non-opioid + adjuvants
- Individualized treatment

非鴉片止痛藥(1)

- Acetaminophen
  - Inhibits cyclo-oxygenase in the brain, no anti-inflammatory effect
  - Can be given together with NSAIDs
  - Q6h, max dose 6 gm/day
- Non-steroidal anti-inflammatory drugs
  - Anti-inflammatory effect
  - Can reduce central sensitization in neuropathic pain, hence increase morphine effect
  - Ibuprofen (max 4.2 gm/d), diclofenac (max 200 mg/d), naproxen (max 1 gm/d)

非鴉片止痛藥(2)

- Non-steroidal anti-inflammatory drugs
  - All NSAID cause salt and water retention, which result in ankle edema
  - Non-selective COX inhibitors cause reversible platelet dysfunction
  - Typical NSAID regimens
    - Ibuprofen 400-800mg tid
    - Naproxen 250-500mg bid
    - Diclofenac sodium 50mg tid, MR 75mg bid or 150mg qd
    - Meloxicam 15mg qd
    - Celecoxib 100mg qd to 200mg bid
    - Nimesulide 100mg bid

非鴉片止痛藥(3)

- Non-steroidal anti-inflammatory drugs
  - The risk for NSAID-related GI toxicity
    - Highest: Aspirin, ketorolac
    - Intermediate: ketoprofen, naproxen, piroxicam
    - Low: diclofenac, ibuprofen, meloxicam, nimesulide
    - Minimal: celecoxib
弱鸦片: Codeine

- Bio-availability: 40%
- Time to max conc: 1-2 hrs
- Half-life: 2.5-3.5 hrs
- Duration of analgesia: 4-5 hrs
- Potency ratio with morphine: 1/10

Ceiling effect of the mixed agonist-antagonist weak opioids.

弱鸦片: Tramadol

Opioid receptors and blocking reuptake of 5HT and NE, but no antimuscarinic nor antidepressant effect

- Bio-availability: 70%
- Onset: 1 hr
- Time to max conc: 2 hrs
- Half-life: 6 hrs
- Duration of analgesia: 4-6 hrs
- Potency ratio with morphine: ¼-1/5 (PO), 1/10 (IV)
- Max dose: 400 mg/d

Less constipating, but lower seizure threshold, caution when used with TCA or SSRI.

强鸦片(1)

"Strong opioids exist to be given, not merely to be withheld; their use is dictated by therapeutic need and response, not by brevity of prognosis."

- Pain is a physiological antagonist to the central depressant effects of opioids.
- The therapeutic range is wider than you expected.

强鸦片(2)

- Tolerance, addiction, dependence

Cautions:

- Morphine naïve
- Constipation
- Nausea/vomiting

强鸦片(3)

**morphine:**

- μ-receptor agonist
- Bio-availability: oral 30%, half-life 1.5-4.5 hr
- Potency via PO:SC:IV=1:2:3
- Metabolite:
  - morphine-3-glucuronide (M3G): not analgesic
  - morphine-6-glucuronide (M6G): more potent than morphine
  - Both cumulate in renal failure
- PO titration preferred:
  - Slower absorption, lower peak concentration
  - Upward step by step, re-assess q8h
  - Starting (5 or) 10 mg po q4h, double dose before sleep
  - PRN dose: 1/6 daily amount
  - Increase ½ total dose to double dose, or according to previous day total dose

强鸦片(4)

**morphine side effects**

- Gastric stasis: metoclopramide 10-20 mg q4h
- Cognitive failure: haloperidol 3-5 mg stat and prn
- Myoclonus: rare when oral, more in IV high dose morphine; diazepam/midazolam 5 mg stat and prn
- Constipation: MgO, senokot
**Fentanyl**

- \( \mu \)-receptor agonist
- Transdermal bio-availability 100%
- Half-life 3-4 hrs after IV injection
- Removal of patch: elimination plasma half-life is 24hrs
- TD 25 ug/h, 50 ug/h
- Highly lipophilic, less constipating
- Greater non-specific binding to CNS lipids
- DON'T start strong opioids with Fentanyl, you CANNOT titrate the dose!

### Oral analgesic equivalence to morphine

<table>
<thead>
<tr>
<th>Analgesic</th>
<th>Potency ratio with morphine</th>
<th>Duration of action(hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>codeine</td>
<td>1/10</td>
<td>3-6</td>
</tr>
<tr>
<td>Pethidine</td>
<td>1/8</td>
<td>2-4</td>
</tr>
<tr>
<td>Tramadol</td>
<td>¼~1/5(PO)</td>
<td>4-6</td>
</tr>
<tr>
<td>Fentanyl (transdermal)</td>
<td>100-150 (70 might be possible)</td>
<td>72</td>
</tr>
</tbody>
</table>

### Adjuvant medication for pain

- Steroids: dexamethasone 5mg sc qd
- Haloperidol
- Midazolam
- GABA: gabapentin 300mg tid
- TCA: amitriptyline (Tryptanol), imipramine (Tofranil)
- Anti-epileptics
- Anti-depressant

### Example: Opioid substitution

- 小朋友因病使用嗎啡，目前已經調藥至每日皮下注射500 mg，但狀況更差，且出現躁動不安，流汗與myoclonus
- 您認為應該換藥
- 想換成fentanyl 貼片(potency: 100-150倍之口服嗎啡)

請問如何換算？

### 標準答案

- Morphine 500 mg sc= 1000 mg po
- Morphine 1000 mg po
  = 1000 mg/150= 6.67 mg parenteral fentanyl in 24 hr
- 考虑incomplete cross-tolerance的問題，需降低25%劑量: 6.67 mg x 75%= 5 mg in 24 hr

### 實際上，答案是………

- Fentanyl 贼片分成TD 25 ug/h, 50 ug/h
- 相當於口服嗎啡60-90mg, 120-180 mg/24hr
- Morphine 500 mg sc=1000 mg po
- Morphine 1000 mg po X 0.75=750 mg
- 差不多4-6片大片的貼片
臨終前的疼痛處置，何者錯誤？

A. 臨終前仍須繼續之前的 opioid 類止痛劑
B. 無意識時，病患仍會歷經疼痛
C. 臨終前 48 小時，大部分病患可以減少止痛劑的使用
D. 緩和的動作且避免非必需的運動，可以減緩和活動相關的疼痛
E. 之前未使用 opioid 類止痛劑，但產生新疼痛之病患，可以使用連續皮下灌注 morphine

(C) 錯誤:

40% 增加，39% 不變，僅 12% 減少止痛劑的劑量
3

児童安寧團隊照護經驗分享
The Experience of Palliative Care in Pediatric

沈青青護理督導長
Ching-Ching Sheng

臺北榮民總醫院護理部
Nursing Supervisor, Department of Nursing, Taipei Veterans General Hospital

本課程提供學員瞭解以下的內容：
1. 兒童安寧照護的內涵、現況與發展
2. 兒童安寧照護的照護模式
3. 兒童安寧照護的照護成果
4. 兒童安寧照護的拓展
5. 臨床案例分享與討論
生命無懼—陪伴孩子走向生命終點
Valiant Life - Accompanying Your Child at the End of Their Life

蘇惠娟理事長
Huei-Jiuan Su

中華生命無懼協會
President, China Valiant Life Association Director

「放手」不代表「放棄」；「死亡」不代表「結束」…。

任何父母聽到「安寧」兩個字，就好像承認放棄治療、放棄努力、放棄希望、甚至放棄最後仍然可能出現的奇蹟！作這樣的決定，除了錐心刺骨，還有些許罪惡感。我了解！

只是，當醫療對孩子再也沒有任何幫助時，我們還能為孩子做什麼？

我多麼不希望父母在孩子離去之後，所有的記憶都停留在孩子最後的痛苦掙扎，一輩子揮之不去！

「告別」需要很大很大的勇氣；「放手」需要很深很深的愛…

父母和孩子之間的告別，是人世間最讓人心碎的課題…

當我們願意接受孩子即將離去的事實；當我們願意選擇放手時…。孩子才能坦然接受自己即將死亡的事實，然後，安然離去…

但是也唯有父母願意主動的、坦然的、勇敢的和孩子告別，才能讓孩子離去時沒有牽掛；讓父母接下來的日子沒有遺憾！

然而，「放手」不代表「放棄」；「死亡」不代表「結束」…。

“愛”，是直到天堂都不會消失的…。
典範演講：
以歷史的透鏡來拓展我們兒科醫學的視野

Exploring the Frontiers of Pediatric Medicine Through a Historical Lens

楊義明教授
Yih-Ming Yang
中國醫藥大學兒童醫院
Professor, China Medical University Children's Hospital

兒科醫學的回顧

兩百五十年前（1764），瑞典的von Rosenstein
領先建立現代兒科醫學，二十五年之後（1789），
美國賓州大學醫學院開始兒科的課程。大約六十年
之後，美國費城兒童醫院（1855），及波士頓兒童
醫院（1869）相繼成立，不久，哈佛大學醫學院成
立兒科部（1893）。十多年之後，臺灣總督府臺北
醫院（臺大醫院前身）成立兒科部（1906），不
久，臺北帝大（臺大前身）醫學院也建立兒科部
（1936）。

兒科學及兒童醫院的建立，帶動了兒童醫學
的重大進展，也同時促進了兒童健康照護的提
昇，更開啓了兒科研究之門。進入廿世紀時，推展
嬰兒營養與餵奶安全（1900），孩童健康獲得顯著
的改善，並且提升對兒童健康福利的認識及重視
（1908年紐約市成立兒童健康處）。隨後開始了一
系列對增進兒童醫療福祉的重大進展，首先是抗
感染疾病的研究及發展（發現抗生素，1930）及對
於兒童發展及發育的新知及重視（1930），接著是
對遺傳病學的瞭解（1940），早產兒的醫療照顧
（1943），先天性心臟病的醫治（1945），以及預防
醫學進入了嶄新的領域（小兒麻痺疫苗的發現，
1954）。

最近的半個世紀，我們的兒科醫學界領導了
臺灣兒童醫學的快速進展，建立最優質的兒科。
全民健保更提供了前所未有的對於兒童健康照護
的保障，大幅度的提昇對兒童疾病之診斷及整體
治療。這幾十年更是積極推動新生兒先天性疾病
篩檢，成效斐然。

臺灣的兒科次專科也在這五十年有著異異的
發展，對專門疾病醫療照顧，都非常專精，極為
先進，包括新生兒 / 周產兒科，心臟，感染，腸
胃，代謝 / 內分泌，腎臟，腸胃，胸肺，神經，
過敏 / 免疫及腎臟，精神，血液腫瘤及心理。小
兒外科體系，包括小兒外科，心臟外科，骨科，
復健，神經外科，眼科，耳鼻喉科及泌尿等，都
建立了優質的次專領域。一些對兒童特殊需要
的次專科，如風溼，青少年，學童健康 / 學校醫
療，安寧緩和醫療，兒童社會醫學及兒童虐待 /
忽略，運動醫學等，則正在發展或成長茁壯中。

在這五十年，臺灣的兒科積極的加入先行國
家兒童醫學研究的行列。我們的尖端醫學研究在
國際上也佔有一席之地。例如，張美惠院士的研
究團隊從1980年代開始的B型肝炎疫苗接種研
究，發現兒童接種B型肝炎疫苗能有效預防肝
炎，同時能防止肝癌。在醫學史上首次證明疫苗
的接種能有效防止癌症，立下了人類創新醫療的
新里程碑。

我們在兒童疾病跨團隊醫療照顧上，正在全
力提昇整合性的醫療品質，我們應當在這方面擴展更多的社會資源，努力於落實整合性步驟及高協調性的醫療照顧程序。諸如：及早的發現問題，及時的建立診斷，適當、適時、適宜的跨團隊的評估及治療計劃，以及適當、適切的長期追蹤及再評估。同時要將家庭全程的包含在這個過程中。

兒科醫學的任務

兒科醫學會與兒科醫師擔當有重大的社會角色與使命，就是肩負起兒童健康福祉的守護者，不遺餘力的倡導兒童福祉，為兒童權利發言。對於推展確保兒童生病時應有的醫療照顧，使每個孩子都得到保健追蹤，更是責無旁貸。

兒科醫學的前瞻性視野

1) 在跨團隊醫療照顧的整合上
2) 在以兒童為中心及以家庭為中心的照顧上
3) 在強化、健全國家兒童醫療健康政策，喚起社會兒童保健意識，及保障兒童健康保健的權益上
4) 在教養深遠的教育使命上
5) 在推展與支持兒科研究上

將逐項的提出探討及引伸，並且提出擴展視野的考量，以及可能的開創性及前瞻性思考。
Probiotics in Paediatrics: 
Prevention and Adjuvant 
Treatment of Common Conditions 

Dr. Ashton Harper 
MBBS BSc MRCS Medical Advisor – 
Protexin Human Healthcare 

Microbial organisms are found in virtually all environments on Earth and many multicellular organisms have evolved in close symbiosis with them. They make a vital contribution to a range of human physiological processes and their impact on health and disease is undeniable. A wealth of evidence of probiotic benefit in humans has been published in recent decades. Many parents have ever asked their paediatrician the common questions: ‘Should I give my baby any probiotic?’, and ‘How do probiotics work inside my baby?’ In this lecture Dr. Harper will describe the association between diseases and gut microbial characteristics, the mechanism of action of probiotic bacteria, and the most up-to-date conclusions from the literature on the utility of probiotics for a range of common paediatric diseases. The talk will also cover: desirable traits of probiotics, recommended dosage, analysis of viability, rationale for the choice of species, choosing multi-strain or single strain products, and safety. The evidence presented in this lecture will help pediatric health care providers make appropriate decisions regarding the usefulness and benefit of probiotics for their patients.
1 台湾肺炎链球菌疫苗接种计划成效
Effectiveness of National Pneumococcal Vaccination Programs in Taiwan

呂俊毅医师
Chun-Yi Lu
台大儿童医院
Doctor, National Taiwan University
Children's Hospital

Taiwan used to have its highest culture-confirmed invasive pneumococcal disease (IPD) incidence of 15.6/100,000 in children aged 2-4 years before the implementation of any national immunization program (NIP) for pneumococcal infections. In 2007, Taiwan started a pneumococcal NIP for high risk groups with PCV7. PCV7 was replaced by PCV10 in 2010 and then PCV13 in 2012. The IPD incidence remained unchanged during these years. The NIP was extended to one-dose PCV13 for all children aged 2-5 years in 2013. In 2014, the program was further extended to two doses of PCV13 for all children aged 1-2 years and one dose of PCV13 for all children aged 2-5 years in 2014. The unique catch-up-as-primary pneumococcal NIP has shown its early success in Taiwan. The IPD incidence in children age 5 years or less decreased by 29.1% in 2013 and 51.3% in 2014. The IPD caused by 19A decreased by 39.2% in 2013 and 43.5% in 2014. While the incidence of IPD decreased significantly in children, the incidence of adults remained unchanged.

In 2015, Taiwan further extended its pneumococcal NIP downward to infants. Every infant gets PCV13 at 2, 4, and 12-15 months of ages. Such a 2+1 PCV13 program not only kept IPD incidences in children low but also showed certain degree of herd effects in the elderly. IPD incidence decreased in people aged 75 years or older.

The Taiwanese experience showed that herd effect of PCV13 vaccination is minimal when the vaccine is used with catch-up programs. A standard prime-booster program starting from early infancy leads to maximal effectiveness directly in children and indirectly in the elderly.

2 評估對肺炎的影響程度：成人預防接種的新思維
Measuring the Impact of Pneumonia: New Insights into the Need for Vaccination of Adults

黃玉成教授
Yhu-Chering Huang
長庚儿童医院小兒感染科
Professor, Department of Pediatric, Chang Gung Memorial Hospital

According to the Global Burden of Disease Study, lower respiratory tract infection, including community acquired pneumonia (CAP), was the second leading cause of death and years of life lost in 2013.1 Streptococcus pneumoniae is among the most commonly identified cause of CAP in adults.2 Due to the empirical use of antibiotics, lack of a systematic definition of CAP, difficulties in obtaining samples for
culture, and differences in diagnostic test sensitivity/specificity, the incidence of pneumococcal CAP is likely underestimated. In addition, determining the true burden of pneumococcal CAP is hindered by the fact that most patients are treated on an outpatient basis, and most studies are based on hospitalized patients. To improve the clinical diagnosis of pneumococcal infection in CAP, a Luminex technology-based multiplex urinary antigen detection (UAD) diagnostic assay was developed and validated. This assay can simultaneously detect 13 serotypes of *S. pneumoniae* (corresponding to the polysaccharide antigens in the 13-valent polysaccharide conjugate vaccine [PCV13]) by capturing serotype-specific *S. pneumoniae* polysaccharides secreted in human urine. There are now several planned or ongoing population-based UAD studies which can estimate the true incidence of all-cause CAP, and vaccine-type CAP, by identifying disease in both outpatient and hospitalized settings. In this presentation, we review the current status of these studies and how vaccination of adults with PCV13 addresses an unmet medical need.
Evolutional Change of EEG and Image Study in a Full Term Baby with Perinatal Asphyxia and Hypoxic-ischemic Encephalopathy Treated by Hypothermia Therapy

Yu-Hsien Lee, Chun-Shan Wu, Chuan-Yu Wang
Department of Pediatrics, Taipei Medical University Shuang-Ho Hospital, Taipei, Taiwan; Pediatric Department, School of Medicine, College of Medicine, Taipei Medical University

Background: Therapeutic hypothermia (TH) had been reported to reduce the risk of mortality or morbidity in infants with moderate or severe hypoxic-ischemic encephalopathy (HIE) since 2005. We are going to introduce a full term newborn with perinatal asphyxia performed TH to ameliorate the severity of HIE.

Methods: This male newborn was born to a mother G2P2, GA: 40+3weeks at 2016/04/20 02:02. Maternal history had Group B Streptococcus positive with complete prophylaxis treatment. Birth body weight is 3560gm. Apgar score are 5, 4 and 6 at 1, 5 and 10 minutes respectively. After birth, no crying, poor muscle tone, cyanosis, no obvious reflex were noted. Endotracheal tube (ETT) was inserted immediately. After admission to NICU, physical examination showed light reflex trace, pupils 3-4 mm, breathing sounds crackles with gasping and subcostal retraction, extremities ecchymoses and hypotonia. Empirical antibiotics were prescribed. Laboratory data revealed respiratory and metabolic acidosis, leukocytosis, acute kidney injury, and no anemia. CXR revealed bilateral infiltration increased and haziness. However, he had subtle seizure with submandibular fasciculation and sucking on 4/20 morning and Phenobarbital was given. Brain echo before TH showed brain swelling and suspected a left parietal infarction. Due to neonatal asphyxia, TH was then started on 4/20 13:15.

Results: This patient was treated with TH for 72 hours while after birth 11 hours. EEG revealed multifocal spikes decreased after TH and brain sonography revealed brain swelling improved. Post hypothermia treatment brain MRI revealed severe HIE. Patient was discharged with taking home anticonvulsants persistent use and OG tube feeding. Further follow up of patient’s development and milestone is important.

Conclusions: TH was reported to have significant benefits to moderate or severe HIE. However, we experienced a case that patient’s outcome evaluated by brain MRI and longitudinal brain echo still appeared to be severe, even though EEG and clinical activity were improving after hypothermia therapy. Maybe there are some predict signs that can remind us the case might be poor prognosis. Predict signs included poor seizure control, CO2 over-washout and IICP signs. Besides, there are also some management can be modified which included the intervention time of TH (less than 6 hours after birth), closely monitor drugs level and adjust drugs dosage during TH.

Posterior Reversible Encephalopathy Syndrome in a Patient with Adrenal Cortical Carcinoma

Han-Pin Lin, Shou-Yu Wang, Julie Chi Chow, Ming-Chi Lai
Chi Mei Medical Center, Pediatric Department

Background: Adrenal cortical carcinoma in children is extremely rare, and posterior reversible encephalopathy syndrome (PRES) is a reversible neurological entity characterized by seizures, headaches, visual symptoms and impaired consciousness.

Methods: We report about a 12-year-old girl who presented with status epilepticus following a tonsillitis of an influenza viral infection. On physical exam cushingoid features were noted, and her blood pressure was elevated. A brain magnetic resonance imaging (MRI) showed findings consistent with posterior reversible encephalopathy syndrome and the lumbar puncture showed unremarkable CSF results. Given the clinical presentation and findings on MRI-brain, a diagnosis of PRES was postulated. Survey of PRES was carried out and a calcified left adrenal tumor was demonstrated by MRI-abdomen. She later underwent left adrenalectomy and lymph nodes dissection.

Results: The pathology reported adrenal cortical carcinoma with lymph node metastasis, stage III. After cumulative radiotherapy, she received adjuvant therapy with mitotane and steroid replacement with cortisone acetate.

Conclusions: This is the first known case of adrenal carcinoma presenting with PRES, and the case highlights...
the importance of performing a survey of the underlying cause of PRES.

3 Reversion of Abnormal High Systemic Vascular Resistance with Strong Vasodilators in Infants of Critical EV71 Infection Complicated with Severe Heart Failure

使用高剂量血管扩张剂救治肠病毒感染的婴幼儿

Jeng-Sheng Chang1,2,3, Ping-Yun Chiou1,2, Chien-Heng Lin3, Shao-Jyun Lin4

Departments of Cardiology1, Pediatric Intensive Care Unit2, Pulmonology3 and Infection4, Children’s Hospital of China Medical University, Taichung, Taiwan

Background: The 2014 management guideline for severe EV71 infection by Taiwan’s Center of Disease Control recommended that the patients of stage III (Autonomic dysregulation stage) and stage IV (Heart failure stage) be treated in the ICU with milrinone infusion. In 2010 Lancet Infectious Disease, T. Solomon addressed that the complications of pulmonary edema (PE) in patients of severe EV71 was caused by both cardiac toxicity and a high systemic vascular resistance (SVR). The presentations of PE and CHF have been reported in many papers of severe EV infection, however, the high SVR phenomenon and its optimal management has not received adequate attention.

Methods: Determined to figure out the SVR status of critical EV71 patients before they were connected to ECMO support, and to verify their response to vasodilators, we present the following 2 cases to share our latest experience.

Results: Case 1. Echocardiography study on a one-year-three-month-old boy of severe EV71 infection on his 3rd day of disease onset showed that the LVEF was only 26%. Hemodynamic calculations revealed that the arterio-venous mean pressure difference (AVmPD), Cardiac Index (CI) and systemic vascular resistance index (SVRI) were 86 mmHg, 1.5 L/min/M2 and 57.3 Wood units*M2, respectively. We treated him with 2 courses of milrinone loading (50 μg/kg/min infusion in 20 min’), however, the cardiac contractility and hemodynamic decompensation did not improve, so we put him into ECMO therapy. The ECMO was removed smoothly in 3 days and he was discharged on the 26th day of admission without neurology sequel. Case 2. A 3-and-half-month-old male infant of 6.7kg body weight was referred to our ER at his 3rd day of fever with presentations of poor activity, pale appearance and tachycardia (210 bpm). Echocardiography revealed a poor cardiac contractility (LVEF= 35.3%), but his BP remained at 117/85 mmHg, and O2 saturation was above 95%. We treated him with 3 doses of milrinone loadings, but his hemodynamic status remained as poor as 87 mmHg, 1.7 L/min/M2, and 51 Wood units*M2 in AVmPD, CI and SVRI, respectively. Thereupon, we began to escalate the NTG infusion dosage up to 10 μg/kg/imin, use apresoline bolus infusion, and administer NG tube medication of phenoxybenzamine. His hemodynamic status improved in 12 hours when the hemodynamic data returned to 68 mmHg, 2.88 L/min/M2, and 23.6 Wood units*M2, respectively. His cardiac contractility returned to normal 5 days later, though compliance remained abnormal and myocardium appeared edematous and thick. He was discharge at 16th day of admission without neurology sequel.

Conclusions: Our continued hemodynamic and echocardiographic studies on patients of critical EV71 infection showed that both cardiac dysfunction and abnormally high SVR are crucial factors to cause systemic low cardiac output. By using high dosage of vasodilators like milrinone and NTG, some borderline cases can be revived without sending the patient for ECMO therapy. However, during the critical period, a cardiologist must be always available to determine that whether the patient’s cardiovascular impairment has responded favorably to the vasodilators or the patient needs an urgent ECMO therapy.

4 Refractory Kawasaki Disease with Coronary Artery Aneurysm in a very Young Infant: A Case Report and Management Suggestion by Literature Review

嬰兒難治性川崎氏症併發冠狀動脈瘤：個案報告與治療建議之回顧

Yi-Li Hung, Da-Jyun Su, Chung-Min Shen, Nan-Koong Wang

Departments of Pediatrics, Cathay General Hospital and Chinese University of Medical Sciences, Kaohsiung, Taiwan

Background: The diagnosis and treatment of Kawasaki disease (KD) in infants below 3 months are challenging. Their clinical presentations are usually atypical so that the initial treatment timing is often delayed. Besides, their therapeutic response to intravenous immunoglobulin (IVIG) is often refractory which needs further adjunct immune modulating agents. Majority of these patients will develop coronary artery dilation.

Methods: Herein, we describe the case of a 50 days old male infant who suffered from spiking fever for 1 day and was admitted under the impression of upper respiratory tract infection. Incomplete KD was diagnosed 4 days of fever with the serial presentation of skin rash, extremity changes, lip and oral changes, conjunctiva congestion. The laboratory data showed marked elevated CRP 33.9mg/dL, ESR 66mm/1hr, hypoalbuminemia 2.1g/dL. The hemogram showed leukocytosis WBC47.6x1000/μL and microcytic anemia Hb 6.5g/dL. He received a total 3 courses of IVIG but didn’t achieve the clinical relief. Adjunctive intravenous methylprednisolone led to prompt defervescence and were continued for 5 days without adverse effect. Despite of timely administration of IVIG and methylprednisolone, he still developed bilateral large coronary artery aneurysms.

Results: Reviewing of the previous literature, KD in infants below 3 months is rare and is often featuring atypical presentation with severe coronary artery involvement. The diagnosis of KD can’t be depended by the American Heart Association (AHA) criteria in infants of this age group. Infliximab, cyclosporine and methylprednisolone pulse therapy have been reported to treat refractory KD in young infants successfully.

Conclusions: Infants below 3 months with KD have to treat it as a distinct entity because of their poor IVIG response and high risk for getting coronary artery aneurysm. Early use of immune modulating agents or steroid with IVIG may be effective for refractory KD in young infant.