HORMONE RESEARCH

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Plenary Lecture 1

PL-01

Modern Management of Type 1 Diabetes Mellitus

William Tamborlane

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Results of the DCCT/EDIC study indicate that youth with type 1 diabetes mellitus (T1DM) should aim to achieve and maintain HbA1c levels as close to normal as possible. However, the rapid physiological and psychosocial changes that occur during childhood and adolescence make these patients among the most difficult to manage. In the DCCT, adolescents randomized to the intensive treatment group had higher HbA1c levels and an increased risk for severe hypoglycemia than intensively treated adults. Remarkably, a much greater proportion of young patients today are able to meet strict standards of care than ever imagined possible only a few years ago. A number of technological advances in treatment of T1DM have been introduced over the past 15 years, including the production of fast and long-acting insulin analogs, the more widespread use of improved insulin pumps and the introduction of new continuous glucose monitoring devices. The impact of that each of these advances have had on increasing the proportion of young patients who are able to achieve target HbA1c levels more safely will be discussed during this presentation.

Plenary Lecture 2

PL-02

New Strategies to Improve Final Height

Leo Dunkel

Professor of Paediatrics, University of Kuopio, Finland

Without estrogen action linear growth continues for an exceptionally long period of time. Aromatase inhibitors have therefore become an option for treatment of children with short stature. Two placebo-controlled studies with letrozole, have reported clear impact of this treatment on predicted adult height. In boys with constitutional delay of puberty 1-yr treatment with letrozole increased predicted adult height by 5.1 cm. In another study in boys with idiopathic short stature 2-yr treatment with letrozole increased predicted adult height increased by 5.9 cm. The efficacy of another potent aromatase inhibitor, anastrozole, has been assessed in only one controlled study in adolescent boys on GH therapy. Linear growth was comparable between groups; however, there was a significantly slower increase in bone age from baseline in the anastrozole plus GH group after 2 and 3 yrs of treatment. This resulted in a net increase in predicted adult height of +5.7 cm at 3 yrs on therapy. Available data suggest that the achieved gain in predicted adult height also results in taller adult height. However, before the safety of the treatment is established, particularly the qualitative effects on bone development, this treatment in growth indications must be considered experimental.

Plenary Lecture 3

PL-03

Central Precocious Puberty: Clinical Management and Consensus

Erica Eugster

Professor of Pediatrics and Director of the Section of Pediatric Endocrinology at Riley Hospital for Children

Long acting analogs of gondadotropin releasing hormone (GnRHa) are standard of care for the treatment of central precocious puberty (CPP) worldwide. Most commonly administered in the form of a depot injection, GnRHa reliably achieve and maintain suppression of the hypothalamic-pituitary-gonadal (HPG) axis, and are fully reversible upon discontinuation of treatment. An alternate delivery system has emerged in the form of a hydrogel implant containing the potent GnRHa histrelin, which is inserted into the subcutaneous tissue of the upper arm in a minor surgical procedure. Continuous release of histrelin across the microporous walls of the implant results in rapid and sustained suppression of the HPG axis in children with CPP for up to one year. Initial studies suggest that this modality is safe and is well received by patients and their parents. Additional progress in the area of CPP was a 2007 Consensus Conference on the use of GnRHa jointly sponsored by the Lawson Wilkins Pediatric Endocrine Society and the European Society for Paediatric Endocrinology. Although GnRHa have a favorable track record in terms of safety and efficacy, many questions regarding their use remain. Findings of the Consensus Conference underscored the need for rigorously conducted, prospective studies investigating physiologic and psychosocial aspects of both treated and untreated CPP.

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Plenary Lecture 4

PL-04

Mechanism of Pancreatic β-Cell Death and Its Consequence in Type 1 Diabetes

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While apoptosis of pancreatic β-cells could be the final step in type 1 diabetes (T1D), it has not been elucidated which molecule(s) are the real culprit(s) in T1D. Perforin, FasL, TNFα, IL-1, IFNγ and NO have been claimed as the effector molecules. While FasL was initially considered as a strong candidate for dominant death effector, following experiments showed contradictory results. Cytokine combinations between IFNγ and TNFα or IL-1 are being revisited as the death effectors. Regarding signal transduction downstream of cytokine receptors, a critical role for STAT1 downstream of IFNγ receptor was shown by the absence of diabetes in STAT1-null NOD mice. Diabetes in NOD mice with β-cell-specific inactivation of IKKβ/NF-κB was accelerated, suggesting that net effect of β-cell NF-κB is antiapoptotic. The first step in the development of T1D (initial event) has been elusive. Recently, a couple of papers suggested the possibility that apoptosis of pancreatic β-cells induces inflammatory/immune responses to β-cells. Such a theory is based on the assumption that apoptotic cells can, under certain circumstances, induce immune responses, inflammatory and autoimmune disorders, which is in contrast to the dogma that apoptotic cells result in immunosuppression and necrotic cells provoke inflammation/immunity. We observed that late apoptotic β-cells with secondary necrosis elicited inflammatory responses in macrophages through TLR2/MyD88/NF-κB signaling. Late apoptotic cells also induced TLR2-dependent maturation of dendritic cells and activation of autoreactive T cells. TLR2 knockout mice showed defective priming of diabetogenic T cells by apoptotic β-cells in the pancreatic lymph nodes. Furthermore, TLR2 deficiency conferred a significant protection against T1D and insulitis in T1D animal models. These findings present evidence suggesting that apoptosis of pancreatic β-cells could be both the initial and final steps in T1D and, provide a novel strategy for therapeutic or preventive intervention in T1D.

Symposium 1: Growth and Puberty

S1-01

The IGF Axis and Short Stature

Ron Rosenfeld

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Prior studies have demonstrated that 25-50% of short children (defined as below -2SD in height) have low serum concentrations of IGF-I. Secondary IGFD has been defined as reduced serum IGF-I in the face of decreased GH production, on either a hypothalamic, pituitary or bioactivity basis. Primary IGFD has been defined as reduced serum IGF-I, despite normal-increased GH levels. To date, eight distinct molecular etiologies for primary IGFD have been identified: 1) IGF-I gene deletions/mutations; 2) defects of the extracellular domain of the GH receptor (GHR) affecting GH binding; 3) defects of the extracellular domain of the GHR, affecting dimerization; 4) defects of the transmembrane domain of the GHR, affecting receptor anchoring; 5) defects of the intracellular domain of the GHR, affecting receptor signaling; 6) defects of the post-GHR signaling cascade; 7) defects of the acid-labile subunit (ALS); and 8) mutations of the IGF-I gene resulting in bioinactive IGF-I. To these defects, one can add mutations affecting the IGF-I receptor, as causes of IGF resistance. We have established a centralized IGFD Research Center, in an effort to facilitate evaluation, diagnosis and management of patients with primary IGFD and IGF resistance. Biochemical assays include IGF-I, IGF-II, IGFBPs, ALS, GH and GHBP. Molecular studies include evaluation of the genes for IGF-I, IGF-II, IGFBP-3, ALS, GHR (both wild-type and exon-3 deletions), JAK2, STAT5a and 5b, and the insulin and IGF-I receptors and signaling cascades. Of >200 patients referred for evaluation to date (many studies are still in progress), we have identified and/or characterized 6 patients with STAT5b defects (4 patients first identified by us and 2 patients first identified elsewhere, encompassing 5 different mutations); >20 patients with defects of the GHR; five patients with mutations of the gene for ALS; and 3 patients with heterozygous mutations of the IGF1R gene, including one resulting in a truncation of the tyrosine kinase domain. In all of the cases of primary IGFD diagnosed, serum IGF-I concentrations were significantly below the lower limits of normal for age and failed to rise upon administration of GH. It is likely that the defects described above represent the most extreme forms of primary IGFD, but should provide important insights into future evaluation of milder forms of growth failure associated with low serum IGF-I, as well as help identify the most appropriate candidates for IGF-I and/or GH therapy.

S1-02

Endocrinological Characteristics of Brain Tumor Surviors

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Survival rates are improving following advance of cancer therapy for childhood brain tumors. The recognition and prompt management of late complications are essential to prevent further morbidity and impairment of quality of life.

Endocrine problems are very common and depend on tumor location, treatment modalities (surgery, radiation, chemotherapy), and age at treatment. Cranial radiation can cause hypothalamic-pituitary dysfunction. Growth hormone deficiency (GHD) is most common endocrinopathy, followed gonadotropin (LH, luteinzing hormone; FSH, follicular stimulating hormone) dysfunction (hypogonadism, or early puberty), adrenocorticotropin and thyrotropin (TSH) deficiency. The spinal radiation can cause primary hypothyroidism, thyroid cancer, primary hypogonadism, infertility, and poor growth of the spine with relative sparing of limb growth. Chemotherapy can damage the gonads or hypothalamus.

The growth failure is most common complication. Multiple factors can contribute to growth failure, including spinal radiation, intercurrent illness, depression, inactivity, poor nutrition, and endocrine dysfunction, as especially GHD or early puberty. Overweight and osteoporosis are other late complications that impair the quality of life.

The early recognition and treatment of the endocrine sequelae can improve the quality of life. Cancer survivors require yearly surveillance for endocrine dysfunctions, including height and weight, arm span, pubertal staging, assessment of dietary calcium and vitamin D intake, free T4, TSH, and LH/FSH/testosterone or estradiol (after 14 years of age in male and 13 years in female). Early intervention of endocrinopathy can enhance the growth rate and maintain proper weight and bone mineral density and ultimately improve quality of life.

S1-03

The Short SGA Child – An Update on Diagnosis and Management

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Introduction: Approximately 3–5% of neonates are born small for gestational age (SGA). Children who are born with a weight or length of ± 2 SD scores (SDS) are by definition appropriate for gestational age (AGA) and, therefore, SGA should be defined as a weight or length of less than or equal to –2 SDS below the mean for gestational age (Lee 2003, Clayton 2006).

The term SGA is often, though inaccurately, used interchangeably with intrauterine growth retardation (IUGR) (Hediger et al. 1998, Martin et al. 2002). IUGR describes a pathophysiological cause of inhibited foetal growth in utero, whereas SGA corresponds to a statistical definition. Moreover, neonates with IUGR are usually born SGA, but not all infants who are SGA have experienced IUGR.

Catch-up growth and height normalisation: Most infants who are born SGA achieve normal height following a period of catch-up growth by the age of 2 years (Boersma 1997). This accelerated growth can lead to a weight or height within 2 SDS for age. Nevertheless, approximately 10–15% of SGA infants fail to achieve catch-up growth, and those who do not achieve this within 2 years have a high risk of short stature in later life (Hokken-Koelega 1995, Karlberg 1995). Additionally, the extent of catch-up growth usually contributes to adult size and body proportions, indirectly suggesting that there may be a further, postnatal growth failure among those whose size remains below the normal range.

While catch-up weight gain between birth and 2 year occurs in the majority of SGA children, they develop a dramatic transition toward central adiposity and insulin resistance between ages 2 and 4 yr. The mechanisms underlying this predisposition to adverse health problems related to altered body composition, such as metabolic syndorm and cardiovascular events is not uinderstood as today and derseves further research (Ibanes 2006). This implies that body mass index should be closely monitored by paediatrician during catch up and weight excess tentatively prevented.

Several studies have demonstrated clearly the persistence of short stature in later life in those born SGA. These data reflect the importance of catch-up growth during the first 2 to 4 years of age in achieving height within the normal range.

In a study in the Netherlands, approximately 15% of infants who were born SGA failed to manifest sufficient catch-up growth to achieve normal height within the first 2 years of life (Hokken-Koelega 1995). Interestingly, the proportion did not differ significantly between SGA infants born prematurely and those born full-term.

A study in France demonstrated that by the age of 22, compared with those born APA, individuals born SGA had a significantly reduced body size and a higher frequency of short stature (Jaquet 2004). An adult height of under 2.5 SDS was observed in 3.7% of the SGA group.

The SGA condition is associated with non-growth issues: Adult metabolic syndrome is a condition combining hypertension, glucose intolerance or type 2 diabetes and central obesity; dyslipidemia commonly present. This condition leads to an increased risk of cardiovascular disease. There is an increased prevalence of adult metabolic syndrome among obese adults and those born SGA (Barker 1993, Curhan 1996, Ong 2002, Yarbrough. 1998). Subject born SGA have an increased risk of being overweight in adult life, justifying that height, weight and body mass index are monitored closely to prevent excessive weight gain. As mentioned above, catch up growth in SGA may also be associated with the development of altered body composition (Ibanes 2006).

Failure to achieve sufficient catch-up growth to normal levels may be associated with psychosocial disadvantages. The impact of SGA and persistent short stature on psychosocial functioning is a much-debated issue, as data are contradictory and inconclusive. Some studies have noted a negligible impact of SGA on individuals, whereas others have reported a psychosocial disadvantage, cognitive and academic impairments, and behavioural problems (Kranzler 2000, Larroque 2001, Lundgren 2001, McCarton 1996, Paz 1995, Stabler 1998). When behavioural problems are evident, psychological evaluation is appropriate.

Thes data outline that the SGA condition carries medical outcome issues deserving strong consideration. Not only the SGA condition is associated with height issues, but also with other important disadvantages such as body composition, metabolic disorders and possible psychological adjustment issues in later life.

Short SGA Children may benefit from Growth Hormone Therapy: The short child born with the SGA condition may now benefit from GH therapy since it is a registered indication in many countries around the world. (Chatelain 1994, Carel 2003, DeZegher 2000, Ranke 1996, Saas 1999, Van Pareren 2003).

Evaluation of children born SGA who do not catch-up growth need evaluation to secure that GH treatment is appropriate (Reiter 1998). GH deficiency may be associated to the SGA condition (de Waal 1994, Albertsson-Wikland K. 1998). As for other GH indication full evaluation should be undertaken in order to understand how much the child suffers from his short stature, what is the level of expectation from GH therapy compared to what can be achieved by this treatment and finaly what is the overall benefit risk ratio as for any given child considered for GH treatment.

It seems wise that GH therapy is not started until the spontaneous catch-up phase is completed (2 to3 years of age). In some country authorities have recommended to wait for age 4 bfre starting GH. However very severe form could benefit from earlier treatment but the experience is still limited.

GH dose is still debated in short SGA. The FDA (USA) has approved 65 mcg/kg/day in contrast to the EMEA (Europe) recommending a starting dose of 35 mcg/kd/day. A prediction, model of response to treatment is available and usefull (Ranke 2000). Clearly there is a greater efficacy with the highest dose on height gain and velocity during the first three years. Long term outcome including final height however, even though better with the highest dose, shows less difference. The younger the child the better the response during the initial phase of treatment. Therefore the proper decision for treatment planning has to consider the severity of shortness, the final height objective, and the fact that long term treatment carries the risk of poor compliance. A major challenge is still to identify what is the most appropriate age to start and , once height near normalization (briging the height close to the target height chanel) has been achieved, how to maintain this benefit to adult height. Economics issue isneeds being be integrated: the older the child, the heavier and less responsive, the higher the cost. The younger the child, the more responsive and the lighter hence less costly per year, but the longer the duration of treatment…

Individual surveillance of plasma IGF-1 is now well recommended especially if high GH dose is used (Van Dijk 2006). Most investigators recommend that the GH dose be diminished if plasma IGF-1 is greater than +2. 5 to +3.0 SD for age. This attitude is based on safety grounds since long term effect of high IGF-1 level during the growing phase is not documented

Tolerance to GH treatment needs consideration. Glucose tolerance may need specific surveillance since high GH dose may alter glucose homeostasis including in non obese SGA. High-dose GH therapy is associated with reversible decreases in insulin sensitivity (de Zegher 2000). The relative risk for metabolic syndrome as adult raises the question of long term tolerance of GH therapy. However the experience acquired from clinical trials and national scale use in several large countries at the dose ranging from 35 to 65 mck/kg/day establishes a fair tolerance (Cutfield 2000, De Zegher 2000). Should the patient be overweight and or should te family history be positive for type 2 Diabetes or obesity, we recommend specific surveillance of glucose hemoestasis including fasting glucose and sometime oral glucose tolerance test.

Conclusion: Most short children who were born SGA will experience catch-up growth leading to normal adult height but around 8–15% will have persistent short stature. Children who are short for their age can suffer psychosocial disadvantage throughout childhood and adulthood.Catch -up growth can be achieved through GH treatment, which has been shown to display a favourable benefit-risk balance. Still the optimal schedule and regimen for individual therapy of short children born SGA requires additionalm research and experience before considered to be fully established.

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Symposium 2: Electrolyte Disorders

S2-01

Recent Insights in the Nephrogenic Syndrome of Inappropriate Antidiuresis

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Mutations of G-protein coupled receptors are responsible for a wide range of diseases. With respect to water balance and vasopressin signaling, more than 180 different inactivating mutations have been previously described in the V2 vasopressin receptor (V2R), resulting in nephrogenic diabetes insipidus. In contrast, we have recently described the first known patients with V2R activating mutations, both infant males. Patients with these novel gain-of-function V2R mutations have a disorder which we have termed "nephrogenic syndrome of inappropriate antidiuresis" (NSIAD): a clinical presentation consistent with the syndrome of inappropriate antidiuretic hormone secretion but with undetectable levels of arginine vasopressin (antidiuretic hormone). Since our original description, several other cases of NSIAD have been described in various parts of the world. In follow-up studies, we have demonstrated that urine Aquaporin 2 excretion is inappropriately elevated in NSIAD and does not suppress normally with water loading. In addition, we have found that our original patient, now a toddler, is able to maintain eunatremia without intervention, associated with hypodipsia and an apparent intact thirst mechanism. The mechanisms by which these gain-of-function mutations constitutively activate the V2R are currently being investigated.

S2-02

Childhood Cerebral Salt Wasting

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Disturbances in salt and water balance are common in children managed in tertiary institutions for intracranial pathologies such as tumours and head injuries and present significant complexities in diagnosis and management. While hypernatremia associated with diabetes insipidus is a commonly encountered entity, hyponatraemia is also frequently seen.

The commonest recognized cause of hyponatremia in these situations is the syndrome of inappropriate antidiuretic hormone secretion (SIADH), however there has been increasing recognition of cerebral salt wasting, characterized by high net urinary sodium losses, polyuria and extracellular volume contraction. Diagnosis can be challenging, especially as other conditions such as central diabetes insipidus can precede or coexist. There has been debate about how commonly

CSW occurs (compared to SIADH) and even some questioning of its existence as a distinct entity.

Natriuretic peptides, particularly atrial (ANP) and brain (BNP), have been implicated in the pathophysiology of CSW, however this remains incompletely understood. Management of CSW includes recognition and then accurate replacement of sodium and fluid losses. Often this is sufficient and the disturbance relatively brief, however in more persistent cases, we and others have reported experience with the use of fludrocortisone as an additional therapeutic option.

S2-03

Genetic and Functional Study of Congenital Lipoid Adrenal Hyperplasia

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Congenital lipoid adrenal hyperplasia (lipoid CAH) is the most severe form of CAH, impairing adrenal and gonadal steroidogenesis. Most cases of lipoid CAH are caused by recessive mutations in the gene encoding steroidogenic acute regulatory protein (StAR), a protein that plays an essential role in cholesterol transfer from the outer to inner mitochondrial membrane, thus providing the substrate for steroid hormone biosynthesis. Affected children typically present with life-threatening adrenal insufficiency in early infancy due to a failure of glucocorticoid (cortisol) and mineralocorticoid (aldosterone) biosynthesis, and 46,XY genetic males have complete lack of androgenization and appear phenotypically female due to impaired testicular androgen secretion in utero. Recently, some patients have been reported that they showed late and mild clinical presentation. These cases and studies establish a new entity of 'non-classic lipoid CAH' showing that the phenotypic spectrum of StAR mutations is substantially broader than previously appreciated.

The cholesterol side-chain cleavage enzyme, P450scc (CYP11A1), have a crucial role in converting cholesterol to pregenolone in all steroidogenic tissues. Although progesterone production from the fetally-derived placenta is necessary to maintain pregnancy to term, some patients with P450scc mutations have recently been described. P450scc mutations can also cause lipoid CAH and constitute a recently recognized human endocrine disorder. The phenotypic spectrum seen in 46,XY individuals is likely to range from severe loss-of-function mutations associated with prematurity, complete underandrogenization and severe, early-onset adrenal failure, to partial changes found in children born at term with genital ambiguity and later-onset adrenal failure. In contradistinction to lipoid CAH caused by StAR mutations, adrenal hyperplasia has not been reported in any of the patients with P450scc deficiency.

Symposium 3: Diagnosis and Management Challenges

S3-01

Diagnosis and Management Challenges of Noonan Syndrome

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Noonan syndrome (NS) was first described as a syndrome with Turner phenotype and cardiac anomalies. NS is now recognized as an autosomal dominant dysmorphic syndrome characterized by hypertelorism, a downward eyeslant, low-set ears, short stature, a short/webbed neck, cardiac anomalies, deafness, motor delay, and a bleeding diathesis. Juvenile myelomonocytic leukemia, Arnold-Chiari malformation, thrombocytopenia, and deficiency of factor XI have been observed in some patients. The genetic analysis has revealed that half of the patient bears mutations in PTPN11, a gene encoding the non-receptor protein tyrosine phosphatase SHP2. In our study, PTPN11 mutations account for approximately 40% of Japanese NS patients. This type of NS is categorized as NS1, and other rarer forms of NS are identified to have mutations in NF1 gene (NF-NS), KRAS gene (NS3), SOS1 gene (NS4), RAF1 gene (NS5). NS2 is an autosomal recessive form of NS characterized by the high incidence of hypertrophic cardiomyopathy.

The growth hormone treatment for short stature is effective in the first year, but the effect is gradually attenuated. Thus the GH treatment for NS is still controversial.

S3-02

Klinefelter Syndrome (KS): Growth and Hormone Replacement

Leo Dunkel

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Since the identification of its chromosomal basis 47,XXY in 1959, the typical KS phenotype has become well recognized, but the mechanisms behind the testicular degeneration process have remained unrevealed. The KS boys have sufficient testosterone levels to allow normal onset and progression of puberty. Their serum testosterone levels remain within the low-normal range almost throughout puberty, but from midpuberty onwards, signs of a relative testosterone deficiency emerge. Findings like a leveling-off in testosterone and insulin-like factor 3 (INSL3) concentrations, high luteinizing hormone (LH) levels, and exaggerated responses to gonadotropin-releasing hormone (GnRH) stimulation suggest diminished testosterone secretion. In KS subjects, measurements of serum INSL3 may be useful in monitoring Leydig cell function. In the KS boys the number

of germ cells is markedly low already at the onset of puberty. The pubertal activation of the pituitary-testicular axis accelerates germ cell death. Germ cell differentiation is—at least partly—blocked at the spermatogonium or early primary spermatocyte stages, since no pachytene spermatocytes are detected in the testes in puberty. Genetic features of the X chromosome affect the KS phenotype. Further studies are, however, needed to reveal the mechanisms responsible for the testicular degeneration and the phenotypic differences in KS.

S3-03

Thyroiditis in Paediatric and Adolescent Age Groups

Nikhil Tandon

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All forms of thyroiditis, acute, sub acute and chronic can occur in childhood, though the first two are infrequent. Chronic thyroiditis is an autoimmune disorder characterised by lymphocytic infiltration of the thyroid gland with a predominant Th 1 cellular response. It is frequent in girls, shows familial aggregation and is associated with type 1 diabetes mellitus, celiac disease, and other autoimmune disorders, as well as with Turner syndrome. An association has also been described with certain HLA haplotypes and exposure to excess dietary iodine.

The disorder usually presents with asymptomatic goitre; less frequently with symptoms of hypothyroidism and rarely with thyrotoxicosis. The diagnosis of chronic lymphocytic thyroiditis is based on presence of anti TPO antibodies that are detectable in > 95% of the cases. Fine needle aspiration of the thyroid shows characteristic lymphocytic infiltration with lymphoid follicles, follicular cell hyperplasia with minimal fibrosis. Ultrasonography is increasingly used to corroborate the diagnosis. The natural history of this disorder in adolescence is inadequately known. Two thirds have persistent disease, with half of them becoming hypothyroid over the next two decades, while the remaining one third undergo spontaneous remission. Close follow up with assessment of serum TSH every 6-12 monthly is necessary to detect hypothyroidism at the earliest.

Our studies in this subject indicate that among goitrous children in the community, the prevalence of thyroiditis as defined by the presence of thyroid microsomal antibodies (TMA) was 6%. Prevalence of high TMA titres was significantly more in goitrous girls compared to goitrous boys and non-goitrous controls. Similarly, cytopathological evidence of lymphocytic thyroiditis was observed in 6% of goitrous children. Either significant TMA positivity or cytological evidence of thyroiditis was seen in 9.4% of goitrous children and adolescents. Prevalence of high titres of TMA was significantly higher in children with thyroid dysfunction as compared with euthyroid children. Conversely, 29% of goitrous subjects with significant TMA positivity had thyroid dysfunction as compared with less than 4% of TMA negative goitrous subjects. Similarly, 22.8% children with cytological evidence of thyroiditis had thyroid dysfunction as compared with less than 4% of goitrous children with a cytological diagnosis of colloid goitre.

While larger cross-sectional studies have failed to reveal any association of thyroiditis in children with urinary iodine excretion, some small studies have shown a higher urinary iodine excretion in children with thyroiditis compared with those without disease. In view of the significant familial association observed in this disease, it would be advisable to screen all first degree relatives of these children for thyroid dysfunction. Immunogenetic studies reveal a positive association with HLA-DRB1*1404 and HLA-DRB1*03. In addition, a higher paternal transmission of HLA-DRB1*14 to affected offspring was observed in comparison to unaffected offspring.

Recent studies have shown that thyroid USG has a useful, though limited, role in excluding thyroid disease in children. Subjects with hypoechogenicity had higher percentage of thyroiditis on cytopathology, thyroid peroxidase antibody positivity and thyroid dysfunction than those with normal echogenicity. However, sensitivity of echogenicity for the diagnosis of autoimmune thyroiditis in children is less than that reported in adults.

In conclusion, thyroiditis in children and adolescence is commonly autoimmune in origin with its clinical presentation varying from asymptomatic goitre to thyroid dysfunction, more commonly hypothyroidism. Close monitoring of thyroid functional status is recommended for early detection of hypothyroidism, and in view of a high familial association, screening of first degree relatives is recommended.

Symposium 4: Regional Challenges/ Neonatal Screening

S4-01

Newborn Screening: Obstacles and Challenges in a Developing Country

Sylvia Capistrano-Estrada

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Newborn screening refers to a system of testing babies within the first few days of life for health conditions that may cause undesirable consequences if these conditions are not detected and treated early. The system has six components: education, screening, early follow-up, diagnosis, management and evaluation(1). It has been said that the barriers to successful newborn screening implementation are similar whether the program is in a developing country or in a more developed one. The following have been identified as obstacles to newborn screening: education (understanding and awareness about newborn screening by the medical, political and lay communities), finances (adequate means to fund and sustain newborn screening), logistics (infrastructure and technology to ensure smooth implementation of testing, follow-up, diagnosis and treatment), culture (beliefs, norms and perception of people in relation to family, parenting and medical care), and politics (government policies and support, networking and integration of newborn screening within the health, lay and political environment). Each country's challenge is to address these barriers

within the context of their priorities and limitations (2). The talk will discuss newborn screening in the Philippines and will highlight the major strategies being used to ensure its nationwide implementation.

S4-02

Challenges for Newborn Baby Metabolic Screening Programmes

Bendikson K[1], Hofman P[2], Webster D[3]

[1]National Screening Unit, Ministry of Health, [2]University of Auckland, [3]National Testing Centre, LabPlus, Auckland City Hospital, New Zealand

All screening programmes face challenges. Developed programmes are more likely than developing to have dealt with establishing a screening infrastructure for dealing with specimen collection, followup and treatment of affected infants; to have good coverage and a secure, probably government funding. Challenges remaining include improving the rate of unsuitable samples and their transit time to the laboratory; using second-tier tests and other strategies to improve screening specificity; developing local networks able to develop performance metrics (eg positive predictive value) for screening and develop standards for these – which requires a uniform definition of disorders consistent with counting in a timely fashion; and developing and having accepted by local funding agencies criteria for adding and removing tests. Related to this is the challenge to be more rigorous in quantifying the benefits of early detection and treatment in order to compare possible new screening with existing newborn metabolic screening and other screening in the jurisdiction. The state screening programmes of Australia (5) and New Zealand (1) together screen almost 400,000 infants annually and have worked together on quality initiatives since the early 1980s. Performance metrics and standards for the programmes will be presented.

Symposium 5: Diabetes Mellitus

S5-01

The Psychological Impact of Type 1 Diabetes in Childhood and Adolescence

Fergus Cameron

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The attainment of optimal mental health and neurocognition is arguably the pre-eminent developmental task of childhood and adolescence. The potentially deleterious impact of a chronic disease such as type 1 diabetes upon brain development is therefore highly significant. Given the dependency of the neural ontogeny and function upon stable and adequate blood glucose levels, there is a strong theoretical concern that type 1 diabetes in childhood and adolescence may impact upon neurocognitive development. DSM IV psychiatric disorders have been well documented in adolescents with type 1 diabetes and it now appears that poor mental health is the most prevalent complication of diabetes in young adult life1. Recent DCCT publications found no deterioration in cognitive function in adults or adolescents2, 3. Children and younger adolescents however have different neurophysiological requirements and the issue of the impact of type 1 diabetes on the developing brain remains an open question4. Twelve year prospective data from diagnosis of type 1 diabetes through to adult neuromaturation in cohorts of type 1 diabetes patients and controls showed that patients experienced measurable and significant decreases in verbal, performance and full scale IQ with concomitant morphological and chemical changes consistent with lower neuronal density, increased gliosis and demyelination particularly in the frontal lobes and basal ganglia and brain volumetric differences. The same cohort of patients demonstrated markedly reduced rates of secondary school education compared to controls. Thus type 1 diabetes does appear to have significant psychological and functional sequelae in childhood and adolescence.

Reference

1. Cameron FJ, Northam EA, Ambler G, Daneman D. Routine psychological screening in the young: a notion whose time has come? Diabetes Care 2007; 30:2716-2724.

S5-02

Towards the Development of an Artificial Pancreas: Continuous Glucose Monitoring and Closed-Loop Insulin Delivery

William Tamborlane

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Real-time continuous glucose monitoring (RT-CGM) systems have the potential to be the most important advance in assessing diabetes control and in improving clinical management in the past 20 years. Nevertheless, the efficacy of current RT-CGM devices in lowering HbA1c levels more safely in children and adolescents with T1DM has not been established. In this presentation we will review the results of the recently completed JDRF RT-CGM randomized clinical trial of continuous versus standard glucose meter monitoring in patients with T1DM who ranged in age from 8 to > 70 years. The JDRF trial involved over 330 patients who were studied during the randomized phase for 6 months. The effect of patient age on the responses to RT-CGM use will be evaluated. It should be noted, however, that no approach to insulin replacement will be optimal until there is feedback control of insulin delivery based on minute to minute changes in glucose levels. The first practically applicable closed-loop insulin delivery system will employ external pumps and external glucose sensors. Preliminary results with one such system will be presented and the next steps forward will be discussed.

S5-03

Current Status of Obesity and Metabolic Syndrome in Children and Adolescents

Ho-Seong Kim

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The increasing prevalence of childhood obesity is a worldwide trend and is becoming a significant public health problem. Moreover, childhood obesity is directly related to metabolic syndrome, but there is limited information on their relation in Korean children and adolescents. The author investigated the association between obesity and metabolic syndrome among 2,165 Korean boys and girls aged 12-19 years, who participated in the Korean National Health and Nutrition Examination Survey in 1998 and 2001. Obesity was defined by body mass index cutoff points provided by the U.S. Centers for Disease Control and Prevention. A diagnosis of the metabolic syndrome is made when three or more of the following risk factors are present: (1) waist circumference ≥ 90th percentile; (2) systolic or diastolic blood pressure ≥ 90th percentile; (3) triglyceride ≥ 1.24 mmol/L (110 mg/dL); (4) high-density lipoprotein cholesterol ≤ 1.03 mmol/L (40 mg/dL); (5) fasting glucose ≥ 6.1 mmol/L (110 mg/dL). The prevalence of obesity increased significantly from 5.4% in 1998 to 11.3% in 2001 ($p < 0.0001$). The overall prevalence of the metabolic syndrome also increased significantly from 6.8% in 1998 to 9.2% in 2001 ($p < 0.05$). The prevalence of the metabolic syndrome increased significantly with severity of obesity (p for trend < 0.05). Approximately 50% of obese boys and 40% of obese girl had the metabolic syndrome. These findings indicate the importance of prevention and management of the metabolic syndrome in children and adolescents.

Kaichi Kida Oral Session

OR-1

Transgenerational Effects of Prematurity on Glucose Metabolism and Body Composition

Sarah Mathai, Wayne Cutfield, Jane Harding, Stuart Dalziel, Janene Biggs, Paul Hofman

Paediatric Endocrinology, The Liggins Institute, University Of Auckland, New Zealand

Aims: To evaluate the insulin sensitivity (Si) and body composition of offspring from prematurely born parents (≤37 weeks gestational age) compared to offspring from term parents.

Methods: Premature and term adults born between 1969 and 1974 with children aged 5 to 10 years were recruited. Si was assessed using either a sampled intravenous glucose tolerance test (children) or hyperglycaemic clamp (adults) and DEXA scans used to measure body composition.

Results: see attached file (Table 1)

Table 1. Mean ± SEM

	Offspring of premature parents	Offspring of term parents	p value
n	37	21	
Age (years)	8.0 ±0.3	7.9±0.3	0.82
Male Gender	17	14	0.56
Fasting glucose (mg/dl)	83±1.4	77.2±8.2	0.53
Fasting insulin (mu/l)	4.4±0.5	5.1±0.6	0.06
Si (10^{-4}/min^{-1}/mU/liter)	12.6±1.0	14.6±1.7	0.32
Acute insulin response (AIRg, mu/l)	420±84	266±27	0.09
Disposition index	3593±379	3861±676	0.7
Glucose effectiveness (10^{-2}/min^{-1})	2.4±0.2	3.2±0.2	0.01
Total body fat (%)	23.4±1.5	18.6±1.7	0.04
	Premature parent n=31	Term parent n=21	
Si (mg.kg^{-1}min^{-1}mu.l^{-1} x 100)	19.0±2.5	36.3±5.2	0.002
AIR g (mu/l)	56.1	25.3	0.003
Total body fat (%)	34.5±1.6	29.9±1.9	0.05

Premature parental Si was correlated with children's Si ($p=0.35$, $p<0.05$) but not in controls. There was no parent of origin effect.

Conclusion: Offspring of premature parents have alterations in glucose metabolism and body composition, suggesting transgenerational inheritance.

OR-2

Long-Term Down-Regulation of mRNAs Encoding Steroidogenic Enzymes in the Adrenal Gland after Transient Asphyxia in Preterm Fetal Sheep

Mhoyra Fraser, Laura Bennet, Charisma Dhaliwal, Wayne Cutfield, Alistair Gunn

Physiology and the Liggins Institute, University of Auckland, New Zealand

Aims: It has been postulated that exposure to high cortisol levels during fetal life, as may occur during exposure to intrauterine stress, may chronically alter the 'set-point' of the hypothalamic-pituitary-adrenal (HPA) axis.

Methods: We examined the hypothesis that the marked physiological hypercortisolemia associated with acute asphyxia induced by 30 min of umbilical cord occlusion in chronically instrumented preterm fetal sheep (0.6 gestation; term is 147 days), would be associated with long-term changes in genes regulating cortisol biosynthesis. After 28 days recovery fetal adrenals were collected; quantitative real-time PCR (qRT-PCR) was used to quantify mRNA.

Results: Adrenal mRNA expression for cholesterol side-chain cleavage (CYP11A1) was significantly reduced ($P<0.001$) in occluded fetuses compared with levels in sham controls. Nonsignificant trends

for reduced mRNA expression was observed for SF-1, StAR, CYP17, CYP21, HSD3B2 and ACTH receptor mRNA.

Conclusion: In conclusion, exposure to transient acute asphyxia in the preterm fetus is associated with long-term downregulation of expression of CYP11A1, a key steroidogenic enzyme that controls the rate-limiting step of steroid biosynthesis.

OR-3

Insulin-Like Growth Factor Binding Protein-3 Inhibits Proliferation of MCF-7 Human Breast Cancer Cells through a Senescence-Like Mechanism by Inhibiting Telomerase Activity

Ho-Seong Kim, Woo Jung Lee, Ji Young Kim, Sun Woo Lee, Hyun Wook Chae, Duk-Hee Kim

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Aims: The insulin-like growth factor binding protein (IGFBP)-3 has been shown to potently inhibit proliferation of various cell types in an IGF-independent manner. However, the specific mechanism for the IGF-independent action of IGFBP-3 has yet to be elucidated. In the present study, we have demonstrated that IGFBP-3 inhibits cell proliferation through a senescence-like mechanism by inhibiting telomerase activity.

Results: Induction of IGFBP-3 in MCF-7 human breast cancer cells inhibited DNA synthesis in an IGF-IGF receptor-independent fashion. The percentage of cells containing senescence-associated β-galactosidase activity was 6 times higher compared with control cells. The effect of IGFBP-3 on inducing senescence-like phenotype was abolished by co-treatment with siRNA against IGFBP-3, suggesting that IGFBP-3 induces senescence specifically. Flow cytometry analysis showed that cells in G0/G1 phase were increased in the IGFBP-3-induced cells compared with controls. In addition, telomerase activity by TRAP (telomeric repeat amplification protocol) assay and the expression of human telomerase reverse transcriptase mRNA by real-time RT-PCR were decreased.

Conclusion: These results show that cellular production of IGFBP-3 leads to senescence-like phenotype through the inhibition of telomerase activity in MCF-7 human breast cancer cells, thereby inhibiting cell proliferation in part, and that IGFBP-3 functions as a negative regulator of breast cancer cell growth.

OR-4

The Effect of Iodine Imbalance on the Development of Thyroid Dysfunction in Preterm Infants

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Aims: Iodine is essential for biosynthesis of thyroid hormone and dietary iodine intake of lactating women is high in Korea. The aim of this study was to know the relationship between iodine imbalance and development of thyroid dysfunction in preterm infants.

Methods: Urinary iodine concentration (UI) and thyroid function of 34 preterm infants born at ≤34 weeks' gestational age were evaluated. Initial tests were performed on the first week of life, and the second tests were performed on the 3rd week of life in 21 infants.

Results: The median values of initial and the second UI were 118.4 μg/L and 701.3 μg/L respectively. Preterm infants were divided into 3 groups according to UI of initial test [low (n=13), <50 μg/L; intermediate (n=9), 50~300 μg/L; high (n=12) >300 μg/L]. The average intake of breast milk on the 1st week of life were significantly different in 3 groups (0.8±2.0 mL/kg; 10.3±13.0 mL/kg; 50.1±41.0 mL/kg, $P<0.05$). Thyrotropin values on the 3rd week of life of low UI group and high UI group tended to be increased (8.8±7.6 μU/mL; 6.8±3.4 μU/mL; 16.1±11.9 μU/mL).

Conclusion: These results suggest that insufficient or excessive iodine intake may cause delayed thyrotropin elevation in preterm infants.

OR-5

The Genetic Base of Neonatal Diabetes Mellitus and Clinical Therapy in China: A Pilot Study

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Aims: To investigate the genetic base in Chinese neonatal diabetes patients and to explore the effect of sulfonylureas in clinical management of the patients.

Methods: 12 infant diabetes patients and their parents were recruited, genomic DNA were extracted from the peripheral bloods.

KCNJ11,ABCC8 and insulin gene were sequenced using direct PCR products. 7 patients were treated with glibenclamide, 5 patients were treated with insulin based on the parents' choice.

Results: 1)Three different mutations were found in ABCC8 gene (D209E/N, L39V/N, I544T/N), one mutation were found in KCNJ11 gene (V59M/N), one patient was found with methylation defects in 6q24, one patient were found with insulin gene muation. 2) All the patients were effect when treating with insulin injection. 3) 5 of the 7 patients treated with glibendamide successfully stop insulin therapy and maintain good glycemic control with oral agents.

Conclusion: we found high frequency gene muations in Chinese neonatal diabetes patients especially in KCNJ11 and ABCC8 gene. Oral sulfonylureas were effect in most of the patients which highly suggests glibendamide could the first chioce for neonatal diabetes patients. However large scale, mulitcentric study will still be needed in the future.

Oral Session 1: Adrenal Gland

OR-6

Differences in Adrenomedullary Function between Phenotypes and Genotypes in Classical Congenital Adrenal Hyperplasia Patients with 21-Hydroxylase Deficiency

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Aims: There is good evidence that proper glucocorticoid secretion of the adrenal cortex is necessary for adrenomedullary epinephrine synthesis. We investigated the association between adrenomedullary function, disease severity, and genotype in classical congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency.

Methods: Thirty-five patients were enrolled in this study, who were able to collect 24-hour urine. Plasma and 24-hour urinary catecholamines and their metabolites, and the CYP21 genotype were determined in all patients. The disease-causing mutations were divided into 3 groups according to expected 21-hydroxylase activity (Null group with no residual enzyme activity; group A with 0-2% of enzyme activity; group B with >2% of enzyme activity).

Results: Plasma epinephrine and 24-hour urine epinephrine concentrations were lower in patients with salt wasting form than in those with simple virilizing form. Plasma and 24-hour urine epinephrine concentrations were correlated with the expected 21-hydroxylase activity based on genotype (Null < A < B). Concordance rate between clinical phenotype and predicted phenotype based on 21-hydroxylase activity was 91.2%.

Conclusion: We observed the parallel decrease in adrenomedullary function and adrenocortical function in patients with classical CAH. Measurement of plasma and 24-hour urinary catecholamines and their metabolites appears to be another biomarker of predicting the disease severity.

OR-7

Functional Effects of DAX-1 mutations Identified in Korean Patients with X-Linked Adrenal Hypoplasia Congenita

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Aims: X-linked adrenal hypoplasia congenital (AHC) with hypogonadotropic hypogonadism and adrenal insufficiency is a rare disorder caused by mutations of DAX-1. In this study, we investigated the functional defect of DAX-1 caused by mutations (i.e., the W105X, Q252X and L386delfs2) that were identified in 3 unrelated Korean patients with AHC.

Methods: To evaluate the functional defect of DAX-1 caused by mutations, we used a promoter assay in vitro. After mutagenesis of the DAX-1 gene, steroidgenic factor 1 (SF-1) and promoter region of steroidogenic acute regulatory protein (StAR) genes were transiently co-transfected into HEK293 cells. Subsequently, the luciferase activity of StAR was measured by fluorescence spectrophotometer.

Results: DAX-1 inhibits not only the transcriptional activity of SF-1, transcriptional activator of many genes involved in steroid hormone biosynthesis, but also the expression of StAR by binding to DNA hairpin structure in the StAR promoter. The mutant DAX-1 proteins showed functional activity comparable to that of normal DAX-1. However, the mutant DAX-1 proteins revealed lower repressive activity on the promoter of the StAR gene than normal DAX-1.

Conclusion: Nonsense mutations of the DAX-1 were shown to partially eliminate the ability of DAX-1 to repress the transcription of StAR in vitro assay.

OR-8

First Year of Congenital Adrenal Hyperplasia (CAH) Newborn Screening Program in Vietnam

Bich Phuong Nguyen[1], Nghiem Minh Pham[2]

[1]Endocrinology, Children's Hospital1, Viet Nam, [2]Newborn Screening, Tu Du Hospital, Viet Nam

Aims: To evaluate the benefits of NS for CAH from 1/6/2007 to 1/7/2008

Methods: 17OHP was measured by ELISA in filter paper blood samples. Infants with 17OHP > or = 40 nmol/L were recalled for a confirmative test.

Results: From 31200 screened newborns (115F, 100M; 325PT), 20 were recalled (none were PT), CAH was confirmed in 6 (4F, 2M), estimated prevalence 1/5200. Salt wasting (SW) CAH was diagnosed in 4 (2F, 2M) and simple virilizing (SV) CAH in 2F. Prader III (2 SW, 1 SV) and IV (1 SV). Median age at diagnosis was 7.1 days; median time to correct gender assignment 7.8 days (max 10). 2F were incorrectly assigned gender at birth. All cases were identified before clinical diagnosis and none had an adrenal crisis. No false negative cases were detected. The cost of NS was 40.000 VND (2.35 $US) / screened infant.

Conclusion: CAH appears to be more common in HCMC compared with rates in other countries with NS for CAH. We estimate that 182 babies/year have CAH in Vietnam. Benefits of screening were avoidance of SW crisis and early correct gender assignment in virilized girls. The results support a nationwide, government funded CAH NS program, for early diagnosis and prompt treatment.

OR-9

Spectrum of 21-Hydroxylase (CYP21) Gene Mutation and Genotype- Phenotype Correlation in Patients with Congenital Adrenal Hyperplasia (CAH 21OHD)

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Aims: To assess the spectrum of CYP21 gene mutation and study the genotype-phenotype correlation in patients with CAH 21OHD in an Indian population.

Methods: 82 alleles from 41 (27 F; 35 SW) patients with CAH 21OHD belonging to 39 families were studied.

Results: Percentage distribution of CYP21 gene abnormalities seen was as follows: IN2 20.7; deletion19.5; Q318X 18.3; I172N 8; R356W 4; novel 3.6 ;cluster 1; not characterized 19. Deletion, R356W, IN2, Q318X and cluster mutation were detected more frequently in SW phenotype while I172N and IN2 were found in NSW phenotype. Genotype was not always concordant with phenotype. Homozygous IN2 mutation showed an overlap with 85% being SW and 15% NSW phenotype.

Conclusion: The frequency of CYP21 gene mutations are different in this Indian cohort from other reported world literature. The frequency of mutations not characterized was comparable with other series. This information is useful to delineate appropriate strategies for prenatal diagnosis and expectant therapeutic measures in this particular population.

OR-10

Understanding the True Burden of Congenital Adrenal Hyperplasia (CAH) in Vietnam

Kate Armstrong[1], Claire Henderson[1], Nguyen Thi Hoan[2], Bui Phuong Thao[2], Garry Warne[3]

[1]CLAN (Caring & Living As Neighbours), Non-Governmental Organisation, Australia, [2]Endocrinology Department, National Hospital of Pediatrics, Hanoi, Viet Nam, [3]Department of Endocrinology and Diabetes, Royal Children's Hospital, Melbourne, Australia

Aims: Incidence of CAH in Vietnam is not known, although anecdotally it appears relatively common. CAH places heavy burdens on children and families; exploring these issues is vital to improving future health outcomes in Vietnam.

Methods: At the annual CAH Club meeting (National Hospital of Pediatrics, Hanoi) in June 2006, parents were offered a voluntary, confidential, written survey covering: demographic profile; income; health expenditures; diagnosis/treatment; family history; schooling; and ways to assist families.

Results: Response rate was high (130 families; 72%); 13/130 families (10%) had two children with CAH, so 143 children (median age 5 years) were represented. Most were rural (68%) and Kinh (94%). Intolerable financial burden of managing CAH was overwhelming response. Median monthly income was higher than the national average; very few rural poor families represented, suggesting higher mortality amongst this group. Sibling deaths were common: 19/130 families (15%) had lost a child previously (4/130 had lost two children). Educational sessions and support group meetings were considered helpful.

Conclusion: Urgent financial assessment and support of families at time of diagnosis of this chronic medical condition of childhood in Vietnam may be as relevant to survival as medical intervention.

Oral Session 2: Obesity & Diabetes

OR-11

Expression of OB-Rb and SOCS3 mRNA in Hypothalamus and Liver of Obese Rats Fed with High-Fat Diet

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Deptment of Pediatrics, The Second Affiliated Hospital Dalian Medical University, China

Aims: To study the expression of OB-Rb and SOCS3 mRNA in hypothalamus and liver of obese rats.

Methods: Young rats in 8 week high-diet and control group diverged based on body weight gain into obese and control group. Serum leptin and insulin levels were measured by RIA, and gene

expression of OB-Rb, SOCS3 mRNA in the hypothalamus and liver was detected by RT-PCR.

Results: The levels of leptin and insulin in obese rats were increased compared with control rats, and the levels of OB-Rb in hypothalamus and liver were reduced significantly, the expression of SOCS3 mRNA in hypothalamus and liver was increased markedly. There was a negative relationship between SOCS3 and OB-Rb mRNA levels in hypothalamus and liver; similarly, there was a significant negative correlation between serum leptin concentrations and OB-Rb mRNA levels in hypothalamus and liver in obese rats. Serum leptin concentrations of obese rats had a significant positive relationship with SOCS3 mRNA levels in hypothalamus and liver. Serum insulin levels had no relationship with OB-Rb or SOCS3 mRNA levels in neither liver nor hypothalamus.

Conclusion: The up-regulation of SOCS3 gene expression may act as one of the factors that result in leptin resistance in obese rats.

OR-12

The Time Serial Changes of Adiponectin in SGA Rats and Its Relationship with Insulin Resistance

Ying Yanqin

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Aims: To observe the time serial changes of adiponectin levels in SGA rats and its relationship with insulin resistance

Methods: An SGA animal model was built by maternal nutrition restriction. AGA rats were as controls. The SGA rats were randomly divided into five groups and executed at 3, 5, 7, 9 and 12 weeks of age. Fasting glucose was detected by GOD-PAP, and fasting insulin and adiponectin were detected by ELISA. The relationships between adiponectin and insulin resistance index (IRI) and BMI were evaluated.

Results: The adiponectin in SGA rats were significantly higher than AGA at 3 and 5 weeks of age, and lower from 9 to 12 weeks of age. In SGA rats, adiponectin were inversely related to BMI at 5 and 12 weeks of age, and inversely related to IRI at 7, 9 and 12 weeks of age.

Conclusion: The adiponectin in SGA were time serial changed and the decreased adiponectin was inversely related to BMI andIRI. This may be a prognostication of high risk of type 2 diabetes and atherosclerosis in adult.

OR-13

Correlations between the Timing of Adiposity Rebound (AR) and Metabolic Syndrome in Japanese Obese Children

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Aims: Reveal the timing of AR as well as the relationships between AR and dyslipidemia, insulin resistance, visceral fat accumulation, non-alcoholic fatty liver disease (NAFLD) in Japanese obese children.

Methods: Age at AR, serum lipids, HOMA-IR, content of visceral fat, prevalence of NAFLD were examined retrospectively in 78 obese Japanese children.

Results: Age at AR was 2.55±1.10 years in the whole study population. Children undergoing earlier AR exhibited a trajectory with higher levels of BMI after reaching AR and got increased serum levels of low density lipoprotein cholesterol (LDL), content of abdominal fat, HOMA-IR and prevalence of NAFLD in late childhood and young adolescence. The timing of AR correlated with HOMA-IR and abdominal fat accumulation (visceral and subcutaneous fat) inversely, and was an independent predictor to NAFDL.

Conclusion: An early AR not only associated with the development of obesity in adolescence, but also a risk factor for the development of dyslipidemia and visceral obesity, and thus was one of the factors that account for the development of insulin resistance and NAFLD. Early intervention for the controlling of rapid weight gain during the period of AR may be useful for prevention of the risk for obesity and other components of metabolic syndrome later in life.

OR-14

Effectiveness of Beta2-Microglobulin and Cystatin C as Early Predictive Markers of Diabetic Nephropahy

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Aims: Determination of microalbuminuria has been suggested as an early predictor of diabetic glomerular disease. But albumin excretion rates are altered by many variables and timed urine collection is tend to be erroneous and inaccurate. The aim of this study is to show clinical values of serum cystatin C(Cys C) and beta2-microglobulin in the assessment of renal function in pediatric diabetic patients.

Methods: 60 pediatric type 1 and 2 diabetic patients with microalbuminuria (30-300 mg/24 h) (n=30) and without microalbuminuria (< 30 mg/24 h) (n=30) were enrolled at Severance children's hospital. Anthropometric measurements and serum Cys C, beta2-

microglobulin, creatinine, urinary microalbumin levels, creatinine clearances were determined.

Results: In patients with microalbuminuria, serum Cys C was increased significantly in comparison to patients with normoalbuminuria($P<0.05$), while no differences were observed for beta2-microglobulin levels. Serum creatinine concentrations and creatinine clearances were not different between both groups. Cys C was positively correlated with serum beta2-microglobulin and serum creatinine. Serum beta2-microglobulin was also positively correlated with serum creatinine in patients with microalbuminuria.

Conclusion: Serum Cys C and beta2-microglobulin are useful endogenous markers in assessment of renal function in pediatric diabetic patients with and without microalbuminuria.

OR-15

Clinical Profile and Autoantibody Status in Younger Onset Diabetes in Bangladesh

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Aims: To examine the clinical profile and GAD and IA2-ic antibody (Ab) status in different clinical subtypes of 199 diabetics under 18 years attending BIRDEM.

Methods: A cross sectional study from January 01 to December 03. Patients were classified based on clinical features. Type 1 (Group1) patients were younger and had short duration of classical symptoms or presented with diabetic ketoacidosis (DKA); Patients with fibrocalculous pancreatic diabetes (FCPD/Group 2) had evidence of pancreatic stones; patients with malnutrition modulated diabetes (MMDM/Group 3) were malnourished with prolonged symptoms of diabetes without ketosis. Two type 2 diabetics were excluded from the analysis.

Table 1. Characteristics at presentation

	Group 1	Group 2	Group 3	p value
Age at diagnosis (yrs)	9.29±4.1	13.54±2 1	13.84±2.33	0.0001
Duration of symptoms at diagnosis (months)	1.45±1.28	5.6±8	10.16±8.05	0.0001
DKA	12/52[21.1%]	0/31	0/45	
BMI (kg/m^2)	14.05±3.8	13.06±2.2	12.76±2.7	0.0001
Hb A1c (%)	14.75±2.84	17.62±2.05	16.37±2.96	0.0001
C-peptide (ng/ml)	0.54±0.51	0.47±0.23	0.66±0.67	0 .70
GAD Ab positive	23/55[41.8%]	2/12[16.6%]	6/44[13.6%]	0.05
IA2-ic Ab positive	17/55[30.9%]	1/12[8.3%]	10/44[22.72]	0.12

Results: Among 133 newly detected patients 40.6% had type 1 diabetes, 23.26% FCPD and 35.3 % MMDM.The charecteristics at presentation are shown in Table 1.Anti-GAD Ab positive patients had lower C-peptide ($p=0.01$) and relatively shorter duration of symptoms ($p=0.06$).

Conclusion: Although the three groups differ clinically , the C-peptide and antibody status do not discriminate between the types of diabetes defined by clinical criteria. Autoimmunity is also present in FCPD and MMDM groups indicating an overlap with type 1 diabetes in these groups.

Oral Session 3: Growth, Thyroid & Adipocyte

OR-16

The Impact of Thyroid Dysfunction on Neurodevelopmental Outcome among Premature Infants

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Aims: The objective of study was to determine the various thyroid dysfunctions and its impact on neurodevelopmental outcome among premature infants.

Methods: Premature infants whose gestational age was <34 weeks or birth weight <1,500g were enrolled during a period of 24 months (n=302). A follow up TSH and FT4 were obtained at <7 days old, 4 weeks and before discharge and sought how various thyroid dysfunctions affected neurodevelopmental outcomes at corrected age 18 months by Bayley Scales of Infant Development (n=152).

Results: 2 cases of primary congenital hypothyroidism showed normal neurodevelopmental outcome in one. Transient thyroid dysfunction was observed in 80 cases (52.6%) of which 23 cases (28.8 %) showed transient hypothyroxinemia. This group occurred more commonly among younger gestational age and influenced by their clinical illnesses, but did not show significant relations to neurodevelopmental outcome. In contrary, 52 cases (65%) of transient hyperthyrotropinemia of which 50% of persistent hyperthyrotropinemia had a significant impact on poor neurodevelopmental outcome ($p<0.01$). Transient hypothyroidism occurred in 5 of which all of them showed normal neurodevelopmental outcomes.

OR-17

Pilot Study on Comparative Proteomic Analysis in Male Children with Idiopathic Short Stature before and after Growth Hormone Therapy

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Aims: As a pilot study, the experiment was undertaken to investigate the change of proteomic profiles in sera of growth hormone (GH) treated subjects.

Methods: The 6 male individuals with idiopathic short stature were included. Before and 3 months after GH therapy, their sera were obtained. The six most abundant proteins in each serum sample were depleted using Multiple Affinity Removal Columns (MARC). Subsequently, MARC-treated sera were run on 2-D gels and the image was analyzed by Melanie 7.0. The spots, expressed by at least 2 folds higher pre-GH therapy than post-GH therapy, were analyzed using MALDI-TOF method.

Results: The over-expressed proteins after GH therapy were diverse in each individual and the level of expression is not remarkably high. Total 19 different spots were found over-expressed after GH therapy and identified as complement 3, haptoglobin CRA-b, myosin, alpha-2-macroglobulin precursor, keratin 7 & 10, actin, tubulin and etc. It is difficult to implicate the function of these proteins in clinical significance. However, cytoskeletal proteins and acute phase reactive proteins seemed to increase in the sera of GH treated patients.

Conclusion: The proteomic expression pattern of sera may be altered by GH therapy, which will give an insight into the identification of biomarker of GH responsiveness.

OR-18

IGFBP-3 Effects on Adipocytokine Expression in 3T3-L1 Adipocyte

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Aims: IGFBP-3 is the most abundant circulating IGF binding protein and is expressed in many tissues. IGFBP-3 not only regulates IGF bioavailability and action, but also mediates IGF independent actions on cell survival and apoptosis. We have recently shown that IGFBP-3 leads to the induction of insulin resistance in vitro in 3T3-L1 adipocytes and in vivo in rats. Adipocytes are emerging as an important endocrine source of adipocytokines as well as a target tissue for various cytokines that modulates insulin sensitivity. We carried out a series of experiments to elucidate the effects of IGFBP-3 on adipocytokine expression, which is related to insulin sensitivity. In addition, we studied the expression of the nuclear hormone receptor PPAR-γ, by RT-PCR in maturing adipocytes treated with IGFBP-3 as its levels often control adipocytokine expression.

Methods: We treated maturing 3T3-L1 adipocytes with IGFBP-3 (1 ug/ml) for 1 day and measured the mRNA levels of adiponectin, leptin, TNF-α, and IL-6 expression by RT-PCR.

Results: IGFBP-3 inhibited adiponectin and leptin expression, but stimulated TNF-α expression. No effect on IL-6 expression was observed. IGFBP-3 also inhibited PPAR-γ mRNA expression.

Conclusion: We conclude that the effects of IGFBP-3 on 3T3-L1 adipocytes are related to the regulation of expression of several adipocytokines that modulates insulin sensitivity. Down regulating PPAR-γ expression may be one of mechanisms of adipocytokine modulation by IGFBP-3.

OR-19

Impact Of c-myb on the Expression of Insulin-Like Growth Factor Binding Protein-3 in Human Chronic Myelogenous Leukemia Cells

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Aims: The c-myb plays an important role in regulation of cell growth and differentiation in immature hematopoietic cells. This study was characterize the impact of c-myb on the cell growth and IGF axis in human leukemia cells.

Methods: We investigated whether suppression of c-myb function by DN-myb modulates the cell proliferation and IGF axis in leukemia cells, K562.

Results: The overexpression of DN-myb inhibited c-myb induced cell proliferation, and c-myb induced cell growth was inhibited by using anti-IGF-IR antibody. DN-myb overexpression resulted in a significant decrease in the expression of IGF-I, -II and IGF-IR. However, IGFBP-3 was upregulated by DN-myb in K562 cells. The IGFBP-3 promotor activity assay and Western immnunoblotting demonstrated the DM-myb regulates IGFBP-3 at the transcriptional levels. In addition, IGFBP-3 inhibited cell proliferation of K562 cells in a manner dependent on its concentration. The PI3 kinase inhibitor LY294002, upregulates IGFBP-3 expression but downregulates IGF-I and IGF-II expressions. However, the IGFBP-3 promoter activity was not induced by LY294002.

Conclusion: The disruption of c-myb function by DN-myb may inhibit cellular proliferation at least by regulating expression of components of the IGF system, in particular, upregulation of IGFBP-3, and DN-myb gene therapy may useful for treatment of leukemia.

OR-20

Pomegranate Extract Induces Apoptosis in Human Prostate Cancer Cells by Modulation of the IGF-IGFBP Axis

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Aims: IGF axis is critical for the regulation of apoptosis in human cancer cells. Potent anti-tumorigenic effects of pomegranate juice and extracts have been reported. We investigated the relationship between pomegranate-induced apoptosis in human prostate cancer cells and the IGF/IGFBP system.

Methods: Cell proliferation and apoptosis ELISA assays were performed in human prostate cancer cells. Cells were treated with 10 μg/ml pomegranate extract standardized to ellagitannin content (POMx) and/or IGFBP-3/IGF-I. Western blotting were performed for investigating the influences of POMx treatment on the key signaling pathways known to be important in cell proliferation and apoptosis.

Results: Treatment of LAPC4 cell with POMx resulted in inhibition of cell proliferation and induction of apoptosis. Interestingly, co-treatment with POMx and IGFBP-3 revealed synergistic stimulation of apoptosis and additive inhibition of cell growth. Western blot analysis revealed that treatment with POMx or POMx/IGFBP-3 combination resulted in increased JNK phosphorylation, and decreased Akt and mTOR activation. IGF-1 completely blocked apoptosis induction by POMx in 22RV1 cell. In contrast, IGF-I failed to inhibit POMx-induced apoptosis in R- (IGF-IR null MEF) cells, suggesting the importance of IGF-IR. POMx-treatment decreased Igf1 mRNA expression in a dose-dependent manner.

Conclusion: These studies revealed novel interactions between the IGF system and pomegranate-induced apoptosis.

OR-21

Hypopituitarism is a Rare Consequence of Structural Traumatic Brain Injury in Early Childhood

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Aims: We aimed to assess the risk of post-traumatic hypopituitarism (PTHP) in young children with structural traumatic brain injury (TBI).

Methods: Prepubertal children who had sustained structural TBI before 3 years of age were recruited >1 year following TBI. PTHP was assessed with growth hormone (GH) stimulation (arginine 0.5 g/kg and clonidine 150 μg/m²), low dose synacthen (0.1 μg) and baseline thyroid function tests. Normal peak response was defined as GH ≥7 μg/L and cortisol >500 mmol/l.

Results: 36 children (56% male) were studied aged 7.1 years ±1.7, 5.8 years ±1.4 after TBI. Mechanism of injury was falls (56%), RTA (22%) and other (22%). Injury severity by GCS was mild (12-15) in 78%, moderate (9-12) in 11% and severe (<9) in 14%. CNS radiology revealed skull fracture only in 44% and intracranial haemorrhage or brain injury in 56%. One subject was GH deficient (peak GH 4.6 μg/l) with a normal IGF-1 (143 ng/ml) and another ACTH deficient (peak cortisol 474 mmol/l), giving a <6% prevalence of PTHP. Both had a GCS of 15.

Conclusion: Young children with structural CNS abnormalities following TBI are at low risk of PTHP. GCS may be a poor indicator of risk.

Oral Session 4: Bone & Ca, Development, & Syndrome

OR-22

The Natural History of Vitamin D Deficiency in African Refugees Living in South-Western Sydney: A Longitudinal Study

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Aims: To describe the natural history of hypovitaminosis-D in a cohort of African refugee migrants living in south-western Sydney, Australia.

Methods: A community based cohort of refugees from North Africa living in South-western Sydney took part in a health screening programme in local schools for children and their families. The programme included screening for 25-hydroxyvitamin-D (25(OH)-D) deficiency at the end of winter(T1). Serum concentrations of parathyroid hormone(PTH), calcium, phosphorus(PO4) and alkaline phosphatase(ALP) activity were also evaluated. Measurements were repeated at the end of summer(T2). We report on differences in 25(OH)D, PTH, calcium, PO4 serum concentrations and ALP serum activity between T1 and T2 and explored whether subgroup differences existed.

Results: Ninety-one asymptomatic African refugees with Type VI skin pigmentation were included. At T1 all were 25(OH)D deficient; 10% mild, 77% moderate and 13% severe. The mean 25(OH) D serum concentration increased from 18.9±5.6 nmol/L at T1 to 36.0±12.4 nmol/L at T2 (P<0.001). Eighty-seven-percent remained deficient at T2, none were severe.

Conclusion: Vitamin D deficiency was universal in our cohort during winter and 87% remained 25(OH)D deficient at the end of summer. The youngest age groups had the greatest improvement. This

supports the need for screening and supplementation of vitamin-D in high risk groups.

OR-23

Effects of Zoledronic Acid on Bone and Mineral Metabolism in Children with Femoral Head Avascular Necrosis

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Aims: To describe systemic effects on bone and mineral metabolism of intravenous Zoledronic acid (ZA) therapy in otherwise normal children and adolescents with femoral head avascular necrosis (AVN).

Methods: 37 children (age 10.8±2.76 years) with AVN of the femoral head (Slipped Capital Femoral Epiphysis (SCFE), N=20 or Perthes Disease (PD), N= 17) were treated with at least 12 months of intravenous ZA (0.1125 mg/kg/yr). Bone mineral density (BMD) z-scores and mineral homeostasis were evaluated at baseline, 6, 12 and 18 months.

Results: All children maintained height SDS during treatment. Bone age increased appropriately. Age adjusted z-scores of total body BMD (0.06+/-0.84 to 1.04+/-1.02), lumbar spine BMD (0.22+/-0.94 to 1.57+/-0.74) and lean tissue mass adjusted BMC (0.42+/-1.41 to 1.94+/-1.61) increased during the 18 months of treatment with no differences between SCFE and PD patients. Serum calcium, phosphate, alkaline phosphatase, osteocalcin and urine deoxypyridinoline/creatinine ratio decreased, whereas the concentration of PTH increased during the first 12 months of treatment. They all stabilised over the next 6 months. There were no incidences of fracture, spondylolisthesis or osteonecrosis of the jaw.

Conclusion: Here we report that ZA in otherwise healthy children with femoral head AVN significantly increases BMD while decreasing bone turnover.

OR-24

Dose Birth Weight Correlate with Serum Adipocytokines, IGF-I, Insulin and Mitochondrial DNA Copy Number in Cord Blood?

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Aims: Birth weight is associated with development of metabolic syndrome in later life. The aim of this study is to evaluate whether the levels of adipocytokines, IGF-1, insulin and mitochondrial DNA (mtDNA) copy number in cord blood are correlated with anthropometric parameters of newborn and/or mother.

Methods: We measured the levels of adiponectin, IGF-1, leptin, insulin and mtDNA copy number in cord blood of 100 full-term newborn babies: 16 SGA babies, 58 AGA babies, 26 LGA babies. We represented ratio of mtDNA to 28s rRNA as amount of mtDNA.

Results: The levels of IGF-1 in SGA (56.1±42.0 ng/ml) were significantly lower than those in AGA (93.6±58.2 ng/ml) and LGA (99.0±62.0 ng/ml) and were positively correlated with birth weight. The levels of leptin in LGA (13.5±11.1 ng/ml) were significantly higher than those in in SGA (4.1±2.7 ng/ml) and AGA (7.5±5.9 ng/ml), and were correlated with birth weight. The concentration of adiponectin, insulin was not significantly different between 3 groups. MtDNA copy numbers in cord blood were not significantly

Conclusion: Decreased mtDNA copy numbers in singletons of SGA and LGA suggest that both extremes of birth weight groups can develop metabolic syndrome in later life and should be followed-up.

OR-25

Phenotype–Genotype Correlations and the Efficacy of Growth Hormone Treatment in Korean Children with Prader-Willi Syndrome

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Aims: We compared phenotypic differences between the patients with microdeletion of the paternally derived 15q11-13 region and those with maternal uniparental disomy of chromosome 15 (mUPD15). In addition, the efficacy of growth hormone (GH) therapy was examined in these two PWS genotypes.

Methods: Fifty-three patients were diagnosed having PWS. Typical phenotypes and changes of heights, weights, and body mass indexes (BMI) before and after GH treatment were obtained by retrospective review of medical records. The data from the patients with microdeletion were compared with those from the patients with mUPD15.

Results: Of total 53 patients with genetically confirmed PWS, 39 cases (73.6%) had microdeletion and 14 (26.4%) with mUPD15. Maternal ages were significantly higher in the mUPD15 group, and hypopigmentation and feeding problem in neonatal period were more frequently observed in the microdeletion group. Growth hormone was administered to 20 patients (14 with microdeletion, 6 with mUPD15). There was no difference between two groups in height velocity, weight and height SDS, and BMI after GH therapy.

Conclusion: Phenotype and genotype correlations were observed in Korean PWS patients such as more advanced maternal ages in the mUPD15 group and more frequent feeding problems and hypopigmentation in the microdeletion group.

OR-26

PTPN11, SOS1, KRAS, and RAF1 Gene Analysis, and Genotype-Phenotype Correlation, in Korean Patients with Noonan Syndrome

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Aims: Germline mutations in the KRAS, SOS1 and RAF1 genes have been reported to cause Noonan syndrome (NS) besides PTPN11 gene after 2006. We assessed correlation between phenotype and genotype by molecular analysis of the PTPN11, SOS1, KRAS, and RAF1 genes in Korean patients with NS.

Methods: This was a retrospective study in 59 NS patients. Each diagnostic criterion of NS was explored, as were auxological parameters, levels of IGF-1 and IGF binding protein-3 (IGFBP-3). Mutation analysis of PTPN11, SOS1, KRAS, and RAF1 genes was performed. We compared each phenotype between 5 different genotype groups (the groups with each 4 gene mutations, and the group without mutation in any of these 4 genes).

Results: We found disease-causing mutations in 30 (50.8%) patients, which were located in the PTPN11 (27.1%), SOS1 (16.9%), KRAS (1.7%) and RAF1 (5.1%) genes. The patients with PTPN11 mutations showed higher frequencies of patent ductus arteriosus and thrombocytopenia. The patients with SOS1 mutations had lower incidences of delayed psychomotor development. All patients with RAF1 mutations had hypertrophic cardiomyopathy.

Conclusion: The molecular defects of NS are genetically heterogeneous and involve several genes other than PTPN11 related to the RAS-MAPK pathway. In addition, certain genotype-phenotype correlations seem to be discernable.

OR-27

IVF Methods Influence Childhood Growth

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Aims: Our aim was to compare growth and body composition of in-vitro fertilization (IVF) offspring born following thawed embryo replacement (IVFT) to normally conceived (controls) and fresh embryo IVF children (IVFF).

Methods: Healthy pre-pubertal children aged 4-10 years were evaluated, all born at term from singleton pregnancies. Children in the IVFT group were compared to two other groups; an IVFF group and a control group. Anthropometric measurements, bone age and DEXA scan were performed.

Results: All parents had similar BMIs and Mid-Parental Heights (MPH). Mothers in the IVF group were older. IVFF children were taller than both IVFT children and controls.

See table 1. Results expressed as mean±SD.

*p=<0.05 across groups

Conclusion: Thawed embryo IVF children (IVFT) exhibit auxological differences when compared to normally conceived or fresh embryo IVF children (IVFF), this may be due to the additional manipulation during the cryopreservation process.

Table 1.

	IV F_T	IV F_F	Controls
Total subjects	32	70	96
% females	43	50	46
Mean age	6.7±1.7	5.9 ±1.3	7.0±1.9
Gestation	39.5 ±1.9	39.3±1.6	39.6±1.6
Birth weight SDS	0.6±1.0	–0.1±1.2	0.4±0.9
H-MPH SDS	0.06±1.0	0.3±1.0	–0.3±0.8*
% Body fat	18.4±6.8	17±5.0	1S±7.0

Poster Sessions

P01-01 Adipose Cytokines and Miscellaneous Hormones

Plasma Ghrelin Levels in Obese Children

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Aims: To measure the plasma ghrelin levels in obese children and investigate the role of ghrelin in obese mechanisms.

Methods: 91 obese and 23 health children were enrolled. Obese subjects were divided into three groups according to their BMI. Group

1 was defined as BMI<25 kg/m2, group 2 as BMI ranging from 25 to 30 kg/m2 and group 3 as BMI >30 kg/m2. Blood ghrelin levels were measured by radioimmunoassay.

Results: The fasting plasma ghrelin levels [ln(ghrelin)] in controls, group 1, 2 and 3 were 5.99±0.96, 5.16±0.77, 5.43±0.49 and 5.15±0.61 respectively with a significant difference (P<0.001). The fasting ghrelin levels in controls were higher than that in three obese groups (all P<0.05), but no significant difference was found among obese groups (all P>0.05). Stepwise multiple regression analysis showed that abnormality of glucose metabolism was the independent determinants of plasma ghrelin levels (P=0.023).

Conclusion: The data support that ghrelin are close associated with obesity in childhood, especially associated with the glucose homeostasis. Moreover, this study suggests that lower ghrelin levels might be a result of obesity, but not a cause of obesity.

P01-02 Adipose Cytokines and Miscellaneous Hormones

Plasma Levels of Ghrelin during GH Provocative Tests and GHRH Test in Children with Short Stature

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Aims: To measure the plasma ghrelin levels during GH provocative tests and GHRH test in short stature children.

Methods: Blood samples of 10 boys of GHD and 10 boys of idiopathic short stature (ISS) during GH provocative tests, and other 10 boys of GHD during GHRH test were collected. Plasma ghrelin levels were measured by radioimmunoassay.

Results: The fasting ghrelin levels of GHD group were lower than that of controls (P=0.008). Repeated measure general liner model analysis showed that the plasma ghrelin levels were not different at different time points both during arginine stimulation test and insulin tolerance test (ITT) (all P>0.05). The ghrelin levels between GHD and ISS groups were different during ITT (P=0.029), but not during arginine stimulation test (P=0.100). In GHD children undergone GHRH test, the ghrelin peak were inversely correlated with the stimulated GH peak in GHRH test (r=-0.665, P=0.036).

Conclusion: The data support that ghrelin has an important role on GH secretion and abnormal secretion of ghrelin might be a reason of GHD which due to hypothalamic abnormality. Moreover, GH secretion stimulated by arginine and insulin might partly by activating ghrelin-GHSR signaling.

P01-03 Adipose Cytokines and Miscellaneous Hormones

The Role of Adipose Tissue in Insulin Resistance Catch-Up Growth IUGR Rat

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Aims: To investigate whether the differentiation progress and function of adipose tissue has changed in catch-up growth intrauterine growth retardation (IUGR) rat.

Methods: Nutrition restriction method to establish IUGR model. 8 newborn with weight<5.1g established the non-catch up growth IUGR group; 5 newborn with weight<5.1g established the catch-up growth IUGR group. Measure the nose- tail length and weight at 0w, 1w, 2w, 3w, 4w; fast serum glucose, insulin, TG, and OGTT was examined in the 3rd w.

Results: The weight of catch-up group grow fast than the control and non-catch-up IUGR group, there is significant difference between the catch-up group and the control group at 4thw (p<0.01), the body length of the three groups have no difference.(p>0.05). Fast and OGTT serum glucose and insulin lever in two IUGR group is higher than the control group (p<0.01), the glucose has no difference between the two IUGR group (p>0.05), the insulin level of catch up is higher than the non-catch up group (p<0.05). TG level in catch-up group is higher than the control group (p<0.05), but has no difference with the non-catch up group.

Conclusion: Catch up growth IUGR rat have high glucose, insulin, and TG level, may due to notable increased adipose tissue.

P01-04 Adipose Cytokines and Miscellaneous Hormones

Association of Serum Retinol Binding Protein 4 and Insulin Resistance in Obese Children and Adolescents

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Aims: Retinol binding protein 4 (RBP4) is involved in the modulation of glucose metabolism and increased in insulin resistance subjects. We investigated the status of serum RBP4 levels according to the degree of obesity and the relationship between serum RBP4 levels and levels of other metabolic parameters for insulin resistance in children and adolescents.

Methods: 42 overweight (85P ≤ BMI < 95P) and 30 obese (BMI ≥ 95P) children and adolescents were included. Height, weight, blood pressure and body composition were determined. Serum RBP4, adiponectin, insulin, hsCRP, glucose, total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol were measured.

Results: Serum RBP4 levels were significantly higher in obese group compared with overweight group (53.18 ± 13.03 vs. 63.35 ± 14.52 mcg/mL, P<0.05). Also, HOMA-IR were significantly higher in obese group (2.020 ± 1.49 vs. 3.24 ±2.47, P<0.05). Serum RBP4 levels were positively correlated with age (r=0.305, P<0.05), fat mass (r=0.317, P<0.05), serum triglyceride (r=0.251, P<0.05), insulin level

Table 1 (for Abstract P01-06). Comparison of metabolic profiles according to adiponectin fertile group

Variables	Tertile 1 (<6.2μg/ml), n=83	Tertile II (6.2~8.6μg/ml), n=81	Tertile III (>8.6 μg/ml), n=75	P-value
Body mass index (kg/m^2)	27.6±3.1	27.0±2.8	26.4±2.6	0.04
Waist circumference (cm)	91.1±9.0	89.1±7.3	87.8±7.3	0.04
HOMA-IR	5.3±4.8	4.5±2.7	3.9±2.4	0.05
Triglyceride (mg/dL)	172.1±87.9	153.2±74.6	133.3±60.8	0.006
HDL cholesterol (mg/dL)	49.5±12.0	51.5±12.7	56.2±14.1	0.004
Prevalence of Acanthosis (%)	71.1	58.0	39.0	0.01
Prevalence of MS (%)	54.2	50.6	29.3	0.002

(r=0.308, P<0.05) and HOMA-IR (r=0.310, P<0.05), but not related to total cholesterol, HDL-cholesterol, LDL-cholesterol and serum adiponectin.

Conclusion: In obese children and adolescents, serum RBP4 may have clinical implications for lipid metabolism and insulin action. Serum RBP4 seems to be a good early marker for insulin resistance.

P01-05 Adipose Cytokines and Miscellaneous Hormones

Follow Up of Pediatric Cancer Survivors for Endocrine Manifestations

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Aims: To look for late effects on endocrine system in pediatric cancer survivors.

Methods: Records of 66(38M) childhood cancer survivors, treated as per the unit protocol, referred for endocrine evaluation in last 8 years, were retrospectively studied. The median duration between treatment of cancer and endocrine evaluation was 8 yrs (range 1 to 11 yrs). Leukemias(71%), lymphomas (14%), intracranial tumors (4.5%), others (10.5%) were the various cancers in this series. 21% of the children had received irradiation either cranial(15%), testicular(3%), pelvic(1.5%) or the cervical(1.5%).

Results: Although 13 children were short, most of them (n=11) were within the target height range. Five children were obese (BMI > 95th centile). Six (9%) children had endocrine manifestations and 2 (33%) received irradiation. Growth hormone deficiency (n=1), primary gonadal failure (n=1), primary hypothyroidism (n=1), delayed puberty (n=1) and short stature cause unknown (n=2) were the various effects seen in this series.

Conclusion: Growth affection was the commonest problem seen in children in this series. Endocrine effects were seen more in children not having received irradiation.

P01-06 Adipose Cytokines and Miscellaneous Hormones

Adiponectin Level as a Diagnostic Marker of Metabolic Syndrome in Obese Children

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Aims: Increasing evidence points to the role of hypoadiponectinemia on the insulin resistance in obesity. This study aimed to clarify the usefulness of serum adiponectin level as a diagnostic marker of metabolic syndrome(MetS) in obese children.

Methods: A total of 239 obese (BMI>85P) children aged 11.5±1.7 were included. Anthropometric variables, fasting insulin, glucose, triglyceride and HDL-cholesterol,serum adiponectin, leptin, resistin and visfatin were measured.

Results: Adiponectin level was inversely related to BMI(p<0.01), waist circumference(P < 0.01), diastolic BP(p<0.05), insulin(P = 0.01), HOMA-IR(P = 0.01), triglyceride(P < 0.01), resistin(p=0.03), and positively related to HDL-cholesterol(P < 0.01). Adiponectin was not related to total fat percent, leptin and visfatin level. Adiponectin was significantly related to triglycerides (P< 0.01) and waist circumference (P < 0.01) independent of age, gender and BMI. Adiponectin level was lower in children with MetS compared to non-MetS (7.1±2.3 vs 7.7±3.1 in boys, 6.6±2.5 vs 8.5±3.3 in girls,P<0.01). There were significant differences in BMI, waist circumference, fasting serum insulin, HOMA-IR, triglyceride levels and the prevalence of MetS among the three groups divided according to the adiponectin levels (Table1).

Conclusion: Hypoadiponectinemia was highly associated with MetS in obese children. Evaluation of serum adiponectin level might contribute to an early detection for obese children with MetS.

P02-01 Adrenal Disorders

Late-Onset Adrenal Hypoplasia Congenita Caused by Premature Truncation of the Ligand-Binding Domain of DAX-1 Molecule

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Aims: Mutations in the orphan nuclear receptor DAX-1 cause X-linked adrenal hypoplasia congenita (AHC). Affected boys usually present classically with salt-losing crisis and adrenal insufficiency in early infancy with rare exception of a late-onset subtype. We report late-onset AHC caused by mutation of Dax-1 gene.

Methods: The 12-year-old boy was referred to us because of generalized skin pigmentation for about 3 years accompanying with fatigue and headache. Primary adrenal insufficiency was diagnosed and replacement therapy was initiated. Hypogonadotropic hypogonadism was confirmed at the age of 18, by that time delayed puberty had become apparent. Direct sequencing of the peripheral blood DNA was done.

Results: A novel 1033del13 mutation on the ligand-binding domain of the DAX-1 gene was found, which caused a premature stop codon and truncation of the C-terminus.

Conclusion: This case demonstrates that even a truncated protein lacking the major functional domain of DAX-1 can present late-onset and covert adrenal failure with hypogonadotropic hypogonadism.

P02-02 Adrenal Disorders

Iatrogenic Hypertension is Frequent in Infants with Congenital Adrenal Hyperplasia due to P450c21 Deficiency

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Aims: To identify treatment and biochemical factors associated with the development of hypertension (BP ≥2SD above the mean for age) in infants with P450c21 deficiency.

Methods: Retrospective analysis of data on 16 patients. BP was measured at every clinic visit.

Results: Eleven infants (5F) were found to be hypertensive (median systolic BP-SDS 2.6 [range: 2.1-6.7]) at a median age of 1.0 months [0.3 –11.3]. The median fludrocortisone dose was 0.2 mg/day [0.05-0.25] versus 0.1[0.05-0.2] (p=0.04) in the 5 normotensive infants (2F) at the time of peak BP (median BP-SDS 1.7[-0.2 to 1.8]). Nine (66%) were treated with NaCl and 7 were not, owing to the different practice of the treating endocrinologist. In the NaCl-treated group 6/9 became hypertensive, not significantly different from 5/7 in the non-NaCl-treated group. Hydrocortisone dose (mg/m2/day), suppression of 17OH-progesterone, and plasma electrolytes did not predict the development of hypertension. In multiple regression models, systolic BP-SDS was predicted by both NaCl dose and maximum fludrocortisone dose in the first year of life (p=0.05, adjusted R2 0.27). Seven infants responded to decreased doses, but 4 also received antihypertensives.

Conclusion: Two-thirds developed hypertension, associated with higher doses of fludrocortisone and NaCl. The severity and duration of mineralocorticoid resistance in infancy may be overestimated.

P02-03 Adrenal Disorders

Free Cortisol Index and Calculated Free Cortisol for Adrenal Function Assessment of Critically Ill Children

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Aims: In critical illness, serum total cortisol (TC) may not adequately reflect adrenal function because of decreased cortisol binding globulin (CBG). We aimed to evaluate adrenal function of critically ill children by using free cortisol index (FCI), a TC to CBG ratio, and calculated free cortisol (FC).

Methods: Thirty-two critically ill and 36 healthy children were included. Cosyntropin (ACTH) test was performed. TC and CBG were measured during the testing. FC was determined by Coolens' equation. Data are presented in median (range).

Results: Basal and peak TC were 23.9 (5.0-141.0) and 36.2 (11.1-151.0) mcg/dL in the patients and 4.5 (1.4-24.0) and 18.4 (13.4-24.7) mcg/dL in the controls. FCI rose from 7.9 (1.5-48.0) to 11.7 (3.1-50.6) and 1.1 (0.3-4.7) to 3.9 (2.5-9.0) mcg/mg following ACTH in the patients and controls, respectively. FC of the patients was also greater than the controls' level. As compared to TC, FCI and FC of the patients were higher than the respective values of the controls at a greater degree (basal: FCI 7.5, FC 18.5 and TC 5.4 folds; peak: FCI 3.0, FC 4.8 and TC 2.0 folds).

Conclusion: Free cortisol index and calculated free cortisol better reflect the dynamic changes of adrenal function during critical illness.

P02-04 Adrenal Disorders

A Novel Mutation of the CYP21 Gene in Two Korean Sisters with Salt-Wasting 21-Hydroxylase Deficiency

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Aims: Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders of steroidogenesis most commonly caused by 21-hydroxylase deficiency due to mutations in CYP21 gene. We experienced two Korean sisters suffering from salt-wasting CAH, in whom a novel mutation of the CYP21 gene was detected. A female baby was born with ambiguous genitalia with clitoromegaly and dark pigmentation. Highly elevated 17-hydroxyprogesterone (840 ng/mL), increased plasma renin activity, hyponatremia and hyperkalemia lead to the diagnosis of salt-wasting CAH. Her 6-year-old sister had been diagnosed as the same disease.

Methods: We performed mutation analysis in two sisters and their parents by direct DNA sequencing after allele-specific PCR amplification of the CYP21A2 gene. Rearrangements with pseudogene (CYP21A1) were analyzed by PCR using cross-primers.

Results: Two sisters were compound heterozygotes for c.1136_1137del(p.Pro379ArgfsX16)/c.329_336del(p.Gly111_Tyr113delinsValfsX31). Their father was a carrier of c.1136_1137del of CYP21A2 gene, which is a novel mutation. Their mother was a carrier of c.329_336del, pseudogene derived CYP21A2 gene conversion.

Conclusion: We report two Korean sisters with salt-wasting CAH due to a novel mutation of c.1136_1137del(p.Pro379ArgfsX16) in combination with gene conversion of CYP21A2 gene.

P02-05 Adrenal Disorders

Congenital Adrenal Agenesis Presented with Adrenal Insufficiency: A Case Report

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Aims: We report a very rare case of congenital adrenal agenesis presented with adrenal insufficiency in a 4-day-old female newborn.

Methods: She was admitted with darkish skin color and seizure. Her external genitalia was normal.

Results: In the results of laboratory tests, decreased sodium, increased potassium, decreased sugar, normal 17-hydroxyprogesterone, elevated ACTH, low cortisol level, decreased aldosterone, and rennin level were observed. Chromosomal analysis showed 46, XX. Pelvic ultrasonography showed adrenal agenesis bilaterally, and uterus and ovary of normal size and structure. Treatment was started with oral hydrocortisone, 9α-fluorocortisol, and salt supplementation under adrenal insufficiency. To evaluate the function of adrenal medulla, we examined epinephrine in plasma and epinephrine and metanephrine in urine. Epinephrine in plasma was 7.2 pg/mL (0-140 pg/mL), and epinephrine and metanephrine in urine were 0.1 μg/day (0-20 μg/day) and 0.1 mg/day (<0.8 mg/day), respectively. Six exons of the SF1 gene and their intronic flanking sequences were amplified by PCR with 8 sets of primers, revealed normal sequencing in our samples.

Conclusion: We propose that when a patient presents with male pseudohermaphroditis or normal female genitalia with adrenal insufficiency, SF-1 gene mutation study should be included in the differential diagnosis.

P02-06 Adrenal Disorders

Congenital Adrenal Hyperplasia (21-Hydroxylase Deficiency) Managed by Bilateral Adrenalectomy

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Aims: Use of high dose steroid to control hyperandrogenemia in congenital adrenal hyperplasia (CAH) can result in iatrogenic Cushing's syndrome.

Methods: 18-year-old lady was referred for hirsutism, primary amenorrhoea, poor breast development and Cushingoid features. She was diagnosed to have CAH 10 days after birth when she presented with salt wasting crisis. She had Cushingoid phenotype with proximal muscle weakness. Pubertal staging was Tanner 1 for breast and 3 for pubic hair. Biochemical parameters showed sub optimal control: Testosterone: 4.91 ng/ml (N <0.2 ng/ml) and 17 OH progesterone: 9000 ng/dl (target: 100- 1000 ng/dl) at Prednisolone dose 15 mg/day. Contrast CT showed 5.4X4.3 cm oval heterogeneous mass, with curvilinear calcification arising from the right adrenal gland.

Results: The patient underwent bilateral lap assisted adrenalectomy. Histopathology showed adrenal adenoma on the right side and adrenal hyperplasia on the left. Post operative assessment showed Cortisol: 0.02 mcg/dl, Testosterone 0.06 ng/ml, 17 OH progesterone < 1 ng/dl demonstrating completeness of adrenalectomy. The dose of Prednisolone was tapered to 5 mg/day and oestrogen therapy was started for induction of puberty.

Conclusion: In this patient with congenital adrenal hyperplasia and adrenal adenoma, bilateral adrenalectomy helped to control hyperandrogenemia and reduce steroid dose.

P02-07 Adrenal Disorders

A Case with Congenital Lipoid Adrenal Hyperplasia Evaluated by Serial Ultrasonography

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Aims: The purpose of this study was to emphasize the usefulness of ultrasonography in the follow up the size of adrenal glands of a patient with congenital lipoid adrenal hyperplasia (CLAH).

Methods: An infant with CLAH was serially evaluated the size of the adrenals by ultrasound, and compared with plasma ACTH levels for about 2 years

Results: A 8-day–old female infant was referred to our hospital due to dark pigmentation. Physical examination disclosed diffuse hyperpigmentation. External genitalia appeared normal. CAH was diagnosed based on clinical and laboratory findings. The karyotype was 46,XX, and mutation analysis confirmed the mutation in the StAR gene(Q258X). The enlarged adrenals were identified by ultrasound and measured its length and AP diameter. At 9 days of age, both adrenals were enlarged with a maximun length of 32/30 mm, and AP diameter of l4/16 mm. On serially follow up ultrasonography, we found the enlarged adrenals for more than 1 year, and there was no consistent correlation between serum ACTH levels and adrenal size.

Conclusion: Ultrasonography was useful in the evaluation of an infant with CLAH to demonstrate adrenal enlargement and changes of the size. When persistently enlarged adrenals are seen, the diagnosis of CLAH is highly likely.

P02-08 Adrenal Disorders

Adrenal Incidentaloma

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Aims: Adrenal masses are detected incidentally in up to 5% of patient undergoing abdominal imaging studies. Up to one in five are functional.

Methods: We report of a 7 year old obese boy who presented with abdominal discomfort and recurrent vomiting after a blunt trauma to the abdomen. He was normotensive during the ward stay.

Results: Except for microscopic hematuria, all the other biochemical and hormonal analyses was normal. A CT of the abdomen showed a well encapsulated hypodense mass with solid component (Hounsfield Unit 60-90) measuring 3.2 x 4.1 x 2.0 cm arising from the medial limb of right adrenal gland.

Conclusion: Patient underwent right adrenalectomy 3 months later after the repeat CT abdomen showed persistence of the lesion. The histopathological report concluded a diagnosis of ganglioneuroma.

P02-09 Adrenal Disorders

Survey of a Survivor Cohort: Young People Living with Congenital Adrenal Hyperplasia in Vietnam

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Aims: Adults with Congenital Adrenal Hyperplasia (CAH) in resource-poor countries represent a survivor cohort. Insights from young people living with CAH in Vietnam could guide efforts to improve outcomes.

Methods: A questionnaire was offered to all young people attending the annual CAH Club Meeting (National Hospital of Paediatrics, Hanoi) in June 2006, exploring: emotional, physical and social well-being; family and school life; CAH management; future aspirations, and desired support.

Results: Nine people (33% of total age group) responded; 8 females / 1 male; median age 21 years (range 14-32 years); 100% ethnically Kinh; 56% from urban areas. Majority (86%) felt positive about themselves, socialized in the last week and believed they had good job prospects. All attended school. Family was an essential support, although 71% want more open communication with family about CAH; 57% felt sad, depressed or physically unwell in the preceding week. Most (71%) did not feel confident managing acute illness. All females had surgery in the past; 86% were satisfied with the outcome to date. Financial stress is a major hardship.

Conclusion: Emotional resilience was remarkable, and may influence survival. Educational, emotional, vocational and financial support would benefit this cohort.

P02-10 Adrenal Disorders

Corrected 17-Alpha-Hydroxyprogesterone Values Adjusted by a Scoring System for Screening Congenital Adrenal Hyperplasia in Premature Infants

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Aims: This study investigated the use of corrected 17-alpha-hydroxyprogesterone (17-OHP) values to detect congenital adrenal hyperplasia (CAH) in newborn infants.

Methods: 17-OHP concentrations in blood spots from 913 neonates were measured using a neonatal screening test.A prematurity index was calculated using a scoring system based on gestational age and birth weight. Blood spot 17-OHP concentrations divided by

the sum of prematurity scores were defined as the corrected 17-OHP values.

Results: Preterm infants (<30 wk) and low birth weight infants (<1.0 kg) showed 3.9- and 3.8-fold higher blood spot 17-OHP concentrations than normal full term infants. However, no significant differences were observed in the corrected 17-OHP values between the groups. Blood spot 17-OHP levels yielded significant correlations with the prematurity index ($r = 0.42$, $p < 0.05$). Positive results for CAH were obtained in 9.5% (n = 53) and 2.0% (n = 11) of 556 premature infants by the cutoffs of blood spot 17-OHP (>15.0 ng/ml) and corrected 17-OHP values (>13.0 ng/ml), respectively. Of the 53 positive subjects, 39 (73.6%) converted to negative after 1 to 5 mo without treatment.

Conclusion: Use of corrected 17-OHP values provide limited but helpful information in screening for CAH by reducing the rate of false-positive results, especially in premature infants.

P02-11 Adrenal Disorders

A Preterm Infant with Disorder of Sex Development and Generalized Skin Hyperpigmentation: A Case Report

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Aims: We report a preterm infant with severe asymmetrical IUGR, generalized skin hyperpigmentation and disorder of sex development.

Results: Born at 33 weeks of gestation with birth weight 1.09kg, generalized skin hyperpigmentation and genital abnormality were noted at birth. The phallus was 1 cm long with severe hypospadia. Testes were palpable in his bifid scrotum, with shallow rugae. Phallus length increased to 1.9 cm afterwards. Karyotype showed 46, XY and the SRY gene was positive. Testosterone level was 12.1 nmol/L, FSH 6.8 iu/L and LH 13.1 iu/L. The ACTH level was grossly elevated to 6357 pg/ml. Short synacthen test showed no rise in serum cortisol with baseline cortisol 304 nmol/L. Spot urine steroid profile was unremarkable.

Conclusion: The grossly elevated ACTH with mild adrenal insufficiency suggested ACTH resistance syndrome. The relative high LH, FSH & testosterone levels implied that Partial androgen insensitivity syndrome might be the cause of undervirilization. The association of ACTH resistance syndrome with DSD has never been reported. Further molecular study is in progress.

P03-01 Bone and Calcium Disorders

The Incidence of Metabolic Bone Disease in Very Low Birth Weight Infants in Gorgan (North of Iran) and Some Contributing Factors

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Aims: To discover the incidence and some contributing factors of metabolic bone disease.

Methods: Fifty one neonates weighing less than 1500gr at birth born during a one year period and admitted in two referral center. They were monitored for biochemical and radiological evidence of metabolic bone disease at discharge time and 2-5 months of age.

Results: Incidence of metabolic bone disease in the first and second monitoring were 17.6% and 49% respectively. Radiologic rickets was found in 47% of patients. All infants were exclusively breast fed and received 400IU vitamin D daily from day 14. There was a significant negative correlation between metabolic bone disease and factors such as birth weight and gestational age. Also there was significant positive correlation between metabolic bone disease and use of dexamethasone, aminophylline and duration of NPO in their admission da

Conclusion: Thus metabolic bone disease is a common problem in the very low birth weight neonates in our area and we suggest monitoring for Alkaline Phosphatase(ALP) and phosphorous routinely in very low birth weight infants especially in 2-5 month of age for early diagnosis and treatment.

P03-02 Bone and Calcium Disorders

A Family of Hypocalciuric Hypercalcaemia with P798T Mutation in the Calcium-Sensing Receptor Gene

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Aims: Case report of a family with hypocalciuric hypercalcaemia due to P798T mutation in the calcium-sensing receptor gene.

Results: An 8-yr-old Chinese girl presented to the Department of Paediatrics & Adolescent Medicine of Tseung Kwan O Hospital in Hong Kong for short stature. She was assessed to have genetic short stature and constitutional growth delay. Upon routine biochemical investigation, she was found to have persistent mild hypercalcaemia of 2.67 to 3.00 mmol/L. She was totally asymptomatic. Further investigation showed an intact PTH level of 12 pg/ml (normal 11-54). Serum phosphate and alkaline phosphatase level were normal. Serum magnesium level was slightly increased to 0.98 mmol/L (normal 0.69-0.87). Hypocalciuria was confirmed with 24-h urine collection on two occasions showing the calcium to creatinine ratio <0.01 mol/

mol (normal 0.09-2.00). Thyroid function test and serum cortisol were normal. Screening of family members revealed hypercalcaemia in all 3 generations on the paternal side. Clinical diagnosis of familial hypocalciuric hypercalcaemia with autosomal dominant inheritance was made. This was confirmed by genetic study showing heterozygote P798T mutation in the calcium-sensing receptor gene in the girl and relatives of all 3 generations.

P03-03 Bone and Calcium Disorders

Long Term Alendronate in Polyostotic Fibrous Dysplasia

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Aims: To highlight a case of Polyostotic fibrous dysplasia treated with oral Alendronate for six years with good outcome.

Methods: A 16-yr old girl presenting with diffuse bone pains and pathological fracture of proximal phalanx of the right middle finger was diagnosed as Polyostotic fibrous dysplasia based on skeletal radiographs (Multiple expansile lesions with inner translucency and thinned out cortex involving the metacarpals, phalanges and right superior pubic ramus) and radioisotope bone scan. She was treated with oral Alendronate 70mg weekly for six years. She was followed up with serial skeletal radiographs, biochemical parameters and monitored for adverse effects.

Results: Resolution of bone pain and radiographic evidence of reduction in size, increased cortical thickness and appearance of ossification within the skeletal lesions was noted. There was no recurrence of fractures during treatment. There were no adverse effects of long term Alendronate use noted. Serum Calcium, Phosphorus and Alkaline phosphate remained normal all through the follow up. There was no evidence of endocrinopathy or caf

Conclusion: Long term Alendronate therapy appears safe, effective, economical and convenient treatment option for Polyostotic fibrous dysplasia in children.

P03-04 Bone and Calcium Disorders

Clinical Profile of Distal Renal Tubular Acidosis in Children: A Single Centre Experience

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Aims: To study the clinical profile and outcome of distal renal tubular acidosis (RTA) in children.

Methods: Children presenting with metabolic bone disease, obstructive uropathy, nephrocalcinosis or short stature were screened by fasting urine pH. Distal RTA was diagnosed in forty four children (Mean age10.43 + 4.77 Yrs), based on normal anion gap metabolic acidosis with fasting urine pH > 5.5 and positive urine anion gap. Ammonium chloride loading was done in cases with fasting urine pH>5.5 with normal systemic pH and bicarbonate (incomplete RTA). Children with GFR<30ml/min, diarrhea or urinary tract infection were excluded.

Results: Voiding difficulty due to obstructive uropathy in 20 and short stature in 17 children was the common presentation. Seven children with short stature had incomplete RTA. Cause of distal RTA was established in 26 (59%) cases. Obstructive uropathy was the commonest cause noted (22/44). Progressive renal dysfunction was noted in 9 children, all of whom had worse renal function (GFR<60ml/min) at diagnosis. Amongst them, 8 had urological abnormality and one child had Medullary Sponge kidney.

Conclusion: Growth restriction was noted with similar frequency in complete and incomplete distal RTA. Presence of underlying primary condition and low baseline GFR predicted progression of renal dysfunction in children with distal RTA.

P03-05 Bone and Calcium Disorders

Non-Nutritional Rickets Seen in a Teaching Institution in Mumbai (India)

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Aims: To present profile of non-nutritional rickets seen over 2 years

Methods: Prospective study of 34 patients

Results: Age of presentation: 1½ months to 13 years-19 males and 15 females, consanguinity in 9. The etiology was Distal renal tubular acidosis {RTA} (n=20; 59%), Chronic kidney disease (n=4; 12%), Proximal RTA due to cystinosis (n=3; 8.5%), Vit. D dependent rickets type II {VDDR II} (n=3, 8.5%), Chronic liver disease {biliary cirrhosis}(n=2,6%), Hypophosphatemic rickets(n=2, 6%). Most patients had fronto-parietal bossing, beading of ribs, wrist widening, double malleolus as features of rickets while some (n=12, 35%) had bony deformities of lower limbs.10 patients (30%) presented with hypocalcemia. All patients with RTA presented with polyuria , failure to thrive with normal anion gap metabolic acidosis ,18 of whom had nephrocalcinosis.Patients with hypophosphatemic rickets had nephrocalcinosis due to vit D therapy given before presenting to us. 2 patients with VDDR II had alopecia totalis. Patients with RTA showed good response to alkali therapy. 1, 25 di hydroxy vit D was given to patients with VDDR II (showing poor response even with high doses), kidney disease and hypophosphatemic rickets (in addition to Joules solution) .Patients with biliary cirrhosis showed partial healing after high dose of vit D.

P03-06 Bone and Calcium Disorders

Bone Mineral Density According to Age, Bone Age, Pubertal Stages in Korean Children and Adolescents

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Aims: The aim of this study is establishing normative data for Bone mineral density (BMD) in Korean children and adolescents.

Methods: Five hundred fourteen healthy children (262 girls and 252 boys) aged 5 to 20 years were enrolled. BMD of different skeletal site was measured by dual-energy X-ray absorptiometry using a Lunar Prodigy Advance (Lunar Corp., Madison, WI). The apparent volumetric BMD (BMAD) of the lumbar spine and BMD of total body less head (TBLH) were calculated.

Results: We made reference values according to age, bone age and Tanner stages (TS) for boys and girls separately. The different site BMD showed different acquisition pattern according to gender, age, bone age, and TS. Bone age was more correlated with anthropometric parameter. Each skeletal parameter was more accurately fitted to bone age reference values than chronological age reference. Boys showed higher BMD in cortical sites like femur neck, total body and TBLH, while girls showed higher BMD and BMAD in trabecular site like lumbar spine.

Conclusion: This study is unique in dealing with one Asian ethnicity with the bone age reference data. It could be used for comparing with other ethnicity and allows additional insight of bone mass acquisition in Asian ethnicity.

P03-07 Bone and Calcium Disorders

Effect of Soy-Based Formula on Infants' Bone Mineral Density

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Aims: With the development of soy-based formula (SF) for neonates and infants, the blood chemistry concerning calcium metabolism and bone mineral density (BMD) was compared among the infants on SF, breast milk (BF) and casein based formula (CF).

Methods: Breast milk and artificial formulae were given till 1st three months of life, thereafter weaning food was added freely. Blood chemistry including calcium, phosphorus, and alkaline phosphatase was analyzed at 5, 12, and 36 months of age. BMD was taken at birth, 5, 12, and 36 months of age.

Results: Serum calcium and alkaline phosphatase were not different till 36 montsh of age. At 5 months of age, serum phosphorus and BMD were significantly lower in SF group, but after 5 months there were no differences in theses parameters till 36 months of age.

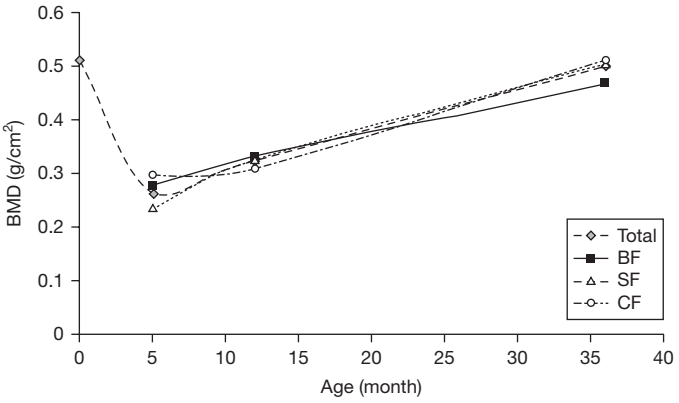

Fig 1. Changes of BMD during 36 months of life.

After birth lumbar spine BMD was rapidly decreased to the lowest level at 5 months and then increased to the birth level at 36 months of age.

Conclusion: In spite of high mineral intake in SF group, the lowest serum P and lumbar BMD at 5 months of age suggest poor intestinal mineral absorption. The means need to be developed to increase intestinal mineral absorption with a reduction in mineral intake.

P03-08 Bone and Calcium Disorders

A Male Patient with Humoral Hypercalcemia of Malignancy (HHM) Caused by Cutaneous Squamous Cell Carcinoma Resulting from Recessive Dystrophic Epidermolysis Bullosa

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Aims: Recessive dystrophic epidermolysis bullosa (RDEB) is a severe skin disorder. Although the patients are at risk of cutaneous squamous cell carcinoma (SCCc), no case of SCCc derived from RDEB with complicating HHM has been reported. We present the first case of a male patient with HHM caused by SCCc resulting from RDEB.

Results: He had a history of generalized trauma-induced blisters and erosions from birth, and skin biopsy confirmed the diagnosis of RDEB. He developed a non-healing ulcer on his right internal malleolus at the age of 20. Serum calcium increased gradually accompanied by high levels of parathyroid hormone-related peptide (PTH-rP). Histopathological examination of the ulcer demonstrated well-differentiated SCCc. Zoledronate (0.5 mg/day) was administered for two days to ameliorate the hypercalcemia. We chose zoledronate, taking his cardiac and renal conditions into consideration, since it requires the least volume for administration. No serious adverse events were observed. Serum calcium normalized after 9 days.

Subsequently, amputation of his right lower extremity was performed. Immunohistochemistry demonstrated PTH-rP expression. Serum calcium remained normal and PTH-rP decreased to the normal range.

Conclusion: We propose that zoledronate is an effective and safe treatment for HHM.

P03-09 Bone and Calcium Disorders

Pamidronate Therapy in Children and Adolescents with Osteoporosis

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Aims: The aim was to evaluate efficacy of pamidronate in children and adolescents with osteoporosis from various etiologies.

Methods: Ten patients (10.1-17.4yr) with osteoporosis, who had bone pain and/or fracture were enrolled. Pamidronate 1.5mg/kg was given every 6 to 8 weeks for 6 or 8 cycles. Bone mineral density (BMD) in lumbar spine (L-spine) and femur neck/total (F-neck/total) and their z scores were measured at baseline, after 4th cycle and last cycle.

Results: Etiologies were as follows; neurofibromatosis and/or malnutrition (n=2), epilepsy (n=2), autoimmune disease (n=2), leukemia (n=3), hyperthyroidism and OI (n=1). Most patients showed remarkable improvement in bone pain after first cycle and no further fracture thereafter. There was higher BMD z scores after 4th cycle than baseline (from -4.29 to -2.32 in L1-4, -3.73 to -2.76 in F-neck, -3.88 to -2.94 in F-total, p=0.005). However there was no significant change in BMD z scores between 4th and 8th cycle. Eight of 10 developed fever, relieved by antipyretics and 3 of 10 revealed symptomatic hypocalcemia during first cycle. The growth was normal during follow-up periods.

Conclusion: Pamidronate appears to be effectively and safely administered to relieve the symptoms in patients with osteoporosis from various etiologies, but its side effects should be monitored.

P03-10 Bone and Calcium Disorders

A Case of a Parathyroid Adenoma Patient with Referred Pain

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Aims: A 14-year-old boy complained about the chronic pain on both knees and ankles. At the time of the diagnosis, his serum calcium level was 11.8 mg/dl, alkaline phosphatase, 1450 U/L; intact parathyroid hormone, 1299.0 pg/ml; 1.25 vitamin D3, 95.3 pg/ml; respectively. The widening of growth plate on both femoral heads were found in the hip radiography, and parathyroid adenoma and/or carcinoma was suspected in thyroid neck ultrasonography. Right inferior parathyroidectomy & closed reduction and internal fixation of both femoral heads were performed. The diagnosis was made from the biopsy, and the result was a parathyroid adenoma with minimal capsule invasive adenocarcinoma. The patient followed up regularly to Hanyang university hospital. We report a patient who visited the clinic for referred pain, diagnosed as parathyroid adenoma, and underwent parathyroidectomy.

P03-11 Bone and Calcium Disorders

Hypervitaminosis D – Consequence of Irrational Treatment

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Aims: Presenting cases of Hypervitaminosis D

Methods: Retrospective study of medical charts of 7 children with Vitamin D overdose leading to hypercalcemia

Results: Age at presentation was 7.5–24 months. Indication for vitamin D administration was failure to thrive, delayed milestones or erroneous diagnosis of rickets without supportive biochemical or radiological parameter. These children had received vitamin D in range of 9–40 lac units and Calcium supplements 40–125 mg/kg/day before presenting to us. Presenting features were failure to thrive (n=7), polyuria (n=3), constipation (n=2), gross hematuria (n=1), lethargy (n=1), persistent irritability (n=1), recurrent vomiting (n=1) and transient hypertension (n=1). Further evaluation revealed microscopic hematuria (n=3), leucocyturia (n=2), hypercalciuria in all, nephrocalcinosis (n=3). Serum calcium ranged from 11.9-16.8 mg/dl. All patients had hypercalciuria (urinary Calcium/Creatinine=0.85-3.85) and high 25–hydroxy vitamin D levels ranging from 70ng/ml to more than 150 ng/ml (normal range-7-40). PTH level were low in all: <3-7pg/ml (normal range-9-65). Treatment was given with hydration (n=7), prednisolone (n=5), IV Pamidronate (n=4),calcitonin(n=1)

Conclusion: We would like to emphasize that irrational use of vitamin D should be discouraged as it can cause serious problems leading to hypercalcemia, hypercalciuria that can produce acute symptoms and grave long-term consequences like nephrocalcinosis

P03-12 Bone and Calcium Disorders

Eight Cases of Incidentally Diagnosed Subclinical Rickets

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Aims: The purpose of this study is to clarify current causes and ways to prevent subclinical vitamin D deficiency rickets

Methods: We reviewed the clinical and laboratory characteristics of children who were incidentally diagnosed as subclinical rickets at Eulji Hospital, Seoul, Korea from March, 2003 to July 2007.

Results: Eight patients (six boys and two girls) were diagnosed as subclinical vitamin D deficiency rickets. The mean age of patients was 12.6±5.8 month, and they were diagnosed from January to July. The associated disease were pneumonia, urinary tract infection, acute gastroenteritis, and iron deficiency anemia. They were all breast fed. Two patients were shown growth failure. The mean serum alkaline phosphatase was 1995.8±739.5 IU/L, mean calcium was 9.5±0.6 mg/dL, and mean phosphorus was 3.6±1.5 mg/dL mg/dL. The mean intact parathyroid hormone was 214.8±155.9 pg/mL (reference range, 9-65), mean 1,25-dihydroxyvitamin D was 82.4±49.3 pg/mL (reference range, 20–70), and mean 25-hydroxyvitamin D was 29.6±10.6 ng/mL (reference range, 10–30). An radiographic examination showed cupping, fraying and flaring of metaphyses in all patients. Six patients of these were given calcitriol (400 IU/day) during three month. After that their radiographic and laboratory examination showed improvement.

Conclusion: Breast feeding without supplementation is high risk group of vitamin D deficency.

P03-13 Bone and Calcium Disorders

60,000 Units of Cholecalciferol Fails to Normalize Serum 25 Hydroxyvitamin D (25OHD) in Volunteers in North India

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Aims: To study the effect of a single large dose of cholecalciferol on 25OHD over 3 months. (Hypovitaminosis D is common in India. Data are scant on doses of cholecalciferol required to prevent deficiency.)

Methods: Healthy medical staff (18 males, 12 females) were compared at baseline and monthly for 3 months after 1 oral dose of 60,000 units cholecalciferol, for 25OHD and parathyroid hormone (PTH), by repeated measures ANOVA using general linear model.

Results: Mean 25OHD was 7.11 + 5.4 ng/ml at baseline (<10 ng/ml in 85% subjects), and 18.7 + 8.96, 14.2 + 7.34, 11.1 + 5.3 ng/ml after 1, 2 and 3 months of therapy ($p < 0.001$). PTH (n=10) showed mean (excluding 1 outlier) of 40.0 + 11.0 pg/ml at baseline (median 35.8, range 29 -131 pg/ml), and 33.6 + 11.2, 41.7 + 17.9, and 48.3 + 16.3 pg/ml after 1, 2 and 3 months of therapy ($p = 0.057$). Alkaline phosphatase normalized only in 2 of the 12 subjects with elevated baseline values. A higher dose is under investigation.

Conclusion: Cholecalciferol 60,000 units at 3 monthly intervals is ineffective in maintaining adequate serum 25OHD levels. A higher and more frequent dosing regimen is indicated.

P03-14 Bone and Calcium Disorders

The Effect of Growth Hormone Therapy on Bone Mineral Density in Young Adults with Childhood-Onset Growth Hormone Deficiency

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Aims: Growth hormone (GH) has multiple beneficial effects in addition to its promotion of linear growth. Therefore adults with GH deficiency (GHD) have abnormal body composition, altered lipid metabolism, increased cardiovascular disease, and decreased bone mineral density (BMD). We evaluated the effect of GH therapy on BMD in young adults with childhood-onset GHD

Methods: 17 childhood-onset GHD adults (10 male, 7 female, mean age 24.5±5.5 yr) with or without continuous GH treatment after final height were studied. All subjects divided two groups; GH-treated group (n=6) and GH-untreated group (n=11). BMD in lumbar spine and proximal femur was measured by dual energy X-ray absorptiometry.

Results: The mean serum level of IGF-I concentration in the GH-untreated group was lower than in the GH-treated group (88.4±55.9 ng/mL vs. 358.7±196.8 ng/mL, $P<0.05$). The BMD of lumbar spine in the GH-treated group and GH-untreated group was 1.02±0.13 g/cm2 and 0.82±0.09 g/cm2 and the BMD of femur was 1.15±0.14 g/cm2 and 0.82±0.10 g/cm2 respectively.

Conclusion: The BMD of the GH-treated group was significantly higher than the GH-untreated group ($P<0.05$)

P03-15 Bone and Calcium Disorders

Cherubism or Craniofacial Fibrous Dysplasia? A Diagnostic Dilemma!

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Methods: Cherubism is a rare non-neoplastic disease of childhood characterized by bilateral, painless enlargement of jaw. Craniofacial fibrous dysplasia (CFD) is a close mimicker. A 14 year old boy consulted us for progressive swelling and disfigurement of lower jaw since the age of 4 years. He had an elongated face with a hard bony swelling originating from lower jaw (Fig 1). There was a 2x2 cm ulcer with pus discharge on the chin. His dentition was misaligned. Rest of his examination was normal. X-ray skull showed bilateral cystic expansible lesion in the mandible. The CT showed

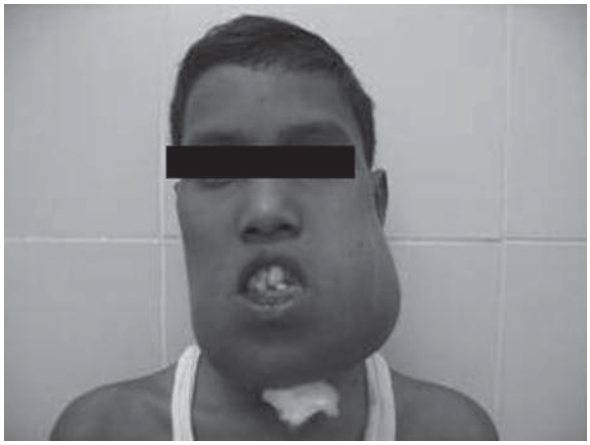

Fig. 1.

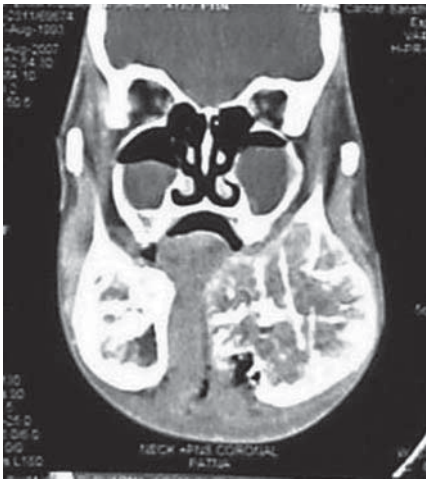

Fig. 2.

similar finding (Fig 2) with areas of involvement of skull vault. These findings were corroborated by bone scan, 18-F-Fluoride PET scan, 3D-CT reconstruction images and SSD images. The possibilities of cherubism and CFD were considered. The factors favoring cherubism over CFD were age of onset, bilateral involvement, cystic lesion, predominant mandibular involvement and severe dental deformity. However involvement of cranial vault in cherubism has not been reported. Biopsy may help in reaching the final diagnosis but was deferred in view of parents.

P03-16 Bone and Calcium Disorders

A Report Case of Hyperphosphatemia and Hypocalcemia from Enema

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Pediatric, Pediatric endocrinology, Thailand

Aims: We report the case of 1 year old with underlying imperforate anus with anovestibular fistular S/P anal transfer who developed hyperphosphatemia, hypocalcemia after received pediatric enema 100 ml. He had chronic constipation with regularly use pediatric unison. The day admission he was given 100 ml of pediatric enema, ten minute later, he had many time of diarrhea and carpopedal spasm. Physical examination was moderate dehydration. Investigation showed serum ionized calcium 0.71 mmol/L, phosphate 23.82 mg/dl, and blood gases revealed a PH 7.25, PCO2 40.5, PO2 43.4. We treated him early with fluid rehydration and intravenous calcium. He had completed phosphate and calcium level in normal range in two days.

Conclusion: Phosphate enema should be aware of adverse effects of electrolyte disturbances in pediatric < 2 years of age like in other literature.

P03-17 Bone and Calcium Disorders

Hypochondroplasia

Indra Himawan

Pediatric, Pediatric endocrinology chapter, Indonesia

Aims: A case report of 7 years old boy with hypochondroplasia

Methods: Case report

Results: His chief complaint was his height was shorter than his mates and never been increasing. Clinical evaluation showed a disproportion in his short limb. the height of his body was 102 cm (< 9 cm below p3 CDC 2000). The height of his upper segment (US) was 61 cm and his low segment (LS) was 1,56 cm. At radiologic examination there was anormality of bone age, it revealed at age 3 years and 6 month. On superior and inferior extremities photo showed shortening of long bones with metaphyseal flare. On phalang photo there were retadation of carpalia bone development and shortening and broad of phalangs.The laboratory examination Ft 4 was 0,8 Iu/l TSHs was 0.10 Iu/l, provocation of growth hormone using clonidin at 0, 30 th, 60th and 90th minute of control growth hormne was 1,98 ug/ml, 2,31 ug/ml, 25,40 ug/ml and 35,50 ug/mll. IGF-1 was 103ug/l

Conclusion: A Case report of 7 years old boy with hypochondroplasia. The diagnosa made was base on clinical manifestation, laboratory and radiographic examination

Table 1 (for Abstract P04-02).

	DF (age 10.2 ± 2.4)			DHF (age 10.8 ± 2.4)		
	Fever	Convalescent		Shock	Convalescent	
free T4 (ng/dL)	1.2 ± 0.2	1.6 ± 0.3	0.001	1.2 ± 0.4	1.7 ± 0.4	0.001
T3 (ng/dL)	103.1 ± 1 39	146.6 ± 34.8	0.001	90.5 ± 34	141.9 ± 37.4	0.001
TSH (mU/L)	1.7 ± 1.5	1.8 ± 0.8	ns	2.4 ± 2.0	2.2 ± 1.1	ns
Cortisol (ug/dL)	16.5 ± 7.0	10.1 ± 4.3	0.001	15.5 ± 9.8	7.7 ± 4.1	0.008
IGF-1 (ng/dL)	95.8 ± 92.6	129.5 ± 194	ns	66.7 ± 52.4	74.7 ± 59.3	ns
IGFBP-3 (mg/L)	2.7 ± 1.2	3.0 ± 1.1	ns	2.5 ± 1.1	3.3 ± 1.2	0.03

P04-01 Developmental Origins of Health and Disease

Effects of Neonatal Dexamethasone Treatment on Brain Synaptic Plasticity and Function

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Aims: Synthetic glucocorticoids (GC) like dexamethasone (Dex) are widely used for treatment and prevention of chronic lung disease in premature human infants. The aim of this study was to evaluate the effect of neonatal Dex administration on the brain development and function.

Methods: New born rats were i.p injected with Dex on neonatal day 1, 2, and 3. At age of 3-4 months, spatial learning was tested in the Morris water maze. The animals were then decapitated and hippocampal slices were prepared. Synaptic Long term potentiation (LTP) and depression (LTD) were induced in these slices. Protein patterns were analyzed in one month aged animals using 2-dimensional polyacrylamide gel electrophoresis (2-DE).

Results: The performance of Dex rats in the water maze showed increased escape latency ($P<0.05$). LFS depressed significantly the synapses more in the Dex-rats. HFS, on the other hand induced more LTP in the control than in the Dex group. In addition we have used 2-DE to separate proteins from control and Dex samples. Multivariate and hierarchical cluster analysis of differentially expressed proteins enabled discrimination between different sample groups.

Conclusion: Neonatal Dex affects significantly the hippocampus synaptic plasticity and learning tests performance. Protein expression in the different parts of the brain was significantly different.

P04-02 Developmental Origins of Health and Disease

A Preliminary Data of Hormone Changes in Dengue Viral Infection

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Aims: Dengue is an acute febrile diseases resulting from an infection by dengue virus. Infected children can present as dengue fever (DF), dengue hemorrhagic fever(DHF) or uncomplicated febrile illness. DHF is a serious and often fatal pediatric problem in Southeast Asian countries due to hypovolemic shock resulting from extravasation of plasma albumin and fluid into interstitial space. Although this disease is common in Southeast Asian countries including Thailand, endocrine changes is rarely studied.

Methods: Thyroid function test (free T4, T3, TSH), serum cortisol, serum IGF-I and IGFBP-3 were measured in 23 children (11 M, 12 F) with DF during fever and convalescent period and in 16 children (8 M, 8 F) with DHF during shock and convalescent period. All of these hormonal levels were compared between these 2 groups.

Results: Table 1 Mean ± SD of hormonal levels in children with DF and DHF

Conclusion: In DF and DHF, changes in H-P-thyroidal axis appear to be euthyroid sick illness. Adrenal reserve function in DHF looks insufficient (serum cortisol < 18 ug/dL) during shock stage and cortisol replacement may be one of the possible therapeutic modalities.

P05-01 Growth and Pituitary Disorders

Treatment of Growth Hormone Deficiency in the University Medical Center

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Aims: Evaluate the effect and the safety of rhGH in the treatment of GHD in the University Medical Center

Table 1. (for Abstract P05-03). Cocktail test (initial)

	GH (ng/mL)	Cortisol (µg/dL)	TSH (µIU/mL)	LH (mIU/ml)	FSH (mIU/ml)	Prolactin (ng/ml)
0 min	0.1	2.7	6.08	1.9	1.0	14.5
30 min	0.1	6.6	35.06	4.0	3.6	33.9
60 min	0.1	14.0	29.93	3.6	6.0	29.2
90 min	0.1	8.1	25.84			17.6
120 min	0.1	6.0	19.21			13.0

Table 2 (for Abstract P05-03). Cocktail test (at 30 10/12 year-old)

	GH (ng/mL)	Cortisol (µg/dL)	TSH (µIU/mL)	LH (mIU/mL)	FSH (mIU/mL)	Prolactin (ng/mL)	ACTH pg/mL)
0 min	0.1	0.7	0.08	1.2	0.1	5.8	10.8
30 min	0.1	4.4	0.27	2.5	2.4	30.9	51.8
60 min	0.1	9.5	0.25	2.8	3.8	33.3	136.9
90 min	0.1	11.5	0.21			23.6	70.4
120 min	0.1	11.6	0.17			22.8	55.8

Methods: Short children (standing height < -2SD) diagnosed as GHD in the Endocrinology Clinic of the UMC from 09/2004 to 06/2007 were included in the trial.

Results : Among 57 cases of short stature admitted to the UMC from 09/2004 to 06/2007, 14 cases were diagnosed of GHD. Mean age of diagnosis was 11.1 years old, and girls were diagnosed at older age than boys (13.2 vs 9.7 y.o.). 9/14 cases completed the 24-month course of treatment. After 24-month of treatment, there was an average increase of 20.4 cm in height in the treatment group. The mean height velocity in the first year and the second year were 10.6 cm and 10.1 cm, respectively.

Conclusion: Recombinant hGH could increase the height of GHD children in the study group by approximately 20cm after 24 months of treatment. Highest height velocity could be achieved at 3rd and 4th trimester of treatment by approximately 3cm/trimester. There was no significant difference between height velocity of 1st and 2nd year. No major side effects were noticed in the treatment group.

P05-02 Growth and Pituitary Disorders

Pan-Hypopituitarism

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Aims: Pan-Hypopituitarism is manifested by diminished or absent secretion of several pituitary hormones. A boy AP, 22 years, was diagnosed as panhypopituitarism since the age of 16 years old. At diagnosis the pubertal status was A1P1G1, with testicle volume of each 1ml. Highest GH level with ITT was 0,05 ng/ml (> 10 ng/ml). The gonadal axis showed hypogonadotrophic hypogonadism. Morning cortisol was low 1,62 µg/dl (5-25 µg/dl) while evening cortisol 1,44 µg/dl (2,5-12,5 µg/dl). Thyroid function and ultrasound was normal and bone age was retarded boy as a 10 years old. Skull CT scanning and MRI revealed no tumor.

Results: Hormone Replacement Therapy was started, and given appropriately on regular basis. After six years hormone replacement therapy the pubertal status advanced to A2P2P3, incrased libido, and volume testicle (4ml/4ml). The height increased 15,5 cm (2.1 cm/years) and his bone age still retarded as a 16 years old. He is still on therapy with L-thyroxine, HCG, and hydrocortisone.

P05-03 Growth and Pituitary Disorders

A Case of Panhypopituitarism Compared with his Normal Twin Brother

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Aims: We report a 29 2/12 year-old male case of idiopathic panhypopituitarism compared with his normal twin brother.

Methods: The laboratory and radiologic investigation with the cocktail test was done on the male complaining of short stature.

Results: He was born prior to his normal twin brother with no specific birth history. His height was 151.5 cm (<3 percentile), weight 49 kg (<3 percentile) with his normal twin brother (173 cm tall). His bone age was about 14.8 year-old and the pituitary gland was small on MRI. T3 94.46 ng/dL, T4 4.3 µg/dL, TSH 6.08 µIU/mL, IGF-1 96.0 ng/mL, IGF-BP3 857 ng/mL and testosterone was 0.1 ng/mL. Mutation analysis of the transcription factors for pituitary formation including PROP1, Pit1, LHX3, Hesx1 and SOX3 was normal. The cocktail test results was as below

Conclusion: We report a rare case of panhypopituitarism showing progressive loss of TSH response compared with his normal twin brother. Their picture will be shown in the APPES2008.

P05-04 Growth and Pituitary Disorders

The Effect of rhGH Treatment on the Children after Hypothalamus Pituitary System Tumor Operation

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Aims: To study the effect of rhGH treatment on the children after hypothalamus pituitary system tumors operation

Methods: A retrospective analysis of 16 cases underwent accepted surgical therapy for hypothalamus pituitary system tumors. 9 cases accepted rhGH treatment after operation. Observe their clinical outcome

Results: Among all children with hypothalamus pituitary system tumors after operation. 9 of 16 cases accepted rhGH treatment. 3 cases were only rhGH therapy. 2 cases accepted rhGH plus euthyrox. 2 cases accepted rhGH plus euthyrox and minirin. 2 cases accepted rhGH treatment, euthyrox, minirin and sex hormone. Beginning rhGH treatment time is after operation 1.6 years. Average time of therapy is 2.8 years (0.5~8.6 years). 9 cases of growth rate are all up. IGF-1, IGF-BP3 lever were increased. 1 case after craniopharynqioma operation and rhGH treatment two years, was found pituitary cyst after drug withdrawal one year.Other's MRI are normal.

Conclusion: It's important that rhGH treatment in time for children after hypothalamus pituitary system tumors operation because of disorders of endocrine hormone. The treatment should be performed after state of the illness one year.To detect the lever of IGF-1, IGF-BP3 and MRI would have value in predict rhGH treatment.

P05-05 Growth and Pituitary Disorders

Clinical Significance of Brachymesophalangy and Cone-Shaped Epiphysis of the Fifth Middle Phalanx in Korean Children with Short Stature

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Aims: The cone-shaped epiphyses mid-5(CSE-5) and brachymesophalagia-5(BMP-5) are common osseous anomalies. That were thought to be normal variants. We evaluate clinical parameters in children with short stature in association with CSE-5 and/or BMP-5.

Methods: We reviewed medical records of 322 normal short stature children. Two indicies for BMP-5 were used. Index 1 was the ratio of the width to the length of the fifth middle phalanx. Index 2 was the ratio of the lengths of the fifth to the fourth middle phalanx. CSE-5 was assessed by visual inspection. We assessed following clinical parameters; advanced skeletal maturation(ASM), z-scores of height, mid-parent height(MPHz) and predicted adult height(PAHz) according to CSE-5 and/or BMP-5.

Results: Of the 322 children, 68.3% had normal 5th finger, 15.5% BMP-5 with CSE-5, 8.1% BMP-5 alone and 8.1% CSE-5 alone. The PAHz in children combined BMP-5 with CSE-5 was lower than children with normal 5th finger(p=0.013). The PAHz had weak correlation with index 1(r=-0.136, p=0.021) and index 2(r=0.198, p=0.001). The children with CSE-5 and/or BMP-5 were more ASM than normal 5th finger (0.07±1.08 yrs vs -0.23±1.36 yrs, p=0.049), lower PAHz(-1.13±1.07 vs -0.71±1.28, p=0.008), lower PAHz-MPHz(-0.53±1.07 vs -0.14±1.30, p=0.013).

Conclusion: This study suggests that BMP-5 and CSE-5 are one contributable factor for adult height.

P05-06 Growth and Pituitary Disorders

Comparison of Predicted Adult Heights Measured by Bayley-Pinneau and Tanner-Whitehouse 3 Method in Normal Children, Precocious Puberty and Constitutional Growth Delay

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Aims: The aim of this study was to compare with bone ages measured by Greulich-Pyle (GP) and Tanner-Whitehouse 3 (TW3) methods and investigate the difference of predicted adult heights(PAT) measured by Bayley-Pinneau (BP) and TW3 RUS score methods in normal children, precocious puberty and constitutional growth delay.

Methods: Bone ages were assessed by GP and TW3 methods in 85 normal children, 30 precocious puberty girls and 30 constitutional growth delay boys. PAT were calculated by BP and TW3 methods and the differences of both results were compared in each group.

Results: The PAT measured by BP and TW3 methods showed no significant difference in normal boys, while PAT by TW3 method was higher than that by BP method in normal girls. In precocious puberty girls, the PAT by TW3 method was also higher than that by BP method (159.3±4.2 cm vs 156.3±4.0 cm, P<0.01). On the other hand, the PAT by BP method was higher than that by TW3 method in constitutional growth delay children (173.3±4.4 cm vs 169.7±3.2 cm, P <0.01).

Conclusion: In precocious puberty and constitutional growth delay, BP method might be preferred to predict adult height but further study for final adult height is needed.

P05-07 Growth and Pituitary Disorders

Influences of Growth-Promoting Complementary Therapies on Predicted Adult Heights of Children

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Aims: We are going to investigate the effects of complementary therapies on predicted adult heights of children.

Methods: 33 patients were divided into 3 groups. The 1st group was the children who took the herbal medicines, the 2nd one was them who took growth promoting foodstuffs and the 3rd one was them who had done the regular exercises. Their mid-parental target height standard deviation score, bone age, height SDS adjusted for bone age and predicted adult height SDS were checked before and after therapies. The differences of their height SDS adjusted for their bone ages and predicted adult height SDS before and after therapies were compared with paired t-test or Wilcoxon signed rank test.

Results: 1) The number of group 1, 2, 3 was 23, 4 and 6. 2) The gain in height SDS adjusted for bone age after therapy in group 1, 2 and 3 was 0.02±0.20, -0.07±0.53, 0.01±0.62 (P>0.05). 3) The mean gain in predicted adult height SDS after therapy in group 1, 2, and 3 was 1.20, -0.42 and 0.06cm (P>0.05).

Conclusion: There is little evidence that the complementary therapy is an effective method to improve the outcome of final adult heights of children.

P05-08 Growth and Pituitary Disorders

A Case of Panhypopituitarism Associated with Radiation Therapy in Germinoma

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Aims: Germinoma is sensitive to radiation therapy. Neurotoxicity depends on the total dose, the fraction size, and the duration of the radiation.

Results: A 22-year-old female visited for her absent secondary sex characteristics. She was diagnosed germinoma at 11-year-old due to symptom of diabetes insipidus. She was treated with 4500 cGy radiation and was administered intranasal DDAVP. Growth hormone was injected for 5 years, but she was lost follow up since 18-year-old. Physical examination showed no breast-budding, pubic and axillary hair. Height and weight were 159cm (25-50 percentile) and 48.2kg (<3 percentile). Pituitary MRI was unremarkable and chromosome study showed 46, XX. Her bone age was markedly delayed as 13.25-year-old. Hormonal studies showing ACTH 44.32 pg/ml, cortisol 1.58 μg/ml, ADH 3.16 ng/ml, prolactin 11.65 ng/ml, T3 158.85 ng/ml, T4 3.13 μg/ml, TSH 2.60 mIU/l, and free T4 0.37 ng/ml. Gonadotropin releasing hormone stimulation test was done, and she was diagnosed secondary hypogonadism. After sex hormone replacement therapy (estradiol valerate + medroxyprogesterone acetate), she showed menarche and breast budding, and now she continues to use sex hormone, sodium-L-thyroxine, and DDAVP.

Conclusion: Here we report a case of female patient who developed panhypopituitarism associated with radiation therapy in germinoma. She is on multihormonal therapy.

P05-09 Growth and Pituitary Disorders

Growth of Children Born with Very Low Birth Weight in Korea

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Aims: Although the growth of children born with very low birth weight(<1500g) has been studied extensively in western countries, much less is known about Asian children. The aim of this study is to investigate growth of VLBW preterm infants in Korea.

Methods: A total of 191 children (109 boys, 82 girls) aged 1 to 6 years were followed up (mean age at 20.0±1.7 months). The growth of SGA-VLBW were compared with that of AGA-VLBW. Catch-up growth was defined as standard deviation score (SDS)<-2 in weight or height.

Results: Of the entire study group, mean gestational age was 29.6±2.6 weeks, mean birth weight was 1194±226g and mean birth height was 38.3±3.2cm. At final follow up, mean Ht SDS was -1.73±1.5 and mean Wt SDS was -1.35±1.3. A 141/191 children(73.8%) showed catch-up in weight and 93/191 children(49%) showed catch-up in height. The catch up rate of weight was lower in SGA-VLBW than AGA-VLBW group(53.66%vs 79.3%, P=0.02)

Table 1 (for Abstract P05-09). Comparison of growth status between SHA-VLBW and AGA-VLBW children

	SGA (+) N=41	SGA (−) N=150	p-value
Birth weight (g)	1135±240	1210±219	<0.05
Gestational age (weeks)	32.3±2.5	28.8±1.9	<0.001
Weight SDS	-1.91±1.09	-1.19±1.28	0.0004
Height SDS	-2.14±1.50	-1.70±1.71	0.1665
Percentage of weight catch up (%)	22/41 (53.7)	31/150(20.7)	0.0009
Percentage of height catch up (%)	19/41 (46.3)	76/150(50.7)	0.7341

(Table1). The catch up rate of height was not different between the two group.

Conclusion: SGA-VLBW children had lower rate of catch up growth than AGA-VLBW group especially in weight. Further large-scaled long- term follow up research is needed.

P05-10 Growth and Pituitary Disorders

Growth Patterns of Children Born to HIV-Infected Mothers

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Aims: To study growth patterns of children born to HIV-infected mothers

Methods: 320 children born to HIV-infected mothers at Hat Yai Hospital during January 1998 to December 2002 were reviewed. We devided patients to 2 groups, group 1: HIV-infected children(n=20) and group 2: HIV-noninfected children(n=300). Demographic data, antiretroviral therapy and growth parameters were compared. Weight, length and head circumference were evaluated at birth through 18 months using Z-score.

Results: The study showed the mothers and children who received antiretroviral therapy had significantly reduced HIV transmission rate(p value<0.001). The mother's age, antenatal care, VDRL serology, premature rupture of membrane and mode of delivery were no difference between HIV-infected and HIV-noninfected children. The vertical transmission rate was 6.25%. There was no difference in mean weight for age and height for age at birth between groups. HIV-noninfected group showed catch up all growth parameters within the first 4 months. Weight for age, height for age and head circumference for age in HIV-infected group were lighter and shorter at birth and onwards but no statistically significant compared to the HIV noninfected children.

Conclusion: HIV-noninfected children have catch up growth within 4 months of age. HIV-infected children shows delay of growth compare to HIV-noninfected group but not significantly difference.

P05-11 Growth and Pituitary Disorders

A Case of Mosaic Ring Chromosome 4 Presented with Short Stature

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Aims: We report a 10 month-old male case of mosaic ring chromosome 4 presented with severe short stature.

Methods: The chromosomal analysis with fluorescence in situ hybridization (FISH) study was done. We compared the phenotypic variation with the previously reported cases of ring chromosome 4.

Results: He was presented with severe short stature and mild developmental delay was suspected on the follow-up. Ring chromosome is a structural abnormality which is thought to be the result of fusion and breakage in the short and long arms of chromosome. Wolf-Hirschhorn syndrome is a well known congenital anomaly in the ring 4 chromosome with a partial deletion of the distal short arm. The chromosomal analysis showed the mosaic karyotype with [46,XY,r(4)(p16q35)[84]/ 45,XY,-4[9]/ 92,XY,dic r(4)[5]/ 46,XY,dic r(4)]. Both paternal and maternal karyotypes were normal. The fluorescence in situ hybridization (FISH) study showed deletion of the 4p subtelomeric region with the intact 4q subtelomeric and WHS region.

Conclusion: We report a 10 month-old male case of mosaic ring chromosome 4 presented with severe short stature (about –4 SDS). It is supposed that the size of deletion in the distal short arm of chromosome 4 correlates with the phenotypic variation including short stature.

P05-12 Growth and Pituitary Disorders

Postoperative Pituitary Hormonal Disturbances and Hormone Replacement Therapy Time and Dosage in Children with Craniopharyngiomas

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Aims: To elucidate the postoperative pituitary hormonal disturbances and the hormone replacement therapy (HRT) time and dosage in children with craniopharyngiomas (CP)

Methods: 20 patients with growth retardation and with CP after resection, comprising 14 boys and 6 girls, with a mean age of 10.63±3.18 years (Group A) and 10 of the patients were aged >10 years old (Group B).and age-, sex- and Tanner stage matched Control Group A and Control Group B. The serum concentrations of IGF-1, GH, free thyroxine (FT4), TSH, ACTH, cortisol (COR), FSH, LH, PRL, testosterone (T) and estradiol (E2) were measured

Results: All cases had multiple pituitary hormone deficiency (MPHD). The serum peak GH, IGF-1, FT4 and COR levels of Group A were significantly lower than that of the Control Group A; The serum FSH, LH, and T levels were significantly decreased; however, E2 and PRL were significantly increased in Group B compared with the Control Group B; 18 cases were found to have central DI; The time and corresponding dosage of HRT of rhGH, hydrocortisone,levo thyroxine,DDAVP were displayed respectively

Conclusion: Patients with CP after resection often displayed MPHD, and needed total HRT at appropriate times and dosages to improve quality of life and normal growth

P05-13 Growth and Pituitary Disorders

Non-Compliance with Growth Hormone Treatment (GH) Occurs Commonly

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Aims: No studies have prospectively evaluated compliance with GH treatment in the medical literature. Our aim was to assess GH treatment compliance in children receiving GH therapy in New Zealand (NZ).

Methods: All children in NZ receiving government funded GH were recruited and studied. Children received monthly allocations of GH based upon surface area dosing. Compliance with GH treatment was assessed over a four month period during 2007. Compliance was determined by 2 techniques each month; GH vials required (GHreq) and used GH vials returned (GHret), both expressed as a percentage of allocated vials.

Results: There were 177 children studied, aged 12.1±8.1 years, with 48% males. Diagnostic groups were; GH deficiency 57%, Turner Syndrome 27%, idiopathic short stature 7%, small for gestational age 6%, Prader Willi Syndrome 3% and others 6%. There were 78% European, 17% Maori/Polynesian and 5% Indian/Asian. Overall compliance was 77±28% (GHreq 86±15% and GHret 66±36%). Compliance was lower in Maoris/Polynesians (64±34%) than in Europeans/Asians (78±28%, $p<0.002$). Diagnosis did not influence compliance ($p=0.2$). The following factors did not influence compliance; age ($p=0.4$), sex ($p=0.7$) or diagnosis ($p=0.2$).

Conclusion: Non-compliance with GH treatment occurs commonly and must be considered in all subjects with an inadequate response to GH treatment.

P06-01 Growth Hormone and the IGF/BP Axis

Slipped Capital Femoral Epiphysis in Children with Short Stature on Growth Hormone Therapy

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Aims: This study was aimed to see the incidence of SCFE relating to GH therapy and their clinical and radiological characteristics.

Methods: We retrospectively analyzed 1337 children with short stature on GH therapy at Kyungpook National University Hospital from January 1st, 2001 to June 30th, 2007.

Results: Their male:female ratio was 1:1.1and mean age was 10.1 years old. Underlying diseases consisted of 163 children with GH deficiency, 19 with Turner's syndrome, 7 with chronic renal failure (CRF), 10 with tumors and 2 with Prader-Willi syndrome. And the remainders were idiopathic short stature (ISS). Two out of 1,337 patients (incidence rate was 0.15%) were diagnosed with SCFE. One was 16 years old girl with CRF and renal osteodystrophy. The other was 11 years old girl with ISS who was on combined therapy with GH and GnRH agonist. SCFE occurred 1.25 year after GH therapy in both. Their chief complaints were hip joint pain and lower extremity pain. GH therapy was stopped and corrective surgery was successfully performed.

Conclusion: The incidence rate of SCFE was 1.5% in chidren with short stature on GH therapy.We should consider SCFE in children with persistent low extermity pain on GH therpy.

P06-02 Growth Hormone and the IGF/BP Axis

IGFBP-2 has Growth-Promoting Effects, Which are Modulated by Binding to a Nuclear Partner Protein, PAPA-1

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Aims: Insulin-like growth factor binding proteins (IGFBPs) have multiple effects on cellular functions. We are interested in the protein-protein interactions of IGFBP-2, which govern its actions.

Methods: We performed a yeast two-hybrid screen using a human prostate cDNA library.

Results: We isolated PAP-1-associated protein-1 (PAPA-1) as a nuclear partner protein, whose expression and subcellular localization was regulated by androgens. Co-immunoprecipitation and GST-pull down assay confirmed the interaction in vitro, and confocal microscopy showed the co-localization of IGFBP-2 and PAPA-1 in the nucleus. Suppression of PAPA-1 by siRNA treatment enhanced the growth-promoting effect of IGFBP-2. Incorporation of BrdU into LNCaP cells was induced by hIGFBP-2 transfection and this effect was abrogated by the simultaneous expression of myc-hPAPA-1. Mouse embryonic fibroblast (MEF) from IGFBP-2 knockout mouse showed slower growth rates compared to wild type, and transfection of FLAG-mPAPA-1 inhibited the cell proliferation of IGFBP-2 knockout (but not wild type) MEFs.

Conclusion: These data suggest that IGFBP-2 has IGF-independent growth-promoting effects, which are modulated by binding to PAPA-1 in the nucleus.

P06-03 Growth Hormone and the IGF/BP Axis

Study on the Interactions between Growth Hormone and Ghrelin in Rat

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Aims: Ghrelin is the third hormone, which regulates growth hormone secretion, together with growth hormone releasing hormone(GHRH) and somatostatin. The object of this study is to know the interaction between growth hormone(GH) and ghrelin.

Methods: We administerd 10 μg of rat ghrelin or normal saline to male Sprague-Dawley rats(body weight 250-300 g) intravenously. After 10 minutes later blood and tissue samples were collected. Plasma GH levels, pituitary GH mRNA expression and hypothalamic GHRH mRNA expression were measured. And after three day administration of human GH(500 μg/kg, twice a day) or normal saline subcutaneously to rats with food or without food for 45 hours, plasma ghrelin levels, plasma insulin levels, plasma IGF-1 levels, and stomach ghrelin mRNA expression were measured.

Results: Plasma GH levels were significantly higher in rats with ghrelin injection than in controls($P<0.05$). But both pituitary GH mRNA levels and hypothalamic GHRH mRNA levels were not different between two groups. Plasma ghrelin levels, plasma insulin levels and stomach ghrelin mRNA expression were not affected by administration of GH. Fasting increased plasma ghrelin levels($P<0.05$) and stomach ghrelin mRNA expression($P<0.05$) significantly. And also it decreased plasma insulin and IGF-1 levels($P<0.05$).

Conclusion: Ghrelin stimulated GH secretion without increasing synthesis of GH nor GHRH. Additionally, GH administration

P06-04 Growth Hormone and the IGF/BP Axis

The Growth of Pediatric Peritoneal Dialysis Patients with GH Treatment

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Aims: We studied effect of growth hormone (GH) treatment and the factors influencing growth of the peritoneal dialysis patients.

Methods: Seventeen patients who treated with peritoneal dialysis and GH for more than one year were enrolled. Factors influencing growth such as age, height at start of GH treatment, total Kt/Vurea, residual renal Kt/Vurea, laboratory findings during GH treatment were compared between the growth group (increase in height-SDS after one year of GH treatment, n=11) and poor growth group (no increase in height-SDS after one year of GH treatment, n=6).

Results: The mean age at the start of dialysis was 7.7±5.2 years and the mean age at the start of GH treatment was 8.5±4.8 years. In the growth group, height-SDS at start of GH treatment were smaller (-1.72±1.00 vs. -0.77±0.88, P=0.048) and residual renal Kt/Vurea were better (1.54±0.51 vs. 0.15±0.26, P=0.02) than poor growth group.

Conclusion: GH treatment in children with peritoneal dialysis was more effective on patients who had more severe growth retardation. The reservation of residual renal function was important for improvement of effect of GH treatment.

P06-05 Growth Hormone and the IGF/BP Axis

The Common Exon 3 Polymorphism of the Growth Hormone Receptor Gene (GHR) and Growth Promotion Efficacy of GH Therapy in Korean Patient with Turner Syndrome

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Aims: A human growth hormone receptor (GHR) gene exon 3 polymorphism (d3-GHR) has been reported to be associated with responsiveness to GH therapy. We assessed the frequencies of this polymorphism, and analyzed short-term growth response to GH therapy according to GHR-exon 3 genotypes in Korean patients with Turner syndrome (TS).

Methods: This is a retrospective study in 175 TS patients. Auxological and endocrine parameters were measured, and the GHR-exon 3 genotype was analyzed. Allelic frequencies of GHR-exon 3 genotype were compared between the TS group and a control group. Changes in height velocity (HV) and IGF-1 and IGF binding protein-3 (IGFBP-3) concentrations were compared in GH-treated patients with these genotypes after the first follow-up year.

Results: There was no difference in GHR-exon 3 genotype frequency between TS and control groups. Follow-up HV (P=0.014) and height-SDS gain (P=0.031) differed significantly. However, follow-up IGF-1, IGFBP-3 concentration and BMI showed no significant difference between the groups with and without d3-GHR after 1yr of GH therapy.

Conclusion: The growth promotion efficacy of GH therapy differed significantly between TS patients with and without the d3-GHR allele. The GHR-exon 3 polymorphism seems to affect the growth promoting efficacy of short-term GH therapy in Korean children with TS.

P06-06 Growth Hormone and the IGF/BP Axis

Effects of Somatropin Therapy on the Bone Metabolism in Children of Growth Hormone Deficiency

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Aims: To investigate the effects of rhGH replacement therapy on the bone metabolism in children with GHD and to explore the role of GH in the balance of bone metabolism.

Methods: 30 children with GHD were received rhGH replacement therapy, measured the body height, body weight, BMI, growth velocity and serum of IGF-1, IGF-BP3, calcium, phosphonium, AKP, osteocalcin, β-CTX after 3 and 6 month treatment and detected bone age, bone mineral density of lumbar spine and femoral bone after 6 month treatment.

Results: The bone turnover markers (AKP, OC and β-CTX), serum phosphonium, IGF-1 and IGF-BP3 , the BMD of lumbar spine, neck of femur and great femur trochanter were increased after GH therapy than before ($P<0.01$). The accrescence of lumbar spine BMD could be positively correlated with the increase of body height, serum calcium and IGF-BP3 ($r=0.418,0.433,0.483$, $P=0.021$, 0.017, 0.007 separately).

Conclusion: GH replacement therapy could increase the level of serum IGF-1, IGF-BP3, bone turnover markers and the BMD of spine and femur in GHD children. The accrescence of lumbar spine BMD could be positively correlated with the increased changes of body height, serum calcium and IGF-BP3.

P06-07 Growth Hormone and the IGF/BP Axis

Variability of Pharmacological Growth Hormone Stimulation Test

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Aims: Growth hormone deficiency (GHD) has been confirmed by two pharmacological growth hormone stimulation test (GHST). We studied the relative potencies of clonidine, insulin, and levodopa as well as reproducibility of GHST.

Methods: This study included 87 boys and 56 girls with short stature (height SD score -2.5±0.7) and bone age delay (bone age SD score -2.0±1.2) for chronological age who underwent GHST from 2003 to 2007 in the Ajou university hospital, Korea. In 372 tests, clonidine, insulin, and levodopa were used in 127, 136, and 109 respectively.

Results: Peak GH values were higher with clonidine (14.5±8.3 ng/ml) than with insulin (9.5±8.1 ng/ml) ($p=0.0002$) and were also higher with levodopa (17.3±10.4 ng/ml) than with insulin (11.6±8.9 ng/ml) ($p=0.0001$). However, peak GH values with clonidine (9.4±5.7 ng/ml) were not different from those with levodopa (7.9±4.5 ng/ml) ($p=0.1656$). No significant correlation was found in the peak GH values of repeat clonidine, insulin, and levodopa stimulation ($p>0.05$).

Conclusion: Clonidine and levodopa are stronger than insulin in the pharmacological growth hormone stimulation test. Because the reliability of the GHST is questionable, new diagnostic criteria should be developed.

P06-08 Growth Hormone and the IGF/BP Axis

Analysis of Cytosine Adenine(CA) Repeat Polymorphism of the IGF-I Promoter Gene in Children with Idiopathic Short Stature

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Aims: The aim of the present study was to investigate the role of polymorphic CA repeat of the IGF-I gene in children with idiopathic short stature.

Methods: Children diagnosed as idiopathic short stature of 172 (99 boys and 73 girls) aged between 7 and 15 years were involved for the present study. Data were analyzed using GeneMapper an software version 3.7. All analyses were performed using MEDCALC software package.

Results: The CA repeat sequences ranged from 15 to 22, and 19 CA repeats were the most common with an allele frequency of 38.9%. Homozygous for 19 CA repeat was 12.8%, heterozygous for 19 CA repeat was 52.3% and 19 CA noncarrier was 34.9%. There are no significant differences in height, body weight and body mass index and serum IGF-I levels among three different genotype groups. Correlations between serum IGF-I level and age according to the IGF-I genotypes revealed statistically significant relationship in whole group, 19 CA repeat carrier group even in noncarrier group, respectively. There is also no significant differences of the first year responsiveness to GH treatment among three different genotype groups.

Conclusion: Our results suggest that the IGF-I 19 CA repeat gene polymorphism is not functional in children with idiopathic short stature

P06-09 Growth Hormone and the IGF/BP Axis

Status of Alternative Therapies Used by the Children Visiting the 'Growth Clinic'

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Aims: Although growth hormone treatment is now widely used, it is still expensive and many parents are seeking alternative therapies. We report the current status of alternative therapies for children visiting the 'growth clinic'.

Methods: Questionnaire about the usage of alternative therapy was used. Parents were asked whether they used alternative therapies and where they got the information. Also, they were asked whether the treatment was effective, and whether they would continue to use.

Results: Two hundred and twenty nine children visiting the 'growth clinic' were analyzed. Their ages were between 6.1 years to 15.4 years. Height Standard Deviation Score(SDS) were between -3.2 to 1.0. Twelve boys and 7 girls were more than zero in height SDS value. Among 145 children, supplemental foods and oriental herbs were most widely used followed by over-the-counter drugs. They attained the information most frequently from their neighbors followed by television, newspaper and internet. More than half of the parents answered that the alternative therapies were not effective. However, 46.9% of the parents answered they would continuously use the therapy.

Conclusion: Many patients visiting the 'growth clinic' for short stature had experiences on the alternative therapies. Although these therapies seemed not effective, they would continue alternative therapy.

P06-10 Growth Hormone and the IGF/BP Axis

IGFBP-3 Promoter Polymorphism is Related to Circulating IGFBP-3 Level; Focused on the Relation to the Height of Korean Girls

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Aims: The most common single nucleotide polymorphism of IGFBP-3 promoter region is -202 locus. In vitro, significantly higher promoter activity of the A allele at the -202 locus compared with the C allele, consistent with the relationship observed between genotype and circulating IGFBP-3 was documented. However, the effects of IGFBP-3 promoter polymorphism on growth in children are unknown.

Methods: RFLP genotyping of the -202 single nucleotide polymorphism was performed in 146 Korean girls. The subjects were divided into three groups (tall, mean and short) according to height percentile by normal references of Korean children. The serum levels of IGF-I and IGFBP-3 were compared according to genotype.

Results: In Korean girls, genotype distribution was 79 AA (54.1%), 60 AC (41.1%) and 7 CC (4.8%). A to C allelefrequency at -202 locus is 25.4%. Mean serum IGFBP-3 level in girls with AA genotype is higher than that in girls with AC (P=0.035) in short group. Mean serum IGFBP-3 level in girls with AA genotype is higher than that in girls with AC (P=0.047) in mean group.

Conclusion: The polymorphism of this locus influences the circulating IGFBP-3 level in Korean girls such as previous reports. However, the effects on growth cannot be proved in this study.

P06-11 Growth Hormone and the IGF/BP Axis

Genetic Polymorphism and Biomarker Relationships to IGF-1 Changes after 1 Month of GH Therapy in Prepubertal Children with Growth Hormone Deficiency (GHD) or Turner Syndrome (TS): The PREDICT Study

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Aims: PREDICT investigated relationships between IGF-I and IGFBP3 SDS changes with biomarker changes and genetic polymorphisms in previously untreated children with GHD (n=169) or TS (n=149).

Methods: Blood samples were obtained before and after 1 month of treatment (Saizen

Results: Changes in IGF-I SDS correlated positively with changes in insulin sensitivity (HOMA-IR) and triglycerides (TG). Changes in IGFBP3 SDS did not correlate with HOMA-IR in TS or GHD. Changes in IGFBP3 SDS correlated with changes in all lipid parameters for TS only. In GHD, genotypes were correlated with

Table 1 (for Abstract P06-11). Correlation of IGF-1 and IGFBP3 SDS changes with insulin/lipid changes (ITT)

		TS (n=149)		GHD (N=169)	
Predictor value	Response value (% change)	Spearman correlation	p-value	Spearman correlation	p-value
IGF-1 (SDS)	HOMA – IR	0.31	0.0005	0.32	0.0001
	TC (mmol/L	0.16	NS	0.11	NS
	LDL –C (mmol/L)	0.21	0.0243	0.20	0.0186
IGFBP3 (SDS)	HOMA –IR	0.06	NS	0.03	NS
	TC (mmol/L	0.41	<0.0001	0.13	NS
	LDL –C (mmol/L)	0.23	0.0129	0.11	NS
	HDL –C (mmol/L)	0.27	0.0029	0.08	NS
	TG (mmol/L)	0.22	0.0148	0.01	NS

change in IGF-I SDS for 6/98 genes. In TS, genotypes were correlated with change in IGF-I SDS for 12 additional genes. No significant difference was seen between GHR-d3 polymorphism and changes in IGF-I and IGFPB3 SDS.

Conclusion: Differential effects of GH treatment on metabolic biomarkers are seen within TS and GHD. Multiple genetic polymorphisms (different in GHD and TS) in pathways related to the control of growth are associated with an early response to GH, as defined by change in IGF-I.

P06-12 Growth Hormone and the IGF/BP Axis

Some Remarks on Growth Hormone Treatment for 4 Cases with Growth Hormone Deficiency

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Aims: Aim of the study was to summary some remarks of GH-deficient children in the National Hospital of Pediatrics, Hanoi.4 patients diagnosed of GH deficiency have been treated by GH for than 6 months.

Methods: Case descriptive study.

Results: Mean age of GH treatment was 11.3 years. (8-15 years). Before treatment: height SDS was -2.8SD. Basal GH was 0.28ng/ml (0-0.6); stimulated GH was 0.35mg/ml (0-0.7); IGF1 was 38ng/ml (13-107). Bone age was delayed of 6 year compared to chronological age. Mean duration of treatment was 14 months (6-21months) with mean GH dose of 0.04mg/kg/day. Height velocity after 6, 12, 18, 21 months were 6.9, 12.1, 16.5, and 19, respectively. Height score was -1.8SD.

Conclusion: Mean age on GH treatment was 11.3 year (8-15 years). Mean GH dose was 0.04mg/kg/day. Height velocity after 12 and 21 months was 12 and 19 cm, respectively. Height SD score was increased from -2.8 to -1.8SD after 14 months. The bone age reached approximately to the chronological age at 12 months.

P06-13 Growth Hormone and the IGF/BP Axis

Multicentric Study of Efficacy and Safety of Recombinant Human GH Solution Use in Growth Hormone Deficient Children in China

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Aims: To evaluate the efficacy and safety of recombinant human GH solution use in GH deficient children in China.

Methods: A 12-month randomized, open-label ,multicenter trial was conducted in study in 31 previously untreated children with GH deficiency (GHD).A rhGH solution was given sc daily at a weekly dose of 0.25 mg/kg. Body height was measured 3-monthly and height velocity (HV) and height SD score (HT SDS) were calculated. Serum IGF-I, IGFBP-3,GH antibodies and safety parameters were assessed regularly.

Results: The mean (±SD) annualized growth rate was 16.02 ±5.08cm/yr at 3 months, 14.06±3.98 cm/yr at 6 months, 13.70 ±3.51 cm/yr at 9 months and 12.87 ±3.33 cm/yr at 12 months compared with 2.68 ±0.91 cm/yr at baseline($P<0.001$). HT SDS was -4.62 ±1.46 at the onset of therapy and increased significantly after the treatment to -3.80±1.53, -3.28±1.60, -2.86±1.75 and -2.47±1.86, respectively ($P<0.001$). IGF-I and IGFBP-3 were increased comparably for the treatment ($P< 0.001$).The rate of skeletal maturation was not accelerate significantly during treatment. No severe adverse events happened in the trial and the most-likely adverse event was hypothyroid.

Conclusion: Recombinant human GH solution is safe and effective for GH replacement in children with GH deficiency.

P07-01 Obesity

Can Education Through Poster Improve the Knowledge and Practice of Preschoolers about Healthy Lifestyle? IHHP-HHPC

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Aims: Lifelong behavior and risk factors of chronic diseases track from early life to adulthood. It seems that dietary habits and unhealthy food consumption as well as passive smoking play an important role

in development of such diseases. Multiple studies showed healthy life-style education in preschool children improves their knowledge, attitude and practice about healthy life style. Objective: To study the effect of life style education in daycare centers for preschool children via educational posters.

Methods: In an interventional study 250 preschool children were selected by 2-stage random cluster sampling and taught tips on healthy life style via educational posters. Their knowledge on healthy life style was assessed Before and (1week and 3 months) after education via a picture-questionnaire and their practice and behavior was assessed before and after education via their favorite snack choice in day care centers. Collected data were analyzed using Spss V13/win by t-paired test and Man Whitney tests.

Results: The knowledge and practice score of studied subjects significantly improved one week after intervention compared with baseline and persisted until the third month after education.

Conclusion: Health life style education via poster for pre-school children has a significant effect on improvement of their knowledge and practice about healthy life style.

P07-02 Obesity

Association Between Waist-for-Height Ratio and Dyslipidemia Among Overweight and Obese Pediatric Patients Seen at the Out Patient Department of the Philippine General Hospital

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Aims: To determine the relationship between waist-for-height ratio and dyslipidemia among overweight and obese pediatric patients age 5-19 years at the Philippine General Hospital

Methods: A complete history and physical examination was done. Data collected were age, sex, weight, height, WC, WHR, WHtR and BMI. Fasting blood lipid sample was collected (n=88, mean age 11.86 years, mean WHtR 0.56).

Results: There were 88 overweight and obese children and adolescents (mean age 11.86

Conclusion: An elevated WHtR increases the likelihood of developing hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL.

P07-03 Obesity

Relation Between Thyrotropinemia and Severity of Obesity in Children

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Aims: Obesity effects pituitary thyroid axis resulting in elevated thyroid stimulating hormone (TSH) level. We studied the relation between body mass index (BMI) and TSH in euthyroid and subclinical hypothyroid obese children and to compare serum TSH among obese and overweight children.

Methods: Fifty consecutive children (aged 2-18 yrs) presenting for obesity was studied. All cases with TSH > 10, low T3/T4, organic and syndromic obesity were excluded. Patients were divided into Group 1: Overweight (n=20) (BMI between 85th to 95th centile) and Group 2: Obesity (n=30) (BMI > 95th centile). Appropriate statistical tests were applied for analysis.

Results: Elevated TSH level (between 4.5 and 10 mIU/L) with normal T3, T4 was seen in 4/20 overweight and 9/30 of obese children (P=0.5219). The mean TSH was comparable in both the groups (3.22 vs. 3.63 mIU/L, P=0.3491). Overall TSH showed no correlation with BMI (r=0.0014, P=0.9924).

Conclusion: Our preliminary data did not show any relation between severity of obesity and TSH level. Further large scale data from population are required to confirm these findings.

P07-04 Obesity

Should Waist to Height Ratio of >0.5 Indicating Central Adiposity Be Used in Chinese Children?

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Aims: Derive reference data for two anthropometric indexes of central adiposity: waist circumference (WC) and WHtR for Han Chinese children and assess the cut-point for WHtR in Chinese children.

Methods: A school based, cross-sectional study was conducted in city of Chongqing (south-west China) between 2003- 2004. 7326 (3603 boys) Han-Chinese students aged 5-17 years were recruited from 15 primary schools and 9 secondary schools. Anthropometric measurements included height, weight, WC. WHtR by dividing the WC by height.The LMS method was used to establish smoothed percentile curves.

Results: WC increases with age in both genders until 15 years and then plateaus and boys had a higher WC compared to girls. The median WHtR was also higher in boys compared to girls by age ($P<0.05$) until the age of 12 years.Boys were identified as more excess central obesity compared to girls,17.4% and 10.8% respectively. the Chinese cut point of 0.485 and 0.475 identified more central obesity(17.4% in boys and 10.8% in girls) compared to when using the 0.5 cut point(14.8% in boys and 5.6% in girls).

Conclusion: Chinese boys have higher WC and WHtR than Chinese girls. The cut point for indicating excess central adiposity of 0.5 for WHtR could also be used in Chinese children and adolescents.

P07-05 Obesity

Effects of Body Composition, Leptin and Adiponectin on Bone Mineral Density in Prepubertal Girls

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Aims: Body weight is positively associated with bone mineral density (BMD). But, it is not clear whether lean mass or fat mass mediate bone stimulatory effect excerted by weight. Leptin and adiponectin are potential contributors to BMD. The aim of this study was to assess the relationship between body composition and BMD and whether leptin and adiponectin determine BMD independently.

Methods: Subjects included 48 prepubertal girls. They were classified as obese group (n=23, BMI ≥ 85th percentiles) and control group (n=25, 25th percentiles ≤ BMI < 75th percentiles). Serum leptin and adiponectin levels were determined by ELISA. BMD (by BIA) and body composition (by DXA) were measured.

Results: Listed in Fig. 1 and 2

Conclusion: In prepubertal girls, lean mass and fat mass are independent predictors of femoral BMD. Lean mass has a greater impact on BMD than fat mass. Leptin can predict femoral BMD independently but not L-spine BMD. Leptin may have a certain biological role in regulating bone metabolism.

Table 1. Correlation of serum leptin, adiponection, HOMA–IR, fat mass and lean body mass with BMD

	BMD_{femur}		$BMD_{L\text{-}spine}$	
	r	*P*	*r*	*P*
HOMA-IR	0.455	<0.05	0.353	NS
Fat mass	0.75	<0.05	0.681	<0.05
Lean mass	0.818	<0.05	0.83	<0.05
Leptin	0.659	<0.05	0.481	<0.05
Adiponectin	−0.181	NS	−0.006	NS

Table 2. Results of multiple linear regression

	BMD_{femur}		$BMD_{L\text{-}spine}$	
	β	*P*	β	*P*
HOMA-IR	0.007	0.495	0.003	0.820
Fat mass	−0.012	0.047	−0.002	0.740
Lean mass	0.022	0.000	0.019	0.000
Leptin	0.007	0.011	0.001	0.918
Adiponectin	−0.002	0.743	0.002	0.768

P07-06 Obesity

Five Cases of Polycystic Ovary Syndrome (PCOS) Presenting with Hirsutism and Obesity in Adolescence

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Aims: This study was aimed to describe five cases of PCOS presenting with hirsutism and obesity in adolescence that is complex disorder with multiple components, including infertility, metabolic syndrome, type 2 diabetes mellitus, and cardiovascular diseases

Methods: The clinical characteristics, laboratory and ultrasonographic findings of five patients with PCOS were investigated through the review of medical records

Results: They showed hirsutism, acne and acanthosis nigricans, and obesity with the body mass index above the ninety-fifth percentile. Laboratory findings showed elevated luteinizing hormone, total testosterone and decreased sex hormone binding globulin. One patient was diagnosed as having impaired glucose tolerance by oral glucose tolerance test, and four patients showed insulin resistance classified by homeostasis model assessment-insulin resistance (HOMA-IR) value. All patients were treated with exercise, low calorie diet. Metformin and estrogen-progesterone oral contraceptives were administered in three of five patients respectively. During the follow-up period, two patients have achieved weight loss and three patients recovered regular menstruation

Conclusions: Polycystic ovary syndrome, occurring in adolescents, has an increasing risk of type 2 diabetes mellitus, endometrial cancer, obesity and infertility. Therefore, early diagnosis and management of patients with PCOS are important to prevent serious complications

P07-07 Obesity

Ad-36 Adenovirus-Induced Obesity in Korean Children

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Aims: Human adenovirus-36 (Ad-36) induces obesity by a direct effect of the viral E4orf1 gene on lipogenic enzymes in host adipocytes. Ad-36 antibodies are specific evidence of infection with this virus. Studies in adult humans show a strong correlation of serum antibodies to Ad-36 and presence of obesity, but the effect of Ad-36 in children has not been reported.

Methods: Blood was obtained for measurement of Ad-36 antibodies in 84 obese Korean children (8.3-16.3 years) at the school physical examination or obesity clinic visit. Frozen serum was shipped to the Obetech Obesity Research Center, USA, for analysis by serum

neutralization assay for Ad-36 antibodies. A sample was considered positive if 50% or more of replicates had a titer of 1:8 or higher.

Results: Of the 84 samples, 30% were positive (N=25) and 70% were negative (N=59). BMI z-scores were significantly higher (1.92 vs 1.65, p<.01) in infected children. Waist circumference was higher in infected children (p=.05). Blood pressure, glucose, cholesterol, SGOT and SGPT were not significantly higher in infected children, but the values were greater.

Conclusion: Ad-36 infection is very common in obese Korean children and correlates highly with obesity. Ad-36 may have played a major role in the obesity epidemic in children.

P07-08 Obesity

Association of Obesity and Hyperandrogenemia in Korean Children and Adolescent Obese Girls

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Aims: This study was to know relationship between obesity and hyperandrogenemia (HA) and assess the degree of HA in Korean children and adolescent obese girls.

Methods: Subjects were 69 normal weight (body mass index (BMI) for age<85 percentile) and 78 obese (BMI age ≥ 95 percentile) peripubertal girls. They were divided into 3 groups (Tanner stage 1=prepuberty, Tanner 2, 3=early puberty, Tanner 4, 5=overt puberty). Blood samples were taken early in the morning after 8hr of fasting.

Results: Compared with normal weight girls, mean total testosterone(T) , free T, DHEA-S, and insulin levels were significantly higher in obese groups(P<0.05). SHBG levels was significantly lower in obese groups(P<0.001). High total T, free T, DHEA-S, insulin and lower SHBG levels were pronounced in overt puberty. BMI correlated with total T(r=0.468, P<0.001), free T(r=0.495, P<0.001), DHEA-S(r=0.422, P<0.001), SHBG(r=-0.362, P<0.001), and insulin(r=0.495, P<0.001) . Fasting insulin correlated with total T(r=0.279, P<0.05), SHBG (r=-0.268, P<0.05), free T(r=0298, P<0.001), and DHEA-S(r=0.272, P<0.05). LH correlated with total T(r=0.674, P<0.001), free T (r=0.576, P<0.001), and DHEA-S(r=0.423, P<0.001).

Conclusion: HA is pronounced in obese girls during overt puberty. Identifying girls at risk for HA may be an effective means of preventing some of the longterm complication associated with PCOS.

P07-09 Obesity

Serum Visfatin Levels Cannot Represent the Degree of Obesity and Insulin Resistance in Children and Adolescents

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Aims: Visfatin is an adipocytokine secreted from adipocytes in the visceral fat. In our study, we focused on whether there were differences in serum Visfatin level between obese and non-obese population, and insulin resistant and non-resistant population.

Methods: 22 obese children and adolescents who had a BMI over 95 percentile of their age and sex and 26 healthy controls who had a BMI below 95 percentile of their age were selected and serum Visfatin and AST, ALT, lipid profiles, insulin and glucose were obtained.

Results: Significant differences were observed in serum ALT and HOMA-IR (p<0.05) but serum Visfatin showed no significant differences between the obese group and controls (obese group 40.03±16.24ng/ml vs. control 34.52±11.65ng/ml, p=0.179). Serum Visfatin showed no significant correlations between anthropometric data, AST, ALT, glucose, insulin, lipid profile and HOMA-IR in the obese group.

Conclusion: There were no direct correlations with serum Visfatin and variables regarding obesity (BMI) and insulin resistance(HOMA-IR) in children and adolescents. This might suggest that serum level of Visfatin might not represent the actual activity of this molecule in intracellular receptors. Further studies with oral glucose tolerance test and other variables regarding insulin resistance and obesity should be obtained to confirm our current conclusions.

P07-10 Obesity

Birth Weight and Insulin Resistance in Obese Korean Children

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Aims: Low birth weight has been known to be associated with insulin resistance in later life. The purpose of this study was to clarify the relationship between birth weight, current weight status and the development of the insulin resistance in obese children.

Methods: A total of 1668 obese (BMI ≥85P) school children (mean age 11.9±1.7 years, 1079 boys, 589 girls) were included. Anthropometric variables(height, weight, waist circumference, fat percent), blood pressure, fasting insulin, glucose, triglyceride and HDL-cholesterol were measured. We defined pediatric metablic syndrome(MetS) based on the modified NCEP-ATPIII criteria. We compared metabolic parameters by birth weight group.

Results: HOMA-IR, prevalence of acanthosis nigricans and MetS were significantly higher in low birth weight group than nor-

Table 1 (for Abstract P07-10). Metabolic parameters by birth weight group

	Birth weight			
	<2500g (n=187)	2500-4000g (n=1379)	>4000g (n=102)	p-value
Birth weight (kg)	2.2±0.4	3.3±0.3	4.3±0.3	<0.0001
BMI (kg/m2)	26.7±2.9	26.3±2.9	27.1±3.2	0.006
Percentage of Weight for height (%)	133.6±12.5	133.1±12.4	135.0±14.3	0.441
Fat percent (%)	37.0±5.6	37.0±5.5	36.3±6.2	0.627
HOMA-IR	5.4±5.	5.1±6.6	4.2±3.3	0.032
Prevalence Acanthosis n(%)	111/187(59.4)	744/1379(53.9	49/102(48.0)	<0.0001
Prevalence of MetS n (%)	38.187(20.3)	245/1379(17.8)	18/102(17.6)	<0.0001

mal or high birth weight group (Table1). Birth weight was negatively associated with serum triglycerid levels (r=-0.05, p=0.04) and HOMA-IR(r=-0.06, p=0.02).

Conclusion: These findings suggest that lower birth weight with current overweight status may predict the risk of insulin resistance and metablic derangement.

P07-11 Obesity

Serum Leptin, Adiponectin and Resistin Levels in Obese Children

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Aims: The aim of this study was to compare the serum levels of adipocytokines and growth parameters of obese children with those of normal children.

Methods: We enrolled 36 obese children (M:F=17:19, 9.1±2.0 yrs) whose BMI was the 85th percentile or over and 35 health children (M:F=16:19, 9.3±1.9 yrs) as control group whose BMI was between the 15-85th percentile. We measured serum leptin, adiponectin and resistin levels and IGF-I and IGFBP-3 with basic blood chemistry in both group.

Results: Serum leptin levels were significantly higher in obese group compared with control (p<0.001) and adiponectin concentrations inversely lower in obese children than control (p<0.001). No significant difference of resistin levels regarding obesity was seen. The leptin/adiponectin (L/A) ratio was five-folds greater in obese children compared to control (p<0.001). Leptin levels correlated with IGF-1 (p=0.021) and BMI (p<0.001). Adiponectin values correlated inversely with IGFBP-3 (p=0.009), BMI (p<0.001) and leptin (p<0.001). The L/A ratio correlated with BMI(p<0.001). Adipocytokines were not correlated with fasting blood sugar and lipoproteins.

Conclusion: Obese children have markedly elevated serum leptin levels and decreased serum adiponectin levels and showed higher L/A ratio than healthy control. L/A ratio could be used as a marker for estimate degree of childhood obesity.

P07-12 Obesity

Clinical and Metabolic Profile of Obese Children in a Tertiary Care Hospital in India

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Aims: To study the clinical & metabolic profile of obese & overweight children.

Methods: Children referred to our hospital endocrinology services for increased weight gain from April 2006 to July 2007 were enrolled after ruling out endocrinopathies. Detailed history & physical examination findings were noted and entered in a specific proforma. The oral glucose tolerance test (OGTT), serum insulin and lipid profile tests were performed.

Results: Out of 109 patients enrolled ,70 were boys (64.2%)and 39 were girls(35.8%).The age range was 5-18 yrs with a mean of 13.6 yrs.80(73.3%)were obese (>95thBMI centile, CDC) & 29(26.6%) were overweight (85-95th BMI centile) with a mean BMI of 29 kg/m2. Known family H/O type2 DM &obesity was elicited in 75 (68.8%) & 80(73.3%) subjects respectively.Gynecomastia was seen in45/70 boys.Hypertension was seen in 27(25%). Impaired fasting glucose was seen in 24/107 (22.4%)whereas impaired glucose tolerance was seen in 13/99 subjects (13.1%) who underwent OGTT. Type 2 DM was found in 1 adolescent girl.

Conclusion: There is a need to screen and follow-up all obese and overweight children for metabolic impairment in particular with a positive family history of diabetes mellitus and obesity.

P07-13 Obesity

Metabolic Profile of Obese Children and Adolescents in Bangladesh

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Aims: Childhood obesity, an epidemic in developed country is also emerging as a health problem in developing countries like Bangladesh. The study was undertaken to see the metabolic profile

of children and adolescents with obesity, attending the Paediatric Endocrine OPD, BIRDEM.

Methods: A cross sectional study from January 2006 to December 2007.

Results: A total of 140 patients presented with obesity (BMI> 95th centile for age and sex). Male to female ratio was 1.3:1. Mean age was 9.44±3.05 years. Mean BMI was 27.15±3.67kg/m2. Impaired glucose tolerance (IGT:2-hour plasma glucose during the oral glucose tolerance test ≥7.8 to< 11.1mmol/L)) was found in 17.1 % of subjects. Diabetes mellitus in 0.85%. Total cholesterol was >200mg/dl in 23.6%, triglyceride was >150mg/dl in 38.5% , HDL cholesterol was< 40 mg/dl in 44% and LDL cholesterol was>130mg/dl in 19.6 % of subjects. Systolic Blood pressure was high in 13.6% and diastolic blood pressure was high in 20% of subjects. Metabolic syndrome was found in 37.7% of subjects.

Conclusion: The high rate of IGT, dyslipidaemia and metabolic syndrome in this cohort is of concern. Factors contributing towards obesity needs to be identified so that strategies could be planned for prevention and management of this health problem.

P07-14 Obesity

Effects of Weight Management Program on Lipid Profiles, Adiponectin and Insulin Resistance in Korean Obese Children

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Aims: It is well known that obese children have many serious problems, but it is difficult to control childhood obesity. Few studies have reported successful interventions in children. We performed an organized weight management program for Korean obese children and analyzed effects of our program.

Methods: Weight management group (19 obese children: Body Mass Index(BMI)>95P) who had organized exercise program for 3 months and age, sex matched control group (19 obese children: BMI>95P) were enrolled. Weight management group had organized exercise program with educated teachers for 90 minutes a day (8 days a month) and life style modification counseling. Control group had conventional counseling at out-patient clinic. We analyzed BMI, serum lipid profiles, adiponectin, HOMA-IR and Body fat % after 3 months.

Results: Weight management group had a better effect on weight(mean: -2.3kg vs +2.5kg) and BMI(-1.7 vs +0.5) compared with control group. Serum lipid profiles were improved. HOMA-IR was decreased through our program(-1.0 vs +0.5). Changes of serum adiponectin levels were not significant between two groups.

Conclusion: Our weight management program is effective for weight loss and helpful in improving lipid profiles and lowering insulin resistance in Korean obese children.

P07-15 Obesity

Insulin Sensitivity and Beta Cell Function in Obese Korean Children and Adolescents with Normal Glucose Tolerance

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Aims: The aim of this study was to investigate the beta cell function and insulin sensitivity in Korean obese children who has normal glucose tolerance (NGT).

Methods: The data from two hundred fifty children and adolescents (M/F 165/85, age 12.0±2.7) were included. Fasting glucose, insulin, total cholesterol, triglyceride, LDL-cholesterol, HDL-choldesterol, and OGTT results were analyzed. In this study, insulinogenic index (IGI) and whole body insulin sensitivity index (WBISI) were calculated from oral glucose tolerance as insulin secretion function and insulin sensitivity. Subjects were divided into 4 groups by Glucose level in 120min (Glu120m) quartiles. Hyperbolic feedback curve were drawn with IGI and WBISI.

Results: 1) Height, weight, age, sex and BMI were not significantly different among 4 groups. 2) No significant difference in fasting glucose levels among 4 groups. 3) HOMA-IR was significantly different according to Glu120m. 4) WBISI was significantly decreased according to Glu120m. 5) Leftward shift toward IGT in the feedback curve was significant in higher Glu120m groups.

Conclusion: High normal oral glucose tolerance test obese children may have a gradual deterioration in glucose stimulated insulin response and have an increased risk of IGT and diabetes. More mechanistic studies for the transition from NGT to IGT and ultimately diabetes should be followed.

P07-16 Obesity

Prevalence of Obesity Among Affluent School Children in Dhaka

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Aims: To study the prevalence of obesity amongst affluent school children and adolescent in Dhaka,capital of Bangladesh.

Methods: A cross sectional study was conducted in September 2006 in one of the private school of Dhaka. Permission was taken from the school authorities to take anthropometric measurements of all school children.Weight, standing height, triceps skin fold thickness (TSFT), waist and hip circumference were measured. Weight was measured using a bathroom scale and height was measured with stediometer. Herpenden's calipre were used for measuring TSFT.The body mass index (BMI) was calculated as weight in kilogram divided by square of the height in meter. Subsets with a BMI ≥95th centille

were classified as obese using CDC growth chart.Children and adolescents were devided into Group 1 (3-5years,n=110),group 2 (6-9 years, n=177,Group 3 (10-13 years, n=149) and group 4 (14-18 years, n=33).Date of birth was collected from school record book.

Results: The prevalence of obesity was 16.4%, higher among male 20.6%, compared to female (15.3%). Obesity was highest in age group 2 (27.7%), 14.5% in group 1, 10.7% in group 3 and 9% in group 4.

Conclusion: The prevalence of obesity is very high among affluent school children in Dhaka.

P07-17 Obesity

The Comparison of Glucose Tolerance in Primary School Children with Normal Body Weight, Overweight and Obesity

Aditiawati

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Aims: To compare glucose tolerance in primary school children with normal body weight, overweight and obesity.

Methods: A cross sectional study in primary school children at Palembang. All subjects underwent a two-hour oral glucose-tolerance test (1.75 mg of glucose per kilogram of body weight). Impaired glucose tolerance was defined based on ADA guidelines.

Results: Sample 1232 children were evaluated glucose tolerance in 24 children randomly each group according to body weight. Impaired glucose tolerance was detected in 29.2 percent of the obese; 20.8 percent of the overweight and 4.2 percent of the normal body weight. There was no type 2 diabetes identified in this study. In this Study was found the association between impaired glucose tolerance and obese (p=0.026); achantosis nigricans (p=0.000); family history of type 2 diabetes (p=0.000). In logistic regression analysis was only found that family history of type 2 diabetes had a strong association (p=0.000) and adjusted ratio result=21.250. Family history of type 2 diabetes became a predictor of impaired glucose tolerance twenty-one times compared to children without family history of type 2 diabetes.

Conclusion: Impaired glucose tolerance was associated with overweight and obesity. The family history of type 2 diabetes became a predictor of impaired glucose tolerance

P08-01 Posterior Pituitary and Other Electrolyte Disorders

Spontaneous Regression of Isolated Langerhans Cell Histiocytosis of the Infundibulum Presenting with Diabetes Insipidus

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Aims: Central diabetes insipidus (CDI) is a rare disorder that may be caused by a variety of diseases. In paediatric patients, the most common causes of a thickened pituitary stalk with CDI are germ cell tumors (GCT), lymphocytic infundibuloneurohypophysitis (LIN), and granulomatous diseases such as Langerhans cell histiocytosis (LCH) etc. The differential diagnosis between these diseases by tumor markers and radiological examinations is difficult, only histopathological proof can lead to a definitive diagnosis.

Methods: A 13-year-old girl was diagnosed with CDI according to her polyuria, polydipsia, and a water deprivation test. MR imaging showed a thickening of the pituitary stalk and loss of the physiological hyperintense signal of the posterior hypophysis. Based on the mild elevation of cerebrospinal fluid beta-hCG, neurohypophyseal GCT was most anticipated.

Results: However, a biopsied specimen of the pituitary revealed LCH. Another LCH lesion was not detected. Three months after the onset, the tumor spontaneously regressed, this finding seemed to be LIN.

Conclusion: In conclusion, the histopathological proof of the underlying disease is essential for the selection of the appropriate therapeutic intervention. We supposed that some paediatric patients who were diagnosed as LIN without a biopsy, may have had spontaneous regression of isolated LCH of the neurohypophysis.

P08-02 Posterior Pituitary and Other Electrolyte Disorders

Clinical, Endocrinological and Radiological Courses in Patients Who was Initially Diagnosed as Idiopathic Central Diabetes Insipidus

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Aims: Idiopathic central diabetes insipidus (CDI) is defined in CDI patients without definite etiology. Some patients initially diagnosed as idiopathic CDI progressed to organic causes. We reviewed clinical, endocrinological, and radiological courses of 20 patients who

was initially diagnosed as idiopathic CDI, to assess the predicting factors for progression to brain tumors.

Methods: We reviewed the medical data and followed up their clinical courses in 20 CDI patients who had no definite organic etiology, such as malformation, tumor, at the time of diagnosis.

Results: Our study included 15 males and 5 females. Mean age of CDI diagnosis was 7.8±3.6 (2.1-14.7) years. Mean follow-up duration was 8.6±5.1 (1.5-18) years. Six (30%) patients were diagnosed as brain tumor during follow-up. Ten (50%) of 20 patients had growth hormone deficiency. Multiple pituitary hormone deficiencies were found more frequently in brain tumor patients than idiopathic patients (60% vs 7%, P=0.037). Pituitary stalk thickening (PST) were observed in 9 patients (47%). The newly development of PST was observed in patients diagnosed as brain tumor.

Conclusion: About 30% of idiopathic CDI patients progress to organic disease. If there are multiple anterior pituitary hormone deficiency or newly development of PST, more close and careful follow-up is needed.

P08-03 Posterior Pituitary and Other Electrolyte Disorders

Genetic Mutation in Three Thai Children with Congenital Nephrogenic Diabetes Insipidus

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Aims: To describe three Thai children with congenital nephrogenic diabetes insipidus (NDI) caused by an inactivating mutation in the Vasopressin-2 (V2) receptor or Aquaporin-2 mutation (AQP2).

Methods: Case series. Three affected individuals from the different family were studied. A 3 year-old girl, 3 year-old boy and 2 year-old boy, were presented with polyuria and polydipsia since the age of about 6 months. Failure to thrive was observed in only the first case. The results of water deprivation test were compatable with NDI. Genetic analysis Genomic DNA of all three children were extracted from peripheral blood leukocytes and mutation analysis of the entire coding sequences of the V2 gene or AQP2 gene were performed by direct DNA sequencing.

Results: A heterozygous novel missense mutation were identified in exon 1 of AQP2 gene (c.3G>T and c.85G>A) in an affected girl. A novel missense mutation (c.1628A>G) and a known missense mutation (c.1132C>T) of V2 gene were identified in the other two boys, respectively.

Conclusion: We report three cases with NDI, one girl with AQP2 mutation and two boys with V2 mutation and emphasize an important role of genetic testing for definite diagnosis and genetic counseling.

P09-01 Puberty Disorders

Short-Term Long-Acting Gonadotropin-Releasing Hormone Agonist Accelerates Longitudinal Growth in Female Pubertal Rats

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Aims: To assess possible mechanism(s) whereby GnRHa exerts its effect on linear growth.

Methods: We used a female pubertal rat model to evaluate the effect of short-term gonadotropin-releasing hormone agonist(GnRHa) with estrogen supplement or not on growth mediators of the GH-IGF-1 axis, in both the liver and epiphyseal growth plate(EGP). Forty 21-day-old female rats were randomized blocks to 5 groups(n=8). One group were sacrificed as base-line control. Group-OVX were operated for ovariectomy. Group-Gn and group-E2 received 2.5mg/kg im. triptorelin which was repeated 2 weeks later, Group-E2 received additional daily 1μg/kg.d E2 s.c. 3 days after the second GnRHa injection for 11 days. Group-ctrl was sham-operated serving as controls. Each of the 32 rest rats received 30 mg/kg oxytetracycline s.c. and 20 mg/kg calcein s.c. on 9 and 2 days respectively before sacrifice at 7-week-old. The responses of hepatic mRNA of GH receptor, IGF-1 and IGFBP-3, circulating IGF-1 and IGFBP-3, local IGF-1/IGF-I receptor (IGF-1R) proliferation rate(PFR) in EGP were evaluated.

Results: Short-term of 4-week GnRHa suppressed gonadal steroids production known as 'chemical ovariectomy'. Similar to group-OVX, group-Gn were longer and heavier than group-ctrl with greater tibial length, wider EGF, faster longitudinal growth rate(LGR) and higher PFR. Estrogen supplement reversed GnRHa's effect. There was no difference among the 4 groups in plasma IGF-1 and IGFBP-3 level, hepatic IGF-1 and IGFBP-3 mRNA level, local IGF-1 and IGF-1R level in EGF. GnRHa down-regulated hepatic GHRmRNA expression, which was reversed by estrogen supplement.

Conclusion: GnRHa accelerates longitudinal growth of female pubertal rats. Estrogen deprivation contributes to GnRHa-induced alteration of linear growth of female rats, by the way of improving the proliferating rate and suppressing the senescence of EGF. The underlying mechanism does not attribute to endocrinol change of GH/IGF-1 axis function, or change of local IGF-1/IGF-1R in epiphyseal growth plate.

P09-02 Puberty Disorders

Correlation of Serum Dehydroepiandrosterone Levels and Psychological Behavior in Precocious Puberty Girls

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Aims: To investigate the correlation of serum dehydroepiandrosterone (DHEA) levels and psychological behavior in precocious puberty girls.

Methods: The levels of DHEA and dehydroepiandrosterone sulfate (DHEAS) were measured by ELISA in 64 idiopathic central precocious puberty (ICPP) girls, 46 premature thelarche (PT) girls and 36 healthy prepuberty ones. Raven's Standard Progressive Matrices (SPM), Achenbach's Child Behavior Checklist (CBCL), Self-Esteem Scale (SES), and Body-Esteem Scale (BES) were used to assess the psychological behavior.

Results: The Log(DHEA) and Log(DHEAS) were 0.77±0.36 and 2.30±0.32 g/L in ICPP group, 0.68±0.33 and 2.33±0.29 g/L in PT group, and 0.28±0.22 and 2.12±0.35 g/L in controlS, with significant difference among the three ($P<0.05$). The SES and BES scores in ICPP and PT groups were lower than that in controls with significant difference among the three ($P<0.05$). The CBCL scores in depressed, withdrawn, aggressive and somatic complaint assessment were significantly higher in ICPP group. The SES score, the Weight Concern and Body Strength scores for BES were negatively correlated with Log(DHEA) in precocious puberty girls ($P<0.05$). The nine CBCL factors were not related to Log(DHEA) ($P>0.05$).

Conclusion: Precocious puberty girls are prone to with lower self-esteem and less confidence, which are correlated with the increase of of serum DHEA levels.

P09-03 Puberty Disorders

Clinical Presentation and Treatment Outcome of Children with Central Precocious Puberty

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Aims: To determine the clinical presentations and the final height of Thai children with CPP

Methods: Fifty-one children with CPP who attended at Songklanagarind Hospital from 1992-2007 were retrospectively reviewed

Results: The etiologies of CPP were idiopathic (37 girls), hypothalamic hamartoma (5 girls, 2 boys), and CNS diseases (3 girls, 4 boys). The median age at the time of diagnosis was 7 years for idiopathic and 3.4 years for hypothalamic hamartoma. The most common clinical presentation was breast development in girls (70%) and phallus enlargement in boys (80%). The median height and weight SDS at initial presentation were 2.34±1.25 and 2.52±1.02, respectively. Bone age was on average 4 years more advanced than chronological age. Twenty-four children reached their final height at a median age of 11.2 years. The median final height of children treated with LHRH analog (n = 11) was 150.1 cm (range 148-158), which was significantly greater than the final height of 142.3 cm (range 135-148) of those who were untreated.

Conclusion: The common clinical presentations of CPP are breast development in girls and the phallus enlargement in boys. LHRH analog treatment results in final height closed to their target height

Table 1 (for Abstract P09-04). Changes of BMD during GnRHa with or without hGH treatment

	Total (N=40)	Group I GnRHa (N=26)	Group II GnBHa + hGH (N=14)
Before treatment			
CA (yr)	9.2 ± 1.5	8.6 ± 1.2	9.9 ± 1.5
BA (yr)	11.6 ± 1.3	11.2 ± 1.3	12.4 ± 1.0
BMD SDS vs CA	0.06 ± 1.05	0.20 ± 0.95	–0.20 ± 1.20
BMD SDS vs BA	–1.36 ± 0.93*	–1.19 ± 1.01	–1.67 ± 0.68†
After treatment			
CA(yr)	10.3 ± 1.5	9.7 ± 1.1	11.1 ± 1.5
BA (yr)	12.2 ± 1.2	11.8 ± 1.1	12.8 ± 0.9
BMD SDS vs CA	0.04 ± 0.99	0.13 ± 0.91	–1.19 ± 0.81
BMD SDS vs BA	–1.12 ± 0.95*	–1.08 ± 1.04	–1.19 ± 0.81†
Duration of treatment	1.57 ± 0.7	1.6 ± 0.9	1.7 ± 0.6

*P <0.05 compared to normal range
†P <0.01 changes in BMD SDS in Group II, during treatment

P09-04 Puberty Disorders

Changes of Lumbar Bone Mineral Density During Gonadotropin Releasing Hormone Analogue Treatment with or without Growth Hormone

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Aims: Treatment of precocious puberty with gonadotropin releasing hormone analogue (GnRHa) might theoretically have a detrimental effect on bone mass during pubertal development. We investigated the bone mineral density (BMD) changes during GnRHa treatment, and further the effect of human growth hormone (hGH) co-treatment.

Methods: Forty girls with idiopathic central precocity or early puberty were included. Fourteen received GnRHa alone (Group I), and the others received GnRHa + hGH (Group II).

Results: In both groups, BMDs before and after treatment were in normal range according to chronologic age (CA), but significantly lower according to bone age (BA). In group I, there were no significant changes in BMDs during treatment. .But, in group II, BMDs according to BA were significantly increased after treatment.

Conclusion: At initial manifestation of precocity, lumbar BMD was proper to CA, but lower if compared to BA, that is, BMD does not increase with BA. During GnRHa treatment, the subjects as a whole showed no significant change in BMD-SDS according to CA or BA, but co-treatment with hGH significantly increased BMD-SDS according to BA.

P09-05 Puberty Disorders

Mechanism Research on Influences of Nutrition to Sexual Development in Girls

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Aims: To study the influences of nutrition on adolescence sexual development in girls and its mechanism by making comparison in body mass index(BMI) and blood lipid between idiopathic central precocious puberty and normal girls.

Methods: The BMI and blood lipid level of 113 ICPP girls were measured and the data were compared with the normal girls of the same age. The correlation betweentanner and BMI were analysed.

Results: 1.BMI of ICPP girls was significantly higher than that of normal girls in different ages (7age: BMI16.54±1.44 kg/ m2, (control 15.95±2.03 kg/ m2) P<0.05; 8age: BM18.18±2.12 kg/ m2, (control16.38±2.43 kg/ m2) P<0.05; 9age::BMI 19.52±1.96kg/ m2, (control16.82±2.67 kg/ m2) P<0.05; 10age:BMI 19.61±1.46kg/ m2, (control17.26±2.67kg/ m2) P<0.05) and there was no correlation between tanner and BMI(r=0.164, P>0.05).2.The blood lipid level of ICPP girls had no difference with that of normal girls,It showd that ICPP girls had no blood lipid disorder although they had great weighty relatively.

Conclusion: BMI of ICPP girls is larger than that of normal girls of the same age. But there has no correlation between severity and BMI and ICPP girls show no blood lipid metabolism disorder.

P09-06 Puberty disorders

Causes of Precocious Puberty: Multicenter Study in Korea

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Aims: We analysed the spectrum of diagnoses made in a consecutive group of children referred for signs of precocious puberty.

Methods: Retrospective analysis of 375 children(365 girls and 10 boys) referred for evaluation of signs of precocious puberty between January 2003 and May 2007 was done.

Results: The conditions causing precocious puberty were early puberty(36.3%), true precocious puberty(30.4%), premature thelarche(29.1%), pseudoprecocious puberty(3.7%), premature pubarche(0.5%). There were differences in the age of onset of puberty (premature thelarche, 5.4±2.6 years vs. true precocious puberty, 6.8±1.3 years vs. early puberty 8.6±0.5 years). True precocious puberty children showed higher height SDS, weight SDS, BMI, basal FSH, LH and estradiol, more accelerated growth velocity and bone age than those had premature thelarche. Precocious puberty patients showed higher height SDS. weight SDS, and more bone age advancement when compared to those with early puberty. Later onset(>2 years) premature thelarche presented in 89 girls(81.7% of premature thelarche) at 6.4±1.6 years, and among them, 8 girls developed true precocious puberty later.

Conclusion: Common conditions causing precocious puberty were early puberty. true precocious puberty, and premature thelarche. Although premature thelarche might be regarded as a benign condition, true precocious puberty can be developed in some patients, so careful follow-up will be needed.

P09-07 Puberty Disorders

An Adolescent Girl with Hirsutism Due to Sertoli-Leydig Cell Tumour

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Results: We reported a case of Sertoli-Leydig tumour in a 14 years old girl who presented with obesity, primary amenorrhoea and symptoms of hyperandrogenism. Physical examination showed a BMI of 26.5 kg/m2, Tanner stage V breast and Tanner stage IV pub-

lic hair development, with no acanthosis nigricans. There was mild hirsutism, mild clitormegaly and masculine habitus. Investigations showed raised serum testosterone of 4.8 -10 nmol/L. Synacthen stimulation test did not suggest atypical congenital adrenal hyperplasia. A 2-day and 5-day low dose Dexamethasone Suppression Test showed normal adrenocorticol suppression but subnormal androgen suppression, indicating ovarian source of androgen. Initial pelvic ultrasound and computer tomography (CT) showed no adrenal or ovarian mass. Repeated MRI of pelvis 8 months after initial CT scan showed a large 9cm right ovarian tumour. Laparoscopic right salpingo-oophorectomy was performed. Microscopic examination confirmed Sertoli-Leydig cell tumour of intermediate differentiation. Staging operation showed stage IA disease with no macroscopic and histologic evidence of pelvic involvement. Patient developed menarche, then regular period 2 months after the operation. Serum testosterone level normalized 10 months after operation. Regular follow up ultrasound showed no evidence of recurrence or metastasis 14 months after operation.

P09-08 Puberty Disorders

The Effect on the Nutrition of Suckling Period to KiSS-1/GPR54 mRNA Expression and Sexual Development in Female Rats

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Aims: To determine the effects of nutritional intake during the suckling period on the expressions of KiSS-1/GPR54 mRNA in the hypothalamus and sexual development of female rats.

Methods: 21 Foster mother rats and 120 foster suckled female rat pups were randomly divided to the 3 groups: (1) control group, 30 neonatal rats receiving breast milk from 3 lactating rats; (2) Overnutrition group, 30 neonatal rats receiving breast milk from 15 lactating rats; and (3) Undernutrition group, 60 neonatal rats receiving breast milk from 3 lactating rats. After weaning, the female juvenile rats had free access to standard laboratory diet. The real time RT-PCR were performed and the time of vaginal opening were observed.

Results: When the vaginal openings in overnutrition group were first appeared, the expression of KiSS-1 and GPR54 mRNA in the hypothalamus among 3 groups were compared. Both KiSS-1 and GPR54 mRNA in overnutrition group were greater than those in control group and undernutrition group ($P < 0.05$).

Conclusion: Nutrition in suckling period may effect the sexual development by regulating the expression of KiSS-1/GPR54 mRNA in hypothalamus.

P09-09 Puberty Disorders

The Comparison of Pubertal and Menarcheal Onset of School-Aged Girls Between Urban and Rural Area in Chachoengsao Province

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Aims: To compare the age of onset of puberty and menarche in school-aged girls between urban and rural area and identify the possible factors related to pubertal and menarcheal onset of these two groups.

Methods: Nine hundreds and nine school-aged girls at an urban school and 409 schoolgirls at two rural schools in Chachoengsao province were enrolled to the study. Weight and height were measured, BMI was calculated and breasts Tanner staging were evaluated by female Pediatric Endocrinologists. Questionnaires were collected for analyses of relating factors.

Results: The age at onset of puberty and menarche in the urban schoolgirls were significantly earlier than the rural school girls, 9.76 vs 10.67 and 11.87 vs. 12.53 years, respectively ($Ps<0.01$). Using stepwise multiple linear regression analysis, BMI z-score and living in urban area had the effect on the early onset of puberty ($R=0.465$ and $R=0.529$, respectively, $Ps<0.001$) and age at menarche ($R=0.432$ and $R=0.393$, respectively, $Ps<0.001$).

Conclusion: Thai urban school-aged girl in Chachoengsao province had significantly earlier age of onset of puberty and menarche than the rural ones. These findings were related to obesity and living in the urban area. Further study is needed to identify whether early pubertal development and obesity will affect final adult height.

P09-10 Puberty Disorders

Gonadotropin-Releasing Hormone, Its Receptor and GPR54 Gene Analysis in Korean Girls with Central Precocious Puberty

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Aims: The Gonadoptopin releasing hormone (GnRH), GnRH receptor and GPR54 gene have been known to be important in the onset of puberty. We studied GnRH, its receptor and GPR54 gene polymorphisms in Korean girls with central precocious puberty.

Methods: 104 Korean girls with central precocious puberty were recruited as case group and 53 normal Korean women were recruited as control group from Ajou University Hospital, Korea. The DNAs

were collected and screened for polymorphisms using PCR. The PCR products were sequenced directly.

Results: No polymorphism was found in GnRH receptor gene. Two known polymorphisms were identified; one from exon 5 in GPR54 gene and the other from exon 1b in GnRH gene. However, the polymorphisms were not associated with central precocious puberty and onset age of breast budding.

Conclusion: Polymorphisms in GnRH, GnRH receptor and GPR54 gene are not likely to affect mechanism of pubertal onset directly. This study is the first analysis in Korean patients with central precocious puberty. Because of small size of our study populations, further studies are needed in larger populations.

P09-11 Puberty Disorders

Phthalate and Bisphenol-A in the Serum of Children with Idiopathic True Precocious Puberty

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Aims: Environmental endocrine disruptors (EDCs) are compounds which mimic or antagonize natural hormones to interfere with endocrine system. Recent attention is focusing on indoor or dietary pollutants such as phthalates and bisphenol-A, which appeared to affect normal sexual development. Thus, we aimed to assessed the serum levels of phthalate and bisphenol-A among the children with idiopathic precocious puberty to estimate the possible environmental hazard on children.

Methods: The study included 29 girls, 1 boy with idiopathic precocious puberty. Thirty children as control were selected within the endocrinology section. Anthropometry and bone age x-ray were performed. Precocious puberty was diagnosed with GnRH-stimulation test. Serum bisphenol-A and di-(2-ethylhexyl)phthalate (DEHP) levels were analyzed by gas chromatography/mass spectrometry.

Results: The mean age was 8.6±0.9 vs. 7.8±1.1years in the group of precocious puberty vs. control. The height standard deviation score(SDS) was 1.3±1.0 vs. -0.4±1.1($P<0.005$), weight SDS was 1.3±1.3 vs. -0.2±1.3($P<0.005$). Tanner stage was B3±0.9 vs. B1. Bone age was 9.5±1.1 vs. 7.9±1.9years($P<0.005$). Bisphenol-A did not show difference (11.2±10.3 vs. 16.2±12.5ng/ml, $P>0.05$), however DEHP levels were significantly increased within the children with precocious puberty (159.01±92.78 vs. 103.55±92.98ng/mL, $P<0.05$)

Conclusion: This study suggests that phthalate(DEHP), one of most commonly used plasticizers, may act as one of compound etiologic factors of precocious puberty.

P09-12 Puberty Disorders

Effect of Early Exposure to Genistein on the Onset of Puberty in Female Rats

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Aims: Exposure to dietary phytoestrogens such as genistein (GS) during early childhood is a growing public health concern. We examined the effect of early exposure to GS on the developing reproductive tract.

Methods: Weaning(3wk-old) female SD rats were assigned to three groups(n=6 for each): fed by high dose of GS(100mg/kg/d), low dose of GS(10mg/kg/d) and control group until the first vaginal opening(VO) was observed. Genes of ERα, ERβ, and progesterone receptor(PR) in the ovary and uterus were investigated histologically and immunohistochemically.

Results: High GS group had earlier VO than control and low GS group. In ovary, the transcriptional activities of ERα and ERβ were higher in High GS group than in controls. In uterus, the transcriptional activities of ERα, ERβ and PR were higher in Low GS group than in controls (Table 1). The number of ERα- and/or ERβ-positive cells in the ovaries and uteri of both high and low dose GS-exposed rats were higher than those in control tissues.

Conclusion: It is concluded that acute(<1wk) exposure to GS during the prepubertal period could activate the reproductive endocrine system resulting in the early onset of puberty in female rats. Further clinical investigation on the effect of GS on the developing reproductive tracts in children is warranted.

Table 1 (for Abstract P09-12). Effect of GS on vaginal opening tissue weight and the expression of ERα, ERβ and PR

	Ovary			Uterus		
	Control	Low GS (10mg/kg/d)	High GS (100mg/kg/d)	Control	Low GS (10mg/kg/d)	High GS (100mg/kg/d)
Vaginal opening (postnatal day)	34.2 ±3.3	32.3 ±3.9	27.3±1.8**			
Tissue weight (mg/g BWt)	0.31 ± 0.05	0.35 ± 0.06	0.42 ± 0.08	0.69 ± 0.41	0.77 ± 0.27	1.44±0.32**
ER-α expression	1	1.53 ±0.40*	1.80±0.45**	1	2.03±0.78*	1.70±0.78
ER-β expression	1	1.16±.0.41	1.72. ± 0.59	1	1.66±0.46**	1.22±0.32
PR expression	1	1.20 ± 0.15	1.37 ± 0.27	1	1.86 ± 0.75*	1.71 ± 0.39

*$p<0.05$, **$p<0.01$. from control group

P09-13 Puberty Disorders

Incidence and Etiologies of Precocious Puberty in Korea During Last 10 Years

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Aims: The purpose of this study is to investigate the trend of incidence, etiologies, and clinical characteristics of precocious puberty (PP) during last 10 years in Korea.

Methods: Chart reviews were done for 223 patients who had been diagnosed as PP in our institute from 1998 to 2008. Clinical characteristics, endocrinologic investigations including hormonal studies, brain and/or abdominopelvic imaging studies were reviewed.

Results: Annual incidence of PP has been raising, from 4 cases in 1998 to 62 cases in 2007. 216(97%) were female, 6(3%) were male. In 216 PP girls, 131(60%) were true PP, 84(39%) were premature thelarche, whereas 2(1%) were pseudoprecocious puberty. 32 true PP girls revealed abnormal intracranial lesions on their brain MRIs. These neurogenic true PP girls had no differences in their clinical characteristics and hormonal levels compared with idiopathic PP girls. In 6 PP boys, 3(50%) were congenital adrenal hyperplasia, 2(33%) were idiopathic true PP and 1(17%) was pseudoprecocious puberty.

Conclusion: There has been increasing numbers of patients with PP. Neurogenic true PP girls had no differences in their clinical characteristics and hormonal studies compared with those who have idiopathic true PP. Male PP were much less common, however, they tend to have higher incidence of organic causes.

P09-14 Puberty Disorders

A Single Leutinizing Hormone Determination 3 Hours After Depot Leuprolide is Useful for Monitoring of Therapy in Gonadotropin-Dependent Precocious Puberty

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Aims: To determine role of LH value post intramuscular (im) depot leuprolide for monitoring therapy in patients with Gonadotropin Dependent Precocious Puberty (GDPP) instead of subcutaneous leuprolide stimulation test.

Methods: In six patients, who were on 11.25 mg depot leuprolide, the LH peak after subcutaneous (sc) test was compared with LH at hourly interval from first four hour after im depot leuprolide. After ten tests we started to collect at 3rd hour as it was persistently high. Fifteen such tests were carried out.

Results: Before therapy, the mean ± SD LH peak after subcutaneous leuprolide stimulation test was 20.6 ± 7.85 IU/liter (range 9.64–30.4 IU/liter), and it was 27.3 ± 12.21 IU/liter 3 h after the first depot (range 10.5–45.4 IU/liter). During therapy, the mean ± SD of LH peak after sc stimulation test was 1.96 ± 0.75 IU/liter (range 1.1 to 3.1 IU/liter), and it was 2.58 ± 0.54 IU/liter (range 1.4–3.4 IU/liter) 3 h after depot leuprolide.

Conclusion: 3-hour LH value following im depot leuprolide injection can be used for monitoring therapy in patients with GDPP because of its convenience and cost effectiveness.

P09-15 Puberty Disorders

Gonadal Dysfunction After Hematopoietic Stem Cell Transplantation

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Aims: High dose chemotherapy and total body irradiation performed for the preparation of hematopoietic stem cell transplantation (HSCT) can seriously affect the hypothalamic-pituitary-gonadal axis. The purpose of this study was to evaluate gonadal dysfunction in the subjects who underwent HSCT during childhood and adolescence.

Methods: Subjects included 29 females (age at latest assessment 16.4±2.1 years; age at HSCT 11.2±2.9 years) and 28 males (age at latest assessment 16.3±1.5 years; age at HSCT 11.2±2.2 years) who underwent HSCT for hematologic malignancies or severe aplastic anemia. Gonadal dysfunction was defined as abnormal levels of luteinizing hormone (LH) or follicle-stimulating hormone (FSH) with or without abnormal pubertal development.

Results: Nineteen (65.5%) females showed evidence of gonadal dysfunction. Abnormal elevation of LH was more frequent in the females who were >10 years at HSCT compared with those who were ≤10 years (14.3% vs 73.7%, OR=16.8, P<0.05). Sixteen (57.1%) males had evidence of gonadal dysfunction. Out of them, nine showed normal pubertal development with normal LH levels but abnormally elevated FSH levels, which is indicative of germ cell dysfunction.

Conclusion: These findings suggest that about two thirds of females and more than half males develop godadal dysfuction after HSCT and pubertal-aged girls are especially at higher risk.

P09-16 Puberty Disorders

Peripheral Precocious Puberty Due to Congenital Adrenal Hyperplasia in a Boy Concomitant with Hodgkin's Lymphoma

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Aims: To report a rare case with PPP in a boy.

Results: Precocious puberty is classified into two main groups, central precocious puberty and peripheral pseudoprecocious puberty. The most common cause of this pseudoprecocious puberty in boys

is congenital adrenal hyperplasia (CAH). A 4 year-old boy presented with mass in the neck. Fine needle aspiration biopsy revealed Reed-Sternberg cells, lacunar cell and its variant, characteristics for Hodgkin's disease. The patient also suffered from tall stature (P > 95th), voice deepening, growth of pubic hair, advance bone age, enlargement of penis, and small testicle. The laboratory findings: LH was 0.1 mIU/ml (0.8-7.6 mLU/mL), FSH was 0.15 mLU/mL (0.7-11.1 mLU/mL), and Testosterone was 398.6 ng/dL (3-32 ng/dL). These findings were characterized for peripheral precocious puberty condition. Increasing of 17 α OHP level combined with normal head MRI and electrolytes indicated of a simple virilized CAH. After the fourth chemotherapy of second series, the patient had presented with seizure and decrease of consciousness, high fever, nausea, and diarrhea, with physical findings of shock and anemia. The presentation of neutropenia, trombocytopenia and high ESR indicated suspicion of sepsis leading to a septic shock. The patient died from septic shock.

P09-17 Puberty Disorders

The Role of Environmental Endocrine Disruptors in the Onset of Precocious Puberty

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Aims: To explore the role of environmental endocrine disruptors (EEDs) in the onset of precocious puberty.

Methods: The concentrations of octylphenol(OP), biphenyl A(BPA) and did-n-butyl phthalate(DBP) in serum from 110 precocious puberty and 100 normal children were measured by HPLC and GC. The volume of uterus and ovary, and the content of serum E2 in precocious puberty were determined. The contents of EEDs and the indices of the target organs were analyzed via correlation and regression.

Results: In control group, OP, BPA, DBP were detected in 5%, 2%, 4% of serum samples, respectively. In precocious puberty group, OP, BPA, DBP were detected in 33.6%, 40.9%, 27.3% of them. The levels of EEDs in precocious puberty group were notably higher than that of control group ($P < 0.001$). In precocious puberty group, positive correlations were found between the contents of OP, BPA, DBP and the volume of uterus and ovary ($P < 0.05$ or 0.01).

Conclusion: A part of normal children has contaminated by EEDs, the children of precocious puberty have been much more heavily exposed to EEDs than normal children. There is a close statistical relationship between EEDs and the onset of precocious puberty, and EEDs are important factors inducing the disease.

P10-01 Sexual Differentiation

Diagnosis of 5-Alpha Reductase 2 Deficiency – A Local Experience

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Aims: 5-alpha reductase type 2 deficiency is characterized by masculinization defects in 46,XY subjects. A child was presented at birth with micropenis. He had normal male karyotype and unremarkable radiological examinations. Urinary steroid profiling showed characteristic feature of 5-alpha reductase deficiency, with all 5-alpha reduced steroid metabolites virtually absent. Mutational analysis on the SRD5A2 gene by direct DNA sequencing confirmed the presence of a novel mutation L55P and one known mutation R277Q. Family genetic study showed both parents are carriers of these mutations.

Conclusion: This case illustrated the usefulness of urinary steroid profiling and mutational analysis for the diagnosis of this condition. These tests are particularly valuable when quantitative assay for dihydrotestosterone is not available locally.

P10-02 Sexual Differentiation

A Case of 4-Year-Old True Gonadal Intersex

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Aims: A 4-year-old child was found to have ambiguous genitalia at birth in Busan university hospital. The result of chromosomal study was 46,XX. 17-OH progesterone, cortisol, Plasma renin activity(PRA), Testosterone, 5α-Dihydrotestosterone(DHT) were all in the normal ranges. A small uterus and vagina were observed in the pelvic ultrasonography. After four years, the child was transferred to Hanyang university hospital for clitoroplasty. The pelvic MRI showed the external genitalia as a long tubular tract and the bladder neck connected with rudimentary uterus, and no definite evidence of gonads. The explorative laparoscopy & vaginoplasty was performed by urology & plastic surgeon. The biopsy from the right gonad revealed the ovotestis tissue, and the gender rearing of the child was decided as a female. We report a child with ambigous genitalia who was diagnosed as a true gonadal intersex.

P10-03 Sexual Differentiation

Cytogenetic Characteristics of Children with Disorders of Sex Development

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Aims: To investigate the characteristics of cytogenetic results of DSD cases referred to our clinic in 2000-2007.

Methods: Data of DSD cases referred by pediatricians or aged below 18 years old were evaluated. Cytogenetic analysis was performed using G-banding and/or FISH technique. The presence of SRY gene was determined by PCR and/or FISH.

Results: During the study period there were 154 DSD cases. In 58 cases we found 46,XX, 44 cases 46,XY, 12 cases 45,XO. In 28 cases the cytogenetic results were mosaic 45,XO with Y chromosome or part of it as the second chromosome in the additional cell lines (15 cases) and mosaic 45,XO with X chromosome or part of it as the second chromosome in the additional cell lines (13 cases). Interestingly there were 12 cases resulted in autosomal chromosomes anomalies. SRY gene were determined in 27 cases. Among 18 XY cases 2 do not have detectable SRY gene.

Conclusion: In 25.9% of DSD children cytogenetic analysis could established the diagnosis. Cytogenetic test along with SRY gene detection is an important first-line test, that may lead clinician to prompt and precise diagnosis in DSD cases. Autosomal chromosomal anomalies could be the cause of DSD, but this finding need further confirmatory molecular test.

P11-01 Syndromes

Clinical Features According to Karyotype in Turner Syndrome

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Aims: Turner syndrome (TS) is a disorder in which various anomalies can be accompanied, especially cardiovascular, renal, thyroid and auditory problems. The aim of this study is to identify the incidence of these disorders in patients with TS according to karyotype.

Methods: We reviewed medical records of 91 patients with TS diagnosed by chromosome analysis in 4 hospitals from Jan 1998 to Dec 2007. The distribution of karyotype was 45,X (47.3%), mosaic pattern (34.1%) and structural aberration group (18.7%). We evaluated these cases by prepared protocol of 4 medical problems.

Results: Renal anomalies, cardiovascular anomalies, thyroid disorders and auditory problems are accompanied in 4.4%, 9.9%, 11.0% and 5.5%, respetively. 45,X group had renal anomalies (7.0%), cardiovascular anomalies (18.6%), thyroid disorders (9.3%) and auditory problems (11.6%). Mosaic group had renal anomalies (3.2%), thyroid disorders (12.9%), no cardiovascular anomalies and auditory problems. Structural aberration group had cardiovascular anomalies (5.9%), thyroid disorders (11.8%) and no other 2 problems. Patients with 45,X group had a significant higher incidence of cardiovascular anomalies (p=0.025).

Conclusion: We concluded that there are differences clinically according to karyotype of TS, especially in incidence of cardiovascular anomalies.

P11-02 Syndromes

Hypogonadotropic Hypogonadism in a Female Patient with CHARGE Syndrome Caused by a Mutation in the CHD7 Gene

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Aims: CHARGE syndrome is a congenital malformation disorder that includes coloboma, heart defect, choanal atresia, retarded growth and development, genital hypoplasia, and ear abnormalities.

Methods: We report the case of Korean female patient with CHARGE syndrome and CHD7 mutation who had hypogonadotropic hypogonadism and abnormal olfactory bulb as manifested by delayed puberty and growth retardation.

Results: This patient was a 13 year old girl who had poor pubertal development and short stature. She was born with a birth weight of 3.5 kg. She suffered from feeding problem and respiratory difficulty at first year. She had severe mental retardation. She had both optic nerve coloboma, external ear abnormalities and hearing loss. In CT scanning of the temporal bones, bilateral agenesis of the semicircular canals were demonstrated. We identified a heterozygous nonsense mutation at exon 20 of the CHD7 gene. (c.4601G>A; W1534X). She had absence of pubertal development. A GnRH test showed prepubertal responses. Brain MRI showed aplasia of the right and hypoplasia of the left olfactory bulb and bilateral absence of the olfactory sulci.

Conclusion: Hypogonadotropic hypogonadism with abnormal olfactory bulb development in CHARGE syndrome should be considered as a common finding and needed to be detected earlier for growth and pubertal development.

P11-03 Syndromes

A Boy with Contiguous Gene Syndrome Due to an Deletion of Distal Xp (46,Y,Del(X) p 22.2) and His Sister with Leri-Weill Dyschondrogenesis (46,X,Del(X)p 22.2)

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Aims: We report on a boy and his sister with short stature. The boy manifested Leri-Weill dyschondrosteosis, dysmorphic feature, mental retardation, ichthyosis, Kallmann syndrome. But her sister manifested only Leri-Weill dyschondrosteosis.

Results: Cytogenetic study showed a terminal deletion of Xp (Xp22.2-Xpter) in both of boy and his sister. Because their parents were divorced, we couldn't confirm the parent's chromosomal analysis. But, according to his aunt, mother was short of stature, too.

Conclusion: Terminal or interstitial deletion of distal Xp (Xp22.2-Xpter) have been recognized as reason for variable contiguous gene syndromes in males. Several genetic diseases including Leri-Weill dyschondrosteosis(SHOX), chondrodysplasia punctata(CDPX1), mental retardation(MRXgenes), ichthyosis(STS), Kallmann syndrome(KAL1), ocular albinism type 1(OA1) have been located to this region. The phenotype depends on extent and position of the deletion. SHOX(Short Stature Homeobox-containing gene) is located in the pseudoautosomal region 1(PAR1) on both the X and Y chromosomes. Genes residing in PAR1 escape X inactivation. Short stature phenotypes in both of them were considered to be a result of haploinsufficiency of SHOX. The remaining genes are X chromosomes specific and inherited as X-linked recessive traits. Most likely owing to preferential inactivation of abnormal X chromosome, her sister manifested only Leri-Weill dyschondrosteosis.

P11-04 Syndromes

A Case of Beckwith-Wiedemann Syndrome with True Hermaphroditism

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Aims: We report a case of Beckwith-Wiedemann syndrome with true hermaphroditism. A 1530g girl was born by emergency cesarean section at 30 weeks of gestation because of fetal distress. She was in respiratory distress and bronchopulmonary dysplasia, had been treated with ventilator therapy. Physical examination showed macroglassia, both ear creases, a nevus flammeus on the forehead, and clitomegaly.

Results: The results of laboratory studies were as follows : LH 35.6 mIU/ml, FSH 127.2 mIU/ml, estradiol 33 pg/ml, testosterone 4.2 ng/ml, alpha fetoprotein(AFP) 16781 ng/ml. Abdominal MRI revealed suspicious ovotestis in both external iliac areas. There was no significant abnormality in brain MRI. Karyotype was 46.XX with negative SRY gene. Methylation specific PCR-RFLP test of H19, LIT1 gene on 11p15.5 showed the paternal allele of LIT1(BWSIC2) was abnormally methylated.

Conclusion: As bronchopulmonary dysplasia was improved, she showed rapid weight gain (4 kg (< 3 percentile) at 2 month (corrected age), and 7.4 kg (50 percentile) at 5 month (corrected age). Her clitomeraly was not progressed than before. We checked abdominal ultrasound screening and measurement of alpha fetoprotein (AFP) every 3 months, there were any tumor until now.

P11-05 Syndromes

Polysyndactyly, Renal Hypoplasia and Central Precocious Puberty: A Case of Pallister-Hall Syndrome

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Results: A 16 month old boy presented with an 8 week history of acne, pubic hair development, penile enlargement, scrotal maturation and increased growth velocity. Background history included bilateral post-axial polysyndactyly and chronic renal failure. His weight, 90thcentile, and height, 90thcentile, had previously tracked <3rdcentile and 3rd-10thcentile respectively. Clinical assessment revealed: facial acne; Tanner 3 genital and 2 pubic hair development; 5mL testes. Random LH and testosterone were elevated. Bone age: carpal bones 2yr8mo; phalanges 4yrs. MRI revealed hypothalamic hamartoma (HH). The constellation of post-axial polysyndactyly, renal hypoplasia and HH indicated a clinical diagnosis of Pallister-Hall Syndrome (PHS). Monthly GnRH analogue commenced. Growth velocity declined, testicular volume decreased (2-3mLs), acne resolved and pubic hair regressed. Baseline and stimulated LH decreased. PHS is an autosomal dominant condition due to a mutation of GLI-3(chromosome 7p14.1). GLI-3 encodes a zinc-finger transcription factor (component of the Sonic Hedgehog Pathway). Endocrinological manifestations include:-precocious puberty (associated with HH) and hypopituitarism (GH, TSH, ACTH, LH/FSH deficiency). Disruption of pituitary development has been proposed. Compared to isolated HH, those occurring in PHS are reported to be less associated with gelastic seizures and neurological dysfunction, yet more commonly associated with precocious puberty and other endocrine disturbances.

P11-06 Syndromes

CT Angiographic Study of Thoracic Vascular Anomalies in Turner Syndrome

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Aims: It is well known that Turner syndrome (TS) is associated with bicuspid aortic valve and aortic coarctation, so echocardiographic evaluation of all patients is currently recommended. To understand the prevalence of thoracic vascular anomalies in TS, we prospectively evaluated a group of asymptomatic TS patients using computerized tomography (CT) angiography.

Methods: A total of 15 TS patients underwent CT angiography. These patients were also done echocardiography as a routine procedure before doing CT evaluation

Results: A high prevalence of thoracic vascular anomalies was seen in TS patients; aortic anomalies including aberrant right subclavian artery (20%), dilatation of proximal left subclavian artery (13.3%) and dilatation of aortic root (6.6%); venous anomalies including partial anomalous pulmonary venous return (20%) and persistent left superior vena cava (13.3%).

Conclusion: Thoracic vascular anomalies are more common in TS. Further meticulous echocardiographic examination should be done in every TS patients for identification of thoracic vascular lesions.

P11-07 Syndromes

Study of the Clinical and Cytogenetic Patterns of Turner's Syndrome Patients in Singapore

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Aims: To study the clinical and cytogenetic patterns of Turner Syndrome (TS) patients in Singapore

Methods: Retrospective review of case records of 37 patients with diagnosed TS was done. All patients had their diagnosis confirmed by karyotype analysis.The incidence, type of cytogenetic abnormalities and clinical characteristics of the patients in the local population was studied.

Results: Out of the 37 patients studied,24(65%) were Chinese,7(19%) were Indians,4(11%) were Malays and 2(5%) were Caucasians.The patients presented at different ages with varied clinical features,5/37(16%) were diagnosed antenatally,11/37(30%) presented primarily with dysmorphic features between birth to 2 months,2/37(5%) presented between 2 months to 1 year with developmental delay and failure to thrive,13/37(35%) between 1 year to 15 years presented with short stature and 6/37(16%) who presented after 15 years had primary or secondary amenorrhoea,infertility & recurrent miscarriages as their chief complaint.Table attached.

Conclusion: The distribution of cytogenetic abnormalities in patients with TS in Singapore is different from that reported in the literature especially with regards to the Chinese population. Our prelimnary data shows that there are more TS patients with X mosacism than standard monosomy.The incidence of cardiac diseases and hypothyroidism is similar to that reported in the litreture,but renal malformations account for only14% versus 40% reported risk.

P11-08 Syndromes

CASE REPORT MOSAICSM KLINEFELTER SYNDROME

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Background: Klinefelter syndrome is a rare case. It is the most common chromosomal disorder in man. The classic classification of genetic karyotype is 47, XXY, 46, XY / 47, XXY or 48, XXXY, or 49, XXXXY. The characteristic of this syndrome are hypogonadism, gynecomastia, infertility, psychosocial problem, hyalinization of tubulus seminiferus and increasing in urine gonadotropine. The purpose of case is to demonstrate Klinefelter Syndrome and to establish the diagnosis.

Table showing karyotype distribution and clinical features (for Abstract P11-07).

Karyotype	No of patients	Cardiac disease	Renal malformation	Hypothyrodism
All	37	9/37(24%)	5/37(14%)	6/37(16%)
45,X	7(19%)	4/7(57%)	1/7(14%)	3/7(43%)
46 X i(xq)	7(19%)	1/7(14%)	–	1/7(14%)
45 x/46,x,i(xq)	5(13%)	–	–	–
45,x/46,xx	8(21%)	1/8(13%)	–	1/8(13%)
45,x/47,xxx	3(8%)	–	2/3(67%)	–
45,x/46,x +ring	2(5%)	1/2(50%)	2/2(100%)	1/2(50%)
45,x/46,xy	1(3%)	1/1(100%)	–	–
45x/46,x+mar	1(3%)	–	–	–
46,x,xp (short arm deletion)	1(3%)	1/1(100%	–	–
46,x,xq (long arm deletion)	1(3%)	–	–	–
Other	1(3%)	–	–	–

Case Report: T, 7 years old boy, with chief complain disorder of sex development, with male normal phenotype. On physical examination we found abnormality of the genital which include in Prader III criteria, bilateral undescended testicular. The result of testicular functional test with HCG test shows increasing level of testosterone from 20 ng/dl to 85,27 ng/dl, the result of chromosomal analysis is 47, XXY(7) / 46, XX(43) Mosaicsm Klinefelter Syndrome, and planning therapy for the patient is testosterone hormone for micropenis therapy, and inhibin-B test for fertility prognosis.

Conclusion: Has been reported Mosaicsm Klinefelter Syndrome patient with 47,XXY(7)/46,XX.

P11-09 Syndromes

A Case of Myelodysplatic Syndrome Associated with Turner Syndrome

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Aims: Myelodysplastic syndromes in children are often associated with chromosomal abnormalities, but there are few reports about association with Turner syndrome.

Methods: A 15-year old girl with Turner syndrome came to the outpatient clinic with generalized weakness and pitting edema.

Results: Lab studies revealed persistent pancytopenia and iron deficiency anemia. Abdominal ultrasound revealed small sized and coarse liver with splenomegaly, dilated splenic vein and ascites in abdomen and pelvis. The abdominal CT scan revealed liver cirrhosis, splenomegaly and dilated splenic vein, lower esophageal varix, portal hypertension and spleno-renal shunt. Examination of the bone marrow revealed dyserythropoietic features, hypercellular marrow with moderately increased megakaryocytes. The patient was diagnosed as Myelodysplastic syndrome after bone marrow biopsy. After events of upper gastrointestinal bleeding, the patient progressed to acute hepatic failure and expired.

Conclusion: A definite association of Myelodysplastic syndrome with Turner syndrome has not yet been described. We report a case of Myelodysplastic syndrome found in a Turner syndrome patient.

P11-10 Syndromes

Characteristics of Turner Syndrome in Jakarta

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Aims: To know the characteristics of Turner Syndrome which include karyotipe, age when diagnosis was done, pubertal status, follicle stimulating hormone (FSH) level, and bone age.

Methods: The study was descriptive study. Data was taken from Jakarta Turner Society and medical record of child patient from endocrinologic outpatient clinic Ciptomangunkusumo Hospital from 1997–2006.

Results: There were 20 cases of Turner Syndrome, 17 patients had 45,X karyotype and the left its had mosaic karyotype. Mean of age when diagnosis was 7.75 years (interval 0-15 years); mean of birth weight was 2590 gm; short stature was found in 18 subjects. They were 8 patients accompanied abnormalities: cardiac abnormalities (4), ear abnormalities (3), and hypertension (1). Seventh patients with delayed puberty. Mean TSH level of 16 patients was 82.94 IU/litre (interval 13.8-188 IU/litre). Bone age of 16 patients showed retarded (11 patients).

Conclusions: In this study, the main characteristics of Turner Syndrome was 45,X karyotipe and the physical characteristics were short stature, delayed puberty accompanied with other medical disorders.

P11-11 Syndromes

A Case of Turner Syndrome with Spinal Hemorrhage Associated with Vascular Anomalies

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Aims: It is known that Turner syndrome is related with vascular anomalies and connected with brain hemorrhage and gastrointestinal hemorrhage. But spinal hemorrhage in Turner syndrome is not reported before.

Methods: 9-year-old girl with 45X/47XXX mosaic Turner's syndrome was referred for weakness of both lower legs. She has been treated with growth hormone for short stature for last 3 years. On physical examination, lower motor function was decreased on grade 3, and sensory and deep tendon reflex was normal. Whole spine MRI showed acute spinal hemorrhage and suspicious vascular anomalies such as arteriovascular malformation at thoracic 11-12 level. But no definite arteriovascular malformation was not revealed on spinal artery angiogram.

Results: She was treated with high dose steroid pulse therapy and recovered hospital day 15. There were still anomalous vascular lesion at same level on follow up spine MRI. Now she has no weakness of legs.

Conclusion: We report a case of Turner syndrome with spinal hemorrhage associated with vascular anomalies for the first time.

P12-01 Thyroid Disorders

Childhood Minimally Invasive Follicular Carcinoma: Clinical Features and Immunohistochemistry Analysis

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Aims: To report on 2 cases of childhood MIFC to emphasis the clinical features, laboratory findings, diagnosis and management of this rare disease.

Methods: The patients' age, gender, clinical features, laboratory findings, pathology, and therapy were reviewed. Immunohistochemistry analysis was performed on the resected masses section.

Results: One male and one female with age of 8 and 12 years were enrolled. They were all hospitalized as thyroid mass. Imaging findings showed well-defined heterogeneous mass and radionuclide scintigraphy with 99mTc demonstrated small cold nodules in right lobe of thyroid. Histopathology of the mass confirmed the diagnosis of MIFC. Immunohistochemical staining showed positive of thyroglobulin, thyroid transcription factor-1, galectin-3, Hector Battifora mesothelial antigen-1, cytokeratin-AE1/AE3, cytokeratin-19, proliferating cell nuclear antigen and E-cadherin in two cases, and S-100 in one case while CD56, vimentin and desmin were all negative. One case was undertaken lobectomy and the other one was undertaken subtotal thyreoidectomy with L-T4 replacement therapy.

Conclusion: MIFC is exceedingly rare in child and should be included in the differential diagnosis of mass in thyroid. The diagnosis of MIFC depends mainly on the pathological findings. An early diagnosis and surgical treatment still remain the best methods of improving the prognosis of childhood MIFC.

P12-02 Thyroid Disorders

The Frequency of the Congenital Hypothyroidism in Term Neonates with Prolonged Indirect Hyperbilirubinemia, Oromieh Iran

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Aims: The aim of this study was to evaluate the frequency of congenital hypothyroidism in neonates with prolonged jaundice in area without hypothyroid screening program but high breastfeeding rate.

Methods: Jaundiced infants, otherwise clinically well, age more than two weeks age, with complain of visible yellow color of skin or eye who presented or referred to newborn nursery of Imam Hospital, Oromieh Iran, for evaluation of the prolonged jaundice from April 2005 to March 2006 were eligible for this study. Work-up of prolonged indirect hyperbilirubinemia including direct coombs test, blood types of baby and mother, complete blood count, blood smear, glucose-6-phosphate dehydrogenase level, reticulocyte, bilirubin level, T4, TSH and urine analysis and culture were performed.

Results: All cases were breastfed. The numbers of male and female patients were 43(43%) and 57 (57%) respectively. Among 100 cases enrolled in the study six neonates (6%) suffered from CH. Out of the 6 cases, 2 were males and 4 were females.

Conclusion: The frequency of congenital hypothyroidism is high in prolonged jaundice in field of the study. According to the results of this study, it can be recommended that CH should be considered in prolonged jaundice.

P12-03 Thyroid Disorders

Long Term Outcome of Childhood Graves Disease in Chinese Children

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Aims: In contrast with most western countries, the incidence of Graves' disease among Hong Kong Chinese children is very high. We have conducted a 20-year retrospective review on our Chinese childhood Graves' disease patients and documented their treatment outcome.

Methods: Medical records of children diagnosed with Graves' disease between 1988 and 1998 were reviewed. They were followed until 2008 to evaluate their long term outcome. Their treatment received, relapse rate and current disease status were determined.

Results: A total of 83 patients were diagnosed to have Graves' disease between 1988 and 1998. Fifty-one (61%) of them suffered from relapse within three years after stopping the initial course of oral medication. Among those with relapse, 28 (55%) of them has family history of thyroid disorder. Only 14 (43%) patients with positive family history in patients achieved complete remission with ATD alone ($P < 0.05$). Among all the subjects, 36 received definitive treatment. Twenty seven (75%) received RAI. Among patient receiving RAI treatment, 10 (40%) required a second dose.

Conclusion: The relapse rate in our cohort was 61% after the first attempt of stopping anti-thyroid medication. Because of the inability to induce long term remission with oral medication, earlier definitive treatment should be considered.

P12-04 Thyroid Disorders

Does This Patient Have Hyperthyroidism?

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Aims: To report a case of resistance to thyroid hormone

Methods: We report a Chinese girl with persisetent abnormal thyorid function tests. She was found to have high FT4 level on routine blood testing. Her FT4 levels are persistently high (27-32.2pmol/l, normal range 12.9-23.3pmol/l). Other thyroid function tests including FT3 and TSH levels were normal. Antithyroid antibodies were negative. She has no family history of thyroid disorders. There are no symptoms of hyperthyroidism. She has no goitre and is clinically euthyroid. Her family memebers' thyroid function tests were normal. Multational analysis of the THRB gene for resistance to thyroid hormone was arranged for this family.

Results: The mutational analysis of index case showed heterozygous for R383C (CGC>TGC). Genetic studies on other family memebers showed no mutation.

Conclusion: This patient does not have hyperthyroidism. She has resistance to thyroid hormone. The mutation, R383C may be a de novo mutation. No treatment is required as she is euthyroid.

P12-05 Thyroid Disorders

A Case Report About Hyperthyroidism with Thymus Hypertrophy

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Aims: To consider wheaher hyperthyroidism as the cause of unexplained thymic hyperplasia and with the symtem and sings of hyperthyroidism being controlled,the hyperplastic thymus gland will get small in size.

Methods: We present the case repot of a nine-year old girl who experienced behavioural disturbances such as difficulty concentrating,difficulty sleeping,tachycardia,weight loss,was confirmed hyperthyroidism by examination of thyroid function tests. However,she relapsed and even got worse for poorlycompliant. She came to our hospital for further theraphy and was found space occuping dieases of anterior mediastinum unexpectedly by chest X-ray. The computed tomography (CT) imaging suggested thymic hyperplasia.The department of surgery advised to operation but her patents refused it.We treated her with antithyroid medicine and propranolol. The girl became euthyroid and her symptom was allieved after two weeks.We monitor the girl for every three months

Results: We hyperthysize the hyperplastic thymus gland will get small in size after three months and maybe an operation will not be necessary. The result will come out before September.

Conclusion: The case emphasizes the need to consider hyperthyroidism as the cause of unexplained thymic hyperplasia,we should be aware of this phenomenon.

P12-06 Thyroid Disorders

Thyroid Gland Phenotype in Primary Congenital Hypothyroidism

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Aims: To determine the thyroid gland phenotype in Malaysian children with primary CHT

Methods: Forty children with primary CHT confirmed by high TSH and low FT4 detected through the newborn screening were treated with thyroxine and underwent Technetium thyroid scan when they were 3 years and older after temporarily stopping their thyroxine for 4 weeks. Repeat TSH and FT4 after scan confirmed CHT. Results of scan were reported by a single radiophysicist.

Results: Twenty four (60.0 %)children had normal /hypoplastic but nonfunctioning glands,13 (32.5 %) aplastic glands and only 3 (7.5 %) with ectopic glands.

Conclusion: This finding is in contrast to that reported in Caucasian children with CHT in whom ectopic glands were more commonly found . Since genetic or epigenetic factors influence thyroid gland development and thyroid hormone synthesis , mutational analysis of transcription factors(TTF-1 ,TTF-2 and PAX8) or TSHR and genes regulating iodine transport into thyroid gland and thyroid hormone synthesis may help elucidate the different thyroid phenotype in this Asian population.

P12-07 Thyroid Disorders

Neonatal Outcomes Associated with Maternal Autoimmune Thyroid Disease

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Aims: To examine the effect of maternal autoimmune thyroid disease on infants' thyroid function.

Methods: Retrospective review of medical records of neonates born to mother with history of autoimmune thyroid diseases.

Results: 135 babies were identified (M: F=69:66). Eight babies (6%) had their cord blood TSH > 15 iu/ml. Reassessment on Day 5, six babies were found to have persistently elevated TSH and 2 (1.5%) were subsequently diagnosed as congenital hypothyroidism. Its incidence is higher than the reported 1 in 1115 in Hong Kong (2005 data). 67 babies had raised fT4 detected on Day 5. Among them, 2 babies (3%) had transient neonatal thyrotoxicosis. Two babies were found to have raised TSH only at one month old and were diagnosed to have compensated hypothyroidism. Altogether, 71 out of these 135 infants (52.6%) were found to have thyroid dysfunction within first month of age with female predominance (F: M = 43:28) in this thyroid dysfunction group (60.6% vs 35.9%, $p<0.05$). Of these 71 infants, 91.5% had transient hyperthyroxinaemia, 17.9% and 78.3% had positive anti-thyroglobulin antibody and positive anti-thyroid microsomal antibody respectively.

Conclusion: Maternal autoimmune thyroid disease will affect infants' thyroid function. It is therefore, necessary to closely follow up this group of babies after birth.

P12-08 Thyroid Disorders

Primary Hypothyroidism as an Early Manifestation of Langerhans Cell Histiocytosis

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Aims: To describe uncommon endocrine manifestations of Langerhans Cell Histiocytosis.

Methods: Case description and online review of literature.

Results: A five year old girl presented with primary hypothyroidism and polyuria, without any bony defects. Water deprivation test confirmed central diabetes insipidus. She responded to desmopressin and levothyroxine supplements. Magnetic resonance imaging (MRI) showed non-visualised posterior pituitary bright spot. Eight months later she developed severe headache, polyphagia, obesity, goiter and thelarche. Repeat MRI of the brain showed a well defined T2-weighted hypointense, homogenously enhancing mass lesion in the hypothalamus. Hypocortisolemia and growth hormone deficiency were also detected. Paradoxically, there was an accelerated growth (growth velocity, 18 cm/year), IGF 1 was also undetectable. Electron microscopy of the thyroid tissue demonstrated Birbeck granules. Stimulated serum leutinizing hormone (LH) was prepubertal (<1.5IU/l). She was started on vinblastine and steroids. However, she died in her hometown after 2 months of start of therapy.

Conclusion: LCH can be a cause of primary hypothyroidism in children. The disease course may be rapidly progressive. Repeated MR imaging of the brain should be done. Anterior pituitary functions should be assessed at initial diagnosis, especially in the presence of DI. Precocious puberty can manifest on follow up.

P12-09 Thyroid Disorders

Two Cases of Multiple Endocrine Neoplasia Type 2B

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Aims: Multiple endocrine neoplasia 2B (MEN 2B) encompasses several distinct syndromes featuring tumors of endocrine glands, is characterized by medullary thryroid carcinoma(MTC), pheochromocytoma and mucosal neuromas of the tongue, lips and other sites. MTC is the main cause of death in patients who have not received early prophylactic treatment, and MTC in MEN 2B represents more aggressive progress than that of MEN 2A.

Methods: We encountered two cases of MEN 2B. One was a 6 year old boy who manifested multiple mucosal neuromas of the tongue which had been aggravated in four months, and the other was a 13 month old boy who had familial history of MEN 2B.

Results: Their genetic analysis revealed a point mutation of 918 cordon in the RET proto-oncogene. At the time of diagnosis, the thyroid computed tomography of a 6 year old boy showed hypoechogenic nodules on thyroid glands, which are suspicious of malignancy. All of them underwent an operation for prophylactic total thyroidectomy and an older boy's specimen was turned out thyroid medullary carcinoma.

Conclusion: Here, we report two cases of MEN 2B with a review of literature.

P12-10 Thyroid Disorders

Variations of Serum Level of Triiodothyronine, Thyroxine, Free Thyroxine and Thyroid Stimulating Hormone in Infants with Congenital Hypothyroidism

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Aims: Sreum level of triiodothyronine(T3), thyroxine(T4), free thyroxine(FT4), and thyroid stimulating hormone(TSH) are variable in infants with congenital hypothyroidism(CHT). We monitored these hormone level and delineate the relation with etiology of CHT

Methods: CHT infants were selected retrospectively on the bases of the serum level of TSH(>20mIU/mL) in neonatal screening from Jan. 2000 to Dec 2006. Total 38 neonate were selected and 4 neonate were thyroid agenesis, 9 ectopic thyroid, and 25 dyshormonogenesis. Serum level of T3, T4, FT4, and TSH were detected by radioimmunoassay(RIA) on 1 month, 2 month, 4 months, 6 month,

and 12 months of age. These hormone level of agenesis and ectopic thyroid infants(group A) were compared to those of dyshormonogenesis infants(group B). All of the infants were administered L-thyroxine adequately

Results: Serum level of T3, T4, and FT4 were normalized within 2 months of age in both group of infants. In group A, serum level of TSH on neonatal screeing was 150.1±143.88 mIU/mL, on 1 month of age 50.3±51.88, 6 months 17.4±21.26. In group B, serum level of TSH on neonatal screeing was 60.5±48.20 mIU/mL, on 1 month of age 28.0±28.16, 4 months 2.7±2.81.

Conclusion: Serum level of TSH was variable in thyroid agenesis and ectopic thyroid

P12-11 Thyroid Disorders

Clinical Profile of Ectopic Thyroid from a Tertiary Referral Centre

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Aims: To study the presentation and management outcomes of patients with ectopic thyroid

Methods: Retrospective study (January 1995- March2008) was carried out in 23 patients(16 female, 7 males) with ectopic thyroid. The outcomes measured were age of presentation, symptoms, endocrine profile, nuclear imaging findings and management

Results: Mean age of presentation was 14.3yrs (Range 5mo-40yrs). Twelve patients had sublingual thyroid(presented with anterior neck swelling), and 11 had lingual thyroid which were detected incidentally or with dyspahgia/bleeding. Fifteen patients had hypothyroidism, 4 had subclinical hypothyroidism and 4 patients were euthyroid . The ectopic thyroid was the only functional thyroid tissue in 20 out of 23 patients and in 3 patients with lingual thyroid showed normal radiotracer concentration in the thyroid bed also. Five patients with lingual thyroid were operated for recurrent bleeding or dysphagia and were put on replacement therapy postoperatively. The rest 18 patients were treated with thyroxine and swelling decreased / disappeared in 16 patients and 2 patients didn`t followed up.

Conclusion: Our patients presented with either sublingual or lingual thyroid and 83 % were hypothyroid at presentation. In 87% of patients, ectopic thyroid was the only functioning thyroid tissue. Thyroid replacement therapy was effective in all patients

P12-12 Thyroid Disorders

Thyroid Dysfunction in Premature or Small for Gestational Age Infants

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Aims: Thyroid hormones is essential for the normal development of the brain in early life. Thyroid dysfunction in the premature infant is characterized by variable levels of thyroid stimulating hormone (TSH), thyroxine (T4) and free T4 (fT4) concentrations during the first 2-4 postnatal weeks of life. The purpose of this study is to identify the prevalence of thyroid dysfunction in this group.

Methods: Premature or small for gestational age (SGA) infants, who were admitted to Dankook University Hospital between April 1999 and March 2008 and tested for the thyroid function, were included in this study. We retrospectively reviewed medical records and categorized the subjects into three groups (low fT4 and normal TSH, low fT4 and elevated TSH values, normal fT4 and elevated TSH values).

Results: Among 620 subjects, 133 (21.5%) had initially abnormal thyroid function test (TFT). In addition, seven out of 487 subjects with initially normal TFT showed delayed TSH elevation on follow-up. Thyoxine was prescribed to 11 patients (1.8%), and medication could be discontinued in 9 subjects after age 3. One patient was confirmed as having ectopic thyroid on thyroid scan.

Conclusion: In this study, thyroid dysfunction was frequent in the premature or SGA infants, but most of them were transient.

P12-13 Thyroid Disorders

Incomplete Catch-Up Growth After Puberty-Onset Substitution in Hypothyroidism: Is the Use of Growth Hormone Necessary?

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Aims: This study was to assess whether catch-up growth was complete and feasibility of the use of growth hormone in longstanding untreated and puberty-onset substitution hypothyroidism.

Methods: Catch-up growth was analyzed in 10 pubertal children with hypothyroidism starting treatment at an age of 15.0 (13.2-18.1) years, bone age 5.58±2.10 and a height (HT) SD score (HT SDS) of -6.1 (±1.1). All patients were followed to adult height.

Results: The first 3 treated years are most important. HT velocity was 12.5± 2.6, 9.3±2.5 and 8.0±3.6 cm/year, and change in HT SDS was -4.37±0.84, -3.18±1.08 and -1.91±1.57, bone age progression 5.42±2.01, 2.17±1.03, 2.58±0.92 during the 1st, 2nd and 3rd year, respectively. Adult height reached a HT SDS of -1.72±1.08, all not within their target HT range(HT SDS: 0.4±1.07). Growth hormone (GH) was used in addition to L-thyroxine in another three patients of same situation. Two years growth hormone treatment improved adult height to a HT SDS of -0.82±1.28.

Conclusion: Catch-up growth in hypothyroidism is incomplete if treatment has been started during puberty. Growth hormone treatment improved the final height.

P12-14 Thyroid Disorders

Graves Disease

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Aims: Graves disease is an immune-mediated disorder and the most common cause of hyperthyroidism in children. Prevalence of this disease is about 0.02%. There is a strong female predisposition, the female-male ratio being 6 to 8:1. It can occur at any age, especially in adolescence.

Methods: Twelve years old girl with hyperhidrosis, weight loss, irritability and emotional lability, prominence of the eyes and palpitation.

Results: From physical examination we found exophthalmoses, goiter and tachycardia. From laboratory findings we got elevation of total T3 and T4 level, decreased of TSH level. We confirmed it by the positive result of antimicrosomal antibody (AMA) and antithyroglobulin antibody (ATGA). Patient was treated with propylthiouracil (PTU) 75 mg tid.

Conclusion: We chose PTU as treatment of our patient and showed excellent result. Clinical symptoms and total T4 level relieved after 1 month therapy.

P13-01 Type 1 and Other Types of Diabetes

Psychological Status of Children with Type I Diabetes Mellitus: Maternal Psychologic State in Diabetic Children with Depressive Mood

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Aims: The aim of this study was to see an incidence of depression in adolescent children with type I DM, and to see the characteristics of demographic variables, maternal psychologic state and family environments in adolescent children with type I DM who was in depressive mood.

Methods: We analyzed 23 children with type I DM who participated in a diabetes summer camp which was held in Daegu between August 6th and 10th, 2004 and answered questainnaires which included CDI/BDI for children, MMPI and SCL-90 for patients' mothers, and FES which mothers were asked to respond. They consisted of 10 boys and 13 girls and their mean age was 13.3 years.

Results: There were significant differences in maternal MMPI and SCL-90 between depressive and non-depressive group. Among the maternal MMPI, the t-scores of hypochondriasis and hysteria in depressive group were higher than those of non- depressive group. And among the dimension of SCL-90, t-score of depression, anxiety, phobic anxiety and psychoticism in depressive group were higher than those of non-depressive group($p<0.05$).

Conclusion: We found high incidence rate of depression in children with type I diabetes and the mothers of diabeteic depressive childen were more depressed and anxious than the others.

P13-02 Type 1 and Other Types of Diabetes

Oxidative Stress State in Children with Diabetic Ketoacidosis and Its Influencing Factors

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Aims: To investigate the oxidative stress state in children with diabetic ketoacidosis(DKA), and analyze whether any observed abnormalities were related to metabolic disturbances.

Methods: Four groups of subjects were studied, comprising 22 patients with DKA (group 1), 18 diabetic children with medium metabolic control (HbA1c<9%, group 2), 22 children with poorly controlled diabetes(HbA1c>9%, group 3), and 36 healthy control children(group 4). Malondialdehyde (MDA), nitrate oxidase (NO), glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), and metabolic parameters were measured in the serum of the subjects.

Results: Mean serum MDA value was significantly higher in group 1 than in group 2 and group 4. NO was significantly higher in group 1, 2 and 3 compared with group 4. GSH-Px was significantly lower in group 1, 2 and 3 than in group 4. Both serum MDA and NO values in the diabetic patients were positively related to HbA1c, and serum SOD values in the DKA patients were negatively related to HbA1c.

Conclusion: There was an increase of oxidative stress and decrease of antioxygenic ability in DKA children, and these changes tended to correlate more with markers of diabetic imbalance than with parameters of acute metabolic disturbances of DKA.

P13-03 Type 1 and Other Types of Diabetes

E23K Kir6.2 Polymorphism in the Korean Type 1 Diabetes

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Aims: The G to A mutation in the Kir 6.2, the ATP-sensitive potassium channel subunit, results in the substitution of a highly conserved glutamate (E) residue with lysine (K). The previous studies have shown to have a relationship with high risk to type 2 diabetes. But there are few studies for the role of E23K polymorphism in type 1 diabetes. Our aim was to investigate association of the E23K polymorphism in the KCNJ11 gene with Korean type 1 diabetes.

Methods: We studied 70 patients with type 1 diabetes mellitus. We used the control group of other Korean study. The control group was composed of 630 non-diabetes. E23K polymorphism was analyzed by direct sequencing of exon1 in the KCNJ11 gene.

Results: The EE, EK, and KK genotype percentages of the KCNJ11 E23K polymorphism in the control group were 0.405 (255 control), 0.433 (273 control), 0.162 (102 control) respectively. The EE, EK, and KK genotype percentages of the KCNJ11 E23K polymorphism in the study group were 0.3 (21 patients), 0.443 (31 patients) and 0.257 (18 patients) respectively.

Conclusion: E23K polymorphism appears at higher frequency in the Korean type 1 diabetes. But our study was small cohorts, so we need a large scale study in type 1diabetes.

P13-04 Type 1 and Other Types of Diabetes

Transient Neonatal Diabetes Mellitus with Macroglossia Caused by Paternal Uniparental Disomy of Chromosome 6

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Aims: Transient neonatal diabetes (TND) is associated with paternal uniparental isodisomy (UPD) of chromosome 6, paternally inherited duplication of 6q24, and a methylation defect at a CpG island of ZAC/HYMA1. We experienced a case of TND who presented with hyperglycemia, macroglossia, and intrauterine growth retardation, caused by paternal UPD.

Methods: An 18-day-old female infant was admitted to hospital due to macroglossia and recurrent hyperglycemia. The patient was born at 40 weeks of gestation and weighed 2,200 g (<3 percentile). The patient's length was 50 cm (50-75 percentile), her weight 2,690 g (10-25 percentile), and her head circumference 35.8 cm (75-90 percentile). She had extreme macroglossia, large fontanelles, micrognathia, and prominent eyes. Serum glucose level was 200-200 mg/dL and improved 1 week later spontaneously. To identify the presence of paternal UPD of chromosome 6, genomic DNA from peripheral blood was prepared and digested with methylation-sensitive BssHII.

Results: Polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) analysis identified the paternal origin of the HYMA1 gene.

Conclusion: We have found a patient with TND carrying paternal UPD of chromosome 6. TND is associated with UPD of chromosome 6 suggesting that an imprinted gene on chromosome 6 is responsible for this phenotype.

P13-05 Type 1 and Other Types of Diabetes

A Study of the Growth and Development of Microvascular Complications in Patients with Type 1 Diabetes Mellitus

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Aims: The aim of this study was to evaluate the effect of T1DM on growth and factors associated with the development of microvascular complications.

Methods: We conducted a retrospective longitudinal evaluation of 154 patients above 16 years of age. We analyzed factors which affect final height standard deviation scores (SDS) and development of microvascular complications.

Results: Final height SDS was -0.11±1.15. Final height SDS was significantly lower than midparental height SDS and height SDS at diagnosis. Height SDS at onset of puberty, midparental height SDS and pubertal growth gain affected final height SDS. The number of patients with complications was 37 (24 percent). Microvascular complications developed at a younger age and after longer duration of diabetes in patients with a prepubertal onset of T1DM compared to patients with pubertal onset. Patients with complications had a higher level of average HbA1C than patients without complications. Patients whose microalbuminuria regressed had lower levels of average HbA1C, systolic BP, second 24h urine microalbumin than patients with persistant or progressed microalbuminuria.

Conclusion: The results suggest that various factors associated with T1DM can impair growth potential, but degrees of glycemic control don't affect final height. Additionally, the degrees of glycemic control and puberty affect the development of microvascular complications.

P13-06 Type 1 and Other Types of Diabetes

The Clinical Characteristics of Pancreatic Autoantibody Positive Type 1 Diabetes in Chilren and Adolecence

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Aims: The purpose of this study is to know whether there are any clinical characteristic differences between patients with autoantibody positive and negative type 1 diabetes at initial presentation.

Methods: We analyzed total 110 patients (<18-year old) with newly diagnosed type 1 diabetes. Pancreatic autoantibodies, Glutamic Acid Decarboxylase(GAD) and Insulin autoAntibody(IAA), both or one of them were measured, and reviewed clinical and laboratory characteristics according to presence of antibodies.

Results: GAD antibody was checked in 94 of 110 patients and 51.5% was positive. IAA was checked in 95 patients and 36.8% were positive. Both GAD and IAA were measured in 79 patients and 24.1% patients had both antibodies. But in 35.4% patients were negative. The patients who had one or both autoantibody were younger than the others, and had lower BMI, lower corrected sodium level, and lower serum effective osmolarity than the others ($P<0.05$). Patients who had IAA antibody were younger compared with patients who had not IAA antibody.

Conclusion: We concluded that both GAD and IAA are more useful for detecting immune-mediated type 1 diabetes, especially in younger aged group.

P13-07 Type 1 and Other Types of Diabetes

Rising of the Incidence of Diabetes Mellitus Type 1 in Children of Southern Thailand

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Aims: To determine the incidence of DM type1 in children of southern Thailand in the year 1997-2005 To study the epidemiologic data of DM type 1 in these children

Methods: We sent 218 questionaires to the directors of all public and private hospitals in all 14 provinces of southern Thailand. The informations of the new diabetic patients under fifteen years old diagnosed in the year1997-2005 were collected. Incidence rate were calculated per 100,000 population under fifteen years old per year.

Results: There were 116 new DM type 1 children diagnosed in this period of time. The average incidence in the year 1997-2005 was 0.65 per 100,000 population per year. The male to female ratio was 1: 1.The most common age group at diagnosis was 11-15 years old. Our previous study revealed that the incidence of DM type1 in children of southern Thailand in the year 1992-1996 was 0.52 per 100,000 population per year.

Conclusion: The average incidence of DM type1 in children of southern Thailand in the year 1997-2005 was 1.25 times that in the year 1992-1996. There was 25 percent rising of the incidence in the year 1997-2005 from that in the year 1992-1996. DM type 1 increased 2.8 percent per year.

P13-08 Type 1 and Other Types of Diabetes

A Study of Development of Macrovascular Complications and Factors Related to These Complications in Young Adults with Childhood/Adolescence-Onset Type 1 Diabetes Mellitus

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Aims: Macrovascular complications are the main cause of mortality in type 1 diabetes mellitus(T1DM). The purpose of this study was to assess risk factors of macrovascular complications and to clarify the presence of the early vascular changes in young adults with T1DM diagnosed in childhood and adolescence.

Methods: Seventy-two patients(23.9±2.4 years) and twenty normal controls were included. The incidence of hypertension and dyslipidemia were reviewed and flow-mediated vasodilation(FMD) and mean intima-media thickness(IMT) were measured by ultrasound.

Results: Of the 72 patients, 32(44.4%) had hypertension. The proportion of male($P=0.034$) and mean body mass index($P=0.042$) were higher in hypertensive patients than in normotensive patients. Thirty-one(44.9%) patients had dyslipidemia and LDLc levels were positively correlated with mean HbA1c($r= 0.318$, $P=0.008$) and total daily insulin dose($r=0.274$, $P=0.023$). The value of mean IMT was significantly higher in patients than that in control (mean IMT 0.43±0.06 mm vs. 0.39±0.06 mm $P=0.025$). There was no difference in the value of FMD between patients and control, but the duration of the disease after pubertal onset was negatively correlated with FMD ($r=-0.34$, $P=0.010$).

Conclusion: Hypertension, dyslipidemia and atherosclerotic vascular change were observed in young adults with T1DM, which strongly suggests that meticulous screening of macrovascular complications and their risk factors should be conducted.

P13-09 Type 1 and Other Types of Diabetes

Systemic Lupus Erythematosus in a Girl with Type 1 Diabetes

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Aims: Systemic lupus erythematosus (SLE) is one of autoimmune diseases which is closely related to type 1 diabetes with PTPN22 genotype. There were many studies regarding insulin resistant diabetes in SLE patients, but SLE was scarcely reported in patients with type 1 diabetes.

Methods: We experienced a case of SLE in a girl with type 1 diabetes.

Results: A 13-year-old girl presented chronic diarrhea and abdominal pain. She had been treated with insulin for type 1 diabetes since 10 years of her age. Colonoscopic examination showed multiple petechiae limited to mucosal area on proximal parts of colon and the pathology confirmed chronic multiple nonspecific inflammation. Anti-nuclear antibody and anti-double stranded DNA were positive, and both C3 and C4 were decreased. One month later, Generalized edema and proteinuria developed. Kidney biopsy confirmed lupus nephritis class II. She was diagnosed with SLE and treated with prednisolone.

Conclusion: This case raises awareness that SLE, although very rare, can occur in type 1 diabetic patients.

P13-10 Type 1 and Other Types of Diabetes

Two Cases of Insulin-Associated Edema in Type 1 Diabetes Mellitus

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Aims: Insulin-associated edema is a rare complication. It occurs shortly after the initiation of intensive insulin therapy and it improves without specific therapy, but sometimes needs diuretics or ephedrine therapy.

Methods: This study was conducted to assess two cases of insulin-associated edema in newly diagnosed type 1 diabetes mellitus patient and poorly controlled patient with established diabetes mellitus during insulin therapy.

Results: A 12-year-old female patient came to our hospital for mental change for 1 day and body weight loss, polydipsia, and polyphagia for 1 month. Her blood glucose level was 572 mg/dl, ketone 1+, and insulin therapy was started. On 5th day of insulin therapy, she showed body weight gain and edema on both lower legs and foots. On 12th day edema was improved without specific therapy. The second patient was an 11-year-old girl with poorly controlled blood glucose for 1 year. Blood glucose was 308 mg/dl, and HbA1c 12.5 % and she was started insulin therapy. On 6th day she showed body weight gain and generalized edema. On 9th day edema subsided. After discharge her edema recurred and showed no response to furosemide administration.

Conclusion: We report two cases of insulin-associated edema. The second patient showed no response to diuretic therapy.

P13-11 Type 1 and Other Types of Diabetes

Profile of Diabetic Ketoacidosis Patients at Dr. Soetomo Hospital During 2002–2007

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Aims: to describe the clinical symptoms and outcome of DKA patients in Pediatric Intensive Care Unit (PICU) Soetomo hospital during 2002–2007

Methods: Medical records review

Results: Thirty two children with DKA had been treated in PICU by using ISPAD 2000 protocol; 27 girls, 5 boys. There were 17 new cases and 6 cases were recurrent DKA. The clinical and symptoms were vary; there were 32 patients, 46.2% with unconsciousness, 38.5% with Kussmaul, and 15.4% with seizure. Five cases mild acidosis, 19 cases moderate acidosis, 10 cases severe acidosis. Sixteen cases with hyponatremia, 1 case hypernatremia, 6 cases hypokalemia, 2 cases hyperkalemia. The mean duration of using syringe pump insulin was 1.41 days, blood glucose level in the first coming 481.88 mg/dL, changing subcutaneous insulin syringe pump 3.05 days, time of blood glucose level reach below 250 mg/dL 2.18 days, time of patients' consciousness recovery 1.59 days, and time of patients starting oral diets was 3.05 days. The mean duration of hospitalization in PICU 2.47 days, and no death cases of DKA.

Conclusion: The management of DKA by using ISPAD 2000 protocol in PICU of Soetomo hospital for five years revealed no mortality

P13-12 Type 1 and Other Types of Diabetes

A Case of Simultaneously Combined Hyperosmolar Hyperglycemic State in Adolescent Girl with Diabetic Ketoacidosis

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Aims: Diabetic ketoacidosis(DKA) is an important complication of diabetes in children and is the most frequent diabetes-related cause of death in childhood. Hyperosmolar hyperglycemic state has high mortality in adults, although there is no data on mortality in children. There was not any case that DKA is combined with hyperosmolar hyperglycemic coma coincidently in children and adolescent.

Results: We experienced adolescent girl who presented initially to have DKA and hyperosmolar hyperglycemic coma. She was severely hyperglycemic(serum glucose 1330mg/dl) and hyperosmolar(Serum

osmolality 441 mmol/H2O) state with significant ketoacidosis (serum keton body 1:8 positive, ABGA pH 7.1, PCO2 13mmHg, PO2 97mmHg, bicarbonate 4mmol/L, anion gap 48). HbA1c was 17.6%, C-peptide was 0.9 pmol/ml, insulin level was 10uU/ml.

P13-13 Type 1 and Other Types of Diabetes

Protection of INS-1 Cells from Oleic Acid-Induced Apoptosis by Inhibiting the Glycogen Synthase Kinase-3

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Aims: With juvenile obesity becoming endemic worldwide, the incidence of obesity-related type-2 diabetes in children is on rise and its long-term consequences make the treatment of type-2 diabetes more challenging.The apoptosis of β-cells plays an important role in the pathogenesis of type-2 diabetes.Recent studies demonstrated that glycogen synthase kinse-3 (GSK-3) is closely related with the development and progression of type-2 diabetes.

Methods: Apoptosis was induced by oleic acid (OA) in INS-1 cells and the activity of GSK-3 was inhibited by LiCl. The PI staining and flow cytometry were employed for the evaluation of apoptosis.The phosphorylation level of GSK-3 was detected by Western blotting.

Results: The results showed that OA at 0.4 mmol/L could cause conspicuous apoptosis of INS-1 cells and the activity of GSK-3 was significantly increased. After the treatment with 24 mmol/L of LiCl, a inhibitor of GSK-3, the OA-induced apoptosis of INS-1 cells was lessened and the phosphorylation of GSK-3 was increased remarkably.

Conclusion: GSK-3 activation plays an important role in OA-induced apoptosis in pancreatic β-cells and inhibition of the GSK-3 activity can effectively protect INS-1 cells from the OA-induced apoptosis.Our study provides a new experimental basis and target for the clinical treatment of type-2 diabetes.

P14-01 Type 2 Diabetes and Impaired Glucose Tolerance and Insulin Resistance

Prevalence of Type 2 Diabetes and Metabolic Syndrome Among Overweight Children in Northeast Thailand

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Aims: To determine the prevalence of type 2 diabetes (T2DM) and metabolic syndrome (MetS) among overweight children and adolescents in Khon Kaen Province, northeast Thailand.

Methods: A cross-sectional, prospective pilot study was performed in school children between 10 and 15 years of age. Body weight, height and body mass index (BMI) calculations for 2,156 school children were analysed. The BMI for the age and sex value at > 85th percentile was considered overweight and the overweight children were evaluated for family history of diabetes, signs of insulin resistance, plasma fasting glucose and lipid level.

Results: Five hundred and ninety four (27.55%) overweight children were identified, of whom 186 (31.3%) participated in the study. T2DM was documented in 4 (2.15%) while MetS was documented in 6 (3.2%) children. At least one type of dyslipidemia was found in 87 (46.8%) children.

Conclusion: The prevalence of T2DM among overweight school children is 2.15%. Screening for T2DM and MetS are recommened in overweight children. Preventive interventions to reduce overweight and consequently prevent T2DM in Thai children should be provided at school and community level.

P14-02 Type 2 Diabetes and Impaired Glucose Tolerance and Insulin Resistance

Management of Congenital Insulin Resistance in a Toddler-A Clinical Experience

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Aims: This paper describes the early clinical diagnosis of congenital insulin resistance in a toddler; its unique challenges, our strategies and positive outcomes

Methods: The patient's dysmorphism, together with early dentition, coarse facies, hirsutism, mental precocity and acanthosis nigricans assisted in early diagnosis. Endocrine investigations were indicated due to early thelarche and symptomatic hyperglycemia.

Results: OGTT done was normal, with FPG 3.5mmol/L, 1-hour 9mmol/L; 2-hour 7.2mmol/L HbA1c 6%. Insulin levels :0 min-19.3mU/L; 1-hour 1065mU/L.C peptide level > 20.5pmol/L. i.e. Classic for insulin resistance syndrome. Her symptoms progressed and her sugars became increasingly deranged within weeks. Fasting hypoglycemia (especially in the middle of the night / early morning) and postprandial hyperglycemia were found, classical of Rabson Mendenhall syndrome. We started Metformin and dietary planning. Daytime dietary restrictions comprised high fiber and low carbohydrates. Small frequent cornstarch milk feeds on night. With this, significant and sustained improvements in sugar profile allowed us to wean off metformin.

Conclusion: Clinical features and unique sugar profiles can present in the younger child and may allow earlier recognition than typically described. Medications and simple dietary regiments are the cornerstones of treatment. This may delay or prevent complete islet cell exhaustion seen with end stage diabetes in Rabson Mendenhall syndrome.

P14-03 Type 2 Diabetes and Impaired Glucose Tolerance and Insulin Resistance

Metformin with or without Insulin in the Management of Newly Diagnosed Type 2 Diabetic Children

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Aims: To evaluate the effectiveness of metformin with or without insulin in glycemic control in newly diagnosed type 2 diabetic children.

Methods: We reviewed all newly diagnosed type 2 diabetes from July 2000 to March 2008 in our diabetic clinic and assessed those children with HbA1c >10% at diagnosis. In addition to lifestyle modification, all children were treated with metformin with or without insulin. We reviewed their control as reflected by their trend of HbA1c in 3 to 6 month interval.

Results: We reviewed 11 newly diagnosed type 2 diabetic children with HbA1c >10% at diagnosis. There were 6 children in metformin group and 5 children in metformin + insulin group. Apart from BMI, the mean ages and HbA1c at diagnosis were similar in both groups. At 6 months after diagnosis, there was a larger decrease in HbA1c in metformin + insulin group (7.65% vs 4.08%, p=0.014). The mean HbA1c were also lower in metformin + insulin group (5.93% vs 7.16%, p=0.037).

Conclusion: For newly diagnosed type 2 diabetic children with HbA1c >10% at presentation, combination of metformin and insulin may achieve better glycemic control than metformin alone. Studies with bigger sample and longer-term follow up are necessary to confirm this finding.

P14-04 Type 2 Diabetes and Impaired Glucose Tolerance and Insulin Resistance

Clinical Presentation of Children and Adolescents with Type 2 Diabetes Mellitus in Malaysia

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Aims: To determine the clinical presentation of children with type 2 diabetes mellitus(DM) in a tertiary centre in Malaysia.

Methods: Children younger than 18 years diagnosed with diabetes (RPG >11.1mmol/L or FPG >7mmol/L or 2 hr PG >11.1mmol/L) from 1997-2006 were identified from the diabetes clinic data base and their case notes reviewed. Demographic profile, clinical presentation, physical signs, laboratory results and family history were evaluated. DKA was defined as acidosis, pH<7.3 and/or HCO3 <15mmol/L.

Results: There were 36 patients, mean age at diagnosis (±SD) was 13.14 ± 3.0 years. Girls and boys were equally affected, 44.2% were obese, 22.2% overweight . There were 6 (16.7%) who were asymptomatic, but majority (88.3%) had polyuria, polydipsia and polyphagia. Weight loss was positive in 55. 5%, DKA in 11.1%, Acanthosis nigricans in 36.1% .Those with weight loss and DKA had normal or elevated C peptide. Type 2 diabetes was positive in families in 72.2%

Conclusion: Clinical presentation of type 2 DM varied from asymptomatic to severe illness(DKA). Those with classical symptoms, weight loss and DKA maybe indistinguishable from Type 1 but presence of Acanthosis Nigricans, C - peptide and positive family history of type 2 are discriminative.

P14-05 Type 2 Diabetes and Impaired Glucose Tolerance and Insulin Resistance

Prevalence of Microalbuminuria in Youths with Type 2 Diabetes Compared with Type 1 Diabetes

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Aims: We aimed to compare the prevalence and associated risk factors of microalbuminuria in youths with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM).

Methods: We evaluated albumin excretion rate and HbA1c in 162 patients(124 with T1DM, aged 22.5±4.6years, and 38 with T2DM, aged 19.9±5.7years). All participants with T1DM and 16 with T2DM had been followed up for 5years after initial evaluation.

Results: Duration of DM was 13.6±3.6 and 7.7±5.6years, and average HbA1c was 9.0±1.9% and 8.9±2.0%, in participants with T1DM and T2DM, respectively. Microalbuminuria and overt nephropathy was observed in 23(18.5%) and 6(4.8%) of T1DM, and 7(18.4%) and 2(5.3%) of T2DM, respectively. In T1DM, microalbuminuria was observed in 16(12.9%) at initial evaluation, and 3(18.7%) of them became macroalbuminuric during follow up. Among 105 who were initially normoalbuminuric, 11(10.5%) became microalbuminuric and 2(1.9%) became macroalbuminuric after 5 years. Among 16 patients with T2DM who had been followed up, 3(18.7%) were initially microalbuminuric, and they remained microalbuminuric during follow up. Among 12 initially normoalbuminuric, 2(16.7%) became microalbuminuric at follow up.

Conclusion: Despite shorter diabetic duration, young patients with T2DM showed similar prevalence of microalbuminuria with those with T1DM, suggesting that screening for microalbuminuria should be started earlier in T2DM.

P14-06 Type 2 Diabetes and Impaired Glucose Tolerance and Insulin Resistance

The Effect of 6 and 12 Months Metformin Treatment on Obese Children and Its Factors Analysis

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Aims: To compare the 6 and 12 months effect of metformin treatment on obese children and learn characteristics of the affecting parameters.

Methods: 132 obese children were grouped based on OGTT, including 31 simple obese cases (Grp1), 50 hyperinsulinemia cases (Grp2), 51 IGR/T2DM cases(Grp3). 20 cases of Grp2 managed by lifestyle interferering and 30 cases treated with metformin. Grp3 was treated with metformin and lifestyle interfering. Evaluated their aoxological and serum parameters.

Results: 1. After metformin treatment, all speculated parameters were improved remarkablely, while there were no significant differences between 6 and 12 months. 2. Metformin treated patients in Grp2, HOMA-IR and logHOMA-β decreased. Grp3, FBG and HOMA-IR decreased, but logHOMA-β increased. 3: Treated patients in Grp2 and3, the change value of parameters were related to ΔBMI.

Conclusion: Obese children HOMA-IR and other indicators are related to decreased BMI, metformin combined with life-style changing are more effective in hyperinsulinemia group than IGR/DM group. We suggest 6months treatment duration.Then maintain low BMI may be the main target. More effective early stage than later.

P15-01

A Case Report of Glucocorticoid Hypersensitivity Syndrome

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Aims: We describe a case of a 13-year-old Chinese boy with a Cushing's syndrome appearance who have normal, even low serum cortisol. Through a series of tests, he was diagnosis as glucocorticoid hypersensitivity syndrome.

Methods: In one year period, we performed several times physical examinations, endocrine studies and imaging examinations on him to confirm the diagnosis.

Results: The chief complaint of the patient was ostalgia, growing slow, weight gain significantly and occasional hypertension for two years. Physical examnination showed a chubby boy (height: 154.5cm, weight: 49kg, waist circumference 76cm, hip circumference: 88cm) with a Cushing like appearance (moon face, buffalo hump, hirsutism, violaceous striaes wider than 0.5 cm). Routine laboratory test were not abnormal. Endocrinology study showed plasma ACTH at the normal low limit, 24 hours UFC and plasma cotisol significantly decreased. Antibodies of HIV and syphilis in serum were negative. Organs radiological examinations were negative as well as serum markers of tumor. Neither he had history of alcoholism nor steroid therapy history.

Conclusion: This patient had a typical Cushing's syndrome appearance with serum low cortisol levels and decreased 24 hours urinary free cortisol. Plasma levels of ACTH were very near to the low limit. Since that, he was diagnosis as glucocorticoid hypersensitivity syndrome.

P15-02

Inborn Errors of Metabolism Diagnosed through Screening for High-Risk Childrens

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Aims: Inborn errors of metabolism were first studied in National Hospital of Pediatrics-Hanoi (NHP) in Vietnam. Objective: finding prevalence and the distribution of IEMs in children with high risk, and providing clinical characteristics, familial factors, and outcomes of treatment.

Methods: 317 high-risk patients were examined and treated at NHP from 2005 to March 2008. Quantitative analysis of blood amino acids and acylcarnitine using Tandem MS and urine organic acids using GC/MS was done in Shiman University-Japan.

Results: IEMs was found in 14.2% of high risk patients. In 45/317 cases (14.2%) with confirmed IEM: 4/45 cases (8.9%) with fatty acid oxidation disorders, 33/45 cases (73.3) organic academia, 8/45 cases (17.8%) with aminoacidopathy. None patients with fatty acid oxidation disorders died. Nine patients among 33 cases with organic acidemia (27%) were cured. The rate of cured patients having aminoacidemia was 50%.

Conclusions: IEMs was found in 14.2% patients with high risk. Fatty acid oxidation disorders, organic academia, and organic acidemia occupied 8.9%, 73.3%, and 17.8% respectively.

P15-03

The Role of Capillary Blood β-Hydroxybutyric Acid Assay in Children with Diabetic Ketoacidosis

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Aims: The aim of this study was to compare the use of capillary β-OHB acid assay and urine ketone in the management of DKA.

Methods: We prospectively studied 12 DKA episodes from July 2006 to February 2008. Blood glucose, β-OHB measured using a hand-held meter (MediSense® Optium), and urine ketone test were perfomed every hour. Blood gas analysis was tested every four hour

Results: The average age was 13.7 ± 2.49 years. Two severe, 7 moderate and 2 mild DKA episodes. The average time of DKA to resolve was 23.6 ± 2.9 hours and the mean of stay was 4 ± 0.7 days. There was significant strong correlation between acid base status with β-OHB levels in the first hour and significant moderate correlation until 28th hour, while the correlation between acid base status with urine ketone were significantly moderate until 24th hour. After acidosis resolved, 5 of 12 patients still had positive urine ketone tests while β-OHB levels were negative.

Conclusion: The correlation between capillary blood β-OHB acid levels and acid base status is better than urine ketone.

P15-04

Addison Disease

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Aims: Addison disease, or primary acquired adrenal insufficiency, results from destruction of adrenal cortex.

Methods: Case report

Results: Ten years old girl has had dark skin and dry for two years. She also had been pubic hair for a year with change voice. Her appetite was decreased and weakness. She didn't have history of tuberculosis. Born 40 weeks, vigorous, and birth weight 2800 gm. On physical examination she looked no dysmorphic, pimple on face. BP 90/60. Current weight 24 kg (3th percentile-CDC 2000), height 138 cm (50th percentile), BMI 12.6 kg/m2 (< 3th percentile), Mid Parental height < 3th percentile, bone age 14.6 years. Skin pigmentation in both exposed and nonexposed parts of the body, mocous tongue. TS 3 pubic hair and TS 2 breast development. The laboratory data revealed: complete blood count in normal limit, morning cortisol serum 2.41 µg/dL (low), night cortisol serum 2.39 µg/dL (low), fasting blood glucosa 39 mg/dL (low), Na serum 121.4 mg/dL (low), 17-OH progesteron 70 ng/dl (N 3-90), testoteron serum 255 µg/dL (N 6-82), ACTH plasma 1634 µg/dL (N 6-46), and thyroid function was normal. Synacten test not performed. On ultrasonografi abdomen revealed no disorders

Conclusion: Addison Disease. Need further investigation like Synacten test

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