HK J Paediatr (new series) 2016;**21**:214-226

Proceedings of Congress

3rd Annual Scientific Meeting: Hong Kong College of Paediatricans

5-6 December 2015

Oral Presentation – Free Paper Session

The Impact of Genetic Polymorphisms on the Association Between Fish Consumption and Body Burden of Methylmercury

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Background and aims: Methylmercury (MeHg) is a toxic heavy metal that can cause adverse health effects in children even at low doses. Contaminated fish is the major source of MeHg for the general public. Hong Kong children are at high risk of MeHg exposure due to high fish consumption. It is well-known that the elimination rate of MeHg varies greatly among individuals, but the reason for that is less clear. Previous studies have shown that mercury biomarker concentrations can be affected by genetic variations affecting the MeHg metabolism pathway. This study aims to investigate the impact of genetic variations in metallothionein (MT) and glutathione (GSH)-related genes on the association between fish consumption and body MeHg burden, as measured by hair MeHg concentration.

Methods: Hair MeHg levels and genotypes for GCLC, GCLM, GPx1, GSTA1, GSTP1, MT1A, MT2A and MT4 were determined in 196 children. Based on the fish frequency questionnaire filled by the child's caregiver, subjects were separated into high fish consumption group and low fish consumption group for analysis. Multivariate regression analysis was performed to assess the association between hair MeHg level, fish intake and the genetic polymorphisms.

Results: Our preliminary analysis showed that subjects with MT1M (rs9936741) TT genotype demonstrated a lower hair MeHg level (P=0.024) compared with those with CT and CC genotype. We also found two other GSH-related gene polymorphisms that show effect modifications on the association between hair MeHg level and estimated fish intake.

Conclusions: Our results are consistent with the literature and suggest that body burden of MeHg is influenced or modified by MT-related and GSH-related gene polymorphisms. Affected individuals could be at higher risk of the adverse effects of MeHg exposure.

Acknowledgements: Funded by a grant awarded by the Food and Health Bureau of Hong Kong, *Health and Medical Research Fund* entitled "Identification of genetic susceptibilities to low-dose mercury exposure in children" (ref no.: 11120601).

Long Term Outcome of Infant Peritoneal Dialysis in Hong Kong

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Background and aims: To review the outcomes of infant peritoneal dialysis (PD) in the Paediatric Nephrology Centre, Princess Margaret Hospital, Hong Kong.

Method: We retrospectively reviewed all Chinese infants and children who were put on chronic peritoneal dialysis (CPD) before two years old from July 1995 to December 2013.

Results: Nine Chinese patients (M:F=3:6) were identified. They were put on automated peritoneal dialysis at a median age of 4.7 months (m) (interquartile range, IQR: 1.1-13.3 m). The median duration of CPD was 40.9 m (IQR: 22.9-76.2 m). The causes of renal failure were renal dysplasia (n=3), pneumococcal-associated haemolytic uremic syndrome (pHUS, n=3), ischaemic nephropathy (n=2) and primary hyperoxaluria I (PH1, n=1).

All patients survived except one patient with PH1 who died of acute portal vein thrombosis after liver transplantation. One patient with pHUS had renal function improved and was able to wean off dialysis. Four patients had deceased donor renal transplantations with a mean waiting time of 76.7 months. Three patients remained on CPD at the end of the study. Weight gain was achieved in

our patients while three required gastrostomy. Four patients were delayed in development or required special education. Peritonitis and exit site infection (ESI) rates were 1 episode per 46.5 patient-months and 1 episode per 28.6 patient-months, respectively. Dialysis adequacy (KT/V urea more than 1.8) was achieved in 87.5% of patients.

Conclusion: CPD is technically difficult in infants. However, low peritonitis rate, low ESI rate and no CPD-related mortality can be achieved. CPD would be a promising strategy to bridge the way to renal transplantation.

Combination of Histone Deacetylase and Proteasome Inhibitors Counteracts the Anti-apoptotic and Cell Cycle Regulatory Function of EBNA-3C Protein in Epstein-barr Virus-positive Burkitt and Lymphoblastoid Cells

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Background and aims: Epstein-Barr virus (EBV) drives the development of post-transplant lymphoproliferative disorder (PTLD) via the concerted action of Epstein-Barr nuclear antigen (EBNA) proteins. We previously reported that combination of histone deacetylase inhibitor (HDACi) and proteasome inhibitor (Pi) could synergistically induce apoptosis of Burkitt lymphoma (BL) and lymphoblastoid cells (LCL; an in-vitro cell model of PTLD) which express the EBNA-3A, -3B and -3C proteins. In this study, we aim to investigate the mechanism by which combined HDACi/Pi counteracts the survival function of EBNA-3A, -3B or -3C proteins.

Methods: Spontaneous LCLs (sLCLs) and a panel of BL cell lines (BL31) harboring EBNA-3A, -3B or -3C knockout (KO) EBV genome and corresponding cell lines harboring the knockout virus together with the individual gene revertant (Rev) were treated with combination of HDACi (vorinostat) and Pi (bortezomib), followed by analyses of apoptosis and cell cycle. In-vivo testing of B cell xenografts in SCID mice was also performed.

Results: Isobologram analysis showed that combined HDACi/Pi induced significantly greater synergistic killing in 3C Rev than 3C KO cells. Such differential response was not observed in either 3A or 3B Rev and KO cells. Furthermore, higher percentage of sub-G1 population and stronger proteolytic cleavage of apoptotic markers including PARP and caspase-3 as well as up-regulation of p21 were found in EBNA-3C expressing cells when compared to 3C KO cells. Combined HDACi/Pi also mediated G2/M arrest in 3C KO cells but not in EBNA-3C expressing cells and produced enhanced suppression of the growth of EBNA-3C expressing but not 3C KO BL31 xenografts in SCID mice, supporting that EBNA-3C might be the major counteracting target of the drug combination. Furthermore, significant increase in percentage of sub-G1 population without G2/M arrest and up-regulation of cleaved PARP and caspase-3 as well as p21 were also observed in paediatric PTLD patient-derived sLCLs upon treatment with combined HDACi/Pi.

Conclusions: Combined HDACi/Pi induces potent apoptosis in EBV-positive BL and LCL through counteracting the anti-apoptotic and cell cycle regulatory function of EBNA-3C. This drug regimen may be tested as treatment for EBV driven lymphoproliferative diseases.

The work is funded by CRCG grant (#104003676) of KFH and CRCG (#104002068, #104002845 and #104003674) and EBV research (#200004525) grants of AKSC.

Breast Pain in Lactating Mothers

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Breast milk is the best food for infants below 6 months. With the joint effort of doctors, nurses and mothers, the prevalence of the ever breast feeding rate in Hong Kong has climbed from 5% in 1978 to 86% in 2014. However, only 27% can sustain breast feeding to 4-6 months. One of the reasons for stopping breast feeding is complications encountered during the process. Breast pain is the commonest complaint in lactating mothers.

This is a retrospective study of lactating mothers presenting with breast pain to a private clinic over a period of 6 months (January to June 2015). A total of 69 patients were seen. Thirteen used formula milk supplements. All except 6 were in their thirties. Twenty-four had their babies below one month of age. Twenty-four had experienced pain for over 7 days.

Patients were asked for their history of pain, prior treatment, feeding practices and their diet. They were then examined for their breasts, including the nipples, areolae and breasts. All had redness or tenderness of 1 or 2 breasts. Massage and milk expression were given to relieve the pain. All except 2 experienced immediate relief. Twenty-one were

given oral antibiotics. Only 1 was suspected to have fungal infection. There were 6 cases of abscess of which 4 needed referral to surgeons.

Additional complaint	n	Diagnosis	n
Nipple pain	8	Breast abscess	6
Sharp needle pain after feeding	8	Mastitis	13
White spot at nipple	15	Blocked duct	35
Fever	14	Poor positioning and latching	8
Failure to prior treatment	22	Cracks or sore nipples	3

Engorgement, blocked duct, mastitis and breast abscess reflect progression of a similar origin of inadequate drainage, which can be due to poor positioning and latching, inadequate emptying or overproduction. More education to mothers and successful early intervention can prevent sufferings of these dedicated mothers.

Clinical Application of Whole Exome Sequencing for Paediatric Undiagnosed Diseases in Hong Kong – Experience From First Sixty Cases

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Background and aims: By using next generation technology to sequence all the coding regions of the genome, whole-exome sequencing (WES) is now a more affordable and an increasingly important tool in diagnosing unsolved diseases. Worldwide, there has been growing collaborative efforts to solve rare and undiagnosed diseases using WES technology, with a diagnostic yield of up to 30%. We introduced the use of whole exome sequencing to paediatric patients with rare diseases in Hong Kong, and share our findings of the first 60 cases.

Methods: Sixty children with undiagnosed diseases referred to the genetics service in Queen Mary Hospital were recruited. These patients had all been assessed by a geneticist and genetic counsellor with conventional cytogenetic and molecular testing performed where appropriate. For those where a genetic diagnosis could not be obtained, the patients were offered singleton whole-exome sequencing. The results were validated and the relevant literature reviewed to determine the pathogenic nature of the mutation.

Results: A diagnostic rate of pathogenic causal variants was found in over 25% of patients, comparable to internationally reported figures. In addition to mutations in known rare diseases, we also discovered extended phenotypes of known syndromes and mutations contributing to newly described syndromes.

Conclusion: We share our experience in establishing WES as a useful tool for obtaining difficult diagnoses, as well as a valuable research tool to discover new genetic causes of rare diseases. The overall aim is not only to help more families to raise awareness and reach a diagnosis in the local population, but also to establish a pipeline to deal with the challenges of future application of next generation sequencing in the diagnosis of rare paediatric diseases.

Acknowledgements: SK Yee Medical Research Foundation and The Society for the Relief of Disabled Children.

Copy Number Variation in Hong Kong Patients with Autism Spectrum Disorder

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Background and aims: When offering chromosomal microarray for patients with autism spectrum disorder (ASD), as according to international standards, copy number variations of uncertain significance (CNV VUS) are frequently identified, which leads to challenges in genetic counselling. We aim to study the CNV findings in children with ASD in Hong Kong, and to gather information for reclassification of recurrent CNV VUS.

Methods: ASD patients from the Department of Paediatrics and Adolescent Medicine QMH/HKU were recruited if their Array Comparative Genomic Hybridization (aCGH) were done anytime from January 2011 to August 2014 in Prenatal Diagnostic Laboratory, Tsan Yuk Hospital. Diagnosis of ASD was made by developmental paediatricians and clinical psychologists using the criteria from Diagnostic and Statistical Manual of Mental Disorders, Fourth or Fifth Edition. NimbleGen

CGX-135k oligonucleotide array and Agilent CGX 60k oligonucleotide array were used. Information was summarised from the literature and existing databases to re-classify CNV VUS occurring in our ASD cohort.

Results: Among 288 patients with ASD in our cohort, we identified 5 patients with pathogenic CNV (1.74%) and 5 patients with likely pathogenic CNV (1.74%). Among all the CNV VUS, one variant overlapping DPP10 (hg[19] chr2:116,534,689-116,672,358) was recurrently found in Chinese individuals. The frequency of this variant in our ASD cohort was 0.35% (1 in 288), and 0.96% (9 in 935) in our controls. (P=0.467, two-tailed Fisher's exact test). Similar CNVs were suggested to be ASD-related in previous studies recruiting mainly Caucasians. However, there were Chinese individuals with typical development possessing similar CNVs identified in independent sources (9 from our internal database, 1 from Singapore Genome Variation Project, 24 from The Singapore Prospective Study Program).

Conclusions: Our study explored the CNV findings in Hong Kong paediatric ASD patients. The CNV overlapping DPP10 may be a Chinese-related copy-number variation in Hong Kong Chinese, and we reclassified it to be likely benign in our locality. Our result emphasized the need to account for ethnicity to give the most precise interpretation of aCGH data.

Acknowledgements: The study was supported by SK Yee Medical Research Fund, SK Yee Medical Foundation and the Society for the Relief of Disabled Children, Hong Kong.

Inclusion of Vaccines into the Childhood Immunisation Programme and Association With Mothers' decision to Vaccinate Their Children

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Background and aims: The Scientific Committee on Vaccine Preventable Diseases determines whether vaccines should be included in the Hong Kong Childhood Immunisation Programme (CIP). Vaccine in the CIP are administered at Maternal Child Health Centres at no cost to the parents. Vaccines not in the CIP are mainly available in the private sector and parents pay out-of-pocket if they want their children vaccinated. We investigated the association between vaccination uptake/intention and vaccine inclusion in the CIP.

Methods: A sample of 500 postpartum mothers were recruited from postnatal wards at two public hospitals from May to August 2014. When the children reached 6 months old, postal questionnaires with telephone follow-up if necessary collected details of vaccination uptake (vaccines scheduled below 6 months) and maternal vaccination intention (vaccines scheduled after 6 months). Chi-square tests and logistic mixed models were performed using statistical software R version 3.2.1.

Results: One family left Hong Kong and 6 mothers quitted the study before 6 months. Of those mothers followed-up, 372 (75%) responded to the 6-month questionnaires of which 314 (84%) provided copies of immunisation records. Uptake of vaccines scheduled before 6 months and in CIP (Bacillus Calmette-Guérin, Hepatitis B, Diphtheria, Tetanus, acellular Pertussis and injectable Polio, conjugate pneumococcal) was 100% but significantly less for those not in CIP (Haemophilus influenzae type b (28%) and rotavirus (47%)). Excluding vaccines for travelers and older children, four vaccines are available for routine use after 6 months of age (Measles, Mumps and Rubella vaccine [MMR], varicella, influenza and Hepatitis A vaccines). 88% and 86% mothers intended to give MMR and varicella to their children in the future respectively but less intended to give vaccines not in the CIP (influenza (33%) and Hepatitis A (32%)). Inclusion of a vaccine in the CIP was significantly associated with both the overall vaccination uptake ($p<0.0001$) and intention ($p<0.0001$). Family household income was not a moderator of the association between CIP inclusion and vaccination intention ($p=0.064$).

Conclusions: Inclusion of a vaccine in the CIP was strongly associated with both vaccination uptake and maternal intention.

Mutation in PIK3CA Leading to Developmental Mosaic Disorders

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Background and aims: Mutation in phosphatidylinositol-4, 5-bisphosphate 3-kinase (PIK3CA), one of the genes involved in the PI3K/AKT/mTOR pathway, is associated with developmental mosaic disorders which are now collectively termed as PIK3CA-Related Overgrowth Spectrum (PROS). PROS can be further divided into two subgroups based on the affected body systems, which are body asymmetrical overgrowth and central nervous system (CNS) overgrowth respectively. Body asymmetrical overgrowth includes diseases such as CLOVES Syndrome, Klippel-Trenaunay Syndrome, Cystic Hygroma and Fibroadipose Hyperplasia. More than 90% of these patients have somatic mutations in one of the 4 mutation hotspots in PIK3CA. CNS overgrowth includes diseases such as Megalencephaly Polymicrogyria Polydactyly Hydrocephalus Syndrome (MPPH) and Megalencephaly Capillary Malformation Syndromes (MCAP). Patients who have CNS overgrowth have megalencephaly and at the same time developmental delay and/or autistic spectrum disorder. We have ten patients that are suspected to have PROS, and we aim to identify the diseasing causing mutation in each patient.

Methods: For patients who have body asymmetrical overgrowth, somatic mutations can only be detected on affected tissues. Since there are mutation hotspots, digital PCR was used to identify low level somatic mosaicism. For the 2 patients with CNS overgrowth, mutation can be detected on blood, saliva and buccal tissues. Whole exome sequencing was used to identify the diseasing causing mutation.

Results: In 7 out of 8 patients with asymmetrical overgrowth, somatic mutations in PIK3CA have been identified. The percentage of mutant in these patients ranged from 3.3% to 31.6%. For the 2 remaining patients with CNS overgrowth, 1 reported somatic mutation with 4.5% mutant and 1 novel germline mutation in PIK3CA have been identified.

Conclusion: In order to obtain a molecular diagnosis of PROS, the correct choices of affected tissues and sequencing technology are important. Surgical debulking is now the only option for treatment for PROS. With the identification of mutations in PIK3CA, inhibitors that inhibit PI3K/AKT/mTOR pathway may be used in controlling the progressive overgrowth in patients.

Acknowledgement: This work was supported by SK Yee Medical Research Fund and Society for Relief of Disabled Children.

Poster Presentations – Studies

Pulmonary Function in β-thalassaemia Major

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Background: Pulmonary dysfunction has been reported in patients with β-thalassaemia major but the associations with iron overload and the natural progression remain unclear.

Objectives: (1) To determine the pattern of pulmonary impairment in patients with β-thalassaemia major and their associations with iron overload and (2) to examine lung function progression of a subgroup over a period of 13 years.

Methods: Subjects with β-thalassaemia major under the care of the four participating hospitals were recruited for full lung function assessment. Serum ferritin and magnetic resonance imaging (MRI) measurements of the liver and myocardium were used as surrogate index of body iron content. This study included 23 subjects who underwent lung function assessment 13 years ago.

Results: One hundred and one patients were recruited and 52 of them were males (mean age: 25.1±7.9 years). Thirty-one (30.7%) had restrictive disease, four subjects (4%) had impaired diffusion capacity, and one (1%) had obstructive disease. There was a significant correlation between the severity of restrictive abnormality and myocardial T2* relaxation time in MRI measurement ($r=0.33$, $p=0.03$). Significantly shorter myocardial T2* relaxation time was observed in patients with restrictive disease when compared with patients with normal lung function (26.3±14.0ms vs 39.0±18.5ms; $p=0.02$). Serum ferritin level was inversely correlated with the diffusion capacity ($r=-0.32$, $p=0.002$). As a group, the 23 subjects did not demonstrate significant changes in pulmonary function over time, but 3 patients who had normal lung function at baseline developed restrictive abnormality at follow-up.

Conclusions: Restrictive deficit is the predominant type of lung abnormality seen in patients with β-thalassaemia major, and the severity correlates with iron overload. Lung function of the majority of patients does not worsen with time.

Demographic Characteristics of Maternal Psychiatric Illness in NTEC Cluster

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Background: The Comprehensive Child Development Service (CCDS) in New Territories East Cluster of Hong Kong in relation with parent-child bonding has been established in March 2012. It aims to combat trans-generational poverty in reducing unfavorable factors in the development of children coming from deprived families. One of the unfavorable factors is maternal mental problems or postnatal depression, which might severely jeopardize the care of the baby and the establishment of mother-child bonding. Now the program has been fully in place and we would like evaluate the characteristics of the mothers with psychiatric illness identified during antenatal period.

Aim: To evaluate the demographic characteristics of the mothers with psychiatric illness identified during antenatal period in Prince of Wales Hospital during 2012-2013.

Methods: Retrospective demographic data was collected whenever the ladies firstly presented to CCDS midwife and while admission for gave birth. From May 2012, all pregnant ladies with the psychiatric illness identified in any circumstances by the staff of Maternity Child Health Center (MCHC) or Prince of Wales Hospital (PWH) during antenatal care, were referred to the midwife of CCDS. They were closely followed up during the antenatal and postnatal period by collaborating with Obstetrician, Paediatrician, Psychaitrist, MCHC and social welfare services.

Results: There were 313 ladies recruited under CCDS program, 231 of them were identified with psychiatric illness, which contributed for 73.8%. Only one of them was below 18 years old. Seventy-four percent of them suffered from depression, 5.2% of them had schizophrenia and 10.4% suffered from other kinds of psychiatric illness. Close to half of them (44.6%) were put on medications. Sixty-five percent were married and the rest were single, unmarried, divorced, or separated. There were 5.2% of them also had substance abuse within one year prior to expected date of delivery, and 42% percent of their partners were also drug abusers. Among those, only one of them was continuously abusing drug during the antenatal period. Half of them quit after pregnancy. Sixteen percent were also smokers. Almost 30% the smokers were also drug abusers.

Sixty-four percent of them were born in Hong Kong and thirty-one percent born in Mainland China. Thirty-three percent of them were employed at full time. For educational

level, a quarter (24%) of the subjects was below low secondary, 44% at high secondary and post-secondary or above was 34%. For income, there were 30% were above mid-income (10K-19K). Fifteen percent of our subjects were receiving social security. When compared this from general population in Hong Kong, there was only 5% of citizen aged under 60 are receiving social financial assistance. Therefore, the rate of receiving social security was higher in this group of ladies. When compared to the female educational level reported by Hong Kong Statistics Department, our subjects were higher in educational level but income was comparative with the female population. Housing status was similar to the reported population. Most of them were living with spouse, family and in-laws (45%, 10.4% and 6.5% respectively).

Only 7% reported with no social network was in function. There was 40% of them were followed up under some kinds of social workers.

Seventy-three of the ladies had attended antenatal educations during antenatal period, and there was statistical significant positive correlation of reported manageable child care at home with antenatal education. (p=0.001)

For infant feeding, close to 8% of them exclusive breast fed their newborn babies, 20% were providing mixed feeding. Ladies who were more manageable to work had higher rate of providing any forms of breast milk feeding. (p=<0.001). Factors that determined the postnatal mothers' ability in managing child care at home and resuming work.

Conclusion: Better engagement of at risk pregnant ladies with psychiatric illness on antenatal education was correlated with higher rate in managing child care at home. Moreover, with the different socioeconomic factors which were identified in predicting the possibility of resuming work in postpartum period and child care at home, resources can be redistributed to those higher risk families i.e. lack of social support and pregnant ladies who is newly immigrated to Hong Kong with psychiatric illness. In conclusion, CCDS is an effective programme improving at risk families in caring their newly born babies.

Acknowledgement: Maternity and Child Health Service, CCDS Team.

Neonatal Outcomes of Preterm Infants ≤29 Weeks Over a Decade from Queen Mary Hospital, Hong Kong: Comparison with The Vermont Oxford Network

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Background: To evaluate neonatal mortality and morbidity in preterm infants ≤29 weeks over a decade at Queen Mary Hospital (QMH), Hong Kong, so as to provide center-specific data for prenatal counseling and to benchmark these results against Vermont Oxford Network (VON).

Methods: In this retrospective analysis, perinatal/neonatal data were collected for 419 infants of gestational age (GA) 23 to 29 weeks that were born at QMH between January 1, 2005, and December 31, 2014. These data were compared with those recorded in the VON in 2013.

Results: Overall survival rate at QMH was 87%, which was significantly higher than VON (80.5%). Morbidity free survival at QMH (40%) was comparable with VON. Overall, 86% had respiratory distress syndrome (RDS), 40% bronchopulmonary dysplasia (BPD), 44% patent ductus arteriosus (PDA), 7% severe intraventricular haemorrhage (IVH), 5% necrotising enterocolitis (NEC), 10% severe retinopathy of prematurity (ROP), 10% late-onset sepsis and 84% growth failure upon discharge. Rates of RDS, IVH, NEC and severe ROP were similar in the two populations. In QMH, significantly more infants were having BPD, PDA and growth failure than in the VON. Rate of late-onset sepsis was significantly lower than in the VON.

Conclusions: Mortality and most morbidity rates of our center compare favorably with international standards, but rates of BPD and growth failure are concerning. Regular benchmarking process is crucial to audit any change in clinical outcomes after implementation of local quality improvement project.

Retrospective Study of Paediatric Patients with Macrolide Resistant Mycoplasma Pneumoniae in a Regional Hospital in Hong Kong

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Background: Community-acquired pneumonia (CAP) remains a frequent cause of morbidity and mortality worldwide, and *mycoplasma pneumoniae* is well known as a common causative agent. *M. pneumoniae* infections can usually be effectively treated with macrolides, which are generally considered the first-choice antibiotics in children, but there has been recent concern over emerging macrolide resistant strains of *M. pneumoniae* and rates vary greatly across continents. The treatment of choice for macrolide resistant mycoplasma pneumonia include tetracycline and quinolone group of antibiotics, which both raise concerns over potential side effects when used in children.

Aim: This study looks at patients admitted with *M. pnuemoniae* to a large regional hospital in Hong Kong. The aim is to extend the data surveillance for a clearer perspective on the resistance rate in our local community and to compare characteristics of macrolide resistant mycoplasma pneumoniae (MRMP) to identify associated clinical parameters predicting resistance with implications in guiding treatment with antibiotics alternative to those in the macrolide group.

Results: MRMP was identified in 43% of the patients tested within our study period. Clinical parameters and radiological changes did not show significant factors to help differentiate clinically those likely with MRMP. A clinical parameter of non-defervescence by 72 hours is identified as a statistically significant clinical indicator for likely macrolide resistance.

Conclusion: Patients in the MRMP group appeared to have a higher rate of developing complications and requiring additional clinical support. Time to defervescence with a cut off at 72 hours showed a discriminative ability to identify those likely with macrolide resistant mycoplasma pneumonia supporting the clinical decision in early switch to doxycycline therapy particularly balancing the risks of adverse effects in the younger population of children. This would overall shorten the length of stay and decrease the burden of such a common and treatable condition in the paediatric population to the overall health care system in Hong Kong.

Endocrine Dysfunction in Paediatric Patients with Primary Brain Tumours: A Single Centre Analysis in Hong Kong

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Aim: To evaluate the frequency and timing of occurrence of endocrine complications in patients with childhood brain tumours and to identify predictors for their occurrence.

Methods: Patients' medical records from 1st January 2000 to 31st October 2014 were retrospectively reviewed for patient characteristics, tumour information and treatment data. The identification of endocrine dysfunctions (included growth hormone deficiency, hypothyroidism, cortisol deficiency, hypogonadism and diabetes insipidus) was based on biochemical investigations and endocrine stimulation tests.

Results: Sixty-seven patients were included in the study. The mean age of tumour diagnosis was 9.7±4.8 years and the mean time of follow up was 5.5±4.4 years. One or more endocrine dysfunctions were detected in 32 patients (47.8%). Hypothyroidism was the commonest endocrine dysfunction, accounting for 46.3% of all patients (n=31), followed by cortisol deficiency (n=21, 31.3%), diabetes insipidus (n=19, 28.4%), growth hormone deficiency (n=16, 23.9%) and hypogonadism (n=12, 17.9%). Endocrine dysfunctions were detected at diagnosis or during follow up. Age, pathological diagnosis and tumour location were associated with development of endocrine dysfunction in univariate analysis, and suprasellar location of the tumour was identified as a significant independent predictor for all types of endocrine dysfunction except diabetes inspidus. There was no significant predictor associated with development of diabetes inspidus in this study.

Conclusion: Endocrine dysfunctions detected either at diagnosis or during follow up were common in paediatric brain tumour patients. Suprasellar tumour is significantly associated with development of endocrine dysfunctions. Regular endocrine evaluation is essential starting from the diagnosis of disease and should be continued as long term surveillance after completion of treatment.

Self-limiting "IDiopathic" Neonatal Hepatitis – The Earliest Clinical Feature of Niemann Pick Disease Type C

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Background: Niemann Pick disease type C is a rare lipid storage disorder, with estimated incidence of 1 in 12000 live births. Patients (apart from the perinatal form) commonly presents with neurological impairment, particulary in the form of developmental regression. With the availability of substrate reduction therapy, Miglustat, it is important to start the treatment early with the first sign of neurological impairment, especially for the juvenile form, of which statistical significant and persistent efficacy had been demonstrated. Therefore, early diagnosis and delineation of early clinical features are important.

Method and Results: We have retrospectively reviewed the clinical features of 4 patients with definitive diagnosis of Niemann Pick disease type C in the Prince of Wales Hospital. For patients with available early infancy data, a self-limiting period of significant neonatal hepatitis, with level of conjugated hyperbilirubinemia and alanine transaminase peaking at around 2nd month of life, and spontaneous resolution by 3-5 months of age were observed. In contrary to the previously reported, hepato-/splenomegaly could be absent in the infancy period. Patients were then remained well, thriving until the onset of neurological impairment.

Conclusion: Our finding was consistent with that previously reported by Vanier et al and Kelly et al that neonatal cholestasis was a common feature of early liver involvement in Niemann Pick disease type C. One exception was the absence of hepato-/splenomegaly in one patient of our series as compared to all patients with hepatosplenomegaly reported by Kelly et al. The limitations of this case series were the small sample size of only 4 patients and incomplete neonatal data. Nevertheless, the observation from this case series highlighted the importance in embarking on the differential diagnosis of Niemann Pick disease type C in patients with a history of self-limiting "idiopathic" neonatal hepatitis with or without hepato-/splenomegaly, an apparent period of "normality" and subsequent development of neurological impairment. Moreover, a well-designed prospective study to follow on the outcome of patients with self-limiting "idiopathic" neonatal hepatitis is important to delineate the proportion of patients with inborn error of metabolism.

Sexually Transmitted Disease in Child Sexual Abuse Victims in a Regional Hospital Over a Period of 15 Years

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Objective: The objective of this study is to review the incidence of sexually transmitted disease (STD) in child sexual abuse victims in a regional hospital in Hong Kong of a 15 years period (1st January 1999 to 31st December 2013).

Method: Subjects were identified through Clinical Development and Reporting System (CDARS) using the diagnostic coding of child sexual abuse (ICD-9: 995.53 child sexual abuse and V61.21 sexual abuse of child, as reason for family seeking advice) in the period from 1st January 1999 to 31st December 2013. Parameters including age, sex, types of abuser, testing of STD and its results were retrieved.

Results: A total of 235 cases were identified with 88 cases excluded because of sexual abuse not involving genital contact or STD screening not performed. There were 147 patients included (F=144, M=3). Their age ranged from 3 to 17 years old with mean age of 12.4 years and modal age of 14 years. There was a surge after 12 years old and after 2005. Sexually transmitted diseases were diagnosed in 29 patients (19.7%), Chlamydia Trachomatis=19, Neiserria Gonorrhoea=7, Herpes Simplex type 2=1, Human Papilloma Virus=1 and Trichomonas vaginalis=1. There was no syphilis or HIV identified. Peer group including classmate, schoolmate, boyfriend or friend were the commonest abusers identified (n=61). Family members & relatives (n=32), Internet friends (n=28), strangers (n=11), neighbors (n=6) and teachers/employers (n=2) were the other abusers identified. In 7 cases, the abusers were not identified. In the STD group, the Internet friend was the commonest abuser (35%, n=10) whereas they were found in 15% (n=18) in non-STD infected victims. It is statistically significant (p=0.032, OR 2.92 (95% CI 1.17-7.30)). Seven girls contracted teenage pregnancy (4.8%) and three patients suffered from pelvic inflammatory disease (2%).

Conclusion: This is the first study investigating the incidence of STDs in child sexual abuse victims in Hong Kong. Internet friends being the abusers, is a risk factor for STDs in child sexual abuse victims. This should raise the healthcare worker awareness. More education should be conveyed to adolescents for self-protection.

Retrospective Review of Neonatal Abstinence Syndrome in a Regional Hospital in Hong Kong

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Background and aims: Neonatal abstinence syndrome (NAS) was known to cause prolonged and intensive hospital cares and adverse effects on the newborns. Recent overseas studies have shown a rapid increase in maternal opioid use and NAS in western countries over the last decade. There is no recent local study concerning NAS in Hong Kong. In this review, we evaluated the epidemiology of NAS requiring pharmacological treatment in the New Territories West Cluster in a hope to provide local data for physicians in counselling NAS parents and facilitate health directors in the resources allocation planning.

Methods: A retrospective review was undertaken of infants born by mothers with opioid abuse in a regional hospital during year 2003-2014 and those with NAS requiring pharmacological treatment were identified. The demographic data and clinical progress were retrieved by case record review.

Results: Ninety nine infants were identified to suffer from NAS and required pharmacological treatment from year 2003 through 2014. Among them, 24.2% were born prematurely and 43.4% were small for gestational age (SGA). There were more term infants with SGA (49.3% Vs 25%) (P = 0.036) when compared with preterm infants. It was found that 5 days' observation was able to detect 98% of babies who required pharmacological treatment. For those with exclusive heroin exposure, 3 days observation may be enough. The duration of treatment ranged from 5 days to 57 days while the hospital stay ranged from 10 days to 65 days.

Conclusions: We observed a decreasing trend of NAS requiring pharmacological treatment, likely due to the declining number of opioid abusers in Hong Kong and the work of the Comprehensive Child Development Service program. However, NAS still posed significant adverse effects on the newborns such as SGA, prematurity and prolonged hospital stay. Based on our findings, the optimal observation period may be shortened to 5 days while for those with exclusive heroin exposure, 3 days observation may be enough. A bigger and more comprehensive longitudinal study involving different regions in Hong Kong would be needed to better evaluate this condition including the short term and long term outcomes.

The Effect of Resistance Training on Vascular Health and Cardiovascular Risk Factors in Non-obese Active Adolescents

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Background and aims: This study determined the benefits of a randomised controlled trial of 10-week's resistance training progamme on vascular function and cardiovascular risk factors in 38 lean and active 11-13 year olds. Thirty-eight lean and active boys and girls were recruited from a Hong Kong Government secondary school and were randomised into a resistance training group (RTG) and control group (CG). The children in the RTG received 10-week supervised, in-school resistance training, twice per week, each session lasting for 70 minutes.

Methods: Main outcome measures taken before and after training included brachial endothelial dependent dilation, body composition, fasting serum lipids, fasting glucose and insulin, high sensitive C-reactive protein, 24-hour ambulatory blood pressure and aerobic fitness.

Results: There were no baseline differences between the two groups for any of the anthropometric variables. Main effects for time (p's<0.05) in a number of anthropometric, metabolic and vascular variables were noted; however, there were no significant interactions indicating the change was more likely an outcome of normal growth and development as opposed to a training effect. The only training related change was in endothelial dependent dilation which increased from 8.5% to 9.8%.

Conclusion: Ten weeks of resistance training in school appeares to have some vascular benefit in active, lean children.

Acknowledgements: We are grateful to Mr. Tsang Fan Pong for assisting in the exercise training class in this study. This project was funded by the University of Hong Kong Small Project Fund and the University of Hong Kong Research Council Strategic Research Theme Public Health.

Poster Presentations – Case Reports

A Teenage Boy with Primary Angiitis of Central Nervous System

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Background and aims: Primary angiitis of central nervous system (PACNS) is a rare disease resulting in inflammation and destruction of CNS vessels without evidence of vasculitis outside CNS. It remains a challenge to clinicians in terms of its non-specific presentations and lack of highly efficient non-invasive modalities for diagnosis. Early intervention with immunosuppressive agents within the narrow window of opportunity to prevent progressive brain injury is important but often delayed. This case report of PANCS should raise the interest and awareness of this challenging but treatable disease. It is also the first local case report of PACNS being treated with arterial bypass surgery.

Case: He is a 15-year-old boy presented with loss of consciousness in street. He was found to be disorientated and have slurring of speech upon admission. The first CT brain showed no parenchymal abnormality. He then developed right upper limb weakness and his slur speech worsened. Repeated CT brain showed extensive infarct of left frontal lobe and left lentiform nucleus. Urgent MRI and MRA brain revealed recent infarct of left middle cerebral artery (MCA) territory. There were luminal irregularities of left anterior cerebral artery (ACA) and left MCA. Extensive workup including blood tests and CSF examination for infections, autoimmune diseases, thrombophilia screening were all negative. He was treated as PACNS with pulses of methylprednisolone and seven monthly doses of intravenous cyclophosphamide infusions. Follow-up MRI brain and cerebral MRA still showed progressive narrowing of left ICA. He was then put on mycophenolate mofetil (MMF) and recently, extracranial-intracranial (EC-IC) bypass surgery was performed. Post-op MRI/A showed improved vascular narrowings and perfusion. He has residual right upper limb weakness and some cognitive impairment.

Conclusion: This is a case of progressive angiographic positive PACNS presented with acute stroke. The exclusion of mimics of reversible cerebral vasoconstriction syndromes is difficult but crucial. Early recognition and treatment improved morbidity and mortality. The efficacy of extracranial-intracranial arterial bypass in preventing future stroke has not been studied in the contest of PACNS but is potentially beneficial in terms of restoring cerebral perfusion. This is the first local case report of surgical intervention for this disease entity.

Adenocarcinoma of the Gastrointestinal Tract in a 10-year-old Girl

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Cancer of the gastrointestinal tract is a rare entity in the paediatric population, and it carries high mortality. We report a case of a 10-year-old girl presented with a history of abdominal pain and vomiting for two weeks. Computer tomography and positron emitting tomography revealed multisystem involvement of disease, including inflamed ileocaecal junction, bilateral lung consolidation, multiple enlarged lymph nodes and left ovarian mass. Adenocarcinoma was diagnosed three weeks after admission following left ovary biopsy and laparotomy. We conclude that any unusual abdominal symptom should be evaluated carefully and investigated by imaging and endoscopy, and joint assessment with paediatric surgeons and radiologists is also recommended.

Hypertriglyceridemia Secondary to Congenital Generalised Lipodystrophy in a Four Months Old Baby

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Introduction: Lipodystrophy is a group of rare heterogeneous disorders characterised by the complete or partial loss or absence of subcutaneous adipose tissue. Lipodystrophy can be congenital or acquired, generalized or partial. Congenital generalised lipodystrophy (CGL) is a group of at least eight different genetic disorders characterised by a generalised lack of adipose tissue at birth and is accompanied by prominent muscularity and subcutaneous veins. Diagnosing CGL early is important as there are a number of associated metabolic derangements like insulin resistance, diabetes mellitus, hepatic steatosis and dyslipidemia that may be amenable to dietary and therapeutic interventions.

Case report: Here we reported a four months baby boy HY who presented with feeding problem and failure to thrive since two weeks of age. Physical examination revealed an active baby with a pointed chin, triangular face and prominent eyes. He appeared generally 'muscular' with almost absent subcutaneous fat. Abdomen appeared distended with mild hepatomegaly. Blood was noted to be lipemic during venipuncture. HY's pre-meal serum triglyceride was 13 mmol/l (<1.7). Total cholesterol, HDL cholesterol and LDL cholesterol were within the normal range. The diagnosis of Congenital generalised lipodystrophy due to mutation in 1-acylglycerol-3-phosphate-O-acyltransferase 2 (*AGPAT2*) was confirmed by molecular genetic testing with two heterozygous mutations identified. c.646A>T. p. (Lys216*) was a known pathogenic mutation resulting in premature termination of protein translation. c.396_398delCAT. p.(Ile132del) was a likely pathogenic mutation resulting in an in-frame deletion of an isoleucine residue at position 132.

HY was switched to a semi-elemental formula pepti junior which has 50% of the fat content in the form of medium chain triglyceride. Serum triglyceride level fell promptly to 1.9 mmol/l two weeks after starting pepti junior and has remained within the normal range since.

Conclusion: The cardinal feature of lipodystrophy is the selective loss of subcutaneous adipose tissue giving rise to an apparent 'muscular' appearance. It is important to recognise this feature clinically as this is often the first step towards diagnosing congenital lipodystrophy disorders. The associated metabolic complications are often amenable to treatment which may improve the long term outcome for this group of patients.

Maternal Carnitine Uptake Defect Uncovered by Newborn Screening

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Introduction: Newborn screening enables early identification of babies who may be affected by a number of inborn errors of metabolism (IEM). Affected individuals picked up pre-symptomatically can have treatment instituted at the earliest instance enhancing the best possible treatment outcome. Since the wide implementation of expanded newborn screening, it is increasingly recognised that a number of maternal IEM conditions may be uncovered through screening performed on their newborn babies.

The Centre of Inborn Errors of Metabolism started the first pilot expanded newborn metabolic screening programme in Hong Kong since July 2013. Over the last 24 months, more than 18,000 newborn babies have been screened. Among the five confirmed IEM cases, one was diagnosed with maternal carnitine uptake defect (CUD). CUD is an autosomal recessive disorder caused by mutations in the *SLC22A5* gene that encodes the carnitine transporter OCTN2. Symptomatic CUD patients may present in infancy with hypoketotic hypoglycemia, hepatomegaly, elevated transaminases, hyperammonemia, skeletal myopathy and cardiomyopathy. CUD is very amenable to carnitine supplementation.

Case: Newborn screening performed on a term Day 2 baby showed a positive result with low free carnitine which was confirmed by a low serum free carnitine of 3.2 umol/l (19.3-53.9). Mother's serum free carnitine was also low at 1.6 umol/l. Both baby and mother's acylcarnitines were all low. Molecular genetic test confirmed baby to be heterozygous for a novel *SLC22A5* mutation c.393+5_393+11delGTGCCGG (Genbank accession number NM_003060.3). Mother was compound heterozygous for the same mutation as well as a known pathogenic mutation c. 695C>T, p. (Thr232Met). The diagnosis of CUD was confirmed in the mother and baby was a carrier of the condition.

Conclusion: Low carnitine ascertained during newborn screening may be due to low maternal plasma carnitine levels. Our patient was born to a mother with undiagnosed and untreated carnitine uptake defect who despite a very low free carnitine level remained entirely asymptomatic. Her baby's low free carnitine detected at newborn screening was a reflection of her low free carnitine level. Asymptomatic or minimally symptomatic mothers with IEM detected through newborn screening broaden the wide phenotypic spectrum of these IEM conditions. Treatment of these asymptomatic mothers remains highly controversial.

A Rare Case of Ambiguous Genetalia and Nephroapthy– Frasier Syndrome

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Aim: WT1 mutation affects the kidney and gonadal development, and the phenotypic presentation depends on the type of mutation. We report a young boy with Frasier Syndrome who presented with ambiguous genitalia and heavy proteinuria.

Methods: Retrospective Review of a 25-month-old boy was performed. He was born with ambiguous genitalia (bifid scrotum,hypospadia with penoscrotal fistula) at birth. His karyotype was 46XY and endocrinological work ups were normal. He then presented at 20 months of age with incidental finding of heavy proteinuria (urine protein/ creatinine ratio 17 mg/mg) and hypoalbuminaemia (albumin level 21 g/dL) during an admission for acute bronchiolitis. His proteinuria was resistant to prednisolone therapy and therefore renal biopsy was done. His renal biopsy was reported to be membranous nephropathy, and he showed partial response to cyclosporine A therapy. In view of the past history of ambiguous genitalia and steroid resistant nephrotic syndrome, genetic test for WT1 mutation was requested.

Results: Heterozygous mutation on the WT1 gene was detected in this patient (NM_024426.4(wt1): c.1432+4C>T). The diagnosis of Frasier syndrome was confirmed and the mutation was likely to be *de novo*. Patients with Frasier syndrome are at risks of gonadal malignancy and therefore cyclosporin A was discontinued. Patient would undergo testicular biopsy and closely monitor for the development of gonadal malignancies.

Conclusion: WT1 mutation is uncommon but should be considered in patient with steroid resistant nephrotic syndrome with ambiguous genitalia, delayed puberty or family history of the above.