HK J Paediatr (new series) 2014;**19**:100-128

Proceedings of Congress

2013 Annual Scientific Meeting: Hong Kong College of Paediatricians

7 December 2013

Symposia

Symposium: A Child with Empyema

Moderator: CW Leung

President of Hong Kong Society for Paediatric Immunology and Infectious Diseases; Consultant Paediatrician & Head of Paediatric Infectious Disease; Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital, Hong Kong

Case Scenario: E Chan

Consultant, Department of Paediatrics and Adolescent Medicine, Kwong Wah Hospital, Hong Kong

A 33-month-old boy with good past health presented with community acquired pneumonia and was treated with cefotaxime and clarithromycin before admission to Kwong Wah Hospital. He subsequently developed necrotising pneumonia with left empyema caused by pneumococcus serotype 3 (identified by PCR in pleural fluid). Blood and pleural fluid cultures were negative. He was treated with a combination of antibiotics including cefotaxime, vancomycin, clindamycin and azithromycin. Chest drain was inserted and intrapleural fibrinolysis was carried out by daily intrapleural irrigation with urokinase. Cardiothoracic surgeon was also consulted for the care of the child. His condition improved with the above measures.

Role of Radiology in the Management of Complicated Pneumonia in Children

WCW Chu

Professor, Department of Imaging & Interventional Radiology, Faculty of Medicine, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

Community acquired pneumonia in the paediatric population is common. A significant number of hospitalised cases are complicated by parapneumonic effusion and empyema. Imaging plays an important role in both diagnosis and therapy in complicated pneumonia in children.

There are different stages of pleural infection: exudative, fibropurulent and organisational. The benefit of ultrasonography over computerised tomography (CT) includes superior ability to visualise fibrin strands within an effusion, which indicates the formation of empyema. Ultrasound also has the advantage of lack of radiation, no need for sedation and portability. However, it is limited by variable technical quality, small field of view and shadowing of deep structures by overlying air.

A recent study showed that ultrasound and CT had similar ability to detect loculated effusion, lung necrosis or abscess resulting from complicated pneumonia. Chest radiography (CXR) and ultrasound should be used in the imaging workup of complicated paediatric pneumonia while CT should be reserved for those cases which are technically difficult to be fully assessed by ultrasound or if there is discrepancy between ultrasound findings and clinical progress.

Q & A:

Q. How does CT compare with CXR in terms of radiation exposure?

A. CT thorax delivers 300 times more radiation than a single CXR. High resolution CT (HRCT) has the same radiation exposure as CT as image reconstruction technology is employed. Prof. Chu pledged the audience to be cautious when ordering CT for children, taking into account unnecessary radiation exposure.

Q. How about the use of low-dose CT?

A. This is already taken into consideration when CT is performed on children.

Bedside Ultrasound for Empyema Thoracis in Children

KS **Hsieh**
Chief, Department of Paediatrics, Kaohsiung Veterans General Hospital Kaohsiung, Taiwan

The role of ultrasound for both diagnosis and monitoring of the clinical course in managing empyema thoracis with the advantage of non-invasiveness, convenience and free from radiation is described. Ultrasound imaging enables localisation of the site of infection and inflammation, estimating the amount of pleural fluid and identifying exudative fibrin within the pleural cavity. Bedside ultrasound is useful for children with empyema thoracis in experienced hands.

Minimally Invasive Chest Drain Insertion in Children

WK **Chiu**
Consultant, Department of Paediatrics and Adolescent Medicine, United Christian Hospital, Hong Kong

Chest drain insertion is a common procedure for various clinical conditions, including pneumothorax, haemopneumothorax, pleural effusion, empyema and postoperative drainage following cardiothoracic surgery. This potentially life-saving procedure, however, may lead to significant morbidity. A minimally invasive technique for chest drain insertion in children by using the Mini Step bladeless trocar is introduced. This technique is safe and efficient. It has a high success rate and minimal morbidity. This procedure is highly recommended for chest drain insertion in children older than two years.

Demonstration video available at http://www.hkmj.org/video/video07.html

Q & A:

Q. How much does the minimally invasive chest drain set cost?
A. Around 1,000 Hong Kong dollars per set.
Q. What sort of sedation is required for the procedure?
A. Parenteral ketamine and midazolam.
Q. What is the best position for insertion of the chest drain?
A. Depending on the diagnosis, most often it is at the safety triangle bound by the lateral border of the pectoralis major, the anterior border of the latissimus dorsi and the nipple line. The needle should puncture just above the superior border of the rib.
Q. What is the smallest age for application of this device?
A. The minimum age is two years.

Surgical Treatment of Empyema Thoracis in Children

CC **Ma**
Chief of Service and Consultant, Department of Cardiothoracic Surgery, Queen Elizabeth Hospital, Hong Kong

Empyema thoracis in children remains a common condition with significant morbidity. Despite the development of new therapies such as fibrinolysis and thoracoscopy, the optimal treatment of empyema thoracis is still controversial. Dr. Ma shared the experience of managing empyema thoracis over the 12-year period from 2001 till 2012. Fibrinolytic therapy is reasonable primary treatment for earlier stage empyema with close monitoring of progress. Failure to evacuate the pleural space and persistent infection should prompt surgical intervention. Early Video Assisted Thoracoscopic Surgery (VATS) in empyema of earlier stage to physically breakdown the loculations and fibrins produces good result. Open decortication is useful in treatment of resistant and later stage empyema.

Q & A:

Q. What actually are the details of VATS?
A. The procedure is to physically breakdown the loculations and fibrin strands of the empyema.
Q. What is your viewpoint on recommending either VATS or fibrinolytic agent?
A. Most of the time operation sessions are limited so surgical procedure cannot be performed early. Intrapleural fibrinolysis through the chest drain is a reasonable alternative. If the operation theatre is readily available, Dr. Ma prefers early operation with VATS.
Q. Can VATS be performed at the bedside?
A. Bedside VATS is not advised.
Q. Is there an age limitation for VATS in children?
A. VATS is usually performed in children above 8 years old.

Epidemiology of Pneumococcal Empyema in Hospitalised Children in Hong Kong

H **Chen**
Associate Consultant, Hospital Authority Infectious Disease Control Training Centre, Hong Kong

A retrospective review by retrieving cases from CDARS (Clinical Data Analysis and Reporting System) of Hospital Authority showed that the incidence of pneumococcal pulmonary empyema (definite: culture from pleural fluid

grew *Streptococcus pneumoniae* and probable: culture from other sites grew *Streptococcus pneumoniae*) seemed to be increasing over the years from 2008 to 2013. But it was not statistically significant. Cases were predominantly caused by non-vaccine serotypes, like 3 and 19A, after the introduction of pneumococcal conjugate vaccine to the Childhood Immunisation Program in Hong Kong.

About 50% of affected children were given antimicrobials before hospitalisation. The most common antimicrobial used was macrolide. Macrolide monotherapy before hospitalisation would delay effective treatment as macrolide resistant pneumococci was commonly identified (~80% of all isolates).

Active surveillance of pneumococcal empyema (using PCR for identification of pneumococcus serotype in pleural fluid) should be conducted to monitor the changing epidemiology of empyema after introduction of pneumococcal vaccination.

About 50% of affected children were given antimicrobials before hospitalisation. The most common antimicrobial used was macrolide. Macrolide monotherapy before hospitalisation would delay effective treatment as macrolide resistant pneumococci was commonly identified (~80% of all isolates).

Active surveillance of pneumococcal empyema (using PCR for identification of pneumococcus serotype in pleural fluid) should be conducted to monitor the changing epidemiology of empyema after introduction of pneumococcal vaccination.

PANEL DISCUSSION

- Increasing incidence of pulmonary empyema has been reported over the past decades. This occurred well before the introduction of pneumococcal conjugate vaccine. The cause can be multifactorial (e.g. change in climate, humidity, biological factors, human behaviour, use of antimicrobials, antimicrobial resistance).
- With the introduction of pneumococcal conjugate vaccine, the overall incidence of invasive pneumococcal diseases has dramatically decreased while the incidence of diseases caused by non-vaccine serotypes have slowly increased as a result of serotype replacement.

Consensus:

- Active surveillance of invasive pneumococcal diseases with cultures and molecular microbiological techniques should be conducted to monitor the effectiveness of pneumococcal vaccination, serotype replacement and changes in antimicrobial resistance.
- Urine antigen test is not a reliable tool for detection of pneumococcal infection as it has a high false positive rate due to colonization or recent pneumococcal vaccination.

Controversy:

- 13-valent pneumococcal conjugate vaccine is not very effective in preventing pneumococcal pulmonary empyema, especially those caused by serotype 3.
- Serotype replacement may be one of the explanations for increasing pulmonary empyema caused by non-vaccine serotypes.

Symposium: A Child with Acute Flaccid Paralysis (AFP)

Moderator: KY Chan

Honorary Consultant, Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital, Hong Kong

Case Scenario: KT Liu

Consultant, Department of Paediatrics and Adolescent Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong

Chi Ping is a 4-month-old Chinese boy who was born in Hong Kong and returned to China at the age of 1 week. He received oral polio, Hepatitis B and DTP vaccines according to the schedule in Mainland China. He was admitted for fever and lower limb weakness. He appeared alert and playful with stable vitals on admission. Investigations included MRI spine, lumbar puncture, blood and stool tests. CSF showed WBC 12/mm^3 (Norm ref: <5/mm^3) with 80% lymphocytes, RBC 50/mm^3, protein 0.8 g/L (Norm ref: <0.5 g/L), glucose 3.0 mmol/L. MRI of thoracolumbar spine was normal.

Immediate nerve conduction, velocity study (NCV) showed normal findings over bilateral median and ulnar, peroneal and tibial nerves. Anti-ganglioside antibody was negative.

He was treated as *Guillain-Barre syndrome* (GBS) with IV immunoglobulin.

Stool PCR was positive for *Enterovirus* but negative in CSF and stool culture was later found positive for Sabin like poliovirus type 2.

Paralysis of left lower limb persisted and repeated NCV showed low amplitude of compound muscle action

potentials (CMAP) with normal latency over the left peroneal and tibial nerves but normal findings of the right lower limb motor nerve study. Sensory nerve conduction study was normal. The abnormal NCV finding was suggestive of motor neuron or motor axonal involvement.

Immune study showed low serum immunoglobulin levels (IgA, IgM, IgG), undetectable antibodies against Tetanus & Diphtheria, absent B-cells in lymphocyte subset and BTK mutation as confirmed by genetic studies.

The final diagnoses were ***Vaccine associated paralytic poliomyelitis (VAPP)*** *and* ***X-linked agammaglobinaemia****.*

Guillain-Barre Syndrome (GBS) in Children: Diagnosis, Management and Local Case Review

S **Chan**

Associate Consultant, Division of Child Neurology, Developmental Paediatrics and Neurohabilitation, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong

GBS is an acquired auto-immune disorder with acute inflammation and damage to peripheral nerves, nerve roots and sometimes cranial nerves. Antecedent infection or fever preceded in some children. Typically, there is symmetrical ascending weakness of limbs progress over days to weeks with severity ranged from mild weakness to total paralysis. Facial, respiratory and bulbar muscles and autonomic nervous system can be affected. Sensory symptoms such as paresthesias, numbness or tingling of the hand and feet, and deep aching pain are common.

The diagnosis of GBS is based on the clinical features, CSF findings and results of neuroimaging and nerve conduction studies. The findings of cyto-albumin dissociation and negative viral PCR & culture in CSF and cauda equina contrast enhancement in MRI spine support the diagnosis.

There are four major clinical variants (Acute inflammatory demyelinating polyneuropathy AIDP, Acute motor axonal neuropathy AMAN, Acute motor and sensory axonal neuropathy AMSAN, and Miller Fisher syndrome MF) of GBS in childhood according to specific clinical features and NCV findings. AIDP is the commonest type with demyelinating pattern of motor and sensory nerves in NCV. AMAN, commonly reported in China, with NCV findings of axonal pattern in motor nerves is often associated with anti-ganglioside antibody. MF is always associated with ophthalmoplegia and ataxia. Other causes of AFP such as acute muscle diseases, acquired causes of neuropathy, anterior horn cell and spinal cord diseases should also be considered. All children suspected of GBS must be admitted to the hospital with close monitoring of vital signs and progression of weakness. Both intravenous immunoglobulin and plasmapharesis are safe and effective in children in shortening the time to recovery and hastening the time to independent ambulation.

A retrospective study on the epidemiology, clinical profiles and treatment outcome of paediatric GBS patients admitted to HA hospitals between 2000 to 2012 was reported. There were a total of 46 patients with 25 (54%) AIDP, 6 (13%) AMAN, 1 (5%) AMSAN, 5 (11%) MF and 9 (20%) undetermined subtype. The estimated average GBS incidence per 100,000 of children <18 years per year was 0.5. The age of admission ranged from 1.58-17.92 years with a mean age of 8.82 +/- 5.13 years. Twenty-seven patients had preceding upper respiratory tract infection or gastroenteritis and 11 patients did not have any preceding illness. Aside from limb weakness, 8 had facial weakness, 3 required ventilator support and 6 had autonomic disturbance. Among 5 patients with blood checked for antiganglioside Ab, 3 were positive. Thirty-five patients received treatment with IVIG and 1 with plasmapharesis. Majority of children with AIDP (92%) had complete recovery, whereas only 50% of children with AMAN had good recovery.

Enteroviruses Infection in Children

YW **Kwan**

Associate Consultant, Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital, Hong Kong

Enteroviruses (EV), traditionally include polioviruses, coxsackie A, B, C viruses and numbered enteroviruses is currently reclassified into human enteroviruses A, B, C and D. Poliomyelitis was the 1st and the most important enteroviral disease causing infantile paralysis. EV infection is a frequent and significant human disease with protean manifestations. Seventy-five percent infected infants are asymptomatic, however, same virus can cause several different clinical syndromes such as non-specific febrile illness, hand foot mouth disease, non-specific exanthema, herpangina, myocarditis, meningoencephalitis and acute flaccid paralysis; whereas same clinical picture can be caused by different enteroviruses.

Infection is acquired via oral or respiratory route, replicating in oropharynx and alimentary tract and spreading to regional lymph node, followed by viraemia and spreading to other body sites.

Based on the clinical features, stool, throat / rectal swab, vesicle fluid or CSF should be collected for viral culture, PCR & serotyping.

Neurological manifestations include meningitis, encephalitis, acute flaccid paralysis (anterior myelitis), transverse myelitis are not infrequent in enteroviruses infection. In Hong Kong, EV71 infection has been a notifiable disease since March 2009. From March 2009-June 2012, 239 EV71 cases aged from 0.5 to 43 years with a median age of 5 yrs were notified. Twenty-eight (11.9%) patients had severe complications including meningitis, encephalitis, meningoencephalitis, acute flaccid paralysis and myocarditis. Surveillance system for severe paediatric EV infection (other than EV71) with complication was launched in July 2010. From July 2010-June 2012, 26 cases had meningitis, encephalitis or myocarditis. From data of acute flaccid paralysis surveillance, non-polio enteroviruses were detected in 8.4% of cases of AFP.

Vaccine Associated Paralytic Poliomyelitis

P Lee

Assistant Professor, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

The live attenuated oral poliovirus vaccine (OPV) has been in use since the 1960s, with significant contribution to the global polio eradication. The administration of Sabin OPV enables the induction of mucosal immunity, in addition to systemic immune response. In immunocompetent individuals, Sabin strains replicate in the gut for a limited period of time and are excreted for up to 30-60 days. Viral replication in the gut triggers an adaptive immune response, including T-cell and B-cell responses that generate mucosal neutralising antibodies. However, in individuals with impaired humoral immunity, the delayed clearance of OPV provides the opportunity for the vaccine strains to revert to virulent strains due to back mutations introduced during unchecked rounds of replications. The consequences are two-fold; firstly, the revertants may have the ability to disseminate to the central nervous system to cause vaccine-associated paralytic poliomyelitis (VAPP) and secondly, the chronic excretion of these virulent strains can be a source of circulating vaccine-derived poliovirus strains and pose a threat to unvaccinated individuals in the community.

Patients with severe combined immunodeficiency (SCID), congenital agammaglobulinaemia including X-linked agammaglobulinemia (XLA) and autosomal recessive agammaglobulinemia, common variable immunodeficiency, and MHC class II deficiency are susceptible to VAPP. VAPP should be regarded as an indicator for underlying immunodeficiency, and such patients should undergo thorough immune evaluation including immunoglobulin pattern (IgG, IgA, IgM), lymphocyte subpopulation, and HIV testing. Evaluation for other opportunistic infections, and establishment of immunological diagnosis should be performed by immunologists so that definitive treatment can be provided.

AFP Surveillance in Hong Kong & Global Polio Situation Update

DYW Chan

Scientific Officer, Vaccine Preventable Disease Office, Surveillance & Epidemiology Branch, Centre for Health Protection, Department of Health. Hong Kong

Acute flaccid paralysis (AFP) surveillance system was set up in Hong Kong in 1997 as a sensitive surveillance system for voluntary reporting of cases under the age of 15 with suspected acute poliomyelitis. It was one of the criteria for Hong Kong's certification of poliomyelitis eradication by the World Health Organization (WHO) Western Pacific Region Office (WPRO) in 2000. The Department of Health (DH) carried out laboratory and epidemiological investigations on AFP cases according to the WHO guideline. The demographic, clinical and virological characteristics of cases reported to the system since it's establishment were reviewed.

From January 1997 to November 2013, 273 patients aged under 15 years presented with acute onset of paralysis of any limbs were reported to the DH. Of the 273 cases, about 45% were aged under five. All cases were discarded as non-polio AFP according to WHO classification. About 60% were identified with neurological disorders, with Guillain-Barre syndrome (26.7%) and myelitis (14.3%) being the most common. Viruses were detected in stool specimens of 13.2% of the AFP cases, with non-polio enteroviruses (NPEV) (63.8%) and adenoviruses (33.3%) accounted for most of the positive detections. Most performance indicators set by the WHO were fulfilled. The AFP surveillance facilitated the clinical, virological and epidemiological examination of paediatric AFP cases. Gullain-Barre syndrome is the commonest cause of AFP in our locality.

There has been substantial progress in global polio eradication, although wild poliovirus is still circulating in some areas. According to the WHO, the global polio cases decreased from 4074 in 1996 to 390 in 2013 (up to 26 November). As of November 2013, wild poliovirus is still endemic in three countries (Afghanistan, Nigeria and

Pakistan), with outbreaks in areas once polio-free including Ethiopia, Kenya, Somalia and Syria. Other than wild poliovirus, vaccine-derived poliovirus also accounted for a small proportion of polio cases worldwide.

The WHO has formulated an endgame strategy in 2012. Key targets of the endgame strategy include interrupting wild poliovirus transmission globally by 2014 and introducing at least one dose of inactivated poliovirus vaccine (IPV) and withdrawal of type 2 component in oral poliovirus vaccine (OPV) by mid-2016. These targets have been successfully achieved by Hong Kong in previous years.

Q & A:

Q. Vaccine associated paralytic poliomyelitis is very rare and Gullaine-Barre syndrome is the commonest cause of AFP in our locality, could this patient be in fact a case of GBS variant (AMAN) with incidental finding of Sabin polio virus in his stool sample?

A. Our patient's presentation of asymmetric weakness with no sensory / autonomic dysfunction and the unilateral lower limb abnormal NCV findings are more specific for poliomyelitis. There is a higher risk of developing VAPP after OPV in immunocompromised patients and the estimated risk is about 2 per 2000 vaccinees in B cell immunodeficiency. A more detailed NCV/EMG study is helpful to differentiate these two conditions. EMG study help to differentiate the involvement of motor neuronopathy in VAPP from the axonal neuropathy as in AMAN. In axonal motor neuropathy, aside from decreased CMAP in NCV, mild delay in motor distal latency is always present, whereas in anterior horn cells lesion such as poliomyelitis, motor latency is usually not affected.

Q. Israel was certified polio-free in 2002, OPV was then discontinued and replaced by IPV only schedule in routine childhood immunisation. The 2012 national IPV coverage rate was 95%. In 2013, wild poliovirus has been isolated from sewage samples, to stop silent transmission, national supplementary immunisation with OPV was launched. Many developed countries have switched to IPV only schedule to eliminate risk of VAPP associated with OPV, what is the disadvantage of IPV?

A. IPV appears to produce less local intestinal mucosal immunity than OPV and it is not able to spread to unvaccinated contacts. IPV recipients are more readily infected with wild polio than OPV recipients. The detection of wild poliovirus in environmental samples in Israel should alert polio-free countries that could confront similar situation. Importation of polio is possible in the era of heavy international travel and high population movement when wild polio continues to be endemic in several parts of the world.

Q. Should we treat poliomyelitis with Pleconaril?

A. Pleconaril interferes with enterovirus attachment and uncoating by binding to the virus protein capsid. A case report on "Pleconaril treatment of vaccine acquired poliovirus" stated that reverted strain of Polio virus 2 (Sabin) was eliminated from CSF and serum of an immunodeficient infant after treatment with Pleconaril. There is ongoing research on various novel drugs for treatment of enterovirus including poliomyelitis.

Q. What is the progress of Hong Kong in maintaining polio-free status?

A. Due to heavy international travel and population movement, the possibility of wild poliovirus importation cannot be ruled out. Hong Kong has taken and will continue with the following measures: i) maintain a sensitive AFP surveillance system; ii) the reference laboratory, Public Health Laboratory Service Branch under the DH maintains high quality performance and full accreditation by the WHO; iii) regular monitoring and ensure high immunisation coverage across the population; iv) a comprehensive and up-to-date polio importation plan.

Symposium: A Child with Autism Spectrum Disorder (ASD)

Moderator: C LAM

Consultant Paediatrician, Child Assessment Service, Department of Health, Hong Kong

Case Scenario: SP WU

Associate Consultant, Department of Paediatrics & Adolescent Medicine, Queen Elizabeth Hospital, Hong Kong

David is a 20 months old boy. He is the first child of a middle class family. Both his parents are healthy. David has been healthy all along. But his parents are concerned that he is lagging behind in his language and motor development from infancy onwards. They vaguely recall some vocalisation when he was at his early infancy, but he has never spoken anything his parents can understand. He does not seem to understand what his parents say to him. He is a loner and quite labile in his temperament.

David's parents are concerned that he might have autism.

- *Is there a screening program run by the government?*
- *How does a developmental-behavioural paediatrician help David?*
- *How would a paediatric neurologist approach the situation?*
- *How would a geneticist be able to help?*
- *What will David's future participation in society and functioning be like?*

Identifying Children with Autism Spectrum Disorder

S Leung
Assistant Director of Health (Family and Elderly Health Services), Department of Health, Hong Kong

Screening for Autism Spectrum Disorders (ASD) is controversial. The UK National Screening Committee (NSC) does not recommend the implementation of a population screening programme because it does not meet the "criteria for appraising the viability, effectiveness and appropriateness of a screening programme". The American Academy of Pediatrics (AAP) recommends that all children be screened specifically for ASD during regular well-child visits at 18 and 24 months, using the Modified Checklist for Autism in Toddlers (M-CHAT) which has high positive predictive values. However, a critical review of 7 validation studies on the M-CHAT (by the speaker) revealed a number of methodological flaws.

The UK NSC and the National Institute for Health and Care Excellence acknowledge the importance of child developmental and behavioural problems. They recommend early recognition be improved through informing parents about what is normal & abnormal and training of relevant healthcare, social care and education professionals; as well as child development and disability services be responsive to the needs of families.

In Hong Kong, the Developmental Surveillance Scheme (DSS), available in all Maternal & Child Health Centres (MCHCs) comprises (i) the provision of information to empower parents to monitor their child's development and behaviours; (ii) structured nurse interview at the key ages of 6, 12, 18 and 48 months of children to identify any parental concerns; and (iii) developmental assessment, at the primary care level, by MCHC doctors for any significant concerns. The importance of training for these primary healthcare professionals is highlighted. Evaluation of the DSS (January to June 2011) revealed that the majority (76%) of preschool children diagnosed with ASD at the Child Assessment Service were referred by MCHCs, mostly before the age of three.

Assessment Perspectives in Autism Spectrum Disorder

SKY Liu
Senior Medical & Health Officer, Child Assessment Service, Department of Health, Hong Kong

A large proportion of children with ASD manifest developmental problems between 1-2 years old. Early identification and diagnosis provide the best opportunity for early intervention, which in turn may improve the outcome of the children. Early indicators of ASD include social skill and communication skill deficits. Impairments in imagination skills/pretend play are also noted. Comprehensive assessment includes parent interview, clinical observation and use of standardised assessment tools e.g. ADOS, ADI-R is necessary to make an early diagnosis. Other differential diagnoses include intellectual impairment, ADHD, anxiety, hearing loss and other medical conditions. Counselling of parents on ASD features, evidence based training, developmental course and prognosis are important to enhance parents' acceptance. Elements of effective treatment program include structured environment with predictable routines, use of visual strategies and behavioural intervention, and early/intensive/individualised program that is applicable in naturalistic settings. Prognosis depends on the severity of autistic symptoms and cognitive ability of the child. Early referral for detail assessment by Developmental and Behavioural Paediatrician, Clinical Psychologist or Child Psychiatrist is of paramount importance.

Neurological Investigations for Children with Autism Spectrum Disorder

CW Fung
Associate Consultant, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

Up to 40% of patients suffering from autism spectrum disorder (ASD) have underlying genetic etiologies. Inborn errors of metabolism only account for less than 5% in the autistic population. Therefore, ASD patients can be sub-classified into essential (non-syndromic) or complex

(syndromic). Patients with complex ASD may have one or a combination of the following features: dysmorphism, abnormal growth parameters, neurological symptoms and signs, and multiple congenital anomalies. Referrals of each ASD patient to a clinical geneticist and paediatric neurologist remain an important part of the etiological evaluation. This talk covers the basic approach from a paediatric neurology perspective to look for an underlying cause in ASD which may have a treatment implication.

Evaluation of Children with Autism Spectrum Disorder – a Clinical Geneticist's Perspective

BHY **Chung**

Clinical Associate Professor, Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

Multiple lines of evidence support the strong role of genetics in the etiology of ASD. Accurate diagnosis of ASD (and co-morbidities) shall be achieved before referrals to clinical geneticists are made. The referring paediatricians shall discuss with the parents the expectations and possible outcomes of the genetic evaluation. The primary roles of the geneticist are to define the cause when possible, to provide genetic counseling and to contribute to case management. Chromosomal microarray is the first-tier genetic testing for non-syndromic ASD, while for syndromic diagnoses, genetic testing is individualised. Genetic counseling is important even for those without an identifiable cause.

Participation and Functioning for Children and Young Persons with ASD

E **Woo**

Senior Medical & Health Officer, Child Assessment Service, Department of Health, Hong Kong

To understand the challenges of children with ASD as they reach school age when they face increasing academic and social demands, underlying psychological and cognitive factors need to be considered. A prevailing psychological model explaining difficulties experienced by persons with ASD involve (1) deficits in theory of mind, (2) weak central coherence and (3) weak executive function. Theory of Mind is the ability to attribute mental states (beliefs, knowledge and intention) to oneself and others. This allows one to make sense of and to predict intention and behaviours of others. As a result, children with ASD have problems taking other's perspectives, maintaining conversation, and understanding what are appropriate things to say in different social situations. Central coherence is the ability to integrate information received with the context, and to neglect irrelevant or unimportant details. Poor executive function is not specific to ASD. Persons with weak executive function tend to have difficulties in organising, planning, and inhibiting inappropriate responses. Self awareness and self-regulation are often weak in children with ASD. As a result of these deficits, different problems emerge as the child grows. At school he/she may face difficulties in language subjects which require communication skills, in liberal studies which require the taking of different perspectives, in organising projects which require executive skills, and in working with teams. Difficulties in social interaction will lead to problems with peers and authorities at school, and with colleagues and supervisors in future employment.

The recently launched DSM-5 provides revised criteria to document profiles of individuals with ASD. Diagnostic criteria were changed from a triad to a dyad consisting of persistent deficits in social communication and social interaction across multiple contexts, together with restricted, repetitive patterns of behaviour, interests, or activities. Specifiers are given for severity, presence of accompanying intellectual or language impairment, association with known medical or genetic condition or environment factor, and additional neurodevelopmental mental or behavioural conditions. Participation and functioning will differ accordingly with different profiles.

Symposium: A Child with Eczema and Food Allergy

Moderator: TF Leung

Professor, Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

Case Scenario: BLC Lo

Consultant, Accident and Emergency Department, North District Hospital, Hong Kong

Mary is a 10-year-old girl who suffered from moderate-to-severe eczema despite the use of emollient and topical mometasone furoate. Her parents brought her to see a general practitioner, who collected blood for some form of "allergy tests". She was then told that the results for cow's milk, egg and "nuts" were positive, thus making the diagnosis of multiple food allergies. Her parents recalled

that she had repeated episodes of mild hives and lip swelling after egg ingestion.

On one day, Mary developed generalised hives, swollen lips and shortness of breath 10 minutes after ingestion of a snack biscuit during lunch. Mary was noted to be increasingly "drowsy". That snack was found to contain peanut butter. Mary was then taken by ambulancemen to the Accident and Emergency Department.

Her vitals were as follows: BP 75/46 mmHg, pulse 135/min, SaO_2 91%.

How should we manage this episode of anaphylaxis?

Pre-Hospital Treatment for Anaphylaxis

TF **Leung**

Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

Definition of Anaphylaxis

Worldwide, anaphylaxis definitions in common use are "a serious, life-threatening generalised or systemic hypersensitivity" and "a serious allergic reaction that is rapid in onset and might cause death".

The common triggers of anaphylaxis are drug, insect sting and food. The time span from onset to death ranges from minutes to 1-2 hours with IV drug the fastest (median few minutes), oral drug (10-20 minutes) follows by insect sting (10-20 minutes) and then food (20-40 minutes).

Thus a prompt recognition followed by appropriate pre-hospital treatment is vital for good outcome. The Co-ordinating Committee (COC) clinical guideline in management of anaphylaxis in children is in the final drafting and reviewing phase. It has adopted an internationally widely accepted operational diagnosis:

Anaphylaxis is highly likely when ANY one of the following three criteria is fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (e.g. generalised hives, pruritus or flushing, swollen lips-tongue-uvula) and at least one of the following:
   a. Respiratory compromise (e.g. dyspnoea, bronchospasm, stridor, hypoxia)
   b. Cardiovascular compromise (e.g. hypotension, collapse)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes or several hours)
   a. Involvement of the skin or mucosal tissue (e.g. generalised hives, itch, flushing, swelling)
   b. Respiratory compromise (e.g. dyspnoea, bronchospasm, stridor, hypoxia)
   c. Cardiovascular compromise (e.g. hypotension, collapse)
   d. Persistent gastrointestinal symptoms (e.g. abdominal pain and vomiting)
3. Hypotension after exposure to known allergen for that patient (minutes or several hours):
   Hypotension for children is defined as systolic blood pressure <70 mmHg from 1 month to 1 year, <(70 mmHg+ [2xage]) from 1 to 10 years old, and <90 mmHg from 11 to <18 years old

The Drug Choice

There has been debate on the initial drug choice and route over the last 40 years, the current international consensus is that adrenaline is the medication of choice for anaphylactic episodes. Intramuscular adrenaline should serve as the first choice of anaphylaxis. Other medications such as antihistamines, inhaled asthma medications, or steroids that may be given by physicians in treating anaphylaxis should not be regarded as first-line medications. Prompt injection of adrenaline has been associated with better outcome. Generally, adrenaline is considered safe in children. The contraindications are patients with cardiovascular problem such as congestive heart failure, hypertension, stroke and arrhythmia (life-threatening) or on defibrillator.

The pharmacologic beneficial effects are summarised as follows:

Through alpha-1 adrenergic receptors: vasoconstriction, increased peripheral vascular resistance (most organs), increased blood pressure and relief of hypotension and shock; decreased mucosal oedema and relief of upper airway obstruction and angioedema/hives. Through alpha-2 adrenergic receptor: decreased insulin release. Through beta-1 adrenergic receptors: increased heart rate and force of cardiac contractions. Through beta-2 adrenergic receptors: bronchodilation, vasodilation, decreased release of mediators (histamine, tryptase and others).

Case Scenario (continued): BLC Lo

Consultant, Accident and Emergency Department, North District Hospital, Hong Kong

Mary was stable after intramuscular adrenaline and chlorpheniramine in AED.

She was then referred to the allergy clinic for detailed evaluation.

Her parents requested "allergy tests" for Mary.

What allergy test(s) should we perform, and how to interpret the results?

Allergy Tests

AM **Li**

Professor, Department of Paediatrics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong

Diagnosis of Food Allergy

1. Acute urticaria / angioedema (IgE-mediated)
   - immediate reactions (<2 hours)
   - may present with upper airway obstruction or anaphylactic shock
   - diagnosis can usually be confirmed by typical history plus the presence of food-specific IgE (by skin prick tests or RAST)
   - needs supervised oral food challenges for diagnosis in doubtful cases
2. Eczematous (IgE/cell-mediated)
   - immediate (<2 hours) or delayed (up to 72 hours)
   - food-specific IgE and atopy patch test may not be accurate
   - needs to consider food elimination and re-challenge to confirm the diagnosis if history is suspicious

The conventional cut-offs for positive allergy results are: skin prick tests - 3 mm (induration) or serum specific IgE by RAST - 0.35 kU/l respectively. But these would tend to give high sensitivity but low specificity. Hence they have good negative predictive value but poor positive predictive value (50%). In contemporary allergy practice, allergists now adopt a higher cut-off for positive diagnosis. For example in peanut test, a > or = 8 mm skin prick test or a > or = 15 Ku/L peanut specific IgE often constitutes a positive diagnosis without resorting to formal food challenge. Some validation studies were performed by investigating the correlation of various cut-off values and the food challenge outcomes. There is so-called 90% or 95% decision point literally meaning above the cut-off the chance of clinical allergy reaches over 90% or 95%. Some validation studies recognised that such cut-off may be age-dependent and food specific. Usually by adopting a standard diagnostic algorithm the need of tedious and expertise-dependent food challenge could be reduced at least by one third to half. Another way to improve the clinical utility of allergy test is to use the concept of "likelihood ratio" (LR) which can further offer the post-test probability for better ascertainment. Likelihood of a given specific IgE result in subjects with positive challenges versus the likelihood of the same specific IgE result in subjects with negative challenges gives rise to the LR. LR can be applied in the given clinical settings provided the pre-test probability is known.

Case Scenario (continued): BLC Lo

Consultant, Accident and Emergency Department, North District Hospital, Hong Kong

Her parents noticed Mary to snore a lot over the past 2 years. She was sleepy and tired most of the time. Mary frequently sneezed in early morning, and rubbed her nose and eyes very often.

What is the cause of her snoring? How should we investigate to find out the cause of her snoring? Is there any long-term consequence?

Snoring – from Primary Snoring to OSAS

K **Kwong**

Consultant, Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital, Hong Kong

There is a continuum of sleep-disordered breathing consisting of primary snoring (PS), upper airway resistance syndrome (UARS), obstructive hypoventilation (OH) and obstructive sleep apnoea syndrome (OSAS); with PS the mildest whilst OSAS is at the severe end. OSAS severity is categorised by apnoea hypopnea Index (AHI). By polysomnography (PSG), a type of sleep study with multi-parametric test as a diagnostic tool in sleep medicine, PS is defined increased respiratory effort without arousals whist OSAS is of partial or complete obstruction resulting in hypoxia, hypercapnia, and/or respiratory arousals.

Primary snoring is prevalent (~5-10%) in Hong Kong school children. It seems snoring is not as benign as one would have thought of. Accumulative evidence has implicated primary snoring is associated with

cardiovascular (higher diastolic blood pressure and endothelial dysfunction) and neurocognitive sequelae (lower global / verbal IQ, poor attention and memory deficit; poor school performance; higher incidence of emotional and behavioural problems) by international and local researchers.

With longitudinal follow up, as high as 1 in 5 children may progress from PS to OSAS in 5 years' time. Tackling allergic rhinitis (AR) and weight control are important in the management of PS.

Case Scenario (continued): BLC Lo

Consultant, Accident and Emergency Department, North District Hospital, Hong Kong

During her follow-up, parents reported that class teachers of Mary complained that she was "inattentive" in classes. She also told you that she found it difficult to concentrate at classes, and she did poorly at school.

Does Mary suffer from attention deficit hyperactivity disorder (ADHD)? Is there any relationship between food allergy and ADHD?

Eczema, Food Allergy and ADHD

MHK **Ho**

Consultant, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, Hong Kong

Reviewing the current literature reports, several studies suggested a positive association between eczema and ADHD. Also many studies showed weak to moderately strong association between asthma and ADHD, partly confounded by concurrent or previous eczema. Allergic rhinitis did not appear to be related to ADHD.

In 3 studies analyzing relationship between eczema and ADHD adjusted for concurrent atopic airway disease and for a broad set of environmental and behavioural confounders, relationship between eczema and ADHD persisted, whereas atopic airway disease and ADHD disappeared in the multivariate model. None of the studies considered eczema as a confounding factor. Only one epidemiologic study considered sleeping problems as a potential modifier or confounder in the relationship between atopic disease and ADHD.

One of the plausible explanations is that atopic eczema is one of the leading causes of sleep loss in childhood. Sleep deprivation leads to tiredness, mood changes and impaired psychosocial functioning and may resemble and /or exacerbate ADHD. Another explanation is that through neuro-immune mechanism resulting in activation of prefrontal cortex. It has been shown that high psychological stress could lead to neuroendocrine dysfunction and elevated dopamine release.

Dietary restriction of synthetic food colors may improve ADHD symptoms in children and adolescents (level 2, mid-level evidence) based on systematic review without assessment of trial quality. Oligoantigenic (hypoallergenic/ elimination) diet employing a few food items e.g. lamb, potato, carrots and pears provided mixed opinions of efficacy.

Skin tests to foods are unreliable, elimination diets are required to test for specific food intolerances. The diagnosis of food sensitivity is complex, time-consuming and too burdensome for patient, family and physician. Some expert opinion, in selected patients with diligent parents, a short 2-3 week period of restricted elimination diet is justified. In patients benefited by the diet, restricted foods are introduced each week, one at a time, until the offending item or items are identified. Improvement in behaviour may be delayed for 10 days to 2 weeks. Food preferred and consumed most is often the offending item.

But most think such oligoantigenic, elimination, additive free diets are complicated, disruptive to the household and often impractical, except for selected patients.

Indications for diet therapy may include medication failure or adverse reaction and strong parent or patient preference.

Overall, there is insufficient evidence to recommend routine dietary interventions for ADHD in children.

Case Scenario (continued): BLC Lo

Consultant, Accident and Emergency Department, North District Hospital, Hong Kong

The family brought Mary to a TCM practitioner for treatment of moderate-to-severe eczema. Mary was given a long list of foods (milk, egg, peanut, nuts, beef, chicken…) that she needs to avoid.

Her parents seek your opinion during clinic visit on how important is this food restriction in eczema management?

Eczema and Food Avoidance

KLE **Hon**

Professor, Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

Food allergy may be the trigger in approximately 1/3 of children with moderate-to-severe eczema and up to 2/3 of infants <2 years old with severe or refractory eczema. Only 10% of infants with mild eczema has food allergy triggered eczema.

Appropriate early intervention can impact significantly on eczema severity, infant growth and quality of life. Positive diagnosis empowers the patient and his families. Negative test lifts unnecessary restriction.

According to US and UK national guidelines, food testing for milk, egg, soy, wheat and peanut should be considered in children under 5 years of age who have

- Moderate to severe atopic dermatitis (AD), and
- AD in spite of optimised management and topical therapy, or
- Reliable history of an immediate reaction after ingestion of a specific food – particularly associated with GI dysmotility and failure to thrive

In infants younger than 6 months, a 6-8 week trial of an extensive hydrolysed formula (EHF) or amino-acid based formula (AAF) is worth to attempt as of both diagnostic and therapeutic implications.

On the other hand, in the local community, it appears that an overwhelming reality is that most of parents are doing unnecessarily over food restriction and food avoidance leading to poor health consequence such as failure to thrive, food faddism and malnutrition. Many parents cannot comprehend the chronic relapsing nature of eczema and demand a rapid cure. Such attitude leads to behaviours not only incompliance to standard care but easy acceptance to alternative practices without sound scientific bases.

A holistic comprehensive care of eczema including education on nature of the disease, assessment the relevancy of suspected food or other triggers, proper skin care and appropriate use of anti-inflammatory treatments remains the cornerstone. Food avoidance is considered a medical therapy and should never be applied blindly without obtaining a proper diagnosis of food allergy.

Abstracts

Aetiological Bases and Clinical Characterisitics of 46,XY Disorders of Sex Development in Hong Kong Chinese

WM **But**,[1*] AOK **Chan**,[2*] CY **Lee**,[3] YY **Lam**,[4] KL **Ng**,[5] A **Lam**,[5] PY **Loung**,[6] MY **Wong**,[1] KT **Chan**,[4] CW **Cheng**,[2] CC **Shek**,[2] WS **Wong**,[2] KF **Wong**,[2] WY **Tse**[1]

[1]Department of Paediatrics, Queen Elizabeth Hospital; [2]Department of Pathology, Queen Elizabeth Hospital; [3]Department of Paediatrics, Caritas Medical Centre; [4]Department of Paediatrics, Kwong Wah Hospital; [5]Department of Paediatrics, United Christian Hospital; [6]Department of Paediatrics, Princess Margaret Hospital, Hong Kong

[*]WM But and Angel OK Chan have equal contribution in this study

Background and aims: Disorders of sex development (DSD) are defined as congenital conditions in which development of chromosomal, gonadal or anatomical sex is atypical. The objectives of this prospective study are to characterise the clinical features, to establish the genetic bases and to determine the relative prevalence of 46,XY DSD in Hong Kong Chinese.

Methods: Patients with 46,XY DSD presented to five paediatric departments in Hong Kong from July 2009 till June 2011 were recruited. They were assessed by paediatric endocrinologists. Mutational analyses of the candidate genes by polymerase chain reaction (PCR) and direct DNA sequencing were conducted based on the hormonal results. For the remaining patients, PCR and DNA sequencing of *AR* and *NR5A1* genes and then multiplex ligation-dependent probe amplification (MLPA) of the genes related to 46,XY DSD were performed.

Results: Sixty-four patients (53 male and 11 female) were recruited. Their age at presentation ranged from birth to 17 years. Five (8%) were born prematurely and nine (14%) had low birth weight. Eight had other major structural abnormalities. Fifty-eight patients (91%) presented with ambiguous external genitalia including 18 with isolated micropenis and nine with severe hypospadias. Two presented with inguinal hernia, one each with delayed puberty and primary amenorrhoea. One was born with a complete normal female phenotype but aminocentesis revealed a 46,XY karyotype. Twenty-two patients (34%) had the diagnosis confirmed genetically. Among them, 11 patients had 5-alpha reductase 2 deficiency and seven had androgen insensitivity syndrome (AIS). There was one patient with each of the following aetiologies: NR5A1-related sex reversal, Frasier syndrome, cholesterol side-chain cleavage enzyme deficiency and persistent Mullerian duct syndrome. A total of 9 novel mutations were identified.

The longest follow up period was 27 years. Five patients exhibited a "tom-boy-like" behaviour during childhood. Two males requested exogenous testosterone to augment penile growth after puberty. None of the patients requested change of gender so far.

Conclusions: 46,XY DSD is a heterogeneous group with diverse aetiologies. Although 5-alpha reductase 2 deficiency is believed to be rare, it is not uncommon in Hong Kong Chinese and indeed the predominant cause confirmed by genetic studies in our cohort.

Endothelial Function in Children with Obstructive Sleep Apnoea and the Effects of Adenotonsillectomy

KCC Chan, CT Au, P Chook, HS Lam, AM Li

Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

Background and Aims: The association between childhood obstructive sleep apnoea (OSA) and endothelial function as measured by flow-mediated dilation (FMD) and the response to OSA treatment are uncertain. This study aimed to examine FMD in children with OSA when compared to non-snoring controls and its response to treatment.

Methods: This was a case-control study followed by an interventional study for the cases. Children aged 6-18 years with habitual snoring as reported by parents and polysomnography (PSG) confirmed obstructive apnoea hypopnoea index (OAHI) of >1/h were recruited as cases. Participants of our previous community growth survey were invited to be controls. All controls had no habitual snoring as reported by their parents and were PSG-confirmed normal (OAHI <1/h). Cases and controls were age, gender and body mass index-matched. All subjects underwent overnight PSG and FMD measurement on the same day. Adenotonsillectomy (AT) was offered to OSA cases with adenotonsillar hypertrophy. For those who refused surgery or had no adenotonsillar hypertrophy, nasal corticosteroids or continuous positive airway pressure (CPAP) therapy were offered. All cases were asked to have repeated assessment on average 6 months later. Subjects who underwent AT were compared to those who did not.

Results: A total of 63 case-control pairs were recruited. In each group, 41 (65.1%) were boys and 30 (47.6%) were overweight. The OSA group had a significantly higher OAHI [5.3/h (2.6-11.7) vs 0.2/h (0-0.5)] and lower FMD (7.9%±1.3 vs 8.3%±0.8) than the control group. For the intervention phase, 32 out of 63 OSA cases underwent AT, 10 received nasal corticosteroid and the remaining refused any treatment. When compared to cases who did not undergo AT, the surgical cases had significantly higher OAHI before treatment [10.5/h (6.0-15.4) vs 3.3/h (1.8-4.1)]. Significant reduction in OAHI was observed only in the surgical group [-8.8/h (-13.7 to -4.7) vs -0.1/h (-1.2 to 2.3)], accompanied by a significant increase in FMD [+0.6% (0.4 to 1.4) vs 0% (-0.3 to 0.2)], which could not be observed in the non-surgical group.

Conclusion: Children with OSA had reduced FMD that was reversible with treatment.

The Effect of a Structuralised Aerobic Exercise Training Program on Social Communication, Attention and Motor of Children with Autism Spectrum Disorfer (ASD)

DFY Chan,[1] CCW Yu,[1] KHK Lam,[2] HK So,[1] AM Li[1]

[1]Department of Paediatrics, The Chinese University of Hong Kong; [2]Hong Kong Sports Institute, Hong Kong

Background: Children with Autism Spectrum Disorder (ASD) are characterised by a triad of symptoms, namely lack of social reciprocal responsiveness, language and communication deficit and rigid repetitive behaviour. Children with ASD typically present with decreased physical activity levels and tolerance. Social and behavioural deficits among children with ASD that make participation with peers difficult, and social constraints could also be the factors affecting physical activity in children with ASD.

Aerobic exercise training which involves movements of large muscle groups at low-to-moderate intensity levels for a sustained period of time, has been used as one of the intervention strategies for promoting motor skills, social behaviours and decrease in stereotypic behaviour in children with ASD, however, scientific evidences on the effectiveness of exercise intervention for autistic children are very limited, which may largely be attributed to the difficulty in program design and the implementation of the program for this group of children. Moreover, most of the studies were based on case reports with small number of subjects involved.

Aim: The aims of this study was to evaluate the effectiveness of a structuralised aerobic exercise training program on improvement of (1) social and communication skills; (2) attention and behaviour and (3) motor function.

Method: Twenty-eight children aged of 4 to 6 years old with diagnosis of ASD were recruited from two of Special

Child Care Centers of Heep Hong Society. They were accompanied with one caretaker to attend two hours of weekly aerobic exercise training program for total 16 or 32 weeks from January to August of 2013. Clinical Global Impression scale on Improvement (CGI-I) reported by parents or caretaker was used for evaluating the global functioning improvement in 3 aspects, namely social and communication skills, attention and behaviour and motor functioning.

Results: Twenty-eight of children with mean age of 5.1 (±0.7) years old were recruited. Thirteen and fifteen children were recruited to receive 16 and 32 weeks training respectively. Twelve children (41%, five and seven from 16- and 32- weeks group respectively) were able to achieve an attendant rate of over 70%. There was no statistic difference of age for those dropped out children (p=0.7). The most common reason for dropping out from training was out of town during the last 6 weeks, by which that period was overlapped with school summer holidays.

Most of CGI-I scores of the 3 domains were comparative in both 16 - and 32 weeks trained group except the improvement of "attention to finish a task" was significantly better in 32 weeks training group ($p<0.05$) (Table 1). For social and communication aspects, up to 83% of parents scored their child had improved in social, communication skills and language skills and 25% of them had "Much improved" (Figure 1). For attention and behaviour aspects, 83% of parents scored their child had improvement. For the items of "follow instruction", there were 58% of them reached "much improved" or "very much improved" level (Figure 2). All the parents scored their child improved in motor skill aspects including coordination and muscle strength (Figure 3). Half of them showed significant improvement in coordination. Overall, 92% of parents scored their child had improvement after completion of the training program (Figure 4).

Conclusion: A structuralised aerobic exercise training program was shown to improve parents' scoring in social communication, attention, behavioural and motor skills of their child with Autism Spectrum Disorder. Besides in spending substantial amount of resources in behavioural training, sufficient amount of exercise for this group of children is also valuable. Structuralised aerobic exercise program in young children with ASD is feasible but the timing of program would be optimal to avoid overlapping with school long holidays.

Acknowledgements: Heep Hong Society and all families we are serving.

Table 1 Comparisons of CGI between children in the 32-week training and the 16-week training group

	Training	N	Mean	Standard deviation	P value
Social and communication					
Social skill	32 weeks	6	3.00	0.894	0.713
	16 weeks	5	3.20	0.837	
Communication	32 weeks	6	3.00	0.632	1.000
	16 weeks	5	3.00	1.000	
Language understanding	32 weeks	7	3.00	0.577	0.633
	16 weeks	5	3.20	0.837	
Language expression	32 weeks	7	3.00	0.577	0.633
	16 weeks	5	3.20	0.837	
Attention and behaviour					
Attention switching	32 weeks	7	3.00	0.577	1.000
	16 weeks	5	3.00	0.707	
Follow instruction	32 weeks	7	2.43	0.787	0.356
	16 weeks	5	2.00	0.707	
Patience to finish a task	32 weeks	7	2.71	0.756	0.857
	16 weeks	5	2.80	0.837	
Attention to finish a task	32 weeks	7	2.57	0.535	**0.026***
	16 weeks	5	3.40	0.548	
Motor					
Coordination	32 weeks	7	2.14	0.690	0.093
	16 weeks	5	2.80	0.447	
Muscle strength	32 weeks	7	2.43	0.787	0.367
	16 weeks	5	2.80	0.447	
Overall					
Overall change	32 weeks	7	2.71	0.488	0.424
	16 weeks	5	3.00	0.707	

*$p<0.05$

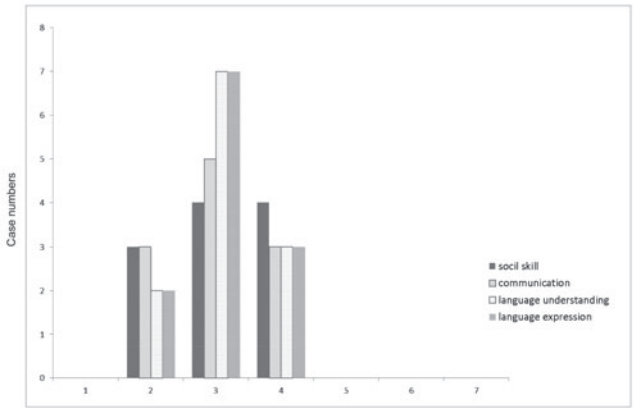

Figure 1 Social and communication domain

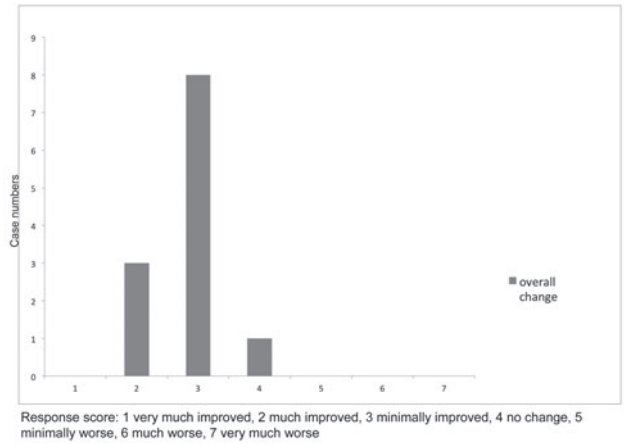

Figure 4 Ovall impression

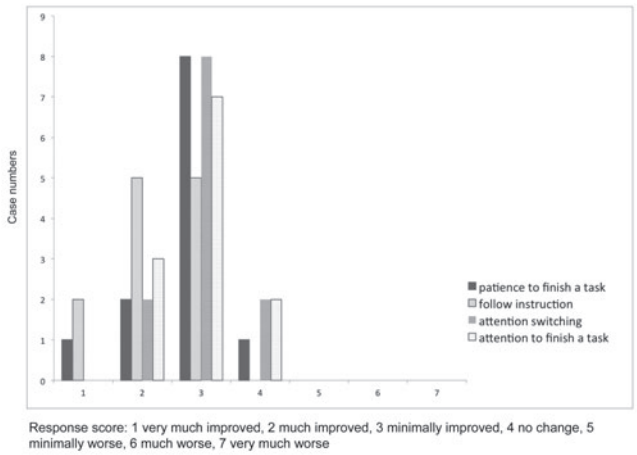

Figure 2 Attention and behaviour domain

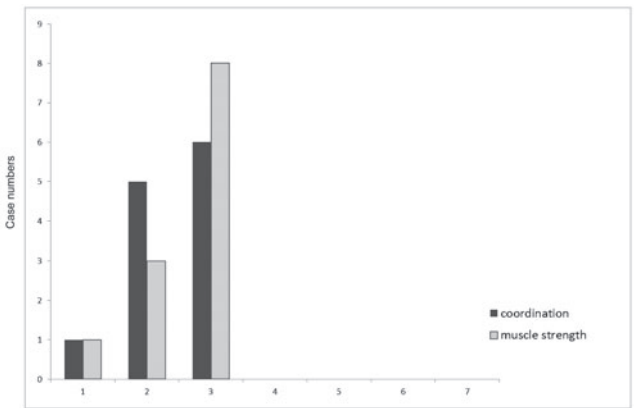

Figure 3 Motor function domain

Low Selenium Level is Associated with Poor Neurocognitive Outcomes in 6-10 Years Old Children in Hong Kong

PHY CHAN,[1] HS LAM,[1] KM KWOK,[1] CLS CHAU,[1] MHM CHAN,[2] AM LI[1]

[1]Department of Paediatrics and [2]Department of Chemical Pathology, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong

Background: Selenium (Se) is a trace element that is vital to our health. Although the mechanism is unclear, studies have been shown that low selenium levels blood concentrations are associated with poor memory in adults and increased risk of Alzheimer's disease in the elderly. Very few studies have focused on the associations between body selenium levels and childhood neurodevelopment. The aims of our study were to assess the selenium levels of Hong Kong children and evaluate the association between body selenium levels and neurocognitive development.

Methods: Subjects were randomly recruited from our previous birth cohort. During the assessment session, blood was taken for serum selenium level measurement. In order to test for a broad range of neurocognitive abilities, subjects were assessed by a panel of neurocognitive tests, including Hong Kong Wechsler Intelligence Scale for Children (HK-WISC), Tests of Everyday Attention for Children (TEACH), Boston Naming Test, and Grooved Pegboard Test.

Results: 421 subjects were recruited (mean age 8.23 years, SD 0.68; 53.4% males). The median serum selenium level was 91.34 ng/mL (IQR 79.53, 99.21). Fifty-four subjects (9.7%) had serum Se levels lower than 70 ng/mL and were considered as selenium deficient. Pearson's correlation showed positive correlation between serum Se

with better performance in Boston naming test, Sky search attention score and map mission in TEA-Ch and Grooved Pegboard test. Poorer performance in Sky search attention score (p=0.003), map mission (p=0.017) and Boston naming test (correct with cue: p=0.006; correct without cue: p<0.001) were found in selenium deficient groups.

Conclusion: A significant proportion of our population can be considered selenium deficient. Our study demonstrated significant positive associations between selenium and a wide range of neurocognitve outcomes in the children of Hong Kong. Selenium deficiency in Hong Kong is associated with poorer neurocognitive outcomes and public health measures to reduce its prevalence may be required. Further studies to investigate the interactions between methylmercury exposure and selenium levels on neurocognitive outcomes are warranted.

Study of Patients with Dystrophinopathy in Hong Kong

SHS Chan,[1] IFM Lo,[2] WWS Cherk,[3] WWS Cheng,[4] LWE Fung,[5] WL Yeung,[6] M Chu,[7] WC Lee,[7] LK Kwong,[7] SNS Wong,[8] CKL Ma,[8] SM Tai,[9] SFG Ng,[10] SP Wu,[11] CNV Wong[1]

[1]Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong; [2]Clinical Genetic Service, Department of Health; [3]Department of Paediatrics and Adolescent Medicine, Kwong Wah Hospital; [4]Department of Paediatrics and Adolescent Medicine, Caritas Medical Centre; [5]Department of Paediatrics and Adolescent Medicine, Prince of Wales Hospital, The Chinese University of Hong Kong; [6]Department of Paediatrics and Adolescent Medicine, Alice Ho Mei Ling Nethesole Hospital; [7]Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital; [8]Department of Paediatrics and Adolescent Medicine, United Christian Hospital; [9]Department of Paediatrics and Adolescent Medicine, Pamela Youde Nethesole Eastern Hospital; [10]Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital; [11]Department of Paediatrics and Adolescent Medicine, Queen Elizabeth Hospital, Hong Kong

Background: This is a first study in Hong Kong on Chinese patients with dystrophinopathy on their prevalence, genetic mutation, motor performance, and the interventions they received.

Method: This study is participated by ten paediatrics departments in different hospitals in Hong Kong. Clinical data was systemically collected from June 2011 to June 2012. Those patients diagnosed dystrophinopathy and were actively followed-up between May 2006 to April 2010 were recruited. Dystrophinopathy, including Duchenne Muscular Dystrophy (DMD) and Becker Muscular Dystrophy (BMD), was confirmed by genetic study or muscle biopsy. Institutional review board approval was obtained from all participating hospitals.

Result: 88 individuals with dystrophinopathy were included in this study. The overall prevalence of dystrophinopathy for 2010, is 1.03 per 10,000 males aged 0-24 years old. Eighty-two percent have DMD and 18% have BMD. Seventy-five patients had undergone mutation analysis and most cases are caused by large exon deletion (49%) , followed by small rearrangement or point mutation (37%), and only a small percentage are due to large exon duplication (9%), with 4% of patients did not have any mutation identified. For the intervention, 23% of children were on steroid and the mean age of starting steroid was 8 years old. The mean age of loss of ambulation was 10.5 years old. For those older than 13 years of age, 30% have cardiomyopathy and half of them were on treatment, 19% required non-invasive ventilation, 15% had scoliosis surgery and 5% had gastrostomy.

Conclusion: This first territory wide study for individuals with dystrophinopathy in Hong Kong confirms a similar prevalence of such condition with the western countries, but we have a much higher percentage of patients with point mutation of the DMD gene. The findings of infrequent steroid use with a late starting age and the interventions they received allow us to compare our current approach in Hong Kong with that of other developed countries.

Acknowledgement: We would like to thank the Department Head and Chief of Service of the participating Paediatrics Departments of the ten hospitals, for their support on this study.

Phenotype Variations in Bartter and Gitelman Syndrome

WKY Chan,[1] KC Tse,[2] SN Wong,[3] WM Lai,[2] S Chim,[4] KP Lee,[5] L Leung[6]

[1]Department of Paediatrics, Queen Elizabeth Hospital; [2]Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital; [3]Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital; [4]Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital; [5]Department of Paediatrics and Adolescent Medicine, Alice Ho Miu Ling Nethersole Hospital; [6]Department of Paediatrics and Adolescent Medicine, Kwong Wah Hospital, Hong Kong

Objective: To describe and identify clinical features that help to differentiate Bartter (BS) and Gitelman syndrome (GS) clinically.

Method: We retrospectively reviewed patients diagnosed

BS or GS in 6 local hospitals in Hong Kong. The clinical features, biochemical and ultrasound findings at presentation are compared.

Results: Thirty patients were reported. Male to female ratio was 15:15. There were 26 Chinese and 4 Pakistani. Eleven patients were clinically diagnosed as BS and 19 patients as GS. The duration of follow up was 5.7±5.4 years. 23% patients presented as growth delay and 37% were detected incidentally. Five patients (11%) presented at neonatal period and all confirmed as Bartter syndrome. 13% patients were detected during family screening. Fourteen patients (47%) had genetic confirmation. One patient had SLC12A1 mutation (BS type I), 4 patients had KCNJ1 mutation (BS type II), 2 patients had CLCNKB mutation (BS type III) and one patient had BSND mutation (BS type IV). Six patients had SLC12A3 mutation and confirmed GS. Comparing all those confirmed BS and GS patients, there was no significant difference in serum sodium (p=0.8), serum potassium (p=0.09), serum magnesium (p=0.11), serum urea (p=0.03) and serum creatinine (p=0.39) at presentation. However, the serum potassium at presentation of GS was low at 2.4±0.29 mmol/L and serum magnesium was 0.77±0.17 mmol/L as compared with potassium of 3.7±1.8 mmol/L and magnesium of 0.98±0.25 mmol/L in BS. The urine calcium excretion was significantly low in GS (p=0.01). None of the GS and BS type III patients had nephrocalcinosis. All patients with BS type I, II and IV patients had nephrocalcinosis. Two clinically diagnosed BS type III patients were confirmed genetically to be GS. One clinically diagnosed GS was genetically confirmed to be BS type III. Growth Failure were described in 3 GS and in 5 BS patients although it was not statistically significant (p=0.59). Serum renin was extremely high in neonatal BS but not in GS. Seventy-two percent BS patients had raised serum aldosterone but 83% patient with GS had normal aldosterone at presentation (p=0.1)

Conclusion: Nephrocalcinosis can differentiate most BS from GS. Phenotypically, BS type III may be indistinguishable from childhood onset GS. Patients with GS can present as growth failure and very low serum potassium.

L1 Protects Endothelial Cells from Iron Induced Oxidative Stress and Mitochondrial Injury

S Chan, MP Chen, YF Cheung, GCF Chan
Department of Paediatrics & Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

Introduction: Iron-overload induced cardiac disease is an important cause of morbidity and mortality in patients with β-thalassaemia major. Arterial stiffening and endothelial dysfunction is another major concern in this group of patients (Cheung et al, Circulation 2002). Excessive iron load is hence associated with endothelial dysfunction, while L1, an iron chelator with antioxidant effect, has been shown to improve endothelial function in these patients clinically. Therefore in this study, we investigated how excessive iron induced endothelial damage. We further explored the protective effect of iron chelator L1 on iron-overloaded endothelial cells.

Methods and results: Using human umbilical vein endothelial cells (HUVECs), we showed that iron-overload induced endothelial microparticles (MPs) generation in a dose dependent manner. Iron increased reactive oxygen species (ROS) production (75-300 μM) (n=3) and increased calcium influx into mitochondria $[Ca^{2+}]_m$ (300 μM, 24 hrs) in HUVECs as evidenced by increased rhod-2 AM fluorescent intensity using flow cytometry. These led to loss of mitochondrial membrane potential ($\Delta\Psi_m$) (300 μM, 24 hrs) as shown by JC-1 assay (n=3). Apoptotic cells were found to be significantly increased under iron treatment (300 μM, 48 hrs) by annexin V/PI assay (n=3). The expression of caspase dependent apoptotic marker active caspase-3 significantly increased in iron treated cells (n=4). Co-incubation with L1 (10 μM) showed an inhibitory effect on iron-induced generation of EMPs by HUVECs (n=3). L1 (100 μM) decreased iron-induced calcium influx into mitochondria and L1 (10 μM) delayed $\Delta\Psi_m$ derangement of HUVECs (n=3). Furthermore, L1 (10 μM) protected endothelial cells from iron-induced ROS generation and apoptosis. ROS determination, dot-plot analysis of annexin V/PI staining and active caspase-3 assay demonstrated that L1 significantly reduced ROS generation, apoptotic cells and active caspase-3 expression.

Conclusions: Our findings suggest that excessive iron induces endothelial cells injury via increased oxidative stress, increased $[Ca^{2+}]_m$, loss of mitochondrial membrane potential and apoptosis. L1 could protect endothelial cells from the above phenomenon and may have therapeutic potential for iron-induced endothelial damage.

Glycogen Storage Disease Type I in Hong Kong: Diagnosis, Clinical Course and Outcomes

J Chow,[1] WM But,[1] G Poon,[2] A Kwok,[2] J Hui,[3] J Chong,[3] SY Lee,[4] KH Poon,[5] LM Wong[5]

[1]Department of Paediatrics, Queen Elizabeth Hospital; [2]Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital; [3]Department of Paediatrics, Prince of Wales Hospital; [4]Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital; [5]Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital, Hong Kong

Glycogen storage disease (GSD) type 1 is a rare metabolic disease affecting glucose homeostasis. This is the first case series on the clinical course and outcomes of glycogen storage disease type I patients in Hong Kong. This collaborative study based on retrospective data collection describes the clinical course and outcomes of all patients managed in the past 20 years in Hong Kong.

Twenty-five patients have been identified from the Hong Kong inborn errors of metabolism registry for the Hospital Authority paediatric patients. All patients were Chinese, and were managed in five regional hospitals of the Hospital Authority. This includes seventeen GSD type 1a and eight GSD type 1b patients, born between 1979 and 2010. GSD 1a is the most prevalent subtype, representing 70% of the cases. Data on their presenting signs and symptoms, dietary management, growth and puberty, treatment, hospitalisations, laboratory results, long term complications and causes of death are presented in this study.

All patients presented with abdominal distension at a median age of 11 for GSD 1a and 19 months for GSD 1b. Growth failure and metabolic derangement are not uncommon despite treatment. Liver and renal diseases are the main long term complications in our patientsas described in other studies. Diabetes mellitus associated with liver disease is rarely reported, but developed in two of our patients. Malignant transformation from adenoma to carcinoma was reported to be low but occurred in one of our patients who had chronic hepatitis B infection. Four patients (16%), age range 7-24 years, had died from metabolic decompensation with severe lactic acidosis and renal failure.

Conclusions: Glycogen storage disease type 1 is a rare disease and a significant proportion of our patients with had moderate to severe morbidities and mortality. Glycogen storage disease type 1 remains a challenge to treatment in Hong Kong despite advances in diagnosis and understanding of the disease.

Identifying Genetic Mutations in Patients with Rasopathies Using a Next Generation Sequencing Diagnostic Pipeline in Hong Kong

IFM Lo,[1] GKC Leung,[2] HM Luk,[1] HMV Tang,[3] WW Gao,[3] WL Wong,[4] LYF Tang,[5] YWY Chu,[4] ASY Kan,[2,6] MHY Tang,[5] STS Lam,[1] WL Yang,[2] ACH Ma,[7] DY Jin,[3] KYK Chan,[2,5] BHY Chung[2,4]

[1]Clinical Genetic Service, Department of Health; [2]Department of Obstetrics & Gynaecology, Li Ka Shing Faculty of Medicine, The University of Hong Kong; [3]Department of Biochemistry, The University of Hong Kong; [4]Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, Li Ka Shing Faculty of Medicine, The University of Hong Kong; [5]Prenatal Diagnostic and Counseling Department, Tsan Yuk Hospital; [6]Department of Obstetrics & Gynaecology, Queen Mary Hospital; [7]Department of Medicine, The University of Hong Kong, Hong Kong

Background and aims: RASopathies are a group of developmental syndromes, namely Noonan, Costello, Cardio-facio-cutaneous, Legius, and LEOPARD syndromes, collectively affecting 1 in 2000 livebirths. They were caused by mutations in genes involved in the RAS/MAPK signaling pathway. Since they are characterised by clinical overlap and genetic heterogeneity, diagnoses are often challenging. We aim to develop a NGS-based strategy for molecular diagnosis of RASopathies.

Method: Targeted NGS of 13 genes (*A2ML1, BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NRAS, PTPN11, RAF1, SHOC2, SOS1,* and *SPRED1)* in the RAS/MAPK pathway, where the targeted enrichment panel covered 98% of the gene coding regions, was performed on 57 RASopathies which were previously tested negative for mutation in *PTPN11* and *HRAS.* Positive controls were run in parallel.

Results: The average read-depth in the regions of interest was >500X, with 99% of target bases reaching minimal coverage of 30X. Eighteen known pathogenic mutations (*SOS1*, n=6; *RAF1*, n=2; *KRAS*, n=3; *BRAF*, n=2; *SHOC2*, n=2; or *MAP2K1*, n=3) were detected in 18/57 (32%) patients. Three novel mutations (1 nonsense and 2 missense) were found in four patients. All detected mutations were confirmed by Sanger sequencing. The novel missense mutations are *in-silico* demonstrated to be deleterious and are absent in unaffected control populations. Detailed genotype-phenotype correlation analysis is in progress. Functional analysis using Elk-1 reporter system and zebrafish modeling is underway to examine the pathogenicity of these novel mutations.

Conclusion: To our knowledge, this study has the largest sample size of *PTPN11* and *HRAS* negative patients from Hong Kong who received diagnosis of RASopathies from

clinical geneticists. Our study has demonstrated that the strategy involving targeted NGS analysis can achieve an addition detection rate of 32%, showing an improvement over the conventional Sanger sequencing analysis merely of *PTPN11* and *HRAS* mutations for RASopathies. Clinical correlations, customised bioinformatics pipelines and follow-up molecular characterisation in cell cultures or animal models are important to delineate the pathogenic role of novel mutations identified by NGS.

Acknowledgement: We would like to thank the families for their participation and the SK Medical Foundation and SK Yee Medical Research Fund for financial support.

Suberoylanilide Hydroxamic Acid and Bortezomib Synergistically Induce Apoptosis of EBV-Positive Burkitt Lymphoma Cells of Wp-Restricted or Type III Latency

KF Hui, YY Leung, PL Yeung, AKS Chiang

Department of Paediatrics & Adolescent Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Background: Endemic Burkitt lymphoma (BL) is strongly associated with Epstein-Barr virus (EBV) with variable latent viral gene expression patterns (type I, Wp-restricted and type III latency). We reported that bortezomib, a proteasome inhibitor, could potentiate the anti-tumour effects of suberoylanilide hydroxamic acid (SAHA), a histone deacetylase inhibitor, on EBV-positive nasopharyngeal carcinoma. Here, we aim to investigate the anti-tumour effects of SAHA, bortezomib and combination of the two drugs on EBV-positive BL cells of different viral latency.

Methods: Cytotoxic effect of SAHA, bortezomib or combination of the two drugs (SAHA/bort) on BL cells of type I, Wp-restricted or type III latency was determined by MTT assay. Effects on apoptosis and cell cycle were measured by flow cytometry. Expression of apoptotic markers, EBV latent proteins and tumour suppressor genes were analyzed by western blotting.

Results: BL cells of Wp-restricted or type III latency, which express the EBV nuclear antigen (EBNA)-3 proteins, were more resistant to killing by SAHA than those of type I latency. However, adding bortezomib to SAHA synergistically enhanced the killing of BL cells of these two latency types. Compared with SAHA or bortezomib, SAHA/bort triggered enhanced apoptosis in the BL cells as indicated by the higher percentages of AV/PI-positive and sub-G1 populations as well as stronger proteolytic cleavage of apoptotic markers, PARP, caspase-3 and caspase-9, and induced the expression of two tumour suppressor genes, $p16^{INK4A}$ and $p21^{WAF1}$, which are known to be down-regulated by the EBNA3 proteins. Furthermore, SAHA/bort suppressed the growth of BL xenografts in nude mice.

Conclusions: Combination of SAHA and bortezomib synergistically induces the apoptosis of BL cells of Wp-restricted or type III latency and possibly overcomes the resistance to apoptosis conferred by the EBNA3 proteins by up-regulation of $p16^{INK4A}$ and $p21^{WAF1}$ genes. Clinical application of this drug combination to the treatment of primary EBV-driven lymphoproliferative disease such as post-transplant lymphoproliferative disorder should be further explored.

Infant Growth and Adiposity in Adolescence: Prospective Observations from Hong Kong's "Children of 1997" Birth Cohort

LL Hui,[1] MY Wong,[2] GM Leung,[1] CM Schooling[1,3]

[1]School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong; [2]Department of Mathematics, The Hong Kong University of Science & Technology, Hong Kong; [3]School of Public Health, Hunter College, The City University of New York, U.S.A.

Background: The role of infant growth in adiposity remains unclear, with suggestions that rapid infant catch-up growth and slow infant growth may be associated with general and specifically central adiposity.

Methods: We used multivariable linear regression in a Chinese birth cohort (n=8327), "Children of 1997", comprising 88% of births in Hong Kong in April and May 1997, to examine in terms births the adjusted association of infant (birth to 12 months) weight growth trajectories (Figure) with body mass index (BMI) (n=6813), waist circumference, waist-to-height ratio (WHtR) and waist-to-hip ratio (WHR) (n=5323) at 13-14 years.

Results: Infant weight growth trajectories had graded associations with adolescent BMI, waist circumference and WHtR but not with WHR, such that compared to adolescents born light with slow infant growth (Trajectory I), adolescents born heavy with fast infant growth (Trajectory V) had higher BMI (0.61, 95% confidence interval (CI) 0.51, 0.71), larger waist circumference (3.85 cm, 95% CI 3.04, 4.66) and higher WHtR z-score (0.15, 95% CI 0.05, 0.25) but similar WHR z-score (-0.02, 95% CI -0.12, 0.07), adjusted for gestational age, parental education, parental BMI, parental height and parental place of birth.

Conclusions: Varying associations of infant growth with different measures of adiposity suggest a complex role of infant growth in long-term health perhaps because infant growth (or its underlying drivers) influences build and body composition as well as adiposity.

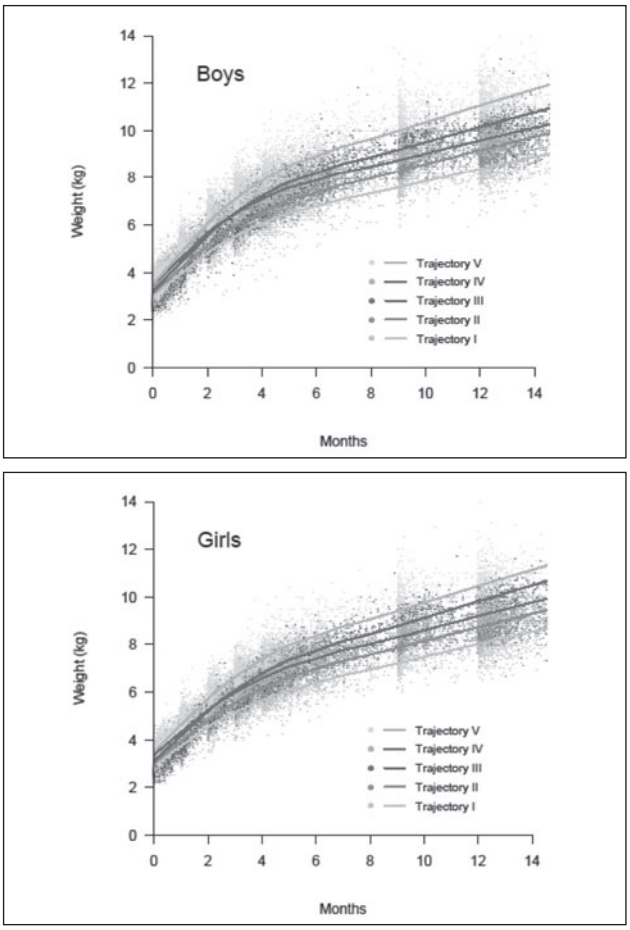

Figure Growth trajectories and weight from birth to 12 months for boys (upper) and girls (lower).

Infant Growth and Body Composition in Adolescence: Evidence from the Hong Kong "Children of 1997" Birth Cohort

LL **Hui**,[1] GM **Leung**,[1] CM **Schooling**[1,2]

[1]School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong; [2]School of Public Health, Hunter College, The City University of New York, U.S.A.

Background and aims: Rapid infant growth is associated with subsequent adiposity in western settings, but less so in other settings possibly because of different socio-economic patterning of infant growth. We examined the association of birth weight and infant growth with fat free mass (FFM), fat mass (FM), skeletal muscle mass, % body fat, % skeletal muscle mass at age 15 years and whether the association varied by birth weight.

Methods: We used multivariable linear regression with multiple imputation and inverse probability weighting to account for missing data and sample selection to examine the association of infant growth with body composition in 469 adolescents from the Hong Kong Chinese "Children of 1997" birth cohort who come from a population with a different socio-economic patterning of infant growth from western settings. Infant growth was defined as change in weight z-score from birth to 12 months. Body composition was assessed by dual energy X-ray absorptiometry at 15 years. Analysis was adjusted for sex, parental education and mother's place of birth.

Results: Faster infant growth from birth to 12 months was associated with higher FFM (0.8 kg, 95% confidence interval (CI) 0.4 kg, 1.2 kg), skeletal muscle mass (0.4 kg, 95% CI 0.2 kg, 0.6 kg) and FM (0.6 kg 95% CI 0.1 kg, 1.0 kg) but not higher % skeletal muscle mass (-0.4, 95% CI -0.6, -0.0) or % body fat (0.4, 95% CI -0.1, 0.8) at 15 years, with no difference by birth weight. Greater birth weight was associated with higher FFM, higher FM, but not with greater % skeletal muscle mass or %BF.

Conclusions: In a developed non-Western setting adolescents who had grown faster as infant were bigger at 15 years, but had similar body composition to other adolescents. Although we cannot rule out residual confounding obscuring an association of faster infant growth with unfavourable body composition, this study is consistent with recent evidence suggesting a minimal role of infant growth in long-term health.

Early Oorigins of Socio-economic Disparities in Cardiovascular Disease Risk Factors in Hong Kong Adolescents – Evidence from the Hong Kong "Children of 1997" Birth Cohort

LL Hui,[1] IOL Wong,[1] MK Kwok,[1] CM Schooling[1,2]

[1]Life course and Lifestyle Epidemiology Group, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong; [2]School of Public Health, Hunter College, The City University of New York, U.S.A.

Background and aims: Cardiovascular diseases (CVD) are the leading cause of death globally. Hong Kong has a high Gini coefficient and widening inequalities in cardiovascular disease. When these inequalities are established is unclear but important for prevention. We examined the contribution of neighbourhood and family socio-economic position to adolescent adiposity and blood pressure and examined whether any associations were mediated by early life exposures.

Methods: We used mixed effect multilevel linear regression to assess the association of neighbourhood (teritary plannining unit) median income and highest parental education with body mass index (BMI) (n=6855, 83% follow-up), waist circumference, waist-hip ratio (n=5374, 65% follow-up) and blood pressure (n=5265, 64% follow-up) among 13-year-old adolescents in Hong Kong's Chinese birth cohort "Children of 1997". We also examined whether the associations varied by mother's migrant status or sex or were mediated by prematurity, small for gestational age (SGA) or infant growth rate.

Results: Neighbourhood median income was unrelated to adiposity or blood pressure. Parental education ≤9 th grade compared to ≥12 th grade, was associated with greater waist circumference (1.73 centimetre, 95% confidence interval (CI) 1.09 to 2.37), waist-hip ratio z-score (0.28, 95% CI 0.21 to 0.35), and higher systolic (1.19 mmHg 95% CI 0.35 to 2.02) and diastolic (0.86 mmHg, 95% CI 0.40 to 1.32) blood pressure, with no difference by mother's migration status or sex. Low parental education was associated with greater BMI (0.16, 95% CI 0.05 to 0.27) only among adolescents with Hong Kong born mothers. None of the associations of parental education with adiposity or blood pressure was mediated by prematurity, SGA status or infant growth rate.

Conclusions: Parental education was inversely associated with central adiposity and blood pressure among Hong Kong adolescents, but was not mediated by prematurity, SGA status or infant growth. Identifying the underlying biological processes by which lower early life SEP raises CVD risk factor is critical to equitable health policy but remains elusive.

Two Chinese Brothers with Recurrent Atypical Haemolytic Uraemic Syndrome

ALT Ma, WM Lai, PC Tong, NKC Tse

Paediatric Nephrology Centre, Princess Margaret Hospital, Hong Kong

Background and aims: DEAP-HUS (Deficiency of complement factor H-related) plasma proteins and Autoantibody Positive form of Heamolytic ureamic Syndrome) represents a relatively new subtype of haemolytic ureamic syndrome (HUS). We report two Chinese brothers who suffer from this condition in Hong Kong.

Methods: Retrospective review of a 10-month-old baby of non-consanguineous parents presented with influenza A with acute kidney injury (AKI) (oliguria and creatinine of 500 umol/L), microangiopathic haemolytic anaemia (Hb of 6.9 g/dL), thrombocytopenia ($50x10^9$/L), high lactate dehydrogenase (1000 U/L) and low C3 level (0.42 g/L). He was managed with haemodialysis and had full recovery of his kidney function in 2 weeks. Three months later, he developed another similar episode of AKI with roseola infantum. His condition improved with plasma exchanges and dialysis but had renal impairment afterwards (eGFR of 32 ml/m^2/min). He remained well until the 2 years later where again he developed the third episode of AKI with influenza. He responded to plasma exchanges with gradual recovery of kidney function back to baseline. His younger brother also had similar presentation of acute kidney injury with viral illness at 7 months of age and had full recovery of his kidney function after plasma exchanges and temporary haemodialysis.

Results: DEAP-HUS work up was done in view of recurrent and familial occurrence of HUS. Anti-factor H antibody was tested positive in the index patient (Antibody titre of 450, normal <100). Heterozygous chromosomal deletions on chromosome 1 was found on the complement factor H-related (CFHR) 1 gene, CFHR 3 gene and CFH (complement factor H) gene in both the patient and his younger brother. Their father carries heterozygous deletions of CFHR1 gene and CFH gene and mother carries different heterozygous deletions of CFHR 1gene.

Conclusion: We report two brothers who developed DHEA-HUS. They developed auto-antibody to factor H which resulted in repeated AKI. Both patients responded to plasma exchanges and renal replacement therapy. Eculizumab, the terminal complement inhibitor, shines light to the management of atypical HUS although the definite duration of the therapy is still not known.

Infant Peritoneal Dialysis in Hong Kong

ALT MA, PC TONG, X LIAO, YF LI, LJ ZHAO, WM LAI, MC CHIU, NKC TSE

Paediatric Nephrology Centre, Princess Margaret Hospital, Hong Kong

Background and aims: Peritoneal dialysis in small children is challenging. We reviewed infants who were on peritoneal dialysis for the past 15 years in a paediatric nephrology centre in Hong Kong.

Methods: Retrospective review on infants who were started on peritoneal dialysis (PD) from 31 July 1996 till 31 July 2012 was performed. Patient demographics, dialysis morbidity, biochemical data, dialysis adequacy, growth parameters and final patient outcomes were analysed.

Results: A total of 9 patients (3 boys and 6 girls) with median age of 0.45 years (0-2.1 years) were started on peritoneal dialysis during the study period. The median duration of PD was 16.5 months (3-75 months). Three patients suffered from congenital abnormalities of the kidneys and urinary tract, 3 had haemolytic uraemic syndrome (HUS), 1 had primary hyperoxaluria and 2 had severe asphyxia which led to renal failure. Half of the patients had hypertension. A third of patients had either a feeding tube or gastrostomy for feeding problems and half of the patients were delayed in development. Dialysis adequacy (KT/V) was estimated to be more than 1.8 in 83% of patients. Two patients were on growth hormone. The mean height standard deviation score was -1.86 on start of PD, -2.03 at 24 months post dialysis and -1.28 at 48 months after dialysis, signifying catch up growth. Peritonitis incidence was 1:35 (episodes: patient months) and catheter survival rate was 67%. The most common cause of access failure was catheter blockage. Incidence of exit site infection was 1:24 (episode: patient months). There was no mortality at the end of the study period. One patient with HUS recovered from renal failure, 4 were transplanted, 1 on both haemodialysis and PD while 3 remained on PD.

Conclusion: Our data suggested that although PD in infants remained to be challenging, infant mortality was low. Laboratory parameters, dialysis adequacy, peritonitis rate and exit site infection rate were acceptable but hypertension and developmental delay were prevalent. Increased efforts must be placed on optimising the dialysis efficiency, nutrition and developmental training on all infants on PD.

Mycobacterial and Candida Infections in a Patient with Novel Dominant Negative Mutation of STAT1 Linker Domain

HW MAO,[1,2] PPW LEE,[1] WL YANG,[1] V LING,[1] KW CHAN,[1] MHK HO,[1] TL LEE,[1] WM TU,[1] YL LAU[1,2]

[1]Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong; [2]Department of Pediatrics, The University of Hong Kong-Shenzhen Hospital, Shenzhen, China

Background and aims: Genetic defects in IFNγ/IL12 pathway causes susceptibility to severe infections with mycobacteria and fungi. Signal transducer and activator of transcription 1 (STAT1) is a transcription factor involved in this signaling pathway. It is crucial in interferon-mediated immunity against microbial infections by regulating the expressions of IFN responsive genes. Chronic mucocutaneous candidiasis is a heterogeneous group of primary immunodeficiency diseases characterised by Candida infections of the skin and oropharynx. STAT1 gain-of-function mutation was shown to be responsible for autosomal-dominant cases of chronic candidiasis. In contrast, STAT1 loss-of-function mutations have been mostly reported in patients with atypical mycobacterial and Salmonella infection. Herein we sought to investigate the STAT1 mutation in a patient who presented with not only recurrent candidiasis, but also mycobacterial infection.

Methods: Exome sequencing was performed for this patient. After bioinformatical analysis, STAT1 was sequenced by Sanger sequencing. The STAT1 signaling pathway including IFN-stimulated STAT1 phosphorylation, transcriptional response and target gene expressions were examined.

Results: The patient was a Chinese girl born to non-consanguineous parents. Since infancy she presented with recurrent oropharyngeal and perineal candidiasis that was refractory to antifungal treatment, and also had recurrent *Salmonella* gastroenteritis. At 5 years old, she developed granulomatous lymphadenitis caused by *Mycobacterium fortuitum*. At 14 months she developed type 1 diabetes mellitus and was treated with insulin. Exome sequencing identified a novel autosomal dominant loss-of-function E559K mutation in the linker domain of STAT1, which was confirmed by Sanger sequencing. The mutation impaired phosphorylation induced by both IFNγ and IFNα, leading to decreased expressions of interferon inducible target genes. STAT1 protein expression was not affected.

Conclusions: In addition to mycobacterial infection, STAT1 loss-of-function mutation also predisposes to

chronic mucocutaneous candidiasis, likely through aberrant regulation of IFN-mediated response. This extends the spectrum of clinical phenotype of STAT1 loss-of-function mutation. We also for the first time reported STAT1 mutation in the linker domain.

Effectiveness of Ciprofloxacin or Doxycycline Treatment in Refractory *Mycoplasma pneumoniae* Infection

HW Mao, Y Liu, JY Zhou, K Sang, CB Chow, MC Chiu, K Lau

Department of Pediatrics, The University of Hong Kong-Shenzhen Hospital, Shenzhen, China

Background and aims: *Mycoplasma pneumoniae* (MP) is a common pathogen causing community-acquired pneumonia and macrolides have been the main therapeutic drugs of choice. In China, due to the potential side effects of cartilage damage and dental discolouration, ciprofloxacin and doxycycline are not recommended for children younger than the ages of 18 and 8, respectively. However, macrolide-resistant MP has been increasingly reported worldwide, and China has the highest prevalence of macrolide-resistant MP with resistant rate being >90% in the southern provinces. Thus, management of macrolide-resistant MP infections has become a major therapeutic challenge. Herein we report the success of using ciprofloxacin and doxycycline in treatment of refractory MP infection in young Chinese children.

Methods: Seven cases of macrolide-resistant MP infections diagnosed in the Department of Pediatrics, The University of Hong Kong-Shenzhen Hospital from June to October 2013 were retrospectively reviewed.

Results: There were 5 girls and 2 boys with median age of 6 (1-7 years). All of them presented with high fever and cough. Laboratory investigations showed increased acute phase reactants including CRP and ESR, with near normal white blood cell counts [median $6.6x10^9$/L; range (3.96-11.72)$x10^9$/L]. Chest X-ray showed either lobar or unilateral pneumonia. All patients were first treated with macrolides including erythromycin and/or azithromycin. Second line medications were used when fever persisted with worsening of clinical symptoms. Five patients developed pleural effusion and one progressed rapidly and required ventilator support. Due to more experiences in young children, ciprofloxacin was used in 4 cases. In the first 3 children, fever subsided on day 4 to day 5 post-treatment with improvements in clinical conditions. However, high fever persisted in the 4th child with newly developed pleural effusion. Doxycycline was started and then the patient defervesced after 2 days. Thereafter, the team decided to use doxycycline instead of ciprofloxacin in subsequent cases. And fever was observed to subside faster when treated with doxycycline than ciprofloxacin (median, 1 day vs 4 days).

Conclusions: Doxycycline and ciprofloxacin are effective for the treatment of refractory MP infection. In our cohort, fever appeared to subside faster with doxycycline. With the high prevalence of macrolide-resistant MP in China, there is an urgent need to evaluate the current national guideline for the treatment of MP infections.

Prevalence, Risk Factors and Impact of ADHD in Children with Recent Onset Epilepsy

MYY Ngan,[1] CH Tsang,[1] LH Yip,[1] TS Lai,[2] SM Lam,[2] KL Kwong[1]

[1]Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital; [2]Department of Child Psychiatry, Castle Peak Hospital, Hong Kong

Background and aims: Children with epilepsy are at higher risk for psychiatric comorbidities with attention deficit hyperactivity disorder (ADHD) being one of the more common co-morbid psychiatric disorders. This study aims to identify the prevalence, risk factors and impact of ADHD on seizure outcome in children with epilepsy.

Methods: A prospective cohort study was conducted from January to July 2010. Children 6-18 years old with recent onset epilepsy with follow up in a regional Hospital were recruited. Children attending special schools were excluded. Chinese Strengths and Weaknesses of ADHD-Symptoms and Normal-Behaviors Questionnaire (Chinese SWAN) was administered to all patients and scores compared with the community population. Basic demographic data were obtained through interview. Seizure characteristics and outcome was obtained through electronic records. Cases were those diagnosed with ADHD and controls were children without ADHD. Cases and controls were compared using univariate and multivariate analysis. All children were followed up for 3 years for seizure control and outcome.

Results: 48 children with recent onset epilepsy were recruited. The prevalence of ADHD is 20.8% (10 patients with ADHD, 7 being hyperactive/impulsive and 3 combined type). There was an equal distribution of males and females in those having ADHD.

The SWAN scores for our study cohort showed no significant difference with the community population.

There was no significant difference in the demographic profile between cases and controls. The age of seizure onset was a significant risk factor for ADHD. The average age of seizure onset was 7.46 years in the ADHD group and 10.88 yrs in the control group (p=0.032, OR=0.728, 95% CI 0.545-0.973). Seizure type and seizure etiology were not significant risk factors on univariate analysis. Younger age of seizure onset (p=0.057, OR 0.544, 95% CI 0.291-1.0) and increased seizure frequency (p=0.037, OR=189.303, 95% CI 1.366-26242.6) were significant risk factor identified on multivariate analysis.

ADHD did not affect seizure outcome, discontinuation of anticonvulsant or polypharmacy.

Conclusions: The prevalence of ADHD among children with epilepsy (20.8%) was higher than their community counterparts (3.9%). As ADHD has a negative impact on children's academic and social performance, it is important to screen for presence of ADHD symptoms in this group of patients and offer appropriate intervention.

Outcome of Hepatobiliary Scanning: Preterm Versus Full-Term Cholestatic Infants

LY Siu,[1] KN Wong,[2] KW Li,[1] NS Kwong[1]

[1]Tuen Mun Hospital, [2]Hong Kong Sanatorium & Hospital, Hong Kong

Background and aims: The biliary tracts in different biliary atresia (BA) patients evolve at different speed to atresia as the cause of BA are believed to be multifactorial. The younger age at the time of the Kasai procedure is associated with better outcomes and should be preferably before 60 days of age. Hepatobiliary scintigraphy (HBS) is sensitive but of variable specificity in screening for BA. If the parameters leading to the variable specificity of the HBS can be identified and removed, HBS will facilitate early identification of candidates for Kasai procedure and unnecessary HBS can be avoided.

The aims of this study were to evaluate the specificity of a non-draining HBS for BA in preterm and full-term babies, to verify the relationship between non-draining scan and higher levels of direct bilirubin and to find an objective criterion to guide the time in performing HBS.

Methods: A total of 175 infants (113 males and 62 females, median age of 45 days) with 181 HBS performed in Tuen Mun Hospital between January 1998 and May 2010 were retrospectively analysed. A "non-draining" scan was defined as one showing no excretion of radiolabelled tracer into the small bowel 24h after injection. The disease category, epidemiological and laboratory data were compared between infants having non-draining and draining scans. In addition, the predictive value of a negative scan for BA was compared between preterm and full-term infants.

Results: Twenty infants (11.4%) were surgically confirmed to have BA. A non-draining scan was found to be 100% sensitive for BA, and the specificity was 96% and 78% among full-term infants and preterm infants, respectively. The mean direct bilirubin values of infants with BA and intrahepatic cholestasis were 141.9 and 111.3 μmol/L, respectively, which were significantly higher than 67.2 μmol/L seen in infants with draining scans. Adopting direct bilirubin ≥63 μmol/L as the threshold for performing HBS among full-term babies was found to be 100% sensitive and 66% specific for picking up non-draining scans.

Conclusion: Our data supported that using direct bilirubin ≥63 μmol/L as an objective criterion in guiding the time to perform HBS among full-term babies can facilitate early identification of candidate for Kasai procedure and avoid unnecessary scans.

Integration of Chromosomal Microarray Into Paediatric Clinical Care in Hong Kong

V Tao,[1] YWY Chu,[1] KY Chan,[2] EY Lau,[2] G Mok,[1] W Tso,[1] A Liu,[1] A Kan,[2] MH Tang,[2] YL Lau,[1] BHY Chung[1,2]

[1]Department of Paediatrics & Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong; [2]Department of Obstetrics & Gynaecology, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

Background and aims: Chromosomal microarray (CMA) has emerged as a major tool to identify unbalanced chromosomal aberrations in children and is recommended as the first tiered investigation for intellectual disability, autism spectrum disorders and multiple congenital anomalies. While the clinical interpretation and genetic counseling remain as ongoing challenge, data about potential downstream benefits and harms of CMA is lacking, especially in paediatric population. Our objective is to evaluate the clinical impact of CMA on medical management in children.

Methods: In January 2011- May 2013, we performed high resolution CMA using the NimbleGen 135k oligonucleotide array on 330 children in a university-affiliated paediatric unit in Hong Kong at a research base.

Patients who had received prenatal CMA test or failed to follow-up, and those with trisomy disorder were excluded. Cases with pathogenic/likely pathogenic CMA results were analyzed. By retrospective chart review, descriptive and multivariate analyses are performed to understand the association between CMA results and change in the medical management.

Results: Total 82 patients were reported to have abnormal CMA results. Pathogenic/likely pathogenic chromosomal aberrations accounted ~10% (32 patients with pathogenic and 2 patients with likely pathogenic changes), while the aberration with unclear/uncertain clinical significance accounted for the remaining 90%. CMA detects clinically significant submicroscopic (<5 MB) abnormality in 18 patients. Some syndromal disorders were initially missed on clinical assessment either due to atypical clinical feature or patient's young age, including two William syndrome, two DiGeorge syndrome, one Cri-du-Chat syndrome, and one Klinefelter syndrome. All clinical significant cases were followed with genetic counseling. Total 69 medical managements were prompted by pathogenic/likely pathogenic CMA in 34 patients. One family has withdrawn as the parents realised that "knowing more may not be better".

Conclusion: CMA findings can be medically actionable and/or have major implications for family members. The insights we have learned from some of our patients have wider implications for the medical community. The potential of CMA findings to impact, positively and negatively, on patients is tremendous and warrants careful evaluation. Our findings will be instructive in anticipating the impact of whole genomic analyses on medical management and downstream utilisation of health services.

Griffiths Mental Developmental Scales (GMDS) – Validation for Chinese Children

WWY Tso,[1] VCN Wong,[1] LJ Ao,[2] M Li,[3] X Zhang,[4] FY Jiao,[5] X Xu,[6] KX Du,[7] B Farragher,[8] XL Xia,[9] D Challis[10]

[1]Department of Paediatrics & Adolescent Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong; [2]Second Affiliated Hospital of Kunming Medical University, Kunming, China; [3]Child Neuro-Habilitation Clinic, Department of Paediatrics, The First Hospital of Peking University, Beijing, China; [4]Department of Child and Adolescent Health, Tianjin Medical University, Tianjin, China; [5]Shaanxi Provincial People's Hospital of Xi'an medical university, Xi'an, China; [6]Child Health Care Department, The Paediatric Hospital of FuDan University, Shanghai, China; [7]Department of Child Neurology, The Third Affiliated Hospital of ZhengZhou University, ZhengZhou, China; [8]Liverpool School of Tropical Medicine, Liverpool, United Kingdom. *Dr. Farragher generated all the statistical results and interpretation of the statistical model*; [9]Department of Paediatrics, The Second Affiliated Hospital of Kunming Medical College, Kunming, China; [10]Association for Research in Infants and Child Development, Research and re-standardisation subcommittee United Kingdom

Background: The Griffiths Mental Developmental Scales (GMDS) are used by Developmental Paediatricians or psychologists in many countries to assess the developmental profile in children aged 0- 8 years old. There is an increasing awareness of developmental disorders in children in China; the prevalence of pre-school children with developmental disorders was reported to be 12.97%. The GMDS have been validated for normal children in the United Kingdom. However, there are differences in culture and beliefs in Asia and the Western societies. In this study, the GMDS have been translated into Chinese and back translated and modified according to Chinese culture. This prospective study aims to provide validation of the GMDS for urban Chinese children.

Method: Children from 7 different cities in China with typical development were recruited into the study from 2009-2013. Their developmental status was assessed using the translated and back-translated Chinese form of GMDS.

Results: 815 Chinese children (424 boys and 391 girls) with age 7 days to 8 years had been recruited. GMDS scores were analyzed. Smooth developmental curves with standard deviations and percentile scores were computed for the 6 sub-scales (A=Locomotor, B=Personal-Social, C=Hearing and Language, D=Eye and Hand Co-ordination, E=Performance, F=Practical Reasoning) using the LMS method. Plots of the 1st, 2.5th, 5th, 10th, 25th, 50th, 75th, 90th, 95th, 97.5th and 99th percentiles were obtained showing similar trend as the British in subscales.

Conclusion: There are similarities and differences in the Chinese developmental curves as compared to the British

developmental curves. These differences are most obvious for subscale F i.e. practical reasoning. In the future, all Chinese children should be assessed using this first and newly validated Chinese 'developmental growth' chart. This will avoid inaccurate estimation of the developmental profile of Chinese children.

Co-Infection with Influenza Virus and Then *Streptococcus pneumoniae* Dysregulates Immune Response and Enhances Mortality in a Mouse Model

Y Wu,[1] LK Tai,[1] KH Chow,[2] PL Ho,[2] WW Tu,[1] YL Lau[1]

[1]Department of Paediatrics and Adolescent Medicine, The University of Hong Kong; [2]Department of Microbiology, The University of Hong Kong, Hong Kong

Background and aims: Secondary *Streptococcus pneumoniae* infection after influenza is one of the most severe complications of influenza that significantly contributes to excess mortality. With the clinical importance of the co-infection, it is necessary to understand the disease pathogenesis. However, mechanisms of co-infection are not fully understood. We hypothesise that co-infection with influenza virus and then pneumococcus can enhance mortality, increase disease severity and dysregulate host immune response to the pathogens.

Methods: C57BL/6N mice (from Charles River Laboratories, USA) were sequentially co-infected with influenza virus and then *Streptococcus pneumoniae*, or infected with either influenza virus alone or pneumococcus alone. Survival was recorded. To examine disease severity, body weight loss, lung viral titer and bacterial cell counts were measured. To determine immune response, lung inflammatory cytokines and chemokines were measured, the neutrophils and macrophages infiltrating the lung were examined, lung structural damage was scored by histological analysis and level of influenza virus specific IgG in lung was measured by ELISA.

Results: Co-infected mice lost their body weight significantly and resulted in 100% morality rate, whereas mice infected with either influenza virus alone or pneumococcus alone lost their body weight transiently and all recovered from the infections. Co-infected mice had significantly higher lung virus titer and bacterial cell counts. This indicated that co-infection increased pathogen growth. Co-infected mice had higher lung inflammatory cytokines and chemokines, neutrophils and macrophages infiltration, as well as greater lung structural damage. This indicated that co-infection enhanced lung inflammatory response and immunopathology. Co-infected mice had lower virus specific IgG in the lung. This indicated that co-infection reduced antibodies production to influenza virus.

Conclusion: Co-infection enhanced pathogen growth, promoted lung inflammation and reduced virus specific IgG production. With the elevated disease severity and dysregulated host immune response, co-infection increased mortality rate. This study contributes to the understanding of the pathogenesis of the co-infection.

Lupus Protein Losing Enteropathy in an Adolescent Girl

CLS Yan, ALT Ma, PC Tong, WM Lai, NKC Tse

Department of Paediatrics, Princess Margaret Hospital, Hong Kong

Background: Protein losing enteropathy is a rare presentation of systemic lupus erythematosus (SLE), particularly in the paediatric age group. We report the early diagnosis and management of an adolescent girl who suffered from this easily missed disease.

Method: Retrospective case review of a 12-year-old girl who presented with 2-month history of rash and recent onset of oedema. She had urticarial rash over the malar region and vasculitic rash over her limbs. There was no history of frothy urine or gastrointestinal upset. Blood tests showed low albumin level 10 g/L and otherwise normal liver and kidney functions. Further blood tests revealed that she was tested positive for anti-nuclear antibody (ANA titre 320 IU/mL, normal <35 IU/mL) and anti-Smith antibody. C3 and C4 levels were low (C3 0.37 g/L, normal 0.70-2.06 g/L; C4 0.10, normal 0.11-0.61 g/L). The diagnosis of SLE was made according to the Systemic Lupus International Collaborating Clinics (SLICC) criteria, that one clinical (acute cutaneous lupus) and 3 immunological criteria (positive ANA, positive anti-Sm Ab, low complement C3 and C4) were fulfilled. She had very mild proteinuria with the urine protein to creatinine ratio of 0.21 mg/mg (normal <0.20 mg/mg) which could not account for her severe hypoalbuminemia. Therefore SLE with protein-losing enteropathy was suspected.

Results: Nuclear scan (Tc-99 m albumin scintography) showed that there was protein loss diffusely from the small bowel and therefore confirmed the diagnosis of protein-losing enteropathy. To rule out other causes of protein-losing enteropathy, endoscopies were done and both upper endoscopy and colonscopy were normal. CT scan of the abdomen showed mild ascites and reactive lymph nodes

with no evidence of lymphoma. With the diagnosis of lupus protein-losing enteropathy, she was started on prednisolone 30 mg BD (1 mg/kg/day), azathioprine 50 mg daily and hydroxychloroquine 200mg daily. The patient showed significant clinical improvement in terms of oedema and serum albumin level (albumin 20 g/L after 2 weeks of treatment).

Conclusion: Protein-losing enteropathy could be an initial presentation of SLE. Clinician should maintain a high index of suspicion in patients who present with severe hypoalbuminemia in the absence of heavy proteinuria. Timely diagnosis with early institution of appropriate immunosuppressants dramatically improve patients' outcome.

Is Intensive Phototherapy More Effective Than the Conventional Phototherapy in Treating Severe Neonatal Jaundice in Term Infant, and its Possibility to Prevent Exchange Transfusion

PT Yu, CK Leung, SF Wong, WP Lai
Department of Paediatrics, Kwong Wah Hospital, Hong Kong

Aim: To compare the efficacy of intensive phototherapy (IPT) with conventional phototherapy (IPT) in treating severe neonatal jaundice (NNJ) in term baby, and its possibility to prevent exchange transfusion (ET).

Patients & method: This is a retrospective study including all term baby (>/=37 weeks) with severe neonatal jaundice, defined as serum bilirubin level exceeding bilirubin level required for exchange transfusion. Patients admitted for prolonged neonatal jaundice were excluded. Control group included term baby admitted for severe NNJ at 2006-2007 with level 3 CPT given, was compared with intervention group, who admitted at 2009-2012 for severe NNJ and treated with IPT. Data were analysed in term of the need of exchange transfusion. Rates of serum bilirubin drop in neonates ≧day 3 were also compared.

Results: 86 patients and 164 patients were treated with CPT and IPT respectively, 9 patients (10.5%) in CPT group required ET compared to 15 patients (9.1%) in IPT group (p=0.737). The mean SB drop rate in the first 4 to 6 hours in 49 patients in IPT group was 10.8 mmol/dL/hr compared to 14.2 mmol/dL/hr in 102 patients in CPT group (p=0.032).

Conclusion: Intensive phototherapy is more effective in lower the serum bilirubin level compared with conventional phototherapy in case of severe neonatal jaundice. However, its efficacy in prevention of ET may need further study and analysis.

Association Between Sleep Architecture and Glucose Tolerance in Children and Adolescents

Y Zhu,[1] AM Li,[1] CT Au,[1] APS Kong,[2] J Zhang,[3] CK Wong,[4] JCN Chan,[2] YK Wing[3]
Departments of [1]Paediatrics, [2]Medicine and Therapeutics, [3]Psychiatry, [4]Chemical Pathology, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

Background and aims: Short sleep duration is a contributing factor for decreased insulin sensitivity and hyperglycemia. Sleep architecture represents a cyclical pattern of sleep which shifts between sleep stage N1, N2, N3 (slow wave sleep) and stage R (rapid eye movement sleep). We aimed to examine the association between sleep architecture and glucose and insulin metabolism in children and adolescents.

Methods: A total of 118 subjects participated in this study. They underwent an overnight polysomnography (PSG) when percentage of total sleep time (TST) spent at each sleep stage were recorded. Oral glucose tolerance test together with assay of insulin levels was carried out after overnight PSG. We assessed glucose tolerance, insulin sensitivity and pancreatic β-cell function by 2-h glucose level, Matsuda index (IS_{OGTT}) and insulin secretion-sensitivity index-2 (ISSI-2) respectively.

Results: After adjustment for age, gender, BMI z-score, pubertal status and obstructive apnea hypopnea index, stage N3 (%TST) was positively associated with IS_{OGTT}, while stage N1 (%TST) exerted an opposite effect on IS_{OGTT}. High sleep efficiency and long TST were independently associated with low 2-h glucose level, high ISSI-2 and/or high IS_{OGTT}.

Conclusions: Stage N3, sleep efficiency and TST were protective factors in maintaining glucose and insulin homeostasis; however, stage N1 functioned in the opposite direction.

Acute and Chronic Effects of Sleep Duration on Blood Pressure in Normal Weight Adolescents

CT Au,[1] CKW Ho,[2] YK Wing,[2] HS Lam,[1] AM Li[1]
[1]Department of Paediatrics and [2]Department of Psychiatry, Prince of Wales and Shatin Hospital, The Chinese University of Hong Kong, Hong Kong

Background and aims: Inadequate sleep is a common and global phenomenon in modern society. Chronic sleep loss can result in impaired cognitive function and physical well-being. This study aimed to evaluate the association between ambulatory blood pressure (ABP) and sleep duration as measured by 7-day sleep diary and nocturnal

polysomnography (PSG) in normal weight adolescents without significant obstructive sleep apnoea (OSA).

Methods: Normal weight subjects aged 10-17.9 years were invited to come to our sleep laboratory for a 24-hour visit. All subjects underwent PSG for 9.5 hours and 24-hour ABP monitoring during the laboratory visit. ABP was divided into pre-PSG, in-bed during PSG and post-PSG periods for separate analyses. Sleep duration (SD_7) was obtained from 7-day sleep diary, reflecting the sleep pattern in the week prior to laboratory visit. Total sleep time (TST) and sleep efficiency (SE), both markers of acute sleep changes, were obtained from PSG.

Results: Totally 162 adolescents participated, of whom 19 were excluded because they had moderate-to-severe OSA (obstructive apnoea hypopnoea index of >5 per hour). Subjects with shorter SD_7 demonstrated rebound from sleep deprivation on the PSG night. SD_7 was inversely associated with systolic BP (SBP) in pre-PSG, in-bed and post-PSG periods (all β=-2 mmHg, $p<0.01$), and diastolic BP (DBP) in pre-PSG and in-bed periods (all β=-1 mmHg, $p<0.05$). TST was inversely associated with SBP in post-PSG period (β=-1.5 mmHg, p=0.047). SE was inversely associated with SBP in in-bed period (β=-0.1 mmHg, p=0.038), and DBP in in-bed (β=-0.1 mmHg, p=0.023) and post-PSG periods (β=-0.2 mmHg, p=0.006). Both TST and SE were not associated with SBP and DBP in pre-PSG period (all $p>0.1$).

Conclusions: Short sleep duration as measured by 7-day sleep diary was associated with higher BP in normal weight adolescents. Occasional adequate sleep may partially ameliorate the risk of high BP, but may not completely reverse the effect of long-term sleep insufficiency.

Sleep Duration, Cognitive Performance and Bone Mineral Density in Preschool Children

XT **Yu**, HS **Lam**, CL **Chau**, PHY **Chan**, AM **Li**

Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong

Background and aims: Childhood sleep is associated with childhood growth and development. Short sleep duration has been linked to a variety of neurocognitive problems. However, few studies have evaluated the impact of short sleep duration on cognitive functioning as well as the association between sleep duration and physical development in young preschool children. This study aimed to examine the associations between sleep duration and neurocognitive outcomes, and explore the association between sleep duration and bone mineral density (BMD) in preschool Chinese children in Hong Kong.

Methods: Eighty-eight healthy preschool children without snoring were recruited from a community-based survey including 1291 3-5 years old children. Their total sleep duration was under 11.5 for 3 years old, 11 for 4 years old and 10.5 for 5 years old, respectively, which was the 55 percentile in the cohort. The participants underwent BMD assessment by ultrasound of sound speed of sound of dominant radius and the tibia in the same side. Neurocognitive test included Connor's Kiddie-Continuous Performance Test (K-CPT) and sky search of The Test of Everyday Attention for Children (TEA-Ch). The parents reported their children's sleep patterns by sleep diary in two weeks before the tests and assessments.

Results: Average total sleep duration in previous 7 days was positively associated with BMD z score by age of tibia (r=0.30, p=0.05) and radius (r=0.32, p=0.03). However we didn't find any significant association between total/night sleep duration and neurocognitive performance including CPT and sky search.

Conclusions: Though it is reported that Hong Kong children sleep less than children in western countries, our results indicate that Hong Kong preschoolers are not sleep deprived due to the neurocognitive performance by CPT and sky search. However, habitually decreased sleep duration is closely associated with lower BMD both in radius and tibia. These findings may lead to the development of better preventive approaches to poor bone growth through recommendation for healthy sleep in preschool children.

Vitamin D Defficiency is Prevalent and Associated with Childhood Eczema in Hong Kong Children

TF **Leung**,[1] SS **Wang**,[1] APS **Kong**,[2] HY **Sy**,[1] GWK **Wong**,[1] KL **Hon**[1]

Departments of [1]Paediatrics and [2]Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong

Background and aims: Vitamin D is increasingly recognised to be importance in innate immune defense and asthma pathogenesis in addition to its crucial role in maintaining bone health. Recent studies suggested vitamin D deficiency to be associated with diminished expression of antimicrobial peptides in the skin. However, the impact of vitamin D deficiency on eczema diagnosis and severity remains unclear. This case-control study investigated the relationship between eczema diagnosis and severity and serum vitamin D levels in Hong Kong Chinese children.

Methods: 499 children with physician-diagnosed eczema and 328 non-allergic children were recruited. Eczema severity was assessed by SCOring Atopic Dermatitis (SCORAD; short-term) and Nottingham Eczema Severity Score (NESS; long-term). Serum 25-hydroxyvitamin D (25[OH]D) concentrations were measured by immunoassay (Immunodiagnostic Systems, Boldon, UK). Subjects were categorised as deficient (<25 nM), insufficient (25-49.9 nM) and sufficient (≥50 nM) according to international guidelines.

Results: The mean (standard deviation) serum 25(OH) D levels in eczema patients and controls were 28.9 (15.3) nM and 34.2 (14.5) nM respectively (p<0.001). Vitamin D deficiency was more common in eczema patients than controls (47.7% vs 26.8%; p<0.001). The majority (61.0%) of controls had vitamin D level in the insufficiency group. Serum 25(OH)D levels showed inverse correlation with both short- and long-term eczema severity. By SCORAD, the median 25(OH)D levels in nM among patients with mild, moderate and severe eczema were 25.6, 20.3 and 18.8 respectively (p<0.001). For NESS, the median 25(OH)D levels in nM among these respective groups were 25.1, 22.7 and 20.3 (p=0.004). Vitamin D deficient patients had higher plasma total IgE levels than those with insufficient and sufficient vitamin D status (p<0.001).

Conclusions: Vitamin D deficiency is prevalent in Hong Kong Chinese children, which is also associated with eczema diagnosis. Besides, there is an inverse correlation between serum 25(OH)D level and severity of childhood eczema. Oral vitamin D supplementation may improve disease control in patients with moderate-to-severe eczema.

Funding: Research Committee Group Research Scheme (3110087), CUHK.

Population References of Forced Expiratory Indices for Chinese Preschool Children in Hong Kong

TF **Leung,**[1] TC **Liu**,[1] KK **Mak**,[2] XF **Su**,[2] AM **Li**,[1] S **Lum**,[3] GWK **Wong**[1]

[1]Department of Paediatrics and [2]School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong; [3]Portex Respiratory Unit, UCL Institute of Child Health, London, United Kingdom

Background and aims: Advances in spirometry techniques have made it possible to obtain measurements in preschool children. Validated references for spirometric parameters are available for Caucasians but lacking in young Asian children. This community-based study established forced expiratory indices in Chinese children aged 2-7 years in Hong Kong.

Methods: Subjects were recruited from 19 randomly selected nurseries and kindergartens in Hong Kong, based on a stratified and clustered randomised sampling frame. Parents completed Chinese ISAAC questionnaire that recorded subjects' demographics and respiratory health. Concurrently, children performed incentive spirometry on-site (Master Screen, Jaeger GmbH, Würzburg, Germany) according to international guideline. Spirometry normograms were created using LMS method and prediction equations were formulated by linear regression. The reproducibility of $FEV_{0.5}$ and FVC measurements on two occasions 2-3 weeks apart was evaluated by Bland-Altman plots.

Results: 1922 (68.7%) of 2797 eligible children consented to participate. Their mean (standard deviation [SD]) age was 4.4 (1.0) years. Children with premature birth, active asthma, history of clinically significant congenital cardiopulmonary disease and respiratory tract infections within 4 weeks were excluded. Following exclusion also due to technical reasons, 895 (46.9%) of 1909 assessed children contributed data to the spirometric references. Compared with girls, boys had higher forced expiratory volume in 0.5-second ($FEV_{0.5}$), $FEV_{0.75}$, FEV_1, forced vital capacity (FVC) and peak expiratory flow but not FEF_{25-75}. Standing height was the most important predictor for all parameters, whereas the best prediction model for both boys and girls was formed by standing height, weight and age. The adjusted R^2 values for boys ranged from 0.556 to 0.760 and those for girls varied between 0.616 and 0.746. The mean (SD) percentage differences in $FEV_{0.5}$ and FVC between two occasions were -0.4 (5.1) % and 0 (3.2) % respectively. Bland-Altman plots showed good between-occasion agreement for these parameters.

Conclusions: This population study presents spirometry normograms and reference equations in young Chinese children in Hong Kong. Forced expiratory indices of these preschoolers are determined by gender, age, weight and standing height.

Funding: Health and Health Services Research Fund (06070261), Food and Health Bureau, Hong Kong SAR.