International Journal of Pediatric Endocrinology 2015, Volume 2015 Suppl 1
http://www.ijpeonline.com/supplements/2015/S1

INTERNATIONAL JOURNAL OF PEDIATRIC ENDOCRINOLOGY

MEETING ABSTRACTS Open Access

Abstracts from the 8th APPES Biennial Scientific Meeting

Darwin, Australia. 29 October – 1 November 2014

Published: 28 April 2015

These abstracts are available online at http://www.ijpeonline.com/supplements/2015/S1

ORAL PRESENTATIONS

PLENARY LECTURES

O1

Child growth trajectories to adult disease: lessons from UK birth cohort studies

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O1

The developmental origins of health and disease theory purports that early life factors determine long-term risks of death and disease. Historical studies, prospective birth cohorts such the UK ALSPAC birth cohort [1], and more recently genetic studies [2] indicate that the rapid weight gain trajectory to later obesity starts in the first months of life, even from birth. Rapid infant weight gain and childhood overweight lead to earlier pubertal maturation in boys and girls, and in turn these adolescent traits are predictive for obesity, diabetes, hypertension and cardiovascular disease events in later life. Understanding of the nutritional, parental and wider determinants of rapid infant weight gain are informing the development of obesity prevention strategies starting in early life [3].

In contrast to the above 'rapid growth tempo' trajectory to later disease, poor childhood growth is also a risk factor for later health and survival. This 'early childhood stunting' trajectory is seen in older UK birth cohorts, such as the 1946 British Birth Cohort Study [4], and is likely relevant to current children in lower and middle-income countries. The relative importance of these distinct childhood trajectories for later health likely depends on the prevailing nutritional environment. However, in those populations that are undergoing rapid nutritional transition from under- to over-nutrition, the adverse combination of early childhood stunting followed by transition to overweight and obesity will be particularly detrimental to later health.

References

1. Ong KK, Ahmed ML, Emmett PM, Preece MA, Dunger DB: **Association between postnatal catch-up growth and obesity in childhood: prospective cohort study.** *BMJ* 2000, **320(7240)**:967-971.
2. Elks CE, Loos RJ, Sharp SJ, Langenberg C, Ring SM, Timpson NJ, *et al*: **Genetic markers of adult obesity risk are associated with greater early infancy weight gain and growth.** *PLoS Med* 2010, **7(5)**:e1000284.
3. Lakshman R, Elks CE, Ong KK: **Childhood obesity.** *Circulation* 2012, **126(14)**:1770-1779.
4. Ong KK, Hardy R, Shah I, Kuh D, National Survey of Health and Development Scientific and Data Collection Teams: **Childhood stunting and mortality between 36 and 64 years: the British 1946 Birth Cohort Study.** *J Clin Endocrinol Metab* 2013, **98(5)**:2070-2077.

O2

IGFBP-2: a critical player in cancer and metabolism

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O2

Insulin-like growth factor binding protein-2 (IGFBP-2) is widely abundant in fetal life and remains highly expressed in the brain throughout life. It plays a key role in targeting IGFs to their receptors in developing organs [1]. It is also highly expressed by a broad range of aggressive cancers such that its ablation reduces cancer growth. IGFBP-2 has also recently been recognised to play a key role in metabolic regulation.

We have been investigating the role and mechanisms of action of IGFBP-2, and have developed unique insights into its structure-function relationships. Our work has mostly focused on neuroblastoma cell lines of varying aggressiveness and motility, and our manipulations of the IGFBP-2 molecule have allowed functional characterisation.

We have demonstrated that the IGFBP-2 molecule contains a critical central basic region, the heparin-binding domain (HBD), which accounts for its binding to cell surface, critical in targeting IGFs to their receptors. Ablation of this domain dramatically reduces both proliferation and motility of these cancer cells, a process also involving integrin receptors [2].

This same region of the molecule also contains a Nuclear Localisation Sequence (NLS) accounting for the ability of IGFBP-2 to enter the cell nucleus. This process leads to induction of transcription of a range of cancer-promoting genes including VEGF, promoting angiogenesis in a chick embryo model, intrinsic to carcinogenesis. Ablation of the NLS blocks these processes [2,3].

Circulating IGFBP-2 is reduced in obesity and other insulin-resistant states and in animal models can enhance insulin sensitivity. It is regulated by the insulin sensitiser, leptin, and in a sheep model we have demonstrated that centrally administered leptin induces IGFBP-2 expression in skeletal muscle, via the sympathetic nervous system. Similarly, leptin applied directly to cultured skeletal muscle cells induces IGFBP-2 expression, leading to enhanced insulin sensitivity. This suggests that IGFBP-2 may mediate leptin's insulin-sensitising effects [4].

IGFBP-2 also acts on visceral, but not subcutaneous adipose tissue, inhibiting fat accumulation, an effect not seen when the HBD region is mutated or integrin blockade is applied. Thus IGFBP-2 appears to play a beneficial role in regulating the function of visceral fat, which is critical in the pathogenesis of metabolic complications of obesity.

IGFBP-2 is thus a critical player in both cancer biology and in metabolic syndrome. There is potential for targeted pharmacologic manipulation of IGFBP-2 activity in order to reduce the morbidity and mortality of these major diseases in our society.

References

1. Russo VC, Gluckman P, Feldman EL, Werther GA: **The insulin-like growth factor system and its pleiotropic functions in brain.** *Endocrine Reviews* 2005, **26(7)**:916-943.
2. Azar WJ, Azar SHX, Higgins S, Hu J, Hoffman AR, Newgreen DF, *et al*: **IGFBP-2 Enhances VEGF Gene Promoter Activity and Promotion of Angiogenesis by Neuroblastoma Cells.** *Endocrinology* 2011, **152(9)**:3332-3342, [Epub ahead of print].
3. Azar WJ, Zivkovic S, Werther GA, Russo VC: **IGFBP-2 Nuclear Translocation is mediated by a Functional NLS sequence and is Essential for its Pro-tumorigenic Actions in Cancer Cells.** *Oncogene* 2014, **33(5)**:578-588.
4. Yau SW, Henry BA, Russo VC, McConell GK, Clarke IJ, Werther GA, Sabin MA: **Leptin enhances insulin sensitivity by direct and sympathetic nervous system regulation of muscle IGFBP-2 expression: evidence from nonrodent models.** *Endocrinology* 2014, **155(6)**:2133-2143.

O3

Weird animal genomes, sex and the evolution of new sex genes

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O3

In humans and other mammals with XX females and XY males, the Y bears a gene (SRY) that induces testis differentiation in the embryo and switches on hormones that masculinize it. The human X has more than 1500 genes, but the tiny Y is a genetic wasteland and bears only 45 protein-coding genes, most active only in testis. To discover how human sex chromosomes got to be so weird, we compared the chromosomes, genes and DNA in distantly related mammals and even birds and reptiles (with completely different sex determining systems). Kangaroo sex chromosomes reveal the original mammal sex chromosomes, while the bizarre platypus sex chromosomes (more related to those of birds) tell us that human sex chromosomes and the SRY gene are relatively young. The human X and Y evolved from an ordinary chromosome pair as the Y degraded progressively. If Y degradation continues at this rate, it will disappear in just 5 million years. If humans don't become extinct, new sex determining genes and chromosomes must evolve, maybe leading to the evolution of new hominid species.

Where will our new sex genes and chromosomes come from? Whereas mammals (and birds) have rather rigid systems, other vertebrates (particularly reptiles) show great variation in sex determining systems, and we can find many examples of switches in sex determining systems. Using a model of dosage-dependent and temperature dependent sex determination, we can readily understand switches between temperature-dependent and chromosome-dependent sex determination, and even between XY and WZ systems. We also see many ways in which genes or gene copies (often of the same genes which seem to be particularly good at this role) have taken on a sex determining function, and defined new sex chromosome systems.

SYMPOSIA: GROWTH

O4

How databases inform clinical management – insights from ozgrow

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O4

Recombinant human growth hormone (GH) has been used as an effective treatment for short stature since the late 1980's. Although clinical trials were crucial in developing GH treatment strategies, database analyses have the potential to provide additional information with regard to treatment efficacy and safety. The OZGROW database was established in 1989 as an initiative of the Australasian Paediatric Endocrine Group (APEG) to allow monitoring of children receiving GH under the national Pharmaceutical Benefits Scheme (PBS). There are currently (June 2014) 1948 children receiving subsidised GH treatment in Australia and the OZGROW database contains records from 6959 individuals. This unique resource has allowed a number of clinically relevant questions to be addressed.

Defining short stature and therefore eligibility for GH treatment relies on the use of appropriate growth standards. There has been debate as to whether the World Health Organisation (WHO) or the Center for Disease Control (CDC) growth charts best describe the heights of contemporary Australian children. There appears to have been a positive secular trend for height in Australian children such that both charts under-estimate the number of children eligible for growth hormone treatment.

Ascertainment bias has been proposed as an explanation for the fact that more boys than girls receive GH treatment. Analysis of the OZGROW database demonstrated that ascertainment bias did not appear to be a major factor explaining the gender discrepancy. It is possible that biological factors influencing the tempo of growth and development may contribute to the greater number of boys receiving growth hormone.

Another issue that has complicated comparisons of international studies of growth hormone response has been the different dosing schedules used. A simple method for converting weight and surface area based doses was therefore developed. Further analysis suggested that the surface area based protocol used in Australia may disadvantage older children, given that the dose per kilogram reduces over time even if the dose per meter squared remains constant.

The importance of commencing GH treatment early and maximising height gain during the first year of treatment was also highlighted by analysing GH responsiveness in a number of conditions including Turner syndrome, Prader-Willi syndrome and idiopathic short stature. Ensuring that referring physicians are able to diagnose these conditions in a timely fashion therefore remains a priority.

Although the OZGROW database has allowed clinically relevant questions to be studied there remain a number of challenges, particularly with regard to long term follow up.

Acknowledgements: Presented on behalf of OZGROW subcommittee members

O5

Growth hormone responsiveness: why does it vary and can it be predicted?

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O5

Initial response to growth hormone (GH) varies considerably. In severe GH deficiency initial response varies across the group by almost 100%. In common non-GH deficient disorders such as idiopathic short stature (ISS) and children born small for gestational age (SGA) initial response varies by more than 100%.

The explanation for the wide response to GH treatment can be clustered into three broad groups; (i) non-compliance with GH therapy, (ii) clinical characteristics associated with GH responsiveness and (iii) mutations and common gene variants in the GH-IGF-I axis.

(i) Non-compliance with GH therapy: The commonest explanation for variable GH response is missed GH doses. In a national prospective study of GH compliance in New Zealand children; 34% of children missed more than one GH dose per week. Maori and Pacific children missed an additional GH dose each week than Caucasian children. Predictably, poor compliance (≥4 doses/week missed) was associated with a far poorer growth response than good compliance (height velocity SDS +0.4 vs

+2.8). Even moderate compliance (2-3 doses/week missed) was associated with a poorer growth response (height velocity SDS +1.4 versus +2.8). Interestingly, paediatricians were unaware of GH non-compliance. GH response can only be maximised when more effective GH delivery devices are developed that record the date and time GH is administered to enable paediatricians to more effectively address compliance.
(ii) Clinical characteristics associated with GH responsiveness: There is a differential response to GH therapy according to the underlying disorder. GH deficient children are more responsive than those with Turner Syndrome or idiopathic short stature who are in turn more responsive than SGA children (as shown by height velocity and serum IGF-I for a given GH dose). Furthermore, across the normal birth weight range we have recently shown that progressive reduction in birth weight SDS is associated with a progressively lower IGF-I response during IGF-I generation testing. Across growth disorders; more severe GH deficiency, taller parents, shorter stature, younger age at the start of treatment and heavier children are all parameters found to be associated with greater initial and sustained response to GH treatment. Michael Ranke has pioneered individualised GH dosing through GH prediction modelling across growth disorders. GH response can be predicted by inserting common clinical characteristics into a prediction equation that includes adjusting the dose. Prediction modelling is of greatest benefit to children with adverse clinical characteristics in whom greater initial GH doses will lead to greater growth response.
(iii) Mutations and common gene variants in the GH-IGF-I axis: Downstream gene mutations in this axis (GH receptor, IGF-I and IGF-I receptor) are relatively rare causes of short stature, poor growth and GH response. Conversely common gene variants are being increasingly sought that influence stature, growth and GH responsiveness. Initial reports suggested a common GH receptor exon 3 deletion was associated with a better response to GH than the full length form in SGA and ISS children. Further studies have found little if any effect of the GH receptor deletion on initial or sustained growth response in SGA, Turner Syndrome or GH deficiency. Future studies are likely to focus on panels of common gene variants across the GH axis rather than examining individual genes to better characterise GH responsiveness.

SYMPOSIA: ADRENAL

O6

Diagnosis and management of rare forms of CAH

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O6

Congenital adrenal hyperplasia (CAH) is one of the most common inherited metabolic disorders. It comprises a group of autosomal recessive disorders caused by the mutations in the genes encoding for steroidogenic enzymes that are involved in cortisol synthesis [1]. More than 90% of cases are caused by a defect in the enzyme 21-hydroxylase. Four other enzyme deficiencies (P450scc, P450c17, P450c11β, 3βHSD) in the steroid biosynthesis pathway [2-4], along with one cholesterol transport protein defect (StAR) [5], and one electron-transfer protein (P450 oxidoreductase) [6] account for the remaining cases. In these rare forms of CAH, so-called "atypical CAH", the clinical and hormonal phenotypes can be complicated, and are not well characterized. The clinical symptoms of the different forms of CAH result from the particular hormones that are deficient and those that are produced in excess. A characteristic feature of CAH is genital ambiguity or disordered sex development (DSD), and most variants are associated with glucocorticoid deficiency. This talk will focus on the diagnosis and management of the variant forms of CAH other than 21-hydroxylase so-called "atypical CAH", including the genetic analyses, and phenotypic correlates.

References

1. Miller WL, Auchus RJ: **The molecular biology, biochemistry, and physiology of human steroidogenesis and its disorders.** *Endocr Rev* 2011, **32(1)**:81-151.
2. Sahakitrungruang T, Tee MK, Speiser PW, Miller WL: **Novel P450c17 mutation H373D causing combined 17α-hydroxylase/17,20 lyase deficiency.** *J Clin Endocrinol Metab* 2009, **94(8)**:3089-3092.
3. Sahakitrungruang T, Tee MK, Blackett PR, Miller WL: **Partial defect in the cholesterol side-chain cleavage enzyme, P450scc (CYP11A1) resembling non-classic congenital lipoid adrenal hyperplasia.** *J Clin Endocrinol Metab* 2011, **96(3)**:792-798.
4. Jeandron DD, Sahakitrungruang T: **A novel homozygous Q334X mutation in the HSD3B2 gene causing classic 3β-hydroxysteroid dehydrogenase deficiency: An unexpected diagnosis after a positive newborn screen for 21-hydroxylase deficiency.** *Horm Res Paediatr* 2012, **77(5)**:334-338.
5. Sahakitrungruang T, Soccio RE, Lang-Muritano M, Walker JM, Achermann JC, Miller WL: **Clinical, genetic and functional characterization of four patients carrying partial loss-of-function mutations in the steroidogenic acute regulatory protein (StAR).** *J Clin Endocrinol Metab* 2010, **95(7)**:3352-3359.
6. Sahakitrungruang T, Huang N, Tee MK, Agrawal V, Russell WE, Crock P, *et al*: **Clinical, genetic and enzymatic characterization of P450 oxidoreductase deficiency in four patients.** *J Clin Endocrinol Metab* 2009, **94(12)**:4992-5000.

O7

Recent advances in management of phaeochromocytoma

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O7

Pheochromocytoma (PCC) and paraganglioma (PGL) are the neuroendocrine tumours that arise in adrenal medulla or extra adrenal sympathetic and parasympathetic paraganglia. Paraganglia are small organs that mainly consist of neuroendocrine cells derived from the embryonic neural crest that have the ability to synthesize and secrete catecholamines. Sympathetic PGLs are usually located in the chest, abdomen, or pelvis while parasympathetic PGLs are distributed along parasympathetic nerves in the head, neck, and upper mediastinum, also referred to as head and neck PGL (HNP). PCC/PGLs can be either functional (sympathetic) or non-functional (parasympathetic) based on catecholamine synthesis and secretion.
In children diagnosed with hypertension, up to 1.7% have a catecholamine-secreting neoplasm. The majority of these tumours in childhood are PCC/PGLs. Incidence rates of PCC/PGLs are estimated at 0.3 cases per million per year or less. Approximately 10 –20% of these cases are diagnosed during childhood. Approximately half of the apparently sporadic PCC/PGLs that present in patients younger than 18 years are due to an identifiable germline mutation and this increases up to 70% in children less than 10 years of age. Hereditary tumor syndromes associated with PCC include Von Hippel-Lindau (VHL) disease, multiple endocrine neoplasia 2 (MEN-2), the familial PGL syndromes and rarely, neurofibromatosis (NF) type 1. Recently, many other genes are found to be involved in pathogenesis of PCC/PGLs. Hereditary PCC/PGLs are often multifocal and, in the case of PCC, frequently bilateral.
Children usually present becauseof symptomatic catecholamine hypersecretion or, less often, due to tumor mass effects (e.g. pain), or as an incidental radiographic finding, or because of family screening. At present, the diagnostic test of choice is the measurement of fractionated plasma and/or urine metanephrines (metanephrines and normetanephrines). A four-fold increase above the reference range is associated with an almost 100% probability of the presence of a catecholamine-secreting tumor.
^{123}I-metaiodobenzylguanidine(MIBG) is a highly specific test that can confirm the catecholamine-secreting nature of a tumor, localize tumors not seen with cross-sectional imaging, and identify other sites of disease as well as metastasis. Because MIBG testingis not 100% sensitive, particularly in some genetic mutations, recently other functional scans have been studied in the evaluation of PCC/PGL: ^{18}F fluorodihydroxyphenylalanine (DOPA) positron emission tomography (PET), ^{18}F fluorodopamine (FDA) PET,^{18}F fluorodeoxyglucose (FDG) PET.
Surgical resection is the mainstay in the treatment of PCC/PGLs. It should be done after adequate alfa and beta adrenergic blockade to minimize the hemodynamic fluctuation during surgery. Laparoscopic adrenalectomy is the preferred procedure for most PCC. Laparotomy should be considered in patients with large PCC and/or a concern for underlying malignancy based upon the clinical presentation or radiographic appearance of the tumor. In the setting of bilateral PCC, cortical-sparing procedures should be considered for the adrenal with the least tumor bulk. The cortical-sparing approach is particularly attractive in

young children and children at risk for noncompliance with lifelong glucocorticoid and mineralocorticoid replacement. The surgical approach for removal of a PGL depends upon the location of the tumor but in selected cases can also be performed laparoscopically.
Patients with unresectable malignant tumors or distant metastatic disease can usually be treated symptomatically with adrenergic blockade. Radiation therapy or radiofrequency ablation can help with symptomatic metastatic disease, and IV bisphosphonates can be considered bony metastases, particularly in patients with bone pain or lesions that increase the risk of pathological fracture. Systemic treatment modalities are only palliative in nature and include ^{123}I-MIBG therapy, peptide receptor radiotherapy (PRRT) and chemotherapy. PCC/PGLs can have unpredictable behavior and metastasize late in the clinical course. In addition, children in particular are at risk for the development of metachronous tumors. This makes long-term follow-up mandatory in children with PCC/PGL.

O8
Genetic and functional study of StAR (steroidogenic acute regulatory protein) deficiency
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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O8

Congenital lipoid adrenal hyperplasia (lipoid CAH) is the most severe form of CAH, impairing adrenal and gonadal steroidogenesis. Most cases of lipoid CAH are caused by recessive mutations in the gene encoding steroidogenic acute regulatory protein (StAR), a protein that plays an essential role in cholesterol transfer from the outer to inner mitochondrial membrane, thus providing the substrate for steroid hormone biosynthesis. Affected children typically present with life-threatening adrenal insufficiency in early infancy due to a failure of glucocorticoid (cortisol) and mineralocorticoid (aldosterone) biosynthesis, and 46,XY genetic males have complete lack of androgenization and appear phenotypically female due to impaired testicular androgen secretion in utero. Previously, the Q258X mutation of StAR was shown to account for about 70% of affected alleles in most patients of Japanese and Korean ancestry. However, it is more prevalent (92.3%) in the Korean population. These results suggest that the genetic defect in the StAR gene in Korean patients with lipoid CAH is highly homogeneous, probably reflecting a founder effect. Recently, some patients have been reported that they showed late and mild clinical presentation. These cases and studies establish a new entity of 'non-classic lipoid CAH' showing that the phenotypic spectrum of StAR mutations is substantially broader than previously appreciated.

SYMPOSIA: NORMAL WETTENHALL SYMPOSIA

O9
Recent advance in FGF23 – clinical perspectives
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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O9

Fibroblast growth factor 23 (FGF23) is a circulating factor that plays a central role in the renal reabsorption of Pi and metabolism of vitamin D. It is mainly produced by osteocytes in bone and exerts its effects on distant organs such as the kidney and parathyroid in an endocrine fashion. FGF23 increases renal Pi excretion by reducing the expression of type 2a and 2c sodium/phosphate (Na^+/Pi) co-transporters in the proximal tubules. In addition, it decreases the renal production of 1,25-dihydroxyvitamin D [1,25$(OH)_2$D] by suppressing the expression of 25-hydroxyvitamin D-1a-hydroxylase and increasing that of 25-hydroxyvitamin D-24-hydroxylase. FGF23 requires a-Klotho as well as FGF receptor to exert its effects.
FGF23 consists of 251 amino acids. Loss of function mutations in FGF23 cause familial tumoral calcinosis, which is characterized by hyperphosphatemia and increased levels of 1,25$(OH)_2$D. Autosomal dominant hereditary hypophosphatemic rickets (ADHR) is caused by mutations in the cleavage RXXR motif, which prevent inactivation of FGF23. Excess of FGF23 action results in renal phosphate wasting and an inappropriately low level of serum 1,25$(OH)_2$D. Recent studies have implicated the iron-deficiency in the late manifestation of ADHR. Tumor-induced osteomalacia is an acquired paraneoplastic syndrome of renal phosphate wasting caused by overproduction of FGF23 by tumors.
Among hereditary hypophosphatemic rickets/osteomalacia, X-linked hypophosphatemic rickets (XLH) is the most common form and is caused by deletion or inactivating mutations of the phosphate-regulating gene homologous to endopeptidase on X chromosome (PHEX). Autosomal recessive hypophosphatemic rickets type I and type II are caused by inactivating mutations of dentin matrix protein 1 (DMP1) and ectonucreotide pyrophosphatase/phosphodiesterase 1 (ENPP1), respectively. In these conditions, serum FGF23 levels are increased, which is responsible for the renal phosphate wasting and impaired vitamin D metabolism. FAM20C is a secreted kinase that phosphorylates extracellular proteins including DMP1. Recently, inactivating mutations in FAM20C have been reported in patients with increased levels of FGF23 and hypophosphatemia. PHEX, DMP1 and FAM20C as well as FGF23 are highly expressed in osteocytes, indicating the critical role of osteocytes in mineral metabolism. Hypophosphatemic rickets/osteomalacia caused by the increased bioactivity of FGF23 are classified into FGF23-mediated hypophosphatemic rickets/osteomalacia. Measurement of serum levels of FGF23 is useful for diagnosis of these conditions. Neutralization of FGF23 will be a potential treatment for XLH and other FGF23-mediated hypophosphatemic rickets/osteomalacia.

O10
Osteoporosis in children with chronic illness: lessons from natural history studies that guide clinical practice
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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O10

Children with serious chronic illnesses have the potential for significant bone morbidity, particularly in the context of disorders with impaired muscle function and the need for glucocorticoid (GC) treatment. Recently, studies have shown that vertebral fractures are often the first sign of osteoporosis in this context. Longitudinal studies have taught us that vertebral fractures are most frequent in the first year of GC therapy among children with GC-treated diseases, that vertebral fractures are often asymptomatic and thereby go undetected in the absence of routine monitoring, and that even asymptomatic vertebral fractures predict an increased risk of future fractures. Other discrete clinical predictors of incident vertebral fractures are evident early in the course of GC therapy, including decreases in spine BMD Z-scores and increases in body mass index Z-scores in the first 6 months of GC therapy. Taken together, these observations highlight that the first year of GC therapy is a critical period for monitoring in order to identify bone morbidity in a timely fashion. Children with risk factors for bone morbidity other than GC therapy (such as neuromuscular disorders and immobilization) are also at increased risk for vertebral and non-vertebral fractures fractures. As such, routine surveillance for vertebral fractures (for example, with a lateral spine radiograph) is now considered a key facet of the bone health evaluation in children with chronic immobilization or GC-treated diseases.
While some risk factors for osteoporosis will be permanent (such as immobilization arising from disorders such as cerebral palsy), other children will experience transient threats to bone health. This is an important distinction, since children with transient threats have the potential for vertebral body reshaping, either spontaneously or with bone-targeted treatment such as bisphosphonate therapy. Recovery from fracture-induced deformity is growth-dependent, underscoring the importance of timely diagnosis and intervention during childhood in those with limited potential for spontaneous vertebral body reshaping.
Prevention begins with optimization of conservative measures, including physical activity, nutrition, treatment of co-morbid endocrinopathies and aggressive treatment of the underlying disease using the lowest effective GC dose. These measures may be insufficient to prevent first-time fractures in some, raising the need for bone-specific therapy in line with a secondary prevention approach. Secondary prevention is predicated

upon identification of early signs of osteoporosis and intervention to prevent disease progression. Since bone-targeted treatment is typically reserved for children with overt fragility, careful monitoring to avoid advanced osteoporosis presentations is paramount. Bisphosphonates are the most commonly prescribed agents in children; however, interest in the use of novel osteo-anabolic therapy is mounting given bone histomorphometric observations that osteoporosis in children with serious chronic illnesses is typically characterized by significant reductions in bone turnover.

O11

Treatment of childhood osteoporosis – current and future perspectives

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O11

Bisphosphonates are the mainstay of medical therapy in the fracturing child with osteoporosis. The majority of the data in children pertains to intravenous pamidronate use in children and adolescents with osteogenesis imperfecta (OI), where pamidronate has been associated with improvements in bone mineral density, cortical thickness, vertebral shape, pain, mobility and height [1]. Side-effects of pamidronate including acute phase response to the initial dose and retardation of bone healing have also become apparent. To date, there have been no reports of osteonecrosis of the jaw. The best functional outcomes occur when bisphosphonates are given as part of a multidisciplinary approach to treatment.

More recently, bisphosphonates have been used to treat other primary and secondary osteoporotic disorders e.g. immobility and glucocorticoid. Zoledronate is a third generation bisphosphonate with a potency 100-200 times that of pamidronate. Even though both pamidronate and zoledronate have a similar mechanism of action, zoledronate has potential advantages over pamidronate in the management of paediatric bone disorders due to its shorter infusion time and longer duration of action. Zoledronate has been shown to be effective in the management of osteogenesis imperfect [2] and secondary osteoporosis [3]. The optimal regimen for intravenous bisphosphonate use in both the acute and maintenance phase of treatment remains to be developed.

Oral bisphosphonates do not appear to be as beneficial as intravenous bisphosphonates in children. Although they result in increased bone density, they do not improve bone pain or alter bone histomorphometry [4]. Larger studies await publication. Further the use of bisphosphonates in primary fracture prevention in children is yet to be investigated.

Biological agents hold promise for the future. Denosumab (RANKL inhibitor) use in children has been reported but it would appear unlikely it will be used widely. Anti-sclerostin antibodies and Dickkopf-1 (DKK1), two Wnt pathway inhibitors, however are potential treatments for primary and secondary osteoporosis with their potent effects on periosteal bone formation [5].

In summary, bisphosphonates have improved the life of children with significant bone fragility. Their use in primary fracture prevention and the utility of new agents such as anti-sclerostin antibodies and DKK1 require further investigation.

References

1. Rauch F, Glorieux FH, : **Osteogenesis imperfecta.** *Lancet* 2004, **363(9418)**:1377-1385.
2. Vuorimies I, Toiviainen-Salo S, Hero M, MÃ¤kitie O: **Zoledronic acid treatment in children with osteogenesis imperfecta.** *Horm Res Paediatr* 2011, **75(5)**:346-353.
3. Simm PJ, Johannesen J, Briody J, McQuade M, Hsu B, Bridge C, *et al*: **Zoledronic acid improves bone mineral density, reduces bone turnover and improves skeletal architecture over 2 years of treatment in children with secondary osteoporosis.** *Bone* 2011, **49(5)**:939-943.
4. Rauch F, Munns CF, Land C, Cheung M, Glorieux FH: **Risedronate in the treatment of mild pediatric osteogenesis imperfecta: a randomized placebo-controlled study.** *J Bone Miner Res* 2009, **24(7)**:1282-1289.
5. Ke HZ, Richards WG, Li X, Ominsky MS: **Sclerostin and Dickkopf-1 as therapeutic targets in bone diseases.** *Endocr Rev* 2012, **33(5)**:747-783.

SYMPOSIA: DEVELOPMENTAL ORIGINS

O12

DOHAD and early pubertal timing

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O12

Age at menarche varies widely between girls, is estimated to be highly heritable and is associated with long-term health outcomes, such as obesity and type 2 diabetes. Earlier pubertal maturation in boys and girls links rapid postnatal growth weight gain to later life metabolic and cardiovascular disease [1,2]. Genome-wide association studies (GWAS), which genotype hundreds of thousands of common genetic variants located across the entire genome, have been successful in identifying many specific genetic determinants of pubertal timing and these findings have informed the mechanisms that link earlier pubertal timing to increased risks of disease. The genetic signals indicate that both obesity-related and obesity-independent mechanisms may link pubertal timing to insulin sensitivity and diabetes risk.

Our earlier findings [3] in the ReproGen international GWAS consortium identified substantial overlap between loci associated with menarche and those associated with body mass index, as had been predicted by analyses of data from twins, and in keeping with recognised associations between infancy and childhood weight gain and pubertal timing, and in turn between pubertal timing and obesity in adult life. However, the locus with the strongest individual effect size is in the gene LIN28B, which regulates microRNA processing and also insulin sensitivity. Our recent larger studies indicate further mechanisms that may link puberty timing to diabetes risk, and also suggest pubertal timing as a possible postnatal development target for the evolution of genomic imprinting [4].

References

1. Lakshman R, Forouhi NG, Sharp SJ, Luben R, Bingham SA, Khaw KT, Wareham NJ, Ong KK: **Early Age at Menarche Associated with Cardiovascular Disease and Mortality.** *J Clin Endocrinol Metab* 2009, **94(12)**:4953-4960.
2. Elks CE, Ong KK, Scott RA, van der Schouw YT, Brand JS, Wark PA, *et al*: **Age at menarche and type 2 diabetes risk: the EPIC-InterAct study.** *Diabetes Care* 2013, **36(11)**:3526-3534.
3. Elks CE, Perry JR, Sulem P, Murabito J, Ong KK, Murray A, *et al*: **Thirty new loci for age at menarche identified by a meta-analysis of genome-wide association studies.** *Nature Genetics* 2010, **42(12)**:1077-85.
4. Perry JR, Day F, Elks CE, Sulem P, Stefansson K, Murabito J, *et al*: **Parent-of-origin-specific allelic associations among 106 genomic loci for age at menarche.** *Nature* 2014, **514(7520)**:92-97.

O13

Placental hormones and the control of fetal growth

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O13

Linear growth in the postnatal period is controlled by the production, secretion, and action of pituitary growth hormone and IGF-1. IGF-I and IGF-II production and signaling are also essential for fetal growth and neural development. But the control of IGF production in the fetus is largely independent of GH.

Among the factors that control fetal IGF production, the availability and utilization of nutrients is most important. Since fetal nutrient supply ultimately derives from maternal nutrient stores, we can understand fetal growth only through analysis of the factors that control maternal nutrient utilization and transport to the fetus.

I will argue that hormones produced by the placenta, including placental lactogen, placental growth hormone, and sex steroids regulate the intake, absorption, utilization and transfer of maternal nutrients to the fetus and modulate fetal and neonatal insulin production. Dysregulation of placental hormone production may be associated with fetal growth

retardation or fetal overgrowth and may predispose in later life to glucose intolerance and type 2 diabetes.

O14
Early nutrition and metabolic outcome
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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O14

In recent years the number of extremely premature born (very low birth weight (VLBW<1500 g) children has increased as a consequence of increased survival rate. Those preterm neonates who survive have an increased risk of long-term neurological disabilities and chronic pulmonary disease. In addition, in the last two decades alterations in body composition and increased metabolic risk have been added to the list of consequences. In order to evaluate whether early patterns of infancy anthropometry and nutrition have an impact in metabolic hormonal profile and body composition we have prospectively assessed two cohorts of preterm infants and results will be presented.

SYMPOSIA: DIABETES

O15
ISPAD and its role in the management of diabetes in the young in the Indian subcontinent and the Far East
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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O15

Over the last three decades, while the fundamental need for insulin replacement in Type 1 diabetes (T1D) in young people remains, the method of delivery has changed dramatically.
From the "First World" view, "intensive insulin" therapy offers the best outcome, in terms of glycaemia and long-term health, and a shift to multiple injection therapy and pumps has become the approach promoted from diagnosis. A recent recognition is the sustained effect of near-normal glycaemia from diagnosis ('metabolic memory'), achieved through strict glucose targets and dose adjustment of insulin for carbohydrate.
To use the developing technology of T1D requires considerable motivation from patients and their families and there is a need for a parallel support programme from a multidisciplinary team. The components of successful adherence to the management regimens are a matching of health beliefs, attuned communication and reciprocity between those with diabetes, the families and their health professionals.
The regions of the Indian Subcontinent and the Far East offer a significant challenge for ISPAD, an organisation dedicated to support education, science and advocacy for diabetes in the young. The heterogeneity of health care services and social standing of the component countries is significant test for ISPAD. The Society has risen to this test though a portfolio of activities, projects and administrative approaches, to work in partnership with organisations in the region dedicated to improving the outcome of diabetes in the young.

O16
Feasibility of intensive insulin therapy in a developing country – the Indian experience
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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O16

The superiority of the Intensive insulin regimen over the conventional split mix is very well established in Western centres, often considered a prelude to pump therapy. Developing countries find it a challenge to initiate Basal bolus therapy. The main problems include: lack of support systems in school environment to take up the injections and glucose monitoring at school, and difficulties in assessing carbohydrate content of native foods prepared at home (considering the variability in preparation of any given food item). The parental acceptance of five injections a day also remains a challenge. There are numerous extraneous influences and myths in minds of parents that discourage them from accepting this regimen. We present our experience in surmounting these challenges and establishing Intensive insulin therapy as a first line of insulin therapy and also share the advantages in terms of the glycemic control and growth of children on follow-up with us.

O17
Strategies for management of diabetes in the young in China
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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O17

The incidence of type 1 diabetes mellitus (T1DM) is rising rapidly in children, with an overall annual global increase of 3%. Approximately 79,100 children under age 15 develop T1DM annually. Although the reported incidence of T1DM in China was as low as 0.6 per 100,000 per annum in 1995, the number of children with T1DM cannot be underestimated within the large population. The number of type 2 diabetics in the young has been increasing significantly in the last decades.
To improve access to quality care for children with diabetes in China, the World Diabetes Foundation (WDF) planned a project to help to establish pediatric diabetes centers to increase the rate of diagnosis and to improve the quality of treatment for children with diabetes through training of health care professionals. A survey was conducted on the basis of pediatric diabetes centers across China to raise the awareness of pediatric diabetes, and to evaluate the diagnosis and treatment status of diabetes care in children. Multiple diabetes camps were organized for children and caregivers. The project commenced in December 2012 and will be completed in February 2015. Thirty three pediatric diabetes centers in 25 cities across China were established. A cross-sectional questionnaire survey about the children with diabetes was completed.
Until the end of December 2013, 1,224 children with T1DM were effectively enrolled into the program with a mean age of 7.28±3.75 (mean± SD). For the age distribution, 79% were in the range of 4-12 years old, of those 384 cases were younger than 5 and 840 cases were older than 5 years old. The male to female ratio was 46.8% to 53.2%. 49% of the patients presented with typical diabetic symptoms such as increased thirst, frequent urination, extreme hunger, weight loss and fatigue. 59.3% cases first presented with diabetic ketoacidosis (DKA). The overall incidence of hypoglycemia was 17.5% (20.3% in <5y vs 16.3% in ≥5y, P>0.05y). The total incidence of DKA was 59.3% (57.4% in <5y vs 60.2% in ≥5y, P>0.05). The average level of HbA1c was (11.1±3.2)%. Using HbA1c 7.5% as a cut-off, the incidence of hypoglycemia was 29.3% in the HbA1c below 7.5% group and 14.2% in the above 7.5% group (P<0.001). The incidence of DKA was 54% in the HbA1c below 7.5% group and 61% in the above 7.5% group (P>0.05). 97.2% of the patients received insulin treatment, while 83.3% with insulin injection and 14% adopted pump therapy. 78.8% of the patients were using multiple insulin injection regimes.
In China, T1DM is still the major form of diabetes among the young, although there is a tendency of increasing T2DM. Greater efforts need to be made to improve the awareness and quality of care. A task fprce on diabetes in children was recently formed by the Chinese Society of Pediatric Endocrinology and Metabolism (CSMEM) to facilitate nationwide research and collaboration.

SYMPOSIA: HOT TOPICS

O18
Insights into the diagnosis and management of congenital hypothyroidism
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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O18

Congenital Hypothyroidism is the commonest preventable cause of intellectual disability. Newborn screening with early identification and treatment has resulted in near normalisation of long term intellectual

outcomes in the affected children. However, a number of issues still remain to be clarified. Firstly, while there has been a marked improvement in intellectual outcomes many studies have shown persistent cognitive deficits compared to control populations. It has generally been considered that this deficit reflected antenatal reductions in fetal thyroxine exposure and was unavoidable. However, variables such treatment delay and low thyroxine doses when initiating may also contribute. There is now data to suggest early diagnosis and treatment with high dose thyroxine and frequent blood testing can result in completely normal cognitive outcome when compared to healthy siblings. Treatment paradigms will be discussed that normalise cognition, with suggestions of management regimes that can be used in areas of the Asia-Pacific region where thyroid function testing is more difficult.

The frequency of congenital hypothyroidism is increasing world-wide. This is in part related to changes in the newborn cut-offs which have reduced in many countries. Other reasons have also been suggested and the ethnic composition of the countries seems very relevant. Asian and Pacific peoples appear to have a much higher incidence of dyshormonogenesis and rates are of congenital hypothyroidism are climbing more rapidly in countries where the proportion of these ethnicities is increasing.

There also remains ongoing concern about the appropriate cut-offs for notification of hypothyroidism. Indeed there has been an international trend for lower cut-offs resulting in many children being diagnosed with sub-clinical hypothyroidism. The relevance of diagnosing these children remains unclear with most likely being normal. I will discuss the use of different cut-offs and how these can affect the diagnosis and management of congenital hypothyroidism, as well as what should be the appropriate cut-offs in less affluent countries and the common reasons for missed diagnoses.

MANAGEMENT SESSIONS

O19

Controversies of the assesment and management of polycystic ovary syndrome in adolescents

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The diagnosis of polycystic ovary syndrome (PCOS) in adolescents is difficult as the pathological criteria used in adults like menstrual irregularities, acne, hirsutism and polycystic ovarian morphology could be normal physiological findings during puberty; in addition the syndrome is heterogeneous and there is limited high quality evidence. [1-3] Three international conferences have been held reporting different criteria for diagnosis of PCOS in women [Table 1]. [4-6] The 2011 Australian PCOS evidence-based guideline [1], the 2012 international evidence-based workshop [2] and the 2013 Endocrine Society Clinical Practice Guideline [3] highlight the issues of applying adult criteria to diagnose PCOS in adolescents.

All criteria require exclusion of other conditions: non-classic congenital adrenal hyperplasia, hypothyroidism, Cushing syndrome, hyperprolactinemia or androgen producing tumours which can cause a PCOS-like picture.

Although diagnosis of PCOS is based on its reproductive manifestations, it is a metabolic disorder. PCOS adolescents are at a high risk of having or developing glucose tolerance abnormalities, dyslipidemia and hypertension. Insulin resistance and the consequent development of hyperinsulinaemia seem to be the central pathophysiological mechanism that links PCOS to its associated metabolic derangements; this can occur independent of weight status. Obesity, which is commonly associated with PCOS, exaggerates insulin abnormalities. Adolescents with PCOS should have evaluation of glucose homeostasis and insulin resistance at diagnosis.

PCOS management should include a multidisciplinary team and should be individualized depending on the predominant complaint and weight status. Lifestyle modifications should be the first line treatment in the presence of overweight, obesity and/or insulin resistance. Metformin can also be added. Cyclical progesterone withdrawn bleed or cyclical oral contraceptive pills are used for menstrual irregularities. Antiandrogens like spironolactone and oral contraceptive pills are used for hirsutism. Permanent treatment with laser or electrolysis is usually advised after a course of antiandrogens.

Various aspects of adolescent PCOS will be discussed based on illustrative cases.

References

1. Teede HJ, Misso ML, Deeks AA, Moran LJ, Stuckey BJ, Wong JL, *et al*: **Assessment and management of polycystic ovary syndrome: summary of an evidence-based guideline.** *Med J Aust* 2011, **195(6)**:S65-S112.
2. Johnson T, *et al*: *NIH EbMW Report* 695 Bethesda, Maryland, National Institutes of Health 2012, **1**:1-14, (http://prevention.nih.gov/workshops/2012/pcos/default.aspx).
3. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, *et al*: **Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline.** *J Clin Endocrinol Metab* 2013, **98(12)**:4565-4592.
4. Zawadzki JK, Dunaif A: **Diagnostic criteria for polycystic ovary syndrome: towards a rational approach.** *Polycystic Ovary Syndrome* Boston: Blackwell Scientific Publications: Dunaif A, Givens JR, Haseltine FP, Merriam GR 1992, 377-384.
5. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group: **Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome.** *Fertil Steril* 2004, **81(1)**:19-25.
6. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis R, Escobar-Morreale HF, Futterweit W, *et al*: **The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report.** *Fertil Steril* 2009, **91(2)**:456-488.

O20

Delayed puberty – clinical approach and management

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O20

Delayed puberty, while not uncommonly a variant of normal pubertal physiology, could be an indicator of a wide range of less common but

Table 1(abstract O19) Diagnostic criteria for PCOS in women

PCOS definition	Clinical (modified Ferriman-Gallway score >8*) or biochemical hyperandrogenemia (elevated total or free testosterone level **)	Oligomenorrhoea (< 6-9 menstrual cycles per year) or oligo-anovulation	Polycystic ovaries on ultrasound (>12 follicles in one ovary or volume >10 cc)
NICHD 1990 [4]	Yes	Yes	
Rotterdam 2003 [5]	Yes	Yes	Yes
	2 of 3 criteria		
AE-PCOS 2009 [6]	Yes	Yes	Yes
		1 of 2 criteria	

* Ethnicity should be considered when assessing hirsutism

**Testosterone assays, puberty and time of the sample should be considered when reviewing levels

important clinical disorders. Congenital pathologies may involve defective developments of the gonads, pituitary gonadotrophs or hypothalamic GnRH neurons. Acquired pathologies could likewise be acting at each level. Clinical diagnostic evaluation to delineate a good range of these disorders and the respective managements will be covered in this session.

O21

Drilling down on the vitamin D debate: where are our priorities?

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O21

Vitamin D deficiency remains a global, public health concern despite intense focus in recent years. While nuanced issues such as the most appropriate cut-offs to define degrees of vitamin D sufficiency, insufficiency and deficiency are still unsettled, these debates occur on a backdrop of children continuing to be diagnosed around the world with the most devastating consequences of overt vitamin D deficiency - rickets and hypocalcemic seizures. The fact that few, if any, countries are exempt from new cases of vitamin D deficiency rickets underscores the potential barriers to effective prevention, including well-publicized national policies, education at multiple levels of the care system, access to vitamin D supplementation and compliance. As pediatricians, the global eradication of childhood rickets due to vitamin D deficiency is arguably our most important mandate at the moment, one that should not be overshadowed by the vitamin D adequacy cut-off debate. Only a small, critical amount of vitamin D daily is required post-natally to prevent rickets, with the optimal approach to rickets prevention targeting mother-infant dyads. Single dose or intermittent therapy is an appealing strategy to overcome compliance issues, although a full understanding of the risks related to higher dose therapy during the early years is still needed. Overall, this presentation will focus primarily on issues and strategies related to the global eradication of vitamin D deficiency rickets, with some discussion around the optimization of vitamin D status throughout the pediatric years.

ORAL SESSIONS

O22

A single antenatal course of betamethasone adversely affects glucose regulation in adulthood and the next generation in childhood

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O22

Objective: To assess whether a single antenatal course of betamethasone affects insulin sensitivity and other metabolic parameters in the offspring, and whether effects are transmitted to the next generation.

Methods: A cohort of 52 adults (aged 35.7 years, 46% men, 23 born after steroid treatment) and their term-born children (n=61, aged 8.0 years, 52% boys, 49% from a parent born after steroid treatment), was recruited in Auckland. Insulin sensitivity and secretion were assessed using hyperglycaemic clamps in adults, and HOMA-IR in children. Other assessments included DXA-derived body composition, lipid profile, adipokines, and 24-hour ambulatory blood pressure monitoring.

Results: Insulin sensitivity over the last 60 minutes of the hyperglycaemic clamp was 31% lower in the Steroid group (p=0.048), with a similar trend for overall insulin sensitivity (p=0.061). Steroid adults had a compensatory increase in first-phase insulin that was 53% higher than in controls (p=0.031), with total insulin secretion 44% higher in the Steroid group (p=0.044). Children of parents born after steroid treatment had higher fasting glucose (p=0.049) and insulin (p=0.008) concentrations than controls. HOMA-IR values indicated that children in the Steroid group were more insulin resistant than controls (p=0.006).

Conclusion: This study shows that maternal treatment with a single dose of betamethasone is associated with reduced insulin sensitivity in the offspring in mid-adulthood. Importantly, there is indication of an inter-generational effect, with the subsequent generation displaying increased insulin resistance.

O23

Endocrine dysfunctions in patients with mitochondrial diseases

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O23

Aims: Mitochondrial diseases are a heterogeneous group of genetic disorders that result from dysfunction of the respiratory chain. The endocrine disorders such as diabetes mellitus, hypoparathyroidism, hypothyroidism and growth hormone deficiency have been described in patients with mitochondrial DNA mutations. Among these, patients with Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS) frequently present with mitochondrial diabetes. Thus, this study was performed to investigate endocrine dysfunctions in patients with mitochondrial diseases.

Methods: A total of 106 patients (65 males and 41 females) diagnosed with mitochondrial diseases were included. Their etiologies were confirmed by clinical features and mitochondrial gene sequencing: Leber Hereditary Optic Neuropathy (LHON) (56 patients, 52.8%), MELAS (33 patients, 31.1%), Leigh disease (7 patients, 6.6%), Myoclonic Epilepsy with Ragged Red Fibers (MERRF) (7 patients, 6.6%), Pearson syndrome (2

Table 1(abstract O22) Study outcomes in the offspring (adults, F1) born from mothers who were either treated with antenatal betamethasone (Steroid) or not treated (Control), and in subsequent generation (children, F2). Data are means and 95% CI, adjusted for confounders

		Steroid	Control	p-value
Adults (F1)	n	23	29	
	1st phase insulin (mU/l)	43.1 (30.9–60.2)	28.1 (20.9–37.8)	0.031
	2nd phase insulin (mU/l)	57.5 (42.6–77.8)	41.6 (31.8–54.4)	0.068
	Total insulin (mU/l)	101.7 (74.7–138.4)	70.4 (53.5–92.6)	0.044
	Insulin sensitivity	16.1 (11.0–22.4)	23.1 (17.3–30.2)	0.061
	Insulin sensitivity last 60 min	14.3 (9.9–19.7)	20.6 (15.7–26.6)	0.048
Children (F2)	n	30	31	
	Fasting glucose (mg/dl)	4.88 (4.69–5.12)	4.67 (4.50–4.85)	0.049
	Fasting insulin (mU/l)	5.05 (3.98–6.41)	3.57 (2.79–4.58)	0.008
	HOMA-IR	1.10 (0.85–1.43)	0.74 (0.57–0.98)	0.006

patients, 0.02%) and Kearns-Sayre syndrome (KSS) (1 patient, 0.9%). Clinical, auxological and endocrinological parameters such as weight, height, body mass index (BMI), serum free T4, thyroid stimulating hormone (TSH), and glycosylated hemoglobin (HbA1c) were analyzed. Their medical records were reviewed retrospectively.
Results: Endocrine dysfunctions were observed in 19 patients (19/33, 57.6%) with MELAS,1 patient with KSS and Pearson disease, respectively. In patients with MELAS, mean age at diagnosis was 15.2 ± 10.7 years (range, 8 month to 36 years). Their mean height, weight, and BMI were 139.0 ± 20.1 cm (- 2.54 SDS), 30.0 ± 11.6 kg (- 4.43 SDS) and 15.7 ± 3.4 kg/m^2 (- 2.18 SDS), respectively. Mean HbA1c was 6.59 ± 1.81% in 24 patients with MELAS who showed hyperglycemia in routine serum chemical tests. Thyroid functions were normal in all patients. In mitochondrial gene analysis of MELAS, mt.3243 A>G was the most common (23/33 alleles, 69.7%), followed by mt.3316A>T (1 alleles), mt.13513G>A (1 allele), mt.8363G>A (2 allele), and mitochondrial DNA deletion (1 allele). One patient with KSS showed hypocalcemia with low parathyroid hormone level and stunted growth velocity. A Pearson syndrome patient manifested adrenal insufficiency. Endocrine dysfunctions were not found in the other mitochondrial diseases including LHON, Leigh disease, and MERRF.
Conclusion: Endocrine dysfunctions and growth failure are associated with mitochondrial diseases, especially in patients with MELAS. However, their growth parameters can be affected by general condition, nutrition, and other associated factors. Mitochondrial endocrinopathy should be considered as a rare cause of endocrine dysfunction and growth failure when clinically suspected.

O24

Criteria of radiological diagnosis for neonates with hypochondroplasia

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O24

Introduction: The diagnosis of hypochondroplasia (HCH) is hampered by absence of radiological criteria relevant to the age-dependent manifestations, particularly those in the neonatal period. This work deals with the radiological features in hypochondroplastic neonates with a FGFR3 mutation, including quantitative measurement that facilitates the definitive diagnosis. We propose the radiological criteria for HCH in the neonatal period.
Patients and methods: Subjects included six HCH neonates with FGFR3 mutations and 30 control subjects, in whom radiological examination was available as a neonate. The following findings were evaluated: 1) short ilia, 2) squared ilia, 3) short greater sciatic notch, 4) horizontal acetabula, 5) short femora, 6) stubby femora, 7) metaphyseal flaring, 8) lumboscaral interpediculate distance narrowing, and 9) oval radiolucency in the proximal femora.
Results: All measurement parameters for short ilia, short greater sciatic notch, horizontal acetabula, short femora and stubby femora (parameters 1, 3, 4, 5, and 6) were statistically different between HCH and control, while the other parameters 2, 7, and 8 were not. Based on these results, we tentatively made the criteria and scoring system for the diagnosis of HCH. The major criteria that are given a score of 2 comprise parameters 1, 3, and 6, whose distribution was not overlapped between HCH and control. The minor criteria that are given a score of 1 point comprise parameters 4 and 5, and 9, because the parameter 4 was overlapped in distribution between HCH and control, the parameter 5 is a non-specific finding, and the parameter 9 is subjective in assessment. We presumed that a total score of 6 points or higher warrant a diagnosis of HCH.
Conclusion: HCH was clearly distinguishable from normal infants assessing the skeletal findings of the ilia and proximal femora on neonatal roentgenograms. We compiled a set of diagnostic criteria for the early diagnosis of hypochondroplastic neonates.

O25

Abundant CD4+FOXP3+ regulatory T cells fail to suppress the proliferation of T cells in patients with Turner syndrome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O25

Context: Why Turner syndrome (TS) patients are predisposed to autoimmune disease remains unclear.
Objective: We investigated whether the frequency, phenotype, and suppressive function of CD4$^+$FOXP3$^+$ regulatory T cells (Tregs) are altered in young TS patients with the 45,X karyotype compared to age-matched controls.
Methods: Peripheral blood mononuclear cells from young TS patients (n = 24, 17.4–35.9 yrs) and controls (n = 29) were stained with various Treg markers to characterize their phenotypes. Tregs sorted for CD4$^+$CD25^{bright} were co-cultured with autologous CD4$^+$CD25$^-$ target cells in the presence of anti-CD3 and CD28 antibodies to assess their suppressive function.
Results: TS patients exhibited a higher frequency of CD4$^+$FOXP3$^+$ Tregs among their lymphocytes (mean 2.06 vs. 1.52%, P = 0.005) and FOXP3$^+$ Tregs among their CD4$^+$ T cells (7.44 vs. 4.19%, P < 0.001) compared to controls. The expression of inhibitory CTLA-4 in the Tregs of TS patients was also significantly higher (mean fluorescence intensity = 214.1 vs. 184.6, P = 0.003). The frequency of Tregs expressing GITR$^+$, CXCR3$^+$, and CCR4$^+$CCR6$^+$ was comparable between the two groups. However, the ability of Tregs to suppress the in vitro proliferation of autologous CD4$^+$CD25$^-$ T cells was significantly impaired in TS patients compared to controls (P < 0.05 at a 0.1:1 ratio of Tregs to target cells, P < 0.01 at 0.25:1, 0.5:1, and 1:1).
Conclusions: The Tregs of TS patients could not efficiently suppress the proliferation of autologous effector T cells, despite the abundance of Tregs in the peripheral circulation.

O26

Higher fibre and lower fat intake is associated with better vascular function in children with type 1 diabetes

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O26

Children with type 1 diabetes (T1D) might not consume a healthy diet. A healthy diet is associated with reduced risk of cardiovascular disease (CVD) in adults, but there is no data evaluating the association between diet composition and early markers of CVD in T1D children. We aimed to investigate the macro/micronutrient intakes of T1D children and the relationship with vascular function.
The Australian Child and Adolescent Eating Survey (ACAES–version1.2) Food Frequency questionnaire [1] was administered to 77 T1D children (aged 14±2.3 years, 37 males, BMI z-score 0. ±0.6) participating in an RCT [2], obtaining in-depth macro/micronutrient intake. Vascular function was measured by Flow Mediated Dilatation (FMD) and Glyceryl Trinitrate Mediated Dilatation (GTN). Pearson's correlation and multivariate regression analysis determined dietary predictors of vascular function.
Children had diabetes duration 5.7±3.9 years, median HbA1c 8.7(range: 6.3-14)% and insulin dose 0.8±0.2 units/kg/day. 37 children used CSII.
T1D children had daily energy intake 10762.3 ±2487.68kJ, protein 113.3 ±27.68g, fat 88.16±88.16g, carbohydrate 318.60±75.97g, fibre 31.41±8.89g and sodium 3069.91±766.43mg. Better (higher) FMD independently

Table 1(abstract O26) Independent predictors of GTN

R^2=0.41		
	Coefficient	p-value
Total fats	-0.06	0.02
Vessel diameter	-68.15	0.00
Diastolic BP	0.23	0.04
Pump use	3.35	0.01
T1D Duration	-1.26	0.04

correlated with a higher daily fibre intake (r^2 =0.25, Coefficient 0.20, p=0.04). Higher daily total fat intake independently correlated with worse (lower) GTN (other GTN associations in Table 1). Daily sodium intake exceeded recommendations of 1500mg, this was not significantly related to FMD/GTN. Higher fibre and lower total fat intake, is associated with better vascular function in T1D children. This is the first evidence that diet composition may reduce the risk of CVD in children with T1D in addition to improving diabetes control.

References

1. Watson JF, Collins CE, Sibbritt DW, Dibley MJ, Garg ML: **Reproducibility and comparative validity of a food frequency questionnaire for Australian children and adolescents.** *Int J Behav Nutr Phys Act* 2009, **6**:62.
2. Alman AC, Talton JW, Wadwa RP, Urbina EM, Dolan Lm, Daniels SR, *et al*: **Cardiovascular health in adolescents with type 1 diabetes: the SEARCH CVD study.** *Pediatr Diabetes* 2014, **15(7)**:502-510.

O27

Height and height velocity of early/average/late maturing children and adolescents from longitudinal study of the Kangwha cohort

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O27

Aims: The timing of the growth spurt and gender differences in physical growth can vary greatly, and it may contribute to the final height. However, there are few studies about height and height velocity of early/average/late maturing children because of the requirements of a population based longitudinal study. We investigated the height and height velocity according to growth tempo from the Kangwha cohort.
Methods: The present study conducted as a part of a community-based prospective cohort study from 1986 to 1999 with 800 school children (359 males, 441 females). We calculated 2 standard deviation of peak height velocity (PHV) and the age of PHV, and then grouped the subjects into early/average/late maturing groups. We compared the results of 3 groups and investigated the differences.
Results: The age at PHV was 12 in boys and 10 in girls, and height velocity at PHV was 8.62 cm/yr in boys and 7.07 cm/yr in girls on average tempo growth. In boys, the age of PHV was 11 and PHV 9.82 cm/yr in the early maturing group, and the age of 13 and 8.97 cm/yr in late maturing group. In girls, the age of PHV was 9 and PHV 9.75 cm/yr in the early maturing group, however, in the late maturing group; the difference was not significant compared with average tempo. The final height of each group was not different.
Conclusion: Final height was similar between early/late and average tempo group. The PHV might be greater in the early than in the late maturing group, however the difference was significant only in boys. Further longitudinal studies including pubertal development are needed.

O28

Messenger ribonucleic acid expression of KiSS-1 and serum level of kisspeptin in rat at different developmental stages

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O28

Purpose: KiSS-1 and its product, kisspeptin is necessary for pubertal onset and proper adult gonadal function due to its stimulatory effect on the secretion of gonadotropin-releasing hormone (GnRH). Although the pathophysiological importance of KiSS-1 and kisspeptin is well known, the developmental patterns of expression of KiSS-1 genes and serum level of kisspeptin have not been explored to date. We report herein the expression profile of KiSS-1 genes and serum level of kisspeptin in the rat at different developmental stages.
Methods: Spraque-Dawley (SD) strain female rats were used. To analyse expression of KiSS-1 mRNA, samples were obtained from hypothalamus, pituitary and ovaries in female rats according to developmental stages. At the same time, blood samples were collected for analysis of serum levels of kisspeptin and luteinizing hormone (LH). The expression of KiSS-1 mRNAs was assessed by RT-PCR and the serum levels of kisspeptin and LH were analyzed by ELISA.
Results: The expressions of KiSS-1 gene in hypothalamus and ovary were increased according to developmental stages and peaked at the prepubertal stage (at day 27, respectively, 0.88 ± 0.22, 0.54 ± 0.25). However, there were no significant changes or correlations between developmental stages and KiSS-1 gene expression in pituitary. Serum kisspeptin level was also increased according to developmental stages. However, peak level of kisspeptin (35.43 ± 3.60 pg/mL) was in the pubertal stage at day 34. Serum LH level was also increased and peaked (23.29 ± 15.24 ng/mL) at pubertal stage (at day 38). However, an increasing pattern was little delayed than that of kisspeptin level.
Conclusion: The expressions of KiSS-1 mRNA in hypothalamus and ovary, serum levels of kisspeptin and serum LH levels were increased according to developmental stages in rat in regular sequence. Therefore, serum kisspeptin levels can be an indication of KiSS-1 gene expression in hypothalamus and pubertal onset.

O29

The effect and the mechanism of allo-bone marrow mesenchymal stem cells in experimental autoimmune thyroiditis

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O29

Aims: To investigate the effect and the mechanism of allo-bone marrow mesenchymal stem cells (BM-MSCs) transplantation in the Experimental Autoimmune Thyroiditis (EAT) mouse model.
Methods: C57BL/6 mice were treated with porcine thyroglobulin and Freund's adjuvant both in the simple model group and the BM-MSCs treated group. Mice in the BM-MSCs treated group were injected with homology BM-MSCs(3×10^5/mouse) at the beginning of model establishment. A normal control group was set as well. All mice were killed at the 28th day after primary immunity. The histopathological analysis of thyroid tissues were observed. The levels of autoantibodies, thyroid hormone, IFN-r, IL-10 were detected.
Results: (1)) A mouse model of EAT was established successfully. (2) The thyroid in the simple model group and the BM-MSCs treated group showed inflammatory response and inflammatory cell infiltration, but the response in the BM-SCs treated group was weaker than in the simple model group. [3] Compared with the normal control group, increased autoantibodies were detected with P<0.05, an increased IFN-γ level and a decrease of IL-10 in the simple model group; Compared with the simple model group, decreased autoantibodies were detected with P<0.05 in the BM-MSCs treated group; Decreased expression of IFN-γ and increased expression of IL-10 was detected in this group with P<0.05.

Conclusion: BM-MSCs could partly restore the immunological homeostatic state through modulating the immunological dissonance of Th1/Th2, and alleviate inflammation of the thyroid. It may provide a new approach to therapy of autoimmune thyroiditis.

O30

The glycemic control has improved in Japanese patients with childhood-onset type 1 diabetes mellitus since 1995

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O30

Purpose: The effect of basal-bolus insulin therapy on better glycemic control was documented in the DCCT study. We aimed to clarify whether the introduction of insulin analogues gave the good quality of life using basal-bolus insulin therapy without hypoglycemia to the most of pediatric and adolescent patients with type 1 diabetes mellitus (T1DM).
Methods: Glycemic control was compared between the 1st in 1995, 2nd in 2000 and 3rd in 2008 cohorts of childhood-onset T1DM in Japan, consisting of 566, 749 and 803 patients, respectively. We examined the data of HbA1c, frequency of moderately severe hypoglycemia, insulin regimen, body mass index (BMI) and the SD score each during July and October.
Results: The median values of HbA1c (% of glycemic goal <7.5%) were significantly improved between the subsequent three cohorts; 9.02% (18.6%), 8.10% (30.35) and 7.60% (44.1%), in 1st, 2nd and 3rd cohorts, respectively. In addition patients with HbA1c more than 9% were significantly decreased in that order of cohorts. The frequency of moderately severe hypoglycemia was 9 times/ 4 months/ 100 patients in 3rd cohort. The frequencies of multiple daily insulin or pump therapy were 34.5%, 59.7% and 80.7%, in that order. The daily insulin dose was higher in 3rd cohort in comparison with 1st cohort. While the height SD score significantly increased in 3rd cohort, the BMI SD scores in 2nd and 3rd cohorts were significantly higher than that in 1st cohort.
Conclusion: We conclude that the introduction of insulin analogues, especially using the long-acting analogues since 2003, resulted in better glycemic control with good quality of life with less moderately severe hypoglycemic episodes in comparison with DCCT study. On the other hand we may have to pay attention to overweight without dietary advice.
On behalf of The Japanese Study Group of Insulin Therapy for Childhood and Adolescent Diabetes.

O31

Response to low dose growth hormone treatment in infants and toddlers with Prader-Willi Syndrome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O31

Aim: We aimed to assess the benefits and safety of low dose growth hormone treatment (GHT, 4.5 mg/m^2/week) in young children with genetically confirmed Prader-Willi Syndrome (PWS).
Methods: Data of 20 infants (2-12 months) and 24 toddlers (13-24 months) were collected from the PWS-OZGROW database. The two groups were evaluated for standard deviation scores (SDS) of height (length under age 2 years), weight and BMI using the World Health Organization standards (SDS_{WHO}) and PWS specific BMI (SDS_{PWS}), bone age (BA), insulin-like growth factor-1 (IGF-1) levels, hypotonia, developmental delay, spinal curvature, sleep studies and adverse events over 2 years of GHT.
Results: At commencement of GHT infants had a reduced BMI SDS_{WHO} (P=0.003), while toddlers had a reduced height SDS_{WHO} (P=0.014). The height/length SDS_{WHO} of infants increased from -1.09±1.15 at baseline to -0.26±0.89 after one year and -0.02±0.80 after two years GHT (GLM repeated measures; P <0.0001,) and in toddlers increased from -2.11±1.45 to -1.11±1.11 and -0.87±0.94 (P <0.0001). BMI SDS_{WHO} increased in both groups (data not shown), while BMI SDS_{PWS} decreased (P<0.0001, age groups P>0.05) from 0.40±0.84 to -0.07±0.67 at Year 1 and -0.31±0.95 at Year 2 (both age groups combined). Preterm and full term children did not differ significantly in response to GHT, nor did children with deletion (14) and uniparental disomy (16). All children had low to very low serum IGF-1 at baseline which increased to within the normal reference range for the majority of children (61%) with the remainder modestly increased during the first 2 years of treatment. An improvement in tone, spinal curvature and developmental delay was noted in those who were more severely affected at baseline. Two children developed scoliosis. Three children ceased GHT temporarily to adjust positive airway pressure settings or for tonsillectomy following onset or worsening of obstructive and/or central sleep apnoea. Bone age was not advanced and no other serious adverse events were reported during the two year GHT.
Conclusion: Treating young children (<2 yrs) with PWS with 4.5 mg/m^2/week of GH normalises height and achieves IGF-1 levels in the normal range in the majority of patients. The risk of respiratory adverse events can be minimised by regular monitoring. The dose was sufficient to keep height and most IGF-1 values in the normal range and PWS specific BMI SDS in a negative range and may lower potential risks of long-term treatment of very young children with PWS.
On behalf of the PWS and OZGROW collaboration.

O32

Molecular basis of transient neonatal diabetes mellitus in Japan: frequent KATP-TNDM and identification of a patient with a monoallelic INS mutation

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O32

Background: It has been reported that the most common (~70%) form of transient neonatal diabetes mellitus (TNDM) is 6q24-related TNDM, followed by TNDM caused by activating mutations in the KATP channel genes (KCNJ11 and ABCC8, KATP-TNDM) which accounts for approximately 30% of TNDM. Recessive promoter mutations in the insulin (INS) gene also have been reported as rare causes of TNDM.
Aims: To elucidate the molecular basis of TNDM in Japan.
Methods: Nineteen Japanese patients with TNDM were analysed by methylation specific PCR of the differentially methylated region at chromosome 6q24 and by PCR amplification and direct sequencing of all exons and exon-intron boundaries of the KCNJ11, ABCC8, and INS genes.
Results: 6q24 abnormalities were identified in 7 (paternal duplication in 4, paternal uniparental disomy or epimutation in 3), mutations of ABCC8 (R1380C, R216C, V607M) in 3, KCNJ11 (E227K, R50Q, C42R) in 3, and INS (Q62X) in 1.

Conclusion: As compared with previous reports, the frequency of KATP channel mutations were higher in this Japanese cohort. In addition, this is the first report of a monoallelic, coding sequence mutation in the INS gene (Q62X) responsible for TNDM.

O33

Continuous subcutaneous insulin infusion is associated with a reduced rate of microvascular complications

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O33

Aim: To determine whether use of continuous subcutaneous insulin infusion (CSII) is associated with lower rates of microvascular complications than use of multiple daily injections (MDI) in adolescents with type 1 diabetes from 2000-2014.
Methods: We assessed microvascular complications in 1152 adolescents aged 12-20 years with diabetes duration ≥ 5 years. Retinopathy was detected using seven–field fundal photography, albumin excretion rate (AER) using overnight urine collections or albumin-to-creatinine ratio (ACR) and peripheral nerve function by thermal and vibration threshold.
Results: Median age was 17 years [IQR 15-18] and median diabetes duration 9.0 [7.0-12.0] years. CSII was used by 29% and MDI 72%. CSII was associated with a lower rate of retinopathy than MDI (16% vs 22%; p=0.025) across the entire study period and in the latest time period with lower rate of AER elevation (≥ 7.5 μg/min)(26%vs 37%; p=0.012); microalbuminuria (1.3% vs 5.5%; p=0.016) and peripheral nerve abnormalities (27% vs 32% ; p 0.139) although the latter did not reach statistical significance.
In multivariable analysis, retinopathy was negatively associated with CSII Odds ratio (OR) 0.68 (95%CI:0.47-0.98) and positively with higher HbA1c OR 1.20 (1.08-1.32), older age at diagnosis 1.12 (1.02-1.22), longer diabetes duration 1.26 (1.15- 1.38) and lower height SDS 0.78 (0.67-0.91). Early elevation of AER was associated with higher HbA1c OR 1.33 (1.20-1.47), insulin dose 1.86 (1.22-2.82) and lower socioeconomic advantage 0.66 (0.46-0.94). Microalbuminuria was associated with higher insulin dose 2.64 (1.07-6.50) and HbA1c 1.34 (1.07-1.68). A peripheral nerve abnormality was negatively associated with CSII OR 0.66 (0.44-0.97), insulin dose OR 0.50 (0.26- 0.94) and positively with higher BMI SDS OR 1.31(1.06-1.63).
Conclusion: While the benefits of CSII on glycaemic control and quality of life are recognised, this is the first study to show a beneficial association of CSII vs MDI on microvascular complications.

O34

Sensory neuropathy in young people with type 1 diabetes: a systematic review

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O34

Peripheral sensory neuropathy and its risk factors are well-described in adults with type 1 diabetes (T1D). While clinically evident neuropathy is rare in young people with T1D, we and others have shown that subclinical peripheral neuropathy is common [1]. However, the prevalence of sensory neuropathies may be underestimated, due to a lack of established testing guidelines.
We performed a systematic review of the epidemiology of peripheral sensory neuropathy, and diagnostic accuracy of tools used for its assessment, in young people with T1D. We searched Medline and Embase from Jan 1985 to Mar 2014. Inclusion criteria were studies in young people with diabetes duration > 1 year which tested for sensory neuropathy using nerve conduction velocity (NCV), temperature perception threshold (TPT), vibration perception threshold (VPT) and/or clinical examination.
We identified 26 eligible studies, involving 5527 young people with T1D. Only 7/26 (27%) studies were of good methodological quality (Newcastle Ottowa Scale score > 7). Clinical examination yielded a wide variation in the rates of sensory neuropathy, with pooled prevalence of 15% (95% CI 13 to 17). Abnormal VPT was more common, with pooled prevalence 33% (30 to 36), as was TPT, with pooled prevalence 32% (26 to 39). The prevalence of abnormal NCV was similar 36% (33 to 39). Overall, the pooled prevalence of sensory neuropathy, using any test, was 26% (24 to 27). We calculated sensitivity and specificity of the different diagnostic tests that were used in the included studies, in comparison with neuropathies detected by 'gold standard' nerve NCV testing. The sensitivity of VPT ranged from 29-62%, and specificity from 65-100%. Sensitivity of TPT was 19% and specificity was 65% (one study). The sensitivity of clinical examination ranged from 0-100% and specificity from 81-100%.
In conclusion, there is marked variation in reported prevalence rates of sensory neuropathy, due to lack of consensus on its definition, classification of abnormal results, and testing methodology. Clinical examination demonstrates the lowest sensitivity for detection of sensory neuropathy in young people with T1D.

Reference

1. Downie E, Craig ME, Hing S, Cusumano J, Chan AK, Donaghue KC: . *Diabetes Care* 2011, **34(11)**:2368-2373.

O35

The Australasian diabetes data network (ADDN): first steps towards a national database resource

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O35

The Australasian Diabetes Data Network (ADDN) is a collaboration that aims to collect and centrally collate a suite of patient data across Australia and New Zealand that will be available to all diabetes researchers. ADDN will collect information prospectively, facilitating data sharing and building capacity in clinical service delivery and investigation. The central database will provide a research resource, facilitate study recruitment and be an ongoing source of data to enable benchmarking against national outcomes. By April 2015 ADDN will be populated with over 4,000 participants presenting an opportunity to analyse national data for the first time. To date ADDN holds the data of 1136 children and adolescents. Of the T1D participants (n=1064), males and females were equally represented, with 3% (35) aged <5, 19% (200) aged 5-10, 37%(396) aged 10-15, 38%(399) aged 15-20 and 3%(34) >20 years of age. A total of 10% were treated with twice daily injections, 42% with Multiple Daily Injections and 47% with continuous subcutaneous insulin infusion (CSII). The TID group had a median HbA1c of 8% (64 nmol/mol) with 31% (330) <7.5% (58.5 nmol/mol), 42% (447) 7.5-9.0 (58.5-74.9 nmol/mol) and 27%(287) >9.0% (74.9 nmol/mol). From these preliminary results it is clear that a large proportion of participants are not meeting recommended glycaemic targets [1] despite the high uptake of intensified insulin therapy. Further analysis of the ADDN dataset is needed to understand the influence of different practices and therapies for T1D used in Australian youth, and the clinical and demographic predictors of glycaemic outcomes. This research and resource will have major implications for clinical investigation in Australasia and will provide an evidence base to inform health policy.
On behalf of the ADDN Study Group.

Reference

1. Craig ME, Twigg SM, Donaghue KC, Cheung NW, Cameron FJ, Conn J, Jenkins AJ, Silink M, Australian Type 1 Diabetes Guidelines Expert Advisory Group: National evidence-based clinical care guidelines for type 1

diabetes in children, adolescents and adults. Australian Government Department of Health and Ageing, Canberra 2011.

O36

Performance of a predictive algorithm in sensor-augmented pump therapy in the prevention of hypoglycaemia

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O36

The Predictive Low Glucose Management (PLGM) system consists of a Medtronic Veo pump, Enlite sensor, MiniLink REAL-Time transmitter, Bluetooth-RF translator and a predictive algorithm operating from a Blackberry smartphone. The system suspended insulin delivery when the pre-set hypoglycaemic threshold of 4.4mmol/L was predicted to be reached in 30 minutes.
The aim of this study was to determine the plasma glucose profile with the PLGM system when hypoglycaemia was induced by (a) moderate-intensity exercise, (b) subcutaneous insulin bolus and (c) increasing the overnight basal infusion rate in individuals with type 1 diabetes. The primary outcome was the plasma glucose nadir following each hypoglycaemic stimulus with and without PLGM.
Participants performed 30-60 minutes of moderate-intensity exercise or were administered a subcutaneous insulin bolus following a glucose stabilisation period on basal continuous subcutaneous insulin infusion. In participants studied with increased overnight basal rates, hypoglycaemia was induced by increasing basal rates by 180%. They were randomised and studied on 2 separate days; with PLGM off and with PLGM on. On both days, participants were observed until plasma glucose dropped to 2.8mmol/L or were symptomatic.
Results: A) PLGM suspended basal insulin in 9/13 participants who performed moderate-intensity exercise resulting in a higher glucose nadir in 6/9 participants (66%).The mean±SD glucose nadir with PLGM off and on was 3.38±0.44mmol/L and 3.5±0.65mmol/L respectively. (p=0.27).
B) PLGM suspended basal insulin in 27 participants in whom SC insulin bolus was administered resulting in a higher glucose nadir in 20 participants (74%). The mean±SD glucose nadir with PLGM off and on was 3.33±0.47mmol/L and 3.71±0.5mmol/L respectively. (p=0.003).
C) PLGM suspended basal insulin in 6/6 participants in whom overnight basal rates were increased resulting in a higher glucose nadir in 5/6 participants (83%). The mean±SD glucose nadir with PLGM off and on was 2.7±0.29mmol/L and 3.9±1.11mmol/L respectively. (p=0.05).
Sensor-augmented pump therapy with the PLGM system is likely to be effective in reducing the risk of hypoglycaemia. The system appears to be more effective when hypoglycaemia is induced by insulin bolus and increased overnight basal rates than with exercise.

O37

Childhood glycaemic control has an enduring effect on the lifetime risk of microvascular complications in type 1 diabetes mellitus

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O37

The development of diabetes-related microvascular complications in type 1 diabetes (T1DM) is known to be related to glycaemic control, but the degree to which variations in HbA1c across the lifetime contributes to this risk is unknown. Our hypothesis was that individuals with poor control in childhood and subsequent improved control in adulthood would still have an increased risk of severe diabetes-related complications when compared with individuals who achieved good control throughout the lifecourse. This study aimed to investigate this premise in a cohort for whom serial lifetime glycaemic data are available. The study population comprised children diagnosed with T1DM <18 years at The Royal Children's Hospital (Melbourne) who transitioned to the Royal Melbourne Hospital for ongoing (adulthood) care. Data were collected through BioGrid Australia, a biorepository allowing inter-institutional data linkage, and included demographics as well as serial HbA1c and complication data. 'Severe complications' were defined as severe diabetes-related eye disease, renal failure, ulceration/amputation or death. Glycaemic control was categorised according to HbA_{1c} changes over time, based on median values throughout the lifecourse; "Optimal" (≤8.2% throughout lifecourse), "Improving" (>8.2% in childhood, ≤8.2% in adulthood), "Worsening" (≤8.2% in childhood, >8.2% in adulthood), "Poor" (>8.2% throughout lifecourse). A total of 503 (male=253) individuals were identified, diagnosed 1975-2010. At the time of follow up, mean (SD) age was 27.9 (6.2) years and median (IQR) duration of diabetes was 17.8 (12.2, 23.2) years. Severe complications were documented in 26 (5.2%) and were associated with mean HbA_{1c} at age 16-30 years (<0.05) and intra-individual lifetime glycaemic variability expressed as HbA_{1c}SD (p=0.02). The relative risk (95% confidence interval) of developing severe complications in the improving, worsening and poor groups was 14.9 (1.7-130.9, p=0.01, n=50), 12.5 (1.4-109.4, p <0.01, n=60) and 15.4 (2.1-114.8, p <0.01, n=206) respectively when compared to the optimal group (n=187). In conclusion, the overall rate of severe complications is low in this cohort despite the lifecourse poor glycaemic control demonstrated in 40.1%. Our findings demonstrate that poor glycaemic control in childhood has a lasting effect on the development of severe microvascular complications in adulthood.

O38

A randomized controlled trial on the effects of antenatal exercise on birth weight and neonatal body composition

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O38

Aims: To determine the effects of an antenatal exercise programme on birth weight and neonatal body composition of offspring of overweight and obese women.
Methods: We are conducting a parallel arm randomized controlled clinical trial in Auckland, New Zealand (NZ). Eligible participants were enrolled to the study from March 2013 to April 2014. The intervention group participated in a 16-week home-based moderate-intensity exercise programme utilising stationary cycles and heart rate monitors. Maternal measures including weight, aerobic fitness, physical activity and diet were assessed at baseline and end of intervention. Neonatal and maternal body composition were assessed 14 days after delivery.
Results: A total of 75 participants were recruited (intervention n =37; control n = 38). Participants had a mean pre-pregnancy BMI of 31.5 kg/$m^{2;}$; age of 30.5 years and weight of 91 kg at study entry. 57% were NZ European/other, 29% Pacific Island and 13% Maori. 25% were nulliparous. Maternal characteristics known to affect birth weight were similar between groups at baseline. To date, 42 participants (intervention n= 19, control n=23) have completed the study. The birth weight (g) of offspring in the intervention group is 3701 ± 561 compared to 3552 ± 495 in the control group. Secondary offspring outcomes in the exercise and control groups are: birth length (cm) 51.5 vs 51.6; head circumference(cm) 35.1 vs 34.8; customised birth weight centiles 59% vs 42%; neonatal lean mass (g) 3717 vs 3546; neonatal fat mass(g) 367 vs 275 and neonatal %body fat 8.8% vs 7.2%. Maternal outcomes in exercise (n=24) and control (n= 26) groups are: weight gain (kg) over the intervention period 8.93 vs 8.94 ; postpartum maternal BMI 32.7 vs 35.5 and % body fat 46% vs 48%.
Conclusion: This is the first clinical trial exploring the effects of antenatal exercise in overweight and obese women on neonatal body composition

Preliminary trial results on 42 participants indicate a trend towards increased neonatal fat mass and % body fat in the intervention group. Trial data collection will be completed by October 2014.

O39

Effect of exercise intensity and blood glucose level on glucose requirements to maintain stable glycaemia during exercise in individuals with type 1 diabetes

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O39

Current recommendations for carbohydrate supplementation to prevent exercise-induced hypoglycaemia in individuals with type 1 diabetes (T1D) do not take into account exercise intensity or blood glucose levels during exercise. The aim of these studies was to investigate the effects of (a) exercise intensity and (b) blood glucose levels, on carbohydrate requirements to maintain stable glycaemia during exercise in individuals with T1D at basal insulin levels and to determine the glucoregulatory mechanisms underlying these effects.

Nine young adults with T1D underwent euglycaemic clamps, whereby stable blood glucose levels between 4.5 to 6mmol/L were maintained during the study at basal insulin levels. Participants performed up to 40 minutes of exercise at four different exercise intensities (35%, 50%, 65% and 80% VO_{2peak}) on four separate days following a randomised counterbalanced design. In a subsequent experiment, eight participants underwent either a euglycaemic or hyperglycaemic (9.5 – 10.5mmol/L) clamp at basal insulin levels, during which they performed 40 minutes of exercise at 50% VO_{2peak}, on two separate days. In both studies, glucose infusion rates (GIR) to maintain stable glycaemia were measured during exercise, constant deuterated glucose was infused to determine glucose kinetics and blood samples were collected for the analysis of glucoregulatory hormones.

The average GIR to maintain euglycaemia during exercise was 2.0±0.9, 4.0 ±1.5, and 4.1±1.7g/h (mean±SEM) at 35%, 50% and 65% VO_{2peak}, respectively. These GIRs were all significantly greater than that at 80% VO_{2peak} where no glucose was required ($p<0.05$). Exercise at 80% VO_{2peak} was associated with a significant rise in catecholamine levels and endogenous glucose production ($p<0.05$). The average GIR to maintain stable glycaemia during exercise performed during the second experiment at 50% VO_{2peak} was similar at euglycaemia (4.9±2.1g/h) and hyperglycaemia (5.5±2.5g/h; $p>0.05$).

At basal insulin levels, the relationship between exercise intensity and the amount of glucose required to prevent hypoglycaemia is not linear, with no glucose required to maintain euglycaemia during high-intensity exercise. Performing moderate-intensity exercise at euglycaemia or mild hyperglycaemia does not alter the glucose requirements to maintain stable glycaemia.

O40

Resistance training improves metainflammation and body composition in obese adolescents

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O40

Adolescent obesity is associated with inflammation, insulin resistance and prediabetes. The purpose of the study was to investigate whether resistance training (RT) improves the adipokine profile, body composition and insulin sensitivity of obese adolescents. Fourteen obese adolescents (16.1+1.6 y; M:F 6:8; body mass index (BMI) SDS 2.01 + 0.31) were recruited for a 16-week RT intervention. Thirty-one lean youth (15.6+1.3 y; M:F 19:12; BMI SDS -0.03+0.07) had baseline anthropometric measurements and blood tests for comparison. Participants completed 3 RT sessions per week with training load progressively increased from 60% to 85% of one repetition maximum (1-RM). The following parameters were examined pre- and post-intervention: 1) Height, weight, BMI; 2) High sensitivity C-reactive protein (hs-CRP) and adipokines including interleukin (IL)-1β, IL-6, tumor necrosis factor-alpha (TNF-α), adiponectin, soluble intercellular adhesion molecule (sICAM)-1, leptin and resistin; 3) Body composition by dual energy x-ray absorptiometry (DXA), and 4) Insulin sensitivity by homeostatic model assessment (HOMA-IR). Obese youth had significantly higher IL-1β, leptin and resistin (all $p<0.0001$) and lower adiponectin and sICAM-1 (both $p<0.0001$) at baseline compared with lean youth. Post-intervention, a reduction in IL-6 ($p<0.01$), IL-1β ($p<0.01$) and resistin ($p<0.001$) was observed whereas adiponectin and sICAM-1 increased ($p<0.05$, $p<0.001$ respectively) in obese adolescents. HOMA and hs-CRP remained unchanged. IL-1 β and sICAM-1 levels in obese youth normalised to levels comparable to lean youth post-intervention ($p = 0.1$ and $p=0.2$), whereas TNF-α and resistin were significantly lower ($p<0.05$, $p<0.01$ respectively) post-intervention in the obese youth. Percent fat for the trunk, arm and total body ($p<0.05$) were reduced, while fat free mass ($p<0.01$) was increased after the intervention. RT is a feasible intervention to improve the adipokine profile and body composition of obese adolescents suggesting it may be a feasible intervention for improving metabolic health in obese youth at high risk of Type 2 Diabetes.

O41

Supplementation with oxidised fish oil in pregnancy markedly increases neonatal mortality in male rat offspring

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O41

Introduction: Omega-3 fish oils are the most popular health supplements, taken by 15-30% of people at all stages of life, including pregnancy. These oils may improve insulin sensitivity through the recently characterized GPR120 receptor, but are chemically unstable and easily degrade into potentially toxic lipid peroxides. The health effects of oxidised fish oil are mostly unknown. We have shown that 89% of fish oil products in NZ exceed recommended oxidation limits, 36% by more than two-fold.

We hypothesised:

1. Fish oil supplementation during pregnancy of insulin-resistant mothers would prevent adverse metabolic programming of the offspring.
2. Oxidised fish oil would cause adverse metabolic and cardiovascular outcomes.

Methods: 80 female Sprague-Dawley rats were allocated to a control or high-fat diet and time-mated. Throughout pregnancy they received 1ml of unoxidised fish oil, a highly oxidised fish oil, or control (water) by daily gavage. This dose of fish oil has been shown to reverse insulin resistance in rats. Neonatal mortality was recorded. Markers of oxidative stress and inflammation will be measured in unused pups. At weaning, male offspring were fed standard chow ad libitum. At 100 days they will undergo metabolic assessment including insulin sensitivity, lipid and inflammatory profiles, blood pressure and body composition.

Results: Neonatal mortality was 8 times greater in the offspring of mothers treated with oxidised fish oil than controls (25.7 vs 3.2%, respectively; $p<0.0001$), with mortality from Day 2 to weaning being 1.4

times greater (p=0.042). Oxidised offspring had lower birth weight (5.4 vs 6.1 g p=0.008), and reduced weight at weaning (36.6 vs 40.7 g; p=0.07) and adolescence (day 51: 221.6 vs 256.7 g; p=0.02). Further, puberty was delayed compared with controls (day 45.3 vs 42.7; p<0.05).
Discussion: Oxidised fish oil in pregnancy markedly increased neonatal mortality and had a powerful programming effect on the surviving offspring. Fish oils are often taken in pregnancy and are usually oxidised which may lead to adverse programming of growth and development. The long-term metabolic effects of the oxidised and fresh fish oil will be available for the ASM. As fish oils at retail are substantially oxidised, we recommend a precautionary response to these data: pregnant women should not take supplementary fish oil.

O42

Increased rates of infantile hypercalcaemia following guidelines for antenatal vitamin D3 supplementation

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O42

Consultations for infantile hypercalcaemia (IIH) have increased at Sydney Children's Hospital since guidelines for vitamin D_3 supplementation during pregnancy were introduced in 2006. Recent nationwide shortages of low-calcium formula (LCF) suggest this problem may be widespread. CYP24A1 mutations have been identified as a potential cause of IIH.
To determine if IIH is occurring more commonly, de-identified, first-measured serum calcium from all infants <6 months (n=5796) measured in our laboratory, were grouped by years 2005-2007 (n=1516), 2008-2010 (n=1945) and 2011-2013 (n=2335). In addition, we analysed 13 infants treated by our department for idiopathic infantile hypercalcaemia (IIH) from 2011-2013.
Rates of hypercalcaemia (>2.75mmol/L) increased from 2011 (1.1% vs 1.3% vs 8.7%, χ^2P<0.001). Rates of hypocalcaemia (<2.25mmol/L) fell steadily (42.4% vs 32.3% vs 24.8% %, χ^2P<0.001). Twelve mothers of our 13 infants with IIH received antenatal vitamin D_3 supplementation. One infant also received 400 units/day Vitamin D_3 post-natally. At diagnosis, median age was 13 days (range 4-50), 77% were breast-fed, 54% were symptomatic and 25% had nephrocalcinosis. Median initial calcium was 3.00mmol/L (range 2.84-4.03) and phosphate 2.04mmol/L (1.1-3.33). PTH was not elevated (median 1.0pmol/L [<0.3-3.1]), urinary calcium: creatinine ratio not suppressed (median 2.3, [0.4-9]), 25OHVitD low-normal (median 44nmol/L [17-218]) and 1,25$(OH)_2$VitD elevated (median 232pmol/L [64-720]), in keeping with an abnormality in CYP24A1. In 7/10 infants with data available, treated with LCF for median 95 days (range 25-310), median PTH rose to 17.1pmol/L ([8.2-49.3], P=0.02) with a trend to lower 25OHVit D (median 23nmol/L [<10-108], P=0.09) despite continued high-normal calcium levels (median 2.66mmol/L [2.11-2.75]).
Concurrent changes in rates of hyper and hypo-calcaemia suggest antenatal vitamin D_3 supplementation as an aetiological factor. IIH was associated with significant morbidity, including symptomatic hypercalcaemia and nephrocalcinosis. Treatment with LCF prevented further symptomatic hypercalcaemia, but resulted in elevated PTH. The biochemistry of our patients with IIH raises variations in Vitamin D metabolism or calcium set-point as potential associated factors.

GROWTH & METABOLISM

O43

Regular, moderate intensity maternal exercise reduces birth weight but increases the risk of later childhood adiposity

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O43

Aims: We have previously randomised primiparous mothers to either an exercise regime or normal activity between 20 and 36 weeks gestation. In this study we aimed to assess the long-term effects of exercise during pregnancy on growth parameters and body composition in the offspring over their first 6-8 years of life.
Methods: Of the initial 84 women and their offspring who participated in the RCT, follow-up data were available on 46 mothers (26 exercisers, 20 controls) and 46 children. At each follow-up visit (6 months, 1 year, 2 years, 4 years, 6-8 years) clinical assessment included measurement of mothers' and children's heights, weights, BMI, and waist circumference, as well as blood pressure. Body composition was assessed in both mothers and children by whole-body dual-energy X-ray absorptiometry (DXA) scans at 4-year and 7-year follow-up visits.
Results: There were no differences in anthropometry between exercise and control children in the first 2 years of life. In addition, at age 4 years there were no differences in height, BMI, percentage body fat, or waist circumference between the two groups. At a mean age of ~7.5 years, exercise and control children showed similar weight, height, BMI, and waist circumference, but the exercise group had more body fat (17.5 vs 16.0%, P=0.02) than controls. Over the course of follow-up there were no observed differences in anthropometry between exercise and control mothers.
Conclusion: While no long-term benefits of maternal exercise in the first pregnancy were noted in mothers, children exposed to maternal exercise during intrauterine life appear prone to greater fat mass accumulation in mid-childhood. Larger studies are required to confirm this important observation as exercise in pregnancy is widely recommended by obstetricians.

O44

Pre-clinical alterations in cardiovascular phenotypes and their associations with metabolic profiles among obese youths

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Introduction: Childhood obesity and various obesity-related co-morbidities have become a serious global healthcare problem. Predictive risk stratification and early detection of high-risk obese youths can potentially help modify the outcomes of obesity before irreversible damage taking place. Newer surrogate markers for assessing pre-clinical cardiovascular alterations have good predictive values for future cardiovascular risks. However, local data regarding obesity-related arterial alterations in youth are lacking at present.
Aims: To evaluate the 1) pre-clinical cardiovascular alterations; and 2) their associations with the metabolic profiles in obese Hong Kong Chinese youths.
Study methods: A total of 56 obese subjects and 58 healthy lean controls (M: F 1:1, age 17.0 ± 2.06 years) were recruited. Clinical, biochemical and arterial (structural and functional) parameters were obtained from all participants. Structural arterial parameters were determined by assessing carotid arterial intima-media thickness with ECG-synchronized ultrasound (Vivid 7, GE Medical Systems, Norway). Cross-sectional and regional arterial functions were determined by assessing the arterial stiffness (β) of carotid arteries and pulse wave velocities of various arterial segments respectively with an automatic device (VP-2000; Colin Medical Technology, Japan). All ultrasonographic and arterial assessments were performed by a single researcher.
Results: Obese youths have worse preclinical arterial phenotypes both structurally and functionally, hence higher risks of developing cardiovascular disease in the future (p<0.0001). Important independent risk factors for preclinical arterial alterations in obese youths, including body mass indices (BMI), waist circumferences, blood pressures and plasma alanine aminotransferase (ALT) levels were demonstrated (p<0.0001). Obese youths having co-morbid metabolic disturbances were associated with worse preclinical arterial phenotypes. The worst cardiovascular phenotypes were shown in obese youths with the highest triglycerides to high-density lipoproteins (Tg-to-HDL) ratios despite most

of them having normal serum triglyceride and HDL levels. Furthermore, obese subjects with higher paediatric NAFLD fibrosis index (PNFI) scores [1] have worse cross-sectional arterial stiffness.

Conclusions: Assessment of preclinical cardiovascular phenotypes in asymptomatic obese youths provides clinicians a window for early identification of those at higher risks of developing future cardiovascular events. Evaluation of lipid compositions and obesity-related liver alterations may potentially help further stratify obese youths into subgroups with different degrees of cardiovascular risks.

Reference

1. Nobili V, Alisi A, Vania A, Tiribelli C, Pietrobattista A, Bedogni G, *et al*: **The pediatric NAFLD fibrosis index: a predictor of liver fibrosis in children with non-alcoholic fatty liver disease.** *BMC Med* 2009, **7**:21.

O45

Serum bisphenol A concentration and premature thelarche in female infants aged 4-month to 2-year old

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O45

Aims: To estimate the association between serum bisphenol A and premature thelarche in female infants aged 4-month to 2-year old.

Methods: We set a case-control study, a total of 251 female infants (aged 4 months to 2 years) with premature thelarche and 33 healthy age-matched control subjects were enrolled. Test the serum bisphenol A (serum BPA) concentration by liquid-liquid extraction coupled with ultra-performance liquid chromatography tandem mass spectrometry.

Results: The mean serum BPA levels in the normal and premature thelarche groups were 1.70 ng/ml and 3.48 ng/ml respectively. Serum BPA concentration in the premature thelarche group was significantly greater than that in the control group. There was no correlation between age and serum BPA level. Univariate logistic regression analysis showed that serum BPA concentration positively associated with premature thelarche, and the effect of BPA falls down as the age growing.

Conclusions: This hospital-based study implies that the association between serum BPA concentrations and premature thelarche. Additionally, the serum BPA levels are much higher than we ever thought in infants, and much more concerns should be raised in infants aged 4-month to 2-year old.

TYPE 1 DIABETES

O46

Gastric emptying is rapid in adolescents with type 1 diabetes and relates to gastrointestinal symptoms

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O46

Gastric emptying is a critical determinant in postprandial glycaemic control. This study aimed to assess whether gastric emptying in adolescents with type 1 diabetes (T1D) relates to gastrointestinal symptoms and to heart rate variability (HRV) as a measure of autonomic function.

We studied 30 adolescents (age 15 ± 2.5 years, BMI 22 ± 3.1 kg/m^2) with T1D. Subjects consumed a ^{13}C labelled pancake meal. Gastric emptying was measured by ^{13}C breath test. Blood glucose was monitored frequently over 4 hours and gastrointestinal symptoms at 30-60 minute intervals, by a visual analogue questionnaire. Chronic gastrointestinal symptoms over the previous 3 months were assessed by a validated Diabetes Bowel Symptoms Questionnaire [1]. HRV was assessed by LabChart Pro [2].15 age and sex matched controls were also studied.

Gastric half emptying time was accelerated in adolescents with T1D compared to controls; 77.6 (61.4-99.3) minutes [median (IQR)] versus 109.1 (70.8-124.2), P = 0.02), independent of hyperglycaemia during the study, HbA1c, duration of diabetes, and BMI.

There was no difference in the prevalence of chronic symptoms or symptoms of a severity that affected lifestyle between the two groups.

The presence of nausea, vomiting, bloating and/or fullness during the study in T1D was associated with faster gastric emptying compared to asymptomatic T1D (r =0.55; p = 0.04), and this was independent of peak glucose and glucose at 4 hours.

Rate of gastric emptying in T1D did not correlate with HRV.

Adolescents with T1D have rapid gastric emptying associated with acute gastrointestinal symptoms. Symptomatology could be used as a clinical tool to determine the need for further investigation.

References

1. Quan C, Talley NJ, Cross S, Jones M, Hammer J, Giles N, *et al*: **Development and validation of the Diabetes Bowel Symptom Questionnaire.** *Aliment Pharmacol Ther* 2003, **17(9)**:1179-1187.
2. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology.: **Heart rate variability: standards of measurement, physiological interpretation and clinical use. .** *Circulation* 1996, **93(5)**:1043-1065.

O47

Prevention of retinopathy in type 1 diabetes: a systematic review and meta-analysis

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O47

Diabetic retinopathy (DR) is the most serious ocular complication of type 1 diabetes (T1D) and leading cause of acquired blindness in working aged adults. Although various interventions have been trialled to prevent the development or progression of DR, the evidence to support many of these remains unclear. We systematically reviewed the evidence for primary and secondary interventions, to guide the management of DR in people with T1D.

Systematic searches were performed using MEDLINE, EMBASE and CENTRAL databases (from January 1990 to June 2014) to identify randomised controlled trials and controlled cohort studies reporting the incidence or progression of DR following administration of systemic interventions. English-language studies with a minimum follow-up of one year were eligible. Meta-analyses of extracted data were performed to determine pooled relative risk (RR) reduction.

Twenty-three studies met the inclusion criteria. Intensive insulin therapy significantly reduced the risk of both incident DR (RR 0.44, 95% CI 0.22-0.86, p=0.02) and progression of DR (RR 0.55, 0.31-0.97, p=0.04) compared with conventional therapy. Continuous subcutaneous insulin infusion (CSII) pumps provided significantly greater protection than multiple daily injection therapy (RR 0.33, 95% CI 0.19-0.57, p<0.0001). Angiotensin-converting enzyme inhibition had no impact on DR incidence but reduced progression (RR 0.57, 95% CI 0.34-0.94, p=0.03). Conversely, angiotensin receptor blockade was effective in decreasing DR incidence (RR 0.65, 95% CI 0.49-0.85, p=0.002) but had non-significant effect on progression. Both pancreas-alone and combined pancreas-kidney transplantation retarded progression of DR (RR 0.20, 95% CI 0.10-0.41, p<0.0001). Islet cell transplantation provided no benefit compared with either intensive or conventional insulin therapy.

In people with T1D, there is strong evidence supporting intensive insulin therapy for prevention of DR. Anti-hypertensives also provide protection

against DR in normotensive, normoalbuminuric adults but their effectiveness in other populations is yet to be investigated. In patients with T1D of longer duration, pancreas transplantation slows progression of DR. There is insufficient evidence to recommend the use of anti-lipid therapy or other medical interventions.

BONE/VITAMIN D

O48

High incidence of vitamin D deficiency in 2 – 17 year olds presenting with fracture to a Melbourne suburban public hospital

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O48

To determine vitamin D deficiency risk and other lifestyle factors in children and teenagers aged 2 – 17 years presenting with fracture to Sunshine Hospital, a clinical observational study was undertaken using convenience sample data collected from children and teenagers aged 2 - 18 years of age presenting with fracture, for whom consent had been obtained to determine clinical characteristics and lifestyle factors. Recruitment was undertaken over a 4 month period from 1st February to 31st May 2014. A suburban Melbourne (latitude 38°S) teaching hospital, Sunshine Hospital provides paediatric orthopaedic services for a high proportion of children and teenagers from ethnically diverse backgrounds with an increased proportion of highly pigmented individuals, which may influence vitamin D status specifically. Proxy measures of vitamin D were used (skin pigmentation, hours spent outdoors, sunscreen use and obesity) [1] to determine patients at risk for vitamin D deficiency. Further consent was then obtained from at risk patients to take blood for 25 OH vitamin D (LIAISON®, Diasorin Assay). Of the 162 patients recruited into this study, 133 (82%) had risk factors for vitamin D deficiency. Of these 108 (81% of at risk) consented to blood testing for 25 OH vitamin D, with a median of 50nmol/l (range 14 – 110nmol/l) obtained. A total of 56 (52% at risk, 34% of total participants) were found to be vitamin D deficient and of these 45 (80% at risk) were mildly deficient (25 OH D 30 -50nmol/l) and 11 (20% at risk) had moderate deficiency (25 OH D 12.5 – 29 nmol/l). Although our study was undertaken at the end of summer, one third of the patients in our study were vitamin D deficient. Furthermore, half of those clinically deemed at risk for vitamin D deficiency were confirmed on biochemical testing. Childhood fracture incidence has been reported to be increasing, and with relatively stable genetic characteristics, any variations in childhood fracture incidence would imply environmental changes. The effect of mild to moderate vitamin D deficiency on fracture risk, healing and longer term refracture risk in children and teenagers is yet to be determined, however, based on our findings we recommend that vitamin D status be assessed in all at risk children and teenagers living in urban environments at higher latitudes presenting with fracture.

Reference

1. Paxton GA, Teale GR, Nowson CA, Mason RS, McGrath JJ, Thompson MJ, *et al*: Vitamin D and health in pregnancy, infants, children and adolescents in Australia and New Zealand: a position statement. *Med J Aust* 2013, **198(3)**:142-143.

O49

The relationship of serum 25-hydroxyvitamin D with glucose homeostasis in obese children and adolescents in Zhejiang, China

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O49

Aims: Evidence of the association between vitamin D, insulin resistance and oral disposition index (oDI) in obese children and adolescents is limited. We investigated serum 25(OH) D levels in obese children and adolescents in Zhejiang, China, and determined the relationship between serum 25(OH) D and glucose metabolism.
Method: A cross-sectional design was used. All together 348 obese and 445 non-obese children and adolescents (aged from 6-16 years old) were enrolled in this study. Obese children were divided into four subgroups: normal glucose tolerance (NGT), isolated impaired fasting glucose (IFG), isolated impaired glucose tolerance (IGT), combined IFG and ITG (IFG +ITG) according to the oral glucose tolerance test. We measured serum 25(OH) D levels and calculated the homeostasis model of insulin resistance (HOMA-IR), the whole body insulin sensitivity index (WBISI), the product of β-cell function and insulin sensitivity by the disposition index (DI).
Results: The levels of 25(OH)D in obese group were significantly lower than those of non-obese group; serum 25(OH)D level in obese with NGT group was higher than that of the other three subgroups, and it was significantly inversed with LogHOMA-IR (r=-0.114, p=0.035), positively correlated with LogWBISI, LogHOMA0DI after control for age, sex, season, puberty stage (r=0.111, p=0.040; r=0.122, p=0.024). Obese patients with vitamin D deficiency have a significantly higher risk of disturbing the glucose metabolism, such as IFG, ITG, IFG plus ITG, either IFG or ITG, for its OR 3.198(95%CI 1.467-6.97), 5.443(95%CI 1.863-15.897), 5.560(95%CI 1.212-25.502), 4.007(95%CI 2.017-7.962).
Conclusion: 25(OH) D deficiencies or insufficiency are common in obese children and adolescents in Zhejiang, China. Obese patients with 25(OH) D deficiency (<30nmol /L) are at higher risk for abnormal glucose metabolism.

O50

Vitamin D status in overweight and obese Malaysian school children and its relationship with metabolic syndrome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O50

Obesity is a rising health problem, with increasing prevalence in children and adolescents. Lower vitamin D is linked to increased adiposity and higher risk of metabolic syndrome. However, evidence from tropical Asian countries is limited, especially in children and adolescents.
To examine the relationship between vitamin D level and BMI, abnormal glucose profile, insulin resistance and metabolic syndrome markers in the overweight/ obese secondary school children.
A cross sectional study in multiethnic secondary school children aged 13 -17 years was performed. Anthropometric measurements: height, weight, waist circumference and blood pressure were obtained. Blood for fasting glucose/ lipids/ insulin, and vitamin D (25 (OH)D) were taken. Oral glucose tolerance test was also performed. Insulin resistance indices were calculated based on homeostasis model assessment (HOMA) index.

A total of 543 subjects were enrolled. Forty eight percent were overweight/obese. Most of them (62%) were vitamin D deficient (<50 nmol/L), 32% were vitamin D insufficient (50 to <75 nmol/L) and only 6% were vitamin D sufficient (≥ 75 nmol/L). Mean 25(OH)D in the overweight/ obese group was 44.3±15.9nmol/L and was significantly lower compared to the non overweight/obese group (47.9±19.4nmol/L); (p=0.018). Females had lower mean vitamin D level (43.2±15.9nmol/L) compared to males (53.6±19.6nmol/L) (p<0.001). The Chinese had the highest mean vitamin D level (65.9±16.4nmol/L), followed by Malays (44.2 ±16.9nmol/L) and Indians (39.5±13.3nmol/L) (p<0.001).

Among those who were overweight and obese, metabolic syndrome was present in 58 (22%) of them. No significant relationship was found between 25(OH)D level and abnormal glucose profile, insulin resistance and metabolic syndrome markers among the overweight/ obese participants. The overweight/ obese females had 78% prevalence of vitamin D deficiency, compared to 59% in overweight/ obese males. Overweight/ obese Indians had the highest prevalence of vitamin D deficiency (82%) followed by Malays (70%) and Chinese (20%).

Vitamin D deficiency is highly prevalent in Malaysian adolescents despite an abundance of sunlight. Lower vitamin D levels are associated with female gender, ethnic groups with darker skin and obesity. However, no relationship was found between vitamin D deficiency and metabolic syndrome.

O51

Pseudohypoparathyroidism type 1a with hypomethylation at the responsible differentially methylated region for Beckwith-Wiedemann syndrome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O51

Aim: It was previously reported that several patients with pseudohypoparathyroidism type 1b (PHP-1b) have a more generalised imprinting defect. However there was no report that a patient of PHP-1a has any generalised imprinting defects. Here we aim to report a case of PHP-1a with hypomethylation at the Kv-differentially methylated region (DMR) (11p15.5), responsible for Beckwith-Wiedemann syndrome.

Method: A 6-year-old girl admitted to our hospital because of tetany due to hypocalcemia.

Result: She was a full-term infant and was delivered after an uncomplicated pregnancy. She did not show macrosomia, omphalocele or macroglossia. The neonatal period was uncomplicated. Her TSH level was in the normal range on neonatal screening. Her parents and younger sister did not show any visible sign of Albright's hereditary ostedystrophy. At 5 months old, she was severely obese and clinical follow-up was started. At 2 years old, her serum TSH level was 11.8 IU/l and free T4 was 0.4 ng/dl. Her serum calcium level and phosphate level were within normal ranges. She was diagnosed as having hypothyroidism and levothyroxine replacement therapy was initiated. Her body weight then gradually decreased. She did not suffer from mental retardation.

At 6 years old, she was admitted to our hospital because of tetany when she had an upper urinary tract infection. On admission to our hospital, she presented with a round chubby face, short neck and obesity. Radiography indicated short metacarpals, which mainly affected the fourth digit. Computed tomography indicated ectopic ossifications at putamen. Biochemistry revealed hyperphosphatemia and increased serum concentrations of parathyroid hormone. Urinary excretions of cAMP and phosphate did not increase after intravenous infusion of PTH, suggesting PTH resistance in the kidney. Molecular analysis revealed a maternally inherited 2-Mb deletion of 20q13.3- 20q13.32 including the GNAS locus and the adjacent STX16 locus. Furthermore, a loss of maternal methylation on the Kv-DMR region was detected. A specific diagnosis was made of PHP-1a in the presence of Beckwith-Wiedemann syndrome. She was treated with 1,25-dihydroxyvitamin D3 [1,25$(OH)_2$D3] (0.02 μg/kg/day) and calcium lactate (0.1 g/kg/day) was initiated. By this treatment, hypocalcemia was improved. Serum intact-PTH level has gradually decreased to 100-200 pg/ml. Her urinary calcium excretion has remained below 0.2 (calcium (mg/dl)/creatinine (mg/dl).

Conclusions: This is the first case report to describe a combination of PHP1a with a generalised imprinting defect, and their co-existence should be considered and further investigated.

Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

O52

The outcomes of a standardized approach to managing metabolic bone disease of prematurity

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O52

Metabolic bone disease (MBD) of prematurity is an increasingly well-recognized complication of pre-term birth. Despite this, there is limited evidence for the optimum method for assessing and monitoring bone health and appropriate supplementation.

This study assesses the effectiveness of the MBD protocol at Monash Health nurseries (Clayton, Dandenong and Casey) in infants born under 32 weeks' gestation between November 2012 and January 2014.

Preliminary data of 93 infants (mean gestational age (GA) 29 weeks (24-32.3weeks), birth weight (BW) 1279.4g (553-2512g)) were assessed. Risk factors assessed include 8.8% IUGR infants (n=56), 12.9% maternal pre-eclampsia, 7.5% necrotising enterocolitis (NEC) episodes and exposure to medications as follows:caffeine (84.9%; mean 42 days), diuretics (23.7%; mean 13.8 days) and steroids (2.2%). Preterm infants received 14.3 days of total parenteral nutrition (TPN) on average, with the majority on fortified expressed breast milk once enteral feeding was established.

Initial MBD screen was performed for 80.6% infants (mean age 36.6 days) with only 24.7% having repeated monitoring (mean age 67.9 days). 6.5% had Alkaline phophosphatase (ALP) levels >500U/l initially (range 143-827U/l), reducing to 1.1% (range 173-573U/l). Average Tubular Resorption of Phosphate (TRP) was 79.7% (n=71). The majority of infants were on Vitamin D 400units/day. 23.6%(n=22) commenced phosphate supplements (mean duration 41 days) and 15.1%(n=14) commenced calcium supplements (mean duration 53.2 days).

Average birth length was 38cm (10-50thcentile) with evidence of slowing growth velocity (mean follow up length 49cm (<3rdcentile) at mean age 79.9 days). Five infants were identified with fractures however two were from birth trauma and two suspected non-accidental injury. One patient had an incidental finding of fractured femur with multiple risk factors for MBD including very low birth weight (700g), NEC episodes requiring prolonged antibiotic therapy (69 days), TPN (48 days), caffeine (88 days) and diuretic use (22 days).

Significant difference (p<0.001) is noted between phosphate-treatment and untreated groups for both GA and BW: Median 27weeks and 929g for treated subjects versus 29.6weeks and 1343g if untreated. In the phosphate-treatment group, ALP levels improved (mean pre-treatment414U/l and post-treatment264U/l, p=0.0006) and difference in phosphate levels were also significant with p=0.003. Between phosphate-treatment group versus untreated group, differences were insignificant for ALP (p=0.05) and phosphate levels (p=0.09), though this may reflect insufficient subsequent MBD screens (treatment group, n=15 versus untreated group, n=7).

Further evaluation is anticipated to help improve MBD understanding in this high-risk cohort particularly given morbidity associated with MBD occult fractures. In addition, secondary outcomes would include cost efficiency of MBD surveillance and identifying optimal supplemental therapy.

ADRENAL/DSD

O53

Novel heterozygous mutations of the SF1 gene and their functional characterization in patients with 46,XY disorders of sex development (DSD) without adrenal insufficiency

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O53

Aims: Heterozygous mutations in SF1 have been identified in patients with 46,XY disorders of sex development (DSD) with normal adrenal function. This study was aimed to identify mutations in the SF1 gene in patients with 46,XY DSD and functional characteristics of their impact.
Methods: This study included 48 patients with 46,XY DSD without adrenal insufficiency or dysmorphic features. Genomic DNA was extracted from peripheral blood leukocytes and direct sequencing of the 6 coding exons of SF1 was performed. To evaluate the effect of SF1 mutations on transcriptional activity, transient transfection studies were performed using dual luciferase reporter assay system with cotransfection of PGL4.75 Renilla luciferase as a marker of transfection efficiency. Wild-type, or mutant SF1 expression vectors with SF1 dependent StAR and MIS promoters linked to luciferase were assayed for luciferase activity.
Results: Four of 48 patients (8.3%) harbored heterozygous novel sequence variants of the SF1 gene: p.G26A, p.C283R, p.L384RfsX7 and p.E445X. They presented female external genitalia with clitoromegaly in childhood or primary amenorrhea in adolescence. Endocrine evaluation at diagnosis showed low basal gonadotropin and testosterone levels. Functional studies of the p.G26A, p.C283R, and p.L384RfsX7 mutants demonstrated impaired transcriptional activation of SF1-responsive promoters. However, p.E445X mutant displayed no functional perturbation as wild-type.
Conclusion: This study identified three novel loss-of-function mutations and their functional characteristics in patients with 46,XY DSD. Loss of function mutation in the SF-1gene is one of the relatively common causes of 46, XY DSD. Therefore, genetic defect of the SF-1 gene should be considered as an etiology in 46,XY individuals without adrenal insufficiency.

O54

Response to growth hormone therapy and gonadal pathology in 45,X/46,XY females

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O54

Turner syndrome (TS) and related sex chromosome abnormalities are associated with a variety of karyotypes and phenotypes affecting 1 in 2500 live births. Mosaicism with Y material (45,X/46,XY) and female phenotype is rare (<1 in 15 000 births) [1]. Their risk of gonadal malignancy is 10-15%, and up to 50% in those with ambiguous phenotype at birth [2]. The SHOX gene is located on both X and Y chromosomes but is more prone to deletions on the X chromosome, potentially influencing height outcomes across TS karyotypes [3]. However, children with SHOX deficiency respond similarly to TS girls when treated with the same dose of growth hormone (GH) [4]. We therefore examined height outcomes and gonadal malignancy rates in TS vs 45,X/46,XY females.
We identified 198 females aged ≤ 30 years with TS or mixed gonadal dysgenesis treated with GH (under TS or auxological criteria). Final height (FH) was available on 51 TS (45,X or mosaic without Y material) females. An additional 13 had 45,X/46,XY karyotype with TS phenotype, and two had non-mosaic 46,XY karyotypes with cytogenetic abnormalities consistent with TS. Of these 15 females, gonadal tissue histology was available for 11 and FH in nine. We evaluated patient records for age, height, mid-parental height (MPH), GH dose at commencement, duration of therapy and growth response at 12 months and at FH. Comparisons between TS and 45,X/46,XY groups were performed using the Mann-Whitney U test.
All 45,X/46,XY patients had a female phenotype and five had clitoromegaly at birth. Three were identified prenatally; age at diagnosis ranged from birth to 13 years, with the most common presenting features being short stature (n=5), ambiguous genitalia (n=5) and dysmorphic features (n=2). Of the 11 that underwent gonadectomy, four (none virilised at birth) had a gonadoblastoma, including one dysgerminoma in situ.
Age, height, MPH,GH dose at commencement, duration of therapy and height z-score after 12 months did not differ between groups. Median FH z-score for 45,X/46,XY was higher than TS, -1.12 [range -1.96,0.31], vs -1.59 [-3.12,0.01], p=0.016. Response to GH therapy (median Δ height z-score) after 12 months was similar: 0.45 [-0.04,0.84] vs 0.39 [-0.21,1.14], p=0.81. However, height response over the total duration of therapy was better for 45,X/46XY: 1.5 [0.72,2.88] vs 0.87 [-0.98,2.14], p=0.009.
45,X/46,XY females appear to respond differently to GH therapy, suggesting a possible contribution of SHOX on the Y chromosome. The rate of germ cell tumours in non-virilised females (36%) is higher than previously reported.

References

1. Lindhart Johansen M, Hagen CP, Rajpert-De Meyts E, KjÃ¦rgaard S, Petersen BL, SkakkebÃ¦k NE, *et al*: **45,X/46,XY Mosaicism: Phenotypic Characteristics, Growth, and Reproductive Function – a Retrospective Longitudinal Study.** *J Clin Endocrin Metab* 2012, **97(8)**:E1540-E1549.
2. Cools M, Pleskacova J, Stoop H, Hoebeke P, Van Laecke E, Drop SL, *et al*: **Gonadal Pathology and Tumor Risk in Relation to Clinical Characteristics in Patients with 45,X/46,XY Mosaicism.** *J Clin Endocrin Metab* 2011, **96(7)**: E1171-E1180.
3. Oliveira CS, Alves C: **The role of the SHOX gene in the pathophysiology of Turner syndrome.** *Endocrinol Nutr* 2011, **58(8)**:433-442.
4. Blum WF, Ross JL, Zimmermann AG, Quigley CA, Child CJ, Kalifa G, *et al*: **GH Treatment to Final Height Produces Similar Height Gains in Patients with SHOX Deficiency and Turner Syndrome: Results of a Multicenter Trial.** *J Clin Endocrin Metab* 2013, **98(8)**:E1383-E1392.

O55

Clinical and mutational spectrum of patients with congenital lipoid adrenal hyperplasia in Southeast Asia

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O55

Aims: Mutations in Steroidogenic Acute Regulatory protein (StAR) cause congenital lipoid adrenal hyperplasia (lipoid CAH), characterized by absent steroidogenesis, potentially lethal salt loss, 46,XY sex reversal and massively enlarged adrenals engorged with cholesterol esters. Nonclassic lipoid CAH is a recently recognized disorder caused by StAR mutations that retain partial function. We aim to delineate the clinical and mutational spectrum of StAR mutations in patients with lipoid CAH.
Methods: The entire coding regions of the StAR gene were assessed by polymerase chain reaction and sequencing analysis.
Results: There were 10 patients of lipoid CAH had mutations in the StAR gene with 5 novel mutations (p.P230L>WfsX, IVS6-1G>A, IVS3+(2-3)insT, p.W147R, p.Q264R). Eight patients had classic lipoid CAH presenting with adrenal crisis during early infancy (range of onset 3-11 months of age). Two siblings had nonclassic phenotypes with later onset adrenal insufficiency without disordered sex development. Adrenal enlargement by imaging was demonstrated in only 3 cases of classic lipoid CAH. The functional studies of novel StAR mutations are being under investigation.
Conclusion: StAR mutations may not be rare in Southeast Asian population. There is a broad clinical spectrum of StAR mutations varying from early onset adrenal insufficiency to late onset of glucocorticoid

deficiency with only mild defects in mineralocorticoid and sex steroid synthesis. Adrenal gland enlargement is not pathognomonic for lipoid CAH.

O56

Gender change and stigmatization in late-treated Indonesian children, adolescent, and adult patients with DSD

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**O56

In Indonesia clinical management of Disorders of Sex Development (DSD) is challenged by limited knowledge and limited diagnostic and treatment facilities. Prior to this study, most patients remained untreated and grew up with ambiguous bodies and doubts about their gender. We investigated patients' experiences of being raised in ambiguity.
118 Indonesian patients, ages 6 – 41, with 46XX DSD (n=27), 46XY DSD (n=77) and chromosomal DSD (n=14) were compared to 118 control subjects matched for gender, age, and living area. Questionnaires for gender identity, gender role behavior and social stigmatization were translated or designed. The psychometric properties were satisfactory. For patient and control group comparisons, Mann-Whitney U and Fisher's Exact tests were applied.
The results showed that 7% of the children, 8% of the adolescents and 44% of the adults changed gender, particularly non-diagnosed and non-treated patients with 46XY DSD (81%). 95% of the patients changed gender from female to male, including untreated patients with 46,XX CAH-SV. Compared to control groups, cross-gender role behavior was seen in young girls with 46XX CAH-SV (p=.047) and adolescent girls with different types of DSD (p=.01). In girls with DSD, confusion with gender identity was seen (young girls p=.004; adolescent girls p=.01). Adult men reported past cross-gender role behavior (p=.01) and past problems in gender identification (p=.01) prior to female-to-male gender change.
Children with genital ambiguity (p<.006) and cross gender behavior (p<0.001) and adults with ambiguous bodies (p=.001) and adults who changed gender (p<0.03) suffered stigmatization. Rejection or isolation elicited depression and withdrawal from social activities in girls (p=.002), women (p=.009) and youngsters who had changed gender (p=.02).
We conclude that a high percentage of our patients changed gender. The wish for gender change was particularly seen in patients with progressive masculinization. Patients with DSD who had visible ambiguity in physical and behavioral appearance suffered stigmatization. Teasing and rejection led to strong emotional reactions. Early clinical evaluation and treatment, patient and parent education, and teaching coping strategies will improve quality of life.

POSTER PRESENTATIONS

DIABETES

P1

Novel heterozygous deletion in the *HNF1β* gene - adolescent with antibody negative diabetes, longstanding hyperglycaemia without ketosis, cataracts, small echogenic kidneys with a cortical cyst, pancreatic atrophy, exocrine pancreatic insufficiency and a uterine anomaly

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P1

A 13 year old pubertal Caucasian female presented with longstanding polyuria/polydipsia and weight loss of 12kg over 4 months (BMI decreased from 23 to 17.5kg/m^2 despite a 5cm height gain). There was no personal / family autoimmunity history. A paternal grandparent was thought to have type 2 diabetes. She was haemodynamically stable and mildly dehydrated without clinical signs of insulin resistance. She had bilateral stellate posterior subcapsular cataracts. Plasma glucose was 57mmol/L with normal blood ketones and venous pH. HbA1c was 18.2% (175mmol/mol). Mildly elevated urea and creatinine corrected after rehydration. Liver function tests, serum magnesium and urate were normal. Islet autoantibodies were negative.
Renal ultrasound (US) identified bilaterally small kidneys (<5th centile), with echogenic parenchyma, reduced corticomedullary differentiation, normal cortical thickness and a 5mm left cortical cyst. Urinary albumin/creatinine and calcium/creatinine were normal.
Further imaging (US and MRI) demonstrated severe pancreatic atrophy and a müllerian duct anomaly (arcuate / subseptate uterus).
Faecal elastase 1 in a soft stool sample was low (range of severe exocrine pancreatic insufficiency). However the patient has gained weight with insulin treatment and had normal measures of fat-soluble vitamins.
Aim: Conduct genetic testing for the autosomal dominant Renal Cysts and Diabetes Syndrome (RCAD), also known as MODY5, caused by heterozygous mutations of the hepatocyte nuclear factor–1 beta (HNF1B) gene (chromosome 17q12).
Methods: Direct testing for HNF1B gene sequence variations was performed by Multiplex Ligation-dependent Probe Amplification (MLPA) and bidirectional DNA sequencing.
Results: A heterozygous c390_395del (p.Gln130_Gln131del) was detected. This novel deletion results in the in-frame loss of two glutamine residues in exon 2 of the HNF1B protein. These residues are highly conserved and located in the HNF1 N-terminal domain that contains a dimerization sequence and an acidic region that may be involved in transcription activation. Parental testing has determined that this variant is likely de novo.
Conclusion: This de novo variant has not been previously described, hence its pathogenicity is unknown. However the phenotype is consistent with RCAD (MODY5).
Written informed consent was obtained from the patient for publication of this Case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

P2

1,5-Anhydroglucitol, an indicator of short term glycaemic control, is the most discriminatory metabolomic marker in adolescents with type 1 diabetes compared to control subjects

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P2

Aim: To compare the metabolomic profile of adolescents with T1D (≥5 years duration) to controls using gas chromatography–mass spectrometry (GC-MS).
Methods: Design Case control study. Setting Tertiary paediatric hospital clinic. Population 27 (14F/13M) adolescents with T1D (age (median, interquartile range) 15.5, 14.7-16.4 years; duration 7.7; 6.0-11.8 years; HbA1c 9.1, 8.1-10.1%); glucose 13.35 (7.60-17.85) and 27 (14F/13M) control participants (age 15.1, 14.4-16.8 years). BMI was <95th percentile. Measures Fasting plasma and urine metabolomes were profiled by GC-MS and compared between cohorts. Statistics Univariate comparisons:-

Spearman correlations, t-tests/Wilcoxon rank sum tests. Multivariate comparisons:-PCA, OPLS-DA and OPLS.
Results: For GC-MS (plasma and urine), the molecule most influential in separating the two groups was identified as 1,5-anhydroglucitol (1,5-AG) a metabolically inert polyol that is a short-term marker of glycaemic control (7-14 days). It competes with glucose for reabsorption in the kidneys. Otherwise stable levels of 1,5-AG are rapidly depleted as blood glucose levels exceed the renal threshold for glycosuria. 1,5-AG was more influential on group classification than fasting glucose or HbA1c.
Multivariate regression modelling of the plasma data (glucose signals removed) was performed against glucose and HbA1c groups (glucose:4.2-5.4mmol/L, 5.3-9.9mol/L, 11.0-36.7mmol/L; HbA1c:4.7-6.0%, 7.3-9.2%, 9.9-15.4%). Three distinct groups emerged for each variable indicating clear metabolomic differences.
Conclusion: Metabolomic profiling was feasible in this context. GC-MS revealed a "marker" distinguishing the two groups without any bias for or targeting of the analyte. The metabolic profile of the adolescents with diabetes appears to be most influenced by short-term (7-14days) hyperglycaemia. The planned GC-MS fatty acid methyl ester (FAME) analysis and Liquid Chromatography-MS will reduce inherent interference by glucose and provide a more comprehensive coverage of the metabolome.
A 1,5-AG blood assay (GlycoMark) is not yet routinely available in pathology laboratories in Australia. Due to discussions following this study, it may shortly become available. Its particular utility is to assess recent glycaemic control and suggest unrecognised postprandial hyperglycaemia in moderately-controlled (HbA1c 6.5-8%) patients.

P3

15-year incidence of new-onset diabetic ketoacidosis in children with type 1 diabetes from a regional paediatric setting (Auckland, New Zealand)

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P3

Aims: This study aimed to assess the incidence of new-onset diabetic ketoacidosis (DKA) incidence over a 15-year period in children with type 1 diabetes (T1DM) from our regional paediatric diabetes centre in Auckland, New Zealand.
Methods: We performed a retrospective review of all patients <15 years of age diagnosed with T1DM from our unselected complete regional cohort for the years 1999 to 2013. Children were included if they had type 1 diabetes as defined by clinical presentation and/or DKA and/or presence of pre-type 1 diabetes autoantibodies. DKA was classified into Mild (pH <7.3 bicarbonate <15), Mod (pH <7.2 bicarbonate <10), and severe (pH <7.1 bicarbonate <5), according to the ISPAD guidelines.
Results: For the 15-year period, there were 731 children <15 years with new-onset T1DM, 343 (47%) males, there were 195 (26.7%) cases of new-onset DKA: 51 (26%) severe, 52 (27%) moderate, and 92 (47%) with mild DKA. Average age at diagnosis was 8.6 years. The annual incidence of DKA was variable, ranging from 18% to 37%. The overall incidence of new-onset DKA did not differ over the study interval (p=0.78). The likelihood of being in DKA at onset of T1DM was unaffected by age, sex, ethnicity, or socio-economic status. Amongst those in DKA, New Zealand European ethnicity (p=0.038) and female gender (p=0.056) were each associated with increasing DKA severity at presentation.
Conclusions: There has been a stable but persistent level of New-onset DKA over the 15-year period studied in our regional paediatric population. Action must be taken to improve awareness of T1DM and in doing so, reduce the incidence of new-onset DKA.

P4

African immigrant parents' understanding of their teenagers' newly diagnosed diabetes status in Perth, Western Australia

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P4

Background: Recently Western Australia has seen a rise in African population due to both economic and refugee migration. Concurrently, a rise in the numbers of teenagers of African origin diagnosed with both type 1 and type 2 diabetes and associated complications has been noticeable. Different ethnic background is a known risk factor for poor metabolic control; this trend is reflected in studies wherein people of African origin have been found to have a high risk of developing diabetes. What is evident from health promotion literature is that parents of teenagers with a chronic health condition, when they are well informed about that condition, play a key part its management. Little is known, though, about what African migrant parents understand about diabetes and its dietary control.
Aim: To develop insight of a sample of migrant African parents now residing in Western Australia knew about, and were able to provide in relation to the dietary needs of their recently-diagnosed diabetic teenager through an exploration of family food habits.
Methods: A survey approach.
Findings: Twelve parents from five different countries of origin participated in this survey. Despite all participants having received education on the topic from a dedicated paediatric diabetes team, it was evident from their families' food habits that either an understanding of or the capacity to accommodate the dietary requirements of their diabetic teenager was minimal.
Conclusion: It is possible that African migrant parents of diabetic teenagers' knowledge about and capacity to support their children's dietary needs is contributing to unplanned hospital admissions. The results of this small survey indicate a need to revise the information provided to African migrant parents of diabetic teenagers to more closely accommodate cultural preferences. Further work is necessary to determine the most effective approach to health education with this group of health care consumers.

P5

Permanent neonatal diabetes mellitus in China

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P5

Aims: Permanent neonatal diabetes mellitus (PNDM) is a rare disease which is defined as the onset of diabetes before the age of 6 months with persistence through life. Patients with KCNJ11 or ABCC8 gene mutations have the opportunity to switch to oral sulfonylurea therapy. There were limited studies about the genetic analysis and long term follow-up of PNDM.
Method: Report four cases of PNDM, including their genetic mutations, treatments and long-time follow-ups. All of the patients and their parents got gene analysis include INS, KCNJ11 or ABCC8 gene.
Results: None of the patients and their parents suffered from any genetic mutations of these three common genes. One of the children got continuous subcutaneous insulin infusion (CSII) and the others got multiple injections of insulin (MII). The PNDM patients had persisted after 35 months to 60 months of follow-up, 3 patients maintained almost stable blood sugar level, and 1 patient had poor sugar control.
Conclusion: All of PNDM patients are suggested undergo genetic evaluation. For patients without KCNJ11 and ABCC8 gene mutation, oral sulfonylurea might not be considered. CSII is a useful tool for overcoming the difficulties of diabetes, and can also improve quality of life.

P6

Electrocardiography evaluation in type 1 diabetes mellitus, preliminary study

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P6

Cardiovascular complication should be evaluated in patient with T1DM. Ventricular instability (QT abnormalities) in Type 1 Diabetes Melitus (T1DM) is a risk factor for mortality. Prolongation of corrected QT interval (QTc) is accurate and the most sensitive test for the autonomic neuropathy whether QT interval dispersion (QTd) in arrhythmia is a predictor for mortality. This study is to evaluate arrhythmia, prolongation of QTc and QTd in T1DM children. Cross sectional study of children diagnosed T1DM in Soetomo Hospital; Surabaya during April 2013 to April 2014 was performed. The ECG was done in all of the patients. Arrhythmia, QTc and QTd were measured and analyzed with Paired t-test. There were 17 patients joint this study. Age was 8 to 15 years. There were 9 girls and 8 boys who suffered from 1 to 7 years of illness. There were 9/17 arrhythmia patients, 2/17 prolonged QTc patients, 4/17 borderline QTc patients, 1/17 with total AV block. The patient with total AV block was diagnosed DMT1 with ketoasidosis and acute pancreatitis. There was 1 patient without prolonged QTc although suffered from five times of DKA. The mean of QTc was 428.5 (SD 27.67) m.sec and QTd was 29.3 (SD 12.79) m.sec. There was significant differences between present of arrhythmia and QTd ($P<0.01$, 95% CI -35.01 to -20.85) and QTc ($P<0.01$, 95% CI -442.43 to -411.85). Arrhythmia and prolonged QTc was present in T1DM children under 10 years of illness. No one with prolonged QTd. Every arrhythmia should be taken into account in QTd to predict the mortality.

P7

What can we learn from adherence data in adolescents participating in a clinical trial?

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P7

Introduction: Treatment adherence during adolescence is challenging. Limited data exist for the rate of medication adherence in adolescents.
Aim: To evaluate medication adherence using two different methods (electronic monitoring system and tablet count) in adolescents with Type 1 Diabetes (T1D) participating in an RCT.
Method: Medication adherence was assessed in 54 T1D adolescents (age 14±2.3y, 26 males) enrolled in a 1 year RCT to receive metformin or placebo [1].
Adherence was assessed using tablet count and prospective electronic monitoring using Medication Event Monitoring System caps (MEMS, AARDEX group, LTD Sion, Switzerland), which recorded episodes of bottle opening for each participant. These data were then compared to prescribed doses.
Adequate adherence was defined as ≥ 80% of prescribed doses taken over a defined period. Adherence was assessed after allowing a 3-month run-in period to account for dose titration and minimise potential for reactivity associated with initial adherence monitoring. Data were reported from 3-6 months (short-term) and from 6-12 months (long-term).
Results: Adolescents had mean T1D duration 5.9±4.2y, median HbA1c 8.5 (6.3-11.6)%. 26 used CSII.
MEMS adherence data for short and long-term use was available for 53 and 48 participants respectively. Adequate adherence using MEMS was 47% (25/53) short-term and 35 (17/48) long-term. Median (IQR 25-75%) adherence was 79 (46.6-88.7%) short-term and 67 (43.4-86.8%) long-term.
Tablet count adherence data for short and long-term use was available for 35 and 42 participants respectively. Adequate adherence using tablet count was 63% (22/35) short-term and 45% (19/42) long-term. Median (IQR 25-75%) was 84 (70.8-90.1%) short-term and 77 (61.7-86.8%) long-term.
There was no statistically significant difference in adherence between the two methods used p=0.22 (short-term) and p=0.07 (long-term). Adolescents who were adherent in the short-term by MEMS were more likely to have a longer diabetes duration (7.2 vs 4.8 years, p=0.03).
Conclusion: Adolescent adherence to intervention in this clinical trial was suboptimal as shown by both electronic monitoring and tablet count. This finding reinforces the importance of parental involvement in treatment regimens in this population.
Reference

1. Anderson , *et al*: *BMC Pediatrics* 2013, **13**:108.

P8

Prevalence and potential risk factors of hypokalemia in pediatric patients with diabetic ketoacidosis

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P8

Aims: To examine the local prevalence of hypokalemia in patients with diabetic ketoacidosis (DKA), both at presentation and during treatment, and to investigate the potential risk factors leading to significant hypokalemia during treatment of DKA.
Methods: Retrospective review of 114 consecutive patient-episodes. Univariate analyses were performed to study any difference in mean between the group with nadir of potassium (Kn) >= 3.0mmol/L from group with Kn < 3.0mmol/L for predictors concerning patients' demographics, the baseline characteristics, the therapies for DKA (including average insulin infusion rate before Kn), and the pace of recovery from DKA. Predictors deemed statistical significant in univariate analyses were subjected to multivariate analysis.
Results: The period prevalence of hypokalemia at presentation and during treatment of DKA were 13.8% and 92.5% respectively. Univariate analysis showed patients who were younger, with lower mean body weight, lower mean plasma bicarbonate at presentation, lower mean serum potassium level at presentation, higher urine output per unit body weight (in the first 24 hours of admission), higher amount of potassium supplement given before Kn, shorter time lag of starting potassium supplements (as reference to time of start of insulin) and longer duration of metabolic acidosis were independently associated with risk of developing Kn < 3.0mmol/L. Multivariate analysis showed that duration of metabolic acidosis was the sole risk factor for having Kn < 3.0mmol/L.
Conclusions: In our cohort, the longer duration of metabolic acidosis predicts significant hypokalemia during DKA treatment, which could have represented a persistent accumulation of free fatty acid and an on-going stimulus for aldosterone secretion, hence kaliuresis-related hypokalemia [1-7]. Therefore, in patients with slow resolution of metabolic acidosis, the measurement of the urinary potassium might allow for better estimation of potassium requirement during DKA treatment, such that significant hypokalemia could be minimized. In our data, the average insulin infusion rate was not associated with statistically increased risk of significant hypokalemia, therefore, the strategy of lowering insulin infusion rate in patients with significant hypokalemia during DKA treatment should require further evaluation.
References

1. Gennari FJ: **Disorder of potassium homeostasis: Hypokalemia and Hyperkalemia.** *Crit Care Clin* 2002, **18**:273-288.
2. Nardone DA, McDonald WJ, Girard DE: **Mechanisms in hypokalemia: clinical correlation.** *Medicine* 1978, **57**:435-446.
3. Adrogué HJ, Lederer ED, Suki WN, *et al*: **Determinants of plasma potassium levels in diabetic ketoacidosis.** *Medicine* Baltimore 1986, **65**:163-72.
4. Sterns RH, Cox M, Feig PU, Singer I: **Internal potassium balance and the control of the plasma potassium concentration.** *Medicine* Baltimore 1981, **60(5)**:339-354.

5. Goodfriend TL, Ball DL, Egan BM, *et al*: **Epoxy-keto derivative of linoleic acid stimulates aldosterone secretion.** *Hypertension* 2004, **43(2)**:358-63, Epub 2004 Jan 12.
6. Giebisch G: **Renal potassium transport: mechanisms and regulation.** *Am J Physiol* 1998, **274**:F817-33.
7. Frindt G, Palmer LG: **Effects of insulin on Na and K transporters in the rat CCD.** *Am J Physiol Renal Physiol* 2012, **302**:F1227-33.

P9

HbA1c variability and the risk of microalbuminuria in patients with type 1 diabetes

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P9

Aims: The higher HbA1c is a risk factor for microvascular complication in type 1 diabetes. However, it remains controversial that glycemic variability seemed to be an additional risk factor for development of complication in diabetes. In this study we have analyzed the HbA1c variability to investigate the influence on progression of microalbuminuria in patients with type 1 diabetes.
Methods: Fifty patients (M=27, F=23) with type 1 diabetes and microalbuminuria who visited Yonsei University Severance Children's Hospital were enrolled. In addition, ninety eight (M=31, F=67) type 1 diabetic patients without complication were enrolled for control. Microalbuminuria is defined that urinary albumin excretion rate is between 30 mg/24h and 300 mg/24h. HbA1c during 3 years (just before the development of microalbuminuria or in the past 3 years in control) were reviewed retrospectively. HbA1c variability expressed as standard deviations (SDs) of HbA1c for 3 years.
Results: There was no difference of mean age between type 1 diabetic patients with microalbuminuria and control (respectively, 22.9±5.5year and 21.6±4.8years, p=0.129). The mean duration to developed microalbuminuria was 9.9±5.1 years. Mean HbA1c was higher in patient with microalbuminuria (14.3±5.1%) than in control (12.2±5.3%, p=0.02). HbA1c variability was also higher in patient with microalbuminuria (1.14 ±0.81) than in control (0.69±0.38, p<0.001). HbA1c variability was closely related to the mean HbA1c level in all patients (r=0.480, p<0.001). There were also significant trends that microalbuminuria was developed in patients with higher HbA1c SDs in shorter period (r=-0.418, p=0.003).
Conclusion: This study has shown that HbA1c variability was positively correlated with mean HbA1c level and progression of microalbuminuria. In addition, higher HbA1c variability may shorten the period of development of microalbuminuria. Thus, long-term fluctuation in glycemic control seems to contribute to the development of microalbuminuria in type 1 diabetes.

P10

Reproductive health knowledge, attitudes and beliefs in young women with type 1 diabetes mellitus aged 15 – 25 years attending a tertiary centre multidisciplinary transition clinic: A descriptive study

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P10

To assess issues related to the existing reproductive health knowledge, attitudes and beliefs in 15 – 25 year old young women with type 1 diabetes mellitus (T1DM), we administered a questionnaire as sexually active adolescents with T1DM are at high risk of unplanned pregnancies and reproductive complications. Glycaemic control during adolescence is recognised as being poorer than during any other life stage. Periconceptional poor glycaemic control is associated with increased incidence of congenital malformations. This is a descriptive study in females aged 15 – 25 years attending our Young Adult Diabetes Service (YADS) clinic, a transition clinic at Monash Medical Centre, a conception to end of life tertiary health facility. Our study was undertaken between June 2011 and June 2013, when there were 173 eligible young women on our YADS clinic database. Data was collected on a cross-sectional basis from a web-based questionnaire on a sample of 100 female adolescents who provided consent to participate (58% of those eligible), using a modified reproductive health attitudes and behaviour (RHAB) questionnaire [1]. Almost half (48%) of respondents were sexually active, with a mean age of sexual debut of 16.9±1.8years (range 13 – 21yrs). Mean HbA1c was 8.9±1.6%. HbA1C in non participants was significantly higher (9.2±1.8%), although responders and non-responders were comparable on age and SES. Responses to questions related to their personal concerns about their future health risks, revealed that respondents perceived their risk and level of concern of unplanned pregnancies (18.7%) and STDs (8.7%), to be much lower than those of weight gain (59.3%) and blindness (57.1%). Despite high perceived benefits of prepregnancy counselling (PC) (78%), low PC delivery rates were reported by study participants (15%), although review of clinic check lists revealed documentation that 34% of study participants had received PC. Diabetic Nurse Educators (DNEs) were perceived to be the most useful source of health information (81% of respondents). We support recommendations of the National Health and Medical Research (NHMRC - 2011) that young adolescents need developmentally appropriate information from commencement of puberty, with a sensitive, proactive, preventative approach before these young women become sexually active, to enable them to make informed choices regarding reproductive health. However, engaging adolescent girls with T1DM to provide effective provision of such information remains challenging, even in an age appropriate specialised clinic setting.

Reference

1. Charron-Prochownik D, Wang SL, Sereika SM, Kim Y, Janz NK: **A theory-based reproductive health and diabetes instrument.** *Am J Health Behav* 2006, **30(2)**:208-220.

P11

Neonatal diabetes as an isolated manifestation of ipex: an expanding spectrum of disease phenotype with FOXP3 mutation

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P11

Neonatal diabetes occurs due to a genetic form of pancreatic βcell dysfunction. Mutations in a number of genes have been identified in the last decade which has helped not only in the etiological diagnosis but has also influenced medical therapy.
Our proband was born at term with a birth weight of 3.99kg with no antenatal risk factors. He presented in severe diabetic ketoacidosis at 8 weeks which required intensive management. He was commenced on continuous subcutaneous insulin infusion for his ongoing management.

His initial genetic analysis for ABCC8, KCNJ11, INS gene mutations was negative.
He demonstrated excellent glycaemic control with an average HbA1C of 6.5% at 2 years of age. His growth and development are appropriate for age with no associated co-morbidities. However, further targeted next generation sequencing of all known neonatal diabetes genes identified a hemizygous FOXP3 missense mutation p.R347H with his mother as a carrier. FOXP3 mutations cause IPEX syndrome, (immunodysregulation, polyendocrinopathy, enteropathy, X-linked syndrome) and can be lethal in infancy and early childhood. Prophylactic bone marrow treatment is the only known cure for this condition.
Our proband has isolated neonatal diabetes with no other features of IPEX. His maternal grandfather aged 63 years, was also hemizygous for the mutation. He had enteropathy secondary to ulcerative colitis since childhood which was resistant to conventional treatment and required colostomy. This makes him the oldest living man with IPEX. Our proband's maternal cousin also had eczema in infancy which has resolved.
This case highlights the impact of genetic diagnosis on the management of neonatal diabetes. A lethal condition with no cure other than bone marrow transplant has now been shown to have atypical manifestations with the availability of genetic testing. The management in our patient is challenging given the poor genotype – phenotype correlation and the dearth of information regarding milder forms limited to a few case reports with similar mutation. We have decided against prophylactic bone marrow transplant and will consider it in the event of enteropathy or another autoimmune manifestation.
Written informed Consent for this patient has been taken including results of the genetic analyses according to the Institutional Ethics Committee procedures of our health service.

P12

Phenotype, genotype of neonatal diabetes mellitus due to insulin gene mutation

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P12

Insulin (INS) gene mutations that cause permanent neonatal diabetes mellitus change single protein building blocks (amino acids) in the protein sequence. These mutations are believed to disrupt the cleavage of the proinsulin chain or the binding of the A and B chains to form insulin, leading to impaired blood sugar control. At least 10 mutations in the INS gene have been identified in people with permanent neonatal diabetes mellitus.
Objective: To describe clinical features and laboratory manifestations of patients with INS gene mutation and to evaluate outcome of management.
Subject and methods: Clinical features, biochemical finding, mutation analysis and management outcome of 3 cases from 3 unrelated families were studied. All exons of INS gene were amplified from genomic DNA and directly sequenced.
Results: 3 cases (one girl and two boys) onset at 126.6 ±56.7 days of age with gestation age of 38.0 ± 1.4 weeks, birth weight of 2850 ± 494.9 g. All of them admitted with the feature of diabetic ketoacidosis with pH of 6.94 ±0.16; HCO^-_3 2.63 ±0.85 mmol/l; BE 26.05±4.03 mmol/l, plasma glucose levels were 37.57±15.2 mmol/l, HbA1C of 9.9 ±2.5%. Mutation analysis of the INS gene showed: heterozygous for a novel missense mutation (c.127T>A; C43S) in exon 2 of INS gene in one case; heterozygous for a novel INS splicing mutation, c.188-31G>A of the INS gene in two cases. After 8 months of insulin treatment, two patients with c.188-31G>A mutation have normal development with DQ 80-100%, HbA1C of 6.85 ±0.49%, quite normal blood glucose levels. The case with c.127T>A mutation treated with insulin for 8 years has physical development delay, poor blood glucose control with HbA1C of 11.4%.
Conclusions: It is important to perform screening gene mutation for patients with diabetes diagnosed before 6 months of age to control blood glucose and follow up the patients.

P13

Clinical, para-clincal and outcomes of diabetes ketoacidosis in Vietnam national hospital pediatrics

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P13

Diabetic ketoacidosis (DKA) is a serious complication of diabetes mellitus that occurs when your body produces high levels of blood acids called ketones**.**
Objective: This study aimed at describing some characteristics of clinical and commenting outcomes of the treatment for DKA in children with diabetes mellitus type 1 (DM1) in Vietnam National Hospital of Pediatrics from 2007 to 2012.
Methods: Description retrospective and prospective on all patients previously diagnosed of DM1 or newly diagnosed of DM1 with DKA.
Results: On average: each year, patients with DKA were admitted. 72% of these cases were first presentation with diabetes. Up to 36% of cases had misdiagnosis for other diseases. Clinical: dehydration 100%; 92% altered consciousness; vomiting 72%; thirsty 72%; weight loss 78%. The clinical presentation of DKA in patients who the newly diagnosed of DM1 was more severe than that in preciously diagnosed patients. The risk factors: 64% infection for all; 57.1% non-compliance with treatment for patients being treated insulin before. Laboratory: Blood glucose 36.8 ± 13.5 mol/l (from 14 to70 mol/l). Severe and moderate acidosis was seen in 56%. Abnormality of sodium levels were found in 11/25 patients (44%), of which only 3/25 patients actually decreased serum sodium (adjusted sodium); hyperkalemia in 6/25 patients (24%). The time of infusion insulin was 18.9 ± 27.56 hours. Average time replacing fluid was 37.7±21.1 hours. The duration of ketonuria was 37.9 ± 17.5 hours. Patients were alert after 12.04 ± 11.52 hours.
Conclusion: DKA is a complex disordered metabolic state characterized by hyperglycemia, ketoacidosis, and ketonuria. The goal of treatment is to correct the high blood glucose level with insulin. Another goal is to replace fluids lost through urination, loss of appetite, and vomiting.

P14

Cyclical variation in the national incidence of childhood type 1 diabetes in Australia (2000 - 2011)

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P14

To determine the incidence and incidence rate trends of type 1 diabetes in children aged 0-14 years Australia-wide using all available data from 2000 to 2011, and to examine the temporal trends for non-linear, cyclical variation.
Cases were identified from the National Diabetes Register (NDR) which was established in 1999 and contains data on patients with insulin-treated diabetes Australia-wide. For 0-14 year olds with type 1 diabetes the NDR is estimated to be 97.7% complete [1]. Population data published by the Australian Bureau of Statistics were used as the denominator data. Annual age-standardised as well as gender and age specific incidence rates were calculated. Poisson regression was used to analyse the incidence by calendar year, gender, and age at diagnosis. To analyse the incidence for non-linear variation, sine and cosine functions

were applied to Poisson regression models for 3-, 4-, 5-, 6-, and 7-year cycles and the Akaike Information Criterion (AIC) used to assess goodness-of-fit [2].
Between 2000 and 2011, 11,575 (6,049 M, 5,526 F) cases of childhood type 1 diabetes were identified from the NDR. The mean incidence of childhood type 1 diabetes in Australia over this time period was was 23.6 (95%CI:23.2 – 24.0) per 100,000 person years. The mean incidence was 4.9% (95%CI:1.1% - 8.8%) higher in boys compared to girls. Compared to 0-4 year olds, the mean incidence was 65% higher in 5-9 year olds, and 208% higher in 10-14 year olds. No significant linear increase in the incidence rate trend was observed overall (Incidence rate ratio 1.003 (95%CI:0.997 – 1.008), or by gender. An average annual increase in incidence was only observed in the 10-14 year old age group (1.2% per year (95%CI:0.4% - 2.1%)). When analysed for non-linear variation in the temporal trends, a 5-year cyclical variation of 6% was observed in the overall incidence rate trend. A 5-year cyclical variation in incidence was observed in both genders and all age groups.
From 2000 to 2011, no linear increase in the annual overall incidence of childhood Type 1 diabetes was observed in Australia. Of interest, a sinusoidal pattern in the incidence rate trend was observed, with a 5-year cyclical pattern. The cyclical pattern of incidence rate trends observed Australia-wide corroborates findings reported in Western Australia [3] and provides further evidence supporting a key role of environmental factors in the aetiology or clinical onset of childhood type 1 diabetes – further investigation is required.

References

1. AIHW: Diabetes series no. 13. *Cat. no. CVD* 2010, **51.**
2. Stolwijk , *et al*: *J Epidemiol Community Health* 1999, **53**:235-238.
3. Haynes , *et al*: *Diabetes Care* 2012, **35**:2300-2.

P15

D-buddy peer support for better health outcomes in adolescents with diabetes mellitus

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P15

Aim: Diabetes can be demanding and burdensome causing emotional distress. Non-adherence to treatment and self-care management can affect diabetes outcomes and quality of life. Peer support can play an important role in better psychological adjustment to diabetes. The aim of this study is to evaluate improvement in Quality of Life (QOL), Problem Areas in Diabetes (PAID) and glycaemic control in adolescents with diabetes.
Methods: Adolescents age 12-18 years with Type 1 or Type 2 diabetes on insulin were recruited between October 2012 to December 2013 and paired with a buddy of same age, gender and type of diabetes to provide peer support. They were instructed to contact peer buddy via telephone, SMS, Facebook, WhatsApp, or Face-to-face for 6 months. QOL, PAID scores and HbA1c were measured before and after 6 months. The adolescents who refused enrolment were treated as control group and HBA1c compared at 6 months with the study group.
Results: A total of 66 patients (33 buddy pairs) were recruited in peer support group and 100 in control group. There were more females in peer support group (72.7%) than in the control group (49%).
In peer support group, mean number of contact episodes was 1.3 +1.4, and most common mode of contact was via SMS (43.9%), WhatsApp (27.3%) and Facebook (21.2%). There was slight improvement in mean QOL score (67.2 +14.3 vs. 69.1 +13.6; p=0.1) and also a marginal reduction in mean PAID score (25.2 +19.3 vs. 23.4 +18.8; p=0.3) indicating less negative emotions related to diabetes.
From baseline to 6 months, there was no improvement in mean HbA1c for peer support group (9.3 ±3.2 vs. 9.3 ±2.4; p=1.0) and control group (9.4 +2.2 vs. 9.3 +2.3; p=0.5).
Conclusions: Our findings showed that there were no significant improvement in glycaemic control, quality of life and problem areas in diabetes of adolescents receiving peer support. Therefore, we need to develop other methods engaging adolescents sustain improvement in health outcomes.

P16

A lack of association between vitamin d-binding protein and 25-hydroxyvitamin d concentrations in pediatric type 1 diabetes without microalbuminuria

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P16

The risk of vitamin D deficiency might increase along with the increased urinary loss of vitamin D binding protein (VDBP) consequent to impaired 25-hydroxyvitaminD (25-OHD) circulation. We aimed to evaluate the possible increased urinary loss of VDBP, a correlation between VDBP and circulating 25-OHD levels, and the risk factors influencing low vitamin D levels in pediatric type 1 diabetes patients without microalbuminuria.
Subjects with T1DM without microalbuminuria (n=45) and age-matched healthy control subjects (n=29), aged 9–14 yr, residing in Seoul and the Gyeonggi-Do in Korea (37°N) were studied. Height, weight and pubertal stage were evaluated. The percentage of body fat was measured by bioelectrical impedance analysis (inbody). A questionnaire was used to assess the amount of daylight outdoor activity and vitamin D intake. Serum levels of calcium, phosphorus, intact parathyroid hormone, 25-OHD, 1,25 dihydroxyvitamin D and VDBP, as well as urinary levels of VDBP, microalbumin and creatinine (Cr) were measured. 25-OHD deficiency was defined as ≤20 ng/mL.
The urinary VDBP to Cr ratio (VDBPCR) in type 1 diabetes patients was higher than that in the control group (P = 0.016) and correlated positively with the urinary microalbumin to Cr ratio in both groups (P <0.001). The serum 25-OHD levels did not correlate with the serum VDBP or urinary VDBPCR. A multivariate regression analysis including known vitamin D deficiency risk factors (age, gender, body fat percentage, vitamin D intake, daylight outdoor hours, and urinary VDBPCR) revealed that daylight outdoor hours (β = 2.881, P = 0.009) and vitamin D intake (β = 2.342, P = 0.050) affected the 25-OHD levels in type 1 diabetes patients.
In pediatric type 1 diabetes patients without microalbuminuria, the urinary VDBP loss was increased proportionally with the urinary mACR. However, the urinary VDBPCR did not correlate with the serum 25-OHD levels. The factors associated with 25-OHD levels during winter periods were daylight outdoor hours and vitamin D intake.

P17

Analysis of insulin pump settings in children and adolescents with type 1 diabetes mellitus

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P17

Aim: To characterise current insulin pump settings used in young patients with type 1 diabetes mellitus (T1DM) and their relationship to glycaemic and weight control.
Methods: This retrospective study included patients aged <18 years old with T1DM duration >1 year who were using the Medtronic pump device. Data from the insulin pumps including number of blood glucose (BG) tests per day, basal and bolus insulin parameters, carbohydrate ratio (CR) and insulin sensitivity factors (ISF) were averaged over 14 days for statistical analyses. Anthropometric data and recent HbA1c was also recorded.

Results: 292 patients (144 males, 148 females) were included in the study. Participants had a median age (IQR) of 12.9 (10.0-15.1) years and pump duration of 2.8 (1.5-4.2) years. No significant differences in median HbA1c (IQR) were observed in preschool (n=14; HbA1c (8.0% (7.0 to 8.0%)), prepubertal (n=105; HbA1c (8.0% (8.0 to 9.0%)) and adolescent subjects (n=173; HbA1c (8.0% (8.0 to 9.0%)). Adolescents took significantly fewer boluses and BG tests per day compared to younger children ($p<0.05$). Age specific diurnal variation in basal insulin doses was noted. Additionally, stronger carbohydrate cover was used in real-life compared to the theoretical 500 rule while weaker corrections were used in real-life compared to the 100 rule. Predictors of lower HbA1c values included higher number of daily boluses, greater number of blood glucose testing per day, lower average CR/500 rule ratio and higher average ISF/100 rule ratio adjusted for age ($R2 = 0.22$; $p<0.01$). Predictors of favourable weight (lower BMI-SDS) included lower total daily dose (units/day), lower percentage of basal to total daily insulin dose, weaker average CR and higher number of different CR adjusted for age ($R2 = 0.33$; $p<0.05$), although age was the strongest predictor (older age associated with lower BMI-SDS).
Conclusion: Insulin pump therapy requires continuous adjustments and glycaemic targets are achieved only by a minority. This study provided additional information on real life carbohydrate ratio and insulin sensitivity factor, which may be helpful in optimising pump therapy in the future.

P18

Body composition in Indian children and adolescents with type 1 diabetes

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P18

Studies suggest that children and adolescents with type 1 diabetes (T1DM) have suboptimal body composition with higher fat mass and lower bone mass. Aim of our study was to compare body composition of Indian children with type 1 diabetes with age gender matched healthy controls.
In a cross-sectional study, body composition parameters were measured by DXA (Lunar DPX PRO, Total Body Densitometer) in 160 (74 boys) children with T1DM (attending type 1 diabetes clinic) and age gender matched healthy controls. Z scores for bone mineral content (TBBMC) for age, bone area for age (TBBA), TBBMC for TBBA, TBBA for height, lean body mass (LBM) for height, TBBMC for LBM [1] and fat and lean mass [2] were computed using Indian reference data. Anthropometry and tanner staging (TS) was assessed for all children. The height (HAZ), weight (WAZ) and BMI (BAZ) were converted to Z scores using contemporary Indian references [3].
Mean ages of boys and girls were 11.4±3.3y and 10.9±3.4y respectively. For both genders HAZ (boys -0.5 vs 0.3, girls -0.5 vs 0.1) and WAZ (boys -0.6 vs 0.0 and girls -0.5 vs -0.1) were significantly lower in diabetics, though BAZ scores were comparable. Similarly, mean Z scores were significantly lower for fat mass (boys -0.1 vs 0.2, girls -0.1 vs 0.1) and higher for lean mass (boys -0.4 vs -1.1, girls -0.3 vs -0.6) in diabetics for both genders. Diabetic boys and girls had lower android fat percent (boys 20 vs 25, girls 28 vs 32, $P<0.05$) when compared with controls. Mean Z scores for bone parameters showed TBBA for age (boys -0.1 vs 0.5, girls -0.1 vs 0.3), TBBMC for age (boys -0.1 vs 0.6, girls -0.1 vs 0.3) and TBBMC for LBM (boys -0.4 vs 0.0, girls -0.5 vs -0.2) were significantly lower in diabetics while all other bone parameters were comparable.
Indian children with type 1 diabetes had lower fat mass (including android fat) and higher muscle mass than controls; however, diabetics need special attention to optimize their bone health.

References

1. Khadilkar AV, *et al*: *Bone* 2011, **4(4)**:810-9.
2. Khadilkar AV, *et al*: *Int J Obes* 2013, **37(7)**:947-53.
3. Khadilkar VV, *et al*: *Indian Pediatr* 2009, **46(6)**:477-89.

P19

Early identification of monogenic diabetes: implications on medical treatment and genetic counselling for an adolescent girl with MODY3

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P19

Aim: To highlight the therapeutic and genetic implications of early diagnosis of HNF-1α mutation in a girl whose family member had previously been thought to have type 1 diabetes.
Method: We reported an adolescent girl in whom a diagnosis of MODY3 was established by molecular finding of a heterozygous HNF-1α NM 000545.5: c.775G>T (p.Val259Phe) mutation. She and her mother now successfully manage their diabetes with low dose sulphonylurea.
Result: A 14 years old girl, who previously had been well, was incidentally found to have hyperglycemia by her diabetic mother. Her body mass index was 19 kg/m^2. General examination was unremarkable without any acanthosis nigricans. Fasting blood glucose was 6.4mmol/L and 2 hour glucose in oral glucose tolerance test was 15.3mmol/L. HbA1c was 7.5%. Fasting C-peptide was 3.2 μg/L (reference 0.9-7.1μg/L).
Family history revealed that her mother developed diabetes at the age of 20 and had been managed as type 1 diabetes with insulin. Mother had satisfactory glycemic control despite the dosage of insulin remained relatively low for decade. However, she then got poor compliance to insulin injection after the age of 40, resulted in worsening of HbA1c to 11-12%. Furthermore, two maternal aunts were thought to have diabetes, but no further detail was available.
A diagnosis of MODY was considered for the girl and molecular analysis confirmed MODY3 with heterozygous HNF-1α NM 000545.5: c.775G>T (p.Val259Phe) mutation. The patient was initiated on the treatment with low dose gliclazide. She could achieve good glycemic control without problem of significant hypoglycemia. Her most recent HbA1c was 5.7%.
Gene sequencing confirmed that her mother also harbored the same mutation. After genetic counselling, insulin therapy of patient's mother was gradually switched to glimepiride by adult endocrinologist. Her HbA1c showed significant improvement from 12.2% to 7.1%. In addition, no mutation was detected for patient's elder sister, indicated that she only had the population risk of developing diabetes.
Conclusion: Maturity Onset Diabetes of the Young (MODY) is frequently misdiagnosed as type 1 or type 2 diabetes. MODY3, resulting from a mutation in the HNF-1α gene, is the most common form of MODY and low dose sulphonylurea is highly effective in maintaining a good glycemic control. Early awareness of MODY and confirmation of subtypes by molecular analysis is important in guiding the appropriate treatment, predicting the clinical course, providing genetic counselling and sometimes, correcting the diagnosis or treatment for other diabetic family members.
Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P20

Fat free mass index and fat mass index tracing on body composition chart in diabetes adolescent girls

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P20

Aims: The prevalence of obesity and type 2 diabetes is increasing, and the impact of obesity on diabetes manifestation should be considered in management of type 1 diabetes children. There are some cases difficult to categorize into certain type in pediatric diabetic patients in the era of acceleration. The objective of this study was to determine the type differences of diabetes by analyzing the growth and body composition

status and choose a proper treatment modality using the body composition chart.
Methods: Fourteen type 1 diabetic adolescent girls (age 12.6±3.3 years) and 16 type 2 diabetic adolescent girls (age 14.2±2.6 years) were included. Height, weight and body compartment of fat mass, fat free mass were measured in each patient. Body mass index (BMI), fat mass index (FMI), fat free mass index (FFMI) and percent body fat (PBF) were calculated. FFMI and FMI were plotted on body composition chart and traced the coordinate during follow up period.
Results: BMI difference between diabetes types was explained with the difference in FFMI as well as FMI. Body composition chart presented that type 2 diabetes girls showed marked elevation in FMI and PBF. And FFMI was lower in type 1 diabetes girls. Superimposed effect of obesity on type 1 diabetes was expressed on body composition chart with marked increment of FMI and the adequate effect of lifestyle intervention in type 2 diabetes was showed marked decrease in FMI and sustained FFMI during follow up period.
Conclusion: Body composition chart might be useful in adequate growth and glucose control monitoring in diabetes children and adolescents. Early adjustment of diabetes management strategy on the basis of body composition during growing period will improve glucose control and promote adequate growth.

P21

Type 2 diabetes mellitus in children: are we 'treating' them right?

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P21

Background: Incidence of Type 2 diabetes mellitus (T2DM) in children is rising alongside childhood obesity. In children, there is limited therapeutic options and tight blood glucose (BG) control may be challenging.
Aims: To determine metabolic control and complications in children with T2DM seen in University Malaya Medical Centre (UMMC).
Methods: Data on children with T2DM referred to and managed in UMMC from 2000 until 2013 were collected. Their body mass index (BMI and blood tests (HbA1c and Lipids) were compared at presentation to their latest clinic appointment. Treatment modalities and duration of follow up were documented. T2DM was dignosed if they had hyperglycaemia (Random BG > 11.8mmol/L or fasting BG > 7mmol/L or 2hpp OGTT >11.1mmol/L with low C-Peptide). Hypertension (HPT) if BP> 90th centile for age,sex and height. Dyslipidemia is considered if either triglycerides> 1.7mmol/L, cholesterol >5.2mmol/L, HDL< 1.03mmol/L or LDL> 2.50mmol/L. Non-alcoholic fatty liver disease (NAFLD) was confirmed with ultrasound, diabetic nephropathy (DN) if urine microalbumin>3.5 in boys , >4.5 in girls and diabetes retinopathy(DR) if reported by opthalmologist.
Results: A total of 49 children with T2DM were seen, but only 37 had available data for analysis. Their age ranged from 7-17 years old at initial presentation. Forty nine percent (n=24) were boys. The mean duration for follow up was 3.6 years(0.2-10years).
Conclusions: This study revealed children with Type2DM had poor metabolic control with mean HBAc of 9.7% and early complications were already seen after 3.6 years of follow up.

P22

Glucose fluctuations in association with oxidative stress among children with type 1 diabetes mellitus: comparison of different phases

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P22

Objective: To examine the association of glucose fluctuation and oxidative stress in children with type 1 diabetes mellitus (T1DM) across different phases.
Methods: Children treated for T1DM at Beijing Children's hospital from 2010 to 2013 were enrolled and divided EQUALLY into three study groups including newly diagnosed children (Group A, acute metabolic disturbance phase), Group B (honeymoon phase), and Group C (long-standing phase). Healthy control children were matched to the T1DM patients by age and sex. The 24-hour urinary free 8-iso-prostaglandin F2α to creatinine (8-isoPGF2α/Cr) ratio indicated oxidative stress. Glucose fluctuation parameters (GFPs) included mean blood glucose levels (MBG), standard deviation of daily blood glucose levels (SDBG), mean amplitude of glucose excursions (MAGE), and incremental area under the curve for postprandial glucose (IAUC). GFPs and 8-isoPGF2α/Cr levels in the study groups were compared and the association of GFPs and 8-isoPGF2α/Cr across groups was assessed.
Results: In each study group, 8-isoPGF2α/Cr and all GFPs in children with T1DM were significantly higher than those in normal controls. 8-isoPGF2α/Cr was significantly correlated with all GFPs in all three T1DM groups. Multiple linear regression analysis showed a stronger association with 8-isoPGF2α/Cr for MAGE than for HbA1c in both the acute metabolic disturbance and long-standing phases of T1DM.

Table 1(abstract P21)

	At presentation	At last visit
Mean Age:	11.79 years old (7-17)	15.3 years old (8.9-22)
Mean Weight:	61kg	70.4kg
Mean BMI (SDS):	28kgm^2 (+2.62)	28.5kgm^2 (+1.91)
Mean WC:	97.0cm	94.3 cm
Mean HbA1c:	11.2% (7.4-16%)	9.7% (5.4-14.4%)
Metformin:	56% (21/37)	92% (34/37)
Insulin:	32%(12/37) ** mainly due to ketosis at diagnosis	32% (12/37) ** mainly due to poor BG control
Dsylipidemia	92% (22/24 screened)	87% (21/24 screened)
Fatty Liver:	Not screened at diagnosis	80% (8/10 screened)
Nephropathy:	Not screened at diagnosis	24% (9/37)
Hypertension	24% (9/37)	8% (3/37)
Retinopathy:	Not screened at diagnosis	1 had early changes of diabetes retinopathy

Conclusion: Glucose fluctuations were positively associated with oxidative stress inpatients in different phases of T1DM. Glucose fluctuations may have a stronger effect than sustained chronic hyperglycemia on triggering oxidative stress, but coexisting high levels of blood glucose are required.

P23

Eye and renal complication in pediatric patients with diabetes mellitus type 1

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P23

Management and life expectancy for patients with diabetes mellitus type 1 (DM 1) is significantly improved. Long-term complication of the disease such as eye and renal complication have been paid much attention because it is an important cause of blindness and renal failure.
Aims: We studied status of eye and renal complication and its relationship with HbA1C in 81 patients diagnosed of DM 1.
Method: Observational, random collection.
Results: Eye complication was seen in 23.5% of patients. Renal complication was seen in 22.2% of patients. 13.6% of patients had both kinds of complication. The longer duration of DM 1 the patients had, the more eye and renal complication was detected. In groups with eye and renal complication, HbA1c was significantly higher than that in groups without complication. Probability of having renal complication in a poor glucose control group was higher than that in a good glucose control group with OR ratio of 2.2. For eye complication, the figure was 3.7.
Conclusion: The best thing to postpone eye and renal complication is glucose control.

P24

SNPS in the exons of toll-like receptors are associated with susceptibility to type 1 diabetes in Chinese population

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P24

Objective: Toll-like receptors (TLRs) recognize a wide range of pathogen-associated molecular patterns (PAMP) and mount the initiation of immune response. Single nucleotide polymorphisms (SNPs) in exons of genes encoding TLRs might be responsible for the generation of an abnormal immune response which could lead to autoimmune diseases. In this study, we investigated the SNPs in TLRs in a Chinese population, and we hypothesized that SNPs in TLRs are associated with type 1 diabetes (T1D), an autoimmune disease caused by destruction of insulin producing pancreatic β-cells, in the studied population.
Research design and methods: We selected 28 SNPs in exons of TLRs with an aim to identify those that might have a direct correlation with T1D etiology and many have not been included in previous GWAS studies. Genotyping of those SNPs in TLRs was performed in 429 T1D patients and 300 age and gender-matched healthy controls in Chinese Han population. The earlier GWAS studies did not include samples from China.
Results: Among the SNPs genotyped, the T allele of TLR1-626 was found to be positively associated with T1D (OR=1.98, Pc=0.01). We identified another T1D associated locus in TLR6, the homozygous AA genotype of TLR6-1329 was negatively and heterozygous GA was positively associated with T1D (OR=0.54, Pc=0.02 and OR=1.70, Pc=0.03). We also identified the haplotype T-G-A in TLR1 gene to be positively associated with T1D (OR=2.22, Pc=0.03). Additional haplotypes in TLR-6 also showed significant positive and negative association. In addition, our haplotype analysis and conditional analysis showed that these two SNPs are the primary T1D associated loci among the SNPs tested in our cohort in each TLR gene.
Conclusion: SNPs and haplotypes in TLR1 and TLR6 gene were associated with T1D in Chinese Han population. Our study, for the first time, indicates that TLR1 and TLR6 gene might play important roles in the etiology of T1D.

P25

Novel mutation in the hepatocyte nuclear factor 1B/maturity – onset diabetes of the young type 5 gene – unreported Vietnamese case

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P25

Maturity-onset diabetes of the young type 5 (MODY5), a type of dominantly inherited diabetes mellitus and nephropathy, has been associated with mutations of the hepatocyte nuclear factor-1 (HNF-1β) gene, mostly generating truncated protein. Various phenotypes are related to HNF-1β mutations. Our aim to describe clinical and genetic findings in the unreported Vietnamese case identified with HNF-1β mutations. The proband with kidney failure from 7.5 years of age and diabetes diagnosed at 13.5 years of age who were described. Case report included information: characteristics of diabetes, renal function and structure, pancreas structure. Genomic DNA were extracted from WBC of whole blood and HNF-1β mutation was performed using PCR and direct sequencing. The proband is heterozygous for a novel HNF1B missense mutation (c.505T>C; p.Y169H). This mutation results in the substitution of the amino acid histidine (charged polar) for tyrosine (uncharged polar) at codon 169**.** The tyrosine residue is conserved across species and it is therefore likely that the p.Y169H mutation is pathogenic. This result is consistent with a diagnosis of renal cysts and diabetes syndrome (RCAD). Testing was done for proband's parents and no mutation was found in HNF1B. It is therefore likely that the p.Y169H mutation has arisen de novo. Kidney MRI showed right kidney atrophy and pancreas MRI showed only tissue of head of pancreas. Investigations at 14.5 years of age – diagnosed diabetes showed: plasma urea 10.1 mmol/l; creatinine 250 micrommol/l; HbA1C 13.6%. He was given insulin of 0.8 UI/Kg/day and HbA1C was 6.8% after one year of treatment with insulin injection. Maturity-onset diabetes of the young type 5 encompasses a wide clinical spectrum. Analysis for mutations of HNF-1β is warranted, even without a family history of diabetes, in non obese patients with diabetes and slowly progressive non diabetic nephropathy, particularly when pancreatic atrophy.
Written informed consent was obtained from the patient for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

P26

Day and night glucose control using a hybrid closed loop system for the management of type 1 diabetes

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P26

Achieving tight glycemic control for the management of type 1 diabetes is often associated with a heavy burden of care, and frequent hypoglycemia. Closed loop insulin delivery, or an "artificial pancreas", represents a new technological frontier for the management of type 1 diabetes which aims to overcome these difficulties. Rapid advancement and improvement in the components of closed loop systems (continuous glucose monitors, insulin pumps, and mathematical algorithms) has been translated into numerous published reports demonstrating effective

glucose control in hospital studies, camps, hotels, and most recently – in home studies. Most studies to date have focused on overnight control due to the difficulties in managing glucose excursions from carbohydrate intake and exercise. We investigated the capability of the Medtronic Hybrid Closed Loop (HCL) System in managing glucose levels during both day and night. The Medtronic HCL system consists of a Medtronic MiniMed insulin pump, Medtronic MiniMed Enlite II glucose sensor, Medtronic MiniMed Minilink REAL time sensor, Medtronic MiniMed Translator, and an Android mobile device with the HCL algorithm (proportional integrative derivate minus insulin feedback and additional safety parameters) software application installed. When using the HCL, meal boluses are delivered manually using the Android mobile device. All basal insulin delivery is controlled by the algorithm. We present in-clinic pilot data from 3 individuals with type 1 diabetes, incorporating 140 hours of closed loop management, over 5 days and nights. A free living environment was simulated, with free access to food, and exercise encouraged. For the three participants, percent of time spent in target glucose range (4 – 10mmol/L) was 81%, 62% and 73% respectively. Including all data, the mean glucose was 8.74mmol/L, which corresponds to an HbA1c of approximately 7%. There were no hypoglycemic or adverse events. We conclude that the Medtronic HCL system is potentially effective and safe for the management of type 1 diabetes. Outpatient studies, with comparisons to sensor augmented pump therapy with low glucose suspend in a randomized cross-over trial are ongoing.

P27

Comparison of alternating home telemedicine consultations with regular face to face consultations in type 1 diabetes

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P27

Aims: To compare a model of alternate home videoconference consultations/face to face consultations with regular face to face consultations in young rural patients with Type 1 Diabetes Mellitus (T1DM).
Methods: A 12 month non randomized controlled trial was performed in 2013 comprising a cohort of children, adolescents and young adults with T1DM from the immediate local region compared with a similar cohort from a region greater than 70 Km away. The local cohort continued with 3 monthly appointments and extra visits as required between appointments. The distant cohort had 6 monthly face to face consultations, alternating with 6 monthly formal videoconference consultations to their homes. Extra visits were also managed via videoconference.
Outcome was measured by comparison of HbA1c between the two groups before during and after the intervention. Missed or rescheduled visits were compared. A patient satisfaction survey was performed and logistic issues were described from both the patient and medical team perspective.
Results: 30 patients (mean age 18.3 years) in the control group (mean HbA1c 8.4%) were matched with 29 patients (mean age 17.2 years) in the intervention group (mean HbA1c 8.3%) (NS). During the intervention period, the glycaemic control in both groups deteriorated slightly (control 8.7%, intervention 8.5%) (p=0.31) Upon return to regular 3 monthly appointments, HbA1c was 8.4% (control) and 8.6% (intervention). Missed or rescheduled appointments occurred more in the telemedicine group.
Patient satisfaction was strong for 4 measures of convenience (time of day, home location, accessibility to other parent/partner and time off school/work) but with major inconvenience accessing HbA1c testing. The major disincentives were lack of personal interaction and more difficulty discussing difficult issues. The major issues for the medical team were reduced ability to read patient's and parent's emotions because of technology and less commitment to appointments by some families.
Conclusion: Telemedicine consultations to home are well accepted and convenient for rural families and young adults with T1DM but are associated with more difficulty accessing HbA1c tests, more missed appointments and more difficulty reading emotional cues during consultations. Glycaemic control did not improve. Catch up videoconferences between appointments were very well accepted. Replacing face to face consultations with direct home videoconference should be done with caution.

P28

Development of diabetes mellitus after hematopoietic stem cell transplantation for childhood leukemia

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P28

Aims: We investigated clinical features of newly diagnosed diabetes mellitus (DM) after hematopoietic stem cell transplantation (HSCT) for treatment of childhood leukemia.
Methods: Between April 2009 and March 2014, total 124 patients (73 males, 51 females) were visited the clinic of pediatric endocrinology for routine follow-up check after HSCT for leukemia. Among them, five patients developed DM (4 males, 1 female). We retrospectively reviewed medical charts including laboratory findings.
Results: Three patients were diagnosed as acute lymphoblastic leukemia who received total body irradiation and chemotherapy. The other two patients were diagnosed as acute myeloblastic leukemia. The mean age at HSCT was 8.0 ± 4.2 years. Four out of five patients developed chronic graft-versus-host disease (GVHD) and treated with steroid more than 2 years. The mean age at diagnosis of DM was 15.8 ± 1.8 years and the time interval between HSCT and DM was 7.8 ± 4.4 years. Three patients showed obesity depend on body mass index (>95th percentile for sex and age). No one showed antibodies related with pancreatic β-cell. All five patients showed hyperinsulinemia with mean fasting insulin levels at diagnosis of DM was 13.3 ± 9.2 μIU/mL. The mean homeostasis model assessment of insulin resistance index (HOMA-IR) of patients was 4.39 ± 2.01.
Conclusion: GVHD, long-term steroid treatment and insulin resistance seem to be close related to develop of DM after HSCT for treatment of childhood leukemia.

P29

Permanent neonatal diabetes due to a heterozygous INS mutation

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P29

Permanent Neonatal Diabetes Mellitus (PNDM) is a rare disorder where patient presents with diabetes within the first few months of life without autoantibodies associated with type 1 diabetes. The majority of PNDM cases have INS, ABCC8 or KCNJ11 mutations. We present a PNDM case with INS mutation. The proband is a second child of three siblings without family history of diabetes. She was born at term via emergency lower segment caesarean section with good APGAR score. Her birth weight was 2.0kg (<3rd percentile), length 49cm (50th percentile), and head circumference 34cm (50th percentile). She was discharged well at day 3 of life, but readmitted at day 17 of life with hyperglycaemia, sepsis and severe metabolic acidosis, requiring insulin infusion. Despite clinical improvement and resolving sepsis, she remained hyperglycaemic and hence neonatal diabetes was suspected. Her GAD-65 and ICA-512 antibodies were negative. HbA1c and c-peptide at diagnosis were 7.9% and 38 pmol/L (normal range: 297.9–1324) respectively. She was still hyperglycaemic despite receiving total daily insulin (TDI) of 1.5U/kg/day, but not ketotic. She was discharged after 20 days of hospitalization with insulatard administered three times daily (TDI 1.2U/kg/day). During the first 8 months of diagnosis, her metabolic control was good (HbA1c 6.7 - 7.6%) despite low insulin requirement, as low as 0.4U/kg/day. Her metabolic control deteriorated since then (HbA1c 11.9 - 13.2%), with TDI doses ranging 0.7 - 0.9 U/kg/day. Rapid acting insulin was not used due to episodes of hypoglycaemia and unpredictable eating habit and activity levels during her toddler years. Direct DNA sequencing revealed she is

heterozygous for p.A24D INS mutation. This mutation has been reported in the literature and known to disrupt preproinsulin processing. Recent evaluation at 51 month showed, negative anti-islet cell antibodies and c-peptide of <30pmol/L (normal range: 297.9–1324). Currently, her developmental milestone is appropriate for her age. However, her height and weight were both below the 3rd centiles. She was recently started on insulin pump to improve her metabolic control and growth.
Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

GROWTH

P30

Disease-specific growth charts of Marfan syndrome in Korea

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P30

Aims: Understanding the growth pattern in Marfan syndrome (MFS) is useful for predicting adult height and for planning the timing of growth reduction therapy. We have reviewed the growth parameters of patients with MFS in Korea and generated the Korean MFS-specific growth curve for understanding the growth pattern in MFS.
Methods: Anthropometric data were available from 187 males and 152 females with MFS through a retrospective review of medical records. The standardized growth curves were constructed for weight and height according to gender. Comparisons between MFS patients and the general population were performed using a one-sample T-test.
Results: Korean MFS patients had similar height and weight compared with the general population at birth. However, linear growth curve of Korean MFS after two years of age showed that the 50th percentile of MFS is above the 97th percentile of normal in both genders. Regarding body mass, although the mean body weight of MFS patients was larger than that of the general population in males and females, the gap of the mean weight curve was small. In the Korean MFS growth curve, the growth pattern and final adult height were nearly analogous to those of the United States (US).
Conclusions: Korean MFS-specific growth charts showed that an excessive growth pattern began in the early infant period, which was prominent in terms of linear growth compared to body mass. There were no ethnic differences in the growth pattern compared with Western MFS patients.

P31

Association of serum concentrations of perfluoroalkyl compounds with poor growth and failure to weight gain in 2-year-old children

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P31

Backgrounds: Potential health concerns of perfluoroalkyl compounds (PFCs) have been raised.
Objectives: We investigated the relationship between exposure to PFCs and growth parameters in Korean 2-year-old children.
Methods: Three hundred sixty children (189 boys, 1.9 to 2.2 years) born as appropriate gestational age infants were enrolled. Height and weight at visit, birth weight, midparental height (MPH) and bone age (BA) were evaluated.
Results: Among fifteen PFCs analyzed, perfluorohexane sulfonic acid (PFHxS), and perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorodecanoic acid (PFDA) were detected in >90% of the serum samples. The number of chemicals above median concentrations among these 5 PFCs were graded on a scale of 0 to 5, and classified into exposure (0) (n = 97), exposure (1-2) (n = 88), and exposure (≥3) groups. After adjusting for sex, birth weight, MPH, and BA, log-transformed PFHxS, PFOS, PFOA, and PFDA were associated with a 1.60, 1.35, 1.57, 1.29 cm decrease in height (all $P < 0.005$). Log-transformed PFOS, PFOA, PFNA, and PFDA were negatively related to weight gain (all $P < 0.05$). Change in weight Z-scores decreased progressively from exposure (0), to exposure (1-2), and to exposure (≥3) (mean +0.43 vs. +0.29 vs. +0.10, $P = 0.012$).
Conclusions: Increased concentrations of PFOS, PFOA, PFNA, and PFDA were associated with short stature and failure to weight gain in 2-year-old children. The more PFCs detected above median concentrations, the shorter and the poorer weight gain. Further prospective studies are needed to clarify causal relationship.

P32

Growth effect of tki treatment in childhood CML

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P32

Aim: Childhood chronic myeloid leukemia (CML) is rare myeloproliferative disorder, and diagnosed mostly in adult, representing for 10% of all CML, and accounts for up to 2-3% of all childhood leukemia. Tyrosine kinase inhibitor (TKI), mostly Imatinib mesylate, is now used in the frontline standard treatment of CML in chronic phase. The aim of this study is to investigate the growth effect of TKI treatment in childhood CML.
Methods: This retrospective study consisted of 20 pediatric CML patients (13 males and 7 females) received TKI treatment at Seoul and Yeouido St. Mary hospital from January 2001 to January 2014. Patients with chronic-phase CML, received TKI treatment for more than 6 months were included. Height and weight data were obtained from the patient's medical records. The differences (Δ) of height and weight standard deviation scores (SDS) at before and after treatment were calculated and associations of factors that influence the growth were analyzed.
Result: Seventeen patients (85.0%) had reduction in height SDS was observed. Mean age at the start of TKI was 10 years, and median follow-up was 53 months. When the mean levels of Δ height and weight SDS were analyzed, we observed significant reduction in height SDS (mean ±SE, -0.35±0.33, P=0.000), but not in weight SDS (mean±SE, -0.04±0.54, P=0.723). Growth deceleration was seen predominantly in patients who started TKI at a prepubertal age compared with those who started at pubertal age or started at prepubertal age but enter puberty on treatment (mean±SE, -0.59 ±0.32 vs. -0.21±0.28, P=0.015). But no significant difference of height SDS were observed between two group depend on the TKI type. After adjusting for type of puberty, significant linear correlations with the reduction of height SDS after treatment was found for age at onset treatment (r^2=0.381, P=0.005).
Conclusion: After received TKI treatment in childhood CML patients, a significant number of patients experience growth deceleration. Initiation of TKI treatment in prepubertal age and age of begin treatment are associated with growth impairment. Continuous follow-up and monitoring growth after received TKI treatment in childhood CML is important for improving quality of life.

P33

Growth status of small for gestational age (SGA) Indian children from two socioeconomic strata

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P33

Aims: To assess growth and factors associated with growth in children born SGA from two socio economic strata in comparison to age and gender matched healthy controls.
Methods: Retrospective study conducted at two hospitals in Pune, 0.5 to 5 years old 618 children – 189 SGA from Upper Socio-economic Strata (USS), 217 SGA from Lower Socio-economic Strata (LSS) and 212 appropriate for gestational age (AGA) healthy controls were randomly selected. Birth history, maternal history, socio-economic status, length/height and weight of children were recorded. Anthropometric data were converted to Z scores (HAZ, WAZ) using WHO AnthroPlus software [1]. Data on neonatal morbidity and feeding history of children were recorded (analysis in progress).
Results: Mean ages of all 3 groups were similar (2.7 years for USS, 2.8 for LSS and 2.9 for controls). The HAZ and WAZ of the SGA group were significantly lower as compared to the controls ($p < 0.05$), and that of the LSS SGAs were lower than that of the USS SGAs ($p<0.05$). The percentage of children who were stunted (HAZ < -2.0) were 32% in USS and 49% in LSS ($p< 0.05$ for all). The percentage of stunted children in the USS SGA group at 2 years was 29% and at 5 years was 17% while in the LSS SGA group, 54% of children were found to be stunted at 2 years and 46% at 5 years. To determine factors associated with stunting in SGA children, generalized linear model (GLM) was used. GLM revealed that a normal vaginal delivery ($\beta = 0.625$) and mother's age ($\beta = 0.072$) were positively associated with risk of stunting, high SES ($\beta = -0.830$), absence of major illness ($\beta = -1.01$), higher birth weight ($\beta = -1.34$) were negatively associated (p for all < 0.05).
Conclusion: Children born SGA showed relatively poor growth as compared to healthy controls. Special attention to growth is necessary especially in children from the lower socio economic strata, very low birth weight babies and those with major illnesses during early years of life.
Reference
1. WHO: **AnthroPlus Software.** 2014, http://www.who.int/growthref/tools/en/ Accessed on 04th June.

P34

Influence of growth hormone receptor exon 3 polymorphism on growth response in children with growth hormone deficiency

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P34

Aims: Pharmacogenetic effects of recombinant human growth hormone according to growth hormone receptor (GHR) exon 3 polymorphism (fl vs. d3) were controversial. We investigated growth hormone response in children with growth hormone deficiency (GHD).
Methods: Total 58 prepubertal children (31 boys and 27 girls) with GHD were enrolled in this study. Subjects were divided to 2 groups according polymorphism (fl/fl, n=48; fl/d3 and d3/d3, n=10), and compared baseline phenotypes and the first year growth response to growth hormone treatment.
Results: The distribution of GHR exon 3 isoforms in children with GHD demonstrated that the frequency of fl/fl (82.8%) is higher than that in most of European studies. There was no significant difference in baseline height SDS between 2 groups. Height velocity during the first year of growth hormone replacement therapy tended to be higher in subjects who have d3 allele (fl/d3 and d3/d3), but there was no statistical difference according to genotype.
Conclusion: It seemed that d3 allele of GHR exon 3 had no impact on the baseline phenotype and growth hormone response in patients with GHD. Relationship between GH dose and IGF-1% to help fully elucidate the value of IGF-1 testing in GH treatment.

P35

Growth status of first grader children in elementary schools in Watu Alo, Manggarai, East Nusa Tenggara

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P35

Background: East Nusa Tenggara (NTT) had the highest number of children under five with mild to severe malnutrition in Indonesia, happened mostly in Manggarai Regency, with the highest number of cases found in Watu Alo Primary Health Care Supervision Area, with 5 out of all 19 cases in Manggarai, NTT (RISKESDAS, 2010). Nevertheless the method to classify the growth status was unclear.
Objective: To determine growth status of first grader children in Watu Alo, Manggarai, NTT using the WHO and CDC growth charts and comparing the results.
Method: A cross-sectional descriptive study. The data was taken from 19 to 22 August 2013 and 24 August 2013 in 5 elementary school under the supervision of Watu Alo Primary Health Care, Manggarai Regency, East Nusa Tenggara. Data interpretation with CDC and WHO growth chart.
Results: CDC: the children are 74% short; 26% normal stature (median: 109 cm), 21.9% underweight; 69.4% normal weight; 6.1% overweight; and 2.6% obese (median: 18 kg). WHO: 72.4% of the children are normal stature; 20.9% stunted; 6.6% severely stunted, 84.7% normal weight; 6.6% risk of overweight; 6.6% wasted; 1% overweight; 0.5% obese; 0.5% severe wasted.
Conclusions: To interpret the growth status, clinical judgement is also needed to be considered. Children growth status should be monitored continuously. Standardized national growth chart for Indonesian children should be made.

P36

Successful treatment with two siblings affected classic Bartter syndrome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P36

Classic Bartter syndrome is a salt-wasting tubulopathy caused by mutations in the CLCNKB (chloride channel Kb) gene. Classic Bartter syndrome is characterized by early childhood onset. Herein, we report two Vietnamese siblings affected classic Bartter syndrome.
Case presentation: Two siblings were admitted to National Hospital of Pediatrics with chief complaints of motor-development delay, growth retardation and failure of thrive. The 1st child - a 39 month old boy with his birth weight of 1.9 kg presented with his height of 69 cm (-7.5 SD), his weight of 7.5 kg (-4.4 SD). The 2nd child – an 18 months old girl presented with her height of 58 cm (-7.8 SD), her weight of 5.8 kg (-3.4 SD). They both developed polyuria (6ml/kg/hour), polydipsia, chronic dehydration and motor delay that they could not stand and walk but had normal intelligence. The investigations revealed hypokalemic metabolic alkalosis (PH: 7.5 – 7.51; pCO2: 45.9 - 56.8 mmHg; $HCO3^-$: 36.6 - 45.7 mmol/l; serum potassium levels: 1.8 – 2.1 mmol/l), hyponatremia (125 – 128 mmol/l), hypochloremia (67 – 84 mmol/l), normal calcemia, and normal calciuria. They were treated with potassium supplement, indomethacin (2.5 mg/kg/day). After 15 months of treatment: height, weight of the 1st boy and 2nd girl were 94 cm (increasing 25cm; -3 SD), 12kg (increasing 4.5kg; -3 SD) and 84 cm (increasing 26 cm; -2.4 SD), 11 kg (increasing 5.2 kg; -1.3 SD), respectively. Their plasma electrolyte became normal after 2 weeks of treatment.
Conclusions: Classic Bartter syndrome will have good prognosis if treated early. This is one cause that can result in growth retardation.
Written informed consent was obtained from the patient for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

P37

Turner syndrome and growth hormone therapy: a review on growth response

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Aims: Turner syndrome (TS) is a sex-chromosome abnormality in females resulting from partial or complete absence of one of the X chromosomes

[1]. One of the main features of TS is short stature. Final height in short girls with TS improves with growth hormone treatment [2]. The aim of this study was to assess the effectiveness of growth hormone therapy in a cohort of Malaysian patients with TS.
Methods: Data from the electronic medical records of 20 patients with TS treated with growth hormone in Putrajaya Hospital, Malaysia from the year 2005 to 2014 was analysed.
Results: The mean age of initiation of therapy was 11.5 ± 3.4 and 55.0% were started after the age of 12 years. The mean height standard deviation score (SDS) increased from -3.84 (±0.94) SD at study entry to -3.47 (±0.97) SD at the end of the first year. This improvement was seen with subsequent year of treatment, though the degree of change in height SDS reduced with time. Age of initiation of therapy had a bearing on treatment response as those who had received growth hormone at an earlier age experienced better growth response. 75.0% of patients who achieved final height were able to achieve the final height within the target height. Of the patients who achieved final height, mean age of puberty was 16 ± 1.5 years and mean height SDS at onset of puberty was -3.3SD. There were no reported adverse events.
Conclusion: Growth hormone therapy improved growth profile of Malaysian children with TS and the importance of early initiation of therapy is demonstrated in this study.
References

1. Ross J, Lee PA, Gut R, Germak J: Impact of age and duration of growth hormone therapy in children with growth hormone therapy in children with Turner syndrome. *Horm Res Pediatr* 2011, **76**:392-399.
2. The Canadian Growth Hormone Advisory Committee: Impact on growth hormone supplementation on adult height in Turner syndrome : results of the Canadian Randomized Controlled Trial. *J Clin Endocrinol Metab* 2005, **90**:3360-3366.

P38

Insulin-like Growth Factor 1 (IGF-1) measurements recorded in the OZGROW database and their relation to growth response in children currently being treated with growth hormone

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P38

Aims: IGF-1 is produced in a GH dependent fashion and measurement of IGF-1 has become increasingly common for both diagnosis of GH deficiency and to guide GH therapy. The OZGROW database records the results of IGF-1 tests performed on patients receiving GH or being assessed for GH treatment. The OZGROW database was used to determine the extent to which IGF-1 testing is performed in this population and to assess the relationship between IGF-1 levels and growth rate.
Methods: Records were obtained for children entering the OZGROW database since 2009 and who were currently receiving GH. Number of patients, visits, and frequency of IGF-1 tests was determined. The nature of IGF-1 tests, such as the units used and whether a reference range was provided was noted. Patients with at least one IGF-1 test result were selected for further analysis. IGF-1 results were standardized (where a reference range was available) by expressing them as a % of the reference range. x% = ((x -L)/(U - L)), where x is the test result and U and L are the upper and lower values of the reference range. Growth was measured as either growth velocity (GV, cm/year) or height SDS/Year over either a 6month (+/- 10 weeks but adjusted to 6m) or 1 year (+/-13weeks adjusted to 1y). Regressions (coefficient=b) and correlations (r) were performed.
Results: 829 patients were assessed representing 7573 clinic visits. 577 (69%) did not have any IGF-1 tests recorded. 25% had one test recorded, 4% had two tests, and 1% had three tests. Another 21 IGF-1 tests were noted but not used in analyses as no reference range was given. Units used were nmol/L, mmol/L, U/ml, ug/L, mg/l, and "other". 11 results had a reference range but no units. Overall a moderate but significant relationship was found between IGF-1% and growth: 6month GV-b=0.014cm/y/%IGF-1, r=0.16, P=0.01; 6month SDS/y- b=0.005dSDS/y/% IGF-1, r=0.31, P<0.001. 1Y GV- b=0.010, r=0.14, P=0.03; 1Y SDS/y- b=0.003, r=0.31, P<0.001. More detailed analyses stratified by indication and gender will be presented.
Discussion and conclusions: IGF-1 has been recommended to titrate GH dose. We found significant variation between IGF-1% and growth response although the correlation was significant. There was also great variation in measurement units used and references ranges stated. Further analyses will focus on the relationship between GH dose and IGF-1% to help fully elucidate the value of IGF-1 testing in GH treatment.

ADRENAL

P39

High incidence of adrenal suppression in children with Kawasaki disease treated with intravenous immunoglobulin plus prednisolone

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P39

Context: Combination treatment with intravenous immunoglobulin (IVIG) plus prednisolone, newly designed for children with severe Kawasaki disease (KD), significantly reduces coronary artery abnormalities [1]. Prednisolone is administered for approximately 20 days in this regimen.
Objective: Our aim was to examine whether adrenal function of the treated patients is suppressed by glucocorticoid administration in this regimen.
Design/setting: This was a prospective study at one medical institution.
Patients: We analyzed data from 21 children with KD who were treated with IVIG plus prednisolone between February and June, 2012.
Main outcome measures: The main outcome measures were cortisol and ACTH values in the morning after the cessation of prednisolone administration and peak cortisol and ACTH values at CRH stimulation tests repeated 0, 2, and 6 months after the treatment.
Results: Morning cortisol and ACTH values after the cessation of prednisolone treatment were suppressed. Peak cortisol values at the first CRH stimulation test ranged from 5.1 to 25.4 mcg/dL and were less than 20 mcg/dL in 17 of 21 patients, but were restored to more than 14.6 mcg/dL in all of them by 6 months after the prednisolone treatment. A significant positive correlation was observed between cortisol values at 09:00 after the prednisolone treatment and peak cortisol values at the following CRH stimulation test ($r = 0.770$, $p < 0.0001$).
Conclusions: Adrenal suppression can occur in a high proportion of children with KD treated with IVIG plus prednisolone, despite rather short duration and low administered dose of glucocorticoids.
Reference

1. Kobayashi T, Saji T, Otani T, Takeuchi K, Nakamura T, Arakawa H, *et al*: Efficacy of immunoglobulin plus prednisolone for prevention of coronary artery abnormalities in severe Kawasaki disease (RAISE study): a randomised, open-label, blinded-endpoints trial. *Lancet* 2012, **379**:1613-20.

P40

Addison's disease in a child: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P40

Addison's disease is chronic primary adrenal insufficiency, a rare disorder which is characterized by adrenocortical insufficiency. The sign and symptom in Addison's disease is nonspecific. This paper is to report Addison's disease in a child focusing in diagnostic approach. Method is case report. Girl, 4 years old suffered from general weakness without paresthesia, fatigue, salt craving and hyperpigmentation including skin, lips, gum, buccal mucosa, hard palate and plantar creases. Tanner stage was prepubertal condition. Basal cortisol plasma level in the morning was 94.8 (50-250) μg/mL and 14.5 (25-125) μg/mL in the evening. This patient was performed ACTH stimulation test. The result revealed declining cortisol plasma level before (20.83) and 30', 120' after the test (16.53,

5.91, respectively). Free T4 was 17.31 (9-20) pmol/L; TSH 2.48 (0.25-5) uIU/mL. Adrenal ultrasound revealed no classification nor hemorrhage. Primary adrenal insufficiency was established. Tuberculosis is frequently reported in Addison. In our patient the Tuberculin skin test revealed negative. Treatment planned to be given were oral hydrocortisone 15 mg/m2 and oral fludrocortisone. Based on anamnesis, physical examination and laboratory findings, addison disease was established. As conclusion, beware of generalized weakness and hyperpigmentation in a child, it may be the symptom of adrenal insufficiency. Careful diagnosis procedure is very important.

Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P41

An infant with Cushing syndrome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P41

Background: Infantile Cushing syndrome is rare. We report an 8 month-old infant who developed growth failure and hypertension from an apparently innocuous topical steroid application.

Case Presentation: An 8 month-old boy was referred to the endocrinology clinic for concerns of growth failure since 3 months of age. He was born full term with a birth weight of 2.67kg and a length of 45cm. His parents noticed that he was not growing well from 3 months of age. However, his weight gain remained more than satisfactory and he gained 700g in the past month. This infant was otherwise in good health, apart from atopic dermatitis, for which the parents had been applying a daily cream with good effect. He was breast fed until 2 months of age and weaned onto solids at 6 months of age.

On examination, the infant had a moon face with hypertrichosis, facial telangiectasia and prominent supraclavicular fat pads. His recumbent length was 62cm (<3rd percentile), his weight was 7.74 kg (25th percentile), and his head circumference was 41.0 cm (3rd percentile). There was no hyperpigmentation or lentigenes, but he was hypertensive with a blood pressure of 140/90 mmHg (95th percentile for age is 99/55 mm Hg) with a heart rate of 140 beats/minute. His apex beat was not displaced and his heart sounds were normal with no murmurs.

A random steroid profile demonstrated a depressed serum cortisol level of 30 nmol/L and an unmeasurably low serum ACTH level of <1.1 pmol/L. This was consistent with exogenous Cushing syndrome. An ECG showed biventricular hypertrophy and a 2-D echocardiogram confirmed severe biventricular hypertrophy with good ventricular function.

On further questioning, he had been receiving twice daily applications of a topical cream for atopic dermatitis, which had been obtained over the counter, without a prescription. Subsequent analysis of the topical agent revealed the contents to be betametasone dipropionate, a high potency corticosteroid.

On establishing the diagnosis of exogenous Cushing syndrome, the offending topical steroid cream was discontinued. Since he was at risk of primary adrenal failure from sudden withdrawal of steroid cream, he was started on a weaning regimen of hydrocortisone. He was also commenced on captopril which achieved good blood pressure control.

Conclusion: Continuous use of high potency topical corticosteroids over several months can lead to Cushing syndrome. Physiologic dosing of hydrocortisone should be prescribed to prevent an adrenal crisis until hypothalamic-pituitary-adrenal axis recovery is confirmed.

Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P42

A case report of neonatal adrenocortical carcinoma

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P42

Adrenocortical carcinoma is rarely seen in a neonatal period. Adrenocortical carcinoma usually causes virilisation, precocious puberty, Cushingoid syndrome.

Aims: Describe a case of neonatal adrenocortical carcinoma diagnosed and treated in Vietnam National Hospital of Pediatrics.

Method: A case report of neonatal adrenocortical carcinoma with Cushingoid syndrome and persistent hypertension.

Results: A boy was admitted to hospital at the age of 23 days because of vomiting, poor feeding and abdominal distension, and edema on both legs. On examination we found the child had Cushingoid syndrome, but not precocious puberty, edema on both legs, and hypertenstion. Blood pressure was 150/90 mmHg, required IV Loxen to maintain BP. Investigation showed cortisol 8AM was high of 4473 nmol/l; cortisol 24AM 3971 nmol/l. Electrolyte, renal function, glucose, urine VMA/HMA were normal. Abdominal ultrasound found a hypo-enhancing mass in the left adrenal area with calcification and dimension of 37x32 mm. Dilated left renal pelvis was also observed. Cardiac ultrasound found ventricular hypertrophy, suspected cardiomyopathy. Neck MRI detected abnormal connection between lymphatic vessels and venous vessels. Abdominal CT showed a heterogeneous mass of 40x41x50 mm with calcification in the left adrenal area. Operation was done to remove the mass. No metastase was noticed during operation. Histology confirmed a diagnosis of adrenocortical carcinoma. Cortical was normal after operation. However, hypertension was still present a week after operation and IV Loxen was indicated to maintain normal BP.

Conclusion: Post-operation hypertension was persistent in a neonatal adrenocortical carcinoma patient.

Written informed consent was obtained from the patient for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

P43

Clinical and molecular characterization of patients with classic 3β-hydroxysteroid dehydrogenase deficiency

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P43

Background: 3β-hydroxysteroid dehydrogenase type 2 (3βHSD2) is the key enzyme converting Δ5-steroids to Δ4-ketosteroids in adrenal and gonadal steroidogenesis. Severe loss-of-function mutations of HSD3B2 gene encoding for this enzyme cause the rare form of congenital adrenal hyperplasia, "3βHSD deficiency". Affected individuals have salt losing, adrenal insufficiency and ambiguous genitalia in both sexes. Patients with 3βHSD deficiency may have elevated 17α-hydroxyprogesterone (17OHP) levels due to normal peripheral type 1, 3βHSD.

Aims: To describe two unrelated patients with 3β-hydroxysteroid dehydrogenase deficiency and perform mutation analysis of the HSD3B2 gene.

Patients and Methods: Patient 1 (Thai) and 2 (Indian) are 46,XY male newborns with ambiguous genitalia (micropenis, penoscrotal hypospadias) who developed salt-losing since early infancy. They were stabilized with normal saline resuscitation and high dose hydrocortisone replacement. Patient 2 was initially misdiagnosed as 21-hydroxylase deficiency due to elevated 17OHP until he was referred for genitoplasty at the age of 2.5 years and the patient were re-evaluated. The ACTH tests revealed low cortisol response, moderately elevated 17OHP, elevated Δ^5/Δ^4 steroids, suggestive of blockage at the level of enzyme 3βHSD. Patients' leukocyte genomic DNA was extracted and the entire coding regions of the HSD3B2 gene were assessed by polymerase chain reaction (PCR) and sequencing analysis.

Results: Patient 1 was homozygous for T259M (c.776C>T) mutation in the HSD3B2 gene. Patient 2 was homozygous for the novel nonsense mutation Y180X (c.540C>A) and his parents were heterozygous carrier.

Conclusion: We report the mutations of HSD3B2 gene, T259M and Y180X (novel) responsible for classic 3βHSD deficiency. The clinical and hormonal phenotypes can be complicated in this disorder. These cases emphasize the importance of confirming the specific enzyme deficiency with molecular genetic analysis.

Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P44

17-hydroxyprogesterone quantification in dried blood spots by high performance liquid chromatography-tandem mass spectroscopy

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P44

Measurement of 17-hydroxyprogesterone (17-OHP) in daily dried blood spot profiles via radioimmunoassay is a convenient and accepted method for monitoring of glucocorticoid therapy in Congenital Adrenal Hyperplasia. Characteristics of this method that serve to limit its clinical usefulness include its lack of specificity for 17-OHP, and a relatively high limit of detection. Mass Spectroscopy is the gold standard method for steroid quantification. We aim to establish a High Performance Liquid Chromatography-Tandem Mass Spectroscopy (HPLC-MS/MS) method for dried blood spot 17-OHP quantification and develop normative age- and tanner-specific, as well as Congenital Adrenal Hyperplasia genotype-phenotype correlated reference ranges to guide glucocorticoid therapy.
Four 3mm blood spots were punched from patient dried blood spot filter paper specimens. 17-OHP was eluted into solvent and concentrated using liquid nitrogen. Steroids were separated using high performance liquid chromatography and quantitated by Tandem Mass Spectrometry. For the radioimmunassay / HPLC-MS/MS correlations, measurements were performed by both methods on 49 samples from children with glucocorticoid-dependent Congenital Adrenal Hyperplasia, as well as children undergoing dynamic endocrine function testing at The Mater Children's Hospital. Reference samples for HPLC-MS/MS calibration, and determination of sensitivity, precision, and recovery were prepared using whole blood samples spiked with 17-OHP spotted onto filter paper. Concentrations were expressed as mean (nmol/L), standard deviation, and coefficient of variation (%).
There was excellent correlation between HPLC-MS/MS and radioimmunoassay methods (r^2=0.9610). For the radioimmunoassay method, the lower limit of quantification has been established at <5 nmol/L while LC-MS/MS allows detection to 1.0 nmol/L (1.2nmol/L, 0.26, 22%) with a proposed lower limit of quantification of 1.5 nmol/L (1.3 nmol/L, 1.3, 13%).
We have established an accurate, reliable, and specific method for quantifying 17-OHP concentrations from dried blood spot using HPLC-MS/MS. This will allow for the establishment of clinically relevant and time-specific reference ranges to guide glucocorticoid dose adjustment in children with Congenital Adrenal Hyperplasia.

P45

An infantile exogenous Cushing syndrome caused by topical steroid

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P45

Corticosteroids are widely use for the treatment of various diseases. Long-term use of corticosteroids may lead to development of Cushing syndrome and hypothalamic pituitary adrenal axis suppression. However, iatrogenic Cushing syndrome from absorption of topical steroids to systemic circulation is less common comparing to parenteral or oral use. Infantile age group have greater risks for systemic side effects of the drugs because their skin has poorly developed barrier function and large surface area.
We reported a 5-month-old female child was admitted to our hospital with puffiness of face and excessive weight gain after 4 months old. She was born at term with an uneventful pregnancy with a birth weight of 3.4 kg. Her body weight was 8.2 kg (+2SDS), height was 63.5 cm (+0.2SDS). Physical examination showed her was moon face appearance, generalized obesity, hirsutism and buffalo hump. There were few erythema and weeping present at skin fold areas. Blood pressure was 105/68 mmHg (>95th percentile). Past history revealed that the child had diaper dermatitis at 3.5 month of age. She was prescribed a topical combination drug containing nystatin, neomycin, gramicidin and triamcinolone acetonide from private pediatric clinic. Since then she was applying the drug 3-4 times daily on neck, axilla, diaper area and all skin fold areas. Totally drug usage was 30 g in 6 weeks. Investigations showed hemoglobin of 15 g/dL, white blood cell count 18,240/mm^3, platelet count 471,000/mm^3, blood glucose 74 mg/dL and normal electrolyte, renal and liver function. Ultrasonography of whole abdomen revealed no abnormality. Random PM cortisol was low (0.2 mcg/dL). Secondary adrenal insufficiency was suspected. 1-mcg ACTH stimulation test was done and the peak cortisol was 1.9 mcg/dL. Therefore, exogenous Cushing syndrome and secondary adrenal insufficiency due to overuse of topical combination drug which containing moderate potency steroid was diagnosed. She was promptly treatment by discontinued applying the drug and administered steroid during stress.
This report highlights the importance of prolonged use of moderate potency topical steroids can causes hypothalamic pituitary adrenal axis suppression and Cushing syndrome, especially during infantile period. Therefore, limiting the use of moderate- to high-potency topical steroids in children and provide information about potential adverse effects to the caregivers are crucial.
Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P46

Leydig cell tumor in a boy with undiagnosed precocious puberty due to congenital adrenal hyperplasia

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P46

Aims: To describe the clinical presentation and sequelae of undiagnosed congenital adrenal hyperplasia (CAH).
Methods: Case report.
Results: A 5-year-old boy presented with penis and testicular enlargement for 1 year. The past medical history had no severe vomiting or failure to thrive. His height was 120 cm (> 95th percentile). His penis was 7 cm and asymmetric testicles. Scrotal ultrasound detected his left testicle was 1.5×0.9 cm and his right testicle was 3.0 x 2.0 cm with a heterogeneous hypoechoic mass 1.8 x 2.0 cm at inferior pole with sheath thickness, clearly margin. His bone age was 14 years. His serum 17-hydroxypregnenolone and testosterone levels were elevated to 1768 ng/dl and 694.5 ng/dl, respectively. His serum hCG was below 1.2 IU/L and DHEA-S < 0.001 mcg/ml. An absent LH response after GnRH stimulation was recorded. He was diagnosed with CAH and treated with hydrocortisone. After one month of treatment, his serum 17-hydroxypregnenolone and testosterone levels decreased to 11 ng/dl and 20.75 ng/dl, respectively. Then, he underwent an open testis biopsy for further evaluating of the mass of his right testicle. Histological examination of the testicle demonstrated large, polygonal, and eosinophilic cells with round nuclei and prominent nucleoli, which are consistent findings with Leydig cell tumors. Thereafter, the child underwent radical orchiectomy of his right testicle.
Conclusion: Undiagnosed congenital adrenal hyperplasia can affect normal development. Universal newborn screening is recommended for congenital adrenal hyperplasia.
Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P47

Long term follow up of growth in children with Congenital Adrenal Hyperplasia 21- Hydroxylase deficiency

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P47

Obesity and decreased final height are described in children with CAH 21OHD. Of 119 children (50 M, 69F;79 Salt Wasters(SW), 40 Simple

Virilizers (SV)) diagnosed over 24 years, various growth parameters were studied in 43 children with regular follow up for 5 years or more.
Clinical data, anthropometry, genotype, hormonal and biochemical profile were evaluated at presentation. On follow up, growth and clinical characteristics, metabolic control (8am 17OH-Progesterone), bone age and replacement doses of gluco-corticoid (GC) and mineralo-corticoid (MC) were studied. Growth parameters were expressed as SDS. Obesity, defined as BMI SDS >/= 2 and short stature, defined as Ht SDS </= -2 were correlated with all the variables, using Unpaired T Test, Pearson Correlation and One way ANOVA Test.
43 children (16M, 27F; 32SW, 11SV; 36 mutations proven) had a mean duration of follow up of 11 +/- 4.14 years. At last follow up, Ht SDS was </= -2 in 27.9% cases (N=12/43: 4M, 8F; 9SW, 3SV). Age at onset of puberty (p=0.035), higher GC dose at presentation (>40mg/m2) (p=0.034) and at 3 years of age (p=0.047) and use of Hydrocortisone and/or Prednisolone (p=0.002) had a negative correlation with Ht SDS. 6 (13.95%) children (1M, 5F; 6SW) had achieved Adult Height (AH) SDS of -2.36 +/- 1.25, and AH SDS – TH SDS (Target Height) was -0.11 +/- 1.23. BMI SDS >/=2 found in 32.6% cases (N=14/43: 2M, 12F; 8SW, 6SV) correlated positively with 17 OHP values (p=0.013). Girls were heavier than boys (p=0.006). Adiposity rebound occurred at 4 years for both the genders. At the time of study analysis, Ht SDS showed a distinct shift to the left and BMI SDS, a distinct shift to the right of mean of the reference population as cited [1].
In the present series, there was a higher incidence of obesity (32.6%) but short stature was noted in 27.9% only. Aggressive lifestyle management, dietary control, optimizing dose of therapy (GC) and regular monitoring should be an integral part of long term management of patients with CAH 21OHD.

Reference

1. Agarwal KN, Agarwal DK: *Indian Pediatrics* 1992, **29**:1203, 1994; 31:377, 2001; 38:1217-35.

P48

X-linked adrenoleukodystrophy in 8 patients

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P48

Background: Adrenoleukodystrophy (ALD) is a genetic disease associated with demyelination of the central nervous system, adrenal insufficiency, and accumulation of very long-chain fatty acids in tissue and body fluids.
Objective: To research the clinical features, laboratory tests, imaging examinations and treatment on children who suffer from X-linked adrenoleukodystrophy. Also aim at revealing the correlation between the severity of disease and level of very long chain fatty acids (VLCFAs) or MRS.
Methods: Analyze 8 cases of X-ALD patients' clinical data, laboratory and imaging results, and make a review of related literatures.
Results: 8 patients were male, onset age ranged from 5-11 years old, and the course of disease was from 4 months to 3 years. 3 patients presented with reduced vision, 2 patients presented with hyperpigmentation and all patients show different degree nervous system symptoms, such as intelligence breakdown, attention deficit, coordination and communication ability decrease, etc. The measurement of VLCFA revealed that low level of C22:0 and high level of C24:0 and C26:0, what's more, we can find increases in the C26:0/C22:0 and C24:0/C22:0 ratios. Cranial MRI showed typical lesion. MRS also demonstrated abnormal image.
Conclusion: Major clinical features of ALD were demyelination of white matter and adrenal insufficiency, generally with rapid development. Serum VLCFA is a specific indicator for diagnosis of ALD, and MRS can find lesion in an early phase. The treatment of ALD is difficult, and some reasearchers demonstrated that application of hematopoietic stem cell transplantation in the early stage is the most effective way until now.

P49

Updated registry of congenital adrenal hyperplasia at the north pediatric referral centre of Vietnam

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P49

The National Hospital of Pediatrics (NHP), Hanoi, Vietnam is an 1200 bed tertiary referral centre servicing approximately 30 million people from northern provinces of Vietnam. This audit was undertaken to analyze anecdotal reports of increasing patient numbers. Retrospective review of all CAH patients registered at NHP from 1999- 5.2014. Ethical clearance was granted by the NHP Directorate.
At the start of 1999 there were 90 children with CAH managed at NHP. By May 2014 this increased to 715 including 375 (52%) male patients and 340 (48%) female patients. Number of cases with 21α-hydroxylase deficiency (21-OHD), 11β-hydroxylase deficiency and 3β-hydroxysteroid dehydrogenase deficiency was 703 (98.3%); 9 (1.3%) and 3 (0.4%), respectively. Among cases with 21-OHD, 72% were salt wasting and 28% were simple virilisation). Total number of cases representing a more than seven fold increase over 14 years. Number of new cases doubled from 30 to 67 in 2013. Most children (85%) were diagnosed at less than 12 months of age (55% at less than 1 month of age); 70% of all children were younger than 10 years. Formal mortality figures were low (7 known deaths).
The caseload of CAH at NHP has increased since 1999 and additional capacity is needed for patient care. Introduction of NBS would enable more accurate estimation of CAH incidence, reduce infant mortality and minimize trauma to affected infants and their families.

P50

Phenotype & genotype of congenital adrenal hyperplasia due to mutation in the type ii 3β-hydroxysteroid dehydrogenase gene: a report of two Vietnamese families

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P50

Congenital adrenal hyperplasia (CAH) is one of the most common inherited metabolic disorders. It includes a group of autosomal recessive disorders caused by the deficiency of one of the enzymes involed in one of the various steps of adrenal steroid synthesis. 3β-Hydroxysteroid dehydrogenase (3β-HSD) deficiency is a rare cause of CAH caused by inactivating mutations in the HSD3B2 gene. Most mutations are located within domains regarded crucial for enzyme function. Our aim is to describe phenotype and to identify mutations of HSD3B2 in two classic β-HSD deficient patients belonging to two apparently unrelated pedigrees. This is a case series study. Family history and clinical manifestations were described. Genomic DNA from these patients was extracted using standard procedures from the peripheral blood leukocytes. Mutation analysis of HSD3B2 was performed using Polymerase chain reaction (PCR) and DNA direct sequencing. Vietnamese 46,XY newborn referred at 2,5th month of life with salt loss associated with hyponatremia (123 nmol/L) and hyperpigmentation. The testes were palpable in the scrotum but associated with a severe hypospadias (micropenis 0.5 cm; posterior). At 4 months of age, a second adrenal crisis has occurred with hyponatremia 127 nmol/L and increased 17OH-Progesterone (26,8 ng/ml) in this 46, XY DSD. This clinical and biological data associated with a sibling with female phenotype deceased at 18 months old after adrenal crisis (1st occurred at 7 days of life) suggest the diagnosis of 3β-HSD deficiency. The sequencing of HSD3B2 confirms the diagnosis because he is homozygous for a missense mutation, pAla161Pro. This mutation affects an aminoacid conserved in all species and is located in one two ahelix involved in the dimerization of the two sub-units of the enzyme. The changing from Alanine to Proline could break the alpha-helix. The same

mutation has been found in the other Vietnamese family. The 46,XY newborn referred at 3th month of life with severe dehydration associated with hyponatremia (93 nmol/L) and hyperpigmentation. The testes were palpable in the scrotum but associated with a severe hypospadias (micropenis 0.5 cm; posterior). Clinical presentation and increased 17OH-Progesterone (9.7 ng/ml) in this 46, XY DSD suggest the diagnosis of 3β-HSD deficiency. The sequencing of HSD3B2 also confirms the diagnosis because he is homozygous for a missense mutation, pAla161Pro. The severity of this mutation correlates well with the phenotype in these patients. Parents of two unrelated pedigrees are not consanguinity. This study contributes to a better understanding of the molecular defects of 3β-HSD and of the phenotypic heterogeneity of CAH related to 3β-HSD deficiency.

Written informed consent was obtained from the patient for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Adrenocortical tumor in patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P51

Adrenocortical tumour have been described in patients with 21-hydroxylase deficiency. These tumours are usually considered to be ACTH – dependent, as diffuse adrenal cortical hyperplasia is commonly seen. We report adrenal cortical tissue tumours developed in three patients with untreated congenital adrenal hyperplasia due to 21-hydroxylase deficiency. All of them had symptoms of adrenogenital vililizing syndrome. A diagnosis of adrenocortical tumour was established by the symptoms, hormonal profile, ultrasonography, and adrenal CT scan. Two of the tumours were located in the right side, all the patients were performed surgery before hormonal replacement therapy because of evidence of secreated adrenal tumors, and the histological diagnosis indicated an adrenocortical adenoma. After removal of tumours, the size of adrenal gland was monitored by serial ultrasonography, and the congenital adrenal hyperplasia was confirmed by extremely high levels of basal serum testosterone, 17-OHP levels, increasing virilizing syndrome after surgery, diffuse hyperplasia of adrenal gland and identified mutations in CYP21A2 gene.

P52

Phenotype of patients with congenital adrenal hyperplasia due to 11β-hydroxylase deficiency

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P52

Congenital adrenal hyperplasia (CAH) is one of the most common metabolic diseases. It is caused by a severe or partial impairment of adrenal steroidogenesis affecting cortisol biosynthesis. Approximately 5–8% of all cases are due to steroid 11β-hydroxylase deficiency (11OHD; OMIM +202010), which occurs in approximately 1:100,000 to 1:200,000 live births in non consanguineous populations. Mutations in the CYP11B1 gene, causing 11b-hydroxylase deficiency in the zona fasciculate in the adrenal cortex, have been identified. Our aim is to describe clinical and biochemical features in patients with CAH due to 11β-hydroxylase deficiency. The case series report included 9 patients (6 male and 3 female) from 7 unrelated families who was identified novel and/or reported homozygous or compound heterozygous mutations in CYP11B1 gene. Diagnosed age was from 2 to 11 years old. All three female cases presented with ambiguous genitalia at birth. Other clinical features were hypertension (6/7 cases); hyperpigmentation (5/7 cases); pseudo-precocious puberty (male) (5/5 cases). Hypokalemia was noted in 3/7 cases. Three cases need antihypertensive drug associated with hydrocortisone replacement therapy. In conclusions, the clinical hallmark of 11β hydroxylase deficiency is variable and virilization and hypertension are the prominent clinical features of 11b hydroxylase deficiency. Biochemical identification of elevated precursor metabolites is not usually available and mutation analysis of CYP11B1 will held confirmation of diagnosis.

P53

Evaluation of parental knowledge after establishing CAH clubs in Vietnam & Indonesia

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The incidence of Congenital Adrenal Hyperplasia (CAH) in some Asian countries is far higher than in Australia, (eg 1:6000 as per the Filipino Newborn Screening Program). For many families in low and middle-income countries in Asia resources are limited, affordable and reliable access to essential medicines is problematic, and families living remotely are required to travel long distances for medical care [1]. CAH is associated with significant physical & psychosocial consequences for affected children & their families where treatment is suboptimal, so there are important equity implications for the global CAH and paediatric endocrinology communities to consider.

Health education is an integral component of health care in any setting. "CAHPepTalk" is an educational resource that was developed initially for CAH families in Australia. This validated educational resource has been produced in DVD format and can be facilitated by one health professional. The program includes a translated validated CAH Knowledge Assessment Questionnaire (CAHKAQ) [2], to enable staff to assess patient knowledge in order to evaluate educational needs.

In collaboration with CLAN (Caring & Living As Neighbours), an Australian NGO committed to optimal quality of life for all children living with chronic health conditions), translation of "CAHPepTalk" into Vietnamese & Indonesian was undertaken, & distributed to CAH Communities in the Asia-Pacific region, was supported by CLAN.

Knowledge of parents of children with CAH in Vietnam and Indonesia was assessed prior to families attending education programs run at CAH Club meetings supported by CLAN, in 3 settings: Hanoi, Ho Chi Minh City & Jakarta. 260 questionnaires have been completed by parents. The results to be presented will include knowledge, management & demographics.

Using the CAHKAQ is the first step in the education process in order to improve health outcomes for families in any setting, within Australia, Vietnam or Indonesia.

References

1. Armstrong K, Henderson C, Hoan N, Warne G: **Living with Congenital Adrenal Hyperplasia in Vietnam: A survey of Parents.** *Journal of Pediatric Endocrinology & Metabolism* 2006, **19**:1207-1223.
2. King J, Mitchelhill I, Fisher M: **Development of a Congenital Adrenal Hyperplasia Knowledge Assessment Questionnaire (CAHKAQ).** *Journal of Clinical Nursing* 2008, **17(13)**:1689-1696.

P54

Evolution of a website: CAHPepTalk.com & the development of the emergency hydrocortisone mobile app

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P54

A comprehensive, validated psychosocial education program (PEP) titled "The CAH Family Workshop" was developed a decade ago to meet the needs of families with Congenital Adrenal Hyperplasia (CAH). Engaging professionals experienced in the field of endocrinology, together with information from parent interviews, was key to development of the program's content. Validation of the program was conducted with the families participating in the program, from one of the three tertiary Children's Hospitals in NSW Australia. The PEP provides families with essential information to assist in understanding and managing the condition.
An awareness of a lack of CAH resources for families living in rural and remote regions of NSW and Australia led to the development of the program into a DVD format. This enabled these families access to the program which covers all aspects of care. The DVD format was designed to be facilitated by one experienced health professional thus reducing the need for a team of specialists to travel to country areas, which was logistically difficult and costly.
The need for CAH resources was further identified in the neighbouring South-East Asian countries of Vietnam and Indonesia where there is a higher incidence of CAH. Through the support of volunteer medical professionals and health services interpreters, the program was translated into these languages. The provision of this valuable resource for families and health professionals in these countries was supported by Caring Living As Neighbours (CLAN) and the CAH Support Group of Australia (CAHSGA).
The most recent stage of this project is the development of the CAHPepTalk.com website, which provides easy access to the English, Vietnamese and Indonesian translations of the program and relevant resources. This presentation will discuss the process of developing this patient-focused education website together with a new Hydrocortisone Emergency Injection App for iphones & android devices.

P55

Congenital adrenal hyperplasia with cholestatic jaundice: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P55

Congenital adrenal hyperplasia (CAH) describes a group of autosomal recessive disorders, each of which involves a deficiency of an enzyme involved in the synthesis of cortisol, aldosterone, or both. Classic CAH is rare, about 1 case per 16,000 population. However CAH with cholestatic jaundice is extremely rare.
A 23 days old boy presented with vomiting, persistent jaundice. He was born at term, and his birth weight was 3 kg. In family history, no liver or endocrine disease was reported.
On examination, his weight was 3 kg; his height was 51 cm; jaundice, hyperpigmentation, dehydration, no hepatomegaly. Strength of his pennis was 3 cm; 2 testis were in the scrotum with volume of 1 ml.
Investigation showed : electrolyte imbalance Na^+ 110 mmol/l, K^+ 7.3 mmol/l, Cl^- 80mmol/l, 17 OHP 111 ng/ml, Testosteron 36.36 nmol/l, cholestatic jaundice : total bilirubin 114.6 mcmol/l, direct bilirubin 75.5 mcmol/l,GOT 40 UI/l, GPT 25UI/l, GGT 142.76 UI/l. The markers for viral hepatitis were negative. Abdominal ultrasound was normal.
He was diagnosed of CAH and treated with hydrocortisone and fludrocortisone. After 1 month of treatment, jaundice disappears and electrolyte is normalized.
Written informed consent was obtained from the patient for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

P56

Pamidronate therapy for hypercalcemia of childhood malignancy

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P56

Background: Hypercalcemia is a common complication of adult malignancies, but uncommon in childhood cancers. The mechanism leading to hypercalcemia varies with the primary tumour and can include the following: 1) Increased osteoclastic activity at the site of the tumour in the bone marrow 2) A paraneoplastic phenomenon secondary to PTH-related peptide (PTHrP) secretion or 1,25–dihydroxyvitamin D by the tumour.
Patients with serum calcium above 3.5 mmol/L tend to be symptomatic and require prompt treatment. The symptoms are generally non-specific and include lethargy, nausea, vomiting, constipation and abdominal pain. Left untreated, hypercalcemia can progress to stupor and coma.
Case Presentation: A 3-year-old girl presented with prolonged fever, hepatosplenomegaly, pancytopenia and multiple osteolytic lesions. She experienced significant weight loss of 5 kg over the past one month associated with anorexia and began to develop persistent daily fever up to 39.5°C with severe pruritus, constipation and irritability.
She was diagnosed to have Ebstein Barr Virus (EBV)-induced T-cell Lymphoproliferative disorder. However, she developed severe symptomatic hypercalcemia of 3.76 mmol/L associated with the paraneoplastic syndrome of an elevated PTH-related peptide, which was successfully treated with intravenous pamidronate (0.5 mg/kg administered as 2 doses), after conventional therapy with hydration and forced saline diuresis failed. Her serum calcium began to normalize to 2.3 mmol/L 2 days after pamidronate administration, with improvement in her symptoms of pruritus and temperament. She tolerated the infusion of pamidronate well with no adverse side effects.
Conclusion: We have demonstrated the effective use of pamidronate as a single agent at a total dose of 1mg/kg to lower serum calcium levels in a patient with severe hypercalcemia of malignancy. In such cases of severe hypercalcemia, we recommend the early use of pamidronate since hydration with saline diuresis is unlikely to normalize serum calcium levels effectively.
Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

CALCIUM/BONE

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Incidence and characteristics of vitamin D deficiency rickets in New Zealand children: a prospective New Zealand paediatric surveillance unit study

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P57

Vitamin D deficiency rickets is the most significant manifestation of vitamin D deficiency in growing children. Concerns have been raised in New Zealand (NZ), and worldwide, that cases continue to present, and may be possibly increasing. We undertook a prospective study to investigate the incidence and characteristics of vitamin D deficiency rickets in NZ children.
Prospective surveillance of Vitamin D Deficiency Rickets was conducted by the NZ Paediatric Surveillance Unit (NZPSU), for 36 months, from July 2010 – June 2013 inclusive. Inclusion criteria were: children aged <15 years with vitamin D deficiency rickets (defined by low 25-hydroxyvitamin D and elevated alkaline phosphatase levels, and/or radiological rickets).

58 children with confirmed vitamin D deficiency rickets were identified. Median age was 1.4 years (range 0.3 – 11), male gender 47%, 95% of children were born in NZ, as opposed to 22% of mothers. Overall annual incidence in those aged <15 years was 2.2/100,000, while incidence in the south of NZ peaked at 6.8/100,000. Overall NZ incidence in children aged <5 years was higher at 6.6/100,000. Skeletal abnormalities, poor growth and developmental delay were the most common presenting features, with hypocalcaemic convulsion in 16%. Key risk factors identified were: dark skin pigment, Indian/South Asian and African ethnicity, age ≤2 years, exclusive breast feeding, and southern latitude, particularly when combined with season (winter/spring).
Vitamin D deficiency rickets remains a health problem for New Zealand children, with significant associated morbidity. Public health policy, utilising infant supplementation, for at minimum the above identified risk factors, should be considered to reduce the incidence of this disease among those at high risk.

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Idiopathic calcinosis cutis universalis

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P58

Background: Calcinosis cutis is an uncommon disorder characterized deposition of crystals of calsium phosphate (hydroxyapatite) in the skin in various areas of the body. Medical and surgical treatments are options to cure calcinosis cutis. Because calcinosis cutis are not always well defined, a recurrence of the lesions may occur.
Case: A 12-years old girl with complaints of multiple lumps on her body since 1 years prior to admission. Two years prior to admission patient complained of movement limitation due to pain when doing leg lifting, squatting and standing up. One years prior to admission patient got bilateral symmetrical lumps on hip, corn size and getting bigger. Two months prior to admission the lumps got ruptured and patient felt pain. From past history no calcium supplementation, no allergy.
In physical examination patient vital sign are within normal limits, moderate malnourished. From head and neck no enlargement of lymph nodes. Heart and lungs are normal. Abdomen is normal and no sign of edema on extremities. On the extremities multiple bilateral and symmetrical lumps, corn size and coin size. On the hip multiple bilateral and symmetrical lumps. The laboratory investigations revealed within normal limits. Biochemical examinations gave normal results for complete hemogram, erythrocyte sedimentation rate, blood sugar, uric acid, electrolyte, liver function and kidney function tests. Serum calcium 1.2 (normal 1.2 – 1.48 mg/dl), phosphorus 4.2 (normal 2.4-5.1 mg/dl), 25-hydroxyvitamin D 18.7(normal 17-54 ng/dl), parathormone (PTH) 29.46 (normal 15-65 pg/dl), and magnesium 2.0 mg/dl (normal 1.3-2.7 mg/dl).
On radiologic findings there are multiple calcification in soft tissue layer on humeral, antebrachial, femoral and crural bilateral. On tissue biopsy there are cystic space containing calcified material separated by fibrous tissue. Patient underwent treatment with bisphosphonate using zolendronate and surgical exicion.
Conclusions: Calcinosis cutis is an uncommon disorder which results in progressive deposition of insoluble calsium salts (crystals of calcium phosphate, hydroxyapatite) in the skin. Medical and surgical treatment are options to cure calcinosis cutis. Medical treatment using bisphosphonate. A better understanding of the process of calcinosis cutis will lead to therapies to improve patient morbidity.
Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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High incidence of vitamin D deficiency in 2 – 17 year olds presenting with fracture to a Melbourne suburban public hospital

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P59

To determine vitamin D deficiency risk and other lifestyle factors in children and teenagers aged 2 – 17 years presenting with fracture to Sunshine Hospital, a clinical observational study was undertaken using convenience sample data collected from children and teenagers aged 2 - 17 years of age presenting with fracture, for whom consent had been obtained to determine clinical characteristics and lifestyle factors. Recruitment was undertaken over a 4 month period 1st February to 31st May 2014. A suburban Melbourne (latitude 38^0S) teaching hospital, Sunshine Hospital provides paediatric orthopaedic services for a high proportion of children and teenagers from ethnically diverse backgrounds with an increased proportion of highly pigmented individuals, which may influence vitamin D status specifically. Proxy measures of vitamin D were used (skin pigmentation, hours spent outdoors, sunscreen use and obesity) [1] to determine patients at risk for Vitamin D deficiency. Further consent was then obtained from at risk patients to take blood for 25 OH vitamin D (LIAISON®, Diasorin Assay). Of the 162 patients recruited into this study, 133 (82%) had risk factors for vitamin D deficiency. Of these 108 (81% of at risk) consented to blood testing for 25 OH vitamin D, with a median of 50nmol/l (range 14 – 110nmol/l) obtained. A total of 56 (52% at risk, 34% of total participants) were found to be vitamin D deficient and of these 45 (80% at risk) were mildly deficient (25 OH D 30 -50nmol/l) and 11 (20% at risk) had moderate deficiency (25 OH D 12.5 – 29 nmol/l). Although our study was undertaken at the end of summer, one third of the patients in our study were vitamin D deficient. Furthermore, half of those clinically deemed at risk for vitamin D deficiency were confirmed on biochemical testing. Childhood fracture incidence has been reported to be increasing, and with relatively stable genetic characteristics, any variations in childhood fracture would imply environmental changes. The effect of mild to moderate vitamin D deficiency on fracture risk, healing and longer term refracture risk in children and teenagers is yet to be determined, however, based on our findings we recommend that vitamin D status be assessed in all at risk children and teenagers living in urban environments at higher latitudes presenting with fracture.

Reference

1. Paxton G, *et al*: Vitamin D and health in pregnancy, infants, children and adolescents in Australia and New Zealand: a position statement. *Medical Journal of Australia* 2013, **198**:142-3.

P60

Parathyroid adenomas – a cluster of boys

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P60

Primary hyperparathyroidism is rare in children and adolescents, representing 1% of all cases, with a slight female preponderance [1-3]. 3-5% of cases are hereditary and may represent the initial clinical manifestation of multiple endocrine neoplasia type 1 (MEN1).
Over the last 30 years, ten cases of primary hyperparathyroidism have presented to our hospital, all aged 11-14 years, with nine cases being male, and eight cases over the last six years. Presenting features included headache and blurred vision in five patients, abdominal pain and nausea (in three), renal calculi (in four), generalized bone pain (in three) and two asymptomatic. One patient had received radiation for acute lymphoblastic leukaemia. Other history included ADHD (in one patient), mild developmental delay (in one), depression (in one) and fine motor difficulties (in one). No patients had a significant family history.
Peak corrected calcium level ranged between 3.12-3.65 mmol/L (2.1-2.65), peak PTH level 6.9-154 pmol/L (1-7), and urine calcium creatinine ratio

0.47-2.76mM/mM (0.04-0.7). Serum alkaline phosphatase was 212-549U/L (80-355), and normal in three of the renal calculi patients. Bony changes were seen in three patients, with flaring of clavicles and widening of epiphyses, decreased phalangeal cortical density and osteopenia. 25-OH calciferol was low at 27-39nmol/L (>50) in 3 of 7 patients in whom it was measured.

Thyroid ultrasound detected suspicious lesions in seven patients and was normal in three patients. Sestamibi scan was negative for three patients (with one ectopic gland) and indicated a single overactive gland in seven patients. All patients had a positive result from at least one modality.

All patients underwent surgical resection, with a single benign parathyroid adenoma identified in each case. The only significant post-operative issues were initial hypocalcaemia (lowest cCa 1.8mmol/L) in eight patients, requiring management with calcitriol and elemental calcium. There was normalisation of calcium over several weeks post-operatively, with gradual weaning of supplementation required. In all, post-operative PTH level was suppressed. MEN1 screening has been negative for all patients.

This case series illustrates the difficulties involved in the diagnosis of parathyroid adenoma in children, requiring both scintigraphy and ultrasound. Scintigraphy has been reported in the literature to have 88% sensitivity, lower in our case series, compared to 78% sensitivity for ultrasound [4]. The gender mix of our cases differs significantly from other reported case series, being predominantly male [3,5] and there is a suggestion of increasing incidence over recent years.

References

1. Sneider MS, Solorzano CC, Montano RE, *et al*: **Sporadic primary hyperparathyroidism in young individuals: different disease and treatment?** *J Surg Res* 2009, **155**:100-3.
2. Paunovic I, Zivaljevic V, Stojanic R, *et al*: **Primary hyperparathyroidism in children and young adults: a single institution experience.** *Acta Chir Belg* 2013, **113**:35-9.
3. Romero Arenas MA, Morris LF, Rich TA, *et al*: **Preoperative multiple endocrine neoplasia type 1 diagnosis improves the surgical outcomes of paediatric patients with primary hyperparathyroidism.** *J Ped Surg* 2014, **49**:546-550.
4. Eslamy HK, Ziessman HA: **Parathyroid scintigraphy in patients with primary hyperparathyroidism: 99mTc Sestamibi SPECT and SPECT/CT.** *Radiographics* 2008, **28**:1461-1476.
5. Kundel A, Thompson GB, Richards ML, *et al*: **Pediatric Endocrine Surgery: A 20 year experience at the Mayo Clinic.** *J Clin Endocrin Metab* 2014, **99(2)**:399-406.

P61

Effect of bisphosphonate treatment in osteogenesis imperfecta children in Cipto Mangunkusumo Hospital Jakarta

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P61

Background: Bisphosphonates are the mainstay of pharmacologic fracture-prevention therapy for most forms of osteogenesis imperfecta (OI). Studies suggests that bisphosphonate treatment may significantly improve the natural history of all type of OI, particularly by decreasing the rate of fracture, increasing bone mineral density, decreasing bone pain, and significantly increasing height.

Objective: To evaluate the effect of bisphosphonate treatment in OI children treated in Cipto Mangunkusumo Hospital (CMH) Jakarta.

Method: We retrospectively studied the data of age, gender, age at diagnosis, bisphosphonate treatment, and its effects in OI patients in CMH from Indonesian OI children registry, which is documented from January 2012 to May 2014.

Results: Seventy-seven OI cases (39 male), which were diagnosed at the age of 1 - 9 years old were recorded. Five patients underwent surgery and three patients died before commencing treatment. Nine patients received intravenous pamidronate and sixteen patients received zolendronic acid therapy. Liver and renal functions, as well as serum electrolyte levels were evaluated before and after treatment. Eight patients reported hyperthermia and three others experienced fatigue, bone pain, and abdominal pain within 24 hours of therapy. Serum calcium level decreased in eight patients. No serious adverse effects were documented.

Conclusions: All registered OI cases patients that received bisphosphonates treatment showed no serious adverse effects.

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Vitamin D status of healthy adolescents from two states in Malaysia

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P62

Hypovitaminosis D is a widespread disorder across all age groups in developing countries. The prevalence of hypovitaminosis D varies from 30-90% depending on the cut off level used to define hypovitaminosis D. In Malaysia, Khor et. al found 35.3% of 402 primary school children aged 7-12 years to have 25(OH)D level < 37.5nmol/L and 37.1% have the level between 37.5-50nmol/L. If a broader definition of hypovitaminosis < 50nmol/L is used then, the prevalence was as high as 74.6%. The risk factors associated with hypovitaminosis D in developing countries are the same as in western countries. The most consistently reported risk factors are female gender, increased skin pigmentation, seasons/latitudes, obesity, concealing clothing style and vulnerable groups (neonates, preschool, elderly).

A total of 469 adolescents (107 PJ, 362 KB) participated in the study. The mean age was 15.6+/-1.4 years. Female gender contributed about 61.0% compared to male gender, 39.1%. As for the race distribution, the proportion of Malay was 79.3%, Chinese 17.7% and Indian 3.0%. Teenagers from KB with family income < RM 1000 was higher (37.8% cf 10.3%; P <0.001). Adolescents from PJ was taller (160.6cm cf 156.3cm; P = 0.02). The mean BMI was 21.0+/-4.4 kgm^2. The mean 25(OH)D was19.9 +/-8.1, in which PJ had a higher level(21.0 cf 19.6) but the mean differences was not statistically significant. More than half (58%) of adolescents had 25(OH)D < 50nmol/L. The proportion of subjects with 25 (OH)D < 50nmol/L was 60.2% in KB and 50.4% in PJ. With regard to the degree of 25(OH)D level, 52% had a level between 25.0-50.0nmol/L, 6% had a level between 12.5-25.0nmol/L. None had a level < 12.5nmol/L.

Chinese had the highest mean of 25(OH)D(23.5+/-8.0; P <0.001) compared to the other 2 races. From multiple logistic regression, significant variables were age (0.84;95%CI :0.72,0.98), gender(boy)(0.13;95%CI;0.08,0.19) and race(Chinese)(0.30;05%C1;0.17,0.53). This study highlights a high prevalence of hypovitaminosis D among adolescents especially in younger adolescents, female and darker skin.

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Sun exposure, ultraviolet (UV) irradiance and serum 25 hydroxycholecalciferol (25OHD) in pregnant women in rural North India

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P63

Vitamin D deficiency is rampant in India despite abundant sunshine. We aimed to estimate the amount of cutaneous vitamin D synthesis in pregnant village women (n=100) in different seasons in conjunction with serum 25OHD. We also correlated variations in surface UV energy with the presence of environmental pollution and crowding.

Methods: The measurements of UVB radiation energy were obtained using UV spectrometer at different times of the day between 9 am and 4 pm, in different seasons. The instrument was calibrated to denote 13 microWatt/cm2 of irradiance per mVolt of deflection. Measurements were taken at our institution (situated in the countryside), at crowded inner city areas and the villages where our subjects resided. The clothing, outdoor activity pattern, and dietary calcium intake were prospectively

documented. Serum 25OHD was measured by radioimmunoassay (Diasorin, Stillwater, MN).

Results: UVB spectrometer reading ranged from 4.5 mVolts in January to 36 mVolts in June. The average erythemally effective UV energy during winter season and during the rest of the year was 308 J/m^2 and 805 J/m^2respectively. Average body surface area exposed was 9.5% in winter and 18.5 % in summer. Using the equation described previously by Godar et al [1] which takes into account effective erythemal irradiance, latitude, age, and duration and surface area of exposure**,** the estimated average daily cutaneous vitamin D synthesis was 769 IU during winter and 1487 IU during summer. The mean serum 25OHD was11.32 ± 5.03 ng/ml during winter (92 % < 20 ng/ml) and, 16.63 ± 8.12 ng/ml during the rest of the year (70 % < 20 ng/ml).The average peak UV irradiance calculated during April and May was significantly higher in our institute campus (338 microwatt/cm2) and the villages (312 microWatt/cm^2), than the crowded inner city location (247 microWatt/cm^2, p=0.03).

Conclusion: During winter at latitude 26.8 ^{0}N, cutaneous vitamin D synthesis is limited by poor UV radiation energy. Poor skin exposure is a limiting factor in all seasons. Particulate pollution may be an important remedial impediment to cutaneous vitamin D synthesis.

Reference

1. Godar DE, Pope SJ, Grant WB, Hollick MF: **Solar UV doses of young Americans and vitamin D3 production.** *Environmental Health Perspectives* 2012, **120(1)**:139-143.

P64

Vitamin D deficiency rickets – tip of the ice burg

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P64

Introduction: Vitamin D deficiency rickets is an increasingly recognized condition across the world in both developed and developing countries. There is no vitamin D fortification program in Sri Lanka. The main source of Vitamin D is sun exposure. The burden of vitamin D deficiency rickets was not studied Sri Lanka.

Aims: Aims of this study were to identify the number of children affected with Vitamin D deficiency rickets in a single center, affected age groups and the level of vitamin D at which the nutritional rickets appears.

Method: The study was conducted in the largest children's hospital in Sri Lanka. The children with radiological rickets were included in the study. Patients with chronic renal failure and liver failure were excluded. The study was conducted from 2012 June to 2014 June. Data obtained from the department of chemical Pathology Lady Ridgeway Hospital Sri Lanka. Vitamin D level was measured using Chemiluminescence method.

Results: Total number of patients presented with rickets was 42.There were 36 children with vitamin D deficiency rickets (F=21). Median age of presentation was 22 months. 22 patients were below 2 years of age (6%). All patients came with complaints of bowing of legs except a 5 month old baby who presented with hypocalcaemic convulsions. The median vitamin D level was 27.9 nmol/L (range 11.5-38.3). There were 18 (50%) children with vitamin D level less than the sample median of 27.9 nmol/L.

Conclusion: Vitamin D deficiency rickets is seen in Sri Lankan children despite the presence of sunshine throughout the year. 61% of the children were below 2 years. Lack of sun exposure due to socio economic changes happened in the recent past would have contributed to vitamin D deficiency rickets. Further community based larger studies are needed to identify the prevalence of vitamin D deficiency and factors contributing to vitamin D deficiency rickets in Sri Lanka.

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Vitamin D nutrition of healthy schoolchildren from North India

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P65

Vitamin D deficiency is not expected in prepubertal schoolgoing children in a sunny country like India since they should have good sunshine exposure in conjunction with school activities. However data from India in this age group are scant.

Aims: To evaluate the vitamin D status of apparently healthy prepubertal vs pubertal schoolchildren and to examine the influence of gender and socioeconomic status on serum 25 hydroxyvitamin D (25OHD).

Methods: Children referred to the pediatric endocrinology clinic for growth evaluation, interpretation of thyroid functions, concern regarding delayed puberty, etc and found to be normal were enrolled, as were their healthy siblings. Pubertal assessment, a food frequency questionnaire for calcium, sunlight exposures (minutes of sunshine exposure from 10 AM - 4PM) and percentage of skin exposed were recorded. Serum calcium, albumin, creatinine, alkaline phosphatase (ALP), 25OHD and iPTH were assayed.

Results: 118 children (69% prepubertal) were enrolled. Vitamin D deficiency (25OHD < 20 ng/ml) was present in 71.6% of prepubertal and 87.8% of pubertal children. Mean 25 OHD was significantly higher in the prepubertal as compared to the pubertal group (16.0 ± 7.9 versus 10.6 ± 7.5 ng/ml, p = 0.001). Their calcium intake and sunlight exposure was also significantly higher. Girls had lower mean 25 OHD as compared with boys (12.9 ± 7.6 vs 16.0 ± 8.4, p=0.02), lower calcium intake (569 ± 270 vs 712 ± 334 mg, p=0.02) and less sunlight exposure (46.7 ± 45.8 vs 75.1 ± 39.1 minutes, p=0.001) than their male counterparts. There was no significant difference in 25OHD of upper, middle and lower socioeconomic classes. We found a significant correlation between serum 25OHD and calcium intake (r: 0.238, p=0.02), duration of sunlight exposure (r: 0.235, p=0.02) and body surface area exposed (r: 0.28, p=0.003). There was a significant negative correlation between 25OHD and PTH levels (r: -0.45, p<0.001).

Conclusions: Pubertal children have lower 25OHD than prepubertal children, probably due to limitation of outdoor activities on the background of high demand. There is significant gender bias against girls for both calcium intake and sun exposure, resulting in lower serum 25OHD than in boys.

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Effects of long term anti epileptic drugs on serum vitamin D levels and bone profile in a cohort of Sri Lankan children

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P66

Aims: To demonstrate association between Vitamin D levels and AED usage.

To demonstrate effects of long term antiepileptic drug use on bone metabolism –eg: Serum alkaline phosphatase (ALP), calcium.

Method: A retrospective cohort study was performed on 205 children aged 1–12 years presented to a tertiary care hospital in Sri Lanka;119 with epilepsy, exposed to AEDs more than 2 years and 86 who are unexposed to AED. Vitamin D levels and bone profile were analyzed by chemiluminescent auto analyzer and photometric methods respectively. The prevalence of Vitamin D deficiency (< 20ng/ml) among children exposed and unexposed to AED was compared. Among exposed the effect of AED combinations on Vitamin D deficiency were assessed. Similarly bone profile was compared in the two groups.

Results: A higher proportion of children on AED were deficient in Vitamin D (53.7%) compared to children who are not on AED (45.3%) (p=0.233).

Difference of Vitamin D deficiency among those on poly AED therapy (59.5%) and single AED (50.6%) were non-significant (p=0.353). Similarly, differences of Vitamin D deficiency in those on Carbamezapine mono therapy (50% n=18/36) and Sodium Valproate mono therapy (60.7%; n=17/27) were non-significant (p=0.4).

The mean ALP among children on AED was significantly higher (599.4 ±178.96) compared to children not on AED (420.6±152.59)(p=0.044).The mean serum calcium among children exposed to AED (2.39+0.15)and those not exposed to AED (2.36+0.17) were similar(p=0.34).

Conclusions: Vitamin D deficiency was not significantly associated with long term AED use in children with epilepsy. Being on polytherapy over monotherapy or being on carbamezapin over sodium Valproate was not associated with Vitamin D deficiency.
However a significantly higher than normal levels of ALP was associated with long term use of AED which needs further evaluation.

P67

Bisphosphonates as treatment of secondary osteoporosis in children: a case series

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P67

Background: Secondary osteoporosis due to chronic disease is a major pediatric health concern and has certain unique diagnostic with various clinical challenges. Bisphosphonates has been used in small numbers of pediatric patients to treat secondary osteoporosis resulted in significantly fewer fractures and improved mobility.
Objective: To present case series of secondary osteoporosis due to chronic disease treated with biphosphonate.
Case Series: We included 6 patients (2 boys, 4 girls), 7–15 years of age with secondary osteoporosis who were treated with biphosphonate. Two patients were diagnosed acute lymphoblastic leukemia, two patients with systemic lupus erythematosus and others with juvenile rheumatoid arthritis. Two patients received methotrexate and dexamethasone; one patient was treated with methotrexate and prednisone; two patients with methylprednisolone; and rest with only methotrexate. Four of them suffered back pain due to trauma and from radiographic examination showed multiple compression fracture on the vertebrae. Lumbal BMD Z-score was ranging from -2.8 to -5.1 in patients who had fracture, while in patients without fracture -2.6 to -3.1. We used zoledronic acid 0.05 mg/kgBW. Two patients already received pamidronate as previous treatment. In 6 - 12 months of follow-up, there were evidence of reduced pain, improved mobility and BMD Z-score, also no evidence of new fractures in radiographic evaluation.
Conclusion: Bisphosphonates appears to be safe and effective as treatment for children with secondary osteoporosis.

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Hearing loss in osteogenesis imperfecta patients

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P68

Osteogenesis imperfecta (OI) is an inherited bone and connective tissue disorder associated with the lifelong occurrence of frequent fractures following even mild trauma. Hearing loss is frequently reported in patients with OI. Objective: to examine the ratio of hearing loss in children with OI, and the relationship between audiological findings and CT images of temporal bone in children with OI. Subject and methods: forty – two children aged 5 to 17 years with OI were included in the study. The patients have type A of tympano and were mesured thresold of hearing by play audiometry. CT imaging was performed in 8 cases as well. Imaging abnormalities were correlated with clinical phenotypes and severity of hearing loss deduced from audiograms. Results: Hearing loss of all etiologies was observed in 28.05 % of ears in studied OI patients. Sensorineural and mixed hearing loss was observed in 4.88% and conductive hearing loss was detected in 23.17% of ears. CT revealed bone – bridge image in the middle ear (10/16 ears), hypodense foci in the fissula ante fenestram (4/16 ears) and cochlear (2/16 ears), abnormal stape (5/16 ears). Conclusions: hearing loss in children with osteogenesis imperfecta is quite frequent. We have all type of hearing loss, but the conductive of hearing loss have highest ratio. The site of abnormal on temporal bone CT images in OI corresponds to presence and type of hearing loss determined by audiometry.

OBESITY/METABOLIC SYNDROME

P69

Correlation between C-reactive protein levels and affecting factors for adiposity in apparently healthy Korean adolescents

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P69

Aims: Recent studies have shown that C-reactive protein is not just an indicator of cardiovascular disease (CVD) incidence and mortality. Thus, early detection of a continous increase in CRP concentrations may be useful in predicting subsequent development of CVD or metabolic syndrome.
The objective of this study was to analyze high sensitivity C-reactive protein (hs-CRP) in apparently healthy young Korean adolescents and determine confounding factors for high hs-CRP in this population.
Methods: We enrolled 197 middle school students (93 boys and 104 girls) who participated in a general health check-up at a tertiary hospital in Seoul. We measured height, weight, waist circumference and blood pressure and investigated hs-CRP concentrations, insulin levels, insulin resistance and lipid profiles. Hs-CRP levels were measured using the Behring BN II nephelometer (Dade Boering, Marburg, Germany) and log-transformed for analysis.
Results: hs-CRP concentration was significantly higher in boys than in girls (P=0.012). Pearson's correlation coefficients revealed a significant correlation between log- transformed hs-CRP and BMI (r=0.24, P=0.0008), waist circumference (r=0.24, P=0.0007), systolic (r=0.17, P=0.019) and diastolic blood pressure (r=0.23, P=0.014), and ALT (r=0.16, P=0.023). In stepwise multivariate linear regression analysis, sex (male gender), waist circumference, and diastolic blood pressure were positively and fasting serum HDL-cholesterol level was negatively associated with log-transformed hs-CRP.
Conclusions: We found that there exists a gender difference in hs-CRP concentrations in apparently healthy adolescents and that log-transformed hs-CRP concentrations were positively associated with male, waist circumference and diastolic blood pressure and negatively associated with HDL-cholesterol level. The gender difference and the contibuting factors for hs-CRP found in these healthy adolescents suggests a possibly relevant pathophysiological mechanism involved in the increase of cardiovascular risk associated with childhood obesity.

P70

Association of serum 25-hydroxyvitamin D concentration and metabolic syndrome in Korean children and adolescents

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P70

Aims: Vitamin D is required not only for bone health but also has been reported to play a role in a range of ailments such as autoimmune disease, cardiovascular disease, type 2 diabetes, hypertension, depression, and certain types of cancer. Several studies have reported that poor vitamin D status during childhood and adolescence is related to obesity and metabolic syndrome. Vitamin D deficiency has been associated with hypertension and increased risk of cardiovascular disease while 25(OH)D concentration is known to be independently associated with both insulin sensitivity and beta cell function. A recent study reported that low serum 25(OH)D to be associated with obesity and metabolic syndrome in Korean children. We investigated the association between serum 25(OH)D

concentrations and the presence of metabolic syndrome components in Korean children and adolescents. We also compared the components of metabolic syndrome according to vitamin D status in Korean children and adolescents.
Methods: The study included 141 Korean children and adolescents who were aged 6 to 18 in Kangdong Sacred Heart Hospital. Anthropometric measurements, including height, weight, body mass index (BMI, kg/m^2) waist circumference, and blood pressure were performed. Serum lipid, fasting plasma glucose (FPG), insulin and 25(OH)D levels were measured. HOMA-IR (homeostasis model assessment for insulin resistance) = [glucose (mmol/L) x insulin]/22.5 values were calculated. Metabolic syndrome defined by modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III).
Results: Among total 141 subjects, 26 (18.4%) children and adolescents had metabolic syndrome. Children and adolescents who have metabolic syndrome have significantly lower serum 25(OH)D concentration than those who do not have (12.35 ± 4.65 vs. 14.81 ± 4.63 ng/mL) (p=0.015). Waist circumference, SBP, fasting plasma glucose, insulin, HOMA-IR are significantly correlated with serum 25(OH)D concentration (p<0.05). Only LDL-cholesterol is significantly different according to tertile groups of serum 25(OH)D concentration. The odds ratio of group I (25(OH)D <11.50 ng/mL) is 1.826 compared to group III (25(OH)D >16.30 ng/mL).
Conclusion: Children and adolescents who have metabolic syndrome have lower serum 25(OH)D concentration. The prevalence of metabolic syndrome may be higher in children and adolescents with severe 25(OH)D deficiency. Further investigation will be needed to identify the influence of 25(OH)D on metabolic syndrome.

P71

The association between bone age advancement and insulin in prepubertal children with obesity

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P71

Aims: Obesity is associated with bone age (BA) advancement of unclear etiology. In animal study, insulin may directly modulate skeletal growth. Our objective was to investigate the association with BA maturation and insulin levels in children with overweight and obesity.
Methods: In this cross-sectional study of 103 prepubertal children, anthropometric data and hormonal values during oral glucose tolerance test were measured. Subjects were divided into two groups by the difference between BA and chronological age (CA) (noted as BA-CA).
Results: The study population included 49 (47.6%) males and 54 (52.4%) females with a mean age of 7.6 ± 1.6 years. The advanced bone age group defined as BA-CA>1 year (n=53) had significantly higher HOMA-IR, fasting insulin levels and lower quantitative insulin sensitivity check index (QUICKI). Also, BA-CA was significantly correlated with fasting insulin (r=0.315, P<0.001), HOMA-IR (r=0.288, P<0.001), and QUICKI (r=-0.353, P<0.001). In multiple regression analysis, fasting insulin was identified as significant independent predictors for BA-CA.
Conclusion: Skeletal age is more advanced in overweight and obese children with hyperinsulinemia and insulin resistance. These findings suggest that insulin may modulate skeletal growth.

P72

Autosomal dominant Kenny-Caffey syndrome with congenital hypoparathyroidism, short stature and normal intellect: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P72

Kenny-Caffey syndrome (KCS) is characterized by proportionate short stature, cortical thickening and medullary stenosis of tubular bones, delayed closure of anterior fontanelle, eye abnormalities, and hypoparathyroidism. The autosomal dominant form (KCS Type 2) caused by mutations in FAM111A is distinguished from the autosomal recessive form (KCS Type1), caused by mutations in TBCE gene, by the absence of mental retardation.
Our proband presented on day 8 of life with hypocalcaemic seizures secondary to hypoparathyroidism. Normocalcaemia was achieved with IV calcium gluconate and maintained by oral calcium carbonate 100mg BD and calcitriol 0.1mcg BD for the first 2 years of life while serum PTH remained low at <0.3pmol/L. There has been no evidence of nephrocalcinosis on follow up. The dose of supplemental calcium and calcitriol is being gradually reduced. She also has persistent mild microcytic anaemia with normal iron stores.
Her phenotype included small hands and feet, triangular hypoplastic and dystrophic nails, hypoplastic mid-face, macrocrania and large persistent fontanelles. Karotype and FISH for 22q11 deletion were normal. Initial investigations included a normal ECHO, renal ultrasound and MRI brain.
Her neurodevelopment is normal but her growth is compromised. At 1 year, her length was 65.5cms (SDS -2.9) and at 3 years, her height was 80cms (SDS -3.8). There is no family history of short stature or hypoparathyroidism. She is growth hormone sufficient on pharmacological testing; however she has been commenced on growth hormone treatment based on her poor growth velocity and short stature. It is currently too early to determine response.
A skeletal survey performed at 2 years of age was suggestive of KCS. Genetic testing revealed a heterozygous mutation c.1622C>A (p. Ser541Tyr) in FAM111A. However, the unusual nails, the reducing calcium requirement and the unexplained microcytic anaemia are unique to our patient.
Written informed Consent for this patient has been taken including results of the genetic analyses and images according to the Institutional Ethics Committee procedures of our health service.

P73

Association of fat mass and obesity-associated gene rs9939609 variant with early onset obesity among bataknese and Chinese children in Indonesia

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P73

Background: Obesity is becoming a worldwide epidemic in modern society, it is prevalent in individuals of both genders and of all ages, socio-economic strata, and ethnic group. Several studies have reported an association between rs9939609 polymorphisms of the FTO gene and obesity. However, this association has not yet been studied among the Indonesian children.
Aims: This is the first study in Indonesia to investigate the association between fat mass and obesity-associated gene rs9939609 variant with early onset obesity among Bataknese (n=94) and Chinese (n=66) children in Medan, North Sumatera, Indonesia.
Methods: We conducted a case control study in ten elementary schools in Medan, North Sumatera, Indonesia. Case group (n=105) were children with early onset obesity and control group (n=55) were normal weight children. The inclusion criteria were Bataknese and Chinese children, aged 6-12 years with early onset obesity. We examined body weight and

height, body mass index, waist circumference. Genotyping was performed using a TaqMan assay for rs9939609 polymorphism.
Results: A total of 160 children between 6 and 12 years old were recruited in this study. The distribution of genotypes and alleles was significantly different among ethnicities (P=0,004), but no association was found for early onset obesity, related anthropometric measurements and gender. FTO rs9939609 allele was not associated with central obesity.
Conclusion: Our study showed there were no associations between fat mass and obesity-associated gene rs9939609 variant with early onset obesity. However, the prevalence of genotypes for FTO rs9939609 in our study were similar with other study in China and Malaysia.

P74

Study of serum visfatin and blood glucose and lipid metabolism, nafld in simple obese children

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P74

Aims: To investigate the relationships between serum visfatin and blood glucose and lipid metabolism, nonalcoholic fatty liver disease (NAFLD) in simple obese children.
Methods: Eighty-six children (57 boys and 29 girls) including 40 obese children, 22 overweight children and 24 healthy children were recruited with ages ranged 7-15 years.The serum visfatin levels were determined by ELISA.
Results: (1) As compared with normal and overweight children, serum visfatin levels increased 49.80%(P<0.05) and 35.88% (P<0.05); There were no difference of serum visfatin levels between the healthy and overweight children. (2) The body mass index, TC, TG, LDL-c, FPG, FINS and insulin resistance index of the obese children were higher than the healthy children (p<0.05 or p<0.01); the HDL-c and insulin sensitivity index of the obese children were lower than the healthy group (p<0.01 or p<0.05).The body mass index, the fasting insulin and the insulin resistance index of the obese children were higher than the overweight children (p<0.01).The ALT and AST levels of the obese children were higher than the healthy group (p<0.05).There was significant difference between the obese children and healthy children on the no-alcoholic fatty liver disease (p<0.01) with the prevalence of 23.33% and 5.26%, respectively.(3) Correlation analysis: Body mass index, TG and ALT were positively correlated serum visfatin (r=0.218, p<0.05; r=0.500, p<0.01; r=0.426, p<0.01, respectively).
Conclusions: The serum visfatin level is correlated with obesity and it is related with the disorder of lipid metabolism and the occurrence of fatty liver in obese children.Serum visfatin levels can be used as a new indicator to evaluate the trend of childhood obesity and valuate the risk of fatty liver, diabetes and cardiovascular of the obese children in the future.

P75

Genetic testing in Indian patients with Prader-Willi syndrome using methylation specific multiplex ligation dependent probe amplification (MS-MLPA)

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P75

Prader-Willi syndrome (PWS) is caused by loss of function of genes on chromosome 15; most cases occur when a segment of the paternal chromosome 15 is absent/inactivated. Recently few cases have been identified with truncating mutations in MAGEL2 gene (Chromosome 15). We present clinical features and molecular genetic analysis on 6 patients with features of PWS using MS-MLPA.

Four boys and 2 girls (age 8-15 years) presenting with obesity, facial features of PWS, developmental delay, snoring and hypogonadism were referred for genetic testing. DNA was extracted from peripheral blood and MS-MLPA was carried out using MS-MLPA Probemix (ME028) from MRC Holland [1]. Data analyses were performed using Coffalyser Software (MRC Holland). MS-MLPA was used to detect copy number changes and determine CpG island methylation status of 15q11.3-13 locus in semi-quantitative manner.
Of six patients, no genetic defect was detected in one. Two patients' DNA on MLPA analysis showed 50% reduction in peak intensities (compared to healthy control) of 29 probes in the targeted 15q11.3-13 region indicating heterozygous deletion of that region. The single copy that was present in these patients was imprinted and likely to be silenced. In the fourth patient, no detectable deletion was found, however, comparative MS-MLPA analysis of this sample pre- and post- methylation-specific restriction digestion showed approximately 100% relative methylation for the 5 probes specific to the imprinted regions (these are 50% in healthy individuals). Both copies of the analyzed region were imprinted and likely to be silenced (most likely due to maternal uniparental disomy). For the last two patients, while no deletion was found, both samples showed hypomethylation (0% methylation) of one probe in necdin-encoding gene (NDN) locus (for this locus, expected methylation for healthy controls is between 30%-50%). We are investigating the relevance of these data.
Our MS-MLPA results in 6 patients with clinical features of PWS indicate that two cases had deletions, one had a maternal uniparental disomy or an imprinting defect, two had hypomethylation of the NDN locus and one did not show any defect.

Reference

1. Ramsden SC, Clayton-Smith J, Birch R, Buiting K: **Practice guidelines for the molecular analysis of Prader-Willi and Angelman syndromes.** *BMC Med Genet* 2010, **11(11)**:70.

P76

Response to vitamin d replacement in overweight and normal weight children with vitamin D deficiency

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P76

Aims: Obesity is a risk factor for vitamin D deficiency (VDD), because the lipid soluble vitamin D can be sequestered in adipose tissue. Although it was suggested that higher dose of vitamin D might be required to treat VDD in obese individuals, little is known about treatment responses in overweight children. We investigated the response to vitamin D replacement in normal weight and overweight children.
Methods: This is a prospective study including 66 Korean children between 8 and15 years of age diagnosed with VDD between Dec 2013 and Feb 2014. VDD was defined as serum 25OHD < 20 ng/mL, and vitamin D sufficiency as ≥30 ng/mL. Overweight was defined as body mass index (BMI) ≥85th percentile (n = 25), and normal weight as BMI between 5th and 84th percentile (n = 41). All participants received vitamin D_3 supplementation (2000 IU/d) for 8 weeks. The level of serum 25OHD, PTH, and biochemical parameters were measured before and after treatment.
Results: The mean age was 9.9 ± 1.4 years in normal weight children and 10.0 ± 2.1 years in overweight children (p=ns). Baseline serum 25OHD level was lower in normal weight children (13.2 ± 3.2 ng/mL) than in overweight children (14.2 ± 2.1 ng/mL, p=0.011). Baseline PTH level was 32.3 ± 9.5 and 39.5 ± 18.0 pg/mL in normal weight and overweight children, respectively (p=0.027). After 8 weeks of treatment, 28 (68.3%) normal weight children and 10 (40%) overweight children achieved vitamin D sufficiency (p=0.023). The mean serum 25OHD level was 33.7 and 28.6 ng/mL in normal weight and overweight children, respectively (p=0.496). The increase of 25OHD levels after treatment was significantly higher in normal weight children than in overweight children (20.6 ± 7.2 vs. 14.4 ± 7.9 ng/mL, p=0.002). However, the decrease in PTH levels seemed to be slightly larger in overweight children compared to normal weight children (-3.2 ± 20.8 vs. -1.1 ± 11.1 pg/mL, p=0.05). In multiple regression analysis, overweight was significantly related to the 25OHD increase after vitamin D replacement (β=0.323, p=0.01).

Conclusion: The response to vitamin D replacement can be influenced by adiposity, and overweight children require larger doses of vitamin D to achieve vitamin D sufficiency.

P77

Familial lipoprotein lipase deficiency – neonatal presentation

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P77

A baby girl, born by normal spontaneous vaginal delivery with birth weight 3.845kg, was admitted for neonatal jaundice on day 2 of life. Her mother had maternal gestational diabetes on diet control. Her father was newly diagnosed with hyperlipidaemia on health screen and was put on diet control. There was no consanguinity. Her serum bilirubin level on admission was 186mmol/L with normal liver function test. However, the serum was noted to be very lipaemic when checking with bedside bilirubin machine and it persisted for few blood samples. The baby girl was on exclusive breastfeeding. In view of lipaemic serum, random lipid profile was checked and showed hypertriglyceridemia (TG) 10.6mmol/L (<1.7mmol/L) and cholesterol (TC) 3.1mmol/L (<5.2mmol/L). Repeated fasting sample showed persistent elevated triglyceride level 8.5mmol/L. Other blood parameters including amylase and liver enzymes were unremarkable. Physical examination showed no dysmorphic features. There was no hepatosplenomegaly or xanthoma. Ophthalmologically examination did not show any lipaedmia retinalis.

In view of elevated serum triglyceride, further workup included lipoprotein electrophoresis and genetic analysis for lipoprotein lipase (LPL) gene were performed. Dietitian was consulted and the baby girl was given a therapeutic trial with commercially available special milk formula, Monogen (85% medium-chain triglyceride oil). The pretreatment lipid profile were TG 8.5mmol/L, TC 4.8mmol/L and HDL 0.6mmol/L (>1.3mmol/L) while TG 6.0mmol/L, TC 3.9mmol/L and HDL 0.6mmol/L after 2 weeks of special milk. She otherwise tolerated the special formula well.

Parents' fasting lipid profiles were also checked. Mother showed hypertriglyceridemia 3.0mmol/L, and father had elevated TG 3.57mmol/L, TC 7.14mmol/L and LDL 4.65mmol/L (<2.6mmol/L). Lipid electrophoresis of baby girl detected a chylomicron band and a dense VLDL band, which was occasionally found in lipoprotein lipase (LPL) deficiency. Genetic analysis of LPL exon 6 by direct sequencing showed a heterozygous LPL NM_000237.2:c.835C>G and heterozygous LPL NM_000237.2:.836T>G mutations. Parental screening showed father carried a heterozygous LPL NM_000237.2:c.835C>G mutation while mother carried heterozygous LPL NM_000237.2:c.836T>G mutation. The patient was confirmed to be compound heterozygous lipoprotein lipase deficiency.

On monthly follow-up evaluations 10 months after hospital admission, the patient remained asymptomatic, maintained adequate growth, and had triglyceride levels gradually on downward trend 4.7mmol/l.

Conclusion: This was a case of neonatal presentation of familial lipoprotein lipase deficiency, presenting with serum lipaemia.

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

P78

Insulin resistance and adverse lipid profile in obese pre-pubertal South Indian children

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P78

High prevalence of obesity, type 2 diabetes mellitus (T2DM) and the metabolic syndrome (MS) are evident among children and adults in India. [1,2] Strong evidence exists for the higher risk for insulin resistance (IR) syndrome in South Asians compared to other ethnicities, thereby demonstrating the higher risk for MS in this population. [3] MS is a risk factor for cardiovascular disease (CVD) and T2DM. [4,5] Adverse metabolic features such as dyslipidaemia are seen even in childhood and persist into adulthood with important long term implications. [6,7] Lipid profile data from pre-pubertal obese children from India is sparse and hence this has been addressed for the first time in this study, along with the relationship between lipid profile and IR in south Indian children.

Heights and weights of healthy pre-pubertal children aged 4-10 years of age were measured and body mass index (BMI) was calculated. Subjects were classified as overweight (BMI ≥85% to <95%) and obese (BMI ≥ 95%) for age and sex. Complete lipid profile as well as plasma glucose and insulin were measured in fasting venous blood samples. LDL/HDL (low & high density lipoprotein cholesterol), TC (total cholesterol)/HDL and IR by HOMA-IR (Homeostatic model assessment) were analysed.

Tests used for analysing differences between groups included: unpaired t-test for quantitative variables; comparison between groups by the non-parametric Mann-Whitney test; ANOVA for quantitative variables; Pearson coefficient of correlation for relationship between the variables and the chi square test for differences in categorical variables between groups. "P" value of <0.05 using a two-tailed test was considered significant. Data were analysed with the statistical software SPSS version 16.0.

Among the 100 participants, 98 were obese and two were overweight (M: F 51:49). Insulin resistance was observed to be higher with increased weight and BMI. A significant positive correlation was present between HOMA-IR and BMI (r = 0.291), triglycerides (r = 0.214) & TC/HDL (r = 0.229). A negative trend in correlation was found with HDL (r = -0.023).

Obese south Indian children were found to have IR and dyslipidaemia during their pre-pubertal years. Long term studies on this population and intervention measures are necessary to analyse and reduce the risk for the MS and CVD in later years.

References

1. Ramachandran A, Snehalatha C, Vinitha R, Thayyil M, Sathish Kumar C, Sheeba L, *et al*: **Prevalence of overweight in urban Indian adolescent school children.** *Diabetes research and clinical practice* 2002, **57(3)**:185-90.
2. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, Das A, *et al*: **High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey.** *Diabetologia* 2001, **44(9)**:1094-101.
3. McKeigue P, Shah B, Marmot M: **Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians.** *The Lancet* 1991, **337(8738)**:382-6.
4. Alberti KG, Zimmet P, Shaw J: **The metabolic syndrome–a new worldwide definition.** *Lancet* 2005, **366(9491)**:1059.
5. Ford ES: **Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome.** *Diabetes Care* 2005, **28(7)**:1769.
6. Nicklas T, Von Duvillard S, Berenson G: **Tracking of serum lipids and lipoproteins from childhood to dyslipidemia in adults: the Bogalusa Heart Study.** *International Journal of Sports Medicine* 2002, **23(S1)**:39-43.
7. Srinivasan SR, Frontini MG, Xu J, Berenson GS: **Utility of childhood non–high-density lipoprotein cholesterol levels in predicting adult dyslipidemia and other cardiovascular risks: The Bogalusa Heart Study.** *Pediatrics* 2006, **118(1)**:201-6.

OTHER/MISCELLANEOUS

P79

A case series of intracranial hypertension in patients with Turner syndrome, with and without growth hormone therapy

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P79

Intracranial Hypertension (IH) is a known side effect of GH therapy [1], but has many other aetiologies. Turner syndrome patients have growth failure related to loss of the SHOX transcription factor and so respond to high dose GH therapy. Turner patients also have a high incidence of middle ear disease that can cause intracranial hypertension via mastoiditis and

venous sinus thrombosis. IH has been reported in Turner syndrome with no predisposing cause.
Aim: To describe a case series of 4 patients with Turner syndrome who developed IH.
Methods: Turner syndrome patients were identified prospectively from the Paediatric Endocrine Database (PED) in a University teaching hospital. All patients had routine ophthalmological and ENT assessments prior to GH therapy. Ocular Coherence Tomography (OCT) scanning was done if papilloedema found. MRI and MRV scans were performed.
Results: 26 active patients with Turner Syndrome, age range 2 to 20 years, were identified and four noted to have co-existent IH. Case 1, age 15 years was referred by a neurologist with pre-existing IH and had never received GH therapy. No cause was found. Case 2, age 14 years was asymptomatic and papilloedema found on fundoscopy as part of pre-GH ophthalmology assessment. The patient had severe middle ear disease and had a mastoidectomy. CSF pressure > 35 mmHg. MRV showed abnormal venous drainage and GH therapy was not started. Both patients were treated with Diamox. Case 3, age 14 yrs and Case 4, age 10 yrs, commenced GH at 9.2 mg/m^2/week (having had normal fundi) and developed headaches and papilloedema, which resolved when GH treatment was ceased. Case 3; CSF pressure 20 mmHg and MRV abnormal sagittal sinus flow. In both patients, GH was successfully restarted at low dose with slow upward titration.
Conclusions: Intracranial hypertension may be seen in Turner syndrome independently from GH therapy. An ophthalmological consultation prior to starting GH therapy is important as some patients have asymptomatic papilloedema. Having significant middle ear disease may add to the risk.
Reference
1. Crock PA, *et al*: Benign intracranial hypertension and recombinant growth hormone therapy in Australia and New Zealand. *Acta Paediatr* 1998, **87(4)**:381-6.

P80

Endocrine complications in survivors of childhood medulloblastoma

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P80

Introduction: Medulloblastoma is the most common malignancy of the central nervous system in childhood. With the current combined treatment with surgery, chemotherapy and radiotherapy, the survival rates had improved dramatically in recent years. However, these survivors are prone to develop various late sequelae secondary to treatment.
Objective: The aim of this study is to assess the rate and the nature of endocrine complications among medulloblastoma survivors in a single center.
Patients and methods: A retrospective chart review of patients with medulloblastoma managed in the department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, Hong Kong, between January 1994 to June 2012 was performed. Patients who had follow-up of less than 2 years were excluded from the study.
Results: Thirty-four patients were included in the study. The median age at diagnosis was 7.5 years (range = 0.8 - 17.2 years) and the median follow-up time was 10.45 years (range = 2 – 18.3 years). Hypothyroidism was diagnosed in 16 patients (Primary hypothyroidism = 5 patients; compensated hypothyroidism = 10 patients; central hypothyroidism = 1 patients) and it was the commonest endocrine complication among this group of patients. The median time to develop hypothyroidism was 50 months (range = 15-155 months) from diagnosis. Male sex was the only risk factor that was found to be associated with the development of hypothyroidism (OR = 3.14; p = 0.031). Eight patients developed growth hormone deficiency and eight patients developed gonadal dysfunction. Age at diagnosis, dose and fractions of radiotherapy, chemotherapy regimen and duration of follow-up were all not associated with the development of these complications.
Conclusions: Hypothyroidism is a common late complication among medulloblastoma survivors. Patients could present with minimal symptoms but it could be easily screened and treated. Therefore, thyroid function test should be regularly monitored among this group of patients.

P81

Sirolimus therapy following subtotal pancreatectomy in neonatal hyperinsulinemic hypoglycaemia: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P81

Hyperinsulinemic hypoglycaemia (HH) occurs due to an unregulated insulin production from the pancreatic β-cells in the presence of low blood glucose. Mutations in ABCC8 and KCNJ11 are associated with severe HH that is unresponsive to conventional medical treatment. The only treatment for patients with medically unresponsive diffuse HH is a subtotal pancreatectomy. However, following surgery, hypoglycaemia may persist and some patients develop diabetes and malabsorption. Overexpression of the mTOR pathway is contributory to HH. Sirolimus, an mTOR inhibitor, is currently used in the treatment of congenital hemangiomas and in post renal transplant. Senniappan et al [1] recently reported efficacy of sirolimus in four surgically naïve patients with diffuse HH unresponsive to diazoxide and octreotide.
We present a patient who was treated with sirolimus due to persistent hypoglycaemia following subtotal pancreatectomy.
A term neonate with a birth weight of 4.67kg had persistent hypoglycaemia since birth secondary to hyperinsulinism and was unresponsive to treatment with maximal doses of diazoxide and octreotide with a glucose infusion requirement (GIR) of 38mg/kg/min. Genetic testing revealed a homozygous ABCC8 nonsense mutation, p. Gln1020Ter. A subtotal pancreatectomy was performed on day 40. Post-surgery, he had a GIR of 20mg/kg/min and was recommenced on daily subcutaneous (SC) octreotide, with monthly long acting (LA) octreotide. At 3 months, he was commenced on oral sirolimus. The dose was adjusted to maintain serum trough levels between 5 and 15ng/ml. Parenteral fluids and SC octreotide were weaned over a month. He was discharged home at 4.5 months on sirolimus (2.5mg/m^2/day) and LA octreotide. He was monitored with capillary blood glucose testing twice a day with the aim to maintain levels above 3.5mmol/L. Further surgery has been deferred. His growth and development are appropriate at 6 months of age with no side effects from sirolimus.
The clinical response in our patient supports sirolimus as a new therapeutic strategy in patients with HH which may facilitate deferment of surgery.
Written informed Consent for this patient has been taken including results of the genetic analyses and histopathological images according to the Institutional Ethics Committee procedures of our health service.
Reference
1. Senniappan S, *et al*: Sirolimus therapy in infants with severe hyperinsulinemic hypoglycemia. *NEJM* 2014, **370**:1131-7.

P82

A study of arterial stiffness in turner syndrome patients using cardio-ankle vascular index

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P82

A large proportion of the increased mortality in Turner syndrome (TS) is related to cardiovascular complications. Increased arterial stiffness may be an important predictor related to cardiovascular complications in TS patients. A novel method of evaluating arterial stiffness, which is

relatively independent of changes in blood pressure (BP), is the cardio-ankle vascular index (CAVI). The aim of this study was to compare arterial stiffness using CAVI between TS patients and healthy controls and to evaluate for possible factors affecting arterial stiffness within the patient group. Known TS patients (n=24) with confirmed karyotypes were recruited from the outpatient clinic of Seoul National University Children's Hospital between August, 2010 and June, 2013. Patients with type 2 diabetes and/or hypertension requiring medication were excluded. There were 5 patients with one or more combined congenital heart anomalies (aortic coarctation (n=2), bicuspid aortic valve (n=2), aortic stenosis (n=3). Anthropometric data, fasting blood lab and measurements of CAVI and pulse wave velocity were collected. A healthy control group (n=23) matched for age and body mass index (BMI) were recruited for comparison. The mean age and BMI of the TS patients were 27.0 years and 22.8 kg/m^2 respectively while that of the control were 28.2 years and 22.04 kg/m^2. CAVI was significantly higher in the TS patients compared to controls (6.05 vs. 6.65, $P < 0.001$), while there was no significant difference in pulse wave velocity. Univariate analysis for factors affecting CAVI within the TS patient group showed that CAVI was associated with waist circumference ($P = 0.04$) and systolic BP ($P = 0.045$). There were no significant factors related to CAVI using multivariate regression analysis including age, systolic BP, waist circumference, HOMA-IR and presence of cardiac anomalies. TS patients showed an increased arterial stiffness compared to age- and BMI-matched controls using CAVI measurement. Further prospective studies in larger TS patient group are mandatory in order to find significant factors related to increased arterial stiffness.

P83

The role of community development in improving awareness, diagnosis and management of childhood non-communicable diseases (NCDs) in Indonesia

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P83

Background: NCDs are now recognised as a major public health problem globally. In Indonesia, WHO estimates that 63% of all deaths are caused by NCDs. Lack of community awareness and health systems ill-equipped to deal with NCDs contribute to misdiagnosis, underdiagnosis, and increased preventable morbidity and mortality, particularly for children and adolescents.
Objective: To raise awareness and improve the diagnosis and management of childhood NCDs in Indonesia.
Method: Established NCD Family Communities: IKADAR (Type-1 Diabetes) in 2003, YTI (Turner's Syndrome) in 2003, KAHAKI (Congenital Adrenal Hyperplasia) in 2008 and FOSTEO (Osteogenesis Imperfecta/OI) in 2013. Community development approach, with focus on education, research (collation of data from IPS registries at Cipto Mangunkusumo Hospital), advocacy and health systems strengthening.
Results: Establishment of clubs and registers increased known prevalence across Indonesia: a 4.5 fold increase in CAH, from 65 patients (2008) to 293 (2014); 2 fold increase in OI, from 35 patients (2013) to 70 (2014); 5 fold increase in Diabetes, from 156 patients (2009) to 960 (2014). Access to medicines improved: donations of hydrocortisone (oral and injectable) and fludrocortisone co-ordinated by KAHAKI and CLAN, with efforts to register nationally; bisphosphonates included in national insurance scheme following launch of FOSTEO. Translation of educational resources and focused training for health professionals coincided with reduced presentations of children to hospital in adrenal crisis and diabetic ketoacidosis and reduced mortality from CAH and Diabetes. Media reports increased across all groups and information sharing amongst community members enhanced by WhatsApp.
Conclusions: The experiences of NCD Communities in Indonesia offer insights into practical steps that can be taken to redress the inequitable plight of young people living with NCDs in the Asia-Pacific region. A community development focus drives sustainable change,and helps increase awareness. Awareness makes a difference.

P84

Pseudohypoparathyroidism: phenotypic spectrum in kindred

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P84

Pseudohypoparathyroidism (PHP) encompasses a heterogeneous group of disorders due to an inactivating mutation in the GNAS gene which encodes the α subunit of G_s proteins (Gsα). Gsα plays a crucial role in intracellular signal transduction of peptides, hormones and neurotransmitter receptors in multiple tissues. Key features of PHP include Albright Hereditary Osteodystrophy (AHO) and biochemical evidence of multiple hormone resistances. There are several conflicting mechanisms for its heterogeneity; a possible explanation is a tissue-specific differential imprinting of Gsα protein. PHP type1a has AHO with multiple hormone resistance and is inherited as maternal imprinting defect. PHP type 1b presents with hormone resistance but no AHO features and is probably due to epigenetic methylation defects. Peudopseudohypoparathyroidism is another subtype with AHO but absence of hormone resistance and is inherited as paternal inactivating mutation. We describe a family with female members having PHP with variable clinical and biochemical features.
Two female siblings from non-consanguineous parents, patient A (15 year) & patient B (13 year) presented at birth with raised TSH levels and were diagnosed to have congenital hypothyroidism and treated with thyroxine replacement. Patient A was noted to have infantile obesity with short stature and evolving phenotypic features consistent with AHO. Further history revealed that her sister patient B has similar phenotypic appearance and was confirmed on clinical exam. Biochemical evaluation for Patient A showed a borderline low calcium and normal phosphate level with elevated PTH while Patient B had normal calcium and phosphate levels with high PTH. Both patients entered puberty at 11 years and patient A progressed to breast tanner 4 but has no menarche at 15 years despite pubertal gonadotropin levels (Table 1), advanced bone age (18 years) & mature uterus. Patient B is currently 12.5 years old and has progressed to tanner 3 breasts with no menarche. Mother exhibits features of AHO without hormone resistance. The father and younger brother do not have any features of AHO.
The two patients with PHP described above had an interesting presentation as congenital hypothyroidism with features of AHO evolving later in life. They exhibit clinical evidence of maternal transmission with end-organ resistance. This family illustrates heterogeneity of presentation of GNAS mutation.
Written informed consent was obtained from the patients for publication of this abstract. A copy of the written consent is available for review by the Editor of this journal.

P85

A multicenter study of endocrine abnormalities in septo-optic dysplasia (SOD) in Asean countries

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P85

Background: Septo-optic dysplasia (SOD) is a heterogeneous malformation condition consisting of optic nerve hypoplasia, various types of forebrain defects and hormonal deficiencies. This study aims to expand knowledge about endocrine abnormalities in patients with SOD in ASEAN countries.
Material and method: Forty-eight patients (27 male, 21 female) who has been diagnosed as having SOD in ASEAN countries were clinically reviewed from medical records.
Results: Clinical manifestations and endocrine abnormalities of the patients are shown in Table 1.

Table 1(abstract P84)

	Patient A	Patient B	Mother
AHO Features			
Brachydactyly	+	+	+
Short stature	+ (136cm, - 4.05 SDS)	+ (134cm, -2.84 SDS)	+ (145cm, -2.79 SDS)
Obesity	+ (32.44 kg/m^2,+2.04 SDS)	-	-
Round face	+	+	-
Ectopic ossification	-	-	-
Cognitive dysfunction with need for special school	+	+	+
PTH (0.9 -6.2pmol/L)	26.4	27.2	8.1
Calcium (2.3-2.63mmol/L)	2.19	2.35	2.31
Phosphate (1.0-1.8 mmol/L)	1.4	1.7	1.2
FT4 (10.3-25.7pmol/L)	12.4	15.4	13.6
TSH (0.50-4.50 mIU/L)	8.05	8.36	3.42
FSH IU/L	7.7	9.5	
LH IU/L	8.92	5.01	
Estradiol pmol/L	87	169	

Table 1(abstract P85) Clinical manifestation of SOD patients

Clinical manifestation			Clinical manifestation		
Age at presentation (months) mean ± SD		33 ± 39 months (range 20 - 178)	MRI findings	Absence of septum pellucidum(%)	62
Ht SDS, mean ± SD		-0.97 ± 1.97		Pituitary hypoplasia (%)	33
Wt SDS, mean ± SD		0.02 ± 2.35		Abnormal of corpus callosum (%)	16
Eye presentation	Nystagmus (%)	54		Cortical dysplasia (%)	8
	Squint (%)	3	Endocrine abnormalities	Hypothyroid (%)	35
	Poor vision (%)	35		GH insufficiency (%)	29
Delayed development (%)		16.2		Delayed/arrested puberty/suspected HG (%)	23
Seizure (%)		7.9		Cortical insufficiency (%)	17
Hypoglycemia (%)		8.1		Diabetes insipidus (%)	19
Neonatal jaundice (%)		2.7	Eye examination	Unilat ON hypoplasia	13
Undescended testes (%) (boys)		5.4		Bilat ON hypoplasia	84
Micropenis (%) (boys)		21		Microcornea	3

HG = Hypogonadism, ON = Optic nerve

Conclusion: This multicenter and multinational study shows that about 20-35 % of SOD patients have endocrine abnormalities. Hypothyroidism and GH insufficiency are the most common endocrine problems associated with this condition.

P86

Diazoxide-unresponsive congenital hyperinsulinism associated with ABCC8 nonsense mutation

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P86

Background: Congenital hyperinsulinism is a dysregulated insulin secretion that results in persistent hypoglycemia. It is a heterogenous condition but common to all is the inappropriately high insulin during hypoglycemia with absence ketone bodies and reduced free fatty acids.
Case presentation: A baby boy with birth weight of 2.4kg at 35 weeks was born via Caesarian section. The boy was allowed feeding on demands, however he had the first onset of hypoglycemia at 2 hours of life. His blood sugar ranged from low reading to 2.5 mmol/L. The patient was treated with boluses of intravenous dextrose D10% followed by maintenance dextrose with its increasing strength in order to treat the refractory hypoglycemia. In addition to that intravenous hydrocortisone and glucagon infusion were started. The patient's blood sugar could only be maintained > 3.0mmol/L after a glucose load of 30mg/kg/min and a glucagon infusion of 50mcg/kg/hour. During hypoglycemia, the insulin level was 19.6 pmol/L (17.8-173.0) and blood ketone was negative. Oral diazoxide was started at 5.0mg/kg/day in divided doses combined with chlorothiazide 7.0 mg/kg/day. Diazoxide was titrated up to 20.0mg/kg/day as he had a poor response even after 1 week of the treatment. Apart from that oral nifidipine 2.5 mg/kg/day in divided doses was also started after a few days with the combination therapy. Only after starting

octreotide infusion a good rise of blood sugar was seen within 1 hour and the glucose load could be brought down and the other drugs were off. The boy was discharged with subcutaneous octreotide infusion at 2mcg/hour via portable insulin pump.
Results: The boy is heterozygous for an ABCC8 nonsense mutation, p. R934*. A second ABCC8 mutation has not been found and sequencing of the KCNJ11 gene failed to detect a change from the normal sequence. He has inherited the mutation from his father; a focal lesion is therefore possible. 18F-DOPA PET-CT scanning is recommended and if a focal lesion is identified and surgically resected, microsatellite analysis of the DNA can be undertaken to confirm loss of heterozygosity.
Conclusion: KATP mutation is the commonest cause for diazoxide resistant congenital hyperinsulinism.
Continuous subcutaneous octreotide infusion is a feasible alternative to pancreatic surgery.
Written informed consent was obtained from the patient's parent or guardian for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P87

A custom next generation sequencing panel to identify the cause of monogenic disorders of insulin secretion, disorders of sexual development and noonan syndrome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P87

Next generation sequencing (NGS), using massive parallel sequencing, is increasingly being used in the clinical setting. It is a high throughput technique that offers a fast and cost-effective testing solution for genetic disorders with a number of candidate genes.
In this study we have employed NGS to sequence 48 samples that had been referred to the Molecular Genetics Department for the investigation of Monogenic Disorders of Insulin Secretion (MDOIS), Disorders of Sexual Development (DSD) and Noonan Syndrome (NS). All samples had previously been genotyped using Sanger sequencing.
Next Generation Sequencing was performed on an Illumina MiSeq using an Illumina Nextera Rapid Capture Custom Enrichment Kit. This custom assay contained capture probes for the coding regions (including +/- 5 bases of intronic sequence) for 66 genes: 34 for DSD; 19 for MDOIS; and 13 for NS. Sequence data generated by the MiSeq was aligned to hg19 and variants detected using CLC Genomics Workbench. Genetic variants were annotated using Cartagenia BENCHlab NGS.
Thirty mutations associated with DSD (SRD5A2, HSD17B3, NR5A1, AR), MDOIS (ABCC8, GCK, GLUD1, INS, HNF1A, HNF4A, HNF1B) and NS (PTPN11, RAF1) were detected. This was concordant with genotypes detected by Sanger sequencing.
Next generation sequencing has proven to be an accurate and efficient method of genotyping monogenic disorders with multiple candidate genes, and is an ideal technique for the clinical laboratory.

P88

Severe neonatal hyperparathyroidism: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P88

Aims: To report case presenting with neonatal severe hyperparathyroidism.
Methods: A severe neonatal hyperparathyroidism was reviewed including demographic and clinical data.
Results: A 6-day-old girl was referred from province hospital due to lethargy, poor feeding and irritability. On examination, there were no dysmorphic features and apart from mild tachypnea, systematic examinations were normal. Her chest X-ray was also normal. Calcium and parathyroid hormone (PTH) levels at presentation were 17.3 mg/dL and 1,776 pg/mL, respectively. Firstly, she was managed with cefotaxime for treatment of sepsis. She received intravenous hydration, diuresis, hydrocortisone but calcium and PTH levels were persistent high. Furthermore, pamidronate was introduced and calcium level was decreased to normal range. Unfortunately, 7-10 days after stop pamidronate, calcium and PTH levels were gradually increased. A sestamibi nuclear scan was performed and showed hyperfunction parathyroid nodule at upper portion of both thyroid lobes. At age of 60 days, this girl went to have operation with a total parathyroidectomy and autotransplantation, using one half of gland placed into the right groin. Serum calcium and PTH were return to normal after operation.
Conclusions: Neonatal severe hyperparathyroidism is managed effectively with total parathyroidectomy and autotransplantation.
Written informed consent was obtained from the patient's parent or guardian for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

PUBERTY

P89

Treatment of central precocious puberty using low dose GnRH analogs (GnRHa)

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P89

Aims: 1. To study the efficacy of lower dose GnRHa in pubertal suppression and bone age advancement.
2. To study if low dose of GnRHa avoided the need for concomitant use of GH therapy while causing adequate pubertal suppression.
Methods: Clinical Records of 17 children (16 girls and 1 boy) were retrospectively analyzed over a period of 24 months (Mar 2012 to Mar 2014). All children satisfied the criteria for precocity based on clinical features, radiological assessment and GnRHa stimulation test. All 16 girls had idiopathic precocious puberty and the only boy had hypothalamic hamartoma.
The mean age of presentation was 6. 9 years.
All children received GnRHa as monthly injection in an average dose of 190 µgm /kg/month and were regularly followed for evaluation of pubertal suppression, height gain and Bone age advancement.
Results: Over a 24 month study period, children showed good pubertal suppression with a comparatively low dose of GnRHa (190 µgm/kg/month). Mean LH post stimulation while on therapy was 2.31 miu/ml suggesting adequate suppression, average annual growth velocity was 5.1 cm. Advancement in bone age was 1.4 years over a period of 2 years.
Conclusion: 1. Children with CPP could be managed with a lower dose of GnRHa to achieve adequate pubertal suppression (190 µgm/kg/month as opposed to the standard recommended dose of 300 - 750 µgm/kg/month).
2. While adequately suppressing puberty and controlling bone age advancement, lower dose of GnRHa seems to allow normal height gain thus negating the need for concomitant GH therapy in an economically challenging situation.

P90

Outcome of girls with central precocious puberty (CPP)

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P90

Due to non-affordability of GnRH analogues (GnRHa), Medroxy Progesterone Acetate (MPA) is still used as a treatment option in girls with CPP in India. The aim here is to study the clinical features of girls with CPP in respect to the age at presentation, etiology and outcome as per the medication used for their treatment (GnRHa vs MPA).
Retrospective study of 38 girls with CPP(19 idiopathic) treated with either MPA or GnRHa (Luprorelin or Triptorelin) were followed up for period

varying from 1 to 8 years. The progression of growth parameters in relation to their age, etiology and medication used for the treatment was studied. Statistical analysis was done using one way ANOVA, unpaired t-test and Pearson correlation tests.
Mean age at onset of puberty in girls with idiopathic ICPP(n=19), neurogenic NCPP(n=12) and hypothalamic hamartoma(HH)(n=7) were 4.68 ±2.83, 5.32±2.20 and 1.76±1.44 years, respectively(P 0.003). Mean height sds at presentation of all girls was higher (0.51±1.80) with comparison to MPH sds (0.90±1.19)(P=0.0021). 70% of the girls presented with SMR stage 3. Bone age was more advanced as compared to height age in all (P=0.0001) and this trend continued till last follow up. At presentation, girls with ICPP were significantly heavier and taller as compared to NCPP and HH (P=0.002 for weight SDS and 0.022 for height SDS). Mean baseline LH, FSH and estradiol were 3.05±2.49 mIU/ml, 4.75±2.29 mIU/ml and 29.43 pg/ml; respectively. At presentation, bone age was more advanced in HH(BA/CA P=0.0001 with BA/HA P=0.03) and LH levels significantly higher(5.6 ±2.26; P=0.02). At last follow up, there was no significant difference in weight sds(p=0.285), height sds(p=0.074) and PAH sds(p=0.056) in girls of different age groups and etiologies. After 4 years of follow up, height sds was better with GnRHa(1.80±0.98) as compared to MPA(P=0.01) but height sds with MPA was also good(0.49±0.81).
Due to prevalence of CNS infections, the proportion of NCPP(31.57%) is higher in our set up, as compared to industrialized countries. With financial constraints, MPA can be considered as a treatment option for CPP.

P91

Test on kisspeptin levels in girls with idiopathic central precocious puberty and its significance

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P91

Aims: This paper is aimed to explore the significance of plasma kisspeptin level in diagnosis and therapeutic evaluation through the detection of kisspeption level of girls diagnosed with idiopathic central precocious puberty (ICPP) before treatment and after 6-months of treatment and girls with simple premature thelarche (PT).
Methods: A total of 70 girls including 24 girls diagnosed with ICPP, 21 girls with PT and 25 normal girls were enrolled. ELISA was adopted to detect plasma kisspeptin level.
Results: The kisspeptin level of ICPP group before treatment (1.80 ±0.13ng/ml)was higher than those of other groups with significantly statistic difference. The kisspeptin level of ICPP group after 6-months of treatment (1.49±0.21ng/ml) was significantly lower than those before treatment (P<0.05).
Conclusions: We can conclude that plasma kisspeptin level is related with initiation of pubertal development, and it can be served as important parameter in ICPP diagnosis and therapeutic effect evaluation.

P92

Effect of triptorelin 3.75 mg subcutaneously injection every 6 weeks on adult height in girls with idiopathic central precocious puberty

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P92

Aims: To evaluate the long-term efficacy of triptorelin 3.75 mg subcutaneously injection every 6 weeks on final height in girls with idiopathic central precocious puberty.
Methods: Forty females with ICPP received triptorelin 3.75 mg every 6 weeks subcutaneously injection in our hospital from 2002 to December 2010 and reached final height were collected. These patients were divided into two groups according to whether there was presence of growth deceleration and rhGH used concomitantly during the treatment. Group A: triptorelin alone, n=17; group B: triptorelin + rhGH, n=23. During the treatment, height, weight, annual GV, sexual development, PAH and adverse effects were observed. BA and height SDS were monitored yearly. After discontinuation of treatment, follow-up was continued for 4~9 years till final height was attained, and age of menarche, time of menarche from discontinuation were recorded.
Results: FAHs were 159.81±4.95 cm and 161.01±4.89 cm respectively in the two groups, exceed the genetic target height (THt), about the 50th percentile of normal female height. FAH increased by 1.51±4.30 cm, 4.86 ±4.49 cm from THt respectively. The values of (FAH-THt) showed significant difference between the two groups (p<0.05). FAH was less than the predicted adult height (PAH) before and after treatment in group A, and greater than that of group B. The value of (FAH-PAH post-treatment) showed significant difference between the two groups (p<0.05). FAH was positively correlated with Ht SDS-BA at the end of treatment, THt, course of rhGH treatment and age of menarche (r2=0.66). BMI increased after treatment compared with that before treatment in both groups, however, compared with healthy children at the same age, there was no significant tendency of increase. Ages of menarche were 11.74±0.66 years and 12.18 ±0.69 years respectively. Times of menarche from discontinuation were 17.41±6.96 months and 14.71±4.77 months respectively.
Conclusion: The final adult height in patients with ICPP was improved effectively by triptorelin 3.75 mg subcutaneously injection every 6 weeks, and more height gain will be achieved when rhGH was used concomitantly to refrain from growth deceleration during the treatment. BMI maintained steadily and ovarian function restored quickly after discontinuation of the treatment with the age of menarche similar to that of normal children. Neither significant adverse effect nor polycystic ovary syndrome was observed.

P93

Mixed embryonal carcinoma – teratoma cause early puberty: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P93

Introduction: Mixed embryonal carcinoma – teratoma is defined a rare kind of germ cell tumor, especially in children. Objective: a rare case report with early puberty due to mixed embryonal carcinoma – teratoma.
Subject: A 3 year 7 month old boy presented with early puberty and adrenal tumor in National Hospital of Pediatrics.
Method: A case report.
Results: A 3 year 7 month old boy presented with enlargement of penis, acnes, pubic hair, deep voice. He admitted with his height of +2.3SDS, penis length of 6cm, testes volumn of 4ml, pubic hair P2 (tanner). Abdoment ultrasound and CT scan showed adrenal tumor. Serum laboratory showed: 17 OHP 3,8 ng/ml, testosteron 32,3 nmol/l, cortisol 8h 433,9 nmol/l, cortisol 22h 39,2 nmol/l, glucose 3,7 mmol/l, αFP 3945,9 u/l, electrolyte normal; urine VMA 15,5 µmol/24h; bone age 5 years. Surgical showed the tumor did not originate from the adrenal. Histologica showed mixed embryonal carcinoma – teratoma. After surgeon, the signs of virilization reduce, serum testosteron become normal.
Conclusion: Mixed embryonal carcinoma – teratoma can be caused testosterone excretion and early puberty.
Written informed consent was obtained from the patient's parent or guardian for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

P94

Risk factors for idiopathic central precocious puberty of girls in Fujian province

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P94

Objective: This study aimed to investigate the potential risk factors of idiopathic central precocious puberty (ICPP) girls in Fujian province.
Methods: A case-control study was conducted in 566 girls who were diagnosed with ICPP at endocrinology department and 547 healthy girls for routine physical examination in Fuzhou Children's Hospital of Fujian from October 2011 to October 2013. Parents were asked to fulfill the questionnaires on children's diets, behaviors, parents and family conditions, and Logistic regression analysis was conducted for risk factors.
Results: Chi-square test showed that 23 variables had significant statistically difference. Logistic regression analysis indicated that some variables were entered the final model: mother's age at menarche were older than 13 years (OR=0.278, 95%CI: 0.201,0.384), intaking organic fruits (OR=0.316, 95%CI: 0.157,0.634), daily exercise time(OR=0.609, 95%CI: 0.490,0.758), intaking ordinary vegetables (OR=1.275, 95%CI: 1.095,1.485), intaking general livestock (OR=1.364, 95%CI: 1.199,1.551), BMI(OR=1.599, 95%CI: 1.365,1.874), income of parents (OR=1.671, 95%CI: 1.317,2.120), heavy study burden (OR=1.818, 95%CI: 1.121,2.948), intaking instant food (OR=2.990, 95%CI: 1.241,7.203), intaking nourishment (OR=3.736, 95%CI: 2.063,6.765), using adult cosmetics (OR=5.284, 95%CI: 3.240,8.618). Among the variables, mother's age at menarche were older than 13 years, intaking organic fruit and doing more exercise for a long time were demonstrated to be the protective factors for ICPP, and others were risk factors.
Conclusion: There were many factors related to ICPP girls in Fujian province, such as mother's age at menarche, diet and behaviors, BMI, parental income, and heavy study burden.

P95

Final height after gonadotropin-releasing hormone agonists with or without growth hormone in Korean girls with central precocious puberty and early puberty

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P95

Aims: We investigated the final height (FH) in GnRHa treatment with or without GH in Korean girls with CPP or EP.
Methods: The forty-one patients were divided retrospectively into three groups: group 1 subjects with CPP (n=20) received GnRHa. Group 2 with early puberty (n=12) received only GnRHa. Group 3 with early puberty (n=9) received combined treatment with GH and GnRHa.
Results: The mean age at the start of treatment was 8.11 ± 0.70 years in group 1, 8.98 ± 0.38 years in group 2 and 9.46 ± 0.46 years in group 3, respectively. The mean predicted adult height (PAH) SDS at the start of treatment was -1.29 ± 1.16 in group 1, -1.14 ± 0.88 in group 2 and -1.87 ± 1.09 in group 3, respectively. Rate of growth during treatment with GnRHa combined with GH was higher significantly in group 3 (6.89 ± 1.45 cm) than in group 1 (5.27 ± 0.89 cm, p = 0.001) and in group 2 (5.64 ± 0.72 cm, p = 0.022). The mean FH SDS was -0.60 ± 0.88 in group 1, -0.40 ± 1.03 in group 2 and -0.92 ± 0.72, respectively and significantly higher than initial height prediction. For the girls received GnRHa alone, FH SDS was correlated significantly with TH SDS, PAH at the start of treatment, PAH at the discontinuation of treatment.
Conclusion: After GnRHa treatment in girls with CPP or EP, FH is significantly higher than initial height prediction. GnRHa treatment combined with GH resulted in higher growth rate.

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Bedding types affect pubertal progression in rat

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P96

Aims: Recently, many experimental animal studies have demonstrated several adverse effects of endocrine disrupting agent, such as reduced reproductive behavior, altered estrous cycle, and decreased slow-wave sleep.
The purpose of this study was to compare the pubertal progression in wild type female rats according to different bedding types.
Method: Twenty female Sprague Dawley rat (SD rat) were randomly divided into two groups according to their bedding types. The 1st group was raised in wood shaving bedding as a control and 2nd one was in corncob bedding as an endocrine disrupting agent.
Each group was checked daily for the first day of vaginal opening, and their vaginal smears were collected to determine estrous cyclicity after vaginal opening. The interval between vaginal opening and the first normal estrous cycle was recorded for determining sexual maturation.
The phases of normal estrous cycles were as follows, proestrus, estrus, metestrus and diestrus.
We compared the proportion of normal estrous cycles in each group.
Result: Vaginal opening was shown early in corncob bedding, but there was no significant difference in the day of the first estrous cycle between 2 groups. Therefore, the periods between vaginal opening and the first estrous cycle were prolonged in that.
The proportion of normal estrous cycles was 80% in 1st and 60% in 2nd group.
In corncob bedding, the number of proestrus and estrus phases was significantly decreased and that of diestrus phases was increased.
Conclusion: The onset of vaginal opening was earlier, and the irregularity of estrous cycles was increased in corncob bedding groups.
Endocrine disrupting agents in corncob bedding were considered to be associated with early vaginal opening and the irregularity of estrous cycles.
Therefore, the bedding type can be an affecting factor in pubertal progression in rodents.

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The characteristics of familial precocious puberty

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P97

Aims: Precocious puberty is defined as the precocious onset of pubertal manifestations. The cause of precocious puberty is unknown despite numerous attempts to find it. Despite most precocious puberty is sporadic disease, some patients have familial tendency. Recently specific gene mutation has proven to cause precocious puberty and the existence of familial precocious puberty is emerging. This study was performed to compare the characteristics of familial precocious puberty and sporadic precocious puberty.
Methods: We studied 32 girls diagnosed with central precocious puberty (CPP) at Ajou University Hospital from 1st Jan 2007 to 31th May 2014. 16 girls have sisters diagnosed with CPP and the other 16 children have no family history of CPP. We divided these subjects to two groups, familial CPP and sporadic CPP. All subjects had been treated with GnRH agonist. We reviewed their auxological data, Tanner stage, laboratory findings, and bone age retrospectively.
Results: The onset of precocious puberty was not available. Baseline characteristics including mid parental height (MPH), bone age, height SD, the bone age advancement, body mass index, Tanner stage and LH peak on GnRH stimulation test revealed no significant difference between familial CPP and sporadic CPP. Age at diagnosis (yr) was 8.54 ± 0.48 and 8.11 ± 0.68 respectively (p = 0.049). The GnRH agonist treatment period (yr) was 3.26± 0.39 and 2.96 ± 0.79 respectively (p > 0.05). The growth velocity (cm / yr) during the treatment was 5.36 ± 0.55 and 5.34 ± 0.85 respectively (p > 0.05). After the GnRH agonist treatment was finished, the increment of PAH (cm) was 12.14 ± 4.42 and 10.83 ± 4.98 respectively (p > 0.05).The difference between PAH and MPH was 6.52 ± 4.92(cm) (p < 0.01) in familial CPP and 1.13 ± 4.18 in sporadic CPP (p > 0.05).
Conclusion: The clinical manifestation of familial precocious puberty is similar with sporadic precocious puberty. GnRH agonist treatment increases the predicted adult height above the mid parental height in familial precocious puberty.

THYROID

P98

A case of 3 months old Japanese boy with sporadic congenital none-autoimmune hyperthyroidism

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Sporadic congenital none-autoimmune hyperthyroidism is rare disease. It causes the gain of function with TSH receptor gene mutation. We report 3 months old Japanese boy with sporadic congenital none-autoimmune hyperthyroidism. Our case was born in the 34th week of gestation with a birth weight 1830g, his length 42.0cm, his head circumference 29.5 cm as low birth weight baby between non consanguineous parents. Oligohydramnios was pointed out his perinatal period. There was no history of thyroid disease in other family members. He showed failure to thrive after the age of one month in spite of increasing nutrition. At the age of 3 months, His weight was 3.5kg, his length 54.6cm. He presented with tachycardia (170~180/min), severe sweating, mild exophthalmos and no goiter. We examined carefully and found he was suffered from hyperthyroidism. The thyroid function showed TSH<0.005 μIU/ml, fT3 20.55 pg/ml, fT4 7.43 ng/dl, Tg603 ng/ml with tests for anti-thyroid antibodies negative. His thyroid ultrasonography showed enlarged as his age, 99mTcO4- scintiscan of thyroid gland showed a homogeneous uptake. His bone age was advanced to 2 years old. Brain MRI showed normal image for his age. His mother had no goiter and had not showed symptoms of hyperthyroidism. Tests for anti-thyroid antibodies were negative with her. We detected TSH receptor gene mutation with our case. The mutation is heterozygous and shows c842G>A,p.Ser281Asn that had been reported before. The boy was treated with amount of 0.8 mg/kg/day of methimazole, his irritability disappears and his heart rate is down. Now his weight gains slowly and his development is appropriate for his age. We conclude that careful examination and follow up need for his development and growth because the severity of sporadic congenital none-autoimmune hyperthyroidism is variety and most reported case were recurrent.

Written informed consent was obtained from the patient's parent or guardian for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P99

Permanent and transient congenital hypothyroidism in Korea: analysis of patients in a single center

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P99

Background: Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation. Neonatal screening programs allow for the early detection and treatment of CH. Transient CH reverts later to normal, which may or may not require replacement therapy. The aim of this study was to determine the prevalence and manifestations of permanent and transient CH in Korea.
Methods: We retrospectively reviewed 610 patients who were diagnosed with CH from January 2001 to January 2011 in Soonchunhyang University Hospital. They all underwent clinical re-evaluation after the age of 2-3, based on the thyroid function testing after levothyroxine therapy withdrawl.
Results: Of the 610 patients diagnosed primarily with CH; 554 (89.1%) patients were diagnosed to have permanent CH, and 66 (10.8%) patients were diagnosed to have transient CH. The median TSH levels before treatment were significantly higher in patients with permanent CH than transient CH (median 58.1:24.1 μIU/mL). Male to female ratio was 1:1.2 (35:31) in transient CH. Of the 66 children diagnosed with transient CH, children discontinued levothyroxine replacement therapy at the age of 25.1±13.2 months. These patients received relatively low dose hormone replacement (initial and at the time of trial of discontinuation).
Conclusion: We concluded that the incidence of CH as well as the transient form similar to the worldwide reported ones.

P100

Pediatric thyroid cancer presenting aggressive pathologic characteristics shows persistently high rates of recurrence during the past 35 years in Korea

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P100

Objective: Clinicopathological characteristics at diagnosis and long-term outcomes of pediatric thyroid cancer were analyzed. Predictors for poor outcome or recurrence were investigated among pediatric papillary thyroid cancer (PTC) patients. Whether young age at diagnosis (<20 years) was independently predictive for recurrence was investigated among PTC patients of all ages.
Methods: We evaluated 153 patients (28males) diagnosed younger than 20 years old, managed during 1980 through 2013 (median 7.0 years of duration). Good or poor outcome (persistence or recurrence) was analyzed in 126 patients followed for at least 12 months. Predictors for recurrence were analyzed among 108 pediatric PTC patients. Adult PTC patients (n = 3093) were finally included in Cox proportional hazards models to find predictors for recur-free survival among PTC patients of all ages.
Results: At the time of diagnosis [papillary (86.9%), follicular (7.9%), medullary (3.9%) and poorly differentiated (1.3%)], 38.6% of multiplicity, 57.8% of extrathyroidal extension, and 66.7% of lymph node (LN) and 13.9% of lung metastasis were found. The proportions of PTC, multiplicity, extrathyroidal extension, LN metastasis (all for P< 0.05), and distant metastasis (P< 0.001) were significantly higher in younger patients at diagnosis. Forty-four of 126 patients (34.9%) showed poor outcome. Recurrence rates at 5 and 10 years were 13.9% and 33.8% respectively. In an analysis of 108 pediatric PTC patients, the poor outcome group showed larger tumors (2.7cm vs. 2.0cm), higher rates of multiplicity (66.7% vs. 30.6%) and distant metastasis (27.0% vs. 7.7%) than the good outcome group (all P< 0.01). After adjusting for sex, age at diagnosis, primary tumor size and LN metastasis, both multiplicity and primary tumor ≥4cm (all P< 0.01) were independent predictors for recurrence among pediatric PTC patients. Male sex, multiplicity, LN metastasis (all P< 0.001), primary tumor ≥4cm (vs. 1.0-1.9cm), and extrathyroidal extension (P< 0.01 for both) rather than age at diagnosis (<20, 20-39, 40-59, ≥60 years) were independent predictors for a poor recur-free survival among PTC patients of all ages.
Conclusions: Pediatric thyroid cancer presented aggressive pathologic characteristics and showed persistently high rates of recurrence during the past 35 years in Korea. The younger onset, the more aggressive was the pathologic presentation. Among pediatric PTC patients, large tumors (≥4cm) and multiplicity were predictive for recurrence. Among PTC patients of all ages, aggressive pathologic presentations at a young age rather than young age itself were decisive factors for recurrence.

P101

Prevalence of thyroid disorders among children with Down syndrome seen in the out-patient clinics of the Philippine general hospital

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P101

Background: Thyroid disorders are noted to occur in 28–40% of children with Down syndrome [1]. Hypothyroidism has a subtle presentation and can be particularly challenging to detect in patients with intellectual disabilities and communication and language impairments [2]. Regular

screening and early diagnosis of thyroid disorders, particularly hypothyroidism, is essential for early intervention.
Objective: To determine the prevalence of thyroid disorders among children with Down Syndrome (DS) seen in the outpatient clinics of the Philippine General Hospital from January 2007 to December 2011.
Secondary objectives: To classify the thyroid disorders present; to describe the clinical profiles and genotype of the children with Down syndrome.
Methodology: A Retrospective chart review of all patients with Down syndrome seen in the Out-patient Clinics of the Philippine General Hospital from January 2007 to December 2011.
Results: Eighty-nine patients were included, 60% males and 40% females .Fifty-six percent had thyroid disorders. Of these, eighty percent had subclinical hypothyroidism, 12% had overt hypothyroidism, while 8% had hyperthyroidism. The mean age for the diagnosis of thyroid disorder was 3.33 (±0.52) years old. The mean age on initial consult was 2.38 (±3.14) years. The mean age of mothers at childbirth was 34.23 (±6.77) years. The most common co-morbid illness was congenital heart disease (46%, 41/89). The most common chromosomal abnormality was full trisomy 21 (95.51%, 85/89).
Conclusion: Fifty-six percent of children with Down syndrome in this study have thyroid disorders, with subclinical hypothyroidism being the most common. This study provides evidence for the need of regular monitoring of thyroid function test among children with DS.
References

1. Weijerman M, de Winter J P: **Clinical practice. The care of children with Down syndrome.** *Eur J Pediatr* 2010, **169**:1445-1452.
2. Carroll K, *et al*: **Increase in Incidence of Medically Treated Thyroid Disease in Children With Down Syndrome After Rerelease of American Academy of Pediatrics Health Supervision Guidelines.** *PEDIATRICS* 2008, **122(2)**: e493-e498.

P102

Graves' disease in children less than 8 years of age: review of clinical features and treatment outcome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P102

Background: Graves' disease is the most common cause of thyrotoxicosis in children. Prepubertal children are the most difficult to treat with remission attained in less than 15% [1,2].
Objective: To characterise clinical features and review treatment outcome among children with very early onset Graves'.
Methodology: Retrospective medical record review of patients diagnosed with Graves' disease at age less than 8 years, who received treatment in our department in the last 14 years.
Results: Sixteen patients (2 males) were identified with median age at diagnosis of 4.96 years (range 2.5-7.83). Presenting symptoms were hyperactivity, weight loss, poor sleep and diarrhoea. They had predominant non-Anglo-Saxon ethnicity. Significant co-morbidities were-Down syndrome [1], juvenile idiopathic arthritis [1], situs inversus with extrahepatic biliary atresia ie EHBA [1].Two had family history of Graves' disease. All had goitre, increased serum Free T4 (median 53.65 pmol/l, range 35-94), increased serum Free T3 (median 33.5 pmol/l, range 19.3-46) and suppressed TSH levels. All were positive for TSII (thyroid stimulating immunoglobulin) or TRAb (thyrotropin receptor antibody). Anti thyroid peroxidise was positive in 83.3% (10/12) and anti thyroglobulin in 80% (8/10). Anti-thyroid drugs (ATD) alone were used in 9 patients, 4 received one dose each of radio-active iodine ablation (10-15 mCi) and 3 underwent thyroidectomy. Our cohort tolerated the ATD's well- Only 1 had significant liver enzyme elevation (underlying EHBA) after Neomercazole, minor side-effects were: skin rash (3) and arthralgia [1]. Data from patients with more than 30 months follow-up was used to assess outcome. Twelve children with median follow up of 66 months (range: 34-161) and median age of 10.13 years (range: 7.17-16) at last clinic visit qualified. Remission was attained in 58.3% (7/12) - 3 were post thyroidectomy, 1 post radio-active iodine ablation and 3 received only ATD's. Growth monitoring showed decline in median weight sds from 0.41 at diagnosis to 0.29 at follow up and height sds from 1.35 to 0.69. Of the sixteen patients 2 girls were followed through their puberty till 16 years of age and both are in remission (1 underwent thyroidectomy and other received Neomercazole).
Conclusion: Our cohort had 16 patients diagnosed with Graves' at a median age of 4.96 years. Overall remission for those with more than 30 months follow-up is 58.3% (7/12), at a median age of 10.13 years. Thyroidectomy had a remission rate of 100%, ATD's alone of 33.3% and one dose of radioactive iodine ablation of 25%.
References

1. Shulman DI, Muhar I, Jorgensen EV, Diamond FB, Bercu BB, Root AW: **Autoimmune hyperthyroidism in prepubertal children and adolescents: comparison of clinical and biochemical features at diagnosis and responses to medical therapy.** *Thyroid* 1997, **7**:755-760.
2. Lazar L, Kalter-Leibovici O, Pertzelan A, Weintrob N, Josefsberg Z, Phillip M: **Thyrotoxicosis in prepubertal children compared with pubertal and postpubertal patients.** *J Clin Endocrinol Metab* 2000, **85**:3678-3682.

P103

Hypertensive encephalopathy in untreated congenital hypothryroidism: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P103

Hypothyroidism is a well-known cause of poor linear growth in children. In long standing untreated congenital hypothyroidism, short stature, mental retardation and myxedema are common. Sexual precocity associated with bone age advancement can occur, but hypertensive encephalopathy is rare. This case highlights an uncommon finding of hypertensive encephalopathy in a 10 year old Filipino girl who was diagnosed to have hypothyroidism at 18 months old with presenting symptoms of short stature and constipation. She was treated with levothyroxine but with poor compliance. Because of a 2-week history of vomiting, headache, blurring of vision, and increased sleeping time, she was admitted. She was noted to have short stature (height for age Z score -3.62) and obesity (BMI = 26.3, Z score +2.55, WHO) with myxedematous appearance, stubby fingers and toes, and SMR IV. While in the hospital she had seizures, and developed hypertensive encephalopathy. She was noted to have elevated TSH levels (12.5 mIU/L) with normal FT4 and FT3 consistent with subclinical hypothyroidism. Cranial CT scan revealed hypodense foci on the occipital area with cerebral edema. She was given levothyroxine, mannitol and antihypertensive drugs. Her blood pressure was controlled and edema subsided. Prolonged untreated hypothyroidism with elevation of thyroid stimulating hormone leads to mental retardation, short stature, sexual precocity, and hypertension. TSH and gonadotropin hormones have some regions of identical structures in common and may cross react to the same receptors. Prolonged increase in TSH and early rise in gonadotropin have led to ovarian follicles to secrete estrogen, and consequently, breast developent, menarche and skeletal maturation. The hypertension related to hypothyroidism is a result of increased peripheral resistance, changes in renal hemodynamics and hormones. Early recgonition of symptoms and treatment as well as adherenece to levothyroxine therapy is essential in preventing complications of hypothyroidism.
Written informed consent was obtained from the parent of the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P104

Follicular thyroid carcinoma in a child presenting as autonomously functioning thyroid nodule

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P104

Thyroid nodules are uncommon in children (1.5%). However, the incidence of thyroid carcinoma in childhood thyroid nodules (26.4%) is 3-4 folds higher than in adults. Autonomously functioning thyroid nodules (AFTN) or hot nodules account for less than 3% of hyperthyroidism in children and carry a small risk of malignancy (2-5%). The majority of malignant hot nodules are papillary thyroid carcinoma (57.1%) with follicular carcinoma reportedly comprising 36.4% of cases. A search of MEDLINE identified 7 paediatric cases of AFTN harbouring carcinoma. Here we report a child, presenting with hyperthyroidism and subsequently diagnosed with follicular thyroid carcinoma.

An 11 year old girl presented with a palpable right sided thyroid nodule and symptoms of hyperthyroidism consisting of tachycardia and anxiety. A thyroid ultrasound showed a solitary, minimally heterogenous nodule on the right, measuring 2.5x1.9x1.6 centimetres. It was hyperechoic to the remainder of thyroid gland and had increased intralesional and perilesional vascularity. A radionuclide scan demonstrated the nodule as hyperfunctioning "hot" nodule with no radiotracer uptake in the rest of thyroid. An ultrasound guided FNAC was performed and features consistent with a follicular neoplasm were identified. She underwent right hemi-thyroidectomy and histopathology was consistent with angioinvasive follicular thyroid carcinoma. No evidence of carcinoma was found in the rest of the thyroid following completion thyroidectomy. Additionally, her head circumference was >98th percentile, a lipoma was present over her sacrum and MRI suggested avascular hamartoma over her right ankle, together raising the possibility of Cowden syndrome.

FNAC is warranted in all cases of solid thyroid nodules in children including hot nodules to help define the pathology. If inconclusive, surgical excision of lesion for histopathology should be considered. Familial cancer syndromes, which can include a hamartoma/tumour phenotype such as Cowden syndrome and other PTEN hamartoma/tumour syndromes, DICER1 syndrome and MEN2 are also possible, depending on the type of thyroid malignancy.

Written informed consent was obtained from the patient's parent or guardian for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P105

Block & replacement regimen is more cost effective than titration regimen in treating thyrotoxicosis in children, without more harm

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P105

Aim: The first line treatment of thyrotoxicosis in our unit is anti-thyroid medication for 2 years – longer if unstable control. Since 2010, we changed the anti-thyroid treatment protocol from block and replacement (B&R) to titration regimen (TIT), after the Cochrane review showed that B&R was associated with similar remission rate but more frequent adverse effects than TIT. We aimed at comparing these 2 regimens in our pediatric patients.

Methods: Patients who received TIT from 2010 to 2014 for relapse of thyrotoxicosis and previously had at least 1 full course of B&R were reviewed. Those who had less than 2 years of TIT, either because they received surgery or radioactive iodine within 2 years, or they have not yet finished the course, were excluded from analysis.

The course of B&R versus TIT was compared within each individual. For those who had previously multiple courses of B&R, the latest course was used for analysis.

Occurrence of adverse drug side effects, length of the anti-thyroid treatment course, number of clinic visits and thyroid function tests during the course, and frequency of abnormal free thyroxine levels were reviewed and analyzed by paired t-test.

Results: 27 patients, who received B&R previously, were put on TIT for relapse of thyrotoxicosis after 2010. 17 patients were excluded from the analysis as they were on TIT for less than 2 years, 9 of them had surgery or radioactive iodine within 2 years after starting TIT.

Among the 10 patients (4 males, 6 females, age 8-16 years) analysed, no significant drug side effect was experienced during both treatment periods. While on TIT, patients required longer duration of treatment (average 23% longer, p=0.005) with more clinic visits (average 50% increase, p=0.003) and thyroid function tests (average 85% increase, p=0.002).

They needed more frequent clinic visits (average 22% increase, p=0.04) and thyroid function tests (average 50% increase, p=0.007) per year. They had higher number of abnormal free thyroxine levels per year (average 28% more frequent, p=0.023). The percentage of abnormal free thyroxine levels dropped insignificantly by 2.6% (p=0.645).

The estimated drug cost for 2 year's B&R was ~397 HKD (51.2 USD / 54.6 AUD), while 2 years' TIT cost ~177 HKD (22.8 USD / 24.3 AUD).

Conclusion: Both B&R and TIT are safe without significant adverse effect. B&R seems more cost effective with shorter treatment duration and less frequent clinical and biochemical monitoring, even drug cost is slightly higher.

DEVELOPMENTAL ORIGINS OF HEALTH AND ADULT DISEASE

P106

LGA infants display early catch down growth in length and weight without epigenetic changes

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P106

Aims: To evaluate the growth patterns of infants born large-for-gestational-age (LGA) from birth to age 1 year compared to those born appropriate-for-gestational-age (AGA). In addition, we aimed to investigate possible epigenetic changes associated with being born LGA.

Methods: Seventy-one singleton infants born at term were classified by birth weight as AGA (10th-90th percentile; n=42) and as LGA (>90th percentile; n=29). Post-natal follow-up until age 1 year was performed with clinical assessments at 3, 6, and 12 months. Assessments included measurement of infants' weight, length, ponderal index, BMI, as well as head, chest, and abdominal circumference. A subgroup of 38 infants (17 AGA and 21 LGA) was selected for genome-wide DNA methylation analysis. Umbilical cord was collected at birth, and methylation profile on umbilical tissue was analysed using the Illumina Infinium 450K methylation array.

Results: At birth, the LGA group had greater birth weight (P<0.0001), length (P<0.0001), head circumference (P<0.0001), ponderal index (P=0.02), BMI (P<0.0001), chest and abdominal circumferences (P=0.04 and P=0.007, respectively) than AGA newborns. At the age of 3 months, LGA infants still presented greater weight (P<0.0001), length (P=0.006), BMI (P=0.02), as well as head (P=0.004) and abdominal (P=0.04) circumferences than AGA peers. However, by age 6 months there were no more anthropometric differences between the two groups. This was due to higher length increment in AGA than LGA infants between 0-6 months (18.3 vs 15.1 cm; P<0.0001), whereas length increment was identical in both groups between 6-12 months (7.7 vs 7.7 cm; P=0.96). For the genome-wide analysis, more than 485,000 DNA methylation sites covering 99% of human NCBI Reference Sequence (RefSeq) genes were examined at birth, but no differences were found between LGA and AGA infants.

Conclusion: Despite being born oversized at birth, LGA infants displayed early catch-down growth (i.e. slower length velocity), so that by the age of 6 months LGA infants were of similar length and BMI as AGA infants.

In addition, no epigenetic differences in genome-wide methylation were found in those born LGA.

P107

First borns and offspring of younger parents have increased metabolic risk

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P107

Introduction: Perinatal factors such as SGA, LGA, and twin birth are known to adversely program metabolism, increasing the risk of metabolic and cardiovascular disease in adulthood. Birth order and parental age at childbirth have recently been associated with metabolic alterations in childhood. First-born children have poorer insulin sensitivity than second-borns, and lower parental age at childbirth is associated with reduced insulin sensitivity in girls. It is unknown whether the effects of these perinatal factors persist into adulthood increasing the risk of diabetes and heart disease.
Methods: Participants were recruited for two clinical trials investigating metabolic effects of dietary supplements. Overweight middle-aged (35-55 years) men born singleton at term were eligible. Exclusion criteria were diabetes, hypertension, known dyslipidaemia, tobacco use, and use of medications likely to affect blood pressure, lipid profile or insulin sensitivity. Insulin sensitivity was assessed using the Matsuda method. Additional assessments included DXA-derived body composition, 24-hour ambulatory blood pressure (BP) monitoring, carotid artery intima-media thickness (CIMT), physical activity (IPAQ), and diet (3-day food diary).
Results: 73 participants were included in the parental age study, while 50 first- and second-borns men were included in the birth order analysis.
As maternal and paternal ages were highly correlated, mid-parental age at childbirth (MPAC) was used in analyses. Decreasing MPAC was associated with a continuous decrease in insulin sensitivity (p=0.008), increased nocturnal systolic (p=0.020) and diastolic (p=0.047) BP, as well as poorer nocturnal diastolic dipping (p=0.046). Decreasing MPAC tended to be associated with a subtle increase in CIMT (p=0.068).
First-born men were 6.9 kg heavier (p=0.013) and had BMI that was 1.6 kg/m^2 greater (p=0.004) than second-borns. Insulin sensitivity in first-born men was 33% lower than in second-borns (p=0.014), despite adjustment for fat mass, physical activity, and diet. The first born effect was independent of parental age.
Discussion: Among overweight middle-aged men, first-borns had lower insulin sensitivity and greater adiposity than second-borns. Those who are have younger parents also had adverse metabolic risk. These data provide evidence that the effects of birth order and parental age on metabolism seen in childhood persist into mid-adulthood and are likely to influence long term cardiovascular and metabolic disease. Further studies should examine sibling pairs and the offspring of parents with disparate ages.

P108

Clinical characteristics and imprinting analysis of Chinese Silver Russell Syndrome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P108

Aims: To study clinical characteristics and imprinting defects in Chinese children with SRS.
Methods: Forty-nine SRS cases were studied retrospectively. Out of these 49 cases, 36 were available to be detected chromosome 11p15 imprinting defects and 21 cases were detected uniparental disomy of maternal chromosome 7 (UPD[7] mat).
Results: There were 32 boys and 17 girls whose ages ranged from 3 m to 12 y. The main clinical characteristics of these SRS were: i) SGA and postnatal growth retardation (mean height standard deviation score (HT SDS) was 2.25; ii) Skeletal malformation including triangular-shaped face, small chin, irregular/crowded teeth, limbs asymmetry and fifth finger clinodactyly. Genetic analysis showed that ICR1 hypomethylation were 22/36 (61.1%) which were following: Ten had hypomethylation in chromosome 11p15 imprinting control region 1 (ICR1) of the paternal allele; seven had both hypomethylation in ICR1 and ICR2; five had hypomethylation in ICR1 and hypermethylation in ICR2. And UPD7 (mat) positive is 1/21 (4.8%). Six patients had been treated with growth hormone (GH) for 3 to 24 months. Growth rates ranged from 4 to 10.8 cm/year.
Conclusions: This study demonstrated that Chinese children with SRS had more growth retardation than bone retardation and had classical skeletal malformation such as triangular faces, and limb asymmetry. Chromosome 11p15 imprinting defects contributed to over 60% of these cases and UPD7 (mat) positive is 4.8%.

P109

Shorter mothers have shorter pregnancies

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P109

Objective: Studies have shown that shorter women are at a greater risk of preterm birth. In light of these previous findings, we aimed to assess whether maternal height was associated with gestational age in a cohort of children born at term.
Methods: Subjects were a control cohort of 294 children of New Zealand European ethnicity, high socioeconomic status, naturally conceived, born appropriate-for-gestational-age of singleton pregnancies at 37–41 weeks of gestation. Gestational age was determined by ultrasound scans performed <20 weeks. Maternal and paternal heights were measured using a Harpenden stadiometer. Associations with maternal height were assessed using linear regression mixed models, accounting for infant's gender, birth order, maternal age, and paternal height, with family number added as a random factor.
Results: Mothers were 167.5 (SD=6.2) cm tall (range 151.4–183.0 cm). Increasing maternal height was associated with longer gestation (p=0.002). Stratified analyses showed that the main effect appears to occur among shorter mothers (<165 cm tall), who experienced gestation that was ~0.6 weeks shorter than that of mothers 165–170 cm (p=0.001) and >170 cm (p=0.0002) tall (Figure 1). There was also a progressive increase in birth weight standard deviation scores with increasing maternal height (p<0.0001). Paternal height was not associated with study outcomes.
Conclusions: This study shows that maternal height is positively associated with gestational length across the term window. An association between shorter mothers and preterm birth has been previously shown. We have extended this observation showing that maternal short stature is associated with shorter pregnancies within the term window. The breakdown of term pregnancies into early term (37 0/7 – 38 6/7 weeks of gestation), full term (39 0/7 – 40 6/7 weeks), and late term (41 0/7 – 41 6/7 weeks) has recently been proposed, in light of differences in neonatal morbidity and mortality as well as in neurocognitive outcomes later in life.
Maternal stature seems to be a factor determining offspring outcomes, with proposed underpinning mechanisms including socioeconomic factors, undernutrition in utero, and anatomical constraints on pelvis during birth. In our study, socioeconomic factors were not at play in light of the homogeneity of our cohort. Lastly, our findings also support the lack of a paternal height effect on length of gestation.

P110

Decreasing birth weight is associated with adverse metabolic profile and lower stature in childhood and adolescence

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P110

Objective: We aimed to evaluate the association of birth weight SDS (BWSDS) with insulin resistance, blood pressure, and auxology in children and adolescents born 23–42 weeks of gestation.
Methods: We studied 143 singleton children and adolescents aged 9.3 ± 3.3 years (range 2.0 – 17.9 years). Clinical assessments included auxology, insulin resistance measured by the HOMA2-IR, and blood pressure from sphygmomanometer measurements. Continuous associations were

examined and stratified analyses carried out. For the latter, participants were divided into those of below-average birth weight (BBW, <0 SDS) and above-average birth weight (ABW, ≥0 SDS).
Results: Irrespective of gestational age, lower BWSDS was associated with progressively increased insulin resistance (p<0.0001) and fasting insulin concentrations (p<0.0001). Decreasing BWSDS was associated with higher systolic (p=0.011) and diastolic (p=0.006) blood pressure. Lower BWSDS was also associated with decreasing stature (p<0.010). The BBW group was ~40% more insulin resistant than ABW participants (p=0.004), with the former also displaying fasting insulin concentrations 37% higher (p=0.004). BBW participants were 0.34 SDS shorter than those of higher birth weight (p=0.002). On average, BBW participants failed to meet their genetic potential, tending to be shorter than their parents (p=0.065). As a result, when corrected for parents' heights, BBW participants were 0.6 SDS shorter than those born of higher birth weight (p=0.001). Sub-group analyses on participants born appropriate-for-gestational-age (n=128) showed that associations of BWSDS with both insulin resistance and stature remained (although attenuated).
Conclusion: Decreasing BWSDS (even within the normal range) is associated with adverse metabolic profile and lower stature in children and adolescents.

P111

Anthropometrics of neonates born to mothers with diabetes in pregnancy in the Northern Territory

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Type 2 diabetes (T2DM) is increasing in prevalence in Indigenous Australian children and adolescents. High rates of diabetes in pregnancy (DIP) in Indigenous Australians increases the risk of diabetes for the next generation. DIP is associated with neonatal adiposity, which correlates with long-term risk of obesity and diabetes. Indigenous Australians have high rates of low birth weight and increasingly, large for gestational age associated with DIP.
The aims are: 1. To evaluate adiposity in babies born to Indigenous mothers and those of European background with DIP in the Northern Territory; 2. To evaluate the relationship between maternal factors and neonatal birth weight and body composition.
Thus far 266 mothers and neonates from the PANDORA cohort (Pregnancy and Neonatal Outcomes in Remote Australia) have been assessed. Neonatal anthropometrics were performed on all neonates, including skin fold measures. Calculations of fat mass were made using a validated equation (fat mass=0.39055(birth weight)+0.0453(flank skinfold)-0.03237(length)+0.54657). Significant differences were found in maternal characteristics between Indigenous and European background participants, including diabetes type (T2DM 14.7% vs 1.1%, p<0.001), smoking in pregnancy (26.5% vs 9.1%, p<0.001) and location of residence (regional/remote 41.4%vs 9.8% p<0.001). Gestational age at birth was significantly different (38.2 vs 39 weeks p<0.001), however birth weight was not significantly different (3380 vs 3428g). Indigenous neonates had greater subscapular (4.69 vs 4.20mm, p=0.003) triceps (4.75 vs 4.22mm, p=0.004) and flank skin folds (4.08 vs 3.60mm, p=0.006). This difference remained significant for the flank skin fold only, after adjustment for diabetes type and maternal body mass index (BMI). There was no significant difference in calculated fat mass. On regression analysis, maternal BMI, smoking, nulliparity and T2DM were each independently associated with birth-weight z-score.
Recruitment to PANDORA is ongoing. Preliminary data reveals higher skin fold measures, indicative of adiposity, in Indigenous neonates. There was no significant difference in fat mass. Smoking, BMI, nulliparity and T2DM were independently associated with birth-weight z-score, ethnicity was not independently associated.

DISORDERS OF SEXUAL DIFFERENTIATION

P112

Phenotype and genotype of patients with disorder of sex development due to 5α-reductase deficiency

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P112

A rare form of the 46,XY disorders of sex development (DSD), 5α-reductase deficiency was first described in patients with pseudovaginal perineoscrotal hypospadias, microphallus, and cryptorchid testes in 1974 by Imperato. This undervirilization in the male is due to an alteration in the 5α-reductase type 2 gene (SRD5A2), which encodes for 5α- reductase activity. Our registry of 750 patients with DSD showed no definitive diagnosis in 80% of cases with 46,XY DSD. Our aim is to identify mutations in SRD5A2 gene and to describe phenotype of detected mutative cases. Mutation analysis was performed for genomic DNA extracted from WBC of 10 patients with 46,XY DSD using PCR and direct sequencing. We identified mutations of SRD5A2 gene in two cases. The first case presented with isolated micropenis at birth, two palpable testes in the normal scrotum. Pelvic ultrasound showed no ovaries and uterus, karyotype was 46,XY and SRY was positive. Serum FSH level was 2.4 UI/L; LH level was 0.9 UI/L and testosterone level was 0.4 nmol/l at 8 years of age. A homozygous missense mutation (p.R237G) was identified in the SRD5A2 gene. The second case presented with microphaslus, penoscrotal hypospadias, gonad bilateral in labioscrotal folds. No uterus and ovaries were found by pelvic ultrasound. Karyotype was 46,XY and SRY was positive. A novel homozygous missense mutation (c.659C>T; p.S220L) was identified in the SRD5A2 gene. Mutation analysis of SRD5A2 gene helps to make definitive diagnosis for patients with 46,XY DSD.

P113

46,XY disorder of sex development and wilms' tumor due to mutation of WT1 gene: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P113

The Wilms' tumor suppressor gene (WT1) is a transcription factor that plays a major role in development of the gonads and kidneys. It is expressed even earlier than sex-determining region of the Y chromosome in the urogenital ridge from which the gonads and kidneys are derived. WT1 mutations will impair gonadal and urinary tract development and have been demonstrated to cause syndromes of WAGR, Denys–Drash and Fraiser. In this study, our aim is to identify mutation in WT1 gene and to describe clinical features of a Vietnamese patient with 46,XY disorder of sex development (DSD) associated with Wilms' tumor. DNA was extracted from WBC and mutation analysis of WT1 gene was performed using PCR and direct sequencing. A 5 days newborn presented with penoscrotal hypospadias, microphallus, right testis in the right inguinal and no left testis was found. Karyotype was 46,XY and no ovaries and uterus were found using pelvic ultrasound. Wilms' tumor was detected at 13 months of age by abdominal ultrasound and CT scan. Mutation analysis was identified a heterozygous missense mutation (c.1390G>A; p.D464N) in exon 9 of WT1 gene. In conclusions, WT1 analysis should be performed in newborns with complex hypospadias with at least one cryptorchid testis and in isolated 46,XY partial to complete gonadal dysgenesis. WT1 analysis is mandatory in all 46,XY DSD with associated kidney disease. Patients with WT1 mutations should be followed up closely because the risk of developing a Wilms' tumor, nephropathy.
Written informed consent was obtained from the patient's parent or guardian for publication of this Case report (and any accompanying

images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

P114

Clinical, endocrinological, and molecular genetic characterization of Kallmann syndrome and normosmic idiopathic hypogonadotropic hypogonadism in childhood and adolescence

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P114

Aims: Isolated gonadotropin-releasing hormone (GnRH) deficiency (IGD) is characterized by delayed or absent sexual development associated with low gonadotropin and sex steroid levels. IGD is classified as Kallmann syndrome (KS) with anosmia and normosmic idiopathic hypogonadotropic hypogonadism (nIHH). This study was undertaken to investigate clinical and endocrinological profiles in patients with KS and nIHH during childhood and adolescence in Korea.
Methods: Twenty nine patients (24 males and 5 females) were included. Their clinical, endocrinological, and radiologic findings were analyzed by retrospective medical record review. In all patients, all exons and intronic flanking regions of the GNRH1, GNRHR, KISS1, KISS1R, PROK2, PROKR2, TAC3, TACR3, FGF8, FGFR1, KAL1, CHD7, and SOX10 genes were amplified by PCR with specific primers and directly sequenced.
Results: Of 29 patients, 14 were KS and 15 were nIHH. At diagnosis, mean chronologic age was 16.55 ± 3.76 years; height SDS was -0.92 ± 1.53; testis volume was 2.10 ± 1.25 mL; and Tanner stage was 1.45. There were associated anomalies in some KS patients: 6 patients with hearing loss, 4 patients with congenital heart disease, and 2 patients with cryptorchidism. Absence or hypoplasia of the olfactory bulb or sulci was found in 9 (82.82%) KS patients. Peak LH and FSH levels were 5.64 ± 5.83 and 5.11 ± 4.61 mIU/mL after GnRH stimulation. Baseline testosterone levels were 0.46 ± 0.62 ng/mL. Twenty four patients (20 males, 4 females) received hormone replacement therapy for 51.1 months of duration. During the follow-up period, all patients reached final adult height of 173.29 ± 8.07 cm (0.27 ± 1.03 SDS). Of 29 patients from 28 unrelated families, molecular defects were identified in 6 patients from 5 families (17.9%, 5/28 pedigrees) in KAL1, SOX10, and CHD7. Two male siblings with KS harbored a novel heterozygous mutation of p.W380* in KAL1. Two unrelated female patients with typical and partial/incomplete CHARGE syndrome were heterozygous for frameshift (p.A608Gfs*4) and nonsense (p.W983*) mutations in CHD7, respectively. A 31-year-old male with KS and deafness harbored a heterozygous p.M112I mutation in SOX10.
Conclusion: This study described clinical, endocrinological, and molecular genetic features in relatively large cohort of IGD patients. Although the mutation screening was performed in ten genes responsible for causing IGD, molecular defects were identified in relatively small proportions of cohort.

P115

The pattern of disorders of sex development in Vietnamese children

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P115

Background: Disorders of sex development (DSD) are defined as congenital condition in which development of chromosomal, gonadal, or anatomical sex is atypical. The Chicago DSD classification includes three main diagnostic categories: sex chromosome DSD, 46,XY DSD and 46,XX DSD.
Aims: Define the pattern of disorders of sex development according to Chicago's classification 2006 at National Hospital of Pediatrics in Hanoi, Vietnam (NHP).
Method: Patients were examined, diagnosed and treated DSD or ambiguous sex at (NHP) from 31/07/2002 to 31/7/2012. Criteria that suggest DSD include.
1. overt genital ambiguity (eg, cloacal exstrophy).
2. apparent female genitalia with an enlarged clitoris, posterior labial fusion, or an inguinal/labial mass.
3. apparent male genitalia with bilateral undescended testes, micropenis, isolated perineal hypospadias, or mild hypospadias with undescended testis.
4. a family history of DSD such as CAIS, and.
5. a discordance between genital appearance and a prenatal karyotype.
Method of the study was descriptive observational.
Results: 51.7% patients had 46,XX DSD, among them 98.6% had definitive diagnosis. Congenital adrenal hyperplasia (CAH) is the most common cause of 46,XX DSD (91.9%). Rate of 46,XY DSD was 25%, however 83.3% had no definitive diagnosis. 23.3% of patients had chromosome DSD, among them 88.3% chromosome DSD was Turner syndrome.
Conclusion: CAH is the most common cause of DSD.

HYPOTHALAMIC/PITUITARY

P116

A case of congenital combined pituitary hormone deficiency who showed respiratory distress and hypoglycemia soon after birth

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P116

Congenital combined pituitary hormone deficiency (CCPHD) is a rare disease, presenting with respiratory distress, hypoglycemia and jaundice soon after birth. It is caused by .pituitary aplasia or hypoplasia or abnormality of transcription factor which related to pituitary development. We describe a Japanese patient with CCPHD, who presented with respiratory distress, hypoglycemia and jaundice soon after birth.
The patient is now 13 months old Japanese girl. She was born by cesarean section because of fetal distress with 39 weeks and 4 days gestation after an uneventful pregnancy. Her parents were unrelated. Birth length and weight were 43.8cm (-2.2SD) and 2,100g and Apgar scores were 8 at both of 1 and 5 min. She had showed tachypnea and cyanosis since soon after birth and taken nasal-CPAP. However respiratory distress had not improved. She had also showed jaundice and hypoglycemia and was treated with phototherapy and infusion therapy. At 6 days old, we found her FT4 level was 0.4 pg/ml and TSH level was below 0.01 μIU/ml. She was suspected CPHD and anterior pituitary hormone levels were assessed. All of anterior pituitary hormones were undetectable. Anterior pituitary was not visible, posterior pituitary was detected at normal position and there were no other abnormality on brain magnetic resonance imaging. We diagnosed her as CCPHD and hydrocortisone was started since 6 days old and levothyroxine since 8 days old. After that respiratory distress and jaundice had improved rapidly. But hypoglycemia had appeared again after interrupting infusion therapy. GH level after arginine stimulation was also undetectable. She had also started growth hormone therapy since 25 days old and she has had no hypoglycemic episodes after that. Her length and weight were 70.3cm (-1.2SD) and 8,485g at 1 year old. GH replacement therapy that was started soon after diagnosis was able to prevent the severe growth retardation. She has no gene abnormalities of transcription factors, HESX1, LHX4 and OTX2, that involves pituitary development. Further studies are needed for investigating genetic basis of this patient.
Careful and prompt clinical, endocrinological and neuroradiological assessment are needed for diagnosis of hypopituitarism in patients who show prolonged respiratory distress, hypoglycemia or jaundice soon after birth.
Written informed consent was obtained from the patient's parent or guardian for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P117

Bone mineral content in growth hormone deficient children treated with growth hormone after withdrawal of 1 year of supplementation with calcium, vitamin D and zinc

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P117

Supplementation with calcium (ca), vitamin d (vit D), zinc has been shown to have a positive effect on bone mineral content (BMC) gain in growth hormone deficient (GHD) children on GH therapy [1]. It is unknown if this gain is sustained after supplement withdrawal. We aimed to investigate the influence of prior supplementation with ca, vitD and zinc on BMC accretion after supplement withdrawal.

31 prepubertal GHD children were randomly allocated to receive A) calcium (500mg/d), vitamin d (30,000 IU/3 months) and B) calcium (500mg/d), vitamin D (30,000 IU/3 months) & zinc (8 mg) for 1 year with GH. Ht measurement, bone mineralization by dual energy x-ray absorptiometry, tanner staging were performed at 4 timepoints, baseline, post 1 year of supplementation and 1 & 2 years after withdrawal of supplementation. Height for age z-scores (HAZ) were calculated from ethnic growth references.

At baseline, children (18 boys, 9.6±2.8 years) from group A & B were similar in their HAZ (-4 ±1.5, -4 ±1.3) and BMC (370±215 g, 440±167g). 1 year post supplementation, 40% & 36% children and by the end of 2nd year of supplementation withdrawal, 47% & 80% from group A & B respectively had entered puberty. Since Ht has strong correlation with BMC, % change in ht adjusted BMC was analyzed. The gain in BMC was greater ($p < 0.05$) in group B (51 %) children than in group A (49 %) children[2]. However, after the withdrawal of the supplementation, the % gain in ht as well as ht adjusted BMC was similar in both groups. The % gain in ht adjusted BMC was lower ($p < 0.05$) in the 1st year of supplement withdrawal (22 %). In 2nd year, the ht adjusted BMC showed a significantly greater (53 %, $p < 0.05$) gain than the supplementation year and first year after supplementation withdrawal.

Effect of short term supplementation with ca, vit D & zn in GH treated GHD children may not continue after the withdrawal of supplementation. However, the greater gain in the 2nd year after supplementation withdrawal was possibly due to the effect of puberty.

Reference

1. Ekbote V, Khadilkar A, Chiplonkar S, Mughal Z, Khadilkar V: Enhanced effect of zinc and calcium supplementation on bone status in growth hormone-deficient children treated with growth hormone: a pilot randomized controlled trial. *Endocrine* 2013, **43(3)**:686-95.

P118

Hypopituitarism due to central nervous system germinoma: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P118

Germ cell tumors in the central nervous system affect children and adults, the peak incidence is from 10 -19 years of age. Clinical presentation is mainly involving to the location and size of the tumor and the patient age. Endocrine abnormalities are the most common symptom.

We presented a case who had hypopituitarism due to central nervous system Germinoma.

A 10 years old girl was admitted to our hospital due to polyuria . Past history : she was diagnosed with diabetes insipidus and treated with oral minirin (desmopressin) 3 years ago. But she did not taken oral minirin for 2 years ago.

Physical examination showed : polyuria (8 ml/kg/h), polydipsia, no dehydration, no weight gain. Her height was 131 cm (-0.5 SD). Her weight was 41 kg. Her BMI was 23.9 (> 97th). She had no manifestation of puberty. Laboratory evaluation revealed : blood osmotic pressure : 304 mosm/kg (normal range : 275 mosm/kg – 295 mosm/kg), urinary osmotic pressure : 80 mosm/kg (normal range : 500 – 1200 mosm/kg); serum cortisol at 8 a.m : 9.2 nmol/l (normal range : 200 – 600 moll/l); plasma glucose level and electrolyte were normal; T4 : 38.8 nmo/l (normal : 50 -150 nmol/l), T3 : 2.35 nmol/l (normal range : 1 – 3 nmol/l), TSH : 4.1 mcUI/ml (normai range : 1 – 5 mcUI/ml); LH : 0.16 UI/ ml (normal range : 0,5 – 9,9 UI/l),, FSH : 0.9 UI/ml (normal range : 1,4 – 5,6 UI/l), Estradiol < 43.3 pmol/l (normal range : 97 – 169 pmol/l). An MRI of brain showed: an under hypothalamic mass measuring 14 × 20 mm, suspected Germinoma.

She was treated with hormone replacement (desmopressin, levothyroxine, hydrocortisone) and radiation therapy.

Written informed consent was obtained from the patient's parent or guardian for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

P119

Multiple endocrine glands insufficiency due to langerhans cell histiocytosis (LCH): a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P119

LCH is the rare disease involving clonal proliferation of Langerhans cells, abnormal cells deriving from bone marrow and capable of migrating from skin to lymph nodes. The clinical presentation of LCH may occur in multiple organs: bone, skin, lymph nodes or pituitary gland, but clinical presentation of LCH rarely occurs in multiple endocrine systems.

We presented a special case who was diagnosed with LCH and presentation of LCH occurred in multiple systems: pituitary gland, thyroid, adrenal gland.

A 11 years old girl was hospitalized for lump on the neck. Past history: one year ago, she was diagnosed with autoimmune polyendocrine syndromes and treated with hormone replacement (levothyroxine 3mcg/kg/day, desmopressin 4 mcg/kg/day, hydrocortisone 10 mcg/kg/day). Physical examination showed: she had a swollen lump on her neck, she had a temperature of 38° C. She had no polyuria, no polydipsia. Her height was 141cm (-0.29 SD); her weight was 37 kg; her BMI was 18.5 (50th – 70th) .She had normal growth velocity and normal pubertal development. Laboratory evaluation revealed : WBC : 10.3 × 109 /l (normal range : 4×10 9 /l – 10 ×109 / l) ; CRP : 105.78 mg/l (normal range : < 10 mg/l); serum cortisol at 8 a.m : 16.3 nmol/l (normal range : 200 – 600 nmol/l); T3 : 1.8 nmol/l (normal range : 1 – 3 nmol/l), T4 : 135.9 nmol/l (normal range : 50 – 150 nmol/l), TSH : 0.002 mUI/ml (normal range : 1 – 5 mUI/ml); blood osmotic pressure : 279 moms/kg, urinary osmotic pressure : 127 mosm/kg; plasma glucose level and electrolyte were normal. An MRI of brain showed: thickened pituitary stalk. A biopsy of the lump on her neck showed: features of Langerhans Cell; skeletal and long bone radiograph showed no osteolytic lesion.

She was treated with hormone replacement and chemotherapy.

Written informed consent was obtained from the patient's parent or guardian for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

METABOLIC

P120

Variations of amino acid, free carnitine and acylarnitine profiles analysed by tandem mass spectrometry in newborns during their first four weeks of life

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P120

Aims: Electrospray ionization-tandem mass spectrometry (MS/MS) has increasingly been advocated for expanded newborn screening and for the early diagnosis of amino acidemias, fatty acid oxidation disorders, and

organic acidurias. Here, we characterized amino acid, free carnitine, and acylcarnitine status with respect to postnatal ages in 158,730 newborns over the last two years.

Methods: Six age groups were defined: 3-4 d (Group A), 5-7 d (Group B), 8-10 d (Group C), 11-15 d (Group D), 16-20 d (Group E), and 21-28 d (Group F). Amino acid, free carnitine, and acylcarnitine concentrations of dried whole blood spots were obtained from the MS/MS analysis. Linear regression analyses of all results of highly disease-related analytes were carried out to identify covariates associated with sampling time in Matlab. For the respective regression coefficients (RC), plus represents the analyte levels elevate as the sampling time prolongs, and vice versa for minus.

Results: Except for PHE, ALA and GLY, values of the remaining amino acids increased with postnatal age as the regression coefficients were plus. In addition, most amino acids levels during days 5-10 were distinctly higher with the exceptions of ALA, ORN and GLY. For free carnitine and short-chain ACs, C0, C5 and C5OH elevated slightly with sampling time (RC<0.05), while analytes left decreased along with age especially for C2 and C3 (RC for C3 was 0.01). For medium- and long-chain ACs, all analytes concentrations decreased with specimen collection time. C14, C16, C18, and C18:1 turned out to remain only half of their primary levels; and the level of C16 varied from 2.73 μmol/L in Day 3-4 to 0.84 μmol/L in Day 21-28. Our results indicate that most amino acids and acylcarnitines had no obvious age-dependent varieties in concentration levels during neonatal period with exceptions of C2, C3, C14, C16, C18, C18:1 and C16.

Conclusions: Although the risk of underdiagnosis of IEM with the use of the same newborn values as reference can be considered as small, for some parameters the use of age-related reference values may have a potential impact on the diagnosis and management of inherited errors of metabolism.

P121

Persistent hyperinsulinemic hypoglycemic in infant: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P121

Persistent hyperinsulinemic hypoglycemic in infant is risk factor for impairment during brain development process. Early diagnosis and treatment will result in better outcome. The aim is to report a case of persistent hyperinsulinemic hypoglycaemic infant. Methode is case report. A, 2 days old term infant, was referred due to hypoglicemia. He got generalized seizure and recurrent hypoglicemia. He can drink well. No vomiting observed. The Apgar score was 6-7-8. Birth weight was 4000 gram. He was the third child. Second child had the same history. No history of diabetes mellitus in the family. Physical examination revealed normal limit. Laboratory examination showed Hb 16.8 gram/dl, WBC17.4/cmm; hematocrite 50.1%; platelet 316/cmm; blood glucose 105 gram/dl, potassium 4.6 mmol/l, sodium 139 mmol/l, chloride 106 mmol/l, calsium 9.6 mg/dl, BUN 5.1 mg/dl, creatinin serum 0.82 mg/dl, Direct Bilirubin 0.079 mg/dl, Total bilirubin 0.19 mg/dl, SGOT 16 U/L, SGPT 10 U/L, CRP 11.10 mg/dl. During hypoglycaemia we got the result as follows: growth hormon 2.99 ng/ml (0.06-5), cortisol serum 198 ng/ml (50-250), fasting Insulin 10.30 Uu/ml (2.6-24.9). Head ultrasonography revealed normal. The patient was given IVFD Dextrose 10 0.18% saline (glucose infusion rate 4-5 mg/kg/min), breast milk 8x30-60cc, Ocreotide 5 mcg/kg/day iv, Nifedipin 4x 0.5-2.5mg per oral. Bolus 2cc/kg body weight of D10% if the blood sugar level was low. Hypoglycemic improved after treatment. As conclusion we should be aware of hypoglycemia in infant, it may due to persistent hyperinsulinism hypoglycemia of infant in which careful management is needed.

Written informed consent was obtained from each patient's parent or guardian for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P122

Congenital central hypoventilation syndrome with hyperinsulinemia in an infant

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P122

Congenital central hypoventilation syndrome (CCHS) is a rare disorder that typically presents in the newborn period and is characterized by alveolar hypoventilation and symptoms of autonomic nervous system dysregulation.

We describe an infant with CCHS who developed hyperinsulinism, which is an uncommon association. She was born by semi-elective Caesarean section at 37 weeks of gestation after a pregnancy complicated by polyhydramnios. Apgar scores were 7and 9 (at 1 and 5 min) and birth weight was 3550 g. She was intubated and ventilated within 24 hours for frequent apnoea's and desaturations. Multiple extubation attempts on the following days failed because of progressive respiratory acidosis. She underwent tracheostomy at 2 months of age. CCHS was diagnosed in the first month of life, after a polyalanine repeat expansion of the PHOX2B gene (20/26genotype) was detected.

At 7 months of age, she was admitted to hospital with seizures associated with hypoglycaemia. A critical sample (glucose 2.5mmol/L) revealed an inappropriately raised plasma insulin of 3.0 mU/L, growth hormone 7mu/L, cortisol 470 mmol/L, and serum ketones <0.1g/L. Urine and serum metabolic screen was normal, as was an EEG. Diazoxide was commenced at 5 mg/kg/day along with hydrochlorothiazide at 1mg/kg/d. These relatively low doses were used in view of parental concerns of potential drug side effect of hirsutism. The dose had to be increased to 7.5mg/kg/day as hypoglycaemic episodes persisted. Capillary blood glucose testing and continuous glucose monitoring showed no further hypoglycaemia at this dose. Sequence analysis of the KCNJ11 and ABCC8 genes implicated in congenital hyperinsulinism was undertaken and no pathogenic mutation was found.

The mechanisms underlying abnormal glycaemia in CCHS are not fully understood. Multiple hypotheses have been postulated including the co-expression of the dopamine beta hydroxylase gene mutation with PHOX 2B mutation. Further, disordered autonomic homeostasis as seen in PHOX2B mutations is thought to impact the regulation of insulin and glucagon secretion.

Our case highlights the importance of considering hyperinsulinism in the differential diagnosis of hypoglycaemia in infants with CCHS.

Written informed consent was obtained from the patient's parent or guardian for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

P123

Sirolimus treatment of severe congenital hyperinsulinism

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P123

Sirolimus treatment reduced dependence on octreotide and frequent feeding in 4 infants with CHI in a recent study [1]. We report our experience in a 1 year-old boy with presumed diffuse disease due to a de novo heterozygous ABCC8 missense mutation (p.D1506E).

This macrosomic infant (term birth weight 5.676kg) presented with hypoglycaemia in the first hours of life. Critical sample results were consistent with CHI (blood glucose 0.9mmol/L, insulin 41mU/L, free fatty acids 0.2mmol/L[RR 0.1-0.6]). The family history was significant for type 2 diabetes in both grandmothers, and CHI in his maternal second cousin.

No ABCC8 missense mutation was identified in either parent or his second cousin.
Initial management included intravenous glucose (12mg/kg/min) and glucagon infusions. Maximal dose diazoxide (20mg/kg/day for 5 days) was ineffective so subcutaneous octreotide infusion was initiated (26mcg/kg/day). At discharge from hospital (age 10 weeks) he was overweight (height SDS 1.11, weight SDS 3.1), receiving octreotide 27mcg/kg/day, nocturnal gastrostomy Polyjoule® feeds (equivalent to 11mg/kg/min glucose) plus 3-hourly daytime bolus feeds.
Sirolimus (0.5mg/m2/day) was added at age 7 months because of continued weight gain and intermittent mild hypoglycaemia while receiving octreotide 37mcg/kg/day. The dose was increased to 6mg/m2/day, aiming for trough levels 15-20ng/ml. After 3 months, the octreotide dose has stabilised (36mcg/kg/day) and the intensity of feeds has been reduced (3.5mg/kg/minute glucose overnight), resulting in weight loss; however, he has also developed linear growth failure (height velocity 6cm/year over 3 months). At 1 year of age his length and weight SDS are 0.48 and 1.21 respectively, and he is developmentally appropriate for age. Apart from one mild episode of respiratory syncytial virus, he has had no significant illnesses during sirolimus treatment.
In conclusion, treatment with sirolimus has improved our patient's blood glucose concentrations, decreased his dependence on hypercaloric nocturnal continuous feeds and decreased his weight gain; however the burden of care remains more significant than reported in the 4 published cases, 2 of whom had heterozygous mutations in ABCC8. The combination of high-dose octreotide and sirolimus may not be sustainable long-term in view of their likely combined contribution to his growth failure and the potential for immunosuppression due to sirolimus.
Written informed consent was obtained from the patient's parent or guardian for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Reference

1. Senniappan S, *et al*: Sirolimus therapy in infants with severe hyperinsulinemic hypoglycaemia. *NEJM* 2014, **370**:1131-7.

P124

Primary hyperlipidemia in children: clinical, biochemistry characteristics and outcome

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P124

Background: Primary hyperlipidemia is genetic dyslipoproteinemia. Without any intervention, cardiovascular diseases and acute pancreatitis may be occurred. The detection and appropriate management of pediatric hyperlipidemia can have a significant impact upon the disease course and can prevent complications.
Objects: to describe the clinical and biochemical characteristics of hyperlipidemia in Vietnamese children and to evaluate outcome of treatment.
Patients and methods: From 2007 to 2013, 30 children with primary hyperlipidemia were recruited and were treated with diet and/or lipid-lowering drug therapy at the National Hospital of Pediatrics, Hanoi, Vietnam. Clinical symptoms and biochemical finding, outcome of treatment were studied. Results: Among 30 cases from 28 families, 8 patients were mixed hyperlipidemia (MHL), 13 patients were hypertriglyceridemia (HT) and 9 patients were hypercholesterolemia (HC). Mean age of diagnosis was 5.5 years (1 month – 16 years). The rate of male/female was 13/17. Clinical manifestations included hepatomegaly (4 cases), xanthemas in the knees and elbows (5 cases), "creamy" blood (21 cases). Twenty cases were clinical asymptomatic. 8/28 patients had family history with hyperlipidemia and cardiovascular diseases. Serum cholesterol levels of HC group was 9.2 ± 4 mmol/l. Serum triglyceride level of HT group was 23.6 ± 9.9 mmol/l. MHL group had hypercholesterolemia (12.1 ± 4.5 mmol/l) and hypertriglyceridemia (20.3 ± 10.5 mmol/l). After interventions, HT group had the best outcome with serum triglyceride level was 10.1 ± 4.6 mmol/l, next to MHL group with serum cholesterole level was 5.8 ± 1.8 mmol/l, and serum triglyceride level was 9.5 ± 5.2 mmol/l; finally, serum cholesterole level of HC group was 12.4 ± 5.5 mmol/l. Five infants with HT had the best outcome of treatment: serum triglyceride level decreased from 19 - 57.6 mmol/l to 5 - 10 mmol/l. Two patients with HC had the worsen results (unchanged blood lipid level).
Conclusions: Primary hyperlipidemia had poor clinical manifestations and good results of treatment. Screening for primary hyperlipidemia help to prevent premature cardiovascular diseases.

P125

Molecular genetics, correlation between genotype and phenotype of 65 Vietnames patients with congenital hyperinsulinism

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P125

Hyperinsulinemic hypoglycemia (HH) is a consequence of unregulated insulin secretion by pancreatic β-cells. Congenital HH is caused by mutations in genes involved in regulation of insulin secretion (ABCC8, KCNJ11, GLUD1, CGK, HADH, SLC16A1, HNF4A and UCP2). Severe forms of congenital HH are caused by inactivating mutations in ABCC8 and KCNJ11, which encode the two components of the pancreatic β-cell ATP-sensitive potassium channel. Our aim is to identify mutations in the ABCC8 and KCNJ11, HNF4A and GLUD genes, and to describe genotype and phenotype correlations of Vietnamese children with congenital hyperinsulinism. A prospective study was conducted on 65 cases with congenital hyperinsulinism diagnosed and treated at the National Hospital of Pediatric from January 2007 to April 2014. Patients were selected by using inclusion criteria of Hussain K (2008). Mutations were identified in 32 cases (49.2%) including mutations of ABCC8 gene (28 cases; 43.1%), KCNJ11 (3 cases; 4.6%), HNF4A (1 case; 1.5%). 100% of cases with homozygous/compound heterozygous recessive mutations or one paternal dominant mutation of ABCC8 gene did not respond to diazoxide treatment and required 95% pancreatectomy. Molecular analysis using pancreas tissue after surgery from cases with one mutation of ABCC8 gene inherited from father confirmed focal lesion type. Other cases without identified mutations usually responded to diazoxide. In conclusions, children with congenital hyperinsulinism should be performed mutation analysis which helps in making diagnosis and treatment decision. Families of children with congenital hyperinsulinism should be given genetic counseling. Prenatal diagnosis should be performed as well as follow - up and treatment should be given to children with congenital hyperinsulinism immediately after birth.

WATER/ELECTROLYTES

P126

Challenges in the diagnosis and management of Pseudohypoaldosteronism Type 1

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P126

Autosomal recessive Pseudohypoaldosteronism Type I (PHA-I, MIM#264350), is a rare disease with a severe clinical phenotype [1,2] and generally no improvement with age [3]. It results from mutations in the amiloride-sensitive epithelial sodium channel causing mineralocorticoid-resistant (ENaC), systemic salt wasting, and is lethal without ongoing supra-physiological sodium supplementation and management of hyperkalaemia [4,5].
Other manifestations of systemic PHA-I include decreased sodium-dependant clearance of alveolar fluid causing recurrent chest congestion, cough and wheeze, but no airway infection by bacterial pathogens

typifying cystic fibrosis [6,7]; and skin rashes from inflammation of sodium-blocked sweat glands [8] with recurrent Staphylococcal skin infections described [9].

Our patient, now nearly four years old, presented as a day 6 neonate with vomiting, apnoea and floppiness. She was shocked and dehydrated with hyponatraemia, marked hyperkalaemia with runs of ventricular tachycardia.

PHA-1 was diagnosed with high cortisol, renin and aldosterone, normal 17-hydroxyprogesterone, inappropriately high spot urine sodium with low potassium, and normal renal ultrasound. Diagnosis was genetically confirmed with the finding of two inherited, distinct, disease causing mutations in the SCNNIA gene. Increased sweat sodium confirmed systemic salt-wasting. Initial management included a high-sodium, low-potassium formula (Kindergen) supplemented with 22 mmol/Kg/day of enteral sodium, the use of daily potassium binding resin (Resonium), and trial of Fludrocortisone.

Requirement for daily large doses of sodium 16 mmol/Kg/day, provided as a mix of sodium citrate and sodium chloride, and daily Resonium continues. Significant oral aversion remains an issue with good growth achieved on calorie-concentrated Kindergen. Gastrostomy feeding was changed to percutaneous jejunal continual feeding due to persistent gastric emptying problems. Central venous access established early has posed ongoing challenges, with intermittent Staphylococcal infections. Our patient has also been hypertensive requiring medical management from 6 months age. She has a recurrent moist cough with past Haemophilus infection.

Minimising inpatient management is vital for establishing 'normality' and optimising development. The need for frequent electrolyte monitoring and adjustment of sodium intake is managed creatively between home and hospital in close liaison with her paediatric endocrinologist and community-based supports. Clear emergency management plans involving early symptom recognition and rapid hospital-access are instituted to manage salt-wasting episodes.

We shall discuss the challenges and pitfalls of managing this rare, life-threatening disease with sparse long-term prognostic information, in the Australian health care context.

Written informed consent was obtained from the parent of the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

References

1. Riepe FG: **Clinical and molecular features of type 1 pseudohypoaldosteronism.** *Horm Res* 2009, **72**:1-9.
2. Zennaro MC, Lombes M: **Mineralocorticoid resistance.** *Trends Endocrinol Metab* 2004, **15**:264-270.
3. Adachi M, Asakura Y, Muroya K, Tajima T, Fujieda K, Kuribayashi E, Uchida S: **Increased Na reabsorption via the Na-Cl cotransporter in autosomal recessive pseudohypoaldosteronism.** *Clin Exp Nephrol* 2010, **14**:228-232.
4. Furgeson SB, Linas S: **Mechanisms of type I and type II pseudohypoaldosteronism.** *J Am Soc Nephrol* 2010, **21**:1842-5.
5. Güran T, Deirmenci S, Bulut YK, Say A, Riepe FG, Giiran Ö: **Critical points in the management of pseudohypoaldosteronism type I.** *J Clin Res Pediatr Endocrinol* 2011, **3**:98-100.
6. Kerem E, Bistritzer T, Hanukoglu A, *et al*: **Pulmonary epithelial sodium-channel dysfunction and excess airway liquid in pseudohypoaldosteronism.** *N Engl J Med* 1999, **341**:156-162.
7. Eaton DC, Helms MN, Koval M, *et al*: **The contribution of epithelial sodium channels to alveolar function in health and disease.** *Annu Rev Physiol* 2009, **71**:403-23.
8. Urbatsch A, Palier AS: **Pustular miliaria rubra: a specific cutaneous finding of type I pseudohypoaldosteronism.** *Pediatr Dermatol* 2002, **19**:317-9.
9. Saravanapandian N, Paul S, Matthai J: **Pseudohypoaldosteronism Type 1: A Rare Cause of Severe Dyselectrolytemia and Cardiovascular Collapse in Neonates.** *J Clin Neonatol* 2012, **1**:224-6.

P127

Pseudoaldosteronism due to mutation of SCNN1A gene: a case report

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International Journal of Pediatric Endocrinology 2015, **2015(Suppl 1):**P127

Introduction: Pseudohypoaldosteronism type 1 (PHA1) is a rare inherited disease characterized by resistance to the actions of aldosterone. It was first described in 1958 by Cheek and Perry, and common clinical manifestations include salt wasting, hyperkalaemia, metabolic acidosis and elevated plasma aldosterone levels in the neonatal period.

Objective: To describe clinical characteristics, laboratory features and management of one Vietnamese patient with pseudohypoaldosteron.

Subject and methods: Clinical features, biochemical finding, mutation analysis and management in a 1 months-old-boy was studied. Based on analysis of this patient's clinical symptoms associated with biochemical examination, the urinary steroid metabolomics analysis was performed using gas chromatography spectrometry and mutation analysis of SCNN1A was performed using PCR & direct sequencing.

Results: Patient is the first child normal delivery with the gestation age of 41 weeks, birth weight of 3200 g, and onset of the disease at 7 days of age. He presented with lost weight, dehydration without vomit, diarrhea or hyperpigmentation. He was admitted with the features of cyanosis, allorhythmic, electrolyte imbalance with sodium of 119 mmol/l, potassium of 7.4 mmol/l. Investigation show pH 7.26, PCO2 34 mmHg, PO2 110 mmHg, HCO^-_3 18mmol/l, BE -10, plasma 17OHP level: 2,4 ng/ml, testosterone level: 1.94 nmol/l, Cortisol 8am: 2662,8 pmol/l, Ure 7.4 mmol/l, Creatinine 44.2 umol/l, Glucose 4.8 mmol/l. the urine steroid metabolomics analysis showed extensive excretion of aldosterone ID-ISTD1 of 1157.41 µg/l. Novel homozygous mutation (c.1668C>A; p.S556R) of SCNN1A gene was identified in the proband. He was treated with florinef of 0.1 mg/kg/day for electrolyte balance. He had complication of intestinal perforation and died due to infection. In conclusions, PHA1 causes severe hyponatremia, metabolic acidosis, and life-threatening hyperkalemia, with normal 17-a-hydroxyprogesterone levels and high excretion of aldosterone levels.

Written informed consent was obtained from the patient's parent or guardian for publication of this Case report (and any accompanying images). A copy of the written consent is available for review by the Editor-in-Chief of this journal.