As excessive doses of glucocorticoids decrease growth velocity and high androgens levels increase it, growth is a useful tool for monitoring congenital adrenal hyperplasia (CAH) treatment. Objective: to determine the growth of patients with salt losing form (SL) of CAH diagnosed in the first four months of age and to analyze the evolution of height and weight after the beginning of the therapy. Data of weight and height z scores (zW, zH) of patients with CAH-SL were analyzed at diagnosis and at the ages of 1 and 2 years (± 3 mo). Doses of hydrocortisone (Hydro) used and serum levels of 7 hydroxyprogesterone (7OH) and androstenedione (A) were also obtained. We studied 2 patients: 8 (38%) males and 13 (62%) females. At the diagnosis the mean age was 37 days, zH was -1.86 ± 1.72, zW was -2.31 ± 1.30. At the age of 1 year zH was -1.67 ± 1.16 and zW was -1.43 ± 1.64. At the age of 2 years zH was -1.07 ± 1.02 and zW was -0.77 ± 1.36. The mean dose of Hydro used was 19.9 ± 1.5 mg/m²/day (17.0 to 22.5) and the median of 17OH and A was respectively 4.1 and 0.29 ng/mL.

Although the patients were shorter when compared to the average population aged 1 and even 2 years, there was an improvement on the anthropometric parameters as the patients presented a catch-up with the treatment. It is important to know the height at the moment of diagnosis for better analyze the subsequent recovery of the growth.

Topical glucocorticoid use might lead to Cushingoid phenotype. However, very little is known about the effects of topical glucocorticoid treatment on liver function.

Case: Eight months old female patient was referred to our department due to hepatomegaly and hypertransaminasemia. She had Cushingoid phenotype and 3 cm hepatomegaly. Clobetasol-17-propionate was used for 5 months to treat diaper dermatitis. This treatment was quitted one week before referral. Laboratory analyses revealed elevated ALT (125 IU/L) and AST (110 IU/L). The increases in enzyme activities were not accompanied by changes in blood bilirubin and albumin levels. Blood ACTH level was 5.57 pg/ml (N:10-42), cortisol basal level was 0.5µg/dl (N:6.2-19 µg/dl). On follow-up, basal cortisol, ACTH, and AST, ALT levels normalized in 2 weeks and 3 months respectively. Approximately 3 months later, a significant improvement in Cushingoid appearance was also observed and hepatomegaly had disappeared. Liver dysfunction was related to topical glucocorticoid use. Our findings suggest that liver dysfunction might also be a component of iatrogenic Cushing syndrome.
Testicular adrenal rest tumors in salt wasting congenital adrenal hyperplasia (CAH) — diagnostic dilemma and therapy

Kristina Klemp1; Andreas Lemmer2; Allhard Hofmann3; Gudrun Wiedemann4; Enrico von Bueren4; Klaus-Peter Ullrich4
1HELIOS Clinics Gotha, Clinic for Pediatrics and Youth Medicine, Germany; 2HELIOS Clinics Erfurt, Clinic for Pediatrics and Youth Medicine, Erfurt, Germany; 3Research Centre for Medical Technology & Biotechn, Biotechnolog, Bad Langensalza, Germany; 4Private, Private, Germany; 5Dako Colorado, Inc., Flow Cytometry, Fort Collins, United States

Background: The occurrence of testicular tumors in patients with CAH is a diagnostic and clinical dilemma. Stikkelbroeck et al. (2001) found testicular tumors in 16 of 17 patients with CAH. The differentiation between tumor cells and Leydig cell tumors is difficult. Together, MRI, ultrasonography and specific clinical signs are the best tools for discrimination. We report about a case in that only after additional application of dexamethasone the tumor suppression could be achieved.

Population: At the age between 11 and 12 years the now 16-year-old adolescent boy was diagnosed with a salt wasting CAH, confirmed by a commencing increase of 17-OHP and renin up to levels like those induced by androgen producing tumors. Search for tumors revealed no abnormal findings.

Objective: We present diagnostic procedures, treatment and follow up.

Results: An enhanced hydrocortisone treatment did not normalize the increased levels of 17-OHP, PT, 11-O-PT and renin. At the age of 15 inhomogeneous tissue regions 2 cm in diameter were observed in both testes. As a result of a dexamethasone test the next day a normalization of the values occurred. After a combination therapy with hydrocortisone and low dose dexamethasone the affected regions disappeared and 17-OHP and renin secretion normalized.

Conclusions: (1) In the course of CAH with salt wasting an activation of dispersed adrenal rest tissue in testes may be expected especially with onset of puberty. (2) Patients with CAH should be followed up from start of puberty with an ultrasonography of testes at regular intervals. (3) A biopsy can be helpful. (4) If hydrocortisone treatment is without effect, an additional therapy with dexamethasone (single dose / evening) can be recommended. The question why a suppression of adrenal cells in the testicles using hydrocortisone did not happen remains unexplained.

Isolated hypoglycaemia as a form of presentation of primary adrenal insufficiency during the first two years of life

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1Hospital Materno-infantil Vall d’Hebron, Pediatric Endocrinology, Barcelona, Spain

Introduction: Primary adrenal insufficiency (excluding congenital adrenal hyperplasia) is a rare disease in children. Congenital forms appear during the first two years of life and salt loss is classically described as the first manifestation. We present a group of infants with isolated hypoglycaemia as the presentation of primary adrenal insufficiency.

Objective: To describe the presentation and clinical evolution in patients diagnosed of congenital primary adrenal insufficiency.

Patients and methods: 7 patients (4 boys) diagnosed of congenital primary adrenal insufficiency based on: 1) low cortisol (< 5 mg/dl) with high ACTH (> 500 pg/ml); 2) diagnosed during first 2 years of life; 3) no associated autoimmune diseases; 4) adrenal ultrasound that ruled out haemorrhagic or infectious disorder; and 5) 17-hydroxyprogesterone > 200 ng/dl.

Results: Age at diagnosis: 9.3 ± 6.2 months (1.5-15). Initial clinical manifestations: hypoglycaemia (n=6), hyperpigmentation (n=6), asthenia (n=3), hypotension (n=2), mild hyperpyrexia and dehydration without hyperpotassaemaia (n=1), hyperpyrexia and dehydration with hyperpotassaemaia (n=1) and hyperpyrexia and seizure (n=1). Parameters at diagnosis in patients presenting with hypoglycaemia (n=6).

In the patient with hyponatraemia and hyperpotassaemaia, DAX-1 gene was studied and a mutation in exon 1 was detected. Study of the MC2R gene is pending in the rest.

Initial treatment: hydrocortisone+fludrocortisone (n=6), hydrocortisone (n=1). Age at last visit: 16.5 ± 9.8 years (3.2-26.2). Treatment at last visit: hydrocortisone (n=5), hydrocortisone+fludrocortisone (n=1), prednisone (n=5). The five patients over 14 presented complete pubertal development. Three patients presented hypoglycaemia and one hypotension crisis during intercurrent infectious episodes.

Conclusions: the absence of salt loss with hyperpotassaemaia in six of the seven infants with primary cortisol deficiency led us to hypothesize that ACTH unresponsiveness may be a frequent cause of primary adrenal insufficiency during the first two years of life and should be investigate.

Risk of hyponatraemia by hypotonic fluid administration in children with gastroenteritis

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1Hamamatsu University School of Medicine, Department of Pediatrics, Hamamatsu, Japan; 2Iwata City Hospital, Department of Pediatrics, Iwata, Japan

Background: Hypotonic fluid infusion is routine administration into children with acute gastroenteritis, especially in Japan. Generally 0.5% saline with 2.6% dextrose is chosen as initial fluid therapy and then 0.2% saline with 4.3% dextrose solution is followed as maintenance treatment. Some recent studies have mentioned that hypotonic intravenous fluid therapy could develop hyponatraemia in the patients with gastroenteritis.
Aim: The objective of this study was to know whether hypotonic intravenous fluid therapy would be appropriate for children with gastroenteritis. Methods: We measured plasma sodium concentration and arginine vasopressin (AVP) in pediatric patients with symptoms like vomiting or diarrhea were treated by fluid therapy. Blood samples were collected before treatment.

Results: Eighty patients received fluid therapy. The mean plasma sodium concentration was 137±4.1 mEq/l (mean±SD). Hyponatremia (≤136 mEq/l) was seen in 42% (n=34) of patients. arginine vasopressin was high (mean±SE: AVP, 11.2±4.1pg/ml) in 7 of 14 of patients, although sodium concentrations were within normal or low level. It is likely that secretion of arginine vasopressin was increased by non osmotic stimulation as vomiting.

Conclusion: Hypotonic solution has a risk to develop hyponatremia with parenteral hypotonic solution, because hyponatremia or and excessive secretion of arginine vasopressin were seen before treatment.

### Table R-8

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age at Diagnosis (days)</th>
<th>PTH (pg/ml)</th>
<th>Vitamin D-25 (mg/dl)</th>
<th>Calcium (mg/dl)</th>
<th>Phos (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-Term</td>
<td>6.5 ± 2.5</td>
<td>37.1 ± 17.8</td>
<td>13.9 ± 3.6</td>
<td>6.7 ± 1</td>
<td>9.2 ± 1.8</td>
</tr>
<tr>
<td>Pre-Term</td>
<td>56</td>
<td>155.5 ± 7.7</td>
<td>20</td>
<td>6.5 ± 0.3</td>
<td>8.6 ± 0.8</td>
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<td>Di George</td>
<td>3</td>
<td>51</td>
<td>7.6</td>
<td>8.6</td>
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### Table R-9

<table>
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<th>Vitamin D deficiency: a condition highly prevalent also among term infants and formula fed infants</th>
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<tr>
<td>Vitamin D deficiency remains a common cause of hypocalcemia in newborns especially in Hispanics, African-Americans, breastfed infants and preterm infants (PT). Vitamin D deficiency is not considered a frequent etiology of hypocalcemia in full term (FT) formula fed infants. We evaluated etiology of hypocalcemia in infants and preterm infants suffering with diarrhea and diuresis were admitted with the diagnosis of hypocalcemia or hypocalcemic seizures in the last 3 years 12 infants (1 girl 11 boys, 11 FT and 2 PT) were admitted with the diagnosis of hypocalcemia or hypocalcemic seizures in the last 3 years. Vitamin D deficiency accounted for 11 (9 FT and 2 PT) cases and DiGeorge syndrome for 1 case. All except one were formula fed. FT infants presented at 2 months of age, boy with DiGeorge syndrome at 3 days and 65% of FT presented from 6 to 10 days of life (range from 1-19 days). 10 of 12 (83 %) had seizures as the presenting symptom. The seizures were focal in 2 (16%) &amp; generalized in 8 infants. In the other 2, hypocalcemia was an incidental finding. The mean gap between the pregnancies was 2.9 years. Term infants had no intact PTH elevation secondary to the hypocalcemia as opposed to pre-term infants. Vit D25 values were from 10 to 20 ng/ml (mean 13 ± 3.6). Phosphate level was elevated in 7 of 12 infants. There is a high prevalence of vitamin D deficiency among hypocalcemic FT, formula fed infants, especially boys (91%) in contrast to published literature. All FT infants had relatively low iPTH values, suggesting lack of compensatory increase in iPTH in response to low calcium. Vit D25 level was not extremely low, but transient hypoparathyroidism in infancy and immature renal response to PTH may have induced hyperphosphatemia and hypocalcemic seizures. Hypocalcemia may be an important factor in the cause of focal seizures. Vitamin D supplementation should be considered full-term and formula fed infants.</td>
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### Table R-10

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<tr>
<th>Bilateral femoral fractures due to rickets in an adolescent boy with cerebral palsy</th>
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| It has been demonstrated that biochemical and radiological rickets can develop during anticolvulsan therapies (ACT). A 14 year-old-boy was admitted to bilateral femoral fractures transferred from orthopaedic clinic to pediatric endocrine unit due to hypocalcemic convulsions. His medical history was as follows: perinatal asphyxia, seizures disorders, diagnosis of Lennox – Gestault syndrome (LGS). He had received ACD since he was diagnosed as LGS 10 years ago. On physical examination, he had microcephaly with otherwise normal body growth, swelling of wrists and his lower extremities were put in plaster casts because of femoral fractures. His laboratory results revealed that hypocalcemia (5.7mg/dl), hypophosphatemia (2.4mg/dl), elevated alkaline phosphates (422U/L) and parathyroid hormone (225pg/ml) levels. Serum 25(OH)vitamin D level was low (4.5mg/ml). Radiographs of hands/wrists demonstrated cunin fraying, and widening of epiphysis. His bone mineral density of the lumbar spine was 0.63gr/cm², Z score was -2.0. Based on these findings, he was diagnosed as rickets stage 3 and was started on calcitriol. After his calcium level reached to 7mg/dl, he was treated with oral plaster casts because of femoral fractures. His laboratory results revealed that hypocalcemia (5.7mg/dl), hypophosphatemia (2.4mg/dl), elevated alkaline phosphates (422U/L) and parathyroid hormone (225pg/ml) levels. Serum 25(OH)vitamin D level was low (4.5mg/ml). Radiographs of hands/wrists demonstrated cunin fraying, and widening of epiphysis. His bone mineral density of the lumbar spine was 0.63gr/cm², Z score was -2.0. Based on these findings, he was diagnosed as rickets stage 3 and was started on calcitriol. After his calcium level reached to 7mg/dl, he was treated with oral plaster casts because of femoral fractures. His laboratory results revealed that hypocalcemia (5.7mg/dl), hypophosphatemia (2.4mg/dl), elevated alkaline phosphates (422U/L) and parathyroid hormone (225pg/ml) levels. Serum 25(OH)vitamin D level was low (4.5mg/ml). Radiographs of hands/wrists demonstrated cunin fraying, and widening of epiphysis. His bone mineral density of the lumbar spine was 0.63gr/cm², Z score was -2.0. Based on these findings, he was diagnosed as rickets stage 3 and was started on calcitriol. After his calcium level reached to 7mg/dl, he was treated with oral plaster casts because of femoral fractures. His laboratory results revealed that hypocalcemia (5.7mg/dl), hypophosphatemia (2.4mg/dl), elevated alkaline phosphates (422U/L) and parathyroid hormone (225pg/ml) levels. Serum 25(OH)vitamin D level was low (4.5mg/ml). Radiographs of hands/wrists demonstrated cunin fraying, and widening of epiphysis. His bone mineral density of the lumbar spine was 0.63gr/cm², Z score was -2.0. Based on these findings, he was diagnosed as rickets stage 3 and was started on calcitriol. After his calcium level reached to 7mg/dl, he was treated with oral plaster casts because of femoral fractures. His laboratory results revealed that hypocalcemia (5.7mg/dl), hypophosphatemia (2.4mg/dl), elevated alkaline phosphates (422U/L) and parathyroid hormone (225pg/ml) levels. Serum 25(OH)vitamin D level was low (4.5mg/ml). Radiographs of hands/wrists demonstrated cunin fraying, and widening of epiphysis. His bone mineral density of the lumbar spine was 0.63gr/cm², Z score was -2.0. Based on these findings, he was diagnosed as rickets stage 3 and was started on calcitriol. After his calcium level reached to 7mg/dl, he was treated with oral plaster casts because of femoral fractures. His laboratory results revealed that hypocalcemia (5.7mg/dl), hypophosphatemia (2.4mg/dl), elevated alkaline phosphates (422U/L) and parathyroid hormone (225pg/ml) levels. Serum 25(OH)vitamin D level was low (4.5mg/ml). Radiographs of hands/wrists demonstrated cunin fraying, and widening of epiphysis. His bone mineral density of the lumbar spine was 0.63gr/cm², Z score was -2.0. Based on these findings, he was diagnosed as rickets stage 3 and was started on calcitriol.

### Table R-11

<table>
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<tr>
<th>Dilemma of hyperparathyroidism in hypophosphatemic rickets: two cases</th>
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<td>Hyperparathyroidism is noteworthy not only during the treatment but also in untreated patients with hypophosphatemic rickets (HR). We presented two patients diagnosed as HR with hyperparathyroidism although both had never received phosphate treatment. Patient 1: A 16 years old male was presented with difficulty in walking since 14 years old and multiple fractures. He was previously diagnosed ankilosing spondilitis. His past medical history was unremarkable until 14 years old.</td>
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Physical examination revealed severe deformities in extremities and height less than 3 percentile. Severe hypophosphatemia (1.3 mg/dl), normocalemia (9.6 mg/dl), ALP (1764 U/l), iPTH (95 pg/ml) levels were detected at presentation. 25 OH D vitamin, urinary Ca/Cr, TRP were 25ng/ml, 0.24, 43%, respectively. No tumour was detected. He was diagnosed as autosomal-dominant HR and treated with high dose active vitamin D and low dose phosphate.

Patient 2: A 4.3 years old male born to consanguineous family was presented with inability to walk since the age of 12 months. He was previously diagnosed as nutritional rickets and treated with vitamin-D and Ca at 18 months. He was hospitalized at 2 years old with serum Ca 9.6 mg/dl, P 2.4 mg/dl, ALP 1903 U/L, PTH 511 pg/ml, 25 OH D 68 ng/ml and 1.25 OH D 20 mg/ml and given Stoss therapy. He had a sibling with similar findings died at 2.5 years old. Physical examination: disproportional short stature (height -4.5 SD), deformities of lower extremities and thorax, widening of wrist. Radiograms documented rickets, fractures and pneumonia. TRP and TmP/GFR were found as 88% and 1.8 mg/dl. He was diagnosed X-linked HR and treated with phosphate and active vitamin D.

Hyperparathyroidism is a challenge at the diagnosis and during treatment of HR. PHEx gene plays a role in the regulation of PTH. The mechanism is predicted to be more complex than merely regulation of FGF-23.

Methods: 128 patients with type I diabetes attending a single pediatric endocrine clinic underwent anthropometric and biochemical assessment. Anthropometric measurements followed WHO criteria. Blood samples were analyzed for glycated hemoglobin (HbA1C), cholesterol (chole), triglycerides (TG), low density lipoprotein (LDL) and high density lipoprotein (HDL), and blood pressure was recorded.

Findings: Patients’ mean age was 12.6 ± 4.1 years. Patients’ mean age at the onset of diabetes was 7.1 ± 2.8 years. Mean duration of diabetes was 6.9 ± 3.2 years. 48.5% of patients had some form of dyslipidemia. 21.4% had isolated hyperglycemia, 11.6% isolated hypercholesterolemia and 15.5% mixed hyperlipidemia. Factors associated with dyslipidemia included longer duration of diabetes, higher mean age, higher mean HbA1C (p < 0.001). Hypertriglyceridemia was more frequent in female patients and subjects with higher BMI (p < 0.05). The mean value of TG 199.9 ± 74.1 mg/dl, TC 178.5 ± 29 mg/dl and LDL 141.2 ± 37 were significantly higher in patients with poor metabolic control (mean value of HbA1C 9.3 ± 1.8) than the diabetic patients with better control (mean value of HbA1C 7.1 ± 0.77). TG 156.8 ± 53.9 mg/dl, TC 143.5 ± 37.6 mg/dl LDL 108 ± 21.2.

Conclusion: Our findings indicated that type I diabetic patients with poor metabolic control are at higher risk of developing dyslipidemia. However, given the well documented problems of lifestyle regulation and compliance in optimizing control especially in this age group, we need to develop alternative and simple interventional strategies to improve outcome. Monitoring of lipids should be extended and yearly screening of patients for dyslipidemia recommended.
The aim of this study was to analyze the onset of the diseases and the age at the diagnosis was found ($r=+0.45$; $p<0.000001$). 2. Heavier children needed higher daily dose of insulin ($r=+0.58$, $p=0.00000002$). 3. No correlation was found between BMI before the onset of diabetes and the level of HbA1c ($r=-0.0099$; $p=0.09$). 4. No significant differences in the mean age, BMI and the level of HbA1c at diagnosis in particular years (2004, 2005, 2006) was observed.

Conclusions: In the study group the BMI increase was not correlated with the younger age of the onset of diabetes. 2. The mean value of BMI did not differ in particular years. The study sponsored by KBN Grant No 2PO5E04427.

**R-16** Read by Title

**A retrospective analysis of our patients with diabetes mellitus type 1**

Erdal Adalı; Leyla Akın; Adem Güç; Selvi Sarıkaya

Bakırköy Maternity and Children’s Hospital, Pediatric Endocrinology, Istanbul, Turkey

We aimed to evaluate the characteristics and complications of our patients with diabetes mellitus type 1. 441 DM type 1 patients (213 male, 228 female, aged 1-21 years) attending regular follow-up at our pediatric endocrinology department were evaluated retrospectively in this study. The age of diabetes onset, diabetic ketoacidosis at the first diagnosis, season at the diagnosis, insulin regimen, average HbA1c levels, blood chemistry, urinalysis and thyroid function tests were determined. Long term complication parameters included: arthropathy, microalbuminuria, retinopathy and neuropathy. Age of diabetes onset was 7.6±3.7 years in females and 7.6±4.0 years in males. The frequency of DKA at the first diagnosis was 80.7% in all patients while 87.6% in those under five years of age. Any acute complication did not occur in brain edema during DKA treatment. Seasonal preponderance was not present at the first diagnosis. 414 of the patients were eutrophic while 2 of them had clinical and 5 of them subclinical hypothyroidism at the first screening. As come to long-term complications, 15 patients developed arthropathy, 15 patients had microalbuminuria in association with hypertension in three of them, 5 had neuropathy and 2 had retinopathy. All patients with complication had bad control and only seven of them had diabetes for less than five years.

**R-17** Read by Title

**The assessment of body mass index (BMI) in Polish children with newly diagnosed diabetes mellitus type 1**

Elżbieta Petrykko; Anita Horodnicka-Józwa; Agata Jankowska; Justyna Szmit-Domagalska; Krystyna Wójcik; Mieczysław Walczak

Pomeranian Medical University, Department of Pediatrics, Endocrinology, Metabolic, Szczecin, Poland

Background: The accelerator hypothesis postulates the shared background for both type 1 and type 2 diabetes. Enhanced weight gain and obesity may be associated with high risk for T1DM.

Objective and hypothesis: The aim of this study was to analyze the association between body mass index (BMI) before the onset of diabetes and the age, level of HbA1c, daily dose of insulin intake at the onset of the disease in all patients with newly diagnosed diabetes mellitus type 1 during the years: 2004-2006.

Population and methods: The study was performed in 104 patients with type 1 diabetes mellitus, 48 girls, 56 boys aged 0-17.4 years. Mean age at diagnosis was 9.7 years. In all patients body mass index, parameter of metabolic control such as HbA1c, daily dose of insulin intake as well as the age at onset were assessed. All these parameters were estimated in all group and then in particular years.

Results: In all study group positive correlation between BMI before

**R-18** Read by Title

**Quality of life and clinical outcomes of the paediatric diabetes patients and their families treated by continuous subcutaneous insulin infusion at Nottingham University Trust Hospital: 2000 to 2005**

Douglas Thomas; Tabitha Randell; Louise Denvir; Dorothy Mackinley; Sandra Corbett

Nottingham University Hospital, Department of Paediatric Endocrinology, Nottingham, United Kingdom; Nottingham University Hospital, Department of Paediatric Psychology, Nottingham, United Kingdom; Nottingham University Hospital Trust, Department of Health Audit, Nottingham, United Kingdom

Aim to look at the all paediatric diabetic patients on Continuous Subcutaneous Insulin Infusion (CSII) pumps and see if clinical change in HbA1c was reflected in patient perception of quality of life.

Patients were identified who were treated with insulin pumps between 2000 and 2005. The records were reviewed to gain information on HbA1c, Weight, Height and BMI. Values from 2 years prior to commencing CSII to 2 years post CSII were extracted. This data was entered into SBSS. A paediatric psychologist administered a Quality of life (QoL) questionnaire and semi-structured interview at routine clinic visits.

19 patients were commenced on pumps by Nottingham University Trust. Data was available on 17 of these patients. Average HbA1c 2 years prior to commencement on pump was 10.2% which had dropped significantly to 9.4% (p-value 0.08) after 2 years on CSII. 13 of the 17 patients between the ages of 5 to 17 were interviewed and completed the QoL Measure. 13/13 patients and 11/13 parents/carers stated QoL was better on the CSII. Positive factors highlighted included freedom, fitness, self-esteem, flexibility and control. Girls had better QoL scores prior to CSII therapy compared to boys, with QoL scores improved significantly on CSII in both sexes and boys demonstrating a larger increase. (Results QoL; Pre: post CSII ; Boys = 66 : 77 ; Girls 79 > 83.)

CSII therapy resulted in an improvement in HbA1c, which was maintained at two years. The Quality of Life (QoL) questionnaire revealed significant patient satisfaction post CSII:

“Changed our attitude to diabetes - it was in control of us, now we are in control” (girl aged 12) “If you take my pump away I’ll kill myself” (boy aged 13). HbA1C alone does not provide a full clinical picture.
Intravenous insulin was started, followed by subcutaneous shots. β-cell autoantibodies from cordon blood and thereafter (yearly) from peripheral blood were always negative. Pancreas morphology detected by ultrasound was normal both in mother and infant. Steatorrhea was absent. Transient open oval foramen in the heart was observed in the infant. During the first year of life she catched-up growth. C-peptide level was 0.5 ng/ml, then undetectable after i.v. glucagon stimulation. During a 6-year follow-up, HbA1c mean values were 7.5%, and mean insulin requirement was 0.32 U/kg/day.

We performed genetic analysis on the child DNA as follows: Glucokinase, Kir6.2, JPF1, PDX1 and HNF-1α without finding any mutation. Even if the family history suggests a key role of genetic factors in the pathogenesis of PNDM, unfortunately the genetic analysis we performed up to now didn’t lead us to a definitive diagnosis. We are waiting for the result of other genetic tests like SUR1 (ABCC8) and GliX3.

R-20 Read by Title

Early-onset abnormal glucose homeostasis in Alstrom syndrome: clinical and laboratory data in four patients
Ozgur Pirgon; Mehmet Emre Atabek; Ahmet Sert
Selcuk University, School of Medicine, Department of Pediatric Endocrinology, Konya, Turkey

Alstrom syndrome is a rare autosomal recessive disorder characterized by retinal degeneration, sensorineural hearing loss, early-onset obesity, and non-insulin dependent diabetes mellitus. We report four patients, aged, 2, 9, 12, 15 year-old, with Alstrom syndrome with different clinical presentations. Molecular characterization in all patients led to the identification of a mutation (8506 G>T) in ALMS1 gene on chromosome 2p12–3. All patients had the electoretinogram results with no demonstrable response (cone–rod dystrophy).

The first case was a 15 year-old boy who became blind at the age of 6 years as the result of progressively impaired vision. At the age of 14, diabetes mellitus was diagnosed with elevated plasma glucose (417 mg/dL), HbA1c (8.4%), insulin (30.8 mU/mL) and acanthosis nigricans presented in the neck, axilla, and groin regions. The patient had elevated triglyceride levels (5790 mg/dL). The patient was managed with daily insulin injection combined with metformin. At follow up hyperglycemia and hyper triglyceridemia were decreased to normal levels.

The second case was a 9 year-old girl. She was obese. Oral glucose tolerance test showed glucose intolerance (148 mg/dL at 120 min.) and she had dyslipidemia. Diet and medical treatment with metformin improved the impaired glucose tolerance.

The third case was a 12 year-old boy, he was obese. He had suffered from a visual defect and he developed total blindness 3 years ago. In addition, he had pulmonary involvement. However, his blood examination was normal with no abnormal glucose homeostasis. The fourth case was a 2 year-old girl and sister of the third case, she had no symptoms related to Alstrom syndrome. The fourth case was a 2 year-old girl and sister of the third case, she had no symptoms related to Alstrom syndrome. The fourth case was a 2 year-old girl and sister of the third case, she had no symptoms related to Alstrom syndrome.

R-21 Read by Title

The genetic determination of tendency to cardiovascular disease in the two Bardet Biedl Syndrome with metabolic syndrome
Ayta Türel Ergür; Ozkan Ergür; Suzan Akyıldız; Semra Baykal Gökeç
1Uluk University, Faculty of Medicine, Pediatric Endocrinology, Ankara, Turkey; 2Atatürk Research Hospital, Section of Retina of Ophthalmology Dept., Ankara, Turkey; 3Atatürk Research Hospital, Molecular Genetics, Ankara, Turkey

In obese children and adolescents; myocardial infarction and thromboembolic events may develop at early ages. Severe obesity and metabolic syndrome are common findings in the Bardet-Biedl syndrome (BBS). In this study whether there were polymorphisms on cardiovascular susceptibility genes (FV, FXIII, prothrombin, fibrinogen, MTHFR, PAI-1, HPA-1, Apo-B, apoprotein-E/F3) genes were investigated in two BBS cases plus metabolic syndrome.

Metabolic syndrome was defined according to WHO criteria. According to this; case1 was aged 17.9 years old, case2 was aged 11.7 years old. Both of the cases were morbid obese. And both of te cases had polydactyly, retinitis pigmentosa, acanthosis nigricans, hypogonadism and lobulation anomaly of bilateral kidney. Case 1 was detected insulin resistance, dyslipidemia, grade 2 hepatosteatose and case 2 was detected glucose intolerance, dyslipidemia. In both cases same polymorphisms were detected on FXIII, MTHFR, PAI-1, HPA-1, Apo-e, inclination, in syndromic cases with metabolic syndrome, possibility that thromboembolic diseases and myocardial infarction could develop at early age should be kept in mind. Detecting genetic susceptibility in such cases and monitoring the patients may be life saving especially in conditions at risk such as dehydration, severe infection and operation.

R-22 Read by Title

The assessment of growth hormone receptor gene and selected postreceptor findings of growth hormone activity in short children born with IUGR
Anna Kryskulikowicz-Fengler1; Mieczyszaw Walczak2; Elzbieta Petriczk2; Andrzej Kędzia3; Eugeniusz Korman4; Cezary Gębowski5; Jan Lubinski6
1Children’s Memorial Health Institute, Department of Pediatrics, Warsaw, Poland; 2Pomeranian Medical University, Department of Pediatrics, Endocrinology, Diabetology, Szczecin, Poland; 3Karol Marcinkowski University of Medical, Department of Pediatric Endocrinology and Diabetology, Karol Marcinkowski, Poland; 4Pomeranian Medical University, Department of Genetics and Patomorphology, Szczecin, Poland

Our study assessed 74 children in prepubertal age: 37 short, born with IUGR (birth weight <10 th percentile of normal pregnancy duration) and 37 AGA with normal stature, as a control group, age and gender were stratified to assess main exponents of growth hormone activity in IUGR children.

We studied 74 children in prepubertal age: 37 short, born with IUGR (birth weight <10 th percentile of normal pregnancy duration) and 37 AGA with normal stature, as a control group, age and gender were stratified to match controls to study group. Insulin growth factors and their binding proteins were assessed in both groups. Samples were taken from venous blood, concentration measured by RIA. Amplification of GH receptor gene was done by standard method, with use 13 par of starters made for particular exons. In IUGR children concentrations of IGF-I (p<0.05), IGF-II (p<0.05), IGFBP-3 (p<0.001) were significantly higher, and higher although no significant concentration of GHBP. In the group of IUGR children concentrations of IGFBP-1 were lower than in the group of AGA children.

We also did not find any mutation in the GH receptor gene. In the pattern sequence of GH-R (GenBank nr:XO6562) in position 504 the same as pattern sequence. We observed similar number of changes in our material in exon 6, we found in the position 504 substitutions variant A/G GLY 168 GLY, in the group of IUGR children variant 504 G/G GLY 68 GLY , and in the group of IUGR children variant 504 A/G GLY 168 GLY.

It is assumed that 10-15 % of IUGR children do not present the catch-up growth, which may impair final growth. Recent literature emphasizes this fact as a possible common cause of short stature in adults. We performed the study to assess main exponents of growth hormone activity in IUGR children.

It is assumed that 10-15 % of IUGR children do not present the catch-up growth, which may impair final growth. Recent literature emphasizes this fact as a possible common cause of short stature in adults. We performed the study to assess main exponents of growth hormone activity in IUGR children. The assessment of growth hormone receptor gene and selected postreceptor findings of growth hormone activity in short children born with IUGR.

In conclusion: probably in most cases short stature in children born with IUGR may be caused by different factors than abnormal structure or function of GLR-20;

In conclusion: probably in most cases short stature in children born with IUGR may be caused by different factors than abnormal structure or function of GLR-21.
of growth hormone receptor gene.
*The study was supported by a grant from the Polish Committee of Science

R-23 Read by Title

SHOX overdosage and estrogen deficiency, two mechanisms responsible for tall stature in trisomy X?
Julia Rohayem; Walter Werner; Angela Huebner
1Children’s Hospital University of Dresden, Endocrinology and Diabetes, Dresden, Germany; 2Institute for Genetics University of Dresden, Clinical Genetics, Dresden, Germany

Mutations of the pseudoautosomal gene SHOX are known to cause mesomelic short stature conditions such as Leri Weil dyschondrosteosis and Langer mesomelic dysplasia. We hypothesise that tall stature in sex chromosome aneuploidy 46,XXX might result from SHOX overdosage and estrogen deficiency. We report a 13 year old girl presenting with tall stature (189 cm) >5 SDs above the target height of 183 cm ( +/- 5.5 cm). The patient’s growth charts displayed a linear growth far above to the 97th centile and a continuous growth spurt of 8 cm in the past 7 months following menarche. Bone age was retarded (12 years, Greulich/Pyle), predicted adult height (Bayley/Pinneau) 201 cm. Menarche age was 12.3 years, followed by irregular cycles. Clinical examination made evidence of long legs but normal arm length. The breast buds appeared underdeveloped for pubertal stage B3 P4 A1. Ultrasound investigation confirmed scarce glandular breast tissue, uterus and ovaries were morphologically inconspicuous. LH was normal for age; 2.1 IU/L, FSH slightly elevated: 4.4 IU/L (range:0.8-4.0), estradiol levels low: 53 pmol/l (prepubertal: >=37). Karyotyping revealed gonosomal aneuploidy: 47,XXX and FISH showed the presence of 3 SHOX genes. Delayed epiphyseal closure is one of the recognized consequences of estrogen deficiency. In triple X syndrome a variable ovarian dysfunction is described, ranging from normal function to severe estrogen deficiency. Growth charts of triple X females typically showed delayed deceleration of the pubertal growth spurt and a retarded epiphyseal closure, resulting in tall final height. Our patient displayed discrete signs of ovarian insufficiency. Tripling of the SHOX gene causes overdosage and contributes to disproportionate tall stature due to its location in the pseudoautosomal region of the X chromosome escaping X inactivation. This case illustrates, that SHOX gene overdosage in sex chromosome aneuploidy 46,XXX, combined with estrogen deficiency may be causative of a tall stature.

R-24 Read by Title

Relation of estrogen levels to endothelial function as measured by peripheral arterial tonometry (PAT) score in 7th grader boys
Amrit Bhargava1; Sunil Sinha; Rachika Putharkothaman; Viral Gala1; Margrita Smotkin-Tangora1; Neesha Ramchandani1; Joyce Munga1; Irina Kazachkova2; Deborah DeSantis1; Lisa Altshuler1; Kate Pavlovich2; Michael Rosenbaum2; Steven Shelov1; Svetlana Ten1
1Infant’s and Children’s Hospital of Brooklyn, Department of Pediatrics, Brooklyn, United States; 2New York Presbyterian Medical Center, Department of Pediatrics, New York, United States

Introduction: It is unknown at this point whether increase in estrogen during puberty influences endothelial function.

Objective: To establish relation of estrogens with the development of endothelial function as measured by PAT in 7th grader boys.

Methods: 34 healthy males were studied. They were divided into 2 groups on the basis of the pubertal levels of Estrone-Sulfate (ES). ES has longer half life and is due to X chromosome aneuploidy 46,XXX, combined with estrogen deficiency may be causative of a tall stature.

R-25 Read by Title

Plasma lipid profile in obese children and adolescents
Robabeh Ghergherechi1; Maryam Razaghy Azar2
1Tabriz University of Medical Sciences, Pediatric Endocrinology, Tabriz, Islamic Republic of Iran; 2Iran University of Medical Sciences, Pediatric Endocrinology, Tehran, Islamic Republic of Iran

Background: The prevalence of overweight and obesity has significantly increased in pediatric population. It can be accompanied by dyslipidemia. The aim of this study was to investigated the lipid profile in obese children and adolescents.

Methods: Two hundred and thirty five (98 male, 137 female) children and adolescents between 4-18 years of age were included in this study. BMI was calculated by using the weight (kg)/height2 (m). On the bases of BMI all cases were divided into three groups: at risk of overweight (AROW) >85% < 95 %, overweight (OW) >95 % >97 % (32), and very overweight (VOW) >97 % (169). After 12 hours fast, serum sample were collected for analyses of lipid profile. The means of three groups were compared by ANOVA at the significance level of P<0.05.

Results: Mean total cholesterol in 235 cases was 181/30 ±33/58 mg/dl, mean LDL-C was 44/22 ±13/20 mg/dl, mean HDL-C was 111/44 ±33/35 mg/dl and mean triglyceride (TG) were140/78 ±88/54 mg/dl. We found no significant difference in means serum total cholesterol, LDL-C, TG and HDL-C in three BMI groups but high levels of TG were identified in 55 percent of (VOW) compared to 37 percent of (OW) and 17 percent of (AROW) children, it was significant difference. Low levels of HDL-C were found in 26 percent of (VOW) compared to 12% of (OW). The study found no gender differences for lipoproteins.

Conclusion: There was a propensity for hypertriglyceridemia in very overweight children. Therefore, strategies should be designed for weight reduction in children and adolescents.
R-26 Read by Title

Prevalence of obesity in children and adolescents with Prader-Willi syndrome
Graziano Grugni; Antonino Cinotti; Laura Bosio; Andrea Corrias; Teresa De Toni; Eliana Di Battista; Adriana Franzese; Luigi Gargantini; Nella Greggor; Lorenzo Lughetti; Chiara Livieris; Arturo Nasedd; Giovanni Pozzani; Letizia Ragusa; Alessandro Salavatori; Alessandro Sartorio; Giuliana Tiffrin; Giuseppe Chiumello

1 Italian Auxological Institute, Division of Auxology, Verbania, Italy; 2 Bambino Gesu Children’s Hospital, Unit of Autoimmune Endocrine Diseases, Rome, Italy; 3 S. Raffaele Hospital, Pediatric Endocrinology, Milan, Italy; 4 Universita di Turin, Pediatric Endocrinology, Turin, Italy; 5 University of Genoa, Pediatric Endocrinology, Genoa, Italy; 6 University of Naples, Pediatric Endocrinology, Naples, Italy; 7 Civic Hospital, Pediatric Endocrinology, Treviglio (BG), Italy; 8 University of Padua, Pediatric Endocrinology, Padua, Italy; 9 University of Modena and Reggio Emilia, Pediatric Endocrinology, Modena, Italy; 10 University of Pavia, Department of Health Sciences, Pavia, Italy; 11 Maria SS, Pediatric Endocrinology, Troina (EN), Italy; 12 University of Varese, Pediatric Endocrinology, Varese, Italy; 13 S. Giuseppe Hospital, Pediatric Endocrinology, Milan, Italy.

The complications associated with obesity are the main risk factors for death in individuals with Prader-Willi syndrome (PWS). In this context, weight control seems to be improved in those subjects who have had the benefit of early diagnosis and treatment. Because of the better awareness of PWS during the past 20 years and more reliable genetic testing, the diagnosis is actually made earlier than in the past. The objective of our study to analyse the prevalence of obesity in the Italian population of PWS <18 years. In a national collaborative study, weight-for-length, height, weight, and BMI data were available for 171 patients (96 males) with genetically confirmed PWS, aged 0.4-17.8 years. From birth to 24 months overweight and obesity were considered when weight-for-length were >85th percentile and >95th percentile, respectively [Kuczmarski et al., 2002]. For PWS aged 2 to 8 years we defined as overweight and obese those patients with a BMI more than the percentile curves that at age 18 years passed through the cut off point of 25 and 30 for adult overweight and obesity, respectively [Cole et al., 2000]. In addition, BMI SDS was derived from population standards [(Cole et al, 1995)]. Obese and overweight patients were 69 (40.3%, 40 males) and 36 (21.1%, 19 males), respectively. Sixty-two subjects were overweight (36.5%, 35 males) and 4 individuals <2 years were underweight (2.3%, 2 males). BMI SDS ranged from -3.4 to 15.1 (mean±SE: 3.65±0.32). A low rate of obesity in the first 5 years of age was in according with the natural course of PWS, but it is of note that about 1/4 of patients aged 6-17 years was overweight (24.8%, 28 cases), differently from what previously reported. As far as our non-obese PWS subjects are concerned, 40 out of 66 patients were undergoing GH therapy, while 3 subjects have stopped GH therapy. In addition, 18 individuals without GH treatment were younger than 3 years. These findings seem to confirm that early diagnosis and anticipatory care are required to achieve better outcomes.

R-27 Read by Title

Nondiabetic and nonhypertensive renal consequences of obesity in childhood
Paula Sol Ventura; Miliam Lozano; Maria Llopis; Maria Munillo; Diego Yeste; Joan Bel

1Hospital Universitario Germans Trias i Pujol, Pediatric Endocrinology, Barcelona, Spain; 2Hospital Universitario Germans Trias i Pujol, Biochemistry, Barcelona, Spain.

Obesity is associated with glomerular hyperperfusion and hyperfiltration from physiological adaptation resulting from afferent arteriolar vasodilatation. The renal injury is further exacerbated by concomitant presence of dyslipidemia, hyperglycemia, and/or insulin resistance, inflammation and hypertension. The renal injury clinically manifests as microalbuminuria, proteinuria and/or poor renal function, and is histologically characterized by glomerulomegaly, mesangial expansion and/or sclerosis.

Aims: to evaluate a group of obese children and adolescents, the existence renal alteration, and the possible relationship with other complications of obesity.

Methods: we evaluated 108 obese children and adolescents (BMI>97P), aged between 3 and 17 years (mean 11). We analysed: anthropometric parameters, SDS-BMI; blood pressure control (using an average of 3 measurements, elevated systolic or diastolic blood pressure >95thpercentile, at least 1 week apart. Task Force Report, Pediatrics 1996); biochemical markers, HDL-cholesterol, triglycerides(TG), renal function, oral glucose-tolerance test(2hs), HOMA index (insulin x fasting glucose/22.5), microalbuminuria (relation albuminuria/creatininuria, at least 1 week apart, using the first miccion of the day). Statistical analysis with SPSS, version 11.

Results: we studied the existence of microalbuminuria in 108 children (median: 6mg/g creat, range: 932), 2 adolescent presented macroalbuminuria (table), the remaining patients presented values alb/creatininuria >30mg/gr (normal<30mg/gr) (n:106, median:23, range:5).

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, age, BMI</td>
<td>boy, 17 years, BMI:45, 5</td>
<td>girl, 15 years, BMI:47.9</td>
</tr>
<tr>
<td>Evolution years of obesity</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>alb/creatininuria &gt;30mg/gr</td>
<td>244</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>Glucose intolerance</td>
<td>244</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>HDL:33, TG:158</td>
<td>HDL:37, TG:149</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>75-85thpercentile</td>
<td>75-85thpercentile</td>
</tr>
<tr>
<td>Inflammation: CRP (mg/L)</td>
<td>8.1</td>
<td>6</td>
</tr>
<tr>
<td>Intima-media thickness</td>
<td>Normal (0.05/0.05)</td>
<td></td>
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<tr>
<td>Echocardiographic</td>
<td>normal</td>
<td>Left ventricular end systolic internal dimension to increase</td>
</tr>
<tr>
<td>Ultrasound, alanine-aminotransferase, aspartate-aminotransferase</td>
<td>Steatosis, normal liver enzymes</td>
<td>Normal liver enzymes</td>
</tr>
<tr>
<td>Treated with angiotensin converting enzyme inhibitors</td>
<td>Favorable response to treatments</td>
<td></td>
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</tbody>
</table>

Conclusions: in both adolescent patient A and B) with macroalbuminuria (alb/creatininuria >300mg/gr), with glucose intolerance, but in the absence of diabetes and hypertension, we can conclude that the kidney disease can be directly attributed the obesity, and independently associated with risk factor of glomerulopathy (hypertension, diabetes). However we can’t absolutely rule out renal pathology concomitant for absence of renal biopsies.

R-28 Read by Title

Bone age status in obese children
Meral Karadag; Murat Aydin; Ayla Guven; Tolga Ozgen

Ondokuz Mayis University, Pediatrics, Samsun, Turkey

In the recent years, the incidence of obesity has been increasing in all age groups. The effect of obesity on bone development is controversial. There have been many opinions that obesity generally accelerates the bone development. On the other hand, there have been only a few studies related with this subject. In this study, we investigated whether there is diversity between chronological age and bone age in children with exogenous obesity. Two hundred eight cases with obesity which were followed up by Department of Pediatric Endocrinology, Ondokuz Mayis University Faculty of Medicine, have been included in this study. The patients who have hormonal abnormality, except having insulin resistance, have been excluded from this study. The bone age of the patients has been determined by pediatric endocrinologist using G-P and TW methods with left wrist radiographies. The age of the patients were 3,6-17,7 years, 113 were female (54%) and 95 were male (46%). The G-P bone ages were equal to chronological age in the patients who have stage 1 puberty, and were advanced in the patients who have stage 2, 3, 4, and 5 puberty. Twenty of the bone ages were similar with chronological ages in patients who have stage 1, 2, 3, 4 pubery and more advanced than chronological age in patients who have stage 5 puberty. The G-P bone ages were found to be advanced in the groups of patients with metabolic syndrome, PCOS, impaired glucose tolerance and insulin resistance. We conclude that, bone ages were advanced in obese children.

46th Annual Meeting of the ESPHE Horm Res 2007;68(suppl 1): 1-282
Aim: The diagnostic usefulness of GH provocation tests is still under evaluation. Although these are imperfect and have poor reproducibility. We investigated the diagnostic potential of IGF-1 and IGF-BP3 to distinguish between ISS and GH-deficiency and to test the diagnostic accuracy of these combined GH-dependent markers, we recruited 233 short children divided in two groups: 1) 130 subjects (71 males and 59 females) mean age 9.9 ±3.1 SD yrs and bone age 8.3 ±3.6, with GH response to two provocative testing (clonidine and arginine) < 10 ng/ml) 2) 103 ISS children (66 male and 59 female), aged 9.4±2.8 yrs. All these patients at the time of test had an height < 2 DS and normal or subnormal growth velocity; all were in pubertal stage. The subjects with malnutrition, coeliac, thyroid, other chronic diseases and chromosomal abnormalities were excluded from the study. Plasma IGF-1 values were within aged matched 5th to 95th p. in both groups because of it’s benefits. However, IGF-BP3 levels were significantly lower in GH-deficient children than in ISS, may serve as a valuable parameter in combination with others in the evaluation of the GH-IGF axis.

Background: Peri pubertal obesity is associated with great problems, from impacts on children health to socio-psychological development and life. The aim: of this article is to document the frequency of obesity and evaluate the metabolic and hormonal changes at obese adolescents.

Methods: Population based study, medical team realized screening intervention among teenagers at five second schools in Casak. Measurement antropometric data according to BMI (Body Mass Index), detected over weight children (BMI >85th perc.). At extreme obese (BMI >95th) realized clinical research (coronary, renal and hepatic function) and evaluate metabolic change, hormonal and biochemical excess. Analysed data of biomedical parameters, lipid status (TG, LDL, HDL, insulin, glucose level, fasting and postprandial, fasting insulin increase, resistance IR, HbA1c, hormonal changes- diurnal cortisol secretion, thyroid function (TSH, FT4).

Results: At the sample of 2490 adolescents (13-15 age), found 6% obese (95F, 59M). At 2% extreme obese (26F, 18M), 40% dyslipidemic (10F=7M), elevated lipid index; at 20% (5F, 4M) IR, 12% (2F=3M) alteration HbA1c>7%, with no change fasting and postprandial glyc. Cortisol profile irregular at 8% (2F/1M), thyroid function- subclinical hypothyreosis at 12% (3F=2M), with lipid excess 9% (3F/1M) and autonomy 6% (2F/1M).

Conclusion: Obese adolescent are frequently girls, and have more other endocrine disorders. Therapy treatment suggest diet and physical activity for only BMI high, strict diet for only lipid excess, low sugar diet with slow glycemic index food intake, for IR, and permanent 30-40 min walking a day. After for weeks regular sleeping time, adequate diet and including sports, regimen cortisol and IR improved. After 12 weeks, BMI lower in F,M sig (p<1), reverse metabolic disorders. Medicament therapy: rare satins, at one patient elevated CPK, L-tyoxin at too patients elevated TSH, dyslipidemia and autoimunity. At least we still observe candidates for Metformin.
R-33 Read by Title

**Growth hormone therapy in Russell-Silver syndrome**

Heung Sik Kim; Sang Woo Park; In Kug Bang; Byung Kyu Choe

Keimyung University School of Medicine, Pediatrics, Daegu, Republic of Korea

Russell-Silver syndrome is characterized by low birth weight, growth retardation, asymmetry, abnormal sexual development, cranio-facial disproportion, short little finger and clinodactyly. There are only a few reports of growth hormone therapy in this condition.

We report the GH treatment in 3 Russell Silver syndrome patients.

Case 1. A 13-months-old boy visited our hospital for poor gain of height and weight. His height SDS was -3.16. He had small triangular face and micrognathia. He had empty sellar on left side. GH was not deficient but IGF1 level was decreased. Karyotype was 47,XXY. Bone age was much delayed for his age. GH treatment started when he was 14 months. The height SDS increased to -1.86 when he was 4 years old.

Case 2. An 18-months-old boy visited our hospital for poor gain of height and weight. Height SDS was -3.3. He had small triangular face, micrognathia and brachycephaly. GH secretion after stimulation test was slightly decreased and IGF1 level was decreased. Bone age was delayed for his age. GH treatment started at the age of 5. His height SDS reached to -2.48 when he was 9 years old.

Case 3. A 3-months-old boy visited our hospital for the evaluation of poor height and weight gain. His height was only 57cm. The height SDS was -2.03 at that time and decreased to -3.84 when he was 6 months old. He had small triangular face, micrognathia, brachycephaly and facial asymmetry. GH stimulation test was unremarkable, but IGF1 level was low. Bone age was much delayed. GH treatment was started at the age of 8 months. The height SDS was -3.16 when he reached the age of 5.

Three patients had characteristic facial appearance and their height was below 3rd percentile. Their bone age was markedly delayed and IGF1 level was decreased. After GH therapy the height was significantly increased. In one patient, the karyotype showed 47, XY. This case need close observation if he show the characteristics of Klinefelter syndrome.

R-34 Read by Title

**GH treatment in Silver-Russell syndrome: personal experience in 3 patients**

Francesca Riva; Anna Cogliardi; Angela Spandri; Luciano Beccaria; Alessandro Manzoni Hospital, Dept. Pediatrics, Lecco, Italy

Silver-Russell syndrome is characterized by stunted pre- and postnatal growth with absent catch-up growth and inappropriate advancement of bone age during childhood, typical craniofacial aspect and body asymmetry. In these patients GH secretion abnormalities have been frequently reported and GH treatment has been often proposed even if no data on final height are available. We describe the effect of GH therapy in three patients affected by Silver-Russell syndrome for a mean duration of 32 months. All patients had a significant clinical diagnostic score (greater than 4 according to Price) and 2 patients showed maternal uniparental disomy of chr 7. GH response to pharmacological tests was normal in all but one patient that showed partial GH insufficiency (patient A) (maximal GH response: 9.6 ng/ml after clonidine test). Mean nocturnal GH secretion was abnormal in one patients (patient C) (mean GH value: 1.5 ng/ml). In these two patients with GH secretion abnormality, IGF1 value was lower than 5th centile for sex and age. Two patients started GH therapy at 3.4 yrs of age (patient A and B) while patient C started at the age of 8.6 years. GH treatment was administered at a dose of 0.35 mg/kg/wk and, up to now, therapy has been continued for 2.5 years in patient A and C and for 3 years in patient B. Growth velocity after therapy increased from 4.9 ± 0.2 cm/yr (pre-treatment) to 8.3 ± 0.7 cm/yr after 1 yr (+67.5%) and 7.2 ± 0.5 cm/yr after 2 yr (+67.5%). In patient B, in the third year of treatment, growth velocity remained higher than 50% in comparison to pre-treatment measurement. Consequently, HSDS increased in all patients from -3.7 ± 0.4 (pre-treatment) to -3.0 ± 0.2 after 1 yr and -2.6 ± 0.1 after 2 yr of therapy. After GH treatment IGF1 level increased in two patients (in patient A it was unmodified) remaining in the normal range and no significant increase of insulin level occurred. According to previous studies, our preliminary data confirm a sustained catch-up growth after GH treatment in Silver-Russell syndrome.

R-35 Read by Title

**Response to rhGH and rhIGF-I therapy in 2 brothers with a pseudoxon mutation in the growth hormone receptor (GHR) causing growth hormone insensitivity (GHI)**

Amit Bhangoo; Henry Anthl; Ron Rosenfeld; Lou Metherell; Adrian JL Clark; Svetlana Ten

1Infants’ and Children’s Hospital of Brooklyn, Division of Endocrinology, Brooklyn, United States; 2Saint Barnabas Medical Center, Division of Pediatric Endocrinology, Livingston, United States; 3Lucile Packard Foundation for Children’s Health, Pediatrics, Stanford, United States; 4Barts and the London, Queen Mary, Univ of London, Centre for Endocrinology, William Harvey Rsch Ins, London, United Kingdom

Background: We describe the response to rhGH and rhIGF-I therapy in 2 brothers with physical & biochemical features of GHI. They were identified to have a homozygous intronic 108 bp pseudoxon insertion leading to the inclusion of an additional 36 amino acids in the extracellular domain of GHR.

Patient 1: A 13.7 yr old boy of Pakistani descent was followed for severe short stature (-3.8 SDS); physical features like frontal bossing & midfacial hypoplasia. He received rhGH therapy at the dose of 0.3-0.7 mg/kg/wk. The response to GH was suboptimal, with an average growth velocity (GV) of 6.9 cm/yr. At 13.2 yrs of age he was started on rhIGF-I at the dose of 0.12mg/kg/dose twice a day. The GV increased substantially to 12.4 cm/yr, with a subsequent decrease to only 1.2 cm/yr. (Fig 1A)

Patient 2: A 9 yr old boy was referred to for severe short stature (-5.5 SDS) & physical features as described above. He was started on rhGH at 3.4 yrs, the dose was increased from 0.3mg/kg/wk to 0.7mg/kg/wk. On average, the GV was only 6 cm/yr. At 8.5 yrs of age he was started on rhIGF-I at the dose of 0.12 mg/kg/dose twice a day. The GV remained low at 3.4 cm/yr. (Fig 1B)

Conclusion: Both brothers showed a poor response to rhGH, as expected with this GHR mutation. One brother had an initial good response to rhIGF-I, but the second showed little response, for unclear reasons.

R-36 Read by Title

**Efficacy and safety of growth hormone in Turner syndrome**

Fatimah Harun

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Background: Final adult heights of girls with Turner syndrome (TS) can be improved with Growth hormone(GH). However not many children with TS in a developing country can have this benefit as the cost of treatment is expensive.

Objective: To determine the effectiveness and safety of GH in girls with TS in a tertiary medical centre.

Materials and Methods: Patients with TS, confirmed by karyotype, whose bone age(BA) less than 12 years were given GH at doses between 0.045-0.050mg/kg/day. All patients were informed and given a list of adverse effects of GH and advised to record and seek treatment should any occur. Their anthropometric measurements, BP and a full physical examination and blood tests were taken at baseline, six weekly, and every 3 months as per ISGF guidelines.

Results: A total of 23 girls with TS received GH. Mean age at start of treatment was 12 years(range 5-15), BA 11 years(range 2-12). The first year...
height increase was 8.9cm (range 4.7-10). Eight completed treatment, mean duration of treatment was 3.4 years (range 1-5). The mean final adult height was 150cm (range 144.4-154) while the mean adult height of Malaysian women with TS who received no GH was 135cm. Adverse events were dizziness (n=2), pseudotumour cerebri (n=4), scoliosis (n=2), swollen joints of hands (n=2). Except for scoliosis which was mild, all the adverse events were transient. Of the 4 with pseudotumour cerebri, GH was discontinued but reintroduced in two while it was stopped completely in 2 who developed it at the end of treatment. 

**Conclusion:** The final height of 150cm achieved in those treated with GH was satisfactory for Malaysian girls. GH was also proven to be relatively safe.

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**R-37** Read by Title

**Initial assessment of a new generation recombinant human growth hormone**

*Neville J. Howard; Anne Craighead*

Children’s Hospital at Westmead, Institute of Endocrinology & Diabetes, Sydney, Australia

A new generation biosynthetic human growth hormone for therapeutic use has become available since December 2005 and is presented in a form to enhance ease of delivery and with the secondary aim of improving long-term compliance in administration of the hormone.

The purpose of this study was to investigate the initial safety and efficacy of a new generation biosynthetic human growth hormone (rhGH), Omnitrope® Sandoz.

Six subjects aged 8 to 18 years with growth hormone deficiency or short stature (one with Prader Willi syndrome) and growth failure commenced on rhGH using 5 mg/1.5 ml liquid preparation in a pen injector with ultra fine needle – Omnitrope® Pen5. The dosage was 5-7 mg/m² surface area/week given 6 days per week. Each subject was assessed closely for ease and efficiency of administration, local and systemic reaction, growth response, and general physical examination.

At 3 to 6 months following initiation of Omnitrope® all subjects had increased growth velocities comparable to responses to first generation rhGH therapy. Ease of delivery of the hormone was reported by all parents/subjects. No complaints of discomfort, pain or reaction at the site of injection were noted.

No systemic reactions were recorded including no headache, peripheral oedema or skin rashes. Ease of administration was reported in 4/6 subjects.

Initial therapeutic response to a new generation rhGH in our study was positive for safety, reliability of administration, and growth response. Longer term studies are planned to assess compliance in administration with Omnitrope®, liquid rhGH delivered by pen injection.

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**R-38** Read by Title

**Idiopathic central hypoventilation syndrome in a girl with hypothyroid dysfuction**

*Daw-Ming Niu; Chuan-Hong Kao; Ni-Chung Lee; Cheng-Hong Huang; Yu-Yuan Ke; Wen-Jue Soong*

Taipei Veterans General Hospital, Taiwan, Department of Pediatrics, Taipei, Taiwan

**Background:** Children with idiopathic central hypoventilation have a central chemoreceptor that is hypersensitive to hypercapnia with variable response to hypoxaemia. We observed this syndrome in a 7-year-old girl who, besides persistent hypercapnea and hypoxia, also suffered from hypodipsia with bouts of hyperventilation, episodes of spontaneous hypocapnia, hyperphagia and obesity, somnolence and growth retardation. These combined manifestations are consistent with hypothyramic dysfunction (HD).

**Diagnostic methods:** Serial endocrine stimulation tests were performed, which included TRH stimulation test, CRH stimulation tests, insulin tolerance test, and clomiphene stimulation test. Brain magnetic resonance imaging and single-photon emission-computed tomography scanning were also performed.

**Results:** The endocrine studies revealed growth hormone (GH) deficiency, hypothyroidism of hypothyramic origin (low serum T4 concentration with delayed supra-thyroid response of thyroid stimulating hormone to TRH), high baseline concentrations of prolactin with a delayed response to TRH, and a normal pituitary-adrenal axis. Brain imaging revealed no tumour or anatomic abnormality, and a normal hypothalamic uptake. With GH and thyroxin replacement, hypothermia has resolved and her daily physical activity has markedly increased.

**Conclusions:** The endocrine and neurologic manifestations of HD in this patient were clearly distinct from congenital central hypotension syndrome, which is generally present within the first 24 h of life, and is not associated with HD. We believe that this patient suffers from a distinct syndrome, and that hypothalamus function studies are indicated in patients with late-onset idiopathic central hypoventilation.
stimulating tests peak levels, first year response to GH therapy (as Å height SDS), duration of GH therapy were similar in both groups statistically. Final heights were evaluated for two groups.

Results: Before the therapy, as can be expected, parentally adjusted deficit of height was significantly more profound in Group 2 than Group 1. Final height SDS was similar in both groups. Although the final height SDS was significantly worse in Group 2 than Group 1 while corrected by midparental target height, improvement of height was better in Group 2 than Group 1. Chronological and bone age at cessation of therapy, and IGFI-3 SDS at cessation of therapy were similar in both group.

Conclusions: Genetically short child can exceeded his/her genetic height potential with GH therapy when GHD was detected. Besides GH therapy would result worse height improvement in children with low MPH SDS, these children attained better final height than their midparental target height.

R-41 Read by Title
Occurrence of various variants of dwarfism in children and adolescents of the Uzbek origin based on a retrospective analysis
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The aim of our study was to determine the occurrence of variants of dwarfism in ethnic Uzbek children and adolescents according to their attendance of the Research Institute of Endocrinology (RIE).

9446 case reports of children and adolescents admitted the RIE clinic during 1995 to 2005 were analyzed. The number of patients with growth retardation (GR) made 1568; of them there were 760 children aged 1 to 11 years (352 boys and 408 girls) and 808 adolescents aged 12 to 16 years (489 boys and 319 girls). The greatest number of patients with GR had congenital hypothyroidism (CHT) — 28.3% followed by children and adolescents with somatogenic dwarfism (SD) — 22.4% (with various chronic somatic diseases). In the structure of the disease the next place is taken by constitutional retardation of physical and sexual development (CRPSD) making 19.7% (its occurrence in boys and girls made 3:1). Patients with somatotrophic deficiency made 15.6% (girls/boys ratio was 1:1.5). Hereditary pathology was diagnosed in 4.6% of cases, the number of girls with Turner Syndrome (TS) prevailed making 58.9% (various mosaicism variants were found in 41% of TS girls).

The occurrence of other hereditary syndromes varied and included 10 girls with Bard-Moon-Bidle Syndrome, 9 cases with Nunan Syndrome, 7 ones of pyknodyosostosis, 2 cases with Russel-Silver Syndrome, 2 cases with Bloom Syndrome. Paltauf’s dwarfism made 3.8% and that with familial dwarfism — 1.3%; skeletal dysplasia was found in 6 cases (0.4%).

Thus, the analysis of the occurrence frequency of dwarfism variants in ethnic Uzbek children and adolescents according to their attendance showed the leading place of non-endocrine diseases (SD, CRPSD) in the structure of dwarfism variants accompanied by stunting. In children with dwarfism of endocrine genesis the greatest per cent was among CHT patients, somatotrophic insufficiency and hereditary pathology.

R-42 Read by Title
Unreliability of classic provocative tests for the diagnosis of growth hormone deficiency
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We investigated 9 short prepubertal children with blunted GH response to classic pharmacological stimuli in contrast with near-normal growth rate. As the subjects showed psychological problems due to their short stature, both physicians and parents requested a deeper endocrinological evaluation for having a definitive diagnosis. Therefore, a supraphysiologic stimulus such as GHRH plus arginine was used to evaluate the pituitary reserve and the children were followed to evaluate their growth velocity for a longer period before starting GH replacement therapy and. Serum GH levels were measured by a time-resolved immunofluorimetric assay before and after 1 µg/kg BW iv injection of GHRH, while serum PRL, IGF-I and insulin were evaluated only in basal conditions using an automatic immunometric assay. Of 9 studied subjects, 7 showed a normal GH response to GHRH plus arginine administration; the parents of the remaining 2 children refused the test.

Normal serum levels of PRL, IGF-I, insulin and a normal insulin sensitivity were observed in all children. After one year, the growth rate in each patient was further improved and reached almost normal values. Our results further confirm that the decision to start GH replacement therapy should be based on both auxological parameters and laboratory findings. The GHRH plus arginine test appears to be useful to identify false GH deficiency in children showing a blunted GH response to classic stimuli in contrast with normal growth rate.

R-43 Read by Title
Calcium-phosphate metabolism in children with short stature, normal GH secretion and retarded bone age – the preliminary study
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Short stature might be caused by many diseases or pathologies with different etiologies. The majority of those causes are nonhormonal. The most common reason for growth disturbances are gastroenterological pathology or incorrect diet. The quality of diet concerning the calcium and vitamin D3 supplementation is an important factor of normal bone development. We evaluated the calcium-phosphate metabolism parameters in children with short stature. The inclusion criteria were: height <−2SD, height velocity <−1SD, bone age(BA) < 80% chronologic age (CA), normal GH secretion, euthyroidism, EMA negative, no chronic diseases in patient’s history. The study group was consisted of 15 children aged 6-13 years, mean height SD was −2.5, BA/CA ratio = 0.66. Serum levels of ionized and total calcium (Ca), inorganic phosphate (P), magnesium, PTH, 25(OH)D3, alkaline phosphatase (ALP) and urine levels of Ca, P were measured. The GFR (glomerular filtration rate) and Ca/Cr (calcium/creatinine) ratio were calculated. Results: 2 patients presented low levels of Ca, low Ca excretion with urine and 25(OH)D3 levels within low-normal range. 2 other patients presented low Ca and P urine excretion. 4 patients had elevated PTH coexisting with electrolyte disturbances suggesting secondary hyperparathyroidism. The kidney function markers in all children were normal. Such a frequent presence of calcium-phosphate metabolism disturbances suggests the inadequate diet (Ca, D3) in examined group of children.

R-44 Read by Title
Growth and nutrition in children with cerebral palsy
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Poor linear growth and low fat stores have been described in children with cerebral palsy (CP). Growth impairment in these children may depends on many nutritional and non-nutritional factors. Aim of the study was to describe growth and nutritional status in a group of children with CP and to explore their relationship with dietary intake and severity of motor impairment. We evaluated 28 children (20 m / 8 f ), mean age 5.4±2.6, affected by diplegia (n=15), hemiplegia (n=6) or tetraplegia (n=7). Anthropometric assessment included: head circumference, height, arm span, weight, knee height, mid-upper circumference, triceps and subscapular skinfold thickness. Parents heights, gestational age, weight and length at birth were recorded. BMI, mid-upper muscle area (AMA) and mid-upper fat area (AFA) were calculated.

Dietary intake was assessed by mean of a 7-days estimated food intake diary. Severity of motor impairment was classified according to the Gross Motor Function Classification System (GMFCS). Mean height SDS (± 0.95±1.32) was lower than mean target height SDS (+0.35±1.1),height SDS was <2 DS in 20% of the patients; BMI was >2 DS in 26% and <−2 DS in 13% of the patients. On the basis of skinfold thickness (ST) and AFA we recognized 2
Persistent Hyperinsulinemic Hypoglycaemia of Infancy is a rare entity, difficult to diagnose and treat. The authors describe the clinical cases of two male children with CP. The initial biochemical severity of CH may also be involved. The authors describe the clinical cases of two male children with CP.

The authors describe the clinical cases of two male children with CP.

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The authors describe the clinical cases of two male children with CP.
ng/ml (normal, 3-18 ng/ml). Pituitary magnetic resonance imaging revealed a large pituitary adenoma with supracellar extension. Because of refused surgical treatment of pituitary enlargement by parents, medical treatment with long acting somatostatin analogue octreotide and dopamine receptor agonist cabergoline were commenced. After three months of medical treatment, nadir GH during OGGT was <1 ng/ml, IGF-I level was decreased from >900 ng/ml to 269 ng/ml, prolactin level was in normal range, and pituitary adenoma was regressed.

Conclusion: Medical therapy alone in patients with gigantism who have not undergone surgery or radiotherapy offers the prospect of near normalisation of GH/IGF-I levels together with substantial tumour shrinkage.

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R-49 Read by Title

Assessment of ovarian function in girls with precocious puberty
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Precocious puberty is a disorder of the sexualization process. The appreciation of the functional ovarian maturity in a group of girls with precipitated puberty (group 1) and a group of girls with normal puberty (group 2) revealed different results regarding the existence of menstrual disturbances (66.1%-group 1; 34%-group 2), duration of the menses (66.6%- group 1; 33.3%- group 2); the quantity of the menstrual flux – altered (61.3%- group 1; 36.8%- group 2), the presence of dysmenorrhea and/or premenstrual syndrome (60.4%- group 1; 39.6%- group 2), end-stage of breast development (24.7%- group 1; 75.3%- group 2), the presence of low blood levels of ovarian hormone (81.4%- group 1; 18.6%- group 2), presence of ovarian cysts (64% - group 1; 36% - group 2). These observations reveal disorders of the sexualization process on girls with precipitate puberty on the grounds of a delayed functional ovarian maturity compared with girls with normal puberty.

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R-50 Read by Title

Case reports of two siblings with familial ovarian dysgenesis
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This case report describes two sisters who admitted separately at different times, ages 15 and 12, presented with amenorrhea, lack of secondary sexual characteristics, and short stature. No evidence of any other congenital anomaly was found in both sisters. Laboratory studies indicated hypergonadotropic hypogonadism. Peripheral blood samples revealed normal 46, XX karyotype in both sisters. Laboratory studies indicated hypergonadotropic hypogonadism. Peripheral blood samples revealed normal 46, XX karyotype in both sisters. On ultrasound scan gonads were not visualized in both patients. In this case report, we aimed to stress the necessity of taking familial ovarian dysgenesis into consideration in female patients with short stature, lack of secondary sex characteristics, normal karyotypes, and similar sibling histories.

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R-51 Read by Title

Metabolic homeostasis in patients with polycystic ovary syndrome
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Present research was focused on studies of some metabolic disorders in pathogenesis of polycystic ovaries syndrome (PCOS) in girls. Girls aged 14-18 years (N=87) were studied in the Medical Center “Prometheus” during 2006 year. Ultrasound examination and hormonal tests (DHEA-S, LH, FSH, testosterone) were performed to diagnose PCOS in 57 girls. Some indices of carbohydrate and lipid metabolism were studied. Results obtained showed insulin-resistance in 41 patients (71.9%), which was based on homeostasis model assessment (HOMA) index found over 2.5; as well as hyperinsulinemia following sugar overload test. Out of these 41 patients 30 girls developed body mass index >20kg/m², while the rest 27 patients showed abnormally low insulin levels and increased level of DHEA-S following the glucose stimulation (12.5±0.38 vs. 9.8±0.6 ng/ml in control, P=0.01).

Lipid metabolism studies showed hypercholesterolemia in PCOS patients: 231.6±8mg/dl vs. 174±2.6mg/dl in controls (P<0.01). Lipoprotein fractions showed as following: LDLp level 5±0.63mmol/l, VLDLP as 1.3±0.18mmol/l vs. LDLp 2.9±0.4mmol/l, VLDLP 0.6±0.15mmol/l in healthy control subjects (P=0.01). 16 girls without clinically expressed insulin resistance showed LDLp and VLDLP values almost not changed: atherogenic fraction was low, though insignificantly (P<0.005).

We may conclude that the metabolic alterations in pathogenesis of PCOS express in hypercholesterolemia and are mediated primarily by insulin resistance, which predetermine the guidelines for further treatment of PCOS.

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R-52 Read by Title

Congenital panhypopituitarism as a rare cause of hypoglycaemia in newborn infants
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To illustrate differential diagnoses of postnatal hypoglycaemia we report on a newborn boy with congenital panhypopituitarism.

Case report: After an uneventful pregnancy he was born spontaneously at 41+3 gestational weeks. Apgar 8-10-10. Initially he drank well when he was nursed. At age of 10 hours he became apnoeic and hypotonic, spontaneous movements were suspended. Cardiopulmonal respiration was started immediately. With artificial ventilation his oxygen saturation was 100% but he soon developed tonic-clonic twitches that stopped after infusion of Etomidate and Luminal. After transferral to the intensive care unit blood glucose was too low to be detectable. Blood glucose was stabilized by infusion of glucose and he received dopamine and cortisone. After oral nutrition was introduced successfully, intravenous glucose substitution and cortisone was stopped. Consequently, he developed relapsing hypoglycaemia. Metabolic screening was inconspicuous. Hyperinsulinism could be excluded and maternal blood glucose levels during pregnancy had always been reported to be normal. Endocrinological evaluation revealed normal ACTH and low cortisol and normal growth hormone levels during hypoglycaemia indicating an inadequate secretion. Thyroid hormones were low. MRI of the brain showed a hypoplastic pituitary gland. According to the diagnosis of panhypopituitarism a substitution of somatotropine, cortisol and thyroxine was started. Under hormone substitution blood glucose values were always stable and no more seizures were observed. Genetic testing is on the way.

Conclusion: In newborn children with acute deterioration hypoglycaemia is a common cause for seizures. Beside frequent causes for hypoglycaemia like maternal gestational diabetes or metabolic disorders, congenital panhypopituitarism must be considered as a rare differential diagnosis. Adequate therapy must be introduced as quickly as possible as recurring hypoglycaemia can lead to asphyxia and infantile brain damage. Quick and adequate hormone substitution is essential for prevention of developmental delay.

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R-53 Read by Title

Growth hormone deficiency in infant
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Introduction: The Growth Hormone (GH) deficiency may be associated with deficiency of other anterior pituitary hormones and usually presents in infancy with hypoglycaemia, cholestatic jaundice and microcephaly.

Aim: To characterize the infants with congenital hypopituitarism attended at Children’s Hospital of Coimbra.

Methodology: Longitudinal study, 8 infants were evaluated in relation to: sex, weight of birth, gestational age, age of diagnosis, hypoglycaemia, jaundice, microcephaly, visual deficit, features of cholestasis, cortisol and GH
concentrations, lesions in the region of the pituitary or hypothalamus identified by Magnetic resonance imaging, associated hormone deficit, treatment with GH.

Results: Six infants were boys. All infants had neonatal hypoglycaemia, jaundice, 4 visual defect and 2 cholestasis features. Five of six boys had microgenia. All infants had abnormalities in the region of the pituitary. Five had ACTH and thyroid-stimulating hormone (TSH) deficit associated with GH deficit. The therapy with GH was initiated at a mean age of 0,48±0,5 Years, with a mean doses of 0,026±0,005 mg/Kg/day and the mean duration was 4.3±0.9

Years. The treatment with hydrocortisone, growth-hormone and thyroxine, improved liver disease within 4-6 weeks. The Height-SDS increased with the treatment and the Height-SDS after the treatment was significantly superior to the initial Height-SDS and to the Target stature.

Conclusions: In the infants with hypoglycaemia, jaundice and microscopic de clinician should be suspect to congenital hypopituitarism, particularly in those with developmental abnormalities of the pituitary. Substitution therapy with GH, improved liver disease and normalize the growth in those infants.

R-54 Read by Title

A case of isolated growth hormone deficiency (GHD) originated from hypophysitis of pituitary stalk. Hormone profile and time course in MRI

Results
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Background: The reasons for hypophysitis can be of primary or secondary nature. The reasons for primary hypophysitis are widely unknown. In children and adolescents the association with a diabetes insipidus is common. Mostly it appears like a panhypophysitis although an appearance like an adenohypophysitis is possible. The lesion is usually confined to the adenohypophysitis. Posterior pituitary gland or stalk involvement is rare. We report about the course of disease in a patient with a diagnosed hypophysitis with isolated stalk involvement.

Population: A boy presented with short stature (137cm, <3rd percentile, target height 176 cm) at age of 13 year with growth arrest for over one year. The growth velocity was about 3.5 cm per year. In two stimulation tests the values for GH were lower than 1 ng/mL.

Objective: We present diagnostic procedures, treatment and follow up.

Results: Under the therapy with rhGH a very good catch-up growth was achieved. The first MRI before therapy was normal, but the following two years later showed a tent-shaped thickening of the infradibulium up to the area of the eminencia mediana with an existing neurohypophyiscal bright spot. These findings persisted without change for more than 3 years. GH secretion improved after 5 years confirmed by GH stimulation tests and overnight secretion profiles of GH, Melatonin, and DHEA, although MRI remained unchanged.

Conclusions: Hypophysitis has a low incidence and its causes are unknown. It can lead to GH deficiency only as a partial dysfunction, and can last for years. rhGH treatment can improve GH secretion over the years - as seen in autoimmune diseases of the thyroid gland treated with thyroxine.

R-55 Read by Title

Two new cases of isolated scrotal hair
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Introduction: Genital hair development in infancy is rare and isolated scrotal hair (SH) is an atypical location that has not been well characterized. We describe 2 infants referred with isolated SH.

Cases: In the first case, the pregnancy was complicated both by an intra-
uterine growth retardation and a short gestation (33.5 weeks) during which the mother was treated for hypertension. The infant was delivered by cesarean section after 1 course of corticosteroid. He was breast fed and his subsequent growth was normal. He developed at 8 months a number of course scrotal hairs and a slight increase of scrotal folds. There were no other signs of premature sexual development. SH resolved by age of 13 months. In the 2nd case, the mother received 2 courses of corticosteroid and the birth was preterm (34 weeks). The infant presented a moderate respiratory distress. He was receiving formula. Long and straight scrotal hairs was first noted at 7 months and disappeared spontaneously by 11 months. No other signs of virilization were noted. Growth velocity was normal for age. No mothers reported ingestion or exposure to hormones or medications. Laboratory evaluation (DHAS, DHA, androstenedienedione, testosterone, 17 hydroxyprogesterone, 11 deoxyxycortisol, βHCG concentrations, LHHR stimulation test) and imaging studies (bone age, abdominal and testicular US) were unremarkable except in the first case who had a mildly elevated level of testesterone at 10 months (40 ng/dL). No underlying pathological cause was found.

Conclusion: The etiology of isolated SH during infancy remains unknown. Minipuberty of infancy in boys may account for SH development corresponding to the early physiologic rise in testosterone. Some reports have suggested an increased sensitivity of hair follicles to androgens and a different distribution of androgen receptors. We did not find any mention of a possible effect regarding use of corticosteroid before birth.

R-56 Read by Title

Age incidence and etiology of precocious puberty in the Institute for endocrinology and metabolism of Iran
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Abstract: Precocious puberty, defined by the appearance of secondary sexual characteristics before 8 years of age in a girl or before 9 years of age in a boy, can be distressing for families and compromise final height. Recently the age limits between normal and precocious puberty have been challenged. Considering these issues we investigated the age incidence and etiology of precocious puberty. This observational descriptive study entailed 44 girls and 8 boys with precocious puberty, examined between 1991 - 2001.

Results: Mean age of girls and boys was 5.8 ± 2.1 yrs and 7.43 ± 1.4 yrs respectively. Most of the patients fell within the age category of 7-7.9 years old (%47.7 of girls and %37.5 of boys) had central precocious puberty (CPP), including Idiopathic CPP (20 girls and 1 boy) and neurogenic CPP (1 girl and 2 boys); 7 patients (%9.1 of girls and %37.5 of boys) had peripheral precocious puberty (PPP), including congenital adrenal hyperplasia (3 boys), ovarian cysts (2 girls), McCune-Albright syndrome (1 girl) and adrenal carcinoma (1 girl); 21 patients (%43.2 of girls and %25 of boys) had normal variant puberty including premature theloarche (12 girls), premature adrenarche (6 girls and 2 boys) as well as premature menarche (1 girl). CPP secondary to PPP was identified in 1 girl with McCune-Albright syndrome and 1 boy with congenital adrenal hyperplasia.

Conclusion: The most common etiology of precocious puberty in girls was idiopathic CPP (%47.7), and in boys was congenital adrenal hyperplasia (%33.3). The presence of %40.9 of girls with idiopathic CPP within the age category of 7-7.9 yrs, may suggest an early but otherwise normal puberty in many of these girls as a consequence of the trend towards earlier maturation. Further studies require re-examining the age of normal puberty onset in girls.