R-1 Read by Title

**Metabolic syndrome in children with abdominal obesity**

Paweł Matusik; Agnieszka Prokopenko; Zofia Skrobl; Anna Waleza; Filip Achtelik; Ewa Malecka-Tendera

Medical University of Silesia, Dept. of Paediatrics, Endocrinology and Diabetes, Katowice, Poland

Obesity in children and adolescents is now a growing medical problem. Increased prevalence of a specially abdominal obesity may results the development of the metabolic complications and can even lead to the metabolic syndrome which is the major risk factor for the cardiovascular complications in adults. The aim of the study was to determine the frequency of the elements of metabolic syndrome appearance in obese pediatric population. We studied 189 children (105 girls, 84 boys) with abdominal obesity (BMI “d 97 pc.”) in the mean age 12,13,46 years, which were the Metabolic Out-Patient Clinic patients between the 2004-2006 years. In all children plasma concentrations of total cholesterol, HDL cholesterol, triglycerides, glucose and insulin levels (during the oral glucose tolerance test) were estimated and blood pressure was measured. In 132 (69.8%) of children dyslipidemia, in 33 (17.46%) hypertensive and in 24 children (12.43%) hypoglycemia, abnormal fasting or impaired glucose tolerance, and in 47 (22.4%) children hypertension was diagnosed. The metabolic syndrome was present in 69 (36.5%) children. The study showed that the abdominal obesity in children and adolescents is significantly associated with metabolic abnormalities therefore the metabolic syndrome. The early prevention and obesity treatment in children and adolescents is necessary to prevent the atherosclerosis complications occurrence in young age.

R-2 Read by Title

**A case of hashitoxicosis**

Diana Vlahova; Elissaveta Stefanova; Krassimira Kazakova; Alexander Kurtev; Zdravka Petrova

Medical University of Sofia, Dept. of Pediatrics, Endocrinology and Diabetology, Sofia, Bulgaria

**Background:** Autoimmune thyroiditis (AT) is the second most common cause for autoimmune endocrine disease in children and Hashitoxicosis is the rarest form.

**History:** 16 year old female, first uncomplicated pregnancy and delivery, with family history for thyroid diseases (mother with operatively removed cold thyroid nodule). Since 6 months - complains of intermittent difficulties in breathing and impaired sleep.

**Status:** Height 167 cm, weight 49 kg, BMI 17.57 kg/m2, reduced subcutaneous adipose tissue, pulse 80 beat/min (during sleep 68-80), BP 110/60 mmHg, pubertal development V stage (Tanner), no menstrual problems, goiter II grade according to the WHO classification.

**Exams:**

<table>
<thead>
<tr>
<th>days</th>
<th>TSH</th>
<th>FT4</th>
<th>FT3</th>
<th>ATA</th>
<th>anti-TPO</th>
<th>TSHR-Ab</th>
<th>Th</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>0.27±4.2</td>
<td>9.3±17</td>
<td>2.4±4</td>
<td>0±115</td>
<td>0±34</td>
<td>0±1.5</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.007</td>
<td>24.3</td>
<td>5.76</td>
<td>656.2</td>
<td>0.4</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>0.01</td>
<td>16.64</td>
<td>3.55</td>
<td>no</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>95</td>
<td>3.94</td>
<td>16.38</td>
<td>3.84</td>
<td>0.4</td>
<td>yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thyroid gland ultrasonography: right lobe 49/17/21 mm, left lobe 46/18/20 mm, mildly hypoechogenic, nonhomogenic structure. Treatment was not performed and a week later the follow-up hormones were significantly improved.

**Diagnosis:** Autoimmune thyroiditis. Hashitoxicosis.

**Discussion:** Hashitoxicosis in children is difficult to diagnose and manage. This case is interesting because her thyroid function was ameliorated without treatment.

R-3 Read by Title

**Autoimmune thyroid disease in children and adolescents with type 1 diabetes:**

First report from north west Iran

Siavash Shiva

Tabriz University of Medical Sciences, Pediatrics (endocrinology), Tabriz, Islamic Republic of Iran

**Background and Objectives:** The prevalence of autoimmune thyroid disease in diabetic patients varies depending on the age, sex and ethnic background of the subjects. The objective of the study was to determine the prevalence of autoimmune thyroid disease in children and adolescents with type 1 diabetes in North West Iran.

**Materials and Methods:** In a cross-sectional study in year 2007, antibodies to thyroglobulin (anti-TG) and thyroperoxidase (anti-TPO) and serum TSH level were measured in 145 children and adolescents (67 boys) with type 1 diabetes. The mean age was 8.3 ± 3.6 years (range 1-18 years) and the mean duration of diabetes was 1.7 ± 2.6 years (range 0.5-15 years).

**Results:** The prevalence of autoimmune thyroid disease determined by high titer of antibodies to TPO and/or TG was 11.7%. Each of anti-TPO and anti-TG antibody titers was high in 9.7% and 7.6% of patients and 5.5% of them had high titers for both antibodies. The mean serum TSH level was 2.9 ± 2.1 µU/ml in antibody negative patients but it was 4.7 ± 4.1 in patients with positive anti-TPO and/or anti-TG titers. Of 17 subjects with autoimmune thyroid disease, 17.6% (3 cases) were hypothyroid. All of the hypothyroid subjects were girls and had high serum levels of both anti-TPO and anti-TG antibodies.

**Conclusions:** Thyroid autoimmunity and hypothyroidism are seen in children and adolescents (especially girls) with type 1 diabetes in North West Iran but, it’s prevalence in not so high.

R-4 Read by Title

**Two cases of Bardet Biedl syndrome with unusual association of epicanthus in two sisters**

Gülşen Karagüzel; Ayşe Aksoy; Ulas Ozdemir; Yusuf Gedik; Ayşenur Ökten

1Karadeniz Technical University School of Medicine, Pediatric Endocrinology, Trabzon, Turkey; 2Karadeniz Technical University School of Medicine, Pediatric Neurology, Trabzon, Turkey; 3Karadeniz Technical University School of Medicine, Pediatrics, Trabzon, Turkey

Bardet-Biedl syndrome (BBS) is a rare autosomal recessive disorder with clinical and genetic heterogeneity. The main features are obesity, retinal dystrophy or pigmentary retinopathy, learning disabilities, dysmorphemic extremities, renal abnormalities, and only in males, hypogonitalism. We present two sisters (Case 1: 12-year-old girl, Case 2: 16-year-old girl) with BBS who referred to our clinic for obesity. Based on phenotypical features (obesity, polydactyly,
brachydactyly, mental retardation), they were diagnosed as BBS. Both of the sisters had epicanthus and metabolic syndrome. Additionally, we determined cerebellar atrophy and bilateral cataract in Case 2. Even though genetic studies have not performed yet, we described first epicanthus in both sisters with BBS. Moreover, brain neuroimaging abnormalities have been reported in only a few patients, these include cerebellar atrophy. We also report another brain abnormality in Case 2.

**R-5 Read by Title**

**Obesity and overweight frequency after adenotonsillectomy in children**

Yasar Sarı; Ismail Sangül; Uzeyir Gök

1Firat University, Faculty of Medicine, Division of Pediatrics
2Endocrinology, Elazığ, Turkey; 3Firat University, Faculty of Medicine, Pediatrics, Elazığ, Turkey; 4Firat University, Faculty of Medicine, Department of Otolaryngology, Head and Neck Surg, Elazığ, Turkey

**Objectives:** This study was performed to determine the frequency of obesity in children who underwent adenotonsillectomy in the first and second years after the operation.

**Methods:** All children underwent adenotonsillectomy because of adenotonsillar hypertrophy in Department of Otolaryngology Head and Neck Surgery in our University hospital setting during January-December 2004 were considered for the study. We successfully obtained follow-up data from 78 patients (mean age 88.6±38.5 months; 37 female and 41 male) out of 143 total patients undergoing adenotonsillectomy during this period. All patients were anthropometrically evaluated before the operation. The frequency of the obesity (BMI ≥ 95 percentile) and overweight (BMI= 85-94 percentile) was determined according to the body mass index.

**Results:** Of the patients 28 were overweight and 50 were at normal weight at admission. Significant increases were obtained in body weight, body mass index and height in all patients at both the first and second year follow-up (p<0.001, p<0.003, p<0.001, respectively). Four out of the 28 overweight children became overweight (4.3%) at the end of the first year, and one being obese (3.6%). The number of overweight and obese children in this group at second year follow up was 9 (32%) and 2 (7.1%), respectively. Among to the initially normal weight patients (n=50), first year follow-up yielded 14 overweight (28%) and 2 obese (4%) cases, these respective numbers being 13 (26%) and 9 (18%) at the end of the second year. When total numbers of patients were considered the rate of overweight and obesity was 28.2% and 14.1%, respectively.

<table>
<thead>
<tr>
<th>Anthropometric measurements</th>
<th>Preoperative (n: 78)</th>
<th>12th month (n: 78)</th>
<th>24th month (n: 78)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height(cm)</td>
<td>118.9 ± 18.6</td>
<td>124.9 ± 18.7</td>
<td>130.7 ± 18.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height SDS</td>
<td>-0.46 ± 0.48</td>
<td>-0.11 ± 0.51</td>
<td>0.08 ± 0.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>22.6 ± 9.4</td>
<td>29.0 ± 11.7</td>
<td>33.0 ± 2.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight SDS</td>
<td>-0.68 ± 0.50</td>
<td>0.112 ± 0.49</td>
<td>0.32 ± 0.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>15.4 ± 2.3</td>
<td>17.0 ± 2.1</td>
<td>18.5 ± 2.1</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Overweight, n (%)</td>
<td>0 (0)</td>
<td>18 (23.1)</td>
<td>22 (28.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity, n (%)</td>
<td>0 (0)</td>
<td>3 (3.8)</td>
<td>11 (14.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusions:** A high percentage of obesity was observed in this study group during the two-year follow up period after the adenotonsillectomy. Therefore, children underwent adenotonsillectomy should be carefully monitored and families as well as family physicians should be cautious about the risk of childhood obesity development following the operation.

**R-6 Read by Title**

**Abstract withdrawn**

**R-7 Read by Title**

**A146G Polymorphism in the steroidogenic factor-1 (SF-1) gene and its association with ambiguous genitalia with apparent partial androgen insensitivity**

Saurabh Sinha; Pascal Philibert; Svetlana Ten; Charles Sultan

1Maimonides Medical Center, Pediatric Endocrinology, Brooklyn, NY, United States; 2Hôpital Lapeyronie, CHU Montpellier, Service d’Hormonologie, Montpellier, France

**Background:** Etiology of ambiguous genitalia in genotypic 46 XY subjects is heterogeneous. Mutation in Steroidogenic factor-1(SF-1) has been reported to be associated with disorders of sex development with or without adrenal insufficiency in male.

**Patient:** index case presented for evaluation of ambiguous genitalia on his 2nd day of life. He is a product of full term pregnancy form a non-consanguinity parents of African American origin. On physical examination, he found to have bifid mildly rugated scrotum with penoscrotal hypospadias and micro-penis. Both of his testes were palpable in the scrotum. Family history is significant for presence of hirsutism (hair over the chin, upper lips) and severs acne in mother. No family history of ambiguous genitalia or infertility. On laboratory evaluation he found to have normal male 46 XY karyotype. His adrenal steroid hormone profiles were normal on ACTH stimulation test. Testosterone level increased from163 ng/dl to 529 ng/dl following a HCG stimulation test. Normal kidneys were identified on pelvic sonogram. A normal male urethra was outlined in voiding cystogram and genitogram. Mother found to have normal 17 OHP, testosterone levels.

**Method:** Hormonal evaluation was done in first week of life. An ACTH and HCG stimulation test was done to evaluate adrenal and testicular function. Sequencing of the androgen receptor, 5 alpha reductase, WT-1 and SF-1 were done from the DNA obtained from peripheral blood.

**Results:** No evidence of adrenal insufficiency noted on ACTH stimulation test. Mutations analyses of DNA were negative for Androgen receptor, 5 α reductase, WT-1 and SRY gene. He found to have A146G Polymorphism in the SF-1 gene.

**Conclusions:** A146G polymorphism in SF-1 gene can be present with several ambiguous genitalia. Apparent partial androgen insensitivity like picture with normal androgen receptor can be due to SF-1 gene mutation in contrary to the usual dysgenetic tests.

**R-8 Read by Title**

**Childhood hypocalcemia after the neonatal period**

Seung-hoon Hahn

Holy Family Hospital, Catholic University of Korea, Department of Pediatrics, Bucheon, Republic of Korea

**Background:** hypocalcemia is one of the most common problems in neonatal endocrine disorder, but after that period we still meet the children with hypocalcemia in the hospital.

**Objective:** to evaluate the characteristics of the children with hypocalcemia after the newborn period in the hospital.

**Methods:** The charts of the children diagnosed as hypocalcemia (1 month-15 years) were reviewed for 5 years from 1st January 2003 to 31st December 2007. We checked up Calcium, Phosphorus, Magnesium, parathyroid hormone(PTH), 1,25-dihydroxyvitamin D, and alkaline phosphatase. We also took radiological examinations.

**Results:** There were 47 patients with an average age of 2.8 years. The number of boys (27 persons, 57.4%) was slightly more than that of girls. 31(66.0%) of them received treatment within the first day of life. He is a product of full term pregnancy form a non-consanguinity parents of African American origin. On physical examination, he found to have bifid mildly rugated scrotum with penoscrotal hypospadias and micro-penis. Both of his testes were palpable in the scrotum. Family history is significant for presence of hirsutism (hair over the chin, upper lips) and severs acne in mother. No family history of ambiguous genitalia or infertility. On laboratory evaluation he found to have normal male 46 XY karyotype. His adrenal steroid hormone profiles were normal on ACTH stimulation test. Testosterone level increased from163 ng/dl to 529 ng/dl following a HCG stimulation test. Normal kidneys were identified on pelvic sonogram. A normal male urethra was outlined in voiding cystogram and genitogram. Mother found to have normal 17 OHP, testosterone levels.

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**Results:** No evidence of adrenal insufficiency noted on ACTH stimulation test. Mutations analyses of DNA were negative for Androgen receptor, 5 α reductase, WT-1 and SRY gene. He found to have A146G Polymorphism in the SF-1 gene.

**Conclusions:** A146G polymorphism in SF-1 gene can be present with several ambiguous genitalia. Apparent partial androgen insensitivity like picture with normal androgen receptor can be due to SF-1 gene mutation in contrary to the usual dysgenetic tests.
**R-9 Read by Title**

**Urinary iodine levels and prevalence of goitre in school children in Kirikkale**

Baris Cakir; Olayc Evlyayoglu; Chihat Sanli

Kirikkale University, Pediatric Endocrinology, Kirikkale, Turkey

**Aim:** Iodine status and the prevalence of goitre was aimed to study in school children in Kirikkale city, a middle Anatolian city.

**Patients and Methods:** Children (7-12 years) were selected from 2 primary schools; from high and low socio-economic status. Anthropometric, and urine iodine measurements, evaluation goitre was performed in all children. Goitre was graded according to World Heath Organization Palpation System. Forms that question household iodine usage were let to be filled at home. Morning urine samples were kept at -20C in deionized tubes until the analysis date.

**Results:** 403 children (203 boys) mean aged 10.36 ± 2.38 (6.37-15.91) years were enrolled in the study. Goitre was diagnosed in 29.5%. Median for urine iodine was 115±1 (7-451) µg/L. Iodine was deficient 46% (n=186) of the children. Iodine deficiency was severe, moderate and mild in 2.7%, 13.9% and 29.5% of the patients respectively. Median urine iodine measurement in schools with high and low socio-economic status were 123 µg/L and 101.5 µg/L respectively. Incidence of using iodized salt in schools with high and low socio-economic status were 82,23% and 71.8% respectively. Median urine iodine level in schools with high socio-economic status were higher in the school with high socio-economic status. Incidence of iodine deficiency was 39.4% in children using iodized salt and 68.4% in children not using iodized salt. Incidence of iodine deficiency was higher in the children not using iodized salt (p<0.05).

**Conclusion:** Iodized salt is not widely used, salt iodization has not fully solved the problem. Iodized salt should be more widely used and it’s efficiency should be increased.

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**R-10 Read by Title**

**Osteopetrosis and congenital hypothyroidism: Report of a case complicated by slipped capital femoral epiphysis**

Ayhan Abaci; Emre Tascilar; Z Uulsen Coskun; Cemil Yildiz; Ediz Yesilkaya

1Gulhane Military Medical Academy, Pediatric Endocrinology, Ankara, Turkey; 2Gulhane Military Medical Academy, Radiology, Ankara, Turkey; 3Gulhane Military Medical Academy, Orthopedic Surgery, Ankara, Turkey

Although the cause of slipped capital femoral epiphysis is not exactly known, attributions to various endocrine disorders have been made. The mean incidence in childhood was reported to be 10.8/100000. A 13-year-old female patient presented with the complaint of acute onset of limp and difficulty in walking. Medical history revealed that she was diagnosed congenital hypothyroidism and L-thyroxine treatment was initiated at the age of 20 days. Incidence of using iodized salt in schools with high and low socio-economic status were 123 µg/L and 101.5 µg/L respectively. Incidence of using iodized salt in schools with high and low socio-economic status were 82,23% and 71.8% respectively. Median urine iodine level in schools with high socio-economic status were higher in the school with high socio-economic status. Incidence of iodine deficiency was 39.4% in children using iodized salt and 68.4% in children not using iodized salt. Incidence of iodine deficiency was higher in the children not using iodized salt (p<0.05).

**Conclusion:** Iodized salt is not widely used, salt iodization has not fully solved the problem. Iodized salt should be more widely used and it’s efficiency should be increased.

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**R-11 Read by Title**

**Two cases presenting with pubertal delay and diagnosed as celiac disease**

 Tolga Unuvar; Ayhan Abaci; Ihsan Esen; Ece Biber; Atilla Buyukgebiz

1Dokuz Eylul University, Pediatric Endocrinology, Izmir, Turkey; 2Acibadem Hastanesi, Pediatric Endocrinology, Istanbul, Turkey

Pubertal delay may be due to underlying chronic diseases as well as primary endocrine disorders. Celiac disease, one of the common malabsorption disorders of childhood, may progress silently in some cases while the ones diagnosed late present with growth failure and/or disturbance of pubertal development. Because of the changing face of current Celiac disease, patients are being diagnosed in the adolescence with atypical symptoms and findings. Here we presented two girls aged 13 and 16 years referred with lack of development of secondary sex characteristics and short stature. Their height and weight were below the third percentile and breast development and pubic hair consistent with Tanner stage 1. We aimed to draw attention to the necessity of routine screening of Celiac Disease in the differential diagnosis of delayed puberty.

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**R-12 Read by Title**

**Is pituitary stalk interruption syndrome (PSIS) a diagnostic marker of the severity of anterior pituitary hormone deficiency?**

Vasilios Maras; Julia Polychroni; Maria Argyropoulou; Lela Stamoyannou

1P & A Kyriakou’ Children’s Hospital, 1st Dept. of Paediatrics, Athens, Greece; 21st Dept. of Paediatrics, Athens, Greece; 3University of Ioannina, Medical School, Dept. of Radiology, Ioannina, Greece

PSIS is characterised by an ectopic posterior pituitary hypertensive signal, absence or faint visualisation of pituitary stalk (PS) and absent or hypoplastic adenohypophysis. The pathogenesis of PSIS is unclear and its natural history not established until adulthood. Studies have correlated the absence of PS with a more severe form of the disease in childhood associated with multiple anterior pituitary hormone deficiency, whereas visualisation of PS is related to isolated GHD. We present the case of a 9-year old boy evaluated in our clinic because of his short stature. The boy is the second child of non-consanguineous parents born by normal delivery in Albania. The mother reported a normal ante-natal period, prolonged neonatal jaundice and a blood transfusion at the age of 18 months because of severe anaemia and failure to thrive. Physical examination, pubertal and psychomotor development were normal. His height percentil was < 3, height velocity 3 cm/year (<1st percentile) and bone age 2 8/12 years retarded. His hormonal profile showed complete GH deficiency (max peak GH response =3.46µg/ml), low cortisol, IGF-1 and T4/T4, inappropriately low TSH and hyperprolactinemia. Brain MRI revealed a typical PSIS picture with an absent PS and confirmed the diagnosis of congenital panhypopituitarism secondary to PSIS. A small oval mass was present in the left thalamus exhibiting low T1, high T2 and FLAIR signal, with no enhancement with IV contrast agent. Our patient was started on appropriate replacement treatment (rGH/T4) with a close follow-up in our clinic. During therapy a mild elevation of SGOT/SGPT and serum ALP was noticed. Extensive laboratory investigations ruled out the most common causes of hypertransaminasemia and increased CPK. The MRI was repeated after 3 months and no change in the lesion size was observed. Our case confirms the correlation between anterior pituitary function and morphological anomalies of the hypothalamic-pituitary region on MRI, with a functional prognostic value of the visibility of the PS.
R-13 Read by Title

A case of left ileo-femoral vein thrombosis, obesity and dyslipidemia
Diana Vlahova; Alexander Kurtev; Elissaveta Stefanova; Krassimora Kazakova; Zdravka Petrova
University Pediatric Hospital, Clinic of Pediatric Endocrinology, Sofia, Bulgaria

Background: Childhood obesity and related complications are an increasing problem through out the world.

History: 12 year old male, second uncomplicated pregnancy and delivery, with family history for obesity, arterial hypertension, type 2 DM and morbus Bazedow. Present disease - since 8 years - with increased appetite and obesity. Till 12 yr 5mo - heavy sport activity 5 times a week - reduced weight. 12 yr 5 mo - diagnosed phlebothrombosis and started treatment (12 yr 7 mo).

Status: Height 152 cm, weight 64.5 kg, BMI 27.32 kg/m² (> 95 P, SD=+2), mildly increased subcutaneous adipose tissue, pulse 84 beat/min (during sleep 68-80), BP 124/89 mmHg, pubertal development III stage (Tanner), marked difference between the two thighs circumference.

Exams: Increased cholesterol (8.5 mmol/l), triglyceride (2.4 mmol/l) and LDL-cholesterol level (5.9 mmol/l), decreased HDL-cholesterol level (0.98 mmol/l) - type II B dyslipidemia. Normal glucose tolerance test. Abdominal ultrasonography - steatosis (no biochemistry data for steatohepatitis).

Theraputic: Diet, Fraxiparine, Detrelax - mild improvement of the vessel diameter.

Conclusion: Combination of obesity, mild hypertonetion, dyslipidimia and endothelial dysfunction define metabolic syndrome. Vessels’ involvement as complication of the syndrome X is rarely seen in pediatric endocrine praxis, which makes it difficult to diagnose and manage. Because of the possible serious consequences, metabolic syndrome should be diagnosed and treated as soon as possible.

R-14 Read by Title

Recurrent pulmoner edema due to central hypoventilation in an obese patient
Hasan Onal1; Erdal Adat1; Seicen Yaroglu Kazanci1; Teoman Akça1; Selvi Sarıkaya2
1Ministry of Health Bakirkoy Maternity and Children, Endocrinology and Metabolism, Istanbul, Turkey; 2Ministry of Health Bakirkoy Maternity and Children, Pediatrics, Istanbul, Turkey

A 12 year old obese boy was brought to the hospital by coughing, vomiting and cyanosis.

The patient had afebril convulsion 6 months and 2 years ago. Cranial MR and EEG of him were normal, 4 months ago in a different clinic, after afebril convulsion he were treated for non cardiogenic pulmoner edema. And there had been no etiology determined.

In his physical examination, hearth rate was 132/min, S3 were present, his respiratory rate was 45/min. His weight was 54 kg (>97%) and his thorars was amphimatos e in type.

In his EKG, sinusoidal tachycardia, T wave negativity; in telecardiyography, cardiomyegaly and in echocardiyographic investigation, right ventricule and right atrium enlarmgement were detected. In spiral thorax CT there were diffuse alveolar infiltration which had consolidation form in some places especially in central parts of the lung. There were no pleural thickness and any effusion.

In his blood gas analysis, acute respiratory asidosis (pH:7.25, pCO2:67,7, pO2:27,9, HCO3:32) and metabolic alcalosis were detected. Iyonizing caliusm was low. As treatment oxygen inhalation, digoxin and dopamin has given. And sufficient respond has seen, pulmoner edema has regressed in 5 days of the treatment.

Despite the regression of pulmoner edema and pulmoner symptoms, componsautary respiratory asidosis was determined. Oral glucose tolerance test showed increased glucose value. In patient’s polosonographic investigation, sleep apnee were detected. He diagnosed as central hypoventilation.

The events occured in the patient can be explained as follows:the continuous chronic hypopnea and sleep apnees causes increased intracranial pressure and though vomiting. And metabolic alcalosis occurs after chronic componsautary respiratory asidosis. Patient’s bicarbonat level increases more and iyonizing calcium level decreases. All these causes pulmoner edema and afebril convulsion.

R-15 Read by Title

Two rare causes of adrenal insufficiency
Ebru Imanoglu; Onur Bagci; Oya Erkan
Cerrahpasa Medical Faculty, Pediatric Endocrinology, Istanbul, Turkey

Here we present three patients with two rare causes of adrenal insufficiency. First patient is a male patient with the triple A (adrenal insufficiency, achalasia, alacrima) syndrome. At 11 years of age, he presented with difficulty in swallowing, vomiting undigested food and skin hyperpigmentation. He had a history of a hypoglycemic convulsion at 10 years old. Endocrinological evaluation was consistent with primary adrenal insufficiency. He had dry eye findings and achalasia. Adrenal US was normal. The other two patients were also males and had adrenoleucodystrophy. They presented when 6 and 7 years old. The first had a normal skin colour and the other had skin hyperpigmentation. The 6 years old patient had a convulsion. Ataxia and decrease in vision were present. The 7 years old patient presented with ataxic gait, dysarthria and nystagmus. In both patients endocrinological evaluation was consistent with primary adrenal insufficiency and adrenal US was normal. The very long chain fatty acid analyses of sera showed increased tetracosanoic to decosanoic and hexacosanoic to decosanoic acid ratios. These findings and MRI findings in both patients taken together with primary adrenal insufficiency were consistent with the diagnosis of adrenoleucodystrophy.

R-16 Read by Title

A case of Albright’s osteodystrophy-like syndrome complicated by diabetes mellitus (DM) in a 16 year-old girl
Tatiana Shiryeva; Ekaterina Anokhina; Tatiana Semicheva; Irina Alexandrova
Endocrinology Research Centre, Institute of Pediatric Endocrinology, Moscow, Russian Federation

Background: ALBRIGHT’S hereditary osteodystrophy (AHO) is a congenital genetic syndrome characterized by short stature, obesity, round face, mental weakness, and sc calcifications and/or brachymetaphalangism. Objective: to report a sporadic case of AHO-like syndrome at 16- yrs-old girl complicated by DM and partial atrophy of the optic nerves.

Results: Patient N, was born in term, birth weight was 2000 g, birth length was 49 sm. No familial history of growth disorders or DM. Nanism was diagnosed at 6 yrs (height 97 sm, HSDS=-3,56), DM manifested in the age of 14 yrs. Further current of DM was mild clinical course with low self-control. Partial atrophy of the optic nervous diagnosed at 6 yrs.

An objective study: 46XX, height 125,8 sm, HSDS=-6,07, not obese, brachydyactylia, round face, deviation of little fingers, mental retardation. She had hypocalcaemia Ca2+-1,02 mmol/l (1,03-1,29), PTH serum level 224,7 pg/ml (15-65). Radiography of hands found out the shortening of bilateral fifth metacarpals, BA was 16 yrs. Thyroid and gonadal functions were normal.

HBAlc-6,3%, insulin dose <0,4 U/kg/day, glycosuria. Antibodies research in blood (IAA, ICA, GAD) was negative. Fasting C-peptide-1,1ng/ml; 2 hours after meal-2,8 ng/ml. HLA-typing (DRB 104, 10; DQA1 0301, 0101; DQB1 0302, 0501): the combination of high risk alleles for DMT1. Insulinotherapy was stopped and metphormin 500 mg td was started with successful result.

Fundscopy: UO partial atrophy of the optic nervous.

Conclusion: We have shown a case of AHO-like syndrome complicated by DM and partial atrophy of the optic nerves. Shortish, round face, brachydactylia, mental retardation are typical in AHO patients with Gs á deficiency. However, the patient does not have PTH resistance, sc calcifications and/or brachymetaphalangism.
**R-17 Read by Title**

Dis hormonal dwarfism associated with Immuno deficiency - centromeric instability - facial anomalies syndrome (ICF)-case presentation

Ottilia Margineanu1; Ioana Miclea1; Ioan Sabau1; Ioan Simeodra1; Mihaela Noditi2
1University of Medicine and Pharmacy, 1st Pediatric Clinic, Timisoara, Romania; 2Institute of Health, Genetics, Timisoara, Romania

Aim: To present a patient with dis hormonal dwarfism associated chromosome variant 46, XX, 16qh+, associated ICF syndrome, hypertrichosis and men- strual cycle disorders.

Material and Method: We present S.A., a 13 year old girl. Results and discus- sions S.A was born from a consanguineous marriage. Physical examination reveal a 13th years old girl, height 36 kg, short statured, height 132 cm (under percentile 3), dis hormonal dwarfism, round dysmorphic face: macrocrania, hypertelorism, macroglossia, protruding tongue, high narrow forehead, low implanted hair, facial and general hypertrichosis, with masculine disposition of the pubic hair, and scoliosis. The patient also presented irregular menses (menarche at the age of 12). The mental retardation was confirmed by the psychological examination. Biological investigation showed normal thyroid function, normal cortisol levels in serum, low tolerance glucose test and immuno- deficiency with low levels of IgG. Chromosomes were 46, XX, 16qh+.

Skeletal radiography showed bone maturation concordant to the chronologi- cal age. The association of this particular phenotype with the genetic findings suggested the diagnosis of the ICF syndrome accompanied by the modificati- on of the HP1 receptor, which is involved in the intranuclear transmission of the steroid hormones. Unfortunately we can’t perform sophisticated genetic analyses.

Conclusions: 1. Although ICF syndrome is difficult to diagnose without so- phisticated genetic analyses, some findings in our patient imply it is a possi- bility. 2. Hypertrichosis is relatively frequent at the preadolescent age and may have complex etiology including complex mechanisms affecting the steroid nuclear receptor. 3. The assessment of the cytotype is necessary in order to frame etiologically a dis hormonal dwarfism associated with other dysmorphic features and to delineate etiological paths.

**R-18 Read by Title**

Gonadal tumor in a 17-years-old girl with a recent diagnosis of CAIS

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The diagnosis of CAIS (complete androgen insensitivity syndrome) remains often unidentified until late puberty, when adolescent girls refer to a first en-docrinological evaluation for primary amenorrhea. When and if gonadectomy should be performed remains an open question even if data in literature show that the risk in complete androgen insensitivity syndrome (CAIS) is the lowest between the Disorders of Sex Development (DSD), estimated less than 5%. A 17-years-old girl was evaluated because she hadn’t had menses yet. She had always been in good health, except for inguinal hernioplasty in infancy. She had normal female external genitalia, well-developed breast, scanty axil- lary and pubic hair; her height was ~97% p.e for sex and age. Basal hormonal analyses showed high levels of serum testosterone, normal gonadotropin and low-normal estradiol. On ultrasonography (US) no uterus was seen; gonads were found in pelvic cavity; the vagina was short and blind-ended. Karyotype was 46,XY. She was submitted to our centre to be approached by a multidis- ciplinary specialist team. She repeated US four times before our evaluation; the last one showed a disomogeneous structure of the right gonad, confirmed by magnetic resonance (MR). Hysteroscopy exam after gonadectomy revealed the presence of testicular tissue with bilateral multifocal classical-type Serto- li-cells tumor and hyperplasia of Leydig cells. Tumoral serum markers were all negative. The patient started replacement estrogen therapy and was also started on hormone therapy by an urologist to plan a future vaginoplasty. It is important to find diagnostic methods to recognize a gonadal tumor precociously. US is ope- rator-dependent and serum markers are not sensitive/specific enough. When a biopsy/gonadectomy is due to be performed and how to manage correctly these conditions still remains an open question. Debates and studies by mul- tidisciplinary teams are necessary to diagnose CAIS earlier and to improve the management.

**R-19 Read by Title**

Two cases of autoimmune polyendocrine syndrome type 2

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University Pediatric Hospital, Clinic of Pediatric Endocrinology, Sofia, Bulgaria

Background: The Autoimmune Polyendocrine Syndrome (APS ) type 2 is a relatively rare disease and a reason for hypocalcaemic seizures in children.

First Case: 5 year old boy with seizures, carpopedal spasms, laryngospasms was unsuccessfully treated with a combination of anticonvulsants for epilepsy without Ca and Ca2+ being examined. Several months later hypoparathyroid- 228
ism was diagnosed. Alopeacia areata, vitiligo and ectodermal dis- pigmentation appeared in a short period of time, followed by symptoms of Addison disease and oral candidiasis within 8 years.

Laboratory Results: Hypocalcaemia with low ionized Ca, hyperphosphate- mia, low PTH, normal cortisol, without nephrocalcinosis and nephrocalculus at the beginning, later nephrocalcinosis, ECG - prolonged QT interval, normal anterior ocular segment, normal TSH and fT 4, as well as thyroid ultrasound.

In evolution - flat cortisol rhythm, low free 24 - hour urine cortisol and extre- mely high ACTH, followed by hypernatremia and high potassium. Normal α 1 antitriphine, antigliadine antibodies.

Second Case: 4 year old girl with seizures, carpopedal spasms and laryngo- spasms, unsuccessfully treated with anticonvulsants, presenting with positive Chvostek sign. Hypoparathyroidism and candidiasis were established with a delay of 4 months.

Laboratory Results: hypocalcaemia with low ionized Ca, hyperphosphate- mia, decreased serum level of PTH, bilateral microthlithiasis, normal ocular fundus and anterior segment, normal EEG, oral candidiasis.

Treatment: Calcium gluconicum and Tachystin, Dactarin oral gel in both ca- ses. Hydrocortison and Cortineff in the boy.

Discussion: Children with hypoparathyroidism isolated or within APS type 2 are rarely seen in pediatric praxis. This may make them difficult to diagno- se and manage, because of common symptoms with more frequent diseases. Children with APS presented with a single disorder (as hypocalcaemia) have to be followed closely, because of a possibility of appearance of another auto- immune disease.

**R-20 Read by Title**

Evaluation of endocrine late effects in children and adolescents survivors of cancer treatment

Hilton Kuperman1; Ana Cristina Fraga Moreira1; Claudiene Battisti2, Ana Lúcia Beltrai Corrachione1; Vicente Odono Filho1; Durval Damiani1
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Background: Patients who have been treated for oncologic diseases may have severe and sometimes irreversible late effects. Endocrine disturbances have been reported in 20% to 50% of these survivors.

Objective: Evaluation of main endocrine late effects in cancer survivors.

Patients and Methods: 73 patients (41F) were followed since 09/2003. Age at cancer diagnosis was 3.8 years (median: 3.0 years; 0.1 to 14.0 y). Mean age at first consultation to endocrine evaluation was 12.7 years (2.0 to 27.0 y). Mean interval between diagnosis and first endocrine evaluation was 8.4 years (0.7 to 21.4 y). Radiotherapy was applied in 67.5% of them. Endocrine disturbances have been reported in 20% to 50% of these survivors.

Results: 73 patients (41F) were followed since 09/2003. Age at cancer diagnosis was 3.8 years (median: 3.0 years; 0.1 to 14.0 y). Mean age at first consultation to endocrine evaluation was 12.7 years (2.0 to 27.0 y). Mean interval between diagnosis and first endocrine evaluation was 8.4 years (0.7 to 21.4 y). Radiotherapy was applied in 67.5% of them. Endocrine evaluation included tests for GH deficiency, precocious or late puberty, ad- renal and thyroid alterations, metabolic syndrome, diabetes insipidus when necessary.

Results: Acute Lymphocitc Leukemia was the most frequent diagnosis (33.8%), followed by Hodgkin Lymphoma (12.1%) and Central Nervous Sy- stem Tumors (8.1%).

After treatment, 24 patients (40 %) presented short stature. Eight (41.3 %) out of these patients had GH deficiency and were under treatment. 16 patients
with short stature (67%) were submitted to radiotherapy. Obesity was present in 33.8%. Precocious was observed in 15.5%, and were under LHRH analog treatment. Thyroid deficiency occurred in 7 patients (9%). Adrenal insufficiency and post-radiotherapy thyroid nodules was observed in 2.7%.

Diabetes insipidus was detected in all three patients with Histiocytosis X.

Conclusion: Cancer survivors patients should be early and regularly follow up to possibly detect endocrine alterations, so an improvement in their quality of life can be achieved.

R-21 Read by Title
Assessment of prevalence of microalbuminuria in patient with Diabetes Mellitus type 1
Zahra Razavi
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Background and objective: Diabetic nephropathy is a serious complication of type 1 diabetes. It is one of the known causes of end stage of renal disease in United States. About 50% of mortality in diabetic patients is due to hypertension. According to different studies, microalbuminuria is an important prognostic factor for end stage of renal disease. This study performed to assess the prevalence of microalbuminuria type 1 diabetic patients visited in Pediatric Metabolic Disease Clinic in Hamadan in 2006.

Materials and methods: Diabetic patients visited in Pediatric endocrine Clinic under went assessment in our study. Variable data such as age, sex, the age of patient, disease period, patient’s puberty stage dose of insulin and time of insulin usage in one day and blood pressure of patients’ were obtained according to patients’ history and their physical examination. 24h urine samples of patients were assessed for detection of urine protein and creatinin and also microalbuminuria by of means of immunoturbidimetry method.

Result: In this study 105 patients were evaluated. 56 patients were female and 49 were male. Mean age of patients was 13.3±5.5 years and their average period of disease was 5.2±4.1 years. Fifteen cases (14.3%) had microalbuminuria and just one case had overt proteinuria. Blood pressure was normal in 95.5% of patients while in patients with microalbuminuria 73.3% of them had hypertension. Prevalence of microalbuminuria was more than patients taking less amount of insulin according to body weight. We detected no case of microalbuminuria before the age of puberty. There was no relation between microalbuminuria and HBa1C.

Conclusion: In our study the prevalence of microalbuminuria in diabetic patients was significant and increased by increasing the period of disease, blood pressure and puberty stage and by decreasing insulin dose. So screening of patients for early detection and treatment of microalbuminuria in puberty age and after that seems important. key words: diabetes mellitus ; nephropathy in HV. In addition all patients changing to the electronic device showed a HV > 4 cm/y post changeover, compared to only 4 (50%) in the other group. Our initial data indicates that patients changing over to an electronic GH device show improved height velocity, indicating improved compliance, compared to those changing between other devices.

R-23 Read by Title
Cranioopharyngioma in childhood
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The symptoms of cranioopharyngioma (C) are characterized by manifestations of intracranial hypertension, visual impairment and endocrine deficits. Complications of the tumor and its treatment involve not only hormonal-neurological-visual but also hypothalamic function with obesity, hyperphagia, hyperlipidemia.

Subjects: nine children with diagnosis of C evaluated in our hospital between 1990 and 2007 with a prevalence in male (M:F=6:3). Mean age at diagnosis was 8 ys (range 2.7-15 ys).

Symptoms at Diagnosis: visual impairment 55%, manifestations of intracranial hypertension 55%, growth impairment 44%, headache 33%, behaviour disturbances 22%, obesity 22%, deficit VI cranial nerve 22%, hyperphagia 11%. Therapeutic option was radical surgery in all patients. Endocrine deficits and sequelae after surgery: diabetes insipidus (88%), GH deficiency (88%), ACTH deficiency (88%), TSH deficiency (88%), GnRH deficiency (55%), dyslipidemia (44%), insulin resistance (11%), hyperprolactinemia (11%), anemia (22%), visual impairment (66%), convulsions (33%). All patients showed important catch-up weight after surgery, but only two patients (22%) showed severe obesity (BMI≥2SDS), the same with pathologic BMI before treatment. GH therapy was begun in eight patients with mean height gain of 1.8 SDS (mean height SDS: at diagnosis -2.1, after GH -0.3). Recurrence was detected in 2 patient (22%).

Conclusions: the clinical picture of C at diagnosis is often dominated by manifestations of intracranial hypertension and visual impairment, with growth delay as main endocrine disturbance, while complications after surgery are characterized by multiple pituitary hormone deficiency. There is a good response at GH treatment with an optimal height gain. Obesity after surgery is more frequent in patients with elevated BMI at diagnosis or hypothalamic involvement, however worsens after operation. So it’s very important at the time of diagnosis educate the child and his family to maintain an appropriate weight control with a correct diet and physical exercise to prevent metabolic syndrome.

R-24 Read by Title
Treatment with growth hormone and rIGF-1 in a case of Russell silver syndrome with Immune mediated diabetes (IMD)
Chickalaiar Vilay1; Somashekar Rachaiath1; Sunil Sinha1; Svetlana Ten1
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Russell Silver Syndrome (RSS) is a known case of short stature that can be improved with Growth Hormone(GH) treatment. We are reporting for the first time, an experience of the combination of rIGF-1 and GH treatment in Russell Silver Syndrome with Immune Mediated Diabetes. Patient was diagnosed with RSS at the age of 1 year and 7 months. Birth history was significant for premature twin delivery at 34 weeks of gestation & SGA. She has triangular face, clinodactyly, under growth of the left side of the body when compared with the normal right side. She has G-tube feeding because of PTT and severe reflux. At 2 yrs of age she was started on GH treatment at the dose of 0.35 mg/kg/week and increased to 0.5 mg/kg/week at 3 yrs of age. She has been receiving Pediasure 8 cans a day through GT tube. Her baseline Ht SDS was -2.5SDS that improved to -1.22 SDS on GH treatment. GH therapy was begun in eight patients with mean height gain of 1.8 SDS: at diagnosis -2.1, after GH -0.3. Recurrence was detected in 2 patient (22%).

Conclusions: the clinical picture of C at diagnosis is often dominated by manifestations of intracranial hypertension and visual impairment, with growth delay as main endocrine disturbance, while complications after surgery are characterized by multiple pituitary hormone deficiency. There is a good response at GH treatment with an optimal height gain. Obesity after surgery is more frequent in patients with elevated BMI at diagnosis or hypothalamic involvement, however worsens after operation. So it’s very important at the time of diagnosis educate the child and his family to maintain an appropriate weight control with a correct diet and physical exercise to prevent metabolic syndrome.
developed IMD at 3 yrs of age (confirmed by positive gad ab) and treated with insulin 0.3 unit/kg/day through insulin pump. However, her insulin requirement did not increase after combination therapy was started. Patient tolerated therapy well, no complications or complains, her last HbA1c was 6.1 %.

Combination therapy of GH and rIGF-1 can be safe and beneficial in patients with RSS. Even such complicated case with RSS and IMD proved to respond well with great improvement in growth velocity without deteriorating the diabetes control.

**R-25 Read by Title**

**Visual hallucinations following night-time hypoglycaemia in a 4-year old girl with type 1 diabetes**

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**Background:** Visual hallucinations in association with prolonged hypoglycaemia have not been reported in children with type 1 diabetes. In general, hypoglycaemia elicits autonomic responses and neuroglycopenic symptoms. Transient focal neurological deficits (e.g. diplopia) occur occasionally during hypoglycaemia.

**Case Report:** A 4-year old girl with type 1 diabetes presented with visual hallucinations to our outpatient clinic. The girl saw insects crawling over her body and on the floor and asked her parents repeatedly to remove the insects. Parents reported on hypoglycaemic episodes the day before and on the morning of presentation. Blood glucose level at bedtime was 45 mg/dL (2.5 mmol/L), therefore the girl had additional carbohydrates, but on the following morning blood glucose level again was 33 mg/dL (1.8 mmol/L). Parents reported that the girl was agitated and took oral carbohydrates immediately. Half an hour later the girl started having visual hallucinations, but reacted adequately. At presentation in our outpatient clinic blood glucose level was 398 mg/dL (22.1 mmol/L). No fever or other symptoms were present. Physical and neurological examination was normal. Past medical history was unremarkable, diagnosis of type 1 diabetes was made one year ago. Up to now there were no severe hypoglycaemic events with unconsciousness or seizures. HbA1c in the past was between 6.9 and 7.4%. Electrolytes and thyroid function was normal and drug screening was negative. Laboratory evaluation revealed no metabolic defects. Electroencephalogram was normal. Twelve hours after the visual hallucinations started the girl stopped reporting on visual symptoms.

**Conclusions:** This is the first report on hypoglycaemia-associated visual hallucinations in a child with type 1 diabetes. Especially in young children prolonged or recurrent hypoglycaemia episodes possibly exert various effects on neuropsychological performance.

**R-26 Read by Title**

**Early-onset gonadoblastoma in a girl with 46,XX, i dic(Y) karyotype**

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Y chromosome-bearing gonadal dysgenesis is a well-known risk factor for gonadoblastoma. We report a case of early-onset gonadoblastoma in a girl with 46,XX, i dic(Y)(q10) karyotype. A newborn presented at birth with some dysmorphic features (mild lower limb micromelia, foot and hand skin redundancy). External genitalia were female, of normal appearance. Family history, pregnancy, delivery and neonatal period were unremarkable. Karyotype, performed for suspected Turner syndrome, revealed 46,XX,i dic(Y)(q10) chromosome pattern. Search for SRY was negative. Pelvic ultrasound scan showed the presence of uterus with infantile morphology, whereas gonads were not detected. During follow-up, growth and psychomotor development were normal. FSH progressively increased (32.1 IU/L at the age of 1 year). At the age of 2 years, laparoscopic gonadectomy was performed. Histology showed multiple foci of gonadoblastoma in both gonads. Search for secondary localizations of gonadoblastoma was negative. Short-term follow-up (the child is now 2.4 years old) has been uneventful. Gonadal dysgenesis may be completely asymptomatic until the expected age of puberty. In our case karyotype was performed at birth because of mild features of Turner syndrome. The risk of gonadoblastoma is thought to be approximately 25-70% in Y-bearing dysgenetic gonads, and has been linked to the presence of multiple copies of TSPY gene throughout Y chromosome. In this condition gonadoblastoma has been described in patients as young as 4 years old. Prophylactic gonadectomy is recommended in such patients. Optimal age of gonadectomy is not well established, as most cases are diagnosed in pubertal age. Our case shows that development of gonadoblastoma in this condition may start very early in life. We suggest that prophylactic gonadectomy be performed as soon as diagnosis of gonadal dysgenesis is made.
and metabolic control; to establish average insulin doses of different ages and sexes and to present them in the form of figures - percentile tables.

**Methods:** 100 examinations (55 f and 45 m), ages 2-18 analysed at the Children’s University Hospital in Belgrade, from 1994 to 2002. All achieved a satisfactory metabolic control of diabetes after the period of the remission of the disease; 80% conventional insulin therapy (CT), and 20% intensive therapy (IIT), using humane insulins.

**Results:** Data analysis - insulin dose at ages 3-9 is 0.8 IU/kg/24h in both sexes and that from the age of 10 the need for insulin considerably increases, with metabolic control deteriorating at the same time (HbA1c 8.56 vs 9.23%). Insulin needs are the greatest during adolescence, f 1.20 IU/kg/24h. The examinees IIT achieved a better metabolic control in comparison to their peers on CT (8.84 vs 9.40%).

**Conclusion:** The ranges of insulin doses show that every child needs an individual approach and estimate of insulin needs. Daily insulin needs grow with chronological age (0.8 before adolescence and 1.16 IU/kg/24h in adolescence) and f get greater insulin doses than m, especially during adolescence. Insulin needs in percentiles (P5 – P95) and presented in the form of figures enable simple visualization of the range of insulin doses at different ages (figures 2 and 3). There is a considerable deterioration of metabolic control during adolescence. (HbA1c 9.23%), especially in girls (9.45%). The IIT is combined with greater insulin needs and lower values of HbA1c.

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**R-28 Read by Title**

**Children and adolescents with obesity and the metabolic syndrome have high circulating cortisol levels**

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**Objectives:** The aim of this study was to investigate the relationship between the varying degrees of obesity and blood glucocorticoid levels in obese children and adolescents with and without metabolic syndrome features.

**Methods:** We studied 241 obese children and adolescents aged between 2 and 17.6 years; 127 boys and 114 girls. All children underwent an oral glucose tolerance test. Measurements included blood pressure, cortisol, ACTH, and lipid profiles. The diagnosis of metabolic syndrome was defined according to the criteria adapted from World Health Organisation and National Cholesterol Education Program Adult Treatment Panel-III guidelines.

**Results:** Blood cortisol and ACTH levels were higher in patients with MS than without MS (p = 0.02)

<table>
<thead>
<tr>
<th>Variable</th>
<th>MS (-) (n=135)</th>
<th>MS (+) (n=106)</th>
<th>Total (n=241)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH (ng/L)</td>
<td>24.3±15.99</td>
<td>29.1±18.10</td>
<td>26.5±17.10</td>
<td>0.042</td>
</tr>
<tr>
<td>Cortisol (µg/dl)</td>
<td>11.9±4.87</td>
<td>13.6±6.23</td>
<td>12.6±5.56</td>
<td>0.02</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>92.8±43.56</td>
<td>151.0±66.53</td>
<td>118.4±61.94</td>
<td>0.001</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>94.2±27.538</td>
<td>98.2±31.36</td>
<td>96.0±29.29</td>
<td>NS</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>164.2±33.30</td>
<td>173.3±36.06</td>
<td>168.2±34.76</td>
<td>0.043</td>
</tr>
<tr>
<td>Fasting blood glucose (mg/dl)</td>
<td>85.9±7.61</td>
<td>89.0±12.04</td>
<td>87.3±18.88</td>
<td>0.008</td>
</tr>
<tr>
<td>Fasting blood insulin (mIU/L)</td>
<td>15.7±8.10</td>
<td>23.3±10.59</td>
<td>19.1±11.12</td>
<td>0.001</td>
</tr>
</tbody>
</table>

ACTH levels increased with weight (r = 0.13, p = 0.02), systolic blood pressure (r = 0.21, p = 0.002), diastolic blood pressure (r = 0.17, p = 0.01), fasting glucose (r = 0.17, p = 0.01). Cortisol production was only correlated with systolic blood pressure (r = 0.12, p = 0.05). Table 01.

**Conclusions:** Results from the present study indicates that there may be a link between cortisol production and the metabolic syndrome in obese children and adolescents.

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**R-29 Read by Title**

**Isolated cryptorchidism revealing the WT1 gene mutation and a bilateral nephroblastoma**

Audrey Cartault1; Pascal Philibert2; Sofia Mouttalib3; Françoise Paris4; Stéphane Decramer5; Jean Pierre Salles1; Charles Sultani2; Catherine Pienkowski3

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Mutations of the Wilms tumor suppressor gene (WT1) is characterized by both various disorders of sex development in XY males, and a high risk of Wilms tumor or glomerulopathy. We report an isolated cryptorchidism with bilateral nephroblastoma in a boy 5 months old. This patient was born at term with bilateral cryptorchidism. He had no consanguineous parents nor familial sexual or renal anomaly. Genital phenotype noted a well masculinized development without hypospadias nor micropenis (size 35 x 15 mm). Karyotype was 46 XY in peripheral blood. Hormonal status was in normal range: testosterone level at 27 ng/dl, AMH 34 ng/ml, Inhibine 150 pg/ml, LH 1 and FSH 3 MU/l. Biosynthetic HCG test (1500 IU per injection at Day 1, 3, 6 and control level at day 7) noted a normal response of testosterone at 450 ng/dl and so confirmed the presence of functional gonad. Ultrasonography found only one gonadal structure in right inguinal area and noted renal abnormalities. The renal biology was normal, microalbuminuria was negative. 2 months later he presented a palpable left lumbar mass and an arterial hypertension to 18/11 Hz. Abdominal TDM highlighted a hypervascularized mass (11cm) in the left kidney with compression of the renal artery and 1 nodule of the lower pole of the right kidney (diameter 10mm). WT1 gene sequencing identified a heterozygous mutation in exon 6 (pTyr 271 stop) described in 1995. This bilateral nephroblastoma was scored stage 1 was not sensible to conventional chemotherapy and we decided to carry out a left nephrectomy.

**Conclusion:** In this original observation , the codon stop mutation preserves the renal structure but this mutation has been changed by another one in 2005. The WT1 gene sequence suggests that a single mutation of WT1 gene is not responsible for the bilateral nephroblastoma.

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**R-30 Read by Title**

**Multiple organ anomalies in an infant born to mother with poor glycaemic control**

Hakan Donenya1; Hasim Ogun1; Nuran Kucuk2; Mehmet Karacar2; Mecl Kantaro2

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Type 2 DM has a worse pregnancy outcome than general pregnant population. Some studies have found higher rates of congenital malformations in pregnancies complicated by type 2 DM than in those with type 1 DM. The most common malformations are cardiac disorders followed by musculoskeletal abnormalities. We present multiple organ malformations in an infant born to mother with type 2 DM. A 33-day-old male infant was referred to our clinic because of inadequate growth and feeding. On physical examination, the patient’s height, weight, and head circumference were 51 cm (25-50.P.), 2100 g (< 3.P.), and 36 cm (3.P.), respectively. He had triangular face appearance, low set ears, patient’s height, weight, and head circumference were 51 cm (25-50.P.), 2100 g (< 3.P.), and 36 cm (3.P.), respectively. He had triangular face appearance, low set ears, flat nasal bridge, bilateral hypoplasia of nasolabial fold, saddle nose, and short neck. He also had thoracic deformities, syndactyly, omphalocele, and a sirenomelic limb. On abdominal ultrasonography, the patient was found to have a single umbilical artery, and arteria carotis communis originated from truncus brachiocephalicus dexter. Transfontanel ultrasonography revealed flimsy corpus callosum. Renal ultrasonography showed horseshoe shaped kidney. Chromosomal analysis showed a normal male karyotype 46, XY. In conclusion, the poorer glycaemic
PWS is a genetic disorder characterized by hypothalamic dysregulations responsible for many clinical features and endocrine deficiencies. It has been recently hypothesized how PWS children could be at risk of sudden death during stressful conditions because of a Central Adrenal Insufficiency (CAI). However, to date adrenal insufficiency due to Congenital Adrenal Hyperplasia (CAH) has never been reported in PWS. CAH is inherited defects of cortisol biosynthesis. More than 90% of CAH are caused by 21-hydroxylase deficiency (21-OHD), found in 1:15 000 live births. “Non-classic”, or late-onset 21-OHD, detected up to 1:100 in certain populations, does not manifest with neonatal genital ambiguity; rather, it can present later in childhood with signs of androgen excess (premature pubarche, acne and accelerated bone age). We report a PWS boy with premature pubarche who was diagnosed to be affected by NCAH. V.T. is a 8,5 y.o. PWS boy, on growth hormone (0,14 mg/Kg/week) since 4 years, who presented with premature pubarche and fast advancement of bone age (B.A.velocity: +2 years in the last eleven months). As before the age of 9 in males the presence of pubic hair can be the first sign of a gonadal or adrenal disease, adrenal short stimulation test with Synacthen® (0,25 mg iv) was performed. Late onset type CAH was identified (basal 17OHP: 6 ng/ml and stimulated 135 ng/ml). Besides, low blood and urine cortisol were detected. NCAH is usually not characterized by cortisol insufficiency and patients do not need glucocorticoid administration unless symptoms and/or clinical manifestations: the boy was though started on glucocorticoid therapy both because of bone age advancement, compromising final height, and the evidence of a mild adrenal insufficiency. We recommend to evaluate adrenal function in all PWS children presenting with not only cortisol insufficiency symptoms but also androgen excess signs.

The increased current use of prenatal testing makes possible to diagnose precociously different chromosomal abnormalities related to the Disorders of Sex Development (DSD). Prenatal diagnosis, clinical and diagnostic management and following genetic advice of a fetus with 46XY and discordant ultrasound (US) imaging of external genitalia are arising problems. 17β-hydroxy-steroid-dehydrogenase-3 (17BHD3) deficiency is a rare autosomal recessive disorder of sex differentiation with impaired testicular conversion of androstenedione (A) to testosterone (T); it is often clinically indistinguishable from androgen insensitivity syndrome (AIS), even if it is estimated 0.65 times the incidence of AIS. We describe the case of a mother who underwent amniocentesis during pregnancy because of her age. The fetus had normal male karyotype 46XY, discordant with the US features of external genitalia. Prenatal medical analyses were negative for genes coding 5α-reductase enzyme (SRD5A2) and androgen receptor (AR). At birth normal female external genitalia were observed; on US imaging no uterus and ovaries were found, gonads in inguinal position with US features of testicles, a normal aspect of adrenal gland and a short blind-ended vagina were observed. The karyotype was confirmed 46XY and the hormonal investigation suggested the diagnosis of AIS; female sex was assigned to the newborn. At 4th month of life, the baby was reevaluated and a kCG test showed an increased A/T ratio, suggesting a 17BHD3 deficiency. ACTH test showed normal adrenal function. The molecular analysis of HSD17B3 gene confirmed the diagnosis. 46XY DSD comprises a heterogeneous group of conditions in which the same clinical phenotype is due to different pathogenetic mechanisms. The increasing number of prenatal testing has made possible to identify precociously clinical conditions with 46XY and female phenotype, which have raised problems of prenatal diagnosis and genetic advice.
with declared female sex before diagnosis at the age of 1 year was reared as female. She had unpalpable gonads and her stimulated testosterone was 15.7 nmol/l. Other four patients with one palpable gonad and stimulated testosterone levels between 8.9 and 29.6 nmol/l were reared as male. Testosterone treatment prescribed to the boys showed good penile size response. Laparoscopic gonadal biopsy, gonadectomy or orchidopexy were performed in the first year of life. Histological studies showed presence of rare germ cells surrounded by embryonic sex cords in the streak portion of gonads. Germ cells were C-kit positive in 2 and PLAP positive in 4 patients. FOX L.2 expression was detected in 4 streak gonads, AMH- in none. Appropriate genital surgery was performed in the second year of life in 4 patients.

**Conclusion:** High testosterone after HCG stimulation and good response to testosterone treatment in 46,XY partial gonadal dysgenesis could orient towards male sex assignment. This type of sexual ambiguity should be differentiated from true hermaphroditism and other disorders of sexual differentiation. Early gonadal and genital surgery is recommended.

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**R-35 Read by Title**

**A single day program combining evaluation and intervention for overweight and obese children**

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**Objective:** We present the six-month follow-up results of a single day outpatient clinic program for overweight and obese children.

**Patients and Method:** 79 children aged 6 to 17 participated in a program aiming at reducing or stabilizing the z-score BMI. The children were received with their parents in small groups of 4. Following an individual assessment of clinical, biological, nutritional and physical exercise status, the group underwent educational sessions on the same topics. The day ended by an individual synthesis in order to organize the follow-up that was undertaken either by the regular doctor or by the obesity specialist.

**Results:** Height and weight were measured at start and at 6 month follow-up for each child. The z-score BMI evolution was measured and analyzed with the chi 2 test, according to the age, sex, initial BMI metabolic status and the type of follow-up. Three patients were lost to sight. 20% were undertaken by the regular doctor, 56% by the obesity specialist. Unfortunately 24% had no medical follow-up. The participants achieved a reduction (34 children) or stabilization (34 children) in 90% of the cases. Results were independent of the sex, age, initial BMI, metabolic status and type of follow-up.

**Conclusion:** This short intervention program had a positive effect on BMI in overweight and obese children at 6 months, independently of their characteristics and the existence and type of follow-up. However a longer follow up is necessary to assess the durability of the result.

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**R-36 Read by Title**

**Pseudopseudohypoparathyroidism: A case report**

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**Introduction:** Both parathyroid hormone and parathyroid related peptide (PTHrP) effects the target tissues through type 1 receptor. This receptor is connected to an adenylate cyclase enzyme system. Hypocalcemia and hyperphosphataemia in case of normal renal functions are biochemical results of hypoparathyroidism. Pseudohypoparathyroidism (PHP) is a heterogeneous group of disease which occurs as a result of target-organ parathormone resistance. Although biochemical changes look like hypoparathyroidism, parathormone levels are either normal or higher than normal. Gs alpha deficiency is known to be responsible from Albright’s Hereditary Osteodistrophy (AHO) which can be seen in PHP type 1a, PHP type 1c and pseudo-PHP. The main characteristics of AHO are obesity, mild mental retardation, short stature, subcutaneous ossification and brachydactly of especially IVth metacarpal bone. Here, we report a patient with AHO phenotype having pseudo-PHP.

**Case Report:** HO, a 15-year old boy, was presented to us with short stature and morbid obesity. On physical examination, his weight was 92 kg (>95 percentile), his height was 153 cm (<5 percentile), BMI was 43 kg/m² (>95 percentile), relative weight was 200% and waist to hip ratio was 1.53. There was no achondroplasia characteristics. Fourth metacarpal bones on both hands were noted as short. His pubertal stage was Tanner III to IV. He had a mild mental retardation with a motor speech deficiency. Detailed ophthalmologic examination was also normal. Thyroid gland was non-palpable. On laboratory examination, complete blood count; serum calcium, phosphate, alkaline phosphatase, PTH, prolactin, FSH, and LH levels; thyroid function tests and OGTT were all normal. There was a mild insulin resistance with a HOMA-IR value of 4.35. Cranial CT was also normal. Since he had AHO phenotype without any hormone resistance including PTH resistance he was diagnosed as pseudoPHP and a specific genetic analysis was planned to confirm the diagnosis.

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**R-37 Read by Title**

**Neurofibromatosis-1 associated with turner syndrome and klinefelter syndrome**

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**Background:** Neurofibromatosis is an autosomal dominant disorder characterized by cafe-au-lait spots and fibromatoses tumors of the skin. Turner’ syndrome is a sex chromosome disorder occurring in 1 in 2,500 female births. Klinefelter’s syndrome is one of the most severe genetic diseases. There is an extra sex chromosome X or Y. The possibility of Klinefelter Syndrome is 1 in every 1000 males.

**Aim:** In this paper we report overlap neurofibromatosis-1 with Turner syndrome and Klinefelter syndrome.

**Case 1:** The patient presented with short stature at 16 years old. Physical examination, her height: 133cm (SDS-3.57), weight: 36kg (SDS-2.94), and her bone age: 14 years. A number of cafe-au-lait macules and axillary’s freckling were observed on her body. Her breasts were at Tanner stage 2. She had webbing of the neck, a low posterior hairline, small mandible, high arched palate, widely spaced nipples and cubitus valgus. Her spine showed a right thoracic curve. The rest of the clinical examination was negative. The magnetic resonance showed 5mm hyperintens nodular lesion where right postero-lateral area of mesencephalon.

**Case 2:** He suffered hyperpigmentation stains on his body. He’s 15 years old. Physical examination, height: 165.5cm (25-50p), weight: 45.5kg (10-25p). He had gynecomastia, a number of cafe-au-lait macules and axillary freckling. His pubic hair was female-like. His penis was normal and both testicles volume were approximately 2 ml. The rest of the clinical examination was negative. Both of them had Lisch nodules in eyes. Karyotype analysis of the patients was 45.XO and 47.XXY respectively.

**Conclusions:** There is a well-known association between neurofibromatosis-1 and Noonan syndrome-like manifestations but no report with Klinefelter’s syndrome. All of them are common genetically disorders. Thus these disorders might be overlapping a patient. Due to on these cases, we emphasise which each patient with turner like symptoms or Klinefelter’s like syndrome might be carefully examined for cafe-au-lait macules.

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**R-38 Read by Title**

**Determination of the relationship between final height and BMI and mid-parental height in high school students, 16-17 yr-old in 2007**

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The main purpose of child's life is global development and growth for convert to active and healthy human. The final height is an important index of normal growth. There are many factors (genetic and environmental) can influence final height. The purpose of this study is the determination of relationship
between final height with body mass index (BMI) and mid-parental height in high school students (16-17 y old). This cross-sectional study was conducted on 500 healthy high school students (190 boys and 310 girls). The samples were collected on the basis of multi stage probability sampling. The information was extracted with measure of height and weight interrelation of height with BMI and mid-parental height. In order to study of data the regression model and one sample t-test was used. The data were collected using a questionnaire based on the special goal of the study. The results showed that the mean of height was 172.8 in boys and 158.2 in girls. The mean of height of students were significantly less than NCHS charts (p. value < 0.05). There are significant statistical relation between the final height and mid-parental height (p. value < 0.03). It was a positive correlation between final height and BMI. The difference of students’ height with NCHS charts may be due to different race and environmental factors. We can use mid-parental height for determining of target height. Promotion of normal BMI could be increased final height.

R-39 Read by Title
Androgen secreting adrenocortical tumor:
Case report
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Androgen secreting adrenocortical tumors are extremely rare in childhood. Experience with these uncommon tumors is limited. We report a two year old girl presenting with deepening of the voice, acceleration of linear growth, acne, Tanner stage III pubic hair and clitoral enlargement (3.5x1.5cm) of one week of left adrenalectomy. During the preparation of this report, the histological diagnosis was not established yet. Differentiation between benign and malignant tumors by histological criteria often is not possible. Although certain histological features suggest malignancy, such as the presence of numerous mitoses with abnormal forms, widespread necrosis, and broad fibrous bands these features can also be found in some benign tumors. The prognostic significance of tumor size, weight, and histological grade are still unclear. Long- term follow up is mandatory because of the uncertainty in classification of adrenocortical tumors.

R-40 Read by Title
A 12 years old boy with Prader-Willi syndrome and early onset diabetic nephropathy
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The Prader-Willi syndrome (PWS) is characterized by diminished fetal activity, obesity, muscular hypotonia, mental retardation, short stature, hypogonadotropic hypogonadism, and small hands and feet. It can be considered to be an autosomal dominant disorder and is caused by deletion or disruption of a gene. Several genes on the proximal long arm of the paternal chromosome 15 or maternal uniparental disomy 15. Diabetes mellitus occurs in up to 14% of patients with PWS and the incidence of abnormal glucose tolerance increases after 15 years. It has been assumed that the etiology for this increased rate of type 2 diabetes is related to the morbidity and concomitant insulin resistance, but this remains controversial. Patients with PWS present lower insulin resistance and a dissociation between beta-cell secretion and the degree of obesity. Nephropathy can occur rarely. A 13 years old boy suffe-ring from obesity consulted on our department. His prenatal and natal history were normal. We learned that he had hypotonia at infancy. In his physical examination we determined that he had short stature, obesity, severe mental retardation, narrowing of the temples, almond-shaped eyes, a thin upper lip, bilaterally cryptorchidism, microopenis, hypopoten atrphy, small hands and feet. Laboratory examination revealed chromosome 15q11 microdeletion, fasting hyperglycemia, macroalbuminuria, hypogonadotropic hypogonadism. Autoantibodies for the pancreas were not detected. Hba1c level was 12.5 %. Fasting and post-prandial C-peptid levels were 2.3 and 4.9 ng/dl, respectively. Fasting, and post oral glucose loading insulin levels were 21.5 and 66.2 µIU/ml, respectively. We started combined insulin and metformin treatment. No other etiology for proteinuria except diabetes nephropathy was determined. The case was accepted to be a PWS with diabetes mellitus accompanying early onset diabetic nephropathy. We added an ACE inhibitor (Enalapril) to his treatment.

R-41 Read by Title
Iatrogenic Cushing syndrome due to topical steroid administration in an infant
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Topical therapy with glucocorticoids is used commonly in chronic dermatoses. Iatrogenic Cushing syndrome may occur after long use (and abuse) of a topical corticosteroid. We report an infant with Cushing syndrome caused by overuse of topical corticosteroid therapy for diaper dermatitis. Case A 3-month-old boy was brought to hospital with a 1 month history of accelerated weight gain and change in appearance. He was the first child of an unrelated couple, born after an uneventful pregnancy and had been breastfed since birth. The infant was normal up to the age of 2 months when he developed skin lesion on his genitral region. His primary physician prescribed clobetasol 17-propionate 0.05 % (dervomate cream 0.05 % 25 g) cream two times daily. Her mother reported using clobetasol propionate ointment two to three times for 1 months. On physical examination, her weight was 6300 g (75 centile), height 59 cm (50-75 centile) and head circumference was 39 cm (10-25 centile). He had generalized obesity with moon face, fat deposition on neck, lanugo-like hair on the forehead as well as multiple telangiectasias on the cheeks. His blood pressure was normal. There was diaper dermatitis. The rest of the physical examination was unremarkable. As we thought that he might be iatrogenic Cushing syndrome due to the application of this topical steroid, we stopped the therapy and performed laboratory studies. Laboratory examination revealed hypercholesterolemia (255mg/dl), elevation in liver enzymes (ALT 57 U/L, ASH 82 U/L, GGT 198 U/L), in addition low early morning cortisol (1µg/dl) and suppressed ACTH (5pg/ml). Low-dose ACTH stimulating test revealed adrenocorticotropin insensitivity (peak cortisol was 12.9 µg/dl). In conclusion misuse or extensive use of topical steroids can cause Cushing syndrome. Physicians should keep extensive use of topical corticosteroid in mind when a child presents with cushingoid features.

R-42 Read by Title
High catecholamine and renin levels in a patient with malignant hypertension in neonatal period: Case report and review of literature
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Severe hypertension is rare in neonatal period. Literature review revealed limited information about diagnostic approach, interpretation and treatment in newborn period. This clinical report describes a newborn with malignant hypertension & extremely elevated catecholamines. It focuses on challenges in differential diagnosis, discussion of clinicopathologic features and therapeutic strategies used to manage the refractory hypertension. This is a baby
girl of 38 weeks GA that developed severe hypertension in NICU at day 5 of life. Initial birth history was remarkable for maternal history of prolonged rupture of membranes and GBS positive vaginal cultures, APGAR's of 5, 6 and 9, sepsis workup & antibioticotherapy. Echo revealed poor biventricular function but no co-arctation. Renal sonogram & CT abdomen showed a large cystic mass along the right superior pole of the kidney read as an adrenal hemmorhage. Doppler USG of abdomen revealed blood flow to both kidneys but initial renal scan showed no function in either kidney. Renin, aldosterone and catecholamines were significantly elevated as shown in figure 1. An MBG scan revealed no pheochromocytoma or neuroblastoma. Anti-hypertensive treatment was started with Milrinon and furosemide. Subsequent antihypertensive medications were added due to refractory hypertension: day two of treatment- Esmolol, day 3 - Hyaladrazine dip, day 4 - Nitropresudipide, day 8 - Labelatalol drip, day 9- captopril, day 13- Phenoxbenzamine. Despite the above medical treatment patient's condition continued to deteriorate, & by day of life 18 developed candidal & staphylococcal sepsis and multiorgan failure and expired by day of life 24. Autopsy revealed severe right renal artery atresia & hemorrhagic infarction of the right adrenal gland Of 10 known cases of malignant neonatal hypertension recovered in Medline, 8 survived, 4 with unilateral nephrectomy & 4 with Captopril therapy. This case emphasizes that in neonatal hypertension, integrating the clinical picture, biochemical profile; imaging can pose a diagnostic & therapeutic challenges.

**R-43 Read by Title**

**PROP1 gene analysis in Korean children with hypopituitarism**

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Mutations of the PROP1 gene leads to combined pituitary hormone deficiency, which is characterized by a deficiency of GH, TSH, LH/FSH, PRL and ACTH. We studied for the PROP1 mutations in Korean children with hypopituitarism. The six patients with congenital hypopituitarism were recruited from the Ajou University Hospital, Korea. The pituitary phenotype range from isolated growth hormone deficiency to combined pituitary hormone deficiency. Clinical data, including endocrine and neuroradiological data were obtained from the medical records, and the DNA was collected and screened for mutations within PROP1 using PCR. The PCR product were sequenced directly. Four patients had abnormal pituitary gland in MRI-hypoplastic anterior lobe(n=4), absent posterior lobe(n=1), and ectopic posterior lobe(n=1). In two patients, MRI findings showed normal pituitary gland. Endocrinologically, two patients were isolated growth hormone deficiency. Among the rest patients, two of them were GHD and hypogonadotropic hypogonadism, the other one was GHD and central hypothyroidism, and the last one was GHD, central hypothyroidism, and ACTH deficiency. We did not identify any mutations in the PROP1 gene. However, three known polymorphisms were identified: The 277T>C(Ala94Val) and the associated IVS1+3A>G in exon 1 were found in 33% of patient alleles sequenced (n=12). The 424G>A(Ala142Thr) in exon 3 change was identified in 8% of those sequenced (n=12). These cases represent the previous reports that PROP1 mutations are rare in sporadic cases of CPHD. The low mutation frequency in sporadic cases may be due to other unidentified genes or candidate genes causing this disease. Furthermore, it is necessary to study PROP1 gene and the involved genes in more Korean patients.

**R-45 Read by Title**

**Complete vaginal agenesis in girl with Mayer-Rokitansky-Küster-Hauser syndrome type II**

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Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is characterized by congenital aplasia of the uterus and the upper part (2/3) of the vagina. Complete vaginal agenesis in MRKH syndrome is rarely reported. A 13 3/12 year-old girl had no complaints about her pubertal progression or urinary tract, disease admitted to our clinic for evaluates genital abnormalities. In her physical examination, weight was 33.7 kg (~3 percentiles), height 136.9 cm (~3 percentiles). Height SDS was -2.89. Bone age was 11. Blood pressure was 110/80 mmHg. Abdominal examination revealed a painless pelvic mass. Development of breast was Tanner phase III, pubic hair was Tanner phase II. Axillary hair was present. The perineal examination showed hypoplastic and partially fused labium minor, short introitus and a single opening. There was no gonad or mass within inguinal canal or labium major. Her karyotype analysis revealed no mullerian and gonadal structure associated with right pelvic kidney, and left renal agenesis. Basal and stimulated gonadotrophins and estradiol results of the girl suggested present of the intact ovary. Therefore an exploratory laparoscopy was performed, showing a single pelvic kidney and absence of fallopian tubes, and uterus. Ovaries were found in normal shape and localization. Voiding cystourethrography was normal. Patient had sigmoid vaginoplasty. In conclusion, physicians should be aware of concomitant other anomalies such as renal, skeletal or odiological, when they meet with female with vaginal and uterine agenesis.

**R-44 Read by Title**

**Can growth hormone deficiency be predicted by Arginine test and IGFl levels?**

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**Context:** What if the somatostatin-dependent Arg and the GHRH-dependent insulin, Glu or clonidine GH-stimulation tests diverge? Is it GHD or is it normal?

**Objective:** To characterize children who respond differentially to Arg and Glu

**Methods:** Prepubertal children (n= 85, 34 F/51M) with growth retardation, age 7.0 ± 3.1 years (mean ± SD), had and subnormal response to Arg (GH <10 µg/l) were retested by clonidine or Glu test, tIothyroid functions and a TRH-stimulation test were performed.

**Results:** The group was divided according to the peak GH levels to five groups. Group A-GHD, GH < 5 µg/l during both tests (IGF-1 SDS -1.85 ± 1.31). Group B - partial GHD, Arg GH 5-50 µg/l and Glu GH 5-10 µg/l (IGF-1 SDS -2.56 ± 0.19). Group C - divergent, Arg GH < 5 µg/l and Glu GH >10 µg/l (IGF-1 SDS -0.94 ± 1.41). Group D - divergent, both tests GH 5-10 µg/l (IGF-1 SDS -1.54 ± 1.26). Group E, Arg GH 5-10 µg/l and Glu GH >10 µg/l (IGF-1 SDS -0.86 ± 0.95). The groups were comparable in BMI, FT4 and TSH. IGFI SDS differed among the groups A-B p=0.01, A-C p=0.003, A-E=0.01, B-C, B-D and B-E p=0.001. There was no difference between the groups C-E. IGFBP3 differed among the groups A-D and A-E p<0.03. There was no difference among the groups in TRH-stimulated TSH. Prolactin differed among the groups A-C p<0.01, A-D p=0.006 and A-E p<0.005. GH AUC during Arg test were compared and showed significant differences among the groups. The Receiver Operating Characteristic curve (ROC) curve for AUC GH levels during Arg test was 0.67 and 0.762 for IGFI SDS. AUC Arg GH cutoff of 207 µg/l-min and IGFI SDS cutoff of -2.31 were found to have the best combinedoptimal sensitivity and specificity for GH deficiency.

**Conclusions:** 1. Children with divergent Arg and Glu tests have partial GH (secondary IGF-1) deficiency. 2. The combination of IGFI SDS below a cutoff of -2.31 and Arg GH AUC below a cutoff of 207 predicts a subnormal second test and makes it redundant.
R-46 Read by Title
Case report on heterosexual pseudopuberty praecox due to Sertoli cell hyperplasia
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We present a case of long term observation of a boy with hyperplasia of SER-TOLI cell with testicular enlargement and gynecomastia. A six-year old boy with beginning gynecomastia and a testicular volumes of 25 ml and 20 ml shows high serum levels of estradiol (8.4 pg/ml), normal to 4.0 pg/ml) and normal levels of testosterone (1.53 nmol/l), dihydrotestosterone (0.5 nmol/l), androstendione (0.08 ng/ml) and an extremely high concentration of inhibin B (2350 pg/ml). There is no stimulation of FSH and LH in LH-releasing hormone test. Testicular MRI shows a homogenic testicular tissue. A biopsy suggests a SERTOLI cell hyperplasia with tubular adenoma. After surgical treatment (resection of the half of testes) the inhibin B decreases instantly to normal concentrations. After one year Serum level of estradiol is normalized and LH-releasing hormone stimulates FSH to almost normal values. After four years there is a complete involution of gynecomastia and a normal development of puberty.

R-47 Read by Title
A case of genital ambiguity: Congenital adrenal hyperplasia and/or para-renal tumour?
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Introduction: congenital adrenal hyperplasia (CAH) is the most common cause of ambiguous genitalia. CAH associated with tumours detected at neonatal period are rare. We report the case of a female newborn, admitted at the 5th day of life for ambiguous genitalia and a left para-renal tumour.

Case Report: this female newborn was the 1st child of a healthy, unrelated couple. At birth, clitoral enlargement and labioescrotal fusion (Prader III) were detected; blood pressure was normal.

Laboratory evaluation revealed: ACTH 1819 pg/ml (N: 10-185); cortisol 4.6µg/dl (N 5-25); 17-hydroxyprogesterone 0.2 ng/ml (N 0.1-9.4); testosterone= 1250ng/dl; 11-desoxycortisol= 75ng/ml (N <8); active renin 180,4µm/ l (N 280-473); α-fetoprotein 45160IU/ml (N 1652-34710). The ultrasound showed a solid tumour 22x17mm near the inferior pole of the left kidney; there was a normal uterus. She started hydrocortisone (10mg/m2/day). On the 8th day of life, salt wasting was detected and fludrocortisone (25µg/day) and NaCl supplementation were introduced. At 14th day of life, the surgical resection of the tumour was performed. At 13 months, she developed cushing signs, despite the low hydrocortisone dose. Therefore, fludrocortisone was stopped and the dose of hydrocortisone was futher reduced. Two weeks later, she had an addison crisis. ACTH stimulation test was performed and it confirmed CAH. Therapy with hydrocortisone and fludrocortisone was restarted. The pathologic examination of the tumour revealed a capillary haemangiom. She underwent feminizing genitoplasty at 23 months and now she is 2.5 years old, growing well.

Conclusion: In this patient, we thought the cause of the virilization was the solid tumour and or CAH. The tumour hypothesis proved to be wrong and symptoms are best explained by CAH. This case teaches us to be very carefully with adrenal insufficiency and always excluded CAH.

R-48 Read by Title
Bone metabolism parameters in children with transitory hyperthyroidism
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Scientific Research Institute of Endocrinology, Children, Tashkent, Uzbekistan

Aim: to study bone metabolism parameters in children with transitory hyperthyroidism.

Materials and Methods: we examined 25 newborns from mothers with diffuse toxic goiter (1st group) and 10 newborns from healthy mothers (2nd group). The patients took tirozol during gestation. By the term euthyroid condition was achieved in 91.3% of pregnant women. RIA kits (Immunotech, Czech Republic) were used to measure TSH, T3 and T4 levels. ELISA by Hospitecs kits (Diagnostics S.A., Switzerland) was used to assay phosphoryl and alkaline phosphate, calcium measured by Nypress kits (Diagnostics, Belgium). Bone tissue was assessed by the ultrasound velocity in bone segment by means of “Echoosteometro-E0-02”.

Results: transitory hyperthyroidism was found in 26.1% of the newborns with low TSH (1.57+0.53 mU/l); high T4 (127.8+15.4 mmol/l), to be caused by translacental transfer of active TSH-stimulating mother antibodies. At the age of 3 months mean calcium serum concentration in both groups was 2.31±0.14 mmol/l. Phosphorous reduction in blood was registered in 50%, mean blood level being 1.36±0.20 mmol/l. Ultrasound osteometry showed decrease in ultrasound velocity in mandibular (2063.5±180.0 m/s), claviclar (3055.5±58.5 m/s), ulnar (2300.7±228.9 m/s) and tibial bone (2197.5±160.0 m/s) in both groups of children to be the evidence for the reduced mineral density of bone tissue.

Conclusions: 1. Adequate compensation of diffuse toxic goiter in pregnant women results in birth of healthy newborns in 82.1%, 20.4 % having transitory hyperthyroidism. 2. 40% in group of children with transitory hyperthyroidism had hypocalcemia, hypophosphatemia and osteopenia being observed in 50% and 95%, respectively, indicating formation of pathological Infant’s skeletal alterations in the nearest future.

R-49 Read by Title
Growth and other endocrine outcomes for Thalassemia Major with or without bone marrow transplantation
David Gillis1; Memet Aker2; Shoshona Vilk-Revel5
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Thalassemia major (TM) can be treated by repeated blood transfusions and chelating agents to reduce hemoidersis. However, endocrine consequences such as pituitary insufficiency, hypothyroidism and diabetes occur. Bone marrow transplantation (BMT) can prevent the requirement for blood transfusions and chelating agents but the highly toxic agents utilized for bone mar-

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row ablation also have serious endocrine consequences. We use a busulfan and fludarabine based regimen for myeloablation prior to BMT for TM. We evaluated the endocrine outcome of these patients compared with patients treated at the same time conservatively (i.e. without BMT). Thirteen patients underwent BMT and 14 were treated conservatively. Average ages at latest evaluation in the BMT group and in the non BMT group were 11.4±5.1 and 11.2±5.3 respectively (P=not significant), male to female ratios were 7:6 and 7:7 respectively. Average age at BMT was 6.1±4 years and the time elapsed since BMT at latest evaluation was 5.3±3.9 years. Delta Height SDS (i.e. the difference between measured height SDS and target height SDS by parental height) was -0.15±0.27 for BMT patients and -1.36±0.2 for non-BMT patients (p=0.0016). Hypergonadotropin hypogonadism as evidence for gonadal failure was noted in 3/13 patients in the BMT group and 0/13 in the non-BMT group. Delayed puberty with low gonadotropin levels for age was noted in 3/14 patients in the non-BMT group and 0/13 in the BMT group. For BMT vs. non BMT basal morning cortisol levels were 326±150.0 nmol/l and 231±124.0 nmol/l respectively (p=0.09), average TSH was 2.88±1.89 and 2.33±1.45 respectively and FT4 was 14.3±2.7 and 16.0± 2.8 respectively (p=not significant for both). BMT improves growth but is associated with a high incidence of gonadal failure. The current conservative treatment is based on oral chelating agents and transfusion every 2-3 weeks. Further study regarding growth enhancement therapy for non BMT patients is warranted. The long-term side effects of BMT need to be discussed with patients and family.

R-50 Read by Title
A girl with unusual presentation of thyroid papillary carcinoma
Elena Faleschini; Eva Da Dalt; Stefania Bassanese; Alessia Saccar; Federico Verzegnassi; Giorgio Tonini
IRCCS Burlo Garofolo, Pediatric Dept-Endocrinology Unit, Trieste, Italy

Thyroid carcinoma presentation consists in a single painless solid nodule, firm with surrounding tissue, lymphnode enlargement, hoarseness and dysphagia. A 12 years old girl was admitted to our unit, with the hypothesis of subacute thyroiditis, one month after the painful swelling of the neck, mild fever, tachycardia, lymphadenopathy with reactive aspect. Hystory negative for neck irradiation, familial cancer. Biochemical evaluations showed increase in C-reactive protein, ESR, neutrophil leucocytosis, normal thyroid hormones, positive TPOAbs. Sonography revealed increased left thyroid lobe, with multinodular aspect and presence of enlarged lumphnodes. After antiinflammtory therapy we obtain a slight improvement of all symptoms and normalization of biochemical indexes. No changes of thyroid aspect after repeated sonographies. In order of atypical thyroid imaging with incomplete resolution of symptoms the first FNA didn’t showed De Qurvein cells, the second, focused on surrounding tissue in the right lobe. There are evidences of multinodular papillary carcinoma following subacute thyroiditis or thyroid cancer mimicking it. It is also known that Hashimoto thyroiditis is correlated with papillary carcinoma also in children. We observed an unusual pattern of disease: starting symptoms of subacute thyroiditis in the left lobe with multiple carcinoma-matosis and metastasis of the satellite lymphnodes and surrounding tissues, the presence of Hashimoto thyroiditis in the right lobe unless the normality of sonography and only a slightly increase of TPOab. Our experience suggests to suspect carcinoma in presence of persistent thyroid nodular enlargement, and symptoms of subacute thyroiditis, unless a mild improvement of clinical sign.

R-51 Read by Title
Ambiguous genitalia as a manifestation of cytochrome P450 oxidoreductase deficiency [Antley-Bixler Syndrome]: A case report
Raquel Corripio Collado1; Jacobo Pérez Sánchez1; Ramon Nomás Cuervo2; Elisabeth Gabau Vila2
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The Antley-Bixler syndrome is a rare congenital malformation syndrome characterized by craniosynostosis, midface hypoplasia, and skeletal malformations but may also include congenital heart disease, and kidney or genital anomalies. Cytochrome P450 oxidoreductase (POR) deficiency is a disorder of steroidogenesis with multiple clinical manifestations, the Antley-Bixler syndrome is the worth of them. Newborn presented ambiguous genitalia prenatally diagnosed at 20 weeks’ gestation on ultrasound and confirmed at birth. Aminoccinosis was performed revealing 46, XY karyotype. The baby was born at term, normal height and weight, had “pear shaped” nose, hypoplastic phallus, labioscrotal folds fused at the midline and palpable inguinal gonads. There was poor testosterone response with normal testosterone / dihydrotestosterone ratio to human chorionic gonadotrophin test. Hormone profile showed elevated basal 17-OH progesterone and 17-OH pregnenolone levels and normal androgen levels. The patient had positive clinical response to exogenous testosterone. Next studies demonstrated elevated luteinising hormone levels with normal 7-dehydrocholesterol and low cholesterol and a poor cortisol response to adrenocorticotropic hormone. Apparent decreased activity of 17alpha-hydroxylase, 17,20-lyase, 21-hydroxylase and lanosterol 14alpha-demethylase was suspected. All these enzymes require POR as an electron donor. Hydrocortisone treatment was started. Craniosynostosis was diagnosed after 4 month. DNA encoding POR was sequenced and two heterozygote mutations were found: G539R mutation and a change of amino acid (G80R). Ambiguous genitalia can be the only manifestation of a POR deficiency and it should be analyzed if multiple abnormalities in steroidogenesis are suspected.

R-52 Read by Title
Precocious puberty in a patient with X linked adrenal Hypoplasia congenita due to DAX 1 mutation
Suher Parçac1; Sema Tanrverdi1; Samim Ozen1; Damla Goksen1; Burak Durmaz2; Ferda Ozkiny3
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One of the most common causes of primary adrenal failure is X-linked adrenal hypoplasia congenita. DAX1 gene mutation and deletion causes congenital adrenal failure and adrenal hypoplasia congenita. Hypogonadotropin hypogonadism is the most common disorder accompanying this mutation. A 1.5 month old male patient admitted to the hospital with vomiting. His weight was 3380 g (-2.37 SDS); height 54 cm (- 0.31 SDS) on admission. His physical findings revealed, hyperpigmentation and testis measured 2 ml. Adrenal hypoplasia was determined with computed tomography. The patient was evaluated for a possible mutation in the DAX 1 gene and had identical DAX 1 mutation with Q 155X, causing a stop kodon. He was put on hydrocortisone and fludrocortisone therapy. The mother noticed presence of pubic hair and enlargement of the penis at 7 months of age. His height was 69 cm (-1.5 SDS), penile size was 7 cm. and pubic hair was Tanner stage 2. Tests measured 2 ml bilaterally. Bone age was 3 months. Serum ACTH, dehydroepiandrosterone, 17 hydroxyprogesterone levels were normal. Total testosterone was 7,7 pg/ml. Peak LH and FSH levels in LHRH test were 12 and 3 mil/ml respectively. Presence of pubic hair, enlarged penis, prepubertal stelicular size, nonaccelerated growth velocity, increased plasma levels of free testosterone but pubertal LHRH test, he was diagnosed as central precocious puberty. Are these peak LH levels and clinical findings acceptable with central precocious puberty? Although it has been shown that DAX 1 mutations in humans can promote a dual effect on Leydig cell function characterized by hyperactivity during infancy and childhood causing gonadotropin indepen-
dent precocious puberty in boys; our patient’s clinical and laboratory findings are different from the ones in the literature.

**R-53 Read by Title**

**Growth patterns and growth velocity in congenital adrenal hyperplasia**

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Masshad University of Medical Sciences, Pediatric Endocrinology, Mashhad, Islamic Republic of Iran

**Introduction:** In patients with congenital Adrenal hyperplasia (CAH) adult height is below target height. This may result from growth inhabitation by glucocorticoid treatment or adrenal androgen excess. One important goal in the management or patients is to achieve normal growth.

**Aim:** The objective was to determine weight, height, body mass index (BMI) growth velocity and influences of kind of glucocorticoids.

**Methods:** We performed a cross-sectional retrospective study of 50 children and adolescents with CAH (27 female and 23 male subjects; age 0.3-17.8 years). Who presents in our outpatients department during 1 year. We grouped the patients into salt wasting (SW) and simple virilizing (SV) and 11-hydroxylase deficient groups, as well as according to current metabolic control.

**Results:** The BMI SDS did not differ significantly between children receiving hydrocortisone, prednisolone, or dexamethasone (p=0.9). There was no significant difference in age and BMI Between genders and clinical forms (p=0.3 & for female and p=0.5 for male). Two subjects had BMI over 85 percentile. Mean weight velocity were 3.3±1.6 kg per year, and did not differ significantly between gender, type of medication and clinical forms (p=0.6). Weight SDS were relatively high in subjects receiving dexamethasone (0.82±1.2) in compare to subjects treated with hydrocortisone (-0.2±1.6) (p=0.4). Height velocity was correlated positively with serum levels of 17-OH-progesterone (p=0.04).

**Conclusions:** Treatment of children with CAH requires close observation and individualized approaches to prevent final short stature, and obesity.

**R-54 Read by Title**

**Cushing or pseudo-cushing syndrome: discussion about a pediatric case**

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The differential diagnosis between Cushing syndrome and pseudo-Cushing syndrome is quite difficult. This situation is well known in adults but not in children. We are discussing clinical, biological and radiological aspects about a case of pseudo-Cushing syndrome. A 13 years old boy was referred because of growth failure (loss of 1.5SDS) and severe weight gain (gain +2.5SDS) during puberty (BMI: 28.5 kg/m2: +4SDS). There was no intake of any corticosteroid. Tanner stage was A3, P3, G2. His clinical presentation was Cushing-like: round erythosic face, severe acne, faciotroncular obesity, but rare purple stretch marks. He suffered from strong headaches. The blood pressure was in normal range. His bone age was consistent with his chronologic age. Biological investigations showed normal GH increase with Ornicetil stimulation test (48mU/l), IGF1:342ng/ml, normal TSH and thyroxine level, as well as according to current metabolic control.

The circadian rhythm was lost. The DDA VP stimulation test showed a very significant increase in cortisol (+232%) and ACTH (+539%) level. On the other hand, urinary free cortisol was low (15 nmol/day) against the diagnosis of Cushing syndrome, low dexamethasone suppression test (1 mg at 0h) was normal. The growth velocity was 2.5SDS during puberty (BMI: 28.5 kg/m2: +3SDS) during puberty (BMI: 28.5 kg/m2: +3SDS) during puberty (BMI: 28.5 kg/m2: +3SDS). We propose a validation of diagnosis strategy in children including few criteria: clinical features, urinary free cortisol 3 days, midnight cortisol, low dose dexamethasone suppression test in a first line screening test.

**R-55 Read by Title**

**Autoimmunological course of prediabetes phase in patient with type 1 diabetes high-risk HLA genotype**

Daniel Witkowski1; Joanna Breh-Chruacieli1; Malgorzata Wajda-Cuszlag1; Elzieta Piontek2; Roman Janas2

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The Type 1 Diabetes is the disease in which the combination of HLA system genes and environmental factors lead to autoimmune destruction of the insulin secreting β-cells of the pancreatic islets. The immunological markers of type 1 diabetes (GAD Ab and IA2 Ab levels) were determined for the first time in 10 years old girl because of the type 1 diabetes new-onset in her brother. GAD Ab and IA2 Ab levels were increased in examined girl. The siblings of child who is suffering from diabetes are approximately 5% risk carrier of disease development. The type 1 diabetes high-risk HLA DRB1*03, DRB1*04, DQBI*0201, DQB1*0302, DQA1*0301, DQA1*0501 HLA genotype was found in this girl. Additionally her HLA genotype was identical with her brother HLA system which increased risk factor from 5% up to 16-20%. Prediabetes state in observed patient was monitoring by measurements of: GAD and IA2 autoantibodies levels and insulin/C-Peptide levels during IVGTT. RIA methods were used.

**R-56 Read by Title**

**Primary ovarian failure in 47,XXX female**

E Thisted1; L.P Hansen1; H Mogensen1; J Harri2; K Rasmussen2; T Hertel3

1Hospital of Soenderborg, Paediatrics, Soenderborg, Denmark; 2Hospital of Soenderborg, Gynaecology and Obstetrics, Soenderborg, Denmark; 3Hospital of Soenderborg, Pathology, Soenderborg, Denmark; 4University Hospital of Odense, Clinical Genetics, Odense, Denmark; 5University of Odense, Paediatrics, Odense, Denmark

Hypergonadotropic hypogonadism in adolescents is often seen in Turner syndrome, but seldom in combination with other genetic defects as triple x. An eighteen year old female was referred to the paediatric outpatient clinic because of absent menarche. She was 174 cm tall, her weight was 52.5 kg and the blood pressure 115/75. Pulmonary stenosis was ruled out. Her HbA1c was normal. Type 1 diabetes (GAD Ab and IA2 Ab levels) were determined for the first time in 10 years old girl because of the type 1 diabetes new-onset in her brother. GAD Ab and IA2 Ab levels were increased in examined girl. The siblings of child who is suffering from diabetes are approximately 5% risk carrier of disease development. The type 1 diabetes high-risk HLA DRB1*03, DRB1*04, DQBI*0201, DQB1*0302, DQA1*0301, DQA1*0501 genotype was found in this girl. Additionally her HLA genotype was identical with her brother HLA system which increased risk factor from 5% up to 16-20%. Prediabetes state in observed patient was monitoring by measurements of: GAD and IA2 autoantibodies levels and insulin/C-Peptide levels during IVGTT. RIA methods were used.

**Conclusions:** 1) in prediabetes phase increased insulin/C-peptide secretion disorders were observed 2) increased autoantibodies levels were determined 3) particularly increased IA2 Ab level shortly before the end of prediabetes state was determined.
Evorel patch 25mcg estadiol/24h/3days and within a period of three months she developed breast, tanner stage 3-4 and gained 10 kg in weight, but still no menarche appeared. Her weight was only accelerated with 0.3 cm in this period. Absent menarche and no breast development, but normal pubarche may be a course of premature ovarian failure (POF) reflected by a variety of possible causes including autoimmunity and genetic defects. POF in itself is a very rare condition among young females. In combination with triple X syndrome only few cases are reported in literature. This case emphasizes the need for chromosomal investigation in adolescents with amenorrhea.

It is known that thyroid function may be transiently impaired (Non-Thyroidal Illness Syndrome, NTIS) in systemic severe illnesses. The aim of our study was to evaluate the prevalence of NTIS at diagnosis of type 1 diabetes mellitus in children and adolescents. We examined 86 diabetic patients (mean age 8.15 ± 4.03 yrs) diagnosed in our Centre between 1999 and 2007. Blood samples for the evaluation of thyroid hormones were drawn within the first 6 days since diagnosis in all patients, within the first 12 hours since admittance in 70 patients and before any therapy in 34 patients. T3 levels were significantly lower than controls in all patients, whereas TSH levels were lower only in controls than patients examined immediately after the admission (Table). T3 and T4 values showed a significant negative correlation with the severity of acidosities, NEFA values, and adrenal gland hormones levels (cortisol, renin activity, aldosteron) and a positive correlation with C-peptide levels. Glycemia, HbA1c, and fructosamine values were negatively correlated only with T3 values. All thyroidal parameters normalized within few weeks.

<table>
<thead>
<tr>
<th>At diagnosis of diabetes</th>
<th>At diagnosis of diabetes, and before any therapy</th>
<th>Controls (n. 59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (mcU/ml)</td>
<td>2.28±1.41 (0.21-7.17)</td>
<td>1.76±0.86 (0.21-3.97)</td>
</tr>
<tr>
<td>FT3 (pg/ml)</td>
<td>2.52±0.90 (0.60-5.00)</td>
<td>2.28±1.00 (0.60-4.00)</td>
</tr>
<tr>
<td>FT4 (pg/ml)</td>
<td>11.52±2.70 (5.10-18.50)</td>
<td>11.06±2.86 (5.80-15.70)</td>
</tr>
</tbody>
</table>

* p<0.0001, § p<0.001 vs controls

In conclusion, NTIS is present at onset of diabetes above all when metabolic derangement is severe. In most severe cases, the adaptive picture of "low T3 syndrome" is associated with an impairment of the hypothalamus-pituitary-thyroid axis. The normalization of the metabolic abnormality is spontaneous and rapid. Therefore, if not investigated in the very first hours, it may go unrecognized.

**Purpose:** Turner syndrome (TS) affects a wide spectrum of organ systems to varying degrees which may include cardiovascular, endocrine, renal and hearing defects. These health issues should be addressed in a comprehensive, systematic manner. The study analyzed endocrine problems and associated anomalies in TS patients of adolescent and adulthood.

**Methods:** Fifty-nine TS patients, who reached final adult height, were included into the study. Axiological parameters, endocrine features including thyroid and gonadal functions, the level of hemoglobin A1c and bone mineral density were analyzed. For evaluation of associated anomalies, pure tone audiometry, kidney ultrasonogram, aortic CT or echocardiography were performed.

**Results:** The age of patients was 25.8±6.9 years and final adult height was 148.3±4.3 cm in GH treated group and 147.6±7.8 cm in GH non-treated group. Four patients experienced menarche spontaneously, but secondary amenorrhea and early menopause occurred. Three patients with mosaic karyotype could give birth to a baby. The estrogen replacement therapy was started at 19.1±4.3 years old and there was no patient who had developed breast cancer during this therapy. Thyroid autoantibodies were detected in 25 patients and 11 of them were treated by L-thyroxine. The mean level of hemoglobin A1c was 5.8±1.1% and 5% were diagnosed to type 2 diabetes. Several autoimmune diseases such as SLE, autoimmune hepatitis, and Crohn disease were associated in 3 patients. Thirty-four patients showed osteoporosis lower than -2SD of bone density. Extracorporeal shock wave lithotripsy of renal stone was performed in 1 patient with horseshoe kidney, and cardiac anomalies were newly detected in 3 adult patients.

**Conclusions:** Variable endocrine and cardiovascular anomalies can be associated in TS, and can cause serious complications. Early recognition of diverse medical issues which could be accompanied during the transition period and close monitoring on a regular basis is critical for enhancement of quality of life as well as prevention of serious complications in TS.

**Subject and Methods:** This retrospective study included 18 Tunisian girls aged from 14 to 20 years presenting a PCOS accordingly to the diagnosis criteria of Rotterdam consensus. All patients had a complete clinical examination. Blood samples were collected to determine lipid profile and hormonal status. An oral glucose tolerance test was performed (75 g of glucose) and glucose and insulin levels were measured.

**Results:** Mean age is 17.8±1.9 years and mean duration of hirsutism is 4 years. Familial history of hirsutism is found in 56 % of cases. Spinae norrorea is present in 78 % of cases. The score of Ferriman and Gallway is above 7 in all cases (mean : 20 : - ; range : 7 - 38) and alopecia is found in 7 cases. Obesity is present in 61 % of cases and android obesity in 50 % of patients. Total cho lesterol level is found borderline or high in 35 % of cases. HDL-CT level is found borderline or low in 50 % of cases. Triglycerides are normal in all cases. Oral glucose tolerance test is performed in 13 patients and is normal in 12 cases and diagnoses a diabetes mellitus in one case. Hyperinsulinemia is found in 37 % of patients. Mean HOMA-IR index is 5.6±8.3 (0.74 - 29.38). Plasma total testosterone level is high in 89 % of cases, DHEAS in 17 % and delta4androstenedione in 25 %.

**Conclusion:** PCOS in adolescents is early associated to endocrine and metabolic abnormalities related to hyperinsulinemia and insulinoresistance.
The long arm of the Y chromosome is involved in spermatogenesis and contains genes and gene families critical for germ cell development and differentiation. Deletion of AZF region of Y chromosome is associated with spermatogenic failure and leads to partial or complete spermatogenic arrest. Here we report a case with complete gonadal dysgenesis with deletion of AZF region of Y chromosome. A fourteen years old girl presented to the pediatric endocrinology clinic because of delayed puberty. On examination, external genitalia were female with slight clitoral enlargement. Breasts development was Tanner stage I and she had scanty pubic hair. Pelvic ultrasound showed a hypoplastic uterus, but ovaries were not detected. Karyotype analysis revealed a normal male karyotype (46 XY). LH, FSH levels were high, estradiol and testosterone levels were low. Gonads were found in the pelvis with laparoscopic examination and removal. Gonadal histology was revealed disgenetic ovarian tissue, with no signs of malign transformation. The sy81 section of AZF region was found deleted. The SRY gene on the p arm of Y chromosome was present.

Hypernatremia occurs primarily in infants with diarrheal dehydration. The purpose of this study was to evaluate the current pattern of hypernatremia in hospitalized children. Medical records were reviewed in 42 patients admitted to our clinic during a 31-month period, all with serum sodium greater than 150 mEq/L. The etiologies, predisposing factors, and morbidity and mortality associated with hypernatremia were evaluated. The mean age was 3 years (range, 1 month to 15 years), and the mean serum sodium concentration was 161.9 mEq/L (range, 151–189 mEq/L). Hypernatremia occurred in 24 (57.1%) children during hospitalization. The majority of children (81%) were admitted for reasons other than hypernatremia. In 12 (28.5%) of the patients, inadequate fluid intake was the main cause of hypernatremia. Gastroenteritis contributed to the hypernatremia in 14.8% (6 out of 42) children. Twelve of these were infancy period. Sixty two percent of patients (26 out of 42) suffered from neurologic impairment, critical illness or chronic disease before developing hypernatremia. The overall mortality was 42.9%. Patients in whom hypernatremia was not corrected had a significantly higher mortality than those in whom hypernatremia was corrected (8 out of 8 [100%] vs. 10 out of 34 [29, 4%]). Mean serum sodium level in survivors (159.6mEq/L) was lower than that in non-survivors (165mEq/L). Hypernatremia occurs in all ages in childhood, with the vast majority having significant underlying medical problems. Hypernatremia caused by gastroenteritis in infants was not common. Hypernatremia is primarily occurred during hospitalisation associated with sepsis and underlying neurologic disorders. We thought that underlying causes of hypernatremia might result in a high mortality rate.

The effect of treatment with human growth hormone in a girl with Kabuki syndrome

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The effect of treatment with human growth hormone in a girl with Kabuki syndrome. Kabuki or Nijikawa-Kuroki syndrome (KS) is a rare congenital mental retardation syndrome typically characterized by: postnatal growth retardation, face reminiscent of the make-up of actors of Kabuki, a traditional Japanese performance, bones and organs malformations (heart, kidneys, vertebral). Endocrinological anomalies such as growth-hormone deficiency, gonadotropin deficiency and premature thelarche were seen. To date no molecules cause has been determined. In the literature on the subject only a few cases report a case with complete gonadal dysgenesis with deletion of AZFa region.

Type 1 diabetes mellitus affects approximately 10,000 Moroccan children below the age of 15 years. Without appropriate care, these patients are subject to repeated hospital admissions during childhood, and disabling diabetic complications in the long term. Appropriate care involves patient information and training as well as practical and psychological support for their families. To reduce the frequency of complications in type 1 diabetes, a dedicated outpatient clinic was established in 1986 at the Rabat Children’s Hospital. In addition to providing medical therapy and monitoring, we have developed a team composed of different specialists (doctors, nurse, dietician and social worker) to initiate and maintain a programme of training in diabetes for the child and family, according to a standardised protocol. In 1986 the clinic consisted of 36 children and there were 7 new cases seen that year. Since then the clinic has grown to provide regular monitoring for 1000 children in 2007, with 130 new cases being seen during that year. The mean age at onset of diabetes is 10.64 years (range 9 months-15 years) and a current age of 12.5 years (range 14 months - 25 years). During the study period we have witnessed a considerable improvement in results: 1. Currently all children and families are able to inject insulin and carry out daily monitoring 2. Growth has markedly improved; while 25% out of the 131 young diabetics looked after at the children's hospital had a short height at 1989, the 236 children looked after after 1989 had a height at the end of their growth with a normal height 3. Only 2% of diabetic children were readmitted with DKA in 2001 compared with 25% of the clinic in 1986. Since 1989 there has been a steady improvement of metabolic control, mean HbA1C 9% in 1998, and 8.0% in 2007 We conclude that our programme of patient and family education has succeeded in improving the readmission rate of diabetic children in Morocco. The approach adopted could be applied to other chronic childhood disorders.

The effect of treatment with human growth hormone in a girl with Kabuki syndrome.

Improvement in health care for diabetic children at Rabat, Children's Hospital Morocco 1986-2007
Noureddine Bencherifa; Zineb Imane; Naima Bernani; Hind Bahaymed; Asmae Touzani; Amina Balafrae
Children’s Hospital, Pediatric, Rabat, Morocco


The effect of treatment with human growth hormone in a girl with Kabuki syndrome. Kabuki or Nijikawa-Kuroki syndrome (KS) is a rare congenital mental retardation syndrome typically characterized by: postnatal growth retardation, face reminiscent of the make-up of actors of Kabuki, a traditional Japanese performance, bones and organs malformations (heart, kidneys, vertebral). Endocrinological anomalies such as growth-hormone deficiency, gonadotropin deficiency and premature thelarche were seen. To date no molecules cause has been determined. In the literature on the subject only a few cases report a case with complete gonadal dysgenesis with deletion of AZFa region.

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A rare cause of neonatal diabetes mellitus: Wolcott-Rallison syndrome
Sofia Leka; Theoni Petropoulou; Christina Kanaka-Gantenbein
Aghia Sofia Children Hospital, 1st Department of Pediatrics, Medical School, Athens, Greece

Wolcott-Rallison syndrome (WRS, OMIM 226980) is a rare autosomal recessive disease characterized by early infancy insulin-dependent diabetes mellitus and spondyloepiphyseal dysplasia. We present clinical data of one patient meeting WRS criteria. He is the first child of non-consanguineous parents, born at term with a birth weight of 2350gr. He presented at 2 months with an upper respiratory tract infection. Blood glucose was 873mg/dl and urine analysis revealed glycosuria. He was started on regular insulin injections and was subsequently discharged without any complications. At the age of 3 years, he presented with a 24-h history of pyrexia (39oC), diarrhea and vomiting. Clinically, he was severely dehydrated with metabolic acidosis (plasma urea was 120mg/dl, creatinine 3,3mg/dl, blood glucose 365mg/dl, pH 7.27, bicarbonate 10,1mmol/l, base excess -12.9). His Glasgow coma scale was 15/15 on admission. 24-h after recovering from his metabolic acidosis he became progressively drowsier, presented generalized seizures and was transferred to the pediatric intensive care unit with multiorgan failure: severe hepatic dysfunction (SGOT 10176IU/lt, SGPT 5828IU/l, bilirubin 10.4mg/dl, PT 47,9sec, factor VII and V undetectable) and acute renal failure (creatinine 3,6mg/dl, GFR 14ml/min/1,73m2) that required peritoneal dialysis. MRI scan showed pachygyria and cerebral atrophy. All investigations towards an infectious or metabolic cause of this episode were negative. At the age of 5 years, he presented right lower leg limping and shuffling gait. Hip X-rays showed epiphyseal dysplasia. He has since a borderline renal function (GFR 70-80ml/min/1,73m2) and a moderately, controlled diabetes in low dose SC insulin injections. He did not develop further episode of acute liver failure. We propose that any infant with neonatal diabetes mellitus should be screened for epiphyseal dysplasia because even mild infectious illness can potentially be complicated by liver/renal failure.

Growth retardation in two patients due to severe atopic dermatitis
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The negative effects of asthma bronchiale and the use of oral and inhaled corticosteroids on growth in children are well observed. In contrast growth failure in patients with atopic dermatitis has rarely been described.

Case 1. An 11 year old girl presented with growth retardation (-4.2 SDS) and severe allergic symptoms. At 8 years she started intensive topical therapy and balanced diet with 200% SDS. After initiating intensive topical therapy and balanced diet with 200% SDS. She suffered from episodic eczema with profound sleep disturbance due to severe pruritus from the age of eight years. IGF-I, IGFBP3, chromosomal analysis, and stimulated growth hormone (GH) secretion were normal. However, she showed neuroendocrine dysfunction and after initiating sufficient atopic dermatitis therapy HV increased (+3.4 SDS). Despite continuing the intensive topical treatment, sleep disorders causing neurosecretory dysfunction remained, so GH treatment was initiated resulting in catch-up growth.

Case 2. A 2.8 year old boy presented with severe generalized exsudative eczema and hyperalbuninaemia due to protein loss through the skin. Atopic dermatitis and cow milk allergy were known since 7 months of age. During the second year of life HV slowed down to 3.2 cm/year (-3 SDS, height -2.9 SDS). After initiating intensive topical therapy and balanced diet with 200% protein supplementation, the eczema improved, and a considerable catch-up growth was observed. At the age of four years his height is -1.4 SDS while IGFBP3 and IGF-1 remained normal all the time. Growth failure in atopic dermatitis can either be attributed to rigorous elimination diet without balanced food intake, protein loss via skin in exsudative skin disorders, chronic inflammation or in neuroendocrine dysfunctions due to pruritus-related sleeplessness. Growth failure must be considered as a relevant symptom in atopic dermatitis. Management of these patients requires a close collaboration of pediatric allergologists and endocrinologists and further studies are needed to understand the mechanisms of growth impairment in patients with atopic dermatitis.

Testicular microlithiasis associated with prepubertal gynecomastia: Case report
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Testicular microlithiasis (TM) is characterized calcification in the seminiferous tubules and rarely seen in childhood. A 9 11/12 years-old boy presented with four-month history of development of right breast tissue. He also complained about pubic and axillary hair growth during the last year. There was no family history of precocious puberty. He was 148.3 cm (97%percentiles). Weight was 45.8 kg (90-95percentiles). Bone age was 11 6/12. His Blood pressure was 100/60 mm Hg. There was 3 cm glandular tissue on the right breast. Axillary hair and pubic hair was Tanner stage III. Testes volumes were 4ml on the right side, 3 ml on the left side. Stretched penis length was 7x2.5 cm. Biochemical analysis was unremarkable. Thyroid function tests within the normal range. Alpha-feto protein was 0.61 ng/ml (<7.0), beta HCG was 0.1 mIU/ml (<2). Gonadotropin releasing hormone test (GnRH) was performed and results were prepubertal. ACTH stimulation test was done to rule out CAH and the results of 17-OHP were normal. Ultrasonographic examination of the breast tissue revealed large but normal glandular structures. Abdominal ultrasonographic examination was normal. Testis ultrasonography showed that right testis was 25x11 mm, left testis was 22x8 mm and disseminated, multiple, calcifications were found in both testes. Both testes were normal appearance on the surgical exploration. Since insitu carcinoma risk in the testicular microlithiasis, testis biopsy was performed at the both side after informed consent were obtained from child’s parents. Biopsy specimen of the both testes showed spherical calcified structures in seminiferous tubules. Best of our knowledge this is the first case showed associating with prepubertal gynecomastia and TM. However all these may be coincidental.

Androgen exposure does not increase prenatal or infant growth, as shown in congenital adrenal hyperplasia
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Differences in androgen exposure has been suggested as the cause of differences in birth-weight and -length seen between boys and girls. Congenital adrenal hyperplasia (CAH) results in decreased cortisol and aldosterone production and increased levels of androgens already during foetal development. There is a good correlation between CYP21 genotype and clinical manifestations. Foetuses with severe CYP21 genotype groups are exposed to higher androgen levels. Treatment includes substitution with glucocorticoids and mineralocorticoid. To investigate if androgen exposure increases foetal and infant growth, the birth weight and growth pattern during the first 18 months of life was compared for different CYP21 genotype groups. 88 patients diagnosed with CAH were included. SDS for weight and length at birth, corrected for gestational age, and at 1, 3, 6, 9, 12, and 18 months for males and females with CAH were included. SDS for weight and length at birth, corrected for gestational age, and at 1, 3, 6, 9, 12, and 18 months for males and females with CAH were included. SDS for weight and length at birth, corrected for gestational age, and at 1, 3, 6, 9, 12, and 18 months for males and females with different CYP21 genotype groups were compared. We found no significant difference in birth weight or length between the CYP21 genotype groups. On the contrary a slight positive trend for weight and length between the more severe and the milder forms of CAH could be seen, however, this was not significant. During the first 18 months a tendency towards poorer growth in more severe genotype groups could be seen. The reason for this was not clear, but it could be caused by treatment with higher doses of hydrocortisone or insufficient mineralocorticoid substitution in the patients with the more severe forms of CAH. Our study indicates that androgens do not increase prenatal and infant growth. Over-substitution with hydrocortisone during infancy may cause poor growth development in CAH. It remains to be investigated if androgens can cause accelerated bone maturation in infancy.
We report a case of a 13-year-old boy with severe hemophilia A, who had suffered from four intracranial hemorrhages in early childhood. At the age of 3 years the impairment of the growth velocity was noted. The patient's percentile position on the growth chart was below the third percentile, with a tendency to deepening the height deficiency during next years. At the age of 7 years endocrinological investigation was performed. In the stimulatory tests for growth hormone (GH) excretion maximal value of GH was 1.5 ng/ml. The level of IGF-1 was also decreased. The function of other pituitary dependent hormonal axes was normal. The bone age was retarded 3 years. We established diagnosis of growth hormone deficiency, as a devastating complication after intracranial hemorrhages. The hemophilic boy was qualified to growth hormone therapy. For over 6 years he received everyday subcutaneous injections. During this time growth velocity increased, his height is now above tenth percentile and bone age 12 years. Under the GH treatment no complications were observed besides small subcutaneous bleedings after injections at the beginning of treatment. Therapy is still continued, the patient gives the injections by himself. The aim of this case presentation was to point the attention on the potential risk of pituitary axes damage in hemophilic patients after intracranial hemorrhages. The diagnosis of GH deficiency in hemophilic patients is very rare. It could be dependent on the difficulties of growth evaluation because of arthritic complications. Significant problem in the diagnostics initiation are the doubts of the hematologists who are afraid of GH therapy in subcutaneous injections. Our patient proves that the GH treatment could be safe and successful in patients with severe hemophilia.

**Conclusion:**
was compared with flexible and non-flexible MDI therapy groups.
was not detected (p<0.05) frequency of hypoglycemia, lipid profiles, total and HDL cholesterol, triglycerides (7.71%, 8.21%, and 8.71%, respectively, p=0.105). Statistically significant difference with transition to CSII compared to flexible and non-flexible MDI injection therapy was detected as 15.53±1.8 years, duration of diabetes 6.77±4.05 years. The mean CSII placement age of the 17 adolescent patients enrolled to the study was detected as 15.53±1.8 years, duration of diabetes 6.77±4.05 years. The level of IGF-1 was also decreased. The function of other pituitary dependent hormonal axes was normal. The bone age was retarded 3 years. A decrease was detected in HbA1c levels of the patients with transition to CSII compared to flexible and non-flexible MDI injection therapy. Carbohydrate counting and flexible MDI therapy was taught to these patients before CSII application. The metabolic and clinical parameters of the cases for the post-CSII application period were compared with the data of flexible and non-flexible MDI therapy.

**Results:**
The mean CSII placement age of the 17 adolescent patients enrolled to the study was detected as 15.53±1.8 years, duration of diabetes 6.77±4.05 years, flexible MDI injection duration 0.70±0.20 years, and duration of insulin pump use 2.07±1.12. A decrease was detected in HbA1c levels of the patients with transition to CSII compared to flexible and non-flexible MDI injection therapy. However, this decrease was not found statistically significant (1.71%, 8.21%, and 8.71%, respectively, p=0.105). Statistically significant difference compared to flexible and non-flexible MDI injection therapy was detected as 15.53±1.8 years, duration of diabetes 6.77±4.05 years. A decrease was detected in HbA1c levels of the patients with transition to CSII compared to flexible and non-flexible MDI injection therapy. Carbohydrate counting and flexible MDI therapy was taught to these patients before CSII application. The metabolic and clinical parameters of the cases for the post-CSII application period were compared with the data of flexible and non-flexible MDI therapy.

**Conclusion:**
In the adolescent age group, it is revealed that CSII treatment is efficient and safe without an increased risk for weight gain and hypoglycemia compared to flexible and non-flexible MDI injection. The present study, additionally, demonstrated that the flexible MDI injection treatment might also be efficiently and safely used in patients, who could not receive CSII treatment owing to social and financial causes.

**Objective:**
To compare the long-term outcomes of continuous subcutaneous insulin infusion (CSII) application with the clinical and metabolic parameters recorded during multiple daily insulin (MDI) therapy.

**Material and Method:**
Continuous subcutaneous insulin infusion was placed to volunteer adolescents, who had a duration of diabetes for at least 1 year, regularly attended pediatric control for the last one year, measured and recorded blood glucose average 3 to 4 times a day, and did not achieve the preferred metabolic control even though the use of MDI therapy. Carbohydrate counting and flexible MDI therapy was taught to these patients before CSII application. The metabolic and clinical parameters of the cases for the post-CSII application period were compared with the data of flexible and non-flexible MDI therapy.

**Results:**
The mean CSII placement age of the 17 adolescent patients enrolled to the study was detected as 15.53±1.8 years, duration of diabetes 6.77±4.05 years, flexible MDI injection duration 0.70±0.20 years, and duration of insulin pump use 2.07±1.12. A decrease was detected in HbA1c levels of the patients with transition to CSII compared to flexible and non-flexible MDI injection therapy, however this decrease was not found statistically significant (1.71%, 8.21%, and 8.71%, respectively, p=0.105). Statistically significant difference compared to flexible and non-flexible MDI injection therapy was detected as 15.53±1.8 years, duration of diabetes 6.77±4.05 years. A decrease was detected in HbA1c levels of the patients with transition to CSII compared to flexible and non-flexible MDI injection therapy. Carbohydrate counting and flexible MDI therapy was taught to these patients before CSII application. The metabolic and clinical parameters of the cases for the post-CSII application period were compared with the data of flexible and non-flexible MDI therapy.

**Conclusion:**
In the adolescent age group, it is revealed that CSII treatment is efficient and safe without an increased risk for weight gain and hypoglycemia compared to flexible and non-flexible MDI injection. The present study, additionally, demonstrated that the flexible MDI injection treatment might also be efficiently and safely used in patients, who could not receive CSII treatment owing to social and financial causes.
be possibly signalized by the TSH monitor, NTS, after thorough adaptation, might be a useful instrument in monitoring the effect of programmes for securing optimal iodine supplementation at population level among the most sensitive to ID individuals represented by the NB.

R-72 Read by Title

The IVS14 + 1G > A splice mutation in the AAAS gene causes triple A syndrome in a Palestinian child: clinical and genetic characteristics

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Background: Triple A (Allgrove Syndrome) is a rare autosomal recessive syndrome characterized by Alacrima, Achalasia and Adrenal insufficiency. Other features may include autonomic instability, neurological symptoms and hyperkeratosis of palms and soles. The recently identified AAAS gene located on chromosome 12 is considered responsible for the disease phenotype. Several mutations have been so far identified mainly in the Western European descent.

Methods and Case Presentation: A 7.6 years old boy, born to consanguineous parents, presented with a severe hypoglycemic event and was diagnosed with glucocorticoid deficiency. On evaluation his mother recalled the absence of tears (alacrima) since birth. Family history was remarkable for a brother who had alacrima and died from pneumonia at 2 y of age. The patient was clinically evaluated and DNA was extracted for micro satellite linkage analysis and AAAS gene sequencing.

Results: Upper GI series revealed moderate achalasia. Esophageal manometry showed increased pressure in the lower esophageal sphincter. In Histamine test the wheal and flare response was delayed. Using micro satellite markers (D12S368 and D12S83) flanking the AAAs gene on chromosome 12 our patient was found to be homozygous and the parents heterozygous at the AAAS gene locus. Sequencing revealed the patient to carry a homozgyous mutation in the splicing site following exon 14 IVS14+1G>A.

Conclusions: Triple A syndrome is rare but should be considered in patients with adrenal insufficiency, especially from consanguineous descent. This will facilitate early treatment of other affected systems (GI) and enable prenatal and early clinical diagnosis prior to devastating consequences. The mutation in the splicing site following exon 14 found for the first time in Palestinians may indicate an earlier founder effect with previously reported families from North Africa.

R-73 Read by Title

Management of Pickwick syndrome in 14 year old boy

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Background: Severe childhood obesity is increasing problem through out the world. Related complications are becoming an urgent problem, not only for the patient but also for the health system.

History: 14 year old male, first uncomplicated pregnancy and delivery, with family history for obesity, arterial hypertension, type 2 DM, metabolic syndrome and Pickwick syndrome (father and grandmother).

Present disease: Since 8 years - with voracious appetite and rapidly increasing weight.

First hospitalisation (2004): Sever obesity, impaired glucose tolerance and hyperinsulinism. Recommended therapy, Metformin and hypocaloric diet was ineffective.

Second hospitalisation (2006): In one year time the boy gained 50 kg and become increasingly sleepy. Height 170 cm (97 P, SDSH +1.19), weight 153 kg (>>> 97 P), BMI 51.7 kg/m2 (>>> 95 P), hip circumference 142 cm, abdominal circumference 147 cm, facies lunata, acanthosis nigricans, RR 147/90 mmHg. OGTT - hyperinsulinism, BGA - hypoxemia and hypercapnia. Heart ultrasonography - pulmonary hypertension. Treatment, Metformin, hypocaloric diet, antihypertensive medications, BiPAP, was effective.

Third hospitalisation (2007): In three months time, lose about 30 kg. Height 170 cm (97 P, SDSH +1.19), weight 128 kg (>>> 97 P), BMI 45.9 kg/m2 (>>> 95 P), hip circumference 136 cm, abdominal circumference 134 cm, facies lunata, acanthosis nigricans, RR 147/90 mmHg. BGA - normal. Heart ultrasonography - normal.

Treatment: Metformin, hypocaloric diet, antihypertensive medications, BiPAP.

Conclusion: Pickwick syndrome as complication of morbid obesity is rarely seen in pediatric endocrine praxis, which makes it difficult to manage. Because of the possible serious consequences, it should be diagnosed and treated as soon as possible.

R-74 Read by Title

Obesity is a risk factor for the severity of migraine attacks in childhood

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This study investigates the influence of obesity on the severity of migraine in childhood. Medical records of all patients with migraine evaluated at the Child Neurology Clinic between March 2000 and September 2006 were reviewed. 124 (77 female) cases, aged between 4.0-17.0 years were included the study. Obesity was defined as a relative body mass index>120. Regarding the headache severity, patients were categorized into 2 groups as having mild and moderate/severe headaches. For the headache frequency, patients were again categorized into two groups as having attacks <4/month and ≥4/month. The frequency of obesity was 17.7%. Relative BMI values were not different in migraine subgroups with aura (n=88) or without (n=36) (105.3±17.4 and 102.7±16.4 respectively). Severity of headaches were not different between obese nonobese patients. There was a relationship between obesity and frequency of attacks. The percent of patients who have ≥4 attacks/month was 75% in obese cases and 41.3% in non-obese cases (p=0.017). In this study, obesity seems to be related to frequency of headache attacks in children and adolescents with migraine.

R-75 Read by Title

Prolonged hungry bone syndrome secondary to Parathyroidectomy in a 10-year-old child with parathyroid adenoma

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Background: The reported predictors of hungry bone syndrome in adult patients with parathyroid adenoma were higher preoperative serum levels of calcium, alkaline phosphatase, N-terminal parathyroid hormone, and urea nitrogen; and their resected parathyroid adenoma were larger. Clinical and biochemical predictors of hungry bone syndrome in children with parathyroid adenoma has not been reported.

Case report: A 10-year-old girl was referred to our endocrine clinic because of hypocalcemia and walking difficulty. Physical examination revealed “x-bain” deformity and palpable nodule in the left-lower pole of thyroid gland. The biochemical and hormonal tests revealed that serum total calcium was 12.8 mg/dl, serum inorganic phosphate 2.1 mg/dl, 1,25 (OH)2 vitamin D >150 pg/ml (normal 30-65), and urine calcium level 1730 U/L, “intact” parathyroid hormone (IRMA) 1027 pg/ml (9-65 pg/ml), 102,7±16,4 respectively). Severity of hypocalcemia and walking difficulty. Physical examination revealed “x-bain” deformity and palpable nodule in the left-lower pole of thyroid gland. The biochemical and hormonal tests revealed that serum total calcium was 12.8 mg/dl, serum inorganic phosphate 2.1 mg/dl, 1,25 (OH)2 vitamin D >150 pg/ml (normal 30-65), and urine calcium/creatinine ratio 0.35. Neck ultrasound and parathyroid sestamibi scintigraphy showed a mass in the left-lower pole of thyroid gland. Histopathology of the mass was in accordance with parathyroid adenoma. Patient developed hypocalcemia in the immediate postoperative period and requiring intravenous calcium infusion for one month.

Conclusion: There is two main reasonable factors associated with severe hy-
The aims of our longitudinal study were to evaluate the patients presenting with lack of pubertal development. It is a rare cause of congenital adrenal hyperplasia. The characteristics of P450c17 deficiency include karyotype 46, XX or 46, XY disorder of sex development, hypertension, hypokalemia, and lack of pubertal development. We performed a clinical, hormonal study of 4 sisters with 17alpha-hydroxylase deficiency.

**Aim:**
A clinical, hormonal study of 4 sisters with 17alpha-hydroxylase deficiency.

**Background:** Chromosome 22q11 deletion syndrome is a syndrome due to a chromosomal abnormality which presents with diverse clinical manifestations. Hypoparathyroidism is one of these clinical manifestations.

**Case:** We report a case of 22q11 deletion syndrome. A 3 days old girl who was delivered from unconsanguineous parents at 34. week of gestation was admitted for tremors in upper extremities. Hypocalcemia and hypophosphatemia was detected. Parathyroid hormone level was at the lower limit of normal despite hypocalcemia. Search for dysmorphic features revealed atypical facies, hypertelorism, short filtrum, narrow and high palate, low set ears and skin tags before the ears. Thorax MRI revealed thymic hypoplasia; however no immunological defects were detected. There were no cardiac defects in echocardiography. Chromosomal analysis revealed 22q11 deletion.

**Conclusion:** 22q11 deletion syndrome should be considered in the etiology of hypoparathyroidism associated with dysmorphism.

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**R-76 Read by Title**

**22q11 deletion syndrome as a cause of hypoparathyroidism**

**Cengiz Bagci**; Oya Ercan; Hulya Kayserili

**Cerrahpasa Medical Faculty, Pediatric Endocrinology, Istanbul, Turkey; Istanbul Medical Faculty, Medical Genetics, Istanbul, Turkey**

**Background:** Chromosome 22q11 deletion syndrome is a syndrome due to a chromosomal abnormality which presents with diverse clinical manifestations. Hypoparathyroidism is one of these clinical manifestations.

**Case:** We report a case of 22q11 deletion syndrome. A 3 days old girl who was delivered from unconsanguineous parents at 34. week of gestation was admitted for tremors in upper extremities. Hypocalcemia and hypophosphatemia was detected. Parathyroid hormone level was at the lower limit of normal despite hypocalcemia. Search for dysmorphic features revealed atypical facies, hypertelorism, short filtrum, narrow and high palate, low set ears and skin tags before the ears. Thorax MRI revealed thymic hypoplasia; however no immunological defects were detected. There were no cardiac defects in echocardiography. Chromosomal analysis revealed 22q11 deletion.

**Conclusion:** 22q11 deletion syndrome should be considered in the etiology of hypoparathyroidism associated with dysmorphism.

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**R-77 Read by Title**

**Four sisters one of them genetic male with congenital adrenal hyperplasia due to 17-hydroxylase deficiency**

**Mehmet Keskin**; Bulent Ozokutan; Mustafa Ciftci; Levent Temel; Ozlem Keskin

**Gaziantepe University, Faculty of Medicine, Pediatrics, Gaziantep, Turkey; Gaziantep University, Faculty of Medicine, Pediatric Surgery, Gaziantep, Turkey**

**Background:** P450c17 deficiency is an autosomal recessive disorder and a rare cause of congenital adrenal hyperplasia. The characteristics of P450c17 deficiency include karyotype 46, XX or 46, XY disorder of sex development, hypertension, hypokalemia, and lack of pubertal development. We performed a clinical, hormonal study of 4 sisters with 17alpha-hydroxylase deficiency.

**Aim:** To emphasize early diagnosis of 17-alpha-hydroxylase deficiency because an expected lack of pubertal development can be due to an already diagnosed disease.

**Case Report:** A 14-year-old girl was referred for evaluation of oral hiperpigmentation and lack of pubertal development. In her history, she was the first born to unrelated healthy father and mother. She was 160 cm tall (50-75th percentile) and weighed 44 kg (10th percentile). Hiperpigmentation was found especially on digits and oral mucosa. She had female external genitalia and lacked spontaneous puberty. Her bone age was 10 years according to Greulich-Pyle atlas. Ultrasonographic evaluation showed that testes in the inguinal region and no uterus and ovaries. The circulating concentrations of cortisol and gonadal steroids were reduced and that of progesterone, adrenocorticotrophic (ACTH) hormone and gonadotropin was elevated. There was no hypertension and hypokalemia. Karyotype analysis was 46, XY. After starting cortisol replacement therapy with diagnosis of 17alpha-hydroxylase deficiency, gonadectomy was applied. Estrogen replacement was started and healthy sisters were invited. All patients had elevated basal serum levels of progesterone and karyotype analysis 46 XX. The diagnosis was the same for them and the genetic study was designed.

**Conclusions:** Basal progesterone measurement is a useful marker of p450c17 deficiency and that its use should reduce the misdiagnosis of this deficiency in patients presenting with lack of pubertal development.

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**R-78 Read by Title**

**Usual values and usefulness of crosslaps in pediatric practice**

**Eric Mallet**; Agnes Fery; Marcelle Leroy; Jean-Paul Basuyau

**University Hospital Charles Nicolle, Department of Pediatrics, Rouen, France; Centre Henri Becquerel, Biochemistry Laboratory, Rouen, France**

Serum Crosslaps is a bone resorption specific marker already validated in adults for osteoporosis helping in decision and therapeutic. Not yet clinically evaluated in children, we wanted to analyse the usefulness of this marker in paediatric practice, easier to collect than the other bone resorption markers which need urinary collection often uncertain in children. Patients and methods.- Serum Crosslaps were measured using the One Step ELISA immunoassay (Osteometer) in a population basis of 175 healthy children. The data were compared with results obtained in subgroups of children affected by bone metabolism diseases: osteogenesis imperfecta, mucoviscidosis, hypoparathyroidism, hypercalcaemia, corticotherapy, neuro-muscular pathology, precocious puberty, anorexia nervosa. Results.- The paediatric reference data obtained in the population basis showed an important dispersion and significant variations with age and growth: no significant change occurred in either sex until ten years, then there was progressive increase during puberty, peaking at 14-17 years in boys, earlier at 10-14 years in girls, before decreasing again until adults data. There was no significant difference between the results of population basis and subgroups of illness children. However, in three cases of children with osteogenesis imperfecta, a decrease of serum crosslaps was observed with bisphosphonate treatment. Conclusion.- Interindividual important changes and variations with age and growth make difficult the use of serum crosslaps in pediatric practice. It could be interesting in individual follow-up of pathology or treatment influencing on bone metabolism, as bisphosphonate treatment in osteogenesis imperfecta. It would be evaluated by carrying on the study on larger samples.

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**R-79 Read by Title**

**Characteristics of central precocious puberty and treatment in the Republic of Macedonia**

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**Pediatric Clinic, Endocrinology and Genetics, Skopje, Macedonia, Fyrom**

**Introduction:** Premature sexual development in girls occurs before the age of 8 years. It may be central precocious puberty (CPP) of idiopathic or central origin.

**Aims of the study:** The aims of our longitudinal study were to evaluate the auxologic parameters and pubertal stage of girls with CPP treated with a GnRH agonist for a period of three years.

**Materials and Methods:** In the longitudinal study, girls with premature sexual development were recruited at the Department for Endocrinology and Genetics, Pediatric Clinic, Skopje. Central precocious puberty was diagnosed in 40 girls by the standard LH-RH test.

**Results:** At the diagnosis we had 40 girls, and in the third year 16 patients. Therapy was arrested in 11 patients. From 40 girls, 9 (19,5%) had an idiopathic etiology. The rest of the 31 patients (80,1%) had an idiopathic form of CPP. There was a significant difference in the growth velocity, with a significant difference between the first and second year of evaluation (p < 0,01). A positive correlation was found between the chronological age at the diagnosis and bone age. (p < 0.05), between body mass index (BMI) SDS and the levels of the hormone LH (p<0.05), BMI SDS and bone age, and BMI SDS with the levels of estradiol (p< 0.05). The regression analysis showed a significant decrease of growth velocity and bone age during the study period of 3 years (p<0.05). Regarding the puberty stage, at the diagnosis 57.5% of the girls had a breast development of M2, 42.5% had M3. At the third year none of the patients had breasts. At the diagnosis, axillary hair A2 had 15.6% of the girls and it did not regress during therapy. At the diagnosis pubic hair was registered in 57.5% of the girls, and it remained similar during therapy.

**Conclusion:** The treatment with a LH-RH agonist contributes to improvement of auxologic and pubertal parameters, while it showed in our experience that has less effect on axillary and pubic development. In our case we did not have undesired effects of therapy and it showed to be well tolerated.

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**Read by Title**

Horm Res 2008;70(suppl 1)
Cardinal features of Turner syndrome are short stature, left sided congenital heart defects, and ovarian dysgenesis. Common ocular findings in Turner syndrome include strabismus, myopia, hyperopia, amblyopia, ptosis, hyperelorism, epicanthus, and red-green colour deficiency. Ocular hypertension and glaucoma have also rarely been reported in whom all had karyotype consistent with Turner syndrome mosaicism. We present a 12-year-old girl with Turner syndrome who referred to our clinic with short stature. Physical examination demonstrated height 116cm (<3rd percentile), Hds: -5.7, widely spaced nipples, pubertal status was Tanner stage 1, pruritus, corneal opacity and history of congenital glaucoma operation when she was five months old. Ultrasonography showed streak gonads and right renal agenesis. Her karyotype analysis showed 45,X without mosaicism. To our knowledge, association of renal agenesis and congenital glaucoma in Turner syndrome without mosaicism has not been reported previously.

A 17.5 year old boy had been diagnosed with type 1 diabetes at the age of 1.10 years with ketosis but no acidosis. He manifested with growth delay between 9.4 and 10.7 %) during the first symptoms of excessive thirst and polyuria. A 10-year-old boy was diagnosed with type 1 diabetes at the age of 1 year. He had signs of central diabetes insipidus (CDI) and was on treatment with glucocorticoids and thyroid hormones before the diagnosis of diabetes. He had signs of central diabetes insipidus and hypothyroidism and hypocorticism in 100%, diabetes insipidus in 92%, growth retardation in 92%, and obesity in 80% of patients. The insufficient efficacy of glibenclamide in this case may be related specifically to this mutation.

Beta-cell insulin secretion is regulated by the closure of ATP-sensitive potassium channels (KATP) which is composed by SUR1 (ABCC8) and Kir6.2 (KCNJ11) subunits. Activating mutations in KCNJ11 gene reduce sensitivity to ATP inhibition and are responsible for 30 to 58% of permanent neonatal diabetes (PNDM) cases. Recent studies demonstrated that oral sulfonylureas could improve insulin secretion by closing KATP channels in an ATP-independent route, representing a therapeutical option in PNDM metabolic control, improving also the neurological symptoms in some cases. 

Objective: To evaluate the efficacy of glibenclamide treatment in a child with PNDM by comparing it with insulin therapy.

Methods: A 4 years old female child with severe development delay, epilepsy and neonatal diabetes (DEND syndrome) in insulin therapy since 5 months of life, carrying a C166Y mutation in KCNJ11 gene, was switched from insulin (0.2U/kg/day) to glibenclamide (1.5 mg/kg/day) treatment, in a 8 weeks observational period, followed by insulin reintroduction. Glucose, insulin, C-peptide responses in OGTT were compared before and after glibenclamide switching; the 8-points capillary glucose profile and the hypoglycemia frequency recorded in Capella-Pro software of the Accu-chek meters as well as the mean HbA1c levels were compared before and during glibenclamide switching and also after insulin reintroduction.

Results: Glucose response in OGTT was higher during glibenclamide therapy (p<0.01) and it was noticed a trend to more frequent hypoglycemic episodes with insulin. Different neither in neurological symptoms, nor side effects were observed.

Conclusion: The insufficient efficacy of glibenclamide in this case may be related specifically to this mutation.
Due to the pulsatile nature of growth hormone (GH) secretion, random levels of GH have limited utility in the evaluation of GH status. Therefore, diagnosis of GH deficiency typically involves the use of provocative testing utilizing a variety of physiologic or pharmacologic stimuli. More than 189 combinations have been described (1) To assess the variation in GH provocative test procedures included in the GH MonitorSM database. The GH MonitorSM (EMD Serono, Inc.,) is a North America (US, Canada) voluntary, multi-center, observational registry for pediatric patients treated with Saizen®. In addition to collecting safety and efficacy data, information is obtained regarding practices related to the diagnosis and treatment of patients on Saizen®. For this analysis, data from Jan 2003 - Aug 2007 were evaluated pertaining to GH provocative testing prior to Saizen® therapy initiation. The number of patients tested at screening and entry into the database and the type and rates of use of various provocative agents were recorded. 1326 (77%) of the 1733 patients registered, had a provocative test and 994/1326 (75%) had data available on the specific type of provocative agent used. A total of 10 stimuli were administered in 20 combinations. The three most commonly utilized combinations of provocative agents were arginine and L-dopa (22%), arginine and clonidine (20%), and L-dopa and insulin (14%). The combination of L-dopa and insulin testing decreased from 27% in 2003 to 3% in 2007. Only 37/994 (4%; 10 females and 27 males) of these patients received estrogen priming. Although many GH provocative testing protocols have been described, data from the GH MonitorSM suggest that only a limited number of combined tests are used. The decreasing use of insulin and L-dopa likely reflect high morbidity and decreased availability respectively.

Reference: (1) Badaru A and Wilson DM. Alternatives to growth hormone stimulation testing in children. TRENDS Endocrinol Metabol 15 (6): pp252-8

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**Diversity of GH provocative testing: Analysis of data from the GH MonitorSM registry**

**Nerissa Kreher; Allison Baxter Bendus**

1EMD Serono, Inc., Endocrinology, Rockland, United States; 2EMD Serono, Inc., Endocrinology, Fairfax, United States

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**Influence of muscle and fat mass on insulin resistance measured by HOMA-IR**

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Physical inactivity leads to a reduction of muscle mass, high caloric food intake to an increase of fat mass. Thus, overweight children and adolescents with a lack of physical activity should have an elevated percentage of fat mass and a reduced percentage of muscle mass. We hypothesized that physical inactivity promotes insulin resistance. Therefore, an increased percentage of fat mass was expected to be more frequent in insulin resistant overweight children. The study-group consisted of 44 overweight/obese children and adolescents (BMI >P90=P97; 20 female, 24 pubertal) presenting consecutively to our obesity outpatient clinic. They were investigated by a standardized program including the measurement of body composition, fasting plasma glucose and fasting insulin levels. Fat and muscle mass were assessed with help of DEXA (L-PX-LUNAR, GE-medical Corp.). Insulin resistance was defined as HOMA-IR=P95 according to Allard. SD-Scores were calculated with reference data established by van der Sluis.

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**Self-assessment of puberty in healthy adolescents: Self-examination vs memory impression. Preliminary data**

**Meropi Dimitriadou; Athanasios Christoforidis; George Katzos**

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Self-assessment of puberty represents an interesting alternative for assessing pubertal staging, which avoids the embarrassment caused by direct inspection of sexual characteristics. However, several studies on the accuracy of this method have shown conflicting results. Until now, the technique of pubertal self-assessment has been based on the parallelism of Tanner’s staging standards to adolescents’ memory impression of their sexual characteristics. Our aim was to evaluate the usefulness of self-examination during pubertal self-assessment in improving the accuracy of the results. Forty-two volunteers (24 F and 18 M) with a mean age of 11.19 ± 1.63 years (range: 8-14 y) were enrolled in the study. All participants were healthy siblings of hospitalized patients. All volunteers were asked to complete a questionnaire showing drawings of Tanner’s pubertal stages with a short description by memory impression and after private self-examination of their sexual characteristics. Consequently, pubertal staging was assessed by an expert. Finally, participants were instructed to complete a modified Franzoi and Shield’s Body-Esteem scale. Results showed that 24 (57%) adolescents’ pubertal assessment by memory were in agreement with the physician’s ratings for both sexual characteristics, whereas 25 (60%) were in agreement after self-examination. Gender, age, BMI or Body Esteem Scale Score did not differ statistically among adolescent with correct pubertal self-staging and the rests. Nine subjects under-estimated their pubertal stage, whereas 8 subjects over-estimated it. As expected, age was significantly lower in the latter group, whereas, Body Esteem Scaling Score was significantly lower in the first group. Generally, self-examination seemed to improve the agreement scores with the physician’s ratings compared to pubertal estimations by memory. In conclusion, self-estimation of pubertal staging after self-examination is a promising practice which seems to improve the reliability of pubertal self-assessment in adolescents. Further research is needed for safer conclusions.

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**Catecholaminergic activity in girls with hyperthyroidism and hypothyroidism**

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Background: The relations between autonomous nervous system and endocrine system, which were found during animals and adult persons examination incline to estimate adrenergic system activity in endocrinological disturbances especially in thyroid dysfunction during puberty period.

Materials and Methods: The study concerns 30 girls with hyperthyroidism and 10 with hypothyroidism. The control group consisted of 30 healthy peers. In investigated girls catecholamines levels in psasma (HPLC) and in 24-hour
urine excretion (Euler and Floding method) were determined.

Results: In control group plasma adrenaline was 43.2 pg/ml, in hyperthyroidism group was 50.8 pg/ml, respectively. The noradrenaline plasma level was in control group 235.0 pg/ml, in hyperthyroidism group was 218.5 pg/ml, respectively. In conclusion, therapy with disodium pamidronate seems to be effective on attainment of final height in the range of target height. Spontaneous menarche occurs in all patients followed by regular menstruation in the vast majority of treated subjects.

Materials and methods: Nineteen girls, with CPP, which had completed at least two years of triptorelin therapy and have attained final height at the time of last evaluation, were incorporated in the study. The diagnosis of PP was based on combined data concerning early occurrence of secondary pubertal signs, advanced bone age (BA) and accelerated growth rate based on multiple height measurements and LHRH response consistent with CPP. Seven girls with central precocious puberty, which did not initiate triptorelin therapy mainly due to their parents’ refusal and had attained the final height, were used for comparisons. The mean (SEM) chronological age at diagnosis was: 8.42 (0.15) years and 8.44 (0.57) years and (BA) 10.76 (0.32) and 11.2 (0.43) yrs for patients and controls respectively. Girls were treated with triptorelin (Arvekap, IPSEN, Greece) every 4 weeks at a dose of 3.75mg.

Results: Mean final height was not statistically different from mean target height (157.26cm versus 159.55cm, P=0.055). Mean age of menarche was statistically different between treated girls and controls (12.45 versus 11.02 years, P=0.004). Menarche was observed 1.37years±0.73 (range: 0.4-3.57) following triptorelin discontinuation. Menstrual cycle was regular ranging from 28 to 40 days in 17 (89.5%) out of 19 girls.

Conclusions: Suppression therapy seems to be effective on attainment of final height in the range of target height. Spontaneous menarche occurs in all patients followed by regular menstruation in the vast majority of treated subjects.

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Fetal growth restriction secondary to maternal smoking is gestational age dependent

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Smoking during pregnancy cause fetales growth restriction. Most published studies have reported cigarette smoking effects in term infants, only few have analyzed effects in preterm. This study was designed to evaluate effects of maternal smoking during pregnancy in preterm infants (gestational age < 33 weeks). Prospective case-control study from a cohort of preterm infants from two French perinatal networks (Poitou-charantes & Franche-Comte) over two years (2005 - 2006). Cases were 358 very preterm infants (GA 24 - 32 weeks) divided into two subgroups according to maternal smoking status as smokers (129 infants) and non-smokers (229 infants). Controls were 361 term infants (GA 37 - 42 weeks) also divided into two subgroups as smokers (129 infants) and non-smokers (232 infants). We studied influence of maternal smoking on fetal anthropometric growth parameters (BW, BL, HC) defined according to AU DIPOG curves, France) in the groups and compared cases and controls. Other causes of fetal growth restriction were excluded. - Maternal characteristics (age, height, pre pregnancy body weight, parity, fetus sex) were comparable in both groups and subgroups. - Smoking mothers of preterm infants were younger (P < 0.001), overall less educated (P < 0.001) and often unemployed (P < 0.001) than non-smokers. - Smoking did not alter fetal growth in preterm infants: smokers versus non smokers BW (P=0.92), BL (P=0.44) and HC (P=0.81). Growth restriction was marked in term infants with BW (P < 0.001), BL (P < 0.001) and HC (P < 0.01). - In multivariate analysis, after adjustment for other confounding factors, fetal growth appeared to be significantly altered by maternal smoking during pregnancy only in term infants. Smoking in pregnancy does not seem to alter fetal growth before term 33 weeks, pregnant women can still be advised to give up smoking before the end of their second trimester to limit fetal growth restriction. Our study confirmations observations by Fitzgiral et al. that maternal smoking effects on fetal growth is gestational age dependent, with term born infants the most penalised.

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Suppression of idiopathic central precocious puberty, effect on adult height and menarche

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In true precocious puberty, the increased gonadal steroid secretion increases height velocity, somatic and psychosocial development, and the rate of skeletal maturation and can lead to short adult height. The aim of this study to assess the impact of suppression therapy of idiopathic central precocious puberty(CPP) with triptorelin on final adult height and the timing of menarche and pattern of menstrual cycle post-treatment.

Osteogenesis imperfecta is a genetic disorder due to the decreased amount or abnormal structure of the collagen. Major symptoms of the disease are bone pain, severe osteoporosis and multiple fractures that cause significant physical handicap. Bisphosphonates improve the bone density, and ameliorate the symptoms, decreasing the rate of bone fractures. The aim of our study was to evaluate the effect of treatment with bisphosphonates (disodium pamidronate) in children with osteogenesis imperfecta. Ten children with different forms of osteogenesis imperfecta were included in the study. Their age at the onset of treatment was between 1 month and 12 years. Multiple fractures occurred in all of them the total number per child being 2-22. The most severe form of the disease was noticed in the youngest children in whom fractures occurred starting at birth and multiplied without any significant trauma. All children were treated with i.v. disodium pamidronate 1mg/kg monthly during the first year, at 3 months interval during the second year and at 6 months thereafter. The duration of therapy was 3 months to 6 years. Special attention was paid to the management during infancy in order to avoid additional fractures. Pain dissapeared in all children. There was significant decrease of the number of fractures before and after initiation of therapy (p<0.001). Seven children did not have any fracture after the initiation of the therapy. Three children had 1-3 additional fractures during the total of 49 months of therapy. Only one febrile episode after the first dose of pamidronate occurred in 4 of the treated children. No other side effects were noticed. No significant decrease of serum calcium levels were noticed. In conclusion, therapy with disodium pamidronate is safe and efficient in treatment of different forms of osteogenesis imperfecta and in different ages of the children.

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Treatment with bisphosphonates of osteogenesis imperfecta

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The age of menarche and its relationship with regularity of menses in Iranian high school girls

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Menses is one of the important indices of puberty and sex hormone secretion in girls. The age of menarche (the first menstruation cycle) is between 9 to 13 years of age, but this is not a general rule, and it depends on various factors such as environment, race, nutrition and etc. Menstruation irregularity is
usually seen during the first 2 years of its occurrence. Ahwaz is a city in the South West of Iran and its population is composed of Lor, Kord, Arab and Persian. The aim of present study was to determine the age onset of menarche and its relationship with regularity of menses in girls living in Ahwaz city. A cross sectional study was performed on 430 children of high school by randomly clustered sampling. The results collected by filling out the questionnaires and recall. The data were analyzed by SPSS 13 with descriptive statistics and chi-square test. The average age of menarche in the study group was 12.88 ± 1.11 years. The incidence of menarche was significantly more in older age onset of menarche (p=0.019). The age of menarche in girls living in Ahwaz was similar to the previous studies in Tehran and United States of America. The age of menarche could affect on regularity of menstrual cycles.

**Objective:** The metabolic syndrome (MetS) is a common basis for the development of atherothrombotic cardiovascular disease. Adiponectin, an anti-inflammatory protein, has been demonstrated to be insulin-sensitizing and an anti-atherogenic factor including coronary spasms, and is considered a key of MetS. Recently, it was suggested that IL-10 might be involved in the inflammatory network of MetS in relation to adiponectin. We examined a possible correlation between adiponectin, IL-10 and MetS in pediatric obese patients, in order to verify if the pathophysiological mechanism related to the MetS in adults is already operative in childhood.

**Methods:** MetS components were assessed in 70 severely obese and 30 non-obese children and adolescents. Serum levels of adiponectin and IL-10 were measured in all subjects.

**Results:** Serum adiponectin levels were significantly lower and levels of MetS components were assessed in 70 severely obese and 30 non-obese children and adolescents. Serum levels of adiponectin and IL-10 were measured in all subjects.

**Conclusions:** Our obese children showed hypo-adiponectin and hyper-IL10 values as reported in adults. Serum adiponectin levels were decreased in patients with MetS but this difference disappeared when controlling the effect of BMI; furthermore MetS wasn't associated with low IL-10. In pediatric patients serum levels of adiponectin did not correlate with IL-10 levels. Our data confirm that the correlation between adiponectin and IL-10 production is complex and not yet fully elucidated.

**Adiponectin and IL-10 production in obese children and adolescents with or without metabolic syndrome**

**Read by Title**

**Valentia Calcatera**, *Mara De Amici*, *Catherine Klersy*, *Cristina Torre*, *Vincenza Brozzo*, *Francesca Scaglia*, *Benedetta Allais*, *Daniela Larizza*

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**Conclusion:** The study group consisted of 31 patients aged 11 to 26 (8 boys and 23 girls). The patients’ parents were asked about symptoms of physical and mental sexual development of their children and their own opinions about the sexual life of people with DS. 37% of the parents who were asked about the pubertal spurt noticed the height and weight gain of their children, 58% noticed axillarche and 95% pubarche. 70% of the girls had menarche (mean 13.3 years) and breast enlargement. Most of the boys had voice breaking and facial hair. 60% of the adolescents reacted for these changes showing interest, every 3rd wasn’t interested at all and every 5th was ashamed. Interest in the opposite sex is shown by 40% of the adolescents with DS. 37% of the parents discussed sexual topics with their children, usually when they were questioned by them. 70% of the parents think that their children should rather be informed on sexual topics by doctors, psychologists or teachers. Most of the parents approve restrictions that don’t allow their children to start their own families. The most preferred contraceptives are the pills and sterilization. Half of the adolescents with DS plan to have a family, but no the correlation with age was observed. 34% of the parents would panic at the information about pregnancy of their children and 37% would accept that fact. 23% of the parents don’t accept relationships between adults with DS, 66% are against people with DS having offspring. The psychosexual development of people with DS is a very difficult problem. Parents are not prepared for the development of puberty symptoms and sexual interest, which results in infanticide and asexual treatment of the adolescents.

**Precocious puberty in Turner syndrome**

**Eleftheria Emmanouilidou; Paraskevi Kokka; Magdalene Patseadou; Melanie Tektonidou; Assimina Gali-Tsianopoulou**

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**Turner syndrome** (TS) affects approximately 1 in 2000-2500 live born girls and it is clinically characterized by reduced growth, ovarian dysgenesis and infertility. Girls with TS may occasionally have normal functioning ovarian tissue, with approximately 30-40% entering puberty, 4% achieving menarche and 1% being fertile. However, the majority of patients with TS do not undergo spontaneous pubertal development. In this report, we describe a TS girl with mosaic karyotype who unusually experienced spontaneous prepubertal puberty, associated with accelerated longitudinal growth and advanced bone age. The patient was treated with LHRH analog (monthly intramuscular injection) and human recombinant growth hormone (daily subcutaneous injections). After two years follow-up her bone age remains slightly advanced, her growth velocity has been normalized and her height is nearly to her target height. This case report would like to emphasize in the fact that the treatment goals and modalities of patients with TS must be adapted to the individual in order to optimize pubertal and growth outcomes.

**Hemoglobinuria in patients with newly diagnosed type 1 diabetes without glucose 6-phosphate dehydrogenase deficiency - A novel observation**

**Malgorzata Wojcik**, *Jerzy Starzyk*, *Marta Giechansowska*, *Malgorzata Stelmach*, *Joanna Nazim*, *Mateusz Jagla*

1Jagiellonian University Collegium Medicum, Dep. of Pediatric and Adolescent Endocrinology, Krakow, Poland; 2Jagiellonian University Collegium Medicum, Dep. of Pediatrics, Krakow, Poland

**Two boys aged 14 (P1) and 17 (P2) years with newly diagnosed type 1 diabetes (glucemia: 33.3 mmol/l, 11.7 mmol) respectively developed hemoglobinuria, epigastrian pain, nausea and vomiting (P1) and (P2) hours following IV administration of an isotonic fluid infusion (isotonic dehydration >10% P1, <5% P2), 8.4% bicarbonate solution in P1 (pH 6-9, BE -28) P2, N, IV insulin (Actrapid P1, Humulin R P2), 15% KCl (2-4 mEq/100 ml IV fluid) and IV bolus of Metamizole - 4 mg after 1 hour (P1) and 2 mg after 4 hours (P2). In both cases, glucose-6-phosphate dehydrogenase (G6PD) deficiency was excluded (13.6 P1, 12.8 P2, N 13.5±± 2.45 IU/gHb) - the only hitherto described cause of hemoglobinuria in diabetes - as well as other known potential hemoglobinuria causes. This suggests that the initial period of diabetes mellitus type 1, even without ketoacidosis, in rare conditions predisposes...
Gluten sensitive enteropathy is a disease characterized with malabsorption and histopathologic abnormalities occurred in small intestine. In children, clinical presentation is very different; sometimes growth retardation can be the only symptom of the disease. In this study, we aimed to determine the clinical presentation is very different; sometimes growth retardation can be the only symptom of the disease. In this study, we aimed to determine the frequency of gluten sensitive enteropathy in children with short stature and the values of markers used in diagnosis. Growth in patients with X-linked hypophosphatemic rickets (XHR) is often impaired, despite early institution of phosphate and vitamin D therapy. This study analyzed the long-term effect of recombinant human growth hormone (rhGH) therapy in XHR. Six children (3 boys with XHR were treated with rhGH (0.05 mg/kg per day) for at least 3 years (yrs). Four of them were treated for a longer period of 5 to 11 yrs. Median age at start of the therapy was 7.2 yrs (range 4.5 to 9.3). Active rickets lesions were not present. Growth hormone deficiency has been excluded. Clinical examination, laboratory tests and bone age have been performed every six months, bone densitometry yearly. Growth data and bone age were compared with baseline values. Median baseline height velocity was 5.3 cm/year (4.2 to 6.0) and increased to 7.5 cm/year (6.9 to 9.0) after 1 year of therapy. Median height SDS at start of the therapy was -2.70 (-3.25 to -1.63) and increased to -2.23 (-2.76 to -1.0) after 1 year. Catch-up growth continued with values of height velocity of 6.4 and 6.7 cm/year in the second and third year, resulting in median height SDS values of -1.90 (-2.50 to -0.89) at 2 yrs and -1.57 (-2.30 to -0.53) at 3 yrs. After 3 yrs median ratio of delta bone age over delta chronological age was 1.01. Bone mineral content increased. After 1 year, median lean body mass improved from 79% to 84% of total body weight with a steady state afterwards. Long-term therapy (5 yrs or more) in 4 patients resulted in a continuing height gain. rhGH was well tolerated in all patients. Long-term therapy with rhGH leads to a significant improvement of height SDS and body composition in patients with XHR. Androgen insensitivity syndrome (AIS) is one of the most common etiologies for male pseudohermaphroditism. AIS is caused by numerous mutations of the androgen receptor (AR) gene. The phenotype may range from partial AIS (PAIS) with ambiguous genitalia to complete AIS (CAIS) with female genitalia. In infants and children the diagnosis can be difficult, since phenotypes are variable, the hormonal profile is not diagnostic until after puberty, and ligand binding assays on genital skin fibroblasts are cumbersome and not informative in up to one third of cases. Molecular genetic testing of the AR gene allows a definite diagnosis and detects mutations in more than 95% of probands with complete androgen insensitivity. However, its yield in individuals with partial or mild forms of AIS is low. We studied 39 children with presumptive diagnosis of AIS from 29 families with the following criteria: 46,XY karyotype, normal male basal and human chorionic gonadotropin-stimulated levels of serum testosterone, and normal ratio of testosterone:dihydrotestosterone, no Mullerian structure in pelvis imaging. According to classification of Sinneker et al, 6 case was diagnosed as CAIS and 33 cases was diagnosed as PAIS. All six cases with CAIS were assigned as female. In 3 patients with PAIS, female to male sex reassignment has been done because of adequate penile response to testosterone treatment. Sequence analysis for the entire coding region of the androgen receptor gene was planned. Initially, exon 4 and 5, which contain hot spots for mutations in the AR gene, were screened by DNA sequencing. No mutations were detected in exon 4 and 5. The other exons are currently under investigation. Clinical and biochemical features, phallic response to testosterone treatment, sex assignment and molecular findings will be discussed.
Clinical features | patient 1 | patient 2 | patient 3
---|---|---|---
Region of origin | Calabria (Italy) | Calabria (Italy) | Calabria (Italy)
Sex | F | M | F
Age at onset (yrs) | 5 | 8 | 0.8
Candidiasis | 13 | 8 | 0.8
Hyponatremia | 3 | 8 | 4.6
Addison's disease | 9.6 | 8 | 1
Age at last exam (yrs) | 29 | 15.8
Hypogonadism | + | - | +
IDDM | - | + | -
GH deficiency | + | + | +
Hypothyroidism | + | - | +
Autoimmune hepatitis | - | - | +
Malabsorption | - | - | +
Alopecia | + | - | -
Enamel hypoplasia | + | - | -
Nephrocacinosis | + | - | -
Autoantibodies
Thyroglobulin | - | + | +
Thyroid microsomal | - | + | -
Parietal cells | + | - | -
Adrenal cortex | + | + | -
21hydroxylase | - | - | +
17α-OH | - | - | +
P450 scc | + | - | -
Islet cells | - | - | +
Glutamic acid decarboxylase | + | - | +
Tryptophan hydroxylase | + | - | +
L-aminoo acid decarboxylase | + | - | +

All patients showed W78R mutation in homozygosity. Our calabrian patients show the mutation W78R previously found only in patients from Salento and this gene mutation distribution seems to confirm the hypothesis of a founder effect.

Conclusion: Familial Sotos syndrome is rare, less than 20 families have been reported. The two children reported present the classical signs of the syndrome. However, an important subdural hygroma was showed in the sister. The few difference between the father and the sister may be due to different mutations of the NSD1 gene.

R-100 Read by Title
Sotos syndrome: a new familial case
Meriem Barsala1; Rosa Acrouf; Samia Ould Kablia; Hadjar Menia; Hanan Kharab; Zahra Kemali;
Central Hospital of Army, Endocrinology, Algiers, Algeria

Introduction: Sotos syndrome was first described in 1964, it is characterized by cranial features including, statural and bone age advance, macrocephaly, a typical fancies and a mental retardation. The exact prevalence is unknown but hundred of cases have been reported. Less than 20 cases of familial forms have been reported in the literature. In 2002, Kurokati identified the NSD1 gene and showed that haploinsufficiency of this gene is the major case of this syndrome. This syndrome is associated with an increased risk of tumours. Concerning the height, growth tends to normalize after puberty.

Case Report: We report two cases of Sotos syndrome in the same family (sister and brother), their clinical features are reported in the table:

<table>
<thead>
<tr>
<th>Features</th>
<th>Child 1:22months</th>
<th>Child 2:6months</th>
<th>Reported frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxemia</td>
<td>present</td>
<td>Present</td>
<td>Several cases</td>
</tr>
<tr>
<td>Neonatal jaundice</td>
<td>present</td>
<td>Present</td>
<td>Can be present</td>
</tr>
<tr>
<td>Statural adrence</td>
<td>present</td>
<td>present</td>
<td>90%</td>
</tr>
<tr>
<td>Excessive Occipito frontal circumference</td>
<td>present</td>
<td>present</td>
<td>90%</td>
</tr>
<tr>
<td>Cranio facial features</td>
<td>present</td>
<td>present</td>
<td>90%</td>
</tr>
<tr>
<td>Scerosis</td>
<td>present</td>
<td>Absent</td>
<td>30%</td>
</tr>
<tr>
<td>Cardiac abnormalities</td>
<td>Absent</td>
<td>Absent</td>
<td>8-21%</td>
</tr>
<tr>
<td>Genito urinary anomalies</td>
<td>absent</td>
<td>absent</td>
<td>2-8%</td>
</tr>
</tbody>
</table>

IGF1 Normal for age Normal for age Normal for age
Intelligence quotient 80 Not done 47-105
Learning difficulties present 60%
Genital length present Absent Present 70-100%
Brain MIR anomalies Corpus callosum atrophy* Ventriculo megalgy** Important subdural Hygroma*** 12-25%, **63%, ***25%

R-102 Read by Title
Estimation of growth hormone secretion after onset of sleep as a screening test for the diagnosis of growth hormone deficiency in children
Monika Obara-Moszynska; Andrzej Kedzia; Barbara Rabska-Pietrzak; Marek Niedziela;
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The diagnosis of growth hormone deficiency (GHD) is still problematic for the clinician. The studies performed in our clinic proved that the physiologic stimulation of GH like sleep is stronger than pharmacological agents and the estimation of GH after onset of sleep can be used as a screening test in diagnosing GHD in children. There is still a doubt what GH cut-off value should be used in the sleep test. The question is, if the cut-off level=20 µIU/ml can be equal for pharmacological and physiological stimulation. The literature data don’t give a clear answer. The aim of the study is to estimate the predictive values for the different GH cut-off values in the sleep test. We studied 80 short stature, prepubertal children, aged 3.5 - 16 years. In every patient the GH test after onset of sleep (0'-30'-60'-90'-120') and two different pharmacological (insulin, clonidine, glucagon, L-dopamine) tests were performed. The children with normal IGF-1 were only analyzed. For estimating prognostic values GHD was recognized due to GH<20µIU/ml in both pharmacological tests. In all performed tests. In some cases the pharmacological an physiological tests diagnosed different; in 15 patients the GH sleep test gave false positive result, in 14 children both pharmacological tests recognized GHD but the sleep test presented GH above 20µIU/ml. The prognostic values for sleep test were: for 17µIU/ml cut-off
the highest accuracy (ACC=64%) was achieved with good balance between specificity (SPEC=72%) and sensitivity (SENS=53%), for 20µIU/ml cut-off - ACC=59%, SPEC=63%, SENS=53%, for 15µIU/ml cut-off ACC=64%, SPEC=70%, SENS=43%. From the clinical point of view the cut-off of 17µIU/ml could be the most useful one. The GH level above 17µIU/ml in the sleep test gives a high probability to achieve a proper GH secretion in pharmacological stimulation test. Considering the purposefulness of the further pharmacological testing in the patient, the cut-off level=17µIU/ml in the sleep test has a better diagnostic value than the concentration 20µIU/ml usually used.

**R-103 Read by Title**

Human placental IGFBP-1 levels in growth disorders at birth

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Throughout pregnancy and later life, the Insulin-like growth factor (IGF) axis plays an important role in normal growth and development. Alterations in this axis can result in serious consequences, such as small for gestational age (SGA) babies. Important components of this axis include the insulin-like growth factors (IGF-I and IGF-II), and their binding proteins (IGFBPs). The aim of this study was to correlate levels of placental IGFBP-1 with IGF-I and IGF-II, and the micronutrients zinc and ferritin, in SGA and large for gestational age (LGA) babies. Human placental samples were obtained from eighty nine women in rural field sites in Pakistan. Samples were further divided into SGA and LGA groups based on population specific percentiles. Multivariate linear regression for IGFBP-1 levels significantly correlated with levels of IGF-I, IGF-II and cord ferritin levels at the time of birth (p<0.05). IGFBP-1 plays a key role in growth regulation, particularly towards the end of the gestational period. Our results emphasise the importance of placental IGFBP-1 in birth outcomes. Furthermore, the influence of key micronutrients, namely ferritin, can be appreciated. The importance of a well-balanced system can be appreciated as both deficiencies and excessive amounts of this protein can tip the balance of growth in either direction.

**R-104 Read by Title**

Can we treat the sequels of the hypothalamic syndrome developed after craniopharyngioma radical surgery? A case report

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BMI reduction and metabolic control are still challenging issues in children affected by hypothalamic syndrome following radical surgery for craniopharyngioma (CF). A 12.8 year old boy radically treated for suprasellar CF at 8 yrs of age (Height: 0.5 SD; BMI: 2.5 SD) showed at first examination: hypopituitarism, diabetes insipidus and obesity (BMI 3 SD) with intractable hyperphagia. Despite severe GH deficiency he presented height 0.9 SD and some acromegalic features. Initial tests: insulin resistance (HOMA:12), dyslipidemia (cholesterol LDL/HDL ratio: 0.23) and indosable IGF-1 levels, carotideal intima thickness (0.7-1.7 mm) and calcifications. During the next 3 yrs, the following therapies were started: GH (to improve lipid panel), testosterone (to induce pubertal development), metformin (to reduce hyperinsulin secretion) and orlistat (to treat obesity); after 6 months of GH treatment lipid panel soon improved with normalization of the carotideal intima, BMI reduced, but HOMA worsened. GH was reduced and metformin was started. Despite all above treatments BMI increased (figure). Therapy with octreotide, 3 injections a day, was started at 15 yrs of age with a single dose of 0.1 mg for 2 weeks, then 0.2 mg for 6 months. During treatment HOMA reduced (6.6) while BMI did not increase; however the patient suffered side effects such as nausea and mild headache and suspended octreotide injections one month before the last check up (HOMA 11.1). Octreotide LAR 10 mg was started but patient early showed cholelithiasis and therapy was definitively suspended. Our data shows the difficulties of treating our patient with hypothalamic obesity. GH doses was reduced to maintain positive effects on lipid panels and carotideal intima thickness and not to affect negatively glucose homeostasis. Metformin showed some efficacy on reducing HOMA. Octreotide seems to stabilize BMI by reducing insulin secretion, however it is not free from major side effects.

**R-105 Read by Title**

Anthropometric indicators of nutritional status in adolescents at high school: Relation with socioeconomic status and gender

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Objective: Anthropometry (the use of body measurements to assess nutritional status) is a practical and immediately applicable technique for assessing children’s development patterns particularly during the first years of life. However, anthropometric indicators can be used to evaluate nutritional status in all age group. We aimed to evaluate nutritional status of Turkish adolescents at high school according to anthropometric indicators and to determine relation with socioeconomic status and gender in this study.

Subjects and Methods: Six hundred eighty adolescents (aged 13-18 years) attending high school in an urban area were included in this study. Height and weight were measured for all subjects and nutritional status were evaluated according to anthropometric indicators which was based on WHO criteria. Adolescents were grouped into three categories according to socioeconomic status.

Results: Frequency of being stunted and underweight were 4.4% and 5% respectively. Frequency of obesity was 19.2% in adolescents. Although height and weight in adolescents girls were higher than boys, anthropometric indicators were not different significantly (p>0.05). Frequency of being stunted, underweight and obese did not significantly different between girls and boys (p>0.05). Height standard deviation scores were significantly lower in adolescents with low and middle socioeconomic status (p<0.001). Frequency of being underweight and obese did not changed significantly according to socioeconomic status (p<0.001). However, frequency of stunted was significantly higher in adolescents with middle socio-economic status (p=0.04).

Conclusion: Obesity was the most common nutritional disorder among Turkish adolescent students in urban area. Frequency of nutritional disorders are similar between adolescents girls and boys according to anthropometric indicators. Although frequency of nutritional disorders are not different according to socio-economic status, adolescents with middle socio-economic status are shorter than those with other socio-economic status.
Heterozygous Q318X mutation of 21 hydroxylase gene in a neonate with scrotal pigmentation and mildly elevated 17OHP level
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Introduction: Scrotal hyperpigmentation is one of the diagnostic clue for congenital adrenal hyperplasia (CAH). Sometimes it was the only clinical finding of CAH, but also seen in healthy newborn, and disappeared in time. During the first week of life basal 17 hydroxyprogesteron (OHP) level tend to be higher and could lead to diagnostic controversy when clinical suspicion of CAH occured.

Case: Fifteen day old term male baby seen in our clinic because of scrotal pigmentation. Physical examination were normal. Penil strech length was 90 centile. On laboratory examination, Na, K, 17OHP were 132 mmol/L, 6.2 mmol/L, 30 ng/ml, 33 pg/ml respectively. One month of age, babies 17OHP level increased to 62 ng/ml, hence 21 Hydroxylase gene analysis were studied. Mutational analysis included most frequently seen nine mutations as 8 bp deletion, large gene deletion, P30L, IVS2, 1127N, V281L, Q318X, R356W, exon 6 cluster mutations. Patient had been found heterozygous Q318X mutation. While father carry the same mutation as heterozigous, no mutation was detected in mother. No treatment was introduced. During follow-up of patient scrotal hyperpigmentation began to disappear, weight gain was normal, ACTH and cortisol level were normal, and serum 17OHP level decreased to 4.2 ng/ml.

Results: While heterozygous Q318X mutation of 21hydroxylase gene led to classical salt wasting CAH, heterozygous mutation would expected to show no clinical findings. Our patient had scrotal hyperpigmentation, upper normal penil lenght and suspensional findings for CAH like mildly increase of 17OHP level, low-normal value of sodium. Slightly high serum 17OHP level could be seen in normal babies during first months of life. If genetic analysis were not done, unnecessary steroid treatment could be started such patient. Prohormone 21-hydroxylase is a key enzyme in the biosynthesis of glucocorticoid and mineralocorticoid steroids. The 21-hydroxylase deficiency is the most frequent enzyme defect responsible for CAH and is caused by mutations in the CYP21A2 gene. The 21-hydroxylase enzyme is responsible for the conversion of 17-hydroxyprogesterone to 11-deoxycorticosterone, which is further converted to aldosterone and cortisol. Patients with 21-hydroxylase deficiency lack cortisol production and have a hyperresponsiveness to ACTH stimulation.

Conclusion: In case of scrotal hyperpigmentation and mildly elevated 17OHP level, we must take a drug history. Evaluation about TRAB, maternal antithyroid Ab and taking thyroid hormone medicine. In case of normal USG and no uptake on scan, we should perform TRAB, antithyroid Ab of baby and mother. When one takes thyroid hormone medicine, it can cause no uptake in scan, so we must take a drug history. Evaluation about iodine uptake dysfunction is helpful for finding the cause.
The genetic aspect of the relationship between parents and children obesity has been studied, but the social aspect of this relationship needs to be evaluated. A controlled study was proposed in which 120 families with an obese child were included (Group 1: 66 girls and 54 boys) and in whom no genetic or hormonal anomalies were detected. Age of children was 7.5 ± 0.5 years. Body mass index > 95 percentile. 85 families with normal child were taken as a control group (group 2: 45 girls and 40 boys). Age was 8.1 ± 0.7 years and body mass index was 50 percentile. In group 1, 16 families (13 %), both parents were obese, in 48 families (40 %), only the father was obese, in 20 families (17 %), only the mother was obese, and in 36 families (30 %) neither parents were obese. The Father was obese in 64 families (53 %) either alone or with the mother. In group 2, in 3 families (4 %) both parents were obese, in 10 families (11 %), only the father was obese, in 18 families (22 %), only the mother was obese, and in 54 families (63 %) neither parents were obese. The Father was obese in 13 families (15 %) either alone or with the mother.

The objective of this study was to evaluate the effects and adverse effects of GH therapy in children with Prader-Willi syndrome (PWS). Me:

Purpose: The objective of this study was to evaluate the effects and adverse effects of GH therapy in children with Prader-Willi syndrome (PWS). Methods: Forty-one patients who treated with GH for more than 2 years (24 boys and 17 girls, mean age 7.3 ± 3.3 years at start of treatment) were enrolled.

Results: Height-standard deviation score (SDS) increased significantly after 2 years (-1.19 ± 1.37 vs. -0.02 ± 1.45). Body weight-SDS also increased (1.02 ± 2.42 vs. 1.63 ± 2.22), but percent body fat decreased (44.6 ± 9.9% vs. 38.1 ± 10.5%) and total bone mineral contents increased (833.4 ± 454 g vs. 1242.3 ± 573 g). Thyroid function test and serum glucose level did not change during treatment, total cholesterol level decreased. GH therapy did not impact glucose control of the patients with diabetes. Most common adverse effects of GH therapy was progression of scoliosis. The other adverse effects of GH were adenoid hypertrophy and so on.

Conclusions: GH therapy improved height-SDS and body composition of PWS. However, GH should be used with caution in those with scoliosis and adenoid hypertrophy.

Clinical manifestations of CYP21A2 heterozygosis are a controversial issue. This condition has been associated to signs of hyperandrogenism in childhood, adolescence and adulthood by some authors. We report a case of mild virilization in a newborn female, exposed to progesterone in the 1st trimester of pregnancy, who resulted to be carrier of a severe mutation of CYP21A2. A 1-month-old female was referred to our Disorder of Sex Development (DSD) Centre for evaluation of clitoromegaly. Family history was negative for DSD or unexplained neonatal deaths. During pregnancy, threatened miscarriage was treated with progesterone from 8th to 12th week of gestation; no maternal virilization had occurred. Neonatal period was uneventful. On evaluation, Prader stage I-II virilization was noted, with clitoral length of 15 mm, and mild decrease of perineum length. 17-OH-progesterone, testosterone, and 4-androstenedione were within the normal range. CYP21A2 molecular analysis resulted in heterozygosis for Q318X mutation. During short-term follow-up, clitoromegaly slightly decreased. This case of mild virilization may have two possible explanations. CYP21A2 heterozygosis has been related to premature pubarche, acne, hirsutism, adrenal incidentaloma. However, most carriers are asymptomatic. Clitoromegaly at birth has been reported in one case. Virilization in female newborns exposed to progesterones in the 1st trimester of pregnancy has been previously described, and demonstrated in experimental models. Risk of virilization is related to the androgenic activity of the drug, dose and duration of treatment: for a short-course, low-dose, weak-androgen-activity progesterone, as in our patient, risk is estimated to be < 1%. This case suggests that heterozygosity for a severe mutation of CYP21A2 may have conferred increased susceptibility to prenatal virilization induced by exposition to weak androgen activity progesterone. The role of unidentified susceptibility genes and/or environmental factors cannot however be excluded.
At least one of protective haplotypes were present in 3.2% diabetic children compared with 66.7% controls (p<0.001). Presence of single protective haplotype decreased risk of diabetes mellitus 0.017 times, CI 0.006-0.05. 

Conclusions: 1. HLA haplotypes DR3-DQA1*0501-DQB1*0201 and DR4-DQA1*0301-DQB1*0302 were most frequent among diabetic children in Lithuania. 2. HLA haplotypes DR2-DQB1*0602 and DR11/12/13-(DQA1*05-DQB1*0301) were generally found among healthy children in Lithuania.

Reference ranges for serum IGF-I and IGFBP-3 values do not show any sex difference. IGF-I and IGFBP-3 values (mean ± SD) are defined for age, sex and pubertal stage. Furthermore, our data shows that in girls serum IGF-I levels are significantly higher than in boys. IGFBP-3 values (mean ± SD) were comparable. Both in females and males subjects, serum IGF-I and IGFBP-3 are statistically different according to age and pubertal stage. Analysis of covariance was based in clinical examination, pubertal response of gonadotropin-releasing hormone releasing test, and measurement of ovarian volume. Age at diagnosis was 7.2± 0.2 years, height was 1.7 SD ± 0.4 above the mean, breast development was Tanner stage 3, and bilateral ovarian volume was 3.8 ± 0.4 cm³. Treatment with GnRH agonists was started. Clinical evaluation showed breast development regression. Three months later ovarian volume was evaluated. GnRH stimulating test was performed in 50 girls. Results of both pelvic ultrasonography and GnRH stimulating test were compared in relation to clinical evaluation. All the girls showed breast regression, GnRH stimulating test showed pubertal response, ovarian volume was decreased to 1.2 ± 0.2 cm³ bilaterally. Clinical, hormonal and ultrasonographic findings were comparable.

Conclusion: Pelvic ultrasonography in girls treated with GnRH agonists can be used as a safe, less invasive, more economic way for monitoring treatment results.
Risk factors for hepatic steatosis in Turkish children (Predictors of non-alcoholic fatty liver disease in obese Turkish children)

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is an emerging clinical problem in children that may lead to cirrhosis and death. It may manifest as simple steatosis or may be accompanied by inflammation with various degrees of fibrosis (non-alcoholic steatohepatitis). The aim was to compare clinical, biochemical and hormonal findings of obese children with hepatic steatosis and obese children with normal liver and search for clinical predictors of hepatic steatosis in obese children.

Material-Methods: We prospectively studied 93 obese children with BMI>95 percentile. Patients divided two groups according to have steatosis. Group 1 consisted of 51 cases (mean age 12.3±2.7 years) with ultrasonographically proved fatty infiltration of the liver. Group 2 consisted of 42 cases (mean 11.06±2.8 years) with normal ultrasonographic findings.

All subjects underwent a complete physical examination including anthropometric measurements. Fasting serum glucose and insulin levels, IR-HOMA, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol, high density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, serum cortisole, free serum T4 and TSH concentrations were compared.

Results: Age, BMI, fasting insulin levels, HOMA-IR and ALT were significantly higher in obese children with hepatic steatosis (p<0.016, p<0.032, p<0.053, p<0.041, p<0.043, p<0.0034 respectively). Increased IR-HOMA (3.5) was found in 28 subjects (58%) in group 1 and in 11 subjects (27%) in group 2. Raised ALT (>40 U/L) was found in 10 subjects (20%) in group 1. Only triglycerides were significantly higher in subjects with increased ALT than in those without in group 1 (p<0.034). In other words ALT concentrations were significantly higher in subjects with elevated triglycerides (p<0.016).

Conclusions: Hepatic steatosis was positively associated with degree of obesity. Hyperinsulinism seems to be an important predictor for hepatic steatosis. Liver enzymes are increased in subjects with hypertriglyceridemia.

R-120 Read by Title
Utilization of serum thyrotropin (TSH) measurements in the pediatric population

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Introduction: Objective: 1. To study the utilization of serum TSH by general pediatricians in the pediatric population. 2. To define populations at risk for sustained abnormal TSH level based on the initial TSH determination and patient characteristics.

Patients and Methods: Database of all outpatients aged 0.5 to 16 years without previous thyroid disease insured by Clalit Health Services (CHS) who had a TSH determination in 2002, and follow-up measurements during a 5-year period. TSH determinations were performed using the Immulite 2000 (Diagnostic Products Corp., Los Angeles, CA) and Centaur (Bayer Health Care) apparatus. TSH values (m IUL) were: normal limits 0.35-5.5, decreased <0.35, elevated >5.5 ± 10 or highly elevated >10.

Results: 121,052 children (11.6% of the cohort) performed at least one TSH measurement between the years 2002-2006. Initial TSH concentrations were normal, elevated, highly elevated and suppressed in 96.4%, 3.1%, 0.3%, 0.2%, respectively. The frequency of TSH testing increased with age and female gender. Despite a normal initial TSH, a second, third and fourth or more TSH tests were performed in 26.1%, 10.7% and 8.4% of cases, respectively. 40% of initially highly elevated and 73.5% of elevated TSH levels normalized in the second TSH determination. Predictive factors for a second highly elevated TSH were: a higher initial TSH and female gender.

Conclusions: TSH measurement is used extensively and repeatedly by general pediatricians as part of the work up for non specific complaints. Normal TSH levels used in this population are likely to remain normal over a 5 year period.
R-121 Read by Title

Recalcitrant hypocalcemia after total thyroidectomy in a thyrotoxic adolescent girl with Graves disease

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Background: Multiple factors lead to severe recalcitrant hypocalcemia in a patient who undergoes total thyroidectomy while thyrotoxic.

Case Report: We describe a 17-year-old girl with Graves disease who presented with an enlarged goiter compressing on her airway. She had florid thyrotoxic symptoms such as anxiety, tachycardia, difficulty in breathing, choking with difficulty swallowing. The severity of her symptoms worsened and she underwent an emergent total thyroidectomy. She developed hypocalcemia with signs of tetany within 6 hours after surgery. She was started on the maximum dose of calcium carbonate (6 g of elemental Ca) po, calcitriol (4mcg/day) & IV calcium gluconate (24 grams a day) drip continuously, much higher than any treatment requirements of hypocalcemia. Her calcium levels failed to rise; she remained symptomatic at levels of 7.5mg/dl. Despite aggressive replacement, the patient’s calcium did not exceed 9mg/dl until postoperative Day # 4. IV Calcium Drip was required for over one week post surgery to keep calcium from dropping below 7.5 mg/dl.

Discussion: Calcitonin release during surgery and ‘hungry bone syndrome’ due to postoperative reversal of thyrotoxic osteodystrophy both contributed to the severe hypocalcemia. Hypoparathyroidism can occur due to trauma, devascularization, or removal of the glands during surgery. All these factors together combined to cause the recalcitrant hypocalcemia seen in this patient; which was extremely difficult to manage. To our knowledge, this is the first report of such recalcitrant hypocalcemia requiring such high doses presenting in the post operative course of an adolescent after total thyroidectomy for Graves disease. One should be particularly alert to severe hypocalcemia in cases of prolonged decompensated hyperthyroidism and peri-operative damage to the parathyroids. This also emphasizes the importance of a euthyroid state if possible prior to total thyroidectomy to avoid such a complication.