Diabetes mellitus is one of the most common chronic diseases worldwide and is associated with an increased morbidity and mortality. Diabetes is characterized by chronic hyperglycemia and alterations of cellular homeostasis, which lead to diffuse vascular damage. The microvascular complications of diabetes, resulting from a damage of the microvasculature of the kidney, retina and neurons, include retinopathy, nephropathy and neuropathy. As a consequence of microvascular pathology, diabetes is an important determinant of blindness, end-stage renal disease and a variety of debilitating neuropathies. In addition, diabetes is associated with cardiovascular disease, which is an important contributor to the overall morbidity and mortality associated with this condition.

Several risk factors are implicated in the pathogenesis of diabetic complications and they can be either modifiable (glycemic control, hypertension, dyslipidemia, diet, smoking) or non-modifiable (diabetes duration, age at onset, puberty, genes).

The pathogenesis of diabetic vascular complications is complex, with the involvement of several mechanisms and a clear contribution of genetic factors. Hyperglycemia is a key determinant of vascular complications of diabetes and there is extensive evidence showing that both acute and chronic hyperglycemia has a deleterious effect. Hyperglycemia contributes to the development of vascular complications through several mechanisms: activation of the polyl and hexosamine pathways, activation of protein kinase C, increased oxidative stress, increased production of advanced glycation end-products, increased synthesis of growth factors, cytokines and angiogenins II. These factors can, in turn, induce a diffuse endothelial dysfunction and contribute to the progressive development of micro- and macrovascular complications and multiorgan damage. Growing evidence suggests that increased oxidative stress, induced by several hyperglycemia-activated pathways, is a key factor in the pathogenesis of endothelial dysfunction and vascular disease. Several mitochondrial and other intracellular pathways are implicated in the increased production of oxidants, which is often associated with reduced antioxidant defences. In addition, recent studies suggest the involvement of epigenetic mechanisms as well as of microRNAs in the pathogenesis of diabetic complications.

The understanding and characterization of the molecular mechanisms underlying the development of vascular complications of diabetes is of paramount importance as this could help the development of better preventive and treatment strategies.

References

New insights into disorders of gonad development using whole genome analysis
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One of the most fundamental influences on our lives is our sex. Whether we are born as male or female has an enormous impact on our behaviour, reproductive options and disease susceptibility. Consequently, if the sex of a baby is not clear it can create many intractable issues, particularly in terms of medical management. Disorders of Sex Development (DSDs) are congenital conditions in which development of chromosomal, gonadal or anatomical sex is atypical. The cause of these problems is most often a breakdown of the complex network of gene regulation responsible for proper development of testes or ovaries in the embryo. In the majority of DSD patients the etiology is unknown and they cannot be given an accurate diagnosis. We aim to identify the underlying changes in gonad genes of these DSD patients, provide a diagnosis and gain insights into gonad development.

We used microarrays to detect changes in copy number in DSD patients. This approach identified potential novel testsis specific regulatory regions in SOX9, a known testis gene. We also showed that deletions and duplications affecting the regulatory sequences of SOX9 can cause it to be ectopically expressed in the developing gonad, allowing it to drive testsis development in the absence of SRY in patients with 46,XX testicular DSD. In addition, we have identified mutations in the novel gene, MAP3K1, in patients with 46,XY DSD; implicating a new signal transduction pathway in testsis development.

We’ve used Massively Parallel Sequencing (MPS) in three different ways. Firstly, we developed a rapid targeted MPS approach allowing in depth sequencing of up to 200 gonad genes per DSD patient. Secondly, we used whole exome capture and MPS on several DSD families, trios and single cases. Finally, we employed whole genome MPS on trios with DSD. This work demonstrates the tremendous power of whole genome approaches, especially when combing MPS data with linkage analysis of a
large family. Whole genome analysis provides a rapid approach to identification of the disease-causing mutations and molecular diagnosis in patients with DSD as well as providing insights into gonad development and sex differentiation.

O3
Factors involved in the development of the metabolic syndrome. We are what we eat and what we are eating
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A variety of metabolic and molecular changes in brain and adipose tissue play a critical role in the pathophysiology of life style-related metabolic diseases [1-3]. Even in obese subjects with insulin resistance in skeletal muscle and liver, insulin action on adipose tissue remains intact or rather exaggerated, resulting in considerable difficulties in weight reduction. Excess in circulating insulin thus causes body fat gain as well as ectopic lipid overload in liver, skeletal and cardiac muscle, pancreatic mice overfat. The adipocyte hormone, leptin controls feeding behavior, augments fatty acid β-oxidation in the skeletal muscle and enhances whole body insulin sensitivity, thereby serving as a promising therapeutic candidate for the treatment of obesity-diabetes syndrome. However, the clinical application of leptin has been hampered by the notion that leptin does not fully exert its metabolic effects in subjects with fat diet-induced obesity [4-6]. It is important to note that the future risk of cardiometabolic diseases exists for infants with low birth weight/intrauterine growth retardation (IUGR). IUGR causes a premature leptin surge in the neonatal period in mice, and conceivably, through a number of epigenetic mechanisms, it may induce hypothalamic leptin resistance in adulthood. Mechanisms of non-genomic, intergenerational transmission of metabolic diseases from parents to children have also been unveiled in an expeditious fashion. The endoplasmic reticulum (ER) is an intracellular organelle involved in protein folding and apoptosis. The accumulation of misfolded proteins in the ER, termed as ER stress, is involved in the molecular pathophysiology of type 2 diabetes and metabolic syndrome. Our recent research in mice demonstrated that high fat diet-induced ER stress in the hypothalamus plays a pivotal role in the preference for fatty foods and resultant increase in body weight. We provided the first evidence that brown rice and its major component, γ-oryzanol, ameliorate glucose dyshomeostasis in mice fed high-fat diet (HFD), accompanied by reduction of hypothalamic endoplasmic reticulum (ER) stress [7]. In my talk, I try to review the update of mechanisms of metabolic endobesity syndrome, with a particular focus on the molecular food sciences.

References

O4
Implementing evidence-based medicine practice in Indonesia: before, now, and the future
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Evidence-based medicine (EBM) is considered as one of the greatest inventions in modern medicine, advocating the use of the best available valid evidence, in line with clinical expertise and patients’ preference, to provide the best patient care. The philosophy probably has existed since the earliest age of medicine, but it was not until 1972 when Professor Archie Cochrane introduced the concept in one of his book, after which it was developed into a practical methodology by a group of scientists in the late 1980s and early 1990s. The work of EBM in Indonesia was first initiated in the early 2000s by conducting a series of intensive trainings at various medical teaching centres all over Indonesia. Most of the pioneers of EBM dissemination in Indonesia are paediatricians. Since then, teaching activities have been flourishing, leading to the formal incorporation of EBM into medical curriculums in some medical schools. Collaborations with similar centres in Europe and Asia have a positive impact. Efforts are also being made in promoting the application of EBM principle in daily practice, such as in ward rounds, journal readings, and case discussions, both in undergraduate and postgraduate education settings. The term and practice of EBM have become very familiar for most health professionals in Indonesia, although occasionally it is misinterpreted in a narrow perspective, seeing evidence as the single factor determining health care. However, the implementation of EBM in clinical practice sometimes is hampered by the scarcity of relevant valid evidence like those happening in the field of paediatric endocrinology. This requires the transition of EBM practice in the future, in which health professionals do not merely act as evidence users but also play roles as evidence producers by conducting more patient-oriented research relevant to actual health problems. This is indeed very important, since most of the evidence available comes from studies in Western countries. Indonesian Clinical Epidemiology and Evidence-based Medicine (ICE-EBM) Network which currently has more than 30 member institutions has an important role in the acceleration of evidence-based practice in Indonesia.

SYMPOSIA – GROWTH

O5
DICER1 familial cancer syndrome: clinical and molecular update
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DICER1 is an RNase endonuclease important for production of microRNAs, which regulate multiple protein-coding genes involved in growth and development. It has been linked to several tumors including pleuropulmonary blastoma (PPB), cystic nephroma, ovarian Sertoli-Leydig cell tumors and thyroid neoplasia. Most of the manifestations of DICER1 mutations occur in young children, adolescents and young adults; only thyroid neoplasia are diagnosed throughout adulthood. Although mutations in this gene behave as autosomal dominant tumor suppressor genes, the penetrance of the various tumors is highly variable, rendering screening and genetic counseling challenging. We have recently hypothesized that mutations in this gene are also responsible for the very rare but often fatal cases of infant (<3y) Cushing Disease, which can be missed initially because of absent or only minimal signs of intracranial hypertension and hypocortisolemia in this age group. Eye signs, such as strabismus or proptosis, may be the first manifestations of these tumors. The ACTH-producing pituitary tumors seen in these infants have a histopathology and electron microscopy that has been termed pituitary blastoma. The incomplete penetrance of this and the other manifestations of the syndrome makes the involvement of
additional predisposing factors likely highly, candidates of which are under investigation.
This presentation will highlight the cardinal features of this new familial cancer syndrome, review the molecular biology of DICE1, consider additional polygenic influences on tumor development and discuss the current recommendations for following these families.

06
The growing controversy about growth charts: WHO or regional?
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Introduction: Since production of WHO Multicenter Growth Reference Study (MGRS) growth standards in 2006, many countries have adopted the WHO charts for under five children [1]. In UK, WHO growth charts are used until 4 years [2] and in US only up to 2 years of age. Over-diagnosis of stunting and underweight in Asian children is likely with the use of these standards as Asian children are still thinner and lighter.

Growth standard vs. reference: A growth reference simply describes the growth of an average population, whereas a standard describes the growth of a ‘healthy’ population and suggests an aspirational model. WHO growth charts are growth standards. A reference is representative of the existing growth pattern of children and suggests us to study the secular trends in height, weight and obesity.

Advantages of WHO growth charts: WHO growth standards have given a platform to compare growth of under five children across all races and ethnicity against a single standard, thus assessment becomes objective and easy. They show more physiological growth pattern as the children in MGRS study were breast fed and hence leaner, promoting prevention of obesity from a younger age. The MGRS provides an unsurpassed foundation for a growth standard based on healthy children living under conditions that favored the achievement of full genetic potential.

Disadvantages of WHO growth standards: In developing nations the WHO 2006 standards tend to over-diagnose stunting and wasting. In a nationwide study done by the author on apparently healthy affluent Indian children the percentage of stunting was 13.6% for boys and 11.2% for girls and that for wasting was 8.5% for boys vs. 10.4% for girls [3]. Similar concerns are expressed by authors from other developing countries such as Indonesia [4], and Malawi [5]. In a study done by Kerac et al on data from 21 countries it was concluded that use of WHO standards to define wasting results in a greater disease burden, in children under the age of 6 months [6].

Conclusion: WHO 2006 growth standards are useful for comparison of growth of children around the world but caution regarding referral for investigations of failure to thrive, changing infant feeding policies and intervention programs based on WHO 2006 standards for the developing part of the world is needed at least for the present time.

References

07
Management of rasopathies
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Noonan syndrome (NS) and NS-related disorders (Cardio-Facio-Cutaneous (CFC) syndrome, Costello syndrome, LEOPARD (Lentigines, ECG conduction abnormalities, Ocular hypertelorism, Pulmonary stenosis, Abnormal genitalia, Retardation of growth and sensory neural Deafness) syndrome) share common clinical features characterized by unique facial features, postnatal growth failure, psychomotor retardation, ectodermal abnormalities, congenital heart diseases, chest & skeletal deformity and delayed puberty. During last decade, student progress has been made in molecular understanding of NS. The functional alterations of the Rasmitogen-activated protein kinase (MAPK) pathway are caused by the mutation in more than 10 genes (PTPN11, SOS1, RAF1, SHOC2, BRAF, KRAS, NRAS, HRAS, MEK1, MEK2). Thus, NS and NS-related disorders are called Rasopathies as a disease group. PTPN11 (40-50%), SOS1 (10%-20%), and RAF1 (3%-17%) mutations are common in NS patients. Noonan syndrome and its related disorders are not rare as a whole. Since their disease natural course and management are different, it is important to recognize Rasopathies and differentiate them primarily based on typical clinical condition. By utilizing DNA testing, the confirmatory diagnosis can be made. Multi-systemic involvement in Rasopathies requires multidisciplinary evaluation and regular monitoring for each special clinical issue. It involves whole spectra of clinical issues of cardiovascular, growth & endocrine, neuro-cognitive, developmental, skeletal & orthopedic, ophthalmo-otolaryngological, GI-nutritional, dental, hemato-oncological and ectodermal systems. For instance, surgical intervention is required for congenital heart defects and cryptorchidism. Before the surgery, bleeding diathesis should be excluded. Also the risk for malignant hyperthermia has to be considered in choosing anesthetics. Special education might be required in 10-40% of NS patients. However, NS patients carrying the mutation in the SOS1 gene and N380D or N380S mutation in the PTPN11 gene tend to show normal cognitive function. Many NS infants have feeding difficulties with poor suck and prolonged feeding time and may require tube feeding in 24% of NS infants. Most NS patients show normal levels of IGF-1 and IGF-BP3, indicating growth hormone (GH) deficiency is not culpable for postnatal growth failure. However, some studies have demonstrated subnormal overnight mean growth hormone concentration, suggestive of impaired GH secretion. The rhGH therapy in NS has been reported to be effective to improve both the height velocity and the final adult height. In this review, the constellation of overlapping clinical features of Rasopathies will be described based on genotype as well as their differential diagnostic points and management.

SYMPOSIA – PUBERTY

08
Endocrine disrupter effects on the gonads and puberty
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Evidence accumulating the past decades indicates that human populations are exposed to environmental chemicals interfering with endocrine systems. There is growing concern of the potential adverse impact of exposure to such endocrine disrupting chemicals (EDCs) on human health, based on observations in wildlife, animal model systems and reports of yet unexplained increased incidences of hormone related disorders in humans. Exposure in fetal and neonatal age may be associated with developmental and reproductive disturbances due to interference with the programming of normal hormone signaling and metabolic pathways. Boys are conceived to be more vulnerable than girls due to their more complicated and androgen driven prenatal sex differentiation.
Male prenatal sex differentiation is crucially dependent on the functioning of fetal Leydig cells. Exposure of these cells to EDCs at critical time windows of development may result in undermasculinization and disorder(s) of sex development (DSD), such as hypospadias, cryptorchidism and ambiguous genitalia. Furthermore, a novel trend of earlier start of puberty has been found during the past few decades, at least in some regions and mostly affecting girls. Among plausible causes behind this phenomenon it has been suggested that exposure to EDCs affecting the programming or triggering of the pubertal clock could result in premature activation of gonadotropin secretion. Another hypothesis is that gonadotropin independent effects of EDCs are associated with an earlier start of puberty. Proof of principle of such potential roles of EDCs has been obtained from a multitude of studies in experimental animals and gained some support by case studies, exposure data and epidemiological investigations in humans. This presentation will review recent data and ongoing studies on the mechanism(s) of action of EDCs, including effects of mixtures, on the hypothalamic-pituitary-gonadal axis in experimental animals and humans. The impact of genetic susceptibility on the degree of disrupting activity caused by certain EDCs will be discussed on the basis of ongoing animal studies.

**The gonadal effects of diabetes**

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The functional reproductive alterations seen in women with type 1 diabetes (T1D) have changed as therapy has improved. Historically, patients with T1D and insufficient metabolic control exhibited a high prevalence of amenorhoea, hypogonadism, and infertility. Recent publications have shown that in spite of intensive insulin therapy, some delay in the age of thelarche, pubarche and menarche is still observed in girls with T1D. In addition, ovarian hyperandrogenism may be observed during late adolescence and an increased prevalence of hirsutism and polycystic ovarian syndrome (PCOS) has been described in adult women with T1D. These endocrine abnormalities may be related to non-physiologic insulin replacement therapy and to hyperglycemia.

Insulin is well known for its effects on carbohydrate metabolism, but this hormone also plays an important role in regulating ovarian function. Granulosa, theca and stromal ovarian cells may be affected by insulin deficiency or excess, which may be present in women with type 1 diabetes mellitus (T1D) [1]. Diabetes disrupts hypothalamic-pituitary-ovarian function, as documented by animal model studies which have helped to decipher the underlying basis of these conditions and have highlighted the variable contributions of defective leptin, insulin and kisspeptin signalling to the mechanisms of perturbed reproduction in T1D [2].

Effects of diabetes on gonadal function vary according to the age of the patient. Young girls during adrenarche exhibit an elevation of DHEAS, androstenedione, inhibin B and anti-mullerian hormone [3], an endocrine profile that is similar to the one observed in young girls in risk of developing polycystic ovarian syndrome later in life. During puberty a delay in pubertal development has been described which is followed by menstrual irregularities and hyperandrogenism during adolescence [1,4,5]. Despite these abnormalities in ovarian function, ovulatory functions is preserved in adolescents with type 1 diabetes [6]. Later in life, adult women with type 1 diabetes exhibit PCOS, polycystic ovaries at the ultrasonographic exam, menstrual irregularities and early decline in ovarian reserve [7-9].

Clearly, despite improvements in insulin therapy, T1D patients still suffer several significant clinical problems, such as pubertal delay, menstrual disturbances and hyperandrogenism which may ultimately lead to the development of PCOS in adulthood. (Fondecyt 1100123 y 1050452)

**References**


**Management of precocious puberty**

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The objectives of treatment for children with central precocious puberty (CPP) are to avoid psychosocial problems caused by early pubertal development and to normalize adult height (AH). A long-acting GnRH analog is the treatment of choice for CPP. GnRH analog administration effectively arrests further development of secondary sex characteristics, slows bone age (BA) maturation, increases pubertal height gain, and is believed to eventually improve AH prognosis. However, the improvement of AH is not well established. It is reported that GnRH analog is effective to improve adult height only in early onset (girls <6 years) CPP [1]. Although BA maturation is decelerated by suppressing gonadotropins with GnRH analog and pubertal period is elongated, growth rate diminishes due to suppressed sex steroid hormone and, in part due to decreased GH secretion. For the evaluation of efficacy of GnRH analog for adult height improvement, one problem is that the prediction method for adult height in CPP is not established. It is reported that predicted adult height (PAH) using the Bayley-Pinneau table for accelerated BA overestimated AH in untreated patients with CPP, and the PAH based on the projected height SD score for BA is useful [2]. Most Asian countries use a starting dose of 100 µg/kg/month of leupropride acetate depo [3]. During GnRH analog treatment, serum concentrations of LH, testosterone or estradiol should be monitored as well as pubertal changes and bone age, height and height velocity. For some older patients, a dose of up to 180 µg/kg/month of leupropride acetate depo is necessary to suppress LH concentration less than 0.5 mIU/ml. When growth velocity is decreased, possible options is to add growth hormone or anabolic steroid hormone only in boys.

The decision to stop therapy should be individualized and based on various factors such as growth velocity, bone age, chronological age, predicted adult height, emotional maturity, and patient’s wish. After treatment discontinuation, long-term follow up is recommended for adult height, reproductive function and bone mineral density.

**References**


SYMPOSIA - DIABETES

O11
Evidence based care of type 1 diabetes in the asia pacific region
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Through advances in therapy and technology, the quality of life, morbidity and mortality outcomes in people with type 1 diabetes continue to improve in countries with well-developed health-care systems, but major disparities in diabetes care exist globally. Ideally, an individual with type 1 diabetes should be managed by a multidisciplinary healthcare team delivering integrated clinical care. Essential to the delivery of optimal diabetes care is education of health care teams, individuals, the community and policy makers. Evidence based clinical care guidelines are an important component of such education. However, while guidelines provide guidance for the practice of evidence based care at the organisational level, evidence based medicine requires the integration of research evidence with clinical expertise and patient values. Since many aspects of health care depend on individual factors such as quality of life, guidelines should be used in the context of the health-care needs and circumstances of each individual with diabetes. Globally, the practicality of implementing evidence based recommendations also depends on the health system structure, availability of resources, economic considerations and socio-cultural factors.

There are a range of guidelines available for the management of young people with type 1 diabetes, including those produced by NICE, ADA, ISPAD and IDF. In Australia, evidence-based guidelines for management of type 1 diabetes across the lifespan were launched in November 2011 [1]. Through the collaborative efforts of the Australasian Paediatric Endocrine Group (http://www.apeg.org.au) and the Australian Diabetes Society (http://www.diabetessociety.com.au), the guidelines address key aspects of diabetes care, based on the best available evidence at the time of writing. The guidelines are structured around clinical questions addressed by systematic reviews and meta-analyses. Notably, evidence for rapidly evolving areas such as use of technologies (pumps, continuous glucose monitoring) is constantly changing. Furthermore, there are aspects of care for which there is little or no evidence, so management is based on best practice or consensus. The applicability of these and other contemporary guidelines to the Asia Pacific Region will be reviewed.

Reference

O12
Increasing incidence of DM type 1 in Indonesia
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Diabetes Mellitus (DM) is one of the most frequent chronic diseases affecting children and adolescents. The number of children being diagnosed with diabetes - regardless to the type of diabetes - is increasing worldwide. It has become a major health problem in both developed and developing countries. The World Health Organization (WHO) data show a prominent worldwide variation in incidence of T1DM from 0.6 per 100,000 in Korea and Mexico to 35.3 per 100,000 in Finland. In Asia, the incidence of type 1 DM is extremely low, from 0.1, 0.6, and 2.4 per 100,000 people per year in China, Korea and Japan. Besides type 1 DM, the incidence of type 2 diabetes among children and adolescent is also increasing worldwide. This can be a result of increasing obesity in these population as recent evidences show a strong relationship between childhood obesity and the development of insulin resistance in early adulthood.

Indonesia is the world’s largest archipelago consist of more than 18,000 island. Despite the huge child population in Indonesia which reaches more than 83 million, prevalence of diabetes in Indonesia is still unknown. Very small number of identified cases found through hospital records has not revealed the real burden of this disease as increased cases were found throughout the years. Indonesian Pediatric Society found 825 type 1 DM children from their registration program all over Indonesia during 41 months registry period (February 2009-July 2012, with diagnosis period from 1991 to 2012). Based on our registry data, overall incidence rate of type 1 DM in 2000 was 0,00388 per 100,000 population with 0,00292 per 100,000 male population and 0,00483 per 100,000 female population. In 2010, the overall incidence rate increased to 0,02819 per 100,000 with 0,03884 per 100,000 male population and 0,01761 per 100,000 female population. This increasing can be a result of increased awareness of type 1 DM among health providers and general public, therefore there is improvement in capacity of detecting and managing type 1 DM in Indonesia.

O13
Chinese children’s diabetes status, trends and hardship
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Diabetes mellitus is now fast emerging as one of the biggest health catastrophes the world has ever witnessed. It has huge global and societal implications, particularly in developing countries such as China and India [1]. China is now bring with it potential massive increase in type 1 diabetes (2-5% per annum increases in incidence in the world’s most populous countries) and childhood obesity (with its associated insulin resistance and type 2 diabetes) [2]. A nine-year prospective study on the incidence of childhood type 1 diabetes mellitus in China by the WHO DiaMond Project China Participating Center and Chinese Academy of Preventive Medicine (CAPM) showed that between 1998 and 1996, the overall incidence rate (IR) was 0.59 per 100,000 person-year. The IR was 0.52/100,000 (95% CI: 0.50-0.54) for males and 0.66/100,000 (95% CI: 0.64-0.68) for females [3]. We recently conducted a nationwide study to evaluate the state and the trend of diabetes based on hospital inpatient data from China’s 14 medical centers and pre-diabetes among obese children from October 1995 through September 2010. We found that in the past 15 years, the prevalence of Chinese childhood diabetes increased dramatically and the growth of T2DM has exceeded T1DM. T1DM has occurrence rate of 89.6% of all diabetes and is still the dominant form of diabetes in children. The prevalence of T1DM was relatively stable from the year of 1995 to 2005, but increased obviously in the recent 5 years according to the hospital records in China. The clear increasing trend from Southwest to East and North disclosed strong regional differences (T1DM from 59.76 to 80.02 and 120.45, T2DM from 2.52 to 3.77 and 15.64 (1/100,000)) (p < 0.0001). Well developed areas had a higher prevalence compared to less developed areas (T1DM: 151.51 vs. 32.2; T2DM: 15.16 vs. 1.64 and other types: 7.54 vs. 0.42 (1/100,000)). An important finding in this study is that the prevalence of childhood T2DM in China doubled from 4.1/100,000 in the first 5 years to...
10.0/100,000 in the recent 5 years, which was 7.44% of total diabetics. Though the ratio is still lower than that of America (8%-46%) [4], the trend is clear and the consequences are serious because China has the largest population in the world. Another important finding in this study showed obese children are potential pools of T2DM. Of the 3153 obese children, 18.24% had IFG alone, 5.99% had IGT, 4% had combined IFG and IGT.

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References

SYMPOSIA – ESPE

014
How safe is growth hormone treatment during childhood?
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Since the introduction of recombinant human growth hormone (GH) in the mid-1980s, supplies are almost limitless and predictably GH usage has escalated dramatically. There have been more than 150,000 children treated with GH worldwide with a wide variety of growth disorders.

Adverse events (AE) with all forms of drug therapy are markedly underreported, considerably underestimating the incidence of the AE. This under-reporting occurs even when the AE is serious and has a possible or probable association with GH therapy. Careful audit of the frequency of reporting of severe AE to other drugs with a possible or probable association with treatment is only 14%. Furthermore missing data is very common and adds to the difficulty in interpreting AE.

Important conditions (adverse events) possibly linked to GH treatment are fortunately rare. There are several major limitations to accurately assessing the prevalence and risk of rare adverse events. Firstly, extremely large datasets are required found in large databases such KIGS and NCCLS each with >50,000 enrolled patients. Secondly, accurate risk assessment of the possible adverse event in an untreated population that matches the GH treated population has rarely been determined.

Important potential adverse events that have received considerable attention will be addressed. These include: tumour recurrence, new malignancies including leukaemia, diabetes mellitus, benign intracranial hypertension and slipped upper femoral epiphyses. The physiological rationale and the risk of these conditions during GH treatment will be addressed.

Serum IGF-I monitoring to prevent elevated levels that may further increase the risk of adverse events is recommended. The potential adverse consequences of sustained elevated serum IGF-I levels will be discussed. In addition, monitoring IGF-I helps to monitor compliance of GH therapy in children with GH deficiency.

Although short term health on growth hormone treatment has been extensively studied, little is known of the long-term health of subjects treated with growth hormone in childhood. Approximately 40,000 children are treated with growth hormone in the European Union and several hundred thousands in the world and it is essential to address this important question. SAGhE is an European consortium aimed at addressing this question as well as to gain further insight in the long term effect of growth hormone both in terms of height and of significance on quality of life.

SYMPOSIA – ENDOCRINE EMERGENCIES

016
DKA management and outcomes
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Diabetic ketosis (DKA) is an acute life threatening complication of type 1 diabetes mellitus (T1D). DKA is characterized by the triad of hyperglycemia, metabolic acidosis and increased total body ketone concentration. These metabolic derangements result from the combination of absolute or relative insulin deficiency and increased levels of counter-regulatory hormones.

DKA is associated with both short-term risks and long-term consequences. Recent data have shown that DKA is responsible for about 15% of cases of death from diabetes. Mortality is predominantly related to the occurrence of cerebral edema, which occurs in 0.3%-1% of patients, whereas only a minority of deaths in DKA is due to other causes.

DKA represents the initial manifestation of T1D in 13-80% of cases and it can also occur in 25% of cases of type 2 diabetes at onset. In addition, DKA is a common complication in patients with known diabetes, where it may be the consequence of illness, poor compliance, or malfunction of diabetes care equipment.
Early identification and treatment of DKA are two key points to minimizing the risks of this complication. Children with DKA should be treated in experienced centers and adherence to guidelines for the management of this condition is of paramount importance. Treatment of DKA requires strict monitoring of the patient, correction of hyperglycemia, acidosis and ketosis and replacement of fluid and electrolytes losses. Another important point is the identification and treatment of precipitating events. Early recognition of signs indicative of cerebral edema is essential to prevent the morbidity and mortality associated with this complication. Cerebral edema occurs in 0.3-1% of patients in DKA and represents the most common cause of mortality in children with DKA, accounting for 60-90% of all DKA deaths. In addition, 10-25% of survivors have significant residual morbidity. The etiology of cerebral edema is poorly understood, but it is likely related to vasogenic, osmotic, and ischemic mechanisms. Prevention of DKA at diagnosis is of paramount importance and should be based on intensive community interventions and education of health care providers to raise awareness. In addition, preventive strategies should be applied to avoid episodes of DKA in patients with an already known diagnosis of diabetes. This requires patient education and access to specific diabetes programs and services.

References

O17 Investigation and management of acute hypoglycemia
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Since prolonged severe hypoglycemia could lead to permanent neurological sequelae, it must be treated immediately. But at the same time, the cause of hypoglycemia should be determined to prevent future recurrence of hypoglycemia preferably at bedside while the patient is still in an emergency room. Most of the cases, this could be done by asking proper questions and taking physical findings in parallel with the treatment, without waiting for the detailed results of critical samples. In taking history of the patients, one should not forget to ask the following questions: (1) preexisting medical problems (especially diabetes mellitus, CNS tumors, adrenal insufficiency, hepatic failure, arrhythmia, citrin deficiency or chronic infections), (2) medication history (especially insulin, oral hypoglycemic agents, beta-blocker, disopyramide, or extended use of antibiotics containing pivalic acid), (3) timing of hypoglycemia following the last meal (VERY important). In taking physical findings, presence or absence of hepatomegaly and circumulatory collapse is the most important. Hypoglycemia within 2-3 hours after meal almost invariably suggests the presence of hyperinsulinemia. Hypoglycemia caused by a defect in gluconeogenesis typically occurs 5-8 hours following the last meal and is usually accompanied by hepatomegaly. Recurrent episodes of hypoglycemia after an overnight fast likely suggest a problem in gluconeogenesis. Circulatory collapse at hypoglycemia suggests the presence of adrenal insufficiency. IV steroid in addition to IV glucose should be considered to prevent neurological sequelae. Critical samples should be taken at the time of hypoglycemia to make a causal diagnosis. Although the turnaround time of endocrine tests or tandem mass-spectrometry is usually long, results available on site often give a clue to the diagnosis. Relatively low ketone bodies by urine dipsticks suggest the presence of hyperinsulinemia or rare disorders of fatty-acid oxidation defects. Hyponatremia accompanied by hyperkalemia suggests primary (not secondary) adrenal insufficiency. Response to initial therapy also gives an important clue to the diagnosis. The need to continue IV glucose over normal resting hepatic glucose production to maintain normoglycemia (4-6 mg/kg min in neonates) strongly suggests the presence of hyperinsulinemia. Never infuse too much glucose to the patients which could obscure the diagnosis. Finally, I will spend some time to show current state-of-the art in the diagnosis and management of congenital hyperinsulinism and discuss how the patients should be managed in the Asia-Pacific region.

**MANAGEMENT SESSIONS**

O18 Longterm endocrine effects of cancer
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Survival after childhood cancer has increased over the last 25 years with around 80% overall survival but outlook is not trouble free. Within 25 years of diagnosis, 4% will have a second tumour. Cardiotoxicity from anthracyclines, radiation related health problems and endocrine deficiencies all contribute to increased mortality, with 18% reported to have died 30 years after diagnosis. Memory processing deficits after childhood cranial radiation result in additional burdens of intellectual, psychosocial and emotional disability. Endocrine late effects of radiation and chemotherapy can be direct, resulting in hypofunction of endocrine glands or indirect resulting in metastasia, cancer and altered bone growth. Deficiencies of hypothalamic pituitary hormones can be expected in 60-100% of patients by 8-10 years after radiation exposure. Pubertal timing and tempo is altered by cranial radiation, with combinations of early puberty and growth hormone deficiency causing diagnostic and management confusion. Evolution of hormonal losses need be recognized. Gonadal dysfunction occurs after both radiation and chemotherapy at any age. The prepubertal tests is not protected from effects of chemotherapy. Age at treatment, type and dose all predict outcome. Loss of function in germinal epithelium and Leydig cells is not reflected in gonadotrophin alterations until age 9-10 years. Abnormal timing of menarche in survivors of central nervous system tumours is common. Follicular reserve is low in young females after cancer treatment is reduced with high risk for premature menopause and little evidence that the ovary can be protected from insult, although 50% of children exposed to early radiation or chemotherapy retain sufficient gonadal function to initiate or complete puberty. Preservation of gonadal tissue prior to cancer treatment is now taking place with semen storage, or gonadal biopsy being offered or considered in both sexes before exposure to gonadotoxins. However, fertility recovery can occur and appropriate contraceptive needs must be met. Cerebral arteritis occurs after brain radiation, with early cerebrovascular accident. HRT may need to be tailored to reduce this risk. Solid organ radiation exposure is hazardous. Thyroid cancer after radiation exposure occurs at 20 times population risk, with regular thyroid ultrasound every 2 years now recommended and FNA as required. Pelvic radiation results in poor pregnancy outcomes with increased foetal loss and small for dates infants. Bladder risks for cancer treatment and taking physy, with semen storage, or gonadal biopsy being offered or considered in both sexes before exposure to gonadotoxins. Long term endocrine effects of cancer can be direct, resulting in hypofunction of endocrine glands or indirect resulting in metastasia, cancer and altered bone growth. Deficiencies of hypothalamic pituitary hormones can be expected in 60-100% of patients by 8-10 years after radiation exposure. Pubertal timing and tempo is altered by cranial radiation, with combinations of early puberty and growth hormone deficiency causing diagnostic and management confusion. Evolution of hormonal losses need be recognized.
019
The management of skeletal dysplasia
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Skeletal dysplasia (SD) is disorders of bone and cartilage development caused by genetic defects. It comprises more than 300 specific disorders [1]. Causative genes responsible for SD include those encoding the bone and cartilage matrix proteins, receptors and intracellular molecules involved in signaling pathways of chondrocyte and osteoblast, specific transcription factors, enzymes involved in bone and cartilage metabolism, cell surface ion channels, and so on. Recently, many novel causative genes have been discovered with the help of whole exome sequencing, whose protein product has function not been well elucidated. SD had been classified according to their clinical and radiologic phenotype, however with discovery of causative genes, nosology and classification has evolved over the last several decades based more on the genotype. Correct diagnosis is the starting point of optimal management of SD, but it can be very difficult in some cases. One should not hesitate to consult to SD specialists in order to make correct diagnosis. Common clinical problems in the skeletal system that interfere with patients’ daily life include short stature, limb deformity, spine deformity, C1-2 instability, and precarious osteoarthritis. Only few medical treatments effective for SD have been established. Bisphosphonate for osteogenesis imperfecta was the most successful medical treatment so far. Hence, the management of SD is still largely surgical intervention and rehabilitation. Orthopedic correction of the limb deformity can improve not only cosmesis, but also patients’ locomotive function. Distraction osteogenesis by ilizarov principle makes complex deformity correction possible, and asymmetrical physeal suppression enables minimally invasive correction of the deformity. Bilateral limb lengthening for height became popular since 80’s, but considering its high rate of complication, surgical indication should be narrowed and the surgery should be discussed thoroughly with the patient and parents preoperatively. Many SDs provoke hip problems and various surgical interventions have been applied, but most of them are anecdotal cases with varying outcomes. Atlantoaxial instability may result in a serious outcome, either acutely or chronically. Great attention should be paid to this condition. Surgical intervention of SD is one of the most challenging areas in orthopedic field, and will evolve with advance of orthopedic technology.

Reference

ORAL SESSIONS
020
Aromatase excess syndrome: a model for genomic disorder: identification of molecular bases and phenotypic determinants
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Aromatase excess syndrome (AEXS) is a rare autosomal dominant disorder characterized by gynecomastia. Although chromosomal inversions leading to abnormal fusion between CYP19A1 coding exons and non-coding exons of neighboring genes have been identified in a few patients with AEXS, its molecular basis and clinical spectrum remain largely unknown. We studied 18 affected males from six unrelated families A–F, and found a heterozygous 77.5 KB tandem duplication involving seven of 11 non-coding exons of neighboring genes have been identified in a few patients with AEXS, its molecular basis and clinical spectrum remain largely unknown. We studied 18 affected males from six unrelated families A–F, and found a heterozygous 77.5 KB tandem duplication involving seven of 11 non-coding exons of CYP19A1 in exons 1 at the distal non-physiological position can also function as transcription start sites, and that the two deletions produced the same chimeric mRNA constituted by DMXL2 exon 1 and CYP19A1 exons 2–10. Clinical features such as gynecomastia and elevated estradiol/testosterone ratios were milder in patients with duplications and deletions than in those with inversions. Furthermore, genotype-phenotype correlations in patients with duplications, deletions, and inversions implies that phenotypic severity of AEXS is primarily determined by the expression pattern of CYP19A1 and the chimeric genes and by the structural property of the fused exons with a promoter function (i.e., the presence or absence of a natural translation start codon). The present study expands the genetic mechanism and phenotypic spectrum of AEXS, and provides novel models for genomic disorder leading to gain-of-function mutations. We also discuss on the effect of estradiol on the hypotalamic-pituitary-gonadal control.
time- and concentration-dependent as assessed by CCK-8 assay, Hoechst 33342/Pl, flow cytometric cell apoptosis assay and electron microscopy. PALmitate triggered ER stress and apoptosis in INS1 cells as evidenced by increased mRNA levels of CEBP homologous transcription factor (CHOP), activating transcription factor 4 (ATF4) and B box-binding protein 1 (XBP-1) in a time-dependent fashion. Western blot analysis also showed significant increase of CHOP and caspase-3 in protein level. We also found that palmitate activated GSK3β by inhibiting phosphorylation at serine 9. While chronic, not acute, 1–2mM VPA and 2mM LiCl remarkably reduced palmitate-induced cytotoxicity. Furthermore, INS1 cells treated with 10–20μM T22D-8, a specific GSK3β inhibitor, also elicited cytoprotective responses against 0.25–0.5mM palmitate for 6–48h and decreased mRNA level of CHOP, but not ATF4 or XBP-1. The protein levels of CHOP, caspase-3 and GSK3β activity were remarkable reduced by co-treatment of INS1 cells with 0.25mM palmitate and 1mM VPA, compared with 0.25mM palmitate only. Finally, down-regulation of CHOP expression in INS1 cells by small interfering RNA (siRNA) did not show apparent cytoprotective responses against 0.25mM palmitate.

Conclusion: ER stress and GSK3β involved in palmitate-induced (α-cell apoptosis, however, GSK3β other than ER stress is likely playing a more prominent role. Valproate protected pancreatic (β-cell from palmitate-induced apoptosis and ER stress by inhibiting GSK3β.

O22 Early markers of the metabolic syndrome in children born post-term
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We recently showed from a Swedish cohort that nearly half of boys born post-term (≥42 weeks gestation) were overweight or obese at 16 years of age. We hypothesized that post-term children would display features of insulin resistance and the metabolic syndrome even in their pre-pubertal years. 90 healthy pre-pubertal children aged 4–11 years with birth weight appropriate for gestational age were studied: 36 children born post-term (18 boys and 18 girls) and 54 children (36 boys and 18 girls) born at term (38–40 weeks). Insulin sensitivity was measured using Bergman’s minimal model. Other assessments included fasting lipid and hormonal profiles, body composition using whole-body-dual energy x-ray absorptiometry, and 24-hour ambulatory blood pressure monitoring. Insulin sensitivity was reduced in post-term children (8.4±0.74 vs 13.5±0.89 x10−11min−1·(mU/L); p<0.0001). Post-term children had an adverse lipid profile, with higher total cholesterol (4.26±0.17 vs 3.92±0.11 mmol/l; p=0.023) and LDL (2.51±0.13 vs 2.25±0.08 mmol/l; p=0.016) concentrations. Further changes suggestive of the metabolic syndrome among post-term children included an increased android to gynoid fat ratio (0.74±0.03 vs 0.61±0.02; p=0.026), and a reduction in the normal nocturnal systolic blood pressure dip (8.2±1.0 vs 13.8±1.0%; p=0.016). Post-term children also had higher serum leptin (7.18±0.91 vs 3.67±0.41 ng/ml; p=0.011), lower adiponectin (8226±693 vs 10536±556 ng/ml; p=0.046), and lower IGFBP1 (9.56±1.06 vs 18.03±1.59 ng/ml; p=0.032) concentrations.

Our study shows for the first time that post-term children have early features of the metabolic syndrome, including reduced insulin sensitivity, adverse lipid profile, and increased abdominal adiposity.

O23 Neurodevelopmental outcomes are normal in congenital hypothyroidism children diagnosed early and treated aggressively over the first three years
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Despite marked improvements in developmental outcome with newborn screening and early levothyroxine replacement most follow up studies of congenital hypothyroidism (CH) show a persistent mild deficit in total IQ. It has been considered that these deficits in neurocognitive function occur in utero and thus even early therapy cannot completely normalise development. Alternatively the deficits could be caused by delayed diagnosis and inadequate early treatment. In Auckland, early diagnosis occurs via our newborn screening programme along with an aggressive high dose treatment paradigm following referral to the endocrine service. Thus we hypothesised that early diagnosis and aggressive therapy with close monitoring would result in normal neurocognitive outcomes.

Methods: A blinded prospective sibling-matched study was undertaken. Subjects were otherwise healthy children and adolescents aged 4 to 18 years. Exclusion criteria for both CH subjects and sibling controls included chronic illness, other congenital problems or documented developmental delay, cerebral palsy or other disability. Assessments included WPPSI for children under 7 years old, WISC IV for children >7 years and several tests of motor function including the Berry assessment of visual motor function, PPVT and ABC. Auxological data were collected and body composition was assessed using DEXA scans. 49 children with CH and 53 sibling controls were recruited. Control subjects were younger (8.5 vs 10.4 years) but had similar gender proportions (54%female vs 60% female), height SDS (0.81 vs 0.84) and weight SDS (1.05 vs 0.97). In the CH group, 22% had athyreosis, 20% had dyshormonogenesis and 57% had eutopophy. Average time to diagnosis was 12 ± 6.7 days and free T4 was normal by 16.6 ± 5.7 days. There was no difference in Verbal IQ between control and CH subjects (93.6 vs 96.7), Overall IQ (95.2 vs 95.1) although there was a trend to better processing speed in the control subjects (97.3 vs 95.1; p=0.07). There was no difference between groups for motor function although there was a trend to better overall ABC scores in the CH group (60.9 ± 29.8% vs 49.7 ± 29%; p=0.06). There were no differences in body composition between the two groups although BMD trended to being lower in the CH group (0.90 vs 0.98; p=0.067). There was no association with developmental outcomes and the age at diagnosis.

Conclusion, the current Auckland diagnosis and treatment paradigm results in neurocognitive outcomes no different to siblings. BMD was lower in the CH group, possibly suggesting the children have been mildly overtreated.

O24 Serum aminoterminal proctye natriuretic peptide in girls with idiopathic central precocious puberty during GnRHa treatment
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The mechanism of linear growth reduction during GnRHa treatment in central precocious puberty has not been elucidated. Aim: To investigate the pattern of serum amino-terminal proCTy natriuretic peptide (NT proCNP) in healthy girls throughout puberty, and the changes of serum NT proCNP in girls with idiopathic central precocious puberty (ICPP) before and during gonadotropin-releasing hormone analog(GnRHa) therapy. Methods: Serum levels of E2, NT proCNP, insulin like growth factor 1(IGF1), NMID Osteocalcin(OC) and carboxy-terminal cross-linking telopeptide of type I collagen (β-CrossLaps) were measured in healthy 57 girls at different pubertal stages, and in 13 girls with ICPP at the beginning and the end of 6th month and 12th month of GnRHa treatment. Height velocities of the 13 ICPP girls in each 6 months before and after GnRHa treatment was calculated.
Results: Serum NT proCNP level increases as the progress of pubertal development and peaks at the late puberty (P<0.01), paralleling with serum E2, and IGF1 levels, like with the pattern of height velocity. All of serum NT proCNP, Osteocalcin and β-Crosslaps level decrease significantly in ICCP girls at the end of 6th months of GnRHa therapy (P<0.01 or P<0.05), and remain the same low level at the end of 12th month of GnRHa. Different from the aboved markers, serum IGF1 level remains high before and during GnRHa treatment despite growth deceleration.

Conclusions: Linear growth reduction in girls with CPP treated with GnRHa is due at least in part to decreased CPP mediated long bone growth after estrogen inhibition. Serum NT proCNP can be used as a biological marker of long bone growth indicating the activity of epiphyseal growth plate.

O25
Molecular defects of the GNRH receptor gene in Chinese patients with idiopathic hypogonadotrophic hypogonadism and the severity of hypogonadism
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To identify and controlling the frequency of mutations in the coding region of the gonadotropin-releasing hormone receptor (GnRHR) gene in forty Chinese patients with normosmic idiopathic hypogonadotrophic hypogonadism (IHH) and establish genotype/phenotype correlations where possible.

The diagnosis of HH was based on absent or incomplete sexual development after 17 yr of age in girls and 18 yr in boys associated with low or normal levels of LH in both sexes and low levels of testosterone in males and of estradiol in females. All patients presented with a normal sense of smell in an olfactory specific test. 40 IHH patients and 40 controls were screened for mutations in the coding sequence of GnRHR gene. The coding region of the GnRHR gene was amplified by PCR and directly sequenced.

A missense mutation serine168arginine (S168R) located in the fourth transmembrane domain of the GnRHR gene was identified in a homozygous state in one male with complete HH, the S168R mutation has been previously shown to cause in the complete loss of receptor function because hormone binding to the receptor is completely impaired. In another patient, a compound heterozygous mutation (Gln106Arg and Arg262Gln) was identified in a male with partial HH, the Gln106Arg mutation located in the first extracellular loop of GnRHR-R, this mutation decrease but not eliminate GnRH binding, while Arg262Gln mutation located in the third extracellular loop of GnRHR and only decreases signal transduction. A good correlation between genotype and phenotype was found in our patients. The patient, who is homozygous for the completely inactivating S168R mutation, has complete HH. In addition, the affected patient who is compound heterozygotes for the Gln106Arg - Arg262Gln mutations, has partial HH.

GnRHR mutations can be classified into partial or complete loss of function mutations. Partially inactivating substitutions of the GnRHR frequently found in familial hypogonadotrophic hypogonadism are Q106R and R262Q. Comparison of compound heterozygous with homozygous patients suggests that their phenotype and the response to GnRH is determined by the GnRHR variant with the less severe loss of function.

O26
Polyorphism of exon 13 lgr8 gene as risk factors for cryptorchidism in children
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Cryorchidism refers to incomplete descend of the testes into the scrotum with the testes located in the normal tracts. The incident is 5-8% among infants born at term. The complications are infertility and testicular cancer. Cryptorchidism has a multifactorial aetiology and the role of exon 13 lgr8 gene polymorphism remains unclear. This study aims to find the frequency polymorphism of exon 13 lgr8 gene in children with cryptorchidism and to prove as a risk factor for cryptorchidism.

This study is an observational case control study, conducted at the children’s in two general hospital and one maternity clinic from September 2010 until March 2011, with 31 children cryptorchidism as cases and 31 healthy children as controls who were matched by gestational age and age of the child. Polymorphism of exon 13 lgr8 gene was evaluated by sequencing of PCR results at YAYASAN GENERA Ekjman Molecular Biology Institution Jakarta. Frequency was analyzed by percentage, polymorphism was analyzed by paired odds ratio and analyzed by computerized programmes, hypothesis with a confidence interval (a) was accepted if p<0.05.

This study found a percentage of intraabdominal cryptorchidism of 41.94%, inguinal cryptorchidism of 41.94%, and prescrotal cryptorchidism of 16.12%. This study also found a frequency polymorphism of exon 13 lgr8 gene (S337A = 54.84%; P340P = 41.94%; H345P = 61.29%; K346K = 90.32%; Q354K = 16.13%; Q356P = 29.03%; S357S = 48.39%). Polymorphisms S337A (TCA→GCA p = <0.001; H345P (CAC→CCC) p = 0.03; Q356P (CAG→CCG) p = 0.004; and S357S (TCT→TCC) p = <0.001 of exon 13 lgr8 gene were found significantly more often in cases. In summary polymorphism S357S is associated with a new marker; polymorphisms S337A; Q356P are associated with an increased risk; polymorphism H345P is associated with an increased risk or new marker of cryptorchidism in boys. This study is expected to be used in the determination of therapeutic decisions, as a guide for prognosis and as a foundation for further studies.

O27
Analysis growth development of 153 disorders of sex development
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Objective: To analyze clinical characteristics and growth development of 153 disorders of sex development (DSD) and non-CAH patients.

Method: To collect DSD patients’ clinical data, including age, gender and family history. To definite categories and assess height, weight and measure penis length and testis volume and describe the deformation. Determine the levels of sex hormones. HCG test, B ultrasonic and chromosomes and the deformations.

Result: Chief complain of the patients to see doctors were abnormal external genitalia. 153 DSD patients include social sex 128 male and 25 female from 42 days to 1610 month (45.9±42.5y). There were 121 (90.3%) 46XY DSD. 39 cases (32.2%) were diagnosed as hypospadias combined with microphrenis, 19 (15.7%) were microphrenis with testis abnormality and 18 cases (14.9%) were simple microphrenis. 13 (10.7%) were testis abnormality, 9 (7.4%) were hypospadias, 1 (0.8%) were hypospadias combined with testis abnormality, microphrenis combined with hypospadias and testis abnormality were 14 (11.6%). 15 (9.8%) cases had DSD family histories and 19 (12.4%) patients’ mother had taken progestrone when early pregnant stage threatened abortion. With face/limb malformation or mental problems were 17 (11.1%). Most of DSD were shorter than the normal population, 16 (10.4%) was <-2SDS, 115 (75.2%)<1SDS. The proportion of height shorter than 25 percentile and 50 percentile was more than normal population, P=0.039 and 0.056 respectively. There were 40 cases with testis abnormality DSD, whose height were shorter than normal population (P=0.041 and 0.015). 130/153 DSD were performed HCG test, height>P50 was 60.3% among 78 who had normal testosterone respond, while only 18.2% height>P50 among 33 cases with abnormal testosterone respond (P=0.000).

Conclusion: This non-CAH DSD included 46XY DSD (121 cases), 46XX DSD (3 cases) and chromosome DSD (10 cases). The most number of 46XY DSD was hypospadias combined with microphrenis, the second was microphrenis. Some patients had DSD family histories and some patients whose mother had been threatened abortion and progestrone exposure duration pregnancy. DSD may have malformation of face/limbs or internal organs.
or mental problems. Patients with DSD may have both disorders of sex development and short statures. Most of DSD were shorter than normal population and testicular development was related to shorter stature. So when evaluated DSD, not only should pay attention to sex development but also to short statures.

Lentivirus-mediated RNAi can effectively suppress the expression of KiSS1 stably, as arsult the expression of GnRH gene can be suppressed, then affecting sexual development. It may provide a potential tool for the study of targeting control of sexual development in vivo and treating precocious puberty and other diseases.

### O28
A study on sexual development of SD rat by using KiSS1RNA interference mediated by lentivirus-based vectors

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To explore the possible mechanism of KiSS1 in control GnRH secretion participate insexual development onset and normal reproduction regulation by investigate the changes of expression of KiSS1, GnRH in hypothalamus and LH, FSH, E2 in serum, by using RNA interference Mediated with Lentivirus-based Vectors, after Interfering expression of KiSS1.

KiSS1, control groups and normal saline group, the interference virus group to 93T cells. Real-time PCR detected the expression of KiSS1 mRNA in order to filter the most effective microRNA plasmid. Constructed recombinant lentivirus and determined the titer, then they were intracerebroventricularly infused into the brain of Sprague-Dawley rats (21-day-old). The three groups included interference virus group, Lentivirus-control, NS-control. Ten rats in each group animals were sacrificed at 30-day-old, 35-day-old, 45-day-old. Then the expression of KiSS1 and GnRH mRNA were conducted in the rat hypothalamus with Real-time PCR, the LH, FSH, E2 in serum were examined with Chemiluminisence method. HE staining was used to observe histomorphology of ovarian.

Successfully filtered the most effective microRNA plasmid and constructed recombinant lentivirus. The titer of recombinant lentivirus was 8x10^8 TU/ml. The level of KiSS1 mRNA in interference virus group was significantly reduced after infecting recombinant lentivirus compared with control group at 30d NS-control group 0.2±0.02, Lentivirus-control group 0.188±0.023, interference virus group 0.106±0.018; at 35d NS-control group 0.433±0.046; Lentivirus-control group 0.41±0.034; interference virus group 0.218±0.025; at 45d NS-control group 0.315±0.048; Lentivirus-control group 0.282±0.052; interference virus group 0.215±0.033, at 30d F=112.40 P<0.01; at 35d, F=209.5 P<0.01; at 45d, F=5.2, P<0.005. The level of GnRH mRNA in interference virus group was significantly reduced after infecting recombinant lentivirus compared with control group at 30d NS-control group 0.2±0.02, Lentivirus-control group 0.2±0.01, interference virus group 0.23±0.03; at 35d NS-control group 0.517±0.048; Lentivirus-control group 0.53±0.052; interference virus group 0.407±0.07; at 45d NS-control group 0.468±0.03, Lentivirus-control group 0.479±0.038; interference virus group 0.455±0.054, at 30d, F=24.6, P<0.01; at 35d, F=209.0 P<0.01). The difference was statistical significant. The level of LH in interference virus group is lower than other two groups at 35d (NS-control group 0.219±0.015mU/ml; Lentivirus-control group 0.215±0.014mU/ml; interference virus group 0.205±0.014 mU/ml; F=7.92 P<0.05). The level of E2 in interference virus group is lower than other two groups (at 35d, NS-control group 56.0±4pg/ml; Lentivirus-control group 52.9±3.2pg/ml; interference virus group 46.8±3.01pg/ml; at 45d NS-control group 57.4±5.5pg/ml; Lentivirus-control group 58.1±3.02pg/ml; interference virus group 52.4±3.57pg/ml; at 35d, F=25.25 P<0.01; at 45d, F=7.63 P<0.05). Meanwhile, the time of vaginal orifice opening of the interference virus group was significantly later than control virus group and normal saline group (the interference virus group 37.4±1.57d, control virus group 35.2±1.9d, and normal saline group 34.9±0.99d, F=18.1 P<0.001). The histology of ovary showed similar results.

Our result show that the lentiviral vector of KiSS1-microRNA can inhibited the expression of KiSS1 stably, efficiently and specifically. Lentiviral with KiSS1-microRNA can affect the expression of GnRH and the levels of sex hormone. Intralateroventricular microinjection of KiSS1-microRNA Lentiviral can delay sexual development of SD female rat.

### O29
A pilot study on children with bone-age advancement without early sexual maturation; auxological and laboratory (GnRH stimulation) characteristics

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Social concern over precocious puberty (PP) is rising nowadays, and there is actually increased visit to hospital due to PP. Among them children with no pubertal sign showing advanced bone-age (BA) have been found in many cases. This study was done to see clinical and laboratory characteristics in these children with so called `asymptomatic PP'. Among children whom visited for evaluation of early sexual maturation between July 2007 and June 2009, children with advanced BA more than 1 yr without any pubertal sign were enrolled. Their clinical, laboratory data including GnRH stimulation test and auxological data were analyzed retrospectively.

Thirty-eight children with asymptomatic PP were enrolled. Male:female ratio was 1:1. Chronological ages (CA) were 9.3±1.1 yrs in boys, 8.1±1.4 yrs, in girls. BA were 11.3±0.9 yrs in boys, 9.8±1.4 yrs in girls. Positive result (peak LH>5 IU/L) of GnRH stimulation test was found in 18 out of 38 children (47.4%) -18 boys (69%) and 8 girls (31%). Patients were divided into 2 groups (positive and negative g group) based on GnRH stimulation test. Basal LH value of positive group was significantly higher than negative group in boys (0.4±0.5 vs 0.1±0.1 IU/L, respectively, p<0.05) and girls (1.0±1.7 vs 0±0.0 IU/L, respectively, p<0.05). However, there were no significant differences between groups in height, chronological age, progression of BA, BMI.

Children with BA advancement without secondary sexual characteristics was found. Their clinical course is unknown yet. Further study is necessary to confirm characteristics of BA advancement without early sexual maturation, so-called `asymptomatic PP'.

### O30
Do patients with celiac disease patients differ from those with concurrent celiac disease with type 1 diabetes mellitus?

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Background and objectives: Celiac disease (CD) and type 1 diabetes mellitus (T1DM) share common genetic loci. Patients with T1DM developing CD may remain asymptomatic and some of the common symptoms of CD may be considered as part of the chronic complications of diabetes like gastrointestinal intolerance, diarrhea, nocturnal diarrhea, alternate diarrhea and constipation.

There are no reports on comparison of presenting features of patients with CD and those with T1DM together. The present study was planned to compare clinical, biochemical and hormonal profile of patients of CD and CD with T1DM.

Patients and methods: Consecutive CD patients with and without T1DM ≤ 20 years seen by us were evaluated clinically and underwent thyroid, gonadal function tests (where applicable) and serum cortisol, besides routine hemogram and biochemical tests. Patients were subjected to screening for CD by anti tissue transglutaminase antibodies (tTGAb) and those positive were subjected to endoscopy of descending part of the duodenum, and 3 biopsies were taken. Histological interpretation was done by an experienced pathologist and recorded as per modified Marsh classification [1]. Patients were diagnosed to have CD as per modified ESPGHAN criteria [2] and T1DM as per ADA position statement [3]. All patients received gluten free diet.
Table 1 (abstract O30) Symptoms in patients with celiac disease alone and celiac disease with type 1 diabetes mellitus

<table>
<thead>
<tr>
<th>S.No</th>
<th>Clinical Features</th>
<th>All Patients (N=109)</th>
<th>CD Alone (Group A, N=86)</th>
<th>CD+T1DM (Group B, N=23)</th>
<th>P value (Group A&amp;B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Short stature</td>
<td>77.1%</td>
<td>87%</td>
<td>40.9%</td>
<td>.000</td>
</tr>
<tr>
<td>2</td>
<td>Diarrhoea</td>
<td>56.9%</td>
<td>40.7%</td>
<td>50%</td>
<td>.431</td>
</tr>
<tr>
<td>3</td>
<td>Constipation</td>
<td>4.6%</td>
<td>3.5%</td>
<td>9.5%</td>
<td>.246</td>
</tr>
<tr>
<td>4</td>
<td>Anemia</td>
<td>70.6%</td>
<td>80.9%</td>
<td>45%</td>
<td>.001</td>
</tr>
<tr>
<td>5</td>
<td>Delayed Puberty</td>
<td>52.3%</td>
<td>61.9%</td>
<td>29.4%</td>
<td>.014</td>
</tr>
<tr>
<td>6</td>
<td>Weight loss</td>
<td>55%</td>
<td>61.9%</td>
<td>45%</td>
<td>.168</td>
</tr>
<tr>
<td>7</td>
<td>Hypothyroidism</td>
<td>8.2%</td>
<td>8.1%</td>
<td>5%</td>
<td>.788</td>
</tr>
<tr>
<td>8</td>
<td>Rickets</td>
<td>3.7%</td>
<td>3.5%</td>
<td>4.3%</td>
<td>.096</td>
</tr>
<tr>
<td>9</td>
<td>Goitre</td>
<td>19.3%</td>
<td>20.9%</td>
<td>13%</td>
<td>.704</td>
</tr>
<tr>
<td>10</td>
<td>Hypoadrenalism</td>
<td>0.9%</td>
<td>1.2%</td>
<td>0%</td>
<td>.246</td>
</tr>
</tbody>
</table>

Table 2 (abstract O30) Laboratory parameters of patients with celiac disease alone and celiac disease with type 1 diabetes mellitus

<table>
<thead>
<tr>
<th>S.No</th>
<th>Biochemical Parameters</th>
<th>All Patients (N=109)</th>
<th>CD Alone (Group A, N=86)</th>
<th>CD+T1DM (Group B, N=23)</th>
<th>P value (Group A&amp;B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Serum IgA tTG (mIU/L)</td>
<td>123.2±110.9</td>
<td>118.3±112.9</td>
<td>139.5±111.1</td>
<td>.433</td>
</tr>
<tr>
<td>2</td>
<td>Hemoglobin (gm/dl)</td>
<td>8.6±2.6</td>
<td>8.3±2.4</td>
<td>10.1±3.2</td>
<td>.018</td>
</tr>
<tr>
<td>3</td>
<td>T3</td>
<td>1.3±0.43</td>
<td>1.3±0.4</td>
<td>1.4±0.6</td>
<td>.146</td>
</tr>
<tr>
<td>4</td>
<td>T4</td>
<td>8.1±2.6</td>
<td>8.1±2.7</td>
<td>7.7±3.1</td>
<td>.596</td>
</tr>
<tr>
<td>5</td>
<td>TSH(mIU/L)</td>
<td>9.7±3.45</td>
<td>7.1±2.17</td>
<td>22.4±6.95</td>
<td>.941</td>
</tr>
<tr>
<td>6</td>
<td>LH(mIU/L)</td>
<td>2.5±2.6</td>
<td>2.6±2.8</td>
<td>1.9±1.8</td>
<td>.596</td>
</tr>
<tr>
<td>7</td>
<td>Calcium (mg/dl)</td>
<td>9.3±1.87</td>
<td>8.9±0.9</td>
<td>9.4±1.9</td>
<td>.014</td>
</tr>
<tr>
<td>8</td>
<td>Phosphate (mg/dl)</td>
<td>4.7±1.0</td>
<td>4.7±1.0</td>
<td>4.4±0.83</td>
<td>.014</td>
</tr>
<tr>
<td>9</td>
<td>ALP(mIU/L)</td>
<td>118±108.4</td>
<td>110.2±106.4</td>
<td>116.6±129.5</td>
<td>.014</td>
</tr>
<tr>
<td>10</td>
<td>Albumin (gm/dl)</td>
<td>4.0±0.6</td>
<td>4.05±0.7</td>
<td>4.3±0.5</td>
<td>.014</td>
</tr>
<tr>
<td>11</td>
<td>SGOT</td>
<td>39.2±26.5</td>
<td>32.8±16.8</td>
<td>39.7±42.1</td>
<td>.014</td>
</tr>
<tr>
<td>12</td>
<td>SGPT</td>
<td>36.3±31.2</td>
<td>28.6±15.6</td>
<td>34.2±58.0</td>
<td>.014</td>
</tr>
</tbody>
</table>

(GDI) and/or diabetic diet. Patients with CD alone (group A) were compared with those having CD with TIDM (Group B).

Results: 109 patients (57 males) with mean age of 14.9±2.9 year fulfilled the eligibility criteria. 23 (21.1%) had T1DM and CD while CD alone was present in 86 subjects. The age at diagnosis of CD was younger (11.5±4.6 vs 13.8 ± 3.4 yr; p<0.05) and the lag period between symptoms and diagnosis of CD was shorter (20.2 ± 31.8 vs 56.1 ± 42.4 months; p<0.05) in those with Group B. Detailed clinical features of patients in two groups are given in Table 1 and laboratory parameters are enumerated in Table 2. Comparing the clinical features in between groups, short stature (87% versus 40.9%, p < 0.0001), anemia (80.9% versus 45%, p<0.001) and delayed puberty (61.9% versus 29.4%, p<0.014) were significantly more common in the Group A. However, diarrhea, constipation and weight loss were comparable in both the groups.

Conclusions: Present study suggests that patients with celiac disease alone are more symptomatic and associated with more biochemical abnormalities compared to those with celiac disease and T1DM. It will be worthwhile to plan a prospective study with long duration of follow up and more number of patients in both groups to further validate the results.

References
Vomiting, anorexia, short-term fever, hair loss occurred in all the patients during AHST, convolution occurred in 1 patients due to severe sodium water retention, leukocytopenia was evident in the first 1-3 months after AHST, one patients suffered from acute bronchitis 2 months after AHST. No other systemic organ lesions were found in all the patients. High-dose immunosuppression and AHST were performed with acceptable toxicity in 7 patients with newly diagnosed childhood T1DM. With AHST, beta cell function was improved and induced insulin independence in the majority of the patients.

O32
High unchanged incidence of diabetic ketoadidosis between 2009 and 2019 in Auckland children
SW Cutfield1, J Derraik, C Jeffries2, PL Hofman1, WS Cutfield∗
1Liggins Institute, University of Auckland, New Zealand; 2Starship Childrens Hospital, Auckland, New Zealand

Background: Diabetic ketoacidosis (DKA) is a potentially life threatening complication of initial presentation with type 1 diabetes mellitus (T1DM). Annual DKA incidence data has been reported in selected populations in many studies; however few studies have reported the trend in DKA incidence over time in an unselected representative childhood population.

Aims: To determine the annual incidence of DKA at initial presentation with type 1 diabetes mellitus in all children <15 years of age between 2000 and 2009 in the Auckland region.

Methods: Data from Auckland children with newly diagnosed T1DM between 1 January 2000 and 31 December 2009 were collected from Starbase, the Starship Children’s Hospital diabetes database. T1DM was confirmed by the presence of glumatic acid decarboxylase and/or tyrosine phosphatase-like protein (IA2) antibodies. DKA was defined by international criteria as venous or capillary pH and bicarbonate as mild DKA with pH <7.30 and bicarbonate <15 mmol/l, moderate DKA pH <7.20 and bicarbonate <10 mmol/l and severe DKA pH <7.10 and bicarbonate <5 mmol/l.

Results: There were 481 children diagnosed with T1DM in the Auckland region (population 1,500,000) between 2000 and 2009. Over the study period the DKA incidence was highly variable (32 to 63% without a discernable change in incidence over the 10 year period [p=0.11]), thus data are expressed as a means over the study period 2000-2009. There were 47.4% of children in DKA at initial presentation which is very similar to the DKA incidence we reported for 1995-96 of 42% [1]. Of those with DKA in the current study 46.7% had mild, 22.0% moderate and 33.3% severe DKA. Younger age was associated with an increasing risk of DKA at 8% per year of age. Children <5 yrs of age had a much higher incidence of DKA at 62% compared to 43% in children 5-15 years of age. Neither sex, BMI, ethnicity nor socioeconomic status (assessed by NZDep score) influenced the likelihood of DKA.

Conclusions: The incidence of DKA at initial presentation of type 1 diabetes mellitus is much higher in Auckland children compared to other published studies. DKA incidence has plateaued over the past 14 years and occurs far more frequently in young children. We speculate that improved community awareness of the symptoms of T1DM will lead to earlier diagnosis of T1DM and avoidance of DKA and associated sequelae.

Reference:

O33
The effect of eggplant (Solanum melongena L.) extract peroral against blood glucose level of white rat (Ratus norvegicus) wistar strain diabetic model
Nanda Rela Qonta, Maimun Zulhaiddah, Sudarto, Harjoedi Adji Tjahjono∗
Faculty of Medicine, Brawijaya University, Malang, Indonesia

Eggplant (Solanum meloneng L.) that are common in Indonesia are already known contain anthocyanins as antioxidants as well as α-glukosidase inhibitor that can inhibit the rise of blood glucose in diabetes mellitus (DM). This study aimed to determine that the eggplant extract has antihyperglycemic effect and the effective dose as well. This was an experimental study with post test only control group design. We used 25 rats that divided into 5 groups: negative control group (PO), positive control group (PA), and 3 treatment groups (P1,P2,P3). The rats in PA, P1,P2 and P3 were injected intraperitonally with aloksan 150 mg/kgBW/day so they have blood glucose level above 200 mg/dl. Treatment group were given eggplant extract by dose P1=383 mg/kgBW/day, P2=686 mg/kgBW/day, and P3=1372 mg/kgBW/day. On day 15 after DM, the rats were terminated and the blood glucose level were measured using a spectrophotometer. The Result of One Way ANOVA test showed that they was a significant differences between treatment groups and PA, no significant differences between P1 and P3 to PO, but there were a significant differences between P2 and PO. It can be concluded that eggplant extract may lower blood glucose level of DM rats near to normal, but the difference in dose in this study do not affect the magnitude of decrease in blood glucose level.

O34
Olive leaf extract improves insulin sensitivity in overweight middle aged males; a randomized, double-blinded, placebo controlled, crossover trial
Martin de Bock1, Jose Derraik, Christine Brennan, Eric Thorstensen, Wayne Cutfield∗
Liggins Institute, University of Auckland, Auckland, New Zealand

Aim: To investigate the impact of supplement olive leaf extract on insulin sensitivity in overweight middle aged males.

Method: We conducted a randomized, double-blinded, placebo controlled, crossover trial on an overweight middle aged male population at risk of developing the metabolic syndrome comparing olive leaf extract containing 51 mg oleuropiein and 9.7 mg hydroxytyrosol to placebo. We measured insulin sensitivity (Matsuda method), pancreatic β-cell responsiveness (oral disposition index), lipid profile, ambulatory blood pressure, carotid intimal media thickness, body composition (DEXA) basal metabolic rate, hand-grip strength, wellness questionnaire, inflammatory cytokines, anti-oxidant potential all measured at baseline and end of both interventions.

Results: 38 participants were suitable for analysis. Even after controlling for total calorie intake fibre intake, physical activity, age, and percentage body fat (DEXA), insulin sensitivity was significant improved on treatment Vs placebo (19% p<0.05), as well as the oral disposition index as a marker of pancreatic β-cell responsiveness (30% p<0.05). The cytokine profile was consistent with improved insulin sensitivity: acutely raised IL-6, IGFBP1 and IGFBP2. No other clinical outcomes were influenced.

Conclusion: Olive leaf extract improves insulin sensitivity in overweight middle aged males. This is applicable to an overweight adolescent population.

O35
The role of activation of PERK in activating glycogen synthase kinase 3(GSK-3) by oleic acid(OA) in type 2 diabetes
Wei Wu, Shan Huang, Xiaoping Luo
Pediatrics Department, Tongji Hospital, Huazhong University of Science and Technology, China

ER-stress induced apoptosis of beta cells is an important mechanism of type 2 diabetes. PERK can be activated by the overactivation of ER-stress which will induce beta cells apoptosis. This study is to reveal the role of ER-stress, GSK-3 and the potential signal pathway during beta cells apoptosis.

The alterations of ER-stress related signal factors and kinases induced by OA are assessed by western blot, and the changes of PERK and AMPK are analyzed by ELISA meanwhile. The phosphorylated GSK-3β and total GSK-3 are detected by western blot, while PERK are inhibited by the transfection of PSIPK plasmid and AMPK are inhibited by the inhibitor SB203580. Finally, the interaction between PERK and GSK-3 are identified by co-immunoprecipitation and direct immuno-fluorescence. The study shows 1. The expression of GRP78, ATF6, XBP1, PERK and AMPK significant increased in the presence of 0.4mM OA(p<0.01) after OA treatment. 2. Activity of PERK and AMPK significantly augmented in the presence of OA (P<0.01). 3. Detections of the alterations of GSK-3 after inhibiting the activity of PERK and AMPK shows (1) GSK-3β was
We investigated adiponectin receptor 1 (AdipoR1) gene polymorphisms might impact was found significantly associated with insulin resistance, i.e., the AA genotype (OR 2.25; 95% CI 1.019) in the distribution of the genotype frequencies. These results suggest activation of GSK-3 can induce beta cell apoptosis by ER-stress which is caused after long-time exposure to free fatty acids. PERK will activate GSK-3 directly. Collectively, PERK-GSK-3 signal pathway will play an important role during beta cell apoptosis in type 2 DM.

O36
Association between insulin resistance with UCP2 -866G/A, UCP2 45BP INS/Dél, UCP3 -55C/T, GHSR1A rs2922126, GHSR1A rs590035 and PRO12Ala PPAR2 gene polymorphisms in obese female adolescents in Yogyakarta, Indonesia

Rina Susilowati1, Dian Enike Septyaningtrias1, Cut Gina Ingyani1, Harry Freitag Luglio Muhammad2, Madarina Julia3
1Department of Histology and Cell Biology, Faculty of Medicine Universitas Gadjah Mada Jalan Bulaksumur, Indonesia; 2Department of Health Nutrition, Faculty of Medicine Universitas Gadjah Mada Jalan Bulaksumur, Indonesia; 3Department of Child Health Faculty of Medicine Universitas Gadjah Mada Jalan Bulaksumur, Indonesia


Aims: The aim of this study was to analyze the association between polymorphism of several genes encoded the uncoupling proteins (UCPs), ghrelin receptors (GHSRs) and peroxisome proliferator-activated receptor gamma (PPARγ) with insulin resistance in obese female adolescents in Yogyakarta, Indonesia.

Methods: Screening for obesity using CDC 2000 criteria was done in 2121 female adolescents aged 13-14 years old in Yogyakarta. BMI > 95th percentile was considered as obese. Among the obese subjects, 78 agreed to be enrolled for this study. HOMA-IR > 3.16 was used to determine the insulin resistance status. DNA was isolated from peripheral blood and UCP2 -866 G/A, UCP3 -55C/T, GHSR1a rs2922126, GHSR1a rs590035 and PRO12Ala PPAR2 genotypes were analyzed by PCR-RFLP. UCP2 45bp ins/dél genotype was analyzed by PCR.

Results: Among the 78 obese adolescent girls, 44 (56.4%) were at insulin resistance state. All subjects had Pro12Pro PPARγ and del/dél UCP2 genotype. Compared to the other polymorphisms analyzed in this study, the AA genotype and the A allele of UCP2 -866 G/A polymorphism was found to have highest association with insulin resistance state (OR 2.75; 95% CI 0.65-11.62; p=0.017 for AA genotype; OR 1.50; 95% CI 0.79–2.83; p=0.22 for A allele). In UCP3 -55C/T polymorphism, TT genotype also showed positive statistically not significant association with insulin resistance (OR 2.23; 95% CI 0.38–14.12; p=0.36), so did T allele (OR 1.30; 95% CI 0.67–2.50; p=0.45).

Conclusion: We found that insulin resistance state is associated with the polymorphism in UCP2 -866 G/A and UCP3 -55C/T genes.

O37
Association of polymorphisms in the FOXO1 and UCP3 genes with nonalcoholic fatty liver disease in Chinese children

Yan-ping Xu, Li Liang, Chun-lin Wang
Department of Endocrinology, The Children’s Hospital of Zhejiang University School of Medicine 310003, Zhejiang, Hangzhou, Zhejiang province, China


Aim: The human protein encoded by the FOXO1 gene functions as a transcription factor of insulin signaling key genes. Human uncoupling proteins 3 (UCP3) are mitochondrial proteins that are involved in the control of energy metabolism and the pathophysiology of obesity. In this study we investigated the role of genetic variation in the FOXO1 and UCP3 gene in susceptibility to non-alcoholic fatty liver disease (NAFLD) and relevant metabolic traits.

Methods: We genotyped nine single nucleotide polymorphisms (SNPs) for association analyses in children (250 patients with NAFLD, 111 patients with metabolic syndrome, 146 with obese and 200 controls). Body mass index (BMI), waist and hip circumference, blood pressure, fasting blood glucose (FBG), insulin (FIN), lipid profiles were measured and performed b-ultrasound examination in all the subjects.

Results: In the NAFLD group, FOXO1A and UCP3 allele were significantly more frequent in both association studies. There was a significant difference in the overall distribution of the genotype frequencies (UCP3 rs1264427 rr: rs1800849), (FOXO1 rs2721068), and there was a significant difference (P = 0.0298, 0.0191) in the distribution of the haplotype (UCP3 rs1235972 UCP3 rs1800849), might be good NAFLD markers.

Conclusion: In conclusion, our study suggests a effect of UCP3 haplotype on NAFLD development and relevant intermediate phenotypes which predispose for NAFLD.
Triglyceride and non-HDL-C are better predictors of cardiovascular disease risk factors in Chinese Han children and adolescents than LDL-C

Objective: To validate serum cholesterol and triglycerides (TG) as predictors for the presence of cardiovascular disease risk factors in Chinese Han children and adolescents.

Subject: A total of 203 simple obesity group included 153 boys and 50 girls with mean age 10.15±1.95 y and 432 obesity with metabolic abnormalities group (hypertension, elevated fasting blood glucose or dyslipidemia, diagnosis was achieved if any of them was reached) included 314 boys and 118 girls with mean age 10.75±2.20 y were studied. The controls consisted of 315 age and gender-matched healthy children including 214 boys and 101 girls with mean age 10.38 ± 2.84 y.

Methods: Anthropometric indices were measured. Blood pressure was evaluated and hypertension was defined based on IDF 2007 definition, which systolic blood pressure(SBP) ≥130mmHg or diastolic blood pressure (DBP) ≥85mmHg. Biochemical measurements were done. Elevated fasting blood glucose(FBG) was considered as FBG ≥ 126 mg/dl (≥5.6 mmol/l) and dyslipidemia was defined according to Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Receiver operating characteristic (ROC) curves were used to analysis the detection of cardiovascular disease risk factors by serum cholesterol and TG in Chinese Han children and adolescents.

Results: Values for SBP, DBP, FBG, low density lipoprotein cholesterol (LDL-C), non-high density lipoprotein cholesterol(non-HDL-C) and TG increased significantly with increasing obesity, whereas high density lipoprotein cholesterol(HDL-C) decreased with increasing obesity. Range of areas under ROC curves for TG and non-HDL-C was 0.80-0.86 and 0.67-0.75 to detect cardiovascular disease risk factors respectively, while the range of areas for LDL-C, TC and HDL-C was between 0.64-0.73, 0.60-0.69 and 0.30-0.38 respectively.

Conclusions: Chinese Han children and adolescents with obesity are naturally at increased risk for hypertension, impaired glucose metabolism or dyslipidemia. Triglyceride and non-HDL-C are better predictors of cardiovascular disease risk factors in Chinese Han children and adolescents than LDL-C.

Study of visfatin, asp level in obese children and their clinical significance

To explore the relationship between visfatin, ASP and the incidence of childhood obesity and the significance of them in diagnoses and therapy of childhood obesity.

Eighty-six children (57 boys and 29 girls) including 40 obese children, 22 overweight children and 24 normal control children were recruited with ages ranged 7-15 years. Serum visfatin and ASP levels were determined by ELISA.

(1) As compared with normal and overweight children, serum visfatin level was significantly higher in obese children (p<0.05); As compared with normal children (p<0.01) and overweight children (p<0.05), serum ASP level was significantly higher in obese children. There were no differences of serum visfatin and ASP levels between normal and overweight children.

(2) The body mass index, TC, TG, LDL-C, FPG, FINS, insulin resistance index of the obese children were higher than the normal children (p<0.05 or p<0.01); the HDL-C and insulin sensitivity index of the obese children were lower than the normal group (p<0.01 or p<0.05). The body mass index, the fasting insulin, insulin resistance index of the obese children were higher than the overweight children (p<0.01).

O44 Evaluation of bone mineral density and bone/muscle geometry using pQCT in children after spinal cord injury

Table 1 (abstract O41) pQCT data of tibial and radial Z-scores at 4% and 66% sites

<table>
<thead>
<tr>
<th>Site</th>
<th>4% Z-scores</th>
<th>66% Z-scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibial Z-score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vBMD trabecular</td>
<td>-2.9 +/- 1.3*</td>
<td></td>
</tr>
<tr>
<td>vBMD cortical</td>
<td>0.5 +/- 1.5</td>
<td></td>
</tr>
<tr>
<td>Total CSA</td>
<td>-1.8 +/- 2.6*</td>
<td></td>
</tr>
<tr>
<td>BMC</td>
<td>-3.9 +/- 3.4*</td>
<td></td>
</tr>
<tr>
<td>pSSI</td>
<td>-2.7 +/- 3.5*</td>
<td></td>
</tr>
<tr>
<td>Radial Z-score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vBMD trabecular</td>
<td>-3.2 +/- 3.6*</td>
<td></td>
</tr>
<tr>
<td>vBMD cortical</td>
<td>-0.2 +/- 3.1</td>
<td></td>
</tr>
<tr>
<td>Total CSA</td>
<td>-1.4 +/- 1.9*</td>
<td>-1.1 +/- 0.8*</td>
</tr>
<tr>
<td>BMC</td>
<td>-2.5 +/- 3.5*</td>
<td>-3.9 +/- 3.0*</td>
</tr>
<tr>
<td>pSSI</td>
<td>-1.7 +/- 1.5*</td>
<td></td>
</tr>
</tbody>
</table>

Values represent mean Z-scores +/- 5D, asterisk represents p<0.05 compared to controls. Tibial data for paraplegics and tetraplegics (n=19), radial data for tetraplegics only (n=10).

greater trabecular vBMD, cortical bone mineral content and cortical thickness tibial Z-scores than those with a complete SCI. pQCT provides a valuable insight into the regional changes in bone and muscle development in children following SCI. Residual muscle function with the ability to weight bear, even if only in a frame, provides a significant benefit to bone development.

**O42**
Losartan improves clinical outcome in Camurati Engelmann Disease
Ahila Ayyavoo1,2, Tim Cundy1, José GB Derraik, Paul L Hofman1
1Liggins Institute, University of Auckland, Auckland, New Zealand, 2Greenlane Clinical Centre, Auckland District Health Board, Auckland, New Zealand

We hypothesized that losartan would help in achieving clinical remission in CED (Camurati Engelmann disease) patients by blocking TGFβ1 (transforming growth factor beta 1) with fewer side-effects than steroids. CED characterised by progressive diaphyseal dysplasia is associated with debilitating bone pain in the limbs, muscle weakness, fatigability and waddling gait [1]. Clinical manifestations are due to mutations in the TGFβ1 gene leading to its over-expression and effect on bone. Losartan is an antagonist of TGFβ1 and it slows the progression of aortic root dilatation in Marfan’s syndrome by blocking the over-expression of TGFβ1 [2]. Steroids which have long been used for treatment of CED and been linked to long term side effects including those on growth, blood pressure and spinal osteoporosis.

A 10 year old child with mutation is in exon 4, position C652T causing an R218C amino acid substitution on chromosome 19q13 had severe limitation of activity since 4 years of age due to pain in the limbs. She underwent a physical examination, a dual energy xray absorptiometry scan(DEXA), pain score and 6 minute walk test prior to start of losartan with a repeat of the tests 9 and 17 months later. She is being treated with losartan at a dose of 0.75mg/kg/day. Table 1.

Losartan improves the quality of life in children with CED by reducing the bone pain along with improvement in their activity levels, fat & muscle mass, without major effects on growth, blood pressure and spinal osteoporosis.

**References**

**O43**
An overgrowth disorder associated with excessive production of cGMP due to a gain-of-function mutation of the natriuretic peptide receptor 2 (NPR2) gene
Kohji Miura1, Noruyuki Namba1, Keiko Yamamoto1, Makoto Fujiwara, Yasuhisa Ohta1, Taichi Kitaoka1, Takuo Kubota1, Toshimi Michigami1, Keiichi Ozono1
1Departments of Pediatrics, Osaka University Graduate School of Medicine, Japan; 2Department of Bone and Mineral Research, Osaka Medical Center and Research Institute for Maternal and Child Health, Japan

**Aim:** in human, overproduction of C-type natriuretic peptide (CNP) due to a chromosomal translocation was reported to cause skeletal dysplasia associated with tall stature. In addition, acomosomesic dysplasia, type Maroteaux, characterized by dwarfism is caused by loss-of-function mutations in the Npr2 gene that encodes the CNP receptor NPr2. We report a three-generation family with tall stature, scoliosis and macrodactyly of the great toes, leading to a gain-of-function mutation in Npr2. **Methods and results:** Since the phenotype of the patients resembled several cases of the CNP overproduction phenotype, in terms of tall stature and large great toes, enhanced CNP/NPR2 signaling was suspected. Since the proband’s phenotype showed similarity to CATSHL syndrome, caused by a loss-of-function mutation in the Fgfr3 gene, except for the absence of neurological symptoms, the Fgfr3 gene was analyzed as well as the natriuretic peptide precursor C (Nppc), Npr2, and Npr3 genes and a novel heterozygous G>A missense mutation at nucleotide +2647 (c.2647G→A) of the Npr2 gene was identified. When expressed in HEK293A cells, the mutant Npr2cDNA generated intracellular cGMP in the absence of CNP ligand. In the presence of CNP, cGMP production was greater in cells that had been transfected with the mutant Npr2cDNA compared to wild-type cDNA. Transgenic mice in which the mutant Npr2 was expressed in chondrocytes driven by the promoter and intronic enhancer of the Col11a2 gene exhibited an enhanced production of cGMP in cartilage, leading to a similar phenotype to that observed in the patients.

**Conclusion:** These results indicate that p.Val883Met is a constitutive active gain-of-function mutation and elevated levels of cGMP in growth plates lead to the elongation of long bones. Our findings reveal a critical role for NPR2 in skeletal growth in both humans and mice, and may provide a potential target for prevention and treatment of diseases caused by impaired production of cGMP, such as pulmonary hypertension, short stature, erectile dysfunction, heart failure, placental dysfunction, and dementia.

**O44**
Genetic diagnosis of Beckwith Wiedemann syndrome and Silver-Russell syndrome
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Beckwith-Wiedemann syndrome (BWS) is fetal overgrowth syndrome, whereas Silver-Russell syndrome (SRS) is characterized by pre- or postnatal growth retardation. BWS and SRS share molecular epigenetic defects in chromosome 11p15, where two imprinting centers, LIT1-differentially methylated region (DMR) and H19-DMR, exist. A small number of patients with SRS harbor paternal uniparental disomy of chromosome 7q as well. Extensive genetic analyses including methylation specific (MS) PCR-RFLP, MS-MLPA, microsatellite markers or MS-pyrosequencing analysis were performed using genomic DNA obtained from peripheral leukocytes to identify the epigenetic defects in patients with BWS and SRS. Ten out of 14 BWS patients (71.4%) showed hypomethylation in LIT1-DMR. One BWS patient harbored hypermethylation in H19-DMR (7.1%). Two BWS patients had both H19-DMR and LIT1-DMR defects, one of whom has paternal UPD at chr. 11 (14.3%). Eleven out of 13 SRS patients (78.6 %) showed hypomethylation in H19-DMR. One SRS patient (6.7%) had UPD at 7q. With MS-pyrosequencing analysis, epigenetic defects were identified in 93.1% of BWS patients and 85.7% of SRS patients. These positive rates are higher than previously reported positive rates, 80% in BWS and 50% in SRS. In addition, with MS-pyrosequencing analyses, quantification of methylation defects was available, which could identify partial methylation defects that were not revealed by MS-PCR-RFLP or MS-MLPA. The validity of MS-pyrosequencing method for the genetic diagnosis of BWS or SRS is needed to be investigated in a large patient cohort.

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**Table 1 (abstract O42)**

<table>
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<th>Age at analysis(years)</th>
<th>9.3</th>
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<tr>
<td>Cumulative pain score</td>
<td>9</td>
<td>1.75</td>
<td>0.25</td>
</tr>
<tr>
<td>6 minute walk (metres)</td>
<td>171</td>
<td>405</td>
<td>414</td>
</tr>
<tr>
<td>DEXA weight(kgs)</td>
<td>17.42</td>
<td>17.01</td>
<td>20.01</td>
</tr>
<tr>
<td>Height(cm)</td>
<td>123.6</td>
<td>128.3</td>
<td>131.7</td>
</tr>
<tr>
<td>Fat(gms)</td>
<td>1702</td>
<td>1253</td>
<td>2693</td>
</tr>
<tr>
<td>Lean(gms)</td>
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<td>14957</td>
<td>16425</td>
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<tr>
<td>BMC(gms)</td>
<td>7549</td>
<td>805</td>
<td>8902</td>
</tr>
<tr>
<td>A/G ratio</td>
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<td>0.23</td>
<td>0.39</td>
</tr>
<tr>
<td>Total body fat%</td>
<td>10.2</td>
<td>7.7</td>
<td>14.1</td>
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<tr>
<td>BMD gms/cm2</td>
<td>0.845</td>
<td>0.873</td>
<td>0.887</td>
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</table>
Insulin like growth factor 2 (IGF2) is a crucial imprinting gene which prompting placenta development and fetal growth. It demonstrates parent-of-origin-specific allelic expression that is epigenetically regulated by differential methylation of IGF2/H19 DMR. We aim to explore if abnormal IGF2 imprinting status that regulated by altered DNA methylation of IGF2/H19 DMR affects IGF2 expression leading to the occurrence of IUGR.

First we established an IUGR model of rat at two different stages (19-d gestational age and 1-day-old) by maternal nutrition restriction, and the rat tissues in the control group and the IUGR group were collected which were divided into four subgroups (N=6–8, each subgroup): Subgroup 1 and Subgroup 2 was the placenta and liver tissue of fetuses with 19-d gestational age, respectively. Subgroup 3 and Subgroup 4 was the liver tissue and skeletal muscle tissue in the posterior limbs of 1-day-old rats, respectively. Then the mRNA and protein levels of IGF2 were tested in the four subgroups of the two groups. In each subgroup, pyrosequencing was used to test the DNA methylation level of imprinting control region IGF2/H19 DMR. We observed that the expression levels of IGF2 in the Subgroup 1, Subgroup 2, Subgroup 3 were decreased significantly compared with the control group, but there were no obvious differences in the Subgroup 4 of the two groups. The pyrosequencing showed no significant differences in methylation levels of the CpG dinucleotides in IGF2/H19 DMR between the two groups. What's more, the methylation ratio didn't change versus age, and maintained the same from fetus till adult, and it also stayed the same among different tissue types except for placenta which had a lower methylation fraction than the other tissues. We concluded that the expression of IGF2 was down-regulated in the IUGR rats, which could play an important role in the pathogenesis of IUGR. However, the down regulation was not always the result of the aberrant imprinting status of the imprinting control region H19 DMR, as there wasn't a clear association between the two. IGF2 could be down regulated through other pathways, such as histone modification, or altered imprinting of another control region, to mediate the development of IUGR.

**O46** Down-regulation of SOCS3 gene in hypothalamus attenuates diet-induced obesity in young rats

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**Aims:** Acquired childhood obesity is becoming increasingly apparent with the changes in children's life-style and eating environment, which become a severe social and medical problem. Our previous studies have found that the leptin concentrations were high in obese children, supporting that leptin resistance is a main mechanism of childhood obesity. The suppressor of cytokine signaling 3 (SOCS3) is a negative-feedback regulator of leptin signaling involved in leptin resistance, therefore we hypothesized that SOCS3 is a potential therapy for leptin-resistant obesity. In the studies, we investigate whether hypothalamic silencing of SOCS3 would attenuate diet-induced obesity and leptin resistance in young rats.

**Methods:** We first established hypothalamic SOCS3-deficient rats through lentiviral vector mediated RNA interference technique. The LVs expressing SOCS3-siRNA or control-shRNA were injected bilaterally into the arcuate nucleus (ARC) of five-week-old male rats, then provided a high-fat diet (HFD) to the rats. The body weight was measured weekly. After 8 weeks of the diet, the rats were killed, the serum leptin and insulin concentrations were measured by RIA, and the expressions of SOCS3 in ARC were detected by immunohistochemistry and a real time RT-PCR.

**Results:** The immunostaining showed that LV-SOCS3-shRNA inhibited SOCS3 protein expression and the RNAi protocol knocked down the expression of SOCS3 mRNA by 49% compared to the controls. The rats with hypothalamic SOCS3 knockdown exhibited significant decrease in body weight gain and lower concentrations of leptin, insulin, glucose and triglyceride when exposed to the HFD.

**Conclusion:** Our results provide evidence that rats with hypothalamic SOCS3 silencing are significantly protected against development of diet-induced obesity and SOCS3 is a potential target molecule for therapeutic intervention of obesity.

**O47** Factors affecting the timing of adiposity rebound

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**Background:** The age of adiposity rebound (AR), when body mass index (BMI) starts to rise after infancy, is thought to be an origin of obesity in later life. We have already reported that children who exhibited an earlier AR were associated with the higher BMI value and atherogenic metabolic status at 12 years of age. We investigated which factors influenced on an earlier AR, birth weight, initial feeding, family history, meals or exercise.

**Methods:** A total of 533 children in the community were enrolled in the study. Serial measurements of BMI from 4 months to 12 years were carried out prospectively. We calculated the age of AR, defined as the age which the lowest BMI occurred during this period. The subjects were divided into 2 groups according to BMI at 3 years is bigger than at 1.5 years (earlier AR group) or not (later AR group). We asked the answering to the question sheet about weight at birth, initial feeding (breast-feeding, bottle-feeding or mixed feeding), family history, meals, and exercises of their parents when children were at 3 years old. We also analyzed which BMI predicted the obesity at 12 years old, 4, 8, 12, 18 month or 2, 3, 4, 5 or 6 years by using ROC analysis.

**Results:** Weight at birth was associated with earlier AR if birth weight was over 3500g, but was not associated with the timing of AR if it was between 1500g and 3000g. Initial feeding was not related to the timing of AR and the frequency of obesity at 2 years old. None of the breast-feeding subjects showed severe obesity at 12 years old. The factors as follows were associated with later AR; eating breakfast every day, not eating snacks, non-obese father, the first baby, going to kindergarten. Contrary to expectation the habits of drinking sweet beverages and eating snacks, non-obese father, the first baby, going to kindergarten. Contrary to expectation the habits of drinking sweet beverages and eating snacks, non-obese father, the first baby, going to kindergarten.

**Conclusion:** This study showed that obesity at 12 years old was associated with weight gain over 2 years old, but not with the weight gain during infancy period.

**O48** Extracts giving of purple eggplant (Solanum melongena L.) orally can lower blood serum levels of malondialdehyde of white rat (Rattus norvegicus) wistar diabetes mellitus induced by aloxan

Ellisma Swandini Nugraheni, Harjoedi Adji Tjahjono

Faculty of Medicine, Brawijaya University, Malang, Indonesia


Purple eggplant (Solanum melongena L.) is known to contain anthocyanins, which is about 850 mg/kg of eggplant. Anthocyanins are water soluble pigments which the antioxidant ability arising from structural conjugated bonding system, so having a high reactivity as a primary antioxidant, oxygen scavengers, and chelator, that these substances are expected to reduce oxidative stress in diabetes mellitus (DM). This study aims to determine that the eggplant extract can reduce level of malondialdehyde (MDA) in the Wistar rat strain-aloxan induced model of diabetes mellitus and effective dose. This study is an experimental research with the design of the Control Group Post Test Only Design. The sample consisted of 25 rats that were divided into 5 groups, namely a negative control group (PO), a positive control group (PA) and 3 treatment groups (P1, P2, P3). Positive control group and three treatment groups were injected aloxan intraperitoneally as
The experiment aimed to investigate the effect of intrauterine (HPA) axis. Long-term follow up I overweight and 8.1% were obese. In neonatal rats and adult rats, prevalence of overweight increased 2013(Suppl 1): cell. The animal model of small for gestation in rat was made according to school grade. Most subjects (72.8%) had normal weight, 11.8% were overweight and obesity in adolescents and to identify the risk factors. Obesity and overweight in adolescents has more than tripled in the past 30 years. They are among the easiest medical conditions to recognize but most difficult to treat and has both physiological stress, which may programme later metabolism and body composition. The changes of childhood obesity in Shanghai, one of the most urbanized areas in China, is believed to represent and forecast the childhood obesity prevalence in today metropolitans and future overall China. In this study, we provide estimates of the prevalence and trends of overweight and obesity among children and adolescents in Shanghai from 2003 to 2008. One urban and one suburban district were randomly selected in the study in 2003. 70,582 students in 2003 and 86,355 students in 2008 in schools of those 2 districts were examined. Data on height, weight, gender and living area were collected. Weight status was estimated by body mass index (BMI) using the International Obesity Task Force standard. The prevalence of obesity and overweight were analyzed by area, age, gender and year. The prevalence of overweight and obesity increased significantly during the study period (2003-2008): the prevalence of overweight increased from 13.67% to 15.41% (p<0.01); prevalence of obesity increased from 3.72% to 4.58% (p<0.01). The prevalence of obesity and overweight in boys was significantly higher than that in girls (p<0.01). The prevalence of overweight and obesity in urban area was also significantly higher than that in suburb area (p<0.01). Over a 5 years period, there was a significant increase in the prevalence of obesity and overweight in children and adolescents of two districts in Shanghai. The high percentage of overweight may cause even more rapid increase in obesity in the absence of effective interventions in the near future.

**O50**
Prevalence and risk factors of overweight and obesity in adolescents in Malang, East Java-Indonesia

Ariani Harjono1, Anik Purnati, Haryudi Adjil Cahyono, Marudani Youswarwoto
Child Health Department Saiful Anwar General Hospital/Medical Faculty
Brawijaya University, Indonesia


Obesity and overweight in adolescents has more than tripled in the past 30 years. They are among the easiest medical conditions to recognize but most difficult to treat and has both immediate and long-term effects on health and well-being. We are interested in determine the prevalence of overweight and obesity in adolescents and to identify the risk factors. A cross sectional study was carried out on 346 adolescents of senior high school aged from 15-18 years old in Malang City, Indonesia. Anthropometric measurements included body weight, height, and mid-upper arm circumference (MUAC). The nutritional status was classified based on Body Mass Index (BMI) using the WHO standard criteria. Dietary recalls were collected to assess the quality of food. A systematic random sampling was made according to school grade. Most subjects (72.8%) had normal weight, 11.8% were overweight, 7.2% were overweight and 8.1% were obese. Among overweight group, 60% were boys, while among obese group, 50% were boys. On multivariate regression analysis, it was found that energy expenditure had significant negative correlation with the occurrence of overweight and obesity (p<0.001) while energy intake and lifestyle had a significant positive correlation (p<0.001 and p<0.001). Energy intake and lifestyle were proportionally related to overweight and obesity.

**O51**
Severe hyperemesis gravidarum affects offspring metabolism in childhood

Ahlia Ayavo1,2, Paul L Hofman1,2, José GB Derer1, Sarah Mathai1, Peter Stone1, Frank Bloomfield1,2, Wayne S Cutfield1,2
1Liggins Institute, University of Auckland, Auckland, New Zealand; 2National Research Centre for Growth and Development, University of Auckland, Auckland, New Zealand; 3Department of Obstetrics and Gynaecology, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand


Hyperemesis gravidarum leads to alterations in maternal (and possibly fetal) nutrition throughout pregnancy, but there are no data on the long-term metabolic health outcomes in the offspring. We hypothesized that hyperemesis gravidarum could lead to fetal nutritional compromise or physiological stress, which may programme later metabolism and body composition. Two groups of healthy pre-pubertal children born at term, aged 4-11 years were studied: offspring of mothers who suffered hyperemesis gravidarum (HG group; n=36) and controls (n=54). Recruited HG children were born to mothers admitted to hospital with metabolic disturbance during pregnancy. Following an overnight fast, a frequently sampled intravenous glucose tolerance test modified by insulin was performed, and insulin sensitivity was measured using Bergman’s minimal model. Other assessments included fasting lipid and hormonal profiles, as well as body composition using whole-body dual-energy x-ray absorptiometry. Data were analysed separately using linear mixed models, controlling for appropriate confounders. Data are expressed as mean±SEM.

Children born to mothers with severe HG had reduced S10.4±0.6 vs 13.4±0.9 x1010 (mU/L; p=0.016), increased fasting insulin (6.5±0.6 vs 4.9±0.3 mU/L; p=0.023), reduced IGFBP1 (13.0±1.3 vs 18.0±1.6 mg/ml; p=0.029) and IGFBP3 (3017±106 vs 3497±102 mg/ml; p=0.008) in comparison to controls. Baseline cortisol was higher in HG children (251±13 vs 218±11 nmol/l; p=0.007). DEYA-derived body composition was similar in HG and control groups. Children born to mothers who experienced severe hyperemesis gravidarum were less insulin sensitive and had elevated baseline cortisol compared to controls. We postulate that severe hyperemesis gravidarum reduces insulin sensitivity in the offspring due to fetal programming of the fetal hypothalamic-pituitary-adrenal (HPA) axis. Long-term follow up of these offspring is essential to determine later risk of metabolic disease.

**O52**
Changes of calcium channel characteristics and its relationship with pancreatic islet β cell paracrescence in rat born small for gestational age

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**Objective:** The experiment aimed to investigate the effect of intrauterine malnourishment on pancreatic islet β cell. **Method:** The animal model of small for gestation in rat was made under maternal calorie restriction by 50% from d1 of gestation until term, while the control group named AGA rats, were obtained from normal pregnant gravidarum (HG group; n=36) and controls (n=54). Recruited HG children were born to mothers admitted to hospital with metabolic disturbance during pregnancy. Following an overnight fast, a frequently sampled intravenous glucose tolerance test modified by insulin was performed, and insulin sensitivity was measured using Bergman’s minimal model. Other assessments included fasting lipid and hormonal profiles, as well as body composition using whole-body dual-energy x-ray absorptiometry. Data were analysed separately using linear mixed models, controlling for appropriate confounders. Data are expressed as mean±SEM.

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AGA groups. Using capacitance measurement induced by a sequence of sine wave stimulus to reflect the insulin secretion. In a word, study the tendency of channel kinetics and secretion property by timing. Results: The membrane capacitance of SGA was smaller than AGA rat after excluding the influence of whole cell membrane capacitance deviation both in neonatal rats, 4 weeks and 8 weeks (P=0.05). Also, The membrane capacitance of 8 weeks SGA rat was less than 4 weeks SGA rat (P=0.05), while the Cm between 4 weeks and 8 weeks AGA rat had no significant difference. Among the calcium channel characteristics, 1) neonatal rats: Compared with group AGA, SGA showed much lower value of the current density (Id) and peak current density of I-V curve (P=0.05), which was perfectly consistent with the result that the decrease of cell secretion from -40mV to 0mV, but there was no statistical difference found in reversal potential (P=0.05). The same result was obtained in activation curve and inactivation curve of calcium channel, whose half activated voltage/half inactivated voltage V1/2 and slope factor k between SGA and AGA both showed no significant difference (P=0.05); 2) adult rats: there was no statistical difference found in all average calcium current density (Id), including the total calcium, L-type and T-type. No significant difference was observed in the peak current density of I-V curve in SGA and AGA (P>0.05). However, the reversal potential in SGA group was much lower than control (P=0.05). The two group had the same shape of activation curve and inactivation curve of calcium channel, and 50% activated voltage between SGA and AGA had no significant difference, but the calcium channel of SGA was easily to be closed, the inactivated voltage in SGA group was much higher than control (P=0.01).

Conclusion: The effect of intrauterine malnourishment on pancreatic islet β cell last in postnatal life and the destroy of β cell tends to aggravate with time. Low calcium current density on β cell membrane devotes to the decrease of β cell secretion in SGA neonatal rat. However, the current of calcium channel returns to normal level in childhood. The kinetics of calcium channel is changed significantly, which may be the reason that intrauterine malnourishment lead to the decrease of insulin secretion in adult life.

O54
Clinical and molecular characteristics of congenital hypothyroidism with DUOX2 mutations
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Aims: Biallelic or monoallelic mutations in DUOX2 have caused congenital hypothyroidism (CH) with variable phenotypes from asymptomatic to permanent CH. This study was aimed to clarify molecular feature and clinical spectrum in CH with DUOX2 mutations.

Methods: This study included 62 transient or permanent CH patients with normal-sized or enlarged eutopic thyroid. All coding exons of DUOX2 and their intronic flanking sequences were amplified by PCR, and directly sequenced. As for novel sequence variants of DUOX2, functional studies were performed by measuring H2O2 generation in vitro. Clinical presentation was retrospectively reviewed based on medical records.


Discussion: DUOX2 variants were observed 11 out of 28 transient CH patients and 10 out of 32 permanent CH patients (39.3 % vs 31.3 %, P=0.593). At reevaluation, thyroid stimulating hormone (TSH) levels were 7.4±1.9 mU/L and 27.4±21.2 mU/L in transient and permanent CH with DUOX2 variants, respectively. Five patients with biallelic variants had higher initial TSH level (116.1±79.2 vs 50.2±50.2, P=0.049), and 3 out of 5 were determined as a transient CH. Functional analysis revealed partially impaired H2O2 generation in 15 different DUOX2 mutants.

Conclusion: This study showed that DUOX2 mutation is a common cause of CH with normal-sized or enlarged eutopic thyroid. Clinical spectrum of DUOX2 mutations was variable, emphasizing the importance of alternative mechanism to compensate the function of DUOX2 or modifying factors to regulate DUOX2 expression. Long-term follow up for CH patients with DUOX2 variants should be needed.
iodine deficiency, iodine excess, fetal prematurity and inactivating DUOX2 mutations. However, the underlying etiology of TCH is not determined in some cases. In this study, we conducted the first systematic investigation on the etiology of TCH, using screening population-based cohort in Niigata Prefecture, Japan.

Methods: Between April 2003 and March 2009, 148,100 newborns were screened for CH in Niigata prefecture, and 159 patients were considered positive for CH. We diagnosed patients as having TCH that fulfilled the following two criteria: 1) serum TSH level >30 mU/L and serum FT4 level <1.5 ng/dL at the initial examination, 2) serum TSH level <5 mU/L while investigating discontinuation of thyroxine replacement at 2 years of age. A total of 9 patients (1/16,500) diagnosed with TCH were evaluated. To determine the etiology of TCH, we examined the following: 1) maternal medical history, 2) gestational age and birth weight, 3) maternal anti-thyroid antibodies, 4) urinary iodine concentration at initial visit, and 5) DNA sequence of DUOX2.

Results: Among nine TCH patients, one had extremely high maternal TSH level, one was exposed to propylthiouracil, and two were exposed to excessive iodine. Furthermore, we found that five had biallelic DUOX2 mutations. Conclusions: DUOX2 mutations were the major cause of TCH in our cohort study.

**DIABETES**

**P1** Mauriac syndrome and early cataract diabetic
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1Pediatric Endocrinology, Medical Faculty of Andalas University, Padang City, West Sumatra, Indonesia / dr. M. Jamil Hospital Padang West Sumatra, Indonesia
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**Introduction:** Mauriac syndrome (MS) is characterized by development of dwarfism, obesity and hepatomegaly in patients with insulin dependent diabetes mellitus (IDDM). Growth retardation and hepatomegaly in IDDM should alert physicians over insufficient management of DM.

**Aim:** To alert medical community of importance in preventing and managing diabetic complication.

**Result:** A 5 year and 10 month old boy, was admitted with protuberant abdomen since one year ago. He had been recognized as type 1 DM and treated by subcutaneous insulin 4-5 U/day twice a day until admission. His abdomen became larger, wasted arms and legs so he couldn't support his body, and just laid down for 3 months. He had retarded growth and development. Oedema, chest was normal, distended abdomen with hepatomegaly and ascites, Extremities were disuse atrophy and pitting oedema. Laboratory investigation were: blood glucose 1074 mg/dl, metabolic acidosis, elevated of liver enzyme, hypoalbuminemia, hyperlipidemia and positive ketone bodies. HbA1c, C-peptide and IAA values were >18.5%, 1.2 mg/ml and 3.9 u/ml respectively. Bone age was retarded boy. At 10th day, oedema and ascites had disappeared. Six months later, he diagnosed with cataract dextra et sinistra by ophthalmologist and undergone cataract surgery. Growth velocity was 18 cm/year (catch up growth); liver was ¼-1/4. Hba1c value was 9.9%. Insulin dose was 1 U/kg/day.

**Conclusion:** Mauriac syndrome can resolve with appropriate insulin dose, good glyemic control, and improved growth velocity. Early cataract occurs in poor glyemic control.

**P2** Characteristics of ketoacidosis diabetic at Fatmawati Hospital
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2Registrar of pediatric department, Fatmawati hospital, Jakarta, Indonesia

**Background:** Diabetic ketoacidosis (DKA) is the most common complication of diabetes mellitus. DKA results from absolute or relative deficiency of circulating insulin and from combined effects of increased counter regulatory hormone levels. The combination of low serum insulin and high counter regulatory hormone concentrations accelerate catabolic state with increased glucose production by liver and kidneys (by glycogenolysis and gluconeogenesis), impair peripheral glucose utilization causing hyperglycemia and hyperosmolality, and increase lipolysis and ketogenesis, resulting in ketonemia and metabolic acidosis. Most of Indonesian children with diabetes mellitus (DM) came for the first time with diabetic ketoacidosis.

**Aims:** To describe the characteristics of diabetes mellitus type 1 cases presenting with ketoacidosis symptoms at Fatmawati hospital.

**Methods:** A retrospective survey was conducted during June 2012. Data was collected by using questionnaire. Subjects with ketoacidosis complication were included.

**Results:** Of 20 children with diabetes mellitus type 1 at Fatmawati hospital, only 13 subjects were included. Subjects were included had ketoacidosis event. Ratio between male to female almost equal (male 46.2% vs female 53.8%). Most subjects were 5-9 years old (46.1%) and 10-14 years old (38.4%). All subjects were not obese (100%) with body weight are 28.9±13.8 kg and body height are 134.8±16.4 cm. Most subject were severe ketoacidosis (53.8%) and small subjects were mild (23.1%), moderate (23.1%). Median glucose concentration is 339 (203-577) mg/dL and keton concentration is 2.88±1.0 mg/dL. Hemoglobin A1C (HbA1c) is 11±1.9% from all subjects. All subjects survived.

**Conclusions:** Subjects were almost equal between male to female. Most subjects were aged 5-9 years old. Most subjects were severe ketoacidosis with median glucose concentration 339 (203-577) mg/dL and keton concentration 2.88±1.0 mg/dL. Most subjects were not obese with HbA1c 11±1.9%.

**P3** Pediatrician level of knowledge on management of type 1 diabetes mellitus and diabetic ketoacidosis
Ratna Dewi Arta1, Indah S Widyahening2, Aman B Pulungan3
1Department of Child Health, Medical School, University of Hasanuddin, Makassar, Indonesia; 2Department of Community Medicine, Medical School, University of Indonesia, Jakarta, Indonesia; 3Department of Child Health, Medical School, University of Indonesia, Jakarta, Indonesia

**Introduction:** Diabetes Mellitus (DM) is a metabolic disorder characterized by high blood glucose level that result from defects in insulin secretion and/or action. Prevalence of type 1 DM (T1DM) has increased every year, including in Asian countries. Effective management of T1DM needs balanced of insulin treatment, diet, physical activities, and education. Physician that involve in T1DM management should to have adequate competencies and should be able to provide specific attentions as T1DM is a condition that may need long-term monitoring and treatment as well as may have potency of complications, both acute and chronic.

**Objective:** To examine pediatrician level of knowledge on T1DM and diabetic ketoacidosis (DKA) management and factors that influence their level of knowledge.

**Methods:** Research design was a cross-sectional study. Data collected in Banten and Surabaya from August to September 2009. Study population were pediatricians who attended trainings on management of T1DM and DKA in Banten and Surabaya and pediatricians among them that agreed to fill and return study questionnaire and knowledge data sheet were included as sample of this study. Bivariate analysis with x2 or Fisher Exact test (significant value p ≤ 0.05) were analysis methods applied in the study.

**Result:** There were 64 subject included in the study, men 31 (48.4%) and woman 33 (51.6%). We found that younger participants have good level of knowledge with OR 3.64 (95% CI 1.29 to 10.26) and subject with shorter length of duty with good level of knowledge with OR 7.42 (95% CI 2.13 to 25.84).

**Conclusion:** There is association between younger age and shorter length of duty with pediatrician level of knowledge on T1DM and DKA management.
**P4**

**Neonatal diabetes in Wolcott–Rallison syndrome: a case report**

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Wolcott-Rallison syndrome (WRS) is a rare autosomal recessive disorder characterized by the association of permanent neonatal or early-infancy insulin-dependent diabetes, multiple epiphyseal dysplasia and growth retardation, and other variable multisystem clinical manifestations. In the present study, we analyzed the EIF2AK3 gene in a 64 day-old-girl WRS patient and his parents to study the clinical features, the mechanism for genetic onset of WRS and provide credible genetic counseling for prenatal diagnosis in his family. Based on analysis of a 64 day-old-girl’s clinical symptoms associated with biochemical examination, the diagnosis of WRS was therefore made. Genomic DNAs were extracted from peripheral blood leukocytes from the patient and his parents with their informed consent for genetic studies. The coding and flanking intronic regions of the EIF2AK3 gene was analysed by sequencing. In a result, the patient had gestation age of 41 weeks, birth weight of 3200 g, and onset of the disease at 64 days of age. She was admitted with the features of convulsion, anemia, jaundice, diabetic ketoacidosis with pH of 7.27, HCO3 of 17.8 mmol/l, BE of -8 mmol/l, blood glucose 42.46 mmol/l, HbA1C 6.5%, total bilirubin 59.2 µmol/l, direct bilirubin 29.7 µmol/l, AST 3741.2 U/l, ALT 1927 U/l. PCR of CMV, EBV, HAV were negative. Abdominal ultrasound did not find any sign of cholestasis. Sequencing analysis of patient’s EIF2AK3 gene has identified a homozygous missense mutation, p.8632W. The parents are carriers of heterozygous EIF2AK3 missense mutation, p.8632W. In conclusion, combining mutation screening of EIF2AK3 gene with clinical manifestations and effective examination may provide a reliable diagnostic method for patients.

**P5**

**Analysis of clinical and genetic features among 12 neonatal diabetes mellitus**

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**Objectives:** To analyze the clinical and genetic features among 12 neonatal diabetes mellitus (NDM).

**Methods:** Describe clinical features of 12 diagnosed NDM cases in my hospital between Jul. 2001 and Jun. 2012. KCNJ11, ABCC8 and INS gene were sequenced in all patients.

**Results:** The age at diagnosis was between 0.5 and 5 month, the median was 3 month. 7 cases (58.3%) were SGA. Infection occurred in 7 cases, 4 cases with convulsion and 8 cases with ketoacidosis. The mean HbA1c at diagnosis was 10.0% (7.4%~13.7%). Insulin treatment was started in all 12 patients, the initial dose was 1.0~1.2IU/kg/d, 6 cases were treated with glyburide after the acute phase, only one boy who diagnosed as NDM syndrome reached euglycemia. 2 cases stopped glyburide because of gastrointestinal adverse reaction. Among the 12 cases followed up, 7 had PNDM, 4 had TNDM, 1 case lost following. 2 cases died, one was the NDM syndrome patient died of DKA, the other died of hepatic and renal failure at the age of 1 year and 6 months. One had skeletal dysplasia and diagnosed as Wolcott-Rallison syndrome. The blood glucose of most patients was well controlled. KCNJ11c.175G>A (V59M) and KCNJ11c.601C>A (R201H) mutation were found in two patients.

**Conclusion:** The clinical expressions of NDM were atypical and easily missed diagnosis. Of all the NDM cases, 30% was TNDM and relieved automatically. Insulin was the best choice before genetic identification. The KCNJ11 mutation rate of PNDM was 28% in China.

**P6**

**Acute kidney injury as a severe complication of diabetic ketoacidosis in children: a case report**

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**Background:** Diabetic Ketoacidosis (DKA) is associated with significant morbidity and mortality and probably could be prevented by earlier diagnosis of diabetes mellitus (DM) and intervention. The level alertness of primary care doctors and knowledge on DM play a role to prevent severe complication of DKA.

**Objective:** To highlight the acute kidney injury as a severe complication of DKA in children.

**Methods:** We reported a diabetic ketoacidosis patient developing acute kidney injury at Hasan Sadikin General Hospital Bandung, Indonesia.

**Results:** A 12-year-old girl from a rural area was admitted to our pediatric emergency with decreased consciousness. We reviewed there was a history of polyuria, polydipsia and marked weight loss. When she arrived at hospital, she was very ill, comatose state, severe dehydration and typical Kussmaul breathing. Her heart rate was 140/min with thread pulse, low blood pressure, dry mucous membranes, sunken eyes, poor capillary return, and cold fingers. Laboratory analysis showed her blood glucose level was 890 mg/dl, severe metabolic acidosis and urine ketones 3+. The patient was resuscitated with IV fluids as soon as possible, followed by insulin and potassium chloride. On day 2 she developed oliguria and her serum creatinin and urea levels were 2.25 and 124 mg/dl that impressed as acute kidney injury. After fluid restriction she had persistent oliguric, increased serum creatinin and urea up to 7.34 and 234 mg/dl warranted initiation of peritoneal dialysis. After peritoneal dialysis and DKA management she showed a good improvement.

**Conclusion:** Patient with severe DKA developing acute kidney injury need early recognition and initiating renal intervention may improve the potentially poor outcome.

**P7**

**Development of a resource tool to assist children to adjust emotionally to the diagnosis of type 1 diabetes**

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Our previous work has shown that children recently diagnosed with type 1 diabetes (T1DM) have difficulty expressing the grief and despair that they feel in the immediate period following diagnosis. Further, many children describe feelings of isolation with their diabetes and are eager to connect with peers in a similar situation. A children’s book was therefore developed for children with newly diagnosed T1DM and their carers aimed to: 1. Create a platform for these children to enable them to express their emotions in a safe environment with parental support. 2. To read how other children in their situation have adjusted to life with T1DM.

The book is a 24 month period, approximately 60 children aged 8-12 years with T1DM attended monthly Therapeutic Support Groups at the Children’s Hospital at Westmead. The emotions and experiences during the period of T1DM were recorded as direct quotes and drawings. From this data, unique insights shed light on the complexity of the psychological process experienced by children during the time of diagnosis through exploration of specific examples it became clear that emotions such as anger, sadness and isolation were strong themes throughout the journey of diagnosis and were chosen for inclusion in the book. The collated material provides a greater understanding and their carers of the emotional journey experienced when first diagnosed with T1DM. The children discuss feelings and strategies regarding how to cope with injections, finger pricks, what friends can do, tips for parents and stories of hope.

The gathering of material resulted in a children’s book being published which enable the child to read how other children managed their diagnosis of T1DM and endorses to encourage other children to reflect. Throughout the book there are opportunities for the child to draw pictures and write how they navigated their feelings with diabetes. In conclusion the book has been trialled by a number of Social Workers and other disciplines over the past 6 months with positive feedback from health professionals and patients. It has been used in the initial newly diagnosed sessions, counselling and groups at camps. This free book could be beneficial for rural communities who have limited psychological support as it may offer the child to feel understood while reading other children’s similar experiences.
P9

A case of insulin allergy in a girl with type 1 diabetes

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Insulin is an important treatment for type 1 diabetes. Allergy caused by insulin administration is very rare. Several studies have reported some cases of insulin allergy caused by insulin administration. This is the first case of insulin allergy in our hospital.

A 12 years old girl came to outpatient ward with oedema. She had oedema in palpebra, lower extremities and ascites. There were no dyspeu, abdominal pain, and urination complaint. She has been 4 years treatment of type 1 diabetes. In last visit, she was hospitalised because of worst glycemic results (frequent episode of hypoglycemia, hyperglycemia, and Hba1c 16.4%). She was changed from conventional regimen (twice daily) to multiple daily regimen, with the use of twice daily mix insulin (intermediate and rapid) plus rapid insulin (aspart insulin), 3 days before the oedema. There were no involvement of hepatic, cardiac and renal disorder. Cetirizine was given, and the oedema disappeared. We changed back to twice daily regimen for several days, and then try to multiple daily regimen. While she uses multiple daily regimen, oedema occurred again. After discontinuing rapid insulin (aspart insulin), she never had this allergy. She uses a mix-split regimen now. Insulin allergy in this case could be caused by the insulin or non-medical ingredients. As a conclusion, we must concern to insulin allergy although a very rare case.

P10

Trends and complications profile in childhood-onset type 1 diabetes from North India

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Data from India regarding epidemiology and complications of childhood-onset type 1 diabetes (T1DM) is scarce. We analyzed the epidemiology, glycemic control and diabetes related complications in our T1DM patients. Relevant clinical data of patients with onset of T1DM <18 years of age attending our OPD from January 1991 till December 2010 was collected from hospital records, phone calls, letters and direct patient interviews. Patients following up between January 2010 to December 2011 were evaluated for glycemic control. Of 409 patients having at least 1 visit in our clinic over 20 years, 269 patients could be contacted in the study period. The proportion of newly registered T1DM patients among all pediatric endocrine new patients increased 2.4 times between years 2000 and 2010. The proportion of patients diagnosed at age <5 years increased over time and was 24% by year 2010. Premixed insulin or other non-medical ingredients. As a conclusion, we must concern to insulin allergy although a very rare case.

Central nervous system (CNS) impairment is common in diabetic patients even in the early stage of the disease and it could be associated with peripheral neuropathy. Nevertheless, less attention has been directed toward the chronic effects of diabetes on the CNS.

The aim of the study was to investigate the changes of central nerve conduction in children with insulin-dependent diabetes mellitus prospectively using the visual evoked potentials (VEP) and to know how those results were related to clinical risk factors and parameters of peripheral nerve conduction studies (NCS). A total of 75 diabetics (29 males) aged 5-26 years (mean 14.3±4.7) underwent VEP and NCS annually for 5 years. For comparison, 52 healthy children were studied. Out of 75 patients, 25 patients completed annual study for 5 years. The latencies of P100 were prolonged at the study entry when compared with controls (P < 0.001). Significant positive correlations were found between the VEP latency and the glycosylated hemoglobin level. The values of latency and amplitude were inversely related with the age of patients and the duration of the disease. The values of latency were not related with parameters of NCS. Only a few parameters of NCS were weakly associated with the amplitudes of P100.
P12
Illustration of children’s blood pressure in diabetes mellitus type 1 in Indonesia
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Background: One of the long-term complications of diabetes mellitus type 1 (DM type 1) in children is diabetic nephropathy. Diabetes longstanding suffered and pubertal status are the influencing factors which make the complications come up to the surface. Diabetic nephropathy case will be accompanied by increasing of blood pressure symptoms.

Objective: To detect the illustration of childrens blood pressure in DM type 1 base on their age, sex, longstanding suffered, and the latest level of HbA1c.

Methods: A retrospective observational studies on national registered of DM type 1 at pediatric endocrinology chapter to 2010. Age, sex, longstanding suffered, the latest level of HbA1c, systolic blood pressure (SBP) and dyastolic (DBP) are variables which has been researched.

Result: Starting at 177 children suffered by DM type 1,118 (66.7%) are girls and 59 (33.3%) are boys. The average age when they got diagnose for the first time is 11.8 years old. Only one girl (0.6%) who suffered DM type 1 more than 5 years, has SBP and DBP > percentile 95, There is no any significant correlation with the others.

Conclusion: Most of the childrens blood pressure in DM type 1 are still normal. In this research, a girl who being suffered in DM type 1 with hypertension (> 95th percentile) has been suffering more than 5 years. It needs doing blood pressure measurement regularly, for screening the diabetic nephropathy, if microalbumin examination has not been done yet.

P13
Epidemiologic characteristics of diabetes in children aged 0–14 years in Busan and Gyeonnam Province, Korea (2001–2010)
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Objective: We performed this study to investigate changes in the incidence of type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) in children aged below 15 years in Busan and Gyeonnam province, Korea during the period from 2001 to 2010.

Methods: We sent questionnaires via the post to 4 tertiary and 43 general hospitals in Busan and Gyeonnam province. We received answered questionnaires based on medical records from all tertiary and 11 general hospitals. Three hundred forty four diabetic patients (239 T1DM, 89 T2DM, 16 unclassified DM) who were newly diagnosed from 2001 to 2010 were enrolled. The incidence rates were calculated as the number of cases per 100,000 person-years. The denominator for incidence rate was secondary data from the population registry (Korea National Statistical Office). Ninety five percent confidence intervals (95% CI) was calculated using Poisson distribution. The incidence rate was fitted and test for the linear trend was done by Poisson linear regression model. We also used the Poisson regressions to assess the rate ratio for development of diabetes with year, sex, age group, geographic location. The data were analyzed using SAS 9.2.

Results: The average crude incidence was 2.01 (95% CI: 1.77-2.28) and 0.76 (95% CI: 0.61-0.93) for T1DM and T2DM, respectively. There was a significant increasing trend in the incidence of T1DM during the period of 2001 and 2010, with an annual 1.08-fold increase of the rate ratio (95% CI: 1.03-1.12). The trend in the incidence of T2DM increased with an annual 1.23-fold increase of the rate ratio (95% CI: 1.14-1.33). The incidence of T2DM among those aged 10-14 years was rapidly increased during the period of 2001 to 2010 and was higher than that of T1DM in 2010.

The rate ratio for development of T1DM was 1.16-fold higher in males than females and that for those aged 10-14 years was a 2.04-fold higher when compared to those aged 0-4 years. Also, there was an 1.43 increased rate ratio in Busan (urban) compared to Gyeonnam province (suburban). The rate ratio for development of T2DM was 1.29-fold higher in males than females and that for those aged 10-14 years was a 9.59-fold higher when compared to those aged 5-9 years. Also, there was an 1.58 increased rate ratio in Busan (urban) compared to Gyeonnam province (suburban).

Conclusion: The incidence of T1DM and T2DM have shown a significant increasing trend for last 10 years in Busan and Gyeonnam province, Korea. Our study shows the needs for careful monitoring of incidence and its related risk factors of T2DM in adolescents.

P14
Diabetic mellitus type 1 in patient with beta major thalassemia (case report)
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Oxidative stress in pancreatic organ may occur in children with thalassemia. It is caused by the overloaded iron store which not bound by transferrin. This condition triggers apoptosis of pancreatic beta cell so that the production of insulin decelerated progressively. Finally, it results in glucose intolerance and the patient suffers from diabetic mellitus. Some studies conclude that the risk factors of diabetic mellitus in patient with thalassemia are age, volume of blood transfusion required, high ferritin serum, history of diabetic mellitus in family, and adherence in consuming iron chelation agent. The aim of this case report to inform case of diabetic mellitus type 1 with beta major thalassemia in 24 year old female who has been diagnosed thalsasemia since she was five months old.

Female, 24 years old, with body weight 42 kg, and height 153 cm. She admitted for routine blood transfusion because of thalassemia (previously the transfusion was done with interval of 3-4 weeks). Splenectomy was performed when she was 18 years old. So far, she has been provided therapy for desferoksmin 3x500 mg orally and intramuscular injection of deferiprone with poor compliance because of side effect and availability. When she was 23 year and 9 month old, she suffered from diabetic mellitus type I and got insulin basal bolus. She also complained of having pain in left lower extremity which gradually made her very weak and couldn’t walk. Laboratory finding: blood glucose concentration: 116 g/dl, ferritin: 8385 ng/ml, FT4: 0.80 ng/dl, TSH: 3.98 uIU/ml, HbA1c10.9%, C-peptide: L < 17 pmol/L. Left curvis x-ray showed multiple trival fracture. This patient was provided by routine blood transfusion, intramuscular injection of deferoxamine dan deferiprone 3x500 mg orally, vitamin C 2x50 mg orally, folic acid 2x1 mg orally, vitamin E 1x200 mg, calcium and vitamin D supplementation, intensive therapy of insulin basal bolus, diet DM, internal fixation. After 3 months, HbA1c level was getting improvement.

Diabetic mellitus type I in patient with thalassemia could reach optimally by doing good effort for metabolic control and by multiple approaches. Education of self monitoring on blood glucose concentration is very crucial to prevent the complication.
The incidence of childhood type 2 diabetes mellitus (DM) is increasing worldwide in parallel with an increasing prevalence of childhood obesity. We investigated the type of diabetes and the clinical characteristics in the newly diagnosed diabetic children.

Retrospective analysis of clinical characteristics was done in 125 newly diagnosed diabetic children and adolescents under 18 years of age in Korea from March 2003 to December 2010. Children diagnosed with type 1 diabetes were 100 out of 125 (80%) and 25 out of 125 (20%) were type 2 diabetes. Mean age of onset was 9.26 ± 0.99 years and there was no seasonal variation of incidence. 32% of children with type 1 diabetes presented initially with diabetic ketoacidosis. Mean body mass index (BMI) was 16.8 ± 3.8 kg/m², mean blood glucose level was 457.6 ± 112.5 mg/dL and mean glycated hemoglobin (HbA1c) level was 12.1 ± 2.28%. Positive result was revealed in 52% of the subjects with type 1 diabetes for antibodies to glutamic acid decarboxylase (GAD), 3% for islet-cell antibodies (ICA), 25% for insulin autoantibodies (IAA) and 63% showed positive results for at least one of these autoantibodies. 25 patients (20%) were diagnosed with type 2 diabetes. Mean age of onset of type 2 diabetes was 12.2 ± 3.4 years. 12 out of 25 (48%) subjects were diagnosed with type 2 diabetes in the process of evaluating the cause of obesity without any other presenting symptoms. Mean BMI was 28.3 ± 8.7 kg/m², mean blood glucose level was 217.7 ± 105.5 mg/dL and mean HbA1c concentration was 9.0 ± 2.9%. 52% of the subjects diagnosed with type 2 diabetes had a family history of diabetes and 80% were either overweight or obese. Although still not as common as type 1 diabetes among children, type 2 diabetes mellitus increasingly has been seen in children. Routine medical screening in obese children and adolescents or ones with other risk factors of type 2 diabetes should be emphasized to make early diagnosis and start management of type 2 diabetes to improve long-term outcomes.

Hemichorea in 15-year-old patient with poorly controlled type 1 diabetes mellitus

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Introduction: Hemichorea, spontaneous unilateral involuntary movements and contralateral neuroimaging abnormalities of the striatum may be the presenting feature of nonketotic hyperglycemia in older adults with type 2 diabetes, but cases in children with type 1 diabetes are very rare.

Case: A 15-year-old woman with a 6-year history of type 1 DM developed right hemichorea. She presented continuous involuntary choreic movements of both herring arm and leg. The movements were nonsuppressible and ceased only during sleep. With the exception of this movement disorder, other neurological examination was unremarkable. On funduscopic examination, nonproliferative diabetic retinopathy was detected. The following laboratory findings were notable: fasting blood glucose 162 mg/dL, serum osmolality 305 mOsm/L, and HbA1c 13.2%. Urinalysis was negative for glucose, ketones, and protein. There were no signs of diabetic ketoacidosis, hypoglycemia, hypersomnolent hyperglycemic coma, or rheumatic fever. Cranial computed tomographic scan showed that hyperattenuation of the left basal ganglia. T1-weighted magnetic resonance image demonstrated that hyperintensity of the left striatum. The hemichorea was slowly controlled with small oral doses of haloperidol (1.5 mg/d) and intensive blood glucose control.

Conclusion: We report the case of a 15-year-old poorly controlled diabetic adolescent girl who developed acute hemichorea of the right arm and leg in whom T1-weighted magnetic resonance imaging of the brain revealed hyperintense signal in left basal ganglia.

Factors associated with glycaemic control in Singapore children and young people with diabetes

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Data from follow-up studies of DCCT (EDIC) [1,2] and UKPDS [3] suggest that tight glycaemic control in the early years after diagnosis of diabetes may delay the onset and development of diabetes-related complications. This phenomenon of “metabolic memory” [4] is particularly relevant for patients who are diagnosed during childhood and adolescence because of potentially longer lifetime duration of diabetes. We conducted the present study to identify the factors associated with glycaemic control in Singapore children and young people with diabetes. A cross-sectional analysis of data from our Paediatric Diabetes Service (PDS) as at the end of 2011 was performed. We included 125 patients (77 male; 46%), age <20 years and diagnosed with Type 1 (T1D) or Type 2 (T2D) diabetes for >1 year duration, who had attended clinic at least twice during 2011, and whose mean HbA1c measured at their clinic attendances was either good (HbA1c <8%; Group 1, n=69) or poor (HbA1c >10%; Group 2, n=56). The following factors in the two groups were compared: patient characteristics (gender, ethnicity, current age, age at diagnosis, duration of diabetes, type of diabetes, family history);
medical treatment prescribed (insulin, oral agents, both); and extent of resource utilization (diabetes clinics, medical social worker (MSW) input, dietician reviews). Patients whose glycaemic control was intermediate (8% ≤ HbA1c ≤ 10%), and those with other types of diabetes (non-T1D and non-T2D), medical co-morbidities, or who had transitioned to the Adult Diabetes Service during 2011, were excluded.

Compared to Group 1 (good control) patients, Group 2 (poor control) patients were more likely to be non-Chinese (52% vs 24%; p=0.001) and to have received MSW input (30% vs 9%; p=0.002) and attended more diabetes clinics in 2011 (4.4±1.3 vs 3.5±1.0 times; p<0.001) – see Table 1. Multivariate analyses found that these three factors remained independently predictive of poor glycaemic control. There was no statistically significant difference between the two groups in all the other factors examined.

Ethnicity and utilization of healthcare and social services were factors associated with glycaemic control in Singapore children and young people with diabetes. These findings suggest that there are paediatric diabetes patient groups in which the desired outcome was not achieved despite providing higher levels of currently available support. Therefore, we need to devise new ways of improving the management of these at-risk patients.

References

P19
Case report and literature review: T2DM with DKA, HHS and rhabdomyolysis
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We report two type 2 diabetes mellitus (T2DM) adolescent patients who had diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS) predisposing rhabdomyolysis (RM). Literatures were reviewed, which made us focus on the severe complications of DM.

The two adolescent patients were admitted urgently with T2DM complicated with ketoacidosis, whose chief complaints were thirsty and polyuria for 6 days and 3 days respectively, drowsiness for 2 days and 2 hours.

The skin was mottled and cold peripherally. The levels of blood glucose were 47.11mmol/L and 68.11mmol/L, corrected levels of serum sodium were 149.2mmol/L and 149.3 mmol/L, the osmolality were 327.6 mOsm/L and 334.4mOsm/L. The urine ketone body were both positive, blood pH were 6.8 and 7.05. They were diagnosed as DKA and HHS. During the treatments of dehydration and insulin, the patients had oliguria because of poor liquid infusion. The blood creatine kinase (CK) of these patients elevated more than 10000U/L with myoglobinuria characterized with black tea color urine. Based on above, RM were diagnosed. Acute renal failure occurred subsequently. We reviewed the literature of T2DM accompanied with DKA-HHS and RM. The mortality of HHS in children was rare. One report documented the mortality was 14% in children, which was similar to that of 15-20% approximately in adults. There was no document of case report or mortality of RM caused by T2DM with DKA-HHS. The literature documented RM usually caused by drugs, trauma and excessive muscular activity, etc. The normal saline infusion should be given at a rate of 1.5litrères/hour at the beginning to maintain the urine output 200-300ml/hour in adults. The infusion of sodium bicarbonate is not necessary after effective liquid supplementation. Mannitol and loop diuretics may be useful. As for these patients, after the effective liquid infusion and anti-shock treatments, the urine ketone body turned to be negative and the urine color turned to be normal at the third day of admission. The CK level was decreased to normal at the 21-22th day. The two patients were all recovered finally.

The diagnosis of RM depends on the clinic manifestation and laboratory. T2DM with DKA-HHS and RM is very rare in pediatric patients. The main reason of RM of the two patients may be HHS and the inadequate liquid infusion. This kind of patients could be cured by adequate infusion.

We are lack of the experience of the treatment to this kind of patients. So it is important for us to prevent the patients from RM, to recognize HHS earlier, to give enough liquid infusion and to prevent shock. These may be useful to decrease the mortality of RM and on the contrary, to increase the survival rate of patients.

P20
The obstacles in managing type 1 diabetes mellitus patients in H. Adam Malik Hospital, North Sumatera, Indonesia
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Background: Diabetes is a chronic illness that requires continuing medical care and ongoing patient self management, education and support to prevent acute complications and to reduce the risk of long-term complications. Caring for children with diabetes is challenging for many reasons, some of them are social, emotional, and financial problem.

Aims: To report our experiences in managing type 1 diabetes mellitus (DM) patients in our hospital, the referral hospital in our province, from 2009 till June 2012.

Methods: We reviewed all the patients with diagnosis type 1 DM. The following information was collected: patient’s condition at first diagnosis, sex, body mass index (BMI), age at diagnosis, blood glucose, C-peptide, and HbA1C level, parents earning, presenting clinical features, family history, health funding, insulin therapy, and problems in managing the patients.

Results: We have 21 patients from 2009 until June 2012, 4 were male. The age at diagnosis was between 4 until 14 years old. Nutritional status were moderate until severe malnutrition. About 62% of patients had history of diabetic ketoacidosis. Most of them came from low social economic background, for some patients, the parents earning were less than 1 million rupiahs (<USD 100). Only 5 patients had health insurance which covered insulin, and others must buy insulin by themselves. This was a big problem for us since 4 patients stopped insulin therapy, using herbal treatments instead and were readmitted with diabetic ketoacidosis. Mean of HbA1C level was 14%, C-peptide was 0.3 ng/mL. Four patients died with severe DKA, and 1 died with severe hypoglycemia.

Conclusion: Most of our patients were diagnosed late. Social, environment, and financial problems were the main issue in managing these patients. We need government and people to work together to solve these problems and guarantee the quality of life of diabetic patients.

P21
Diabetes ketoacidosis in L-asparaginase therapy
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Background: Diabetic ketoacidosis as a complication of L-asparaginase therapy in children with acute leukemia is rare. We report a patient with acute lymphoblastic leukaemia who developed diabetic ketoacidosis whilst on treatment with L-asparaginase.

Case: E.C, 10 years old female brought to the ER due abdominal pain. Patient is a diagnosed case of B-Cell Acute Lymphoblastic Leukemia (ALL) with diabetic ketoacidosis. Mean of blood glucose was 240mg/dl, ketone body was 2.6 mmol/L and the osmolality was 358mosm/L. The patient had received L-asparaginase (leunase) and Prednisone (60mg/day for a week then 5mg/day) for 3 weeks prior to this recent admission. One week prior to hospitalization, the patient had nocturia (2-3x/night), polyuria and polydipsia. On the day of admission, she had sudden onset difficulty of breathing associated with severe abdominal pain and vomiting. She came in non-ambulatory, in cardiorespiratory distress with BP: 100/70mmHg, HR: 150/min, RR: 60/min, Temp: 37.3°C. Pertinent physical exam showed signs of dehydration with abdominal tenderness, and signs of circulatory compromise. Fluid resuscitation was
immediately instituted. The initial assessment at the ER was pancreatitis but the serum amylase and lipase were normal. Other lab work-ups showed blood glucose of 26.8 mmol/L (NV:3.08-7.92), sodium at 115 mmol/L(NV:132-143), potassium of 3.3, Chloride at 88mmol/L (NV: 98-116). Blood gas showed ph of 7.1, a pCO2: 50, HCO3 at 3.7, and a base deficit of -22.5mmol/L. Urinalysis showed -4 of glucose and -3 of ketones. The patient was then managed as a case of DKA and fluid resuscitation was continued and insulin drip was started. The haemoglobin A1c level at diagnosis was 11.4% but the C-peptide was normal. Patient condition improved and was discharged with insulin injection. The insulin was discontinued after completion of her induction phase and with normalization of blood glucose.

Conclusion: Early recognition of the precipitating factors for DKA is important to prevent L-asparaginase fatal consequences, and the leukemic process itself maybe considered as one of the predisposing factors.
Monogenic diabetes in children mostly results from mutations in genes that regulate beta-cell function. It may be dominantly or recessively inherited or may be a de novo mutation and hence a spontaneous case. Quality of life is important in management of patient with monogenic diabetes. Objective is to analyze quality of life in a patient with monogenic diabetes.

A 19-year-old girl, 29.5 kg, suffered from polyuria, polydipsia, and polyphagia. Family history of diabetes was positive. Physical examination revealed non obese, with collateral vein, and hepatosplenomegaly. Laboratory examination revealed fasting blood glucose 275 mg/dL, hemoglobin A1C 10.3%, C-peptide 4.1 ng/mL (normal 0.7-9.7 ng/mL), ALT:110 U/L, AST:115 U/L, HDL:70 µg/dL, LDL:57 mg/dL, total cholesterol:319 mg/dL, and triglyceride:2030 mg/dL. Liver biopsy revealed hepatosteatosis. She was diagnosed with monogenic diabetes and Nonalcoholic Steatohepatitis (NASH). Patient was given glibenclamide 5 mg twice daily; insulin detemir 14 IU; metformin 500 mg twice daily, with uncooked corn starch. After three months of treatment random blood glucose became 132 mg/dL and A1C became 7.7%; insulin was stopped. Seven months later random blood glucose increased to 287.5 mg/dL, ALT: 204 U/L and AST: 257 U/L. Insulin was readministered and glibenclamide were increased to three times daily. A1C evaluation revealed 5.7%. Diabetic nephropathy (DN) occurred, but after a month of captopril, proteinuria was improved from 8 g/24 hrs to 1.5 g/24 hrs. Diet for DN was put to therapy. No retinopathy was found. Measurement of quality of life using Diabetes Quality of life (DQOL) revealed satisfaction with life 65.8%, impact of diabetes 55%, worries about diabetes 50.9%, and overall her health was poor. Conclusion is hyperglycemia, nonalcoholic steatohepatitis, hypertyglycemia, and diabetic nephropathy reported as clinical course of monogenic diabetes. The quality of life revealed satisfaction.

P26 Early initiation of insulin in a child with T2DM and clinical course - a case report
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Aim: To report a 13 year old girl with T2DM who had been initiated on insulin and the course of her glycemic status.

Methods: We describe a case of T2DM in a 13 year old girl – her clinical presentation, diagnosis and change in glycemic control over a period of 12 months.

Results: 13 year old presented with osmotic symptoms for 3 weeks duration. There was no change in weight. She had a strong family history of DM in mother and grandmother. On examination, general examination was unremarkable with no acanthosis nigricans, skin tags, or visceral obesity. Her vitals were normal. Her BMI was 23.42 kg/m². Her initial blood glucose levels are fasting 245 mg% and post prandial 340 mg%. Her urine ketones were negative and her initial HbA1c was 8.3%. Her fasting insulin and c-peptide levels (before initiation of insulin treatment) were 101 µU/mL (2.6 – 24.9) and 8.58 ng/mL (1.1 – 4.4) respectively. Her TPO and GAD antibody were negative. Her hemogram, liver, renal and thyroid functions were normal.

She was initiated treatment with inj.premix (30/70) 12 units before breakfast (BBF) and 10 units before dinner (BD). Over the course of next 1 year, her insulin requirement was gradually tapered to 6 units BBF and 6 units BD. Her current glycemic status was fasting 93 mg% and post prandial 76 mg% with HbA1c of 6.5%. Insulin and c-peptide levels were 12.6 µU/mL (2.6 – 24.9) and 1.8 mg/mL (1.1 – 4.4). She had gained 5 cm height and lost 2 kg in last 1 year.

Results: As per the ADA (American Diabetes Association) and ISPAD (International Society of Pediatric and Adolescent Diabetes) recommendations, insulin is currently not recommended as initial treatment in the management of children with T2DM unless they present with ketosis or HbA1c >8.5%. However, this case scenario shows insulin when initiated early in children with newly diagnosed diabetes in a state of glucotoxicity, when response to oral hypoglycemic may be suboptimal, may have better glycemic control even at lower doses.

P27 Time to peak postprandial glucose levels in childhood-onset diabetic patients analyzed with a continuous glucose monitoring system
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The risks of complications due to chronic diabetes are indicated by an increase in average blood glucose levels and the range of blood glucose level fluctuation. Postprandial hyperglycemia should be the target of glycemic control in clinical practice. There are few studies on the time to peak postprandial glucose levels in children. Therefore, we investigated the time to peak in childhood-onset diabetic patients using a continuous glucose monitor system (CGMS).

Twenty-seven patients with childhood-onset diabetes were included (male to female ratio, 9:18): 20 had type 1 diabetes, 3 had type 2 diabetes, and 4 had other types of diabetes. All patients underwent CGM on admission using the CGMS; their blood glucose levels were monitored up to 3 h after each meal. The time to peak postprandial glucose levels was retrospectively determined.

The CGMS recorded the postprandial glucose levels 266 times. Average peak time of postprandial blood glucose and average blood glucose excursion were 96.3 ± 56.7 min and 86.5 ± 56.7 mg/dL, respectively. The average peak time and average blood glucose excursion were as follows: type 1 diabetes, 91.2 ± 56 min and 80.0 ± 62.3 mg/dL; type 2 diabetes, 92.7 ± 42.6 min and 105.8 ± 52.2 mg/dL; other types of diabetes, 112.1 ± 50.7 min and 828 ± 42.7 mg/dL. The average peak time and blood glucose excursion for meals were as follows: breakfast, 108.4 ± 53.7 min and 92.6 ± 60.6 mg/dL; lunch, 93.2 ± 51.8 min and 83.4 ± 48.6 mg/dL; and dinner, 88.3 ± 54.0 min and 83.9 ± 60.0 mg/dL. There was no correlation between time to peak postprandial blood glucose and HbA1c levels.

The average time to peak postprandial blood glucose levels was approximately 90 min in both type 1 and 2 diabetes patients. The time to peak postprandial blood glucose levels reported here was delayed as compared to other studies on Japanese healthy adults with childhood-onset diabetes. The time to peak postprandial blood glucose levels in childhood-onset diabetic patients was approximately 90 min. As an indicator of glycemic control in childhood-onset diabetic patients, the CGMS was considered useful for determining the postprandial blood glucose levels in clinical practice.

P28 Clinical picture of diabetic ketosidosis in Saiful Anwar Hospital
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Saiful Anwar Hospital Malang, Indonesia, 2005-2009

Objective: To present the clinical appearance of diabetic ketoacidosis in patients diagnosed in the Pediatric Department of Saiful Anwar Hospital between 2005 and 2009.

Methods: A descriptive study of clinical appearance of diabetic ketoacidosis of 19 patients, 1-14 years of age, diagnosed in Pediatric Department of Saiful Anwar Hospital between 2005 and 2009.

Results: From the 19 patients 58% were girls, 53% were between 5 and 10 years of age. 37% had an equal frequency between 400-600 mg/dl and 600-800 mg/dl of blood glucose levels. 63% were unresponsive. About 53% had moderate DKA. 53% patients had blood bicarbonate concentrations of 5-9,9 mmol/L. Blood osmolality levels of >295-400 mOsm/l in 84% patients. 53% had blood potassium levels of 3.5-5.5 mmol/L. 42% patients had leucocyte counts of 10.000-<20.000/ul. The most common of symptoms of those patients were vomiting, abdominal pain, decreased of consciousness, seizures, diarrhea, decreased of body weight, polyuria, polydipsia, polyphagia and febris. The majority complained of polyuria about 16%. The majority patients of DKA had blood ketone levels of more than 5 mmol/l were 67%. 61% had ketonuri of 4+. The majority of those patients had anion gap levels of about 12.0-24.0 (63%).
Conclusions: Of these 19 patients the majority were girls, aged between 5 and 10 years. The majority of patients had high blood glucose levels (between 400-600 mg/dL and 600-800 mg/dL). Most patients were undernourished and had moderate DKA, the majority had blood bicarbonate concentrations of about 5-9 mmol/l and high blood osmolality levels (>295-400 mOsm/l). And most complained of polyuria and had high blood ketone levels (>5), potassium levels 3.5-5 mmol/l and leukocyte counts of 10,000-20,000 u/l.

P29
Clinical picture and laboratory result of diabetes mellitus type-1
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The most commonly type 1 diabetes mellitus caused by destruction of β cell pancreatic leading to inadequate insulin production. Clinical and laboratory features at the times of diagnosis have been widely studied. We reviewed the clinical appearance of Type 1 Diabetes Mellitus in patients were diagnosed in the Pediatric Department of Saiful Anwar Hospital between 2005 and 2009. The study has been conducted at Pediatric Department of Saiful Anwar Hospital between 2005 and 2009. A. descriptive study of clinical appearance of Type 1 Diabetes Mellitus of 27 patients, 11-14 years of age.

Result: The incidence rate of Type 1 Diabetes Mellitus in our clinic during the period from 2005 to 2009 was 0.0034%. There were thirty Type 1 Diabetes Mellitus patients with duration of illness of more than 2 years, with a male to female ratio of 1:1.7. Most of these patients had no diabetic family history and had moderate malnourished nutritional status. The average frequency of blood glucose home monitoring was less than ideal. Twenty-three out of the 27 patients were fully controlled metabolically; however, these patients still have polyuria, polydipsia, and polyphagia. All of patients type-1 diabetes mellitus have polyuria, polydipsia, polyphagia and weight loss. The majority of age was 5-10 years and female. Most patients had no history of Diabetes mellitus. Most patients hospitalized with Diabetes Keto Acidosis, moderate malnourished, and blood glucose level more than 300 mg/dL.

P30
Correlation between glycemic control and quality of life of adolescents aged 13-18 years with type 1 diabetes mellitus
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The efforts to achieve good glycemic control might damage the quality of life (QOL). This issue has not been elaborated in Indonesia because there was no diabetes-specific questionnaire available in Indonesian language previously. This study would like to find out whether there is a correlation between glycemic control and QOL of adolescents aged 13-18 years with type 1 diabetes mellitus (T1DM).

Cross-sectional study was held on patients who came to The Pediatric Endocrinology Clinic of Cipto Mangunkusumo Hospital or who joined The Endocrinology Working Group Unit of Indonesian Pediatric Society programs during October to December 2010. Glycemic control was measured by hemoglobin A1C (HbA1c) levels. The audit of diabetes dependent quality of life-teen (ADDQol-Teen) Indonesian questionnaire was used to assess the QOL. A total of 36 adolescents participated in the study. Only seven subjects had a normal HbA1c level. Median HbA1c level was 8.7 (range, 5.6 to 13.1%). Eighteen subjects considered their QOL as good or brilliant, while 14 subjects felt that diabetes had a negative impact. The most severe negative impact on the matter of dietary aspects, but could be managed better by subjects with intensive treatment. There was no correlation between HbA1c level on the last examination and average weighted impact (AWI) score (rho = -0.15; p = 0.383) or between mean HbA1c level within 6 months and AWI score (rho = -0.15; p = 0.369).

This study did not show any correlation between glycemic control and QOL of adolescents with T1DM.

P31
Trends in diabetes mellitus among Taiwanese adolescents and young adults during 2000-2009: a national population-based cohort study
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Aims: To describe trends in the prevalence and incidence of diagnosed diabetes mellitus (DM) among Taiwanese adolescents and young adults.

Methods: A subset of Taiwan National Health Insurance Research Database containing complete inpatient and outpatient data of one million beneficiaries randomly drawn from the national population of 23 millions was used for this retrospective longitudinal study during 2000-2009. Patients aged 10-24 years old who had at least two outpatient visit claims and/or one inpatient hospitalization claim for diabetes based on the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) code 250.XX were included. Patients were further subdivided as having type 1 DM, if they had been hospitalized due to diabetic ketoacidosis (ICD-9-CM code 250.1X) and/or had received claims for ICD-9-CM 250.X1 or 250.X3. Those who failed abovementioned criteria for type 1 DM were classified as having type 2 DM. Age-specific and age-sex-adjusted standardized annual incidence and prevalence with 95% confidence interval (CI) by the calendar year 2004 were calculated to describe their trends in different gender and age groups.

Results: During the study period, the age-sex-adjusted prevalence and mean annual incidence of diagnosed type 1 DM were 521.59 per 100,000 enrollees (95% CI 514.89-528.59) and 3.24 per 100,000 enrollees (95% CI 2.71-3.77), respectively. No remarkable sexual difference in the annual incidence of type 1 DM was noted, whereas a male/female ratio of 0.85 (95% CI 0.82-0.88) in the prevalence was observed. The annual incidence of type 1 DM decreased with age and remained stable over these 10 years; while the prevalence remained constant through adolescence and varied from year to year. Meanwhile, the adjusted prevalence and mean annual incidence of type 2 DM were 834.14/100,000 (95% CI 825.64-842.63) and 120.19/100,000 (95% CI 116.96-123.43), respectively. No remarkable sexual predominance in the prevalence of type 2 DM was noted, whereas a male/female ratio of 0.86 (95% CI 0.79-0.92) was observed in the prevalence. The annual incidence of type 2 DM increased with age and decreased gradually over the recent 10 years; while the prevalence was still on the increase in this age group.

Conclusion: The incidence and prevalence of type 2 DM came to outnumber that of type 1 DM during adolescence. Although the incidence of newly diagnosed type 2 DM decreased, a rising trend in the prevalence of type 2 DM still existed. A public health policy may be needed to combat the emerging health issue of adolescent diabetes.

P32
Pharmacological therapies for children with type 2 diabetes mellitus should be individualized
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Aim: We presently present a variety of pharmacologic therapies tailored to each patient’s characteristics. We studied the current pharmacologic therapies at our outpatient clinic in obese and non-obese children with type 2 diabetes mellitus (T2DM).

Methods: We treated 108, 80 obese and 28 non-obese, children diagnosed as having T2DM. Among these patients, 26 obese and 23 non-obese children were assigned to pharmacological therapies during the course of diabetes. The frequency of progression to pharmacologic therapies was significantly higher in non-obese than in obese patients (82.1% vs. 32.5%, P<0.05). As to the indication for pharmacologic therapies, oral hypoglycemic
drugs (OHD) and/or insulin were started if the HbA1c value exceeded 7.0% despite dietary and exercise management. 

**Results:** 1) For the 27 obese patients, metformin alone or in combination with an additional medication was frequently used, i.e. 6 patients received metformin alone and 9 metformin with additional OHD including an α-glucosidase inhibitor and/or thiazolidinedione. Only 2 patients independently received glibpiride as a sulfonylurea (SU). In addition, 9 patients were treated with insulin, using basal insulin supported with OHD or biphasic pre-mixture insulin. 2) On the other hand, the 23 non-obese patients were frequently treated with insulin alone or in combination with an additional medication followed by SU, i.e. 11 patients received insulin alone or with additional OHD, and 9 used glibpiride alone or in combination with other OHD. 3) New anti-diabetic drugs, a DPP-4 inhibitor and a GLP-1 receptor agonist, seemed to exert positive effects on glycemic control without occurrence of hypoglycemic episodes in some patients regardless of the type of diabetes. The non-obese patients tended to require pharmacologic therapy, in particular insulin, at an earlier stage of diabetes as compared to the obese patients. 4) Some patients using insulin experienced mild hypoglycemia, but no other significant adverse events were observed with any of the medications.

**Conclusion:** We identified differences among pharmacologic therapies between obese and non-obese children with T2DM. New anti-diabetic drugs, an incretin mimetic and an enhancer, seemed to be effective for some young patients, showing efficacy similar to that in adult T2DM patients. These results suggest that pharmacologic treatment strategies in childhood T2DM should be tailored to individual patient characteristics.

**P33**

**Medication adherence and economic problem among patients with type 1 diabetes in Central Java Province, Indonesia**

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Diabetes type I prevalence is increasing around the world. The lack of knowledge, social economic problem, and the limitation of health systems infrastructure are the problematic issues in developing countries including Indonesia. The objective of this paper was to investigate medication adherence and economic problem among patients with type 1 Diabetes in Central Java Province, Indonesia. This study is a qualitative study using in-depth interviews of 10 parents of children with type I Diabetes, recruited in Central Java Province, Indonesia. Broad interviews are used to provide information including parents’ experiences regarding their children’s treatment particularly medication-taking behavior, complementary and alternative medicine use and social economic problem in their families. The parent’s biggest concern (70% of parents) is related with the high cost of lifelong medication and laboratory evaluation. Some children have no insurance and even though some of them have insurance but not cover all the cost. Some barriers of medication adherence were related with economic problem and insulin injection which were scary for some young children. Complementary therapy including herbal treatment were usually used alongside of conventional treatment. This study suggests that medication adherence were might related with economic condition in families with type I Diabetes in Central Java, Indonesia.

**P34**

**The study of cognitive function in children with type 1 diabetes mellitus**

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Aims: To determine if frequent exposures to hypoglycemia and hyperglycemia during early childhood lead to neurocognitive deficits, and explore the possible affected factors.

**Methods:** We Chosen 32 cases of children with type 1 diabetes mellitus. They were aged from 6-16 years. The duration of the disease was more than one year. We used Chinese Wechsler Intelligence Scale for measurement and analyzing cognitive function, and compared with age-and sex-matched healthy control subjects (control group). We explored the influence of glycosylated hemoglobin and hypoglycemia on cognitive function as well.

**Results:** The full intelligence quotient and the verbal intelligence quotient of diabetic group were lower than the control group. In the sub-tests, as words of knowledge, category, comprehension, arithmetic, vocabulary scale points of diabetic group was significantly lower than that of control group. The verbal comprehension factor and memory/attention factor of the two groups had significantly difference. Glycosylated hemoglobin of diabetic children had a linear regression relationship with total IQ and verbal IQ.

**Conclusion:** Diabetes mellitus had effects on children’s verbal intelligence quotient and attention, which affected the full intelligence quotient. Glycosylated hemoglobin was the independent risk factor to the full intelligence quotient. Larger cross-sectional and longitudinal studies of neurocognitive function are needed to define the effect of type 1 diabetes on the developing brain.

**P35**

**Frequency of dawn phenomenon and its associations with age, HbA1c and diabetes duration in Japanese type 1 diabetes mellitus (T1DM) using the continuous glucose monitoring system (CGMS)**

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**Aims:** We defined the dawn phenomenon as an increase in either insulin requirements or the plasma glucose concentration, in the absence of preceding hypoglycemia or waning insulin levels, occurring between the hours of 0400 and 0800. According to previous studies, the frequency of dawn phenomenon is reported to be approximately 54.0% inpatients with type 1 diabetes mellitus (T1DM), and the poor glycemic control is associated with an exaggerated dawn phenomenon. The present studies were undertaken to assess the associations between dawn phenomenon and age at the time of the study, HbA1c and diabetes duration in Japanese T1DM showing the dawn phenomenon.

**Methods:** Study subjects consisted of 21 patients (3 males and 18 females) with T1DM who had a duration of more than half a year based on CGM. The mean age was 22.1±15.9 yr; diabetes duration 11.1±9.7 yr; HbA1c 8.3±2.2% (JDS). All subjects were receiving therapeutic injections of insulin, 4 were managed by multiple daily injections (MDI) and 17 with continuous subcutaneous insulin infusion (CSII).

**Results:** The dawn phenomenon was present in 8 of the 21 patients (38.1%). The plasma glucose concentrations increased a mean of 69.5% from the overnight nadir to the pre-breakfast time point. The patients with dawn phenomenon were compared in terms of diabetes duration (13.0±9.9 vs 10.0±9.7; p<0.01)yr , HbA1c(8.3±1.6 vs 8.5±2.4; p<0.01)%, age at the time of the study (24.6±18.0 vs 20.5±14.9; p<0.01)yr. The subjects with dawn phenomenon had longer diabetes duration, lower HbA1c and were older. Furthermore, these subjects experienced hypoglycemia (<70mg/dl) during the daytime.

**Conclusion:** The frequency of dawn phenomenon in the present study was lower than that in the previous studies. This might be attributable to there being many users of CSII among our subjects and to Japanese foods containing a large amount of the carbohydrate as compared with protein. The associations of dawn phenomenon with longer diabetes duration and advanced age may be based on poor glycemic control. Furthermore, excess boluses cause hypoglycemia and low HbA1c. These results suggest that change in the basal insulin rate should be considered instead of an increase in the pre-meal bolus. We conclude that CGM should be used to adjust CSII.

**P36**

**Significance of the measurement of serum fructosamine in the management of childhood diabetes**

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**Aims:** To determine if frequent exposures to hypoglycemia and hyperglycemia during early childhood lead to neurocognitive deficits, and explore the possible affected factors.

**Methods:** We Chosen 32 cases of children with type 1 diabetes mellitus. They were aged from 6-16 years. The duration of the disease was more than one year. We used Chinese Wechsler Intelligence Scale for measurement and analyzing cognitive function, and compared with age-and sex-matched healthy control subjects (control group). We explored the influence of glycosylated hemoglobin and hypoglycemia on cognitive function as well.

**Results:** The full intelligence quotient and the verbal intelligence quotient of diabetic group were lower than the control group. In the sub-tests, as words of knowledge, category, comprehension, arithmetic, vocabulary scale points of diabetic group was significantly lower than that of control group. The verbal comprehension factor and memory/attention factor of the two groups had significantly difference. Glycosylated hemoglobin of diabetic children had a linear regression relationship with total IQ and verbal IQ.

**Conclusion:** Diabetes mellitus had effects on children’s verbal intelligence quotient and attention, which affected the full intelligence quotient. Glycosylated hemoglobin was the independent risk factor to the full intelligence quotient. Larger cross-sectional and longitudinal studies of neurocognitive function are needed to define the effect of type 1 diabetes on the developing brain.
Aims: HbA1c can usually be used as the indicator of glucose control and correlated with the development of long-term diabetic complications. But there are limits that it usually reflects the mean glucose levels of 2-3 months and can be variable in the situation of hemoglobinopathy or the conditions of altered RBC lifespan. In contrast, serum fructosamine levels reflect the mean glucose levels of 2-3 weeks. This study was designed to see the significance of the measurement of serum fructosamine in the management of childhood diabetes and to see the correlation between the HbA1c and fructosamine.

Methods: Clinical data were evaluated for the sixty Korean patients who are on the management of diabetes in the department of Pediatrics, Dankook University Hospital. Fructosamine and HbA1C levels were also reviewed on the basis of clinical information and analyzed using IBM SPSS Statistics version 20.

Results: HbA1c and fructosamine levels showed strong association (p<0.001). Fructosamine levels indicated the average glucose concentration over the previous 2-3 weeks better than HbA1c, so were useful for the evaluation of therapeutic efficacy of recent change of therapeutic modality as well as for the diagnosis of fulminant diabetes.

Conclusion: The measurement of fructosamine levels was useful in the management of childhood diabetes especially, if there is some discrepancy between the clinical information and HbA1 levels. In addition, it was useful for the short-term evaluation about the recent glucose control after the change of the treatment modality of diabetes.

P38
Childhood hypertension due to a rare cause
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A 3 year 6 month old child, presented with complaints of fever, loose stools and vomiting. The child had no signs of dehydration and was noted to be hypertensive with blood pressure of 120/76 mm Hg (95th centile for age, sex and height: 104/65 mm Hg). All the peripheral pulses were equal and well felt. There was no radiofemoral delay, no abdominal bruit. The child had been reared as a female, had normal female external genitalia and no palpable gonads. Urine evaluation, Renal function test and USG abdomen were normal. Child had Metabolic alkalosis with hypokalemia. Elevated Urine chloride suggested a saline non responsive metabolic alkalosis. Markedly elevated 24 hour urine potassium and TTKG (Transstubular potassium gradient) was suggestive of tubular potassium wasting in the presence of hypokalemia. Plasma Renin Activity (PRA) was low, with low normal plasma aldosterone concentration (PAC). Serum Cortisol (8AM) was low with elevated ACTH. Basal and post ACTH 17 hydroxy progesterone was low with elevated total progesterone levels. The karyotype was 46XX. This clinical and biochemical picture was suggestive of 17 alpha hydroxylase (CYP 17) deficiency. The patient was started on hydrocortisone therapy. With this, the blood pressure got controlled, the patient gained height, weight, the pigmentation decreased, serum potassium normalized. Thus, the diagnosis of, 17 alpha hydroxylase deficiency, a rare form of Congenital Adrenal Hyperplasia, should be considered in any child with systemic hypertension, especially in the presence of concomitant hypokalemia with metabolic alkalosis.

More commonly, it presents in the peripubertal period, during evaluation of delayed puberty. The presentation as early childhood hypertension is rare. Plan to confirm the diagnosis by genetic analysis.

P37
Extra-hepatic portal vein obstruction and type 1 diabetes in a child: a co-incidence or causal association?
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P37

Introduction: We report an eight year old boy who had extra hepatic portal vein obstruction (EHPVO) and developed type1 diabetes (type1 DM).

Case report: An eight year old boy presented with polyuria and polydipsia for 1 month. On examination, liver was not palpable but spleen was enlarged (6cm). Blood sugar was 460 mg/dl and type1 DM was confirmed. Ultrasonography showed portal vein cavernoma with normal liver and pancreas. C-peptide level of 0.05 ng/ml with normal kidney and liver functions. Thus diagnosis of EHPVO with portal hypertension was also confirmed. Other investigations including liver functions, hemogram, renal functions, serum amylase, lipid profile, thyroid function, Protein C, S and factor V Laiden estimation were normal. There was no history of abdominal infections like peritonitis, pancreatitis and umbilical sepsis or umbilical artery catheterization in neonatal period. C-peptide level was low (0.111 ng/ml) with weakly positive Islet cell antibodies, positive GAD 65 antibodies (>2000 IU/ml). Tissue peroxidase and Tissue transglutaminase antibodies were negative. Patient is asymptomatic after endoscopic band ligation of esophageal varices and split-mix insulin regimen.

Discussion: In the index case sequence of events seems to be portal vein thrombosis at least few years before, leading then to cavernoma formation and narrowing of portal vein leading to development of portal hypertension over the years which remained asymptomatic till child developed diabetes. Similar sequence was seen in two previously reported patients of EHPVO who went on to develop type 1 diabetes on follow up of few years [1]. Only common condition which can cause both EHPVO and type1 diabetes is pancreatitis. However, there is no proof of pancreatitis in the index case. Authors in above report have also suggested that any disease in portal vein may incite inflammatory response in the pancreas [1]. In above mentioned report of three cases, authors have reported 3 cases of Type1 DM in a cohort of 100 cases of EHPVO and in our cohort of around 500 type1 DM patients this is the first case identified to have EHPVO. To conclude, this is only the fourth case reported to have EHPVO who developed type1 DM. In the index case it looks more of a co-incidence rather than a causal association between the two entities.

Reference
can be precisely identified using molecular genetic testing. Modes of presentation vary and can mimic type 1 or 2 diabetes. Making a specific diagnosis of MODY can have important implications for guidance of appropriate treatment, prognosis and genetic counselling. The paediatric diabetes team across the Southern District Health Board provides diabetes care to approximately 160 children and adolescents spread over the largest geographical region in New Zealand. We present the cases of three children and their families diagnosed with MODY over the past two years. This includes two novel mutations, one of which segregates in a unique kindred that is strongly affected by both MODY and classic autoimmune mediated diabetes.

These families highlight the features of three of the more common MODY subtypes; MODY2 - a 13 year old boy with a novel unclassified variant c.698G>A (p.Cys233Tyr) in exon 7 of the Glucokinase (GCK) gene, MODY5 - a 14 year old girl with a novel de novo dosage change of a 1.3M deletion in the HNF1a gene, and MODY3 with a reported nonsense mutation c.864delGinsCC (p.Gly282ArgfsX25) in exon 4 of the HNF1a gene observed in an 11 year old girl. In addition to these index cases, genetic testing has lead to the diabetes diagnosis of a sibling with a GCK mutation, and the identification of an HNF1a mutation in another currently asymptomatic sibling. To date, we have identified a prevalence of MODY in the paediatric diabetes population of the lower South Island of approximately 2.5%. This prevalence, along with increasing access to molecular genetic testing, highlights the importance of consideration of MODY in atypical diabetes presentations in the paediatric/adolescent population.

**GROWTH**

**P40**

Classic Bartter syndrome complicated with profound growth hormone deficiency

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**Case history:** A Japanese boy was born at 41 weeks of gestational age by spontaneous cephalic delivery, with birth weight 3.680g. Family history was remarkable for his elderly sister suffering from classic Bartter syndrome. He also was diagnosed as classic Bartter syndrome, based on the findings such as failure to thrive, metabolic alkalosis with hypokalemia, and the activated renin-aldosterone system. The diagnosis was later confirmed by CLCNK1 gene analysis which revealed compound heterozygous mutations: deletion of the exon 1 - 3 (derived from his mother) and ΔL130 (derived from the father). Treatment with spironolactone, indomethacin, sodium chloride, and potassium supplementation was commenced at 8 months of age. However, his serum potassium level failed to normalize, and tended to be around 3-3.5mEq/L. He had mild intellectual impairment, and needed specialized education. When he was 11 years old, through the investigation for macrocephatemia, renal stones with nephrocalcinosis were detected. This complication resolved following the amelioration of hypokalemia, which was achieved by vigorous potassium fortification. Because access to growth rate was consistently subnormal and he was very short (< -4.7SD), scrutiny for growth hormone (GH) secretion was conducted at his 13 years of age.

**Results:** Profound GH deficiency was evident. Serum IGF-1 level was 80ng/mL (norm, 179-646), with IGFBP-3 1.92ng/mL (2.69-4.16). Pharmacologically stimulated GH levels were 0.15 and 0.39 ng/mL, after insulin and arginine administration, respectively. His bone age was 11.4 years old (TW2-RUS for Japanese). MR imaging detected no abnormality within hypothalamic-pituitary region.

**Clinical course:** GH treatment with 0.15-0.19mg/kg/week resulted in growth rate as much as 1.17 cm during the first 12-months, followed by 10.8 cm during the subsequent 12 months. Although his pubertal stage progressed from Tanner stage 1 to stage 2 during 2 years, Δ bone age / Δ chronological age was 1.02. No significant change in serum potassium level was observed.

**Discussion:** In literature, GH deficiency in Bartter syndrome and Gitelman syndrome has been anecdotally reported, with diverse severity among patients. At present, its precise pathogenesis, as well as its prevalence, is unknown. Classic Bartter syndrome complicated with profound GH deficiency, as seen in this case, is rare. The sister of the case, who also suffered from classic Bartter syndrome, is 145 cm tall (-2.05D) now and seemed not to be GH deficient. Her potassium level had been managed rather better than this case. It may be tempting to speculate that long-term hypokalemia may be harmful for somatotrophs to produce GH.

**P41**

The growth patterns, hemoglobin pretransfusion, serum ferritin and bone age in thalassemia major patients

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Despite frequent blood transfusions combined with chelation therapy lead to an improved rate of survival, endocrine disorders related to secondary hemosiderosis such as short stature, delayed puberty and hypogonadism are major problems in adolescent children with thalassemia major. The aim of this study was to know the description of height, growth velocity, bone age, hemoglobin pretransfusion level and serum ferritin in thalassemic patients.

The retrospective study of children hospitalized in Pediatrics ward Sanglah Hospital Denpasar from December 2010-February 2011. Fifteen subjects were diagnosed as thalassemia major, aged between 1.91 years - 13.5 years; 7 boys and 8 girls. Two children aged less than 3 years and 7 children had entered puberty. All patients had to undergo iron chelation therapy deferrioxamin with inadequate quality. Short stature was found in 4 children (26%), all with growth velocity of <5 cm/year. Clinically 1 person categorized as delayed puberty. Mean hemoglobin pretransfusion levels can be maintained >8805; 8 mg/dl (10), the remainder (5) has an average hemoglobin below 8 mg/dl. Four children with serum ferritin over 3000 ng/ml, all with short stature. In the radiological evaluation (bone age) 5 children have delayed bone age.

Our study suggests that thalassemic patients, short stature is found in 26% cases and all of them have entered the age of puberty. All patients with short stature has serum ferritin levels >3000 mg/ml.

**P42**

A girl with short stature and dysmorphism

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**Case presentation:** A 5-year-9month old Chinese girl presented with severe growth retardation, height SDS -4.17 and body weight SDS -2.37. The mid-parental height was 151.2cm (3rd-10th centile). She was born small for gestational age with no catch-up growth. Congenital anomalies including right dysplastic kidney and large secundum atrial septal defect were present. She had delayed development with microcephaly and dysmorphism, including triangular face, epicantthic folds, low set ears, micrognathia, and brachydactyly. Ophthalmological assessment showed astigmatism, myopia, and left exotropia requiring surgical correction. Audiology assessment showed bilateral mild conductive hearing loss. Thyroid function, morning cortisol, serum calcium and renal function tests were normal. Metabolic disease workup including lactate, plasma for amino acid, urine metabolic screen, VLCFA, transferrin isoelectrofocusing and clotting profile were normal. CT and MRI brain were normal. Serum IGF-1 at 13 years old was 62nmol/L (+0.5SD). Growth hormone study with glucagon showed peak growth hormone of 32mg/L. Bone age was 12 years at chronological age of 12-year-10month. Radiograph of both hands showed brachydactyly but no proximal implantation of 1st digit. Genetic study show normal karyotype, but MLPA and FISH later confirmed heterozygous terminal deletion of 15q26.2 with the genetic defect compatible with IGF-1 receptor mutation. Growth hormone therapy was refused by the patient and mother. Breast development started at 12-year-4month and menarche started at 13-year-5month of age. The growth spurt was absent with peak growth velocity of only 5.5cm/year. On the latest follow-up at 13-year-9month of age, her height was 126.8cm (-4.7SD).
Discussion: Our patient displayed typical phenotypic features of IGF-1 receptor mutation of heterozygous deletion of 15q26.2 with severe growth retardation. The condition could potentially benefit from growth hormone treatment according to recent literatures [1]. Our report highlights the importance of investigating for genetic causes of short stature in patients with concomitant dysmorphism and growth retardation.

Reference

P43
A case of Shwachman-Diamond syndrome
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Shwachman-Diamond syndrome (SDS) is an autosomal recessive disorder (OMIM 260400), characterized by exocrine pancreatic insufficiency, skeletal abnormalities and bone marrow (BM) dysfunction, with a risk, as high as 30%, to develop myelodysplastic syndrome and/or acute myeloid leukaemia (MDS/AML). The SDS gene (OMIM 607744) is localized on chromosome 7 at the band q11 and mutations of this gene are found in 90% of patients.

Direct sequencing of whole exon 2 and flanking intronic regions of the SBDS gene was performed on an ABI Prism 3100 Genetic Analyzer (Applied Biosystems, USA) using a BigDye Terminator v3.1 Cycle Sequencing Kit (Applied Biosystems). The forward (F) and reverse (R) primers for amplifying exon 2 are AAATGGTAAGGCAAATACGG (2Fa), AGACCTCGATGAAGTTC-GC (2Fb) and ACCAAGTCTTATTATGAAATGAC (2R).

We described a 14 years old boy who presented with skeletal system abnormalities (Legg-Calve-Perthes syndrome, congenital coxa vara and genu valgum deformity), short stature, chronic dyepsea, neutropenia and thrombocytopenia. Abdominal CT of patient showed congenital lipomatosis of pancreas and spine bone density shows osteoporosis. Direct sequencing for whole exons including intron-exon boundaries of patient showed two heterozygous mutations, c.[183_184TA-CT] →[258_259TC-CT].

We treated the patient with pancreatin (Now Foods Pancreatin 1T=Lipase 9,000/Amylase 50,000/Protease 50,000 USP units) and Dicamax (1T=Ca. carbonate 1,250 mg and cholecalciferol 1,000 IU). We has observed for hematologic abnormality and prepared for bone marrow transplantation.

We report a child with diverse clinical manifestations of SDS including short stature, chronic dyedpsea, skeletal system abnormalities, and neutropenia; the clinical diagnosis was confirmed by genetic analysis for the second time in Korea.

P44
Growth after hematopoietic stem cell transplantation in children with acute myeloid leukemia
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Previous studies have shown that hematopoietic stem cell transplantation (HSCT) may result in growth impairment. Disease type, differences in treatment before HSCT and treatment duration before HSCT can affect growth after HSCT and act as confounding variables. By contrast, acute myeloid leukemia (AML) patients receive HSCT during their first remission and are not treated by steroids during their relatively short period of induction therapy time. The purpose of this study was to evaluate 5 years growth after HSCT and to find factors influencing final adult height (FAH) in childhood AML patients.

Among 97 AML patients whom received HSCT in Seoul National University Hospital, we report 24 patients whose puberty began at least 3 years after HSCT and 19 patients who reached FAH without relapse. Medical records were retrospectively reviewed. Summary measure analysis was used to evaluate for 5 year growth after HSCT and to find statistical differences between factors. Univariate and multivariate regression analysis was performed to find factors influencing FAH.

Five years growth after HSCT: Patients received HSCT at 4.2 years of age. Six patients received radiotherapy (RT) and chronic GVHD (cGVHD) were in 4 patients. History of RT and cGVHD significantly impaired the first 5 years growth after HSCT. But cGVHD seems to influence to only the first 2 years growth after HSCT. Age at HSCT, gender and history of steroid use were not significantly affected 5 years growth after HSCT.

Final adult height after HSCT: Patients received HSCT at 10.1 years of age. Four patients received RT. In patients reached FAH without relapse after HSCT, only history of RT significantly reduced FAH. Age at HSCT, gender and history of steroid use were not significantly affected FAH.

Growth impairment after HSCT in AML patients might be occurred. But without RT history, growth impairment seems to be temporary and improve by catch-up growth. HSCT with conditioning regimen consists of chemotherapy thought to be not to significantly decrease FAH. So the growth hormone treatment is seems to be not needed in non-RT patients. But in patients who received RT, catch-up growth will not be shown and eventually attain reduced FAH.

P45
The clinical and molecular genetic study of 20 Silver Russell Syndrome cases
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Objective: To analyze the genetic pathogenesis and improve the accuracy of the diagnosis of the disease, this study reported the clinical features of 20 patients with Silver Russell Syndrome (SRS) in the Beijing Children’s Hospital and detected the chromosome 11p15 imprinting defects in 16 patients of them.

Methods: 20 SRS cases diagnosed in Beijing Children’s Hospital from 2006 to 2011 were studied retrospectively for clinical manifestations, physical signs, laboratory examinations and respond of GH treatment. We compared with 3 different diagnostic criteria and used the methylation-specific multiplex ligation dependent probe amplification (MS-MLPA) method to detect the chromosome 11p15 imprinting defects in 16 patients of them, meanwhile take 10 normal control.

Results: We collected 20 SRS patients over a period from 2006 to 2011 with 3 criteria. The concordance is 90%. Include fifteen males and five females, age range 0.8~12.17yr. The most chief complaint is short, 85%. Then, it is asymmetry (5%), and external genital abnormalities (10%). The clinical characteristics with the frequencies accounted for over 80% included small for gestation age(SGA), postnatal growth retardation, craniofacial dysmorphism, asymmetry and super thin of whole body, extremely limbs, fifth finger clinodactyly, BMI<−2SDS and height was obviously lagging behind bone age. Of them had used the growth hormone for 3-months to 12 Months. The growth velocity is from 4cm to 10cm/year. In the 16 patients, 6 patients were found hypomethylation in chromosome 11p15 ICR1, the other one with chromosome 11p15 ICR1 hypomethylation and ICR2 hypermethylation may be the result of the maternal chromosome 11p15 uniparental disomy. Another case had duplication of the maternal chromosome 11p15 fragment. Two cases had good effects of GH treatment, one with chromosome 11p15 ICR1 hypomethylation and the other one was neglected after HSCT.

Conclusion: The top 3 clinical features in SRS are ① growth retardation include SGA and/or postnatal. ② Malformation include craniofacial dysmorphism, asymmetry of face and/or limbs, fifth finger clinodactyly. ③ Super severe low BMI and height was obviously lagging behind bone age. No laboratory and imagination specificity. Chromosome 11p15 imprinting defect is the major genetic disturbance in SRS, about 50%.
and ICR1 hypomethylation is the predominant molecular alteration. The MS-MLPA is a technique for detecting all chromosome 11p15 imprinting defects of SRS. It is useful for the study of the genetic aspects of SRS. The relation between the respond of GH treatment and genetic changes is uncertainty.

**P46**
Quantifying adherence to growth hormone treatment: the easypod™ connect observational study (ECOS)

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Recombinant human growth hormone (r-hGH) is indicated for pediatric patients with a variety of growth disorders. Until recently, analysis of adherence to treatment has been limited by recall bias and reliance on self-reporting. Accurate recorded data on r-hGH use can now be collected using the easypod™ auto-injector. The multinational easypod™ connect observational study (ECOS) was launched in 2010 to collect and analyze r-hGH dosing, clinical and auxological data from patients prescribed r-hGH via easypod™. Twelve countries are currently recruiting patients.

The primary objective is to assess adherence in patients receiving r-hGH via easypod™. Secondary objectives include describing the impact of adherence on clinical outcomes and identifying adherence patterns. Data will be obtained from patients' medical notes and uploaded from auto-injectors. Auxological parameters are collected, and prescribed dosing data recorded at clinic visits as per routine clinical practice. Annual adherence will be calculated (number of days the patient administered injections divided by the expected number of injection days over 1 year, as a percentage). Dose intensity (total amount of dose received divided by planned amount of dose over 1 year, as a percentage) will be analyzed. Adherence data will be correlated with clinical outcomes. An adherence pattern will also be developed based on patients' age, sex, indication, self-injection, and time on treatment. The study will run until 2015, with yearly analyses, and will be overseen by a multinational scientific steering committee.

With data from ECOS, it will be possible to accurately assess r-hGH treatment adherence in various growth disorders and explore its potential impact on growth. Ultimately, drivers of and barriers to treatment adherence will be identified, allowing appropriate support programs to be developed.

**P47**
Berardinelli-Seip syndrome in a Chinese boy with Seipin gene mutation: a case study and literature review of genotype-phenotype

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Objective: Congenital generalized lipodystrophy (CGL), or Berardinelli-Seip syndrome, is a rare and heterogeneous disease of autosomal recessive inheritance characterized by the generalized absence of adipose tissue at birth and severe adverse metabolic consequences. The identified causative genes for CGL include 1-acylglycerol-3-phosphate O-acyltransferase 2 (AGPAT2), Berardinelli-Seip congenital lipodystrophy 2 (BSCL2 or Seipin), Caveolin-1 (CAVI) and polymerase I and transcript release factor (PTRF). Although more than 60 cases of CGL with different gene mutations have been found in Asian patients, only 7 patients were Chinese. Data are also limited regarding genotype-phenotype analysis in Asian CGL patients. Therefore, we aimed to analyze variations of two identified major causative genes, Seipin and AGPAT2, involved in CGL etiology in a mainland Chinese affected family and explore the genotype-phenotype of Berardinelli-Seip syndrome in Asian populations.

Methods: We report a detailed clinical and genetic analysis of a Chinese boy with CGL who was followed from infancy through preschool. Sequences of the entire coding region of Seipin and AGPAT2 were examined. Phenotypes in various Asian subtypes were compared and the related literature about Berardinelli-Seip syndrome was reviewed.

Results: We identified a homozygous frameshift mutation (c.974-975insG) in the Seipin gene in the CGL-affected boy. His parents were heterozygous for the same mutation. No variation was found in the AGPAT2 gene.

Conclusion: In Asian populations, Seipin and PTRF are the main genes identified to date as being responsible for CGL and Seipin is a major causative gene. Genetic heterogeneity is accompanied by phenotypic heterogeneity.

**P48**
Factors predicting the response to growth hormone therapy in Taiwanese patients with Turner syndrome

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Background: Turner syndrome (TS) occurs in one 2000-2500 live female births and is associated with short stature, premature ovarian failure, and a range of other phenotypic features. Girls with TS achieve an average adult height 20cm shorter than their mid-parenteral height if they didn't receive treatment. Growth hormone (GH) treatment was associated with highly significant gains in growth and adult height in girls with TS. The purpose of this study was to evaluate the factors that predicting the response to GH in patients with TS.

Patients and methods: We performed a retrospective cohort study of clinical and laboratory data of 57 Taiwanese TS children who received growth hormone from Nov 1998 to Nov 2011. Patients’ height and weight were measured before and every three months throughout the GH treatment. Bone age (BA) was evaluated every six to twelve months during and after GH treatment. Conjugated estrogen would be introduced if no spontaneous puberty onset (breast Tanner stage 2) was noted after 13 year of age. 37 of these patients were followed until final height.

Results: From Nov 1998 to Jan 2011, 57 Turner syndrome patients started GH therapy at the mean age of 11.13 years and the dose of GH was 0.33mg/kg/week. Forty-six patients received estrogen replacement therapy at the mean age of 15.09 years, if indicated. The growth rate before treatment was 4.62cm/year, which increased to 7.04, 5.67, 4.72, 4.29 cm/year during the first four years of GH therapy, respectively. The first year growth response was found to be positively correlated with height SDS at start of GH treatment and target height; but negatively correlated with age, height, and BA at start of GH treatment. Adult height correlated positively with height SDS and Turner height SDS at start of GH treatmet and first year growth response. Height gain over projected adult height had negative correlation with Turner height SDS and BA at start of GH treatment; but positive correlation with duration of GH treatment and age at start of puberty (spontaneous or induced).

Conclusions: There was no difference in baseline characteristic between different karyotype except height velocity and number of spontaneous puberty. As children with GH deficiency, the administration of GH to
children with TS results in marked acceleration in linear growth, which is most pronounced during the first year of treatment. A paradoxical finding was noted in our finding: children who were tall (according to TS height SDS) at the start of treatment remained tall till adult height, but their height gain was relatively minor.

P49
Hospital malnutrition at pediatric ward Dr. Wahidin Sudriohusodo Hospital Makassar
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Background: Hospital Malnutrition (HM) is one of the health problems in hospital care. Malnutrition in hospital leads to many problems like prolonged length of stay, clinical complications, delayed recovery and increase economic cost.

Objective: To determine nutritional status on admission and monitoring their weight changes, in order to reveal incidence of hospital malnutrition.

Methods: A prospective study was conducted in January until December 2011 period. The initial measurement were made by residents in charge. The nutritional status was defined according to CDC 2000 guidelines. Exclusion criteria including children with fluid retention, organomegaly, obesity, and tumours. HM was defined as weight decreased ≥ 2% for LOS (length of stay) less than 7 days, ≥ 5% for LOS 7 to 30 days and ≥ 10% for LOS 1 to 6 months. Data were analyzed using SPSS for Windows.

Results: From 1286 patients hospitalized during the period, most of them (81.5%) suffer for weight loss ≥ 2%. According to age, HM occurs more in 25 – 36 months age group (0.16%).

Conclusion: Incidence of HM still high, a close monitoring to patients intake and needs is necessary to prevent and to lower the incidence.

P50
Factors affecting growth and adult height in pediatric renal transplantation
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Growth retardation is common in children with chronic kidney disease. Renal transplantation (TPL) resolves many endocrine, metabolic and uremic disturbances that contribute to growth retardation. However, growth continues to be suboptimal even after TPL. The aim of this study was to review factors affecting post-TPL growth and final adult height (FAH) in children who received kidney allografts. A retrospective chart review of 65 patients (44 male) who received renal TPL at Seoul National University hospital was done. Only patients less than 15 years of age at TPL with regular follow up for at least 3 years afterwards were included. Subjects with immediate graft failure or those receiving post-TPL growth hormone treatments were excluded. Height z-scores were recorded at diagnosis, commencement of renal replacement therapy (RRT), TPL and thereafter at 6 month intervals for 3 to 5 years. The delta height z-scores during 2 years and 5 years post TPL were calculated as the difference in height z-scores between those time points and height z-score at TPL. The mean age at TPL was 10.1 (1.8 – 14.4) years. The mean height z-score of recipients was -1.61±1.36 (-4.64 – 1.64). The mean delta height z-score at 2 years and 5 years were 0.61±0.89 (-1.03 – 2.41) and 0.38±0.88 (-0.98 – 2.04) respectively. Age at TPL (before or after age 10) had a significant correlation with both 2 and 5 year change in height z-score (p=0.001 and p=0.012, respectively). Multivariate linear regression analysis showed that age and height at the time of TPL were significant determinants of 2 and 5 year growth after TPL (r²=0.56, p=0.006). Further analysis showed that height at commencement of RRT and duration of RRT were significant factors in determining the pre-TPL height (r²=0.76, p<0.001). The mean FAH was -1.21±1.10 (-2.85 – 1.61, n=33) and the percentage of patients who attained a FAH z-score ≥ 1.88 was 76%. FAH z-score correlated with height z-score at the time of TPL (p<0.001). This study suggests that age and height at the time of TPL are important factors affecting post-TPL growth and FAH. Maximizing growth before TPL by decreasing the duration of RRT and early preemptive TPL may lead to better attainment of expected adult height.

P51
Response to growth hormone therapy in children with Noonan syndrome: correlation with or without PTPN11 Gene mutation Yoo-Mi Kim*, Jin-Ho Choi, Boom Hee Lee, Chang-Woo Jung, Hye Young Jin, Jae-Min Kim, Gu-Hwan Kim, Jin Soon Hwang, Sei Won Yang, Jin Lee, Han-Wook Yoo
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Aims: Noonan syndrome (NS) (MIM 163950) is an autosomal dominant disorder characterized by postnatal short stature, congenital heart disease, early feeding difficulties, mild learning disabilities, and characteristic facial dysmorphisms, short and webbed neck, and chest deformities. Proportionate short stature is well recognized as one of the key features of NS and has been reported in more than 80% of patients affected by NS. The objective of this study was to evaluate the efficacy of recombinant human growth hormone (rhGH) therapy and the influence of genotype on the response to rhGH therapy in children with Noonan syndrome (NS).

Methods: Fourteen male and four female subjects with NS with short stature whose height was less than third percentile, were included. The rhGH was subcutaneously administered at a dose of 66 µg/kg/day, subcutaneously for a 12-month period. Mutations in the PTPN11 gene were identified in 10 subjects (55.6%). Mutations in the SOS1 (two children, 11.1%), MEK1 (one child, 5.6%) and KRAS (one child, 5.6%) genes were also found.

Results: The mean age was 8.3±2.4 years (range, 4.4 to 13.2 years) at the start of rhGH treatment. Height-SDS increased from -2.8±0.9 at the start of rhGH therapy to -2.0±0.9 12 months later (P<0.001). Height velocity increased from 5.0±0.9 cm/year in the year before treatment to 8.9±1.6 during treatment (P<0.001). Changes in height SDS, height velocity, and serum IGF-1 level did not differ significantly between those children with or without PTPN11 mutations.

Conclusion: The rhGH therapy significantly improved the growth velocity and increased the serum IGF-1 level. Long-term correlation between genotype and rhGH therapy responsiveness needs to be addressed in a large population.

P52
Serum levels of FGF21 are reduced and negatively correlated with adiponectin in children with Prader-Willi syndrome Su Jin Kim*, Young Bae Sohn, Sung-Yoon Choi, Young Ok Choi, Chi Hwa Kim, Dong-Kyu Jin
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Background/Aims: FGF21 (fibroblast growth factor 21) is a novel metabolic regulator that has beneficial effects on glucose homeostasis and insulin sensitivity. In human obesity, serum FGF21 level was increased. The aims of this study were comparing fasting serum levels of FGF21 in Prader-Willi syndrome (PWS) and obese control children and finding correlations these levels with insulin sensitivity and obesity-related parameters.

Methods: Sixteen children (median age, 10 years; interquartile range, 9.0–13.5 years) with PWS were matched with 16 control subjects (median age, 10.5 years; interquartile range, 9.5–12.5 years). We measured serum levels
of FGF21, adiponectin, insulin sensitivity and obesity-related parameters during oral glucose tolerance test.  

**Results:** Waist to hip ratio and HOMA-IR were lower in PWS individuals relative to control subjects. Remarkably, serum levels of FGF21 were lower and adiponectin were higher in PWS subjects than in control subjects. FGF21 levels were significantly positively correlated with HOMA-IR and negatively correlated with adiponectin.  

**Conclusion:** Previously, FGF21 level was reported to increase with obesity. However, compared with obese controls, our results show PWS individuals have lower FGF21 levels. Our data suggest that insulin sensitivity, lower waist to hip ratio, lower FGF21 levels and higher adiponectin levels are the characteristics of PWS children.

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**Tall stature in children: differential diagnosis and management**

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Tall stature is defined as height above 97th percentile for age and sex or more than 2.5D above the mean for a defined population. It means 3 out of every 100 children in a community are tall and should be evaluated.  

Familial tall stature also known as constitutional tall stature is the most common cause of tall stature. The height is consistently above 97th percentile and mid parental height too is above 90th or 97th percentile. Usually occurs in a female child and the mother often remembers her unusual tall stature during her childhood. The bone age is marginally to moderately advanced so that the final height prediction is not very high.  

Physical examination is normal and lab tests, if obtained, are negative.  

The second most common cause of tall stature is nutritional. The height as well as the weight are at higher percentile. Again the bone age is marginally to moderately advanced so that final predicted adult height is not too much.  

Hormonal causes of tall stature include hyperthyroidism, precocious puberty and growth hormone excess. Hyperthyroidism is more common in girls and is almost always caused by Grave’s disease. The bone age is moderately advanced so that the final adult height is usually compromised.  

In cases of precocious puberty, although due to anabolic effects of sex steroids, the child is tall at the onset, the ultimate adult height is compromised due to premature epiphyseal fusion caused by oestrogen. Again, although, delayed puberty may be associated with short stature in childhood, as with constitutional delay, failure to eventually enter puberty and complete sexual maturation may result in sustained growth in adult life, with ultimate tall stature [1].  

GH hormone excess causes gigantism in childhood and acromegaly in adults. Gigantism is characterized by tall stature, broad hands and feet, prognathism, broad root of nose, excessive sweating, hypertension and glucose intolerance. Almost each and every part of the body is affected and large for age. GH levels are consistently high and can exceed 100 ng/ml [2]. Serum IGF-1 and IGFBP-3 are raised and serve as a sensitive screening tool for GH excesses. But the gold standard for making the diagnosis of GH excess is the failure to suppress serum GH levels below 5 ng/dl after 1.75 gm/kbw glucose challenge. This test measures the ability of IGF-1 to suppress GH secretion, because the glucose load results in insulin secretion, leading to suppression of IGFBP-1 which results in an acute increase in serum free IGF-1 levels.  

Management of tall stature: Constitutional tall stature requires only reassurance after bone age assessment and prediction of final height. Obstinate cases require sex steroids to halt the progression of growth. In girls ethinylestradiol orally combined with cyclic progesterone has shown to reduce the final height up to 7 cm. In boys testosterone 250-1000 mg monthly has shown similar results. For best results these drugs should be started early i.e before 10 years in girls and 12.5 years in boys [4].  

Nutritional tall stature is managed by lifestyle changes and avoidance of bad dietary practices. Thyrtoxicosis is maned by use of antithyroid drugs. Methimazole and carbimazole are two commonly used antithyroid drugs.  

Oestrogens are somatostatin analogues which can be used at a dose of 15-5 mg once or twice daily subcutaneously to reduce growth hormone hypersecretion and it has shown to reduce the final height up to 5cm [5].

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**Easypod™ adherence in children with growth disorders treated with r-hGH. A preliminary Italian experience**

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Short stature was seen in 32.2% of our patients. Diabetes was present during the observational period. Eighty-seven patients entered the study in our hospital. The main objective of this study is to determine the prevalence of endocrine complications among our patients with growth disorders during the 1st year of treatment. The long-term adherence will be evaluated in the study. Data on the 54 available patients show that 25 patients (46.3%) were adherent to treatment while 29 patients (53.7%) were not. The impact of low adherence on clinical and biochemical parameters is under evaluation. The study will run until January 2013. Data obtained from this study will allow to explore the potential impact of adherence to r-hGH on growth outcomes after 1 year of treatment. The long-term adherence will be evaluated in the easypod® connect observational study, also ongoing in Italy.

**P55**

**Endocrine complications in patients with thalassaemia major**  
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Thalassemia major is an inherited hemoglobin disorder characterized by chronic anemia and iron overload due to transfusion therapy and gastrointestinal absorption. Iron overload causes severe endocrine complications in patients with multi-transfused thalassemia major.

Endocrine complications includes short stature, acquired hypothyroidism and hypoparathyroidism, hypogonadism, glucose intolerance and diabetes mellitus.

**Aim:** The main objective of this study is to determine the prevalence of prominent thalassemia complications.

**Methods:** Eighty-seven patients entered the study in our hospital. The patients have a mean age of 10.5 (range, 5-16) years. Physicians collected demographic and anthropometric data and the history of therapies as well as menstrual histories. Patients have been examined to determine their pubertal status. Serum levels of ferritin, glucose, insulin, A1c, cortisol, ACTH, calcium, phosphate, PTH were measured. Thyroid function was assessed by T3, T4 and TSH.

**Results:** Short stature was seen in 32.2% of our patients. Diabetes was present in 10.3%. Primary hypothyroidism and hypoparathyroidism was present in 6.9% and 1.15% of the patients. Hypocalcemia was 9.2%. Cortisol and ACTH were normal. About 10.3 % of patients had more than one endocrine complication with mean serum ferritin of 3125 micrograms/litre.

**Conclusion:** High prevalence of endocrine complications among our thalassemics signifies the importance of more detailed studies along with therapeutic.
Endocrinopathies in Thalassemia major patients in Thalassemia Center Jakarta, Indonesia
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Background: Regular transfusion in thalassemia major patients increases life expectancy and improves quality of life, but results in iron overload, which had toxic effects to organs including endocrine glands. The introduction of iron chelation therapy has reduced its toxicity, but complications may still occur. In Indonesia, most of our patients did not receive optimal iron chelation therapy, which might result in higher prevalence of endocrine complications.

Aims: To find out the endocrinopathies profile in thalassemia major patients in Thalassemia Center Jakarta.

Methods: This was a retrospective study based on the registry database in Thalassemia Center, Jakarta. We included patients who diagnosed as thalassemia major with complete data on glucose metabolism, thyroid function, pituitary-gonadal axis, bone profile, bone age, and serum ferritin level. We analyzed the association between ferritin level, chelation therapy and type of thalassemia with endocrine profile using chi-square with the significant value of 0.05.

Results: Complete data on endocrine profile were found in 67 subjects (31 boys, 36 girls), 23 (34%) were diagnosed as β-thalassemia homozygote and the rest as β-thalassemia/HbE. The mean age was 16.7± 5.8 years. Most of the patients (63%) received iron chelation therapy with desferrioxamine followed by deferiprone (20%) and only two patients have not taken any iron chelation therapy yet. Short stature was found in 65% of subjects, while 20% of subjects suffered from delayed puberty, 41% had hypothyroidism, and 29% had retarded bone age. None of them was diagnosed as DM or IGT, but one diagnosed as IFG. Hypocalcemia was found in 27% subjects. Subjects with serum ferritin level ≥ 2,500 ng/mL had increased risk to develop hypothyroidism, hypocalcemia and hyperphosphatemia, even though not statistically significant (p=0.58, p=0.08, respectively). Serum ferritin level also not associated with short stature and delayed puberty. Subjects with thalassemia beta-major had increased risk to develop hypothyroidism (p=0.036), but no differences found in the prevalence of short stature, delayed puberty, hypocalcemia, and hyperphosphatemia (p=0.17, p=0.91, p=0.60, respectively). The frequency of transfusion per year and type of chelation therapy did not influence the endocrine profiles.

Conclusions: This study showed that the prevalence of short stature among thalassemia patients is higher in Thalassemia Center Jakarta, while the risk to develop impaired glucose metabolism is lower, despite of poor compliance in iron chelation therapy. The risk to develop hypothyroidism, delayed puberty, and hypoparathyroidism were comparable to other studies.

Clinical, biochemical, and genetic analysis of two Korean patients with Tricho-rhino-phantalangeal syndrome type I and growth hormone deficiency
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Tricho-rhino-phantalangeal syndrome type I (TRPSI) is a rare autosomal dominant hereditary disorder characterized by sparse hair, bulbous nose, long philtrum, thin upper lip, and skeletal abnormalities including cone-shaped epiphyses, shortening of the phalanges, and short stature. TRPSI is caused by mutations in the TRPS1 gene. Herein, we report two Korean cases of TRPS1. Although both patients (a 17-year-old-female and a 14-year-old male) had typical clinical findings, Patient 1 had an additional growth hormone (GH) deficiency. Treatment with recombinant human growth hormone (rhGH) 0.7 IU/kg/week led to an increase in growth velocity. Over 10 years of GH therapy, the mean growth velocity was 5.7±0.9 cm/year. While patient 2 showed a low response after the GH stimulation test, the patient had a poor response with rhGH therapy and GH therapy was discontinued after 6 months.

For the genetic analysis of the TRPS1 gene, two mutations were found. Patient 1 had a heterozygous mutation c.2520dupT (p.Arg841LysfsX3) which had not been previously reported. Patient 2 had a known nonsense mutation c.1630C>T (p.Arg544X). In summary, we were the first to report Korean patients with mutation of TRPS1.

Clinical and laboratory characteristics of Prader-Willi syndrome
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Prader-Willi syndrome (PWS) is a complex multisystem genetic disorder due the lack of expression of paternally inherited imprinted genes on chromosome 15q11-13. Clinical presentation includes hypotonia, hyperphagia, obesity, hypogonadism, learning difficulty. We studied clinical and laboratory of patient diagnosed and treated in National Hospital of Pediatrics, Hanoi (NHP). This is descriptive study. We collected 26 patients diagnosed of PWS by FISH in NHP from December 2007 to April 2012 were recruited in the study. Male/female ratio was 6/1. Patients diagnosed before 5 years occupied 53.5%. 85.7% of patients were found to have hypotonia at age of 4.920.0 months. 86.4% of patients had hyperphagia at age of 20.711.1 months. In patients aged of >2 years, height SDS was +8.47.7 SD compared to gender and age. The figure of BMI was +10.33 3.4/7 of patients aged ≥6 years had microgenis. 91.7% of patients had hypothyroidism. 4/24 of patients (14.3%) had type 2 diabetes mellitus. Based on clinical presentation, more PWS patients could be diagnosed and treated early.

Factors affecting height in children and adolescents with transfusion-dependent Thalassemia – results from a Thalassaemia center in Malaysia
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Thalassemia, a common inherited haemoglobinopathy in Malaysia, causes significant morbidity due to chronic anaemia and complications of iron excess from regular blood transfusion. Short stature is one of the most prominent complications in transfusion-dependent thalassemia with prevalence of 31\% to 75\%. Causes of growth impairment include iron overload, nutritional deficiency, GH-IGF1 axis dysregulation, abnormal puberty and desferrioxamine toxicity. We aim to determine the prevalence of short stature, defined as height z-score ≤ -2, and the factors affecting height in thalassemia patients attending the Haematology clinic at a tertiary referral center. This observational cross-sectional study involved patients aged 3-19 years, needing blood transfusion at least every 8 weeks, and without co-morbidities or endocrinopathy which affect growth.
Weight & height were measured. Puberty status was clinically assessed. Body mass index (BMI) was calculated as a marker of nutritional status. Mean of ferritin levels measured over the preceding one year was calculated as a marker of iron overload. There were 52 boys (mean age 11.2±4.8y, mean height z-score -1.67±1.11, mean BMI z-score -0.87±1.44, mean ferritin 3316±2092 μg/L) and 47 girls (mean age 11.8±4.2y, mean height z-score -1.59±0.97, mean BMI z-score -0.83±0.95, mean ferritin 3005±2356 μg/L). Overall 35/99 (35%) were short while 64/99 (64%) had normal height, 19/52 (37%) boys and 16/47 (34%) girls were short. 16/19 (84%) short boys were aged ≤9 years, 15/16 (94%) short girls were aged ≥8 years. Only one boy (aged 15y) and one girl (aged 14y) had delayed puberty. They were both short with height z-score -3.41 and -2.26 respectively. Overall there was a moderate positive correlation between height z-score and BMI z-score (Pearson r = 0.388, p=0.00). There was no significant correlation between height z score and mean ferritin level (Pearson r = -0.044, p= 0.666).

Significant proportion (35%) of our transfusion-dependent thalassaemia patients have short stature, majority of them in the pubertal age group. Height is significantly associated with nutritional status but not ferritin level. Improvement in nutrition may improve height in these patients.

### P62

**Association of change on insulin-like growth factor (IGF)-I and IGF-binding protein 3 with genetic markers after a month of growth hormone (GH) therapy on Chinese children born with GH deficiency**

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**Aims:** To identify genetic markers associated with changes in IGF-I and IGFBP3 standard deviation score (SDS) after 1 month of r-hGH treatment in Chinese GHD children either born Appropriate for Gestational Age (AGA) or Small for Gestational Age (SGA).

**Methods:** This phase IV open-label interventional study was performed on samples from 205 GHD children (175 subjects born AGA and 30 subjects SGA) of Chinese Han origin, recruited at 8 centers. All the subjects were given r-hGH for 4 weeks (0.033mg/kg/d).1536 SNPs were selected from 100 Candidate Genes involved in the GH-IGF1 axes, growth plate and other short stature-related diseases. We genotyped Single nucleotide polymorphism (SNP) using Illumina GoldenGate™ Assays. Linear regression was used to identify single SNPs significantly associated with changes, from baseline to week 4, in serum IGF-I SDS and IGFBP3 SDS. Gestational age (GA) was also included in the model. The significance threshold was set as a corrected P-value<0.05. Multiple linear regressions with interaction effect were used to identify significantly associated genes with changes, from baseline to week 4, in serum IGF-I SDS and IGFBP3 SDS. The significance threshold was set as a corrected P-value<0.1.

**Results:**

1. 6/19 SNPs which correspond to 4/17 genes were significantly associated with IGF-I SDS change/IGFBP3 SDS change separately from baseline to Week 4 in all samples (AGA+SGA) with a corrected P-value<0.05. Among them, 3/10 SNPs showed significant interaction effects, suggesting that the pattern of SNPs associated with IGF-I SDS change/IGFBP3 SDS change was different between two groups. Aged 11.2±4.8y.
2. (2) 14/14 genes which significantly associated with IGF-I SDS change/IGFBP3 SDS change at Week 4 were identified in all samples (AGA+SGA). Among them, 6/12 genes showed significant interaction effects, suggesting that IGF-I SDS change/IGFBP3 SDS change have different effect on these genes expression between two groups. We also found that 5 genes in common associated with both IGF-I SDS change and IGFBP3 SDS change.

**Conclusions:** The results of our study demonstrate the genetic association between polymorphic variations of some candidate genes and serum IGF-I and IGFBP3 SDS changes after r-hGH therapy in children with GHD born SGA and AGA, suggesting that these genetic markers could be used into clinical practice in order to optimize efficacy, safety and cost of r-hGH therapy.

### P63

**Safety and effectiveness of recombinant human growth hormone replacement in postoperative craniohypophysectomy children**

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**Aims:** To observe the safety and effectiveness of recombinant human growth hormone (rGH) replacement therapy (GHRT) in postoperative craniohypophysectomy (CP) children.

**Subjects and methods:** We reviewed the records for all patients undergoing GHRT at our hospital over the study period. Patients were included if they had received CP resection, GHRT for at least 12 months, and records of serial magnetic resonance imaging data and data for treatment, pituitary hormone profiles and growth chart were available. GH-naïve control patients were selected from our hospital database of patients carried out the same surgery. Patients were matched for date of surgery, age, site of primary diagnosis and sex.

**Results:** 18 patients were recruited with growth hormone deficiency. In treatment group, all patients all gained acceleration in growth velocity and elevated growth factors level. There were no recurrent tumors found in both groups.

**Conclusions:** Our study demonstrates no increased risk for recurrent in patients receiving GHRT, thus supporting a high safety profile of GHRT in postoperative craniohypophysectomy children. Additionally, GHRT can provide a significantly change in growth velocity compared with control group.

### P64

**Pathological gynecomastia in children at Cipto Mangunkusumo hospital Jakarta**

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Gynecomastia is generally attributed to conditions that disrupt sex-steroid signaling pathways, resulting in increased or unopposed estrogen action on breast tissue. Pubertal gynecomastia is common and usually physiological, with sympathetic reassurance and watchful waiting the mainstays of treatment. Meanwhile, pathological gynecomastia should be identified, sought the cause and gave proper management shortly. The aim of our study was to raise vigilance into pathological gynecomastia that require more complex management and have long-term effect. We conducted a retrospective chart review of 12 patients with gynecomastia who presented to pediatric endocrinology clinic at Cipto Mangunkusumo Hospital, Jakarta from September 2009 to June 2012. Seven patients (58%) aged 10.3 to 13.5 yr old were diagnosed physiologic pubertal gynecomastia, one patient (8%) aged 1 month old was diagnosed neonatal gynecomastia and the rest 4 patients (34%) were pathologic. Of the pathologic case, two patients aged 7.4 and 8.4 yr old were diagnosed prepubertal gynecomastia with history of taking herbal medicine and fast foods at least three times a week and still being observed. The others, aged 10.6 and 14.9 yr old were investigated and confirmed to have DSD (disordered of sexual development) 47 XY, Klinefelter syndrome and DSD 46 XX ovotesticular. Our results suggested that gynecomastia in children should prompt an immediate evaluation distinguish a normal developmental variant from possible endocrine disorder in order to give the best treatment.
PUBERTY

P65

Precocious puberty in children

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Objective: To determine the etiology of precocious puberty at tertiary care hospital and to compare the clinical and laboratory parameters of central and peripheral precocious puberty.

Study design: Cross sectional study.

Place and duration of study: Endocrine clinic at National Institute of child health, Karachi, Pakistan from January 2009 to December 2011.

Methodology: Children who fulfilled the criteria of precocious puberty were included. Precocious puberty defined as the development of secondary sexual characteristics before the age of 8 years in girls and 9 years in boys. All patients evaluated clinically and on laboratory investigations. Data was entered and analyzed using SPSS version 17.0. Independent sample t-test/ Mann-Whitney U-test were applied.

Result: Total numbers of patients registered during this period were 84. The conditions causing precocious puberty were central precocious puberty (36.5%), peripheral precocious puberty (38.8%), premature pubarche (10.6%) and premature thelarche (14.1%). In central precocious puberty 26 were female and 5 were male. The causes identified in them were idiopathic (67.74%), hypothalamic hamartoma (12.9%), crianoiphagrioma (9.67%), arachnoid cyst (3.22%), hypothalamic astrocytoma (3.2%), hydrocephalus (3.2%). In peripheral precocious puberty 21 were male and 12 were female. Congenital adrenal hyperplasia (81.8%), adrenocarcinoma (9.1%), ovarian teratoma (6.1%) and McCune Albright syndrome (3%) were diagnosed in them. There was difference in the age of onset of puberty of central precocious puberty 3(2-6) versus peripheral precocious puberty 5.25(3.62-7.0). Central precocious puberty children showed higher height SDS, weight SDS, FSH, LH than peripheral precocious puberty.

Conclusion: Peripheral precocious puberty is more common than central precocious puberty. Height SDS, weight SDS, FSH, LH was higher in central precocious puberty versus peripheral precocious puberty.

P66

Hyperandrogenism secondary to topical testosterone exposure

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Topical testosterone gels are now a widely used method of testosterone replacement therapy and have been shown to be convenient and effective [1]. The unintentional transfer of testosterone gel to children or partners by skin contact is a rare but significant adverse effect [2]. A 3-year-old well girl was referred for assessment of precocious puberty. Pubic hair had been first noted by her mother 9 months earlier. Examination revealed a tall girl (>99.9th centile) with no breast development but Tanner stage th pubic hair and cliteromegaly. Testosterone levels were elevated at 2.5 nmol/l, as was her Androstenedione level at 1.1nmol/l. 17 OH P was normal and tumour markers were negative. Urine steroid profile was quantitatively normal but there was a modest increase in androgen metabolites. Bone age was advanced by 16 months. Ultrasound and MRI imaging of her ovaries and adrenals did not reveal a source of androgen production.

Upon further direct questioning, her father revealed he was using topical testosterone replacement therapy. Her father was advised of measures to reduce secondary exposure. Her repeat testosterone level fell to 0.7 nmol/l upon retesting 4 months later and the cliteromegaly resolved. At follow up a further six months later, testosterone level had risen to 2.5 nmol/l. Switching to the use of IM preparations was encouraged. Follow-up testing after these measures were adopted revealed normal undetectable testosterone levels (<0.7nmol/l).

Once daily application of testosterone gels to the skin results in relatively stable and physiological testosterone levels in most users [3]. It is often favoured above the other methods of delivery of testosterone as it is painless, discrete and convenient to use. Even small quantities of transferred testosterone may result in clinical signs of hyperandrogenism.

When reviewing children with evidence of virilization, we must remember to question parents about the potential for exogenous androgen exposure.

References

P67

Three cases of pediatric patients with testicular microliithiasis showing gynecostasia and testicular enlargement

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Background: Testicular microliithiasis (TM) is a rare pathology characterized by localized or diffuse intratesticular foci of calcification. Its incidence in the pediatric population ranges from 1.1% to 4.2%.

Aims: To report three cases of TM in boys who complained of gynecostasia and bilateral testicular enlargement.

Results: Case 1) A 9.4-year-old boy presented with bilateral testicular enlargement accompanied by other pubertal signs. His bone age was 11 years and serum levels of LH and FSH after GnRH stimulation were within pubertal limits. Scrotal ultrasonography (US) showed TM in both tests. He revealed early puberty and no malignant evolution. Case 2) A 9.4-year-old boy with Down syndrome presented with bilateral testicular enlargement and accelerated growth velocity. His bone age was 11 years and serum levels of LH and FSH after GnRH stimulation were within pubertal limits. He had TM at US in both tests. He underwent right orchiectomy. He also revealed early puberty and no malignant change. Case 3) A 11-year-old boy complained of gynecostasia without other findings of puberty. His bone age was 11 years. He also had TM at US in both tests. No focal testicular lesion or malignancy developed during the review period.

Conclusions: Our report underline the usefulness of scrotal US for finding an occult TM in a patient with gynecostasia without other findings of puberty. In addition, TM may be predictive factor for early puberty evolution, but a large number of patients with a longer follow-up period may be needed to accurately discern the possible association between TM and precocious puberty.
patient, as premature telarche, and the rests, as precocious puberty, were evaluated. Nineteen age-matched, non-pubertal girls, were included as control group. Polysomnography was carried out to all patients. Levels of hormones and neurotransmitters were assessed during REM period.

Results: Weight Standart Deviation Score (SDS) in girls with PP was significantly higher than those in girls with PT and non-pubertal (p<0.05). Nocturnal kisspeptin, leptin, gamma-aminobutyric acid (GABA), and glutamate levels during sleep revealed no statistically significant difference among three groups (p>0.05). First sleep interval of Stage N1 in polysomnography was shorter, whereas total sleep time was longer in girls with premature telarche compared to other groups (p=0.031 and p=0.029, respectively). There were negative correlation between total sleep time (TST) and kisspeptin levels and positive correlation between TST and glutamate levels in girls with PT (r=0.481 and r=0.503, p<0.05, respectively).

Conclusion: Interval of transition to sleep is shortened, whereas total sleep time is prolonged in girls with premature telarche. Sleep pattern of girls with precocious puberty is similar to those of non-pubertal girls. No change was found serum levels of hormones and neurotransmitters related with pubertal activation during deep sleep periods in girls with precocious puberty compared to girls with PP and non-pubertal.

P69 Different clinical courses of central precocious pubertal girls according to the age at presentation and treatment

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The progressivity of central precocious puberty (CPP) seemed to depend on the age at presentation. We investigated the clinical courses between the early onset and late onset groups.

One hundred thirty five girls with central precocious pubertal diagnosis were followed between Jan. 2003 and Dec. 2009 were included. Among 135 patients, 123 were idiopathic CPP (91.1%) and 12 (8.9%) had neurogenic problems, such as arachnoid cyst, hydrocephalus, pineal cyst, pituitary cyst, partial empty sella, cerebral palsy, diffuse cortical atrophy, tuberous sclerosis, and Langerhans cell histiocytosis. Also noted was small for gestational age in another 12 patients among the idiopathic patients. CPP criteria were development of secondary sexual characteristics before 8 yr of chronological age (CA) with advanced bone age (BA), and stimulated LH >5 IU/L. They were treated with GnRH analogues every 4 weeks and followed for more than 1 yr. According to the age at initiation of treatment, 9 were before 6 yr, 11 were 6-7 yr, 61 were 7-8 yr, 54 were >8 yr. Subjects were divided into two groups if they were treated before (Group I) or after 7 yr of age (Group II). Clinical courses and laboratory findings were evaluated every 6 months. We compared anthropometric parameters, calculated predicted adult height (PAH), predicted treatment periods, and laboratory findings between the two groups.

Among the baseline parameters, BA and CA were greater in group II, but BA/CA ratio were significantly greater in group I. The time needed for disappearing the CA and BA difference was 4.64 yr (3.74-5.54 yr) for the total patients, but the time is significantly different between the two groups, 7.98 yr (3.88-12.07 yr) for group I and 4.24 yr (3.74-4.73 yr) for group II. The time needed for disappearing the PAH and TH difference was 2.49 yr (1.96-3.01 yr), but the time is significantly different between the groups, 4.37 yr (1.32-5.87 yr) for group I and 2.32 yr (1.48-3.16 yr) for group II.

Among the girls with CPP, younger age group had more advanced bone age compared to chronologic age, and needed significantly longer treatment periods for the disappearance of BA-CA gap and PAH-TH gap.

P70 Central precocious puberty secondary to hypothalamic hamartoma

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Introduction: Central precocious puberty (CPP) presenting at a very young age is likely to have an underlying pathology. One of the pathologies is hypothalamic hamartoma (HH), a non-neoplastic tumour-like lesion located at the floor of the third ventricle, near the tuber cinereum. Two young children with CPP due to HH without gelastic seizures or mental retardation were successfully managed and described in this report.

Cases: Case 1: An 18-months-old boy presented with vaginal bleeding. Physical examination showed breast Tanner stage (TS) 4 with pubic hair TS2. Her follicle-stimulating hormone (FSH), luteinizing hormone (LH) and estradiol were in pubertal range (6 IU/L, 8.9 IU/L, 281 pmol/L respectively) with an advanced bone age of 7 years 10 months. Brain magnetic resonance imaging (MRI) showed a round, non-enhancing, isointense lesion at the tuber cinereum just anterior to the mamillary body representing hypothalamic hamartoma. She responded well with intramuscular GnRH analogue with resolution of precocious puberty. She is currently 9 years, remains prepubertal with maintenance dose of GnRH analogue at 4.2mcg/day.

Case 2: A 20-months-old boy presented with rapid growth. Pubertal staging showed gonads TS2 (testicular volumes of BmLbilia) with pubic hair TS2. His FSH, LH and testosterone were elevated (12 IU/L, 16.5 IU/L and 12.5 nmol/L respectively) with an advanced bone age (BA 3 years). His MRI brain confirmed hypothalamic hamartoma. GnRH analogue at conventional dose failed to correct the excessive growth and stop the progression of pubertal development until a higher dose at 18.5mcg/kg/day was given. He is currently 41/2 years and remains prepubertal.

Conclusion: CPP secondary to hypothalamic hamartoma usually presents early, before the age of two years. Medical therapy with GnRH analogue is still the first choice of treatment. The dosage of GnRH varied and in patients whom standard dose showed insufficient effects, high dose is recommended. Surgical intervention is reserved only for those who failed medical therapy or for those with intractable seizures.

P71 Serum bisphenol A levels in girls with central precocious puberty

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Bisphenol A (BPA) is a chemical widely used to make polycarbonate plastics and epoxy resins lining food and beverage containers. A number of in vitro and in vivo studies have demonstrated that BPA has an estrogenic effect by binding to the nuclear estrogen receptor, and early BPA exposure could induce early puberty. However, effects of human exposure to BPA on pubertal onset and the association of gonadotropin levels have not been fully evaluated. We aimed to study whether serum bisphenol A levels are associated with central precocious puberty (CPP) in Korean children.

A total of 103 girls (51 CPP cases and 52 controls, aged 7 to 9 yr) were enrolled. Pubertal staging, anthropometry, bone maturation were assessed. Gonadotropin releasing hormone-stimulation test were conducted to determine the basal and peak levels of luteinizing hormone (LH). Serum bisphenol A levels were analysed by gas chromatography/mass spectrometry method. Geometric mean serum BPA levels were higher in CPP girls than in controls (6.5±5.5 vs 3.4±4.1 ng/mL, P<0.0001). In partial correlation analysis controlling for age and body mass index, serum BPA level showed significant positive correlation with bone age (r=0.343, P=0.001).

Table (abstract P71) Multivariate logistic regression analysis for obesity according to the quartiles of BPA concentrations

<table>
<thead>
<tr>
<th>BPA Tertile†</th>
<th>Crude OR (95% CI)</th>
<th>P-value</th>
<th>Adjusted OR* (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (ref)</td>
<td>1.0</td>
<td></td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.02(0.75-5.46)</td>
<td>0.165</td>
<td>2.60(0.858-7.93)</td>
<td>0.091</td>
</tr>
<tr>
<td>3</td>
<td>6.67(2.31-19.25)</td>
<td>&lt;0.0001</td>
<td>7.68(2.34-25.19)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Adjusted for age and body mass index
†Tertile 1, 0.19-3.82ng/mL; tertile 2, 3.83-7.87 ng/mL; tertile 3, 8.79-38.1 ng/mL
Purpose: Gonadotropin-releasing hormone (GnRH) stimulation test is the gold standard to document premature activation of the hypothalamic-pituitary-gonadal axis in early puberty. However, this test is time-consuming, costly and uncomfortable for the patients. The aim of this study was to investigate to simplify the GnRH stimulation test in the assessment of pubertal activation and suppression.

Methods: We identified 72 girls diagnosed with central precocious puberty, and they were treated with GnRH analogue (GnRHa) to suppress pubertal progression from 1 January 2011 to 31 January 2012. GnRH stimulation tests were done before and 4 weeks after the third dose of the GnRH analogue. Information on clinical manifestations and laboratory data were obtained by reviewing medical records. All variables were expressed as mean +/- SD, and a p value of <0.05 was considered statistically significant.

Results: 1) Before GnRHa treatment, the mean luteinizing hormone (LH) level was higher at the 30th minutes (18.17 IU/L±16.77) of the test in comparison to the basal level (0.35 IU/L±0.60), the 15th, 60th, 90th and 120th minutes (p<0.001). However, there was no significant difference in the LH level between the 30th and 45th minutes of the test. Among 72 patients, 49 girls (68.1%) were showed the peak LH level at 30th minutes and the others were showed the peak LH level at 45th minutes (33.3%), and 60th minutes (6.9%).

2) After GnRHa treatment, 62 patients (86.1%) were suppressed (peak LH level < 2 IU/L), and 10 (13.9%) were inadequately suppressed. The LH level was higher at the 30th minutes (0.91 IU/L±1.14) of the test in comparison to the basal level (0.26 IU/L±0.55), the 45th minutes (0.78 IU/L±1.12) and 60th minutes (0.71 IU/L±0.18)(p<0.001). But the LH level was no significant difference between 15th and 30th minutes.

3) After GnRHa treatment, the AUC in ROC analysis was greatest at the 30th minutes, and sensitivity and specificity of the 30th minutes samples were 90.0% and 100.0%. The basal LH level of the test was showed low sensitivity (25.0%).

Conclusion: It is adequate to check the LH level at 30th and/or 45th minutes of the GnRH test for diagnosis of CPP and 30th minutes for assessment of pubertal suppression. Therefore we suggest that the simplified GnRH test is sufficient to evaluation of pubertal activation and suppression.
The obesity and overweight rate in girls with earlier pubertal development has been increasing. The purpose of this study was to analyze the relationship between obesity and pubertal development in girls. Two years of age, she was noted to have enlarged head. Cranial CT revealed a fallopian tube and ovary appeared normal. Histopathologic studies were consistent with Sertoli Cell Tumor of the left ovary. She was born term to a G2P1 mother with no perinatal complications noted. At two years of age, she was noted to have gradual bilateral breast enlargement. There was no breast discharge noted. At two years and four months of age, she started to have vaginal bleeding which the mother claimed to occur on a monthly basis lasting for five to seven days. There was no history of trauma or any accompanying urinary symptoms. Initial consult was done in a local hospital where she was also noted to have enlarged head. Cranial CT Scan done was normal. Assessment made was precocious puberty. The patient was subsequently referred to our institution for further evaluation. On physical examination, pertinent findings include increased head circumference (53.3 cm, z-score >0) and height (100 cm, z-score = 0) within normal for age, Tanner Stage 3 for breast and Stage 1 for pubic hair. The rest of the physical exam findings were essentially normal. Bone age was appropriate for chronologic age. Hormonal work-up were as follows: FSH: 0.27 (NV:0.27–3.39 IU/L), LH: 0.22 (NV: 0.03-0.55 IU/L), Estradiol: 234 (NV:<10 pg/mL), and Prolactin: 783 (NV:80-500 microIU/mL). THt: 9.4 (0.3-3.8 mIU/L), FSH: 24.4 (11-24 pmol/L). Pelvic ultrasound revealed upper borderline-sized uterus with slightly thickened round complex mass in the left adnexal region, to consider an ovarian neoplasm. Alpha-feto Protein, B-HCG, CA-125 tumor marker levels were all within normal limits. The patient subsequently underwent Exploratory Laparotomy with Left Salpingo-oophorectomy. Intra-operatively, the left ovary was noted to be converted to a 5cm x 3cm x 3cm solid mass with smooth surface and intact capsule. The right fallopian tube and ovary appeared normal. Histopathologic studies were consistent with Sertoli Cell Tumor of the left ovary, positive for Inhibin and Calretinin immunostaining. The vaginal bleeding and progressive breast enlargement ceased post-operatively. The estradiol and prolactin marker levels dropped ( Estradiol: 254 to 37.3 pg/mL and Prolactin: 783 to 304 microIU/mL) one month after the surgery.

Onset of puberty has shifted toward a younger age in the 21st century. The useful pubertal assessment in the individual child must be based on recent and reliable reference data from the same population. However, currently representative pubertal data for Thai girls are lacking. Therefore, we determine the current prevalence of mean ages at onset of pubertal characteristics in healthy urban Thai girls in Khon Kaen Province, northeast Thailand.

A cross-sectional study was carried out between January and July 2011. Five hundred and three school girls aged 7 to 16 years were enrolled. All were in good physical health. Stages of breast and pubic hair development were rated on girls by Tanner’s criteria. Assessment was performed by a trained pediatrician. Data on menstruation were collected by the status quo method. The median (range) ages of the onset of thelarche and pubarche were 9.3 (7.8-13.4) and 10.8 (8.9-14.5) years, with the mean±SD of 10.1±1.2 and 11.6±1.2 years, respectively. One hundred and eighteen girls had experienced menstruation. The median (range) age of menarche was 11.6 (10.0-14.0) years and the mean age was 11.6±0.8 years. The mean ages of pubarche and menarche decreased from the previous study significantly (P < 0.001). These data can be used as the reference of normal pubertal development in Thai girls in Khon Kaen for the purpose of determining precocious or delayed puberty.

Sertoli Cell Tumor is a rare sex cord tumor, comprising less than 5% of all sex cord tumors. It usually occurs in women of reproductive age but a few can also occur during early childhood. The usual manifestation among children is isosexual pseudoprecocity. This is a case of a three-year-old girl who came in with a chief complaint of vaginal bleeding. She was born term to a G2P1 mother with no perinatal complications noted. At two years of age, she was noted to have gradual bilateral breast enlargement. There was no breast discharge noted. At two years and four months of age, she started to have vaginal bleeding which the mother claimed to occur on a “monthly” interval lasting for five to seven days. There was no history of trauma or any accompanying urinary symptoms. Initial consult was done in a local hospital where she was also noted to have enlarged head. Cranial CT Scan done was normal. Assessment made was precocious puberty. The patient was subsequently referred to our institution for further evaluation. On physical examination, pertinent findings include increased head circumference (53.3 cm, z-score >0) and height (100 cm, z-score = 0) within normal for age, Tanner Stage 3 for breast and Stage 1 for pubic hair. The rest of the physical exam findings were essentially normal. Bone age was appropriate for chronologic age. Hormonal work-up were as follows: FSH: 0.27 (NV:0.27–3.39 IU/L), LH: 0.22 (NV: 0.03-0.55 IU/L), Estradiol: 234 (NV:<10 pg/mL), and Prolactin: 783 (NV:80-500 microIU/mL). THt: 9.4 (0.3-3.8 mIU/L), FSH: 24.4 (11-24 pmol/L). Pelvic ultrasound revealed upper borderline-sized uterus with slightly thickened round complex mass in the left adnexal region, to consider an ovarian neoplasm. Alpha-feto Protein, B-HCG, CA-125 tumor marker levels were all within normal limits. The patient subsequently underwent Exploratory Laparotomy with Left Salpingo-oophorectomy. Intra-operatively, the left ovary was noted to be converted to a 5cm x 3cm x 3cm solid mass with smooth surface and intact capsule. The right fallopian tube and ovary appeared normal. Histopathologic studies were consistent with Sertoli Cell Tumor of the left ovary, positive for Inhibin and Calretinin immunostaining. The vaginal bleeding and progressive breast enlargement ceased post-operatively. The estradiol and prolactin marker levels dropped ( Estradiol: 254 to 37.3 pg/mL and Prolactin: 783 to 304 microIU/mL) one month after the surgery.
Bone plays metabolic roles through osteocalcin (OC) when it is released into the systemic circulation in uncarboxylated form. Identified novel metabolic roles of OC include increasing insulin secretion and sensitivity, energy expenditure, reduction of fat mass and mitochondrial proliferation and functional enhancement. The onset of puberty can be influenced by metabolic factors. This study was aimed to determine serum OC levels in girls with central precocious puberty (CPP) and to investigate the effects of OC on the onset of puberty.

Methods: Serum OC levels of girls CPP (n=30) and their age-matched controls (n=30) were measured. GnRH stimulation test was performed in CPP group. Bone age was determined in all subjects.

Results: Serum OC levels were significantly higher in CPP group compared with control group (76.8 ± 10.5 vs. 61.6 ± 15.1ng/mL, p=0.001). Serum OC levels were correlated with peak LH levels during GnRH stimulation test (r=0.348, p=0.037), bone age (r=0.403, p=0.010) and bone age advance (r=0.323, p=0.042), but not related to age, height, weight and BMI.

Conclusions: Serum OC seems to be associated with the onset of puberty leaving causal relations unresolved.

P81
Two sporadic patients of Perrault syndrome with ovarian dysgenesis and sensorineural deafness
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Perrault syndrome is an autosomal recessive disorder characterized by sensorineural deafness and ovarian dysgenesis. Some patients also have neurologic abnormalities, including cerebellar ataxia, nystagmus, polyneuropathy and mild mental retardation. The syndrome is known to be caused by mutations in HSD17B4 or HARS2 until now but few patients were reported. We report on two sporadic Korean patients of Perrault syndrome with ovarian dysgenesis and sensorineural deafness.

Patient 1: A 14-year-old 6-month female patient presented with delayed puberty. She had bilateral sensorineural hearing impairment. Her neurologic findings were normal and she had no mental retardation. She had normal karyotype (46, X) and hypergonadotropic hypogonadism. Pelvic ultrasound showed a small uterus and ovaries. Brain MRI was normal.

Patient 2: A 16-year-old female patient presented with delayed puberty and neurologic manifestations. She had ataxia, dysphagia and weakness. She had no mental retardation and brain MRI was normal. She had multiple Café au lait spots and long slender fingers but no Marfanoid features. Laboratory tests revealed hypergonadotropic hypogonadism and normal female karyotype (46, XX). Pelvic ultrasound examination showed a hypoplastic uterus and small ovaries.

Because Perrault syndrome has clinical variability and genetically heterogeneous, we have to inspect additional findings and neurologic abnormalities. And further studies will be required to ascertain the common causative mutation of this syndrome.

P82
Precocious puberty and ovarian tumors – 2 case reports
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Aim: To report 2 cases of peripheral precocious puberty due to ovarian tumors of different etiology.

Methods: We describe the clinical presentation, imaging findings, hormonal work-up and follow up after oophorectomy of 2 children with precocious puberty due to ovarian tumors.

Results: Case 1: 3 years old girl presented with progressive bilateral breast enlargement over 1 year, irregular vaginal bleeding for 10 months and pubic hair development for 2 months. Her past history was unremarkable. Her general examination and vitals were normal. Tanner staging was B3P3. There was no axillary hair or genital ambiguity. Cardiac, thoracic and neurological examinations were normal. A solitary well-defined pelvic mass firm to hard, mobile was palpable in right lower abdomen. Her bone age, height age and chronological age were respectively 8yr 10months, 4 year(100cm) and 3 year. Her investigations showed normal hemogram, liver, renal and thyroid functions. Hormonal profile: LH <0.1IU/mL, FSH <0.1 IU/mL, Testosterone 0.334ng/mL, DHEAS 17.97µg/dl, Estradiol >1000pg/ml. CT pelvis showed a heterogeneously enhancing abdomino-pelvic mass with non visualization of ovaries separately suggestive of ovarian mass. She underwent resection of right tuboovarian mass which was suggestive of juvenile granulose cell tumor. Repeat hormonal profile done showed markedly reduced Estradiol levels 17pg/ml. At one year follow-up, there was no vaginal bleeding so far.

Case 2: 6 year old girl presented as precocious puberty with progressive bilateral breast enlargement over 7 months, cyclical vaginal bleeding (3/25-30days) for 4 months and pubic hair development for 2 months. She had a recent height gain over last 1 year. Her past history was unremarkable. Her general examination and vitals were normal. Tanner staging was B3P3. There was no axillary hair or genital ambiguity.

Systemic examination was normal. Her investigations showed normal hemogram, liver, renal and thyroid functions. Her bone age, height age and chronological age were respectively 7.8yr, 7 year (119cm) and 6 year. Hormonal profile: LH <0.1IU/mL, FSH <0.1IU/mL, Testosterone 0.334ng/ ml, DHEAS 17.99ug/dl, Estradiol >162.8pg/ml. CT pelvis showed a bulky left heterogeneous, well defined pelvic mass firm to hard, mobile was palpable in right lower abdomen. Her bone age, height age and chorological age were respectively 7.8yr, 7 year (119cm) and 6 year.

Serum OC levels were correlated with peak LH levels during GnRH stimulation test (r=0.348, p=0.037), bone age (r=0.403, p=0.010) and bone age advance (r=0.323, p=0.042), but not related to age, height, weight and BMI.

Conclusions: Serum OC seems to be associated with the onset of puberty leaving causal relations unresolved.

P83
Central precocious puberty in girls aged 6 to 8 years and magnetic resonance imaging of the pituitary: 11-year experience in a single centre
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Estradiol levels of 162.9 pg/ml due to mixed sex cord stromal tumor. Both have successful outcome at 12 months and 6 months respectively of follow up without recurrence.
Introduction: Central precocious puberty (CPP) could be a phenotype of pathology in the central nervous system. While it is generally accepted that all boys with CPP and girls with CPP at less than 6 years of age should undergo brain imaging as part of the workup, there have been controversies as to the use of brain imaging in girls who develop CPP between 6 to 8 years.

Objectives: To evaluate the prevalence and clinical characteristics of intracranial lesions in patients with central precocious puberty aged 6 to 8 years in a single centre in the past 11 years.

Methods: Retrospective chart review of girls with CPP and their MRI findings between year 1999 to 2009 in a single centre.

Results: One hundred and eighty-eight girls had central precocious puberty in the study period and 157 of them (83.5%) had MRI of the pituitary done as part of the workup. The prevalence of intracranial pathology among girls with CPP aged 6 to 8 years was 20.0% while among all girls with CPP aged less than 8 years, 34 girls (21.7%) were found to have intracranial pathology. These pathologies included: pituitary adenoma (n = 16), pineal cyst (n = 8), Rathke’s cleft cysts (n = 4), arachnoid cyst (n = 1), intra-ventricular cyst (n = 1), venous angioma over the left frontal lobe (n = 1), hydrocephalus (n = 2) and an old infarct over the frontal lobe (n = 1). The two cases of hydrocephalus and the case with an old infarct were known before the onset of CPP. None of the lesions detected required further interventions with surgical removal, chemotherapy or radiotherapy within the follow-up period of 7.2 ± 3.0 years.

Conclusions: Brain imaging the girls with CPP in our centre mainly detected benign lesions not requiring any intervention during our follow-up period. Though the current data do not justifiably a practice of performing routine MRI for girls diagnosed to have CPP at 6 to 8 years, longer follow-up assessment of such lesions detected in childhood may be necessary before concluding on their benign outcome.

P84
Correlation nitric oxide level and homeostatic model assessment insulin resistance in obese adolescent
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Background: Childhood obesity is a significant health problem that has reached epidemic proportions around the world. Childhood obesity associated with increased risk for several cardiovascular and metabolic syndrome, such as insulin resistance. Homeostatic model assessment insulin resistance (HOMA-IR) is a marker widely used for insulin resistance. Nitric oxide (NO) has important role in insulin resistance. Objective: To determine correlation between NO and HOMA-IR in obese adolescent.

Method: A cross sectional study was performed in 44 obese senior high school students in Padang from December 2011 until March 2012. Chosen through multi stage random sampling, devided into 2 groups; 22 in insulin resistance and 22 in non insulin resistance. Variables measured were HOMA-IR with calculated based on fasting glucose and insulin level, serum NO levels. Data was analyzed statistically with computerization system using regression correlation test and T-test. P<0.05 is significant.

Result: There was significant difference in body mass index between insulin resistance and non resistance group (32.53±2.57 vs 30.55±3.03 kg/m²). Glucose level was no significant difference between insulin resistance and non resistance group (4.93±0.79 vs 4.66±1.02 mmol/L). insulin was significant difference between insulin resistance and non resistance group (20.23±4.03 vs 15.82±5.72 uU/mL). Nitrite oxide level was significant difference between insulin resistance and non resistance group (70.07±24.98 vs 55.04±19.66 mmol/L). There was significant correlation between NO level and HOMA IR (r=0.482; p=0.001) and no significant correlation between BMI and NO levels (r=0.135; p=0.325).

Conclusion: Nitric oxide is significantly associated with HOMA-IR in obese adolescent.

P85
The effect of Vitamin C supplementation toward high sensitivity c-reactive protein (hsC-RP) level on male adolescent obesity in Padang
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Background: Prevalence of obesity in children and adolescent has significantly increased, it becomes a serious problem because of the over releasing of interleukin-6 (IL-6), disruption on the oxidative balance, risk factor of getting cardiovascular disease with typically marked by elevation of the hight sensitivity C-Reactive Protein (hs-CRP). On the way to decrease IL-6 release from the visceral adipose cell is by treating the oxidative stress with antioxidant agent, such as Vitamin C.

Objective: To examine mean hs-CRP level on male adolescent obesity in Padang and to know the effect of Vitamin C supplementation toward hs-CRP level on male adolescent obesity in Padang.

Method: This is an experimental double blind study with 40 samples on March until May 2011, which were divided into 2 groups. One group consumed Vitamin C 500 mg and another group consumed placebo, both twice a day for 8 weeks. The hs-CRP level is measured before and after drug consumptions. The data were analyzed with chi-square and general linear model repeated measure, the confidence interval, p<0.05.

Result: The mean of initial hs-CRP level is higher in the Vitamin C group than the placebo group ((2.28±1.51 vs 1.78±1.23 mg/L). At the end of the study, mean hs-CRP level were decreasing in both groups (1.09±1.13 vs 0.89±1.09 mg/L). The changing in hs-CRP level after 8 weeks isn’t significant statistically (p=0.481).

Conclusion: The mean hs-CRP level is high and Vitamin C supplementation was not significantly decreasing hs-CRP level on male adolescent obesity in Padang.

P86
The effect of vitamin c supplementation on intercellular adhesion molecule-1 (ICAM-1) concentration on male adolescent obesity in Padang
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Background: The role of Vitamin C as antioxidant has been known. Obesity is an oxidative stress condition which becomes risk factor of cardiovascular disease, which could be detected through ICAM-1 concentration.

Objective: To examine the effect of Vitamin C supplementation on the ICAM-1 concentration on male adolescent obesity in Padang.

Method: The randomized double blind controlled trial of 40 obese adolescent boys aged 14-18 years old were performed on March-May 2011. Subjects were classified into 2 groups, the Vitamin C 500 mg treatment group and the control group which got placebo, twice daily for 8 weeks. The ICAM-1 concentration of both groups was examined before and after the treatment. The data were analyzed with paired sample t-test and independent t-test with significant degree p<0.05.

Result: The mean of initial ICAM-1 concentration in Vitamin C group were 131.5) ng/ml and 47.91 (SD 62.25) ng/ml, respectively. The reducing Delta ICAM-1 concentration in vitamin C and placebo group were 187.04 (SD 131.5) ng/ml and 131.50 (SD 62.25) ng/ml, respectively. There was significant statistically (p=0.001) and no significant correlation between BMI and NO levels (r=0.135; p=0.325).

Conclusion: Nitric oxide is significantly associated with HOMA-IR in obese adolescent.
Conclusion: Vitamin C supplementation in obese adolescent boys reduce the ICAM-1 concentration.

**P87**
Correlation between lipid profiles and body mass index of adolescents obesity in Padang
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**Background:** Obesity is an emerging public health problems throughout the world where it is on the increase during childhood, adolescence and adulthood. Obesity is associated with hypertension and dyslipidemia caused by changing eating pattern, life style and activities. Obesity could give negative effect of cardiovascular disease and metabolic syndrome.

**Objective:** To determine correlation between blood lipid profile and body mass index of adolescents obesity in Padang.

**Methods:** The study was part of the study of obesity for adolescents in Padang 2010 with cross sectional study of anthropometric measurement (body weight, body height and body mass index), versus blood lipid (cholesterol, LDL, HDL, Triglyceride) serum. The data were analyzed by SPSS 19 using Chi square, T test independent and regression correlation of Pearson’s method.

**Result:** The samples included 36 male (45%) and 44 female (55%) adolescents obesity with mean of ages 16 years 4 months. Mean of body mass index was 32.02(SD 3.47). The dyslipidemia; hypercholesterolemia, increased LDL, increased of triglyceride and decreased of HDL (40%, 41.3%, 25% and 43.8% respectively). The triglyceride level increased with increasing BMI (p = 0.008 and R = 0.294), but there were no significant correlation between cholesterol, HDL and LDL versus body mass index (p = 0.258, 0.416 and 0.594; with R = 0.128, 0.09 and 0.06 respectively).

**Conclusion:** There was a positive correlation between body mass index and triglyceride level.

**P88**
Association between lipid profile and blood pressure in obese adolescents in Padang
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**Background:** Obesity in children is one of the medical and public health problems of the most attention today, because of an increasing incidence. Obesity is associated with dyslipidemia and increased blood pressure will increase risk for cardiovascular and metabolic disease.

**Objective:** To determine association between blood pressure with lipid profile in obese adolescents in the city of Padang.

**Method:** This study is part of a study on obese adolescent in Padang. A cross - sectional study was conducted in 2010 with population of high school students in Padang by anthropometric measurements, blood pressure and blood lipid profile examination. Data were analyzed with SPSS 19 with chi square test and ANOVA with 95% confidence level.

**Results:** Increased blood pressure occurred in 32% of all samples with 27% of prehypertension and 5% hypertension. Dyslipidemia, cholesterol levels, high LDL and triglycerides and low HDL levels found respectively 40%, 41.3%, 25% and 43.8% of the total sample. Obese adolescents with increased blood pressure have high triglyceride levels compared with obese adolescents with normal blood pressure. (40.6% vs 14.6% with P 0.009).

**Conclusion:** Obese adolescents has risk for the occurrence of dyslipidemia and hypertension. Hypertension in obese adolescents is mainly associated with high triglyceride levels.

**P89**
Prevalence of Non Alcoholic Steatohepatitis (NASH) and association with body mass index in obese adolescents in Padang
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**Background:** The prevalence of obesity in children increased from year to year and cause a variety of chronic diseases such as Non Alcoholic Steatohepatitis (NASH). NASH is a liver inflammation due to accumulation of fat in the liver, which had no relationship with alcohol consumption, but associated with obesity and diabetes factors. In most cases, diagnosis of NASH was established by elevated levels of aminotransferase enzymes.

**Objective:** To determine the prevalence of NASH and association with body mass index (BMI) in obese adolescents in Padang.

**Methods:** Cross sectional study was conducted in 80 obese adolescents which is comprised of a study of obese adolescents in 2010 with a population of obese students with anthropometric (bodyweight, bodyheight, BMI) and aminotransferase enzymes measurement. All data are presented as means±SD. Statistical analyses were conducted using t and Mann Whitney U tests. P<0.05 was considered significant.

**Results:** Mean age was 16 years 4 months, body weight 84.61±11.88 kg and body height 1.62±0.08 m. Mean of ALT was 30.6 U/L±24.089, ALT 43.1 U/L±11.83 and ratio of AST/ALT 1.05±0.68. High levels of ALT (>40 U/L) was found in 27 cases (33%). Subject with high level of ALT had a higher BMI values compared with normal ALT (p<0.05).

**Conclusion:** The prevalence of NASH in obese adolescents was 33%. There’s a significant association between elevated of BMI in obese adolescents with NASH.

**P90**
University screening test at State University of Jakarta
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**Background:** Insulin resistance is the greatest risk factor for the development of type 2 diabetes and is perhaps the greatest current health threat to our children. The prevalence of childhood obesity has more than double in the past 15 years in many regions of the world. The marked increase in pediatric obesity in the past decade has resulted in unprecedented increases in incidence of type 2 diabetes mellitus among children and adolescent.

**Aims:** To describe the characteristics of obesity and insulin resistance among pre-university student at state university of Jakarta

**Methods:** A cross sectional study was conducted during May 2012 – June 2012. Data was collected from adolescent before becoming university student. Subject was measured of body weight, height, body mass index, fasting insulin concentration (μM/mL) dan fasting glucose concentration (μM/mL). Subject was also calculated for homeostatic model assessment (HOMA). The HOMA cutoff point for diagnosing of insulin resistance is 3.16.

**Results:** Of 390 adolescent enrolled at UNI, before becoming university student, 20 subject were obese (5.1%). Most Children were male (65%). From all subjects, mean body weight is 88.9±3.4 kg and mean height 165.8±2.2 cm. Body mass index of children with P95-97 was 30%, while BMI children with >P97 was 70%. Children with insulin resistance was 12 subjects (60%). Median of HOMA among all subjects is 4.04 (1.3 up to 13.7) and mean of BMI is 32.1±4.1. No significant difference between body weight and HOMA index (p=0.305) and also no significant difference between BMI and HOMA index (p=0.161).

**Conclusions:** Most subjects were male. Most subjects were obese with mean body weight 88.9±3.4 kg and BMI 88.9±4.1. Only 60% subjects had insulin resistance. No significant difference between body weight, BMI and HOMA.
P91

Pre-diabetic risk factors among adolescents with obesity
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Background: Childhood obesity has increased as a health problem worldwide and WHO has declared that obesity is a global epidemic problem which is needed to be managed promptly. In the last decades, prevalence of childhood obesity has raised dramatically. Childhood obesity may results in overweight and impose other health problems. It is also a risk factor for development of Type-2 Diabetes Mellitus (DM).

Objective: To determine prediabetic risk factors among adolescents with obesity.

Methods: The study was conducted as an observational study using cross sectional sectional and case control approaches. Data was collected from level I to III students of two selected Junior High Schools (SMP Katolik Rajawali and SMP Islam Athirah) in Makassar, Indonesia, started on August to October 2011. These students were adolescents with obesity and permissions to participate in the study were gained from their parents. Analysis were done using X2 test or Fisher Exact Test (significant value p ≤ 0.05) as well as logistic regression analysis.

Results: Data consisted of 114 sample, 75 (65.8%) boys and 39 (34.2%) girls. There were 35 (76.1%) girls and 11 (23.9%) boys with pre-diabetic. Logistic regression analysis showed that there were 3 factors associated with the occurrence of pre-diabetic among adolescents with obesity, which were degree of obesity AOR 4.23 (95% CI 1.92 to 10.77), history of breastfeeding AOR 3.9 (95% CI 1.55 to 9.86) and history of DM in the family AOR 6.48 (95% CI 2.52 to 16.64).

Conclusion: Degree of obesity, history of breast feeding and history of DM in the family are correlated with prediabetic occurrence among adolescents with obesity.

P92

Variants of 11β-hydroxysteroid dehydrogenase (HSD11B1) gene type 1 and 2 in Chinese obese adolescents
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Objective: To investigate the relationship between 11β-hydroxysteroid dehydrogenase (HSD11B1) gene type 1 and 2 and obesity in Chinese child.

Methods: A total of 400 obese and 200 healthy adolescents were enrolled as obese and control groups. Seven tagged SNPs in HSD11B1 (rs4393158, rs2293543, rs10082248, rs10863782, rs2236903, rs2298930, rs4545339) and 4 variants in HSD11B2 gene (rs28934592, rs28934591, rs28934594 and rs28934593) were measured by automated platform MassArray.

Results: The rs28934592 in HSD11B2 and rs10863782 in HSD11B1 were excluded as false positive or HWE P>0.05. Moreover, one allele type was found in the other 3 locations of HSD11B1. The minor allele frequency of rs4393158, rs2293543 and rs10082248 were higher in patients than these in controls (P=0.045, P=0.001, respectively). The rs10082248, rs2298930 and rs4545339 were associated with the risk of obesity in the recessive model (P<0.05, respectively). Moreover, the total cholesterol in patients with GG or AG genotype was significantly higher than that in patients with AA genotype in rs10082248. The rs4393158 was associated with the hypertension in additive model (P=0.037), and glucose abnormal and hypercholesterolemia in dominant model (P<0.05, respectively), while the rs2235543 was associated with hypercholesterolemiainoverdominant model test (P=0.017).

Conclusion: The polymorphism of HSD11B1 may be a cause of childhood obesity, or even associated with the complication of childhood obesity. However, variants of HSD11B2 may not be a cause of obesity.

P93

Microalbuminuria and obesity in children
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Microalbuminuria is considered as a marker of endothelial dysfunction and found to be associated with nephropathy and cardiomyopathy in diabetic and non-diabetic obese patients. In this study, we sought to investigate the effect of childhood obesity on microalbuminuria in children. A total of 96 children who were clinically healthy were enrolled from July 2007 through March 2012. Height, weight and body composition of fat mass (FM) and fat free mass (FFM) were measured in each subject. Body mass index (BMI), fat mass index (FMI), fat free mass index (FFMI) and percent body fat (PBF) were calculated. Serum creatinine, cholesterol, triglyceride (TG), high-density lipoprotein (HDL) cholesterol, fasting insulin, glucose, spot urine microalbumin/creatinine ratio, and glomerular filtration rate (GFR) were were obtained. We divided the children into two groups according to the presence of microalbuminuria, based on the age specific reference range of spot urine microalbumin/creatinine ratio(1) and the differences between two groups were analyzed. Urine creatinine and FFM in microalbuminuria group were found to be significantly decreased compared to control group. There were no significant differences between two groups in anthropometric and other biochemical parameters associated with obesity. In two groups comparison according to BMI z-score: lean (BMI z-score <2) and obese (BMI z-score ≥2), obese children showed significantly higher serum creatinine, TG, FM, PBF and FMI and lower HDL cholesterol. However, no significant differences in the urinary microalbumin excretion and FFMI were observed. In our study, urinary microalbumin excretion is associated with FMI rather than obesity in children. This suggests that microalbuminuria might be strongly associated with FMI rather than obesity during growth. Further studies to elucidate the implication of microalbuminuria in obese children should be followed.

P94

Association between overweight-obese girls and age of menarche
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Menarche is the first period of menstruation in woman reproduction cycles. Several epidemiology study revealed the earlier onset of age of menarche. Better nutritional status, e.g. overweight-obese, is considered as one factor contributes to this condition. We want to know the association between overweight-obese girls and age of menarche. A cross sectional study was performed in SDN 1 Kleco Surakarta (elementary school) students in April 2012. All girls, aged 8-12 years old were included to this study. Nutritional status was measured anthropometrically for calculating and plotting the body mass index (BMI) for age based on CDC 2000 growth chart. We concluded overweight-obese girl if BMI for age >85 percentile. An interview was done to know the age of menarche. Of 179 girls, 35 (19.6%) subjects were overweight-obese; 10 (5.7%) obese and 25 (13.9%) overweight girls. Twenty six subjects (14.5%) have had period of menarche when we did this study. Means of age of menarche is 10.72 (SD 0.89) years old; the youngest age of menarche is 9 years old (2 subjects, 7.7%). Seven subjects that had period of menarche (27%) are overweight-obese. Chi-square test showed no association between overweight-obese girls and episod of age of menarche (odd ratio 1.64, 95%CI 0.63-4.39). Kuskall-Wallis test revealed no association between overweight-obese girls and means of age of menarche (p=0.906,p>0.05). This results suggest that there is no association between overweight-obese girls and means of age of menarche.

P95

Correlation between acanthosis nigricans and insulin resistance in obese children in Manado
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Background: Acanthosis Nigricans, which is a skin condition characterized by darkening and thickening of skin caused by papillomatosis and hyperkeratitis has been reported to be linked to insulin resistance and is thought to be a major factors in type 2 diabetes mellitus.
Objective: To determine whether the presence of acanthosis nigricans in obese children is related with insulin resistance.

Methods: We performed a cross sectional analytic observational study. One hundred twenty three obese children, ages 10 - 14 years with and without acanthosis nigricans got examined for insulin resistance using Homeostasis Model Assessment of Insulin Resistance Index (HOMA-IR). Diagnosis of acanthosis nigricans is confirmed by a dermatologist. This study took place in Wenang district, Manado, North Sulawesi from October 2009 until January 2010.

Results: Acanthosis nigricans was found positive in 33 children (61.1%). We found insulin resistance in 84.4% of obese children with acanthosis nigricans. There was a positive correlation between acanthosis nigricans and obese children with insulin resistance (r=0.568, p<0.0001).

Conclusion: Children with acanthosis nigricans are more likely have insulin resistance. Therefore, we need to identify acanthosis nigricans in obese children for the possibility of diabetes mellitus type 2 so early intervention can be done.

Methods: The body mass index (BMI), waist and hip circumference, blood pressure (systolic/diastolic), lipid profile, fasting glucose, insulin, leptin, neuropeptide Y(NPY), amylin were measured in 56 children (24 obese children and 32 non-obese controls). We calculated HOMA-IR and evaluated the relationship between each anthropometric data, metabolic bio-marker and diet regulating factor (leptin, NPY, amylin).

Results: Insulin and total cholesterol, triglyceride, LDL-cholesterol levels of the obese group were significantly higher than those of the non-obese group (p<0.05), leptin, NPY, leptin/NPY ratio, amylin levels of the obese group were significantly higher than those of the non-obese group (p<0.05). leptin showed significant correlation with BMI (r=-0.379, p=0.043), NPY (r=0.377, p=0.046), L/N ratio (r=0.754, p=0.000) in the obese group. amylin showed significant correlation with insulin (r=0.400, p=0.048), HOMA-IR (r=0.459, p=0.028) in the obese group.

Conclusion: There is abnormality in central diet regulatory system caused by leptin and neuropeptide Y resistance in the obese group. And amylin showed significant correlation with insulin resistance.

Methods: The lower 25-Hydroxyvitamin D(25(OH)D) is considered for its relationship. Therefore, we aimed to assess the association among 25(OH)D level, metabolic syndrome components [Waist circumference(WC), Blood pressure, Triglycerides, Glucose, High-Density lipoprotein Cholesterol], and insulin resistance indices [homeostasis model assessment-insulin resistance, quantitative insulin-sensitivity resistance, glucose to insulin ratio] among preadolescent child.

Methods: We followed up 221 subjects from July to August 2011 aged 7 to 9 child, who were part of Ewha Birth & Growth Cohort study, Seoul, Korea, which is a prospective cohort established 2001-2006. We investigated the associations among vitamin D level in blood, metabolic syndrome components, and insulin resistance using multivariate regression analysis adjusted for sex, age, birth weight, calories, and BMI z score.

Results: 38(17.2%) child were deficiency (<20ng/mL) for vitamin D level, but distribution of metabolic components among 25(OH)D status was no significant difference. But, other features were not associated with 25(OH)D. When regarding the criteria for metabolic components, those who were more than WC 90% tile had higher frequency in deficient group than in sufficient group, but distribution of metabolic components among 25(OH)D status was no significant difference.

Conclusions: The lower 25(OH)D level may contribute to the association with some of metabolic components in general preadolescent child, but further study is needed to explore the relationship with insulin resistance.

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insulin and HOMA-IR of normal weight subjects were made according to sex, age and weight status. Insulin resistance was defined as HOMA-IR > 95 percentile. The odds ratios of metabolic syndrome and its components were assessed based on insulin resistance state.

Results: Insulin and HOMA-IR values appear to peak at age 13-14 years in male and age 12-13 years in female subjects. Female had lower fasting glucose and higher insulin (P = 0.049) than male. Thus, HOMA-IR between sex was not different (P = 0.257). Overweight and obese subjects had higher HOMA-IR compared with subjects of normal weight (3.83 [95% CI 3.64–4.02], 5.16 [95% CI 4.70–5.62], and 2.66 [2.62–2.71], respectively). The prevalence of insulin resistance in total subjects was 9.7% (male; 10.9%, vs. female; 8.6%). The prevalence of insulin resistance in normal-weight, overweight and obese subjects were 4.7%, 25.6%, and 47.1% respectively. Subject with insulin resistance had more metabolic syndrome (odds ratios, 18.33 [95% CI 9.62–34.94]) and its components.

Conclusions: Insulin and HOMA-IR values vary depending on sex, age, and weight status. Obesity is the most important risk factor for insulin resistance, but number of insulin resistance subject in normal-weight subject were compatible to those. This information may be useful in not only Korean but also Asian planning programs for the prevention of type 2 diabetes from childhood.

Background: Childhood obesity is a worldwide epidemic problem and it prevalence has been increasing over the time, however, there is no best single standard criteria for screening obesity in population. In this study, we aim to assess the prevalence of obesity in primary school children by using percent weight for height (PWH) criteria compare with body mass index (BMI) curve from International Obesity Task Force (IOTF) and study the correlation between these two criteria.

Method: A cross-sectional study was performed during July 2009 - January 2010 in grade 3-6 children from 3 primary schools which was selected by stratified proportionate sampling. The program consists of measuring of individual height and weight in all children and these data were used to calculate percent weight for height (PWH) and body mass index (BMI). The correlation between these two criteria was assessed by using Pearson Correlation coefficient.

Result: Total number of subjects was 1,223 (637 boys and 586 girls), age 9.68±1.2 years. The prevalence of childhood obesity assessed by PWH (overall rate: 15.3%; boy: 19.3%; girl: 10.9%) was higher than using BMI (overall rate: 11.9%; boy: 15.7%; girl: 7.8%). When the rate of childhood obesity was compared by age group, the prevalence of obesity in prepubertal children by PWH criteria was higher when compare to BMI criteria. By contrast, in pubertal children the prevalence of obesity was higher when using BMI criteria. The correlation between PWH and BMI criteria was fair (r = 0.66) but increasing according to age(r = 0.61 at age of 8 to 0.74 at age of 12 year).

Conclusion: The prevalence of childhood obesity using PWH and BMI criteria from IOTF was significantly different. The correlation between these two parameters was fair. Further studies would be needed to determine the clinical validity of these parameters as a tool to screen and provide intervention for childhood overweight.

Profile of fasting blood glucose in obese children with insulin resistance

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Background: There are more obese children in school age. They are at risk for developing type 2 diabetes in future. Fasting blood glucose level increased in obese children who have insulin resistance. We examine are there any significant differences in fasting blood glucose level of obese children among a group with insulin resistance than obese children without insulin resistance.

Objective: To determine the difference between fasting blood glucose level in obese children with insulin resistance and without insulin resistance.

Method: Conducted research using observational analytic research method with cross sectional approach.

Results: There were 54 obese children, mean age 12.2 (11.9 to 12.5) years. Thirty seven (68.5%) boys and 17 (31.5%) girls. With 34 children (63%) had insulin resistance: 23 (67.6%) male sex, and 11 (32.4%) girls, 18 (52.9%) no history of diabetes mellitus in families and 16 (47.1%) were found in the family history of diabetes mellitus. The average fasting blood glucose level on average obese children with insulin resistance is higher than obese children without insulin resistance at 5.08 (4.9 to 5.2) mmol/L compared with 4.79 (4.6 to 4.9), (p <0.003) mmol/L. Fasting Blood Glucose Level in obese children with insulin resistance was significantly higher than obese children who did not have insulin resistance.

Conclusion: The data from this study showed that the level of fasting blood glucose in obese children who had insulin resistance is higher than obese children without insulin resistance.

Prevalence of insulin resistance in obese adolescence

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Background: Childhood obesity is a global health problem with several metabolic and cardiovascular complications. The prevalence of childhood and adolescent obesity is differed in each country with several affecting factors. Insulin resistance as one common feature of obesity is known to have a link with the risk of diabetes type 2 and cardiovascular complication. Insulin resistance is also a basic mechanism of metabolic syndrome. Several mechanisms proposed the link between obesity, insulin resistance, and metabolic syndrome. This study aimed to look at the characteristics of obese adolescence with metabolic syndrome and to look for the prevalence of insulin resistance among them with several risk factors that may affect.

This was a cross-sectional study on 92 obese adolescent, aged between 12 and 15 years old, in Central Jakarta, Indonesia. All adolescent underwent blood sample tests, including fasting blood glucose, lipid profile, and fasting blood insulin. Insulin resistance was defined as a HOMA-IR index of 3.8 or more. The diagnostic of metabolic syndrome was defined according to International Diabetes Federation (IDF) criteria.

Insulin resistance was found in 38% of the adolescent, with a higher rate among females (57.2%) than males (42.8%) (p = 0.673). Most of them had acanthosis nigricans as the marker of insulin resistance (71.4%) (p = 0.939). Among them, 82.8% had a family history of metabolic syndrome (p = 0.646). The prevalence of metabolic syndrome among obese adolescent was 19.6% with female predominant. The prevalence of each of the component was 48.9% for high blood pressure, 78.3% for abdominal obesity, 8.7% for impaired fasting glucose level, 22.8% for low levels of high-density lipoprotein cholesterol, and 21.7% for high triglyceride level. There was a strong correlation between impaired fasting glucose level and insulin resistance (p = 0.04), with the risk of 5.7 times to get insulin resistance.

Insulin resistance has a prevalence of 38% in obese adolescent population in this study. Insulin resistance has a significant association with impaired fasting glucose level.

Screening tool for diagnosis childhood obesity: percent weight for height vs body mass index

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Method: Using percent weight for height (PWH) criteria compare with body mass index (BMI). The correlation between these two parameters was fair. Further studies would be needed to determine the clinical validity of these parameters as a tool to screen and provide intervention for childhood overweight.

Conclusion: Screening tool for diagnosis childhood obesity: percent weight for height vs body mass index provide intervention for childhood overweight.
Factors on educational outcome for obesity prevention in female adolescents in Korea

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International Journal of Pediatric Endocrinology 2013, 2013(Suppl 1) P103

Aims: High demands for academic achievement seem to lead adolescents to study more but exercise less, which eventually increases the prevalence of obesity whose health status might be poorer than a few decades ago. As a way of cutting off obesity prevalence in high school students in Korea, this study aims to measure the association between health status, daily behaviors and educational outcome.

Methods: 276 female high school students in Seoul were enrolled to attend the obesity education in their physical classroom. Mean age was 17.2±0.5 years old. We obtained weight, height, waist circumference. The obese, overweight was defined as body mass index(BMI) more than 95th, 85th–94th percentile respectively for age and sex. All respondents were asked to answer a structured checklist of family history, past history, review of symptoms, and health-related behavior before the education class, and the other questionnaire was given twice to measure the obesity-related behaviors at the same time and one month later.

Results: The number of adolescents with obesity was 33(12.0%). 20 (7.2%) subjects belonged to overweight group. 222(80.4%) students showed improvement on obesity-related behaviors after education. The number of physical health problems for recent 1 year was significantly correlated with the number of family history (r=0.20, p=0.001) and the number of current physical symptoms for recent 1 month (r=0.27, p=0.001). Daily unhealthy behavior for recent 1 month was not only correlated with the number of current physical symptoms for recent 1 month (r=0.28, p<0.001) but also mental health symptoms for recent 1 month (r=0.36, p<0.001). In the multivariate linear regression model, daily healthy behavior for recent 1 month only showed significant impact on educational outcome with odds ratio 0.81(95% CI: 0.661-0.992).

Conclusion: Educational program for obesity prevention improved daily healthy behaviors on survey after one month. Daily healthy behavior for recent 1 month was associated with educational outcome.

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Metabolic abnormalities in obese children attending a tertiary care centre in South India

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Aims: To describe the profile of metabolic abnormalities in obese and overweight children presenting to Paediatric Endocrinology Clinic.

Methods: This is a prospective descriptive study of 80 children and adolescents, between 5.0-16.0 years of age, who were obese or overweight attending the Pediatric Endocrinology Clinic of the Christian Medical College, Vellore, S India during October 2011 to February 2012. All children with syndromic obesity, hypopituitarism, hypothyroidism, familial hyperlipidemia, and on steroids or on pharmacotherapy for obesity were excluded from the study. Body weight (kg), standing height (cm), waist circumference (cm), hip circumference (cm) and repeated blood pressures were measured in all subjects. Blood investigations included fasting glucose and 2 hour post prandial glucose levels, fasting insulin levels, HbA1c levels and fasting lipid profile.

Results: 80 children and adolescents (females n=33, males n=47) were recruited; 65% in the obese category, 15% were overweight and 20% were morbidly obese. The mean age in males was 11.32 ± 2.605 yrs and in females 10.85 ± 2.970 yrs. The mean waist circumference among the pubertal children was 97.13 cm ± 10.913 and 88.75% of the subjects had waist circumference more than 90th centile for age and sex. Dyslipidemia was the most prevalent metabolic abnormality detected. Insulin resistance was present in more than a fourth of our children, with a higher incidence among girls. Comparison between boys and girls showed that boys had a higher prevalence of decreased HDL (46.81% vs 33.33%) and increased triglycerides (51.06% vs 27.27%). Those who had attained puberty had higher prevalence of decreased HDL (42.86% vs 40%) and hypertension (11.42% vs 6.66%). Among the groups, prepubertal boys had the highest prevalence of dyslipidemia, both elevated triglycerides and decreased HDL. This has not been shown in any other study so far. The prevalence of metabolic syndrome according to the IDF definition was found to be 28%, that according to Cook was found to be 38.75% and that according to De Ferranti was found to be 43.75%. The study didn't show any significant correlation between waist circumference and elevated HOMA-IR. Among the overweight category, 83.33% (n=10) had at least one metabolic abnormality, 25% (n=3) had 2 metabolic abnormalities. The incidence of metabolic abnormalities between the obese and morbidly obese category were similar.

Conclusion: The study shows that the prevalence of insulin resistance in the group is 26.25%, girls having higher insulin resistance than boys. 41.25% of children also had decreased HDL, more seen among boys and those who were morbidly obese. 12.5% had both elevated triglycerides and decreased HDL. The prevalence of hypertension (8.75%) is lower than previously seen. HBA1C may be a better indicator of glucose homeostasis than fasting blood glucose alone. As insulin resistance is not one of the criterion of metabolic syndrome, 64.7% of those with insulin resistance are not included in the IDF definition of metabolic syndrome – hence a new definition including insulin resistance as one of its criteria may be required. Screening for dyslipidemia should be done even in overweight children to diagnose and prevent progression to metabolic syndrome.

P105

UCP2 and UCP3 polymorphisms as risk factors of insulin resistance in Indonesian obese adolescents

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Uncoupling Protein 2 (UCP2) dan Uncoupling Protein 3 (UCP3) is a mitochondrial transmembrane carriers which uncouple the transport of protons across the inner mitochondrial membrane from electron transport and the synthesis of ATP from ADP. The UCPS play a role in energy homeostasis and have been considered as candidate gene for controlling obesity and insulin resistance. The aim of our study is to analyze UCPS and UCP3 polymorphisms as risk factors of insulin resistance in obese adolescent. A case control study was conducted in Junior High School in Semarang, Central Java, Indonesia during 2007- 2008. Seventy five subjects included in this study. Height, weight and body mass index (BMI) were measured. Insulin resistance was estimated by using the homeostasis model assessment (HOMA-IR) score which calculated as fasting insulin (microU/mL) x fasting glucose (mmol/L)/22.5. Three polymorphic sites i.e. UCP3 -55t/c, UCP3 Y210V, and UCP2 A55V were investigated by using the Restriction Length Fragment Polymorphism. The data were analyzed by 2x2 table and odd ratio with 95% confidence interval.

There were 38 obese (27 male, 11 female) and 37 normoweight (25 male, 12 female) subject with the mean age was 13.2 (SD 0.32) years. Of 38 obese, there were 3 (7.9%) subject had insulin resistance. None of normoweight subjects had insulin resistance. There was a significant correlation between BMI and insulin resistance (r = 0.601, p< 0.001). Of 38 obese subject, C allele of UCP2 A55V and C allele of UCP3 Y210V are a risk factors of insulin resistance (OR 2.45, 95% CI 1.97-3.04, p<0.001; OR 2.6, 95% CI 2.10-3.24, p< 0.0001 respectively), whereas UCP3 -55t/c was not considered as risk factors of insulin resistance. Our study suggest that C allele of UCP2 A55V and C allele in UCP3 Y210V are a risk factors of insulin resistance in Indonesian obese adolescent. Larger studies is needed to prove the role of UCPS in controlling insulin resistance.
P106  
The polymorphism of EGFL6 D53SN is not associated with obesity in Chinese children  
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Objective: To investigate the association between EGFL6 D53SN polymorphism and obesity in Chinese children.  
Design: Case-control study.  
Subjects: A total of 384 obese and 205 healthy children were enrolled as obese and control groups.  
Measurements: The tagged SNP in EGFL6 (rs16979033) was measured by automated platform MassArray. Anthropometric estimates (BMI, BMI Z score, waist circumference, waist-height-ratio) and biochemistry marker measurements (fasting glucose, fasting insulin, total cholesterol, triglyceride, HDL-C, non-HDL, HOMA-IR ) were performed.  
Results: The frequencies of the N allele were 13.9% in 589 children. Among the obese group, 329 were homozygous for the 535D allele, 22 girls were heterozygous and 33 were homozygous for the 535N allele in the control group, 173 were homozygous for the 535D allele, 15 girls were heterozygous and 17 were homozygous for the 535N allele. The frequencies of the N allele were 13.5% in obese group and 14.5% in control group, having no significant difference ($\chi^2=0.119$, p=0.730). The EGFL6 D53SN polymorphism was not associated with obesity in either the dominant or recessive model test. The anthropometric estimates and biochemistry marker measurements in patients with EGFL6 33SD were not significantly different than those in patients with EGFL6 33SN.  
Conclusion: The polymorphism of EGFL6 D53SN was very common in Chinese children. EGFL6 D53SN polymorphism was not associated with obesity in Chinese children and it may not be a cause of childhood obesity.  

P107  
Aspartate aminotransferase-platelet ratio index, adiponectin and body mass index in children with fatty liver  
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Obesity in children is becoming a global epidemic. Non-alcoholic fatty liver disease (NAFLD) is a highly prevalent and potentially serious complication of childhood obesity. Adiponectin level was decreased on obese children. Adiponectin is a protective factor against non-alcoholic fatty liver disease on obesity. The early identification of fibrosis is important in children with NAFLD in order to prevent the development of liver disease in adulthood. One of non-invasive procedure to predict liver fibrosis is the aspartate aminotransferase-platelet ratio index (AST-PRI). The purpose of our study was to assess a correlation between APRI, adiponectin and body mass index (BMI) in obese children with fatty liver.  
A cross-sectional study was conducted from August to September 2007. Subjects were obese children from one junior high school in Semarang, Indonesia. Complete blood count, transaminase enzyme measurement, adiponectin level and abdominal ultrasound (USG) were performed on each subject. Only subjects with bright liver on USG underwent APRI analysis. Spearman’s correlation was used for statistical analysis. Of 37 obese children, 19 children had bright liver on USG. The mean APRI was 0.16 (0.119). The mean Adiponectin was 4.04. Only one obese subject (5.0%) with bright liver had an APRI > 0.5. APRI was significantly correlated to alanine amino transferase (ALT) levels (r = 0.62), but not significantly correlated to BMI (r = 0.35) and adiponectin (r = 0.45). There was no correlation between BMI, ALT (r = 0.16), AST (r = 0.16), and adiponectin (r = 0.30).  
This study suggest that obese children with fatty liver might have high APRI levels indicating the presence of liver fibrosis. However, there is no correlation between APRI, adiponectin and BMI.  

P108  
Sleep and physical activity pattern of obese children  
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Obesity has become worldwide pandemic. Studies indicated that the pandemic was associated with change in food consumption and physical activity pattern. Studies in adults showed that obese individuals had shorter sleeps. The aim of this study is to compare sleep pattern of normal, overweight and obese children in association with their overall daily physical activity pattern. This is a cross sectional study comparing the activity pattern of normal, overweight and obese children. 136 Obese, 118 overweight and 125 normal weight children sprinkled with grouping were sampled from screening of obesity in 25 elementary schools in Yogyakarta, Indonesia in 2005. Children were classified as normal, overweight or obese using WHO 2007 reference standard. Information on daily activities was obtained by 7 non-consecutive 24-hours activity recalls. They were between 6.9 to 15.5 years old, mean(SD): 10.6 (1.1) years. Normal weight children slept longer, mean(SD): 9.4(1.0) hours than overweight children, mean(SD) 8.3(1.5) hours, mean difference (95% CI) of 1.1 (0.8-1.4) hours, p<0.001. Likewise, normal weight children slept longer than obese children, mean(SD) 8.2(1.2) hours, mean difference (95% CI) of 1.2(0.1-1.5) hours.  
Overweight and obese children were more likely to sleep less than 8 hours/day; OR (95%CI) of 9.7(3.9-23.9); p=0.001 and 12.1(5.0-24.5), p<0.001, respectively. There were no significance differences in screen-time, over-all sitting and doing moderate or vigorous activities between normal weight, overweight and obese children. However, there was negative correlation between screen-time and sleeping time, r=-0.11, p=0.03 and weak positive correlation between time spent doing moderate and vigorous activities and sleeping time, r=n.s, p=0.03.  
Overweight and obese children slept shorter than normal weight children. Sleeping time is inversely related to screen time and positively associated with moderate and vigorous activities.  

P109  
Comprehensive genetic analyses of primary adrenal failure without enzymatic defects  
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Our objective is to estimate frequencies of mutations in STAR, CYP11A1, NR0B1, NRS1A1, MC2R, and MRAP in a cohort of Japanese patients with primary adrenal failure without enzymatic defects. Twenty-one patients were included, who were diagnosed as having primary adrenal failure without enzymatic defect, namely 21-hydroxylase deficiency, 3βHSD deficiency, 11β-hydroxylase deficiency, and 17α-hydroxylase deficiency. Sixteen patients presented with primary adrenal failure before the age of 2 years. Fourteen patients had apparent mineralocorticoid deficiency. Fourteen patients were 46, XY and 7 patients 46, XX. Three had 46, XY disorders of sex development. Mutation analyses of STAR, NR0B1, NRS1A1, MC2R, and MRAP were done by PCR-based sequencing and next generation sequencing. In case of no amplification of NR0B1 by PCR, we performed oligonucleotide array CGH. We described clinical findings in each patients and determined possible genotype-phenotype correlation. Five patients were diagnosed as having DAX-1 deficiency. NR0B1 mutations were found hemizygotically in 3 patients (c.116delG, c.484_865del, and p.Q283X). NR0B1 deletions were found in 2 patients (40kb deletion including NR0B1 and 2kb deletion of exon 1). Four patients presented with primary adrenal failure in newborn,
the and the other patient presented at the age of 6 years. STAR mutations were found in 3 patients. One patient was 46, XY, and 2 patients were 46, XX. One patient, who presented with primary adrenal failure in newborn, had c.217delG/p.R728X. Two patients, who presented at preschool age, had p.Q258X/p.R272C and p.Q258X/p.R188H. No mutations were found in CYP11A1, NR5A1, MC2R, and MRAP. In conclusion, NR0B1 mutations and deletions are relatively common in 46, XY normal male phenotype patients (S/N). STAR mutations might be found in cases, being older than 2 years of age. 3. CYP11A1, NR5A1, MC2R, and MRAP mutations are rare.

ADRENAL

P110 Adrenal cortex tumors: clinical features and laboratory finding

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The adrenal cortex tumors (ACT) include both malignant adrenal cortex cancers and benign masses that can be either secreting, of one of the hormones normally produced in the adrenal cortex or non-secreting. We describe clinical features and laboratory finding of patients with adrenal cortex tumors. This is a case series report. 29 cases of childhood with adrenal cortex tumors treated at the Vietnam National Hospital of Pediatrics in a period of 1995–2011 have been reviewed in detail the presenting features and laboratory. The study recruited 15 boys and 14 girls. The median age at diagnosis was 4.97 ± 3.61 yrs (range, 20 days to 14 yrs); 19 patients were younger than 5 yrs. Hypertension and cushingoid features were common in patients (62%, 5.86%), virilization was presenting feature in 44.8% of the group. An abdominal mass was palpable in 20.7% of the patients. High level of testosterone was common in patients (94.1%). 30% of the patients had hypercortisolemia. All tumors were unilateral; the right adrenal glands predominated over left (1:9:1). 62.5% tumors over 4 cm. 22 patients had received operation to remove the tumors: 11 adenofibroma, 2 adenocarcinoma. In conclusion, high percentage of patients had malignant tumors among ACT operated patients.

P111 Diagnosis and prevalence of Congenital Adrenal Hyperplasia (CAH) in Austrian children screened or not screened for CAH

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Prevalence of Congenital Adrenal Hyperplasia (CAH) is not exactly known in the Austria; a number of patients with CAH might not be diagnosed, especially males. CAH is in about 95% of the cases due to a defect in the 21-hydroxylisation (‘classical CAH’). Newborn screening for CAH, based on the measurement of 17α-hydroxyprogesterone (17-OHP) was shown to be efficient for diagnosis, and is part of the newborn screening programme in Austria since April 2001.

In our study we compared 2 groups of children:

- Group A: children born in Austria (a province of Austria), 1992 – 2001, n = 119,001, m 61,256, f 57,745;

In group A (patients screened), CAH was diagnosed in 8 children (m 4; f 4), 4 of them with simple virilising (SV) 21-ÓH deficiency (m 3; f 1) and 4 with salt wasting (SW) 21-ÓH deficiency (m 1; f 3). In group B, 98.7% of all newborns born in Styria could be screened by measuring 17-OHP in a dried blood spot on filter paper. Recall rate was 0.578%. CAH was diagnosed in 10 children (m 3; f 7), 8 of them with SW (m 2; f 6), and 2 with 11β-hydroxylase deficiency (m 1; f 1).

Whereas group A displayed the expected Mendelian sex ratio, group B showed a strong female predominance (m 3; f 7) and the other patient presented at the age of 6 years. STAR mutations were found in 3 patients. One patient was 46, XY, and 2 patients were 46, XX. One patient, who presented with primary adrenal failure in newborn, had c.217delG/p.R728X. Two patients, who presented at preschool age, had p.Q258X/p.R272C and p.Q258X/p.R188H. No mutations were found in CYP11A1, NR5A1, MC2R, and MRAP. In conclusion, NR0B1 mutations and deletions are relatively common in 46, XY normal male phenotype patients (S/N). STAR mutations might be found in cases, being older than 2 years of age. 3. CYP11A1, NR5A1, MC2R, and MRAP mutations are rare.

P111 Malignant paragangliomias with succinate dehydrogenase subunit B mutation in a 13-year old child treated successfully with surgery and 131-I-MIBG

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Paragangliomas and pheochromocytomas are exceptional rare tumours in children arising from the neural crest origin. A number of susceptibility genes have been identified to be associated with familial cases of paragangliomas and pheochromocytomas. Malignancy frequency has been found to be high especially in patients with succinate dehydrogenase subunit B (SDHB) mutations. We report a case of a 13-year old Chinese girl with right adrenal pheochromocytoma, paraganglioma in the subepithelial region with invasion into the inferior vena cava, and metastases to the right scapula and vertex. She underwent surgery for excision of the abdominal tumours, and also therapeutic 131-meta-iodobenzylguanidine (131-I-MIBG) therapy for the metastatic lesions. She required a left adrenalectomy 2 years later due to the occurrence of a left pheochromocytoma. She remained asymptomatic for 8 years after the initial presentation and is currently alive. Although she does not have any family history of neuroendocrine tumours, susceptibility genes were screened in view of the young age at presentation and multifocal malignant tumours. She was found to carry a known mutation c.572G>A (p.Cys191Thr) in the SDHB gene. This case illustrates the need for screening of susceptibility genes for familial paragangliomas/ pheochromocytomas in apparently sporadic cases, and the therapeutic benefit of using 131-I-MIBG as an adjuvant treatment for metastatic lesions.
We report a case of congenital lipoid adrenal hyperplasia showed different cortisol level in genotypic female twin with same STAR gene mutations.

P114
Cushing’s Syndrome due to a non-adrenal ectopic adrenocorticotropic-secreting ewing sarcoma in a child
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Ectopic ACTH Syndrome (EAS) is extremely rare in pediatric age group. Sarcomatous tumors causing EAS are even rarer. A nine year and 4 months old male Filipino presented with a 6 months history of gradually enlarging mass on the left distal thigh. He experienced increasing appetite, rapid weight gain of about 27kg in 5 months, recent onset of widespread acne and darkening of skin around the neck. Physical Examinations revealed cushingoid face, widespread acne, facial hair, phlethora, buffalo hump, truncal obesity, purple abdominal striae and severe acanthosis nigricans on the neck and axilla. Non-inflamed mass and slight tenderness over the left distal thigh were noted. Patient was normotensive. Weight & height for age were at Z score above -3 and -1, respectively. Body Mass Index at Z score above 2. His pubertal development was classified as Tanner stage 1 testicular and pubic hair development. Work ups revealed hypernatremia, hypokalemia, metabolic alkalosis and elevated levels of serum cortisol and ACTH. Low and high dose dexamethasone suppression tests failed to suppress serum and urine free cortisol levels, findings which were consistent with ectopic ACTH secreting tumor. Radiological findings were normal skull and chest roentgenograms and normal computed tomographic scan of chest and abdomen. Magnetic resonance imaging of Hypothalamo-pituitary was also normal. An Immunohistochemistry result of left distal thigh mass was consistent with Ewing Sarcoma. The patient received chemotherapy with Vincristine, Doxorubicin and Cyclophosphamide. Unfortunately, patient succumbed to death 5 days post chemotherapy due to severe sepsis.

P115
Results from 28 years of newborn screening for congenital adrenal hyperplasia in Sapporo City
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Newborn mass screening (MS) for congenital adrenal hyperplasia (CAH) was started in 1989 at nationwide of Japan. To date, the goals for prevention of life-threatening salt-wasting crises and prevention of incorrect sex assignment in virilized females are almost achieved. However, in Sapporo city, which is located in the northern part of Japan, a pilot study was started in 1982 after the assessment of its feasibility and efficiency.

Here we report the results of MS from 1982 to 2010 in Sapporo city. In 28 years, 17-hydroxyprogreterone (17-OHP) was determined in MS samples in 498,147 newborns and a total of 2,466 screened newborns had abnormal 17-OHP. Among them, 26 patients were diagnosed with 21-hydroxylase deficiency (21-OHD), which corresponds to a prevalence of 1:19,160 live birth in Sapporo city. It is almost identical to the worldwide incidence of CAH. Among 26 patients, 20 patients were classified into salt-wasting forms, 5 patients were classified into simple virilizing forms and one was classified into nonclassical forms. 19 patients were female and 7 patients were male. Two familial cases were detected. The mean examination day of 25 patients (data of one patient was not available) was 6.4 days after birth (from 0 to 18 days). Among 18 female patients, 11 patients were clinically suspected because of virilization prior to MS result becoming available and were referred to neonatal center. 4 female patients were referred after MS screening. One female patient was assigned to male after birth, however the patient was diagnosed as having 21-OHD by MS and the sex was changed after the diagnosis. One female patient was a familial case and during pregnancy prenatal treatment was done and her genitalia was normal female. Another one patient having normal female genitalia and no symptom, was diagnosed as nonclassic forms by MS. By contrast to female patients, all 7 male patients were detected by MS. Another type of CAH was not detected in our study.

In conclusion, MS for CAH in Sapporo city can be considered reliable.

P116
Giant bilateral symptomatic adrenal myelolipomas manifested in an adult with congenital adrenal hyperplasia
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Adrenal myelolipoma is an uncommon, non-functioning tumor composed of variable amounts of mature adipose tissue and scattered islands of hematopoietic elements, including erythroid, myeloid, lymphoid series, and megakaryocytes. Diagnosis of adrenal myelolipomas based on radiologic imaging, such as ultrasonography, CT or MRI is effective in more than 90% of cases. It should be differentiated from other fat-containing adrenal masses such as teratoma, lipoma and liposarcoma. The optimal treatment depends on the size and symptoms of the tumor. Surgical treatment is usually not necessary for asymptomatic adrenal myelolipomas smaller than 4 cm. In contrast, symptomatic, complicated, and hormonally active myelolipomas larger than 7 cm should be surgically removed. This report present a 50-year old adult raised as a male with giant adrenal myelolipomas manifested as adrenal masses, which was misdiagnosed with liposarcoma by radiologic examination. The patient has been raised as male despite of ambiguous genitalia and thorough investigation was not performed because of poor socioeconomic status. Physical examination showed short stature (<3rd percentile), hyperpigmentation, and micropenis without palpable gonads. There were uterus and ovary in pelvic cavity on abdominopelvic CT. ACTH stimulation test showed adrenal insufficiency. Steroid replacement was initiated before bilateral adrenalectomy. The histologic findings revealed myelolipomas, and endocrine and molecular investigation lead to the diagnosis of 21-hydroxylase deficiency. Karyotype was 46,XX and mutation analysis of CYP21A2 identified a compound heterozygosity consisting of p.I173N and p.Q319*. The patient has been treated with dexamethasone 0.5 mg once daily and fludrocortisone 0.1 mg once daily. As subject has been raised as a male, additional operation such as oophoro-hysterectomy is under consideration. Patients with congenital adrenal hyperplasia should be screened for incidental adrenal masses to avoid unnecessary surgical procedures.

P117
Phaeochromocytoma presenting as hypotension in a 12 year old female
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Background: Phaeochromocytoma is a rare catecholamine tumor that presents with hypertension and the triad of headaches, palpitations, and sweating. We present a case with shock and tachycardia as the manifestation of phaeochromocytoma.

Case: 12 year old female sought consult at the ER due to loss of consciousness. In the past, other symptoms included bouts of fatigue, headache, pallor, palpitations and profuse sweating of two years duration. The patient had history of body weakness, abdominal pain and vomiting associated with dyspeptic hours prior to her admission. She had history of
pheochromocytoma for which a left adrenal mass was excised three years prior her present admission. She then lost to follow-up after her operation. On clinical examination, the patient was drowsy, incoherent, diaphoretic, cyanotic, tachypneic (30 beats/min), tachycardic (200 beats/min) and no blood pressure appreciated. Her weight was 26 kg and height of 140 cm (-2SD); BMI: 13.2 (-2SD) Eye exam noted a grade III retinopathy. Initial blood work-up showed anaemia, hypoglycemia and hypocalcaemia. Echocardiography showed concentric LV enlargement, systolic dysfunction, tricuspid regurgitation with LVEF of 31%. The CKMB was elevated but the troponin I was normal. Fluid resuscitation was initiated and intravenous inotropes agents were administered. Thereafter, her hemodynamic condition improved gradually and later found to have hypertensive episodes (range: from 120/100-180/120) even after discontinuing the inotropes. In view of hypertension and history of left adrenal tumor, work up for pheochromocytoma was done. Biochemical evaluation for pheochromocytoma revealed elevated 24-hour urine free metanephrines of 16.61mg (normal: 1mg/24hr). The computed tomography (CT) of the abdomen revealed a right suprarenal mass measuring 5.7 x 4.7 x 4.7cm. Patient was started on Terasozin and Carvedilol with normalization of blood pressure and resolution of other symptoms. She underwent laparoscopic mass resection. During tumor manipulation, the patient had several hypertensive crises (247/147mm Hg), which was treated with nitroglycerin and nicardipine drip. Post resection of the tumor, there was hypotension (60/40mmHg) which was given dopamine drip. The surgical specimen weighed 37.5grams, measured 5.5 x 4 x 2.3cm and histopathological examination confirmed the diagnosis of pheochromocytoma. At OPD, patient has no BP elevations and repeat 24 hour urine free metanephrines was normal at 0.06mg (normal: < 1mg/24hr). Currently she is maintained with Hydrocortisone at [8mg/m2/day].

Conclusion: This is a rare manifestation of pheochromocytoma and can be a challenge to the clinicians. Recurrent pheochromocytomas are unlikely in children but recurrent tumors may appear years after initial diagnosis.

P118 Congenital adrenal hyperplasia-presenting as central precocious puberty
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International Journal of Pediatric Endocrinology; 2013(Suppl 1)
P118

Aims: To demonstrate the presentation of Congenital adrenal hyperplasia (CAH) as central precocious puberty.

Materials and methods: 4 children with mean age of 6.5 (5.5, 6.5, 6.5, 7.5) who presented to the out patient department with precocious puberty between December 2008 to December 2011 were studied.

Results: 3 were boys, out of which 2 were twins. 3 boys were diagnosed to have CAH after presentation to the OPD. They had mean bone age of 12 years. They had elevated testosterone (mean: 2.4 ng/ml) and 17 hydroxyprogesterone (mean: 24 ng/ml) at presentation. They had clinical (testicular volume 5ml) and biochemical (mean basal LH : 6 ng/ml) evidence of central precocious puberty. The girl was already diagnosed to have CAH (testicular volume 5ml) and biochemical (mean basal LH : 6 ng/ml) evidence of central precocious puberty. She presented with menarche at the age of 7.5 and had basal LH of 8 ng/ml. All the patients were started on replacement with hydrocortisone, fluorocortisone and GRH analogue (Leuprolide depot).

Conclusions: Central precocity may be due to undiagnosed CAH. Improperly treated CAH may also lead to central precocious puberty. Treatment may involve GRH analogues along with adrenal steroids.

P119 Evaluation of a psychosocial education program for families with congenital adrenal hyperplasia
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P119

Congenital Adrenal Hyperplasia (CAH) is an inherited condition caused by an enzyme deficiency which leads to a potentially life threatening adrenal crisis. Poor compliance and any illness, injury, or major medical procedure can be life threatening. Medical interventions, counselling and timely education are essential for these families. This study evaluated a psychosocial education program (PEP) developed to meet the needs of families with a child with CAH, with the additional opportunity of exploring the impact of CAH on the child and family. Two hundred and two participants (parents/carers/children with CAH and siblings), from 68 families took part in the study. Participants attended a full-day workshop which included information about CAH, a practical intervention session, group discussions and provision of a resource folder. Data were collected to explore the impact of CAH on the child and family using the Child Behaviour Checklist (CBCL) and the Child Health Questionnaire (CHQ). Sibling data were collected for comparison of the CAH group with siblings and population norms. Evaluation of the PEP involved baseline and follow-up (immediate, six months and 12 months post education) measures of knowledge using the CAH Knowledge Assessment Questionnaire (CAHKAQ) and a formal evaluation. Evaluation of the PEP showed that knowledge increased immediately following the PEP, which was maintained over time. Sick day management was seen to be the major challenge for families. Fathers’ and Mothers’ scores for behaviour (CAH group compared to siblings) were within population norms, although Father’s rated children with CAH, having lower social competence than siblings and norms. Fathers’ and Mothers’ were in agreement about the impact of CAH, with ratings lower than siblings and population norms for bodily pain & discomfort, general health of the child, and emotional impact on parents. The PEP achieved its major goal of increasing knowledge about CAH, and was positively evaluated by families. The workshop has now been incorporated into a DVD that is available to families and health professionals.

P120 Treatment outcome and some affecting factors of congenital adrenal hyperplasia
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P120

Congenital adrenal hyperplasia (CAH) is a common hereditary disease in the National hospital of pediatrics (NHP). CAH is treated with hormone replacement therapy for life. It is necessary to evaluate treatment outcome in order to have monitoring method and further treatment plan. Thus we study the treatment results and factors affecting treatment outcome of children with CAH being treated in the NHP. This is descriptive study. All patients diagnosed CAH being treated and monitored for more than one year at the NHP from July 1990 to July 2010. In our patient group, good outcome: 80/124 (64.52%), not good outcome: 44/124 (35.48%). Treatment outcome of patients diagnosed at the age of less than 1 year was 13.7 times better than that of a non-compliance group. These results of treatment depend on the age of diagnosis, using appropriate doses of hydrocortisone and treatment compliance.
CAH could be a medical and social crisis, and especially in South Sumatera, Indonesia it is also associated with cultural problems. Natural history of CAH without treatment can cause death due to loss of salt crisis unless it can be detected and treated early.

Objectives: To report case of long-term salt wasting type of CAH patient, deformity of external genitalia which is now called as disorder of sex development (DSD) and failure to thrive.

Results: A 45 day old baby admitted with symptoms of diarrhea and vomiting since birth. Physical examination found external genital deformity and failure to thrive, with hypotonia and hyperkalemia. This baby was consulted to pediatric endocrine subdivision and then suspected as a salt wasting type of CAH. Previously, patient was hospitalized with diarrhea and vomiting for 5 days before referral to Moh. Hoesin Hospital Palembang. Patients had frequent vomiting since birth and difficulties in gaining weight. The parents considered that this child sex was a male. Based on laboratory finding, result of the hormone testosterone and 17-OH pregesterone level, a salt wasting type of CAH is established. Internal genitalia ultrasound, genitography, and chromosome analysis assigned that patient’s sex was a female. A 2 years observation in this patient after discharged was focused on problems of drug availability, growth, ambiguous genitalia, electrolyte disorders, even puberty and reproduction. Also, other problems in families such as knowledge, attitude and behaviour of all family members of CAH disease, adherence to visit polyclinic for monitoring the risk of morbidity and mortality, financial limitations that may inhibits early growth intervention in infants with CAH who need optimal nutritional support, parenting pattern in accommodating the patient as a female, and also psychosocial impact.

Conclusion: Post-treatment patient with CAH should involve a multidisciplinary care. Not only medical and genetic factors which contribute to succeed of long-term treatment of patients with CAH, but also good environmental and family factors are required to optimize the growth and development of children with CAH.

**P122**

Psychosocial problems in children with congenital adrenal hyperplasia in Cipto Mangunkusumo Hospital, Jakarta, Indonesia

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Congenital Adrenal Hyperplasia (CAH) is a chronic illness that requires lifelong medication and, in some cases, frequent hospitalizations. This situation will bring psychosocial consequences for the patients and their families. This study aims to determine the psychosocial problems in children with CAH in Cipto Mangunkusumo Hospital.

Data was taken from medical records in Pediatrics Endocrinology Clinic of Cipto Mangunkusumo Hospital, Jakarta, Indonesia during 2007-2012. Out of 96 patients were diagnosed as CAH, 76 patients aged 4-16 years old included in this study. Patient’s parents were interviewed by telephone for screening of psychosocial problems using the Pediatrics Symptom Checklist-17 (PSC-17). Patients and their parents were also asked about their psychosocial experience.

Out of 76 patients, Twenty five patients had 46,XX karyotype, 2 patients had 46,XY karyotype, while 49 patients have no karyotype data available. Most children were raised in accordance with the results of their karyotype finding. Few parents reported some behaviour problems with their children according to PSC-17.

Our study suggests that few children with CAH had a psychosocial dysfunction that might be related to their physical condition. Improving knowledge and encouraging parent to join with CAH support group were important to help families with CAH in Indonesia.

**P123**

A pilot study on the effect of three hydrocortisone dosing regimen on 17 hydroxyprogesterone levels in patients with congenital adrenal hyperplasia

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The 2004 Newborn Screening Act has saved a lot of Filipinos from Congenital Adrenal Hyperplasia (CAH). The increase in the number of patients living with CAH challenges us to find the optimal steroid replacement therapy. In the Philippines, there is no locally published data on this. The objectives of the paper are to compare the effect of different hydrocortisone dosing regimens on the 17 hydroxyprogesterone (17 OHP) levels of patients with CAH and to report adverse effects.

The pilot study is a single-blinded randomized control trial comparing the 17 OHP levels of infants with CAH given higher evening hydrocortisone dose (HED), higher morning hydrocortisone dose (HMD) and equal hydrocortisone dose (EHD) who consulted in a tertiary hospital from January 2011 to July 2011. Nine patients completed the study (3 males and 6 females) with mean age of 16 (±11) months. One patient was randomized to HMD, 5 to HED and 3 to EHD. A marginally significant difference (p-value=0.0515) in the 17 OHP levels was observed between treatment groups. Adverse effects included increased BMI with concomitant presence of cushingoid facies in 33% (3/9) of the patients and an increased growth velocity in one patient in the HED group.

A significant difference was observed between treatment groups. The decrease in 17OHP was best appreciated in the EHD group but no definitive conclusion can be made on the optimal treatment schedule due to the small sample size. It is recommended that a larger study be done on newly diagnosed neonates with CAH using 525 patients (11 for HMD, 257 for HED and 257 for EHD) and ACTH levels be included in the outcome measures.

Also, the use of oral steroids available in the country such as Prednisone or Dexamethasone as an alternative treatment be investigated.

**P124**

Study relationship between the value of 17-OHP and the value of testosterone in monitoring for congenital adrenal hyperplasia

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Deficiency of 21-hydroxylase (21-OHD) is present in 90–95% cases of congenital adrenal hyperplasia (CAH), an autosomal recessive disorder. CAH affects severely on the physical development and reproductive function. In monitoring the disease and evaluating treatment outcome, presentation of salt wasting, electrolyte disturbance, androgenism, cushingoid features, plasma levels of 17-OHP, testosterone, Δ4-androstenedione, urinary levels of 17-OHCS, 17-CS, and bone age were used.

We aimed to study relationship between the value of the plasma 17-OHP and the value of the plasma testosterone levels to monitor treatment of CAH. The study was prospective. We collected 82 CAH Vietnamese patients who were diagnosed of 21-OHD. They have been treated and monitored at the Vietnam National Hospital of Pediatrics, Hanoi, Vietnam in the period of 1/2007- 1/2010. The value of plasma levels of 17-OHP and testosterone were measured in combination with clinical symptoms every 6 months.

In 82 study’s CAH patients aged 1-15 years old, the group aged <10 years old occupied 82.9%. The salt – wasting form occupied 75.6%; the simple virilizing form 24.4%. 59/82 of patients (71.1%) had successful treatment with the mean plasma level 17-OHP of 0.02-5.67 nmol/l and the mean levels of testosterone of 0.01-8.02 nmol/l according to groups’ ages. The mean levels of plasma 17-OHP and testosterone also increased with age and sex in the group of patients having failed treatment. It confirmed a positive relationship between the value of plasma 17-OHP and levels of the testosterone with 95% significant confidence.

Each time of patient examination, besides clinical symptoms and plasma levels of 17-OHP should be done to evaluate treatment.

**P125**


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Congenital Adrenal Hyperplasia (CAH) is a hereditary disorder that can cause a huge impact to the sufferer, his family and surrounding living environment but is still often diagnosed late. We believe that a better
understanding of the disease through analysis of the chief complaints and early signs of CAH will aid early diagnosis.

Analysis of chief complaints and early signs of CAH from paediatric endocrinology private practice (1997-2011) consisting of 10 females and 9 males was carried out. All CAH patients are referrals from other paediatricians in East Java. Ambiguous genitalia was found in all females (10), 6 came with this as the chief complaint. Hyperpigmentation was never mentioned as a chief complaint although it is present in all patients except 3 males. One male patient came with precocious puberty. Diarrhoea and vomiting between male and female patients were equally distributed (6:5). Vomiting and diarrhoea was in all salt wasting type boys (6) as the chief complaint. Only 1 out of 5 girls had vomiting and diarrhoea as the chief complaint. Failure to thrive was found as the chief complaint in 2 out of 7 patients with the condition. Family history was useful in the diagnosis of three patients. There were 12 patients diagnosed under 1 month, the other 7 patients were diagnosed between age 2 months and 10 years 7 months.

Careful examination of signs & symptoms and high suspicion are needed to diagnose CAH. Ambiguous genitalia in females, hyperpigmentation, vomiting and diarrhoea, as well as failure to thrive are important clinical findings. In patients with precocious puberty, CAH should be considered in the differential diagnoses. Blood Na and K values are very useful in areas where hormonal exam is not available to help diagnose and to start electrolyte therapy in salt wasting type. With early diagnosis, we can prevent the negative impact of the disease such as adrenal crisis, severe electrolyte imbalance, failure to thrive, precocious puberty and heavy psychological impact due to incorrect gender assignation.

P126
Congenital adrenal hypoplasia, glycerol kinase deficiency and myopathy: condition requiring prompt identification. Clinical and biochemical findings in two cases
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Coincident expression of otherwise unrelated inborn errors of metabolism may occur as a result of large deletions of multiple gene, referred to as the contiguous gene deletion syndrome. We describe two male infants who presented with failure to thrive and raised urinary glycerol levels, leading diagnosis of glycerol kinase deficiency, congenital adrenal hypoplasia and myopathy. These clinical diagnoses, suggest Xp21 contiguous gene deletion syndrome.

The two male infants currently 48 months and 3 months old, presented with failure to thrive at 10 months and 1 month of age respectively. On evaluation, poor weight gain, urine organic acids showed high levels of glycerol. Further results revealed pseudo-hypertriglycerideremia which raised the suspicion of glycerol kinase deficiency. Both infants were persistently hyponatremic and hyperkalemic, and the synacthen test showed a suboptimal cortisol peaks. Plasma renin was high with low aldosterone indicating mineralocorticoid deficiency. The older male infant who presented at 10 months of age also had significant developmental delay with muscular weakness and markedly raised creatinine kinase. He was confirmed to have Duchene Muscular Dystrophy.

Both the infants were started on steroid and salt replacement and monogen feeds containing medium chain triglycerides. Their weight improved with normalization of sodium & potassium levels. The above spectrum of clinical & biochemical features is consistent with a diagnosis of Xp21 contiguous gene deletion syndrome. Although rare, raised urinary glycerol and serum triglycerides leads to suspicion and allows early recognition of this condition, where prompt treatment can prevent life-threatening adrenal crises.

P127
Mutations of ABCD1 gene and phenotype of Vietnamese patients with X-linked adrenoleukodystrophy (X-ALD)
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X-linked adrenoleukodystrophy (X-ALD) is caused by a defect in the gene ABCD1, which maps to Xq28 and codes for a peroxosomal membrane protein that is a member of the ATP-binding cassette transporter superfamily. X-ALD is panethnic and affects approximately 1:20,000 males. X-ALD disease characteristic by progressive neuropsychiatric dysfunction, occasionally associated with adrenal insufficiency. We aim to describe the clinical, laboratory and cerebral MRI characteristics of Vietnamese patients with X-ALD and to identify mutations of ABCD1 in these cases. Clinical features, biochemical finding and cerebral MRI lesions of 9 cases from 7 unrelated families were studied. Genomic DNA from these patients was extracted using standard procedures from the peripheral blood leukocytes. Mutation analysis of ABCD1 was performed using Polymerase chain reaction (PCR) and DNA direct sequencing.

Among these patients, two families had two children with X-ALD, the others were unrelated but one case had family history of X-ALD (his maternal grand mother has a sister whose two sons having paralysis for more than 1 year, hyper-pigmentation and died at the age of 7 and 12 yrs). Endocrinology symptoms of adrenal insufficiency were observed in 8/9 cases; 7/9 cases showed neurological symptoms of cerebral ALD or adrenomyeloneuropathy; 2/9 cases had only symptoms of chronic adrenal insufficiency and no neurological symptoms until 12 and 5 years of ages respectively. 8/9 cases had serum cortisol and ACTH measured confirmed adrenal insufficiency. 8/8 cases showed increased plasma VLCFA. Neuroimaging studies (cerebral MRI) showed classical posterior pattern in 7 cases who had neurological symptoms and normal pattern in 2 cases without neurological manifestations. We identified 7 different mutations of ABCD1 in 9 patients. Of which, four novel mutations [c.1202G>T (p.Arg401Trp); c.1208T>A (p.Met403Lys); IVS8+28-551bp del; containing whole the exon 2 (4243bp), plus insertion of 79bp from BAP31 and 8bp from unknown origin in this deleted region] were identified in four unrelated patients with neurological symptoms. The reported mutation c.1628C>T (p.Pro543Leu) was identified in two cases (sibling; elder had no neurological symptoms and younger had progressive neurological disability). The reported mutation c.1553G>A (p.Arg518Gln) was found in a boy without neurological symptoms at 5 years of age. The reported mutation c.1552 C>T (p.Arg518Thr) was identified in two cases (sibling; both have adrenal insufficiency and neurological symptoms).

For the first time, mutations in ABCD1 are identified in X-ALD Vietnamese patients. Despite many mutations having been identified in patients with these clinical phenotypes, the genotype-phenotype correlations have not been clarified.

P128
Mutation spectrum of CYP21A2 and correlation between genotype – phenotype in 81 Vietnamese patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency
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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 involved in one of the various steps of adrenal steroid synthesis. The most common form of CAH (95%) is caused by mutations in CYP21A2, the gene encoding the adrenal steroid 21-hydroxylase enzyme (P450C21). Two major phenotype are recognized in 21-OHD: classic and non-classic. Classic CAH is clinically categorized in two groups: the simple-virilising and the salt-wasting form. The National Hospital of Pediatrics (NHP) in Hanoi is an 1100 bed tertiary referral centre servicing approximately 30 million people from northern provinces of Vietnam. At the start of 1999 there were 91 children with CAH due to 21-hydroxylase deficiency (21-OHD) managed at NHP. By June 2012 this increased to 624 [98.2% due to 21-OHD], representing a more than six fold increase over 12 years. Number of new cases ranged from 15 to 70 per year.

We aim to determine the mutations in the CYP21A2 gene in Vietnamese patients with CAH and attempt a genotype-phenotype correlation. Molecular analysis was performed using PCR, multiplex ligation-dependent
probe amplification and direct sequencing of PCR products of the CYP21A2 gene in 81 CAH patients (39 male and 42 female). Correlation between phenotype and genotype was evaluated based on identified mutations and clinical manifestations.

Mutations were identified in 92.6% mutant alleles, 22 genotypes were found in 81 cases. Seven different causative mutations were identified in CYP21A2 including one novel mutation. The most frequent genetic defect in the classic salt-wasting and simple virilizing forms was the IVS2-13A/C-G (54 alleles; 36%) mutation, followed by Large lesion (42 alleles; 28%) including exon 1 deletion (2 alleles), exon 1-3 deletion (10 alleles), exon 1-6 deletion (4 alleles), exon 1-8 deletion (2 alleles) and larger deletion (24 alleles); p.R356W (26 alleles; 17.3%); p.I172N (15 alleles; 10%). The rarer mutations were novel p.R484fsX541 (6 alleles; 4%); p.Q318X (4 alleles; 2.7%) and p.R426C (3 alleles; 2%). The majority of patients (61 cases; 75.3%) were homozygotes. Four cases were compound heterozygous. Thirteen patients had only a heterozygous mutation detected. Genotype accurately predicted phenotype in 93.8 and 100% of patients with salt-wasting and simple virilizing, respectively.

The spectrum of mutations of the CYP21A2 gene in Vietnamese patients is comparable to the some reported in other Asian population. Large deletion accounts for nearly one-third of the genetic defects. Therefore, laboratory should include methods for detecting point mutations as well as large deletions. Genotype-Phenotype correlation was high in the studied patients.

P129 A clinical follow-up study of premature thelarche in infants under the age of two
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Objective: Assess the clinical status and natural course of premature thelarche in infants under the age of 2 years as well as analyze the predictive factors for thelarche regression.

Method: Through Hospital Information System, analyze the hospital-based prevalence of premature thelarche in infants under the age of 2 years as well as analyze the follow-up databases of clinical features and laboratory data in 890 patients under 2 years old from October 2009 to September 2010.

Result: 1. Hospital-based prevalence in infants under the age of 2 years in 2009, 2010 and 2011 is 0.26‰, 0.40‰, 0.39‰ respectively. On average it’s 0.35‰. Period from July to September in every year is the peak time of doctor visiting. 2. Most (99.8%) of infants with premature thelarche are manifested as isolated premature thelarche, while only 0.2% are represented as peripheral precocious puberty. 3. Among the patients under the age of 2 years with isolated premature thelarche 89.5% of them get a regression between the age of 2 and 3 years (The average of regression age is 17±5.8 months), 10.5% of them do not make recovery by the age of 3 years and even some (0.4%) turn into central precocious puberty(CPP). 4. The two influencing factors of breast regression are breast size by the first time of doctor visiting and whether basal estrogen is high or not.

Conclusion: Premature thelarche in infants under the age of 2 is not a rare disease. Remaining of premature thelarche is probably associated with minipuberty and environmental estrogen disruptors. Premature thelarche in the majority manifested as a self-limited condition. Meanwhile, follow-ups at regular intervals to those remaining symptoms above 2 years old are needed.

P131 A case of virilizing adrenocortical carcinoma diagnosed by urine steroid profiling
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Introduction: Childhood adrenocortical carcinoma is rare and has poor prognosis. Histopathological examination often helps in differentiating between benign versus malignant adrenal tumors. However, the diagnostic accuracy of adrenal biopsies varies and could be affected by the sampling and the quality of the specimen. Urine steroid profiling (USP) has been used to differentiate between malignant tumors from benign ones. We report a case of virilizing adrenocortical carcinoma in which the diagnosis was made with the help of the characteristic USP findings.

Case report: A 6-year old girl presented with left lower quadrant pain. Physical examination revealed a large abdominal mass of 9 x 9 cm in size. She has tall stature and deepened voice. There was no palpable change except few pubic hairs and clitoromegaly. No gonads were palpable. There was no cushingoid features or hirsutism. Computed tomography showed a 12 cm well-defined heterogeneously-hypoenhancing mass at the upper pole of the left kidney. Ultrasound-guided biopsy of the tumor revealed necrotic tissue. Open biopsy showed fibroblastic tissue with no specific
diagnosis. Luteinizing hormone, follicular stimulating hormone and testosterone were elevated for age at 1.7 IU/L, 6.1 IU/L and 1.8nmol/L respectively. Urine for free cortisol was normal. USP showed markedly increased metabolites of dehydroepiandrosterone. Tetrahydro-11-deoxycortisol and 3-alpha, 16-alpha, 20-alpha pregnenetriol, which are metabolites reported to be increased in malignant adrenocortical tumors, were also elevated. The findings were suggestive of a steroid-secreting malignant adrenocortical tumor, which predominantly synthesizes androgens. Laparotomy was done and an 11 x 10 cm well encapsulated tumor arising from the left adrenal gland was found. Complete removal of the tumor was performed. Histological exam showed an extensively necrotic malignant adrenocortical carcinoma with no evidence of invasion into capsule, adjacent lymph nodes or nerves. USP was repeated 1 month post-operatively and showed no excess excretion of androgen metabolites, which suggested complete tumor removal.

Conclusion: Histopathological exam from tumor biopsy could be misleading in adrenocortical carcinoma due to sampling problem. On the other hand, hormonal overproduction and production of unusual metabolites could be revealed by USP and this helps in the diagnosis and follow-up of patients.

P132
Improving patient access to educational resources: the development of an educational resource for congenital adrenal hyperplasia
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CAH, a chronic condition with essentially life threatening aspects, is a frightening concept for families to come to terms with, even more so in the isolation of country areas. Having adequate knowledge and understanding is important in maintaining a sense of normality for these families and is an essential component to management both medically and within the family. The ultimate goal of this study was to improve patient access to education and support, and improve patient outcomes through increased knowledge and understanding. The principle aim of this study was to extend the education service we provide for our patients locally at specialist centres, to the patients who live in isolated regions of NSW and Australia wide. A comprehensive psychosocial education program (PEP) which was developed for patients and families with Congenital Adrenal Hyperplasia (CAH) and run at our local centre, was developed into an audiovisual format. In doing so, the program could be facilitated by one experienced professional, therefore eliminating the need for a team of specialists to travel country areas, which is logistically difficult and considerably costly.

Outreach services in NSW Australia, often provide only specialist medical care, with country families having only limited access to education, counselling and support services, that is routinely provided in metropolitan centres. In order to meet their needs the development of this innovative education program into an audiovisual format was planned and developed in order to provide an educational resource not only for patients and families, but also for clinicians. The PEP has been run 4 times with the program designed to cover the essential information required for families to know and understand the condition. Four 20 minutes sessions: What is CAH, Adolescent/Adult Issues, Psychosocial Issues and Sick Day Management, are followed by a 4 minute session on how to inject Hydrocortisone.

The process of developing an audiovisual educational tool will be discussed and the essential factors which need to be considered, in developing such programs into an audiovisual format will be discussed in detail.

This program is used in conjunction with the CAH Knowledge Questionnaire [1] (CAHKAQ) developed to evaluate our education process.

Reference

P133
Translation of a psychosocial education program for congenital adrenal hyperplasia in DVD format
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Introduction: Congenital Adrenal Hyperplasia (CAH) is a life threatening requiring good parental knowledge, in order to manage the daily care and any clinical problems arise. The impact of the condition is significant regardless of cultural background, with near death experiences and genital ambiguity occurring. Parents need to adjust to the burdens, that having a child with CAH creates, for all the family members. The authors have developed a validated CAH psychosocial education program (PEP) for families, which focuses on the essential information required to understand and manage CAH and which has been transformed into a DVD format, to improve access of families to educational resource information. This PEP has proven to be of vital importance in helping families manage this chronic condition [1]. However, it became apparent that families living form non-English speaking backgrounds, and those living in developing countries of South East Asia, did not have access to sufficient resource materials.

Aim: This project aimed to translate the PEP in its Audiovisual format (DVD), into firstly Vietnamese, and then other languages. In doing so, its content could then be facilitated by one health professional.

Method: A Medical Illustrations quote was obtained and funding was sourced. Five speaker presentations of the PEP were video-recorded live. Each was transcribed verbatim and edited in line with the slides. Transcripts were translated into Vietnamese by two medical professionals, and then narrated by a health services interpreter inline with the slide presentations. Discussion will include the process and the considerations required to develop such a comprehensive program in a translated format.

Results: The DVD has been used for newly diagnosed families at our centre, and in country NSW. As expertise with this condition is limited only to specialist centres, the DVD has since been sourced by the CAH Support Group Australia (CAHSGA), and internationally by CLAN, (Caring Living as Neighbours) an organisation providing healthcare needs for resource poor countries. Having completed the Vietnamese translation, we are currently pursuing an Indonesian translation.

Conclusion: Developing comprehensive education programs in a DVD format is necessary for supporting families in caring for their child. Ensuring families of non-English speaking backgrounds receive necessary and appropriate information to enable them to manage their child’s condition is the responsibility of all health professionals.

Reference
City) in collaboration with CLAN (Caring and Living As Neighbour Organization) and Children’s Hospital Westmead (CHW) has been holding annual Club meetings for all diabetes and congenital adrenal hyperplasia (CAH) patients and families since 2009. These Clubs are an opportunity for health professionals to educate families and for families to meet and interact.

The study aimed to answer 3 questions:
1) Perceived benefits of the Clubs
2) Changes to management as a result of attending the Clubs
3) Recommendations on ways to improve the Clubs

A survey of families (written format with closed and open questions) attending the 2011 CAH and Diabetes Club meetings was undertaken at CH2 Outpatient Clinic visits 6 months after the Club meeting.

29/31 diabetes families (93.5%) and 18/19 CAH families (94%) were surveyed. 100% of parents indicated they felt their overall knowledge had improved. Amongst the diabetes families: 50% felt more confident with sick day management; 48% reported changes in diets and improved blood glucose control (48%); 20% visited the hospital more frequently for complication screening; and 10% reported prompting doctors to screen for complications when they felt this had been forgotten. Of the CAH’s families: 50% felt more confident with sick day management and increasing dose of hydrocortisone independently; 36% let children go to the kindergarten; 29% began letting children play sports; 29% of mothers had attended genetic consultants for the next pregnancy; and 7% of children had benefited from surgery that the families had previously been too afraid to undertake. The majority of families suggested the club meetings should be longer and focus more on specific areas of interest: nutrition, exercise and physiology in diabetes and physiology, genetic consulting in CAH.

Families reported significant benefits from attending CAH and Diabetes Clubs, with some substantial improvements in quality of life for the children.

P135 Functional ovarian cysts in a neonate with classical 21-hydroxylase deficiency: case report and review of the literature
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Ovarian cysts (OCs) have been described in patients with congenital adrenal hyperplasia (CAH), however, neonatal OCs are rare in CAH. We report a unique neonate with 21-hydroxylase deficiency (21OHD), having functional OCs which developed after the start of treatment for CAH. The patient was referred for clitoromegaly at age of 5 days. Because of elevated ACTH, 277 pg/ml; 17-alpha-hydroxyprogesterone (17OHP), 184.4 ng/ml; plasma rennin activity (PRA), 39 ng/ml/hr; testosterone, 4.58 ng/ml; classical salt-wasting 21OHD was diagnosed. Estradiol (E2) and gonadotropins were not elevated. At age of 72 days, genital bleeding was seen for 5 days, followed by 5 times of genital bleeding per month. At age of 85 days, MRI showed development of right OC (34 x 36 mm) and reduction of the left one. Blood examination revealed E2, 99 pg/ml; LH, 0.3 IU/l; FSH 4.6 IU/l. At age of 10 months, OCs spontaneously diminished and E2 became under sensitivity. We determined that she had functional OCs. Treatment for 21OHD may give rise to them. To our best knowledge, including our case, 7 cases of neonatal OCs in CAH have been reported in the literature. Of these cases, 4 were diagnosed to have functional OCs after the initiation of treatment for CAH. In the 4 patients, all had genital bleeding and 3 had spontaneous regression of OCs. The remaining 3 cases had congenital OCs without genital bleeding and received cystectomy. Therefore, the mechanism of neonatal functional OCs in CAH may be different from that of congenital OCs and spontaneous regression could be expected without surgery.

P136 Tackling “pillar 5” – exploring options to help families of children who are living with congenital adrenal hyperplasia (CAH) in Vietnam to achieve financial independence
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Background: Despite significant improvements in care and health system strengthening for children who are living with Congenital Adrenal Hyperplasia (CAH) in Vietnam in recent years, consultation with families has confirmed that financial burdens continue to present urgent and pressing challenges for many. As part of its strategic framework for action and “5 Pillar” approach to helping children who are living in resource poor countries enjoy the highest quality of life possible, CLAN (Caring & Living As Neighbours) is committed to helping families achieve financial independence, and overcome any financial barriers to providing their children with the best care they can.

Aim: This project sought to understand the financial burdens affecting CAH families in Vietnam and potential opportunities for the development of income generating activities.

Method: The project concentrated on the most vulnerable and impoverished families. With support from members and staff connected with the CAH Club of NHP, willing families in rural areas of North Vietnam were identified for participation in face-to-face interviews in their homes in the month of July 2012. Families’ financial situation and possible avenues to improve same were discussed.

Results: Approximately 50% of all 650 CAH families attending NHP for care live in rural areas. Interviews were conducted with 22 families, with good saturation of responses emerging. The income of most families was under 4,000,000VND (SAUD200) per month, and most were unable to save money. Two key costs for families emerged: that of Florinef and the cost of travel to attend NHP. All mothers interviewed had a network of 2–3 other mothers from the CAH Club with whom they regularly communicated for advice and support. The CAH Club was considered a vital resource. A technique for identifying which families should be helped was developed, and was based on income level and individual plans to improve financial status.

Conclusion: It was estimated 35% (around 120) of the rural CAH families from NHP are in need of urgent priority support. Costs within and beyond the control of families were identified for focus. CLAN will continue to collaborate with NHP to explore most appropriate next steps for action.

P137 Plasma renin activity profile of patients with congenital adrenal hyperplasia in Semarang, Indonesia: a preliminary study
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Congenital Adrenal Hyperplasia (CAH) is an adrenal disorders due to impaired activity of one of the enzymes required for cortisol and aldosterone biosynthesis. One of the subtypes of CAH is the salt-wasting (SW) form which there is a renal salt loss due to aldosterone deficiency. Plasma Renin Activity (PRA) is the main index used to evaluate the mineralocorticoid control in CAH. PRA testing is almost very rare done for the CAH patients due to high cost, sophisticated laboratory is not available in all region and no compulsory health insurance in Indonesia.
The objective of this research was to describe PRA level in patient with Congenital Adrenal Hyperplasia.

This study is a part of CAH cohort study in Center for Biomedical Research (CEBIOR), Semarang, Indonesia. Eighteen patients diagnosed as CAH were drawn blood samples for hormonal test, including 17 OHP, Plasma Renin Activity, Cortisol, and Electrolytes. Clinical history and physical examination was performed to each patients. All 18 patients (17 female and 1 male) have high 17-OHP level and normal electrolytes levels, but only 14 patients have PRA data. Four patients did not show their PRA level due to fail in too much blood collection. Out of 14 patient, four patients which had history of SW have very high PRA level, while six patients have PRA level more than normal without history of salt wasting. The mean of PRA level in patients with history of SW (47.72 (SD 18.63)) are higher than the patients without history of SW (13.97 (SD 13.3)).

This study suggest that PRA level might be useful for evaluating mineralocorticoid level in CAH. It is proposed to the government to subsidize and provide PRA and other hormonal testing for CAH in many regions with affordable cost.

P138

Phaeochromocytoma in a teenage girl with Cushings Syndrome
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External excess of corticosteroid is frequently the cause of Cushings syndrome, while less report of such case due to internal tumor of adrenal gland. Here, we report clinical presentation, and etiological diagnosis of a 14 year old girl with Cushings syndrome caused by supra renal tumor. The first clinical presentation were recurrent cephalgia, irregular periods, hirsutism, skin striae, moon-face, acne, hypertension (140/90 mmHg), and overweight. All symptoms and signs have suggested an excess of corticosteroid hormone, and those occured for almost for one year. Laboratory examination showed normal of random blood glucose level (113 g/dL), and electrolytes (Na: 140.4 mmol/L, K: 3.7 mmol/L, Cl: 107.8 mmol/L). Morning corticosteroid hormone analysis was found increasing (32.0 ug/dL, normal range 2.5 – 25), and dexamethasone test failed to suppress hypothalamic-pituitary-supra renal axis (pre-test cortisol 31.9 ug/dL, and post-test: cortisol 32.1 ug/dL). All laboratory findings suggested an internal corticosteroid excess. The next, ultrasound image showed a profound mass at left supra renal gland, and normal of both kidneys. Further, opened biopsy of the tumor showed macroscopically very fragile mass and tend to hemorrhage. Pathological study concluded a phaeochromocytoma in left supra renal gland. These results suggest that phaeochromocytoma was the cause of corticosteroid excess and presented clinically as Cushings syndrome in our case.

P139

Adverse events related with propylthiouracil therapy of Graves’ Disease in children at Cipto Mangunkusumo Hospital Jakarta
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Despite propylthiouracil (PTU) and methimazole (MMI) have been used for more than half a century to treat hyperthyroidism caused by Graves’ disease, controversy still exists in antithyroid drug (ATD) therapy because of their significant side effects. Reports of adverse events involving cutaneous reactions, vasculitis, agranulocytosis and hepatotoxicity have appeared. In Indonesia, PTU was still included in National Essential Drugs List to treat Graves’ disease in children. The aim of our study was to provide insights into adverse events that can be associated with ATD use. We reviewed adverse events associated with ATD therapy in pediatric patients with Graves’ disease from September 2009 to June 2012 at outpatient clinic, Cipto Mangunkusumo Hospital, Jakarta. We found 21 patients with Graves’ disease aged 3-106 yr old, 5 male and 16 female. During this period, 9 patients (43%) treated with an average daily dose of PTU, the rest with MMI (57%). Adverse events attributed to PTU use were seen in 2 patients. Liver dysfunction was observed in 1 patient, alanine aminotransferase, aspartate aminotransferase and blood bilirubin were increased. The second one, developed epistaxis and had 2 times relaps episodes of thyrotoxicosis and suggested to perform thyroidectomy procedure. Four of the patients treated with PTU switched to MMI and had increased ALT/AST. None of them required hospitalization. One patient treated with PTU had full remission after 5 years of therapy. There was no adverse event observed in patients treated with MMI. Our results suggested that PTU use in children need routine biochemical monitoring to prevent severe adverse events.

THYROID

P140

Hyperthyroidism with Turner Syndrome
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Background: Thyroid dysfunction is more frequently encountered in girls with Turner syndrome (TS). Moreover, patients with both Graves’ disease and the TS have been reported only rarely. Recent evidence indicates that Graves’ disease is also a disorder of cell mediated immunity.

Objective: To report a case of 10-year and 8-month-old girl with hyperthyroidism and TS.

Case: A 10-year and 8-month-old girl presented with short stature (body weight 22 kg, body height 116 cm). On physical examination there were bilateral exophthalmus, enlargement of thyroid grade IA, widely spaced nipples, small finger nails. Laboratory findings showed elevated free thyroxin (FT4), decreased sensitive thyroid stimulating hormone (TSHs) and positive anti thyroglobulin. Ultrasonography (USG) thyroid gland revealed a diffuse enlargement. The ophthalmology examination result was exophthalmus with normal visus. No abnormality on the chest X-Ray and electrocardiography. Bone age was equal to a 8-year and 10-month-old girl. Chromosom analysis result: Mosaiik 45, X / 46, X(X). Treatment with carbimazole have provided some improvement.

Conclusion: The diagnosis was established based on anamnesis, physical examination, laboratory findings and chromosom analysis. Prognosis for this case is undefined.

P141

Profile of Congenital Hypothyroidism patients at Hasan Sadikin General Hospital, Bandung, Indonesia 2010-2012
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Background: Congenital hypothyroidism (CH), is caused by inadequate production of thyroid, represent one of the most common preventable causes of mental retardation. Undetected near birth, CH clinically manifests as mental retardation, coarse facial features, poor growth, deafness and neurological abnormalities.

Objective: To describe characteristics of patient with congenital hypothyroidism diagnosed in Pediatric Department of Hasan Sadikin General Hospital, Bandung, Indonesia

Methods: We reviewed 26 children with congenital hypothyroidism confirmed by thyroid scintigraphy from October 2010 to June 2012 who came to Dr. Hasan Sadikin General Hospital Bandung, Indonesia.

Results: Twenty six subjects were diagnosed with congenital hypothyroidism, consisted of 15 (57.7%) girls and 11 (42.3%) boys, mean age 11.42 ±10.35 month. The youngest age when the diagnosis (CH) was established was 2 months and the oldest was 46 months. Thirteen subjects (50%) were referred by primary care pediatrician, 5 subjects (19.2%) by
general practitioners, 4 subjects by neuropediatrician and 4 subjects by growth and development clinic. The main presenting complaints in CH were global delayed development (69.2%), constipation (50%), prolonged icteric (15.4%) and growth retardation (13.5%). The most common of clinical appearance was hypotonia (69.2%), coarse faces (46.2%), mottled (34.6%), large fontanel (34.6%), umbilical hernia (23.1%) and macroglossia (26.9%). We found 25 subjects were diagnosed as primary CH and only 1 case with secondary CH. The most common etiology of CH was thyroid agenesis (53.8%), thyroid ectopic (19.2%), thyroid hypoplasia (11.5%) and dysmorphogenesis (11.5%). Decreased T4 value were found in all subjects (mean 0.55±0.35 ng/dl) and mean TSHs value at presentation was 31.02±20.71 mIU/L. Of the 26 late diagnosed CH cases, 46% had mental and motor development delay, 23.1% short stature and mental retardation, and 15.4% mental retardation and neurological sequel as complications.

Conclusion: Late diagnosis of congenital hypothyroidism in children result varied clinical manifestation and had mental retardation, gross motor delay, short stature and neurological abnormalities as complications.

**P142**

Thyroid dysfunction after hematopoietic stem cell transplantation in children: older age and acute GVHD might be risk factors of thyroid dysfunction during 3 months after HSCT

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We evaluated short term changes in thyroid function in patients who underwent hematopoietic stem cell transplantation (HSCT) during childhood. And we attempted to find clinical and treatment risk factors for thyroid dysfunction during 3 months after HSCT.

We studied 170 patients (102 boys and 68 girls) who underwent HSCT at the Catholic HSCT center from January, 2004 to December, 2009. Patients with a past history of thyroid dysfunction were excluded. The mean age at HSCT were 10.0±4.8 years. Thyroid function tests were measured before HSCT and at 1, 3 months after HSCT. The normal reference value of T3 was 0.8–2.1 ng/mL, free T3 was 0.8–2.2 ng/dL, and TSH was 0.17–6.0 mIU/L.

The disease and disease status for HSCT were acute lymphoblastic leukemia (ALL) (first complete remission (CR) = 21, second CR = 22), acute myeloid leukemia (AML) (first CR = 74, second CR = 51), chronic myeloid leukemia (first chronic phase = 8), and non-malignant hematological disease (severe aplastic anemia = 32, hemophagocytic lymphohistiocytosis = 3, Fanconi anemia = 5). Out of 170 patients, 169 (99.4%) underwent allotransplantation. aGVHD (grade II–IV) developed in 79 patients. In 170 subjects, 59 patients received a TBI-based, 81 underwent BU-based, and 30 received reduced intensity conditioning regimens before HSCT. Forty-eight (28.2%) out of 170 patients showed thyroid dysfunction during 3 months after HSCT (31: euthyroid sick syndrome, 7: subclinical hyperthyroidism, 4: subclinical hypothyroidism, 4: hypothyroxemia, 2: overt hyperthyroidism and 1: high T4 syndrome). In a univariate logistic regression analysis, the Age at HSCT (p=0.003) and acute GVHD (p=0.006) showed risk factors of thyroid dysfunction during 3 months after HSCT. We could not find any statistical relationships with sex, diagnosis and conditioning regimens. In a univariate logistic regression analysis, euthyroid sick syndrome (p=0.006) showed strong relationships with mortality. In our study, 28.2% patients experienced thyroid dysfunction during 3 months after HSCT. Euthyroid sick syndrome was most frequent, although subclinical hyperthyroidism, overt hyperthyroidism or subclinical hypothyroidism were also observed. Older age and acute GVHD might be risk factors of thyroid dysfunction during 3 months after HSCT. There was a significant correlation between euthyroid sick syndrome and mortality.

**P143**

Hashimoto’s Thyroiditis in children and adolescents: at presentation and during long-term follow up

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Objective: Hashimoto’s thyroiditis (HT) is the most common cause of goiter and acquired hypothyroidism in children and adolescents. The aim of this study was to evaluate the clinical manifestations of HT leading to referral in children and adolescents, in addition to disease course and long-term outcome.

Methods: The clinical and laboratory data of 57 patients with HT at presentation and long-term outcome were retrospectively evaluated using patient records.

Results: The mean age of the patients at the time of diagnosis was 10.9 ± 2.3 years and female/male ratio was 49/8. The complaint at the time of hospital presentation was goiter in 66.7% of the patients. Other reasons for referral were clinical symptoms of hypothyroidism (7.1%) and findings on work-up for an unrelated problem (24.6%) or for high-risk groups (1.8%). At baseline, 49.1% (n=28) of the patients were euthyroid, whereas 31.6% (n=18) had subclinical hypothyroidism, 10.5% (n=6) of subjects were evaluated as hypothyroid. Out of 57 patients, 5 were diagnosed with hasithoxis. Five of the 28 subjects, who were initially euthyroid developed subclinical or overt hypothyroidism during the follow-up period and were started on thyroid medication.

Conclusions: Thyroid function tests should be repeated periodically to detect progression to hypothyroidism in initially euthyroid patients as well as reversibility of hypothyroidism.
2. TRAb levels could be tested in breast milk from 9 mice at 1d after delivery, TPOAb levels >0.5IU/L in breast milk from 15 mice, and TGAb in breast milk from 4 mice. At 1wk after delivery, TRAb levels could be tested in breast milk from 4 mice, TPOAb in breast milk from 7 mice, and TGAb in breast milk from 1 mice. TRAb can not be tested in mice' breast milk in 3wk after delivery, 2 mice could be tested TPOAb from their breast milk, and 3 mice could be tested TGAb from their breast milk. The levels of TPOAb in the breast milk after 1d delivery in the experiment group were significantly higher than those of the control group (P<0.05).

3. 114, 129 offspring 1wk and 3wks-old in the experiment group were suffered with Graves' hyperthyroidism. The incidence rate respectively were 63.3% and 71.7 %. The levels of serum T4, TRAb, TPOAb and TGAb in offspring 1wk and 3wks-old in the experimental group were significantly higher than those of the control (P<0.05).

Conclusions: 1. An animal model of Graves' disease is successfully prepared by immunization with Ad-TSHR-289.
2. The higher levels of thyroid autoantibodies could result in neonatal thyroid disease, whose mothers were suffered with Graves' disease.
3. The levels of thyroid autoantibodies in the mother with Graves' disease could affect the offspring's thyroid function through the placenta and breast milk.

P145
Thyrotoxic periodic paralysis and chorea: two uncommon neuromuscular complications in an adolescent with newly diagnosed Graves disease
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Both thyrotoxic periodic paralysis (TPP) and choreoathetosis are unusual complications of childhood thyrotoxicosis. We hereby report a boy who presented with both TPP and choreoathetosis at the initial presentation of his Graves disease. A 14 year-old Thai boy presented with acute generalized proximal muscle weakness and myalgia for 5 hours. Detailed history revealed the increased appetite, heat intolerance and labile mood for 6 months. Physical examination revealed tachycardia, goiter and mild spasticity.

Generalized proximal muscle weakness and hyporeflexia were noted. Abnormal movement including ballism and mild spoiling of hands were also noted. The milk maid sign was positive. The abnormal movement was consistent with choreoathetosis. Labs showed serum T3 > 651 ng/dL, Free T4 > 7.77 ng/dL, 75th < 0.005 u/L/mL, K 2.1 mmol/L and CPE 1555 U/L. Autoimmune profile showed high titer of the anti-microsomal autoantibodies of 125000. The final diagnosis of Graves disease with TPP and choreoathetosis were made.

Methimazole and propranolol were started. Intravenous K was administered to correct hypokalemia. Serum K was normalized within 7 hours after K replacement. The patient was able to stand and walk normally on the 2nd day of admission. After 4 weeks of treatment with Methimazole, the thyroid function test was consistent with hypothyroidism, therefore the dose of Methimazole was decreased. The choreoathetosis resolved completely within 4 weeks. Our case report demonstrates the first pediatric patient with Graves disease who developed combined neuromuscular complications which were TPP and choreoathetosis. There has been a previous case report of a 21-year-old man with Graves disease who had both muscular complication and choreoathetosis. The muscular involvement in that patient was different from our patient. In that particular patient, he developed acute severe thyrotoxic myopathy which involved both bulbar and skeletal muscle. TPP is an alarming and potentially lethal complication of hyperthyroidism. It usually resolves completely after the normalization of serum K levels. Effective control of hyperthyroidism can prevent the recurrence of TPP. While, choreoathetosis usually resolves after the patient recovers from hyperthyroid state. We should always be aware of Graves disease in any children who present with either muscle weakness or choreoathetosis since the signs and symptoms of Graves disease itself might not be very obvious.

P146
Profile of Congenital Hypothyroidism in DR. Cipto Mangunkusumo Hospital
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Background: Congenital Hypothyroidism (CH) affects children from infant and results from a partial or complete loss of thyroid function. Unrecognized CH can make some problems in health of children.

Method: a retrospective study of congenital hypothyroidism in dr. Cipto Mangunkusumo Hospital, during January 2010-December 2011.

Results: there were 40 children with CH included in the study. Boys 12(30 %) and girls 28(70%). Age when diagnosed 0-3 months 4(10%), 3-6 months 2(5%), 6-12 months 9(22,5%), 1-6 years 20(50%), 6-14 years 5(12,5%). Clinical manifestation: delayed development 27,5%, underweight 17,5%, acute respiratory infection 15%, constipation 12,5%, hypotonia 7,5%, speech delay 5%, short stature 5%, enlarged tongue 2,5%, vomite 2,5%, icteric 2,5%, enlarged lymph node of colli 2,5%. We found suspect down syndrome 4(10%), severe malnutrition 4(10%), short stature 3(7,5%), mental retardation 2(5%).

Conclusion: in our study, most common age of CH patients was 1-6 years, most sex was girls, which often founded were delayed development.
due to brain plasticity. The aims of this study is to determine the effect of stimulation on speech development of 1-3 years old children in IDD and Non IDD areas.

Quasi experimental study used one group pretest posttest design with consecutive sampling was done on 1-3 years old children who fulfilled inclusion criteria in Kepil (Non IDD area) and Kertek District (IDD area), Wonosobo regency from April to September 2011. Stimulation interventions in accordance with the guidelines for implementation of stimulation, early detection and intervention for growth and child development in Primary Health Care 2006. Standard score equivalent of global language from Early Language Milestones Scale 2 was measured before and after stimulation in IDD and Non IDD areas. Statistical analysis used paired and independent t test.

Eighty children consisting of 57.5% boys and 43.5% girls were enrolled in this study. Mean of speech development score in IDD 8.4 (SD 7.94) while in Non IDD 2.93 (SD 6.3) with p value 0.004. Standard score equivalent of speech development before and after stimulation in Non IDD area increase from 89.8 to 92.7 (SD 8.3) (p=0.032) and 85.7 to 94 (SD 7.94) (p=0.001) in IDD area. These result suggest that stimulation intervention has an effect on increasing speech development of 1-3 years old children in IDD and Non IDD area.

P149
Iodine deficiency profile of Central Java province Indonesia during the year 2011
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Iodine Deficiency Disorders (IDD) has recognised as the most common preventable cause of brain damage. IDD also one of the nutrition problems that influences human growth and development. In Indonesia, about 30-60% of the areas are IDD endemic areas. Prevention of IDD in 10 step should be done every year. The aims of this study was to evaluate IDD prevention program in Central Java, Indonesia.

This study was done in 15 district (289 sub district) of Central Java Province during the year 2011. A total of 55617 neonate, 106825 pregnant women, and 2958 urine samples of pregnant women were examined. Neonatal Hypothyroid Index (NHI) in the first week of neonatal visit, Total Goiter Rate (TGR), Urine Iodine Excretion (UIE) of pregnant women and household consumption of iodized salt were collected. The blood analysis was done in IDD Laboratory in Bandung and UIE analysis was done in BP GAKY Magelang, Indonesia.

Of 55617 neonate, there were 18 neonates (0.03%) suspected with cretins. TGR degree 1-2 was found in 174 cases (0.18%). The median of pregnant women UIE was 156mg/l and UIE <100mg/l was found in 1002 (33.67%) pregnant women. There were 4 district with mild iodine deficiency. The consumption of iodized salt in the population was 81.6%.

In the future, the 33.87% of pregnant women with UIE <100 mg/l will put 1/3 of babies born in this area in the risk of brain damage. Problem of iodine deficiency in the past with TGR 0.18% and 18 neonates with suspected cretins is iceberg phenomena with more brain damage. Screening for congenital hypothyroidism should be performed every year in the newborn, followed by UIE examination of childbearing age women and pregnant women because it can happen iodine replate area and new endemic areas.

P150
The cognitive and language abilities after stimulation in children aged less than 3 years iodine deficiency area
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Iodine Deficiency Disorders (IDD) become a health problem in Indonesia and other developing countries. The influences of IDD on children’s intellectual are irreversible, but on the other hand it is said that early stimulation affects brain development. The aims of this study was to determine the cognitive and language abilities after stimulation in children aged less than 3 years in IDD area.

This study was a randomized controlled trial. Children aged 1-3 years, born and live in Wonosobo, one of the IDD area in Central Java, Indonesia (IDD 2008 mapping included this area in moderate endemic area) were test by Caput Scale, Otoacoustic emission (OAЕ) and Urine iodine Excretion (UIE), then they were stimulated and monitored during 3 months. The data was analyzed by Mann-Whitney analysis, statistically significant if p<0.05 (the confidence interval is 95%).

One hundred thirty children were enrolled in this study. The mean age of subjects was 23.24 ± 6.91 months. Median UIE value was 175 µg/L. In IDD area, the value before and after stimulated were as follows : the cognitive ability (79.9 ± 85.1), language skills/CLAMS 80 vs 86.2, visual motor/CAT(80,2 vs 86,1). In non IDD area, before and after stimulated; cognitive ability (84.7 ± 93.5), CLAMS(82,3 vs 91,0), CAT(82,4 vs 91,2). There were increasing the level cognitive and language after stimulation in IDD area and non IDD area,6 and 9 point respectively.

Our result suggest that family stimulation plays a role in improving children’s cognitive and language abilities in both areas of iodine deficiency or not, but there is variance between two groups before and after stimulation, where cognitive and language abilities of children in non IDD area higher then children in IDD area. Therefore controlling IDD program still become a main problem beside stimulation.

P151
Neonatal screening for congenital hypothyroidism: primary thryotropin screening: comparison of false positive rate using radioimmunossay (RIA) Vs fluorometric assay (FIA)
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Background: In Indonesia one of the challenges in implementing neonatal screening for congenital hypothyroidism (CH) is early discharge of infants, therefore we could not avoid to take the specimens between 24-48 hours of age, resulted in high false-positive rate. Since the begining of the neonatal screening program, radioimunooassay (RIA) was used for primary TSH screening. Fluoroimmunoassay (FIA) are expected to be more sensitive method.

Objective: To compare the results of TSH measurements, using RIA and FIA in efforts to minimize false positive rate.

Methods: Blood-spotted filter paper specimens, obtained by heel prick for primary TSH screening were collected from neonates born in 12 hospitals in Bandung. Low birth weight infants, sick neonates, and specimens collected less than 24 ours of age were excluded. In 2008, RIA (Coat-A-Count, Neonatal TSH IRMA), and in 2009 FIA (DELFIA Neonatal hTSH) was used. The cutoff value of TSH was 20mU/L. We calculated the false positive results on specimens collected within 30-48 hours after birth and those taken after 48 hours. The false positive rate compared within two assays.

Results: Specimens from 7915 babies were measured by RIA, 53.46% were collected before 48 hours of age, 36.18% between 24 to 48 hours, and 7684 babies were measured by FIA, 61.17% were collected before 48 hours of age and 39.43% between 24 to 48 hours. Healthy, fullterm babies screened by RIA at age after 24 hours were 6525 with 0.86% recall rate and 0.83% false positive rate. Six thousands and thirteen specimens were measured by FIA, with 0.17% recall rate and 0.13% false positive rate, significantly lower than RIA (p <0.05). Using FIA recall rate and false positive rate on specimen collected between 24 to 48 hours are 0.16% and 0.16%, while on specimen collected after 48 hours are 0.17% and 0.10%, not significantly different (p>0.07).

Conclusions: Primary TSH screening for congenital hypothyroidism using FIA is more sensitive RIA. Lower recall rate as well as false positive rate decreased the burden of tracking the infants for confirmatory, therefore switching the test to FIA is appropriately reasonable.

P152
A clinical profile of pediatric patients admitted for thyrotoxicosis in a tertiary hospital using the 1992 Burch and Wartofsky criteria
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Thyrotoxicosis is the clinical syndrome of hypermetabolism that occurs with increased levels of thyroid hormones. Thyroid storm (TS) represents the extreme manifestation of thyrotoxicosis. Medical charts of all pediatric patients with the diagnosis of "Thyroid Storm or "Impending Thyroid Storm" (TSH > 10 mIU/L) from 2004 to 2010 were retrieved. Patients with a BWC of 25 and above were included. Charts with incomplete data were excluded. Fourteen patients (13 females and 1 male) between 12-18 years of age were included. All had goiter and were biochemically hyperthyroid. The most common chief complaint was dyspnea (57%). The most common precipitating factors were infection and noncompliance to medicines (43%). The mean length of hospital stay was 6.2±4 days. The most common organ system dysfunctions were diarrhea (50%), tachycardia (43%) and hyperthermia (38%). Eight (57%) fit the criteria for TS and 6 (43%) for ITS. The mortality rate was 29%.

The hyperthyroid pediatric patients were admitted due to organ system decompensation secondary to thyrotoxicosis and/or concomitant disease. The levels of thyroid hormone did not distinguish between thyrotoxicosis and TS nor predict the outcome. The most common intercurrent diseases were pneumonia and acquired cardiac disease, the symptoms (fever, tachypnea, tachycardia) of which overlapped with symptoms of the hyperthyroid state. The clinical changes in cardiovascular hemodynamics that occur in patients in thyrotoxicosis aggravates cardiovascular disease, increasing mortality risk. The patients who were admitted with heart failure signs eventually expired.

Wartofsky emphasizes that the diagnosis of ITS and TS is clinical and based on the severity of the symptoms and signs of thyrotoxicosis and presence of functional decompensation of organ systems. The potential high mortality necessitates early treatment. The mortality rate in our study is 29%/4/14 cases), which is higher than that reported among adults (11.3% of 71 cases) in the same tertiary hospital but within the range of 20-30% in the adult population in first world countries. Only two (50%) of those who died had high BWC scores (range 70-85) questioning now the usefulness of BWC as a helpful tool in assessing disease severity among adolescents.

In conclusion, the clinical profile of pediatric patients in thyrotoxicosis using the BWC was reviewed. A validity study on the use and applicability of BWC for pediatric patients is recommended.

**P154**

**Iodine status as indicted by neonatal thyroid stimulating hormone screening in Mitre Keluarga Hospital in Surabaya at 2005-2010**

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**Preamrudee Poomthavorn**

**Effect of iodine supplementation during pregnancy on neonatal thyroid stimulating hormone**

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**Background:** Thyroid hormone is essential for neurological development, particularly in the developing brain. Iodine is the important constituent of thyroid hormone. Its requirement during pregnancy is increased. Elevated neonatal thyroid stimulating hormone (TSH) is a sensitive indicator of iodine insufficiency in pregnant women. Our previous study in the year 2000 demonstrated that median urine iodine (UI) concentration in pregnant women was 85 µg/L, a level of which indicates mild iodine deficiency. Since October 2010, Thai national iodine supplementation program has been started by prescribing a 150 µg iodine tablet daily to all pregnant women throughout their gestation. We, therefore, aimed to determine the effect of maternal iodine supplementation on neonatal TSH.

**Study design:** Retrospective data collection.

**Methods:** Cord blood TSH measurement for screening of congenital hypothyroidism has been routinely performed at Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. Data of neonatal TSH during the years 2007-2011 were collected. Neonates born before October 2010 were classified as pre-iodine supplementation group (Group 1) while those born after October 2010 were post-iodine supplementation group (Group 2).

**Results:** Cord blood TSH values were obtained from 6,802 neonates, 4,864 in Group 1 and 1,938 in Group 2. Median (range) neonatal TSH of Group 1 was significantly higher than that of Group 2 [7.4 (0.01-87.7) vs. 5.2 (0.7-35.1)] mIU/L, respectively (p<0.001). Eighty-one percent of neonates in Group 1 but only 54% in Group 2 had cord blood TSH of greater than 10 mIU/L. Similarly, 26% of neonates in Group 1 but only 13% in Group 2 had cord blood TSH of greater than 10 mIU/L.

**Conclusions:** There was a trend towards declining of cord blood TSH values after iodine supplementation during pregnancy. This finding suggests that mothers residing in Bangkok are likely to have mild iodine deficiency. Median neonatal TSH value is useful for monitoring iodine nutrition in the population.

**P155**

**Three cases of resistance to thyroid hormone and the genetic mutation of these patients and their family members**

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**Aims:** We report the clinical characteristics and the genetic analysis of their family members of 3 cases. Resistance to thyroid hormone (RTH), a dominant inherited syndrome and it is usually due to mutations located in the ligand-binding domain and adjacent hinge region of the thyroid hormone receptor β (TRβ).

**Methods:** We describe patients’ clinical features, biochemical and hormones level such as thyroid function tests (TFTs), imaging data. We also detected the TFTs of his family members as well. Direct DNA sequencing of the TRβ gene was done for all those with abnormal TFTs.

**Results:** The RTH children had goiter, irritability, aggressiveness, and hyperhidrosis. The TFTs showed high levels of circulating free thyroid hormones (FT4 and FT3) and normal or high thyroid-stimulating hormone (TSH) concentrations. All of these patients used bromocriptine, and then clinical presentations got improved obviously without obvious adverse effect. From these three patients and their family members we identified a novel nonsense mutation, A317D, located in exon 9 of the gene of a boy patient and his mother, but his mother showed no any clinical presentation. However, we didn’t have any abnormal finding in for other patients and their parents.

**Conclusion:** The RTH children had goiter, irritability, aggressiveness, and hyperhidrosis. The TFTs showed high levels of circulating free thyroid hormones (FT4 and FT3) and normal or high thyroid-stimulating hormone.
(TSH) concentrations. Fund a novel mutation in the Trp in one patient and his mother. This research verified the phenomena that there is a heterogeneous within the same mutation of RTH patients. All of these patients used bromocriptine, and then clinical presentations got improved obviously without obvious adverse effect.

**P156**
Factors related to decreased bone mineral density in childhood cancer survivors
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The risk of osteoporosis or osteopenia is known to increase after childhood cancer treatment. The purpose of this study was to evaluate patterns of bone mineral density (BMD) and factors related to decreased BMD in childhood cancer survivors. We studied 78 patients (34 males, 44 females) treated for acute lymphoblastic leukemia, acute myelogenous leukemia or chronic myelogenous leukemia during childhood. Clinical data, laboratory finding, bone age, lumbar BMD (LBMD) and femur neck BMD (FNBMD) were investigated. Chronological age at evaluation was 11.6±3.4 yr in males and 13.0±3.3 yr in females. Primary disease, chronological age at treatment, body mass index (BMI), method of treatment (chemotherapy, radiotherapy), endocrine function, presence of chronic graft-versus-host disease (cGVHD) and relevance of BMD standard deviation score (SDS) were evaluated. LBMD and FNBMD of the subjects were -0.91±1.41 and -1.13±1.79, respectively. Twenty (25.7%) patients had LBMD SDS lower than -2. Nineteen (24.4%) patients had FNBMD SDS lower than -2. The patients treated with hematopoietic stem cell transplantation had lower LBMD SDS (-1.7±2.13 vs -0.43±1.33, P=0.025). The risk of having LBMD SDS <2 was higher in the patients treated with glucocorticoid for cGVHD (36.6% vs 13.5%; odds ratio [OR], 3.7; P=0.020). In multivariate logistic regression analysis, longer duration of glucocorticoid treatment (OR, 1.12; 95% confidence interval [CI], 1.03-1.22) and lower BMI SDS (OR, 0.42; 95% CI, 0.21-0.83) were associated with decreased LBMD SDS. These findings suggest that prolonged glucocorticoid use and reduction in BMI are risk factors for decreased BMD in childhood cancer survivors. Anticipatory follow-up and appropriate treatment are necessary, especially for the patients with risk factors.

**CALCIUM/BONE**

**P157**
The first reported case of pseudoparathryoidism type IB in Hong Kong: hypocalcemia in an adolescent boy with recurrent seizures
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Pseudohypoparathyroidism (PHP) is a heterogeneous group of disorders characterized by hypocalcemia, hyperphosphatemia and inappropriately elevated serum parathyroid hormone (PTH) level due to end-organ resistance of biological activity of parathyroid hormone. It is due to epigenetic change of the GNAS locus and is divided into types la, lb, lc and II. We hereby describe the first reported case of pseudohypoparathyroidism type Ib Hong Kong.

**P158**
Alandronate treatment for osteogenesis imperfecta type III in twin babies: a case report
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Osteogenesis Imperfecta (OI) is a connective tissue disorders. There are several types of OI. OI can be autosomal dominant, some cases can be found in recessive by mosaicism in the parent. The main goal of treatment is to reduce the incidence of fractures, prevent deformities of bone and scoliosis, and improve the functional patient. This is a case of OI given alendronate as an alternative treatment. Twin boys babies born in Moewardi Hospital by sectio caesaria. Baby I and II seemed swollen on both of hand and leg. Both of the babies appeared to be less active and limitation of range of motion, with blue sclera. Result of x-rays, it appeared multiple fractures in extremities and costae. We diagnosed osteogenesis omperfecta type III, clinically. We gave alendronate 1 x 1 mg orally, because sodium pamidronate was not available at that time. Alendronate were given by thirty to forty five degree position. Orthopedic surgeon gave on conservative therapy by slap. During treatment in hospital, appeared new fractures in each baby. After giving alendronate therapy for 4 months, the baby I didn’t show new fractures, the baby II suffered three new fractures. There were no side effect of alendronate treatment on gastrointestinal. At the aged of 5th month, the patients were given intravenously sodium pamidronate for 3 days with a dose of 2 mg. Three months after pamidronate, the baby I didn’t show new fractures, the baby II suffered one new fracture. Bone mineral density was not performed in these patients. We conclude that oral biphosphonate could be alternative treatment for OI if intravenous biphosphonate is unavailable. It still needs more research regarding to effectiveness of oral biphosphonate compare to intravenous biphosphonate.

**P159**
Age and seasonal variation of serum vitamin D levels in healthy school children and adolescents
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Purpose: Vitamin D is an important fat-soluble vitamin that functions as a prohormone and affects bone mineralization and calcium homeostasis. In this study, we measured serum vitamin D levels in healthy school children and adolescents, and evaluated the prevalence of vitamin D deficiency, and its correlation with age, season and other clinical parameters.

Methods: We included 706 school children and adolescents aged 7 to 18 years (434 girls and 272 boys) from March 2011 to February 2012. We excluded subjects with any acute or chronic diseases. None of subjects were taking calcium or vitamin D supplements. They were classified according to age (elementary school, 7-12 years old, n=565; middle school, 13-15 years old, n=75; high school, 16-18 years old, n=36), sex (boys, n=272; girls, n=434) and season (spring, March to May, n=267; summer, June to August, n=106; fall, September to November, n=139; winter, December to February, n=194). We performed anthropometric measurement and laboratory tests including fasting lipid profile (cholesterol, triglyceride and LDL cholesterol), ALP, Ca, P and serum 25OHD3 level. Vitamin D deficiency were defined as a serum 25OHD3 level lower than 20 ng/ml.

Results: 1) In total 706 subjects, mean serum vitamin D level was 16.30 ± 6.10 ng/mL, and prevalence of vitamin D deficiency was 74.5%. The serum vitamin D level was negatively correlated with age, serum estradiol and LH values.
2) Mean serum vitamin D levels were 16.65 ± 6.07 ng/mL in elementary school group, 15.23 ± 6.37 ng/mL in middle school group, and 12.65 ± 5.56 ng/mL in high school group. The prevalence of vitamin D deficiency in 3 aged groups was 72.9% in elementary school group, 78.7% in middle school group, and 91.7% in high school group. However, in elementary school group, there was no significant difference in vitamin D levels between low grade (7-9 years old) and high grade subjects (10-12 years old).
3) The level of serum vitamin D was significantly higher in summer (20.99 ± 6.40 ng/mL) and fall (19.11 ± 6.11 ng/mL) than in spring (15.46 ± 5.22 ng/mL) and winter (12.88 ± 4.37 ng/mL). The prevalence of vitamin D deficiency was 93.8% in winter and 49.1% in summer.
4) Mean serum vitamin D level was significantly lower in girls (15.73 ± 5.71 ng/mL) than in boys (17.20 ± 6.59 ng/mL). The prevalence of vitamin D deficiency was 68.8% in boys and 78.1% in girls.
Conclusion: The prevalence of vitamin D deficiency in healthy school children and adolescent was very high, especially in high school adolescents and winter season. These findings suggest that adequate outdoor activity and vitamin D supplements should be necessary for school children and adolescents.

P160
Adequate vitamin D status and adiposity contribute to bone health in peripubertal nonobese children
Jieun Lee, Young Ah Lee, Choong Ho Shin, Sei Won Yang
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The dietary reference intake (DRI) of vitamin D for Korean children was reduced from 400IU/day in 2005 to 200IU/day in 2010. We evaluated the risk factors for low vitamin D status and its relationship with bone health in peripubertal nonobese children living in Seoul or Gyeonggi-do. One hundred children (9.3±1.9 years, 71 prepubertal, 45 boys) participated in the winter (n = 38, December through March) and summer (June through September). Bone mineral content (Z_BMC), fat mass (Z_FM), lean mass (Z_LM), and bone mineral density for the total body (Z_TB) and lumbar spine (Z_L1-L4) were measured using dual-energy X-ray absorptiometry. Twenty-nine percent of children (47.4% in winter, 17.7% in summer) were vitamin D deficient (25-hydroxyvitamin D level of <20 ng/ml). In winter, low vitamin D intake (P = 0.019) and fewer daylight hours (P = 0.015) were associated with low 25-hydroxyvitamin D level. The 25-hydroxyvitamin D level correlated positively with Z_BMC (P = 0.023), Z_TB (P = 0.018), and Z_L1-L4 (P = 0.043) independently of sex, puberty, Z_FM, Z_LM, physical activity level, and calcium intake. Z_FM correlated independently with Z_BMC (P < 0.001), Z_TB (P = 0.037), and Z_L1-L4 (P < 0.001). In conclusion, almost half of peripubertal nonobese children were vitamin D deficient in winter. Considering the beneficial effects of adequate vitamin D status and adiposity on bone health, the current DRI of vitamin D should be upgraded to prevent vitamin D deficiency.

P161
An atypical 7q11.2-q21.11 deletion in a Williams-Beuren syndrome patient
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Aims: Williams-Beuren syndrome (WBS; OMIM no. 194050) is a multisystemic neurodevelopmental disorder caused by a hemizygous deletion of 1.55Mb on chromosome 7q11.23 spanning 28 genes. Here we report a patient showing mild WBS physical phenotype, who carries a longer, 21Mb atypical deletion.

Methods: Genomic DNA from the proband was extracted from peripheral blood leukocyte. Karyotype analysis was performed on metaphase cells. Array-based comparative genomic hybridization of DNA from the patient's peripheral blood lymphocytes was performed.

Results: The proband, a female neonate, is the first child of healthy nonconsanguineous Chinese parents. She was born by uterine-incision delivery with intrauterine distress after 41 weeks of gestation. Her birth weight was 2.4 kg. She showed an distinctive facies including broad brow, periorbital fullness, epicanthal folds, short nose, long philtrum, small jaw and prominent earlobes. The cardiology ultrasound examination showed open foramen ovale without elastin aortic stenosis, pulmonic stenosis. Her abdominal ultrasound examination showed right Duplicated kidneys. Her Karyotyping was 46, XX, del(7)(q11.1q11.23). We then performed array CGH for this patient and confirmed the deletion region of 21Mb from 7q11.2 to 7q21.11.

Conclusion: A deletion of the 7q11.23 chromosomal region is found in approximately 90-95% of the clinically typical WBS patients but in a lower percentage of atypical cases. The commonly deleted chromosomal region has a size of approximately 1.5 Mb. However, smaller or longer deletions have also been described in atypical WBS patients. Array CGH analysis can be performed to make sure the location and size of microdeletion and confirmed the diagnosis of patients with mild or atypical physical phenotypes.

P162
Challenges in managing osteogenesis imperfecta patients in H. Adam Malik hospital, North Sumatera, Indonesia
Siska Mayasan Lubis1, Melda Deliana, Hakimi
Pediatric Endocrinology Division, Child Health Department, Medical School, University of Sumatera Utara, H.Adam Malik Hospital, Medan, Indonesia.

Background: Osteogenesis imperfecta (OI) is a genetic disorder with increased bone fragility and low bone mass, the incidence has been estimated at 1 in per 10000-20000 births, however milder forms of OI are probably under recognized. Cyclical intravenous therapy with the biphosphonate pamidronate has been reported to be beneficial in children and adolescents with moderate to severe forms of OI.

Objective: To report the challenges in managing osteogenesis imperfecta patients in H. Adam Malik Hospital, a referral hospital in North Sumatera, Indonesia.

Case: From July 2011 until now, we have 5 cases of OI in our hospital; all of them were type 3. The youngest was 3 days old and the oldest was 9 years old, all of them were male. These patients have well defined phenotypes, including extremely short stature, progressive limb and spine deformities. We found respiratory problems in 2 patients, a 3 days and 2 months old baby. Diagnosis was based on clinical and radiology examination (bone survey). All of them came from low social economic status, and only 2 patients had government health insurance. The major problem in managing OI patients is the treatment, intravenous pamidronate was not available in our province therefore we must order it from our national referral hospital in Jakarta. Moreover, the price was expensive, and it was not covered by health insurance. Only 1 patient received this treatment and only for 1 cycle. One patient died at home because of respiratory problem. BMD or DXA was also not available in our province.

Conclusion: Managing OI patients in our hospital is still be a big challenge especially regarding the treatment, needing collaboration from all the part concerning the patients, including attention and support from the government, community, and medical provider.

P163
Solitary parathyroid adenoma presenting with spine fracture in a paediatric patient
Marichi P Mabulac1, Carol Boongaling, Siksano Chan-Cua
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Background: Solitary parathyroid adenoma is a rare cause of primary hyperparathyroidism in children. We report a case of patient who presented with difficulty in ambulating due to fracture from hypercalcaemia.

Case: A. A. 16 years old, female referred to our service for evaluation of hypercalcaemia. The patient presented with fracture at the thoraco-lumbar spine after being accidentally slipped on the floor. She sought consult at a private hospital and an orthopedic brace was applied. Three months after the incident, the patient complained of limping and eventually with difficulty in ambulating. She was admitted at the Philippine Orthopedic Center for spinal traction. During her admission, there was an incidental finding of hypercalcaemia and the patient was referred to our institution for endocrine evaluation. The patient had history of easy fatigability, palpitations, polyuria, polydipsia, constipation (2x/week), sweating associated with weight loss about half a year prior to her recent admission. On physical examination, patient was ambulatory but limping, not in respiratory distress. Vital signs showed: BP: 100/60, HR: 96/min, RR: 20/min, afebrile. Weight: 28.6 (<2SD), Height: 136.5cm (<3SD), BSA: 1.04, BMI: 15.37, MPH: 145.75cm. Laboratory assessment showed serum calcium 13.3 mg/dl (8.6-10), ionized
calcium 2.13 mmol/L (1.10-1.35), serum intact PTH > 2500 pg/ml (15-68.3), phosphorous 1.52 (1.30-2.26), alkaline phosphatase 178 IU/L (32-91). KUB ultrasound showed bilateral enlarged kidneys. Thyroid ultrasound revealed a 1.7x1.6cm fluid nodule on the left lobe but the thyroid hormone profile was normal. The Technetium-99m Sestamibi scan showed parathyroid adenoma in the inferior left thyroid bed. The patient underwent total parathyroidectomy with autotransplantation of the remaining parathyroid at (L) forearm. Post-operatively, she had “hungry bone syndrome” due to persistent hypocalcemia 5.5 mg/dL (8.6-10) and urinary calcium/creatinine ratio of less than 0.05 spite of calcium and calcitriol supplementation. The histopathologic finding was compatible with left parathyroid adenoma of 2.7x2.5x1cm dimension. Five months after the operation, the patient was asymptomatic and the serum phosphorous and alkaline phosphorus are within normal range.

Conclusion: Delayed diagnosis of hyperparathyroidism in children can often result in significant morbidity. Serum calcium and PTH levels should be checked in children presenting with non-specific symptoms as parathyroid adenoma section is curative and usually restores serum calcium levels back to normal, thereby avoiding further complications.

**P164**

**Six monthly intravenous zoledronic acid in childhood osteoporosis**

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Childhood osteoporosis can be treated with intravenous bisphosphonates in order to improve bone mass and density. The aims of this study were to evaluate the safety and efficacy of six-monthly zoledronic acid (ZA) in children with osteoporosis.

A retrospective cohort study of 27 patients (16 males and 11 females) were treated with six-monthly ZA (0.05mg/kg/dose) for a minimum of one year. 17 patients were immobile, 4 had steroid-induced osteoporosis, 2 had osteogenesis imperfecta and 4 had other diagnoses. 16/27 (59%) had long bone fractures and 12/27 (44.4%) had vertebral wedging at baseline. Mineral homeostasis, bone mineral density by DXA and vertebral morphometry were evaluated at baseline and 1 year.

The median age at commencement of treatment was 12.3 years (range 8-15.8). Following the first infusion, 2/27 (7%) and 1/27 (4%) developed asymptomatic hypocalcemia at 48 hours and 72 hours, respectively. A fever above 38°C developed in 14/27 (52%), generalised aches/pains in 13/27 (48%) and nausea in 6/27 (22%). At 1 year there was a significant reduction in bone turnover and improvement in bone mineral density (BMD) (see Table 1). Patients with vertebral wedging at baseline showed significant improvement in anterior, middle and posterior vertebral height ratios at 1 year. Only one patient fractured after starting ZA. There was normal growth.

Six monthly ZA was associated with an acute phase reaction to the first dose and improvement in BMD, reduction in bone turnover and improved vertebral shape at 1 year.

**Table 1 (abstract P164) Mineral homeostasis and DXA data at baseline and 1 year**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mmol/L)</td>
<td>2.38 (2.35-2.44)</td>
<td>2.36 (2.28-2.42)</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>188 (143-271)</td>
<td>148.5 (127.25-205.5)*</td>
</tr>
<tr>
<td>Osteocalcin (nmol/L)</td>
<td>7.9 (4.35-11.35)</td>
<td>2.5 (1.1-3.95)*</td>
</tr>
<tr>
<td>25-OH-Vitamin D (nmol/L)</td>
<td>75 (67-94)</td>
<td>76 (57.5-80)</td>
</tr>
<tr>
<td>Parathyroid hormone (pmol/L)</td>
<td>3.5 (2.3-4.1)</td>
<td>3.7 (2.9-5.4)</td>
</tr>
<tr>
<td>Total body aerial BMD Z-score</td>
<td>-0.56 (-1.7 to 0.35)</td>
<td>-0.03 (-1.13 to 0.86)*</td>
</tr>
<tr>
<td>L2-4 aerial BMD Z-score</td>
<td>-1.73 (-2.43 to -0.96)</td>
<td>-0.37 (-1.44 to 0.09)*</td>
</tr>
<tr>
<td>Bone mineral content for lean tissue mass Z-score</td>
<td>-1.68 (-2.51 to -0.60)</td>
<td>-0.10 (-0.9 to 1.35)*</td>
</tr>
</tbody>
</table>

Values represent median (interquartile range), asterisk represents p<0.05 compared to baseline.

**P165**

**Non-transfusion dependent hemoglobin E/β thalassemia had high prevalence of vitamin D deficiency than more severe patients who received regular blood transfusion and iron chelation therapy**

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Hb E/β thalassemia is the most common β thalassemia syndrome in Asia-Pacific due to a high prevalent of Hb E and β thalassemia genes. Management of this condition can be cumbersome due to its clinical heterogeneity and various disease severity ranging from severe end in which patients are transfusion dependent thalassemia (TD) similar to that of β thalassemia major (TM) to moderate and mild severity which are non-transfusion dependent thalassemia (NTDT) akin to β thalassemia intermedia. Although, clinical diagnosis of Hb E/β thalassemia might be identical, the natural history and disease related complications can vary greatly due to different baseline severity and management received. In this study, we evaluated vitamin D deficiency, one of the most common endocrine complications described in TM, in Thai HbE/β thalassemia children who were TD and NTDT.

109 children aged 5.9 to 14.1 years with HbE/β-thalassemia were enrolled. 60 patients who received no or occasional transfusion were classified into NTDT group. While 49 patients who received regular transfusion every 3 weeks to keep pre-transfusion Hb at 9-10 g/dL were classified into TD group. All TD patients except two received iron chelation. Blood samples were collected to determine hemoglobin, serum ferritin and 25-OHD levels. Mean Hb of NTDT was lower than TD patients (8.1±1.0 vs. 10.0±1.0 g/dL, P<0.001). In contrast, TD had higher mean serum ferritin than NTDT patients (4104±2336 vs. 347±488 ng/mL, P<0.001). However, mean serum 25-OHD of NTDT was lower than in TD patients (22.7±5.2 vs. 25.0±10.6 ng/mL, P=0.043). Moreover, the percentage of patients who were vitamin D deficient (serum 25-OHD < 20 ng/mL) in NTDT was higher than TD patients (33.3% vs. 12.2%, P=0.01). We found no correlation between serum 25-OHD vs. ferritin and Hb levels. Although patients with HbE/β thalassemia do not require regular blood transfusion due to their ‘milder’ clinical severity, they remain at high risk of having vitamin D deficiency. A better standard of care for these neglected patients is in an urgent need and a regular monitoring of serum 25-OHD with adequate vitamin D supplementation for deficient patients is highly recommended for all HbE/β thalassemia regardless of their clinical severity.

**P166**

**Osteogenesis imperfecta in children: Indonesian experiences**

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Management of this condition can be cumbersome due to its clinical heterogeneity and various disease severity ranging from severe end in which patients are transfusion dependent thalassemia (TD) similar to that of β thalassemia major (TM) to moderate and mild severity which are non-transfusion dependent thalassemia (NTDT) akin to β thalassemia intermedia. Although, clinical diagnosis of Hb E/β thalassemia might be identical, the natural history and disease related complications can vary greatly due to different baseline severity and management received. In this study, we evaluated vitamin D deficiency, one of the most common endocrine complications described in TM, in Thai HbE/β thalassemia children who were TD and NTDT.

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This was a cross sectional study involving 120 children aged 7-12 years from two different elementary schools in Jakarta. We used structured questionnaire on life style and performed thorough clinical examinations to all participants. We measured the serum level of calcium, phosphate, bone-alkaline phosphatase (BALP), and 25(OH)D. The 25(OH)D level classified as sufficient if ≥ 32 ng/dL, insufficient 15-31 ng/dL, and deficient if <15 ng/dL. Sun-exposure was analyzed based on duration of exposure per week. The association between vitamin D and contributing factors was analyzed using chi-square with significant value at 0.05.

Results: Of 120 children (45 boys and 75 girls), 78.3% were classified as brown (4th degree of Fitzpatrick scale) in skin tone. Most of the children (52.5%) were well-nourished, while 21.7% were obese. Vitamin D insufficiency was found in 75.8% of the subjects, while 15% of the subjects were classified as vitamin D deficiency. Calcium level was low in 16.7% subjects, while the phosphate level was found to be in the normal range for all subjects. Bone alkaline phosphatase was normal in 31.6% subjects. Vitamin D status was not associated with duration of sun exposure (χ², P=0.143), and there were no difference in vitamin D status between the obese and non-obese subjects (P=0.65). Skin tone, clothing style, sunblock usage, and milk consumption did not influence vitamin D status (P=0.08, P=0.43, P=0.05, respectively).

Conclusion: There is high prevalence of vitamin D insufficiency in healthy children aged 7-12 years in Indonesia. Girls have increased risk compare to boys. This result should increase the awareness of health professionals and society regarding vitamin D status in Indonesian children.

**P167**

**Vitamin D profile in healthy children aged 7-12 years old in Indonesia**

Frida Soesanti, Aman Pulungan, Bambang Tridjaya, Jose RL Batubara

**Background:** The recent data on the vitamin D showed a surprising result, which exhibited in high prevalence of vitamin D deficiency and insufficiency in children and adolescence. This is not only occurs in country that lies in high latitude but also in sun rich country. Many factors contributing to this condition, including changing in life style. No data available regarding vitamin D status in healthy children in Indonesia.

**Aims:** To find out vitamin D profile of healthy children in Indonesia and factors associated with vitamin D status in those children.

**Methods:** This was a cross sectional study involving 120 children aged 7-12 years from two different elementary schools in Jakarta. We used structured questionnaire on life style and performed thorough clinical examinations to all participants. We measured the serum level of calcium, phosphate, bone-alkaline phosphatase (BALP), and 25(OH)D. The 25(OH)D level classified as sufficient if ≥ 32 ng/dL, insufficient 15-31 ng/dL, and deficient if <15 ng/dL. Sun-exposure was analyzed based on duration of exposure per week. The association between vitamin D and contributing factors was analyzed using chi-square with significant value at 0.05.

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**P168**

**The Effect of Cumulative Dose of Glucocorticoids on Bone in Children with Inflammatory Bowel Disease (3-year Follow-up study)**

S Tomkova, E Majarová, P Vanušová, J Payer

**Background:** The aim of the study was to evaluate the effect of cumulative dose of glucocorticoids during 3 years on bone mineral density (BMD) and bone turnover (BMT) measurement in children suffering from inflammatory bowel disease (IBD).

**Patients and Methods:** In cohort of 64 children with IBD (54 children with Crohn disease and 10 with Ulcerative colitis) we measured bone mineral density at the time of diagnosis and two times during follow-up. Bone turnover/osteocalcin (OC) and C-terminal telopeptide of type I collagen (CTX) was measured using ELISA same time as BMD. All patient were treated by glucocorticoids with average of cumulative dose 4.46g. The obtained results were analyzed using correlation analysis.

**Results:** At the time of diagnosis we observed the total body BMD Z-score – 1.7 (mean ± SD). There was no change during the treatment (1.77 resp. 1.69 Z-score). The level of CTX and osteocalcin paradoxically increased, but there was no statistical significance.

**Conclusion:** In our study we didn’t find correlation between BMD, cumulative dose of glucocorticoids, CTX and osteocalcin during period of 3 years. Insignificant increase of bone markers was established. According to our results we can speculate that bone status impairment of bone mass is independent in children with IBD on treatment with glucocorticoids regarding to inflammation itself.

**P169**

**Effect of osteogenesis imperfecta on children and their families**

Vu Chi Dung, Kate Armstrong, Can Thi Bich Ngo, Bui Phuong Thao, Nguyen Ngoc Khanh, Nguyen Thu Trang, Nguyen Thi Hoan, Nguyen Phu Dat, Craig Munns

**Background:** The aim of the study was to evaluate the effect of cumulative dose of glucocorticoids during 3 years on bone mineral density (BMD) and bone turnover (BMT) measurement in children suffering from inflammatory bowel disease (IBD).

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**Osteogenesis Imperfecta (OI) is a heterogeneous genetic disorder, with features that include increased bone fragility, pathological fractures, blue sclera, dentinogenesis imperfecta and conductive or mixed hearing loss. Clinical variability is wide from children with few fractures and normal stature to children with multiple fractures, long bone deformity, scoliosis and extreme short stature. Although there is no curative treatment, there are several therapeutic tools capable of improving the course of the condition and patient quality of life. We aim to evaluate the effect of OI on the well being of children with the disorder and their families through a family-centered questionnaire. Sixty children with OI from the Vietnam National Hospital of Pediatrics and/or their parent(s), who attended the first annual family support group in 2011, completed a child and parent questionnaire. 60 patients participated, 26 female and 34 male. The median age was 6.0 years (Interquartile range (IQR) 0.25 - 18 years). Of these, 36 (60%) had dentinogenesis imperfect and 22 (38.3%) had a scoliosis. The median number of fractures was 6.0 (IQR 0 – 30) and median number of...
hospitalizations due to OI was 5.0 (IQR 0-30). Among patients of school age, 9 (15%) could not go to school due to OI. Almost all parents (93.7%) worried about school social communication of the patients. Among these parents, 100% fear of inferiority with friends and 98.3% fear of broken bones. Most parents (76.2%) were significantly concerned about their child’s health. The parents’ themselves reported psychological concerns, with feelings of desperation (58.4%), anxiety (81.7%) and depression (56.7%).

Osteogenesis imperfecta appeared to have a significant deleterious effects on the life of the patients and their families. These data provide a baseline from which to evaluate the effectiveness of interventions to improve the medical and psychological needs of this cohort and their families.

P170

A rare cause of primary hypoparathyroidism due to a novel mutation in the GATA3 gene – the Barakat syndrome

SMY Wong1, WM But1, Angel Chan1, W Chan1

1Department of Paediatrics, Queen Elizabeth Hospital, Hong Kong;
2Department of Pathology, Queen Elizabeth Hospital, Hong Kong


Barakat syndrome, also known as HDR syndrome (hypoparathyroidism, deafness and renal dysplasia), is a rare autosomal dominant disorder, secondary to mutation of the GATA3 gene which is located at chromosome 10p. The GATA3 protein is one of the transcription factors which play an essential role in the embryonic development of the parathyroids, inner ears and kidneys.

We report a Chinese patient who presented with hypocalcaemic convulsion at day 11 of life due to primary hypoparathyroidism. Her serum calcium became normalized with calcium and vitamin D supplement. There was no other clinical feature to suggest DiGeorge syndrome and no family history of hypocalcaemia. The exact cause of hypoparathyroidism was not known at that time. At 6 months of age, she developed the first episode of E-coil urinary tract infection. Ultrasonogram of the kidney was normal but voiding cystogram revealed an intra-renal reflux of right kidney with dilated right ureter. Prophylactic antibiotics was prescribed. However, she developed repeated urinary tract infection with febrile seizures at 13 months and 15 months old respectively. Re-implantation of the right ureter was hence performed at 2 years of age. At the same time, she failed hearing screening test at her regular health assessment and audiometry showed bilateral hearing deficit. When she was reassessed at ten years of age, she enjoyed good health with only mildly deranged renal function.

In view of the presence of hypoparathyroidism, sensorineural hearing deficit and renal anomaly, Barakat syndrome was suspected and genetic analysis of the GATA3 gene was performed at nine years of age. A heterozygous novel mutation, c.1917_1922delCA, was detected in intron 3 of the GATA3 gene. This mutation was not detected in her parents, suggesting that it is a de novo mutation. In conclusion, this is the first case report of a southern Chinese patient with Barakat syndrome diagnosed nine years after the initial presentation with hypoparathyroidism. Barakat syndrome is an extremely rare clinical entity and delayed diagnosis is not uncommon. Physicians should be aware of this condition for early diagnosis and family screening.

P171

Waist to height ratio; a simple and valid index for metabolic syndrome in Korean adolescents

In-Hyuk Chung1, Sang Shin Park2, Eun-Gyung Yoo1

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The incidence of metabolic syndrome (MS) is increasing in adolescents, which can lead to major health threats in the future. Body mass index (BMI) and waist circumference (WC) are commonly used for identifying adolescents at higher risk for MS, but BMI is not a measure of fat distribution, and different BMI and WC cut offs are used according to age. Waist-to-height ratio (WHtR) can be a good indicator for MS, because it includes WC, a good proxy for visceral adiposity. Same WHtR cut off might be used throughout adolescence because it accounts for growth in height by age. We evaluated the validity of WHtR, when compared to BMI and WC, in identifying adolescents with MS.

We analyzed data for 4,068 adolescents aged 10-18 years from the Korean National Health and Nutrition Examination Surveys conducted between 1999 and 2008. MS was defined by International Diabetes Federation criteria. The receiver operating characteristic (ROC) curve was used to determine the ideal WHtR cut off. Area under the curve (AUC), sensitivity and specificity of WHtR for identifying MS were calculated from the ROC curve, and compared with those of BMI (≥ 95P for age and sex) and WC (≥ 90P for age and sex).

The prevalence of MS was 2.4% in boys, 2.1% in girls. The ideal WHtR cut off was 0.51 (sensitivity 94.3%, specificity 94.4%) for boys, and 0.48 (sensitivity 100%, specificity 87.6%) for girls. In ROC curve analysis, the AUC of BMI, WC and WHtR were 0.957, 0.971 and 0.966 in identifying MS for boys and 0.935, 0.965 and 0.961 for girls, respectively. For boys, the sensitivity of BMI, WC and WHtR (≥0.51) was 65.4%, 100% and 98.1% and specificity was 95.5%, 89.6% and 89.3%, respectively. For girls, sensitivity of BMI, WC and WHtR (≥0.48) was 67.5%, 97.5% and 100% and specificity was 94.7%, 90.8% and 87.8%, respectively. WHtR is a simple and valid index for predicting MS in adolescents. WHtR is almost as useful as WC, and it has the advantage that age specific reference tables are not required.

METABOLIC

P172

Targeted suppression of glutaryl-CoA dehydrogenase by lentivirus-mediated shRNA and excessive intake of lysine induce the apoptosis of rat striatal neurons

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Aims: In Glutaric aciduria type 1 (GA1), Glutaryl-CoA dehydrogenase (GCDH) deficiency has been responsible for accumulation of glutaric acid (GA) and striatal degeneration. However, the mechanisms by which GA1 induces striatal degeneration remain unclear. In this study, we aimed to establish a novel neuron model of GA1 and explore the underlying mechanisms of striatal lesion.

Methods: Four short hairpin RNA (shRNA) sequences targeting the GCDH gene (NM_001108896) were designed to construct four recombinant lentiviral vectors. The effectiveness of gene silencing in rat striatal neurons was detected by real-time reverse transcription polymerase chain reaction (RT-PCR) and Western blotting techniques. GCDH deficiency neurons (GCDH-/- neurons), neurons transfected with negative control virus (NC neurons) and not intervention neurons (C neurons) were all incubated with lysine for 24h in concentrations of 0mmol/L, 5mmol/L, 10mmol/L respectively. The viability was measured with 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl-tetrazolium bromide (MTT). The apoptosis of the neurons were detected by Hoechst33342 and PI. Tetramethylrhodamine methyl ester (TMRE) was used to determine the change of mitochondrial membrane potential. The expression of caspase-3, 8, 9, Bax and Bcl-2 were examined by RT-PCR and Western blotting.

Results: The efficiency of gene silencing of lentivirus-mediated shRNA was up to 60%, compared with the parental and control groups. The viability of C neurons, together with mitochondrial membrane potential and expression of caspase-3, 8, 9, Bax/Bcl-2 was not influenced by lysine, even when the concentration was 10mmol/L. The viability of NC neurons was significantly higher than GCDH-/- neurons, when with 5mmol/L lysine interference. When without lysine, there is no difference between the two. Moreover, 5mmol/L lysine could induce GCDH-/- neurons apoptosis, and 10mmol/L lysine could induce NC neurons apoptosis. In these apoptotic neurons, the mitochondrial membrane potential decreased, the expressions of caspase-3, 8, 9, Bax all increased significantly and Bcl-2 expression decreased, compared to normal cells.

Conclusions: These results indicated that targeted suppression of GCDH by lentivirus-mediated shRNA and excessive intake of lysine may be useful as a neuron model for the study of GA1. It also showed mitochondrial apoptotic pathway may be involved in the GA1-induced striatal lesion.
P173
A Chinese boy with episodic ataxia and low CSF glucose
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A 3-year-8-month-old Chinese boy presented with acute exacerbation of ataxia precipitated by a viral illness. Past health revealed a clumsy boy with unsteady gait all along associated with moderate language and gross and fine motor delay but relatively preserved cognitive function. He was born normally at full term to non-consanguinous parents. There was no history of perinatal asphyxia or convulsion. The movement problem was paroxysmal, worse in early morning and during sick days. No history of any drugs was taken. Examination revealed a conscious boy with normal growth and head size. He had cerebellar ataxia with wide-based unsteady gait, truncal ataxia, intentional tremor and horizontal nystagmus. Cranial nerves, muscle tone, power and reflexes were normal. Gross sensation and hearing were normal. No skin rash, telangiectasia or neurocutaneous stigmata was noted. MRI was normal. CSF showed a lowish glucose of 1.9 mmol/l at a blood glucose of 4.8 mmol/l (CSF/blood glucose ratio 0.4). Lactate and other biochemistries were normal, viral and bacterial cultures were negative. In view of the episodic nature with acute exacerbation during viral illnesses, congenital metabolic disease was highly suspected. Metabolic screening including plasma and urine amino acids, urine organic acids, plasma carnitine/acylcarnitine, ammonia, very-long-chain-fatty-acid, lysosomal enzymes, transferrin, copper, ceruloplasmin and pre and post meal lactate, pyruvate, betahydroxybutyrate, acetoacetate and glucose were all normal. Glucose transporter defect was suspected. However, common mutation SLC2A1 gene (1p35-31.3) for glucose transport protein (GLUT1) deficiency was not detected. Erthrocyte uptake test showed decreased glucose uptake. The clinical features together with low CSF glucose and decreased erythrocyte uptake were compatible with GLUT1 deficiency. Ketogenic diet with modified Atkins diet was started. Ataxia showed marked improvement. The diet was well-tolerated. No adverse effect was noted. GLUT1 deficiency commonly presents with infantile epileptic encephalopathy, movement disorder, progressive microcephaly and psychomotor retardation. It is inherited as an autosomal recessive disorder, 70-80% associated with SLC2A1 gene (1p35-31.3) mutation. The prognosis is good with early diagnosis and treatment with ketogenic diet (KDI). Recent research reported similar efficacy to classical KD with lower ketogenic ratios (2:1 or 1:1), such as medium-chain-triglyceride oil diet, modified Atkins diet, and low-glycemic-index treatment. These allow better tolerability and less adverse effects. Further research makes KD more widely available, effective and safer.

P174
A case of sitosterolaemia with stomatocytic anaemia and thrombocytopenia treated with Ezetimibe with good response
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Sitosterolaemia is a rare autosomal recessive lipid disorder characterized by increased absorption of plant sterols in the gut and decreased biliary excretion of sterols causing accumulation of plasma sterols, which can lead to premature atherosclerosis. Here we reported a boy presented with multiple tuberous xanthomas at 4-year sold and was diagnosed sitosterolaemia [1]. The fasting plasma total cholesterol and low-density lipoprotein (LDL) cholesterol levels were 18.3 mmol/L and 16.41 mmol/L respectively. Gas chromatography and mass spectrometry showed that the fasting plasma sterols contained elevated beta-sitosterol 880 µmol/L (Reference range <12 µmol/L), campesterol 489 µmol/L (Reference range <17.5 µmol/L) and stigmasterol 38.9 µmol/L (Reference range <3.5 µmol/L). Molecular study identified compound heterozygous mutations (R419H and IVS12-1G→A) in the adenosine triphosphate (ATP) binding cassette subfamily G, member 5 (ABCG5) gene.

Initial management included dietary restriction in cholesterol and plant sterols and cholestryramine treatment. The total cholesterol and LDL cholesterol levels decreased.

However, common mutation SLC2A1 gene (1p35-31.3) mutation. The prognosis is good with early diagnosis and treatment with ketogenic diet (KDI). Recent research reported similar efficacy to classical KD with lower ketogenic ratios (2:1 or 1:1), such as medium-chain-triglyceride oil diet, modified Atkins diet, and low-glycemic-index treatment. These allow better tolerability and less adverse effects. Further research makes KD more widely available, effective and safer.

Table 1(abstract P174)

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References
Geneotype and phenotype in 20 patients with glycogen storage disease type Ia

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Background: Glycogen Storage Disease Type Ia (GSD Ia) is a group of autosomal recessive inborn errors of metabolism that is caused by deficiency in glucose-6-phosphatase, and it is the major subtype of Liver Glycogen Storage Disease(LGSD) cases. Patients afflicted with GSD Ia cannot maintain glucose homeostasis and manifest hypoglycemia, hepatomegaly, lactic academia. However, we cannot separate GSD Ia from LGSD through clinical manifestations and routine laboratory tests, except for analysis of G6PC gene mutation and assay of glucose-6-phosphatase enzyme activity, which is an invasive method. Therefore, the analysis of G6PC gene mutation is an important method for diagnosing GSD Ia.

Objective: To investigate the G6PC gene mutations in patients with Glycogen Storage Disease type Ia (GSD Ia), and analyze the relationship of its genotype and phenotype.

Methods: We diagnose 48 patients with LGSD by clinical manifestations, laboratory tests and glucagon test. The entire coding region of the G6PC gene from peripheral blood was screened by PCR combined with direct DNA sequencing. The G6PC genes of 50 unrelated healthy children were investigated as comparisons to rule out gene polymorphism. We used software named DNAMAN to analyze their conservativeness through many species homology comparison.

Results: Among 48 patients, there were 41.67%(20/48) of them were found to have G6PC gene mutations. Totally eight types of G6PC gene mutations were detected, which were 727G>T, R83H, H119L, L173P, I341N, V888fsX54, C109T and W878fsX270, and 727G>T and R83H were more frequent, with frequencies of 37.50%(15/40) and 22.50%(9/40), respectively. C109T and W878fsX270 were never reported before. Our clinical and routine laboratory data showed that the patients manifested the same phenotype even with different genotype.

Conclusions: Our study revealed 727G>T and R83H mutations were prevalence in Chinese patients with GSD la. C109T and W878fsX270 might be novel pathogenic mutations. There was no clear relationship between genotype and phenotype.

Short term outcome of congenital hyperinsulinism: case series

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Introduction: Congenital hyperinsulinism (CH) is a major cause of recurrent hypoglycaemia in neonates and infants, results in varying degrees of neurological impairment. Advances in molecular study and imaging technique have been used to guide treatment option for CH. However, there were centres treating CH with long-term medications and reported good neurodevelopmental outcome.

Objective: To describe short-term outcome of infants with CH in Putrajaya Hospital, Malaysia.

Method: Medical data of all patients diagnosed with CH between 15 October 2007 and 31 December 2011 was retrieved from electronic medical record. Their clinical features and treatment outcome were reviewed. The current study was performed in Exeter, United Kingdom.

Results: Five infants were reported. Hypoglycaemic seizure was the commonest presenting feature. All had detectable insulin level (>5 mU/l) during hypoglycaemic episodes and high glucose requirement (>10 mg/kg/min). Three patients were found to have genetic mutation associated with CH. Patient 1 had hyperammonaemia hyperinsulinism syndrome and corresponded missense mutation of GLUD1 gene. For past 2.5 years, there was good response to diazoxide treatment. Patient 2 had diffuse disease with homozygous mutation at the ABCC8 gene. She presented at birth with severe disease and required combination of medications including octreotide. It was complicated by epilepsy, and developmental milestones were mildly delayed. Patient 3 inherited a heterozygous mutation in the KCNJ11 gene from the father (presumed focal disease). He responded only to octreotide and showed normal development at nine months old. Another two patients had no common mutation detected. Patient 4 required combination of therapy initially, but subsequently treated with diazoxide alone and weaned off nasogastros feeding at five years old. Patient 5 had features suggestive of Beckwith-Wiedemann syndrome and did not respond to all medical therapies. Pancreactomy was performed at 3 months old and he died from complications of surgery.

Conclusion: Molecular genetic study is useful in the management of neonates and infants with CH. Patients with focal and diffuse disease were shown to respond to medical therapy.

21 hypoglycemia cases with hyperinsulinisma

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Congenital hyperinsulinemic hypoglycemia (CHI) is the common cause of severe hypoglycemia in infancy. Profound hypoglycemia requires appropriate diagnosis and aggressive treatment to prevent severe and irreversible brain damage. Here we report 21 Japanese hypoglycemia cases with severe hyperinsulinemia.

We report 16 CHI cases, 2 HIHA cases, 1 GSD1b case and 2 PSS cases. 12 cases of CHI had severe episodes of cardiac arrest or seizure in neonatal period, 3 cases of CHI had seizure in infancy, 1 case of CHI had hypoglycemia in infancy. Neonatal-onset CHI cases were treated by octreotide and glucagon at the start. 4 cases of CHI (3 of them had KCNJ11 mutation) were treated as diabetes after pancreatic excision. We will perform pancreatic partial excision to 1 case of CHI who had paternal mutation of ABCC8. 1 case of CHI with ABCC8 mutation is on good control by only diet therapy. We stopped the treatment by diazoxide to 4 cases of CHI until 10 years old. Acuity of the them was varied on the onset. 5 cases of CHI is still treated by diazoxide. HIHA cases had seizure in infancy. They are on good control by diazoxide. GSD1b case had severe hypoglycemia in neonatal period. He was treated as CHI patient by diazoxide. He was diagnosed as GSD1b by hepatomegaly. After live-donor liver transplant, he is on the good control without medication. 1 of PSS cases had hypoglycemia in babyhood. He was cured by surgery. 1 of PSS cases had severe hypoglycemia attack in neonatal period. His family did not choose surgery, so he is still treated by diazoxide.

Three-quarter of CHI cases had severe hypoglycemic attack in neonatal period. Some cases needed surgery, some cases could be controlled by internal therapy and could be cured. 5 cases had hyperinsulinemia except CHI cases. Some cases showed hyperammonemia except HIHA. Correct diagnosis for hypoglycemia cases with hyperinsulinemia needs not just blood test but also imaging or genetic testing.

A discordant of blood glucose analysed by Glucometer and the Central lab method in an infant with Galactosemia

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Galactosemia is an autosomal recessive disorder, which caused by a deficiency of one of three enzymes that involved in the metabolism of galactose: galactokinase (GALK), galactose-1-phosphate uridylyltransferase...
In Southern China, the major IEM were organic aciduria (6 cases), glutaric aciduria (2 cases), maple syrup urine disease (2 cases), very long-chain acyl-CoA dehydrogenase deficiency (4 cases), 3-hydroxy-3-methylglutaryl-CoA dehydrogenase deficiency (2 cases), propionic aciduria (48 cases), and methylmalonic aciduria (MMA) was most common (48 cases), followed by urea cycle disorders (21 cases), phenylketonuria (20 cases), and propionic aciduria (48 cases). The age at diagnosis was early and incidence of IEM disorders and amino acid disorders. The results of this study extend the knowledge of the molecular genetics, phenotype, and outcome behind congenital HH in Vietnam.

P179
Molecular genetics and phenotype of 26 Vietnamese patients with congenital hyperinsulinism
Vu Chi Dung1, Nguyen Thanh Lien1, Bui Phuong Thao1, Nguyen Ngoc Khanh2, Can Thi Bich Ngo3, Nguyen Thi Hoan1, Khu Thi Khanh Dung1, Le To Nhu1, Dang Anh Duong1, Nguyen Phu Dat5, Sarah Flanagan1, Can Thi Bich Ngoc1, Dang Anh Duong1, Nguyen Ngoc Khanh2, Minh Thi Nguyen3, Huy Thanh Nguyen4, Nguyen Thi Hoan1

Hyperinsulinemic hypoglycemia (HH) is a consequence of unregulated insulin secretion by pancreatic ß-cells and is a major cause of hypoglycemic brain injury and mental retardation. Congenital HH is caused by mutations in genes involved in regulation of insulin secretion, seven of which have been identified (ABCC8, KCNJ11, GLUD1, CGK, HADN, SLC16A1 and HNF4A). Severe forms of congenital HH are caused by mutations in ABCG8 and KCNJ11, which encode the two components of the pancreatic ß-cell ATP-sensitive potassium channel (sulfonylurea receptor SUR1) and the inwardly rectifying ion channel Kir6.2). Activating mutations in the subunit genes of ATP-sensitive potassium channel can result in monogenic diabetes, whereas inactivating mutations are the most common cause of congenital hyperinsulinism of infancy.

We aim to identify mutations of ABCG8; KCNJ11 and HNF4A in Vietnamese patients with congenital HH, to describe the phenotype, and to evaluate outcome of these patients. This is a case series study including phenotype, genotype characteristics and outcome. Twenty six Vietnamese probands with congenital HH were analyzed for alterations in ABCG8; KCNJ11 and HNF4A. All exons of KCNJ11; ABCG8 and HNF4A genes were amplified from genomic DNA and directly sequenced. In patients with detected mutations, the parental origin of each mutation was determined.

P180
Detection of inborn error of metabolisms by urine organic acid GC-MS in Southern China
MinYan Jiang1, Li Liu, HuiFen Mei, XuZhen Li, Jing Cheng, YanNa Cai, Wen Zhang, XiaoJan Mao, Zhun Lu

Background: Inborn error of metabolisms (IEM) have been detected worldwide using gas chromatography mass spectrometry since 1980s, but few related date presently exit in Southern China. This study aimed to evaluate the prevalence, spectrum and clinical presentation of IEM in Southern China.

Method: From January 2009 to March 2012, 16075 urine samples were collected from patients with developmental delay, seizures, vomiting and metabolic acidosis in Guangzhou Women and Children's Medical Center.

Results: We diagnosed 148 cases of IEM by urine GC-MS analysis, including 97 cases of organic acid disorders, 41 cases of amino acid disorders and 10 cases of fatty acid oxidizing disorders. Methylmalonic aciduria (MMA) was most common (48 cases), followed by urea cycle disorder (21 cases), phenylketonuria (20 cases), propionic aciduria (11 cases), multiple carboxylase deficiency (8 cases), glutaric aciduria type I (7 cases), oxoprolinemia (7 cases), isovaleric aciduria (6 cases), glutaric aciduria type II and Short chain acyl-CoA dehydrogenase deficiency (4 cases), 3-hydroxy-3-methylglutaric aciduria (3 cases), and amionic aciduria (2 cases), maple syrup urine disease (2 cases), very long-china acyl-CoA dehydrogenase deficiency (2 cases), Malonic aciduria (1 case), Canavan disease (1 case) and mevalonic aciduria (1 case). Average age at diagnosis was 18 months. Prompt therapy was taken, including dietary and medical treatment. Clinical improvements were observed in more than half of the patients.

Conclusion: In Southern China, the majority of IEM were organic acid disorders and amino acid disorders. Fatty acid oxidation disorders were relatively rare. The age at diagnosis was early and incidence of IEM gradually decreased with the age. Urine GC-MS was an important technique to diagnose IEM, which helped to improve patients' prognoses.

P181
First case report of short-chain acyl-CoA dehydrogenase deficiency in China
MinYan Jiang, Li Liu5, MinZhi Peng, CuiLi Liang, HuiYing Sheng, YanNa Cai

Short-chain acyl-CoA dehydrogenase deficiency (SCADD) is a rare autosomal recessive inborn error of mitochondrial fatty acid oxidation. It is caused by mutations as well as polymorphic susceptibility variants. The two polymorphic susceptibility variants of SCADD gene, c.625G>A and c.322G>A, was detected. As its highly variable clinical characteristics, there is no related report in China. This report broadens the phenotype...
and genotype of SCAD deficiency in China and underlines the difficulty of diagnosis.

P182
Long-term outcome of a child with hyperinsulinism-hyperammonaemia syndrome
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Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong SAR, China

Aims: Clinical features of hyperinsulinism-hyperammonaemia syndrome are variable. A potential genotype-phenotype correlation of GLUD1 mutation and clinical features has been suggested. We here report the long-term outcome of a child with hyperinsulinism-hyperammonaemia syndrome.

Methods: A male infant was born at 38 gestational weeks with birth weight of 3605 g. He presented with convulsions at 28 days of life. Physical examination was unremarkable. He was initially treated as meningoencephalitis. CT brain was unremarkable. Bacterial and viral cultures were negative. Plasma glucose upon admission was 1.2 mmol/l with negative urine ketone. Glucose infusion was high up to 12.1 mg/kg/min.

Two sets of critical samples were obtained during hypoglycaemia. Workup for metabolic diseases was unremarkable. But ammonia levels were persistently high up to 252-353 μmol/l. Octreotide injection was started to achieve euglycaemia. Protein free diet was tried but without success in lowering ammonia levels. Octreotide was later switched to oral diazoxide and hydrochlorothiazide. Full enteral feeding was established with stable glucose levels.

Results: Genetic analysis showed a mutation in axon 10; Atn4101le (N4101), a mutation of AAC to ATC at codon 410. The diagnosis of hyperinsulinism-hyperammonaemia syndrome was confirmed. We follow the child until he is 6 years of age. Home blood glucose monitoring prevented him from hypoglycaemia. Fasting test was performed every year to fine tune his diazoxide dosage. He remained seizure free while ammonia levels remained high up to 123-218 μmol/l. Formal developmental assessment performed at 5 years of age showed delay in cognitive and speech development for 1-1.5 years, and attention-deficit hyperactivity syndrome.

Conclusion: Clinical features of hyperinsulinism-hyperammonaemia syndrome are variable. A genotype-phenotype correlation requires confirmation in larger series of patients.

P183
A new cell model of glutaric acidemia type I and the toxicity research
Cai Zhang, Xiaoping Luo
Tongji Hospital, Wuhan, China

Glutaric acidemia (GA-1) is an autosomal recessive disorder of lysine, hydroxylsine, and tryptophan metabolism caused by deficiency of glutaryl-CoA dehydrogenase. It results in the accumulation of 3-hydroxyglutaric and glutaric acid. Affected patients can present with brain atrophy and macrocephaly and with acute dystonia secondary to striatal degeneration in most cases triggered by an intercurrent childhood infection with fever between 6 and 18 months of age. The most common animal model of GA-1 is GCDH deficient mouse. We are trying to establish a new cell model of GA-1 to study the mechanism of neurotoxicity and for the future establishment of the new animal model.

Three Gcdh shRNA sequences were recombinated to the lentivirus vector carrying the GFP reporter gene. And the Gcdh-shRNA vector with the highest knock-down efficiency was transfected into the primary striatal neuron cells. Real-time PCR and Western Blot showed the knock-down efficiency was about 65%. And compared with the control group, the cells transfected with Gcdh shRNA vector shrunk obviously and gathered together, the neurites disappeared, and cell debris increased significantly. Hoechst staining of the nucleus showed the increased apoptotic rate in the knock-down group. MITT indicated the decreased mitochondrial function after Gcdh shRNA interference. These results suggest that Gcdh shRNA interference in rat primary striatal neuron cells could increase the apoptotic rate, which could due to the activation of mitochondria mediated apoptosis, triggered by the dysfunction of the mitochondria.

P184
Clinical, hormonal and chromosomal analysis of undervirilized male / 46XY DSD – a 3 years experience of national institute of child health
Inum Atta, Saira Lone, Yasir Naqi Khan, Mohsina Ibrahim, Jamal Raza
National Institute of Child Health, Karachi, Pakistan

Objective: To do the clinical, hormonal and chromosomal analysis in undervirilized male / 46XY DSD. To make a Presumptive diagnosis on the basis of clinical, chromosomal and hormonal assessment.

Methodology: This study was conducted in National Institute of Child Health at Department of Pediatrics, Division of Endocrinology from January 2008 to December 2010. A Total of 127 Patient under age of 4 years with ambiguity, micropenis, hypospadias, cryptorchidism and delayed puberty were selected and studied. USG Pelvis, HCG Stimulation test and Chromosomal analysis were carried out in all patients. Two types of HCG stimulation test were performed. Short HCG was done in children ten and less than ten years of age. Prolong HCG was performed in children more than ten years of age. Laproscopy and biopsy were carried out in patients who had Mullerian duct structure on USG and also in patients with no gonads. FISH analysis was done in patients who were 46XX karyotype with testes.

Result: Total no. of patients were 127. 43% presented with hypospadias, 17% with ambiguity, 20% with cryptorchism, 13% with micropenis and 5% with delayed puberty. HCG stimulation showed high response (pre and post-testosterone) in 29%, flat in 28%, partial in 27% and normal in 16% of patients. On chromosomal analysis 123 (97%) patients were turned out to be 46XY, 3(2%) patients were 46XX and 1(1%) patient was 46XXY. FISH analysis performed in 46 XX patients showed Y translocation in one patient. 8(6%) 46 XY DSD patients had both wolffian and Mullerian duct structure on ultrasonography. Laproscopy and biopsy performed in 4(3%) patients and proved ovotesticular DSD on histopathology. Laproscopy was also done in 41(34%) 46 XY patients with no gonads on ultrasonography and diagnosed as a case of testicular regression syndrome on per-operative findings. The diagnosis of Gonadal dysgenesis considered in patients who have partial testosterone response, androgen insensitivity in high testosterone response and testicular biosynthetic defect in flat pre and post testosterone response to HCG.

Conclusion: Phenotypic presentation of 46XY DSD depends on the underlying defects. Defect in androgen action on the target tissues or production of active metabolite share common morphological features. Molecular study may help in differentiating these abnormalities and to make a final diagnosis.

DISORDERS OF SEXUAL DIFFERENTIATION

P185
Etiologies of 46,XY disorders of sex development (DSD): a collaborative study in Hong Kong
WM But1, Angel Chan5, CY Lee6, Almen Lam5, YY Lam5, PY Lounq, KL Ng5, MY Wong1, KT Chan1, WY Tse1, CC Shek6
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Disorders of sex development (DSD) are defined as congenital conditions in which development of chromosomal, gonadal or anatomical sex is atypical. In 46, XY DSD, the genotype is XY, but the external genitalia is incompletely virilised, ambiguous, or completely female. The objectives of this prospective study are to test the testicular Sertoli and Leydig cell functions, to establish the genetic basis and to determine the relative prevalence of etiologies in Chinese patients with 46, XY DSD in Hong Kong. All patients with 46,XY DSD (either new or known) presented to five paediatric departments in Hong Kong from July 2009 to June 2011 were recruited. They were assessed by paediatric endocrinologists. Comprehensive evaluation of testicular and adren al functions was performed using serum hormonal assays and urine steroid profiling. Based on the hormonal results, mutational analyses of the candidate genes by polymerase chain reaction and direct DNA sequencing were conducted to delineate the genetic basis of the etiologies. Sixty-five patients were enrolled, 24 (37%) patients with 46,XY DSD were recruited. Their age ranged from birth to 27 years. Thirty-six (55%) patients presented with ambiguous external genitalia, two presented with delayed puberty and one each with primary amenorrhoea and inguinal hernia. Definitive diagnoses were made in 25 (38%) patients. Eleven (17%) patients had 5-alpha reductase 2 deficiency. Androgen insensitivity was confirmed by genetic analysis in eight (12%) patients. There was one patient with each of the following etiologies: Sry-gene syndrome, 5-F1 mutation, Frasier syndrome, cholesterol side-chain cleavage deficiency, persistent Mullerian duct syndrome and mixed gonadal dysgenesis. Genetic basis of the etiologies was delineated in 23 (35%) patients. A total of 10 novel mutations were identified. The longest follow up period was 27 years, none of the patients requested change of gender sex so far. In conclusion, 46,XY DSD is a heterogeneous group with diverse etiologies. Although 5-alpha reductase 2 deficiency is believed to be rare, it is not uncommon in Hong Kong.

**P186**

**Diagnosis of 5α-reductase 2 deficiency: is measurement of dihydrotestosterone essential?**

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5α-reductase 2 deficiency (SARD) is a known cause of 46,XY disorders of sex development. Classical biochemical hallmarks include a normal to high male level of serum testosterone, low level of dihydrotestosterone (DHT) and a raised testosterone/DHT ratio at baseline and/or after human chorionic gonadotropin stimulation. However, equivocal results are not uncommonly encountered, potentially misleading the diagnosis and therefore wrong sex assignment. Our objective is to propose laboratory diagnostic algorithms other than measuring DHT for diagnosing SARD. A retrospective review was conducted on all our local SARD patients with urinary steroid profiling (USP) or SRD5A2 genetic testing performed. Literature review was also carried out on all the reported SARD cases in the past ten years. A total of 16 local SARD patients were studied. Fifteen patients were diagnosed by USP, with characteristically low 5α- to 5β-reduced steroid metabolite ratios. Since insignificant amount of 5α- and 5β-reduced steroid metabolites is excreted under three months of age, a neonate had the genetic testing performed directly. Altogether, 12 patients underwent mutational analysis of the SRD5A2 gene, all had two mutations detected to confirm the diagnosis. Four patients had DHT measured, with one of them reaching the diagnostic cutoff of 5ARD after human chorionic gonadotropin-stimulation. A hundred and forty-three 5ARD patients were studied. Ninety-five percent of them had two mutations detected to confirm the diagnosis. Less than half of all these patients had DHT tested. With the high mutation detection rate in 5ARD patients, we propose analysing the SRD5A2 gene in all newborns with 46,XY DSD for an early diagnosis before sex assignment and any surgical intervention. When USP is readily available, it should also be used as a first-line test to guide subsequent blood testing. In conclusion, SARD can be confidently diagnosed by mutational analysis of the SRD5A2 gene and by USP. Testing the DHT level is not essential to the diagnosis of this condition. The role of this hormone test in diagnosing 5ARD has been over-emphasized.

**P187**

**Penile length of newborns and children in Surakarta, Indonesia**

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Normal penile length reference is required for assessing a child with micropenis complaint. Some studies revealed differences in normal penile length based on their race. We want to know the normal penile length of newborns, children and adolescent in Surakarta which majority people are Javanese. We studied male newborns and children attended to Moeawari Hospital in the period of January 2011 – January 2012. We excluded chronic diseases, hypospadia, ambiguous genitalia, any congenital anomalies and syndromes (such as Down syndrome). We stretched flaccid penile lengths, measured with wooden spatulas, depressed the pubic fat and placed vertically along the dorsal penis. The penile length was measured from basis of penis until gland without preputium. It was done three times. The data were analyzed by SPSS 17.0 version. There are 300 subjects, 100 newborns and 200 children. Two hundreds and ninety six subjects (96.7%) are Javanese. The mean of penile length of preterm (30-36 weeks) and atterm (>36 weeks) newborns are 1.88 ± 0.14 and 2.37 ± 0.26 cm, respectively. The mean of penile length of 0–6 months; 6–12 months; 1–3 years; 3–5 years; 5–7 years; 7–9 years; 9–11 years; 11–13 years; 13–15 years and 13-18 years are 2.67±0.58; 2.67±0.58; 2.80±0.84; 3.5±0.55; 3.5±0.71; 3.85±0.53; 4.5±0.71; 4.63±1.13; 5.53±1.45 and 6.16±1.19 cm. Our study revealed that normal penile length in Javanese children are smaller than normal range reference we used from Moore WT and Eastman RC.

**P188**

**The incidence of cryptorchidism among boys in some provinces in Indonesia**

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Background: Cryptorchidism is a condition in which one or both testes are not fully descended to the bottom of the scrotum. It may be an important cause for male infertility. Numerous epidemiological studies indicate that the incidence has increased in many countries. The data about its incidence in Indonesia is still incomplete.

Aims: The aim of this study was to establish the incidence of cryptorchidism in some provinces in Indonesia.

Methods: This was a retrospective, multicentre descriptive study, we collected data from hospital based registry data that reported by pediatric endocrinologists from North Sumatera, North Sulawesi, Jakarta, and Bali provinces, Indonesia, from 2006 till 2012.
Results: From the registry data there are 274 patients that were diagnosed with cryptorchidism. It was 29.56% for boys under 6 months, 31.39% for those between 6 months and one year, and increased significantly in older boys (39.05%). Overall 43.07% were diagnosed with bilateral cryptorchidism, 29.56% with left unilateral and 27.37% with right unilateral cryptorchidism.

Conclusion: Our data showed a relatively higher prevalence of cryptorchidism in children older than 2 years of age, which may be caused by late diagnosis. We need to increase the awareness of this condition among public population and medical providers.

P189
A novel mutation in the SRY gene causing 46 XY complete gonadal dysgenesis in a Chinese patient
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Introduction: Complete gonadal dysgenesis with 46 XY karyotype, also known as Swyer-James syndrome, is characterized by complete sex reversal with a female phenotype and unambiguous female external genitalia. Sex-determining region Y (SRY) gene mutations causing loss-of-function of the gene were identified in 10-15% of affected individuals. These individuals also have a high risk of developing tumors such as germioma and gonadalablastoma in the streaked gonads.

Case presentation: We report an 18-year old Chinese patient diagnosed with 46 XY complete gonadal dysgenesis. This patient was born with a female phenotype and presented with tall stature, absence of secondary female sexual characteristics and primary amenorrhea in adolescence. The patient is the first child born to healthy and non-consanguineous parents. There was no significant family history. Hormone investigations showed a hypergonadotrophic hypogonadism state (LH 41.6IU/L, FSH 72.3IU/L, E2<37pmol/L, testosterone 1.6nmol/L). Chromosomal analysis revealed a 46, XY karyotype. Magnetic resonance imaging of the pelvis showed a rudimentary vagina and uterus but no ovarian structure was seen. Laparoscopic exploration revealed bilateral streaked gonads and rudimentary uterus. Both gonads were surgically excised. Gonadal histology revealed a dysgerminoma arising in a residual gonadalblastomain the right gonad while the left gonad showed presence off allopian tube and ovarian stroma but no evidence of malignancy. There was no pelvic lymphadenopathy and evidence of distant metastasis. Disease staging was stage 1a and post-operative chemotheraphy was not indicated. Long term hormonal replacement therapy was started.

Methods and results: Mutation analysis of SRY gene identified a hemizygous c.338C>T sequences variant. This results amissense mutation affecting 46,XY individuals, who generally present with clinical spectrum ranging from a male phenotype with hypospadias to a female phenotype with normal Wolffian structures. More than 50 different mutations responsible for this disorder have been documented. This study is to present our previous report, which described two siblings with 2 novel mutations of SRS5A2 gene, on Indonesian children with 5 alpha-reductase deficiency. We describe clinical, hormonal, and molecular profiles of 14 children with 46,XY DSD and undervirilization due to 5 alpha-reductase deficiency. DNA extracted from peripheral blood lymphocytes, and the 5 exons of SRS5A2 gene were amplifed using specific primers and sequenced.

Conclusion: We report a novel mutation of SRY gene that resulted in 46 XY complete gonadal dysgenesis in a Chinese patient and it was complicated with both dysgerminoma and gonadalablastoma.

P190
A 45 X male patient with 7Q distal deletion and rearrangement with SRY gene translocation; a case report
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We report a 3 month old boy, who is the second child born to nonconsanguineous caucasian parents. He were delivered by cesarean section at 38 weeks gestation because of acute deterioration of heart rate, from 27 years old mother. He was hospitalised for respiratory distress and multiple congenital abnormalities. His birth weight was 2350 g (3-10 centile), length was 42 cm (below 3rd centile), and head circumference was 32 cm (< 10 centile). Clinical examination showed respiratory distress, hypertension (85/41 mmHg), microcephaly, cleft lip and palate, low-set ears with large earlobes, anal stenosis and accessory nipple. The external genitalia was completely normal male with a 2.5 cm length penis size and bilaterally descendent testis. Ophthalmic examination showed retinal coloboma and optic disc hypoplasia.

For to evaluate hypertension that refractory to medical treatment, urinary tract ultrasonography and MAG-3 scintigraphy were performed. Renal agenesis in the right side and severe dilatation of renal collecting system and ureter in the left side and thickening of bladder were detected. The urethral stenosis was found and corrected by cystoscopy. The antihypertensive therapy decreased and the follow up USG showed improvement in ureteral diameter. He had abdominal operation with a misdiagnosis of necrotizing enterocolitis because of feeding intolerance, bloody stools and abdominal distension with a edematous intestinal loops on abdominal grapy. The laparoscopy was revealed midgut malrotation and cecum was placed in the normal anatomic location. The magnetic resonans was showed only inferior cerebral vermis hypoplasia without any other defect.

Karyotype was 45,X without evidence of mosaicism.SRY gene (testis determining factor) was positive with polymerase chain reaction. FISH analysis showed SRY/distal 7q translocation. Testicular biopsy was not performed.

Discussion: The XX testicular disorder of sex development is rare condition, with a frequency of 1/20000-25000 male newborns, and 90% of the patients were positive for SRY gene on the X chromosome. Only few 45 X male patients were published to date.

The chromosome 7 q deletion syndrome is rare but well known condition, which shows broad clinical spectrum. All the malformation in our patient had been published with this syndrome. This syndrome may occur as a result of simple deletion, but different aotosomal translocations had been also described. To our knowledge this is the first case of SRY gene translocation on distal 7q chromosome.

P191
Clinical presentations and molecular characterization of Indonesian children with 5 alpha-reductase deficiency
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Inactivating mutations in 5 alpha-reductase (SRD5A2) gene lead to steroid 5 alpha-reductase deficiency, a rare autosomal recessive condition affecting 46,XY individuals, who generally present with clinical spectrum ranging from a male phenotype with hypospadias to a female phenotype with normal Wolffian structures. More than 50 different mutations responsible for this disorder have been documented. This study is to extend our previous report, which described two siblings with 2 novel mutations of SRD5A2 gene, on Indonesian children with 5 alpha-reductase deficiency.

We describe clinical, hormonal, and molecular profiles of 14 children with 46,XY DSD and undervirilization due to 5 alpha-reductase deficiency. DNA extracted from peripheral blood lymphocytes, and the 5 exons of SRD5A2 gene were amplified using specific primers and sequenced.

All of the patients (aged 2 months-18 years old) presented with genitalia ambiguity, including variable degree of hypospadias, phallic enlargement, palpable testis in ‘girls’, micropenis, cryptorchidism, virilization during puberty in ‘girls’ (8 out of 12 patients), and dysmorphic appearances in 1 case. Twelve of them raised as girls, while eight patients who had had undervirilated age changed their identity to male. The T/DHT ratio were more than 20 in 8 patients with documented hormonal results. Three mutations including p.Gly343Asp, c.699-1G>T, and p.Glu135Lys, which have not been reported in other populations were detected. The p. Arg227Gln was the most frequent mutations found (in 13/14 patients or 13/28 alleles). The combination of p.Val89Ile and p.Arg227Gln, which rarely reported in other populations, were detected in 6 patients.
Our study suggest that the most common cause of DSD in our clinic was 46, XY DSD. Karyotype and clinical phenotype may help in establishing the diagnosis.

**P194**

*Genotype and phenotype of Vietnamese patients with androgen insensitivity syndrome prior to diagnosis*

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Androgen insensitivity syndrome (AIS) is the most common specific cause of 46,XY disorder in sex development. The androgen signaling pathway is complex but so far, the only gene linked with AIS is the androgen receptor (AR). Mutations in the AR are found in most subjects with complete AIS but in partial AIS, the rate has varied 28–73%, depending on the case selection. More than over 800 entries of mutations causing AIS, representing over 100 different AR mutations from more than 850 patients with AIS have been reported. We aim to describe clinical manifestations and to identify mutation of AR in Vietnamese patients with AIS. This case series study included 12 patients from 9 unrelated families with AIS. The gonadal position and external genitalia were evaluated clinically and using ultrasound. The mutation analysis of AR was performed using PCR and direct sequencing. The age of diagnosis was 1 to 83 years old. 8/12 cases were complete androgen insensitivity syndrome (CAIS) (female external genitalia) and 4 cases were predominantly female partial AIS phenotype. Four cases had two labial testes, six cases had inguinal testes and 2 cases had abdominal testes. Five different mutations of AR were identified from 7 cases of 3 unrelated families including three novel ones. The novel missense mutation p.L701F (c.2103G>T) was identified in a patient of 83 year of age. The novel missense mutation p.L705S (c.2113C>T) was identified in two sibs. The novel mutation p.W752S (c.2256 G>T) was identified in a child with CAIS phenotype and had family history. The reported missense mutation p.V747M was identified in two sibs. The reported mutation p.V867M (c.2599 G>A) was identified in a child with female phenotype. Our study identified three novel and two reported mutation in the AR gene that may provide us new insights into the molecular mechanisms of AIS. The expanded database of these mutations should benefit patients in the diagnosis and treatment of this syndrome.

**P195**

*Etiology and clinical profile of children and adolescents with disorders of sex development (DSD) presenting with ambiguous external genitalia*

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Aims: The international consensus statement on management of DSD, based on karyotype, has been clinically accepted. Our aim was to study the clinical profile and etiology in patients with ambiguous external genitalia. using the new DSD classification.

Methods: We retrospectively assessed the records of patients, presenting with genital ambiguity, between 2009-2012, to the endocrine clinic of a tertiary care municipal hospital. The patients were classified on the basis of clinical features, hormonal investigations, imaging studies, karyotype and laparoscopy/biopsy, as indicated.

Results: 42 patients (age: neonate to 18 years, 14 (46 XX DSD), 26 (46 XY DSD) and 2(sex chromosome DSD) were evaluated. 46 XX DSD was due to Congenital Adrenal Hyperplasia (CAH) (12/14) and Syndromic DSD (2/14). All presented with citorrormegaly and labialcrotal fusion. 5/12 presented in infancy, with Adrenal crisis and severe (prader stage 3) virilization (Salt Wasting CAH), 7 had Simple Virilizing CAH.

In our series, who all presented with genitalia ambiguity and mostly raised as girls, three mutations, including p.Gly34Fs, c.699-1 G>T, and p.Glu135Lys, which never been reported in other populations were detected.

**P192**

*Sex rearing in individuals with 46,XY disorders of sex development prior to diagnosis*

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46,XY Disorders of Sex Development (DSD) has wide variations of clinical manifestations ranging from complete female, genitalia ambiguity, to complete male. Therefore the individuals with this disorder can be reared as boys or girls. Most of Indonesian DSD cases are facing with budget constraint, because they require series of costly examinations and treatment. We aimed to know the distribution of sex rearing in individuals with 46,XY DSD and tried to find out the possible etiologies based on the clinical manifestations and the age of presentation.

The study reported data of types of sex rearing, age at and clinical presentation of subjects obtained from 46,XY resulted chromosome analysis patients referred to our clinic in year 2009-2010. Seventy 46,XY DSD cases (aged 1 day-32 years old) were collected and analyzed, and 45 of them were reared as boys, 22 as girls, while the types of sex rearing was not yet assigned in 3 cases. Most of the cases were referred for chromosome analysis at age >3 months,8 years, and 12 patients at 18 years or above, 10 of them were raised as female. Genitalia ambiguity was the most frequent referral reason (44/70 cases). Based on detailed clinical examinations and age of presentation we also described the possible diagnosis, in order to help parents or patients to assign gender with minimum cost.

**P193**

*Characteristic of patients with disorders of sex development (DSD) in Cipto Mangunkusumo Hospital, Jakarta*

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Disorder of Sex Development (DSD) is a congenital condition in which development of chromosomal, gonadal or anatomical sex is atypical. They are complex condition related to social stigma, cultural and beliefs in Indonesian population. In Indonesia, there is only a few study regarding characteristic of DSD patients. The aims of our study was to evaluate the characteristic of patients with DSD in Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

We retrospectively reviewed the medical records of patients followed up over the period from 2010 to 2012 in Endocrinology Pediatric Clinic, Cipto Mangunkusumo Hospital, Jakarta, Indonesia. We found 74 patients with DSD. In this paper we excluded 29 patients confirmed as Congenital Adrenal Hyperplasia and 3 patients with Turner syndrome. Of 42 patients, 23 (54.8%) patients had 46,XY DSD; 11 (26.2%) patients had sex chromosome DSD; 3 (7.1%) patients had 46,XY DSD, and 5 patients have not done chromosomal analysis. The age when first diagnosed was ranging from newborn to 14 years old. Most cases referred by pediatrician (33.3%) and urologist (23.8%) with frequent complaint were ambiguous genitalia (52.4%) and severe hypospadias (14.3%). The most frequent of phenotype was hypopospadia (66.7%). Twenty five (59.5%) of patients have been raised as boy prior to diagnosis. Twelve patients were raised as girls have 46, XY karyotype and 2 patients raised as boys have 46, XX karyotype. Definite diagnosis of 23 patients with 46, XY DSD was found only in 4 (17.4%) patients. The problem regarding lack of definitive diagnosis was related with the high cost of laboratory examination and socioeconomic problem in Indonesia.
Hypospadias was the most common presentation in 46XY DSD. Partial Androgen Insensitivity syndrome (PAIS) (8/26, 30%) was the most common etiology. 4 had 5 alpha reductase deficiency, (1 had isolated micropenis and 1 cryptorchidism with PraderWilli Syndrome while other 2 had hypospadias). 4 patients had Complete Androgen insensitivity Syndrome, 2(Pure Gonadal dysgenesis), 1 ( Syndromic DSD), 1 (CAH, 21 hydroxylase deficiency with peripheral precocious puberty). 1 (Vanishing testis syndrome). 5 patients had inconclusive biochemical profile.

6 patients presented with virilization at puberty. Though gender identity prior to puberty was female, history suggestive of conflict regarding the gender role was present. 4/6 were reassigned a male gender, while 2 continued as females.

1 patient of Sex Chromosome DSD, had Ovotesticular DSD with rare mosaic karyotype of 46XX[p-](IP21-23)/46XY 80%/20%, while other had 46XY/46XX 58%/42% chimerism.

Outcome: 46XY DSD comprised 60% cases with genital ambiguity. PAIS is the most common etiology of 46XY DSD and CAH of 46XX DSD. Subjects presenting for the first time in the peripubertal period with virilization, pose a bigger challenge to the treating team, in terms of gender role, identity and sex reassignment, along with difficulties in acceptance in society. The limitation of the study was lack of genetic confirmation, especially in inconclusive cases.

P196 Hypothalamic hamartoma with pubertas precox and gelastic seizure in a boy (Case Report)
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Hypothalamic hamartoma is a rare neoplastic heteropia caused by organic developmental failure. The most common clinical findings in hypothalamic hamartoma are pubertas precox with or without gelastic seizure, and behavioural disturbance. The aim of this case report to inform a rare case of hypothalamic hamartoma with pubertas precox and gelastic seizure in a boy.

A 5 year and 7 month old boy, admitted to the hospital with a chief complain of premature pubic hair growth and frequent sudden laughing without apparent reason which see to the hospital with a chief complaint of premature pubic hair growth and frequent sudden laughing without apparent reason.

Nur Rochmah, Muhammad Faizi, Achmad Yuniar, Netty Harjantien
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Multiple pituitary hormone deficiency (MPHD) is an endocrine disorder due to combination of pituitary hormones deficiencies. Clinical manifestations vary due to the combination of individual hormone deficiencies. The diagnosis is established based on history, signs and symptoms, hormonal and radiological examination. MPHD should be managed by hormones replacement according hormone abnormalities. The objective is to present a case of multiple pituitary hormone deficiency in a child, focusing in diagnosis and management.

P198

Clinical course and endocrinological characteristics of prolactinoma in children and adolescents
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Aim: Prolactinoma is the most prevalent pituitary tumor that accounts for 40% of all pituitary tumors. It is more prevalent in adults with an estimated prevalence of 100/million, however, it is very rare in childhood and adolescents and clinical spectrums and long-term prognosis remain unclear. The most common clinical manifestations have been known to be growth and pubertal disorders. This study investigated clinical and endocrinological characteristics, and treatment outcome of prolactinoma in children and adolescents.

Methods: Six patients (3 males and 3 females) with prolactinoma diagnosed before 18 years of age were included. The diagnosis and relapse of prolactinoma were confirmed by brain magnetic resonance imaging (MRI) and serum prolactin level. The clinical course, endocrinological characteristics, and radiological findings were reviewed retrospectively.

Results: The mean age at diagnosis was 12.2 years (range, 7-15 years).

P199

Multiple pituitary hormone deficiency: beware of combined hormones deficiency

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Soetomo Hospital, Surabaya, Indonesia

Multiple Pituitary Hormone Deficiency (MPHD) is an endocrine disorder due to combination of pituitary hormones deficiencies. Clinical manifestations vary due to the combination of individual hormone deficiencies. The diagnosis is established based on history, signs and symptoms, hormonal and radiological examination. MPHD should be managed by hormones replacement according hormone abnormalities. The objective is to present a case of multiple pituitary hormone deficiency in a child, focusing in diagnosis and management.

P197

Clinical course and endocrinological characteristics of prolactinoma in children and adolescents
Yoo-Mi Kim, Sin-Ho Choi, Beom Hee Lee, Han-wook Yoo
Department of Pediatrics, Asan Medical Center Children’s Hospital, University of Ulsan College of Medicine, Seoul, Korea

Aim: Prolactinoma is the most prevalent pituitary tumor that accounts for 40% of all pituitary tumors. It is more prevalent in adults with an
by hypogonadotropic hypogonadism. Facing patient with pituitary hormone deficiency must be aware of the abnormality of other pituitary hormone.

**P199**
Relapse in pituitary adenoma after resection
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Pituitary adenoma in children is rarely reported. Acromegaly is one of clinical manifestation in GH releasing-pituitary adenoma. Recurrence of clinical manifestation after resection must be evaluated for possibility of pituitary adenoma relapse.

N, male, 15-yr, came to pediatric endocrinology outpatient clinic with the main complain of acromegaly and decreased of visual field which was getting worse since two weeks before(April 11, 2011). He was consulted to ophthalmology and neurosurgery outpatient clinic. MRI with contrast revealed pituitary adenoma. Laboratory results showed TSHS:0.9773 (0.35-4.94)uIU/ml, prolactin 0.514(0.4-15.2)ng/ml, testosterone less than 2.50(boys:13-17:28-1110)ng/ml, growth hormone was more than 40.00 (>10.0)ng/ml. He was performed transsphenoidal removal cystic tumor. Pathological result showed macroscopic: yellowish cystous mass; 0.6x0.4x0.2cm whether microscopic: appropriate to pituitary adenoma, non chromophobe. After surgery, patient was given DDAVP nasal spray 10 microgram/day, L-thyroxin 100 microgram once daily. One year after surgery, patient complaint of acromegaly, decreased visual field, especially in right and left temporal side, cephalgia. On physical examination, body weight was 91.5kg, height was184.5 cm. There was hemianopsia bitemporal. Tanner stage was A2P4G4. MRI with contrast showed pituitary adenoma relapse. Bone age was normal with height percentage based on it is about 96.8%. Tanner Whitehouse showed adult height 186.4cm. Thorax X ray showed heart and lungs were normal. Laboratories results revealed IGFI:1339(237-996)microgram/L, FT4:10.89-1.76 ng/dl; TSHS:0.35-4.94)microU/ml(12-18yo), testosterone:435.1(28-1110)ng/dl. Working diagnosis was pituitary adenoma relapse post tumor resection, panhypopituitarism, diabetes insipidus. Testosterone 150mg once per month was added. Relapse of pituitary adenoma in children must be considered in the recurrence of clinical manifestations.

**P200**
Sexual precocity with pituitary macroadenoma and bilateral multicystic ovaries - a case report
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Aim: To report a 6 years old girl who presented with sexual precocity, multicystic ovaries and pituitary macroadenoma due to primary hypothyroidism.

Methods: We describe the clinical presentation, imaging findings, hormonal work-up and follow up of a child with sexual precocity, multicystic ovaries and pituitary macroadenoma due to primary hypothyroidism.

Results: 6 years old girl presented with vaginal bleeding for last 1½ years. The initial episode lasted 3 days. The vaginal bleeding then continued every month lasting 3-4 days for next 9 months. She also had inter-menstrual bleeding for last 6 months. Parents also noticed breast development (initially left followed by right a month later) for the past 6 months. There was no galactorrhoea, pubic or axillary hair development. There was no height gain during the last 2 years, but weight increased from 14kg to 19kg. Her appetite was normal. Parents also noticed a generalized edema of face, abdomen and legs. There was no history of constipation, cold intolerance or goiter. Her past history was unremarkable. She goes to Anganwadi School but has decreased mentation compared to younger sister. On examination, she was 95.5 cm tall (<3rd percentile), weight was 19 kg (25th percentile). Her skin was rough and dry, heart rate was 80/min and BP 100/80mm of Hg. There was no goiter or lingual thyroid. Tanners staging was B3P1. Galactorrhoea present on gentle manipulation. There was no axillary hair, genital hyperpigmentation or clitoromegaly. Her cardiac and respiratory examinations were normal. On abdominal examination, a soft cystic fluctuant mass palpable in hypogastrium, dull on percussion, well defined in all sides except inferiorly where lower margin was not palpable. Neurological examination showed dull lathargic child with excessive somnolence. The tendon reflexes are normal. Her bone age was delayed 3.2 years. Investigations: Hemogram, renal and liver functions are normal. Her hormonal profile: Total T4 0.549µg/dl (5.1-11.4), TSH > 100 µU/ml (0.27-4.2), TPO antibody – 74.01 pg/ml (<34), LH <0.102(4.2-126), FSH 7.78mIU/ml (3.5-12.5), prolactin 337.7mg/ml(6-29.9), Estradiol 2113pg/ml(<20), Cortisol 15.95µg/dl(6.2-19.4), testosterone 0.029ng/ml(0.084 – 0.481), DHEAS 39.37µg/dl(2.8-85.2), AACT 11.71 pg/ml (7.2 – 63.3). USG neck revealed presence of thyroid in normal location. USG and CT pelvis showed bilateral multiple cystic ovaries and bulky uterus. MRI sela reported as pituitary macroadenoma. Child was started on tab. thyroxin 50 mcg/day. Child lost 4 kg and gained 1.5cm in 2 months and became active. Repeat hormonal work up showed: Total T4 10.59 µg/dl, TSH 3.18µU/ml and prolactin 71 ng/ml she was diagnosed as hashimoto thyroiditis/hypothyroidism with pituitary macroadenoma and sexual precocity.

Conclusion: Short stature in sexual precocity - think of primary hypothyroidism. Multi cystic ovaries and pituitary enlargement although rare, may be seen in children with longstanding primary hypothyroidism. It is important to be aware of this to avoid pituitary surgery which may have disastrous results in these patients.

**P201**
Fluid and electrolyte imbalance related to intracranial abnormality
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Background: Maintenance of the tonicity of extracellular fluids is crucial for proper cell function. In children and adults, normal blood tonicity is maintained by a coordinated interaction among the thirst, vasopressin, and renal systems. Dysfunction in any of these systems can result in abnormal regulation of blood osmolality, which if not properly recognized and treated, may cause life-threatening dysfunction in neuronal and other cellular activities. The aim of this study is to increased awareness on the possibility of fluid and electrolyte imbalance in patients with intracranial abnormality.

Case series: There were five cases consulted to endocrinology division due to polyuriaduring February-June 2012. All of them had intracranial abnormality: Langerhans cell histiocytosis (LCH), cerebellomedulloblastoma, retinoblastoma with intracranial metastases, pituitary adenoma post extirpation, and intracranial abscess. During admission these patients develop polyuria, ranging from 6 to 16.6 mL/kg/hr. Etiology of polyuria were central diabetes insipidus in three patients (LCH, Meduloblastoma, pituitary adenoma patients), and CSW in two patients, the rate of urine excretion was significantly higher in CSW than CSW cases. In CSW, the urine gravity was <1.005, the serum sodium was 138-142 mEq/L with urine sodium of 8-36 mEq/L, and the serum osmolality significantly higher than urine osmolality. None of our patient needed water deprivation test to confirm the diagnosis. Those with CDI were treated with DDAVP nasal spray. None of our patient had water intoxication due to DDAVP; instead the dose should be increased to 3x20 mcg in one patient. In the CSW patients, serum sodium level was quite low, reached 110 mEq/L, manifest as seizure, and unresponsive to rapid sodium corrections. In these patients, the urine gravity was normal and urine sodium excretion was >140 mEq/L. None of these patients had specific signs of CSW. We increased sodium intake up to 10 mEq/kg/day and maintained the fluid balance to prevent dehydration. One patient received fludrocortisone for one week. Four of 5 patients outcomes were good, but one patient died due to multiorgan failure associated with main disease.

Conclusion: Polyuria and electrolyte imbalance are not rarely occur during the course of other diseases, especially those with underlying intracranial pathology. Early identification and treatment of these...
condition will reduce morbidity and mortality associated with fluid and electrolyte imbalance and increase overall treatment outcome.

P202
Vitamin D serum levels and vitamin D receptor FokI polymorphism on tuberculosis children in Palembang, Indonesia
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Aim: The role of vitamin D on host immunity defense against tuberculosis infection has long been known. Deficiency vitamin D and vitamin D receptor polymorphism are strongly associated with the susceptibility of tuberculosis in four seasons countries. As a country with sufficient sunlight, the incidence of tuberculosis in Indonesia remains high. The aim of this study is to assess the association of vitamin D serum level and vitamin D receptor FokI polymorphism with the incidence of tuberculosis in children at Palembang, Indonesia.

Method: A case control study was conducted at Child Health Department Mohammad Hoesin Hospital Palembang during November 2011 - April 2012. Case group consisted of children suffering tuberculosis disease while control group are healthy children who had been sensitized to tuberculosis proven with a positive tuberculin test. Vitamin D (1,25(OH)2D3/calcitriol) serum level was measured by using IDS 1,25-Dihydroxy Vitamin D ELIKit and VDR FokI polymorphism was identified through RFLP analysis. A bivariate and multivariate analysis were performed with p < 0.05 and CI 95%.

Result: Sixty subjects were divided equally to case and control groups. The mean of calcitriol serum level in case group was lower compared to control even though still in normal level range (105,50 ± 66,86 pmol/L vs. 162,90±52,86 pmol/LP=0.001). We found nine subjects with calcitriol deficiency, 8 (26,7%) in children with tuberculosis disease and 1 (3,3%) in children without tuberculosis disease (OR 10,54; 95% CI 1,22-90,66). The incidence of VDR FokI polymorphism is 93,4% in case group and 73,3% in control group (OR 5,0, 95% CI 0,9-26,4). No significant association was found between calcitriol serum level and VDR FokI polymorphism (p=0,999).

Conclusion: Vitamin D (calcitriol) deficiency and low serum level are associated with higher risk of tuberculosis in children at Palembang, Indonesia. Polymorphism FokI VDR gene also contribute to the susceptibility of tuberculosis. Our data supports that vitamin D also has a contribution in susceptibility to tuberculosis infection even in a country with sufficient sunlight exposure.

MISCELLANEOUS

P203
An unusual presentation of girl with down syndrome: Van-Wyk Grumbach syndrome
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Van Wyk-Grumbach syndrome is a rare disease characterized by precocious pubertal onset with profound hypothyroidism and multicystic enlarged ovaries. A 9 year-old girl with Down syndrome visited our hospital for early menarche. At birth, she showed subclinical hypothyroidism (11.8 mg/dL of thyroxine (T4) and 6.05 mIU/mL of thyroid stimulating hormone (TSH)), but she had not been followed up in our clinic. On physical examination, pubertal Tanner stage was breast II and pubic hair I. Laboratory findings were as follows: 0.30 mg/dL of free T4, 8.30 ul/L of TSH, 0.1 u/L of luteinizing hormone and 6.35 IU/L of follicle-stimulating hormone. Her bone age was 6 years. Her pelvic sonogram revealed multiple cysts in both enlarged ovaries. She was diagnosed with Van Wyk-Grumbach syndrome. Levothyroxine treatment at a dose of 0.05mg/day was started. Regression of breast development was obtained after 2 months and her vaginal bleeding did not recur.

P204
Blood spots screening for identification of Fragile X Syndrome among intellectual disability students in Flores Island, INDONESIA
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Fragile X Syndrome (FXS) is the most common known inherited form of intellectual disability (ID), caused by a CGG repeat expansion located in 5’ untranslated region of the FMR1 gene. The prevalence for both males and females varies in different populations being about 1 in 2600-4000 for the full mutation and 1 in 130-800 for premutation alleles. Previous screening in Indonesia showed FXS prevalence of 1.9%(Faradz et al. 1999). Advances targets treatments in FXS have led to a newborn and high risk populations FXS screening studies. In this study, a rapid and inexpensive method for screening both males and females for FMR1 allele sizes throughout the premutation and full-mutation range using a dried blood spot, (Tassone et al, 2008) was applied for the screening of FXS in Flores Island, one of the very remote area in East Indonesia. The screening includes 211 children (130 males and 81 females) from an institution and school for children with special needs in Flores Island, East Nusa Tenggara, Indonesia.

The Blood spots PCR analysis result showed the presence of 3 expanded alleles (1.42%) consist of 2 males with a full mutation and 1 male with a premutation allele. Southern blot analysis confirmed the presence of a full mutation allele and determined the methylation status in this individual. Our results suggest that blood spots screening is an inexpensive and simple method to perform high premutation FMR1 in high risk population especially in the remote area that are far from laboratory facilities.

P205
The neuro-cardio-facial-cutaneous syndrome – unity in diversity
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The neuro-cardio-facial-cutaneous syndrome (NCFCS) concept was recently established in order to group a number of hereditary disorders characterized by a variable degree of growth and mental retardation, cardiac defects, dysmorphic facial features and skin abnormalities, and having a common background, germline mutations in genes of the RAS-MAPKinase pathway. The included entities are Noonan and Leopard syndrome (the most frequent), Costello syndrome, cranio-facio-cutaneous syndrome, as well as some forms of type 1 neurofibromatosis and the newly defined Legius syndrome.

We present illustrative cases of 2 of this syndromes, Noonan (NS) and Leopard syndrome (LS), illustrative for both the common elements and the variety of the characteristics. Four of the six cases of Noonan syndrome are treated with growth hormone, with a good response, proving the importance of an early diagnostic. Two cases are from the same family (mother and son), the mother of another case has patognomonic features but the diagnostic had not yet been confirmed. One of the children with NS, recently diagnosed, with important vertebral deformation needing specific treatment cannot, for the moment, be treated with hGH in spite of the important growth delay (>-3SD).

LEOPARD is an acronym for the major features of the disorder: Lentigines, ECG conduction abnormalities, Ocular hypertelorism, Pulmonary stenosis, Abnormal genitalia, Retardation of growth, Deafness. The probant case of LS, a 15 years old boy, presented almost all these features, with the exception of deafness. He associated a cerebral tumor, rare in LS, but which could be considered as a NCFCS feature, the MAPK pathway being

http://www.ijpeonline.com/supplements/2013/S1
involved in tumorigenesis. He presented with short stature and neurologic symptoms, both improved after the (partial) tumor resection (pylocytic astrocytoma). The genetic investigation of the family confirmed the syndrome at 4 other members (father, two brothers and a sister), each one with various manifestations, from only café-au-lait spots to cardiac malformations.

The absence of patognomonic symptoms as well as the overlap of numerous features makes the diagnosis of the components of NCFCS difficult, the molecular diagnosis offering the chance to exceed the clinical difficulties. More than that, specific mutations are associated with specific phenotypes, which has a great importance for the diagnostic and prognostic of an early diagnostic is important not only for the rapid treatment of life threatening elements (cardiac malformations, tumors) and chronic treatment of some features (like short stature), but also for an appropriate genetic counseling.

**P206**

**Effect of intrauterine body development and nutritional status on the later body-length development of children.** The MDN system

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The author’s aim was to study 1. the effect of intrauterine weight and length development and nutritional status on the later height development of children, - 2/. how can we use the MDN system to identify and distinguish neonates who are likely to need growth hormone treatment in the future.

The authors examined the height of 6335 Hungarian 18 years old young men, whose intrauterine weight and length development was known after birth. They have used a new diagnostic method, so called MDN (Maturity, Development and Nutritional status) system which is suitable to determine the body development and nutritional status of a neonate on the basis of its gestational age, length and weight development considered simultaneously (Berk P, Joutbert K. J Maternal Fetal Neonatal Med. 2009; 22/7, pp.552).

Relying on the birth data and the MDN matrix position of 6335 young men, the authors have established, the height of the 18 years old men became smallest who were proportionately retarded neonates at birth time. Their average height was 170.8cm comparing to the young men who were absolutely averages at birth time (176.1). The difference is strongly significant.

The MDN system is a suitable method for the differentiation the mostly endangered neonate groups, based on their body development and nourishment. The development and the nutritional status have a major impact on the neonatal mortality. The MDN system has another important area of application. It allows the prompt and accurate identification of those newborns for whom systematic follow-up measurements and growth hormone therapy treatment is likely to be necessary in the future.

**DEVELOPMENTAL ORIGINS OF HEALTH AND ADULT**

**P207**

**Association between exon-3 polymorphism of the GH Receptor(GHR) gene with catch growth in children born small for gestational age**

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**Objective:** The aim of this study was to investigate relationship between GHR exon 3 genotype and catch up growth in children fullterm born small for gestational age.

**Methods:** Children were classified as SGA if birth weight was less than -2SDS. Catch up defined as height of less than -2SDS at the time the child was examined. DNA for the GHR exon 3 genotyping was isolated from peripheral blood lymphocytes and was analyzed by multiplex PCR.

**Results:** 1) Total of 92 children, 74(80.4%) had sufficiently catch up. 2) 69(75%) were f/f/f, 15(16.3%) were fl/f2 and 8(8.6%) were d3/d3 in the SGA groups, compared with 81%, 18%, and 1%, respectively in the Korean controls(P=0.04). 3) The highest catch up rate was seen in the fl/d3 subgroup(86.6%), the lowest in the d3/d3 subgroup (62.5%). The differences were not significant. 3) d3/d3 GHR genotype in the SGA groups is higher than in the Korean controls. 4) fl/fi GHR genotype is higher than other published data in SGA groups.

**Conclusion:** Differences in the frequency distribution of the GHR polymorphism genotype between normal Korean population and SGA groups were not significant. GHR-exon 3 polymorphism did not influence the postnatal growth in Korean children with SGA. Additional studies are required to establish effect of the d3-GHR allele on prenatal growth in SGA.

**P208**

**Uteroplacental insufficiency decreases forkhead box protein O1A (FoxO1a) hepatic levels in perinatal and postnatal IUGR rats**

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**Objective:** IUGR re-programs hepatic gene expression, leading to alterations in perinatal mRNA levels that persist postnatally. Forkhead box protein O1a (FoxO1a) is a nuclear transcription factor, which is an important regulator of the in vivo metabolism of energetic substance, and play an important role in stabilizing the hepatocyte glucose metabolism and maintaining blood glucose levels in the body. Recent study investigated FoxO1a expression can stimulate key enzymes of gluconeogenesis pathway phosphoenolpyruvate carboxylyase kinases (PEPCK), peroxisome proliferator-activated receptor γ auxiliary activating factor-1a (PGC-1a) and glucose - 6 - phoshatase (G-6-Pase) gene expression. The effect of IUGR upon hepatic FoxO1a expression is unknown. So in this study we investigate the persistent changes in hepatic FoxO1a expression caused by IUGR, which could initiate and maintain the obesity, insulin resistance and type 2 diabetes, and explore whether the changes in FoxO1a expression are gender specific.

**Methods:** Dietary restriction was used to induce uteroplacental insufficiency and subsequent IUGR. Control(CON) animals came from dams who received anesthesia. Pups were harvested at d0, d21 and d56 of postnatal life, and liver were harvested. Real-time RT-PCR and Western blotting were used to measure hepatic FoxO1a expression.

**Results:** For female and male pups, IUGR significantly decreased FoxO1a hepatic mRNA and protein levels of CON values (P<0.01) at day 0, day21 and at day 56.

**Conclusions:** We conclude that IUGR decreases hepatic perinatal and postnatal FoxO1a expression in female and male rats. FoxO1a functions as a nuclear transcription factor. Important future studies involve determining which genes are affected by this alteration response to IUGR.

**P209**

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