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 were 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.

**R-2 Read by Title**

**Iatrogenic Cushing syndrome associated with liver dysfunction**

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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. Clobetazol-17-propionate was used for 5 months to treat diaper dermatitis. This treatment was quitied 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 0.5ug/dl (N:6.2-19 pg/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.

**R-1 Read by Title**

The importance of anthropometry at the moment of diagnosis for better evaluation of the effect of treatment on growth of congenital adrenal hyperplasia patients

Sofia Helena Valente Lemos-Marin1; Carolina Teddeo Mendes-dos-Santos1; Maria Tereza Matias Baptista1; Gil Guerra-Jr1; Marcelida Palandi De-Mello1; Andre Moreno Morcillo1

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The adrenogenital syndrome must be ruled out in any child who is precocious puberty. A 7-year-old boy was admitted because of precocious puberty and enlargement of testicles. Hormonal studies established the diagnosis of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Testicular biopsy revealed interlacing strands, cords, and rests of cells resembling interstitial (Leydig) cells but with no Reinke crystalloids. Here we report a case of testicular adrenal rest hyperplasia in congenital adrenal hyperplasia due to 21-hydroxylase deficiency: a case report

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Background: Bilateral testicular tumors are a rare complication of congenital adrenal hyperplasia. It can be extremely difficult to distinguish histologically between Leydig cell tumors and adrenocortical rest hyperplasia, which may lead in some cases to unnecessary orchidectomy.

Case: Eight months old female patient was referred to our department due to hepatomegaly and hypertransaminasemia. She had Cushingoid phenotype and 3 cm hepatomegaly. Clobetazol-17-propionate was used for 5 months to treat diaper dermatitis. This treatment was quitied 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 0.5ug/dl (N:6.2-19 pg/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.
**R-4 Read by Title**

Testicular adrenal rest tumors in salt wasting congenital adrenal hyperplasia (CAH) — diagnostic dilemma and therapy

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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 tumors 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 as 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 hydrocortison 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 testicles. As a result of a dexamethasone test the next day a normalization of the values occurred. After a combined therapy with hydrocortison 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 testicles may be expected especially with onset of puberty.
(2) Patients with CAH should be followed up from start of puberty with an ultrasonography of testicles at regular intervals.
(3) A biopsy can be helpful.
(4) If hydrocortison treatment is without effect, an additional therapy with dexamethasone (single dose / evening) can be recommended.
(5) The question why a suppression of adrenal cells in the testicles using hydrocortison did not happen remains unexplained.

**R-5 Read by Title**

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

Maria Clemente; Miquel Gussinyer; Ana Fábrega; Diego Yeste;
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Introduction: Primary adrenal insufficiency (excluding congenital adrenal hyperplasia) is a rare disease in children. Congenital forms appear during the first 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 ultrastrus that ruled out haemorrhagic or infectious disorder; and 5) 17-OH-progesterone < 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 hypotonic dehydration without hypopotassemia (n=1), hypopotassemia dehydration with hypopotassemia (n=1) and hypopotassemia seizure (n=1). Parameters at diagnosis in patients presenting with hypoglycaemia (n=6): Glucose (mg/dl) 34.7±7.4
Sodium (mEq/L) 131.0±3.3
Potassium (mEq/L) 4.4±0.6 (3.9-)
Cortisol (µg/dL) 1.2±0.8 (0.5-)
ACTH (pg/ml) 1124.3±128 (863-1250)

In the patient with hypopotassemia and hyperpotasssemia, 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: hydrocortison+fludrocortison (n=6), hydrocortison (n=1). Age at last visit: 16.5 ± 9.8 years (3.2-26.2). Treatment at last visit: hydrocortison (n=5), hydrocortison+fludrocortison (n=1), prednisone (n=1). The five patients over 14 presented complete pubertal development. Three patients presented hypoglycaemia and one hypotension crisis during intermittent infectious episodes.

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

**R-6 Read by Title**

Adrenocortical insufficiency caused by topical steroids: is abuse or misuse? (Coordinador: Güler; Otuzen Gülümser; Folke Ögren)

1Ondokuz Mayıs University Medical Faculty, Pediatric Endocrinology, Samsun, Turkey; 2Ondokuz Mayıs University Medical Faculty, Pediatrics, Samsun, Turkey

Prolonged application of topical steroids is transient suppressor of hypothalamic-pituitary-adrenal axis (HPA). Infants with diaper dermatitis and exposed to topical corticosteroids have a great risk for Cushing syndrome or adrenocortical insufficiency caused by suppression of HPA axis because diaper area is the most absorbable part of the body for potent corticosteroids. Hypertension and hyperlipidemia due to corticosteroid therapy has been reported. Here, we report six infants (four girls, two boys) aged between 3 to 8 months who exposed to topical potent corticosteroids (Clobetasol propionate and Difluorocortolone valerate) by mother’s application without doctor’s prescription. All infants had similar physical examination findings like moon-like face, buffalo hump and diaper dermatitis. Three of infants had hypertension. We examined the HPA axis and other side effects of the glucocorticoid therapy for these infants. After stopped the topical corticosteroid and serum AST, ALT, lipids, morning cortisol and ACTH levels was obtained from infants. Low dose ACTH stimulation test was shown suppression of HPA axis in all infants. Hydrocortison was started of 15 mg/m²/d for prevention of the glucocorticoid withdrawal syndrome and the hydrocortison dose was gradually decreased. Abdominal ultrasonography was performed for hepatosteatosis. Hepatomegaly was found all infants and hepatosteatosis revealed three of them. Five patients have been followed-up for three to 14 months. One infant died due to generalize cytomegalovirus infection. In conclusion we emphasize that the physicians should be alert for dangerous side effects of topical steroids and they should avoid long-term use. Furthermore all families should be given enough information when the topical steroid treatment has been chosen.

**R-7 Read by Title**

Risk of hypoponatremia by hypotonic fluid administration in children with gastroenteritis

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Takahiko Orzhaki

1Hamatsu 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 hypoponatremia 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 and 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 pg/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.

### R-8 Read by Title

**Rickets, osteopenia and bone cyst in an adolescent girl due to 25-cholecalciferol hydroxylase deficiency**  
Noora AlHemaidi1; Ashraf Soliman1  
Hamad Medical Center, Pediatrics, Doha, Qatar

F M S is a 14-year-old Qatari female who was presented to endocrinology clinic on November 2005, with a history of abnormal gait and genu valgus deformity of both lower limbs. The condition started since a year and has been progressive in nature, associated with knee pain on walking. There was no history of trauma, infection, drug intake, other skeletal abnormalities or other systemic illness. Parents were first-degree cousin, with no family history of bone or joint disease. On examination height = 164 cm, weight 68.5 kg and blood pressure = 110/65 mmHg. Musculo-skeletal exam showed genu valgus deformity more in left side. Spine and upper limbs were free. No joint swelling or tenderness was detected. She had normal heart sounds with no murmurs. Review of the other systems was unrevealing. Investigations revealed normal renal and hepatic functions, bicarbonate, ESR and ANA. Her hemogram was normal and there was no evidence of anemia. Her blood pressure was normal. Her radiographs of hip, knee and ankle revealed significant fraying of the metaphyseal front and 2 radiolucent zones (small cysts) in the upper left tibia and one in the lower part of the femur, with evident osteopenia. Her phosphate tubular reabsorption was 81%. In this patient rickets, osteopenia, bone cysts and bilateral genu valgus deformity, with persistent low phosphate, high alkaline phosphates, high parathyroid hormone, and low level of 25 OH D concentrations did not respond to treatment with 3 mega doses of vitamin D (600, 300, 000 IU) and then 600,000 IU. All her symptoms as well as radiological abnormalities improved markedly after treatment with calcitriol.

### R-9 Read by Title

**Vitamin D deficiency: a condition highly prevalent also among term infants and formula fed infants**  
Radhika Purushothaman1; Bhubanesh Bhatta2; Svetlana Ten1  
1Infants and Children’s Hospital at Maimonides, Pediatric Endocrinology, Brooklyn, New York, United States;  
2Infants and Children's Hospital at Maimonides, Pediatrics, Brooklyn, New York, United States

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 children and divided them into term and preterm infants, term infants were divided into formula fed and breastfed. The mean age of term infants was 12 days and the mean age of preterm infants was 5 days. Results: Of all 200 infants admitted for diagnosis of hypocalcemia, hypocalcemia was seen in 155 infants. Among term infants 20 (10%) had hypocalcemia. In formula fed term infants the hypocalcemia was 6% (12/200 cases) and in breastfed term infants it was 20% (38/200 cases). Among preterm infants, 15% (20/131 cases) had hypocalcemia. Of all FT infants 30% (60/200 cases) had hypocalcemia, 25% of them (15/60 cases) were formula fed and 75% (45/60 cases) were breastfed. Of all preterm infants 30% (40/131 cases) had hypocalcemia, 25% of them (10/40 cases) were formula fed and 75% (30/40 cases) were breastfed. Conclusion: Hypocalcemia is a common finding in full and preterm infants, with a higher prevalence in preterm infants and especially in Hispanic and African-American infants fed formula. Clinical recognition and prompt treatment are critical to prevent adverse neurodevelopmental sequelae in infants with hypocalcemia.

### R-10 Read by Title

**Bilateral femoral fractures due to rickets in an adolescent boy with cerebral palsy**  
Filiz Tunutuncu1; Esra Sayar Hazar2; Ayse Mentes2; Yasemin Kucukgurunoglu1; Serap Karasalioglu1  
Takuya University, Faculty of Medicine, Pediatrics, Edirne, Turkey

It has been demonstrated that biochemical and radiological rickets can develop during anticoagulant 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–Gastaut 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 (5.7 mg/dl), hypophosphatemia (2.4 mg/dl), elevated alkaline phosphatase (422 U/l) and parathyroid hormone (220 pg/ml) levels. Serum 25(OH)vitamin D level was low (4.5 ng/ml). Radiographs of hands/wrists demonstrated cuffin fraying, and widening of epiphysis. His bone mineral density of the lumbar spine was 0.63 gr/cm2, Z score was -2.0. Based on these findings, he was diagnosed as rickets stage 3 and was started on calcitriol boluses. After his calcium level reached to 7 mg/dl, he was treated with oral calcium (75 mg/kg/d) and vitamin D supplements (5000 IU/day). On the third month of the discharge his clinical and laboratory findings were normal and he was discharged. We suggest that vitamin D supplementation should be considered for children and adolescence with CP, especially if they are on ACT.

### R-11 Read by Title

**Dilemma of hyperparathyroidism in hypophosphatemic rickets: two cases**  
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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 anklosing spondilitis. His past medical history was unremarkable until 14 years old.
Physical examination revealed severe deformities in extremities and height less than 3 percentile. Severe hypophosphatemia (1.3 mg/dl), normocalcemia (9.6 mg/dl), ALP (1764 U/l), iPTH (95 pg/ml) levels were detected at presentation. 25 OH vitamin D, 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: disproportionated 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 1 diabetes attending a single pediatric endocrine clinic underwent anthropometric and biochemical assessment. Anthropometric measurements followed WHO criteria. Blood samples were analyzed for Ca, creatinine (Cr), cholesterol (cho), 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).

Hyperglycemia and dyslipidemia were 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 1 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 metabolic control such as HbAc, daily dose of insulin intake as well as the level of HbA1c at diagnosis was 9.7 years. In all patients body mass index, parameter of diabetes onset was 7.6±3.7 years in females and 7.6±4.0 years in males. 1. Acute complications (hypoglycemia, DKA) appeared in 33 patients. 2. Significant correlation was found between the duration of the disease and presence of hypoglycemia (p=0.019). Up to 50% of the patients from the study group with duration of diabetes greater than 10 years suffered at least one hypoglycemic episode which needed hospitalization. 3. Significant correlation was found between the duration of the disease and presence of retinopathy (p=0.02). 4. Significant correlation was found between the metabolic control and DKA incidence. Conclusions: 1. The duration of diabetes may increase the risk of hypoglycemia, DKA. 2. Patients with bad metabolic control more often are hospitalized due to DKA. 3. The duration of the disease is a stronger factor than degree of metabolic control for developing of retinopathy.

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 1-21years) 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 including brain edema during DKA treatment. Seasonal predisposition was not present at the first diagnosis. 414 of the patients were euthyroidic 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.

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

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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 0-7-17.4 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 male groups.

Results: 1. In all study group positive correlation between BMI before 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=0.099). 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: 1. 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.

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

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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 to 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.

Infant and her mother with permanent neonatal diabetes mellitus: which pathogenesis?

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Neonatal diabetes (ND), an uncommon form of diabetes with unclear aetiopathogenesis, is defined as hyperglycaemia that occurs within the first month of life, requires insulin, and persists more than 3 months. The outcome of ND is highly variable, may be either permanent or transient, with/without recurrence. A female infant, with birth weight 2.030 g, delivered full-term by cesarean section from a mother with permanent neonatal diabetes (PNDM), developed hyperglycaemia at day 8th, (13.9 mmol/L) in absence of ketosis.
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 oral foramen in the heart was observed in the infant. During the first year of life she caughted up growth. C-peptide level was 0.5 ng/ml, then undetectable after i.v. glucagon stimulation. During a 6-year follow-up, HbAlc 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 Glis3.

R-20 Read by Title

Early-onset abnormal glucose homeostasis in Alstrom syndrome: clinical and laboratory data in four patients

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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 2p12–13. All patients had the electroretinogram 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 mIU/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 except pigmented retinal dystrophy and nystagmus. None of the patients had cardiac and hepatic failure.

We reported early-onset abnormal glucose tolerance of the patients affected by ALMS. It can be concluded that metformin could have some effect on insulin resistance, impaired glucose tolerance and the other metabolic disturbances of patient with Alstrom syndrome.

R-21 Read by Title

The genetic determination of tendency to cardiovascular disease in the two Bardet Biedle Syndrome with metabolic syndrome

Ayça Türel Ergüür; Özkan Ergüür; Suzan Akyıldız
Semra Baykal Gökçe
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-Biedle 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-E3/3 genes) were investigated in two BBS cases with 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 the 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 FVIII, MTHFR, PAI-1, HPA-1, Apo-E. In conclusion, 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.
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, FISH 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 show delayed deceleration of the pubertal growth spurt and a retarded epiphyseal closure, resulting in final tall 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-23 Read by Title**

**SHOX overdosage and estrogen deficiency, two mechanisms responsible for tall stature in trisomy X?**

Julia Rohayem1; Walter Werner2; Angela Huebner3
1Children’s Hospital University of Dresden, Endocrinology and Diabetes, Dresden, Germany; 2Institute for Genetics University of Dresden, Clinical Genetics, Dresden, Germany

Background: To establish relation of estrogens with the development of 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:** 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 in to three groups: at risk of overweight (AROW) >85% < 95% (34), 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 percent of (OW). The study found no gender differences for lipid profile. Mean triglyceride levels of TG and lower HDL. Group 1 had lower PAT score, E1, E2, and baseline level.

**Conclusion:** The higher levels of E1, E2 is associated with better endothelial function measured by PAT in males. The higher levels of estrogens were Group 2 had higher PAT score irrespective conventional markers of endothelial dysfunction i.e higher triglycerides and lower HDL levels.

<table>
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<th>Age [y]</th>
<th>BMI</th>
<th>Q05</th>
<th>TG</th>
<th>HDL</th>
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<th>E2 [pg/ml]</th>
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</table>

**Conclusion:** There was no difference between Group 1 and Group 2 in regards to WC, % of body fat, BMI, LDL, QUICKI, and AIR. Group 2 had higher PAT score E1, E2, ES, BP, Triglyceride (TG) levels and lower HDL. Group 1 had lower PAT score, E1, E2 and higher cholesterol (Chol) levels (Table 1).

**Conclusion:** The higher levels of E1, E2 is associated with better endothelial function measured by PAT in males. The higher levels of estrogens were Group 2 had higher PAT score irrespective conventional markers of endothelial dysfunction i.e. higher triglycerides and lower HDL levels.

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**R-25 Read by Title**

**Plasma lipid profile in obese children and adolescents**

Robabeh Ghergherechi1; Maryam Razaghi 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 with 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 in to three groups: at risk of overweight (AROW) >85% < 95% (34), 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 LDL-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 percent 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.
Prevalence of obesity in children and adolescents with Prader-Willi syndrome

Graziano Grugni1; Antonio Cornia1; Laura Bosi1; Andrea Corrias1; Teresa De Toni1; Eliana Di Battista1; Adriana Franzese1; Luigi Gargantini1; Nella Gregggi1; Lorenzo Lugheti1; Chiara Livieri1; Arturo Nascetti1; Giovanni Pozzato1; Letizia Ragusa1; Alessandro Salvatori2; Alessandro Sartorio2; Giuliana Tiffo2; Giuseppe Chiumello2

1Italian Auxological Institute, Division of Auxology, Verbania, Italy; 2Bambino Gesù Children’s Hospital, Unit of Autoimmune Endocrine Diseases, Rome, Italy; 3S. Raffaele Hospital, Pediatric Endocrinology, Milan, Italy; 4University of Turin, Pediatric Endocrinology, Turin, Italy; 5University of Genoa, Pediatric Endocrinology, Genoa, Italy; 6University of Naples, Pediatric Endocrinology, Naples, Italy; 7Civic Hospital, Pediatric Endocrinology, Treviso (TV), Italy; 8University of Padua, Pediatric Endocrinology, Padua, Italy; 9University of Modena and Reggio Emilia, Pediatric Endocrinology, Modena, Italy; 10University of Pavia, Department of Health Sciences, Pavia, Italy; 11University of Genoa, Pediatric Endocrinology, Genoa, Italy; 12University of Varese, Pediatric Endocrinology, Varese, Italy; 13S. 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 normalweight (36.3%, 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 16 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-29 Read by Title**

**Obesity at adolescence - screening, endocrine disorders and management**

Rada Petrovic1; Silvia Sajic2; Slavica Markovic3; Snezana Lesovic4; Bosko Petrovic5

1Medical Center Cacak, Pediatric endocrinology, Cacak, Serbia and Montenegro; 2University Pediatric Clinic, Belgrade, Endocrinology, Belgrade, Serbia and Montenegro; 3School of Medicine University Krugujevac, Pediatric Endocrinology, Krugujevac, Serbia and Montenegro; 4Medical Center Uzice, Pediatric Endocrinology, Uzice, Serbia and Montenegro; 5Medical center Cacak, Hospital, Cacak, Serbia and Montenegro

**Background:** Peripubertal 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 Cacak. 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. Analised data of biomedical parameters, lipid status(TC,HDL,LDL,index,Tg), fasting and postprandial glucose level, 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 gyl. Cortisol profile irregular at 8%(2F=1M), thyroid function- subclinical hypothyreosis at 12%(3F=2M),with lipid excess 9%(3F=1M) and autimmunity 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 shugar 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 including sports, regimen cortisol and IR improved. After 12 weeks, BMI lower in F,M sig (p<1), reverse metabolic disorders. Medicament therapy:ratem, at one patient elevated CPK. L-tyoxin at too patients elevated TSH, dyslipidemia and autimmunity. At least we still observe candidates for Metformin.

**Conclusions:** The results confirm great discrepancy in GH concentration depending on test performed. It suggests that during the diagnostic process the value of clinical observation and auxologic data must be stressed.

**R-31 Read by Title**

**Are IGF-1 and IGFBP-3 useful in diagnosis of growth hormone deficiency in children?**

Fiorella Galliuzz1; Maria Rita Quaranta2; Stefano Stagi3; Ilaria Pagnini4; Federica Favelli5; Laura Nanni6; Salvatore Seminara7

University of Florence, Paediatrics, Florence, Italy

The diagnosis of growth hormone deficiency (GHD) in children is routinely based on clinical and auxological characteristics combined with the results of provactive tests, although these are imperfect and have poor reproducibility. To investigate 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 arginina ) < 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 prepubertal 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 95 th. In both groups and the difference between GH and ISS was not significant (p =0.14); on the contrary, the difference of IGF-BP3 in the two groups was very significant (p=0.001).

Using a cut-off of 3.4 ng (GHG) and 3.7 ng (ISS), sensitivity and specificity of IGF-BP3 were respectively : 68.7% and 100% (0-5 yrs), 61.5% and 58.3% (5-10 yrs); 66.77% and 52% (> 10 yrs). These data show that IGF-BP3 rather than IGF-1, may serve as a valuable parameter in combination with others in the evaluation of the GH-IGF axis.

**R-32 Read by Title**

**The effect of growth hormone therapy in a 14-year-old boy with Crohn’s disease and growth hormone deficiency**

Mieczyslaw Szalecki1; Barbara Rabiecka-Pietrak2; Marek Niedziela2

1Children’s Memorial Health Hospital, Pediatric Endocrinologu, Warsaw, Poland

2Poznan University of Medical Sciences, Department of Pediatric Endocrinology and Diabetes, Poznan, Poland

It is still controvercial if Crohn’s disease is the indications to growth hormone therapy.

We present a case of 14-year-old boy with severe growth deficient (-4,5SD).

The patient was growing properly up to 9 year of life,than dramatic decreased growth velocity.During the first three months in dose 0,7U/kg/week then because of slow increase of growth velocity but also a great improvement in Crohn’s disease which make possible to therapy.

The patient was growing properly up to 9 year of life.then dramatic decreased growth velocity. When he was fourteen finally growth hormone deficiency both Crohn’s disease was diagnosed[GH after iuln-4,25mg/ml and after clonidine-4,62mg/ml GFI-77,9 ng/ml].First typical for Crohn’s disease therapy (Immuran and Prednisone 2mg/kg) was started and parallel the diagnosis the growth hormone treatment was performed.After first half of year therapy we observed not only increase of growth velocity but also a great improvement in Crohn’s disease which make possible to reduce and finally put aside Prednisone. During next two years of growth hormone treatment in dose 0,6-0,5U/kg/week boy grew 18,5cm without any symptoms of bowem disease. We present this case not only because of the fact coexistance of two rare diseases but also to prove that growth hormone therapy in Crohn’s disease can not only increase growth velocity and final height but also cause of trofic influence of growth hormone on bowel mucous can reduce inflammation symptoms. Conclusion: growth hormone therapy should be seriously consider in patients(children) with Crohn’s disease because of it’s benefits.
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 scrotum 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 57 cm. 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, XXY. This case need close observation if he show the characteristics of Klinefelter syndrome.

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 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 5 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/wks and, up to now, therapy has been continued for 2.5 y in patient A and C and for 3 yrs 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 1yr (+67.5%) and 7.2 ± 0.5 cm/yr after 2 yr (+28%). 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 patient 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.

Response to rhGH and rhIGF-I therapy in 2 brothers with a pseudoexon mutation in the growth hormone receptor (GHR) causing growth hormone insensitivity (GHI) Amrit Bhandari1; Henry Anhalt2; Ron Rosenfield3; Lou Metherell4; Adrian JL Clark5; Svetlana Ten6;7Infants’ 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 Research 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 pseudoexon 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 0.12 mg/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 0.3 mg/kg/wk to 0.7 mg/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.

Efficacy and safety of growth hormone in Turner syndrome Fatimah Harun1; 2University of Malaya, Department of Paediatrics, Faculty of Medicine, Kuala Lumpur, Malaysia

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 treatement should any occur. Their anthropometric measurements, BP and a full physical examination and fundoscopy were carried out at 3-monthly visit. BA and IGF-I were taken yearly. Puberty was induced with ethinylestradiol 100ng/kg. When BA was 13 years, GH was stopped when BA was 14 or growth velocity less than 2cm/year. Those with side effects were evaluated if GH should continue.

Results: Only 12 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 of growth hormone therapy in Russell-Silver syndrome Heung Sik Kim1; Sang Woo Park1; In Kug Bang2; Byung Kyu Choe31Keimyung University School of Medicine, Pediatrics, Daegu, Republic of Korea

Growth hormone therapy in Russell-Silver syndrome
Alessandro Manzoni Hospital, Dept. Pediatrics, Lecco, Italy

R-33 Read by Title

R-34 Read by Title

R-35 Read by Title

R-36 Read by Title

46th Annual Meeting of the ESPE Horm Res 2007;68(suppl 1): 1-282
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.

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 2000 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 were 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.

R-38 Read by Title
Idiopathic central hypoventilation syndrome in a girl with hypothyroid dysfunction
Daw-Ming Niu; Chuan-Hong Kao; Ni-Chung Lee; Cheng-Hong Huang; Yu-Yuan Ke; Wen-Jue Soong
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Background: Children with idiopathic central hypoventilation have a central
chemoreceptor that is hypoosensitive to hypercarbia with variable response
to hypoxaemia. We observed this syndrome in a 7-year-old girl who, besides
persistent hypercapnea and hypoxia, also suffered from hypopidiasis with bouts
of hypermetria, episodes of spontaneous hypothermia, hyperphagia and
obesity, somnolence and growth retardation. These combined manifestations
are consistent with hypothalamic dysfunction (HD).

Diagnostic methods: Serial endocrine stimulation tests were performed, which
included TRH stimulation test, CRH stimulation tests, insulin tolerance test,
and clonidine 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 hypothalamic origin (low serum T4 concentration with
delayed sustained 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 hypventilation 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 hypventilation.

R-39 Read by Title
Growth hormone therapy for short stature in Diamond-Blackfan anaemia
Angela Huebner1; Ute Maier2; Stefan W. Eber2; Charlotte Niemeyer2
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Diamond Blackfan anaemia (DBA) is a congenital erythroid aplasia that
usually presents in infancy. The disease is characterized by genetic and
marked phenotypic heterogeneity. About two third of the patients respond
glucocorticoids whereas one third require regular transfusions which may lead
to secondary hemodilution. Short stature is a common feature in DBA patients
which may be the result of glucocorticoid therapy, of endocrine disturbances
due to secondary hemodilution or of an unknown DBA-associated effect.

We report on a patient who was diagnosed having DBA at the age of 3 months
when he was commenced on prednisolone treatment with an average dose of
0.15 mg/kg/d. Whereas in early childhood he grew along the third percentile,
between the age of 9 and 12 years his height velocity dropped down to 3.5
cm/year with a bone age delay of 2 years. Arginine and insulin hypoglycemia
tests revealed growth hormone (GH) peaks of 6.6 and 12.1 ng/ml (NR >10
ng/ml), respectively. IGF-1 and IGFBP3 were found in the normal range thus
excluding GH deficiency. As six months of discontinuation of prednisolone
did not improve height velocity, from the age of 13 years the patient was

treated with GH (kindly provided by Novo Nordisk Pharma GmbH) with a
dose of 0.028 mg/kg/d for 5 years. On this treatment and despite continuous
prednisolone treatment with 0.1 mg/kg/d the patient showed an excellent
catch-up growth and an average height velocity of 7.4 cm/year including
an appropriate pubertal growth spurt. He underwent late puberty starting at
age 16 years. At the age 18 years his height is 171 cm (-1 SDS), and with a
prospective height of 175 cm he will reach the parental target height.

Our DBA patient was not GH deficient but experienced a significant
improvement in growth velocity without any side effects. We conclude that
GH therapy might be considered in DBA patients with poor growth velocity.

R-40 Read by Title
Comparison of final height of isolated growth hormone deficient children with or without
short parents
Zerrin Siklar; Merin Berberoglu; Gönül Öcal; Pelin Bilir; Ozlem Engiz
Ankara university school of medicine, pediatic endocrinology, Ankara, Turkey

Objectives: Parental height is one of the most important factor for final
height of Growth hormone (GH) treated children. Some children with growth
hormone deficiency (GHD) also have genetically short parents as determined
by low mid parental height (MHP) SDS. It is aimed to evaluate that how
extent of the patients reach to their mid parental target height, and the effect
of GH administration on final height in two groups of isolated GHD children
either have short parents or normal parents.

Patients and Methods: The analysis comprised of 49 GHD patients with
similar clinical characteristics on admission. Eighteen of patients had familial
short stature component with low MHP SDS (Group 1), while 31 of patients
had normal MHP SDS (Group 2). Height SDS before GH therapy, age of
admission, bone age at admission, GH doses, IGF-1 SDS at diagnosis, GH

Read by Title
stimulating tests peak levels, first year response to GH therapy (as Δ 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 IGF-1 SDS at cessation of therapy were similar in both group.

Conclusions: Genetically short child can exceed 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. 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. Out 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-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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Research Institute of Endocrinology, Endocrinology Diseases, Tashkent, Uzbekistan

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 somatogenic 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-Bidie Syndrome, 9 cases with Nunan Syndrome, 7 ones of pyknodysostosis, 2 cases with Russel-Silver Syndrome, 2 cases with Bloom Syndrome. Paltau’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
Sara Pascoli; Alessandra Mazzola; Cristina Meazza; Paola Travaglini; Kamilla Larej; Ilaria Possenti; Michela Re; Daniela Frattini; Mauro Bozzola
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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 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.

R-43 Read by Title
Calcium-phosphate metabolism in children with short stature, normal GH secretion and retarded bone age – the preliminary study
Monika Obara-Moszynska; Marek Niedziela
Poznan University of Medical Sciences, Department of Pediatric Endocrinology and Diabetes, Poznan, Poland

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/creatinin) 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
Manuela Caruso-Niccolotti; Laura Guardo; Alessandra Nicolosi; Roberta Nicolosi; Domenico Romeo; Matteo Cioni
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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 fat area (AFA) 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
different subgroups: group 1 (65%) exhibited ST < 10° and AFA<5° centile, BMI<1 DS, a mean height SDS -1.5±1.0; group 2 (35%) exhibited ST>10° and AFA>5° centile; BMI >1, mean height SDS 0.17±1.2. Mean dietary intake was reduced compared to food requirement in group 1 and increased in group 2. In both groups we found increased intake of proteins and lipids and reduced intake of CHO, fibers and water. Motor impairment was moderate to severe (III-V GMFCS) in 66% of patients in group 1 and in 20% of group 2. In conclusion children with CP may present both poor linear growth and low fat stores and normal stature with obesity, more frequent in severe and in mild forms, respectively. We suggest that nutritional approach should have a crucial role in the management of children with CP.

R-47 Read by Title
Pubertal development in girls with Laron and GH-gene deletion syndrome
María Francesca Messina1; Manuela Caruso-Nicolletti2; Stefano Zucchini3; Giulia Cremonini4; Patrizia Chiabotto5; Filippo De Luca1
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Growth hormone (GH) and insulin-like-growth-factor-I (IGF-1) exert their principal action on growth but there is much evidence that they also play a role in reproductive function, particularly during sexual maturation. Numerous studies demonstrated that GH, its main ghrelin and the ghrelin’s receptor play a crucial role in female puberty. In this work we describe the first case of a 14-year-old girl with Laron syndrome (GHD-L), the atypical GH-gene deletion’s syndrome (GHD-GD), who started her pre-pubertal development during the current 10° year of age. Due to the GH deficiency, the patient’s pubertal development was delayed (4° centile) compared to the normal values. After GH substitution therapy the growth velocity increased and, closer to 26° year of age, the first signs of pubertal development were visible: axillary pubic hair, breast development and the first pubic hair (3° centile). However, all these signs remained stable and didn’t progress during the following years. This delayed puberty is comparable to what was observed in our previous case report on a 12-year-old Laron patient. 

R-48 Read by Title
What treatment should be the primary choice for growth hormone secreting pituitary adenomas in children?
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Background: There has not been consensus on the treatment choice for growth hormone secreting pituitary adenoma in children. 

Objective: To report the result of medical treatment of growth hormone secreting adenoma in a pre-pubertal boy.

Material and method: Case report; A 10-year-old boy was referred to our pediatric endocrine department because of extreme tall stature, enlarged hands and feet. On physical examination; height was 156 cm (+2.87 SDS) and his weight 54 kg (+2.72 SDS). He had increased thickness of the skin, enlarged hands and feet, discreet facial features with prognathic mandible. The parents noticed that her growth velocity had accelerated for 3 years. He was started on diazoxide but maintained very low blood sugar, sometimes high parenteral glicosis and the blood analysis revealed an hyperinsulinism. The other child is now 15 months-old and he started with seizures at the age of 7 months. In the first episode a low blood sugar was found and the study performed confirmed an hyperinsulinism. The metabolic analysis showed a SCHAD mutation. The child was started on diazoxide with very good response.

PHHI is a rare pathology, difficult to diagnose and treat, so the authors alert for the necessity of treating these children in Paediatric Endocrinology Units with as much experience as possible so that the possible consequences of it are diminished.

R-45 Read by Title
Evaluation of prognostic factors implicated in adult height in congenital primary hypothyroidism detected by neonatal screening
Esteban Mayayo1; José I. Labarta2; Angel Fernández-Longas3; Carmen Rueda4; Juan P García-Gríguez5; Zenaida Galve6
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Aim: To investigate adult height (AH) and possible related factors in patients affected of congenital hypothyroidism (CH) detected by neonatal screening. 

Methods: Retrospective study of 24 patients (19 females and 5 males) detected by neonatal screening between 1979-1988 and treated with L-thyroxine since 15.8 ± 6.0 days of life (9 to 32). The following parameters were analyzed: a) related to severity: etiology, clinical index, TSH and T4 levels at diagnosis, b) related to therapy: age, L-thyroxine dose, mean total T4 level during the first year, period of TSH normalization, c) genetic and environmental factors: target height, age of mother’s menarche, socio-economic situation, d) related to growth: length/height (birth, 6 months, 1 year, 2 years, onset of puberty, menarche), growth increment since onset of puberty and since menarche, age at maximum peak growth velocity, e) related to puberty: age at onset, at menarche, years from telarche to menarche. Results are expressed in mean ± SD.

Results: Adult height of the total group was 0.0 ± 1.0 SDS: 162.8 ± 5.8 cms (0.0 ± 1.0 SDS) in females and 175.2 ± 6.2 cms (-0.2 ± 0.8 SDS) in males. Target height of the total group was -0.7 ± 0.9 SDS: 158.1 ± 5.7 cms (-0.8 ± 1.0 SDS) in females and 171.5 ± 3.4 cms (-0.6 ± 0.4 SDS) in males. Growth and development was similar than the population of reference. Adult height was associated in the total and female groups with target height (r: 0.57, p: 0.003 and r: 0.58 p: 0.008, respectively), father’s height, mother’s height and with height at 2 years, onset of puberty and menarche. It was also related to initial biochemical severity (higher TSH and lower T4 serum levels).

Conclusion: Adult height of CH patients detected by neonatal screening and treated and followed conventionally is normal, compared to standard population, higher than target height. AH and target height are related. The initial biochemical severity of CH may also be involved.
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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Ovidius University of CONSTANTA, Endocrinology, CONSTANTA, Romania

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
Ayhan Abaci; Tolga Unuvar; Ece Bober; Ali Atas; Atilla Buyukgebiz
Dokuz Eylul University, Faculty of Medicine, Department of Pediatric Endocrinology, Izmir, Turkey

This case report describes two sisters who admitted separately at different times, aged 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 hypergonadotrophic hypogonadism. Peripheral blood samples revealed normal 46, XX karyotype was found in both sisters. Laboratory studies indicated hypergonadotropic hypogonadism. Peripheral blood samples revealed normal 46, XX karyotype was found in both sisters.

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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 patogenesis 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 abdominal pattern of obesity 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 hypercholesterolaemia 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, VLDLPD 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 hypercholesterolaemia and are mediated primarily by insulin resistance, which predetermine the guidelines for further treatment of PCOS.
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, 6 jaundice, 4 visual defect and 2 cholecystitis features. Five of six boys had micro penis. 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 Years. The treatment with hydrocortisone, growth-hormone and thyroxine, improved liver disease within 4-6 weeks. The Height-SDS increased with the treatment duration and the Height-SDS after the treatment was significantly superior to the initial Height-SDS and the Target stature.

Conclusions: In the infants with hypoglycaemia, jaundice and micropenis 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 the two 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**

Kristina Klemp1, Althard Hoffmann2, Gudrun Wiedemann2, Eric von Buere3, Klaus-Peter Ullrich4

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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 and symptoms of brain tumour is common. Mostly it appears like a panhypophysitis although an appearance like an adenaral insufficiency is possible. The lesion is usually confined to the adenohypophysis. 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, 3 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 infundibulum up to the area of the eminentia mediana with an existing neurohypophysical 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 intrauterine 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 coarse 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, androstenedione, testosterone, 17 hydroxyprogesterone, 11 deoxy Cortisol, βHCG concentrations, LHRH 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 testosterone 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 entails 44 girls and 8 boys with precocious puberty, examined between 1991 - 2001.

**Results:** Mean age of girls and boys was 5.8 ± 2.1 y and 7.43 ± 1.4 yrs respectively. Most of the patients fell within the age category of 7-7.9 years old (%40.9 for girls and %50 for boys), %60 of girls with idiopathic central precocious puberty were between 6-7.9 yrs. Patients, in terms of etiology of precocious puberty were classified under the following three categories: -24 patients (%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 thelarche (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.