

# Printed Abstracts Only

## PAO-1

### Two cases of Fanconi-Bickel syndrome - first report from China

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**Background:** Fanconi-Bickel syndrome (FBS) is a rare autosomal recessive disorder of carbohydrate metabolism caused by mutations in *Glut2*. To date there is no case has been reported from China.

**Objective and hypotheses:** To summarize the clinical characteristics of FBS. **Methods:** We reported the first two cases of FBS in China. We summarized the clinical characteristics of FBS by reviewing the 2 cases and published literature.

**Results:** The both cases presented similar manifestations as reported, including severe short stature, hypoglycemia, hepatomegaly secondary to glycogen accumulation, severe glycouremia secondary to proximal renal tubular dysfunction. And more points may help to differentiate FBS and type I glycogen storage disease (GSD I) including glucose intolerance with normal lactic acid and uric acid, possible and slightly glucose response to glucagon stimulation without accumulation of lactic acid, severe symptoms of hypophosphatemia and rickets, and metabolic acidosis caused by type II renal tubular acidosis. After receiving symptomatic treatment both children presented catch-up growth.

**Conclusions:** FBS is a rare inherited disease caused by mutations in *Glut2*. It should be carefully differentiated from GSD I and diabetes mellitus in clinical practice. Symptomatic treatment can be helpful.

## PAO-2

### Final height outcome of boys with central precocious puberty treated with gonadotropin-releasing hormone analogue

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**Background:** Data on the final height outcome of boys with central precocious puberty treated with gonadotropin-releasing hormone analogues (GnRH<sub>a</sub>) are far less than those in girls.

**Objective and hypotheses:** To report the final adult height of 20 boys with central precocious puberty treated with gonadotropin-releasing hormone analogue (GnRH<sub>a</sub>).

**Methods:** Twenty boys with central precocious puberty treated with GnRH<sub>a</sub> at a dose of 60~80 µg/kg every 4 weeks for (20.5 ± 6.7) months. At the beginning of therapy, mean chronological age and bone age was (11.2 ± 1.0) y and (13.0 ± 0.4) y, respectively. GnRH<sub>a</sub> was discontinued when the boys reached the chronological age and bone age of (13.2 ± 1.1) y and (13.7 ± 0.6) y, respectively. At the conclusion of the study, all the boys had been followed up for (3.3 ± 1.5) yrs and had achieved adult height. Comparisons were made among their final adult height (FAH), target height (THt), predicted adult height (PAH) at the start and the end of GnRH<sub>a</sub> treatment (PAHi and PAHe).

**Results:** Final height was similar to the target height [(168.6 ± 5.6) cm versus (167.8 ± 4.6) cm] with no significant difference from the predicted adult height (PAHi) [(168.6 ± 5.6) cm versus (169.8 ± 6.6) cm] based on the Bayley-Pinneau method, using a table for average bone age at the beginning of GnRH analogue therapy. Predicted adult height (PAHe) at discontinuation of GnRH<sub>a</sub> therapy was significantly higher than predicted adult height at the beginning of GnRH analogue therapy [(172.5 ± 7.6) cm versus (168.6 ± 5.6) cm, P < 0.05]. Ninety percent (90.0%) of the boys reached target height range (FAH ≥ THt - 1SD). The height gain in comparison with predicted adult height before the start of treatment was (-1.2 ± 3.3) cm, with the residual growth capacity of (10.6 ± 4.3) cm.

**Conclusions:** GnRH<sub>a</sub> treatment can improve final height into the range of target height in boys with central precocious puberty.

## PAO-3

### Prevalence of impaired glucose tolerance and insulin resistance among obese children and adolescents

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**Background:** Obesity is one of the most important nutritional disorders in the world which has an obvious relationship with the incidence of metabolic diseases. Obesity prevalence has increased among children and adolescents during recent decades, leading to a rise in Type 2 diabetes mellitus (DM II) prevalence in these two age brackets. Hence, the aim of this study was to assess impaired glucose tolerance and insulin resistance, and gather metabolic findings in obese children and adolescents.

**Methods:** We studied 110 obese children and adolescents (body mass index, 95th percentile for age and gender) 4-18 years of age referred to the endocrine clinic of the Children's Hospital at Tabriz University in a descriptive cross-sectional study. Fasting glucose, insulin, and lipid profile in all subjects were determined. Oral glucose tolerance test after eating 1.75 g/kg glucose was performed. Homeostatic model assessment was used to estimate insulin resistance.

**Results:** Impaired glucose tolerance and insulin resistance prevalence in 68 obese adolescents was 14.7% and 31.8%, respectively. Impaired glucose tolerance and insulin resistance was not seen in 23.8% of 42 obese children. No case of DM II was seen. There was a significant statistical difference in glucose (P = 0.003) and insulin (P, 0.001) level at minute 120 in individuals with impaired glucose tolerance compared to obese children and adolescents without impaired glucose tolerance. Rate of insulin resistance in patients with impaired glucose tolerance was greater and had a significant statistical difference (P = 0.03).

**Conclusions:** Obesity has a close relationship with increased risk of impaired glucose tolerance and insulin resistance in children and adolescents. Oral glucose tolerance test, unlike fasting glucose test, is a benefit test to predict impaired glucose tolerance. With prompt identification and treatment of obese children with impaired glucose tolerance, we can prevent it from progression towards DM II.

PAO-4

**Thyroid function in epileptic children using carbamazepine, primidone, phenobarbital and valproic acid**

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**Introduction:** In this study, we investigated the changes of serum levels of Free T4 and T3, T3 resin uptake (T3RU) and TSH in epileptic children during chronic treatment with anti-epileptic drugs (carbamazepine, Primidone, phenobarbital and valproate) and 3 months later than prescription.

**Material and method:** This study consisted of four case-series comparisons, was accomplished on 115 (in 4 same groups) epileptic children who were involved 37 girls and 78 boys with ages between 2 months up to 15 years (mean: 62.06 ± 44.97 months), who were taking either phenobarbital (n=29), PRM(n=28), CBZ (n=29), or VPA (n=29) at least for 3 months were evaluated T3, T3 resin uptake (T3RU), T4 and thyroid-stimulating hormone (TSH) levels in start and end of study.

**Results:** All patients were in euthyroid state, there were no clinical findings or laboratory results of hypothyroidism. In collation with thyroid hormones before of prescription in all bundles (Phenobarbital, CBZ, VPA and primidone), there was no significant distinctions in serum FT3, FT4, T3ru and TSH levels. No statistically meaningful relation were found between thyroid function and thyroid hormones levels variants and among AEDs receiving time and thyroid function and thyroid hormones levels, in any of 4 groups (P > 0.05).

**Conclusions:** Thyroid function should be evaluated intermittently in epileptic children using AEDs specially in long term prescriptions.

PAO-5

**Influence of birth brain size on newborn serum insulin-like growth factor-I: role of birth size beyond the presence of intrauterine growth retardation and of preterm birth**

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**Background:** The deviation from the proportionality between brain size and body size at birth has been related to fetal-neonatal stress.

**Objective and hypotheses:** We evaluated the possibility that preterm birth (PT) and intrauterine growth retardation (SGA) do not completely explain the birth size - related predictor role of birth brain weight (BRW) on serum Insulin-like Growth Factor-I (IG1) in the human newborn (NWB).

**Methods:** 78 NWBs 1) free of diabetes mellitus (DM)/life-threatening disease, 2) free of mother with DM and 3) with the availability of all of the following variables were included in the study: gender (SEX), birth gestational age in completed weeks (GA), birth head circumference in cm and birth body weight in gr (resp HC and BW), IG1 measured in ug/dL at one of the first 5 postnatal days (x), 5 days after x (y) and 10 days after x (z) by radioimmunoassay, as well as postnatal age in completed days at x (PNA)(PT definition: GA≤36; SGA definition: BW<10.th centile for GA and SEX; males, n=43; GA range=28-42; PT, n=46; SGA, n=20). BRW was calculated in gr according to the formula “ BRW = 0.037 x HC<sup>2.57</sup> “ (McLennan JE, 1983; Lindley AA, 2000). An estimate of birth body size not represented by brain was obtained by subtracting BRW from BW (BW minus BRW, NBBW). Natural log-transformed IG1 (resp. IG1x-ln, IG1y-ln and IG1z-ln) resulted near-normally distributed. SEX, PT and SGA were dichotomized.

**Results:** Table 1 shows t value (t), partial correlation coefficient (r) and significance level (p) of partial correlations of BRW with IG1x-ln, IG1y-ln and IG1z-ln, and Multiple Linear Regression (MLR) whole model R2 and p regarding MLR models bearing IG1x-ln, IG1y-ln or IG1z-ln as outcome and, as predictors, either 1) BRW, SEX, PT, SGA and PNA (Table 1A), or 2) BRW, SEX, PT, NBBW and PNA (Table 1B).

Table 1.	vs.	A) IG1x-ln	A) IG1y-ln	A) IG1z-ln	//	B) IG1x-ln	B) IG1y-ln	B) IG1z-ln
BRW	t/r/p	2.506/ .283/a	2.812/ .315/b	2.211/ .252a	//	-0.059/ -.007/ns	0.790/ .093/ns	0.301/ .035/ns
	R2/p	.285/c	.459/c	.302/c	//	.375/c	.486/c	.347/c
Signi- ficances:		a, p<.05;	b, p<.01;	c, p<.001;		ns, not significant.		

**Conclusions:** A direct BRW relation to IG1 was observed in studied NWBs after controls including PT and SGA, which could be in part explained by peripheral, i.e., not BRW-related, birth size.

PAO-6

**Influences of birth brain size on the ratio between newborn serum insulin-like growth factor binding protein-2 and -3: role of birth size after controlling for the presence of intrauterine growth retardation and of preterm birth**

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**Background:** The birth brain size - body size ratio has been related to fetal-neonatal stress.

**Objective and hypotheses:** The birth size - related predictor role of birth brain weight (BRW) on the ratio between serum Insulin-like Growth Factor Binding Protein-2 and -3 (resp. IB2 and IB3) in the human newborn (NWB) could be not completely explained by preterm birth (PT) and intrauterine growth retardation (SGA).

**Methods:** 78 NWBs 1) free of diabetes mellitus (DM)/life-threatening disease, 2) free of mother with DM and 3) with all of the following variables available were included in the study: gender (SEX), birth gestational age in completed weeks (GA), birth head circumference in cm and birth body weight in gr (resp. HC and BW), IB2 and chronologically corresponding IB3 measured in ug/dL at one of the first 5 postnatal days (x), 5 days after x (y) and 10 days after x (z) by radioimmunoassay and postnatal age in completed days at x (PNA)(PT definition: GA≤36; SGA definition: BW<10.th centile for GA and SEX; males, n=43; GA range=28-42; PT, n=46; SGA, n=20). BRW in gr was calculated according to the formula “ BRW= 0.037 x HC<sup>2.57</sup> “ (McLennan JE, 1983; Lindley AA, 2000). An estimate of birth body size not represented by brain was obtained by subtracting BRW from BW (BW minus BRW, NBBW). IB2 was divided by the chronologically corresponding IB3 (IB2/IB3). Natural log-transformed IB2/IB3 (resp. IB2/IB3x-ln, y-ln and z-ln) were near-normally distributed. SEX, PT and SGA were dichotomized.

**Results:** Table 1 shows t value (t), partial correlation coefficient (r) and significance level (p) of partial correlations of BRW with IB2/IB3x-ln, IB2/IB3y-ln and IB2/IB3z-ln, and Multiple Linear Regression (MLR) whole model R2 and p regarding MLR models bearing IB2/IB3x-ln, IB2/IB3y-ln or IB2/IB3z-ln as outcome and, as predictors, either 1) BRW, SEX, PT, SGA and PNA (Table 1A), or 2) BRW, SEX, PT, NBBW and PNA (Table 1B).

Table 1.	vs.	A) IB2/ IB3x-ln	A) IB2/ IB3y-ln	A) IB2/ IB3z-ln	//	B) IB2/ IB3x-ln	B) IB2/ IB3y-ln	B) IB2/ IB3z-ln
BRW	t/r/p	-2.489/ .281/a	-2.483/ .281/a	-2.946/ .328/b	//	-0.733/ .086/ns	.0.665/ .078/ns	-0.397/ .047/ns
	R2/p	.380/c	.405/c	.394/c	//	.403/c	.425/c	.463/c
Signi- ficances:		a, p<.025;	b, p<.005;	c, p<.001;		ns, not significant.		

**Conclusions:** Inverse BRW relations to IB2/IB3 in studied NWBs after controls including PT and SGA could be in part explained by not BRW-related birth size.

## PAO-7

### Insulin oedema in a newly diagnosed type 1 diabetic adolescent

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Edema has been accepted as an uncommon complication occurring after initiating of insulin therapy in the absence of heart, liver or renal disease. In newly diagnosed type 1 diabetic children and adolescents insulin-induced edema should be considered after the initiation of insulin therapy.



**Case report:** A 13 year old boy was admitted with a one month history of polyuria, polydipsia, enuresis nocturna and also weight loss developed within last fifteen days. On admission, physical examination was normal except the mild dehydration. He had elevated blood glucose levels, 342 mg/dl and an elevated glycosylated hemoglobin A1c concentration of 11.5%. He had ketonuria but no acidosis with arterial blood pH of 7.40. He was initially given an intravenous infusion of insulin and 2/3 isotonic saline in 5% dextrose. Just before the oral feeding, we have initiated subcutaneous regular insulin for the regulation of blood glucose. In the third day of regular insulin therapy, at a dose of 1.2 units/kg/day, a non-tender, pitting edema developed over the ankles (Figure 1 and 2). We didn't find any clinical or laboratory evidence of heart, liver or renal dysfunction. His urine analysis showed no proteinuria. Twenty-four-hour urinary excretion of microalbumin was within normal limits, 5 µg/min. Chest X-ray, abdominal ultrasonography and echocardiographic

examinations were normal. Doppler ultrasound findings of the lower leg arteries and veins were normal. After four days, the edema subsided spontaneously in parallel with a decrease in daily insulin doses, at a dose of 0.9 units /kg/day. **Discussion:** Insulin edema is a poorly understood phenomenon, which is a rare complication of insulin therapy. Probably it is an underestimated complication, since most of the cases are mild. Here we reported a newly diagnosed type 1 diabetes case who developed insulin edema, in order to make physicians be aware of that rare complication. In most of the cases no therapy is needed and spontaneous resolution of the edema has been mentioned, as was the case in our patients.

## PAO-8

### CYP21A2 promoter conversion causing genotype-phenotype discordance in 21-hydroxylase deficiency with P30L mutation

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**Background:** Steroid 21-hydroxylase deficiency (21-OHD) is an autosomal recessive disorder that is traditionally divided into three forms, salt-wasting (SW), simple virilizing (SV), and a milder non-classical (NC) form. Genotype-phenotype correlation is found in most 21-OHD. In Japan, very rare cases of the NC form have been detected at neonatal mass screening, and the P30L mutation appears to be associated with Japanese NC patients. However, the P30L mutation in NC 21-OHD was found to have poor genotype-phenotype correlation in prior studies.

**Objective and hypotheses:** In this report, we describe a patient with the SV form of 21-OHD in compound heterozygous mutations for P30L and deletion in the CYP21A2.

**Methods:** The patient was a Japanese girl with 21-OHD detected by newborn screening. She showed ambiguous genitalia (Prader stage 3) and skin pigmentation at birth. Her serum 17-OHP level was elevated (78 ng/ml at 13 days of age). Serum Na, K and plasma renin activity were 140 mEq/l, 5.0 mEq/l, and 71.8 ng/ml/hr, respectively. Based on these findings, she was diagnosed as having the SV form of 21-OHD.

**Results:** Molecular analysis for CYP21A2 revealed a compound heterozygous mutation (P30L, del or conv) that was predicted to become the NC form of 21-OHD. Further molecular analysis of CYP21A2 for discrepancy between genotype and phenotype revealed promoter conversions on the same allele as the P30L mutation.

**Conclusions:** We concluded that promoter conversion of CYP21A2 can partly cause discordance between genotype and phenotype in 21-OHD with the P30L mutation.

## PAO-9

### Use of Continuous Glucose Monitoring System for the quality improvement of the glycaemic control

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**Background:** Nowadays CGMS is used for the control optimization and medical treatment of the type 1 diabetes mellitus in children.

**Objective and hypotheses:** The aim of the research is to study the glycemic control readings (of mean glycemia and HbA1C) while using self-control and CGMS.

**Methods:** 20 children (11 boys and 9 girls) with type 1 diabetes mellitus were included in the study. The mean age of the patients was 10,13±1,85 years; the mean diabetes duration was 3,85±3,56 years. All patients wore 72 hrs CGMS sensor (Medtronic, MiniMed, System Gold.)The medical history studying revealed 6 cases of acute complications (hypo- and hypercoma) and 13 cases of chronic complications. During the study patients were measuring the glucose level with the help of glucometer six times per day. The analysis was made by Statistica 6.0.

**Results:** The study revealed that according to the glucometer's readings the minimum glycemia level was  $6,72 \pm 1,31$  mmol/l; CGMS displayed  $3,46 \pm 0,44$  mmol/l ( $p < 0,001$ ). The maximum glycemia level was  $14,93 \pm 1,15$  mmol/l (glucometer) and  $18,18 \pm 1,48$  mmol/l (CGMS) ( $p < 0,01$ ). The mean glycemia level was  $9,76$  mmol/l (glucometer) and  $10,8$  mmol/l (CGMS). According to the CGMS results the patients were in the normoglycemia conditions during the 73% of the whole research period, hyperglycemia was registered at 24,68%, and hypoglycemia was registered at 3,47%. The readings of the regular glucometer showed normoglycemia at the 52% of the whole period, hyperglycemia at the 48%; hypoglycemia wasn't revealed. The initial HbA1C level was 7,95%; after the three month it decreased to 7,41% ( $p > 0,05$ ). The lack of accuracy may be caused by the limited sampling.

**Conclusions:** CGMS is able to reflect the adequate ratio of the hyper- hypo and normoglycemia and helps to reveal the most serious latent hypoglycemias which are difficult to detect with the glucometer. CGMS helps to detect the actual glycemia variability in patients. CGMS shows more accurate results in the mean glycemia measuring and improves glycemic control quality.

## PAO-10

### FTO-risk alleles had no impact on body composition and parameters of metabolism before and after a lifestyle intervention programme in obese children and adolescents

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**Background:** Variants in the FTO (fat mass and obesity associated) gene are associated with early onset and severe obesity.

**Objective and hypotheses:** To investigate the impact of variants of the FTO gene (rs1421085, rs17817449, rs9939609) in obese children before and after lifestyle intervention.

**Methods:** 75 overweight children (40 male, mean BMI  $30,4 \pm 5,5$  kg/m<sup>2</sup>, mean age  $12,6 \pm 2,6$  years). Measurements: Genotyping by means of a Taq-Man SNP genotyping assay. Lean and fat mass were determined by means of DXA. The lifestyle intervention program consisted of an increase in physical activity from one to two hours per day including all daily life activities and fitness training; nutritional recommendations based on the 'Optimized Mixed Diet for German Children and Adolescents' of the Research Institute of Child Nutrition, Dortmund, Germany.

**Results:** For the whole study population, the 6-month lifestyle intervention resulted in a significant improvement (before intervention minus time point 6 months; mean  $\pm$  SD) in BMI-SDS ( $0,10 \pm 0,17$ ,  $p < 0,001$ ), HOMA ( $1,41 \pm 3,19$ ,  $p < 0,001$ ) and relative fat-mass-SDS ( $0,09 \pm 0,23$ ,  $p = 0,005$ ). Before and after lifestyle intervention, there was no significant difference between heterozygote ( $n = 52$ ) and homozygote ( $n = 21$ ) carriers of the FTO gene in terms of BMI, body composition, and the metabolic profile (Insulin, HOMA, lipids, liver function tests).

**Conclusions:** Variants in the FTO gene are common in obese children. However, they seem to have no impact on body composition and metabolism before and after lifestyle intervention.

## PAO-11

### Hypovitaminosis D in a population of foreign adopted or migrant children in Italy

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**Background:** Rickets vitamin D-dependent is highly prevalent in developing nations; however, the prevalence of hypovitaminosis D is underestimated in developed nations.

**Objective and hypotheses:** To compare serum level of 25(OH)D in a population of Italian healthy children versus a population of adopted or migrant foreign children.

**Methods:** Group 1 included 121 healthy children born in Italy or living in Italy since at least 1 year (78 females and 43 males, mean age  $9,5 \pm 4,1$  years). Group 2 included 168 adopted or migrant children living in Italy since less than 1 year (62 females, 106 males, mean age  $5,45 \pm 3,1$  years); the geographical area of origin were Sub-Saharan Africa ( $n = 29$ ), Latin America ( $n = 36$ ), Eastern Europe ( $n = 37$ ), Russia ( $n = 24$ ), Southeast Asia ( $n = 25$ ), Indian sub-continent ( $n = 17$ ).

**Results:** In group 1 mean serum level of 25(OH)D was  $25,3 \pm 11,1$  ng/mL; 34,7% of children was vitamin-D deficient and 39,6% was insufficient. In group 2 mean serum level of 25(OH)D was  $29,0 \pm 17,9$  ng/mL (significantly higher compared to group 1,  $P = 0,04$ ); 29,8% of children was vitamin-D deficient and 29,8% was insufficient. The subgroup from Southeast Asia had better levels of 25(OH)D ( $40,2 \pm 24,3$  ng/mL) compared to the other subgroups. Comparing group 1 versus group 2 without subgroup from Southeast Asia ( $n = 143$ , mean 25(OH)D  $27,0 \pm 15,9$  ng/mL), we found no significant differences ( $P > 0,05$ ).

**Conclusions:** Hypovitaminosis D is highly prevalent in both Italian (74,3%) and adopted or migrant children (59,6%); if we exclude subgroup from Southeast Asia the prevalence in group 2 raises to 65,7%. We have no explanation for the higher levels of 25(OH)D found in this subgroup (Philippines, Cambodia and Vietnam).

## PAO-12

### Parental consanguinity among parents of infants with congenital hypothyroidism in Hamedan

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**Introduction:** Congenital hypothyroidism is inadequate thyroid hormone production in newborn infants. This can occur because of an anatomic defect in the gland, an inborn error of thyroid metabolism, or iodine deficiency. It is the most common congenital endocrine disorder. According to published studies the incidence of congenital hypothyroidism (CH) is high among Iranian population. The purpose of this study was to determine rate of consanguinity among parents of infants with congenital hypothyroidism.

**Methods and materials:** This descriptive study was conducted in infant diagnosed to have congenital hypothyroidism, between 1385-1389. All infants with biochemically confirmed CH (low T4, and TSH  $> 10$  IU/mL in venous blood) were enrolled in this study. A detailed record of the required information was made. The data was manually extracted and displayed in a descriptive manner.  $p$ -value less than 0.05 was defined as statistically significant.

**Results:** The study population consisted of 150 infants with CH 72(47%) females and 78(53%) males. Of the neonates with congenital hypothyroidism 28% had relative parents and in 72%, parents were not relative. In Control group, 20 neonates (14%) had relative parents and 86% parents were not relative. The difference between two groups was significant  $p = 0,005$ . There were no significant differences in sex ratio seasonality, order of birth and mean age of mother at delivery of infant with congenital hypothyroidism and control group ( $p > 0,05$ ).

**Conclusion:** The results of this study suggest infant of consanguineous parents are at greater risk for congenital hypothyroidism than the rest of population.

## PAO-13

### Bone health and physical activity in Danish children, an intervention study

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**Background:** Peak bone mass is an important determinant of adult risk for osteoporosis. Factors, which determine bone mineral density (BMD) and bone mineral content (BMC) in children, are not fully understood. Studies indicate that both genetic factors and lifestyle, such as diet and physical activity during early childhood can contribute to optimal bone development.

**Objective and hypotheses:** The aim of the study is to assess the effect of physical activity on BMD, BMC and bone area (BA) in healthy Danish children. The study also aims to evaluate the relationship between fracture risk and BMD.

**Method:** The study is a three year controlled intervention study from August 2008- August 2011 in 10 public schools in the municipality of Svendborg, DK. Children aged 8 to 11 years were invited, 740 children accepted. Six schools were selected as intervention schools, where the children receive 6 lessons of physical education (PE) per week versus 2 lessons of PE at the four control schools. Blood samples were collected during September 2008 and September 2010. Biomarkers of bone health are measured. Whole-body DXA scans, (Lunar Prodigy) were performed at 718 children at baseline and BMD, BMC, and BA were measured. The DXA scans were repeated during the fall 2010 to February 2011. 684 children participated. Anthropometrics was registered every four month. X- ray of the left hand- wrist was taken at baseline and after the intervention for assessment of bone age. The children's level of physical activity was recorded by accelerometers. Information about fractures was received through questionnaires and SMS- track.

**Results and perspectives:** Preliminary analysis has revealed that, the children in the two groups were similar regarding to anthropometrics, motor performance and aerobic fitness at baseline. Results from the DXA scans will be correlated to fracture risk and the two groups will be compared regarding BMD, BMC and BA values.

**Conclusions:** The data collection has just been completed and the results will be processed through the following months.

#### PAO-14

### Serum leptin and adiponectin in relation to appetite grade, gender and puberty in children with obesity

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**Background:** Leptin and adiponectin suspected to be potential markers of obesity, but the importance as metabolic risk factors is still discussed.

**Objective and hypotheses:** Our aim was to investigate gender differences of leptin and adiponectin concentrations in relation to appetite grade in obese children.

**Methods:** Children (n=300) with obesity (4,8 -17,8 years old) from Belarus were assessed for anthropometric parameters, pubertal stage, serum lipids, insulin, sex-binding globulin (SBG), leptin and adiponectin, appetite (A) grade (4-point assessment). Statistical analysis were performed by using SPSS 16.0 (p=0,05).

**Results:** Leptin levels were significantly different during puberty and increased especially in late pubertal girls (prepubertal - 27,7 ng/ml, p=0,002, early pubertal - 37,8, p=0,001, late - 54,7) versus adiponectin decreasing (prepubertal - 22,3 ng/ml, p=0,001, early pubertal - 14,2, p=0,001, late - 12,1). Peak leptin and adiponectin concentrations were shown in early pubertal boys - 47,6 ng/ml, p=0,021 and 26,8 ng/ml, p=0,02 with further decreasing in late puberty - 24,7, p=0,024 and 21,8, p=0,048 respectively that was connected with negative influence of high testicular androgen to leptin and adiponectin production. There were positive correlations between serum leptin and body mass index (BMI) (p=0,0001), waist circumflex (WC) (p=0,01) triglycerides (p=0,05), insulin (p=0,0001), low-density lipoproteins (LDL) (p=0,02) and negative with SBG (p=0,002) in children with obesity. Adiponectin had negative correlation with the same parameters: BMI (p=0,02), WC (p=0,03) triglycerides (p=0,03), insulin (p=0,02), LDL (p=0,03) and positive with SBG (p=0,001). The highest leptinemia was shown in children with risen afternoon and evening A (118,3 ng/ml p=0,05). Conversely adiponectinemia were independent from rising A time (p>0,05).

**Conclusions:** Serum leptin increases with obesity grade, whereas adiponectin decreases, both are influenced by gender and puberty and correlate with metabolic dysfunction markers. Appetite grade has influence on leptinemia.

#### PAO-15

### A peculiar cognitive and behavioural phenotype as the first clue to suspect Klinefelter syndrome in prepubertal males

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**Background:** Klinefelter syndrome (KS) with the classic 47 XXY karyotype is the most frequent chromosomal aneuploidy with a prevalence of 1 in 700 males and, although the classical clinical picture is well-known and easily recognizable, most patients remain undiagnosed. The rate of diagnosis is extremely low in childhood and only 10% of cases are identified before puberty because the classical signs and symptoms of androgen deficiency appear only in late adolescence. A common element, often underappreciated, in these young boys is the peculiar cognitive and behavioural pattern.

**Case report:** We describe two patients who were diagnosed in prepubertal age, respectively at 7.1 and 10 years, due to a peculiar neurocognitive profile. Both of them showed on WISC III low-normal scores, i.e. FSIQ, PIQ and VIQ ranging between 80 and 85 and a behavioural profile characterized by immaturity, insecurity, shyness and low-self esteem, learning disabilities and academic difficulties. On clinical examination both of them showed a height taller than target height and a progressive growth acceleration between 5 and 7 years, and from the pubertal point of view they had prepubertal testes volume (< 2 cc) and one of them had hypoplastic scrotum with monolateral cryptorchidism. Hormonal pattern confirmed normal prepubertal basal levels of gonadotropins.

**Conclusions:** We believe that to achieve the goal of an early diagnosis in KS, it is necessary to increase medical awareness of the disease and in particular to augment paediatricians' knowledge that in prepubertal age pathognomonic endocrinological features of KS are often lacking but a peculiar cognitive and behavioural pattern is always present, especially when accurately searched.

#### PAO-16

### Effect of a large ventricular defect (VSD) on linear growth: a lesson from an affected baby who is one of triplets

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**Background:** Large VSD may delay growth and compromise adult height.

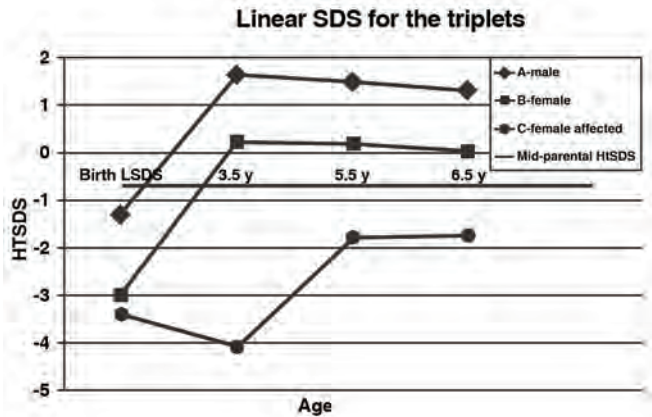
**Objectives:** Study the effect of large VSD on linear growth, in a girl with large VSD, who was a part of triplet and compare it with her siblings' growth.

**Methods:** This girl (C) was born as a part of triplet at 38 weeks of gestation. The other parts of triplet were a male (A) and female (B). The girl (C) birth weight = 1.82 kg, length = 41 cm. We compared girl C anthropometry, bone maturation and IGF-I level data with her normal siblings' data.

**Results:** Clinical examination, CXR and echocardiography revealed a large-size VSD with cardiomegaly and lung congestion. There was no cyanosis, pallor, jaundice or dysmorphic features. The girl was treated with lasix and nutritional support. At the age of 3.5 years a complete corrective surgery was performed. At the age of 6.5 years the bone age of girl C = 5 years, girl B and boy A = 6 years. Their IGF-I were 85, 125 and 185 ug/L respectively. Analysis of growth data of girl C before and after surgery in comparison to the other parts of the triplet reflected the effect of VSD on linear growth as follows:

- The VSD prevented catch-up growth in girl C which occurred in her 2 siblings (3SDS) during the first 3 years,
- Correction of VSD accelerated growth for 2 years with a significant (2.2 SDS) but incomplete catch-up growth (still 1 SDS below mid-parental HtSDS),
- catch-up growth stopped during the 3rd year after surgery,
- in girl C, VSD was associated with delayed bone age (a year) and lower IGF-I versus her siblings.

**Conclusion:** In girl C, VSD prevented catch-up growth during the first 3 years of life with significant but incomplete catch-up growth for 2 years following surgical correction and lower IGF-I secretion. However, VSD was associated with a delay in bone age with a better potential for final adult height.



#### PAO-17

### Thrombocytopenia in a girl with idiopathic central precocious puberty treated with long-term gonadotropin hormone agonists (GnRHa)

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**Background:** Central precocious puberty (CPP) is a frequent endocrine problem in childhood. The idiopathic and organic etiology of CPP are most commonly treated with GnRH agonists. They have been considered in many studies to be safe and effective.

**Case report:** We present a 7 year old girl with idiopathic CPP diagnosed by standard GnRH testing. She developed severe thrombocytopenia during GnRH treatment. The familial history showed that the mother has been treated 8 years for infertility. The pregnancy was controlled and uneventful. At the time of diagnosis her weight was at the 75th percentile and she was 130.5 cm tall on the 97th percentile. The Tanner stage was B3, A1, P1. The bone age was advanced to 8.5 years. Before the treatment she was otherwise healthy. All laboratory evaluations were normal from blood count to thyroid function and brain imaging techniques. After receiving her 9th monthly depot therapy of GnRH agonist, triptorelin acetate, 3,75 mg i.m., she developed bleeding from the injection site, bruises and rash on the skin all over her body. Her platelets were  $27 \times 10^3/\mu\text{l}$  ( $150-300 \times 10^3/\mu\text{l}$ ). The coagulation factors and myelogram were normal. She was hospitalized at the haematology department in our hospital for 5 days and treated with corticosteroids. Recovery was after one week and treatment with GnRH agonists was discontinued.

**Conclusions:** To our knowledge, thrombocytopenia has not been yet reported in children receiving GnRH agonist treatment. This may represent a possible serious adverse effect which needs further investigation.

#### PAO-18

### Peripheral blood karyotype poorly represents tissue mosaicism determined by FISH and QF-PCR - a case report

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**Background:** Cytogenetic analysis in disorders of sexual differentiation is routinely performed on peripheral blood lymphocytes. The presence of Y chromosome material in the gonads is of major interest because of the risk of gonadoblastoma development. However, there is a lack of evidence whether the gonadal karyotype is congruent with lymphocyte karyotype.

**Patient and methods:** A three-week-old boy with normal male genitals pre-

sented with left inguinal hernia and cryptorchidism. The inguinal hernia surgery revealed an unusual anatomic situation. His free testosterone was normal (23.21 pg/ml). Peripheral blood karyotype was mos 45,X[25]/46,X,i(Y)(p10). ish idic(Y)(q11)(DYZ3++)Y[6]. An SRY duplication was detected by FISH. Histological examination found an immature testis on the left, a dysgenetic gonad on the right side and a uterus-like organ. Based on the different degree of differentiation of the two gonads and the normal hormone production we hypothesized that the mosaicism -namely the ratio of Y chromosome- may vary from loci to loci, moreover in some tissues might be significantly different from that of the peripheral lymphocytes. To test this hypothesis blood, gonad and subcutaneous fibroblast samples were analyzed by FISH and QF-PCR.

**Results:** The X:Y ratio was normal in the testis and nearly 2:1 in the blood, fibroblast and a dysgenetic gonad samples by QF-PCR. However, FISH analysis in the testis have found one X centromere in 60% and presence of different mosaic SRY+ cell lines (with single or double SRY signals) in 40% of cells (nuc ish(DXZ1+)(SRY-)[201]/(DXZ1+)(SRY+)[88]/(DXZ1+)(SRY+)[52]/(DXZ1+)(SRY+)[12]).

**Conclusions:** Our case underlines that peripheral blood lymphocyte karyotype might not provide a reliable representation of specific tissue karyotypes. Future studies may prove whether Y chromosome material present in the gonads would be completely absent or undetected in lymphocytes. Peripheral blood is an easy and reliable source of material for cytogenetic analysis, however, the interpretation of test results might require caution.

#### PAO-19

### Complete catch-up growth in a neglected case of hypoadosteronism a year after starting therapy

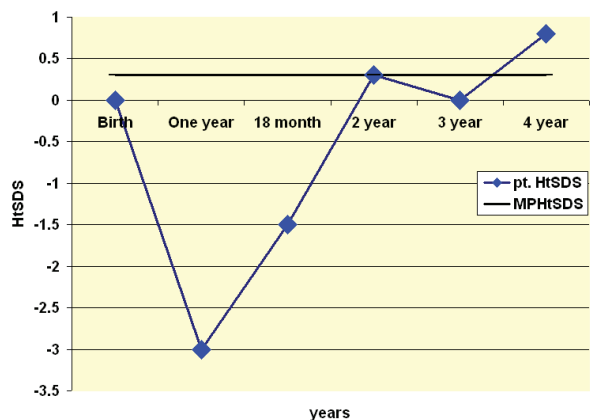
*Noura Alhemaïdi; Ashraf Soliman; Amal Sabt; Ahmed Elawwa*  
Hamad Hospital, Pediatric, Doha, Qatar

**Background:** Early growth impairment may be a Sequelae of untreated hypoadosteronism in infants.

**Objective and hypotheses:** To study the growth pattern of an infant with neglected hypoadosteronism after treatment for 3 years.

**Methods:** This boy presented at the age of one year, with recurrent vomiting and poor growth. He was a product of full-term pregnancy and normal vaginal delivery. Birth weight = 3.1Kg, length = 50 cm. His parents were first-degree cousins. He had five sisters and one brother, all were healthy. He was on formula feeds and started weaning at six months of age, with good appetite and normal bowel motion. He showed delayed gross motor milestones (can sit but can not stand at 1 y) with normal other developmental parameters. Examination revealed fair general condition, with mild dehydration with no pallor, jaundice, dysmorphic features or pigmentary changes. Vital signs including blood pressure were normal. His weight = 6Kg, length = 67.5cm (LSDS = -3), HC = 41.5cm (all < 5th centile). The rest of exam was unrevealing.

Linear growth before and after treatment



**Results:** Showed hyperkalemia ( $K = 7\text{mmol/L}$ ) (N 4-4.8), hyponatremia ( $Na = 126\text{mmol/L}$ ) (N 135-145), acidosis ( $HCO_3 = 17\text{mmol/L}$ ) (N 24-30), BUN = 10 mmol/L (N 1-4.5), creatinine = 20umol/L (N25-65), Cl = 90mmol/L (N95-110), and normal blood glucose. Hormonal analysis showed: Aldoste-

rone 73 pmol/L (N 200-2580), rennin 7ng/ml/hr (N1-6), Cortisol 500nmol/L (N 200-600), 17 OH progesterone 1.5nmol/L (N 0-3). The diagnosis of hypoadosteronism was established and the infant started on fludrocortisone 0.1 mg OD and NaCl 10 mmol/kg/day. During follow-up visits the dose of fludrocortisone was increased to 0.2mg and NaCl was discontinued at 2 year of age. He maintained normal electrolyte concentrations. His growth in stature and weight showed marked improvement with complete catch-up to his genetic potential (mid-parental height) (fig).

**Conclusions:** Hypoadosteronism may present with severe growth retardation during the first year of life. Complete catch-up of growth was achieved during the first year of treatment.

## PAO-20

Abstract withdrawn.

## PAO-21

### Do we need to change the policy of hydrocortisone administration by emergency personnel?

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**Background:** An 8 year old male with congenital hypopituitarism requiring hydrocortisone, growth hormone and thyroxine replacement had an episode of unresponsiveness whilst at school. There was a health care plan in place with appropriate advice suggesting an oral dose of hydrocortisone and if the patient remained unwell to call an ambulance so that intramuscular hydrocortisone could be administered. The patient was brought to hospital where it was evident that the ambulance team were unable to administer intramuscular hydrocortisone as the diagnosis was not that of Addison's disease.

**Objective and hypotheses:** To review the pre hospital management of adrenal crisis.

**Methods:** The paediatric population of Swansea with conditions that require long term steroid dependence.

**Results:** There are currently 13 paediatric patients in Swansea requiring hydrocortisone administration, none of whom have Addison's disease as the underlying diagnosis. All Ambulance crew carry hydrocortisone in their emergency equipment. However current guidelines (1) state this can only be administered in an Addisonian crisis. This is interpreted to mean that if the diagnosis is not Addison's disease then Hydrocortisone is not administered. None of our patients would have the necessary medication administered by the ambulance crew if they presented in an adrenal crisis. This represents a clinical risk causing a delay in administration of potentially life saving medication. This risk currently applies across Wales and the rest of the UK as all ambulance crew follow these guidelines and are advised not to deviate away from it.

**Conclusions:** A significant proportion of paediatric patients requiring long term hydrocortisone replacement do not have Addison's disease as the underlying cause and would not be given the appropriate resuscitation medication in the UK. It is important that this is recognised so that future guidelines can be amended. In the meantime, patients can be registered with the ambulance authorities so there is an alert that hydrocortisone may need to be administered.

## PAO-22

### Diabetes influence on nutritional stereotype and children's quality of life

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**Background:** Diabetes mellitus type 1 (DMT1) can influence on life quality and emotional stability in children.

**Objective and hypotheses:** The study aim was to assess nutritional stereotype's influence on emotional status and life quality in children with DMT1 depending on gender and pubertal stage.

**Methods:** 58 children with DMT1 were included into this research and divid-

ed to 4 groups depending on gender and pubertal stage. Group A (n=14) and B (n=15) included early pubertal boys at age 10,1±2,1 years and girls (10,1±2,1 years) respectively. Group C (n=14) and D (n=15) - late pubertal boys at age 15,1±2,2 years and girls (15,1±2,2 years) equally. Patients were interviewed by self-report questionnaires (Diagnostic Interview for psychological disturbances in childhood and adolescence (DIPS-K)) with point estimation. All foodstuffs were divided into 3 groups: allowed, with the limited use and prohibited. Questions about fast food using were separated from other. Glycosylated haemoglobin (HbA1c), daily usual glycemia, insulin doses were also estimated. All patients got insulin therapy in intensive regimen. Statistical analysis were performed by using T-test (p=0,05).

**Results:** Forbidden products increasingly used for food in groups A and B (p<0,05). Useful products prevailed in groups C and D (p<0,05). 20% children from A and B groups used fast-food in everyday life, 11% -during week-ends; 50% and 17% from group C, 8% and 0% from group D respectively. Life satisfaction was higher in early pubertal children (A and B groups) in relation to late puberty (C and D) regardless of gender. 70% children from A, B and D groups didn't note that DMT1 influenced on life quality at the research time. The anxiety about DMT1 influence on the future life increased with the age (with maximum in group D: 48 from 100).

**Conclusions:** Fast-food consumption frequency in late pubertal boys higher than in other groups. Intensity of life quality's dissatisfaction and anxiety about the future relate from the disease duration.

## PAO-23

### Values of levels of IGF-1, IGFBP-3 and urinary GH to diagnose of short stature

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**Background:** Levels of IGF-1, IGFBP-3 and also urinary GH (uGH) are recognized by markers of GH deficiency and have diagnostic value in various variants of short stature.

**Objective and hypotheses:** To define differences of IGF-1, IGFBP-3 and uGH values in various variants of short stature.

**Methods:** We have examined 147 subjects (85 boys and 62 girls), aged 3-18 yrs (mean age 11±3,9yr.) with short stature and 20 healthy children (10 boys and 10 girl). Serum levels of IGF-1, IGFBP-3 and uGH were measured by IRMA (Immunotech, Beckmand Coulter).

**Results:** The obtained data of laboratory researches of levels of IGF-1, IGFBP-3 and uGH are given in the table. GH excretion and basal levels of IGF-1 and IGFBP-3 were lower in growth hormone deficiency, hypothyroidism and raised in case of familial short stature in compare with healthy children.

Diagnosis	Total No. (%)	urinary GH, ng/ml	IGF-1, ng/ml	IGFBP-3, ng/ml
Growth hormone deficiency	53(36,0%)	0,6±0,84*	97,9±66,9*	1849,0±876,2
Constitutional growth delay	20 (13,6%)	1,4±0,9**	222,9±92,2***	3217,0±584,6***
Familial short stature	15 (10,2%)	2,3±1,2***	242,2±38,4***	3916,0±94,0**
Hypothyroidism	15 (10,2%)	0,9±0,8*	135,7±25,4**	3100,0±125,4***
Genetic syndromes	15 (10,2%)	1,2±1,0**	53,3±48,8*	1308,0±266,9
Other medical causes	14 (9,6%)	1,43±0,6**	187,0±36,4***	2591,0±516,7
Turner syndrome	9(6,1%)	1,4±0,16***	69,3±7,35**	1726,4±98,5
Skeletal dysplasia	6 (4,1%)	1,63±0,9***	126,9±101,0***	2430,0±169,7
Healthy children	20	7,51±2,5	414,0±212,1	1925,3±930,1

P - differences between group of healthy children: \* - p<0,001; \*\* - p<0,01; \*\*\* - p<0,05.

**Conclusions:** Complex measurement of levels of IGF-1, IGFBP-3 and uGH allows to improve the diagnoses of endocrine variants of short stature.

### Descriptive study on growth of small for gestational age (SGA) babies in a multi-ethnic population

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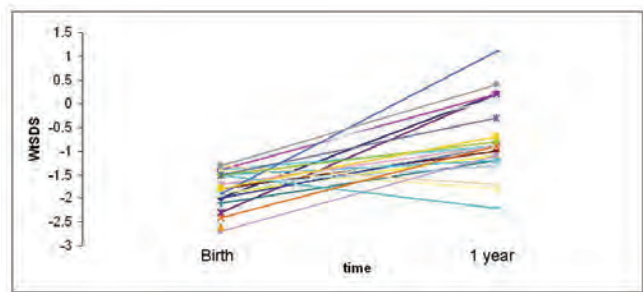
**Background:** The childhood population under study is approximately 200,000 with an annual birth rate of approximately 11,000.

**Objective:** In this prospective observational study, the aim was to collect data on parental ethnicity, educational attainments, social habits, medical history and auxology of SGA babies till the first birthday.

**Methods:** SGA babies were defined as birth weight or length less than the third percentile for gestation. Measurements were converted to SD scores. Mothers of SGA babies were interviewed by one of the authors using a standardised questionnaire. Babies were measured using a stadiometer and weighed using digital weighing scales.

**Results:** 24 mothers were interviewed. Growth data was available for all babies except 1 final measurement. Only 5 out of 24 mothers were Caucasian, 14 were Asian, 3 were mixed and 1 was African. Mean maternal age was 31 (range 21 - 40yrs). 2 admitted to smoking before and during pregnancy. 10 admitted to alcohol intake prior to getting pregnant, with 3 continuing to drink in pregnancy. Birth weight SDS ranged between -2.7 to -1.3, mean -1.8, weight SDS at 1 year ranged between -2.2 to 1.1, mean -0.7 (see chart).

**Conclusions:** It was possible but difficult to study this largely multiethnic group of families (hence the small numbers). Data obtained can be used in future to compare with other populations and with the comparisons, possible factors may be identified to be more strongly linked to having a SGA baby.



### Serum IGF-1 and IGFBP-3 levels in central precocious puberty girls with gonadotropin releasing hormone agonist (GnRHa) treatment

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<sup>1</sup>Wonkwang University Sanbon Medical Center, Pediatrics, Gunpo, Gyeonggi province, Republic of Korea; <sup>2</sup>Chosun University School of Medicine, Pediatrics, Gwangju, Republic of Korea

**Purpose:** To investigate changes of serum IGF-1 and IGFBP-3 levels during one year gonadotropin releasing hormone agonist (GnRHa) treatment in central precocious puberty (CPP) girls.

**Methods:** From 2007 through 2009, twenty six girls were enrolled in this study. They were diagnosed as central precocious puberty and were treated with GnRHa (Leuprolide acetate) for one year. Height, bone age, IGF-1, IGFBP-3 were evaluated every 6months.

**Results:** At the time on diagnosis, their mean serum IGF-1 and IGFBP-3 were 302.90 ± 102.54 ng/mL and 3103.58 ± 705.08 ng/mL. At 6month after treatment, IGF-1 secretion was slightly decreased and IGFBP-3 production was slightly increased. One year later, IGF-1 concentrations were more increased than before treatment and IGFBP-3 levels were decreased. Gonadal suppression with gonadotropin releasing hormone inversely influences circulating IGF-1 and IGFBP-3 levels. But IGF-1/IGFBP-3 were maintained relatively steady levels with normal height velocity (mean ± SD, 6.10 ± 1.36 cm/yr HV SDS 0.02 ± 1.03).

### First-year response to growth hormone in children with brain tumours: analysis of data from KIGS Turkey

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**Background:** Determinants of first-year response to growth hormone (GH) are not well established in children with brain tumor.

**Objective and hypotheses:** To retrospectively analyze first-year response to GH in children with brain tumor registered in KIGS (Pfizer International Growth Database) Turkey.

**Methods:** Among 53 eligible patients, 9 were excluded due to a follow-up period of under 9 months and 7 due to lack of relevant data. Remaining patients were divided into two as Group 1 (change in height SD score >0.5, n=15) and Group 2 (change in height SD <0.5, n=22), which were compared regarding clinical and laboratory variables. Correlation analysis, receiver operating characteristic (ROC) curve, and logistic regression analysis were used to further assess the association of follow-up variables with the degree of height gain.

**Results:** Thirty seven cases [M/F: 17/20; median (interquartile range) age 11.8 (8.9-13.7); ratio of pubertal patients, 28%] were included in the study. Majority of the patients were suffering from craniopharyngioma (n=15, 41%) or medulloblastoma (n=12, 32%). Median (interquartile range) value for height SD score at the start of treatment was 2.83 (-4.01 - -1.93) and duration of follow-up 2.7 years (1.35-4.93). Higher age and height SD scores and greater number of cranial tumors distant from pituitary/hypothalamic area were found in Group 2. Age (r= -0.462, p=0.004) and height SD scores (r= -0.419, p=0.01) at the start of GH were moderately negatively correlated with first-year response. ROC curve analyses provided cut-off levels for age (>9.75 years) and height (>-3 SD score) for prediction of poor first-year response. Risk of poor first-year response increased 2.9 times per 1 SD score increase in height and 1.6 times per 1 year increase in age.

**Conclusions:** Poor response to GH treatment in children with brain tumor is associated with some clinical variables, which might serve to make treatment modifications.

### Albright hereditary osteodystrophy phenotype and 2q37: a familial case report

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**Background:** We report on one case of pseudopseudohypoparathyroidism related to a 2q37 deletion. MC presents an Albright Hereditary Osteodystrophy phenotype (AHO) including short stature, obesity, mental retardation, brachydactyly and mild facial dysmorphic features. Plasma calcium, phosphate, parathormone (PTH) levels and Gsα protein activity were all normal. The chromosomal analysis showed an unbalanced (2;10) translocation inherited from his mother that led to monosomy for the distal 2q and trisomy for the distal



10q. The breakpoint located by CGH-array was in 2q37.1 (gene DIS3L2).

**Objective and hypotheses:** MC's mother, carrying the balanced (2;10) translocation, has no loss of genetic material according to karyotype and CGH-array; but curiously she has the same phenotype than her son except mental retardation.

**Method:** AHO phenotype is present in two disorders: pseudohypoparathyroidism 1a (PHP 1a) where it is associated with hormone resistances especially to PTH; and pseudopseudohypoparathyroidism (PPHP) where no resistance to PTH is observed. In most of the cases of PHP 1a and PPHP, patients have a gene GNAS (located in 20q13) mutation, responsible for a decrease of Gsa protein activity. This gene is controlled by genomic imprinting. In case of paternal transmission the patient has PPHP and inversely. However, some cases like MC have PPHP without gene GNAS mutation but are carrier of a 2q37 deletion. Then Gsa protein activity is normal.

**Results:** Some molecular investigations have tried to identify the gene responsible for the AHO phenotype in 2q37. Recently the gene HDAC4, located in 2q37.3, was found to be mutated in patients with AHO phenotype. However, the mother's breakpoint is in 2q37.1 and HDAC4 is entirely translocated.

**Conclusions:** We propose a diagnostic flow chart in case of AHO phenotype in order not to forget 2q37 deletion as rare cause of short stature and obesity. Furthermore this familial case may be useful to understand the molecular pathways leading to AHO phenotype.

#### PAO-28

### Diabetic ketoacidosis as initial presentation in children with type 1 diabetes mellitus in South Region of Saudi Arabia

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**Background:** Type 1 Diabetes Mellitus (DM) represents about 5-10% of total diabetes with more susceptibility to develop Diabetic Ketoacidosis (DKA) than Type 2 DM as the underlying cause is insulinopen.

**Objective:** To study the percentage of patients with Type 1 DM that presents initially with DKA as this is a good indicator of public health knowledge about diabetes in the pediatric age group.

**Method:** A retrospective study to evaluate charts of patients seen regularly in Aseer Diabetes Center (ADC) over a period of 10 years from 1st Jan 2000 till 31 Dec 2009 whether they present initially in DKA or not.

**Result:** A total of 614 patients with Type 1 DM were registered. Among them 487 patients with completed data, 228 patients were seen in DKA as initial presentation (47%), whereas 259 patients were discovered before reaching DKA (53%). This percentage is higher than what have been published from the United States (25%) and in between if compared to the International figures (16-80%) In relation to age we found that 83% of patients who are less than 1 year of age had DKA as initial presentation. Beyond that age there was no much difference.

**Conclusions:** A relatively high percentage of DKA as initial presentation necessitate follow up study to evaluate what can be the cause of this relatively high percentage, with suggestion to have more public health programs in the media and training courses for primary health care physicians in order to reaches developed countries percentages.

#### PAO-29

### Hypoglycaemia in a Nigerian paediatric emergency ward

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**Background:** Hypoglycaemia is a common problem in paediatric emergency admissions. It has not received enough attention in Nigeria. It has been shown to complicate many childhood illnesses.

**Objective:** This study aimed to determine the prevalence of hypoglycaemia in paediatric emergency admissions, describe clinical factors that commonly predispose to it and investigate its effect on outcome of management.

**Method:** Three hundred and ninety-two consecutively admitted patients were studied. Two milliliters of blood was obtained from each patient for plasma glucose determination. Hypoglycaemia was defined as plasma glucose 52.5 mmol/l (545 mg/dl).

**Results:** Out of these 392, twenty-five (25) of them were hypoglycaemic giving a prevalence of hypoglycaemia to be 6.4 per cent in our emergency ward. Hypoglycaemia was found to be associated commonly with severe malaria, septicaemia, pneumonia, and protein energy malnutrition. Interval of last meal and unconsciousness were the only two significant associated factors to hypoglycaemia. However, the likelihood of hypoglycaemia is increased with night admissions and prolonged duration of illness before admissions. Presence of hypoglycaemia at admission was also found to be significantly associated with death and dying within 24 hours of admission.

**Conclusions:** The prevalence of hypoglycaemia was found to be 6.4 per cent. It was found to complicate many childhood illnesses and it is associated with a higher mortality. It should be suspected in all very ill children, particularly when they are unconscious and have not eaten for over 12 hours.

#### PAO-30

### Ethnic and gender inequities in the evaluation of referred short children

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**Aims:** To examine ethnicity and gender differences in the evaluation of referred children with short stature and to investigate adherence of the primary care evaluation to published guidelines.

**Methods:** Cross-sectional study in a referral center. 371 short patients aged 2 to 18 years were included. Outcome measures were patient's growth characteristics, final diagnosis, and prevalence of pre-referral patient data.

**Results:** The study population was composed of 239 Bedouin children and 132 Jewish children ( $P < 0.0001$ ). More males (61%) than females were evaluated ( $P < 0.0001$ ). There were no significant differences between males and females in age and growth parameters at the time of referral. Bedouins, males and females, were significantly shorter than their Jewish counterparts at the time of referral: Ht SD  $-2.44 \pm 0.73$  and  $-2.62 \pm 1.05$  versus  $-2.13 \pm 0.55$  and  $-2.21 \pm 0.57$ , respectively ( $P < 0.05$ ). There were no significant ethnic or gender differences in the final diagnosis. Significant deficiencies in the primary care evaluation of referred short children were found.

**Conclusions:** We demonstrated novel ethnic- and gender-based inequities in the evaluation of referred short children. We found that the current evaluation of short stature in our area does not comply with existing guidelines.

#### PAO-31

### A novel mutation in EIF2AK3 gene associated with Wolcott-Rallison syndrome in a family from Saudi Arabia

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**Context:** Wolcott-Rallison syndrome (WRS) is a rare autosomal recessive disorder characterized by neonatal diabetes mellitus, multiple epiphyseal dysplasia, osteoporosis, skeletal dysplasia and growth retardation. WRS is caused by mutations in EIF2AK3 gene.

**Objective:** The aim of the study is to describe a new case of Wolcott-Rallison Syndrome and define the underlying genetic defect.

**Design:** A WRS patient was followed up for the first 7 years of his life. DNA sequencing was performed to detect mutations in EIF2AK3 gene.

**Setting:** The patient was followed up in a pediatrics hospital.

**Patients:** DNA analysis was performed on the index case, his parents and siblings.

**Results:** A child of first-cousin parents presented at the age of 38 days with hyperglycemia. At the age of one year, x-rays showed skeletal deformities. He developed recurrent acute hepatitis during the follow-up time, the last one was associated with renal failure that resulted in his death at the age of 7 years. DNA sequencing showed homozygosity for a novel mutation (c.1262delA) in the EIF2AK3 gene.

**Conclusion:** A novel mutation c.1262delA was detected in a new case of Wolcott-Rallison syndrome.

## PAO-32

### Growth and weight-regulation disorders in children are not commonly associated with mutations of the ghrelin and GH secretagenous receptor (GHSR) genes

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**Background:** Ghrelin and its receptor, growth hormone secretagenous receptor, GHSR, play a major role in appetite control and growth regulation. To date, only four confirmed mutations in the GHSR gene have been identified in children with obesity and short stature, while no such mutations have been found in the ghrelin gene.

**Objective and hypotheses:** In the current study, we tested the hypothesis that mutations in ghrelin or GHSR will result in subjects being either over or underweight, and exhibiting abnormal growth.

**Methods:** Ninety-five subjects (37F/58M) were enrolled with FTT (10 pts), GHD (45 pts), ISS (18 pts) or obesity (22 pts). Both ghrelin and GHSR genes were sequenced.

**Results:** Seven different sequence changes were identified (66.3%) in GHSR, two of them novel and five described previously. None of the sequence changes identified in the GHSR gene changed the sequence of the encoded protein. The prevalence of these sequence changes did not differ between the subgroups. One previously described sequence change, Leu72Met, within the preproghrelin/ghrelin gene was identified in two patients (2%), one with FTT and the other with obesity and partial GHD. This sequence change, which had been identified previously in obese women, is located in exon 2 outside the coding region of the mature ghrelin.

**Conclusions:** Our results suggest that mutations of the ghrelin and GHSR genes are not commonly associated with growth and weight-regulation disorders in children.

## PAO-33

### The relationship between initial BMI and BMI change during 1-year of GnRH agonist therapy in girls with idiopathic central precocious puberty

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**Background:** Childhood obesity is associated with early pubertal development, and early sexual maturation is associated with increased prevalence of obesity. Above-average BMI is frequent at diagnosis of central precocious puberty (CPP).

**Objective and hypotheses:** The purpose of this study is to evaluate the relationship between initial BMI and BMI after 1-year of GnRH agonist (GnRHa) therapy in girls with idiopathic CPP. We also compared the group in which BMI-standard deviation score (BMI-SDS) increased after treatment with the group in which BMI-SDS remained the same or decreased.

**Methods:** The subjects were ninety-nine CPP girls treated with GnRHa for more than 1 yr. We investigated chronologic age (CA), bone age (BA), BA advance (BA-CA), height, Ht-standard deviation score (Ht-SDS), BMI, BMI-SDS, predicted adult height (PAH), PAH-SDS before initiation of GnRHa treatment and 1 yr later.

**Results:** There was no difference in initial CA, BA, BA-CA, Ht-SDS, target height between normal BMI group and overweight/obesity group. BMI-SDS increased more in normal BMI group than in overweight/obesity group (0.2 vs -0.1,  $P=0.004$ ), and initial BMI and delta BMI-SDS showed negative relationship ( $R^2=0.251$ ,  $P<0.001$ ). PAH-SDS increased less in normal BMI group than in overweight/obesity group (0.3 vs 0.7,  $p=0.02$ ), but there was no linear relationship between initial BMI and PAH-SDS, delta BA-CA, delta Ht-SDS also was not different between normal BMI group and overweight/obesity group. Comparing pts. in whom BMI-SDS increased or remained the same after treatment with those whose BMI-SDS decreased, there was no difference in delta BA, delta Ht-SDS, delta PAH-SDS. Delta BMI-SDS was related only with initial BMI SD, and showed no relationship with CA, BA, BA

advance, height, drug dose.

**Conclusions:** In CPP girls treated with GnRHa for 1 year, BMI SDS increased in those with normal BMI. Delta BMI-SDS had negative relationship with initial BMI-SDS, but was not influenced by other factors such as initial CA, initial BA, initial BA-CA, initial Ht-SDS, initial PAH-SDS, target height, drug dose.

## PAO-34

### A case of salt-wasting and virilizing form of congenital adrenal hyperplasia in a patient with male phenotype and 46,XX karyotype

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**Background:** In congenital adrenal hyperplasia (CAH) with 21-hydroxylase or 11 $\beta$ -hydroxylase deficiency, futile trophic hormone stimulation results in excess sex hormone precursors. Androgen predominance in these forms of CAH leads to virilization of affected females in utero.

**Objective and hypotheses:** We describe a patient with virilizing and salt-wasting form of CAH.

**Methods:** A case report.

**Results:** Patient 7.2 years old boy. The complaints were: Delay of physical and sexual development (unorchia), pubic hair since the age of 2 years. Anamnesis: over the postnatal period the child was frequently hospitalized due to intensive vomiting, diarrhea and weight loss. The patient was on symptomatic treatment. Auxology: HSDS 1.22. Sexual development stage P3 A1 G2; Testes not palpable. Bone age by Greulich and Pyle 10.5 years. Genetical research: karyotype – 46XX; Laboratory research: 17OH Prog-50 ug/l, Potassium 4.1 mmol/l, Sodium- 136 mmol/l, LH <0.1 IU/l, FSH 2.8 IU/l, Estradiol 10 ng/l, Androstendion 0.7 ug/l, ACTH 133 ng/l, Renin 241 ng/l. Abdominal MRI: In the pelvic cavity on both sides ovary like structure, with the size: 0.8X1.33 cm. At the posterior side of the urinary bladder tubular mass with the size 27X7 mm (apparently vagina); The conclusion of children's psychologist: The psychologic development of the child corresponds to male. Therapy: Hydrocortisone 15mg/day, Fludrocortisone 1 mg/day, Cyproterone 10 mg/day. By substitutional therapy hormone concentration in the blood came down to the normal range and puberty stopped. The condition of the patient was explained to the parents and to an ethical committee for the decision, to raise the patient as a girl or as a boy by gender reassignment surgery (extirpation of uterus and ovaries).

**Conclusions:** Continued excessive adrenal sex steroids in untreated CAH patient causes several problems which may reveal not only physical, but also psychological deviations.

## PAO-35

### A case of a 1 year 9 month old girl with a hypothalamic hamartoma associated with precocious puberty

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**Background:** Gonadotropin-releasing hormone (GnRH) dependent, or central precocious puberty (CPP) results from early onset of hypothalamic-pituitary-gonadal activity. This occurs as a consequence of physiologic gonadotropin stimulation emanating from the GnRH secretion of hypothalamic origin. Both boys and girls with an organic etiology of CPP are more likely to present at a younger age, than those with idiopathic etiology.

**Objective and hypotheses:** We describe a child with hypothalamic hamartoma associated with precocious puberty on Triptorelin treatment.

**Methods:** A prismatic case report.

**Results:** We report 1 year 9 months old girl. Complaints: premature puberty. Sexual development stage: Tanner 3 (B3, P3, A2, Me at the age of 8 months) Anamnesis: from the age of 2 weeks till today vaginal discharge (white), at the age of 3 months pubic hair appeared, at the age of 6 months breast de-

velopment has started, at the age of 8 months menarche occurred. Auxology: Height: 92.7 cm; Weight: 17.8 kg; HSDS: 2.35; Bone age by Greulich and Pyle: 4 years; Gynaecological Ultrasonography: Uterus: 23.6X17X26 mm; Endometrium thickness 4 mm; Ovaries: dex - 23X11 mm with cystic insertion 11X6 mm; sin - 14X9 mm with cystic insertion 2.5 mm; Adrenal Ultrasonography: Without pathology. Cerebral MRI: Disontogenic neoformation of the hypothalamic area (Harmathoma). Hormonal research: FSH 9.6 IU/L (N < 1); LH 1.70 mIU/ml (N < 0.1); Estradiol 77 pg/ml (N < 15); Therapy: GnRH agonist – Triptorelin (Dosage 3.75 mg every 4 weeks). By the therapy hormone concentration in blood came to the normal range 0.06 mIU/ml (LH) and 0.19 mIU/L (FSH), patient had no menstruation since the beginning of the treatment. The puberty has stopped.

**Conclusions:** CNS abnormalities causing CPP include redundant or excessive hypothalamic tissue (hypothalamic hamartoma). Treatment by suppression of gonadotropin secretion with Gonadotropin-releasing hormone agonist (GnRHa) is an appropriate and efficacious treatment of CPP.

#### PAO-36

### Female with disorder of sexual differentiation DSD 47,XXX: a first report

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Iñigo Bilbao Gonzalez<sup>2</sup>; Luis Fernando Galera Moreno<sup>1</sup>

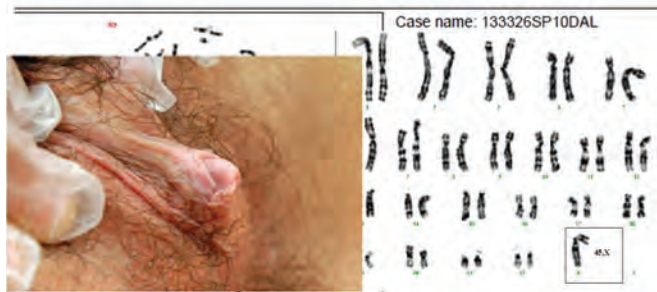
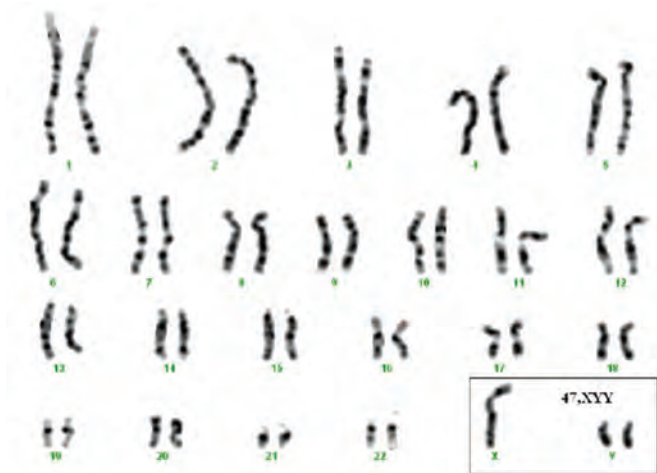
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**Background:** Disorder of sexual differentiation can produce phenotype alterations. Some of them are imperceptible at birth. We present the case of a girl with a karyotype and internal/ external phenotype never described before. We present a large iconography of this peculiar case.

**Clinical case:** 14 years old patient with not sign of thelarche and important hirsutism. Mother with hirsutism, with no menstrual affectation, and not fertility disorders. Normal pregnancy and delivery. There was no evidence of genital malformation at birth. Growth and development were normal. Quickly adrenarche at 8 years old. Moderated acne.

Actual physical exploration: Weight P 90, tall P25. Peculiar phenotype “Turner” like. Hirsutism (Ferriman 12 points) Tanner A5P5B1. Clitoromegaly (Prader 2-3), with penis-form appearance, without terminal urinary meatus. Inguinal conduits normal. Norm-shaped vulva. Permeable hymen.



#### Methods:

Complementary tests TSH 1.98µU/mL FSH 51.6 UI/L LH 33.2 UI/L Estradiol 13.3 pg/mL Testosterone total 10.41 ng/mL SHBG 52.92 nmol/L DHEA-S 174 mcg/dL Free Testosterone 19.3 17 OHP 1.64 ng/mL Karyotype: (400 bands): 47,XXX[28]/45,X[2]

Genital Echography: small size uterus (40x20x8 mm) and gonades (15 x 5 mm) without follicles Lineal endometrius.

LHRH Test: positive respond for testosterone

Gynecologic exploration through laparoscopy:

Uterus and Fallopian tubes were normal. Left ovary compatible with testicle; with a similar form between fimbriae in right side. Tissues biopsy: Compatible with testicular tissue. Karyotype of gonadal biopsy 47 XYY

Evolution: Quick estrogenization (etinilestradiol VO and combined progesterone). 6 months after quiryrgy, there was a reduction of basal testosterone, partial reduction of body hair, telarche development grade III and a substantial improvement of patient' self-esteem. Clitoromegaly is lower too.

#### PAO-37

### Diabetes in 6 patients of beta-thalassemia major

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**Objective:** The aim of this study was investigation of clinical features, pathogenesis, laboratory examination and early treatment of diabetes mellitus in patients with beta-thalassemia major.

**Methods:** Diabetes mellitus was observed in 6 of 53 patients with beta-thalassaemia major. In this retrospective analysis study, patients were examined to determine their pubertal status and the standard deviation score for height for evaluation of short stature. Laboratory test index of blood were measured.

**Results:** The average age in the 6 patients was 13.36 years(11-18years). Two patients, at onset of clinical diabetes, presented with an asymptomatic glycosuria and four with polydipsia, polyuria, weight loss and ketoacidosis. Serum ferritin was in the range of 4800-7148ug / L; Fasting blood glucose was in the range of 8.9-43.8mmol / L, HbA1c was in the range of 8.9-16.8%. 2 patients were detected high insulin level(>20mu/L), suggesting insulin resistance. 4 cases of ketoacidosis were detected insulin level <2mu / L, C peptide mean 24pmol / L, suggesting lack of insulin secretion. Pancreas MRI showed the signal to reduce, which was related with iron deposition. The puberty stage of 6 patients was in Tanner 1 to Tanner 2. 6 patients were all short stature, 4 cases of hypothyroidism, 2 cases of GHD. Mild liver function abnormalities(2 cases) and abnormal heart function(1 case) were detected. All patients treated with transfusion, deferoxamine, exercise, diet control, Glucobay and insulin. Comprehensive therapy was good.

**Conclusions:** Despite therapy with deferoxamine to treat iron overload, the risk of secondary endocrine dysfunction remained high. Diabetes in patients of beta-thalassemia major were often accompanied by other endocrine organ damaged, which occurs with iron deposition. The pathogenesis of diabetes in beta-thalassemia major may be similar to the development of type 2 diabetes. Early diabetes, it was insulin resistance, and finally lack of insulin secretion induced to insulin dependent diabetes mellitus.

#### PAO-38

### Craniopharyngioma: auxoendocrinological changes at diagnosis and endocrine complications after treatment - a retrospective study

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**Introduction:** The craniopharyngioma is a cystic tumor, calcified, squamous-epithelial origin in the slow growth. Internationally, the incidence is 0.5-2/100.0. Mortality/morbidity: survival varies by age group, with an excellent prognosis in patients aged less than 20 years (99% at 5 years).

**Clinical:** The most common presenting symptoms are headache (55 - 86%), endocrine dysfunction (66-90%) and visual disturbances (37 - 68%). Endocrine abnormalities are found in 80 to 90% of craniopharyngiomas. In fact,

in 39% of patients shows impairment of 3-axis pituitary in 28% of 2 or more axes in 11% of 1 or more and 22% no axis compromise. [5]. The most frequent response is that of a GH deficiency present in more than 75% of cases, followed by a gonadotrophic deficiency in 40% of cases and an ACTH and TSH deficiency in 25%. Despite craniopharyngiomas are usually of significant size already at diagnosis, the pituitary stalk is rarely interrupted, for which only 20% of patients presents hyperprolactinemia resulting from the compression pedicle.

**Our experience:** In 25 children (16 males and 9 females) whose age at diagnosis was between 0.35 and 13.30 years with an average of 6.56 years (SD 3.04). Location of craniopharyngioma. Suprasellar 8 Sellar suprasellar 8 Saddle + 3rd ventricle 1 Suprasellar diencephalic 1 Suprasellar + 3rd ventricle 1 Chiasmatic 2 3rd ventricle 1 Retrochiasmatic 1 Retrosellar 1 Suprasellar retrochiasmatic 1 Total 25 Auxo-endocrine abnormalities at diagnosis. Growth retardation 4 / 25 (16%) Precocious puberty, 1 / 25 (4%) Delayed puberty 1 / 25 (4%) PU / PD 1 / 25 (4%) Overweight / obesity 5 / 25 (20%) Gigantism 1 / 25 (4%) Endocrine abnormalities detected after treatment. Diabetes insipidus 20 (80%) Precocious puberty 2 (8%) Hypoadrenalism 18 (72%)

**Conclusion:**

- High incidence of short stature and / or = 2
- High incidence of obesity hyperphagia
- marked hyperphagia (binge eating) with difficulty in controlling appetite.
- Increased behavioral and psycho-social.

**PAO-39**

**Is the level of anti TPO antibodies predictive for the course of Hashimoto thyroiditis?**

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**Background:** Hashimoto's thyroiditis (HT), characterized by the presence of high serum thyroid auto-antibody titers and goiter, is one of the most common types of thyroiditis in children and adolescents. It is associated with a wide spectrum of thyroid functions, ranging from euthyroidism to overt hypothyroidism, with a variable clinical course.

**Objective and hypotheses:** To assess the thyroid hormone status during the long-term follow-up and to establish the prognosis of children and adolescents with HT.

**Methods:** We evaluated thyroid function (TF) in 77 children with HT. The patients were assessed at presentation and then followed up at 6-12 months intervals. We divided them according to the level of anti TPO antibodies into 2 groups: up to 10 fold elevated and above that level.

**Results:**

Age (years)	5-19, mean 14
Sex (M/F)	19/58
Puberty (no/yes)	8/69
TSH (high/normal)	28/49

Follow up period was 0.5 to 10, mean 1.9 years. We compared TF in 2 groups of patients and did not find that level of anti TPO antibodies was predictive.

**Conclusions:** In our group of patients we noticed female predominance, most patients were in puberty and majority of them are still euthyroid in follow up. We were not able to establish the connection between the level of anti TPO antibodies and thyroid function.

**PAO-40**

**Prevalence of subclinical hypothyroidism in child cancer survivors and efficacy of levothyroxine treatment**

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**Background and objective:** Child cancer survivors (CCS) have some complications. Although hypothyroidism in CCS has been well reported, little is known about subclinical hypothyroidism (SCH). The aim of this study was

to investigate the prevalence of SCH and efficacy of levothyroxine (LT4) supplementation in CCS with SCH.

**Methods:** Twenty CCS were divided into two groups. The chemo group (n=8) was treated with chemotherapy alone and the radiated group (n=12) received chemotherapy plus radiotherapy. Control group was healthy children who showed short stature but normal hypothalamic-pituitary and thyroid function. TSH, FT3, and FT4 were measured in all patients. TRH stimulating test was performed only in the patients who were diagnosed with SCH. The definition of SCH is TSH > 5  $\mu$ IU/ml, while FT3 and FT4 are within normal range. Lipid profile and QOL were evaluated after 2 or 3 month of LT4 supplementation in these patients.

**Results:** No patients in the chemo group showed SCH. Four patients in the radiated group (33%) were diagnosed with SCH. They received radiotherapy both in spine and brain. Their TRH stimulating test showed hyperresponse and persistence of high levels of TSH. Their cholesterol levels were significantly higher than those of the chemo group. Mild dose of LT4 administration improved their lipid profile and QOL.

**Conclusions:** High prevalence of SCH was seen in CCS with radiotherapy. Our findings suggest that irradiation of spine plus brain is high risk of SCH. Mild dose of LT4 can improve the lipid profile and QOL in SCH patients.

**PAO-41**

**Adenohypophysitis in a boy with pan-sinusitis and meningitis**

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**Background:** Although hypophysitis is usually thought as a primary process, it may occur secondarily in relation to infections or other processes such as Langerhans cell histiocytosis, Crohn disease.

**Case report:** We report the case of a 15-year-old boy who was admitted to our Clinic due to headache, fever, visual disturbances and rigor nuchalis. A 3D-CT showed pansinusitis whereas CSF showed a pleiocytosis (500 cell/mm<sup>3</sup>); therefore, broad spectrum antibiotics therapy were administered. After 5 days headache, fever, rigor nuchalis were resolved, but diplopia persisted. MRI demonstrated diffuse pansinusitis and extension of inflammation and infection into the adjacent cavernous sinuses and pituitary gland that, after gadolinium, presented asymmetrical enlargement in size. Basal concentrations of plasma ACTH, cortisol, PRL, FSH, LH, testosterone were very low; also TSH appeared very low but thyroid hormones were still within the normal limits. Anti-pituitary antibody was also negative. Corticosteroid treatment (1mg/kg/die) was administered for six months and after two months of discontinuation endocrinological investigations were repeated. There were normal responses of FSH and LH to appropriate stimuli, normal levels of T, ACTH, cortisol, TSH, FT4. Only GH secretion after stimulation tests appeared subnormal (Peak 3,71 ng/ml). Follow-up MRI showed that the pituitary had reduced in size.

**Conclusion:** On the basis of our case we may conclude that: a) pansinusitis can have devastating intracranial sequelae, as involvement of the adjacent pituitary gland and cavernous sinuses; b) endocrinological and radiological examination could be performed after pansinusitis in order to detect early involvement of pituitary gland; c) corticosteroid therapy can be effective in reducing the pituitary size, attenuating inflammation and restoring pituitary function; d) a pattern of pituitary hormone deficiency with early loss of ACTH and TSH and sequential loss of GH could be observed. Long term follow-up is mandatory to monitor other possible hormonal deficits.

**PAO-42****Adrenal agenesis secondary to DAX 1 mutation in a newborn**

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**Background:** Agenesis or hypoplasia of adrenal glands associated to alterations of Gen DAX-1 (crom X) are a very unusual clinical subject, and could be accompanied of other hormonal and genetic alterations. We present a clinical case, supported with images.

**Objective and hypotheses:** Male newborn with breathing distress and very important hyper-pigmentation. Mother 35 years healthy first birth. Father healthy. No consanguinity. Prenatal ecography normal. Negative serology. 41 GA prenatal monitoring normal.

**Methods:** Weight 3880 G (>2 SDS) Height 56,5 cm (>2 SDS) CP 37 cm Hypotonic, with labial sub cyanosis and general hyper pigmentation, Silverman score 3-4/10. Normo configured genitalia, except hyper-pigmentation. Apgar 2/6/8. Requires RCP type II.

**Results:** Laboratory: pH 7,26, CO<sub>2</sub>H 19,4; EB -6. Sodium 119 mEq/L, potassium 7.3 mEq/L, PCR 23,8 mg/L after 24 hours/life Cultives: Negative. Cortisol 2,86 mcg/dl. DHEA-S 8,32 mcg/dl (32-431), 17OHP 3,73 ng/ml (0,4-3,3). ACTH 1.129,1 pg/mL (5-77), cholesterol 177 mg/dl (50-170), Norepinefrine: 5 mcg/24 horas (12 mcg/L) Ephinefrine: < 1 mcg/24 hours (<2 mcg/L) Dopamine: 65 mcg/dl (163 mcg/L). Abdominal ultrasound and MRI: There is no sign of adrenal glands. Genetic study: 46 XY (DAX-1 +) at index case, father not affected, mother 46 XX\*, (null/DAX -1).

**Conclusions:** After Hydro-electrolytic correction and treatment with hydrocortisone; the values of Na/K were normal. We use supplementary dose of sodium too. After 3 months, the levels of ACTH were normal. Up to date (18 months age), patient is asymptomatic. His psychomotor and somatometric development is according to his age. Bone-age equivalent and the hyper-pigmentation has disappeared.

**PAO-43****Bone mineral density and turnover in patients with idiopathic hypogonadotropic hypogonadism**

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**Background:** Patients with idiopathic hypogonadotropic hypogonadism (IHH) may have reduced peak bone mass in early adulthood, and increased risk for osteoporosis despite long-term hormonal replacement therapy (HRT).

**Objective and hypotheses:** We investigated markers of short-term bone turnover, and the relationship between HRT history and bone mineral density (BMD) in patients with IHH.

**Methods:** 33 subjects (24 men, 9 women; mean age 39.8 yrs, range 24.0—69.1) with IHH (Kallmann Syndrome or normosmic IHH), were physically examined and measured for circulating PINP, ICTP, and sex hormone levels. 26 subjects underwent DEXA for BMD of lumbar spine, hip, femoral neck, and whole body.

**Results:** In men, serum PINP correlated with ICTP (R=0.61; p=0.002), but these markers correlated neither with circulating T, nor with serum E levels in women.

Treatment history had a clear impact on bone health in men: lumbar spine (LBMD, mean Z-score -2.0 SD, range -4.1—1.4) was reduced in subjects with inadequate HRT (n=7, including those with long (≥5 yrs) treatment pauses) as compared to those with a history of adequate HRT (n=11; LBMD: -0.5 SD, -2.4—0.7) (p=0.037).

The overall duration of treatment pause (range 0.15—30 yrs) correlated negatively with lumbar and femoral neck Z-scores (R=-0.64 and -0.53; p=0.014 and 0.041, respectively), and the overall duration of HRT (range 2.6—37.3 yrs) had positive correlations with hip and femoral neck Z-scores (R=0.42 and 0.61; p=0.039 and 0.001, respectively). Age, BMI, or age at onset of HRT

did not correlate with BMDs. In addition, BMDs did not differ between subjects with KAL1 (n=3), FGFR1 (n=5), or GNRHR (n=4) mutations (data not shown).

**Conclusions:** In patients with IHH, the prevailing sex steroid milieu does not affect short-term bone turnover. Our data suggest that both the quality and quantity of HRT influence BMD in IHH patients irrespective of age.

**PAO-44****Two cases with HDR syndrome (hypoparathyroidism, sensorineural deafness and renal disease)**

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**Background:** HDR syndrome (hypoparathyroidism, sensorineural deafness and renal disease) was first reported by Barakat et al. described two brothers with steroid-resistant nephrosis with progressive renal failure, sensorineural deafness and hypoparathyroidism in 1977. Autosomal dominant disorder that is caused by mutations of the GATA3 gene, which is located on chromosome 10p15, has been identified recently. GATA3 is expressed in the developing parathyroid glands, inner ears and kidneys, together with thymus and central nervous system.

**Objective and hypotheses:** The patients with symptoms of hypocalcemia must be evaluated carefully.

**Results:** Hypoparathyroidism, sensorineural deafness and renal anomaly were diagnosed in our two patients with symptoms of hypocalcemia.

**Conclusion:** These cases are reported because of HDR syndrome is a very rare condition and the history of deafness in patients with hypocalcaemia for understanding of this syndrome.

**PAO-45****Effects of growth hormone on muscle strength, tone and mobility of children with Prader-Willi syndrome**

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**Background:** Prader-Willi syndrome (PWS) is a genetic syndrome presenting with severe hypotonia and decreased agility. Growth hormone (GH) which is often used in these cases to treat short stature and obesity, seems to have some improvement in hypotonia, physical strength, activity, and locomotor developmental ability.

**Objective:** The aim of this study is to find the growth hormone effect on the agility and strength of these patients.

**Material and methods:** In a prospective, randomized controlled clinical trial, at an out-patient pediatric endocrine clinic in Tehran, 21 PWS children (12 boys and 9 girls, 4 to 9 years old) were divided either in GH-treated or control groups and followed for two years. Agility run, sit ups, weight lifting, and inspiratory and expiratory strengths were considered as the main outcome measures.

**Results:** All the outcome measures of the GH treated group showed a significant improvement compared to those of the control (p<0.01).

**Conclusions:** GH causes a significant improvement in agility and strength of PWS children.

### An unusually early diagnosis of 17-alpha-hydroxylase deficiency

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**Background:** Mutations of the CYP17A1 gene result in 46,XY disorder of sex development, hypertension, hypokalemia and absent pubertal development. It is a rare, autosomal recessive form of congenital adrenal hyperplasia (CAH).

**Objective and hypotheses:** Usually, most patients are detected rather late as adolescents due to lack of puberty or hypertension.

**Methods:** We report about a neonate born to a 40 year old woman, 1st para, 1st gravida. Amniocentesis revealed a fetus with a 46,XY karyotype. At 20 weeks of gestation the development of male external genitalia was missing. Further molecular testing excluded an androgen receptor and SRY gene mutation. A phenotypically female child was born at 41st week of gestation. Gonads were palpable in the labia majora.

**Results:** Postpartal ultrasound revealed testes in both labia majora, absence of uterus and normal adrenal glands. Screening for 21-hydroxylase-deficiency was normal. Multiteroid analysis in serum showed reduced basal glucocorticoid, testosterone and androstenedione levels at the age of two weeks. The urinary steroid metabolome – assessed by GC-MS - showed excessive excretion of 17-desoxy -steroids, decreased glucocorticoid metabolites and absent C19-steroids. Such a metabolic constellation proves 17-alpha-hydroxylase-deficiency. Molecular analysis identified a novel mutation of the CYP17A1 gene: c.896T>A (p.I299N) in exon 5. Substitution with hydrocortisone was started at a moderate dose to prevent hypertension. The child is growing well so far.

**Conclusion:** Herein we report the unusually early diagnosis of a newborn with the rare CAH form of 17-alpha-hydroxylase-deficiency allowing installment of early treatment.

## PAO-47

### The effect of gonadotropin-releasing hormone agonists in Korean boys with idiopathic central precocious puberty and early puberty

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**Background:** Central precocious puberty (CPP) is less common in boys than in girls. There is little data available on the long-term safety and efficacy of GnRHa treatment in boys with CPP. The effects of GnRHa, with and without growth hormone, on the predicted adult height in boys with CPP and early puberty were evaluated after two years of treatment.

**Methods:** This study included nine boys with CPP and 13 boys with early puberty that were treated with depot leuprolide acetate. Anthropometry, bone age, the sexual maturity rating and predicted adult height (PAH) were assessed at baseline, and after 6, 12, 18, and 24 months.

**Results:** The PAH standard deviation score (SDS) in the GnRHa group of boys with CPP (n=9) was significantly increased ( $-0.23 \pm 1.60$  vs  $0.49 \pm 0.71$ ;  $P=0.0014$ ). The PAH SDS of the GnRHa group with early puberty (n=9) was significantly decreased to the pretreatment PAH SDS ( $0.57 \pm 1.06$  vs  $0.36 \pm 0.68$ ;  $P<0.05$ ). Multiple regression analysis revealed that height gain was influenced significantly by age at the start of treatment.

**Conclusions:** GnRHa treatment significantly improved the growth potential in boys with idiopathic CPP. However, GnRHa treatment alone did not affect the growth prognosis in boys with early puberty.

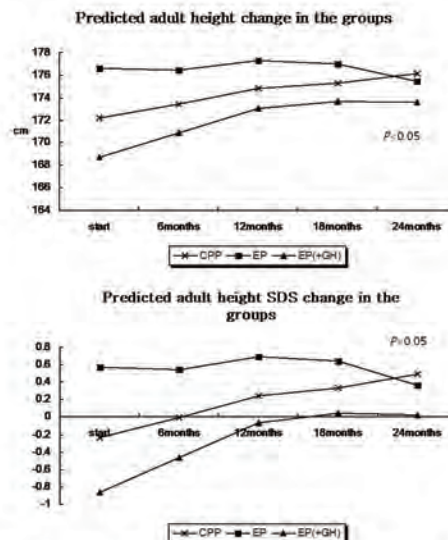


Fig. 2. Predicted adult height and height standard deviation scores (SDS) before and after 2 years treatment with GnRHa or GH+GnRHa in 22 boys with central precocious puberty (CPP) and early puberty (EP).

## PAO-48

### Influence of body mass index on growth hormone responses to classic provocative tests in children with short stature

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**Background:** The diagnosis of growth hormone (GH) deficiency is based on a reduced peak GH response to provocative tests. However, the provocative tests are poorly reproducible and GH secretion is regulated by physiological parameters, such as body weight and puberty. The aim of this study was to assess the influence of BMI on growth hormone response to provocative testing and to analyze the reproducibility of GH stimulation test.

**Methods:** Clinical data was collected retrospectively by chart review from the Pediatric Endocrine Unit at Ajou University Hospital. A total of 187 subjects with short stature who completed a GH stimulation testing between 2003 and 2009 were included in the study.

**Results:** Of the 187 subjects, 66 (35.3%) had GH deficiency, while 121 (64.7%) were categorized as having idiopathic short stature. Reliability was calculated for 48 patients with ISS who underwent the GH stimulation test twice. A GH response  $\geq 10$  ng/ml after retesting was found in 39 (81.3%) patients and a GH response  $< 10$  ng/ml was found in 9 (18.7%) patients. In a stepwise multivariate analysis, BMI was a significantly independent predictor of peak GH. Elevated BMI was negatively associated with peak plasma GH levels.

**Conclusions:** The lack of reliability of GH values in response to pharmacological stimuli should be taken into account in the diagnosis of GH deficiency. Also, higher BMI is associated with lower GH secretion. BMI should be measured and GH results appropriately interpreted for all subject undergoing GH stimulation testing.

### Medullary thyroid carcinoma in two children from a family with multiple endocrine neoplasia 2a syndrome - a case report

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**Introduction:** All carriers of a point mutations in the RET proto-oncogene with multiple endocrine neoplasia type 2A (MEN2A) develop medullary thyroid carcinoma (MTC), while 50% and 30% of patients develop pheochromocytoma and hyperparathyroidism. MTC tends to disseminate early. It is chemo- and radio-resistant and remains the cause of death in 15-20% of MEN2A patients. Consequently, early prophylactic total thyroidectomy is performed in all MEN2A patients.

**Case report:** A 32-yr-old father presented with bilateral pheochromocytoma, MTC and parathyroid adenoma. Genetic analysis revealed a point mutation in codon 634 of exon 11 of the RET proto-oncogene. Genetic testing confirmed that both siblings were carriers of the same mutation. In a 10-y 2-mo old son ultrasound of the neck disclosed nodules in both thyroid lobes and enlarged paratracheal and left jugular lymph nodes. Laboratory examination revealed high calcitonin concentrations (437pg/ml), while serum calcium and PTH levels were on the upper limit of normal values. In a 7-y 10-mo old daughter serum calcitonin level was slightly elevated (20.7pg/ml), and plasma calcium and PTH levels were normal. On ultrasonography, a nodule in a right thyroid lobe, enlargement of the left jugular and right submandibular lymph nodes were observed. Both children underwent total thyroidectomy with neck dissection. Pathological examination showed bilateral MTC in a boy and MTC of the right thyroid lobe in a girl, with no lymph node metastatic disease. Laboratory examination showed no pheochromocytoma in siblings. After surgery both children began with thyroid replacement therapy. Due to the permanent hypocalcaemia in a boy, treatment with calcium-carbonate and calcitriol was initiated. Eighteen months after thyroidectomy, the children are doing well.

**Conclusions:** At present, genetic testing and prophylactic total thyroidectomy prevents the development of an invasive MTC in MEN2A patients. However, the risk of permanent hypoparathyroidism and the issue of thyroid replacement therapy remain a concern.

### A case of adrenal hypoplasia congenita caused by DAX1 deletion

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**Background:** Adrenal hypoplasia congenita caused by DAX1 (Dosage sensitive sex reversal-Adrenal hypoplasia congenita critical region on the X chromosome gene-1) mutation, is a rare disorder and presents usually acute severe adrenal insufficiency in the neonatal period and hypogonadotropic hypogonadism. Because DAX1 is located on Xp21, the mutation affects primarily boys (X-linked). Associated with deletion of DAX1, the Duchenne muscular dystrophy, mental retardation-IL1RAPL1, glycerol kinase and ornithine transcarbamylase genes may also be deleted as part of a contiguous gene syndrome.

**Case:** We report an 1-month old male patient presenting with weight loss, dehydration, lethargy, poor feeding, and hyperpigmentation. The first laboratory investigation showed hyponatremia (121 mEq/L), hyperkalemia (7.8 mEq/L), high ACTH (342 pg/mL), and high renin (24.6 ng/ml/hr), so he was diagnosed with primary adrenal insufficiency (PAI). To reveal the cause of PAI, further investigations were performed and showed normal 17-OHP, VLCFA, and negative adrenal Ab. On abdominal CT, adrenal hypoplasia was detected. DAX1 gene analysis using PCR presented complete deletion and contiguous genes (glycerol kinase and IL1RAPL1) were also deleted. He showed clinical improvement after glucocorticoid and mineralocorticoid treatment, but at present (12 months of age), shows mild motor developmental delay.

**Conclusion:** DAX1 mutation analysis should be considered in males with adrenal hypoplasia congenita.

### Comparison of the efficacy of multiple daily insulin injection therapy and flexible intensive insulin therapy in children with type 1 diabetes mellitus

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**Objective:** To compare the effects of multiple daily insulin injection therapy (MDII) and flexible intensive insulin therapy (FIIT) on metabolic parameters and quality of life in children with type 1 Diabetes Mellitus (DM).

**Method:** Twenty eight patients who were followed regularly at least 1 year in our Pediatric Endocrinology outpatient clinic and being treated with MDII (three doses of pre-meal insulin aspart and a single daily dose of basal detemir/glargine insulin) were included in the study. All the patients were evaluated for HbA1c, BMI-SDS, hypoglycemia, mean fasting plasma glucose (FPG) levels, lipid profile, total daily insulin requirement and quality of life (QOL) before and after the 6 months of FIIT. Treatment periods of MDII and FIIT were compared. The Medical Outcomes Survey Short Form-36 (SF-36) was performed in order to assess QOL.

**Results:** Mean age of the patients was 12.9 ± 2.59 years old. The mean HbA1c and FPG levels of the patients during MDII treatment were found significantly decreased after switched to FIIT (p<0.001 and p=0,024). Insulin requirements, frequency of hypoglycemia, total cholesterol, low density lipoprotein (LDL), triglyceride levels, HDL levels and BMI-SDS of the patients was not significantly decreased with FIIT (p>0.05).

**Conclusion:** HbA1c and mean FBG levels significantly decrease with FIIT without causing significant difference in insulin requirement, frequency of hypoglycemia and lipid profiles. FIIT also improves mental health and is a reasonable choice in treatment of pediatric Type 1 DM patients.

### Suspicious reflections and a solitary nodule in Hashimoto thyroiditis: finally carcinoma

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**Background:** There is controversial literature on the association between Hashimoto thyroiditis (HT) and the incidence and course of papillary thyroid carcinoma (PTC) in children.

**Case report:** Our patient was first seen as a young girl at age 14 with a clinical picture of HT with positive anti-TPO antibodies. Ultrasound revealed an inhomogeneous pattern in the left lobe with many reflections, mimicking micro calcifications, and Tc-99-pertechnetate scan was inconclusive. Fine needle aspiration (FNA) suggested a benign etiology with lymphocytic thyroiditis as in HT. Levothyroxin supplementation was initiated. At age 16.5, our patient complained of a swollen neck and the thyroid gland was found to have increased in size. Ultrasound showed a 2 cm hypervascular solitary nodule in the left lobe near the isthmus. FNA again showed an HT picture. The risk for malignancy, given these repeated negative biopsies, was low and no surgical intervention was performed. Three months later the patient returned. On holiday abroad she had fallen ill and was seen at a hospital outpatient department. Complaints of further diameter increase of the thyroid led to another FNA, which this time suggested PTC. After her return from holiday, a total thyroidectomy was performed, showing a 3,5 cm diameter differentiated PTC (T2N0M0). No KRAS or BRAF mutations were detected in DNA analysis as markers of a malignant clinical course.

**Conclusions:** This case shows the co-occurrence of HT and PTC and the difficulties in diagnosis. In children it is not well defined whether HT increases risk for PTC incidence or prognosis. Ultrasound findings should aid in risk assessment, but its sensitivity in HT is poorly established. In this case, micro calcifications and hypervascularity of the nodule suggested further analysis, but FNA did not support clinical suspicion. Evidence-based medical decision making could guide clinical decisions in children with HT presenting with nodular abnormalities

## PAO-53

Abstract withdrawn.

## PAO-54

### Influence of body mass index on peak GH level in provocation test: children without growth hormone deficiency

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**Background:** Obesity and other related factors are known to suppress the secretion of growth hormone. But the influence of obesity on the peak GH level of provocation test is still controversial in children without growth hormone deficiency (GHD).

**Objective and hypotheses:** This study aims to evaluate the influence of obesity on the peak GH level of provocation test in children without GHD.

**Methods:** The subjects were patients who were admitted to Seoul National University Children's Hospital and got provocation tests done due to short stature from January 2000 to July 2010. Their medical records were retrospectively reviewed, and patients with obvious growth hormone deficiency were excluded. The main outcome measure was peak GH level of provocation test, and the height, weight, and serum IGF-1 levels were also recorded.

**Results:** Simple logistic regression analysis showed that body mass index standard deviation score (BMI SDS) had negative correlation with natural log value (Ln) of peak GH level ( $P=0.004$ ), but gender, age, pubertal status, Ln IGF-1 had no correlation, respectively. In multiple logistic regression analysis, BMI SDS ( $P=0.042$ ) and age ( $P=0.017$ ) were suggested to be significant predictors of Ln peak GH level.

**Conclusions:** In children without overt GHD, a higher BMI SDS may have negative correlation with the peak GH level. Therefore, we can take BMI SDS into consideration when analyzing the results of growth hormone provocation test.

## PAO-55

### Paediatric nephrology; chronic kidney disease (CKD) & coping – psychology vs. immunology & neuroendocrinology; discussion paper

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**Background:** The study of coping with Chronic Kidney Disease (CKD) in young people is a unique and challenging task because their circumstances are quite divergent from their adult counterparts. The aim of this article is to use a combination of retrospective and present literature to inform discussion linking psychology, immune and neuroendocrine systems to recognize a deeper perspective on coping in young people facing CKD.

**Ckd in children and young people:** CKD is a chronic illness and it is irreversible. Coupled with its devastating effects, CKD is associated with cardiovascular dysfunction, anaemia, malnutrition, muscle wasting, muscle weakness, glucose intolerance, reduced bone density; all leading to reduced coping, well-being and overall quality of life.

**Coping strategies (psychological and physiological):** The majority of young people with CKD would be expected to cope adequately with daily events and stresses under normal circumstances. Anxiety is a common psychological pattern of children/ young people with CKD. Physiologically, due to the influence of internal conditioning factors, what might generally be called 'a normally well-tolerated degree of stress' can become chronic for individuals with vulnerable body systems, thus leading to long-term adapting/ coping in young people with CKD.

**Central mechanisms:** The hypothalamic-pituitary-adrenal (HPA) axis is a major part of the neuroendocrine system, involving the interactions of the hypothalamus, the pituitary gland and the adrenal glands; thus how well a young individual with CKD copes may be related to stress hormone levels and cell types in the blood.

**Conclusions:** Overall, an integrated PNI approach is desirable to better understand coping. The immune system has a 'means' to signal and ready the body to respond to stressful challenges enabling it to cope. Understanding coping in children/ young people with CKD should not be restricted to psychological/ psychosocial research.

## PAO-56

### Breasts condition in adolescent girls with autoimmune thyroiditis

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**Background:** The reproductive health is frequently associated with thyroid disorders.

**Objective:** To study of mammary glands (breasts) condition in adolescent girls with autoimmune thyroiditis (AT).

**Population and methods:** The study included 30 girls (aged 15-18 yrs) with AT (group I) and 30 girls without thyroid diseases (control group). AT was diagnosed on the basis of thyroid peroxidase antibodies level and typical picture of thyroid ultrasound. Mammary glands (MG) disease (mastopathy or dysplasia) was diagnosed on the basis of signs and typical picture of MG ultrasound. Statistical analysis was performed using Mann-Whitney Test.

**Results:** Thyroid function was normal in all these girls. TSH levels in girls of group I and control group were  $2.9\pm 0.9$  and  $1.7\pm 0.5$  mIU/L respectively. The investigation shows that only 2 girls without AT and all girls (100%) with AT had MG diseases. Among the patients with MG disease the diffuse fibrous dysplasia was found in 26 (87%) in group I and 2 girls – in control group. The cystic diffuse dysplasia diffuse was diagnosed only in girls with AT (in 2 patients). The study demonstrated that all adolescents with AT and MG disease had cyclic (premenstrual) mastalgia, 27% girls – persistent mastalgia and 45% girls – cyclic and persistent mastalgia. The investigation shows that only 2 girls with MG disease of control group had premenstrual mastalgia.

**Conclusions:** This study has shown a high frequency of mastopathy (38%) among the examined adolescent girls with AT. The AT is risk factor for the mastopathy and the indication for observation and examination of MG.

## PAO-57

### Computer diagnostics of diabetic cardiac autonomous neuropathy in children

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Diabetic cardiac autonomous neuropathy (DCAN) – is one of chronic complications of diabetes mellitus (DM) which indicates the unfavorable prognosis of disease.

**Objective:** To study the possibilities of apparatus programmed test in diagnostics of DCAN in children. Population and methods. There were examined 40 children with DM1, at the age from 7 to 16 yrs. 12 children have the debuting form of diabetes (I group), 16 children have suffered the disease from 1 to 5 yrs (II group) and 12 children have had the disease more than 5 yrs (III group). To diagnose DCAN there was used cardiac vegetative test by means of apparatus programmed complex «VNS - spectrum» (Neurosoft), with program analysis «Poly-spectrum». The evaluation of cardiac rhythm variability (5 cardiac vascular tests on Ewing) was used as the basis of investigation. Each one is estimated from 0 to 2 points.

**Results:** In all patients of I group there was revealed compensation of carbohydrate metabolism; subcompensation in 6 patients of II group and in 5 patients of III group; decompensation in 10 patients of II group and in 7 patients of III group. DCAN of 1 degree (5-7 points) was revealed in 20 children with DM; 4 patients of I group; 8 – of II group, 8 – III group. DCAN of 2 degree (8 – 10 points) was revealed in 5 children with DM: 1 from I group; 4 from III group. There was detected the correlation of DCAN with the age of children at the debut of the disease, duration of the disease, degree of compensation.

**Conclusions:** Cardiac vegetative test allows to diagnose DCAN in children and administer the treatment at early stage, when there is no irreversible death of the nerve fibre.



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**PAO-58****Failure to thrive and the diencephalic syndrome***Yvonne Yijuan Lim; Cindy Wei Li Ho; Kah Yin Loke*

National University Health System, Paediatrics, Singapore, Singapore

**Background:** Diencephalic syndrome is a rare condition which typically presents with severe failure to thrive despite preservation of normal linear growth. This is associated with tumours involving the hypothalamus and/or optic chiasma, with the majority being astrocytoma.

**Objective and hypotheses/method:** We describe 3 patients seen at our centre who were diagnosed with diencephalic syndrome over the past 20 years.

**Results:** Initial differential diagnoses for failure to thrive included celiac disease, generalized lipodystrophy and Russell Silver syndrome in one patient who was short. Only one patient presented with nystagmus, which suggested an intracranial pathology. After extensive workup for failure to thrive, Computed Tomography of the brain eventually revealed the presence of a suprasellar tumour in all 3 patients, which were subsequently confirmed to be inoperable hypothalamic astrocytomas. The age of diagnosis ranged from 9 to 18 months old. There was one death, with the other two patients demonstrating a more protracted course. The child who died presented at the earliest age and had the largest tumour which recurred within 1 month of surgery, suggesting a more aggressive course. Of the other two patients who have survived into adulthood, one underwent cranial irradiation before the age of 5 years, and suffered the consequences of late onset endocrinopathies and mental retardation. Both surviving patients have reached adulthood, with minimal increase in tumour size, suggesting a more indolent course. In diencephalic syndrome, the overall mortality rate is 55% with death ranging from 8 months to 13 years.

**Conclusions:** Diencephalic syndrome must always be considered in any child with failure to thrive from no other apparent reason. This peculiar syndrome provides a unique model of partial growth hormone resistance (elevated growth hormone levels) with normal linear growth, and suggests that there are hypothalamic-pituitary factors in the feedback mechanisms of appetite regulation and metabolism.

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**PAO-59****Profile of iron metabolism in pediatric age: clinical and epidemiological impact on our environment***Javier Caballero<sup>1</sup>; Alicia Romero<sup>2</sup>; María Aguilar<sup>2</sup>;**Eva L van Donkelaar<sup>3</sup>; Virginia Moreno<sup>1</sup>; Ramón Cañete<sup>2</sup>*<sup>1</sup>IMIBIC, Hospital Reina Sofía, Universidad de Córdoba, Clinical Analysis Service, Córdoba, Spain; <sup>2</sup>IMIBIC, Hospital Reina Sofía, Universidad de Córdoba, Pediatric Endocrinology Unit, Córdoba, Spain; <sup>3</sup>University of Maastrich, Faculty of Health, Medicine and Life Sciences, Maastrich, Netherlands

**Introduction:** Iron deficiency is a significant public health problem in terms of epidemiology and potential comorbidities. Its prevalence and easy diagnosis and treatment, put into question the relevance of performing screening programs or targeted screening in high risk populations or suspected cases.

**Objectives:** Determine our environment and the existence of iron deficiency or iron-deficiency anemia in children previously diagnosed between 2 months and 11 years, analyzing their clinical implications.

**Material and methods:** Cross-sectional study in a sample of 900 children seen in primary care. They have no diagnosis or suspicion of iron deficiency or anemia. Simple systematic sampling was conducted to recruit 30 children. We excluded cases of chronic disease. The history collected: age, gender, background neonatal (birth weight, gestational age, type of delivery, neonatal period, feeding (breast milk or formula), vaccinations, previous admissions and intercurrent). We determined weight, height and body mass index. It was performed a blood analysis which included cell count and iron, ferritin and transferrin serum levels. Descriptive statistics was carried out, showing frequency distribution.

**Results:** We found 46.6% of cases of hyposideremia and 40% of iron-deficiency anemia. Of the latter, we observed more frequently in men (83%) and predominant age group (53.3%) fell between 12-36 months. It was also observed more frequently in cases of low birth weight and/or exclusive feeding of formula.

**Conclusions:** Iron deficiency anemia is a common disease in children in our environment. Our largest case series was in children under 36 months, which disagrees with results of other authors. To obtain guidance on the diagno-

sis and etiology, sufficient medical history, physical examination and a small number of laboratory tests. Based on the foregoing, we propose the establishment of a hypothetical program of mass screening of iron deficiency or anemia in children, assessing their potential economic impact on the public health system in terms of cost-effectiveness.

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**PAO-60****Implications of bone metabolism in pediatric patients with inflammatory bowel disease***Caballero Javier<sup>1</sup>; María Aguilar<sup>2</sup>; Alicia Romero<sup>2</sup>; Virginia Moreno<sup>1</sup>;**Eva L van Donkelaar<sup>3</sup>; Ramón Cañete<sup>2</sup>*<sup>1</sup>IMIBIC, Hospital Reina Sofía, Universidad de Córdoba, Clinical Analysis Service, Córdoba, Spain; <sup>2</sup>IMIBIC, Hospital Reina Sofía, Universidad de Córdoba, Pediatric Endocrinology Unit, Córdoba, Spain; <sup>3</sup>Maastrich University, Faculty of Health, Medicine and Life Sciences, Maastrich, Netherlands

**Introduction:** Alterations of bone metabolism in patients with inflammatory bowel disease (IBD) have a high prevalence. Among the known factors leading to this comorbidity are: corticosteroid therapy, the activity of IBD and duration of symptoms and lifestyle.

**Objectives:** To study the potential impact of IBD in mineral metabolism in pediatric patients, evaluating clinical, biochemical, densitometric and radiographic parameters.

**Material and methods:** Cross-sectional study in children with IBD. We collected anthropometric and clinical data (cumulative dose of corticosteroids, index of IBD activity, nutrition survey and lifestyles). It was carried out a blood analysis. It included CBC and serum biochemical study on the levels of glucose, urea, creatinine, sodium, potassium, calcium, phosphorus, alkaline phosphatase, urate, magnesium, PTH, osteocalcin, TSH, T4, CRP, albumin, prealbumin, total protein, total cholesterol, HDL-cholesterol, triglycerides, iron, ferritin, transferrin, orosomucoid and C-telopeptide. The urine analysis included: glucose, urea, creatinine, ions, calcium, inorganic phosphate, total protein, microalbuminuria and urate. We performed bone densitometry (DEXA) of spine and hand-wrist radiograph. Multiple linear regression was performed in successive steps, using as dependent variable bone mineral density (BMD) quantified by the z score value obtained from the DEXA.

**Results:** Preliminarily there are 8 patients (4 boys and 4 girls) aged between 3 and 17. About 25% had a BMD below the normal range for age and sex. Another 25%, an IBD activity index higher. About 37.5 had increased CRP. The C-telopeptide was increased all cases. There was only one case of overweight. We found a significant relationship ( $p < 0.02$ ) between BMD and IBD activity index.

**Conclusions:** The index of activity of the IBD had a negative impact on BMD of the child. Iatrogenic corticosteroid did not result in a detriment of the BMD of pediatric patients and so we propose to prioritize good rate control IBD activity. The C-telopeptide is consistently high in children with IBD.

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**PAO-61****Gonadal mosaicism 45X/46XY resulting in a Turner phenotype with mixed gonadal dysgenesis: a report of two cases***Cristina Dumitrescu<sup>1</sup>; Lavinia Vija<sup>1</sup>; Camelia Procopiuc<sup>1</sup>;**Andra Carageorgheopol<sup>2</sup>; Florentina Dinu<sup>3</sup>; Oana Popa<sup>1</sup>*<sup>1</sup>"C I Parhon" National Endocrinology Institute, Bucharest, Romania;<sup>2</sup>"C I Parhon" National Endocrinology Institute, Hormonology Laboratory, Bucharest, Romania; <sup>3</sup>"Grigore Alexandrescu" Paediatrics Hospital, Surgical Department, Bucharest, Romania

**Background:** Mixed gonadal dysgenesis is regarded as the most common manifestation of 45X/46XY mosaic associated with a wide spectrum of phenotypic manifestations.

**Objective and hypotheses:** We describe two cases with a Turner phenotype associated with mixed gonadal dysgenesis. One of the two cases presents a mosaicism 45XO/46XY and one a 46XY caryotype.

**Methods:** We describe a 16 year old girl who presented with short stature and pubertal delay. She had female external genitalia, an urethral opening on the posterior vaginal wall and some clinical features of Turner syndrome (widely spaced nipples, cubitus valgus, low hairline, multiple nevi). Endocrine studies showed levels of sex hormones consistent with primary gonadal failure. The

pelvic ultrasound revealed the presence of an uterus. At laparotomy a uterus, fallopian tubes and small gonad-like tissue masses in the region of the Fallopian fimbria were found. Histological analysis revealed no organized testicular or ovarian morphology, fallopian tubes on the right side and epididymis on the left side. The second case is a 10 year old girl presenting with features of Turner syndrome (broad chest, mouth abnormalities, cubitus valgus), short stature, and primary gonadal failure. The pelvic ultrasound reveals the presence of an uterus; no gonads were visualized. Laparotomy confirms the presence of an uterus and fallopian tubes with streak gonads.

**Results:** In the first case G-banding analysis of blood lymphocytes confirmed a 46XY karyotype while in the second there was a mosaicism 45XO/46XY. FISH analysis for the eventual presence of isodicentric Y chromosome, as well as gene sequencing for SRY, SOX9, AMH and AR are in progress.

**Conclusions:** Comprehensive cytogenetic, endocrine, histological and molecular studies on the gonads are further needed in order to explain the causality between the genetic profile and the phenotype in these two particular cases.

#### PAO-62

### The experience of recombinant growth hormone treatment in a secondary endocrine referral centre in Saudi Arabia

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**Background:** King Fahad Military Medical Complex is a secondary referral centre for paediatric endocrinology for the eastern province in Saudi Arabia. Recombinant Growth Hormone has been used for many years as a treatment option for children and young adults with many endocrine disorders mainly short stature resulting from growth hormone deficiency or insufficiency.

**Objective and hypotheses:** The aim of the present study is to evaluate the use of R-GH treatment use, indication, dose, effect on height as well as effect of discontinuation of treatment due to compliance or lack of supply issues.

**Methods:** We have identified over 50 patients who are receiving R-GH and performed a retrospective chart review to assess the effect of treatment of GH.

**Conclusions:** Most patients were diagnosed with growth hormone deficiency followed by children with Turner syndrome, then other genetic disorders, and ideopathic short stature. Doses used were generally less than recommended and periods of treatment interruption were noted. The study results will help shape protocols for future growth hormone doses, compare different protocols used in the past with current national and international protocols as well help guide the newly published growth curves for children from Saudi Arabia.

#### PAO-63

### Rapid increase of serum TSH level in an infant on amiodarone treatment: a case report

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**Background:** Amiodarone is widely used as an effective and relatively safe anti-arrhythmic drug. Amiodarone-induced hypothyroidism is well described and close monitoring of thyroid function in all patients receiving amiodarone is recommended. For the first control of serum TSH level is usually recommended 10 to 60 days after starting the treatment.

**Objective and hypotheses:** We present a case of term infant who rapidly developed increased TSH level after starting amiodarone treatment.

**Results:** Male infant from normal pregnancy and uneventful delivery was born from 40 gestational week with the birth weight of 3210 g. Supraventricular tachyarrhythmia, severe combined congenital heart diseases (coarctation of aorta, ventricular septal defect, and foramen ovale apertum), and congestive heart failure were diagnosed at the first day of life. In order to control frequent episodes of supraventricular tachycardia paroxysms, treatment with amiodarone was introduced at the age of 10 days. During the following days the amiodarone dose ranged from 2.5 to 18.75 mg/kg/day (mean 7.2 mg/kg/day). Neonatal screening for hypothyroidism was normal (TSH 1.7 mU/l). On the 9th day of amiodarone treatment (at the age of 18 days) serum TSH level increased to 17.6 mU/l and for the 12 day to 28.6 mU/l. During that period treatment with L-Thyroxine was not initiated because of normal serum free

T4 level (18.8 pmol/l). Amiodarone treatment was gradually withdrawn.

**Conclusions:** In infants receiving amiodarone treatment the thyroid function should be monitored more frequently than the recommended intervals, particularly at the beginning of the follow-up, since the serum TSH level may increase in few days after commencing the treatment.

#### PAO-64

### A case of Liddle's syndrome in an 8-year old girl with argininosuccinic acidemia and childhood absence epilepsy

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**Background:** Liddle's syndrome, also called pseudoaldosteronism, is a rare autosomal dominant disorder caused by an activating mutation of the renal epithelial sodium channel. Affected patients typically show hypertension, hypokalemia and metabolic alkalosis.

**Case report:** We report on an 8-year old girl with argininosuccinic acidemia and childhood absence epilepsy who developed arterial hypertension. Initial diagnostic workup showed a slight hypokalemia, serum aldosterone was incapable of measurement. 24-hour urinary potassium excretion, serum creatinine, arterial blood gas analysis, blood catecholamines and steroid levels, abdominal and renal ultrasound, echocardiogram and renal magnetic resonance angiography were without pathological findings. The family history was unremarkable. An essential hypertension was assumed and the girl was treated with propranolol which failed to control the elevated blood pressure as well as the combination of captopril and spironolactone. Additionally, the girl developed a metabolic alkalosis, hypokalemia worsened. Serum and urine aldosterone levels as well as plasma renin activity were abnormally low. Liddle's syndrome was suspected and treatment with amiloride was started. After 4 weeks of uncomplicated treatment blood pressure returned to normal levels and blood gas analysis was in a normal range. Gene-sequencing for Liddle's syndrome was negative.

**Discussion:** Despite a negative gene-sequencing for Liddle's syndrome (molecular detection rate around 40%) the diagnosis could be established by typical laboratory findings and a good response to amiloride. Neither argininosuccinic acidemia nor childhood absence epilepsy seems to be related to Liddle's syndrome since there are no comparable reports in literature. In retrospect the initial slight hypokalemia in combination with hypertension was already indicative for Liddle's syndrome but in fact the clinical course provided the diagnosis.

**Conclusion:** Children with hypertension and lack of therapeutic response to first-line antihypertensive agents should be worked up for secondary causes.

#### PAO-65

### Side effect profile of diazoxide in children with congenital hyperinsulinism. A retrospective study

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**Background:** Diazoxide is the first-line drug for long-term treatment of congenital hyperinsulinism (CHI). However, the use of diazoxide is often limited by side effects, e.g. hypertrichosis, fluid retention and feeding problems. Up to now the frequency of these side effects is based on estimation.

**Objective:** To precisely determine the frequency of major side effects of diazoxide in children with CHI.

**Patients and methods:** Interviews on side effects were performed with the parents of CHI patients who received diazoxide. In addition, patients' records were retrospectively searched for side effects of diazoxide.

**Results:** So far we identified 24 patients (13 female, 11 male) with CHI who are or had been treated with diazoxide. Preliminary data shows that 92% of them developed hypertrichosis. The treatment of 16 patients is still ongoing, for 25% of these patients hypertrichosis has been regressive in the course of the treatment. In 8 cases the diazoxide treatment has ended because of remission of the disease. In all of these patients hypertrichosis regressed completely. Hypertrichosis was most distinctive along the spine (48%) followed

by the face (30%) and the extremities (13%). In 54% of patients feeding difficulties were reported during the diazoxide treatment, 40% of them had a verifiable weight loss. 37% of the patients developed edema, nearly all of them had facial edema. Tachycardia was rarely reported (4%), hyperuricemia and leucopenia were not reported during diazoxide treatment.

**Conclusions:** The most common reported side effects of diazoxide in patients with CHI are hypertrichosis (92%) followed by feeding problems (54%) and facial edema (37%).

#### PAO-66

##### **Ambiguous genitalia – a 15 years overview**

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**Background:** The term ambiguous genitalia or indeterminate sex is a terminology that parents fear to hear. This is most devastating within the African continent were despite being in the 21st century the sex of a child is of utmost importance. Fortunately this disorder is uncommon. Classifying the cases into different groups is formidable especially when investigative support is minimal.

**Objective:** To determine the prevalence of ambiguous genitalia, categorize patients, the mean length of time for completion of investigation and therapy outcome.

**Methodology:** This is a review of all patients referred with ambiguous genitalia to the clinic over 13 years. Assessment criteria were based on clinical presentation, hormonal and biochemical estimations, sonogram of the abdomen, genitogram and karyotype / buccal smear. Stimulation with human chorionic gonadotropin (hCG) and ACTH (adrenocortical hormone) stimulation tests were performed as required.

**Results:** Reviewed were 44 out of 245 patients with endocrine disorders (1997 to 2010) had ambiguous genitalia. They were categorized as genetic females with virilisation or FPH (15, 34 %) all were due to congenital adrenal hyperplasia (CAH), Genetic males overvirilized (4, 9%) Genetic males undervirilized or MPH (11, 25%), Micropenis with severe chordee 3, 6.8%), micropenis with hypospadias (3, 6.8%), micropenis with cryptorchidism (5, 11%), true hermaphroditism (2, 4.5%) and the syndromic form of ambiguous genitalia (1, 2.2%). Age at presentation ranged from 48hrs to 10 years. Mean length of time for investigation 9 months while 75% had appropriate therapy.

**Conclusions:** Ambiguous genitalia appear very rare when compared to similar collections for the length of time of review. This may be an invalid conclusion due to the inadequate health delivery service, referral system and or older age presentation. Finance seems to be a big constraint to management. The obvious indeterminate external genitalia in females with CAH may account for higher percentage amongst cohorts.

#### PAO-67

##### **Characteristics and prevalence of non-classical congenital adrenal hyperplasia with a v281l mutation in patients with premature pubarche**

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**Background:** The frequency of NCCAH with V281L among children presenting with premature pubarche (PP) is variable.

**Objective and hypotheses:** To determine the prevalence, clinical and laboratory characteristics of NCCAH with the V281L mutation in patients with PP.

**Methods:** The study group was composed of 159 unrelated patients with PP. ACTH stimulation test was performed in 14 of the 159 patients with PP who had basal 17-OHP levels  $\geq 2$  ng/ml. Patients whose stimulated 17-OHP level on the ACTH test was  $\geq 10$  ng/ml underwent a mutational analysis of the CYP21 gene, and those with the mutation were considered to have NCCAH.

**Results:** NCCAH was defined in nine (5.7%) among 159 patients with PP and all of them had the V281L mutation. The gender distribution showed a similarity between NCCAH and patients with idiopathic PP (IPP). When compared with the IPP group, the NCCAH group had higher bone age and

BA-chronological age ratio. However, chronological age, age at pubic hair onset, height, height standard deviation score, parental adjusted deficit in height, weight, and body mass index (BMI) were similar in both groups. All nine patients whose peak 17-OHP levels in the ACTH stimulation test were  $>10$  ng/ml had the CYP21 gene mutation. Four of them were homozygote and four of them were heterozygote. Other one patient was compound heterozygote for the V281L mutation and the I2 splice mutation. The one of the patients with V281L heterozygous mutation developed true precocious puberty and the other one patient had rapid progressive early puberty and developed polycystic ovary syndrome.

**Conclusions:** ACTH stimulated  $> 17$ -OHP 10 ng/ml in PP patients is load star to mutation analysis and heterozygote patients should be followed for clinical and biological hyperandrogenism up to completion of the whole gen sequence.

#### PAO-68

##### **Continuous subcutaneous insulin infusion (CSII): a successful mode of therapy for neonatal diabetes (experience in Qatar)**

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**Background:** Neonatal diabetes is defined as persistent hyperglycemia occurring in the first months of life that lasts more than two weeks and requires insulin for management.

**Objective and hypotheses:** Although pediatricians face numerous difficulties in managing insulin therapy at this age, very few data are available on possible methods of insulin delivery in neonatal diabetes.

**Methods:** We report our experience over 3 years of continuous subcutaneous insulin infusion (CSII) in cases of neonatal diabetes requiring insulin therapy (n = 5). Two neonates were negative for ABCC8,-ve KCNJ11, two had pancreatic agenesis and one has Wolcott-Rallison syndrome. CSII therapy in neonatal diabetes allows easy adaptation of insulin delivery, closely following the current feeding regimen (a basal infusion needed with very minimal dose; preprandial boluses being started with intermittent bottle feeding).

**Results:** Management using very small insulin doses (e.g. bolus = 0.20 U and basal rate = 0.02 U/h) was required and was only possible after insulin dilution (5-10 U/ml) and is more accurate with CSII than with using syringes. CSII allows easy delivery of such small doses without dilution errors. CSII achieved good glycemic control for all neonates (mean HbA1c = 8 %) with few hypoglycemic events; which are particularly frequent and dangerous at this age. Neonates tolerated the subcutaneous infusion lines well without any local side effects.

**Conclusions:** During the neonatal period, and under the supervision of an experienced team, CSII is safe, more physiological, accurate and easy to manage than using syringes or pens.

#### PAO-69

##### **Complete catch-up growth in a case of Johansen Blizzard syndrome with severe postnatal growth retardation**

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**Background:** Patients with Johanson Blizzard syndrome (JBS) have significant postnatal growth retardation.

**Objective and hypotheses:** We report the growth pattern of a boy with the JBS who was born at term with aplasia of the alae nasi and severe congenital sensori-neural deafness.

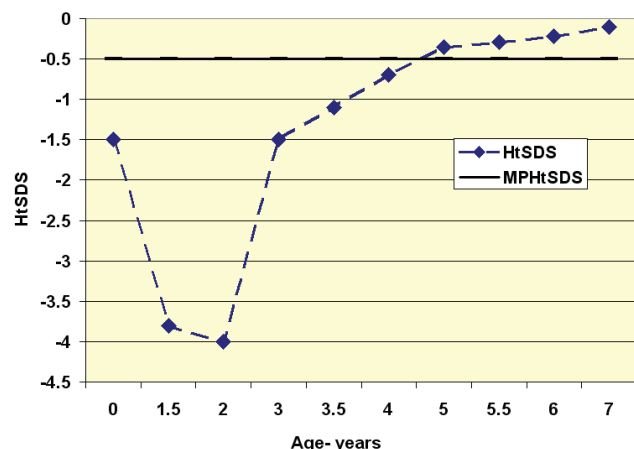
**Case:** At the age of 1.5 years the boy presented with features of JBS and severe postnatal growth failure and apparent severe mental retardation.

**Results:** Investigations revealed mild pancreatic exocrine insufficiency and oral Pancrex V (lipase) was initiated. Despite some improvement in weight, his linear growth was still slow. At 2 years of age, endocrine evaluation proved growth hormone deficiency (glucagon test) with low IGF-I level, primary hypothyroidism (low free T4 and high TSH) and cortisol deficiency. MRI of the brain, showed hypoplastic pituitary gland. The child was started on human

growth hormone (GH), L-thyroxine and hydrocortisone replacement. Marked improvement of linear growth occurred with complete catch-up to his mid-parental height SDS occurred in 2 years. He maintained normal linear growth during the following 3 years.

**Conclusions:** Our case represents the first report of complete catch-up growth in a case of Johansen blizzard syndrome after severe postnatal growth retardation during infancy.

Linear Growth JBS on Therapy



#### PAO-70

### Pediatric Graves ophthalmopathy in association with thyroid autoantibodies

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**Background:** As pediatric Graves disease is an uncommon condition, Graves ophthalmopathy should be more unusual. Graves ophthalmopathy has been reported to be associated with high titers of thyroid autoantibodies. Nevertheless, studies on children are not abundant.

**Objective and hypotheses:** We aimed to compare the thyroid autoantibody levels in Graves disease patients with ophthalmopathy to those in patients without ophthalmopathy.

**Methods:** The subjects were 60 patients under the age of 18 years diagnosed with Graves disease from January 2000 to December 2010 at the Catholic University Saint Vincent Hospital. We reviewed the medical records retrospectively.

**Results:** Among them, 20 patients associated with Graves ophthalmopathy (33.3 %) were compared with 40 patients without ophthalmopathy (66.7 %). TSH Receptor antibody levels were higher in patients with ophthalmopathy than in patients without it (111.25±140.50 U/L vs 57.52±103.08 U/L,  $p = 0.024$ ), and the percentage of elevated anti-microsomal antibody level was also higher in patients with ophthalmopathy (80 % vs 45 %,  $p=0.013$ ).

**Conclusions:** Pediatric Graves ophthalmopathy was associated with high titers of thyroid autoantibodies in our study. Nevertheless, large-scale studies with more patients are required.

#### PAO-71

### Intestinal malabsorption and dark skin caused elevated parathormone levels

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**Background:** Hyperparathyroidism is a rare finding in children. It is a typical sign of vitamin D-deficiency caused by different reasons. It may also be due to calcium wasting syndromes, and it can rarely be induced by adenomas of

the parathyroid glands and in parathormone receptor mutations (pseudohypoparathyroidism).

**Objective and hypotheses:** To show how celiac disease can mimic hyperthyroidism followed by rheumatic complaints.

**Patient:** A 12-year old Gambian girl living in north Europe was developing abdominal and joint pain. Serum analysis revealed low serum-calcium, significantly elevated parathormone and decreased vitamin D. Immigrant rickets was assumed. Because of abdominal pain and iron deficiency, lambliasis was ruled out. Celiac disease was demonstrated by gliadin- and tissue transglutaminase-antibodies as well as by intestinal mucosa biopsy. Despite of a gluten-free diet the joint pains persisted. They were declared by rheumatologists to be caused by a chronic juvenile arthritis (sister disease of celiac disease). However, there were no positive inflammation signals and no clear elevated rheuma-immunology.

**Follow up:** Gluten-free diet and additional treatment with calcium and active vitamin D did not stop increasing parathormone levels, did not stop abdominal and joint pain, and did not stop increment of positive celiac disease antibodies. Assuming compliance problems the patient was then treated with vitamin D injections, which caused decreasing parathormone levels and vanishing joint pain.

**Conclusion:** Celiac disease can cause intestinal rickets with elevated parathormone levels mimicking chronic juvenile arthritis, if gluten-free diet is not strictly performed by compliance problems. Parenteral supply of depot-vitamin D is the therapy of choice in these patients exhibiting normalization of parathormone and vitamin D25 levels with disappearance of rheumatoid joint pain.

#### PAO-72

### Pituitary hyperplasia in primary hypothyroidism

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**Background:** Despite recent progress in imaging techniques, it is not possible to distinguish between TSH-producing macroadenoma and hyperplasia of pituitary thyrotroph cells on CT and MR scans. In such cases, repeat MRI after therapy with thyroxine may provide a definitive diagnosis and eliminate unnecessary surgery.

**Objective and hypotheses:** We describe an example of reactive pituitary hyperplasia from primary hypothyroidism that mimicked a pituitary macroadenoma in a child.

**Case report:** A 10 year old boy presented with occipital headache over the last three months and height growth arrest. Cranial Magnetic Resonance Imaging (MRI) detected an intrasellar and suprasellar pituitary mass. Endocrine evaluation revealed a severe primary hypothyroidism (TSH 589 mU/L, free T4 1.5 pmol/L), mild hyperprolactinemia (1.23 nmol/L) and low IGF-1 (8.6 nmol/L). Thyroid ultrasound showed normal thyroid size with markedly heterogeneous echo texture and hypo-echoic areas. Thyroid peroxidase and thyroglobulin antibodies were high. The patient was started on levothyroxine at 50 ug/day. Three months later IGF-1 and thyroid function had returned to the normal range and height growth velocity had increased. MRI study documented resolution of the mass effect.

**Conclusions:** Primary hypothyroidism should be considered in the differential diagnosis of solid mass lesions of the pituitary gland. Examination of thyroid function in patients with sellar and suprasellar masses revealed by MRI may avoid unnecessary operations which can cause irreversible complications.

#### PAO-73

### Familial non autoimmune hyperthyroidism- a family

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**Objective:** Familial nonautoimmune hyperthyroidism which is inherited autosomal dominant, that caused by activating mutations of the thyrotropin receptor gene (TSHR). Recent studies have shown that FNAH, toxic adenoma and sporadic congenital hyperthyroidism are in fact facets of the same disease, genetic hyperthyroidism due to TSHR mutations.

**Methods:** Case 1: Eleven -year-old male patient was admitted to our clinic with complaints of a neck swelling, weight loss, irritability, sweating. In his physical examination his weight and height were in the normal range, cardiac rate was 100/min above the upper limit. Thyroid examination revealed grade 2 goiter. The patient's laboratory examination: TSH:0.199uIU/ml (0.5-4.8), free t4: 1.23ng/ml(0.8-2.3), free t3:4.92pg/ml(2-4), anti-TPO:175IU/ml, anti-TG:21.6IU/ml(0-134), anti-TSH receptor was negative. Imaging of the thyroid gland both thyroid glands and isthmus thickness increased, 3mm colloid nodule was seen in right lobe. The patient's mother also had goiter with hyperthyroidism which was resistant to treatment so radioactive iodine treatment was applied. Also autoantibody and anti-TSH receptor were found negative in mother.

Case 2: Ten-year-old female patient was admitted because of goiter with his (case 1) older brother. Beside intolerance the heat, she had no symptom. In her physical examination her weight and height were in the normal range, cardiac rate was 104/min above the upper limit. The patient had grade 2 goiter whose laboratory examination: TSH:0.3uIU/ml (0.5-4.8), free t4:1.43ng/dl (0.8-2.3), free T3: 4.66pg/ml (2-4), anti-TPO:12.8 IU/ml(0-134), anti-TG:19.7 IU/ml (0-134) and anti-TSH receptor was negative. Imaging of both thyroid glands and isthmus thickness increased TSHR gene mutations were sent for genetic analysis because of known two-generation family affected and hyperthyroidism no autoimmunity.

**Result:** TSHR activating mutations as the cause of subclinical hyperthyroidism may be more common and should be considered in the differential diagnosis especially if familial.

#### PAO-74

##### The effect of long term sandostatin treatment in a child with hypothalamic obesity

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**Background:** Hypothalamic obesity is one of the most important effects of central nervous system damage. Generally lifestyle modification and diet are ineffective to treat the hypothalamic obesity. Sandostatin has been trying in pediatric hypothalamic obesity with short period in a few study. The results were promising but some are inconclusive.

**Objective and hypotheses:** To evaluate sandostatin treatment a case with morbid hypothalamic obesity.

**Methods:** A 5.1 year old male patient admitted to our clinic with complaint of visual disturbances and cephalgia. Extended evaluation revealed diagnosis of craniopharyngeoma. After neurosurgical investment, he had developed multiple hypophyseal hormone deficiency (TSH, GH, LH, FSH, ADH deficiency) and was given appropriate replacement therapy. Growth was normal despite GH deficiency, and no GH therapy was introduced. Intractable obesity as BMI increased from 19.3 kg/m<sup>2</sup> to 45.4 kg/m<sup>2</sup> within 2 years was developed. The attempts to reduce height gain were unsuccessful. Sandostatin was introduced to patient and he treated for 2 years (5 mcg/kg/day in dose in the first year, 10 mcg/kg/day in the second year). First year of sandostatin treatment, decrease of weight gain gain, even loss of weight occurred ( $\Delta$  BMI: -2.3 kg/m<sup>2</sup>/year). Second year of therapy, the response was not the same that only stabilisation of weight was achieved. No side effect was seen related to sandostatin treatment.

**Results:** In this case report, sandostatin treatment was safe but not as effective as expected, especially in second year of therapy.

**Conclusions:** But that result can not be generalised because consist of one patient. More hypothalamic obese children should be evaluated to conclude the effectiveness of sandostatin treatment.

#### PAO-75

##### TNF-A and others inflammatory molecules in overweight children

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**Background:** Childhood obesity is associated with obesity later in life for adults, and it constitutes a major risk factor for cardiovascular disease and diabetes. The obese adipose tissue expresses an increased quantity of proinflammatory proteins such as the TNF- $\alpha$ .

**Objective and hypotheses:** The objective of this study was to evaluate the levels of TNF- $\alpha$  and others proinflammatory molecules in an overweight infant-juvenile population and their relationship with clinical and laboratory variables. Twenty overweight children and 20 control children were studied. Children in both groups were between 8-13 years old, and each child had his/her waist circumference (WC) measured and body mass index (BMI) calculated. The inclusion criteria for the overweight group was a BMI of >85th percentile for age and sex. In both groups was determined: fasting glucose level (glucose-oxidase); plasmatic insulin (ECLIA); plasma fibrinogen (Claus); uCRP (Immunoturbidimetric); plasma myeloperoxidase (Enzyme immunoassay); TNF- $\alpha$  (ELISA); lipid profile (enzymatic); erythrocyte sedimentation rate and HOMA index. The data were analyzed with the SPSS 15.0 program for Windows. The Spearman's rank correlation coefficient was used to measure statistical dependence between the variables.

**Results:** The TNF- $\alpha$  levels were higher in overweight children [15.4(13.2-24.0) vs. 12.7(11.2-14.8) pg/ml; p=0.03]. Also the levels of fibrinogen (Fg), plasma insulin, HOMA index, uCRP and triglycerides were statistically higher than in the control group. The TNF- $\alpha$  was positively correlated with the waist circumference.

**Conclusions:** The high TNF- $\alpha$ , uCRP and fibrinogen levels confirm a proinflammatory state associated with abdominal obesity in the studied population.

#### PAO-76

##### Prevalence of abnormal serum transaminases concentrations in obese children and adolescents

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**Background:** Non-alcoholic fatty liver disease (NAFLD), the most common cause of liver disease in children, is associated with obesity.

**Objective:** The aim of the study was to examine the prevalence pattern of NAFLD in obese children and adolescents and analyze the anthropometric, biochemical and metabolic factors related to it.

**Methods:** We retrospectively reviewed the charts of 2007 obese children and adolescents (BMI >95th centile) who attended our Department between January 2000 and January 2010. A total of 114 obese subjects were found with elevated (>40U/L) serum alanine (ALT) and/or aspartate (AST) aminotransferases, considered as surrogate marker of NAFLD, since other causes of hepatitis and alcohol consumption were excluded. Variables studied included BMI, pubertal status, and fasting levels of glucose, insulin and lipids. Insulin resistance was evaluated by means of HOMA-IR and Quicki.

**Results:** Presumed NAFLD was present in 5.8% of the obese pediatric population but, predominantly in boys (boys vs girls: 8.4%vs 3.9%, p<0.001). They were 63 boys and 51 girls aged 3.15 to 16.4 (mean age 9.8  $\pm$  3.0) with BMI ranging from 1.62 to 5.11 (mean 3.17  $\pm$  1.6). 48% of them were prepubertal and had significantly lower serum ALT levels compared with pubertal children (p<0.001). Hyperinsulinemia was present in 77(67.5%). Insulin resistance as estimated with HOMA-IR>3 or Quicki >0.31 were equally prevalent in pre-and post pubertal children. In multiple logistic regression models BMIs and male gender were strongly associated with NAFLD.

**Conclusion:** Elevated transaminases is a common finding among obese children even in younger ages, strongly associated with insulin resistance. Their evaluation is recommended as a screening parameter in obese pediatric population.

## PAO-77

### The first documented case of Wolcott-Rallison syndrome in Serbia

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**Background:** Wolcott-Rallison syndrome (WRS) is a rare autosomal recessive disease. Its main characteristic is permanent neonatal diabetes mellitus (PNDM) associated with skeletal epiphyseal dysplasia.

**Clinical report:** The female infant was born from unrelated parents. Pregnancy was uneventful and delivery was at term. Birth weight was 2100 g (below 5th centile) and length was 48 cm. At 3 months of age, the diagnosis of NDM was established and insulin treatment was introduced.

From the very beginning, diabetes was difficult to control. At the age of 1.5 year she was admitted to the hospital for vomiting, edema and hepatomegaly. Laboratory workup showed extremely high levels of liver enzymes. This episode of hepatitis resolved spontaneously within 4 weeks. By that time, she was also diagnosed a hypothyroidism and was started on L-thyroxine. Eight months later, when investigated for steatorrhea, pancreatic hypotrophy was found on abdominal ultrasound.

After exocrine pancreatic insufficiency has been confirmed, therapy with pancreatic enzymes was initiated. At the age of 2.6 years an episode of liver failure (requiring hospitalization) reappeared. She had seizures soon after and was put on Phenobarbital. The etiology of seizures was unrevealed. Mutation analysis of the EIF2AK3 gene showed that the child is homozygous for a nonsense mutation, R902X, in exon 13.

This result confirmed the diagnosis of WRS. After the diagnosis had been established skeletal X-ray was performed. It revealed multiple epiphyseo-metaphyseal dysplasia affecting long bones, vertebrae and pelvis.

**Conclusions:** WRS is a very rare disease. However, it should be considered in any child with NDM and associated disorders, especially if skeletal changes are detected. The diagnosis of WRS in our patient delayed since genetic testing had not been performed at the time of making the diagnosis of NDM and hypothyroidism.

Although genetic diagnosis of WRS does not alter therapeutic approach, it might help in predicting the outcome, as well as offering informed genetic counseling.

## PAO-78

### Obesity in Greek children: a meta-analysis of data from the last decade

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**Background:** The obesity epidemic has reached children in Europe, including Greece. National epidemiological data and trend monitoring are of extreme interest in order to be able to provide a burden to this epidemic.

**Objective and hypotheses:** The aim of the present study was to review all available data published the last decade on objectively measured weight status in prepubertal (1-12 years old) Greek children and therefore to estimate an updated accurate prevalence of obesity in this age group according to sex, after controlling for publication bias.

**Methods:** We reviewed all published available citations from January 2001-December 2010, reporting the prevalence of childhood obesity (ages 1-12 years old) according to the International Obesity Task Force Criteria, in Greece. Pooled analysis and Der-Simonian Laird analysis was performed.

**Results:** The pooled analysis revealed that among 219996 boys, 11.8% were obese, whereas in the girls the prevalence of obesity was 10.6% (total

n=210772). When forest plots were plotted for identification of studies with publication bias, the prevalence of obesity was 10.9% in the boys and 10.2% in the girls (total n=216168 boys and 208637 girls). Overall the boys demonstrated increased odds for being obese compared to the girls (OR:1.14, CI:1.1-1.2). Between pooled and meta-analysis, the girls demonstrated a significantly lower prevalence of obesity in the second (p<0.001).

**Precise conclusions:** According to the analysis, one out of ten prepubertal Greek children appears to be obese. The results also demonstrate the existence of publication bias in pediatric obesity research.

## PAO-79

### Prevalence of obesity and overweight in the primary school children and their relationship with some life style factors, Iran, 2010

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**Background:** Currently obesity is a major health problem throughout the world and a risk factor of many chronic diseases such as cardiovascular disease, hypertension, diabetes mellitus and cancer. Prevalence of obesity and overweight has been rapidly increased in both children and adults. Most of the obese children (80%) will be obese in adulthood.

**Objective and hypotheses:** The aim of this study presents the prevalence of childhood overweight, obesity and their relationship with factors which focused on watching TV, using the computer or playing video games, fast foods consumption, breast feeding and birth weight.

**Methods:** In this cross sectional study 960 (480 male and 480 female) primary school children aged 6-12 years old were selected by a two stage cluster sampling method. Height and weight were measured by the standard methods. Additionally BMI was calculated based on the weight, height and obesity; overweight were defined based on the BMI scores using CDC chart. Obesity, overweight and normal weight were defined as having a BMI  $\geq$ 95th percentile and BMI=85-95th  $15 \geq$  BMI  $\leq$ 85th respectively. The other data were collected by questionnaire that completed by parents. Data were analyzed by using chi square and fisher exact test (ANOVA).

**Results:** According to our findings 11.9% of the subjects were overweight and 6% were obese. The results have shown a positive significant relationship between BMI and the mean time of watching TV, using computer or playing video games and fast food consumption during childhood (p=0.0001). There was no relationship between BMI and gender, birth weight and breast feeding.

**Conclusions:** In this study the prevalence of overweight and obesity was compared to the same study in the last seven years which shown increasing in this community. Several studies have shown breast feeding is a protective factor for obesity, but this study has shown fast foods consumption, the mean time of watching TV and using computer or playing video games during childhood in spite of breast feeding in infancy period can be more effective on obesity.

## PAO-80

### Growth patterns in 100 short children receiving GH therapy - a retrospective study

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**Aim:** To present the evolution of height and metabolic parameters in 100 short children treated with daily doses of growth hormone for up to 3 years.

**Methods:** The children were divided into four groups: group 1 - 58 children with GH deficiency: 19 girls and 39 boys, mean age 8.8 yrs +/-3.4; group 2 - 11 girls with Turner syndrome, mean age 8.2 yrs +/- 3; group 3 - 17 children born SGA, 8 girls and 9 boys, mean age 7.8 yrs +/-3.4 and group 4 - 14 children with idiopathic short stature: 5 girls and 9 boys, mean age 7.4 yrs +/-3.2. The SDs for height and growth velocity (GV) were calculated using the Prader standards from 1988 and statistical relevance was calculated using test.

**Results:** In group 1, the average height was  $-3.1 \text{ SD} \pm 1 \text{ SD}$  (between  $-6.1$  and  $-1.5 \text{ SD}$ ). In the first year, the height gain was of  $0.8 \text{ SD}$  with an average GV of  $3.9 \text{ SD}$  ( $9.6 \text{ cm/year}$ ). In the second and third years of treatment the height gain and GV were  $0.9 \text{ SD}$  and  $3.3 \text{ SD}$  ( $8.5 \text{ cm/year}$ ) respectively  $0.4 \text{ SD}$  and  $2.3 \text{ SD}$  ( $7.4 \text{ cm/year}$ ). In group 2 the initial growth deficit was  $-2.7 \text{ SD} \pm 1.2 \text{ SD}$  (between  $-5.0$  and  $-1.1 \text{ SD}$ ), with a gain of  $0.5 \text{ SD}$  in one year. The GV was  $2.5 \text{ SD} - 8.6 \text{ cm/year}$  ( $p=0.02$  compared with the 1st group) but dropped to  $1.2 \text{ SD}$  ( $6.9 \text{ cm/year}$ ) in the second year ( $p=0.05$ ), with a further gain of  $0.5 \text{ SD}$  in height. Group 3 had a  $-3.3 \pm 0.7 \text{ SD}$  height deficit with a gain of  $0.5 \text{ SD}$  in the first year and of another  $0.4$  in the second year. The GV was  $2.7 \text{ SD} - 9.1 \text{ cm/year}$  (compared with the group 1  $p=0.15$ ) respectively  $1.2 \text{ SD} - 6.8 \text{ cm/year}$  ( $p=0.1$ ). In the 4th group, the initial growth deficit was  $-3.3 \pm 0.5 \text{ SD}$ , with a growth of  $0.6 \text{ SD}$  in the first year of treatment. The GV was  $1.4 \text{ SD}$ , ( $8.5 \text{ cm/year}$ ) significantly lower than in the first group ( $p=0.01$ ). There was an increase of blood glucose levels ( $p=0.03$ ), but the values remained normal.

**Conclusions:** GH therapy in short children is effective, especially in children with GH deficiency. The maximum of catch-up growth is obtained in the first year of treatment. The therapy is safe, but clinical and biochemical follow-up is necessary.

#### PAO-81

### Congenital adrenal hyperplasia – still an undiagnosed condition with serious consequences

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**Introduction:** Classic congenital adrenal hyperplasia is one of the causes of virilisation of the female fetus and can have dramatic implications if it is not diagnosed in time.

**Case presentation:** We present the case of a 4 yrs 8 month old boy, who was admitted for bilateral cryptorchidism and pubic hair development. The patient had been surgically investigated for cryptorchidism at the age of 2.6 yrs, but no testes were found. He had been admitted to various pediatric hospitals for repeated episodes of severe dehydration with low levels of sodium ( $\text{Na} - 128.8 \text{ mEq/L}$ , normal range  $136-145$ ) and hyperkalemia ( $\text{K} - 6.1 \text{ mEq/L}$ , normal range  $3.3-5.1$ ) and was treated for salt wasting nephritis. The clinical exam revealed a patient with normal height ( $+0.37 \text{ SD}$ ) and weight with a well developed penis, and no evident testes. The pubic hair was P3/4. The rest of the clinical exam was unremarkable and the patient was not dehydrated. The hormonal panel revealed: Testosterone –  $2.23 \text{ ng/mL}$ ; LH –  $0.87 \text{ mUI/mL}$ ; FSH –  $3.11 \text{ mUI/mL}$ ; cortisol –  $3.92 \mu\text{g/dL}$  (normal range  $4.3-22.4$ ); ACTH –  $173 \text{ pg/mL}$  (normal range  $8-60$ );  $17 \text{ OH Progesterone} - 533 \text{ ng/mL}$  (normal range  $0.07-1.7$ ). The abdominal CT exam showed adrenal hyperplasia and a uterus. The pelvic ultrasound revealed fluid in the uterus and 2-3 follicles in each ovary. The bone age was 11 years. The cariotype was  $46 \text{ XX}$ . The diagnosis was of virilizing congenital adrenal hyperplasia, probably due to 21-hydroxylase deficiency, with female pseudohermaphroditism and secondary central precocious puberty. Treatment with hydrocortisone was started. Triphoreline  $3.75 \text{ mg/month i.m.}$  was administered for precocious puberty. Because vaginoplasty was not possible and respecting the parents' wishes, the assigned male sex was preserved and the patient will undergo surgery to remove the internal reproductive organs.

**Conclusions:** Congenital adrenal hyperplasia is still a largely undiagnosed condition, especially in absence of neonatal screening. All cases of bilateral cryptorchidism should undergo extensive investigations, including cariotype.

#### PAO-82

### Pituitary hyperplasia caused by primary hypothyroidism: clinical presentation and follow up

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**Background:** Pituitary thyrotroph hyperplasia secondary to primary hypothyroidism is a rare cause of pituitary enlargement. Clinical presentation is variable.

**Objective:** To present a clinical presentation and evolution in 5 cases (4 girls) of pituitary hyperplasia appearing as a result of longstanding hypothyroidism. **Methods:** Clinical appearance was variable (Table 1). Common finding in all children was growth delay during months or years before the diagnosis. All had moderate clinical hypothyroidism. Diagnosis was made by measuring T4, TSH, thyroid antibodies and ultrasonographic examination of the thyroid gland. Pituitary function was revealed by measuring GH, FSH, LH, Prolactin and ACTH. MRI of the pituitary was performed.

**Results:** TSH was very high, and T4 low in all patients. Ultrasound finding of the thyroid gland was typical for Hashimoto thyroiditis. GH deficiency, as well as FSH, LH deficiency were revealed in two patients. One girl had elevated levels of prolactin. Magnetic resonance imaging revealed symmetrical pituitary enlargement associated with contrast enhancement simulating macroadenoma. After introduction of therapy with levothyroxine, both symptoms and pituitary hyperplasia regressed within a period of 1.5 - 13 months. Children were followed for 2-9 years. Growth resumed in all patients, and puberty followed regularly.

**Conclusion:** Pituitary tumor associated with elevated thyroid stimulating hormone and low levels of free T4 is most frequently caused by Hashimoto thyroiditis and should always be treated with thyroxine replacement before other diagnostic tests are ordered. Careful follow up is warranted.

Patient	Age (years)	Clinical signs	TSH(TAGfontoffTAGsymfontmTAGfontoffTAGstdfontU/ml) / T4 (mmol/l)	TPO Antibodies (mU/l)	Other	Time to the normalization of the pituitary size
1.	11	Menstrual bleeding Interruption of growth	48 / 1.8	1254	GH deficiency Hypeprolactinemia	6 weeks
2.	8	Anemia, Interruption of growth, Headache	48 / 0.9	>2000		2 months
3.	9.3	Growth retardation	71.9 / 1.5	>1000		6 months
4.	13	Obesity, Anemia, Interruption of growth and puberty	>75 / <1	>1000	FSH, LH deficiency	13 months
5.	13	Mixedema, Anemia Interruption of growth and puberty	72 / <1	>1000	GH, FSH, LH deficiency	4 months

#### PAO-83

### Retrospective analysis of effectiveness of growth hormone therapy: identification of poor responder

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**Background:** Growth hormone (GH) therapy is well established for more than 20 years including experience in different indications as insufficiency of GH secretion, Ullrich Turner and Small for Gestational Age (SGA) Syndrome.

**Objective and hypotheses:** The aim of this study was to identify Poor Responder after one year of GH Therapy and to find out possible reasons as GH effect on IGF-1 or IGF-BP3 secretion.

**Method:** For 197 children (136 male/61 female) at the age of  $9.2 \pm 7.7$  years GH therapy was started with the average daily dose of  $0.029 \pm 0.004 \text{ mg/kg}$  for the first and of  $0.030 \pm 0.005 \text{ mg/kg}$  for the second year.

**Results:** Average growth velocity increased from  $4.6 \pm 1.9 \text{ cm/year}$  to  $7.64$

+/- 2,7 cm/year (first year) and 6,13 +/- 2,7 cm/year (second year). The metabolic effect of GH therapy resulted in an increase of the IGF-1 level to 148,8 ng/ml (first year) and a further increase of 148,8 ng/ml (second year). Similar results were obtained due to the IGF-BP3 levels (1,57 +/- 1,6 and 1,1 +/- 2,4 mg/ml). After one year of therapy only 4,4 % patients did not show a sufficient increase of IGF-1 (< 15 ng/ml increase). However 20,6 % of all patients did not react adequately by raising the IGF-BP3 level of more than 0,4 mg/ml increase. Poor responder of GH therapy were identified by an increase of growth velocity of less than 2 cm/y and no increase of Height SDS for the first year of therapy. Investigation of the auxological parameters identified 10,4 % of patients, which did not react adequately to GH therapy. 25 % of all patients did not show an increase of growth velocity of > 2 cm/y. Only 4,3 % and 12,8 % of these individuals had no sufficient increase of IGF-1 and IGF-BP3 level respectively.

**Conclusions:** Further studies will be performed to find out the compliance of GH administration due to the response of growth after GH administration.

#### PAO-84

### Clinical characteristics of subclinical rickets in infants less than two years of age

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**Background:** In young children, cases with both of vitamin D deficiency and iron deficiency anemia (IDA) are common.

**Objective and hypotheses:** To evaluate the clinical characteristics of vitamin D deficiency and its association with IDA.

**Methods:** A total of 261 children aged  $\leq 2$  years underwent 25-hydroxyvitamin D3 tests between January 2007 and July 2009. The study cohort was classified into two groups: normal and vitamin D deficient, by their 25-hydroxyvitamin D3 levels.

**Results:** In total, 171 children were in the normal group (mean age, body weight and heights 12.5 $\pm$  7.0 months, 9.3 $\pm$ 0.9 kg and 76.8 $\pm$ 1.1 cm), and 51 children in the vitamin D deficient group (9.9 $\pm$ 5.4 months, 9.0 $\pm$ 0.9 kg and 75.1 $\pm$ 0.9 cm). Vitamin D deficiency was most commonly diagnosed in the spring (44%). The proportion of complete breast-feeding was higher in the deficient group (92%), and 25.5% of the children in the deficient group also experienced iron deficiency anemia compared that 12% of normal group. Wrist radiographs showed findings suggestive of rickets in 7 children in the normal group. Nine children in the deficient group experienced persistent bony changes. Six children received calcitriol medication in the normal group, in whom the mean vitamin 25-hydroxyvitamin D3 level increased from 39.6 $\pm$ 14.6 ng/ml (pre-medication) to 41.8 $\pm$ 17.2 ng/ml (post-medication), and 13 in the deficient group, in whom the mean vitamin 25-hydroxyvitamin D3 increased from 13.3 $\pm$ 5.2 ng/ml (pre-medication), to 34.5 $\pm$ 23.8 ng/ml (post-medication).

**Conclusions:** This study demonstrated that approximately 30% of children aged  $\leq 2$  years experienced vitamin D deficiency associated with subclinical rickets. Many children also experienced concurrent iron deficiency anemia. Guidelines for vitamin D supplement in such children must therefore be established.

#### PAO-85

### Decreased serum testosterone levels in long-term adult survivors with fatty liver after childhood stem cell transplant

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**Background:** Fatty liver and gonadal dysfunction have been identified as potential late effects of therapy in adult survivors treated with SCT. Obesity and metabolic syndrome are also associated with low testosterone levels in general population.

**Objective:** Our objective was to determine the relationship between degree of

fatty liver and testosterone levels in adult survivors.

**Methods:** We reviewed the clinical records of 34 patients who received allogeneic SCT at Tokai University Hospital. The median age of the 34 patients at SCT was 10.0 years, the median age at the last evaluation was 25.5 years, and the median follow-up duration after SCT was 15.9 years. The study population was categorized into 4 groups: CRT (cranial radiotherapy) +TBI (total body irradiation) group, TBI group, TAI (thoraco-abdominal irradiation) group, and Chemo groups.

**Results:** Among the 34 patients, 1 patient treated with only chemotherapy had a greater than 25 kg/m<sup>2</sup> BMI. On the other hand, 11 patients had a BMI less than 18.5 kg/m<sup>2</sup>. No patient satisfied the criteria for metabolic syndrome. Fatty liver was diagnosed in 15 patients during the follow-up period. Concerning the mode of irradiation, a greater number of patients who received CRT+TBI developed fatty liver compared among other groups. Patients in CRT+TBI group were statistically associated with decreased testosterone levels, increased LH and FSH levels compared among other groups (p<0.001, respectively), although testosterone levels in all patients were within normal range during follow-up period. Moreover, severe fatty liver was statistically associated with decreased testosterone levels compared among moderate, mild and non-fatty liver (p<0.001, median 273ng/dL, 333ng/dL 345ng/dL, and 530ng/dL, respectively).

**Conclusion:** Even patients who are not overweight/obese may develop fatty liver, and degree of fatty liver was associated with decreased testosterone levels in adult survivors.

#### PAO-86

Abstract withdrawn.

#### PAO-87

### Short-term effect of the diabetes education program in children and adolescents with type 1 diabetes mellitus

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**Background:** Diabetes mellitus is a chronic disorder and strict glycemic control, which cannot be successfully obtained without behavior modification, is the most important factor in prevention and management of complications.

**Objective and hypotheses:** The purpose of this study was to investigate the short-term effects and associated factors of the diabetes education program and to assess the necessity of regular and structured education and support in diabetic children and adolescents.

**Methods:** Thirty patients (10.0–18.9 years) with type 1 diabetes mellitus (T1DM), attending the diabetes clinic in Seoul National University Children's Hospital, were included in the diabetes education program with intensified treatment. A six-day-course program was provided by a diabetes care team with doctors, a specialist diabetes nurse, a clinical dietitian, and a social worker. Patient data of disease duration and complication studies at the time of enrollment were reviewed and changes in HbA1c levels before and after the education program were analyzed.

**Results:** In 28 of 30 patients, significant decrease of average HbA1c levels (average 0.9%, median 0.8%, P<0.001) was observed after education. The changes in average HbA1c levels were prominent in patients who were educated for the first time. On follow-up, HbA1c level at 3 months was significantly decreased (P=0.009) but after 9 months, it tended to increase again. The decrease of average HbA1c levels after education was negatively correlated with disease duration (r=-0.60, P=0.001).

**Conclusions:** The short-term effect of the diabetes education program with intensified treatment in diabetic children and adolescents was optimistic but regular education and support in these patients should be sustained.



**PAO-88**

**Phenotypic and metabolic characteristics in non-obese adolescents with PCOS**

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**Purpose:** Polycystic ovary syndrome is characterized by hyperandrogenemia, insulin resistance, and dyslipidemia. We evaluated the clinical characteristics and metabolic components of non-obese adolescent girls with PCOS.

**Subjects and methods:** Thirty six non-obese (BMI<25kg/m<sup>2</sup>) adolescent girls (16-18years) with PCOS were compared to thirty two control group girls in similar age and BMI with regular menstrual cycles and were evaluated for anthropometric data and blood pressure. Fasting glucose, triglyceride, HDL-cholesterol, LDL-cholesterol, GOT, GPT were measured.

**Results:** BMI and waist circumference of the PCOS group were not different to the control. Frequency of menstruation and FG score of the PCOS group were significantly lower than the control. Blood pressures of the PCOS group were not different compared to the control. Fat mass and fat percents were higher in the PCOS group but were not significantly different to that of the control. AST ALT, triglyceride, total cholesterol, HDL-cholesterol, fasting glucose were not significantly different between the two groups. LDL-cholesterol was significantly higher in the PCOS group compared to the control. Frequency of abnormal components in metabolic syndrome was not different between the two groups.

**Conclusion:** In non-obese adolescents with PCOS, metabolic derangements were not remarkable.

**PAO-89**

**Does gonadotrophin-releasing hormone analogue affect of the body mass index in the girls with idiopathic precocious puberty?**

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**Background:** To assess whether Gonadotrophin-releasing hormone analogue (GnRHa) affects body mass index in children with idiopathic central precocious puberty (ICPP).

**Patients and methods:** At least 12 months followed up 41 girls (mean age 8.66±1.3years) with CPP were included in the study. 34 girls with ICPP were followed up 18 months. Complaints had been begun before 8 years old. 28 girls underwent GnRH stimulation test. All children were treated with Leuprolide acetat (LA) 3.75 mg/q4wk and the dose was increased only if there is inadequate suppression of LH. The dose had to be increased 7.5 mg/q4 wk in 11 patients. Body mass index (BMI) of the children with ICPP was calculated before the initiation of therapy (PRE) and at 3rd, 6th, 12th and 18th months of the GnRHa therapy.

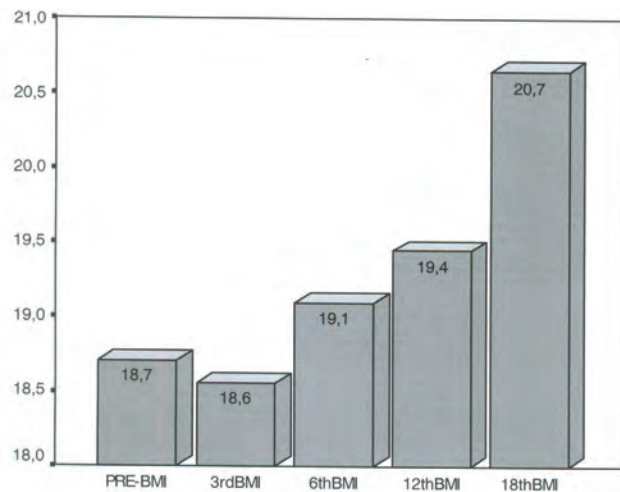
	Mean±SD
Bone age, year	10.3±2
Right ovary volume, mL	2.82±1.6
Left ovary volume, mL	2.76±1.6
Uterine length, cm	40.4±8.1
Basal LH, mIU/mL	2.18±1.8
Basal FSH, mIU/mL	4.31±2
Basal Estradiol, pg/mL	29.6±22

Table 1

**Results:** Pelvic ultrasound findings and basal hormone levels were given in Table 1. At the admission thelarche was a major complaint (32/41) and 5 girls had menarche. PRE-BMI was significantly positive correlated with BMI at 3rd, 6 th, 12th and 18th months of therapy (r: 0.879; r: 0.896; r: 0.909; r: 0.887, respectively). PRE- BMI significantly differed from BMI at at 3rd, 6 th, 12th and 18th months of therapy (F:69.808, p<0.0001). BMI gradually increased after 6 th months of therapy (Figure1). LA dose was significantly correlated with all body mass indexes during therapy. Bone age was correlated with volume of right (r:0.404; p:0.015) and left (r:0.360;p:0.034) ovary

and uterine length (r:0.447;p:0.05).

**Conclusions:** An initial dose of LA 3.75 mg/4 wk was efficient in most girls with ICPP. Unfortunately if this dose would be increased, patients would have a tendency having increased BMI. Clinicians should be alert of obesity risk in children treated with LA.



Distribution of BMIs of the study group during therapy months

**PAO-90**

**Age of puberty in a sample of Iranian girls**

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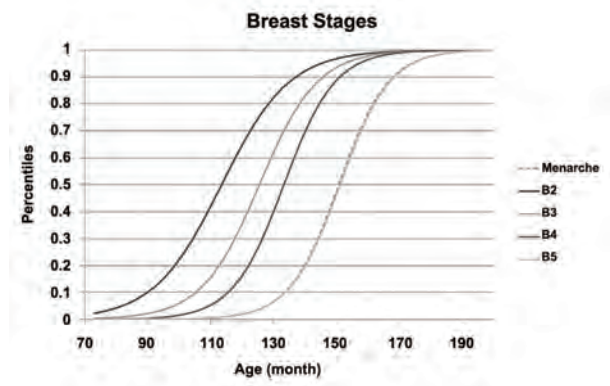
**Introduction:** Entering puberty is an important milestone in reproductive life. Many physiological and psychological processes are influenced by puberty and hormone secretion. Based on data from late 1800s to present, pubertal entry and menarche is occurring earlier than in the past. National data on these milestones can serve as a baseline for assessing secular trends in pubertal development for the population.

**Objective:** To obtain normal values of pubertal stages in 6-16 years old girls of Qazvin province, Iran.

**Methods:** This cross-sectional study was conducted during 2009-2010 in 2259 elementary and middle school girls in Qazvin. Healthy girls (6.0 to 16.0 years old) were selected by clustered random sampling. In all subjects height and weight were measured and pubertal stages were evaluated by trained general practitioners. Breast Stages 1-5 were determined by both inspection and palpation, using the criteria and definitions described by marshal and tanner. The self-reported date of menarche was recorded as well. Pubic hair stages were not evaluated because of cultural difficulties and most subjects disagreement.

**Results:** The mean age of Tanner stage2 breast development (B2) was 9.67 years. The 3rd and 90th percentile for B2 was 6.5 and 12.5years old, respectively. The mean age of menarche between 548 (24.5%) girls was 12.55 years (9.5 -14.75). The mean BMI was significantly higher in pubertal females (at the stage B2 and menarche) comparing to prepubertal girls (at stage B1). In comparison with percentile value proposed by tanner, the 50th percentile age of stage B2 is decreased by 1.7 years in our subjects.

**Conclusions:** The mean age of pubertal onset in girls living in Qazvin (9.67 year) is lower than internationally accepted. Mean age of menarche was 12.55 years old and the onset of puberty less than 6.5 years is considered precocious in the study area.



## PAO-91

### Comparison of antithyroid antibodies in type I diabetic children and control group in 2010

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**Background:** Type 1 diabetes is the most common metabolic disease worldwide. thyroid autoimmune diseases accompany with type 1 diabetes is the most common endocrinopathy. Therefore, thyroid function tests and antithyroid antibodies in patients suffering from Type 1 diabetes is essential to diagnosis of thyroid autoimmune disorders.

**Objective:** To compare the anti-thyroid antibodies in patients with Type 1 diabetes and healthy individuals.

**Methods:** In this descriptive-analytic study, 65 children with Type 1 diabetes and 65 healthy children were selected using simple sampling. Anti-TG, Anti-Tpo, TSH and T4 hormones were measured. The amount of antibodies in both groups compared by using Chi-square statistical analysis, t-independent, Kruskal Wallis.

**Results:** There was not significant difference between two group of samples (case and witness group) in case of sex and age but BMI percentile of two group was significantly different.

Positive Anti-TG in patients was 10.8% and in controls was 1.5% and the difference was statistically significant ( $p=0.029$ ). 16.9% of patients and 3.1% of controls had positive Anti-Tpo that was significantly different between two groups ( $p=0.024$ ). 10.8% of patients had overt hypothyroidism and 4.6% of controls had subclinical hypothyroidism. The difference was not significant statistically.

**Conclusions:** According to the results of research, it seems that the prevalence of Hashimoto thyroiditis in patients with type 1 diabetes is more than healthy people. Hence, thyroid function tests (TFT) and antithyroid antibodies (Anti-Tpo) in patients with Type 1 diabetes is necessary in order to early diagnosis of autoimmune thyroid disorders, prevention of their complications and timely treatment.

## PAO-92

### Maturity onset diabetes of the young (MODY) 2: clinical and genetic spectrum in five children

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**Background:** MODY is a genetically heterogeneous form of diabetes (DM) characterised by early onset, autosomal dominant inheritance and a primary defect in pancreatic  $\beta$ -cell function. MODY2, caused by mutations in the glucokinase (GCK) gene, is one of the most common types. The authors describe

5 cases of MODY2 diagnosed in paediatric age.

#### Case report:

Case	1	2	3	4	5
Age of detection of diabetes (years)	5	5	8	8	8
Family history of type 2 diabetes mellitus and/or hyperglycaemia	+	+	+	+	+
Body mass index (Kg/m <sup>2</sup> ) at first exam (percentile)	12.6 (3)	19.4 (85)	15.8 (40)	24.1 (99.5)	14.2 (11)
Fasting glucose >126 mg/dl	+	+	+	+	+
Initial HbA1c (%)	7.3	6.5	5.3	6.1	5.9
Serum insulin ( $\mu$ U/ml)	<2	9.4	<2	8	6.6
Serum C peptide (ng/ml)	0.9	Ø	1.2	1.1	1.2
Antibodies: anti-ICA, anti-GAD	negative, negative	negative, negative	positive, negative	negative, negative	negative, negative
Glucose at 0h and 2h in oral glucose tolerance test (mg/dl)	Ø	116, 157	130, 189	Ø	Ø
Genetic testing (GCK)	mutation c.579 +1_579 +33del33 in intron 5	mutation c.579 +1_579 +33del33 in intron 5	mutation c.616A>C in exon 6 (not previously described)	mutation c.1268T>A in exon 10 (not previously described)	mutation c.616A>C in exon 6 (not previously described)
Age at genetic diagnosis (years)	7	11	12	14	8
Treatment	diet measures	diet measures	diet measures	metformin before MODY2 diagnosis; diet measures	diet measures
Complications	no	no	no	no	no

Case 1. 5-year-old boy with random hyperglycaemia detected during hospitalization due to gastroenteritis. HbA1c was 7.3% and spot urine analysis was normal. The initial diagnosis was the early presentation of type 1 DM.

Case 2. 11-year-old asymptomatic boy with fasting and random hyperglycaemia since 5 years.

Case 3. 9-year-old asymptomatic boy with fasting hyperglycaemia during the previous year.

Case 4. 8-year-old girl, obese, with fasting hyperglycaemia detected during co-morbidity study. Clinical insulin resistance signs were absent. The initial diagnosis was type 2 DM.

Case 5. 8-year-old asymptomatic girl with fasting hyperglycaemia during the previous 7 months.

Evolution Patient 4 was treated with metformin and the other patients didn't start pharmacological treatment. During follow-up, patients 1, 2 and 3 maintained occasional fasting hyperglycaemia; mean HbA1c was 6%. In case 4, despite treatment with metformin, evolution was similar and HbA1c didn't improve. Genetic testing for MODY2 was performed after few months to several years of follow-up. Any of the patients started or maintained pharmacological treatment.

**Conclusions:** GCK-MODY is characterized by non-progressive mild hyperglycaemia, rare microvascular complications and unnecessary pharmacological treatment. The authors describe 5 patients with mild asymptomatic hyperglycaemia and mildly elevated HbA1c. All presented family history of DM or untreated hyperglycaemia. Genetic testing detected heterozygosity for mutations in GCK gene, 2 previously described and 3 apparently novel variants. This is a vital clinical tool in selected cases since it confirms a diagnosis, predicts clinical course, defines family risk and determines treatment.

**PAO-93****Persistent pubertal gynecomastia: an unusual presentation of a steroid 17-alpha-hydroxylase deficiency**

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**Background:** Pubertal gynecomastia is a frequent reason for consultation in pediatric endocrinology. Although it is usually idiopathic, hypogonadism, hyperprolactinemia, hyperthyroidism and rare testicular or adrenal tumors must be considered. Most often, idiopathic pubertal gynecomastia regresses at the end of puberty when the testosterone (T) level increases.

**Objective and hypotheses:** We report a case of persistent pubertal gynecomastia revealing a mutation of steroid 17-alpha-hydroxylase (CYP 17).

**Methods:** This 15-year-old boy was referred to our pediatric endocrinology clinic because of bilateral gynecomastia, stage III with pigmented and developed areolae. Pubertal development was P3,G3 with a normal penis (length=7 cm). Basal LH and FSH were 7.5 mU/ml (N=1.5-8.5 and 3-8, respectively). Plasma T=5.5 nmol/l (N=12-38), DHEA=1.8 nmol/l (N=10-19) and 17OHP=11 nmol/l (N<15). E2 level was 175 pmol/l (N<180). Basal PRL level was 230 µU/ml (N<500). Plasma TSH and T4L levels confirmed euthyroid status. Plasma βhCG and αFP were negative. Testicular sonography found normal pubertal testis structure. The low plasma T led us to evaluate other steroid precursors. Plasma progesterone (P) level was 10.9 nmol/l (N=0.7-2) with low and non-ACTH-stimulated plasma cortisol level (154.6→212.5 nmol/l).

**Results:** The discordance between the high P level and the low values of other 17OH steroid precursors suggested 17OH deficiency. Sequencing of the CYP17a gene identified a heterozygote composite mutation: p.Pro35Thr and p.Arg239X. Substitution by testosterone enanthate was introduced.

**Conclusions:** This report points out the usefulness of investigating adolescents with persistent pubertal gynecomastia to identify a specific cause and thus propose adequate management.

**PAO-94****Congenital hypothyroidism in a neonate born to a mother with autoimmune thyroid disease**

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**Background:** Congenital hypothyroidism (CH) induced by maternal TSH receptor-blocking antibodies is responsible for approximately 2% of all CH cases.

**Objective:** A case report of a newborn with CH born to mother with autoimmune disease.

**Methods:** TSH in blood on filter paper, serum TSH, fT4 and TSH receptor antibodies (TRAb) tests, imaging pictures.

**Results:** A female newborn is presented (pregnancy 1, delivery 1, terminated by a cesarean section at 40 weeks of gestation, birth weight 3150g, length 54cm, Apgar score 8 and 10 at 1 and 5 minutes, respectively). Maternal medical history indicated hyperthyroidism treated with thiamazol for 5 years, followed by hypothyroidism supplemented with L-thyroxin (LT4) for 3 years prior to conception and during pregnancy.

Available data suggested LT4 substitution during pregnancy to be insufficient, resulting in periodic hypothyroxynemia. Suspected fetal arrhythmia led to echocardiography at 31 weeks of gestation, showing regular, but rather slow heart action (112-120/min). In mass screening for CH, TSH concentration in blood on filter paper was 130.5 mIU/L [N<15]. Serum levels of TSH >60 mIU/L [N:0.4-9] and fT4 9.6 pmol/l [N:10-26] determined in the 4th day of life confirmed the diagnosis of CH. A high neonatal TRAb value [67.8 IU/L, N<1] was correlated with maternal TRAb [68.5 IU/L]. Ultrasound showed the thyroid situated normally and normal in size, yet no marker uptake by the gland was demonstrated by Tc99m scintiscan.

On day 7 of life, the neonate received LT4 substitution at the dose of 12 µg/kg/d, the dosage being modified based on serum fT4 and TSH levels. A de-

creasing demand for LT4 was seen along with normalization of TRAb concentration; at 4 month of life, TRAb was 0.7 IU/L. At 13 month of life serum fT4 and TSH levels during LT4 substitution (1 µg/kg/d) were normal.

**Conclusions:** The presented case confirms the diagnostic importance of TRAb determinations in newborns with CH born to mothers with autoimmune disease, additionally pointing to maternal hypothyroxynemia in pregnancy as a significant CH risk factor in newborns.

**PAO-95****Central precocious puberty in a female child of very young age**

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**Background:** Central precocious puberty under age of 6 years old is rarely related to morphological abnormality of hypothalamus and pituitary gland, and the type of abnormality was variable.

**Objective and hypotheses:** We report a case that a two year and 10 month aged female child was diagnosed central precocious puberty with pituitary intermediate cyst.

**Methods:** This child was visited the pediatric out-patient clinic due to breast budding and progressively increased size of breast for three months. Physical examination with laboratory and radiological study for precocious puberty of this patient was done.

**Results:** On visiting day, breast size was 3 x 3 cm and pubic hair was not noticed. Height and weight of this patient were 99.6 cm (95-97 percentile) and 16 kg (90-95 p). Head circumference of this patient was 49 cm (50-75 p). This patient was born by the full term normal spontaneous vaginal type delivery and birth weight was 3,200 gm, and height 49 cm. Bone age was 5 years old but chronological age was two year and 10 months old. The basal serum level of E2 and LH was 25.58 pg/mL and 7.8 mIU/mL respectively, but the maximum serum level of LH was 43.8 pg/mL after GnRH stimulation. Brain MRI shows pituitary cyst between anterior and posterior pituitary lob. Breast size of this patient regresses to 2 x 2 cm and sustained after GnRH agonist therapy.

**Conclusions:** We report a case of central precocious puberty that is very young age with intermediate cyst of the pituitary gland and respond well to GnRH agonist therapy. However, careful follow-up will be needed in this patient.

**PAO-96****The association of thyroid autoimmunity with statural development in a group of type 1 diabetes mellitus children**

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**Background:** Type 1 diabetes mellitus is frequently associated with other endocrine autoimmunity and the risk is increased by the duration of diabetes. These associations may have a negative impact on diabetes control and children development.

**Aim:** The aim of the study was to evaluate the impact of thyroid autoimmunity on statural growth of children with type 1 diabetes mellitus.

**Material and method:** We examined a group of children with type 1 diabetes mellitus. We collected demographic data; we performed general physical examination, height, weight, thyroid gland, and laboratory data: glycated hemoglobin, thyroid peroxidase antibodies (TPOAb). The score of standard deviation (SDS) was calculated as the difference of actual height and mean height for age and gender divided by standard deviation value. We defined short stature as a SDS under -2 DS. An informed consent was obtained from children's parents or legal tutors.

**Results:** We studied 68 patients (36 boys) with mean age 11.22±4.02 years, mean duration of diabetes 3.43±2.55 years and mean glycated hemoglobin

8.94±1.9%; 16 patients (23%) had thyroid autoimmunity. None of our patients had short stature.

We found a significant association between thyroid autoimmunity and lower SD score: 0.26 SD vs 0.98 SD ( $p=0.043$ ). Mean glycated hemoglobin was significantly higher in patients with thyroid autoimmunity 9.7% vs 8.6% ( $p=0.05$ ), but BMI did not differ significantly between the two groups. Logistic regression analysis revealed that low SDS (SDS under 0) was independently associated with duration of diabetes ( $p=0.049$ ), but not with birth weight, glycated hemoglobin, and TPOAb.

**Conclusion:** Our data suggest a significant association between thyroid autoimmunity and height in children with type 1 diabetes mellitus, but this seems to be explained by other factors such as diabetes duration.

#### PAO-97

### Pattern of presentation and management when neonatal screening for congenital adrenal hyperplasia is not available

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**Background:** We present the presenting features and management of sixteen cases of congenital adrenal hyperplasia following up in the paediatric endocrine clinic at King Fahd Military Medical Complex Dhahran, Saudi Arabia. Cases were diagnosed at our centre or referred from other hospitals.

**Objective and hypotheses:** The aim of the study is to highlight the different presentations and on rare occasions delay of management even when family history exists. The different treatment regimens and follow up plans were also evaluated and compared with current guidelines.

**Methods:** Retrospective chart reviews of sixteen patients diagnosed with congenital adrenal hyperplasia.

**Results:** Family history was positive but was denied or concealed by some families which delayed diagnosis for some cases. Salt loss and ambiguous genitalia was the main presenting feature in neonatal period. Genetic diagnosis was performed for some cases and new mutations were identified. Doses of steroids were adequate according to current guidelines but follow up was hindered by lack of local laboratory evaluation of urinary and serum steroid precursors.

**Conclusions:** We conclude that laboratory support needs to improve as well as parents' education about need to disclose important medical information.

#### PAO-98

### Endocrine disorders in 62 children with Turner syndrome

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**Background:** Turner syndrome (TS) is a common genetic disorder, is associated with reduced adult height and with ovarian failure. However, it is becoming increasingly evident that patients with TS are also susceptible to a range of disorders.

**Objective and hypotheses:** Explore the endocrine disorders in Chinese children with TS.

**Methods:** 62 patients with TS diagnosed in our clinic in 1999~2010 by karyotype, FSH, LH, growth hormone stimulation, IGF1, TPO and Tg antibodies, TSH, FT3, FT4, fasting glucose (GS), A1c (if GS high), ultrasound (varian, uterus and thyroid), bone age, pituitary MRI (if Growth hormone deficiency).

**Results:** Chronological mean age: 10.9(0.2~18 ) years, mean height z score (HtSDS): -3.96 (-0.39~-7.3)SD, >13.5 years no puberty signs (15/17, 88.2%). Distribution of karyotypes: X monosomy-45,X (27/62, 43.6%); mosaicism (22/62, 35.5%): including 45,X/46,XX, 45,X/46,X+marker, 45,X/47,XXX, 45,X/46,X,i(Xq), 45,X/46,XY, 45,X/46,X,dup(X)(q24), 45,X/46X,idic(X)(q24), 45,X/46,XX/47,XXX, 45,X/46,X,add(X)(p22.1), 45,X/46,X,i(Xq)/47,X i(Xq)\*2.; aberration of X structure: 46,X,i(Xq)(10/62, 16.1%), 46,X,del(X)(q22)(3/62,4.8%), Hashimoto thyroiditis (15/40, 37.5%), Hyperthyroidism (3/60, 5%), Hypothyroidism (8/60, 13.3%), growth hormone deficiency (31/55, 56.4%), Diabetes (2/62, 4.8%), LH (11.7±11.2) IU/L, FSH (66.5±51.8)IU/L, IGF1 (201.4±116.4)ng/ml. Pituitary MRI: small (4/29, 13.8%); empty sella turcica (2/29, 6.9%); pituitary tumor or pituitary hyperplasia (2/29, 6.9%); Arachnoid cyst (1/29, 3.4%).

**Conclusions:** Endocrine disorders are common in Chinese children with TS. Children with TS are at risk for growth hormone deficiency, Hashimoto thyroiditis, thyroid dysfunction, diabetes, which require treat early.

#### PAO-99

### A case of myasthenia gravis with graves disease

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**Background:** Thyrotoxicosis due to autoimmune thyroid disease (AITD) occurs in % 5-10 of patients with Myasthenia Gravis ( MG) whereas MG has a frequency of % 0.2 among the patients with AITD. MG and AITD can also be seen together in Autoimmune Polyglandular Syndrome (APS) type 2 and type 3.

**Objective and hypotheses:** Hereby, we report a patient with MG and Graves diseases.

**Methods:** A 15 years old male patient was referred to our clinic for hyperthyroidism. He had diplopia since 8 months and ptosis since 3 months. His height was 169.5 cm, weight was 64 kg, blood pressure was 130/80 mmHg and he had a heart rate of 132/minute. He had unilateral ptosis and diffuse enlarged thyroid gland. Laboratory findings were as follows: TSH: <0.004 mIU/ml, free T4: 4.4 ng/dl, free T3: 13.7 pg/ml, anti thyroglobulin antibody: 2175 IU/ml, anti microsomal antibody: >1000 IU/ml, TSH receptor antibody: 36.9 U/. He had a positive response when we performed prostigmine test.

**Results:** Our case was diagnosed with MG and Graves diseases. He started to receive methimazole, propranolol, pridostigmine.

We found that plasma cortisol was 10 µg/dl, ACTH was 23 pg/ml, c ANCA, p ANCA, anti dsDNA, ANA, anti Ro, anti La and anti tissue transglutaminase antibodies, anti GAD, anti insulin antibody, islet cell antibody were negative. Vitamin B12 was 175 pg/ml and parietal cell antibody was positive. So, we started to give B12 vitamin replacement. We regulated methimazole dosage, beta-blocker therapy was terminated and there was a decline in TSH receptor antibody levels. His diplopia was recovered on the second month of pridostigmine treatment.

**Conclusions:** Autoimmune thyroid diseases should be investigated in the presence of Myasthenia Gravis. Further exploration about Autoimmune Polyglandular Syndrome type 2 and type 3 is needed in the association of Myasthenia Gravis and Graves diseases.

#### PAO-100

Abstract withdrawn.

#### PAO-101

### Recombinant GH treatment in a female patient with Seckel-like syndrome and a novel homozygous mutation 7055 - 7056insC in the PCNT gene

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**Background:** Seckel syndrome is a rare autosomal recessive disorder, characterized by pre- and postnatal growth deficiency, microcephaly, mental retardation, and characteristic facial appearance beaklike protrusion of the mid-face (bird-headed). This disorder is associated with defective ATR-dependent DNA damage signaling. Mutations in ATR gene and also gene encoding pericentrin (PCNT) cause Seckel syndrome.

**Objective and hypotheses:** We describe rGH treated patient with confirmed Seckel-like syndrome.

**Methods:** We report a female patient, 1,5 years old, who has classic features of the syndrome Seckel: height at birth -3,3SD, postnatal growth retardation -10,5SD, OFC -9,9SD, bird-head phenotype, mental retardation. She also has

micrognathia, face asymmetry, low-fitting ears, disproportionately large eyes, clinodactyly of fifth finger. The patient's tooth system is at the initial stage of eruption. She does not have haematological and bone abnormalities.

**Results:** The girl had treatment of recombinant growth hormone "Saizen" 0,05 mg/kg/day. After six months of treatment height was -9,52SD, height velocity 5,5 cm/6 months (+0,53SD), the level of IGF-1 increased to 80,2 ng/ml (before growth hormone treatment IGF-1 was 46,9 ng/ml). Molecular-genetic researches confirmed Seckel-like syndrome in our patient: a novel homozygous mutation in the PCNT gene 7055 – 7056insC. Her unaffected parents and two brothers are heterozygous for this mutation.

**Conclusions:** We described a positive effect of rGH treatment in patient with Seckel-like syndrome with a novel homozygous mutation (7055 – 7056insC) in the PCNT gene.

#### PAO-102

### Precocious puberty caused by granulosa cell tumors

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**Background:** Juvenile granulosa cell tumors a rare tumor which originates from the sex stromal cord, occurs in the first two decades of life and represents less than 5% of ovarian tumors in girls. It contains granulosa and theca cells and is associated with endocrine manifestations of excess estrogen production. Treatment is surgical. The tumor markers are estrogens and inhibin.

**Objective and hypotheses:** Describe two patients with granulosa cell tumors presenting with precocious puberty.

**Methods:** Describe two cases: case1: Five year old girl with thelarche, pubic hair, axillary odor and menarche. Physical examination breast Tanner 3, hyperpigmentation of the nipple and pubic hair Tanner 2. LH 0.1ng/dl, FSH 4.1ng/dl, estradiol 38,8 pg/ml, pelvic ultrasound: walled cystic image of right ovary. Inhibin post quirsurgical 10 ng/dl Case 2: Seven years old girl with seven months history of mammary growth, Tanner 3 nipple pigmentation, pubic hair Tanner 2, LH 0.3 ng/dl FSH 0.3 ng/dl pelvic ultrasound Heterogeneous isodense mass of right ovary. Bone age 10 years 6 months. inhibin post quirsurgical 45ng/dl Two cases were diagnosed precocious puberty. Treatment was surgical and pathological. Two cases were diagnosed precocious puberty. Treatment was surgical and pathological report was JUVENIL GRANULOSA CELL TUMORS. CEA and alpha fetoprotein negative.

**Conclusions:** Patients with granulosa cell tumors presented with precocious puberty, increased estrogen production and decreased gonadotropins. Pelvic Ultrasound reveals an ovarian mass. Treatment was surgical and supervision of inhibin of less than 10ng/ml.

#### PAO-103

### Polycystic ovary disease and its fearsome consequences

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**Background:** Polycystic ovary is a common endocrine disease, 70% of cases present insulin resistance, determining infertility, and in the long-term, endometrial and breast cancer and metabolic syndrome.

**Objective:** Determine the consequences of polycystic ovary syndrome in young women.

**Method:** Descriptive, cross sectional study, targeting women between 13 and 21 years old, who were assisted in the Instituto de Maternidad, Tucumán, Argentina. The analysis was performed using descriptive statistics, the association of variables with SPSS V75.

**Results:** N: 293. The main complaints were secondary infertility and hypertrichosis. 65% of patients were obese and 80% showed insulin resistance. 77% of the patients were dyslipidemic and the remaining 23% had values within the limits of normal. 48% had fertility desires without success after a year of sexual active life. 32% were diabetic type II and 26% were hypertensive.

**Conclusions:** The fearsome consequences of polycystic ovary disease in the short term are present in most of the young patients, which is a personal, familiar and social tragedy, considering the low age of the affected. We propose educational and preventive measures to avoid the potential torpid progress of polycystic ovary syndrome in short, medium and long term.

#### PAO-104

### Final height in patients with type 1 diabetes mellitus (DM1)

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**Background:** Final Height (FH) could be compromised in DM1 pediatric patients. Poor control, growth retardation secondary to celiac disease, chronic acidosis and hypothyroidism are possible causes that could compromise FH in these patients. A retrospective study with 130 patients was performed between 1993-2010.

**Objectives:** To evaluate FH in patients who have DM1 at childhood or adolescence and to compare with their target height (TH). To identify factors that could compromise FH.

**Material and methods:** FH was considered when growth velocity were < 1cm/year at last year and/or Bone age (Greulich-Pyle atlas) >15y for girls, and, >16y for boys. The FH was compared with their TH; mother and father height were obtained from each patient. Were analysed: chronological age (CA) at diagnosis; time of disease (TD) is the time since diagnosis until FH; numbers of hospitalization due to ketoacidosis and hypoglycemia since the diagnosis and, glycosylated hemoglobin (HbA1c) mean during follow up. In addition autoimmune disease: Hashimoto Thyroiditis was considered with positive antibodies TPO and/or TG and elevated TSH; Graves Disease was considered with positive antibody anti-TRAB, low TSH and elevated T4free; Celiac Disease was considered with positive antibody antiendomysium IgA and intestinal biopsy confirmed. Presence of microalbuminuria during the follow up were analysed. The HSDS was used for statistical analysis. A p value less than 0.05 was considered statistically significant.

**Results:** 55 patients (34 girls) reached FH.

	Median	Mean
HSDS-FH	-0.14 (-2.08 - +2.02)*	-0.16 (±0.81)
HSDS-TH	-0.27 (-2.28 - +0.96)*	-0.34 (±0.78)
HSDS-FH minus HSDS-TH	0.22 (-1.9 - +1.95)	0.16 (±0.76)

\*p=0.059 (Wilcoxon)

In Table 02 are shown the findings of overall and the comparison of two groups of patients. We separated and compared two groups of patients; Group A: HSDS-FH minus HSDS-EA < zero (-0.37 [-1.9 - -0.01]), and; Group B: HSDS-FH minus HSDS-EA ≥ zero (0.54 [0.05 -1.95]), p<0.01 (Mann-Whitney).

	Overall	Group A	Group B	p value (Group A x Group B)
n	55	21	34	
CA	10.52(±3.72)	10.43 (±3.46)	10.03 (±2.96)	0.65
TD	6.93 (±3.83)	7.1 (±3.52)	7.12 (±3.38)	0.98
HbA1c	10.6 (±1.92)	11.09 (±2.23)	10.34 (±1.66)	0.16
Hospitalization Hypoglycemia	0.64(±0.88)*	0.86 (±0.96)	0.5 (±0.8)	0.14
cetoacidosis	0.36(±0.67)*	0.38 (±0.8)	0.32 (±0.59)	0.76
Hashimoto Thyroiditis	5	3	2	ns
Graves Disease	1	zero	1	ns
Celiac Disease	7	3	4	ns
Microalbuminuria	23	8	15	ns

\*p<0.0195(t-test).

**Conclusion:** The patients reached FH according their TH. None of the factors evaluated compromised FH in these patients.

## PAO-105

### Growth hormone excess in two children with neurofibromatosis type 1 and optic pathway glioma

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**Background:** In children with neurofibromatosis type 1 (NF1) growth hormone excess (GHE) is extremely rare, but reported in the presence of optic pathway glioma (OPG). GHE can be the result of hypothalamic regulatory defect due to OPG infiltration of somatostatinergic pathways reducing somatostatin tone and leading to GHRH-mediated overproduction of GH.

**Objective and hypotheses:** We present 2 cases of children with NF1, OPG and GHE.

**Methods:** It is a case-report.

**Results:** First case. A pre-pubertal 5 years old girl with NF1 and a diffuse suprasellar low grade glioma involving the optic pathway was referred for tall stature. After completion of chemotherapy, GHE was documented by failure of GH levels to suppress during a standard OGTT and elevated age-adjusted plasma IGF1 levels. She was started on long acting somatostatin analogue (SSa) therapy which normalized her growth velocity and plasma IGF1 levels. Six months after starting SSa she developed central precocious puberty (CPP), and from the age of 7.8 years she also received LHRHa therapy. However following an episode of acute pancreatitis at the age of 10.2 years SSa was stopped. IGF1 levels and growth velocity remained normal while off SSa and subsequently when at the age of 13.5 years LHRHa was also discontinued. This is the first reported case in the literature documenting spontaneous resolution of GHE after treatment with SSa in a child with NF-1 and OPG. Second case. A tall 7.3 years old girl with NF1 and OPG treated with chemotherapy was referred for precocious puberty. CPP was confirmed and treated with LHRHa. Despite documented biochemical and clinical suppression of puberty, growth velocity remained accelerated with raised IGF1 age-adjusted plasma levels. GHE was suspected and then confirmed by a failure of GH levels to suppress in response to an OGTT. Treatment with SSa was started with a normalization of both auxological and biochemical data.

**Conclusions:** Tall stature and growth acceleration in children with NF1 and OPG require investigation for both precocious puberty and GHE.

## PAO-106

### Screening results for vascular complications and associated autoimmune diseases in children and adolescents with type 1 diabetes

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**Background:** Diabetes-related microvascular complications, as retinopathy, nephropathy and neuropathy are life-threatening complications in children and adolescents with type 1 diabetes mellitus (T1DM). Longer duration of diabetes, older age and puberty are the risk factors for the development of complications. Further risk factors include smoking, hypertension, higher body mass index and dyslipidemia. Therefore prevention and screening for complications is an important part in the care of children and adolescents with T1DM.

**Objective and hypotheses:** Our aim was to investigate diabetic complications and associated autoimmune diseases in children and adolescents with T1DM of more than 5 years duration.

**Methods:** The study included 46 children and adolescents with T1DM (18 male, 28 female), mean aged  $14.1 \pm 2.8$  years, with a T1DM duration of  $8.4 \pm 2.9$  years. Forty-two (91.3%) cases were adolescent and 4 (8.7%) cases were in prepubertal age.

**Results:** Insulin treatment consisted of four daily injections in all of the patients and mean HbA1c level was 8.3% (range 5.9%-12.4%). The prevalence of microalbuminuria was 32.6%, dyslipidemia was 21.7%, hypertension was 17.4%, and peripheral neuropathy was 2.2%. None of the patient had diabetic retinopathy. Prevalence of autoimmune thyroiditis and celiac disease were found to be 21.7% and 6.5% respectively. Despite intensive insulin treatment, 47.8% (n:22) of patients with T1DM developed at least one detectable diabetic complication after approximately 8 years of diabetes. Microalbuminuria

was the most common complication and the strongest risk marker was high blood pressure.

**Conclusions:** Annual complication screening should be done after diabetes duration of 5 years in patients with T1DM. Additionally screening at an onset and repeated measurements for autoimmune thyroiditis and celiac disease are recommended.

## PAO-107

### Cushing's disease in a 14-year old female: difficulties of diagnosis

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**Background:** Cushing's disease (CD) is rare in childhood and remains a difficult condition to diagnose and treat. Although the diagnosis of CD is of crucial importance in effective diagnosis and treatment. Sometimes it is difficult to confirm the location of microadenoma in CD.

**Objective and hypotheses:** We report the case of 14-year old girl, who was referred to our hospital because of growth retardation with muscle weakness and rapid onset weight gain. On admission, she had typical Cushingoid appearance with Tanner pubic hair stage 3.

Endocrinological examinations showed elevated levels of serum cortisol, and 24-h urinary free cortisol (UFC), and plasma ACTH. Lack of diurnal variation of ACTH and cortisol was observed. Serum cortisol levels were not suppressed by low and high dose dexamethasone as well. We established ACTH dependent CD. Performing the corticotrophin-releasing hormone (CRH) test, increased cortisol response confirmed the diagnosis of CD. Gonadotropin levels were subnormal suggesting a suppressive effect of chronic hypercortisolemia. Although, on 3.0 Tesla brain MRI, no microadenoma was detected in the pituitary gland. Considering the patient's age, hormonal findings compatible with pituitary ACTH production and the possible complications the bilateral inferior petrosal sinus sampling for ACTH was not performed.

**Results:** Despite of the lack of positive radiomorphological MRI signs, the patient underwent successful and curative transphenoidal pituitary surgery and a 2 mm microadenoma was removed. The histopathological features- ACTH secreting microadenoma- was consistent with the diagnosis.

**Conclusions:** Hypercortisolism was resolved after pituitary surgery. Possessing the typical clinical presentation and endocrinological investigation of CD in special cases -lack of detected microadenoma- the transphenoidal surgery is henceforward a safe and effective procedure in children.

## PAO-108

### Noonan syndrome: clinical phenotype and response to GH treatment

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**Background:** Noonan syndrome (NS) is a disorder characterized by congenital heart defects, facial dysmorphism, skeletal malformation and short stature.

**Objective and hypotheses:** The aim of the study was to describe a cohort of patients with NS in Belarus, evaluate the effect of rhGH treatment for 24 months on metabolic, clinical and cardiac status in patients with NS.

**Methods:** Since 2008 at the State Endocrinology Center 8 NS patients (5m, 3f) were observed. Median age was 13.7yr (11.0-17.8). All but one were in puberty Tanner stage 2-3 at the first observation. One boy had early puberty, a gonadal atrophy was found in one boy also. Two patients had had a mild growth retardation (mean height SDS -1.2), 6 others - severe growth retardation (mean height SDS -2.9 (from -4.8 to -2.0SDS)) according to population standards. Means birth weight and length were normal. Typical face dysmorphism were found in all patients. 3/8 were diagnosed with pulmonary valve

stenosis, 3- with atrial septum defect, one at a time - with hypertrophic cardiomyopathy, tetralogy of Fallot and ventricular septal defect. Only 1/8 had mental retardation. 6/8 patients with severe growth retardation were undergone rhGH treatment. Basal serum IGF-1 levels according to age and puberty stage were -1.9SDS. RhGH dose ranged from 47 to 67 µg/kg/d. Anthropometry, bone age, serum IGF-1 level, lipids, fasting glycemia and insulin, cardiac evaluations were performed at baseline, at 12 and 24 months of treatment.

**Results:** At 12 and 24 months of treatment mean height SDS elevation was found ( $\Delta 1$  height SDS = 0.43 and  $\Delta 2$  height SDS = 0.64, respectively). Basal serum IGF-1 levels normalized after 1st yr of rhGH therapy: -0.48SDS. No significant difference was observed in lipids profiles, fast glycemia, fast insulin levels and clinical cardiac status during two years of rhGH treatment.

**Conclusions:** Cohort of patients with NS in Belarus showed the typical clinical phenotype as well as in other researches. Effect of rhGH treatment starting at the age of puberty in NS is minimal. Early genetic analysis is required to be helpful in selecting the appropriate patients for rhGH therapy.

#### PAO-109

### Delayed diagnosis of a giant virilizing adrenocortical carcinoma in a girl presenting with mutism

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**Background:** Adrenocortical carcinoma (ACC) is an unusual, and highly malignant childhood tumor. In children, the incidence is reported 0.3 cases per million per year.

We describe a giant virilizing ACC in a girl who presented with a history of virilization and mutism.



**Case report:** A 5.5 year-old girl admitted to our clinic with mutism caused by deepening of voice. Her previous history revealed that pubic and axillary hair appeared at the age of 1 year and she was admitted to another hospital. However, the parents could not have brought the child to the regular follow up because of economic deprivation. During subsequent years, clinical progression of virilization have resulted in deepening of voice and ultimately a voluntary mutism have occurred which was chief complaint for admission to our clinic. At the time of presentation, in physical examination there were signs of virilization (deepening of voice, hyperpigmentation in genitalia and areola, acne, cliteromegaly, axillary and pubic hair). Laboratory examination revealed acceleration of bone age (10.5 years), elevated adrenal hormones (17-OH-progesteron: 15,5 ng/ml (N:<1,6), testosterone: 629ng/dl (N:<20), DHEAS: 1543 µg/dl (N:15-60), cortisol: 35,9 µg/dl (N:5-15), ACTH: 9,2 pg/ml (N:0-46)). Abdominal ultrasonography and CT showed a large (13x11,4 cm) cystic heterogeneous mass on right adrenal localization. There was no sign of metastasis in PET scan. Clinical and laboratory findings were consistent with virilizing adrenocortical tumor and patient has underwent surgical resection. Gross appearance of resection specimen is shown in Figure 1. In histopathological examination there was a fibrous capsule of tumor, however, Ki67 proliferation index was 25%, thus diagnosis of carcinoma was concluded with both clinical

and histological findings rather than adenoma. After operation hormonal and clinic resolution was observed and she is under close follow-up without adjuvant chemotherapy.

**Conclusions:** The patient is interesting in her major presenting symptom, mutism, caused by coarsening of the voice and unwillingness to speak.

#### PAO-110

### Growth disorders in Legius syndrome (LS) – a differential diagnosis to neurofibromatosis I (NF1)

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**Background:** Albeit growth disorders occur in 1 of 33 children, only in 1 of 6,000 children a growth hormone deficiency (GHD) results to be the cause, being early discovered and treated successfully. Seldom genetic disorders require complex diagnosis, like the LS, termed after Dr. Eric Legius since 2009 (Messiaen et al 2009), which belongs to the group of neuro-facial-cutaneous syndrome related to NF1. Children with short stature and macrocephaly, axillary freckling café-au-lait spots, signs of Noonan syndrome and learning disability funnel diagnosis towards NF1. If no punct-mutation of NF1 gene is present, LS is to be considered as a less severe and predictable prognosis. a mutation in the SPRED1 gene confirms LS. 155 patients have been reported so far.

**Objective and hypotheses:** Investigation of heredity transmission of LS. Population and methods: We report a 6-year-old patient with typical NF1 symptoms. With no NF1 mutation, the analysis of SPRED1 gene showed the mutation c.293dupA in Exon 4, which was decided to also investigate in other family members.

**Results:** The same mutation was found in the father; a family tree provides more evidence on the heredity transmission. The inter-disciplinary treatment concept is shown.

**Conclusions:** The exact clinical description, confirmation of SPRED1 gene mutation and the assessment of heredity allow for an individual treatment and reduction of psychological strain.

#### PAO-111

### Diabetes related problems and diabetic controls among the school children with type 1 diabetes mellitus living in Istanbul

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**Background:** Adequate glycemic control in children with T1DM requires optimal conditions guided by diabetes team both at home and at the school since children spend a remarkable time at school.

**Objective and hypotheses:** We aimed to search problems related to diabetes management encountered at school.

**Methods:** 114 children with T1DM from randomly selected schools from 1st to 12nd grade (6-18 yrs) were interviewed and a questionnaire was filled by the patients and the parents.

**Results:** Overall mean HbA1c level was 8.1±1.8% (4.7-13.8). Glycemic control was good (HbA1c ≤7.5 %) in 42% of the patients. 68% of the diabetic children were followed by a pediatric endocrinologist, 12% by a paediatrician in government hospital and 15% by a pediatrician in private practice. HbA1c levels were lower in patients followed by a pediatric endocrinologist than those followed by a government based or private-practicing pediatricians (7.9%, 8.7% and 9.1%, respectively, p<0.05). 72% of the patients were visiting their doctors at least every 3 months while in 28%, doctor visits were less frequent and in 15%, there was no regular follow-up. 27% of the patients were checking their blood sugar ≤1-2/day. 55% of children were avoiding

BS measurement at school. The classmates and teachers of the patient know that they were diabetic in %95 and %94 respectively. 30% of the children were avoiding injections at school, 33% were injecting at classroom, 15% at infirmary, 11% at cantina and 11% at restrooms. There was no school nurse in 80% of the schools. 18% of the children reported severe hypoglycemia in the last year. Glucagon was present at 19% of the schools and 72% of the homes of diabetic children.

**Conclusions:** This survey demonstrated a need for a more vigorous education and organisation for diabetes-care (especially for blood sugar measurement, insulin injections and glucagon) at school environment in Istanbul. It also demonstrates importance of a specialist (pediatric endocrinologist) in care of children with T1DM.

#### PAO-112

### Wolcott Rallison syndrome (WRS): a case report of a rare genetic disorder presenting with permanent neonatal diabetes mellitus

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**Introduction:** WRS is the most common genetic cause of Permanent Neonatal Diabetes Mellitus in consanguineous families. Much information can be gained by the identification of a susceptible gene in a particular disorder. WRS is a rare autosomal recessive disorder resulting from mutations in EIF2AK3 (or PEK), the gene encoding the eukaryotic translation initiation factor 2  $\alpha$  kinase 3 (eIF2  $\alpha$  kinase).

**Description:** We report a case of 35 days old female, who presented with seizures, hepatic dysfunction and diabetes mellitus and diagnosed as WRS on the basis of genetic studies with identification of mutations in the gene EIF2AK3. The baby was born an uneventful 36 weeks pregnancy from healthy consanguineous parents with birth weight of 1700 grams. Initial glucose level was 1020mg/dl, insulin needs dropped gradually from 4u/kg to 0.5u/kg until adequate glycemic control was achieved.

**Result:** Sequencing analysis has shown that she is homozygous for the nonsense mutation, L425X, in exon 7 of the EIF2AK3 gene. This mutation is a T > A substitution at nucleotide 1274 (c.1274T>A) resulting in a premature termination codon (p.Leu425X). This result confirms a diagnosis of Wolcott Rallison syndrome. Her mother is heterozygous for the EIF2AK3 nonsense mutation L425X and her father, heterozygous for a nonsense mutation in exon 7 of the EIF2AK3 gene.

**Discussion:** WRS results from the lack of trans-membrane enzyme activity which leads to the cell death by apoptosis in a number of different tissues. The development of early onset diabetes mellitus and skeletal dysplasia in almost all patients of WRS explains the high level of expression of EIF2AK3 in both pancreatic  $\beta$  cells and bone tissues.

However the gene is expressed at a lower level in several other tissues, which determines the variability of the clinical manifestations observed in this syndrome. The clinical features of variable intensity found in different tissues include mental retardation, hepatic and renal dysfunction, cardiac abnormalities, exocrine pancreatic dysfunction and neutropenia.

#### PAO-113

### Terms of diagnostics of 21-hydroxylase deficiency at performance of neonatal screening

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**Background:** Before introduction of neonatal screening there was observed a great many cases of late diagnostics of the 21-hydroxylase deficiency (21-OHD), especially in boys. This led to premature sexual development in the simple virilizing form (SV) and to salt-losing crisis at the salt-wasting form

(SW). Objective and hypotheses. To evaluate age of patients with 21-hydroxylase deficiency, at which the disease was diagnosed, during performance of the neonatal screening.

**Population and/or methods:** In 2006-2010, in Republic of Bashkortostan, by using the neonatal screening the 21-hydroxylase deficiency was revealed in 15 newborns. To evaluate efficiency of the neonatal screening, we determined terms of performance of each screening stage, age (median, minimal and maximal age) at making out the diagnosis of SW and SV 21-OHD in boys and girls.

**Results:** Age at making out the diagnosis of SW 21-OHD in girls after introduction of screening did not essentially change (medians 11 and 8 days, respectively). SV 21-OHD in girls in all cases began to be diagnosed at the neonatal period (median 15 days, min-max 0-21 days). In boys, all cases of the SW 21-OHD after the beginning of screening were revealed at the neonatal period as early as before development of the salt-wasting crisis (median 20 days, min-max 14-28 days). After introduction of screening, median of the age, at which the diagnosis was finally established, were 43 days. SV 21-OHD in boys was diagnosed later as compared with SW 21-OHD in boys and with both forms in girls. This is accounted for by that due to a large amount of the increased 17-hydroxyprogesterone values in boys the repeated study of this marker was performed every 2 weeks.

**Precise conclusions:** Neonatal screening has allowed decreasing essentially the time of diagnostics of the 21-hydroxylase deficiency, especially in boys.

#### PAO-114

### Following up plasma LH and estradiol in overweight girls with idiopathic precocious puberty during GnRH agonist therapy

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**Background:** They have reported that obesity was associated with development of idiopathic precocious puberty (IPP).

**Objective and hypotheses:** We compared suppression of plasma LH and estradiol between overweight girls and nonoverweight group to evaluate whether overweight is associated with suppression of plasma LH and estradiol during GnRH agonist therapy in patients with idiopathic precocious puberty.

**Methods:** We measured plasma LH and estradiol of overweight girls (n=16) and nonoverweight group (n=27) before and after 3 months of GnRH agonist therapy.

**Results:** Follow-up plasma LH and estradiol were not significantly different between overweight group ( $0.57 \pm 0.31$  mIU/mL,  $7.77 \pm 3.55$  pg/mL, respectively) and nonoverweight group ( $0.4 \pm 0.29$  mIU/mL,  $7.80 \pm 4.91$  pg/mL, respectively). Significant suppression of plasma LH ( $< 0.6$  mIU/mL) was observed in 62.5% of overweight group (n=10) and in 70.4% in nonoverweight (n=19). Significant suppression of plasma estradiol ( $< 10$  pg/mL) was observed in 81.3% of overweight group (n=13) and in 81.5% in nonoverweight (n=22).

**Conclusions:** In 3 months of GnRH agonist therapy, suppression of plasma LH and estradiol was not significantly different between overweight and control group

#### PAO-115

### The analysis of the CYP21A2 gene in children with 21-hydroxylase deficiency from Republic Bashkortostan (Russia)

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**Background:** Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders of adrenal steroid genesis in which 21-hydroxylase deficiency (21-OHD) accounts for over 95% of cases.

**Population and methods:** We studied 87 patients with 21-OHD from Republic Bashkortostan with salt wasting (SW) (n=42) and simple virilizing (SV) (n=45) forms. Mutations of the CYP21A2 gene were revealed in 71.82% of



the studied CAH-chromosomes with the following frequencies: delA2orLGC (27.62%), R356W (16.02%), I2splice (11.6%), I172N (7.18%), Q318X (4.97%), V281L (2.76%), P30L (1.1%) and P453S (0.55%).

**Results:** The mutations frequency distribution in the CYP21A2 gene in 2 groups of patients with classical disease forms showed statistically significant differences. SW 21-OHD patients demonstrated delA2orLGC of the gene CYP21A2 twice more often than patients with SV (37.65% and 19.32%, respectively,  $\chi^2=6.28$ ,  $p=0.012$ ), mutation R356W - 2.6 times higher (23.53% and 9.09% respectively,  $\chi^2=5.62$ ,  $p=0.018$ ), mutation I2splice - 2.9 (16.47% and 5.68%, respectively,  $\chi^2=4.1$ ,  $p=0.43$ ), and mutation Q318X - 8.3 (4.41% and 1.14% respectively,  $\chi^2=4.44$ ,  $p=0.04$ ).

The mutation I172N, on the contrary, was more typical for SV patients than SW patients (13.64% and 1.18%, respectively,  $\chi^2=7.95$ ,  $p=0.005$ ). Mutations P30L and V281L were detected only in SV patients.

Thus, we have been able to detect the spectrum of diagnostic significant CYP21A2 gene mutations typical for SW and for SV forms in CAH patients. We found 6 21-OHD patients who carried 3 mutations, two of which formed a cluster: Q318X+R356W (2.87%, 5/174), I172N+Q318X (0.57%, 1/174).

**Precise conclusion:** The studying of molecular-genetic nature of 21-OHD represents the doubtless scientific and practical importance in respect of use of the received data for differential diagnostics of its various forms, medical and genetic consultation and prenatal diagnostics.

#### PAO-116

##### A rare case of adiposegenital puberal obesity

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**Background:** We present a girl with the diagnosis of a growth hormone producing tumour of the pituitary gland.

**Objective:** We would like to present the case of a 1411/12-year-old girl who was referred to our outpatient clinic for endocrine evaluation of obesity. The auxology findings showed a body weight of 97.6 kg, a BMI of 32.8 (= 99.8 Perc.) and a body height of 172.6 cm (= 90. Perc.) with familiar aim size of 156 cm. X-ray of the left hand showed a retardation of the bone age of 1.6 J, the prospective final size was calculated at 177 cm. 2-3 years ago, at the beginning of the first puberty signs remarkable changes of the physical development and the appearance were noted for the first time.

The patient increased extremely in weight and showed a persistent growth push by shoe size at last 45. Clinically she suffered from occasional episodes of headaches, strong sweating and a primary amenorrhoe.

Because of the clear discrepancy between informal aim size and prospective final size, the external appearance of the patient and her distinct obesity we performed detailed endocrinology analysis incl. chromosome analysis, cerebral MRI and ophthalmologic investigation and could diagnose a growth hormone producing tumour of the pituitary gland. The patient was transferred to a specified neurosurgery for transsphenoidal tumor extirpation.

**Methods:** Clinical history and clinical findings, measuring of height, familiar aim size and prospective final size, x-ray of the left hand to calculate bone age and MRI of the brain, especially the pituitary gland.

**Result:** After diagnosis of a growth hormone producing tumour of the pituitary gland, the patient was transferred to a specified neurosurgery for transsphenoidal tumor extirpation.

**Conclusion:** If you see a clear discrepancy between informal aim size and prospective final size in a patient you have to search after a tumor in the pituitary gland.

#### PAO-117

##### Delirium in diabetic ketoacidosis

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**Background:** Neurologic changes during the course of diabetic ketoacidosis (DKA) should be considered as early signs of cerebral edema and should be treated immediately. Yet, delirium is not a usual neurological complication of DKA and has not been reported in pediatric DKA so far. We report our experience with a teenage girl who developed hyperactive delirium during the treatment of DKA due to severe acidosis.

**Case report:** A 15 year-old female patient with known type 1 diabetes mellitus of two years duration was referred because of fatigue and symptomatic hyperglycemia. She had abdominal pain for the last 24 hours, could not eat her meals appropriately and had hypoglycemia in the morning of admission. Due to appetite loss and hypoglycemia, she omitted the insulin dose at lunch time. On physical examination she was alert, had dehydration, deep sighing respiration and a smell of ketones. Her height was 168 cm (+1.02 SDS), weight 68 kg (+1.66 SDS), respiratory rate was 38/min, pulse 80/min. She had normal body temperature and blood pressure. Blood glucose was 414 mg/dl (23 mmol/l), capillary pH: 6.99 and bicarbonate: 5.0 mmol/l. Base excess was -25.2 mmol/l and anion gap was 29.8 mmol/l. Blood urea, liver enzymes and electrolytes were within normal limits. At the sixth hour of treatment the acidosis with administration of fluid and insulin, the patient became delirious. The delirium persisted despite the normalization of acidosis and was difficult to manage. Brain imaging studies revealed neither brain edema nor other intracranial pathologies. No evidence of intoxication could be found. The patient gradually regained consciousness and "merely" suffered from massive DKA associated with infection.

**Conclusions:** We did not find any similar case in childhood period in the literature thus we thought that clinicians should be aware that delirium can be seen in DKA due to severe acidosis.

#### PAO-118

##### Differences in clinical features and responses to treatment in different age groups of children with diabetic ketoacidosis and ketosis

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**Objective and hypotheses:** To compare clinical features and responses to a certain treatment protocol in different age groups.

**Material and methods:** Hospital records of patients with diabetic ketoacidosis (DKA) and ketosis (DK) who admitted to our hospital between January 2007 and December 2009 were reviewed. Symptoms, clinical and laboratory findings of all patients were recorded. Patients were divided into subgroups regarding to age [Group 1 (0-5.0 years), Group 2 (5.1-10.0 years), Group 3 (> 10.1 years)]. All patients with DKA were treated with a standardized intravenous fluid and insulin therapy while patients with DK were treated with subcutaneous insulin. The therapy protocol was analyzed in terms of amount and duration of fluid therapy, dose of insulin infusion and complications of therapy.

**Results:** 132 episodes in 107 patients with DKA (101 episodes) and DK (31 episodes) were studied. 64 patients (60%) were female, 43 (40%) were male, 81 (60%) were in new onset, 51 (40%) were in established diabetes. There were 22 episodes in group 1 (16.7%), 30 episodes in group 2 (22.7%) 80 episodes in group 3 (60.6%). Patients in group 1 and 2 reported more polydipsia and polyuria than patients in group 3 involving patients mostly with established diabetes. Blood glucose and corrected Na levels, as well as pH and osmolality did not differ between groups. HbA1c was found significantly higher with age. Children in group 1 had significantly lower HCO<sub>3</sub> levels compared to group 2 ( $p=0.047$ ) and group 3 ( $p=0.014$ ). Duration and amount of fluid therapy did not differ between groups. Patients in group 3 received significantly higher doses of insulin and patients in group 1 received significantly more bicarbonate therapy. Only one patient experienced cerebral edema which recovered without any sequel owing to appropriate therapy.

**Conclusion:** Children less than five years of age are at higher risk of acidosis and require more attention and closer monitoring during treatment.

**PAO-119****Long term longitudinal evaluation of overweight and insulin-resistance in patients treated for acute lymphoblastic leukaemia during childhood**

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**Background:** Cranial radio-prophylaxis (CR) and total body irradiation (TBI) for hematopoietic stem cell transplantation are risk factors for obesity and insulin resistance (IR) in long term childhood cancer survivors.

**Objective and hypotheses:** To evaluate overweight and IR in a group of childhood acute lymphoblastic leukaemia (ALL) survivors who received or not radiotherapy (RT).

**Methods:** We evaluated 74 patients (pts) treated for ALL at our Centre, at mean age  $5.2 \pm 3.1$  years (yrs), follow-up  $7.8 \pm 3.4$  yrs. They were subdivided in 3 groups according to RT: group 1 (CR 1800 cGy) 17/74 pts, group 2 (TBI 800-1800 cGy) 16/74, group 3 41/74 pts not irradiated. In each group BMI SD and HOMA were evaluated yearly. HOMA was normal if  $< 2.5$  in adults and children,  $< 4$  in adolescents.

**Results:** The prevalence of obesity was 9% in group 1 (after the 5th year), 7% in group 3 (in the first 5 years), 0% in group 2. 18% of pts in group 1, 14% in group 2 and 20% in group 3 were overweight. In the first 3 yrs, group 2 pts showed lower mean BMI SD ( $p < 0.05$ ) than the others. HOMA was abnormal in 9.5 % of all pts and in 39% of overweight and obese pts. HOMA improved during follow-up in group 1 and 3. In Group 2 IR was found in 47% of pts, increasing after the 4th year of follow-up. HOMA was abnormal also in some lean pts (8.3% from group 1, 27% from group 2 and 18.5% from group 3).

**Conclusions:** Obesity is rare in our pts. CR seems to be a risk factor for late obesity onset. TBI showed some protective effect on BMI SD while it negatively affected insulin sensitivity. HOMA should be evaluated in ALL survivors regardless BMI SD, in particular in pts who underwent TBI.

**PAO-120****Comparison of efficacy of growth hormone (GH) treatment in short children with neurosecretory dysfunction (NSD) and partial GH deficiency - 3 years of observation**

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**Background:** Improvement of height velocity (HV), related to an increase of insulin-like growth factor-I (IGF-I) secretion, is the most important index of growth hormone (GH) therapy effectiveness.

**Objective and hypotheses:** The aim of the study was an assessment of the efficacy of 3 years GH treatment by estimation of HV, IGF-I secretion and IGF-I to IGF binding protein-3 (IGFBP-3) molar ratio.

**Methods:** The analysis comprised 54 children (40 boys) with short stature and: partial GHD (pGHD – GH peak in 2 stimulating tests 5-10 ng/ml), and neurosecretory dysfunction (NSD – GH peak in stimulating tests  $> 10$  ng/ml but after falling asleep  $< 10$  ng/ml, decreased IGF-I secretion). All the patients were treated with GH in a dose of  $0.18 \pm 0.02$  mg/kg/week for – at least – 3 years. Before GH administration and after following years of therapy HV, IGF-I secretion and the IGF-I/IGFBP-3 molar ratio were compared.

**Results:** There were no significant differences in any of the analysed parameters between the groups either before the therapy or at any time of treatment, except for the significantly lower ( $p=0.01$ ) IGF-I/IGFBP-3 molar ratio in NSD group before treatment. For detailed data see the Table.

**Conclusions:** The effectiveness of treatment presented similar in NSD and pGHD groups. It seems that normal GH results of stimulating tests should not be a reason for disqualifying short children with disorders of spontaneous GH secretion from GH therapy.

	NSD			pGHD		
hSDS before treatment	$-2.76 \pm 0.61$			$-2.61 \pm 0.40$		
	HV [cm/year]	IGF-I SDS	IGF-I/IGFBP-3	HV [cm/year]	IGF-I SDS	IGF-I/IGFBP-3
before treatment	$3.8 \pm 1.1$	$-1.82 \pm 1.24$	$0.17 \pm 0.05$	$3.5 \pm 0.9$	$-1.65 \pm 0.76$	$0.22 \pm 0.07$
1st year of GH	$9.8 \pm 2.0$	$0.73 \pm 0.92$	$0.41 \pm 0.14$	$10.2 \pm 2.2$	$0.78 \pm 0.76$	$0.44 \pm 0.10$
2nd year of GH	$8.9 \pm 1.7$	$0.45 \pm 1.45$	$0.39 \pm 0.13$	$8.2 \pm 1.7$	$0.42 \pm 1.00$	$0.41 \pm 0.10$
3rd year of GH	$7.4 \pm 2.3$	$0.49 \pm 0.83$	$0.43 \pm 0.11$	$6.3 \pm 2.5$	$0.55 \pm 0.96$	$0.47 \pm 0.15$

**PAO-121****A case of osteopetrosis tarda in childhood presenting with polyarthralgia and rickets**

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**Background:** Osteopetrosis refers to a clinically and genetically heterogeneous group of rare, heritable disorders of the skeleton characterized by increased bone density resulting from abnormalities in osteoclast differentiation or function. Based on clinical features, mode of inheritance and pathogenetic mechanisms osteopetrosis is classified into several distinct entities ranging in severity from asymptomatic to fatal in infancy. Osteopetrosis tarda (autosomal dominant osteopetrosis) typically has onset in adolescence and adulthood and the main complications are confined to the skeleton, including fractures, scoliosis, hip osteoarthritis and osteomyelitis.

**Objective and hypotheses:** To present the clinical features of a child presenting with osteopetrosis tarda.

**Methods:** An 8-year old girl was admitted suffering from back, neck and ankle pain for six months. She was born to nonconsanguineous parents with a birth weight of 3600 grams. At the age of 4 she was referred for pain in thumb, wrist and knees and was diagnosed as having reactive arthritis. She had broken her finger in an accident 1 year ago. Family history was unremarkable except her fathers' broken fingers and metacarpals after a minor trauma. Physical examination revealed no pathological sign with a height of 138 cm (SDS 1.46) and weight 34 kg (SDS 1.24).

**Results:** Laboratory studies showed mild anemia and normal biochemistry with mildly elevated values of PTH (78.4 pg/ml, normal range 12-72) and osteocalcin (30.2 ng/ml, normal range 3.2-13.7) and a low 25-hydroxy vitamin D level of 58 nmol/L (normal range 80-250 nmol/L). Radiographic examination revealed findings of generalized osteosclerosis, sandwich vertebra and thus diagnosis of osteopetrosis tarda and rickets was made. After stoss therapy her complaints have diminished and PTH level was normalized (51 pg/ml).

**Conclusions:** Osteopetrosis tarda is generally diagnosed incidentally in adolescence and adulthood but it may also present in childhood with mild anemia, fractures, polyarthralgia and rickets as in our case.

## PAO-122

### Multiple endocrine complications of allogeneic hematopoietic stem cell transplantation

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**Background:** Since the 1980s, hematopoietic stem cell transplantation (HSCT) has been performed for malignant and non-malignant disorders leading to increasing numbers of long-term survivors. Some of them have endocrine complications that arise many years after the end of the initial disorder treatment.

**Objective and hypotheses:** We present the 16,5 year-old girl with endocrine complications after treatment of acute lymphoblastic leukemia diagnosed at the age of 10.

**Method:** First chemotherapy was complicated with an acute pancreatitis after L-asparaginase. Eight months after diagnosis an allogeneic HSCT from HLA-matched sibling donor was performed. In the conditioning regimen fractionated total body irradiation and high-dose etoposide were used. After HSCT several early and late complications occurred: bacterial and mycotic infections, engraftment syndrome with renal and respiratory failure, graft versus host diseases (GVHD) and pancreatitis.

**Results:** We observed multiple endocrine complications successively appearing after HSCT: i) transient carbohydrates metabolism disorders in first days, followed by regular diabetes requiring insulin therapy, ii) euthyroid sick syndrome in first months, then an overt primary hypothyroidism treated with L-thyroxin, iii) transient hyponatremia due to SIADH syndrome, iv) growth hormone deficiency supplemented with recombinant human growth hormone since second year after HSCT until the age of 16 according to the patient's decision, v) delayed spontaneous puberty followed by secondary amenorrhea requiring an estrogen-progesterone replacement therapy, vi) low bone mineral density detected in repeated densitometry examination, in spite of calcium and vitamin D supplementation, vii) some elements of metabolic syndrome in spite of diabetes with insulin resistance, as high blood pressure, and dyslipidemia.

**Conclusions:** The significant endocrine complications of HSCT in the presented patient were associated with radiation exposure, but were also related to some chemotherapeutic agents, GVHD, and prolonged corticosteroid exposure.

## PAO-123

### Central hypothyroidism following chemotherapy for acute lymphoblastic leukemia

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**Background:** Thyroid dysfunction is frequently reported in patients treated with radiotherapy for childhood cancer. However, it has been suggested that chemotherapy per se might also impair the hypothalamus-pituitary-thyroid axis.

**Objective and hypotheses:** We examined 8 patients, out of a cohort of 31 subjects treated for acute lymphoblastic leukemia (ALL) with chemotherapy alone, who showed, during the follow-up, thyroid findings consistent with central hypothyroidism (CH).

**Methods:** The patients were diagnosed with ALL at a mean age (range) of 3.8 (0.3-6) years and were, at the time of the study, for 6 years (range 6-13) off therapy. Auxological data were recorded and TSH, fT4, thyroid peroxidase and thyroglobulin antibodies, cortisol and IGF-I were evaluated and a thyroid ultrasound was performed. Four subjects, who gave their consent, underwent a TRH test and a MRI scan of the hypothalamic-pituitary region.

**Results:** All subjects showed basal TSH above the normal range, while fT4 was abnormally low in two patients only. fT3 was always in the normal range. After TRH infusion, an increase in TSH serum level was observed; however,

2 patients showed an exaggerated TSH increase while 3 patients showed a slow TSH decline. Two patients showed an impaired fT3 net increase.

**Conclusions:** Our study shows that central hypothyroidism could arise at any time after childhood leukemia following only chemotherapy treatment. Although overt hypothyroidism was detected in only two patients, a careful follow-up of the thyroid function is recommended also for not irradiated ALL survivors.

## PAO-124

### Hyponatremia, hypothyroidism and metabolic acidosis

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**Background:** Severe hyponatremia with hyperkalemia and dehydration is an uncommon but life-threatening occurrence in infancy.

**Objective and hypothesis:** To highlight the importance of diagnosis and treatment of hyponatremia in infancy.

**Method and results:** A two month old female patient with a history of first degree parental consanguinity admitted to hospital with failure to thrive. At initial examination her weight was 2990 gr. height was 53 cm and she was hypotonic. Laboratory evaluation revealed serum sodium concentration 108 mEq/l, potassium 5.3 mEq/l, chloride 71 mEq/l. She received saline solution, hydrocortisone and fludrocortisone with an initial diagnosis of adrenal failure. Additional evaluation was not remarkable with adrenal failure since ACTH was 18.8 pg/ml (10-70 pg/ml), 17-OH Progesteron, 7.7 ng/ml (1.7-17 ng/ml), cortisol, 14 mcg/dl (3-23 mcg/dl), DHEA-S: 35 mcg/dl (<45 mcg/dl) and aldosteron was 408 pg/ml(20-1300 pg/ml). Urinary sodium excretion was 27 mEq/l and serum osmolarity was normal. Thyroid replacement therapy was initiated because her TSH and FT4 levels were 100 mIU/l and 0.47 ng/dl respectively. With the initiation of L thyroxin therapy and with the exclusion of adrenal failure fludrocortisone was tapered. An immediate decrease in serum Na levels was seen and fludrocortisone was restarted. Metabolic diseases that can because hyponatremia was excluded with normal lactic acid, pyruvic acid, tandem mass and quantitative urinary amino acid levels. She was noted to have increasing values of urea, creatinine and uric acid and intermittent metabolic acidosis on the second week of her hospitalization. She died with metabolic acidosis and septic shock on the 6th week of admission.

**Conclusion:** The patient was negative for NR3C2, SCNN1B, SCNN1G and a heterozygous genetic variant in SCN1A gene (pThr663Ala) was found. Glycolisation deficiency disorder, systinosis and membrane transport defects (Pendrin mutation) was thought in the differential diagnosis of these two siblings.

## PAO-125

### Intractable hypercalcemia following transplantation for osteopetrosis

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**Background:** Autosomal recessive osteopetrosis is characterized by insufficient osteoclast activity resulting in defective bone resorption and marked increase in skeletal mass and density.

Osteopetrosis results in generalized sclerotic bones and bone marrow failure. Allogeneic bone marrow transplantation(BMT) is the only treatment for cure, secondary to engraftment of donor-derived functioning osteoclasts resulting in remodeling of bone and establishment of normal hematopoiesis. One of the complications following a successful BMT is hypercalcemia that is a unique complication in this group of patients.

**Methods and results:** We report a three-yr-old girl with osteopetrosis who developed hypercalcemia following the successful bone marrow transplantation. These findings indicated an active donor-derived osteoclastic function and thus bone resorption following the successful donor engraftment in the patient. Her calcium level was 14.8 mg/dL at postBMT 10 days, therefore calcitonin (4 IU/kg sc every 12hr) as well as hyperhydration and furosemide were started. However, the calcium level increased to 16.8 mg/dL at post-BMT 13 days, and then intravenous pamidronate (15mg/BSA) and steroid (methylprednisolone 1mg/kg every 12hrs) was started. At that evening, she

was very irritable with more increased calcium level of 18.2 mg/dL. Her status was considered malignant hypercalcemia, therefore we started continuous renal replacement therapy. After two days, the calcium level decreased to 13 mg/dL without any adverse events, and CRRT had been maintained for six days. At present (postBMT 45 days), her calcium level below 11 mg/dL with weekly pamidronate, daily calcitonin and daily methylprednisolone with tapering dose.

**Conclusions:** In conclusion, hypercalcemia is common in patients with osteoporosis after BMT. If the conventional therapeutic strategies including isotonic saline, furosemide and calcitonin would not be successful, continuous renal replacement therapy should be considered seriously to prevent severe adverse events of hypercalcemia.

#### PAO-126

### Vitamin D status in pediatric patients with malignancy

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**Background:** Multiple studies demonstrated an inverse association between vitamin D and its metabolites and cancer morbidity and mortality. Despite this impressive body of evidence, only a handful of studies estimated vitamin D status in pediatric patients with malignancy.

**Objective and hypotheses:** Our aim was to assess vitamin D status in a large cohort of pediatric cancer patients and survivors, and to define risk factors to vitamin D deficiency. We hypothesized that 25OHD levels will be low in this population, particularly among actively treated patients.

**Methods:** 25OHD levels were obtained in 154 consecutive patients (aged 12.1±5.9y, M=76) during their routine visits to the hemato-oncology department (mean time from diagnosis 4.4±3.9y). Patients or their parents were asked to answer a questionnaire regarding calcium intake and sun exposure habits.

**Results:** Average daily calcium intake was 742.1±415.5mg/day. Mean 25OHD levels were 21.8±8.2ng/ml. Eighteen patients (11.8%) were vitamin D deficient (<11ng/ml), and another 87 (80.3%) were vitamin D insufficient (11-32ng/ml). Only 12 patients (7.9%) were vitamin D sufficient. Younger age and the amount of sun exposure were associated with higher serum 25OHD levels ( $r=-0.24$ ,  $p=0.003$ ;  $r=0.21$ ,  $p=0.008$ , respectively). No association was found with sun protection habits, calcium intake, disease type, gender, years since diagnosis, or undergoing stem cell transplantation.

**Conclusions:** The prevalence of vitamin D deficiency and insufficiency in pediatric hemato-oncology patients is high, while daily calcium intake is significantly lower than the RDA. While these values may be similar to those of the general pediatric population in Israel, they are of particular concern in this patient population, which is at high risk for osteoporosis. Furthermore, given the current knowledge regarding the importance of vitamin D in the context of malignancy, maintaining an adequate vitamin D status may be important for recovery and prevention of recurrence of pediatric malignancy.

#### PAO-127

### Quantitative ultrasound evaluation of bone status in obese children with or without metabolic syndrome

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**Background:** The relation between metabolic syndrome (MS) and bone metabolism is not clear, because MS has both conflicting factors of osteoporosis; one with a protective property, obesity, and another one which can activate bone resorption, inflammation. We evaluated bone status with quantitative ultrasound (QUS) technique in pediatric obese subjects with or without MS.

**Methods:** Phalangeal QUS measures for amplitude-dependent speed of sound (ADSos) and bone transmission time (BTT) were obtained in 56 obese

patients (30M/26F; mean age 12.92±1.63) with BMI>97th percentile for their age and sex. Bone parameters were expressed as Z-score based on age-sex-matched normal controls. Patients were classified as having MS according to Pediatric International Diabetes Federation. Insulin sensitivity was calculated by the homeostasis model assessment (HOMA) and impaired insulin sensitivity (IIS) was defined as a HOMA-IR of 4 or higher. In all pts complete blood count and CRP were performed.

**Results:** MS was present in 10/56 (17.8%); 7 of these pts had IIS ( $p=0.02$ ). Mean ADSos Z-score was  $-1.07±1.1$  (males  $-1.19±1.25$  vs females  $-0.92±0.9$ ,  $p=0.36$ ) and mean BTT Z-score  $-0.18±1.3$  (M.  $-0.41±1.25$  vs F.  $0.07±1.35$ ,  $p=0.18$ ), without significant difference in subjects with or without MS (ADSos Z-score  $-1.16±0.82$  vs  $-1.05±1.16$ ,  $p=0.89$ ; BTT Z-score  $-0.06±1.11$  vs  $-0.21±1.35$ ,  $p=0.74$ ). ADSos and BTT Z-scores were reduced in 10 (2 with MS,  $p=1$ ) and 4 subjects respectively (none with MS,  $p=0.17$ ); bone event was not found. None subject presented signs of inflammation.

**Conclusions:** In our patients normal bone parameters were found, without significant difference in pts with or without MS. Probably, in obese children the inflammation is low and protective role of obesity is predominant on the bone status.

#### PAO-128

### Osteoporosis-pseudoglioma syndrome: clinical outcome after treatment with growth hormone and bisphosphonates

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**Background:** Osteoporosis-Pseudoglioma Syndrome (OPPG, MIM 259770) is a very rare genetic autosomal recessive condition characterized by early blindness and bone fragility with fractures. The affected gene is called LRP5, located at the chromosomal region 11q13.4. Recently, the combined growth hormone (GH) and bisphosphonates treatment in OPPG patients was proposed.

**Objective:** To present the case and the clinical evolution of a 10 year-old Rumanian girl with OPPG, confirmed by the identification of a mutation in exon 11 of the LRP5 gene (c.2409\_2503+79del174), who was treated for one year with GH and intravenous bisphosphonates.

**Case report:** She was the third child of healthy non-consanguineous parents. Sibs were apparently normal but she has two maternal cousins, living in Rumania, who are blind. She was first seen in our Hospital at the age of 10 years. She weighted 23.5 kg (<3%), measured 110 cm (<3%) and had a head circumference of 48,5 cm (<10%). She was disproportionate with shortening of the upper segment secondary to a severe kyphoscoliosis. She could not walk. Extremities were not deformed neither had visible fracture calluses. She had hypotonia and hyperextensible joints. She had bilateral microphthalmia, cataracts and entropion. Bilateral horizontal nystagmus was also present. She was blind.

**Laboratory analyses included:** Calcemia: 10,3 mg/dL, phosphatemia: 5 mg/dL, alkaline phosphatase: 221 U/L, PTH 43,4 pg/mL, 25(OH)D3: 28 ng/mL, osteocalcine: 17 ng/mL, all in normal ranges.

**Skeletal survey:** Generalized osteopenia, thin long bones, flattened dorsal vertebrae, pectus carinatum and deformed chest. Epiphyses were normal. No anomalies were found in the skull. Bone densitometry (L1-L4): 0,378 g/cm<sup>2</sup> (-4 SD for age). She was treated with Pamidronate, calcium, vitamin D and GH.

**Conclusion:** After 1 year of treatment, the intravenous pamidronate therapy was safe, bone mineralization increased (-2,5 SD for age) and fracture rate and pain decreased. Further follow-up is needed in order to confirm the long term efficacy of this treatment.

### Evaluation of cardiovascular risk factors in children with classical congenital adrenal hyperplasia due to 21-hydroxylase deficiency

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**Background:** Classical Congenital Adrenal Hyperplasia (CAH) may present some traits of the metabolic syndrome.

**Objective:** Aim of this study was to investigate cardiovascular and metabolic risk profiles in children and adolescents with classical CAH.

**Subjects and methods:** We compared 20 classical CAH patients (10 males and 10 females, age range 9-19 years) with 20 age- and sex-matched controls. Anthropometry, lipids, blood pressure, fasting glucose concentrations, serum insulin levels and insulin sensitivity were studied. Adiposity was expressed as BMI SDS. Waist Circumference (WC) and Waist-to-Hip Ratio (WHR) were used to evaluate visceral adiposity.

**Results:** BMI SDS was significantly higher in patients than controls ( $0.9 \pm 0.9$  vs  $-0.13 \pm 1.53$ ;  $p=0.008$ ). Five patients (25%) and two controls (10%) had a BMI SDS of  $>2.0$ . WC, but not WHR, resulted significantly higher in patients than in controls ( $82.9 \pm 13.7$  vs  $72.77 \pm 13.6$ ;  $p=0.01$ ). No differences were found for lipid parameters and mean systolic and diastolic blood pressures between the two groups. Fasting insulin levels ( $12.0 \pm 7.6$  vs  $5.1 \pm 5.08$ ;  $p=0.003$ ) and HOMA index ( $2 \pm 1.34$  vs  $0.98 \pm 1.03$ ;  $p=0.01$ ) were significantly higher in CAH patients, compared to controls. A significant correlation was observed between WC and BMI SDS ( $r=0.78$ ,  $P<0.0001$ ), fasting insulin levels ( $r=0.4525$ ,  $p=0.04$ ) and HOMA ( $r=0.45$ ,  $p=0.04$ ).

**Conclusions:** Children with classical CAH are at risk for increased BMI, obesity, hyperinsulinism and reduced insulin sensitivity. WC is an accurate predictor of these metabolic abnormalities and thus it should be monitored during follow-up in patients with classical CAH.

### Successful switching from insulin to oral sulfonylureas in neonatal diabetes mellitus patients

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**Background:** Neonatal diabetes mellitus (NDM) may be defined as hyperglycemia diagnosed within the first 6 months of life and can result from mutations in the Kir6.2 or sulfonylurea receptor 1 (SUR1) subunits of the ATP-sensitive K<sub>v</sub> channel. Transfer from insulin to oral sulfonylureas in patients with NDM due to Kir6.2 or SUR1 mutations is well described.

**Objective and hypotheses:** Determine gene mutation of KCNJ11 and ABCC8 in NDM patients; assess the results of oral sulfonylureas therapy replacing insulin injection.

**Methods:** Case study: 5 patients suffer NDM at 45, 35, 47, 36, 44 days of age, respectively with ABCC8 or KCNJ11 mutations are treated in National Hospital of Pediatrics, Vietnam.

**Results:** 2 patients has heterozygous for a missense mutation on KCNJ11: R201H (p.Arg201His) & R201C (p.Arg201Cys); 3 patients with ABCC8 mutations: missense R1183W (p.Arg1147Trp), nonsense E747X and compound heterozygote for E747X & E128K. All 5 patients switched from insulin to sulfonylurea therapy at 5 years, 2.5 years, 7 years, 5 years and 8 months of age, respectively. Before of switching, HbA1C levels were 9.9; 6; 6; 8.3; 5.8 percent with insulin dose of 1.1; 0.5; 0.2; 0.5; 0.67 UI/kg/d, respectively. After 15; 10; 3; 5 and 5 days, they successfully discontinued insulin, respectively. HbA1C levels improved in 3 first patients (to 6.3; 6.2; 6.1 percent after 12 weeks of treatment) other patients has received sulfonylureas for 5 days. Improved glycaemic control was sustained at one year.

**Conclusions:** KCNJ11 & ABCC8 mutations for NDM has been determined in Vietnam and treatment with sulfonylureas.

### A child with concomitant precocious puberty secondary to factor V leiden mutation and type II diabetes mellitus

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**Background:** In children, the prevalence of type 2 diabetes (T2D) is increasing worldwide. At diagnosis, most patients have a positive family history of T2D. Heterozygosity for Factor V Leiden mutation (FVLM) leads to a 3-fold increase in relative risk of venous thrombosis. The most common causes of precocious puberty are organic cranial lesion such as tumors, trauma, cerebral anomalies, anoxic encephalopathy, in males.

**Case:** An eight year-old-boy was presented with polyuria. He was diagnosed as cerebral venous thrombosis secondary to FVLM two years ago. The patient's father also was diagnosed as T2D and FVLM. Due to cerebral stroke the patient was on artificial ventilation with BIPAP, has spastic paraplegia and no verbal response. His weight was 40 kg (97th p), height couldn't measured because of spasticity. Testes volume was Tanner stage 2, pubic hair Tanner stage 3. Basal LH (2.8 IU/L), FSH (2.38 IU/L) and testosterone (0.55 ng/ml) levels of the patient were found pubertal. The other hormonal evaluation was normal. He was diagnosed as central precocious puberty with basal hormonal evaluation. Cranial and pituitary Magnetic Resonance was revealed encephalomalacic changes secondary to cerebral thrombosis. We considered that his central precocious puberty was secondary to cerebral thrombosis and anoxic encephalopathy. His blood glucose was measured 350 mg/dl with ketone in urinary analysis and no acidosis, he was diagnosed as diabetes mellitus and treated with insulin. All antibodies for type 1 diabetes were negative. HbA1c was high for his age (%10.4). Because of high C-peptide (14.7 ng/ml) the patient was diagnosed as type 2 diabetes. He was discharged with metformin and basal insulin glargine treatment.

**Conclusions:** In this report we presented an eight-year-old boy with concomitant precocious puberty, T2D and positive family history for these diseases.

### Element and thyroid status in newborns from mothers with Graves' disease

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**Aim:** To study effect of Graves' disease (GD) of a mother in region with severe iodine deficiency, on element and thyroid status of a newborn.

**Materials and methods:** We examined 36 newborns in two groups. 1st group (n=18) included newborns born from mothers with GD receiving adequate thyrostatic therapy and the 2nd one (n=18) including those born from the untreated mothers with GD. Content of microelements in hair was measured by means of instrumental neutron activation method at the Institute of Nuclear Physics, Uzbekistan Academy of Sciences.

**Results:** Confidently high content of iodine was found in the 1st group newborns hair as compared with those in the 2nd ( $22.77 \pm 13.33$  versus  $10.48 \pm 4.95$ ... $p=0.04$ ), calcium and iron proportions being confidently lower in the 1st group (Ca:  $1038.89 \pm 27055$  versus  $3468.89 \pm 243.52$ ,  $p<0.001$ ; Fe:  $90.48 \pm 28.41$  versus  $140.73 \pm 118.41$ ,  $p<0.02$ ). In the 1st group newborns thyroid status parameters were close to normal (TSH:  $2.52 \pm 0.29$  mIU/l; T3  $1.69 \pm 0.11$  nmol/l; T4:  $111.1 \pm 10.9$  nmol/l), no case of neonatal transitory thyrotoxicosis (NTT) being registered. Only in one newborn isolated T4 increase with normal TSH and T3 was found. On the contrary, in the 2nd group NTT was found in 6 (33.3%) examinees, transitory neonatal hypothyroidism being registered in one (5.6%). In this group thyroid status parameters were as follows, TSH:  $0.77 \pm 0.24$  mIU/l; T3:  $2.59 \pm 0.1$  nmol/l and T4:  $148.8 \pm 7.95$  nmol/l,  $p<0.05$ .

**Conclusions:** 1. Inadequate thyrotoxicosis compensation in patients with gestational GD results in neonatal transitory thyrotoxicosis and transitory neonatal hypothyroidism in 33.3% and 5.6% of newborns. 2. In newborns from mothers with the untreated gestational GD confidently high proportions of calcium and iron were found to be the evidence for the enhanced elimination of the elements from the organism.

## PAO-133

### Isolated 17,20-lyase deficiency with testicular regression

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**Background:** The CYP17A1 gene encodes P450c17 and is expressed in adrenal and gonads. Mutations of this gene is the cause of combined 17-hydroxylase/17,20-lyase deficiency or in very rare cases isolated 17,20-lyase deficiency. Disturbance of sex steroid production leads to disorder of sex development in 46 XY individual and failure of pubertal development in 46 XX individual.

**Case report:** A 2 years old male patient referred as bilateral undescended testis. He has been investigated for disorders of sex development. Physical examination revealed bilateral non-palpable gonads and hypoplastic scrotum, penile size was 3.2 x 1.5 cm (lower limit for age). In baseline hormonal analysis; total testosterone and androstenedione levels were low, while FSH and LH were elevated. ACTH (250 µg) and hCG stimulation tests were performed in order to evaluate adrenal and gonadal steroidogenesis. There was not meaningful increase in testosterone, androstenedione. DHEAS was low (0.54 µg/dl, N: 5-57 µg/dl). Cortisol production was normal. Normal deoxycorticosterone level and absence of water retention, hypertension or hypokalemia dissuaded us from thought of 17-hydroxylase deficiency. The karyotype was 46 XY, testes could not be detected by ultrasonography. In laparoscopic examination gonads could not be found, but some remnant structures had been excised. Histopathologic investigation of these remnants revealed immature testis tissue with focal dystrophic calcifications and significant hyalinization which adjust to testicular regression syndrome.

**Conclusion:** Isolated 17,20-lyase deficiency is a rare cause of deficiency in sex steroid production. Normal penile formation and absence of Müllerian structures are proofs of normal testicular functions in critical time (12th-14th gestational weeks). This patient who had been presented with two different clinical entities made us think; either a coincidental condition or evoked testicular regression syndrome by impaired steroidogenesis.

## PAO-134

### Bilateral adrenal hemorrhage in a neonate

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**Background:** Adrenal hemorrhage is a rare yet potentially life-threatening event that occurs both in traumatic and in a variety of nontraumatic conditions. The incidence of acute adrenal hemorrhage in infancy range from 0.2 to 3%. Only 5% to 15% of cases reported have bilateral hemorrhage. We report on a neonate with bilateral adrenal hemorrhage associated with thrombophilia.

**Case report:** On day 3 of life the child, a female, presented signs of neonatal sepsis. On day 7, an occasional abdominal ultrasound revealed bilateral adrenal hemorrhage. However, the adrenal function was still normal. On day 36, the child appeared pale and lethargic. Subsequent hormonal and biochemical assessment showed adrenal insufficiency and she, therefore, started therapy of Addisonian crisis with improvement of clinical condition and biochemical parameters.

She is now two years old and she is still receiving replacement therapy with Hydrocortisone and Fludrocortisone. Serial ultrasound evaluations showed a gradual decrease in size of the adrenal hemorrhage with calcifications involving the whole gland bilaterally by the third month of life. Investigations performed to evaluate the cause of adrenal hemorrhage showed heterozygous Factor V Leiden mutation inherited from her father, resulting in resistance to activated protein C, and homozygous MTHFR C677T polymorphism with no elevation of plasmatic homocysteine levels.

**Discussion:** The adrenal gland of the newborn is particularly vulnerable to hemorrhage. In this condition of vulnerability, it seems likely that sepsis and combined thromboembolic risk may have interact in causing bilateral adrenal

hemorrhage. Moreover, accumulating evidences suggest that the association of multiple haemostatic defects increases the risk of thrombosis. Thus, thrombosis might be considered as a cause of neonatal adrenal hemorrhage and pro-thrombotic risk factors should be investigated in case of familiar history of thrombophilia.

## PAO-135

### Registry of congenital adrenal hyperplasia in Vietnam

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**Aims:** The National Hospital of Pediatrics (NHP) in Hanoi is an 900 bed tertiary referral centre servicing approximately 40 million people from northern provinces of Vietnam. This audit was undertaken to analyze anecdotal reports of increasing patient numbers.

**Methods:** Retrospective review of all CAH patients registered at NHP from 1999-2010. Ethical clearance was granted by the NHP Directorate.

**Results:** At the start of 1999 there were 90 children with CAH managed at NHP. By December 2010 this increased to 551 (47% male and 53% female; 72% salt wasting CAH), representing a more than five fold increase over 11 years. Number of new cases doubled from 30 to 60 in 2009. Most children (72%) were diagnosed at less than 12 months of age (39% at less than 1 month of age); 70% of all children were younger than 10 years.

Formal mortality figures were low (6 known deaths), although loss to follow-up unknown. There are data to suggest persisting mortality from undiagnosed CAH (evidenced by low ethnic minority group representation; few children from remote provinces; higher average income of CAH families; gender ratio shift; reports of sibling deaths).

Patient to paediatric endocrinologist (551:6) ratios at NHP are very high compared with higher income countries.

**Conclusions:** The caseload of CAH at NHP has increased since 1999 and additional capacity is needed for patient care given high patient to staff ratios. Introduction of NBS would enable more accurate estimation of CAH incidence, reduce infant mortality and minimize trauma to affected infants and their families.

## PAO-136

### Ethnic background influences the distribution of body fat in obese children and adolescents

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**Background:** The ethnic background, sex and pubertal progression determine body fat in growing children. These factors could also influence the deposition of excess adipose tissue in obese children and adolescents, with potential metabolic impact.

**Objective and hypotheses:** Our aim was to compare the amount and distribution of body fat between obese Latino and Caucasian children and adolescents and their eventual metabolic repercussions.

**Methods:** One-hundred obese children [11.5 ± 2.9 years; 4.1 ± 1.4 BMI-SDS; 53 females/47 males; 57 Caucasian (C)/ 43 Latino (L)] were studied. Glucose, insulin, uric acid, cholesterol and triglyceride levels were measured. Body composition (DXA) and abdominal MRI and ultrasonography were performed in all patients.

**Results:** Both ethnic groups showed similar ratios of visceral and subcutaneous (SQ) abdominal fat in the MRI.

DXA scans showed that Latinos had higher trunk to whole body (T/WB);

L:0.49 ± 0.03 vs. C:0.47 ± 0.03; p<0.05) and trunk to lower limb (T/LL; L:1.43 ± 0.27 vs. C:1.29 ± 0.21; p<0.05) fat ratios, as well as a higher rate of liver steatosis (X2:7.629; p<0.01).

When analyzing exclusively prepubertal children (n=41), MRI showed a higher percentage of SQ abdominal fat in Caucasians (C:82.6±9.1 vs. L:73.4±18.0%; p<0.05).

No inter-ethnic differences in body fat distribution were observed in pubertal males, whereas pubertal Caucasian females showed more subcutaneous (C:85.3±3.9 vs. L:81.6±4.7%; p<0.05) and less visceral abdominal adipose tissue (C:14.1±3.5 vs. L:18.2±4.5%; p<0.01) than Latino girls.

Independently of the ethnic background, a higher percentage of body fat was observed in prepubertal children vs. adolescents (p<0.01), as well as in pubertal females vs. males (p<0.001).

Caucasian prepubertal children and pubertal males had higher uric acid levels than Latino children (p<0.01 and p<0.05, respectively), whereas Latino adolescents had higher fasting glucose (p<0.05) than Caucasians.

**Conclusions:** Ethnic background, sex and pubertal stage influence the distribution of body fat and the metabolic profile in obese children.

#### PAO-137

### Diabetes complications in pediatric patients in Ukraine (results from 3 years follow up data based on Ukrainian pediatric diabetes register)

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**Background:** The aim of this study was to determine the frequency of acute and chronic complications of diabetes mellitus type 1 (DM1) at children 0-17 y.o. during the last 3 years based on the Ukraine Pediatric Diabetes Register (UPDR).

**Methods:** UPDR was established in 2004, it contains information about children with diabetes, 0-17 y.o.: their age, duration of DM1, frequency of acute (the severe hypoglycemia (Hypo) and diabetic ketoacidosis (DKA2, DKA3)), presence of chronic complications (diabetic cataract (DK), retinopathy (DR), nephropathy (DN), peripheral neuropathy (DNp), angiopathy of legs (DA), steatohepatosis (DS), lypodystrophy (DL), heiroopathy (DH) etc), frequency of children without complications (CWC), type and dose of insulin, the level of HbA1c.

**Results:** Based on the UPDR the number of children 0-17 y.o. with DM1 in 2007 was 6650, in 2008 – 6762, in 2009 - 6974, therefore prevalence increased over 3 years by 4,7% (especially in group of children 0-6 y.o. by 15,7%).

Table 1. The frequency of acute complications (%) and HbA1c level (%).

Years	DKA 2-3	Hypo	HbA1c
2007	6,04	0,45	8,9±1,52
2008	9,23	0,43	8,8±1,45
2009	11,39	0,57	8,9±1,44

Table 2. The frequency of acute complications (%) in children with different age.

Age	DKA 2-3			Hypo		
	2007	2008	2009	2007	2008	2009
0-5 y.o.	9,83	17,32	18,11	0,44	0,58	0,19
6-10 y.o.	5,32	9,24	12,06	0,31	0,23	0,43
11-14 y.o.	5,82	8,98	12,14	0,58	0,63	0,75
15-17 y.o.	5,94	7,90	9,32	0,41	0,33	0,58
Total	6,04	9,23	11,39	0,45	0,43	0,57

Table 3. The frequency of chronic complications (%).

Years	DK	DR	DN	DA	DNp	DL	DH	DS	CWC
2007	0,94	7,56	10,69	15,42	18,67	3,01	7,59	11,49	51,29
2008	1,92	8,52	11,43	19,14	19,31	7,29	8,55	16,12	47,68
2009	2,01	8,92	12,95	19,04	20,46	8,26	8,30	14,75	51,55

**Conclusions:** The main reason of increasing the frequency of chronic diabetic complications in Ukraine for the last 3 years is the using of the unified methods of diagnostics.

#### PAO-138

### Clinical presentation and its relationship with chromosomal abnormalities in Turner syndrome

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**Background:** Turner syndrome is a relatively common chromosomal disorder. The disease affects only females, causing hypogonadism and short stature. Early treatment can improve short stature and hypogonadism.

**Objective and hypotheses:** Describe chromosomal abnormalities, clinical characteristics and its relationship with chromosomal abnormalities in patients with Turner syndrome.

**Methods:** 116 patients with Turner syndrome diagnosed in National Hospital of Pediatrics, Hanoi. Method: A crosssection study was used.

**Results:** Mean age on diagnosis was 12.2 ± 4.9 years. Monosomy 45,XO occupied 54,31%; 45,X/46,XX was seen in 14.66%; 27.59% had structural disorders of chromosome X. Short stature was found in all patients aged more than 15 years. Severity of short stature and percentage of patients with short stature went up with age. There was no difference in term of height between karyotype groups. In group aged ≥ 12 years, 95.2% of cases had hypogonadism. Other symptoms frequently seen were nail hypoplasia (77.4%), cubitus valgus (74.7%), broad chest (69.2%) Abnormalities in face and neck were epicanthic fold (55.6%), low posterior line (51.3%), excessive skin in the back of the neck/webbed neck (42.5%). In a group aged <1 year, lymphoedema of hands/feet, epicanthic fold, broad chest, cubitus valgus were found in 100%. Majority of symptoms, congenital defects of heart/kidney were seen more frequently in 45,X group.

**Conclusions:** Lymphoedema of hands/feet in infants, low growth velocity, delayed puberty, abnormalities in face and neck, and other symptoms should be checked to early diagnose and treat Turner syndrome. Patients with 45,X had more severe presentation compared to patients with 45,X/46,XX and structural abnormalities of X chromosome.

#### PAO-139

### Changing trends in epidemiology of type 1 diabetes mellitus in children and adolescents in Cyprus

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**Background:** The incidence of Type 1 diabetes mellitus (T1DM) has dramatically increased worldwide and it is estimated that it may reach the status of an epidemic in the 21st century.

**Objective and hypotheses:** To calculate the incidence of T1DM in Greek-Cypriot children aged less than 15 years between 1990 and 2009 and to examine any changes in the incidence between the two decades, to analyse gender differences in the age of onset and any seasonal variation at the manifestation of the disease.

**Methods:** All newly diagnosed cases of T1DM in children less than 15 year old were registered with the capture – recapture method from 1990 until 2009 and relevant information was obtained. The data were statistically processed in relation to the population data provided by the Department of Statistics and Research of the Ministry of Finance.

**Results:** The overall mean annual incidence of T1DM during this 20 year period is 12, 46/100000. By using the Wilcoxon two-sample test the mean incidence rate in the second decade 2000-2009 was significantly increased when compared to the first one (14.4 vs 10.46/100.000). There was an overall male predominance (M/F: 1.03) but not in the group who manifested T1DM at ages 10-15 years, where females prevail. The percentage of children who

developed T1DM at ages 0 – 5 years increased in the second decade (24.5 vs 17.4 %). The seasonal distribution at the time of diagnosis (higher incidence during winter and autumn months) disappeared in the second decade.

**Conclusions:** The incidence of T1DM in Cyprus is rising. The identification of environmental factors, which increase the risk of T1DM development in genetically susceptible individuals, will theoretically explain this phenomenon. New preventive strategies will therefore be developed if such factors that are implicated in the etiopathogenesis of T1DM will be recognized.

#### PAO-140

### A rare cause of primary ovarian failure in a 16 years old patient: 48,XXXX karyotype

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**Background:** 48,XXXX is a rare karyotype. Since first described in 1961, fewer than 60 patients have been described in literature as suffering from this condition. The main feature described is mental retardation. Some women have tall stature, as in other extra X chromosome karyotype (47,XXY, 47,XXX). Only three patients have been reported so far with primary ovarian failure. Irregular or normal menses are more often described.

**Case report:** Our patient was first seen in the paediatric endocrine ward at 16 years old for primary amenorrhea. She had a mild mental retardation and attended a special school. She had hyperphagic access and obesity, her parents also had obesity. Her pubertal status was A2P3S1 with important adipomasty giving a “false” stage 3 breast development. She had a tall stature (183 cm) above her target height (168.5cm) and had little finger insertion anomaly. Her bone age was 15 years as determined by the Greulich and Pyle method. Blood analysis showed high levels of gonadotrophins: luteinizing hormone: 25.6 mU/ml and follicle-stimulating hormone: 33.3 mU/ml and low level of estradiol 10 pg/ml, consistent with primary ovarian failure. Neither pelvic ultrasound nor MRI showed any ovaries. She had prepubertal uterus. She had chromosome analysis regarding to the amenorrhea associated with the mental retardation and it showed a 48,XXXX karyotype. Estrogen therapy was started to develop sexual secondary characters, close epiphyseal growth plates and prevent osteoporosis.

**Conclusion:** These features add data on height and ovarian function in 48,XXXX women. Mental retardation is often described in women with 48,XXXX but tall stature and primary ovarian failure are described in a few cases. This patient had obesity which is not, to our knowledge, described in literature. Not only small patients (Turner syndrome) but also tall women with primary amenorrhea should benefit from chromosome analysis.

#### PAO-141

### Pituitary enlargement due to partial IGF-I insensitivity

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**Background:** Until recently patients bearing partial GH or IGF-I insensitivity have been diagnosed as idiopathic short stature.

**Objective and hypotheses:** Few data are available regarding pituitary image in these patients.

**Methods:** We describe a 5.5 year-old girl that was seen at the emergency room with nausea, vomiting, headache and unilateral eye lid ptosis. Cranial MRI was normal and ophtalmoplegic migraine was diagnosed.

**Results:** Five years later a second MRI showed a 0.7x0.4cm pituitary lesion with suprasellar extension. Furthermore, a severe prognathism was observed. On the other hand, teeth gapping were normal, her hands and feet were delicate and there were no other signs of possible GH/IGF-I excess or hypopituitarism. Pubertal stage was B3P3. Serum IGF-I was 1490ng/dl (+6.1SDS). Daytime GH profile was suggestive of increased GH secretion as only 4 determinations were below the detection limit of the assay (0.1ng/ml). GH suppression (<0.1ng/ml) was confirmed by OGTT. Due to the severe prognathism, pituitary image and maintained elevated IGF-I levels, the diagnosis of

acrogigantism was considered and a surgical procedure was proposed. However, facing the slow size increase of the pituitary lesion an option for a regular follow-up was taken with laboratory and image control. Nowadays she is 16 years-old, bone age is 18yr and puberty is complete with regular menses. Laboratory determinations regarding pituitary function remain normal except for the IGF-I (consistently around +5.4SDS). MRI performed when she was 15 years-old showed an enlarged pituitary gland (1.2x1.1x0.8cm) with small suprasellar extension. Final height was 1.58m (-0.7SDS), below middle parental height.

**Conclusions:** After 10 years of follow up we believe that the lack of IGF negative feedback due to a partial IGF-I insensitivity could explain the high concentrations of GH and IGF-I with normal height and the pituitary image. Height velocity analysis was misled by puberty during the investigation.

#### PAO-142

### Comparison of injection dose force between three growth hormone injection pens:

#### NordiFlex®, FlexPro® and GoQuick®

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**Background:** A reduced injection force potentially makes it easier for patients to administer their injected medication.

**Objective and hypotheses:** This report compares dose force and dose accuracy of three growth hormone injection devices: Norditropin® NordiFlex® (NF), Norditropin® FlexPro® (FP) (both Novo Nordisk A/S, Denmark) and Genotropin® GoQuick® (GQ) (Pfizer Inc, NY, USA).

**Methods:** Mean of maximum dose force was determined for a 1.5 mg dose at speeds of 4, 6 and 8 mm/s for NF and GQ pens and the dose activation force was measured for FP in 25 pens of each type. Dose accuracy was assessed at 0.1, 0.75 and 1.5 mg doses (60 measurements at each level) in 30 pens of each type. All pens were fitted with a NovoFine 32 G x 6 mm needle. Testing was done at 20°C, 45% relative humidity. Dose force was measured with a tensile testing machine in compression mode (within specifications) Lloyd, LRx plus (ID: 24K-04-115) and transducer (measuring cell) of max 100 N (ID: 24K-04-082). Dose accuracy was assessed using an analytical balance (ID: MS7813) and METDose data system (ID: LP38188).

**Results:** Estimated relative dose force (N/N) for FP was significantly lower than for GQ (3.6, 4.4, 5.2; p<0.0001) and NF (2.5, 2.9, 3.5; p<0.0001) at all speeds (4, 6, 8 mm/s). Dose force for NF was reduced compared with GQ (1.4, 1.5, 1.5; p<0.0001). Dose accuracy at 0.10, 0.75 and 1.50 mg doses was 97, 99 and 99% for FP, 100, 95 and 97% for GQ, and 101, 99 and 99% for NF. Dose precision (CV, %) was 2.5, 0.8 and 0.8 for FP, 11.1, 2.6 and 1.6 for GQ and 3.8, 0.7 and 0.7 for NF.

**Conclusions:** Dose force was significantly lower for FP and NF than for GQ. Dose accuracy was not dissimilar between devices but dosing precision was improved with FP and NF vs. GQ.

#### PAO-143

### Virilization of a toddler girl by paternal use of testosterone cream

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**Background:** A 15-month-old healthy female was referred because of rapid growth of dark pubic hair and a high testosterone (T) level (9 nmol/L, normal value (N) < 0.45).

**Objective and hypotheses:** Demonstrate the cause of the patient's virilization.

**Methods:** Clinical and laboratory work up as well as imaging studies were performed to exclude the main causes of an androgen excess.

**Results:** Past medical history and review of systems were unremarkable. Family history revealed a 4 year-old brother and unrelated parents, all in good health. Weight (11 kg,+ 0.78 SDS), height (78.1 cm,+ 0.4 SDS) were nor-



mal, no growth acceleration was observed. Tanner stage II pubic hair and an enlarged clitoris (12 mm) were found. She had no palpable breast tissue or posterior labial fusion, axillary hair, or acne. Pelvic ultrasound showed prepubertal uterus but no adrenal or ovarian mass were visualized. Adrenal hyperandrogenism was ruled out based on normal values of 17-OHP (0.7 nmol/L; N<3), Androstenedione (<0.5nmol/L; N 0.38 ± 0.20) and DHEAS (<0.5 µmol/L, N 0.06 ± 0.04). Prolactine, thyroid function test and tumoral markers (β-hCG (< 2 U/L; N<5), αFP (5.5 kU/L; N<10)) were normal. Her father, a former elite athlete, reported that he was using a T-cream (T 10% in PCCA Lipoderm-Base®) for muscle problems the last 2-3 months. Four weeks after the father had ceased the treatment, T level decreased to 1.7 nmol/L. The child's clinical virilization signs regressed. We observed no sign of hyperandrogenism in her brother.

**Conclusions:** We describe a virilized toddler girl with isolated high T level due to transdermal intoxication. The differential diagnosis of virilization in childhood includes both endogenous and exogenous causes. Increased utilization of easily available cutaneous androgen applications should prompt clinicians to inquire about exogenous androgen exposure in the medical history of virilized children.

#### PAO-144

### Silent corticotrope adenoma – report of two cases

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**Background:** Some Pituitary adenomas exhibit immunoreactivity to hypophyseal hormones but because of the absence of clinical syndromes. They are known as silent adenomas. In 1979 Hassouny and collaborators describe the silent pituitary adenomas. In reference to corticotrope adenomas 43% are silent because they produced a biologically inactive hormone. They can be large and have a tendency to invade and recur.

**Objective and hypotheses:** We describe two cases of silent corticotrope adenomas in children.

**Methods and results:** CASE1: Nine years old boy presented with frontoparietal headaches, loss of vision, no hypertension, no obesity or evidence of Cushing syndrome. Laboratory: 8 am cortisol 4.2 µg/dl, TSH 2mIU/ml, prolactin 25.9 ng/ml. MRI revealed intrasellar mass of 3,7x2,4x2,4 mm. Treatment surgery, pathology revealed an ACTH producing adenoma Pituitary KI67 3%. Tumor recurred 6 months later. ACTH 15 pg/ml, cortisol 12µg/dl, similar results pathology but KI67 15%. Case 2 A fourteen years old girl had a craniopharyngioma removed a year before. She presented with headaches, visual loss and obesity, acantosis nigricans, no hypertension and no clinical manifestation of Cushing's syndrome. A solid suprasellar mass of 15x19,6mm in MRI. Surgical pathology revealed an ACTH producing Adenoma Pituitary KI67 1%. Post surgery ACTH 13,4 pg/ml, cortisol 7µg/dl, prolactin 20,4ng/ml.

**Conclusions:** Silent corticotrope adenoma are not associated with a clinical picture of hormone excess but they can cause pituitary damage and they have a tendency to recur. Clinical diagnostic is difficult.

#### PAO-145

### Karyotype-phenotype presentation and interim results of growth hormone (GH) treatment of girls with Turner syndrome (TS) in Belarus

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**Background:** TS is a genetic condition associated with different developmental anomalies including short stature.

**Objective and hypotheses:** This work aimed to verify clinical details and response to GH therapy of TS girls in Belarus with relation to karyotype.

**Methods:** Retrospective study of 81 TS patients in our Center.

**Results:** The mean age of TS diagnosis was 9.3±4.9 yrs; 7/81 (8.6%) girls, all 45,X, were diagnosed perinatally. Karyotypes distribution: 45,X - 45/81 (55.5%), mosaicism 45,X/46,XX - 22/81 (27.2%), abnormalities of an X chromosome - 11/81 (13.6%), mosaicism with Y chromosome - 3/81 (3.7%).

Congenital heart abnormalities were diagnosed in 59/81 (72.8%) of pts; 13/81 (16.0%) had bicuspid aortic valve, 6/81 (7.5%) - coarctation of the aorta. The number of severe heart problems tended to be higher in 45,X (p=0.15). Thyroid disorders were found in 63/81 (77.8%) of pts; 21/81 (25.9%) had AIT. Totally, 46/81 (56.8%) pts had hypothyroidism. Thyroid failure was more frequent in other than 45,X girls (61.1% vs. 53.3%, p>0.05). Seventeen pts (21%) had kidney abnormalities. GH therapy (0.33 mg/kg/wk) was initiated at the age of 11.1±4.9 yrs. Only 34.6% of pts were younger than 10 yrs at start of treatment. Baseline HSDS in the whole group was -3.4±1.2; time of GH treatment - 2.9±2.1 yrs, regardless of karyotype. The ΔHSDS were 0.7±0.5, 0.5±0.3 and 0.3±0.5 for year 1, 2 and 3 of GH therapy, respectively. Growth response was not correlated to karyotype. In 25 pts who completed GH treatment final height at 17.2 yrs was 148.4±4.8 cm. In 3.9±1.4 yrs of GH therapy they benefited 6.2±4.6 cm; height increase was + 1.5 cm/year.

**Conclusions:** TS in Belarus are manifested with high genetic variability and somatic abnormalities rates. Due to rather late diagnosis, GH therapy of TS in Belarus is often belated. Nevertheless, TS girls have good growth response.

#### PAO-146

### Late development of celiac disease in type 1 diabetes mellitus

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**Background:** Patients with type 1 diabetes mellitus (T1DM) are at a high risk for developing autoimmune diseases such as coeliac disease (CD). Although CD mainly occurs at T1DM onset, it can also develop in the following years, but in our experience never after 6 years from T1DM onset (Salardi et al, J Pediatr Gastroenterol Nutr 2008). There is no consensus as to the duration of follow-up for autoimmune diseases in T1DM. We report a case of a male who developed CD 15 years after the diagnosis of T1DM.

**Case report:** A 19 yr-old male diagnosed with T1DM at 4 years of age. HLA phenotype was DR 3, 4 and DQ 2, 3. His siblings were also tested for autoimmune diseases and the older sister developed CD and few years after autoimmune thyroiditis. Lab examinations for associated autoimmune diseases were performed annually. 13 years after T1DM onset Hashimoto's thyroiditis was diagnosed, not leading to clinical hypothyroidism. Unexpectedly, after 15 years from T1DM onset, he showed a marked positivity for CD autoantibodies (antitransglutaminase autoantibodies 128 u/ml, normal value <10). During the previous year he was completely asymptomatic: he did not refer gastrointestinal symptoms or an increased frequency of hypoglycaemic episodes. There were no biochemical signs of CD (ferropenic anemia, hypertransaminasemia, hypocalcaemia). Antibody positivity was also confirmed in another laboratory. Bowel biopsy showed a total villous atrophy.

**Conclusions:** The development of CD so far from diabetes onset (>15 years) has been never described before to our knowledge and the literature reports a follow up period never longer than 10 years. We conclude that screening for autoimmune disease should be annually performed in T1DM patients possibly lifelong, even in the absence of clinical symptoms, especially in those with a strong family history of autoimmune disease.

#### PAO-147

### A case of congenital hypothyroidism with Hirschsprung's disease: an unusual association

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**Background:** Hirschsprung's disease (HD) as well as congenital hypothyroidism can present with functional intestinal obstruction and abdominal distension in neonate. Both the diseases are considered as differential diagnosis, rather than as coexistence. We report one such interesting case with unusual coexistence between these 2 conditions.

**Objective and hypotheses:** Thyroid hormone is necessary for neuronal migration and lamination during brain development. Although hypothyroidism impairs colonic motility resulting in pseudo-obstruction the effects of hypothyroidism on neuronal migration through bowel have not been adequately studied.

**Methods:** A 21 days baby girl, product of consanguineous marriage presented

with vomiting and abdominal distension. Weight was 2.5 kg and length 48 cm. On examination, there was facial puffiness, open posterior fontanelles, dry skin, cold peripheries and prominent abdominal veins with visible peristalsis. There was no maternal history of hypothyroidism. Patient was subjected to various investigations.

**Results:** Routine hemogram, liver & kidney function tests were within normal limits. Plain abdominal radiographs revealed gas filled bowel loops with barium enema showing dilated proximal colon, empty rectum, delayed emptying time with funnel like transition zone between proximal dilated & distal constricted bowel (Image 1). TSH was > 150  $\mu$ IU/ml. Thyroid scintigraphy revealed athyreosis, confirming congenital hypothyroidism due to athyreosis. Biopsy following colostomy revealed aganglionic segment, confirming the diagnosis of Hirschsprung's disease. Baby was discharged with oral levothyroxine treatment.

**Conclusions:** With the present case, we propose that thyroid hormones may have a role in the development of HD. Further studies are needed to establish this.



#### PAO-148

### Metabolic syndrome in obese Ukrainian schoolchildren: prevalence and risk factors

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**Background:** Obesity in children and adolescents is currently on a rise in Ukraine, posing challenges to personal health and state health care system.

**Objectives:** To assess prevalence of metabolic syndrome (MS) among obese children and adolescents residing in Lviv, Ukraine, and risk factors leading to its development.

**Methods:** Obese children and adolescents were selected during annual (2009) medical check-up in 10 city schools. These were referred for further investigations. The major components of MS (abdominal obesity, hypertension, dyslipidemia, and glucose intolerance) were evaluated in a cross-sectional study. Potential risk factors for developing MS (weight at birth, parental obesity, degree of obesity, age, sex) were assessed in a multivariate logistic regression analysis.

**Results:** The nutritional status of 8523 school students aged 11 to 18 years showed that the prevalence of obesity (BMI  $\geq$  95%) is 9.1% (n = 776, boys = 381, girls = 395). The prevalence of MS among obese children reaches 14.3% (n = 111, boys = 62, girls = 49). The prevalence of MS tends to increase with increasing of BMI class (3.1% in class I, 6.2% in class II and 18.2% in class III). In a multivariate analysis more advanced age (OR = 4.08, CI = 3.13-6.24), BMI (OR = 2.71, CI = 1.34-5.47) and parental obesity (OR = 2.11, CI = 1.07-4.14) were found to be the most significant risk factors for having MS in obese children and adolescents.

**Conclusions:** Although lower than in neighbouring countries, the prevalence of MS in Ukrainian schoolchildren is growing, which warrants preventive measures. The older the obese child the higher are chances for MS. The most important preventable risk factors are degree of obesity (BMI) and parental obesity.

#### PAO-149

### Skeletal morbidity in children receiving chemotherapy for acute lymphoblastic leukaemia and its association with mineral homeostasis and duration of inpatient stay

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**Background:** Reduced activity, older age and abnormal bone mineral status are considered as important determinants of poor bone health in children with acute lymphoblastic leukaemia (ALL).

**Aim:** To investigate the influence of activity, age and mineral status over the first 12 months of chemotherapy on subsequent SM.

**Patients and methods:** The medical records of 56 children presenting with ALL between 2003 and 2007 and treated on UKALL 2003 were reviewed for the number of in-patient days over the first 12 months of chemotherapy as a surrogate marker of inactivity and lack of well-being. Data for serum Ca, Alb, Mg and Pho were also collected over this period. SM was defined as any episode musculoskeletal pain (MSP) or fractures.

**Results:** The median duration of in-patient days over the first 12 months of treatment in children with no SM was 58 days(40,100) whereas the median number of in-patient days during the first 12 months in those children with any SM, MSP only or fractures only was 83 days(54,131), 81 days(52,119) and 91 days(59,158), respectively(p=0.003). Children with SM and fractures particularly had lower levels of serum Ca, Mg and Pho compared to those without SM over the first 12 months of chemotherapy. There was a higher risk of SM in those who were diagnosed after the age of 8 years(p=0.001,OR=16.95%CI:3.80). Multiple regression analysis showed that the incidence of SM only had a significant independent association with age at diagnosis (p=0.001) and the number of inpatient days (p=0.03) over the first 12 months (r=23). All children who were diagnosed after the age of 8 years with an inpatient stay of greater than 75 days in the first 12 months of the chemotherapy (n,14) children had some form of SM (OR=64).

**Conclusion:** The incidence of SM in children receiving chemotherapy for ALL is associated with a higher likelihood of being older and having longer periods of in-patient stay. The close link between age and changes in bone mineral status may be one explanation for the increased bone morbidity in ALL children.

#### PAO-150

### Trends of body mass index in children with craniopharyngioma from the west of Scotland

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**Background:** Hypothalamic obesity is one of the major causes of reduced quality of life in survivors of childhood craniopharyngioma, predisposing the patient to a wide variety of complications, including cardiovascular disease.

**Objectives and hypothesis:** The aim of this study was to examine the trends of change in body mass index (BMI) in childhood onset craniopharyngioma patients over 5 years. The hypothesis being all children with a craniopharyngioma gain weight irrespective of their BMI at presentation.

**Methods:** This was a retrospective study of 23 children with a diagnosis of craniopharyngioma presenting to the West of Scotland regional endocrine unit over a 5 year period. Data on height, weight, gender and age was collected. BMI SDS for each patient was subsequently calculated and analysed over time. Patients were categorised into 2 groups according to their BMI at presentation, obese BMI >2SDS, non-obese BMI < 1.99SDS. Obesity was defined as patients having a BMI SDS.

**Results:** At presentation, (M: F 11:12) 47.5% (n=11) patients were obese, with 52.5% (n=12) non-obese patients. BMI increased further in 7 of the

obese patients. There was a rise in mean BMI SDS in the first year after diagnosis, followed by a fall in BMI over the 5 year period in both groups; however the obese group at presentation remained obese. In the non-obese group only 10 had an increase in BMI SDS from presentation, with 8 patients becoming obese during the 5 years.

**Conclusions:** Craniopharyngioma patients who are obese at presentation continue to gain weight and remain obese. This probably reflects a greater degree of hypothalamic damage in these individuals.

## PAO-151

### Pseudotumor cerebri and diabetes insipidus.

#### Association or coincidence?

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**Background:** Pseudotumor cerebri (PTC) is characterized by intracranial hypertension in the absence of clinical, laboratory or radiological evidence of space occupying lesion. It can occur in the pediatric population with an increasing incidence among adolescents, especially in obese females. Idiopathic PTC can be associated with anterior pituitary deficiency but there is no evidence in literature of association with central diabetes insipidus (CDI).

**Objective and hypotheses:** We report a case of PTC and concomitant CDI.

**Methods:** 13-yr-old obese female (BMI 2.64 SDS) presented progressive headache, important visual impairment followed by complete blindness, sixth cranial nerve palsy, bilateral papilloedema, right hemisindrome with alteration of the state of consciousness. MRI ruled out the presence of a cerebral mass as well as pituitary lesions, showing concave superior surface of pituitary gland with normal pituitary stalk; posterior pituitary bright spot was not described. Furthermore there was no evidence of cerebral venous thrombosis. High cerebrospinal fluid pressure: 30 mmHg. Autoimmune, vascular, infective and tumoral aetiologies were excluded (negative tumoral markers at the beginning and during follow up). Therapy: lumbar puncture+Acetazolamide. A week after diagnosis she developed polyuria and polydipsia (up to 17 L/day). Hormonal evaluations demonstrated CDI with normal anterior pituitary function. The patient started therapy with desmopressin with adequate hydro-electrolytic balance. Subsequently she was treated with Clobazam for frontal lobe dysfunction, associated to dysarthria and aimless movements of legs.

**Results:** During follow up (1 year), the intracranial hypertension gradually reduced. No more headaches were reported, but visual impairment and diabetes insipidus were still present, even if less severe. Neuroradiological follow-up remained negative for brain tumors.

**Conclusions:** We assume that the increased intracranial pressure might have altered the activity of hypothalamic osmoreceptors and baroreceptors, inducing a lower synthesis of ADH.

## PAO-152

### Maturity onset diabetes of the young (MODY) - presentation of two cases

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**Background:** Maturity onset diabetes of the young (MODY) is characterized by youth-onset diabetes that is inherited in an autosomal dominant pattern.

**Method:** The authors present characteristic features of MODY diabetes in two sisters.

**Results:** The family history has shown that the father and paternal relatives had moderately elevated blood glucose levels, down through successive generations.

**Case 1:** second child, gestational age at birth 38 weeks, birth weight 3200g, breastfed for five months. Case summary: two weeks of polyuria, polydipsia, decreased appetite, in the context of an upper respiratory tract infection. Clinical examination: 8 year-old girl, weight 24 kg, length 120 cm, BMI 17.1 kg/m<sup>2</sup>. Glucose levels ranged between 95-195 mg %, presence of glycosuria, with no ketones, HbA1c level 7.5%, negative anti GAD antibodies and

ICA antibodies. Treatment: diet and a dose of 0.5 IU/kg/day of insulin for 2 months, followed by the diet only, while keeping glucose values between 85-112 mg% and HbA1c level decreased to 6.5%.

**Case 2:** the 12 year-old sister was hospitalized after two months without clinical signs of diabetes, but with the ambulatory blood glucose levels between 112-138 mg%, HbA1c level 6%, OGTT with fasting blood glucose 124 mg% and 2-h postprandial blood glucose 174 mg%, negative anti GAD antibodies and ICA antibodies. Personal history: first child, with normal evolution of the pregnancy, gestational age at birth 36 weeks, birth weight 2600g, Apgar score 9, breastfed for four months, psychomotor and weight development according to child development stages. Clinical examination: weight 35 kg, length 143 cm, BMI 17.5 kg/m<sup>2</sup>. It was established a diet that maintained a good glycemic control; after 3 months HbA1c was 6.5%.

**Conclusions:** The main goal of treatment in these cases of MODY diabetes was to maintain blood glucose levels as close to normal reducing the risk of complications. An early diagnosis of the disease is very important for family screening and also for therapy and prognosis.

## PAO-153

### Long-term (five-year) height outcome in children treated with Norditropin®

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**Background:** The American Norditropin Studies: Web-enabled Research (ANSWER) Program®, a US-based registry, has collected long term efficacy and safety information on patients treated with Norditropin® (somatotropin rDNA origin, Novo Nordisk A/S) at the discretion of participating physicians.

**Objective and hypotheses:** To assess the long-term (5 years) height standard deviation score (HSDS) and ΔHSDS by age, gender, and pubertal status in children treated with GH.

**Methods:** Treatment-naïve pediatric patients with isolated/idiopathic GH deficiency (GHD; n=4454), multiple pituitary hormone deficiency (MPHD; n=387), small for gestational age (SGA; n=461), idiopathic short stature (ISS; n=758), and Turner syndrome (TS; n=435) were analyzed.

**Results:** Mean baseline ages (yrs) were generally younger in patients with MPHD (7.4), SGA (8.5), and TS (8.6) than with GHD (10.8) and ISS (11.2). Lowest peak GH levels were observed in patients with MPHD (3.1 ng/mL) and GHD (5.3 ng/mL). In the overall population, HSDS increased from -2.2 at baseline to -1.1 at Y3 and -0.9 at Y5, with GHD, MPHD, and SGA showing better growth response. Boys had significantly greater ΔHSDS than girls after 3 years or longer treatment duration (p<0.001). When stratified by baseline age, younger patients showed greater ΔHSDS than older patients for both genders (Table). In addition, children with GHD who remained pre-pubertal after 5 years of treatment had the greatest ΔHSDS (2.02±1.14) as compared to patients who were already pubertal at treatment start (1.42±0.69) or who transitioned into puberty during the study (1.58±0.68).

**Conclusions:** These results show that boys generally have greater height gain than girls after long-term treatment. A better growth response is observed in younger and pre-pubertal children, emphasizing the importance of starting GH treatment at a young age and pre-pubertal status.

Table. Mean (SD) ΔHSDS over 5 years by Age and Gender.

	Male N	All Males	Males < 11 yrs	Males ≥ 11 yrs	Female N	All Females	Females < 10 yrs	Females ≥ 10 yrs
Y1	3632	0.53 (0.49)	0.73 (0.57)	0.39 (0.35)	1659	0.55 (0.50)	0.70 (0.55)	0.39 (0.39)
Y2	2595	0.96 (0.65)	1.16 (0.71)	0.80 (0.53)	1142	0.96 (0.70)	1.12 (0.73)	0.78 (0.61)
Y3	1645	1.27 (0.77)	1.39 (0.83)	1.13 (0.66)	733	1.20 (0.84)	1.26 (0.88)	1.10 (0.78)
Y4	965	1.47 (0.83)	1.55 (0.89)	1.35 (0.68)	411	1.34 (0.89)	1.35 (0.92)	1.31 (0.81)
Y5	443	1.65 (0.91)	1.70 (0.97)	1.52 (0.62)	194	1.41 (0.95)	1.41 (0.99)	1.38 (0.70)

**PAO-154****Role of prophylactic medical examination for early diagnosis of endocrine disorders***Alexey Resnenko<sup>1</sup>; Leila Namazova-Baranova<sup>2</sup>*<sup>1</sup>Scientific Center of Children's Health, Diagnostic, Moscow, Russian Federation; <sup>2</sup>Scientific Center of Children's Health, Head, Moscow, Russian Federation

**Background:** Considerable increase of endocrine disorders in pediatric population within last years was observed. Routine children and adolescent check up does not include examination by endocrinologist.

**Objective and hypotheses:** To estimate rate of endocrine disorders in pediatric population we explored 911 Moscow schoolers.

**Methods:** All children were split into groups by sex (sex ratio was 54% boys to 46% girls), age (junior school -from 6 to 11 years, middle school from 11 to 14 years, senior school- from 14 to 17 years). Physical examination, anthropometric measuring, and thyroid ultrasound were performed. On the base of measurements BMI, height velocity and standard deviation score of measurements were estimated.

**Results:** 12% of children had signs of endocrine disorders. Leading position belongs to overweight and obesity (61% of revealed endocrinological disorders). 25% of children with endocrinological disorders had thyroid gland enlargement. 9% had growth abnormalities (7% cases of short stature and 2% cases of high stature), abnormalities of sexual development were revealed in 5%. 9% of children with detected endocrine disorders had two of more diagnosis. Our data shows that overweight and obesity more common for middle and senior school groups and had no significant differences between sexes (sex ratio for overweight and obesity was 51% boys to 49% girls). Thyroid abnormalities predominate at the age of 11-17 years and more common for female population (sex ratio was 13% boys to 87% girls). Most children with growth abnormalities revealed at age 7-14 years, and sex ratio was 82% boys to 18% girls. 5% of boys and 95% of girls with endocrine disorders had sexual development abnormalities with predominance at the age of 11-17 years.

**Conclusions:** Results of our study show importance of endocrine function assessment in school-age children on a regular basis. This tactics helps to reveal possible endocrine disorders at early stages and form groups of children with high risk of endocrine disorders for prophylactic medical examination.

**PAO-155****Rett syndrome associated with thyroid hypoplasia – a synergic association for neurological disturbances: case report***Otilia Marginean<sup>1</sup>; Ioan Simedrea<sup>2</sup>; Tamara Marcovic<sup>3</sup>; Daniela Chirui<sup>4</sup>*<sup>1</sup>Ist Pediatric Clinic University of Medicine and Pharmacy Timisoara, Endocrinology, Timisoara, Romania; <sup>2</sup>Ist Pediatric Clinic University of Medicine and Pharmacy Timisoara, Gastroenterology, Timisoara, Romania; <sup>3</sup>Ist Pediatric Clinic University of Medicine and Pharmacy Timisoara, Pediatrics, Timisoara, Romania; <sup>4</sup>Ist Pediatric Clinic University of Medicine and Pharmacy Timisoara, ICU, Timisoara, Romania

**Background:** Rett syndrome is a neurodevelopmental disorder that characterized by normal early growth and development followed by a slowing of development, loss of purposeful use of the hands, distinctive hand movements, slowed brain and head growth, problems with walking, seizures, and intellectual disability.

**Case presentation:** CA 4 years 3 month old girl admitted in our department in September 2010 for developmental regression, loss of purposeful hand movements, hand stereotypies, and seizures. The patients neonatal and perinatal history were normal (BW 3100g, BH 50cm). She could play with toys with support, she can not sit up or walk. At one and one half years she had stopped using her hands completely and at age two and one half her head growth decelerated markedly and appears seizures. According the progressive neurological problems the child was diagnosed with Rett syndrome (the genetic analysis reveal a nucleotide change in the coding region of 4 exons of MECP2 in a heterozygote state) and she received treatment with carbamazepin 10mg/kg/day. At the admission in our department the child have weight 19kg, height 98.5 cm (age weight 104.96; SDS -1.70 according to Prader criterias), dry rough pale skin, coarse, dry hair, hair loss, constipation, small feet and hands and severe neurologic problems; blood samples show normal BC, liver function, low Ft3, elevated TSH (73.5mU/ml), Low IGF1(23.5ng/ml) according to

the age; small thyroid volume 1 ml (more than -2SD). We add to the treatment L thyroxine. The evaluation after 2 month show mild improved movements but her communications with family was improved.

**Conclusions:** 1. Rett syndrome is a rare genetic disease. 2. Brain damage can be induced by synergic mechanism of synaptic damage and neuronal metabolism. 3. Are necessary more sophisticated genetic analysis to solve the link between hypothyroidism and Rett syndrome.

**PAO-156****Central hypothyroidism secondary to maternal hyperthyroidism***Pilar Sevilla-Ramos; Maria Alija; Esther Cid; Nerea Lopez-Andres; José María Jiménez-Bustos*

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**Background:** Neonatal central hypothyroidism is very rare in paediatric patients. We present the case of a breast-fed baby developing central hypothyroidism when aged 2 months old, secondary to maternal Graves' disease detected after birth.

**Results:** PA: Pregnancy monitored. Caesarean at 34 weeks due to premature breakage of membranes, APGAR 9/10. WAB: 2,570 g (P 75-90); LAB: 45 cm (P50-75). FH: Father healthy, height 170 cm. Mother healthy, height 165 cm. Evolution during neonatal period: Admission at birth due to early asymptomatic hypoglycaemia birth. Metabolopathy screening for low TSH, with TSH of 0.03 mU/L and T4L of 1.84 ng/dl detected. Presents TA 90/43-78/40, FC 157-130 lpm during the first 5 days of life. Irritability and diarrhoea observed. Mother: TSH undetectable, T4L 2.82 ng/dl, antithyroglobulin Ab 45, antiperoxidase Ab 75, TSI Ab 13 (N<10). Follow-up at surgery: 15-day follow-up: Weight: 2.570 kg (P3), Length: 46 cm (P3), macroglossia. TSH 0.02 mU/L, T4L 1.31 ng/dl, T3 1.05 ng/dl, antimicrosomal Ab 71 (N 0-5.6) 2.5 month follow-up: Weight: 4.250 (P3), Length: 53.

**Conclusions:** In maternal Graves' disease the transplacental transfer of Ac TSI affects the development of the hypothalamic-pituitary-adrenal axis (HPA). Rarely, exposure to high levels of intrauterine thyroid hormones in Graves' disease can halt the hypothalamic-pituitary-adrenal axis, leading to a hypothyroidism in the fetus that continues for a variable period of time among newborns.

**PAO-157****Congenital chloride diarrhea with congenital hypothyroidism in two siblings: case report***Erdal Adal<sup>1</sup>; Atilla Erseren<sup>2</sup>; Hasan Onal<sup>1</sup>; Sezen Ugan<sup>3</sup>; Tugba Kontbay<sup>4</sup>; Ahmet Aydin<sup>4</sup>*<sup>1</sup>Ministry of Health Bakirkoy Maternity and Children Education Hospital, Pediatric Endocrinology, Istanbul, Turkey; <sup>2</sup>Kasimpasa Military Hospital, Pediatrics, Istanbul, Turkey; <sup>3</sup>Ministry of Health Bakirkoy Maternity and Children Education Hospital, Pediatrics, Istanbul, Turkey; <sup>4</sup>Istanbul University, Cerrahpasa Medical Faculty, Division of Metabolic Diseases, Istanbul, Turkey

**Background:** Congenital chloride diarrhea (CCD) is a rare autosomal recessively inherited disorder causing watery stool and dehydration characterized by impairment of Cl/HCO<sub>3</sub> exchange.

**Objective:** Infrequency of CCD makes diagnostics difficult and CCD accompanying with congenital hypothyroidism has never been reported so far.

**Population:** A 7-year-old male who was followed with the diagnoses of congenital hypothyroidism, Bartter syndrome and idiopathic chronic diarrhea in different medical centers and treated with L-thyroxine and indomethacin, admitted our unit with electrolyte abnormalities and mental retardation. His medical history was notable for prolonged jaundice and congenital hypothyroidism in neonatal period. L-thyroxine was started but euthyroidism status was hardly supplied with alterations of thyroid hormones. Additionally, dehydration and metabolic alkalosis were recognized in his second months of age with the history of intrauterine polyhydramnios; he was diagnosed as Bartter syndrome and indomethacin treatment was started. But all the medications until now could not heal the problems of watery diarrhea, abdominal distention and electrolyte abnormalities. Additionally, we recognized that this family had a 3-month-old sibling and he was followed-up with the initial diagnoses of congenital hypothyroidism and Bartter syndrome.

**Results:** We figured out CCD in our investigation of these two siblings that

fecal Cl-level was over 90 mEq/L. Indomethacin was stopped and Cl-supplementation was started. Watery diarrhea was recovered and L-thyroxine treatment was optimized to supply euthyroidism.

**Conclusion:** These two cases are worthy of particular attention in the literatures because of the first reported cases of CCD accompanying with congenital hypothyroidism. One point in this regard is that mutations in the SLC26A3 gene have been associated with CCD and surprisingly similar gene mutation of SLC26A4 is also seen in Pendred syndrome (Hereditary hearing loss with thyroid abnormalities). We have investigated for genetic mutations in our patients.

#### PAO-158

### Tall stature, gonadal dysgenesis and obesity: unusual phenotype in a female with X chromosomal aberration

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**Background:** Whilst X chromosome structural aberrations in female patients are most frequently characterized by a short stature and Turner's phenotype, only several patients with strikingly different phenotype have been reported so far.

**Objective and hypotheses:** To describe clinical and genetic findings in a girl with a rare structural X chromosome rearrangement.

**Methods:** Physical examination, biochemical analysis, cytogenetic studies, imaging methods, neurological and psychological investigation were performed.

**Results:** The patient was referred at the age of 13 years because of obesity (BMI 26.3 kg/m<sup>2</sup>, + 2.53 SD). She had a tall disproportional stature (183cm, +3.3 SD), only initial pubic hair (Tanner P2), breast enlargement was caused by fatty tissue. No psychomotor delay or mental retardation were mentioned, however she had to attend a special school. Basal gonadotrophin levels were high (FSH 49.5 U/l, LH 7.5 U/l), estradiol was prepubertal (0.05 nmol/l), that was consistent with hypergonadotrophic hypogonadism indicating gonadal dysgenesis. IGFI levels and thyroid function were normal. Chromosome analysis revealed chromosomal aberration - an isochromosome i(Xp). The result was confirmed by FISH analysis 46, X, i(X) (p10), ish (STS++, DXZ+, SRY-). Bone age corresponded to calendar age. Ultrasound visualized a hypoplastic uterus, ovaries were not visible. MRI of central nervous system demonstrated slight cortical atrophy.

**Conclusions:** We describe a girl with tall stature, obesity, mild mental retardation, gonadal dysgenesis and a rare structural rearrangement of X chromosome. Tall stature can be explained by a triple gene dosage of SHOX (short stature homeobox containing gene) in PAR1 (short arm pseudoautosomal region) together with estrogen deficiency. Oral estrogen replacement therapy was initiated to accelerate puberty and promote epiphyseal fusion, unfortunately the therapeutic effect was diminished due to non-compliance.

#### PAO-159

### 17-years old girl with autoimmune polyendocrine syndrome type 2 - how to obtain the best metabolic control of diabetes

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**Background:** The association between Addison's disease (AD) and type 1 diabetes (T1DM) is well recognised. The prevalence of T1DM in patients with autoimmune polyendocrine syndrome type 2 (APS-2) ranges above 50%.

**Objective and hypotheses:** We report the case of 17 years old girl with primary adrenal insufficiency recognised at age of 11 and AITD who developed T1DM after 6 years. The immunological status has been observed for several years before clinical diabetes onset.

**Method and result:** The results are presented in the table:

Date	4.11.2004	6.03.2009	2.12.2010
HbA1c	5,00%	5,40%	9,30
anti GAD /U/mL/ N: <0,9	0,56	2,11	1,18
anti IA2 /U/mL/ N: <0,75	<0,2	<0,7	<0,7
anti TG-AB /U/mL/ N:30-70	75,9	183	1,48
anti TPO-AB /U/mL/ N:30-50	277,9	1660	139,17
TSH-R-AB /U/L/ N:<9,0			<5,0
p-ANA	1:320(+), 1:640(+)		
anti-21-H U/mL/ N:<1,0		5,33	

It is well known that glucocorticoid replacement therapy in patients with primary adrenal insufficiency and T1DM may lead to quite often and significant changes in insulin requirement and insulin sensitivity. That is why the multiple pen injection regimen was replaced by continuous subcutaneous insulin infusion (CSII) after one month since the diabetes onset. There are several options of "smart" pumps like: 1) temporary basal change, 2) additional basal rate i.e. „for disease“, 3) automatically calculate meal or correction boluses, 4) continuous glucose monitoring devices with real-time display which can participate in improving and maintain good metabolic control in such patients.

**Conclusions:** 1. In the immunological course of diabetes, there was no increase of autoantibodies against  $\beta$  cell, in particular, anti-IA2 just before clinical manifestation of diabetes 2. The patient with APS requires observation for clinical signs of diabetes and glucose monitoring by the determination of HbA1c at least once/twice a year 3. Type 1 diabetes treatment commences using personal insulin pump allows to obtain good metabolic control of diabetes in spite of insulin requirements changes consequently steroid replacement therapy 4. Insulin pump treatment will improve the quality of life in patient with APS type 2.

#### PAO-160

Abstract withdrawn.

#### PAO-161

### The evaluation of body composition and metabolic parameters in girls with central precocious puberty receiving GnRH agonist therapy

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**Background:** The changes in body composition and metabolic parameters in girls with central precocious puberty during GnRHa therapy is still under debate. Objective : To evaluate the changes in BMI and metabolic parameters in girls with central precocious puberty during GnRHa therapy.

**Population and methods:** Thirty-nine girls (mean age 9,13±0,73 years) with central precocious puberty treated with GnRHa were enrolled in the study. BMI-SDS, lipid profile, serum leptin, adiponectin and HbA1c levels were evaluated and standard OGTT was done at the beginning, sixth and twelfth month of therapy.

**Results:** At diagnosis; mean BMI-SDS was 1,13±0,83. Four girls (10,2%) were obese (BMI>95p). None of the patients had impaired glucose tolerance, 8 girls (20%) had insulin resistance. Dyslipidemia was observed in 35,9% (14/39) of patients. At the sixth month, 5 cases (12,8%) had insulin resistance, 2 of whom developed impaired glucose tolerance. BMI-SDS did not change significantly in six month period (p:0,96). No changes in frequency of dyslipidemia (35,9%) was observed at sixth month of therapy. No statistically significant difference was found in serum leptin, adiponectin, HbA1c values between baseline and sixth month of therapy. (p values 0.141, 0.433, 0.443 respectively)

**Conclusion:** At the beginning of therapy one fifth of girls with central precocious puberty had impaired glucose metabolism. However BMI-SDS, lipid and carbohydrate metabolism parameters did not show significant change during six months period. The results of twelfth month evaluation will shed light on the long term changes in patients with central precocious puberty under GnRHa therapy.

### Re-evaluation of metabolic parameters of obese children after 5-7 years

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**Background:** Obesity beginning in the childhood continues to adulthood and becomes more complicated.

**Objective and hypotheses:** In this study we aimed to re-evaluate obese children with respect to obesity status and metabolic parameters after 5-7 years from the first admission.

**Methods:** 100 cases who admitted to our clinic for exogen obesity were called again. 40 of them were male. Their relative BMI was calculated, serum levels of lipids, glucose, insulin, free T4, TSH were studied. There was significant. The cases were divided into 4 group according to metabolic disorders in the first visit:

Group 1: only dislipidemia (HDL<40 mg/dL, triglyceride>150 mg/dL, LDL>130 mg/dL)

Group 2: only insulin resistance (HOMA>3)

Group 3: dyslipidemia and insulin resistance

Group 4: normal

**Results:** At the last evaluation, rel BMI decreased significantly in group 1 and 2 compared to first visit (p=0.006 and 0.034 respectively). The percentage of cases whom metabolic parameters improved to normal limits were 56% in groups 1,2,4 and 18% in the group 3.

**Conclusions:** Loosing weight is easier in children whom have only dyslipidemia or only insulin resistance than children who have both of them. Having that metabolic disorders together makes the metabolic improvement harder. So, prevention of early stages of obesity and metabolic disorders plays important role in adulthood life quality.

## PAO-163

### Factors to predict the result of GnRH stimulation test in girls with suspicious precocious puberty

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**Background:** In girls with early breast development and bone age advancement, sometimes the clinical findings and the results of gonadotropin-releasing hormone (GnRH) stimulation test are inconsistent.

**Objective and hypotheses:** The aim of this study was to investigate the factors to predict the positive results of GnRH stimulation test in girls with suspicious central precocious puberty (CPP).

**Methods:** We reviewed records of 574 girls who visited at Pediatric Endocrinology Clinic of Korea university hospital from March 2005 to May 2010 and underwent GnRH stimulation test under the age of 9 years old. Each of the initial and follow-up tests was divided into two groups based on whether peak luteinizing hormone (LH) level was less than 5 IU/L (negative) or not (positive). Growth velocity ratio was calculated as the difference between height before treatment divided by average growth velocity of Korean girls.

**Results:** In the initial GnRH stimulation test, 375 girls were diagnosed as CPP and other 199 girls had negative results. In the follow-up test, 64 girls corresponding to 32% of 199 girls were diagnosed as CPP. Girls with the initial positive results had more accelerated growth, advanced bone age and higher serum basal LH, follicle-stimulating hormone (FSH), estradiol concentration compared to those with the initial negative results. Girls with the follow-up positive results had more accelerated growth and advanced bone age compared to those with the follow-up negative results. In binary logistic regression, the growth velocity ratio was significant predictive factor [initial test, OR 10.7, (95% CI 4.3, 26.7), P = 0.01; follow-up test, OR 6.6, (95% CI 1.5, 28.9), P = 0.01] of positive results.

**Conclusions:** Considering when the GnRH stimulation test is thought to be helpful for girls with suspicious precocious puberty, rapid growth velocity could be the most useful predictive factor for the positive results.

## PAO-164

### Autoantibody positivity and clinical characteristics of childhood diabetes

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**Background:** Most childhood diabetes was usually thought as type 1 diabetes (T1DM), but there is a tendency of increasing type 2 diabetes (T2DM) and sometimes, it might not be easy to determine the type of diabetes. It's important to know the type of diabetes and it's very useful to choose the best treatment modality.

**Objective and hypotheses:** In this study, we searched the clinical and laboratory characteristics of the patients with childhood diabetes to compare those according to the type of diabetes.

**Methods:** We retrospectively reviewed the medical records of the patients who was diagnosed as diabetes and followed at the department of Pediatrics, Dankook University Hospital to find the clinical and laboratory characteristics.

**Results:** Total 43 patients were enrolled in this study. The patients were grouped as T1DM (n=29), T2DM (n=10) and unclassified (n=4), according to the clinical characteristics and laboratory findings. There was a little female predominance (M:F 1:1.15). Autoantibody positivity was high in T1DM, implying it as the very valuable marker in T1DM. T1DM had an earlier onset age, as expected. In 55%, diabetic ketoacidosis (DKA) was the presenting symptom in T1DM, but no DKA in T2DM as an initial symptom. Initial and FU HbA1c did not show statistically significant differences between the group. Initial serum c-peptide or insulin levels were lower in T1DM. Obesity was not the major portion in childhood T2DM but BMI was higher in T2DM. In T2DM, oral hypoglycaemic agents with or without insulin were chosen as a treatment. During follow up, adolescence, especially in girls, was thought as a very vulnerable period to manage the diabetes requiring more intensive emotional support including family cooperation.

**Conclusions:** In this study, we can confirm that the autoantibody test is very valuable to diagnose specific type of diabetes and to determine the diverse treatment modality. And female adolescence was thought as a vulnerable period to manage the diabetes requiring more intensive emotional support including family cooperation.

## PAO-165

### A hemophilia b carrier girl with central precocious puberty associated with supernumerary marker chromosome, hypercholesterolemia and investigated by FISH and array comparative genomic hybridization

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**Background:** Supernumerary marker chromosome(SMC) in general are extremely rare findings and approximately 1/100,000 newborn cases. Hemophilia B is caused by mutation of the coagulation factor IX (F.IX) gene.

**Objective and hypotheses:** To estimate genomic copy number changes in a Hemophilia B carrier 8 years old girl had central precocious puberty, associated with a supernumerary marker chromosome and hypercholesterolemia in array comparative genomic hybridization.

**Methods:** We report on a 8 years old Taiwanese girl with central precocious puberty. Her elder brother was a victim of Hemophilia B and confirmed she was a carrier of Hemophilia B at the age of 4 years old. Central precocious puberty was diagnosed at the age of 8 years old due to develop of menarche and high levels of FSH and LH. Bone age was significant advanced to 12 years old. Her height was 130 cm (50th percentile), her weight was 28 kg (50th percentile). Her gross appearance was not specific but with moderate intellectual deficiency. Chromosome analysis showed non mosaic and de novo 47,XX,+ marker chromosome. The laboratory test revealed high total cholesterol 308mg/dl, high LDL-C 220 mg/dl, and HDL-C 60 mg/dl.

**Results:** FISH study confirmed the supernumerary marker chromosome is originated from the 14 or 22 chromosome and includes two copies of the acro p-arms, 47,XX,+mar.ish idic(14/22). Array comparative genomic hybridization were performed with arrgh 1-22 (2853BAC)x 2, X(158BAC) x 2, Y(27BAC)x0. No pathologic gene dosage variation was detected from array-CGH. PCR and sequence analysis for Hemophilia B and LDL receptor showed c.424 >T, Glu> stop gene mutation in factor IX gene and missense mutation of 4th exon of LDL receptor with genotype LDLR-C188 (C,Y).

**Conclusions:** Although no pathologic gene dosage variation was detected from array comparative genomic hybridization. Our patient still had a multiple anomalies with supernumerary marker chromosome, Hemophilia B, hypercholesterolemia and central precocious puberty. She had received GnRH agonist treatment till now.

#### PAO-166

### Patient with congenital hypothyroidism, adrenal insufficiency, and SRY deletion: a case report

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**Background:** SRY deletion is a rare genetic condition which can cause androgen insensitivity syndrome and ambiguous genitalia. Congenital hypothyroidism and adrenal insufficiency together with an SRY mutation are rare.

**Objective and hypotheses:** To determine whether congenital hypothyroidism and adrenal insufficiency have been reported in a patient with an SRY deletion. There may be a condition where congenital hypothyroidism, adrenal insufficiency, and SRY deletion occur together.

**Methods:** Literature search.

**Results:** This patient was born via in vitro fertilization at 37 weeks gestation to an Indian mother. Physical exam revealed jaundice, a broad nasal bridge, ambiguous genitalia with well-rugated empty scrotum/labia, micropenis, no hypospadias, and bilateral undescended testicles. Karyotype was 46, XY and FISH analysis showed deletion for part of the SRY region that is usually caused by a copying error during spermatogenesis. LH and FSH levels were elevated, while DHEA-S, DHT, and testosterone levels were low at 0.4mg/ml, 9ng/dl, and 115ng/dl respectively. As beta-hCG stimulation test yielded no increase in testosterone, the patient was diagnosed with hypergonadotropic hypogonadism. Intramuscular injections of testosterone enanthate 25mg/month for 3 months were started with monitoring of phallic growth to follow. As his TSH level was high (19.5uU/ml) and free T4 level was low (1.3ng/dl), the patient was diagnosed with hypothyroidism. After starting levothyroxine, TSH and FT4 levels normalized. At two months of age, the patient developed hyperpigmentation. He subsequently failed an ACTH stimulation test and was therefore diagnosed with adrenal insufficiency.

**Conclusions:** To our knowledge this patient is a novel presentation of congenital hypothyroidism and adrenal insufficiency occurring with an SRY deletion in an in vitro baby.

#### PAO-167

### Response to rhIGF-1 therapy in patients with primary IGF-1 deficiency

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**Background:** Patients with growth hormone insensitivity or Laron syndrome are a heterogeneous group of children with a variety of clinical phenotypes and variable severity of short stature. A relatively high prevalence of IGF-1 deficiency has been reported in ISS patients without classical Laron syndrome features.

**Objective and hypotheses:** To study the response to rhIGF-1 therapy in short children with Primary IGFD.

**Methods:** 21 children with short stature, who passed GHRH (1 mg/kg IV) stimulation test (GH peak >15ng/ml) were included in the study. They were treated with Increlex® 0.24 mg/kg/day. Height velocity (HV) and Height (Ht) SDS were measured after 6 months of therapy.

**Results:** Patient's characteristics: age 9.84±2.5 SD years, Ht -2.49 ± 0.36 SD (range -2.9 to -1.85 SDS) and IGF-1 levels -2.22 ±0.97 SD (range -3.6 to +0.7SDS). The mean birth weight was 2.86 ±0.41 kg. The average peak of

GH after GHRH was 48.9±24.1 SD ng/ml. HV after 6 months of Increlex® therapy was 10.3 ± 3.9 cm/yr. There were only 3 patients in this group whose HV was less than 5 cm/yr on Increlex® therapy. The mean change in Ht SDS was +0.35±0.33 SD after 6 months of Increlex® therapy.

**Conclusions:** This pilot data revealed that the rhIGF-1 therapy has good efficacy in less severe Primary IGFD. The average HV after 6 months of therapy is similar to the data on severe Primary IGFD (Ht<-3SDS, IGF-1 <-3SDS) patients treated with rhIGF-1.

#### PAO-168

### Hot nodule harboring a papillary microcarcinoma in a girl from an iodine sufficient area

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**Background:** Hot nodules on radionuclide imaging of thyroid are generally benign but there are reported some cases of hot nodules associated with thyroid cancer with only a few cases in pediatric age. However a relative high incidence in children's was reported in iodine deficiency area after introduction of iodine supplementation.

**Objective and hypotheses:** To report a case of thyroid cancer associated with a hot nodule in a pediatric patient from an iodine sufficient area.

**Methods:** 13 years old girl consulted for a one week evolution tumor in her neck, her aunt had thyroid cancer. On physical examination an approximately 2 cm firm mobile nodule on thyroid topography was palpated. Thyroid ultrasonography showed a cystic nodule of 19 x 14 x 13 mm with heterogeneous parietal polypoid mass of irregular limits in the right lobule. The rest of the gland was normal. <sup>99m</sup>Tc thyroid scan showed a focal increase of the thyroid with an area of high Tc uptake in the nodule topography corresponding to a hyperfunctioning nodule with normal uptake in the rest of the gland. Thyroid function tests showed T4: 9.24 ug/dl (6-14) free T4: 1.44 ng/dl (0.8-2.2) T3: 178 ng/dl (80-220) TSH 4.42 mU/ml(0.27-4.2) Calcitonin and thyroid antibodies were negative. Fine needle aspiration biopsy (FNAB) showed: macrophages with hemosiderin and erythrocytes without follicular cells. Because the presence of the risk factor, irregular limits in polypoid mass and no conclusive FNAB a right hemithyroidectomy was performed.

**Results:** Histologic section revealed a nodular hyperplasia with lymphocytic thyroiditis. A papillary microcarcinoma of 0.25 mm was detected.

**Conclusions:** Hot nodules in iodine sufficient areas could be associated with malignant disease in pediatric populations too. We recommend the systematic practice of FNAB in pediatric patients with hot nodules especially if suspicious ultrasonography characters or familial history of thyroid cancer are present. The concomitance of an inflammatory process with cancer was previously reported but others studies too.

#### PAO-169

### 45,X male with ambiguous genitalia: a case report

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**Background:** A 45,X karyotype usually result in a female phenotype, with clinical symptoms of Turner syndrome. Rarely, the nonmosaic 45,X chromosomal constitution is associated with maleness. Maleness is usually caused by a reciprocal of the SRY gene on an autosome. These cases generally have

testes and normal male external genitalia with infertility.

**Objective and hypotheses:** We herein report a male newborn who presented with ambiguous genitalia and had 45,X karyotype.

**Methods:** A 38-week-gestation newborn with 3000 gr birthweight was admitted for evaluation of ambiguous genitalia during the neonatal period. He had predominantly male phenotype with micropenis, chordee, penoscrotal hypospadias and nonpalpable right gonad. His left gonad was palpable in scrotal region. Ultrasonographic examination showed Mullerian structures and right sided immature gonad at pelvic area; gonad with immature testis structure at left sided in the scrotum. Laboratory evaluation on 18th day of life revealed as LH: 3.07 mIU/ml, FSH: 4.69 mIU/ml, basal testosterone: 111 ng/dl. Neither mosaicism nor a structurally aberrant Y chromosome was observed by routine cytogenetic analysis. Although FISH revealed SRY negative, it was found to be positive with PCR. Thereafter biopsies of both gonads revealed left testes with immature testicular tissue (5x3x2cm) and right streak gonad (3x2x2cm) (compact ovarian stroma with no follicles). SRY evaluation of both gonad biopsy materials were positive.

**Results:** The patient has been raised as male by removing Mullerian structures and streak gonad decisioning of our gender assignment team. The investigation of translocation of Y chromosome in our patient is still ongoing. We will follow clinical course of this patient for developing Turner phenotype and hypergonadotropic hypogonadism.

**Conclusions:** The presented patient was evaluated as mixed gonadal dysgenesis due to autosomal SRY translocation with 45,X karyotype. SRY should be detected by PCR, in the patient with FISH negative for Y material, before gonadal genotyping.

#### PAO-170

### The difficulties of investigating and treating an endocrine patient in resource limited countries

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**Introduction:** Adrenal masses (AMs) are often discovered incidentally and are then termed adrenal incidentalomas (AIs). They are often discovered after an imaging procedure is performed that is unrelated to the adrenal gland. Less commonly, AMs are discovered as part of the clinical workup for suspected adrenal disease (eg, Cushing syndrome). However it took us more than three months and we are not yet at the final diagnosis.

**Case presentation:** A 3 years old child presented with overweight. Was born prematurely, Birth weight 2.4kg and a mild birth asphyxia, current weight 18kg. On examination the weight was above 97th centile. He had a moon shaped face, striae, trunk obesity, hirsutism, pubarche and was hypertensive (117/67mmHg). Morning cortisol levels were increased. Abdominal USS showed an adrenal adenoma. Computed tomography showed a mass in the right adrenal tumor. Was put on ketokonazole tablets later on was operated and the capsulated tumor was removed, currently awaiting the biopsy results.

**Conclusion:** No diagnosis has been confirmed to date, most of the investigation were not done due to lack of facilities or high costs. This implies that it is very difficult to have a final diagnosis and manage endocrine patients fully.

#### PAO-171

### Vicious circle of poor compliance in a patient with congenital adrenal hyperplasia due to 21-hydroxylase deficiency- a case report

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**Background:** Congenital adrenal hyperplasia (CAH) is a group of disorders resulting from the deficiency of one of the five enzymes required for the synthesis of cortisol. One form of gonadal abnormality in affected males with CAH is the development of testicular adrenal rests, during periods of sustained elevation of plasma ACTH levels. The prevalence of these testicular tumors between 0 and 47% has been reported, dependent on method of detection (palpation vs. ultrasound).

**Objective and hypotheses:** To evaluate a 17-year-old boy history, known with classic 21-hydroxylase deficiency, salt wasting type, diagnosed at birth, referred to our department with a discordant history in the context of the dis-

ease: recurrent hypotension, hypoglycemia, nausea and vomiting crisis, reported to be refractory to corticosteroid treatment.

**Results:** From history we found that he frequently present hypotension, hypoglycemia, nausea and vomiting crisis treated in emergency department with intravenous glucocorticoid in high doses, followed by treatment cessation soon after the acute episode due to self reported testicular pain. Physical examination showed short stature (151cm), painful palpable mass in left testis, BP= 80/ 50 mmHG. The sodium level was 127mEq/l, potassium level was 5.6mEq/l. Morning plasma cortisol was decreased with increased ACTH plasma level, testosterone, LH, FSH, AFP and beta hCG levels were in normal range. The ultrasound examination showed normal adrenal glands and three homogeneously hypoechoic masses 1.1/ 0.9 cm maximum in right testis and three similar masses 3.1/1.8 cm each maximum in left testis.

**Conclusions:** Presence of testicular tumors in a patient with poor control of CAH is not unusual but in our case the testicular pain associated by mistake with glucocorticoid treatment in high doses administrated in acute crisis became a major factor in raising a vicious circle of poor compliance.

#### PAO-172

### Achondroplasia in a girl with G 1138 A mutation, response to growth hormone therapy, two and half years follow up

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**Background:** Achondroplasia is the most common form of skeletal dysplasia in man, has autosomal dominant inheritance and causes extreme short stature. More than 90% of patients with achondroplasia have a G to A transversion or G to C transversion at position 1138 of the fibroblast growth factor receptor-3 (FGFR3) gene.

**Objective:** To evaluate the response to growth hormone of Egyptian patient with achondroplasia.

**Methods:** A prospective follow up study of a girl with achondroplasia.

**Case presentation:** The girl was born on 14.9.2006, is a first infant born to non consanguineous parents. She was delivered by caesarean section with birth weight 2.000 kgm, height 40 cm, OFC 41cm at full term, the second baby is 3 years and is unaffected. Our patient presented with short stature and large head at birth. Examination on 16.2.2011: The child is active, cheerful with average intelligence. Paternal height 180 cm, maternal height 163 cm, patient height 92.8 cm (+2.5 SD), upper segment 60 cm, lower segment 32.48 cm, span 85 cm, weight 18.9 kgm, OFC 55 cm. Bone age is 5.6 years. Low set ears. skull is large with prominent forehead, flat nasal bridge, small chest compared to the abdomen, medial arm and forearm creases are prominent.

**Molecular testing:** Fibroblast growth factor receptor-3 (FGR3) mutation: G1138A and G1138C mutations.

**Method:** PCR and DNA sequencing for known mutation G 1138 A and G1138 C mutation in codon 380 of FGFR3 gene for achondroplasia.

Result: One mutation G 1138 A is detected consistent with achondroplasia. Discussion: On September 2008 he was given growth hormone (GH) 0.09 u/kg/day, patient height was 78 cm. (+2SD), GH dose increased to 0.12 u/kg/d. On February height is 92.8 cm. +2.5 SD, height velocity 6.048 cm/year.

**Conclusion:** Patients with achondroplasia with G 1138 A mutation may benefit from GH at a dose range from 0.09u/kg/d to 0.12u/kg/day to maintain an appropriate height velocity.

#### PAO-173

### A case of transient pseudohypoadosteronism complicated by cerebral artery infarction

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**Background:** Pseudohypoadosteronism is a rare condition characterized by renal resistance to the action of aldosterone. Transient pseudohypoadosteronism (TPHA) has been identified in neonates and young infants with obstructive uropathy and urinary tract infection. Objective: To describe 8-month-old boy with TPHA complicated by cerebral infarction.

**Case:** The patient was the second child of nonconsanguineous parents and was born at a gestational age of 39 weeks after uncomplicated pregnancy. Birth



weight was 3,348g (75-90 percentile). Family history was unremarkable. He showed poor weight gain from the age of 4-month-old. He referred to our hospital for fever and irritability at 8-month. At admission, his weight was 6500g (<3 percentile). He was severe-dehydrated. He had neither genital pigmentation nor abnormalities of the external genitalia. Blood examination showed hyponatremia(117mEq/L), hyperkalemia(5.7mEq/L) and metabolic acidosis. Cloudy urine obtained by catheterization yielded *Escherichia coli*. Renal ultrasonography revealed left hydronephrosis and hydroureter. Endocrine test results showed high levels of aldosterone (22900pg/mL) and plasma renin activity (88ng/mL/hr). We gave him a diagnosis of TPHA caused by urinary tract malformation and urinary tract infection. Serum sodium and potassium levels normalized after 24 hours of intravenous fluids and antibiotic therapy. On the fifth hospital day, he became irritable again and was made a diagnosis of right posterior cerebral infarction by head CT scan. We treated him with aspirin and free radical scavenger immediately. He underwent left ureteroplasty at 1-year. Now, he have normal development at the age of 1-year-4-month.

**Precise conclusions:** Hyperaldosteronism causes endothelial dysfunction and impairs vascular reactivity. Predominant causes of this patient's infarction were infection and severe-dehydration. Remaining cause might be involved in vascular damage from hyperaldosteronism because the action of aldosterone was not defective except in renal tubular tissue in patients with TPHA.

#### PAO-174

### The efficacy of gonadotropin-releasing analogues in children with central precocious puberty

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**Background:** GnRH analogues have been used for treatment of precocious puberty for almost 30 years. However, it is still discussed whether this treatment significantly improve adult height (AH) and how it can impact body mass.

**Objective and hypotheses:** To evaluate the efficacy of GnRH analogues regarding final height and weight of children with central precocious puberty (CPP).

**Methods:** Total number of 50 patients was evaluated in this retrospective single-centre study. Group 1 included 33 patients (26 females, 7 males). All of them had been treated with triptorelin 100mkg/kg/28 days during 3.5 yrs (0.9-7.8 yrs). The median age at the start of treatment was 5.2 (2.0 – 8.0 yrs). This group was subdivided for Group 1A - 19 patients with still opened epiphysis and Group 1B - 14 patients who have already reached adult height. Group2 included 17 CPP patients (14 females, 3 males) that have never received any treatment. Predicted adult height (PAH) was calculated according to the Bayley and Pinneau tables. Target Height (TH) was evaluated as midparental height adjusted for sex (+/- 6.5).

**Results:** GnRH treatment significantly improved PAH in Group 1a. AH in Group 1b was significantly higher to compare to untreated Group 2 (p =0.0002). However, TH still was not reached in Group 1. BMI-SD was similar before and after the treatment (Table 1).

Groups	Group 1A	Group 1B	Group 2
PAH (cm) before treatment (1)	151.0 [144.9-152.4]	--	--
PAH (cm) after treatment (2)	156.9 [150.8-157.0]	--	--
p (1-2)	0.0036	--	--
BMI SDS before treatment (3)	1.92 [0.9-2.41]	1.21 [0.66-1.98]	--
BMI SDS after treatment (4)	1.54 [0.87-2.0]	1.13 [0.87-1.28]	--
p (3-4)	0.26	0.89	--
Target height (TH) (cm)	164.7 [161-169.5]	166.5 [163.7-172.0]	163.0 [159-166.2]
Adult height (AH) (cm)	--	156.0 [152.8-164]	146.2 [141-152]
p (TH-AH)	--	0.003	0.0001

**Conclusions:** In our study GnRH treatment did not allow reaching TH but significantly improved AH and did not influence body mass in patients with CPP. Our results correspond to majority of similar studies reported by others.

#### PAO-175

### Physical activity and sedentary behaviours among obese prepubertal children

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**Background:** Physical inactivity is implicated in the development of childhood obesity.

**Objective and hypotheses:** To investigate the relationships of physical activity (PA) and sedentary behaviours (television (TV) viewing and computer use) with the presence of abdominal obesity in healthy prepubertal children.

**Methods:** A case-control study of 168 healthy prepubertal children (78 males; mean age 8.1±1.2 years) was conducted. Body weight, height and waist circumference (WC) were measured; BMI was calculated. Children were divided into three groups according to the WC percentiles for Bulgarian children as a measure of central obesity ("normal-WC", 31.5%; "children at risk", 27.4% and "abdominally obese", 41.1%). A structured parental interview was used to obtain data about children's physical and sedentary behaviours.

**Results:** No significant difference was found in the frequency and duration of PA among the WC categories in both boys and girls (p>0.05). More than 58% of the parents reported the presence of a seasonal difference in their children's activity with higher mean PA levels during the spring and summer months. This seasonal behaviour was significantly more frequent among the abdominally obese children compared to the normal-WC group (68.1% vs. 47.1%, p=0.04). Children spent an average of 2.7±1.2 h/d watching TV and 0.9±1.0 h/d in using computers.

Although insignificantly, the abdominally obese children spent more hours a day in front of the TV sets and computers compared to their normal-WC counterparts (2.8±1.3 vs. 2.6±1.0 and 0.9±1.0 vs. 0.6±0.9 h., respectively, p>0.05). Boys from all WC-groups used computers more often than girls (1.1±1.0 vs. 0.7±0.9 h/d, p=0.05).

**Conclusions:** Physical inactivity may be associated with the excess accumulation of abdominal fat mass in prepubertal children, which warrants further investigations.

#### PAO-176

### Retrospective study of 215 patients admitted in a pediatric intensive care unit for diabetic ketoacidosis between 1998 and 2008

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**Methods:** This retrospective study presents data collected in one center on 215 type 1 diabetic patients admitted in the pediatric intensive care unit (PICU) between 1998 and 2008 for diabetic ketoacidosis (DKA). All patients were treated on the basis of a single standardized protocol.

**Results:** Among 270 episodes of DKA, 2 populations were distinguished: 1) patients in whom type 1 diabetes was revealed by DKA and 2) known type 1 diabetic patients admitted for decompensation of their pre-existent disease. DKA in new type 1 diabetic patients represented 53% of all episodes of DKA and predominantly concerned young patients (58% below 10 years), males (56%), patients with polyuria and polydipsia with a mean duration of 20 days, and patients with a weight loss of a mean of 12.5%. Secondary DKA in known patients represented 47% of all episodes of DKA and predominantly concerned adolescents (90% above 10 years), females (56%) and patients with psychosocial risk factors (61%). 62% of all patients admitted inadequate self-management. In this group, 11 patients were admitted to the PICU between 3 and 12 times and represented 48% of all episodes of DKA. We did not find any significant difference in DKA severity between both above-mentioned populations. All 4 encountered complications during DKA correction (cardiovascular failure, hypoglycemia, cerebral edema and hypokalemia) had a favorable outcome in our study.

**Conclusions:** In order to limit the incidence of DKA and its complications, it is necessary to reduce the delay between the onset of type 1 diabetic symptoms and the time of diagnosis by providing better education to health care providers and to the general population.

We suggest to diffuse treatment guidelines to healthcare providers to limit iatrogenic risks, to educate patients on management of situations at risk for DKA and to intensify the follow up of patients at risk of relapse.

#### PAO-177

### Follow-up of girls with complete androgen insensitivity syndrome (CAIS) and gonads in situ during and after puberty – two case reports

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**Background:** In recent publications the prevalence of germ cell tumors in CAIS has been estimated < 1% until puberty. Leaving the gonads in situ will allow endogenous hormone production and spontaneous puberty. However there is no data on the tumor prevalence in CAIS after puberty.

**Patients and methods:** In two sisters with a 46,XY karyotype we identified a M749V mutation in exon 5 of the androgen receptor gene. According to the family's request the gonads remained in situ. The girls were first seen in our clinics at the age of 13.6 and 11.3 years. Follow-up visits every six months included clinical assessment of growth and puberty, gonadal ultrasound, hormone profiles (LH, FSH, SHBG, testosterone and estradiol) and tumor markers (HCG and AFP).

**Results:** Both girls showed a CAIS phenotype with normal female external genitalia and absence of Mullerian duct remnants. At the age of 15.8 years the older sister had normal breast development without growth of pubic hair. Hormone profiles showed elevated LH levels and FSH, testosterone, estradiol and SHBG levels within the adult male reference ranges. Gonadal ultrasounds and tumor markers revealed no pathology. The younger girl hadn't shown any signs of puberty at the age of 12.7 years, but stimulated gonadotropins and testosterone levels were detected with prepubertal estradiol and SHBG levels. Ultrasonic scans displayed unsuspecting testes in the inguinal canals.

**Conclusions:** The two sisters are undergoing spontaneous puberty, at which they profit from their specific endogenous hormone production. A follow-up protocol has been designed for early diagnosis of malignancy. However further studies are necessary to evaluate the safety of such protocols and establish criteria for intervention.

#### PAO-178

### Final height after treatment for acute lymphoblastic leukemia

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**Background:** Acute Lymphoblastic Leukemia (ALL) is the most common neoplasia in infancy. Today the percentage of survivors has risen so it is possible to evaluate the long term sequelae of treatments. Reduced adult height has been reported in survivors of childhood ALL.

**Objective and hypotheses:** We hypothesized that adult survivors of childhood ALL would reach shorter adult height compared to mid-parental height and that cranial radiotherapy would be a significant risk factor in a dose dependent manner.

**Population and methods:** We evaluated 20 ALL survivors (10 males and 10 females) treated from 1972 to 2001 who reached final height. The median age at diagnosis was 5 years (range 0,4-14), follow-up length ranged from 10 to 39 years. All patients, except two, were prepubertal at diagnosis; all of them received chemotherapy, 13 received also cranial radiotherapy with doses ranging from 18 Gy to 24 Gy. Final height was compared with mid-parental height. Height data were analyzed as height standard deviation score (HSDS); Wilcoxon test was used for statistical evaluation.

**Results:** The adult stature of the patients, expressed as HSDS, was not statistically different from their mid-parental height. Patients who received cranial radiotherapy, especially at high doses, reached a shorter final height compared with mid-parental height, whereas those who received only chemotherapy (n=5) reached a taller adult height compared with mid-parental height, but this difference was not statistically significant. No difference was observed between females and males.

**Conclusions:** Survivors of childhood ALL, especially those treated with cranial radiotherapy at young age, are at increased risk for adult short stature. Our results do not appear in accordance with similar studies, but this is probably due to the small number of patients examined. We are collecting further data, also to evaluate the influence of newer treatment regimens on final height.

#### PAO-179

### Secondary transient pseudohypoadosteronism – a report of two cases

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**Background:** Secondary pseudohypoadosteronism (PHA) is a syndrome with a state of renal tubular unresponsiveness to aldosterone and is manifested by hyponatremia, hyperkalemia and metabolic acidosis. Major contributing factors are urinary tract infections, urinary tract malformations.

**Objective:** A report of two cases of transient PHA in infants, including one unusual case where PHA occurred in the course of diarrhea due to Crohn disease.

1: A 2-months-age boy admitted to hospital with diarrhea and weight loss. Clinical and laboratory findings revealed dehydration, hyponatremia at 118 mmol/l, hyperkalemia at 7,05 mmol/l, metabolic acidosis (bicarbonate 15,7 mmol/l). Urinary tract infection was excluded. Renal sonography was normal. Congenital adrenal hyperplasia (CAH) was excluded. Pathologically high aldosterone in plasma, plasma renin activity (PRA) and elevated levels of corticosteron metabolites, THALdo (128,3; range: 4,3-12,3), 18-OXO-THF and 18-OHF in urinary steroid profile confirmed PHA. Oral supplementation of high dose sodium was applied. Secretive diarrhea was diagnosed. Colonoscopy was typical for Crohn disease. Treatment with high dose glucocorticosteroids and 5-ASA was applied. Sodium supplementation was withdrawn.

2: A 1-month-age boy admitted to hospital with dehydration and failure to thrive. Laboratory findings revealed hyponatremia at 114 mmol/l, hyperkalemia at 9,48 mmol/l, metabolic acidosis (bicarbonate 15,0 mmol/l), elevated levels of urea and creatinine, positive urine culture. Urosepsis was diagnosed. Laboratory tests confirmed PHA. Oral supplementation of sodium was applied. Obstructive uropathy was diagnosed and urological therapy applied. Salt supplementation was discontinued after about 5 months. Both electrolytes and PRA, aldosterone levels remain within range.

**Conclusions:** PHA should be suspected in cases of severe hyponatremia, hyperkalemia and weight loss in infants. Secondary PHA is usually associated with urological problems, however it one presented patient PHA occurred in the course of secretive diarrhea.

#### PAO-180

### Invasive pituitary adenoma secreting growth hormone, TSH, prolactin and $\alpha$ -subunit in a 12-year-old girl

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**Background:** Prolactinoma is the most common secreting pituitary adenoma, growth hormone (GH) secreting adenomas are less common and thyrotropinoma only constituting 1% of all pituitary adenomas.

**Objective:** 12-year-old girl first presented with headaches and worsening of vision of a left eye that lasted for 4 months. Clinical symptoms included: overgrowth, signs of acromegaly, hyperthyroidism and galactorrhea. Ophthalmological examination revealed signs of raised intracranial pressure. Hormonal tests showed: high GH levels with lack of inhibition in an oral glucose tolerance test, high IGF-1, both free thyroid hormones and TSH levels were high with no reaction after TRH administration and very high concentration of prolactin (PRL) and  $\alpha$ -subunit.

Head MRI revealed a sellar invasive tumour, size 80x55x50 mm, penetrating to interior jugular arteries and optic nerves. A stereotactic biopsy was performed, with tumour hemorrhage complication. Histopathological and immunohistochemical examinations confirmed the diagnosis of invasive pi-

pituitary adenoma secreting GH, TSH, PRL and  $\alpha$ -subunit with sstr 2 and 5 receptors. Pharmacological treatment with somatostatin analogue (octreotide, 30 mg every 28 days i.m.) and bromocriptine (30 mg/d now) was introduced. There was an evident tumour regression with tumour size 40x37x40mm after 4 months of the treatment. Normalisation of GH, IGF-1, TSH and free thyroid hormones and decreasing prolactin level (from 35700 ng/ml to 163 ng/ml) were observed. Due to the successful pharmacological therapy, administered for 16 months now, neurosurgery procedure is planned in a few months.

**Conclusions:** Treatment with somatostatin analogue and bromocriptine is very effective in the therapy of GH, TSH, PRL secreting pituitary adenomas, resulting in not only normalisation of hormones levels but also tumour size regression with better prognosis for the radical surgery.

#### PAO-181

### Coincidence of germinoma and lymphocytic hypophysitis in a 12 year-old-boy with diabetes insipidus and growth hormone deficiency

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**Background:** Intracranial germinoma is a rare malignant tumor, only constituting 3-5% of paediatric intracranial tumor. It usually occurs in children and young adults and it's highly sensitive to radiotherapy and/or chemotherapy. Lymphocytic hypophysitis is an uncommon autoimmune disease in which the pituitary function is usually impaired due to it's infiltration by lymphocytes, plasma cells and macrophages. There are just a few cases of coincidence of this two pathologies described in the literature.

**Objective:** We present a patient with coincidence of germinoma and lymphocytic hypophysitis. 9-year-old boy presented polydipsia, polyuria and headaches that lasted for 2 years. Neurological and ophthalmological examinations were normal. Wasopressin test confirmed central diabetes insipidus, DDAVP treatment was introduced. TSH, free thyroid hormones, ACTH, cortisol and IGF-1 levels were normal. Tumour markers,  $\alpha$ -fetoprotein and  $\beta$ HCG, both in serum and cerebral fluid were negative. Antithyroid and antiadrenal autoantibodies were also negative.

Chest X-ray radiograph showed no pulmonary lesion. The first head MRI showed thickened pituitary stalk size 4x6 mm, absent of a posterior pituitary lobe and 5 mm pineal cyst. During 2,5-year observation growth velocity decreased to 3,5 cm/year. Stimulation tests confirmed growth hormone deficiency. The head MRI was repeated every 6 months, after 2,5 years there was increase of tumour mass, now in the region of the pituitary gland, stalk and hypothalamus. Right-side temporal craniotomy was performed with total remove of the tumour. Histopathological examination revealed both germinoma and lymphocytic hypophysitis. The patient was referred for further oncological treatment.

**Conclusions:** The diagnosis of central diabetes insipidus with thickened pituitary stalk requires long term follow-up to establish the underlying cause. Lymphocytic hypophysitis in children may be the first sign of a host reaction to an occult germinoma.

#### PAO-182

### StAR (= steroidogenic acute regulatory protein) deficiency: case report

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**Introduction:** Lipoid congenital adrenal hyperplasia is an autosomal recessive disease due to deficiency of StAR protein that transports cholesterol into the mitochondria for adrenal steroid synthesis. StAR is also essential for gonadal steroidogenesis and is encoded by a gene on chromosome 8p11.2.

**Case:** 6 month female patient was hospitalized for vomiting and lose in weight started at 4th month. She had severe hyponatremia (Na: 108 mmol/L) and dehydration. She has been referred for persistent hyponatremia and subsequently developed hyperkalemia. She was born at 33rd gestational week,

birth weight was 1750 gr. Parents were second degree related, infant death or sexual development disorder was not described in family history. Physical inspections revealed paleness, vital findings were normal. Dehydration or hyperpigmentation was not present. Height: 58 cm (10-25p), weight: 4 kg (< 3p), external genitalia seemed normal female and systemic examination findings were normal. Na: 130 mEq/Lt, K: 6.4 mEq/Lt, Glucose: 82 mg/dl, baseline ACTH was high, DHEA-S was normal. In classical ACTH stimulation test, mineralocorticoid, glucocorticoid and androgen precursors had not been increased. Significant hyperplasia of both adrenal glands observed in magnetic resonance imaging. Caryotype was 46 XY, t(4;9)(p16.6;p13.3) and a paternal translocation was determined.

Laparoscopic investigation showed intra-abdominal located testes, any Mullerian structure was not found. There was no increase in testosterone after three days of stimulation with hCG 1500 U/dose and gonadectomy was performed. She is still receiving hydrocortisone (14mg/m<sup>2</sup>/day) and fludrocortisone (0.1 mg/day) treatments.

**Result:** StAR protein deficiency is the most severe and rare form of steroid biosynthesis disorders. Mineralocorticoids, glucocorticoids and androgens can not be synthesized and ACTH level is high. Normal DHEA levels helps for differentiating from 3 beta-hydroxysteroid dehydrogenase deficiency. Caryotype analysis and advanced investigations if needed should be performed.

#### PAO-183

### A rare case of early onset of Cushing disease

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**Background:** Cushing disease is the most common cause of hypercortisolae-mia in adults and children over 7 years of age, whereas in children under 7 years adrenal tumours predominate. We present a case of Cushing disease in a 5-year-old boy.

**Objective:** The patient first presented at the age of 4,5 years with a rapid weight gain, growth arrest and symptoms of premature adrenarche. Clinical examination revealed central obesity, hirsutism, plethora, hypertension, psychological disturbances, puberty stage: A2, P2, testes 3 ml. Laboratory findings showed hypercortisolaemia (54,3  $\mu$ g/dl in the morning, 39,2  $\mu$ g/dl at midnight), hyperandrogenaemia, high level of ACTH (162; 375 pg/ml). CRH stimulation and Dexamethasone suppression tests were performed, confirming the pituitary ACTH overproduction. However, a head MRI didn't revealed a pituitary adenoma.

An abdomen CT scan showed normal adrenals. To exclude an ectopic ACTH syndrome a somatostatin receptor scintigraphy was performed. There were two noncharacteristic lesions in a left lung. The levels of neurospecific enolase and chromogranin A were normal. Inferior petrosal venous sampling was unsuccessful due to atypical course of left jugular veins. Repeated head MRI showed normal pituitary gland. Due to excessive clinical symptoms of hypercortisolaemia, on the basis of the results of hormonal tests, a neurosurgical treatment was planned. The patient started pharmacological therapy with ketoconazole and hydrocortisone replacement as a preparation for the neurosurgical procedure. Transsphenoidal pituitary exploration showed a microadenoma and adenotomy was performed. Six months after the surgical treatment there are no signs of relapse, levels of cortisol and androgens are low, other pituitary functions are saved.

**Conclusion:** Although the adrenal tumours are the most common cause of Cushing syndrome in young children there is a necessity of wide diagnostic procedures in case of hypercortisolaemia and normal imaging examinations.

## PAO-184

### Different skeletal maturation patterns in patients with constitutional delay of growth (CDG) and growth hormone deficiency (GHD)

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**Background:** The determination of bone age is one of the most important criteria to diagnose and work clinically with short stature.

**Objective and hypotheses:** The study aimed to identify disparities in the level of phalangeal bone (PH), metacarpal bone (MC) carpal bone (CP) and radius/ulna (RU) - development in patients with CDG or GHD.

**Methods:** Left hand radiographs of patients with CDG (bone age retardation > 1 yr; no organic diseases; family history of delayed growth and puberty) were compared with those of untreated GHD patients (maximum stimulated GH peak <8µg/l). In each patient PH, MC, RU,- and CP-bone age were calculated by the method of Greulich/Pyle.

**Results:** In the CDG cohort (13 males, 2 females, mean age 10.2 yr) bone age was retarded on average by 2.0 years. Differences in the developmental stages of PH, MC, CP and RU bone were identified as shown in table 1. Likewise, the GHD group (13 males, 2 females, mean age 5.71 y) showed delayed bone maturation as revealed in table 1. In GHD patients primarily carpal bone development was delayed, whereas in CDG patients the maturity of metacarpal bones was primarily delayed.

**Conclusions:** The pattern of bone maturation as assessed by left hand radiographs is different between patients with CDG and GHD. We suggest that the extreme delay in carpal bone maturation could be used as a marker for GHD in the assessment of short stature.

	Chronological age Mean in yr	PH Mean in yr (delay in %)	MC Mean in yr (delay in %)	CP Mean in yr (delay in %)	RU Mean in yr (delay in %)
Patients with CDG	10.2	8.1 (21%)	7.4 (27%)	8.2 (20%)	8.5 (17%)
Patients with GHD	5.7	4.8 (16%)	4.4 (23%)	3.5 (39%)	4.0 (29%)

## PAO-185

Abstract withdrawn.

## PAO-186

### Transsexualism in an African setting; case report

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**Background:** Transsexualism is the condition in which a person with apparently normal somatic sexual differentiation of one gender is convinced that he or she is actually a member of the opposite gender. It is associated with an irresistible urge to be and live in that gender hormonally, anatomically and psychosocially. The patient has persistent discomfort with his or her sex and a sense of inappropriateness in the gender role of that sex. It occurs in all societies and cultures however it is a rare occurrence in Africa.

**Objective:** We describe a case of Male-to-Female Transsexual who presented at the paediatric endocrine clinic of the University College Hospital.

**Case report:** EA is a 27 year old male who presented with the desire for sex reassignment surgery. He has already stated wearing female clothes, cosmetics and jewellery. He also changed his name to a female one and moved to another town. Physical examination revealed an individual with tanner stage 1 for breast and a well developed normal male external genitalia with a solitary right testis. Hormonal profile revealed normal testosterone (31.2nmol/l, nor-

mal values 15 – 40nmol/l) and low estradiol levels (0.3nmol/l). He is awaiting laparoscopy and other investigations which have largely been delayed as a result of lack of funds to pay for them. He is being co-managed with the Psychiatry and Surgical teams.

**Conclusions:** Transsexualism is a rare condition and it is often marginalized even in developed economy. This report exposes the socio-cultural and religious influences associated with management. The dilemma it causes to the immediate family and relatives which has not been highlighted in previous reports is also described. The financial implication of management in this part of the world could also be frustrating to the individual. To our knowledge, this is the first case reported in Nigeria.

## PAO-187

### An unusual presentation in an adolescent with parathyroid adenoma: tendinitis

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**Background:** Primary hyperparathyroidism (PHPT) in children and adolescents is a rare condition. PHPT is usually sporadic and caused by parathyroid adenoma. Patients may present with bone pain, proximal myopathy, bony deformities, fractures, renal calculi, neck swelling or acute pancreatitis.

**Case:** We describe an unusual presentation for PHPT in a 15 years-old male patient. He presented with difficulty in walking due to swelling of the ankles bilaterally. Ultrasonography revealed intratendinous calcific nodules in both achilles tendons. Serum biochemistry showed hypercalcemia and hypophosphatemia. Serum parathormone level was found high (512 pg/ml N:4.5-36). Parathyroid scanning suggested parathyroid adenoma. Parathyroidectomy was performed and the diagnosis of parathyroid adenoma was confirmed histopathologically. The family history was negative for multiple endocrine neoplasm syndrome. The intervention was followed by normalization of phosphocalcic profile and improvement of signs and symptoms of the patient.

**Conclusion:** We suggest that hyperparathyroidism should be kept in mind in the differential diagnosis of tendonopathies.

## PAO-188

### Trend in body height distribution and short stature prevalence among children and adolescents aged from 6 to 18 years in two districts of Shanghai

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**Background:** It is unclear how is the trend of height distribution and short stature prevalence change among children and adolescents in Shanghai.

**Objective and hypotheses:** The aim of this survey was to establish baseline data on the trend in body height distribution and short stature prevalence among children and adolescents in Shanghai.

**Methods:** We selected two districts in Shanghai in 2003, randomly, one in urban area and the other in suburb area. All students in the primary schools, junior and senior high schools of the two districts were screened in 2003 and 2008. The main variables we studied were the subjects' height, age and sex. We analysed the body height distribution and the prevalence of short stature.

**Results:** (1) Body heights were significantly higher in boys than that in girls. (2) Compared with data in 2003, the mean height of 2008 was higher. (3) In the past 5 years, the overall increments were 0.09-4.03cm (Urban male), 0.57-2.55m (Rural male), 0.42-3.76cm (Urban female) and 0.04-1.81cm (Rural female) for stature. (4) The prevalence of short stature was significantly higher in urban district than in suburb area (2003: X<sup>2</sup>=139.73, p<0.01; 2008: X<sup>2</sup>

=186.73,  $p < 0.01$ ) and also was significantly higher in male than in female (2003:  $X^2 = 21.36$ ,  $p < 0.01$ ; 2008:  $X^2 = 8.77$ ,  $p < 0.01$ ). (5) The overall prevalence of short stature in all children and adolescents (6-18 years) decreased significantly from 3.74% to 2.22% between 2003 and 2008 ( $X^2 = 315.46$ ,  $p < 0.01$ ).

**Conclusions:** The distribution of height among children and adolescents aged from 6 to 18 years old in the two districts showed significantly increase between the two sexes from the year 2003 to 2008. The prevalence of short stature has decreased during the last past 5 years in the two districts of Shanghai.

#### PAO-189

### LEOPARD syndrome: clinical characteristics and molecular study

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**Background:** LEOPARD syndrome (LS) is an autosomal dominant disorder and features overlap closely with those observed in Noonan syndrome (NS). PTPN11, BRAF and RAF1 are genes known to be associated with LS. The characteristics are including lentiginos and cardiac defects.

**Methods:** Three patients were diagnosed with LS and required the presence of lentiginos with least one of the cardinal features outlined by Voron et al. We made a mutational analysis: Cyclic sequencing was performed after PCR amplification of all the encode regions and the exon/intron boundaries of PTPN11.

**Results:** There were two female (2.5 years and 7.3 years) and one male patient (13.4 years). Phenotypically, the two girls are typical facies of NS; in all patients we observed low-set ears, high palatal arch and epicanthal folds; in two patients we found pterigium colli and ocular hypertelorism. Cardiac anomalies were detected in two patients: hypertrophic cardiomyopathy (HCM) and two patients with ECG anomalies (left axis deviation and left anterior hemiblock). In all patients, reveals the presence of multiples lentiginos appeared during childhood; one girl has conductive deafness, actually is solved. The three patients had short stature below -2SDS and twice with normal growth velocity for age. One patient had mild mental retardation (IQ75-86) and other patient delayed psychomotor development. **Mutational analysis:** We found three different mutations in the PTPN11 gene: G464A, T468M and Y279C. These mutations have been reported in the literature associated with LS. The mother of the boy also had the same mutation as his son and once girl the mutation occurred de novo.

**Conclusions:** LS is a rare genetic disorder, the major features are lentiginos, cardiac defects as HCM, hypertelorism, short stature and variable degree of neurological disability. All patients need close follow-up by pediatricians and might require early intervention, moreover the molecular analysis enables us to confirm the diagnosis and make genetic counseling diagnosis more accurate

#### PAO-190

### Disorders of sex development –DSD-(46,XX ovotestis) in 3 children of Africa

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**Background:** The ovotestis DSD (OMIM # 235600) is characterized by histological presence of testicular and ovarian tissue in the gonads of the same individual. Karyotype is usually 46 XX (60-100%), SRY negative. The most common form of presentation is ambiguous genitalia at birth. Biopsy of gonad around its longitudinal axis is mandatory to avoid misdiagnosis of mixed forms. Frequency of DSD in Africa is high in some series (51% in South Africa vs 8% in Brazil).

**Population:** We report 3 cases of ovotestis DSD from Mauritania, raised as males. They have different degrees of penile curvature and micropenis, proximal hipospadias, bifid scrotum and unilateral or bilateral cryptorchidism. In 2 of them a gonad was palpable. No uterus was found. 17OH-progesterone and DHEA-S were in the normal range. Karyotype 46 XX, SRY gene negative. Gonadal biopsy was performed in cases 1 and 3. In case 2, macroscopic diagnosis of bilateral ovotestis was made (Table 1)

	Case 1	Case 2	Case 3
Age (years)	6,5	3,9	6
Penis (cm)	2,9	0,5	2
Palpable gonad	Right	Left	No
Right gonad	Ovotestis	Ovotestis	Ovary
Left gonad	Ovary	Ovotestis	Ovotestis

Penil curvature correction was performed with penoscrotal transposition and testis / ovotestis orchidopexy, with removal of ovary and internal female genitalia any (Case 1). Subsequently, two-stage urethroplasty was performed. In Case 2, treatment of micropenis with testosterone ointment 2% was carried out with good response.

**Conclusions:** The diagnosis of ovotestis DSD should be considered in children of African origin with ambiguous genitalia. The most common presentation is the ovotestis (44-64%). They are usually reassigned male because they have already been raised as males in their origin country

#### PAO-191

### Evolution of height in patients with classic congenital adrenal hyperplasia –CAH- and its relation to control of hyperandrogenism and dose of glucocorticoids

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**Background:** CAH is often associated with loss of height in relation to target height –TH-, which is associated with hyperandrogenism and complexity of glucocorticoid treatment.

**Objective:** To assess the final height –FH- in CAH patients and its relationship with the dose of steroids and control of hyperandrogenism. To determine if there is a period of age when the height impairment is greater.

**Methods:** 16 patients (9M/7F) with 8 salt-wasting form (SW) and 8 simple virilizing (SV) diagnosed between 1978 and 2006. 10 patients were classified according to the mutation, the rest by the symptoms. We assessed target height in SD and final height in SD. We compared 17 OHP levels and glucocorticoids dose (mg/m<sup>2</sup>) with SD of height at different ages.

**Results:** There were no significant differences between FH and TH neither by gender comparison nor by clinical form (SW vs. SV)-Table 1-

	M (n=5)	F (n=3)	SW (n=4)	SV (n=4)
TH (SD)	-0,78±0,8	-1,32±0,5	-0,54±0,7	-1,43±0,3
FH (SD)	-1,1±1,4	-1,15±1,9	-0,27±1,3	-1,96±1,1

Average age (weeks) at diagnosis was 2.64 for SW and 8.14 for SV (1.5-255). No correlation (Spearman Rho) was found between height (SD) and 17 OH Progesterone levels or mean glucocorticoids dose per body surface during the prepubertal period (Table 2).

Age (years)	2 y	4 y	8 y
Height (SD)	-0,4±1,7	-0,3±1,4	0,07±0,7
Glucocorticoids/m <sup>2</sup>	14,8±5	14,5±5	14,7±4
17-OHP Progesterone	20,6±34	21,2±18	22,7±20
n	12	14	10

Short FH was present in a SV woman (-2.68 SD) with TH 153.8 (-1.6 SD) and a SV male (-2.98 SD) diagnosed at 4 years 3 months with TH 167.2 (-1.6 SD).

**Conclusions:** No significant loss of height in relation to TH was observed in childhood. Two cases of short FH (-2SD) were associated with late diagnosis (SV forms) and familial (genetic) short stature.

PAO-192

**Generalised arterial calcification of infancy - a novel mutation of the ENPP-1 gene**

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**Background:** Generalised Arterial Calcification of Infancy (GACI) is a severe autosomal recessive disorder characterized by calcification and stenosis of large and medium sized arteries. Although many affected children die in early infancy approximately 34% children would be expected to survive beyond infancy. Inactivating mutations of the Ectonucleotide Pyrophosphatase/Phosphodiesterase -1 (ENPP-1) gene have been implicated in many cases of GACI and more recently, in causation of hypophosphataemic rickets.

**Case report:** A female baby was born of on-consanguineous Caucasian parents, at 29 weeks of gestation with evidence of GACI on antenatal scans. She died within 24 hours of birth secondary of congestive cardiac failure. Her female sibling was born at 31 weeks of gestation and was diagnosed antenatally to have complex congenital heart disease including hypoplastic left ventricle, double outlet right ventricle, arterio-pulmonary window and idiopathic arterial calcification. A postnatal scan confirmed these findings. Due to very poor prognosis of this condition, after extensive discussion with parents and paediatric cardiologist it was decided not to actively treat her cardiac condition. Molecular analysis of the ENPP1 gene showed two novel nonsense mutations on Exon1 (c. DelGC 190/191, p. A64A fsX11) and Exon21 (c. 2230 C/T, Q744X). At two and half years of age she started showing evidence of phosphaturia and hypophosphataemia.

**Discussion:** Within last 20 years, anecdotal GACI cases of survival beyond infancy with spontaneous regression of calcification have been reported. The factors which lead to survival beyond infancy are poorly understood but hypophosphataemia and treatment with bisphosphonates was associated with survival in a large retrospective study. The presence of a novel mutation in our case is unlikely to explain the association with complex CHD but this is the first reported case of such association. In our case, the long term outcome and survival could be affected by pulmonary hypertension, despite bisphosphonate treatment.

PAO-193

**Gonadal function in patients with classic galactosemia**

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**Background:** Classic galactosemia is an inherited inborn error of the major galactose assimilation pathway, caused by gactose 1-phosphate uridylyltransferasi (GALT) deficiency, with an incidence of 1:30.000 newborns. Many GALT mutations have been described, with different clinical consequences. In the neonatal period, after ingestion of milk containing galactose, newborns present a severe clinical situation with jaundice, hepatosplenomegaly and hepatocellular damage, vomiting, hypoglycemia, renal tubular disease and hypotonia. Therapy is represented by a galactose-restricted diet which, unfortunately, does not prevent long-term complications, particularly cognitive and motor abnormalities and primary ovarian failure (POF). The pathogenesis of galactose-induced ovarian toxicity remains unclear but probably involves galactose itself and its metabolites such as galactitolo.

**Objective and hypotheses:** The aim of the study is to evaluate pubertal development in classical galactosemia.

**Method:** We report data of our patients (2 couples of brothers) identified by neonatal screening.

**Results:** The table shows our results, 5 patients with classic galactosemia, genotypically characterized, present a cognitive and gonadal behavior in accordance with literature. Indeed, patients 1A and 1B, 2A and 2B show a more severe phenotype although an early diagnosis and therapy and a good dietary compliance; patient 3 has a normal phenotype and is a compound heterozygous for a known mutation linked to a severe phenotype and a mutation not present in literature. Moreover she is carrier of Los Angeles variant, Duarte 1, associated with an increased activity of enzyme GALT.

Patients	Sex	Genotype	Age at evaluation	Characteristics of pubertal development	Hormonal evaluation and pelvic ultrasound
1A	F	p.Q188R/p.K285N	15 years	PH 4 B 4 Primary Amenorrhoea	LHRH test: hypergonadotrophic hypogonadism. Estradiol <12 pg/ml. Normal pelvic ultrasound
1B	M	p.Q188R/p.K285N	12 years	PH 3 T 18 cc Spontaneous and regular pubertal development	LHRH test: normal for pubertal stage. Testosterone 1.5 ng/ml
2A	F	p.K285N/p.X380R	12.5 years	PH 3 B 3 No progression.	LHRH test: hypergonadotrophic hypogonadism. Estradiol <12 pg/ml. Pelvic ultrasound : consistent to pubertal stage.
2B	F	p.K285N/p.X380R	5 years	PH 1 B 1	Hight basal levels of LH and FSH
3	F	p.A122V/p.Q188R/p.N314D/p.L218L	18 years	Early puberty, therapy with LHRH analog. Regular menses.	Normal LHRH test. Estradiol 200 pg/ml. Normal pelvic ultrasound.

**Conclusions:** Since it is a rare disease, the number of patients is low, so that further investigations are needed with larger series and long-term follow-up.

PAO-194

**Pattern of inheritance and analysis of clinical and cerebral MRI features of familial cases of central precocious puberty**

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**Background:** Many clinical observations show that central precocious puberty (CPP) may be in some cases familial. However, the scientific support to this assumption remains sparse up to now.

**Objective and hypotheses:** The aim of the present study was to define a pattern of inheritance of familial CPP, and to identify possible clinical differences between familial (FPP) and sporadic (SPP) forms of CPP.

**Methods:** We studied 110 patients affected by CPP (104 F, 6 M). The family tree of each patient was analysed and all information regarding the age of puberty and of menarche, and the presence of CPP among first and second degree relatives was collected.

**Results:** Forty-one cases (37.3%; 40 F, 1M) met the criteria for FPP and the remaining 69 cases (62.7%; 64 F, 5 M) were SPP. The FPP showed a pattern of inheritance that was autosomal dominant in 24 (58.5%) cases, autosomal dominant with incomplete sex-dependent penetrance in 16 (39%) girls and autosomal recessive in only 1 (2.5%) case. The age at onset and the age at diagnosis of CPP did not differ between FPP and SPP, the girls with FPP showed a higher BMI-SDS than girls with SPP (2.77 ± 2.28 SD vs 1.72 ± 1.71SD; P=0.0402) and a greater bone age acceleration (2.12yrs ± 1.28 SD vs 1.56yrs ± 1.32 SD; P=0.0275). MRI showed CNS anomalies in 14/69 (20%) children with SPP and in 7/41 (17%) children with FPP.

**Conclusions:** A familial origin was found in 1/3 of cases with CPP. Girls with FPP have a higher BMI and bone age maturation than those with SPP. CNS abnormalities were found either in SPP either in FPP and do not allow to exclude the need of performing cerebral MRI in FPP. The high prevalence of FPP suggests a careful inquiry regarding precocious puberty in young siblings and first-degree cousins of a child diagnosed with CPP.

### Effectiveness of gonadotropin-releasing hormone analogue treatment in children with central precocious puberty with respect to bone age acceleration before the therapy

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**Background:** Central precocious puberty (CPP) is defined as the onset of puberty in girls and boys before the age of 8 and 9 respectively. It has a higher incidence in girls. Bone age is almost always advanced. The treatment of choice is long term depot gonadotropin-releasing hormone analogue (Gn-RHa). The goal of mentioned therapy is to inhibit pubertal development and improve the height prognosis.

**Objective and hypotheses:** The aim of this research was to evaluate the influence of GnRHa therapy in children with CPP on the height prognosis depending on pretreatment bone age.

**Methods:** The group of 62 patients with diagnosed CPP was enrolled in the study: 48 girls and 14 boys. Patients were treated with GnRH analogues depot – triptorelin 3.75 mg. For all the patients, the following pre- and post treatment parameters have been calculated and expressed as SDS: height, predicted adult height (PAH), bone age/chronological age (BA/CA) and bone age/height age (BA/HA). Patients were divided in two groups. Group A comprised those children who began their treatment with BA consistent or slightly advanced in relation with CA and HA. Group B gathered those patients whose BA was definitely advanced with respect to CA and HA.

**Results:** Height prognosis improvement was observed in group B (in children whose BA before treatment was definitely advanced with respect to CA and HA). There was no height prognosis improvement noticed in the group A (which was characterized by consistent or only slightly elevated BA). The results are presented in the Table 1 for BA/CA and in the Table 2 for BA/HA.

BA/CA	advanced	normal	p
age before GnRHa [years]	7.4±2.2	9.3±1.7	0.001
hSDS before GnRHa	1.84±1.14	0.87±1.22	0.007
PAH SDS before GnRHa	-0.95±1.35	0.14±1.18	0.005
therapy duration [years]	3.7±2.2	2.80±1.90	0.066
hSDS after GnRHa	1.02±1.34	0.48±1.21	0.156
PAH SDS after GnRHa	-0.42±1.15	-0.31±1.23	0.806
Δ PAH SDS	0.53±0.99	-0.44±0.86	0.001

BA/HA	advanced	normal	p
age before GnRHa [years]	7.8±2.5	8.7±1.6	0.265
hSDS before GnRHa	0.97±1.15	2.03±1.16	0.001
PAH SDS before GnRHa	-1.40±0.93	0.60±0.97	0.001
therapy duration [years]	3.7±2.3	2.8±1.7	0.094
hSDS after GnRHa	0.32±1.17	1.41±1.23	0.001
PAH SDS after GnRHa	-0.98±0.93	0.31±1.05	0.001
Δ PAH SDS	0.42±0.94	-0.28±1.05	0.032

**Conclusions:** The therapy with GnRHa proved to be effective in improving height prognosis only in children with advanced BA.

### A 9 year old prepubertal girl with genital bleeding: premature menarche?

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**Background:** Isolated premature menarche is a rare condition with unknown etiology. There is a predominance of FSH secretion. Before the diagnosis is accepted, all other causes of vaginal bleeding should be excluded.

**Case presentation:** A 9 year old German girl otherwise healthy was presented with suspected genital bleeding. Vaginal bleeding was at first assumed by the mother 5 months ago when she noted a blood-stained panty of her daughter. Any traumatic injuries or sexual abuse were denied. The girl did not report on abdominal pain, dysuria, incontinence or fever. Physical examination showed a prepubertal girl (height 131 cm, weight 30.3 kg, BMI 17.7 kg/m<sup>2</sup> BSA, RR 104/65 mmHg) with fine pubic hairs (Tanner P2), no thelarche and normal, non-estrogenized external genitalia. Basal hormone levels were in the normal range for age (LH < 0.1 mU/ml, FSH 1.3 mU/ml, estradiol < 5.0 pg/ml, fT4 11.7 pg/ml, TSH 0.75 mU/ml, DHEAS 813 ng/ml). After GnRH stimulation, FSH increased more (13.2 mU/ml) than LH (3.4 mU/ml). Pelvic ultrasound showed a normal prepubertal size of uterus and ovaries. Bone age was not accelerated. The girl was presented to the pediatric gynaecologists. By vaginoscopy and urethrascopy a polypous mass was found located at the upper vaginal fornix beginning at the external urethral orifice. At the same time an exploratory excision of the polypous mass was extracted, and histologically confirmed as haemangioma. Currently, it is decided to wait and see in order not to vulnerate the sphincter of the urethra by any therapeutic procedures (e.g. laser- and cryotherapy).

**Summary:** In our case vaginal bleeding was due to a haemangioma. Thus, the diagnosis of premature menarche could be excluded.

**Conclusions:** Haemangiomas of the urethra and vagina are extremely rare in childhood. In a large series of 62 girls (< 10 yrs) genital bleeding resulted in 74% from a local lesion of the vagina (vulvovaginitis > urethral prolapse, trauma > foreign bodies, tumors). Haemangiomas were not reported (Imai et al. Int J Gynecology & Obstetrics 1995).

### Autoimmune thyroiditis and phenylketonuria: a new association

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**Background:** Phenylketonuria (PKT) is an inherited metabolic disorder characterised by an absence or deficiency of the enzyme phenylalanine hydroxylase. The neonatal screening and the early treatment, with a low-phenylalanine diet, prevent developmental delay and support normal growth.

**Objective and hypotheses:** There is no evidence of endocrine disorders or of autoimmune diseases associated with PKT.

**Method:** We describe two cases of unrelated girls affected by PKT with a clinical presentation of thyroid disease.

**Results:** G.A. 14 years, born SGA showed a poor growth from the first years. GH treatment was purposed but never started for the poor familial compliance. Stature: 133,5 cm (<-4SDS); weight: 29 kg; bone age: 13 years, pubertal stage:PH2B3; caryotype: 46,XX. She had menarche at 13,9 years. She presents goitre with a palpable "Delphic" node. Thyroid scan evidences an enlarged thyroid with a pattern of thyroiditis; TSH: 1,2; fT3: 7,4; fT4: 0,95; anti-TG and anti-TPO antibodies in the normal range; glycaemia, IGF-1, celiac disease markers: negative.

S.C. 10,7 years, presented hyperglycaemia with positive ICA, IAA, anti-GAD, treated with a4-doses insulin schedule. She underwent an endocrinological investigation for the evidence of a goitre. She has myxedema, mild anaemia, goitre with a nodular consistence. Stature is 139 cm; weight:34 kg; pubertal stage: PH2B2-3. Hormonal tests evidence: TSH: 199; fT3: 3,19; fT4: 0,39; anti-TG and anti-TPO antibodies: 277 and 12620 respectively; celiac

disease markers: negative. Thyroid scan confirmed the diagnosis of goitre with a typical pattern of thyroiditis.

She promptly starts L-Thyroxin treatment, with a significant improvement in clinical presentation, normalization of hormonal values (one month later she has TSH: 2,8; fT4: 0,94; fT3: 7,4) and reduction of goitre volume and myxedema.

**Conclusions:** We signal these cases for the uncommon association of PKT and autoimmune thyroiditis in two unrelated adolescents: one patient presents two autoimmune endocrinopathies (thyroiditis and T1DM).

#### PAO-198

### Two cases report of Turner syndrome associated with metabolic syndrome

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**Background:** Turner syndrome(TS) occurs in approximately one in 2500 female births and is characterized by short stature and sex hormone deficiency. However, it is becoming increasingly evident that patients with TS are also susceptible to a range disorders.

**Method:** We present two patients with metabolic syndrome(MS).

#### Results:

Case 1, A 13.3ys female patient, karyotype was 45,X/46,X,+mar. height 127.3cm (<-4.95SD), weight 32.7kg, shield thorax, several pigmentary nevi on her face, no puberty signs. Elevation of hepatic enzymes (ALT 60 U/L), TG 5.89 mmol/L, CHOL 6.12 mmol/L, HDL:1.06 mmol/L, fasting blood glucose, insulin, HbA1C, GH peak of GH stimulating test, LH, FSH, TPO and Tg antibodies are presented in Table 1, T3, T4, TSH were normal, BA: 10y, Ultrasound: small uterus and ovaries were not detected, fatty Liver, MRI: pituitary gland dysplasia, partial empty sella turcica. She also suffered epilepsy since 6 months-old. Diagnosis: TS, MS, adiposis, diabetes mellitus(DM), hyperlipidemia, growth hormone deficiency(GHD), hashimoto thyroiditis, epilepsy. Case 2, A 16.5ys female patient, karyotype was 45,XO. height 134cm (<-4.76SD), weight 40.5kg, short neck, micrognathia, shield thorax, cubitus valgus, no puberty signs. Elevation of hepatic enzymes (ALT:170 U/L, AST:101 U/L), TG: 5.42 mmol/L, LDL: 4.58 mmol/L, HDL: 1.14 mmol/L, fasting blood glucose, insulin, HbA1C, GH peak of GH stimulating test, LH, FSH, TPO and Tg antibodies are presented in Table 1. T3, T4, TSH were normal, BA: 14ys, Ultrasound: small uterus and ovaries could not be detected, fatty Liver; Saddle area MRI showed normal. Diagnosis: TS, MS, adiposis, DM, hyperlipidemia, GHD.

Case	Fasting blood glucose (mmol/L)	Insulin (uIU/ml)	HbA1C	GH peak of GH stimulating test (ng/ml)	LH (IU/L)	FSH (IU/L)	TPOAb (IU/ml)	TgAb (IU/ml)
Case 1	10.2	<2	6.8%	4.5	6.0	48.9	416	75.6
Case 2	13.9	11.9	14.3%	4.8	8.2	90.4	10	89.3

**Conclusions:** It appears that  $\beta$ cell dysfunction or insufficiency response to glucose is intrinsic to TS and is at the core of the high risk for DM, excess weight and an abnormal lipid profile, in particular excess triglyceride levels, worsened insulin sensitivity. So to detect and interfere with these disorders earlier are significant for TS patients.

#### PAO-199

### First results from the screening for congenital adrenal hyperplasia in Bulgaria

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**Background:** Congenital adrenal hyperplasia (CAH) is difficult to diagnose and potentially life- threatening in the neonatal period.

**Objective and hypotheses:** The objective of the present study is to analyze the first results from the novel Bulgarian neonatal screening (NS) for CAH for the period April 2010 - March 2011.

**Methods:** The level of 17-OH-Progesterone (17-OHP) in dried blood spot was assessed in all Bulgarian newborns (n=74 133). Until the end of 2010 we

used only the cut-off value of 30 nmol/l for full-term infants at age 3-5 days. We began to apply the ISNS referent values since the beginning of 2011.

**Results:** An increased levels of 17-OHP were found in 637 cases (recall rate 0.85%). On a second assessment the results were confirmed in 410 cases (recall rate 0.55%). Most of the babies were preterm. Only 52 of them (12.6 %) had birth weight  $\geq$  2500 g. and 47 (11.5 %) were born after the 36 week of gestation. The diagnosis classic CAH was confirmed in 7 children. Estimated prevalence for the country- 9.4:100 000. The treatment was started at average age 15.6 ( $\pm$  8.3days). Three of the children with CAH were preterm (birth weight < 2500 g and gestational age < 36 gestational week).

**Conclusions:** The first data on CAH (classical forms) prevalence for the Bulgarian population obtained by NS do not differ significantly from the published for other countries. The results show the importance of NS for the early diagnosis and initiation of treatment. Constant improvement of the existing screening logistic is possible during expansion of the screening programs.

#### PAO-200

### Efficacy and safety of adenotonsillectomy in italian children affected by Prader-Willi syndrome

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**Introduction:** Children affected by Prader-Willi syndrome (PWS) frequently suffer from sleep-associated breathing disorders, because of muscular hypotonia, obesity, sticky saliva, adenotonsillar hypertrophy and craniofacial dysmorphism. Adenotonsillar hypertrophy is the main cause of nocturnal rhonopathy with obstructive sleep apneas (OSAS).

If left untreated, it may result in severe complications: excessive daytime sleepiness (EDS), neurocognitive impairment, behavioral problems and pulmonary heart disease. EDS is a common feature in PWS: it begins in childhood and can interfere with school and social activities, providing a significant decline in quality of life. Adenotonsillectomy (A&T) represents the first line of treatment but several studies identified PWS population at high risk for postoperative complications: difficult awakening from anesthesia, hemorrhages, respiratory complications requiring reintubation and/or supplemental oxygen administration.

**Material and methods:** Eighty-one children underwent a complete otorhinolaryngoiatric examination (anterior rhinoscopy, oral and nasal endoscopy with a flexible fiberscope); nine children underwent surgery because of severe adenotonsillar hypertrophy (grade III or IV). All patients underwent nocturnal polysomnography and Multiple Sleep Latency Test (MSLT) preoperatively; five children underwent a second sleep study three months after surgery.

**Results:** No postoperative complications were observed in our group of patients. Preoperatively, mean sleep latency (MSL) was 5 minutes (range 3-8). The same study, performed after surgery, showed a significant improvement in daytime sleepiness (MSL 8,4 minutes; range 6-12).

**Conclusions:** None of the children in our group presented surgical complications, however caution regarding postoperative complications must be taken due to the high-risk profile related to PWS. Furthermore, our data demonstrates that surgery improves quality of life in PWS by contributing in decreasing EDS and increasing mean sleep latency.



## PAO-201

### The medium and short-term effects of sinusoidal and vertical vibratory training on the musculoskeletal and endocrine system in healthy men

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**Introduction:** The underlying mechanisms that explain the beneficial effect of whole body vibration (WBV) on bone health are unclear.

**Aim:** To compare the immediate and medium term effects of WBV using the Galileo platform (sinusoidal WBV)(sWBV) and the Juvent1000 platform (vWBV) on muscle function, endocrine status and markers of bone turnover.

**Material and method:** 10 healthy men(36yrs±2.4), randomized into two groups; the first group stood on the sWBV and the second group stood on vWBV 3times/wk/2months. The measurements were performed at five timepoints(T) over 4 months. T0(1 month pre-WBV), T1(the first day of exercise),T2(1month WBV),T3(2month WBV) and T4(1month post-WBV). T1, T2 and T3 consisted of four sampling times 60mins before WBV and 5-30-60mins post WBV. Each participant had anthropometry, assessment of body composition by Tanita and assessment of muscle function by mechanography and grip strength force and measurement of serum markers of bone turnover, glucose, IGF-1, cortisol.

**Results:** There were no significant changes in anthropometry, body composition or muscle function in the two groups at the end of the study period. The change in creatine kinase following exercise was similar in both groups. Both vibration platforms were associated with an immediate decrease(p=0.001) in cortisol following the exercise, but there was no difference in the decrement between the two devices. In the medium term, sWBV was associated with a reduction in median serum cortisol from 333 nmol/l(247,442) to 269 nmol/l (192,322)(p,0.04) whereas there were no significant changes in the vWBV group. Serum CTX, a marker of bone resorption fell significantly after 2months in the sWBV group from a median of 0.42ng/ml(0.3,0.87)to 0.29ng/ml(0.2,0.4)(p,0.03).

**Conclusion:** WBV is associated with a fall in endogenous cortisol and a reduction in bone resorption particularly in those subjects who were exposed to sinusoidal vibration. Longer-term comparative studies are required to further investigate the effect on bone.

## PAO-202

### An interesting case of delayed puberty associated with neurofibromatosis type 1 and hamartoma

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**Background:** Neurofibromatosis type 1(NF1) is one of the most common neurogenetic disorder. Complications are quite variable however the most frequent are optic pathway tumors (glioma), short stature and precocious puberty.

**Objective and hypotheses:** We report the case of a 14 yr old boy that occurred with delayed puberty.

**Method:** Clinical and laboratory investigations.

**Results:** Clinical history revealed a previous neurosurgical treatment for a ventricular hydrocephalus caused by a midbrain hamartoma, at the age of 12 yrs. The family history was negative. Upon examination, patient's weight was 47.6 kg (>25th centile), height was 154.7 cm (< 25th centile) significantly below his genetic target (186 ± 7 cm) and he exhibited a decrease in growth rate. Tanner stage was G1 PH1, testis 2-3 mL. We observed several café-au-lait spots, of which 5 were recent onset, localized in the thoracic and sub-mandibular areas and on the right ankle, for which we formulated the hypothesis of NF1. Laboratory investigations revealed a peak of LH after GnRH test of 6,25 mIU.mL-1, corresponding to prepubertal development, in agreement with plasma testosterone that was less than 0.5 nmol.L-1 (r.v. 0,6-2,7 nmol.L-1). Karyotype was normal. Celiac disease, hypothyroidism, growth hormone deficiency were excluded. Bone age was correspondent to chrono-

logical age therefore we excluded constitutional delay of growth and puberty. On suspicion of NF1 we also carried out: dermatological examination, which revealed signs compatible with NF1; ophthalmological exam, which showed one Lisch's nodule in the anterior segment of right eye. MRI revealed a small midbrain hamartoma, normal morphology and amplitude of ventricles and pericephalic spaces, minimum herniation of the cerebellar tonsils and no areas of pathological impregnation.

**Conclusions:** This case is interesting for the association of hamartoma and NF1 with delayed puberty, when usually both diseases are associated with precocious puberty.

## PAO-203

### A novel mutation of abcc8 gene in congenital hyperinsulinism

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**Background:** Congenital hyperinsulinism (CHI) is a heterogeneous disease characterized by dysregulation of insulin secretion resulting life-threatening hypoglycemia. Mutations of SUR1 gene (ABCC8) are responsible for 50-60% of CHI.

**Objective and hypotheses:** Herein we reported an infant who diagnosed CHI, due to a novel homozygote mutation (Q392H) in ABCC8 gene. The patient had very severe brain damage, despite early diagnosis and appropriate management.

**Patient:** A two-day-old baby boy was referred to our center due to resistance seizures. His parents were first degree relatives. At the admission, his hypoglycemia was detected and glucose infusion was started and elevated to 15 mg/kg/min. During hypoglycemia (glucose: 5 mg/dL) blood ketone was negative, ammonia level was normal, insulin:400 uIU/mL c-peptide:26,5 ng/mL. Blood glucose levels were elevated more than 30 mg/dl with IV glucagon. He was diagnosed as CHI. Diazoxide, somatostatin were started and later nifedipine and uncooked corn starch were added to the therapy. The doses of the diazoxide, somatostatin and nifedipine were increased to maximum doses according to levels of blood glucose. Glucose infusion stopped after total enteral nutrition was tolerated. During follow up, in generally his blood glucose levels were within normal limits. Although hypoglycemia was seldomly detected, his neurological status never improved. The patient was found homozygous for a novel mutation (Q392H) in exon 7 of ABCC8 gene. His parents were heterozygous for this mutation. The patient died due to respiration failure at 4. months of life.

**Conclusions:** In CHI patients, genotype-phenotype correlations are unclear. In our case hypoglycemia was detected at the second day of life and severe medical treatment was started in emergence. Although, severe hypoglycemia was seldom, his neurological status did not improve. We hypothesized that, cerebral damage of hyperinsulinemic hypoglycemia might start in utero period due to severely affected phenotype by the novel mutation.

## PAO-204

### Hypercalciuria and renal function and in children affected by osteogenesis imperfecta

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**Background:** Osteogenesis Imperfecta (OI) is a heterogeneous group of inherited disorders of connective tissue characterized by bone fragility, reduced bone mass, laxity of ligaments, blue sclera and different levels of low stature. Hypercalciuria is a condition characterized by an increased urinary calcium without hypercalcemia. It is characterized by an urinary calcium excretion >4mg/kg/die or urinary Ca/Cr ratio >0.21. The relation between hypercalciuria and OI had been already analyzed in several studies.

**Objective:** The aim of this study is to observe the incidence of hypercalciuria

among patients affected by OI and the possible correlation with the severity of the underneath condition. We also want to verify the presence of any kidney damage related with the increased urinary calcium or with the ongoing treatment with bisphosphonates.

**Methods:** We have recruited 36 patients, followed at our clinic, treated with bisphosphonates. We collected, in a period of 3 months (T0-T1), auxological, clinical and laboratory parameters. All patients performed an abdominal ultrasound.

**Results:** Through urinary Ca/Cr ratio we have identified 11 hypercalciuric patients in T0, 15 in T1. We didn't find any alterations in kidney function both in biochemical and in imaging data. But estimating the urinary calcium in mg/kg/die in T1, we've also observed that hypercalciuric patients were only 6.

**Conclusion:** We haven't found correlation between hypercalciuria and severity of OI. Urinary Ca/Cr ratio is not specific enough to detect hypercalciuria in our patients, maybe because of low creatinine levels as a consequence of OI. It is important, in these children, to integrate Calcium and Vitamin D. Hypercalciuria and the treatment with bisphosphonates do not cause any significant kidney alteration. The next studies with DXA are going to make a better evaluation of the influence of hypercalciuria on bones of patients affected by OI.

## PAO-205

### Myxedematous coma due to secondary hypothyroidism with panhypopituitarism

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**Introduction:** Craniopharyngiomas (CP) are rare brain tumors in children. The tumor itself or its subsequent surgical treatment causes the most common multiple hormone deficiency and replacement is frequently necessary. Myxedema coma (MC) is a rare, but often fatal endocrine emergency. The majority of cases occur in primary hypothyroidism but in central origin is extremely rare.

We report the case of a patient with panhypopituitarism due to a craniopharyngioma surgery, who developed myxedema coma due to pituitary hypothyroidism.

**Case:** A 12-year-old girl with loss of consciousness was admitted to a nearby hospital. She was transferred to our hospital for further hormonal evaluation and treatment. Her medical history was learned that she took multiple hormone replacement for two years because of CP had been operated, but took no medicine for the last three weeks. On physical examination; she was unconscious, hypotensive, bradycardic and hypothermic. Oxygen saturation was 75% without administration of supplemental oxygen. She had pretibial, non-pitting edema.

Peripheral blood tests detected decrease in hemoglobin, serum sodium, potassium, calcium levels. All of the pituitary hormone levels was demonstrated as decreased. A thyroid function test reported undetectable levels of both freeT4(<0.67ng/dL), freeT3(<0.67pg/mL), TSH(0.002 IU/ml). Magnetic resonance imaging of the pituitary gland revealed an empty sella. We initiated replacement of electrolytes and erythrocyte then adrenocortical hormone replacement therapy, followed by oral administration of levothyroxine at an initial dose of 600 mcg. As a result, the patient's awareness level gradually improved. Following this, dosages were reduced. Our final diagnosis for the patient was MC due to central hypothyroidism together with panhypopituitarism.

**Conclusion:** We suggested that panhypopituitarism together with stress could rapidly cause MC in children. The reason of this case presentation is that MC is a rare cause of secondary hypothyroidism with panhypopituitarism.

## PAO-206

### Differences in phenotype and genotype: growth in Pompe disease (PD)

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**Background:** Lysosomal storage disorders are very rare diseases that are characterized by a great variability in their clinical presentation. In order to gain experience in this complex field, a center of excellence must be estab-

lished that covers all aspects of these conditions such as diagnosis, treatment and research. The Villa Metabolica at the Children's Hospital of the University of Mainz is dedicated to provide diagnosis and multidisciplinary management for all patients affected by any of the about 50 known lysosomal storage disorders. We wanted to show the differences in Phenotype and Genotype in PD. Pompe disease (also known as glycogen storage disease Type II) is caused by a deficiency of a critical enzyme in the body called acid alpha-glucosidase (GAA). Normally, GAA is used by the body's cells to break down glycogen (a stored form of sugar) within specialized structures called lysosomes. In patients with Pompe disease, an excessive amount of glycogen accumulates and is stored in various tissues, especially heart and skeletal muscle, which prevents their normal function.

**Results:** Actually we have 5 patients with infantile PD, 3 were too small for their gestation age (f. e.: genotype c.1637-2A>G c.1637-2A>G. Also we examined 15 patients with adult PD, one patient is 181 cm, 3 patients are 175 cm, the other are too small for their age (familial predisposition was considered). The growth hormone (GH) insulin-like growth factor (IGF) system is impaired in these cases in PD.

**Conclusions:** The overall objective of our investigations is to evaluate the long-term growth and development especially of patients with infantile-onset Pompe disease under treatment.

## PAO-207

### Menstrual cycle in adolescence and its relationship with parameters of metabolic syndrome

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**Background:** Clinical evaluation of adolescents should include an assessment of the menstrual cycle (MC), with emphasis on changes in the pattern of the cycle that can represent the first sign of a systemic and evolutive disease as the metabolic syndrome (MS), whose clinical manifestation can occur only in adulthood.

**Objective and hypotheses:** The valuation of changes in the pattern of CM may be the opportunity for early diagnosis and initiation of preventive and effective actions. Objective: Evaluate the menstrual cycle in adolescence and its relationship with parameters of MS.

**Methods:** Observational, comparative and transversal-cut study with 59 female adolescents aged between 12 and 19 and presence of at least one of factors: Overweight/Obesity. All of adolescents underwent a clinical evaluation with anthropometric and laboratorial data, composed of Fasting Glucose, Total Cholesterol, HDL-Cholesterol, Triglycerides, Oral Glucose Tolerance Test (Glucose 120) and Fasting insulin and Insulin post OGTT (insulin 120), Folicle- Stimulating-Hormone (FSH), Luteinizing Hormone (LH), Total Testosterone (TT), Androstenedione. Two groups were created. G-1 adolescents with irregular cycles, and G-2 with regular cycles.

**Results:** 59 adolescents evaluated, 36 formed G-1, and 23 formed G-2. In statistical analysis it was observed :G-1 presented: Waist/Height (p=0,009), Waist (p=0,026), Fasting Insulin (p=0,009), Glucose 120 (p=0,002) , insulin 120 (p=0,0001), HOMA-IR (p=0,0008), Triglycerides (p=0,013), MS (p<0,0001) and POS (p<0,0001) greater and QUICK (p=0,008), G/I (p=0,002) HDL (p=0,001) lower than G2. 9 0% of G-1 presented irregularity since menarche Logistic regression analysis observed insulin 120 >75 (p=0,010) were significant to predict irregular cycle.

**Conclusions:** We believe that greater knowledge about the correlation between changes in menstrual cycle in adolescents and variables related to metabolic risk in this age group is very useful for an early screening that will enable the prevention of MS and related diseases.

**PAO-208****An audit of the use of DDAVP for central DI at a single institution***Esieza Ikazoboh; Vaita Tziaferi; Mehul Dattani*

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**Background:** The use of DDAVP in childhood DI is currently non-evidence based.**Objective:** We audited the use of DDAVP in patients with central DI diagnosed between January 2000, and December 2010. 32 patients with a history of DI were identified; 4 were excluded: DDAVP had been discontinued in 3, and a diagnosis of central DI was uncertain in one.**Population and methods:** Diagnoses of the 28 (11 males) included patients were: Septo-optic dysplasia (SOD)-n=11; Craniopharyngioma (CP)-n=7; Holoprosencephaly (HPE)-n=3; Langerhans Cells Histiocytosis (LCH)-n=3; Others-n=5. Medical records were retrospectively reviewed.**Results:** The median age at diagnosis was 1.38 years (range: 0 – 13.84; N=23), with a mean duration of follow up of 26 (0 – 130) months. 64% were ACTH deficient. The mean daily dose of DDAVP required (N=25) was 226.36 (9.46 – 1019.40) mcg/m<sup>2</sup>. Patients with CP and LCH required higher doses (375.85mcg/m<sup>2</sup> {mean age=9.6years} and 341.04mcg/m<sup>2</sup> {7.41years} respectively) whilst patients with SOD and HPE required lower doses (141.24mcg/m<sup>2</sup> {mean age=5.1years}; 70.78mcg/m<sup>2</sup> {6.6years} respectively). All patients were on oral preparations except for one who received intranasal DDAVP. Eight patients were on a twice daily dose whilst 20 were on a thrice daily dose at last follow up; 12.5% of children under 7 years were on a thrice daily dose whilst the proportion was higher (55%) in children over seven. 17 patients had relevant tests performed in the last 6 months, and 8 in the last year; data were unavailable in three. Mean plasma Na<sup>+</sup> concentration (N=26) was 138.4 (131 – 155) mmol/l. 20 patients had paired urine and plasma osmolalities checked in the last year. No adverse events related to DDAVP use were identified.**Conclusion:** Doses of DDAVP in our population vary according to age and underlying condition. In this high risk cohort, 89% of our patients had relevant tests over the past year and had no adverse events.**PAO-209****Effect of urtica dioica leaves distillate on blood glucose of patients with type 1 diabetes***Maryam Razzaghy-Azar; Hossein Zaeri Aghmashhadi*

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**Background:** *Urtica dioica* is an edible plant that is traditionally used for its different effects including lowering of blood glucose.**Objective and hypotheses:** The aim of this study was to determine the glucose lowering effect of *urtica dioica* in patients with type 1 diabetes mellitus (T1DM).**Methods:** This phase one study is registered as the number "IRCT2010 08174585N1" and has ethical approval. It was done on 24 patients with T1DM aged 12 ± 2 years and duration of diabetes was more than 1 year. They had no chronic complication of diabetes or concomitant disorder. Distillate of *urtica dioica* leaves was prepared in the laboratory. Patients were divided into 8 groups of 3 subjects and were studied in 6 days. In the first 3 days, they did not receive the solution but in the second 3 days, they drank *urtica* distillate in the morning once daily while they were on usual insulin therapy. The carbohydrate counting of their foods were equal on these two periods. Their blood glucose was monitored by continuous glucose monitoring system (Medtronic USA) every 5 minutes in these 6 days. Total daily blood glucose and insulin compared by paired T test on these two periods (SPSS 12). The first group received 30 ml/M2 of the solution and the other groups received 15 ml/M2 more than the previous one up to 150 ml/M2.**Results:** Mean blood glucose in the second period and on day 6 were 201 ± 48.6 mg/dL and 194.75 ± 55 respectively that were significantly lower than first period (218 ± 50) (P=0.017, and 0.014 respectively). The total dose of insulin did not change during these periods.**Conclusions:** *Urtica dioica* leaves have a substance with blood glucose lowering effect in T1DM.**PAO-210****Coagulation-factor deficiencies and abnormal bleeding in Noonan's syndrome***Gabriella Gamba<sup>1</sup>; Francesca Marabotto<sup>2</sup>; Laura Losa<sup>2</sup>; Gabriele Ruffi<sup>2</sup>;**Luisa Strocchio<sup>2</sup>; Arianna Zaroli<sup>2</sup>; Mariangela Cisternino<sup>2</sup>*<sup>1</sup>University of Pavia, Department of Internal Medicine - IRCCSFondazione Policlinico San Matteo, Pavia, Italy; <sup>2</sup>University of Pavia, Department of Pediatrics - IRCCS Fondazione Policlinico San Matteo, Pavia, Italy**Background:** Noonan syndrome (NS) is a congenital autosomal disorder, characterized by dysmorphic facies, congenital heart defects, short stature and other anomalies including coagulation abnormalities not fully studied so far.**Objective and hypotheses:** The aim of this study was to evaluate phenotypic features, gene mutations and coagulation parameters in a cohort of NS patients.**Method:** We studied 19 NS patients (10 M, 9 F), 12 probands and 7 first degree relatives, we found in 7/19 a mutation of PTPN11, in 8 of SOS1 and in 1 case of SOS1/RAF1, the remaining 3 cases were mutation-negative.**Results:** A positive history for abnormal bleeding was found in 9 patients (47%), a prolonged PTT in 5 cases (26%), coagulation factors deficiency in 9 patients (47%) and abnormal platelet aggregation in 8 cases (44%); the coagulation anomalies were found both in the 9 patients with a history of abnormal bleeding and in 6 cases (60%) without clinical evidence of bleeding disorders. The coagulation abnormalities were reported both in patients with or without a mutation and were not correlated with a mutation of a specific gene. Important differences in haemostatic status were found between probands and their relatives: the former showed coagulation abnormalities in the majority of the cases while the latter showed a history of bleeding diathesis, but normal laboratory hematological findings. The coagulation abnormalities were more frequent in patients with heart defects; however, a history of bleeding diathesis was detected in patients without cardiopathy.**Conclusions:** A high frequency of coagulation abnormalities was found in NS. These abnormalities do not seem to be related with the patients' genotype. The heart defects should not be the only cause of the haemostatic disorders. The bleeding disorders, as well as the other phenotypic NS features, tend to decrease with age. Our advice is to screen patients with NS for bleeding diathesis to avoid bleedings and post-operative complications.**PAO-211****Puberty as precipitating factor of type 2 diabetes. Prospective 5 years clinical and biological study***Corina Paul<sup>1</sup>; Puiu Iulian Velea<sup>1</sup>; Ionela Tamasan<sup>1</sup>;**Oana Alexandra Velea<sup>2</sup>*<sup>1</sup>University of Medicine and Pharmacy V.Babes, Clinic II Pediatrics,Timisoara, Romania; <sup>2</sup>University of Medicine and Pharmacy V.Babes, Department of Parodontology, Timisoara, Romania**Aim:** The relation between puberty and the onset of type 2 diabetes in obese children.**Material and method:** Within 2006-2010, we studied 95 children with primary obesity. We monitored: family history of DM, clinical signs of insulin resistance (obesity, acanthosis nigricans), biologically we assessed the OGTT, lipids metabolism, HbA1c, HOMA index every six months.**Results and discussions:** At diagnosis 38 cases presented mild obesity, 32 cases medium obesity while 25 cases were severely obese. Neither one presented clinical symptoms of diabetes. We found positive family history of type 1 and/or type 2 DM in 12 cases. At the first visit, fasting blood glucose was normal in all cases; 18 cases were diagnosed as having impaired glucose tolerance and 1 case type 2 DM (with severe insulinresistance HOMA >5). HbA1c level was normal. In all cases we recommended hypocaloric diet. After 3 years of follow-up 4 more cases (2 F, 2 M) pubertal age, were diagnosed as type 2 DM. Anti GAD 65 and ICA were negative in the 5 children with type 2 DM. The metabolic disequilibrium was confirmed by the increased level of HbA1c in all 5 cases. 4 of these 5 children had positive family history for DM (3- type 2 and 1- type 1 DM). In 4 cases we initiated therapy with Metformin 2 x 500 mg/ day. After 3 months of therapy HbA1c levels decreased significantly. In the 5th case, with severe insulinresistance HbA1c normalized with diet. At the time of diagnosis 3 of 5 cases with type 2 DM had normal weight (for age,height and sex), puberty being considered the precipitating factor for

the onset of diabetes.

**Conclusions:** Not only obesity, as a factor of insulinresistance, favours the occurrence of type 2 DM but also puberty precipitates its onset.

#### PAO-212

##### Ovarian function in cystic fibrosis patients

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**Background:** A lower reproductive capacity in women with cystic fibrosis (CF) has been associated with delayed puberty and amenorrhea.

**Objective and hypotheses:** To evaluate ovarian function in women with CF, regarding their clinical and nutritional status.

**Methods:** Cross-sectional study in women (3 years post-menarche) with CF controlled in our hospital. Data of menarche and menstrual cycles were collected by telephone survey. Anthropometric and spirometric data were obtained by medical history review. Blood samples were taken 3-5 days post-menstruation and after 21 days. The biochemical and hormonal parameters measured were glucose, insulin, HOMA, HbA1c, follicular estradiol (E), FSH, LH, luteal progesterone (P), total testosterone (T), androstenedione (A4), DHEA-S, SHBG and free androgen index (FAI). Results are expressed by mean values and ranges.

**Results:** We studied 8 patients aged 22.1 years (15-33). Their BMI was 20.5 (18.3-23.6) and their body fat percentage was 26.4% (20.4%-33%). Mean age at menarche was 13.2 years (11-15). They had menstrual cycles every 28.3 days (21-35), lasting 5.1 days (1-7). Oligo/amenorrhea was found in 2 cases (number 5 and 6). We detected impaired lung function (FEV1 <80%) in 3 cases (number 3, 5 and 6). One case presented CF-related diabetes (number 6) and impaired fasting glucose in 3 cases (number 4,6 and 7) with HOMA normal ranges.

number	E pg/ml	P ng/ml	FSH mIU/ml	LH mIU/ml	LH/ FSH	T ng/ml	A4 ng/ml	DHEA-S mcg/ml	SHBG nmol/l	FAI	PRL ng/ml
1	46	15.57	5.85	8.26	1.4	0.2	2.1	1.09	91.94	0.7	37.57
2	71	31.06	9.14	6.99	0.7	<0.025	0.8	0.49	82.49	0.1	13.38
3	62	4.07	5.18	5.71	1.1	<0.025	0.5	0.05	46.4	0.18	12.26
4	30	12	7.56	4.89	0.6	0.28	3.9	2.1	46.4	0.18	12.26
5	104	0.08	5.1	3.12	0.6	<0.025	<0.3	0.11	18.4	0.47	11.21
6	46	0.87	8.75	10.72	1.2	0.39	3.2	3.13	59.21	2.28	34.03
7	28	12.36	4.75	4.27	0.9	0.24	2.1	1.64	18.14	4.5	26.11
8	21	0.23	4.54	4.78	1	0.14	1.5	1.45	21.16	2.3	10.56

**Conclusions:** None had delayed puberty. We detected normal ovarian function in 5 cases. There was no relationship between ovarian function and nutritional status. Anovulation was observed in 3 cases, 2 of them with impaired lung function, and one with hyperandrogenism (number 6), probably associated with polycystic ovary syndrome.

#### PAO-213

##### Blood count in prepubertal children with premature adrenarche

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**Background:** Premature adrenarche (PA) refers to earlier than normal increase in adrenocortical androgen production, mainly DHEA and DHEAS, in mid-childhood. Adrenal DHEA and DHEAS are androgen precursors that are converted to more potent androgen receptor agonists in peripheral tissues. Androgens are known to enhance erythropoiesis.

**Objective and hypotheses:** We hypothesized that PA could affect blood hemoglobin concentration or erythrocyte count at prepubertal age when androgen production in gonads is low.

**Methods:** We examined 64 prepubertal children with PA (clinical sign(s) of adrenarche and serum DHEAS  $\geq 1$   $\mu\text{mol/l}$ ; 54 girls and 10 boys), and 62 age- and sex matched controls (52 girls, 10 boys) without clinical or biochemical

signs of adrenarche. All subjects were clinically examined, and analyzed for serum steroid concentrations and blood count. Mann-Whitney test was used to compare the differences between the study groups along with Univariate linear model. Pearson correlation test was used for analyzing correlations.

**Results:** Children with PA had higher blood erythrocyte count than their prepubertal controls [mean 4.7 (95 % confidence interval 4.7-4.8) vs. 4.6 (4.5-4.6) E12/l,  $P=0.01$ ]. The difference in erythrocyte count remained significant after adjustment for age and sex ( $P=0.04$ ). There was also a small but significant difference in the mean blood hemoglobin concentration between the PA and control children [130 (128-132) vs. 128 (126-130) g/l,  $P=0.03$ ]. No differences between the groups were found in the mean corpuscular hemoglobin, corpuscular volume or blood leukocyte count. In the entire study population, erythrocyte count was positively correlated with DHEAS, IGF-I and BMI SD score, and hemoglobin concentration with DHEAS, IGF-I and height SD score.

**Conclusions:** Relatively small increases in androgen concentrations due to adrenarche may have a positive effect on erythropoiesis at prepubertal age.

#### PAO-214

##### Evaluation of 1218 oral glucose tolerance tests in children and adolescents

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**Background:** In our outpatient department we evaluated 1218 oral glucose tolerance tests (oGTT) for impaired glucose tolerance (IGT), impaired fasting glucose (IFG), insulin resistance syndrome (IRS) and Type 2 Diabetes (T2D).

**Objective and hypotheses:** The indication for oGTT was obesity ( $n=1052$ ), small for gestational age (SGA) ( $n=36$ ), SHOX- Gen deficiency/ Ullrich Turner Syndrome (UTS) ( $n=55$ )- and Prader Willi Syndrome ( $n=25$ ) before or during growth hormone therapy, as well as IRS at follow up ( $n=39$ ) and risk factors for disturbance of the glucose homeostasis ( $n=48$ ).

**Methods:** All subjects underwent in our ambulance a two hour oGTT (1,75g glucose per kilogram bodyweight, maximum 75g). Following parameters were measured/collected: fasting-, 1- and 2 hour glucose and -insulin, HbA1c, height, weight, body mass index.

**Results:** The older the children the percentage of impaired fasting glucose and impaired glucose tolerance were rising up from about 12% -to 35%. We detected Type 2 Diabetes in children between eight to ten years in one percent, between 10-13 years in three cases and in group older than 13 years of age in 2,1 percent. All patients were obese. The percentage of insulinresistance defined as a fasting insulin greater than 15mU /L and /or a peak insulin greater than 150mU /L (S. Ten, J.Clin. Endocrinol. Metab. 2004;89:2526-2539) was as higher as older the patient evaluated. The HOMA IR  $>2.5$  climbed up from 28% in the younger prepubertal group to 80% in the older subjects. The highest risk factor to develop impaired glucose tolerance, insulin resistance and Type 2 Diabetes was obesity in pubertal children.

**Conclusion:** In obese children change in lifestyle has to begin before onset of puberty. Performance of OGTT is important to detected insuline resistance as major risk factor to develop Type 2 Diabetes. Insulin und glucose results of non obese children differ from obese children.

#### PAO-215

##### Treating pediatric obesity using an interdisciplinary supported treatment -Cigotica programme

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**Introduction:** The advantage of the 'Cigotica' programme is the multidisciplinary approach to treating obese children, which implies specific education, dietetic interventions with the reduction in the total daily calorie intake, physical activity, medical, educational and psychological support, change of behaviour and lifestyle.

**Objective:** To define obesity complications, metabolic risk factors and treatment effects when it comes to body composition and metabolic parameters in adolescents. Programme.

**Methods:** 1.030 adolescents were examined (498 girls and 532 boys), aged 12 to 18, average age 15.45, diagnosed with primary obesity, hospitalised

at the Centre for the prevention, treatment and rehabilitation of obesity in children in the period from 27/07/2008 to 03/10/2010. Hospitalisation lasted 21 days.

**Results:** After the multidisciplinary treatment, the average reduction in body mass ( $p < 0.05$ ) in all adolescents was  $5.92 \pm 2.71$  kg. During the 21-day hospitalisation, the average BMI was reduced by  $-2.12 \pm 0.31$  in all examinees, the BMI z-score was considerably lower in all examinees upon release and it was ( $p < 0.05$ )  $-0.26 \pm 0.08$ . % of fat was considerably lower ( $p < 0.05$ ) in all examinees  $-1.65 \pm 0.23$ , the waist circumference was reduced by  $-7.85 \pm 3.01$ . Hypertension was observed in 28% of adolescents. Two factors of metabolic syndrome were present in 27.6%, and metabolic syndrome was present in 18.3% of the examinees. The disorder in sugar transport was observed in 8.9% of the examinees.

**Conclusions:** The effects of the 'Cigotica' programme are very encouraging and they show that the multidisciplinary approach directed towards the reduction in energetic intake, education, change of lifestyle and habits related to nutrition and physical activity, leads to a considerable reduction in body mass, improvement in blood pressure laboratory analyses, aerobic capacities and self-confidence in obese adolescents.

#### PAO-216

### Prevalence of cryptorchism, retractile testis and orchiopey in children

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**Background:** Cryptorchism represents the most common congenital defect of the male urogenital system. It may be an important cause for male infertility. Very variable figures on the incidence of cryptorchism have been described in different type of studies.

**Objective:** The aim of the present study was to establish the prevalence of the abnormality in Uzbekistan population living in the Tashkent city and Tashkent region.

**Patients/methods:** In total there were surveyed 3417 children and adolescents at the age from 3-14 years. The testis determination was carried out by palpation method.

**Results:** As a whole, the frequency of cryptorchism was 1.2% for boys between 3 years and 14 years. The frequency of pathology was 2.5 % for those of between 3 and 6 years, retractile testis was 5.2 %, there were no cases of orchidopexy 0.75% was at the age between 7-10 years; orchidopexy was 0.35 % and retractile testis was 0.15 %; the frequency of pure cryptorchidism drops more than 3.3 times and retractile testis does 7 times to the puberty age.

**Conclusion:** The prevalence of cryptorchism and the mean age of orchidopexy are high among schoolchildren aged 10-12. The prevalence of cryptorchism differs significantly from the prevalence reported fifteen years ago. It was shown prevalence of cryptorchidism, on Uzbek population correlates with those of foreign sources.

#### PAO-217

### Cushing syndrome due to adrenocortical carcinoma in an infant

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**Background:** Adrenocortical tumors are the most common cause of endogenous Cushing syndrome in infancy and early childhood. We present an infant with Cushing syndrome due to adrenocortical carcinoma.

**Case:** A 15 month-old female child was referred to the hospital with a history of progressively increasing weight gain, appetite, terminal hair growth on the back and limbs but arrested growth rate since 4 months. There was no history of oral intake and topical application of steroids. Physical examination revealed weight of 9 kg (25p), length of 69.5 cm (3-10p), blood pressure 80/40 mmHg, cushingoid features with moon face and facial plethora. Rest of the physical examination was unremarkable. She had no clitoromegaly. Serum assays confirmed hypercortisolism with loss of diurnal variation for cortisol

secretion (8 am: 27,05 µg/dl, 03 pm: 21,64 µg/dl, 11 pm: 22,63 µg/dl) and a concomitantly suppressed ACTH level <5pg/ml. DHEA-S [ $<15$ µg/dl (5-57)], androstenedione [0,9ng/ml (0,8-5)], total testosterone [ $<0,1$ ng/dl (0,1-1,3)] were normal. Abdominal ultrasound showed 30x40 mm intra-abdominal mass arising from the left adrenal gland. Magnetic resonance imaging also detected a solid mass sized 40x45 mm in the left adrenal gland. She was operated on left adrenalectomy under perioperative glucocorticoid coverage. Histopathological examination confirmed adrenocortical carcinoma. She was discharged 20 days after surgery on hydrocortisone 4 mg/day. She is doing well on hydrocortisone and has not shown any sign of disease recurrence during follow up. **Conclusions:** Although Cushing syndrome is rarely seen in infants, the pediatricians should take it into consideration in cases presenting with rapidly weight gain and decreasing growth rate in infancy.

#### PAO-218

### Do children with growth hormone deficiency diagnosed on the strength of one growth hormone stimulation test grow better than patients diagnosed on the strength of two stimulation tests on GH replacement therapy?

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**Background:** A recent consensus statement recommends the use of two growth hormone (GH) stimulation tests for the diagnosis of GH Deficiency (GHD) in childhood. Some clinicians have used a single GH stimulation test because of the high frequency of distress that such tests cause children and the lack of a strong evidence base to the recommendation, while others have followed the recommendation.

**Objective:** To compare the change in height (Ht) Standard deviation score during the first year of GH treatment in subjects diagnosed with Idiopathic Isolated GHD (IIGHD) following one GH stimulation test (GHST) to those diagnosed following two GHSTs.

**Methods:** A retrospective case note review of all patients diagnosed with IIGHD was undertaken in a single tertiary endocrine centre between 2003 and 2009. Patients were categorised in to those who had 1 test (Group1) and two tests (Group 2). Height at diagnosis, 3-8 months and 9-15 months after starting treatment with GH was identified. Ht SDS at baseline and change in Ht SDS ( $\Delta$ Ht SDS) at each time point during treatment was compared using the Mann Whitney U test.

**Results:** 19 patients were studied. Results are summarised in table 1. Data presented as median(range). Table 1. Ht SDS at diagnosis and  $\Delta$ Ht SDS for patients at the three time points during treatment with GH.

	Group 1 [n=12]	Group 2 [n=7]	P value
Ht SDS at diagnosis	-2.7 (-0.9 to -4.5)	-2.5 (-1.9 to -3.5)	Not significant
$\Delta$ Ht SDS 3-8 months	0.2 (0.1 to 0.4)	0.5 (0.3 to 0.8)	0.02
$\Delta$ Ht SDS 9-15 months	0.3 (-0.1 to 0.8)	0.3 (0.1 to 0.8)	Not significant

**Conclusions:** Patients with IIGHD diagnosed on the strength of one and two GHST show no difference in the growth response in the first year when on optimal GH replacement therapy.

#### PAO-219

### Prevalence of metabolic syndrome (IDF 2007 criteria) in obese children and adolescents

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**Background:** Metabolic syndrome (MS) frequency is increased in proportion to the increasing prevalence of obesity in children and adolescents.

**Objective and hypotheses:** This retrospective study was performed to de-

termine the prevalence of MS and its risk factors in obese children and adolescents.

**Methods:** A total of 198 (101 males, 97 females) obese children from 10 to 16 years old were involved in the study. International Diabetes Federation (IDF 2007) criteria were used to diagnose the MS classification. Each patient underwent auxological evaluation, blood pressure (BP), blood samples and oral glucose tolerance test (OGTT). Homeostasis model assessment of insulin resistance (HOMA-IR) has been calculated. Patients were divided into two groups according to the presence of MS.

**Results:** The overall prevalence of MS in our study was 38% with no intersex difference. Mean age was 12,7±1,62 years. Eighty nine percent (n=176) of the patients were pubertal and MS was more often in this group. The prevalence of high systolic BP was 30%, high diastolic BP 25%, hypertriglyceridemia 20%, low HDL-C 48,5%. Impaired glucose metabolism was identified in 17,6% of patients; 21 of them having impaired fasting glucose (IFG) and 14 of them having impaired glucose tolerance (IGT). There was no silent type 2 diabetes. Hepatic steatosis prevalence was 44%. All of the anthropometric measurements and BP levels were found higher in the MS group than those in the non MS group as expected. When we analyzed the cardiovascular risk factors; fasting blood glucose levels, insulin resistance, levels of total cholesterol, prevalence of IGT, hyperinsulinemia were significantly higher but HDL level was significantly lower in MS group when compared to non-MS group. LDL-C levels were found to be similar between two groups.

**Conclusions:** MS prevalence at diagnosis is high (38%) in obese children. When cardiovascular risk factors are considered, the increase in the MS frequency gets more important for the future of children.

#### PAO-220

### Central precocious puberty unresponsive to LHRH analogue treatment in a patient with chromosomal anomaly and cerebropathia

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**Background:** The treatment of central precocious puberty (CPP) is based on LHRH analogous (LHRH-a) with a good hormonal inhibition.

**Objective and hypotheses:** Our aim is to describe the case of a children with chromosomal alteration, cerebropathia and CPP, who does not respond to the treatment with LHRH-a.

**Population:** The children, born at 38 gestational weeks, showed hypospadias, microcephaly and some dysmorphic notes. He presented a neuropsychic development delay and seizures, so at the age of 2 years he started antiepileptic treatment. The karyotype was 46XY, the array CGH showed [del(1)(q41)] and [del(7)(q36.1q36.3)]. At 6 months of age he developed pubic hair and then increase in testicular (5 ml) and penile size. The hormonal investigations (1 years 7 months) showed the activation of hypothalamus-pituitary-gonadal axis (LH peak 18.3 mU/ml, testosterone 1.94 ng/ml), normal adrenal function and advancement of the bone age, suggestive for CPP. The NMR did not demonstrate anomaly of the brain and the hypothalamic-pituitary region. He started treatment with LHRH-a.

**Results:** The treatment with LHRH-a did not permit an adequate inhibition of the hypothalamus-pituitary-gonadal axis and it also caused an advancement of the pubertal development (basal LH 4.3 mU/ml, testosterone 6.27 ng/ml), in presence of a good compliance. At 2 years and 2 months the treatment with LHRH-a was stopped and the treatment with letrozole and cyproterone acetate was started.

**Conclusions:** In our patient the treatment with LHRH-a failed to induce hormonal inhibition. To our knowledge, similar cases are not reported. The possible causes of this failure are unclear: the genetic alteration, the potential alteration of pharmacokinetic of LHRH-a and the cerebropathia may be involved. Investigations to assess the reliability of these assumptions are in progress.

#### PAO-221

### A 30 year review of congenital adrenal hyperplasia in Northern Ireland

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**Background:** Congenital adrenal hyperplasia (CAH) is an autosomal recessive condition with significant consequences if not correctly diagnosed and treated. We have reviewed the patients with CAH presenting in Northern Ireland between 1976 and 2010.

**Aims:** To determine the age, sex and clinical features at presentation; treatment modalities including perineal surgery in childhood; and long-term outcomes including final height and surgery in adulthood.

**Methods:** The medical notes of patients diagnosed with CAH in this time period were reviewed. A literature review was performed and our data compared with that previously published.

**Results:** 37 patients (22 female, 15male) from 30 families presented with CAH over this time period giving an incidence of 1:23,092 live births. 18 (49%) were diagnosed shortly after birth (83% virilised females); 13 (35%) presented in the first few weeks of life with adrenal crises (85% male); and 6 (16%) presented with virilisation in later childhood. 6 (16%) children had diagnosis confirmed on genetic testing.

All children required glucocorticoid replacement. 35 (95%) required mineralocorticoid replacement; 3 children were treated with human growth hormone and 2 children required suppression of early puberty. Mean final height was -1.5SD below mean adult height in boys and girls. In the first 16years reviewed, 8 (80%) girls had perineal surgery in childhood, compared with 2 (16%) in the second 18 years. 2 (9%) women had adrenalectomy. 11 (58%) of those transferred to adult services have been lost to follow-up.

**Conclusions:** The incidence of CAH is less here than in the rest of the United Kingdom with more females affected than males. The majority present in the first few weeks of life. Mean final height is often impaired. There is a trend towards later surgery in these children. There is a heightened need for effective transition to adult services given the large percentage lost to follow-up in adolescent years.

#### PAO-222

### A rare cause of precocious puberty: $\beta$ -hCG secreting tumor

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**Background:** Beta human chorionic gonadotropin ( $\beta$ -hCG) secreting tumours are a recognized cause of precocious puberty (PP), almost exclusively in boys. These tumours may occur in gonads, liver, retroperitoneum and mediastinum or within the central nervous system (CNS).

**Objective and hypotheses:** We present one case of PP due to  $\beta$ -hCG secreting tumour, whose site was difficult to determine.

**Population:** The boy came to our attention at age 6 years. Neurological examination was normal. Physical examination showed scrotal hair, enlarged penile and testes (4 mL) size and gynecomastia.

Hormonal test revealed suppressed levels of gonadotropins at LHRH test (FSH peak 0,8 mU/mL, LH peak 0,5 mU/mL), increased testosterone (3,47 ng/mL), normal adrenal function, prolactin and  $\alpha$ -fetoprotein and slightly higher  $\beta$ -hCG (6,8 U/L; nv 0-5 U/L).

**Results:** Hormonal picture was compatible with gonadotropin-independent PP due to  $\beta$ -hCG secreting tumour. To determine its site testicular and abdominal ultrasound, thoracic CT, abdominal and CNS NMR were performed. These studies didn't reveal any suspicious lesion, with the exception of a cystic-like aspect of pineal gland. A lumbar puncture was performed and revealed slightly higher  $\beta$ -hCG (11,3 U/L).

The abnormal cerebrospinal fluid (CSF)/serum ratio of  $\beta$ -hCG was consistent with a CNS germ cell tumour. Although the tumour was not clearly identified, he underwent four courses of multi-agent chemotherapy (bleomycin, etoposid and cisplatin) and ventricular radiotherapy.  $\beta$ -hCG and testosterone values fell to within the normal range after the first course, indicating significant regression of the tumour. Nowadays the clinical and hormonal picture is stable.

**Conclusions:**  $\beta$ -hCG secreting tumours are a rare cause of gonadotropin-independent PP. Determining the site of the tumour may be difficult. Detection of both serum and CSF levels of  $\beta$ -hCG may be useful.  $\beta$ -hCG value was also an accurate indicator of the response to therapy.

#### PAO-223

### Conjugated hyperbilirubinemia caused by neonatal thyrotoxicosis in an infant

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**Background:** Neonatal thyrotoxicosis (NT) caused by maternal Graves disease is a rare disorder. In the newborn, characteristic signs and symptoms include tachycardia, irritability, poor weight gain, and prominent eyes. Rarely, infants with NT present with thrombocytopenia, jaundice and hepatosplenomegaly. We report an infant with hemorrhagic diathesis and conjugated hyperbilirubinemia, who was diagnosed with NT due to maternal Graves disease.

**Case:** One month-old male infant was admitted to our hospital for further evaluation of a bleeding after vaccination. He was born vaginally at 38 gestational weeks to a 23 year-old primigravida mother, with a birth weight of 2550g. It was learned that his mother had Graves disease for 2 years and did not take propylthiourasil regularly during pregnancy. Physical examination revealed weight of 3100g (3p), height of 51 cm (3p), head circumference of 34 cm (<3p, -2,2SD), prominent eyes and 2x2cm hematoma at left inguinal region. The other physical findings were unremarkable. Laboratory studies showed normal hematological and coagulation parameters but mildly elevated transaminases (ALT 74IU/l, AST 55IU/l) and conjugated bilirubin (3.8 mg/dl) levels. Blood and urine culture were negative as were titers for toxoplasmosis, rubella, CMV, herpes, hepatitis B and C. Metabolic screening tests were negative. Thyroid function tests revealed that the infant was suffering from NT [free T4 2.5 mg/dl (0.63-2.3), free T3 4.9 pg/ml (1.8-4.2), TSH 0.17 mIU/ml (0.4-8.6) and TSR-Ab 54U/l (0-9)]. We decided to follow up him without treatment, because he had only biochemical thyrotoxicosis but not clinical. After 2 months, his conjugated hyperbilirubinemia level resolved as well as thyroid hormone levels returned to the normal range.

**Conclusions:** We suggest that as infants born from mothers with Graves may develop different clinical signs, they should be followed up carefully and closely after birth.

#### PAO-224

### Congenital adrenal hyperplasia: a case report

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**Background:** Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder; the 21-hydroxylase (CAH 21-OHD) deficit, early or late onset, is the most frequent form. The complete enzymatic deficit is characterized by a more elevated mortality in neonatal age; differential diagnosis is difficult at this age, due to the complete virilization of the external genitalia in the females and the lack of genital ambiguity in the males.

**Objective and hypotheses:** The aim of this case report is to show how is multifaceted the diagnostic and therapeutic process that requires a multidisciplinary team, formed by psychologists and medical staff.

**Methods:** S. came at our observation at three days of age for ambiguous genitalia: micro-penis, absence of appreciable gonads, a single orifice at the penis base. Hormonal blood investigations was performed and diagnosis of congenital adrenal hyperplasia due to CAH 21-OHD (complete form) was done. Biochemical analysis showed electrolyte abnormalities characterized by salt-wasting; ultrasonography evidenced uterus presence, vagina and persistence of the urogenital sinus; karyotype 46 XX. Molecular analysis showed CYP21A2 gene mutations. The baby performed substitutive hormonal therapy and electrolytes supplementation.

**Results:** Clinicians, hormonal and instrumental controls confirmed the success of the treatment. At 12 months the baby underwent to genital correction

intervention. A suitable psychological support has been offered to her parents, both during the diagnosis process and the surgical intervention.

**Conclusions:** Virilization occur of external genitalia, in absence of appreciable gonads and with genital feminine insides, has allowed to set clinical diagnosis of CAH before hormonal biochemical confirmation. Therapy was promptly started, preventing hydro-electrolytical imbalances. Clinical, hormonal and instrumental parameters monitoring, along with psychological parents support allowed to early manage this case successfully and to create the premises for a good future therapeutic alliance.

#### PAO-225

### Auxometric and biohormonal data of patients with Turner syndrome undergoing treatment with Somatropin

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**Background:** 95% of Turner syndrome patients are known to have a final adult height 20 cm below the median parental height. It has been proven that these patients respond to rhGH treatment, despite the fact that they are not GH deficient.

**Objective and hypotheses:** Analysis of the effects of Somatropin therapy on the growth of Turner Syndrome patients and identification of the parameters that influence growth.

**Methods:** We analyzed a group of 30 patients with Turner syndrome who were treated in our board between 2002 and 2010. We measured and calculated: height, median parental height, growth velocity under treatment, bone age, IGF-I, predicted adult height without treatment, predicted final height when study was carried out.

**Results:** Mean age was 8,4 yrs (4,5 - 14 yrs); mean initial height was -3,18 SD below normal and 0,12 SD when compared to other girls with Turner syndrome of the same age; the mean period of treatment was 3,26 yrs (1-7 yrs) and the mean dosage was 0,327 mg/kg/week (0,27-0,42); growth velocity per year of treatment averaged at 7,02 cm and growth velocity per year of bone maturation at 5,94 cm. Predicted adult height (PAH) without treatment had an average of 142,6 cm, while the predicted final height, when the study was carried out had an average 150,7 cm. Thus, the mean benefit of the therapy is 8,1 cm.

**Conclusions:** We analyzed the significant correlations between the height benefit of the therapy and a series of auxometrical parameters. Even if we noted that IGF-I rose to considerably higher levels during the therapy, this phenomenon did not correlate significantly with the gain of centimeters per year of treatment or per year of bone maturation, which leads us to believe we may encounter a certain degree of resistance to the action of IGF-I in some patients. Under treatment the patients recovered an average of 1,98 SD from the growth retardation compared to normal adult females and an average of 1,95 SD from the genetic target height.

#### PAO-226

### Does Letrozole in boys and GnRHa in girls with idiopathic short stature (ISS), constitutional precocious puberty (CPP), or being born small for gestational age (SGA) improve their prospective adult height?

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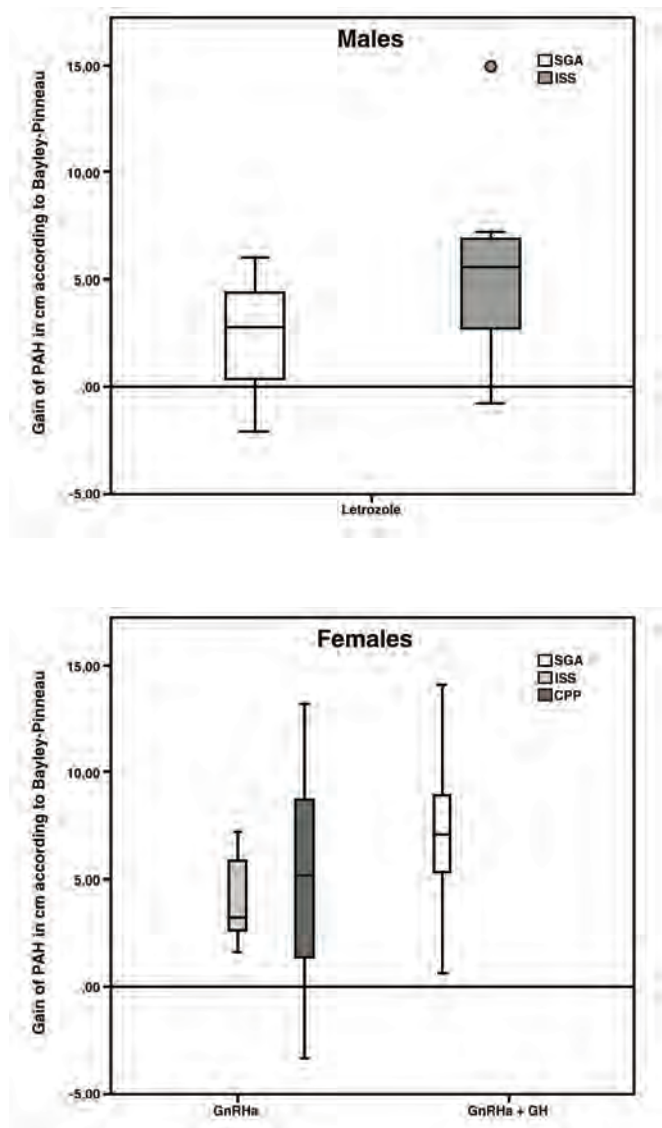
**Objective and hypothesis:** To investigate the hypothesis that Letrozole in boys and GnRHa (leuprolide acetate) in girls are able to improve the prospective adult height (PAH).

**Method:** We retrospectively compared growth data of girls with CPP (n= 14,

median treatment period 2.4 years) and ISS (n=7, median treatment period 1.7 years) as well as data of boys with ISS (n= 8, median treatment period 1,8 years) and SGA (n=5, median treatment period 3.0 years) before, during and after treatment. Girls born SGA (n= 7, median treatment period 1.9 years) had an additional treatment with growth hormone. Near final height or adult height was reached by n=8 patients.

**Results:** Girls with CPP (n=4), treated with GnRHa, showed an improvement of their near final height or adult height in median by 6.2 cm. In girls born SGA (n=2), treated with GnRHa and growth hormone, the final height improved by median 8.9 cm. One boy with ISS, treated with letrozole, had an improvement of adult height by only 1.9 cm. However, one boy born SGA, showed an improvement of adult height by 15 cm according to Bayley-Pinneau. A transient decrease of bone density, as measured by the DEXA method, was observed. A patient questionnaire revealed no other relevant side effects due to the treatment with both Letrozole and GnRHa. Fig 1+2 show the reached gain of height.

**Conclusions:** Both medications seem to be able to improve the PAH. However, a small number of patients failed to improve the prospective adult height. In some patients, the adult height was reached and was higher than calculated before. Therefore, the therapy should be continuously supervised by a pediatric endocrinologist. Prospective controlled trials are necessary in future to confirm the results.



#### PAO-227

### The one year catamnesis in children from mothers after combine treatment of thyroid cancer

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**Background:** The frequency of the thyroid cancer in Ukraine is 36:1000000 per year and in twice more in women with the tendency to growth.

**Objective and hypotheses:** The protocol of the combine treatment include different variation of the extended thyroidectomy (in 2nd trimester), radioiodine therapy, suppressive therapy by thyroxin (2,3 mg/kg).

**Method:** Complex observation in neonatal period and one year follow-up performed in 50 infants from mothers after combine treatment of thyroid cancer.

**Results:** The most frequent complication of gestation period were threat of abortion, discoordination of the delivery, distress of the fetus, postpartum hemorrhage. Optimal development of the placental complex due to using of gestagens in the treatment complex of threat of abortion decreased morbidity of children during first month of life. In neonatal period 60 % of newborns received treatment of prolonged jaundice, 34 % - severe allergic reactions, 18 % - hypoxic-ischemic encephalopathy. Most every newborns had vegetative disorders (abnormality of microcirculation, regurgitation, breach of cardiac rhythm on the electrocardiogram, heightened disposition to sweating). The data of one year catamnesis in 3, 6, 9, 12 months show direct close correlation between frequency of neurological pathology, allergic reaction, vegetative dysfunction and exhaustiveness of the postoperative hypothyroidism compensation, peculiarities of medication of threat abortion. The physiotherapy of perinatal encephalopathy must have been made out in 36 % of infants 3-6 months of life. Common conditions for all children from mothers after combine treatment of thyroid cancer are high frequency of rachitic, acute respiratory infections, disorders of feeding and decreasing of frequency & duration of breast-feeding.

**Conclusions:** All this peculiarities make it possible to include children from mothers after combine treatment of thyroid cancer in high risk group for creation prophylactic-treatment arrangements for them.

#### PAO-228

### New onset type 1 diabetes in the pediatric population of a second level hospital: 12 years' review and evaluation of recent treatment and connection between hospitals

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**Background:** In the pediatric department of a Lisbon area's second level hospital, new onset diabetes is managed in coordination with the tertiary hospital's endocrinology team.

**Objective:** To characterize the children with new onset type 1 diabetes (1999-2011). To describe treatment procedures (2009-10) in order to evaluate the compliance to the 2008-Diabetic Ketoacidosis (DKA) National Protocol. To assess the need for improving the management of new cases without DKA.

**Methods:** Retrospective study. Clinical files were reviewed.

**Results:** 41 children were admitted, 3.4 new cases/year, with a modest increasing tendency. 61% females; median age 9 years. 90% previously healthy, only one obese child; 15% had type 2 diabetes in non-first degree relatives. All were admitted from the emergency department (44% referred with symptomatic hyperglycemia; 1 incidental finding). Classic new onset symptoms were the most common: polydipsia-93%; polyuria-83%; weight loss-68%; polyphagia-37%; lethargy-27%. 44% presented with DKA (severe in 10%). Median hospital stay was 2 days, with subsequent referral to endocrinology (66% to ward; 29% to consultation) and 5% to PICU. Concerning treatment after 2008 (n=13), insulin perfusion was administered to all ketoacidotic patients, with median duration of 6 hours. Insulin perfusion in non-ketoacidotic patients was variable (prescribed to 44%). All but 2 patients started IV iso-



tonic saline with potassium. Saline was replaced by 5-10% dextrose when initiating insulin (91% after at least one hour of IV hydration). One patient required HCO<sub>3</sub> correction before transference to PICU. Intermediate-acting insulin was always started after 24h.

**Conclusions:** These epidemiological and clinical aspects are according to published reports. Overall compliance with DKA guidelines is satisfactory. The lack of uniformity in the management of new cases without DKA highlights the need for implementing uniform procedures and improving the connection pathways between second and tertiary level hospital in the management of new onset diabetes.

#### PAO-229

### Adequacy of implementation of recommendations of dietary intake in children with type I diabetes mellitus

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**Background:** Nutrition in diabetes mellitus type I in children is an important factor in treating the disease.

**Objective and hypotheses:** The aim of our study was to identify communication and the adequacy of the diet with the peculiarities of the clinical and metabolic status in children with type I diabetes.

**Methods:** An analysis of diet 1 day in 28 children with type I diabetes. Energy expenditure determined by the computational method of WHO at a rate of physical activity. Actual energy consumption calculated on the menu layout. The data obtained was subjected to statistical analysis in Excel, Biostat.

**Results:** Table 1: Actual feeding of children

Indicators	Girls prepubertal period (16,7%)		Girls pubertal period (83,3%)		Boys prepubertal period (30%)		Boys pubertal period (70%)	
	Excess	Lack	Excess	Lack	Excess	Lack	Excess	Lack
Energy value (%)	66,7	33,3	33,3	66,7	33,3	66,7	14,3	85,7
Proteins (%)	100	0	46,7	53,3	66,7	33,3	0	100
Fat (%)	33,3	66,7	20	80	66,7	33,3	28,6	71,4
Carbohydrates (%)	66,7	33,3	20	80	0	100	14,3	85,7
Calcium (%)	0	100	0	100	0	100	6,7	93,3
Magnesium (%)	100	0	73,3	26,7	100	0	42,9	57,1

**Conclusions:** In children prepubertal period dominated by an increase in energy value, at puberty - a decline. Excessive intake of protein, including animals, in children prepubertal period. Carbohydrate intake increased in girls prepubertal period. Fat intake increased in boys prepubertal period. Girls prepubertal period, an increase calories by excess consumption of protein and carbohydrates, the boys - protein and fat. At puberty there is an increase calories from fat and carbohydrates. Girls and boys prepubertal period body mass index as normal 33.3% and 66.7%, and at puberty there is a tendency to increase 53.3% and 57.1%. Excessive food intake in boys and girls to dominate the dinner 83.3% and 100% respectively.

#### PAO-230

### Trends in type 1 diabetes mellitus

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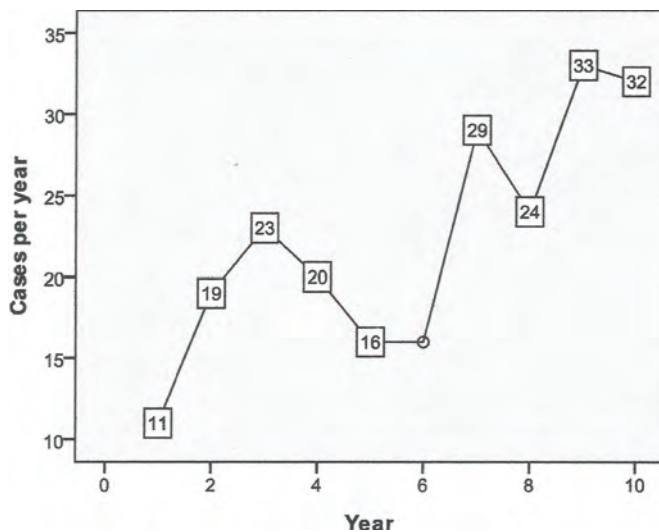
**Background:** Type 1 diabetes mellitus (T1DM) is the most common endocrine problem in childhood, with increasing worldwide incidence. The risk of developing diabetic ketoacidosis (DKA) is higher in children because of non-specific and non-classical signs and symptoms.

**Objective and hypotheses:** This study was designed to review trends in presentation and incidence of childhood diabetes in the last 10 years in southwestern Iran.

**Methods:** During a detailed review of compiled records of Abuzar Children's Hospital from Jan 2000 to Dec 2009, the following clinical information relevant to diabetes were extracted and analyzed: admissions for diabetes, all data regarding demographics, clinical status, laboratory findings, hospital course, morbidity, and mortality.

**Results:** Excluding 129 repeated admissions, 297 cases were enrolled for analysis: 223 new and 74 known cases. Among the new cases, 67.3% presented with DKA, without any gender bias. Among the DKA subjects, 45% had some degree of unconsciousness, and the mortality rate was 4%. The mortality risk was significantly higher in the <2-year group and in girls (boy:girl=1:7; p=0.039). Despite the increase in the number of medical centres that manage diabetic children, there is a regular increase (nearly 50.5% rises over 5 years-Figure) in the disease incidence.

**Conclusions:** Most of the new cases of T1DM presented with DKA, and this is similar to the trend seen in other developing countries. With an increasing incidence of DM, more attention to education of families and periodic retraining of health staff is essential to enable earlier diagnosis and management of new subjects, and to reduce morbidity and mortality rates associated with the disease.



#### PAO-231

### The relation between skinfold thickness and leptin, ghrelin, adiponectin and resistin levels in infants of diabetic mothers

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We aimed to investigate the relation between skinfold thickness and serum leptin, ghrelin, adiponectin and resistin levels in infants of diabetic mothers. The mother two were diagnosed as having gestational diabetes by an Oral Glucose Tolerance Test (OGTT) performed between 24-28 gestational weeks, and their babies were included into this study. Mean HbA<sub>1c</sub> level between diabetic and control mothers were not significantly different. Mean Body Mass Index (BMI), abdominal circumference, upper extremity circumference, and biceps skinfold thickness was not significantly different between infants of diabetic mother and control infants. However, mean subscapular and triceps skinfold thickness was significantly lower in infants of diabetic mother. Mean leptin, ghrelin, adiponectin and resistin levels were also not significantly different between infants and diabetic mother and control infants. Our results indicates that early diagnosis of gestational diabetes and control by appropriate diet or insulin treatment may be effective in protection of fetuses of diabetic mother from the negative effects of gestational diabetes.

**PAO-232****Correlation of childhood obesity with obesity at late adolescence and young adulthood**

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**Aim:** The aim of this study is to answer the question whether an obese child becomes an obese adolescent and/or obese young adult.

**Methods:** It's a follow-up study of obese children followed in our department for the time period 1997-2006. We contacted 234 (109 M) of them during the last trimester of 2010, and they were asked to answer a semi-structured questionnaire. The questionnaire included questions regarding sociodemographic data of the family, current height and body weight of the index case, factors that in their opinion affect weight control. At present 141 cases were contacted, from them 43 were not available because of address change, 3 refused to participate and 22 were excluded because of young age (< 16 yrs old). The response rate is 96.6%. To analyze the data we used descriptive statistics.

**Results:** The two sexes were equally represented in both the childhood sample (46.5 % M and 53.4 % F) and the follow-up sample (46.7 % M, 53.3 % F). Of this cohort of obese children, at follow-up, 24.7% were obese, 32.6 % were overweight and 42.7 % were of normal weight. More than half, 52.8 %, were overweight and obese at follow-up. Examining the sexes separately, 7.9 % of the women were obese and 22.5 % were overweight whereas 16.9 % of men were obese and 10.1 % were overweight.

**Conclusions:** These data, based on this particular sample of obese children, that they were investigated and received dietetic counseling in a tertiary center, suggest that more than half of this cohort have body mass index higher than normal, at young adulthood. Furthermore we conclude that obesity is more prevalent in men, whereas overweight is more prevalent in women. The limitations of the present study is the relative small sample size (the study is ongoing) and the absence of control group in order to assess whether early intervention has a positive effect on long term weight control.

**PAO-233****Resistance to usual treatment in a patient with primary hypoparathyroidism: a coincident association with a celiac disease**

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**Background:** Hypocalcemia may present as an asymptomatic laboratory finding or as a severe, life-threatening condition. Chronic hypocalcemia may be well tolerated by the patient, but treatment nonetheless remains necessary in order to prevent long-term complications.

**Objective:** We present a case study of a patient with primary hypoparathyroidism who is surprisingly resistant to the usual treatment consisting of calcium and vitamin D supplementation.

**Methods:** We report the case of a 14-year old girl, in which the diagnosis of primary hypoparathyroidism was retained because of the association of low PTH coupled with severe hypocalcemia with seizure and brain calcifications.

**Results:** The patient was treated with intravenous calcium gluconate with a good response. Then, she was treated with oral calcium gluconate and alfacalcidol with persistence of the clinical symptoms of hypocalcemia (paresthesia, Chevostek and Trousseau signs) without significant changes in calcemia. The patient's serum analysis indicated the presence of immunoglobulin A isotype antibodies against gliadin. Diagnosis of gluten-sensitive enteropathy or celiac disease was suggested at endoscopy, and confirmed by histological findings in duodenal biopsy. The histocompatibility antigen HLA-DQ2 was founded. The patient was placed on a gluten-free diet, which rapidly lead to the normalization of her bowel habits and improved her metabolic and nutritional parameters.

**Conclusions:** This finding suggests that coexisting celiac sprue is one of the mechanisms responsible for the malabsorption associated with idiopathic hypoparathyroidism concluding in a rare association.

**PAO-234****Pseudohypoparathyroidism: monogenic obesity and tall stature**

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**Background and aim:** Obesity is a common feature in patients with type 1a pseudohypoparathyroidism (PHP) and affected patients typically also have short stature. We describe a infant with PHP who developed morbid obesity with tall stature in early infancy.

**Methods:** 6 months female infant with history of abnormal weight gain and increased appetite was referred for endocrinological evaluation. She was born 38 week gestation with birth weight 4500 gram and rapid weight gain at 1 month. She was only breastfed from birth. Frequently nursed due to crying 3kg/last 1 month. Prenatal history unremarkable. No vitamin D taken by mother during pregnancy or child after birth. On physical examination at 6 months of age length was 70cm (1.4SD) weight was 13 kg (4.8SD) and head circumference was 48(>2SD). She had no dysmorphic feature but she had a hard subcutaneous nodule in her lumbar area and umbilical hernia. Laboratory investigation showed the following values: serum calcium: 6.8 mg/dL (8.6-11mg/dL), phosphorous: 7.6mg/dL (4.2-7mg/dL), magnesium: 3.7 mg/dL (1.6-2.6mg/dL), alkaline phosphatase:333 U/L(145-420U/L), parathyroid hormone:400 pg/ml (9-69pg/ml), albumin: 3.7 mg/dl (4-5mg/dL), 25(OH)D: 55 ng/ml (15-80ng/mL), thyrotropin: 6.87 mIU/ml (0.5-5.2mIU/mL), free thyroxin: 0.69 ng/dL (0.8-1.8ng/dL), cortisol: 2.65 ug/dL (4-27ug/dL), corticotropin: 12.9 pg/mL (10-60), leptin: 23 ng/mL. Excessive weight gain, mild hypothyroidism and increased parathyroidism and decreased serum calcium suggested a diagnosis of Pseudohypoparathyroidism type 1a.

**Conclusion:** Hypothalamic G-protein coupled melanocortin receptor may mediate the central effects of leptin. GNAS mutation result in underactivity of MCR4 It explains the obese, hyperphagic and tall stature phenotype and suggest that the genetic mutations which underlie PHP may be a more common cause of severe obesity.

**PAO-235****Clinical evaluation of short children referred by school screening: an analysis of 2589 children according to the WHO norms of 2007**

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**Background:** An isolated delay in growth can reveal a treatable pathology. A school inquiry was launched. A prospective study was made during the school year 2008/2009 in the north of Tunisia.

**Objective and hypotheses:** To determine the prevalence of stunting growth and the etiologies.

**Methods:** All school children 5 to 8 years old: 2589 children have benefitted from a school screening. Infants with short stature (heights< -2SD) have been identified for exploration. Exploration included: a detailed medical history, nutritional inquiry, physical examination and successive tests, according to primary results, of blood count, bone age, thyroid function, celiac serology, chromosome tests, and growth hormone screening. We use the new tables of the WHO published in 2007.

**Results:** 1.4%(36) infants have a pathological short stature: thyroid dysfunction (2 children), growth hormone deficiency (9 children), intra-womb short stature (8 children), Turner syndrome (1 child), bone constitutional disease (2 children), congenital hepatic disease (1 child) and 14 children with constitutional delay.

**Conclusions:** The majority of short stature in our region is due to either constitutional delay or endocrine causes. The screening for stunting growth in 5 to 8 year old children would allow treatment resulting in a more effective, and improved height development.

## PAO-236

### Graves' disease management with antithyroid drug (ATD) therapy - retrospective analysis of 35 children

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**Background:** Graves' disease is the most common cause of thyrotoxicosis in children, which can have many negative effects on both physical and psychological development. Antithyroid drug (ATD) therapy is recommended as the initial treatment but still exist many controversies concerning optimal duration of ATD therapy.

**Objective and hypotheses:** The aim of our study was the retrospective evaluation of ATD therapy in children with Graves' disease.

**Methods:** The medical history of 35 children (29 girls) in mean age of GD diagnosis 12,1 years was analyzed. Total duration of treatment, time to initial remission, number of relapses, way of ATD therapy discontinuation and block and replace treatment were taken into consideration.

**Results:** Mean time of observation was 2,5 yrs (max. 5.83 yrs.). The initial hormonal remission was achieved in 30 (85,7%) children.

Mean ATD therapy duration for hormonal remission was 4 months.

Only in 14 (34,3%) discontinuation of ATD was possible and mean time free from ATD was 6 months.

Mean number of relapses 2.42 was observed. In 34,3% of children ATD dose reduction was fast (by 50% during a weeks), 34,3% of children had prolonged ATD low dose therapy (form 1.25 to 2.5 mg/d for several months), in 54.3% of children combination of L-thyroxine with ATD was used.

No differences concerning time of initial remission, time and number of relapses depending on way of ATD dosage was found. 5 children from that group were qualified to radioiodine therapy.

**Conclusions:** ATD therapy in children is effective way to achieve initial clinical and hormonal remission in GD thyrotoxicosis but longer permanent remission (after ATD discontinuation) than 6 months is unusual. The late outcome of ATD therapy seems to have no relationship to way and duration of dosage.

## PAO-237

### Results of Gn-RH analogs (triptorelin) therapy in girls with idiopathic true precocious puberty

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**Background:** True precocious puberty (PP) has negative psychological consequences and is often associated with a reduction of final adult height.

**Objective and hypotheses:** To study the efficiency of triptorelin treatment (3.75 mg i.m. monthly) over clinical features, hormonal profile and predicted adult height (PAH) in girls diagnosed with idiopathic true PP.

**Methods:** We conducted a retrospective study over patients diagnosed with idiopathic true PP in the pediatric endocrinology department in the last 5 years; we only considered patients treated for at least 6 months continuously.

**Results:** We identified 42 patients (aged 3 to 8.6 years at the beginning of treatment), which were treated for an average period of 25 months (6-51 months). Growth velocity during treatment was between 3.8 cm/years and 11.8 cm/year, (average 6.4 cm/years); the bone age had a slow rate of progression during treatment (0.85 years bone age/ 1 year chronological age).

The predicted adult height (PAH) at the end of therapy was significantly higher than the predicted final height at the beginning of the therapy. The PAH at the last evaluation during triptorelin therapy was negatively and significantly correlated with the difference between bone age and statural age at the beginning of treatment; we also identified correlations between PAH and bone age at the beginning of therapy (negative correlation) and between PAH and midparental height. 8 patients were re-evaluated after cessation of therapy (between 3 months and two years, at a chronological age of 9.5 - 12 years);

their growth velocity was between 5.5 and 8.2 cm/year (average = 6.9 cm/an) and none of them was menstruate.

**Conclusions:** Triptorelin therapy has proved to be efficient in regression of pubertal signs, in restoring prepubertal hormonal profile and improving final height; it is mostly efficient in patients with high midparental height and low bone age at the beginning of therapy.

## PAO-238

### Final height in patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency

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**Background:** Achievement of optimal growth is one of the major problems in the management of children affected by congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD). The current literature reports that patients with classic CAH often do not achieve their target height (TH) and that they are obese. Glucocorticoid replacement is vital for preventing adrenal crisis and reducing androgen excess, but results in growth inhibition when administered in larger doses. If the androgens are not suppressed, there is advancement of bone age with premature fusion of the epiphyses and ultimate short stature.

**Aim:** The aim of this study was to evaluate final height (FH) of patients with the classic form of 21-OHD and compare to TH.

**Methods:** We reviewed the growth charts of patients with CAH who had attained FH.

**Results:** We evaluated 14 patients who had attained FH: 7 salt-wasting (SW) and 7 simple virilizing (SV). Five patients were male. Mean age at onset of treatment was 2,6y. Target height was available in twelve patients and mean TH-SDS was -0,15±1,1. Mean FH-SDS was -0,58±1,24. Corrected FH (FH-SDS - TH-SDS) was -0,66. All the patients were treated with hydrocortisone. Two patients were overweight at FH. The last bone age done at a mean chronological age of 13 years were advanced more than 1 year in 6 patients.

**Conclusions:** We concluded that mean FH of our CAH patients was within normal range, but in 8 patients was below the genetic target, as reported in the literature. Only one patient was obese.

## PAO-239

### Response of C-peptide/ insulin during a mixed meal test in combination with repaglinide to identify the diabetes type and the option for oral treatment

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**Background:** The aetiology and type of diabetes is not always clear in young diabetes patients. While clinical features, autoimmune antibodies (IC, GAD, IA2 and insulin) as well as molecular diagnostics for Mody 1 - 6 help to distinguish diabetes forms, a subgroup remains without a certain diagnosis.

**Objective and hypotheses:** For such cases we aimed to develop a method to evaluate  $\beta$ -cell function and subsequent options of treatment by repaglinide, a short acting insulin secretagogue (maximum plasma concentration within 0.5 - 1h, half life 1 h) which also stimulates early insulin secretion and is thus suitable to be combined with a  $\beta$ -cell provocation. A mixed meal test combined with incremental dosages of repaglinide was previously applied by Lawrence S. Coma et al. to show the effectiveness of the medication in type 2 diabetes.

**Methods:** Seven patients with unclear aetiology of diabetes and 1 healthy control person underwent after an overnight fasting period a MMTT with Sustacal 6 ml/kg (max.: 360 ml) ingested in combination with repaglinide 1 mg directly before the meal intake. Glucose, insulin and c-peptide were determined after fasting and 30, 60, 90, 120, 150 minutes after test start, i.e. repaglinide medication and start meal intake.

**Results:** In this pilot study we identified five patients who responded with sufficient insulin release to change medication from insulin to repaglinide.

**Conclusions:** We conclude that this test identifies individuals with repa-

glinide responsive diabetes in whom traditional tests couldn't clarify the aetiology and thereby were placed on insulin therapy. Using this test we can offer an oral treatment option despite in some of the cases the molecular diagnosis is not yet clear.

#### PAO-240

### Incidence and clinical characteristics of the new cases of type 1 diabetes in Galicia, Spain

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**Objective:** Studying the epidemiology of childhood-onset type 1 diabetes (DM1) less than 15 years of age in hospitals of Galicia (Spain) during the period 2001-2010.

**Methods:** We identify of new cases with DM1 criteria diagnosed by a pediatrician in Galicia Autonomous Community from January 2001 to December 2010 and conducted a data collection protocol to hospitalization include age, prior to the debut diabetic symptoms, duration, associated autoimmune disease, family history and biochemical parameters at diagnosis.

**Results:** We identified 559 subjects with childhood-onset DM1 during 2001-2010 and distributed by sex: 44.3% females and 55.6% males. The annual incidence rate was 17.2/100,000/year (range: 15.0-19.4); younger than 5 years were 151 children (21.7% from 8 months to 4.9 years); 179 (32%) were 5-9.9 years and between 10-14.9 years were 224 patients (40.8%). Nineteen patients (3.3%) had celiac disease, 15 patients (2.68%) autoimmune thyroiditis (6 subjects hypothyroidism) and 72.7% of patients tested positive for at least one autoantibody (insulin autoantibody, GAD antibody or insulinoma-associated protein 2 (IA2)). In relation to family history: 31 children have a first degree relative with DM1 and 16 with DM2. The debut diabetic symptoms are shown in table 1.

	0-4.9 years	5-9.9 years	10-14.9 years
Average time onset (days)(range)	14.7 (1-24)	24.6 (2-68)	28.7 (3-120)
Polyuria (%)	97.6	96.4	97
Polydipsia (%)	97.6	94.9	100
Enuresis (%)	75.4	59	-
Weight loss (%)	68.5	76	87
Hyperphagia (%)	32.5	55	64
Average glycemia (mg/dL)	475	386.3	536.4
HbA1c (%)	8.9	10.9	11.8
Diabetic ketoacidosis (DKA) (%)	34.4	29.6	24.1

**Conclusions:** The incidence peak was found in the 10 to 14 years age-group and a third of the children was diagnosed with DKA. The 0-4.9 years group was diagnosed in less time and with lower values of HbA1c. The most common symptoms were polydipsia, polyuria and weight loss. The incidence remained stable over the 10 years.

#### PAO-241

### Use of 70/30 premixed insulin in DM1 pediatric patients with a basal bolus regimen with multiple snacks

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**Background:** Metabolic control is related with the number of short-acting analogs bolus administered, as we reported in a previous study [3 bolus (n:33) HbA1c: 8,54+/-0,8; And ≥4 bolus (n:73) HbA1c: 7,52+/-0,8; p<0.001]. In our country, children have 4-5 meals/d, with midmorning and midafternoon snacks. Some of them, especially adolescents, refuse to receive more bolus/d, and have snacks without insulin. In these patients a premixed 70/30 insulin at breakfast and/or lunch could better satisfy insulin requirements, improving glycemic profile and HbA1c.

**Objective and hypotheses:** To analyze the characteristics of a regimen using a premixed insulin 70(aspartic)/30(NPH), related to insulin requirements (U/kg/d), time of the injection and its effect on metabolic control.

**Methods:** 28 DM1 patients with a basal-bolus regimen, 3 short-acting analogs/d and poor metabolic control were proposed to change to 70/30 premixed insulin at breakfast and/or lunch. 21 patients were included.

Mean age +/- DS: 15,14 +/- 2,49 years (range 9-17). Diabetes evolution: 7,52 +/- 4,19 years (1-16). 11 males (52,4%), 10 females (47,69%), 2 prepubertal (9,5%), 19 pubertal (90,5%).

**Results:**

	Before change	After change	Mean of differences	P
Insulin requirements (U/Kg/d)	1,12 ± 0,23	1,11 ± 0,27	-0,01 ± 0,19	NS

	Before change	After change 1st control	After change Annual mean	Mean of differences 1st control	Mean of differences Annual mean	p 1st control	p Annual mean
HbA1c (%)	8,48 ± 0,85 (range 7,3-11)	7,8 ± 0,87 (6,6-10)	7,92 ± 0,80 (6,6-9,7)	-1,01 ± 1,7	-0,9 ± 1,65	0,002	0,000

Premixed insulin administered at breakfast in 33% of the patients, at lunch in 42,9%, and at breakfast and lunch in 23,8%.

**Conclusions:** In DM1 patients having multiple snacks who refuse to receive more than 3 bolus, the change to a regimen with 70/30 premixed insulin at breakfast and/or lunch improve significantly their metabolic control, reducing HbA1c. The change from a short-acting analog to 70/30 premixed insulin does not vary total insulin dose significantly.

#### PAO-242

### Disorder of sex development in southern Nigeria: a report of four cases and constraints in management

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**Background:** Disorder of sex development (DSD) is a congenital condition in which development of chromosomal, gonadal, or anatomic sex is atypical. The prevalence of DSD is about 1% among live births and about 0.1-0.2% present with marked genital ambiguity. In most developing countries, the exact incidence is not known. This is because some cases are missed at delivery, which is mainly by traditional birth attendants and amongst clinicians, poor awareness is a major challenge.

**Objective and hypotheses:** To report four cases of DSD seen in a tertiary hospital in Southern Nigeria and highlight management constraints.

**Methods:** Case notes of patients with ambiguous genitalia seen at the Paediatric endocrine unit between January 2008 and December 2010 were analysed. Literature was reviewed for comparison with current trend in investigations and management. Parents were interviewed using a structured questionnaire and results analysed.

**Results:** Of 62 children seen with various endocrine disorders during the study period, 4 (6.4%) had ambiguous external genitalia. Their ages at presentation ranged from 8 days to 16 years. The commonest initial clinical diagnosis was congenital adrenal hyperplasia. Confirmatory diagnosis was not done in any of the patients due to financial constraint and non availability of facilities for performing the investigations in our centre. Three (75%) were lost to follow up while one patient died from chronic renal failure. Reasons for default were religious 2(50%), financial constraints in investigations 4(100%), lack of diagnostic tools 3(75%), and unwillingness to continue follow up 2(50%).

**Conclusions:** There is still delay in diagnosis of children with ambiguous external genitalia in our environment. Lack of diagnostic facilities, belief in spiritual attacks and high cost of confirmatory test have led to high rate of loss to follow up.

#### PAO-243

### The TRH test identifies hypothalamic defects of the thyroid axis in children within euthyroid state

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**Background:** Congenital Central Hypothyroidism (CCH) has a prevalence of 1:16.000 neonates. 40% of cases are isolated pituitary or hypothalamic deficiencies. CCH is not screened for in Europe where TSH is mainly used as screening. Besides, it is not routine to discriminate between secondary or tertiary CCH using the TRH test. Pituitary CH is due to TSHB and TRHR genes mutations, while hypothalamic CH remains genetically "orphan".

**Objective and hypotheses:** To test the discriminative capacity of the TRH test in the etiology of CCH.

**Methods:** After 7 µg/kg TRH, TSH and PRL were determined at -15, 0, 15, 30, 60, 120 and 180 min. and FreeT4 and TotalT3 at 0 and 180 min. We analyzed TSH peak, its return to basal levels and dynamics of TSH increase (ratios 15'/0' and 30'/0') and fall (ratios 30'/60' and 180'/0') upon Van Tijn. The test was performed in: 1. A 20 month old girl with postnatal progressive and severe growth retardation (-3.7 SD weight and height), hyperphagia and reduced TSH related to her FT4 (TSH 1.2 mU/L, FT4 0.92 ng/dl). 2. A 12 year old boy with hypothermia-bradichardia-sweating crises and sporadic hyperthyrotropinemia (TSH 5.4-8 mU/L) and 3. An 11 year old boy with hyperthyrotropinemia (TSH 9.82 mU/L) and hyperglycemia (109 mg/dl) (TRH defect suspicion).

**Results:** Patients 1 and 2 had type 3 TSH response (hypothalamic defect) with 15'/0' ratios of 23.8 and 9.1 (N<6.5) respectively, without return to basal TSH after 3 h. (180'/0' ratios of 2.87 and 1.7). Patient 3 had type 0 response (thyroidal defect) with 15'/0' and 180'/0' ratios of 4.6 and 0.8, respectively.

**Conclusions:** The 180 min. TRH test identifies hypothalamic defects of the thyroid axis even in the biochemically euthyroid state. Tertiary hypothyroidism can present as mild TSH elevation or as TSH decreases (even within normal values) relative to FT4 levels.

#### PAO-244

### Type 1 diabetes mellitus in schools - monitoring of current practice

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**Background:** It has been shown that by improving diabetes control, the rate of complications later in life is reduced. In the recent years, there is more interest in multiple injection therapy and continuous subcutaneous infusions compared to the conventional twice daily regimes.

**Objective:** We wanted to establish the level of support in school for children and young people with diabetes in our area.

**Methods:** We prospectively collected questionnaires, anonymised from parents or patients attending paediatric diabetes outpatient clinics over 2 months period, (July-September 2010). Our questionnaires included: who does blood glucose testing?, what insulin regimes children are on?, who does the insulin injection in school? and the patient's views about different aspects of education and understanding of school staff of diabetes.

**Results:** We had a total of 78 questionnaires completed and returned. Most children had insulin given in school (44 out of total 78) In the overall sample, most injections were done by the children or young people with supervision from school staff.

Who does blood glucose test? school staff 7 you/school staff 2 you/your child 3 your child 62 your child/school staff 3 Total 77 However, when we analysed the data by ages it appeared that in the young children (less than 8 years), all (7) had the insulin given by school staff(4) or parents (2).

**Conclusions:** We concluded that even in some schools there continues to be fear of managing diabetes. The main problem continues to be the administration of Insulin in the young age group, who are most vulnerable group. However, insulin is only a part of the complex assistance children with diabetes need in school. We believe that our efforts should concentrate in improving schools' understanding of diabetes and education in management of this condition.

#### PAO-245

### Variation of the heart rhythm in children with type 1 diabetes mellitus-preliminary report

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**Background:** In very early stage of diabetes type 1, we may observed symptoms of autonomic neuropathy, which unfavorably effect on course of diabetes type1. Especially sense have complications which are connected with heart-vascular system. In adults the complications may increase risk of death because of cardiac complications.

**Aim:** Early detection neuropathy in diabetes type 1 with different time of going the IDDM.

**Methods:** In both groups were done 24 Holter electrocardiography examination. Mean value of diabetes type 1 was 7,1+/-3,7 y and level of the HbA1c was 9,2%+-2. We analyzed patients with good and bad compensation of diabetes type 1. We observed children 19 with diabetes type 1 (11 girl and 8 boys)-mean age 14,12+/-4,32 y. Control group was consist of 11 girls and 8 boys mean age 14,02+/-2,8 y.

**Results:** Mean value of all parameters of variation of the heart rhythm were lower than in healthy group and it was correlate with duration of diabetes type 1.

**Conclusions:** 1. Indirect symptoms of diabetic autonomic neuropathy, which disturb adaptation of the heart rhythm, may observed in very early stage of diabetes type 1. 2. Preliminary results indicate, that is necessary to do 24h electrocardiography examination in patients with diabetes type 1.

PAO-246

**A case of short stature due to phosphatediabetes**

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**Background:** Primary hypophosphatemic rickets is rare disorder caused by inborn defect of renal tubular reabsorption and usually manifested in childhood and infancy with stunted growth and deformities of lower limbs.

**Objective and hypotheses:** The female patient from healthy parents, born without complications at term, normal weight and length. Psychomotor development until the age of 2 years was normal. Since the age of 2 years deformation of legs and difficulties with walking have been observed.

**Methods:** The Patient was consulted by Pediatric Orthopedist, Nephrologists and Endocrinologist. The blood biochemical findings revealed normal pH, normal calcium (CA)-, potassium (K)-, sodium (Na)-concentrations, very low phosphate (P)- with markedly elevated alkaline phosphatase (AP)- and slightly elevated parathyroid hormone (PTH)-concentration; urine test indicated impaired tubular function: mild glucosuria, proteinuria, erythrocyturia and markedly increased phosphaturia. Phosphate tubular reabsorption (PTR) was 52%, phosphate clearance/creatinine clearance 0,52, renal threshold phosphate concentration (TmP/GFR) 0,25mmol/l. Genetic tests results not available yet.

**Results:** The diagnosis of phosphate diabetes made on the basis of clinical-laboratory data. The therapy with Inorganic phosphate (100mg/kg/d) and 1,25(OH)2VitD 50-60ng/kg/d had been started. Childs walking abilities improved with treatment, the deformation of legs decreased, but O-legs and other skeletal deformations are still remarkable. Auxological parameters are not satisfactory. Physical growth is below the normal range (height SDS -3, 84); the patient's predicted height less than target height. Biochemical monitoring performed regularly under the treatment, serum phosphate remains below normal, serum AP is still elevated.

**Conclusion:** This case is in line with other publications and indicates the difficulty to achieve normal phosphate levels and normal growth without an additional treatment with growth hormone.

PAO-247

**Particularities of diabetes mellitus type 1 according to gender, date of birth, onset of disease and complications**

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**Background:** Diabetes Mellitus (DM) is one of the hardest diseases and is not only a medical, but social problem. DM takes the third place on mobility and mortality in developed countries. Children and adolescent make 8 to 10% out of all patients with diabetes. One out of 500 children or one out of 200 adolescent has diabetes.

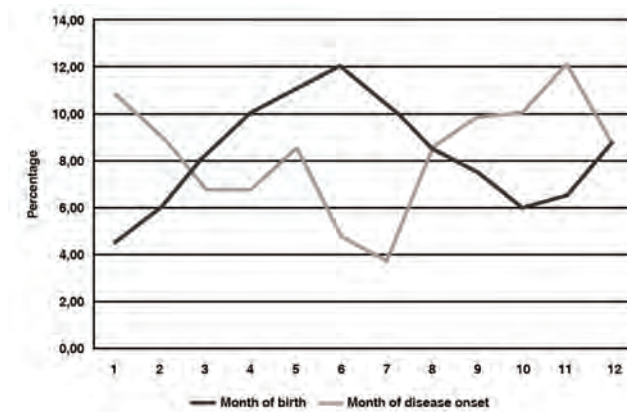
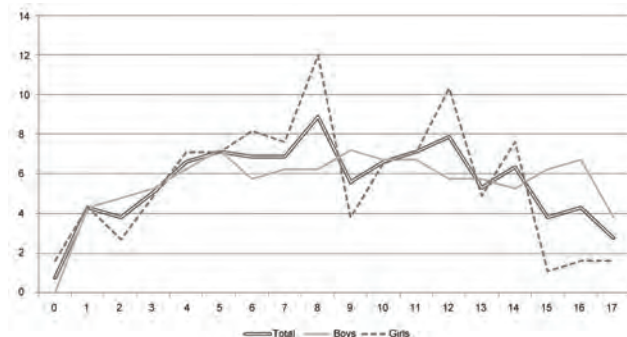
**Objective and hypotheses:** The aim of the study was to investigate particularities of DM1 according to gender, date of birth, onset of disease and complications.

**Methods:** 397 children from 0 to 18 years of age with diagnose DM1 were discovered according to standard medical protocols for this pathology.

**Results:**

	Total %	Boys %	Girls %
Diabetic retinopathy	31.8	50.8	49.2
Diabetic nephropathy	34.6	46.7	53.3
Diabetic angiopathy of the lower extremities	14.4	49.1	50.9
Peripheral neuropathy	27.0	51.4	48.6
Central neuropathy	2.0	50	50
Chairopathy	5.6	54.5	45.5
Mauriac syndrome	0.5	100	0

**Conclusions:** There is practically the same prevalence of onset of DM in all age groups among boys, with an increase in number of cases at 8 and 12 years of age in girls, and decrease at the age of 15 to 17 years. Children born in spring and summer months have higher risk of developing DM1. The onset of the DM1 usually occurs in autumn and winter months. Most commonly children develop nephropathy, retinopathy, and peripheral neuropathy, 1/3 of all patient would have these complications. Gender is not a risk factor for chronic complications' development in DM1. Though girls seem to develop diabetic nephropathy more frequently than boys, but have lower risk of chairopathy and Mauriac syndrome.



PAO-248

**Thyrotoxicosis/thyroid storm in a previously asymptomatic pediatric patient: a case report**

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**Background:** Thyroid storm is a rare but severe complication of thyrotoxicosis. The most common etiology of thyrotoxicosis is Graves' disease, which is also the most common cause of hyperthyroidism in children. Typically pediatric patients present with thyromegaly, weight loss, or behavioral changes. Previously asymptomatic patients whose initial presentation is thyroid storm are not a typical finding.

**Objective:** To determine whether thyroid storm has been reported as the initial presentation in Graves' disease in previously asymptomatic pediatric patients.

**Hypothesis:** Thyroid storm may be a more common initial presentation of thyrotoxicosis in pediatric patients than previously thought.

**Methods:** Literature search.

**Results:** Our patient was a 14 year-old previously healthy female hospitalized for thyroid storm. She was later diagnosed with Influenza and Graves' disease. Prior to presenting to the hospital, this patient exhibited no symptoms of hyperthyroidism. She presented to the emergency room with a 3 day history of fever, diarrhea, sore throat, and cough, consistent with a viral illness. Physical exam revealed hyperthermia, diaphoresis, sinus tachycardia, hypertension, exophthalmos, Von Graefey's sign, Dalrympley's sign, thyromegaly,

tremors, and fluctuating mental status. Her thyroid function studies revealed a Free T3 of 747 pg/dl, Free T4 of 4.8 ng/dl, and TSH of <0.01 uu/ml. She was started on Methimazole, Propranolol, and Potassium Iodide for thyroid storm. Antibody testing revealed anti-TPO of 1355.5 iu/ml, anti-thyroglobulin of 291.8 iu/ml, and TSI of 335% baseline. She was diagnosed with Grave's disease and continued treatment with Methimazole and Propranolol.

**Conclusions:** Graves' disease accounts for 10-15% of all childhood thyroid disorders, with incidence ranging from 0.1-3.0 in 100,000 children. Approximately 1-2% of patients with hyperthyroidism progress to thyroid storm when physiologically stressed. To our knowledge cases of asymptomatic Graves' disease with initial presentation of thyroid storm in pediatric patients are not commonly reported.

#### PAO-249

### Complication of subcutaneous fat necrosis of the newborn

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**Background:** Subcutaneous Fat Necrosis(SCFN) of the newborn is uncommon, self-limited disorder that occurs in full term infant who experienced a perinatal distress in the first weeks of life. It can be complicated by life threatening hypercalcemia and other rare complication such as hypoglycemia, thrombocytopenia, hypertriglyceridemia, anemia and fever. SCFN with hypercalcemia frequently has been reported.

**Objectives:** To describe a case of subcutaneous fat necrosis with all of the above complications.

**Methods:** We recorded risk factors concerning the mother, pregnancy and delivery, clinical aspects of SCFN and early and late outcomes.

**Results:** The child was born at term. Lesions appeared on the 22th day of life. Delivery was complicated by meconium aspiration. Complications were hypoglycemia, hypercalcemia, nephrocalcinosis, dyslipidemia, thrombocytopenia and feve.

**Conclusions:** Physicians caring for infants with subcutaneous fat necrosis of the newborn should be aware of the above associations in order to provide prompt and appropriate treatment to prevent associated, undesirable sequelae. Figure 1: The erythematous subcutaneous nodular plaque on the middle of the back and arm.



#### PAO-250

### Nutritional status in PKU patients in Mazandaran province: is it acceptable or not?

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**Background:** Phenylketonuria is one of the most frequent metabolic diseases which is transmitted as autosomal recessive pattern. Appropriate diet with restricted phenylalanine is the base of treatment, so special formulas and diet replace phenylalanine containing foods. Limited native studies exist about the results of such treatment means protein limitation and replacing an expensive and unavailable foods. This study was designed to evaluate nutritional status the calorie, protein, carbohydrate and fat of patients' diet and iron storage and iron deficiency anemia in PKU patients.

**Objective and hypothesis:** This is a cross sectional study which evaluated all of the PKU patients in Mazandaran province during 2009-2010 in metabolic clinics in Babol and Sari. Nutritional status was evaluated according to 72 hours diet recall sheet which is the method for recording nutrients eaten within 3 days. Nutritional and demographic information was studied according to questionnaire and blood sampling results and iron deficiency anemia.

**Results:** Twenty one PKU patients were studied which 7 ones (33.3%) were female and 14 ones (66.7%) were male with mean age of 7.26±6.64 years. Iron deficiency and iron deficiency anemia was present in respectively in 10 (47.1%) and 6 patients (28.6%). Five patients (23.8%) were underweight and 4 patients (19%) were short stature.

**Conclusion:** Energy, protein, carbohydrate, fat and iron deficiency was significant in patients; According to the price of special foods in our country, families cannot prepare enough foods. So, attention to nutritional demands in PKU patients to reduce malnutrition and iron deficiency is critical.