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 glycoerythema to proximal renal tubular dys-function. 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 (GnRHa) 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 (GnRHa).

Methods: Twenty boys with central precocious puberty treated with GnRHa 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. GnRHa 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 (TH), predicted adult height(PAHe)at the start and the end of GnRHa treatment (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 (PAH) [(169.8 +/- 5.6)cm versus (169.8 +/- 6.0)cm] based on the Bayley-Pinneau method, using a table for average bone age at the beginning of GnRHa analogue therapy. Predicted adult height (PAHe) at discontinuation of GnRHa therapy was significantly higher than predicted adult height at the beginning of GnRHa 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: GnRHa 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 test after eating 1.75 g/kg glucose was performed. Homeostatic model assessment was used to estimate insulin resistance.

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 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 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). The birth brain size - body size ratio has been related to fetal-neonatal stress.

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 significance level (p) of partial correlations of BRW with IG1x-ln, IG1y-ln and IG1z-ln resulted near-normally distributed. SEX, PT and SGA were dichotomized.

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.

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 2.505/- .283/a 2.812/- .315/b 2.211/- .252/c // -.059/- .079/c .390/a .301/b
Significances: a, p<.05; b, p<.01; c, p<.001; ns, not significant.

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. IG2 and IG3) in the human newborn (NWB) could not be 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). BRW in gr was calculated according to the formula “ BRW = 0.037 x HC 1.77 ” (McLennan JE, 1983). 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 BRW.

Results: Table 1 shows t value (t), partial correlation coefficient (r) and significance level (p) of partial correlations of BRW with IB2x-ln, IB2y-ln and IB2z-ln, and Multiple Linear Regression (MLR) whole model R2 and p regarding MLR models bearing IB2-ln, IG1-ln and IG2-ln, and Multiple Regression (MLR) whole model R2 and p regarding MLR models bearing IG1-ln, IG1-ln and IG2-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).

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.

Table 1. vs. A) IB2x-ln A) IB2y-ln A) IB2z-ln // B) IB2x-ln B) IB2y-ln B) IB2z-ln
BRW t/r/p 2.483/- .281/a 2.483/- .281/a 2.945/- .282/b // -2.733/- .089/c .665/- .078/a .397/- .047/a
Significances: a, p<.05; b, p<.01; c, p<.001; ns, not significant.

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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.
Results: The study revealed that according to the glucometer’s readings the minimum glycemia level was 6.7±2.31 mmol/l; CGMS displayed 3.46±0.44 mmol/l (p < 0.001). The maximum glycemia level was 14.93±1.15 mmol/l (glucometer) and 18.18±1.48 mmol/l (CGMS) (p < 0.01). The mean glycemia level was 9.76 mmol/l (glucometer) and 10.8 mg/dl (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 months 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- 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.

Methods: Group 1 included 121 healthy children born in Italy or living in Italy since at least 1 year (78 females and 43 females, mean age 9.5±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±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 subcontinent (n=17).

Results: In group 1 mean serum level of 25(OH)D was 25.3±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±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±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±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).

Results: For the whole study population, the 6-month lifestyle intervention resulted in a significant improvement (before intervention minus time point 6 months; mean ± SD) in BMI-SDS (0.10 ± 0.17, p < 0.001), HOMA (1.41 ± 3.19, p<0.001) and relative fat-mass-SDS (0.09 ± 0.23, p=0.005). Before and after lifestyle intervention, there was no significant difference between the ratio of height/age (n=52) and homozgyote (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.

Results: The study population consisted of 150 infants with CH (72(47%) females and 78(53%) males. Of the neonates with congenital hypothyroidism, between 1385-1389. All infants with biochemically confirmed CH (low T4, and TSH> 10 µU/ml) 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.

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Methods: 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 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 biochemical confirmed CH (low T4, and TSH> 10 µU/ml) 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. 75(47%) females and 75(53%) males. Of the neonates with congenital hypothyroidism, between 1385-1389. All infants with biochemically confirmed CH (low T4, and TSH> 10 µU/ml) 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, between 1385-1389. All infants with biochemically confirmed CH (low T4, and TSH> 10 µU/ml) 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.

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Results: The study population consisted of 150 infants with CH (72(47%) females and 78(53%) males. Of the neonates with congenital hypothyroidism, between 1385-1389. All infants with biochemically confirmed CH (low T4, and TSH> 10 µU/ml) 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.
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 were 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-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 the 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.
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), idemY(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 tests and nearly 2:1 in the blood, fibroblast and a dysgenetic gonad samples by QF-PCR. However, FISH analysis in the tests 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 (incl. shi(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.

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**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 for 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 x 10³/µl (150-300 x 10³/µl). The coagulation factors and myoglobin were normal. An X-ray of the chest was normal. She was hospitalized at the hematology 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.

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**PAO-18**

**Peripheral blood karyotype poorly represents tissue mosaicity 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-
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 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 crews 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 divided 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 weekends; 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±3,9yrs) 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, Beckman 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.

Conclusions: Diuresis of urinary GH allows to improve the diagnoses of endocrine variants of short stature.
PAO-24
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.

PAO-26
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.

PAO-25
Serum IGF-1 and IGFBP-3 levels in central precocious puberty girls with gonadotropin releasing hormone agonist (GnRHa) treatment
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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 month.

Results: At the time of diagnosis, their mean serum IGF-1 and IGFBP-3 were 302.90 ± 102.54 ng/mL and 3103.58 ± 705.08 ng/mL. At 6 month after treatment, IGF-1 secretion was slightly decreased and IGFBP-3 production was increased. Onadal 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 ± 1.63).

Conclusions: Serum IGF-1 and IGFBP-3 levels were not changed during one year GnRHa treatment.
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 present 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 ne-

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.

Aims: To examine ethnicity and gender differences in the evaluation of referred short 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±0.73 and -2.62±1.05 versus -2.13±0.55 and -2.21±1.07, 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.

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

Aims: 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 night admissions and prolonged duration of illness before admissions. He presented initially with DKA as this is a good indicator of public health knowledge about diabetes in the pediatric age group. 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.

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.

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-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), IFS (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 growing 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 GnRHa agonist 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-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 obesity/obesity group. BMI-SDS increased more in normal BMI group than in obesity/obesity group (0.2 vs 0.1, P<0.004), and initial BMI and delta BMI-SDS showed negative relationship (R2=0.251, P=0.001). PAH-SDS increased less in normal BMI group than in obesity/obesity group (0.3 vs 0.7, P<0.002), 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 obesity/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 11β-hydroxylase deficiency, futile trophic hormone stimulation results in excess sex hormone precursors. Androgen dominance 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 (unoria), pubic hare since the age of 2 years. Anamnesis to over the postnatal period the patient was frequently hospitalized due to intensive vomiting, diarrhea and weight loss. The patient was on symptomatic treatment. Aurology: HSDS 1.22. Sexual development stage P3 A1 G2; Testes not palpable. Bone age by Greulich and Pyle 13.5 years. Pituitary MRI: In the pelvic cavity on both sides ovary-like structure, with the size: 0.8x1.3 mm. At the posterior side of the urinary bladder mass with the size 27x7 mm (apparently vagina). The conclusion of children’s psychologist: the psycologic development of the child coresponds 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 reasignment surgery (exptiation of uterus and ovaries).

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

PAO-35

A case of a 1 year 9 months old girl with a hypothyroid 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 pubertal hypothyroid-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 hypothyroidic hama-thoma associated with precocious puberty on Triptorelin treatment.

Methods: A 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-
development 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 neof ormation 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.

Conclusion: 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.

Methods:
Complementary tests TSH 1.98uIU/mL, FSH 51.6 U/mL LH 33.2 U/mL Estradiol 13.3 pg/mL. Testosterone total 10.41 ng/mL SHBG 52.92 nmol/L DHEAS 174 mcg/dL Free Testosterone 19.3 17 OHP 1.64 mg/mL Karyotype: (400 bands): 47,XY[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 Gynecological exploration through laparoscopy: Uterus and Fallopian tubes were normal. Left ovary compatible with testicle; with a similar form between fimbriaes in right side. Tissues biopsy: Compatible with testicular tissue. Karyotype of gonadal biopsy 47 XY

Evolution: Quick estrogenization (etinilestradiol VO and combined proges- terone). 6 months after quirurgy, 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-36
Female with disorder of sexual differentiation
DSD 47,XY: a first report
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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.


Objective: The aim of this study was investigation of clinical features, patho- genesis, 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-thal- assemia major. In this retrospective analysis study, patients were examined to determine their pubertyal 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 (11-18 years). Two patients, at onset of clinical diabetes, presented with an asymptomatic glycos- uria 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 of 6 patients was in Tanner 1 to Tanner 2. 6 patients were all short stature, 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 pubertal 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.

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-37
Diabetes in 6 patients of beta-thalassemia major
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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 a 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%). Endo- crine 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 gonadotropine deficiency in 40% of cases and a ACTH and TSH deficiency in 25%. Despite craniohypophysealomas 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 6.65 years (SD 3.04). Location of craniohypophysealoma. Suprasellar 8 Sellar suprasellar 8 Saddle + 3rd ventricle 1 Suprasellar dienecephalic 1 Suprasellar + 3rd ventricle 1 Chiasmatic 2 3rd ventricle 1 Chiasmatic 2 3rd ventricle 1 Chiasmatic 1 Bodysym 1 Retrosellar 1 Suprasellar retro- chiasmatic 1 Total 25 Aceso-undocrine 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%) Giganatism 1 / 25 (4%) Endocrine abnormalities detected after treatment. Diabetes insipidus 20 (80%) Precocious puberty 2 (8%) Hypoadrenalism 17 (82%)

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:

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<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>5-19, mean 14</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>19/58</td>
</tr>
<tr>
<td>Puberty (no/yes)</td>
<td>8/69</td>
</tr>
<tr>
<td>TSH (high/normal)</td>
<td>28/49</td>
</tr>
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</table>

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 µIU/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 radiation 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 Langherans 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 rigour nucalis. A 3D-CT showed pansinusitis whereas CSF showed a pleiocytosis (500 cell/mm3); therefore, broad spectrum antibiotics therapy were administered. After 5 days headache, fever, rigour nucalis were resolved, but diploria persisted. MRI demonstrated diffuse pansinusitis and extension of inflammation and infection into the adjacent cavernous sinuses and pituitary gland that, after gado- linium, 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 administrated 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.
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.


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, CO2H 19,4; EB -6. Sodium 119 mEq/L, potassium 7,3 mEq/L, PCR 23,8 mg/dl after 24 hours/life Cultivates: Negative. Cortisol 2,86 mcg/dl. DHEA-S 8,32 mcg/dl (32-431), 170HP 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 horas (<2 mcg/L) Dopamine: 65 mcg/dl (163 mcg/L). Abdominal ultrasound and MRI: There is no sign of adrenal glands. Genitic 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.
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. Multisteroid 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.L299N) in exon 5. Substitution with hydrocortisone was started at a moderate dose to prevent hypertension. The child is growing well.

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-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 ≥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.
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 phaeochromocytoma and hyperparathyroidism. MTC tends to disseminate early. It is chemeno- 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 phaeochromocytoma, 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 10-2 yr-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), 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 phaeochromocytoma 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 remain a concern.

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 antiTPO antibodies. Ultrasound revealed an inhomogeneous pattern in the left lobe with many reflections, mimicking micro calcifications, and Tc-99m-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 ultrasound showing suspicious calcifications, and Tc-99-pertechnetate scan was inconclusive. Fine needle aspiration (FNA) revealed a papillary carcinoma (PTC) in children.

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.

Conclusion: DAX1 mutation analysis should be considered in males with adrenal hypoplasia congenita.
and cell types in the blood. The young individual with CKD copes may be related to stress hormone levels. The hypothalamus, the pituitary gland and the adrenal glands; thus how well a person copes, well-being and overall quality of life.

Central mechanisms: Normally well-tolerated degree of stress can become chronic for individuals in stressful situations. Stress can influence the internal conditioning factors, what might generally be called ‘a stress pattern of children/young people with CKD. Physiologically, due to the stress response, people with CKD would be expected to cope adequately with daily events.

Conclusions: In children without overt GHD, a higher BMI SDS may have negative correlation with natural log value (Ln) of peak GH level (P=0.004), but gender, age, pubertal status, Ln IGFI-1 had no correlation, respectively. In multiple 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 IGFI-1 had no correlation, respectively. The overall results show that lower BMI SDS may not be a significant predictor of Ln peak GH level. The results were significant for prediction.

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.

Conclusions: The reproductive health is frequently associated with thyroid disorders. Cardiac vegetative test allows to diagnose DCAN in children at the debut of the disease, duration of the disease, degree of compensation.

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.

Conclusions: 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 in 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.

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

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.
Failure to thrive and the diencephalic syndrome

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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 lipodystrophy and Russell Silver syndrome in one patient. A second patient was also diagnosed with hypothalamic-pituitary factors in the feedback mechanisms of appetite and growth hormone levels) with normal linear growth, and suggests that there are hypothalamic-pituitary factors in the feedback mechanisms of appetite regulation and metabolism.

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. One patient 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.

Profile of iron metabolism in pediatric age: clinical and epidemiological impact on our environment

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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. Of the latter, we observed more frequently in men (83%) and intercurrent. We determined weight, height and body mass index. It was seen in primary care. They have no diagnosis or suspicion of iron deficiency.

PAO-59

Profile of iron metabolism in pediatric age: clinical and epidemiological impact on our environment

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PAO-60

Implications of bone metabolism in pediatric patients with inflammatory bowel disease

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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, phosphate, 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: Preliminary 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.

PAO-61

Gonadal mosaicism 45X/46XY resulting in a Turner phenotype with mixed gonadal dysgenesis: a report of two cases

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Background: Mixed gonadal dysgenesis is regarded as the most common manifestation of 45X/46XY mosaicism, 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 45X/46XY and one a 46XY karyotype.

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, cubitus valgus, short stature, and primary gonadal failure. The pelvic ultrasound reveals the presence of an uterus; no gonads were visualized. An aparatomy confirms the presence of an uterus and fallopian tubes with streak gonads.

Results: In the first case G-banding analysis of blood lymphocytes showed a 46XY karyotype while in the second there was a mosaicism 45X/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 mended 10 to 60 days after starting the treatment.

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-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 pseudohyperaldosteronism, 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 academia and childhood absence epilepsy who developed arterial hypertension. Initial diagnostic workup showed a slight hypokalemia, serum aldosterone was not capable of measuring. 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 academia nor childhood absence epilepsy seems to be related to amiloride. Neither argininosuccinic academia 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 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.
by the face (30%) and the extremities (13%). In 54% of patients feeding dif-
ficulties 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 leukopenia 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 termi-
nology 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 genita-
lia to the clinic over 13 years. Assessment criteria were based on clinical pre-
sentation, hormonal and biochemical estimations, sonogram of the abdomen,
genitogram and karyotype / baccal 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 FP (15, 34%) all were due to congenital adre-
nal hyperplasia (CAH), Genetic males overvirilized (4, 9%) Genetic males
undervirilized or MPH (11, 25%), Micropenis with severe chordee 3, 6.8%,
micropenis with gynecomastia (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 simi-
lar conditions for the length of time of review. This may be an invalid conclu-
dion due to the inadequate health delivery service, referral system and or older
dge 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
Senay Savas Erdem 1; Merih Berberoglu 2; Nuket Yurur Kutlay 2; Zeyneb Siklari 3; Bülent Hacidamoglu 1; Aijlan Tukun 4; Gonul Ocal 2
1 Ankara University School of Medicine, Department of Pediatrics, Division of Pediatric Endocrinology, Ankara, Turkey; 2 Ankara University School of Medicine, Department of Medical Genetics, Ankara, Turkey

Background: The frequency of NCCH with V281L among children pre-
senting with premature pubarche (PP) is variable.

Objective and hypotheses: To determine the prevalence, clinical and labora-
tory characteristics of NCCH 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 peak 17-OHP levels >22 nmol/l. Patients whose stimulated 17-OHP
level on the ACTH test was ≥10 ng/ml underwent a mutational analysis of the
CYP21 gene, and those with the mutation were considered to have NCCH.

Results: NCCH 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 NCCH and patients with idiopathic PP (IP). When
compared with the IPP group, the NCCH 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 hetero-
ygote for the V281L mutation and the I2 splice mutation. The one of the pa-
tients 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)
Fawzyah Alkhafaj; Maryam Al Ali; Ashraf Tawfeq; Mohamoud Zyyoud; Noura Alhemaidi; Amal Sabb; Ahmed Alawa
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Background: Neonatal diabetes is defined as persistent hyperglycemia oc-
curring in the first months of life that lasts more than two weeks and requires
insulin for management.

Objective and hypotheses: Although pediatricians face numerous difficul-
ties 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 ABCCR-ve KCNJ11, two had pan-
creatic agenesis and one has Wolcott-Rallison syndrome. CSII therapy in neo-
natal 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 insulin infusion lines well with
any local side effects.

Conclusions: During the neonatal period, and under the supervision of an ex-
erienced 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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Hamad Medical Center, Pediatrics, Doha, Qatar

Background: Patients with Johansen Blizzard syndrome (JBS) have signifi-
cant 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 se-
vere 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 hy-
pothyroidism (low free T4 and high TSH) and cortisol deficiency. MRI of the
brain, showed hypoplasic 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 JS8 on Therapy

Conclusions:

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But that result cannot be generalized because it consists of one case, as expected, especially in the second year of therapy.

In this case report, sandostatin treatment was safe but not as effective as hoped. The decrease of weight was achieved. No side effects were seen related to sandostatin treatment.

Second year of therapy, the response was not the same as only stabilization of weight gain, even loss of weight occurred (Δ BMI: -2.3 kg/m²/year).

mcg/kg/day in the second year). First year of sandostatin treatment, decrease of height gain were unsuccessful. Sandostatin was introduced increased from 19.3 kg/m² to 45.4 kg/m² within 2 years was developed. The GH deficiency, and no GH therapy was introduced. Intractable obesity with BMI, and was given appropriate replacement therapy. Growth was normal despite visual disturbances and cephalgia. Extended evaluation revealed diagnosis of GH deficiency and no autoimmunity.

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

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: 4.92 pg/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 colloidial 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 (casel) older brother. Beside intolerance the heat, he had no symptoms. 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:9.3ng/ml (0.5-4.8), free T4:1.43ng/dl (0.8-2.3), 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 hypothyroidism 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 tried in 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 craniopharingioma. After neurological investment, he had developed multiple hypothalamic 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/m² to 45.4 kg/m² 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 (A BMI: -2.3 kg/m²/year).

Second year of therapy, the response was 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 cannot be generalized because consist of one patient. More hypothalamic obese children should be evaluated to conclude the effectiveness of sandostatin treatment.

PAO-75
TNF-α and others inflammatory molecules in overweight children

Maria Cristina Bazán1; Teresa Carrizos2; Maria Prados2; Elsa Díaz2; Maria Fonio2; Adela Agregui2
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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-α.

Objective and hypotheses: The objective of this study was to evaluate the levels of TNF-α 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), plasminatic insulin (ECLIA); plasma fibrinogen (Clauss); uCRP (Immunoturbidimetric assay); TNF-α (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-α 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-α was positively correlated with the waist circumference.

Conclusions: The high TNF-α, 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 ± 3.0) with BMI ranging from 1.62 to 5.11 (mean 3.17 ± 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 BMIsds 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.
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 skeletal changes, 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 epiphyseal-methaphyseal dysplasia affecting long bones, vertebral and pelvis.

Conclusions: WRS is a very rare disease. However, it should be considered in any child with NMD 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.

Background: 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-Simomian 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.

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: 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 - 51 girls with Turner syndrome, mean age 8.2 yrs +/-3.3; 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 t-test.

Results: The results showed that height and GV were significantly higher in the GH treated children compared to controls. The most striking difference was observed in the Turner syndrome group, where the height SDs were +1.2 at the start and +7.6 at the end of treatment.

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 - 51 girls with Turner syndrome, mean age 8.2 yrs +/-3.3; 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 t-test.

Results: The results showed that height and GV were significantly higher in the GH treated children compared to controls. The most striking difference was observed in the Turner syndrome group, where the height SDs were +1.2 at the start and +7.6 at the end of treatment.
Results: In group 1, the average height was -3.1 SD +/- 1 SD (between -6.1 and -1.5 SD). In the first year, the height gain was of 0.8 SD with an average GV of 3.9 SD (9.6 cm/year). In the second and third years of treatment the height gain and GV were 0.9 SD and 3.3 SD (8.5 cm/year) respectively 0.4 SD and 2.3 SD (7.4 cm/year). In group 2 the initial growth deficit was -2.7 SD +/- 1.2 SD (between -5.0 and -1.1 SD), with a gain of 0.5 SD in one year. The GV was 2.5 SD – 8.6 cm/year (p=0.02 compared with the 1st group) but dropped to 1.2 SD (6.9 cm/year) in the second year (p=0.05), with a further gain of 0.5 SD in height. Group 3 had a -3.3 +/- 0.7 SD height deficit with a gain of 0.5 SD in the first year and of another 0.4 in the second year. The GV was 2.7 SD – 9.1 cm/year (compared with the group 1 p=0.15) respectively 1.2 SD – 6.8 cm/year (p=0.1). In the 4th group, the initial growth deficit was -3.3 +/- 0.5 SD, with a growth of 0.6 SD in the first year of treatment. The GV was 1.4 SD, (8.5 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 tests were found. He had been admitted to various pediatric hospitals for repeated episodes of severe dehydration with low levels of sodium (Na – 128.8 mEq/L, normal range 136-145) and hyperkalemia (K – 6.1 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 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 ng/mL; LH – 0.87 mUI/mL; FSH – 3.11 mUI/mL; cortisol – 3.92 μg/dL (normal range 4.3-22.4); ACTH – 173 pg/mL (normal range 8-60); 17 OH Progesterone – 533 ng/mL (normal range 8-60); 17 OH Pregesterone – 128.8 mEq/L, normal range 136-145) and hyperkaliemia (K – 6.1 mEq/L, normal range 3.3-5.1). During the first year of treatment. The therapy is safe, but clinical and biochemical follow-up is necessary.

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, Ulrich 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. Methods: For 197 children (136 male/61 female) at the age of 9.2 +/- 7.7 years GH therapy was started with the average daily dose of 0.029 +/- 0.004 mg/kg for the first and of 0.030 +/- 0.005 mg/kg for the second year. Results: Average growth velocity increased from 4.6 +/- 1.9 cm/year to 7.64 cm/year. Growth hormone therapy was ineffective in 10 children, because of low growth velocity (ΔGHV <+0.5cm/year).

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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 ≤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 height 12.5±7.0 months, 9.3±0.9 kg and 76.8±1.1 cm), and 51 children in the vitamin D deficient group (9.9±5.4 months, 9.0±0.9 kg and 75.1±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, and 13 in the deficient group, in whom the mean vitamin 25-hydroxyvitamin D3 level increased from 13.3±5.2 ng/ml (pre-medication), to 34.5±23.8 ng/ml (post-medication).

Conclusions: This study demonstrated that approximately 30% of children aged ≤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.

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: The 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/m2 BMI. On the other hand, 11 patients had a BMI less than 18.5 kg/m2. 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-88**

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

Hae Soon Kim; Hye Jin Lee; Ji Young Oh; Young Sun Hong; Yeon-Ah Sung

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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/m2) adolescent girls (16-18-years) 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 percent 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.

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**PAO-89**

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

Aylin Guven

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**Background:** To assess whether Gonadotrophin-relasing 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±3.13years) with CPP were included in the study: 34 girls with ICPP were followed up 18 months. Complaints had been began before 8 years old. 28 girls underwent GnRH stimulation test. All children were treated with Leuprolide acetat (LA) 3.75 mg/4 wk and the dose was increased only if there is inadequate suppression of LH. The dose had to be increased 7.5 mg/4wk in 11 patients. Bone 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.

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<th>Bone age, year</th>
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<th>Right ovary volume, mL</th>
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<td>Left ovary volume, mL</td>
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<td>Uterine length, cm</td>
<td>40.4±6.8</td>
</tr>
<tr>
<td>Basal LH, mIU/mL</td>
<td>2.18±1.8</td>
</tr>
<tr>
<td>Basal FSH, mIU/mL</td>
<td>4.31±2.2</td>
</tr>
<tr>
<td>Basal Estradiol, pg/mL</td>
<td>29.6±22</td>
</tr>
</tbody>
</table>

**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 positively correlated with BMI at 3rd, 6th, 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 3rd, 6th, 12th and 18th months of therapy (F:69.808, p<0.0001). BMI gradually increased after 6 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:0.366;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.

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**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 marsh 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 disagree.

**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 12.5 years 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) compared 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.

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50th Annual Meeting of the ESPE
### PAO-91

**Comparison of antithyroid antibodies in type 1 diabetic children and control group in 2010**

Fatemeh Saffari1; Ali Asgari2; Tahereh Sadeghi1; Neda Esmailzadeh1

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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 Valis.

**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 statistically significant (p=0.029).

**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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Centro Hospitalar do Porto, Paediatrics Department - Paediatric Endocrinology Unit, Oporto, Portugal

**Background:** MODY is a genetically heterogeneous form of diabetes (DM) characterised by early onset, autosomal dominant inheritance and a primary defect in pancreatic β-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.

**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.

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<tr>
<td>Age of detection of diabetes (years)</td>
<td>5</td>
<td>5</td>
<td>8</td>
<td>8</td>
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<tr>
<td>Family history of type 2 diabetes mellitus and/or hyperglycaemia</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Body mass index (Kg/m²)</td>
<td>12.6 (3)</td>
<td>19.4 (85)</td>
<td>15.8 (40)</td>
<td>24.1 (90.5)</td>
<td>14.2 (11)</td>
</tr>
<tr>
<td>Fasting glucose &gt;126 mg/dl</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Initial HbA1c (%)</td>
<td>7.3</td>
<td>6.5</td>
<td>5.3</td>
<td>6.1</td>
<td>5.9</td>
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<tr>
<td>Serum insulin (µU/ml)</td>
<td>&lt;2</td>
<td>9.4</td>
<td>&lt;2</td>
<td>8</td>
<td>6.6</td>
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<tr>
<td>Serum C peptide (ng/ml)</td>
<td>0.9</td>
<td>0</td>
<td>1.2</td>
<td>1.1</td>
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<tr>
<td>Antibodies: anti-ICA, anti-GAD</td>
<td>negative, negative</td>
<td>negative, negative</td>
<td>positive, negative</td>
<td>negative, negative</td>
<td>negative, negative</td>
</tr>
<tr>
<td>Glucose at 0h and 2h in oral glucose tolerance test (mg/dl)</td>
<td>0</td>
<td>116, 157</td>
<td>130, 189</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Genetic testing (GCK)</td>
<td>mutation c.579 +1_579 +33del33 in exon 5</td>
<td>mutation c.579 +1_579 +33del33 in exon 5</td>
<td>mutation e616A&gt;C in exon 6 (not previously described)</td>
<td>mutation c.1268T&gt;A in exon 10 (not previously described)</td>
<td>mutation c.616A&gt;C in exon 6 (not previously described)</td>
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<tr>
<td>Age at genetic diagnosis (years)</td>
<td>7</td>
<td>11</td>
<td>12</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>Treatment</td>
<td>diet measures</td>
<td>diet measures</td>
<td>diet measures</td>
<td>metformin before MODY2 diagnosis, diet measures</td>
<td>diet measures</td>
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<tr>
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<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>
Background: Puerperal gynecomastia is a frequent reason for consultation in pediatric endocrinology. Although it is usually idiopathic, hypergonadism, hyperprolactinaemia, hyperthyreotoxicity and rare testicular or adrenal tumors must be considered. Most often, idiopathic puerperal gynecomastia regresses at the end of puberty when the testosterone (T) level increases.

Objective and hypotheses: We report a case of persistent puerperal gynecomastia revealing a mutation of steroid 17α-hydroxylase (CYP17).

Methods: This 15-year-old boy was referred to our pediatric endocrinology clinic because of bilateral gynecomastia, stage III with pigmentated and developed areolae. Puerperal development was P3G3 with a normal penis (length = 7 cm). Basal LH and FSH were 7.5 mIU/ml (N = 1.3-8.5 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 µIU/ml (N = 500). Plasma TSH and T4L levels confirmed euthyroid status. Plasma βCG and αFP were negative. Testicular sonography found normal puerperal 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 (154.6–212.3 µmol/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 an heterozygote composite mutation: p.Pro35Thr and p.Arg239X. Substitution by testosterone enanthate was introduced.

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

POA-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 percentile). Head circumference of this patient was 49 cm (50-75 percentile). 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.
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 disorders.

Objective and hypotheses: To explore the endocrine disorders in Chinese children with TS.

Methods: 62 patients with TS diagnosed in our clinic from 1999-2010 by karyotype, FSH, LH, growth hormone stimulation, IGF1, TSH, FT3, FT4, fasting glucose (GS), A1c (if GS high), ultrasound (varian, uterus and thyroid), bone age, pituitary MRI (if growth hormone deficiency). Results: Chronicol mean age: 10.9(0.2-18.7) years, mean height z score (HSDS): -3.96 (0.04-7.7), >13.5 years no puberty signs (15/17, 88.2%). Distribution of karyotypes: X monosomy-45,X (27/62, 43.6%); 45,X/46,XX (10/62, 16.1%); 46,X,del(X)(q22)(3/62, 4.8%), Hashimoto thyroiditis (15/40, 37.5%), growth hormone deficiency (31/55, 56.4%), Diabetes (2/62, 4.8%); thyroid dysfunction, diabetes, which require treat early.

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.
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.

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PAO-104

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

Maria Claudia Schnitt-Lobe; Raissa Rodrigues Weber; Thaisa Silva Gios

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 < 1 cm/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. They 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 Tiroiditis was considered with positives 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 antidiomysium 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.

Conclusions: The findings and comparison of the over all and the comparison of the two groups of patients. We separated and compared two groups of patients; Group A: HSDS-FH minus HSDS-TH zero [-0.37 [-1.9 - 0.01]]; and, Group B: HSDS-FH minus HSDS-EA ≥ zero (0.54 [0.05 - 0.95]), p<0.01 (Mann-Whitney).

In Table 02 are show 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-TH zero [-0.37 [-1.9 - 0.01]]; and, Group B: HSDS-FH minus HSDS-EA ≥ zero (0.54 [0.05 - 0.95]), p<0.01 (Mann-Whitney).
PAO-105

Growth hormone excess in two children with neurofibromatosis type 1 and optic pathway glioma
Patrizia Bruzzi; Assunta Albanese
Royal Marsden Foundation Trust, Paediatric Endocrine Unit, Sutton, United Kingdom

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 age of 7.5 years she also received LRHHa 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 LRHHa 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 NF1 and OPG.

Second case. A tall 7.3 years old girl with NF1 and OPG treated with chemotheraphy was referred for precocious puberty. CPP was confirmed and treated with LRHHa. 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±2.8 years, with a T1DM duration of 8.4±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. Insulin treatment consisted of four daily injections in all of the patients. 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 diabetes 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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1Markusovszky Teaching Hospital, Department of Pediatrics, Szombathy, Hungary; 2Markusovszky Teaching Hospital, 1st Department of Internal Medicine, Szombathy, Hungary; 3University of West Hungary - Savaria Campus, Institute for Health Promotion, Szombathy, Hungary; 4Semmelweis University, 1st Department of Pediatrics, Budapest, Hungary; 5Semmelweis University, 2nd Department of Internal Medicine, Budapest, Hungary; 4National Institute of Neurosurgery, Department of Neurosurgery, Budapest, Hungary

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. Perforning the corticotrophin-releasing hormone (CRH) test, increased cortisol response confirmed the diagnosis of CD. Gonadotropin levels were subnormal suggesting a suppressive effect of chronic hypercortisolism. 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
Yuliya Makaryupa; Julia Boiko
State Center of Medical Rehabilitation, Pediatric Department, Endocrinology Group, Minsk, Belarus

Background: Noonan syndrome (NS) is a disorder characterized by congenital heart defects, facial dysmorphism, skeletal malformation and short stature. NS is henceforward a safe and effective procedure in children.
stentosis, 3- with atrial septum defect, one at a time - with hypertrophic cardio-myopathy, 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 12and 24 months of treatment.

Results: At 12 and 24 months of treatment mean height SDS elevation was found (A1 height SDS = 0.43 and A2 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 Belorus 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.

Case report: A 5.5 year-old girl admitted to our clinic with mutism caused by coarsening of the voice and unwillingness to speak. 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 vocal 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 (10,5 years), elevated adrenal hormones (17-OH-progesteron:15,5 ng/ml (N:<1,6), testosteron: 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)). Abnormal ultrasonography and CT showed a large (13x11,4 cm) cystic heterogeneus 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.

Growth disorders in Legius syndrome (LS) – a differential diagnosis to neurofibromatosis I (NF1)
Klaus-Peter Ullrich1; Gudrun Wiedemann1; Sebastian Ullrich1; Erico von Bueren2; Allhard Hoffmann2; Sabine Weidensee3
1Helios Clinics Gotha, Clinic for Pediatrics and Youth Medicine, Gotha, Germany; 2Private practice, Pediatrics, Erfurt, Germany; 3Regional government, Continuing Education Emscher Lippe, Dorsten, Germany; 4Thermo Fisher Scientific, Inc., Strategic Marketing, Kalamazoo, United States; 5Research Center for Medical Technology and Biotechnology, Research, Erfurt, Germany; 6Center for Human Genetics, Genetics, Erfurt, Germany

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 cafe-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.

Diabetes related problems and diabetic controls among the school children with type 1 diabetes mellitus living in Istanbul
Eda Sunnetci1; Serap Turan1; Zeynep Atay1; Tulay Gurman1; Abdullah Bereket1
1Marmara University, Pediatric Endocrinology, Istanbul, Turkey

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.

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 parents and the patients.

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 paediatricians (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, 23% were injecting at classroom, 15% at home, 11% at playground 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. Glukagon 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.

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 α kinase 3 (eIF2α 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 β 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 determines the variability of the clinical manifestations observed in this syndrome. All patients of WRS explains the high level of expression of EIF2AK3 in both pancreatic β cells and bone tissues.

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 ± 0.31 mIU/ml, 7.77 ± 5.55 pg/ml, respectively) and nonoverweight group (0.4 ± 0.29 mIU/mI, 7.80 ± 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 81.3% 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.

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.

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

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

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.

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

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

Oleg Malievsky1; Dilara Nurmuhametova1; Rushana Basharova2;
1Bashkir State Medical University, Department of Pediatrics, Ufa, Russian Federation; 2Republic Children Hospital, Department of Pediatrics, Ufa, Russian Federation

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, 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.

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

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

Vita Akhmetova1; A. Rakhimkulova1; Oleg Malievsky1;
1Bashkir State Medical University, Department of Pediatrics, Ufa, Russian Federation; 2Republic Children Hospital, Department of Pediatrics, Ufa, Russian Federation

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Delirium in diabetic ketoacidosis

Ayye Nurcan Cebeci, Ayla Guven
Goztepe Educational and Research Hospital, Pediatric Endocrinology, Istanbul, Turkey

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 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.

Case report: A 15-year-old female patient with known type 1 diabetes mellitus of two years duration was referred because of fatigue and symptoms of 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 acidois with administration of fluid and insulin, the patient became delirious. The delirium persisted despite the normalization of acidois 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 acidois.

Delirium in diabetic ketoacidosis

Ayye Nurcan Cebeci, Ayla Guven
Goztepe Educational and Research Hospital, Pediatric Endocrinology, Istanbul, Turkey

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

Objective: to determine the spectrum of diagnostic significant CYP21A2 gene mutations typical for SW and for SV forms in CAH patients.

Materials and methods: We studied CAH chromosomes with the following frequencies: delA2orL-GC (27.6%), R565W (16.02%), L2splice (11.6%), I172N (7.18%), Q318X (4.97%), V281L (2.76%), P30L (1.1%), and P453S (0.5%).

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 delA2orL-GC of the gene CYP21A2 twice more often than patients with SV (37.65% and 19.32%), respectively, p=0.012, mutation R565W - 2.6 times higher (23.53% and 9.09% respectively, p=0.018), mutation L2splice - 2.9 (16.47% and 5.68%, respectively, p=0.043), and mutation Q318X - 8.3 (4.41% and 1.14% respectively, p=0.04, p=0.04).

Conclusion: There is a clear discrepancy between informal aim size and prospective final size, x-ray of the left hand to calculate bone age of the patient was omitted. Because of the clear discrepancy between informal aim size and prospective final size, the patient was transferred to a specified neurosurgery for transspheendoscopic tumor extirpation.

Delirium in diabetic ketoacidosis

Ayye Nurcan Cebeci, Ayla Guven
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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±3.1 years (yrs), follow-up 7.8±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<0.03) 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 onset obesity. 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.

Risk factors for overweight and obesity are: 
- lower height velocity (HV) in first 3 yrs of follow-up
- increasing age
- BMI SD > 2.5

Conclusions: Obesity is rare in our ALL survivors. CR is a risk factor for late onset obesity. HOMA should be evaluated in ALL survivors regardless BMI SD, in particular in pts who underwent TBI.

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A 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 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±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.

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A case of osteopetrosis tarda in childhood presenting with polyarthralgia and rickets

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Dokuz Eylul University, Department of Pediatric Endocrinology, Izmir, Turkey

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 metacarps 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 and HOMA was abnormal as well her fathers’ broken fingers and metacarps after a minor trauma. Radiographic examination revealed findings of generalized osteosclerosis, sandwich vertebra and bone density > 2.5 in adults and children, <4 in adolescents.

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
Anna Wędkowicz1; Agata Zygmunt-Górka2; Joanna Wojtysiak; Marta Ciechanow ska1; Aleksandra Krassowska-Kwiecien2; Jerzy Starzyk
1Polish-American Children's Hospital, Medical College, Jagiellonian University, Department of Pediatric and Adolescent Endocrinology, Department of Transplantation, Cracow, Poland; 2University Children's Hospital, Pediatric and Adolescent Endocrinology, Cracow, Poland

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 carbohydrate 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
Federico Baronio; Laura Battisti; Giorgio Radetti
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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 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. IT3 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
Oziem Korkmaz1; Damla Gokser1; Gulgun Yenen; Afg Berdel1; Sukran Darcan1
1Ege University, Faculty of Medicine, Pediatric Endocrinology, Izmir, Turkey; 2Ege University, Department of Pediatrics, Izmir, Turkey

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 (5-23 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 forNR3C2, SCNN1B,SCNN1G and a heterozygous genetic variant in SCNN1A 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.

Conclusions: Our 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 calcitomin (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 hypercalcaemia, 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 (post-BMT 45 days), her calcium level below 11 mg/dL with weekly pamidronate, daily calcitonin and daily methylprednisolone with tapering dose.

Conclusions: In conclusion, hypercalcaemia is common in patients with osteopetrosis 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 hypercalcaemia.

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 hematopoietic-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 15.8±11.9 ng/ml. Eighteen patients (11.8%) were vitamin D deficient (<15 ng/ml), and another 87 (80.3%) were vitamin D insufficient (11-32 ng/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 hematopoietic-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 12.9±2.1, 97% of 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 (IS) 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 IS (p=0.02). Mean ADSoS Z-score was -1.07±1.1 (males -1.19±1.25 vs females -0.92±0.9, p=0.036) 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 LRPS, 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 urmanian girl with OPPG, confirmed by the identification of a mutation in exon 11 of the LRPS gene (c.2409_G_2503→79delT174), 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 fracturecalluses. 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/cm2 (~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±0.9 vs -0.13±1.53; p=0.009). 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±13.7 vs 72.77±13.6; p=0.001). No differences were found for lipid parameters and mean systolic and diastolic blood pressures between the two groups. Fasting insulin levels (12.0±7.6 vs 5.1±5.08; p=0.003) and HOMA index (2±1.34 vs 0.98±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=0.4, 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 SULFONYLURES IN NEONATAL DIABETES MELLITUS PATIENTS
Ngoc Can1; Chi Dung Vu1; Phuong Thao Bui1; Ngoc Khanh Nguyen1; Maria Craig2; Sian Ellard3; Hoan Nguyen1
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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* 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 sulfonylurea therapy replacing insulin injection.

Methods: Case study: 5 patients suffer NDM at 45, 35, 47, 36, 44 days of age, respectively with ABC8 or KCNJ11 mutations are treated in National Hospital of Pediatrics of Vietnam.

Results: 2 patients has heterozygous for a missence mutation on KCNJ11: R201H (p.Arg201His) & R201C (p.Arg201Cys); 3 patients with ABCC8 mutation having registered in one (5.6%). In this group thyroid status parameters were as follows, TSH: 0.77 ± 0.24 mIU/l; T3: 2.59 ± 0.1 nmol/l and T4: 148.8 ± 7.95 nmol/l, p<0.05. No differences of TSH were found between 2 groups. T3 and T4 were significantly higher in patients than in controls (82.9±13.7 vs 72.77±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±7.6 vs 5.1±5.08; p=0.003) and HOMA index (2±1.34 vs 0.98±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=0.4, 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.

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. Heterozygosis 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 Resonans 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.
**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 deoxycortico-sterone level and absence of water retention, hypertension or hypokalemia discerned us from thought of 17-hydroxylase deficiency. The carotype was 46 XY, testicles 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 testes tissue with focal dysraphic formations 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 week of gestation). 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-135**

**Registry of congenital adrenal hyperplasia in Vietnam**

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1) National Hospital of Pediatrics in Hanoi, Endocrinology, Metabolism and Genetics, Hanoi, Vietnam; 2) National Hospital of Pediatrics in Hanoi, Surgery, Hanoi, Vietnam; 3) CLAN (Caring & Living As Neighbours), Sydney, Australia; 4) The Children’s Hospital at Westmead, Endocrinology and Diabetes, Sydney, Australia; 5) Royal Children’s Hospital, Endocrinology and Diabetes, Melbourne, Australia

**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/L; 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 fat distribution (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 Latin 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.

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**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 (DM 1) 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 complications (Hypo, DKA2, DKA3), 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 (%).

<table>
<thead>
<tr>
<th>Years</th>
<th>DKA 2-3</th>
<th>Hypo</th>
<th>HbA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>6.04</td>
<td>0.45</td>
<td>8.9±1.52</td>
</tr>
<tr>
<td>2008</td>
<td>9.23</td>
<td>0.43</td>
<td>8.8±1.45</td>
</tr>
<tr>
<td>2009</td>
<td>11.39</td>
<td>0.57</td>
<td>8.9±1.44</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Age</th>
<th>DKA 2-3</th>
<th>Hypo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5 y.o.</td>
<td>9.83</td>
<td>17.32</td>
</tr>
<tr>
<td>6-10 y.o.</td>
<td>5.32</td>
<td>9.24</td>
</tr>
<tr>
<td>11-14 y.o.</td>
<td>5.82</td>
<td>8.98</td>
</tr>
<tr>
<td>15-17 y.o.</td>
<td>5.94</td>
<td>7.90</td>
</tr>
<tr>
<td>Total</td>
<td>6.04</td>
<td>9.23</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Years</th>
<th>DK</th>
<th>DR</th>
<th>DN</th>
<th>DA</th>
<th>DNP</th>
<th>DL</th>
<th>DS</th>
<th>CWC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>0.94</td>
<td>7.56</td>
<td>10.69</td>
<td>15.42</td>
<td>18.67</td>
<td>3.01</td>
<td>7.59</td>
<td>11.49</td>
</tr>
<tr>
<td>2008</td>
<td>1.92</td>
<td>8.52</td>
<td>11.43</td>
<td>19.14</td>
<td>19.31</td>
<td>7.29</td>
<td>8.55</td>
<td>16.12</td>
</tr>
<tr>
<td>2009</td>
<td>2.01</td>
<td>8.92</td>
<td>12.95</td>
<td>19.04</td>
<td>20.46</td>
<td>8.26</td>
<td>8.30</td>
<td>14.75</td>
</tr>
</tbody>
</table>

**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.

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**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.

**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.

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**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 10.46/100000). There was an overall increase in incidence between the two decades, to analyse gender differences in the age of onset and any seasonal variation at the manifestation of the disease.

**Conclusions:** The overall mean annual incidence of T1DM during this 20 year period is 12.46/100000.
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. **Conclusion:** 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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CHU Rennes, Paediatric department, Rennes, France

**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,XXX; 47,XXXX). 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 A2P2S1 with important adipomastity 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 ophthalmoplegic migraine was diagnosed.

**Results:** Five years later a second MRI showed a 0.7x0.4cm pituitary lesion. Five years later a second MRI showed a 0.7x0.4cm pituitary lesion. 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 mislead by puberty during the investigation.

**PAO-143**

**Comparison of injection dose force between three growth hormone injection pens:**

NordiFlex®, FlexPro® and GoQuick®

Anne-Marie Kangel Andersen; Marianne Fye Hansen; Niels Aage Hansen


**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, L.Rx plus (ID: 24K-04-115) and transducer (measuring cell) of max 100 N (ID: MST7813) 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-145**

**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) < 4.5). An androgen excess 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 in 18yr and puberty is complete with regular menses. Laboratory determinations regarding pituitary function remain normal except for the IGF-I (consistently around +5 SDS). 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 mislead by puberty during the investigation.
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 (<0.5 nmol/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 hypothalamic/hypophysial pathos 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 to 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 hypothalamic 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: CASE 1: Nine years old boy presented with frontoparietal headaches, loss of vision, no hypertension, no obesity or evidence of hypothalamic-hypophysial dysfunction. Neuroimaging revealed a mass in the sellar region. A transsphenoidal surgery was performed and histopathologic diagnosis was silent corticotrope adenoma. The patient was treated with transdermal testosterone. CASE 2: 19 yr-old male who had first presented at 4 years of age with headaches and visual disturbances. He had his first episode of Cushing syndrome Laboratory: 8 am cortisol 4.2 µg/dl, TSH 2 mUI/ml prolactin 25.9 ng/ml MRI showed sellar mass of 3.7x3.2x2.4 mm. Treatment: Surgery, Pathology revealed a ACTH producing adenoma Pituitary Ki67 15%. Case 2 A fourteen years old girl had a cranoopharyngioma 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 15 x 19 mm MRI. Surgical pathology revealed an ACTH producing adenoma. Pituitary Ki67 1%. Post surgery ACTH 13.4 pg/ml cortisol 7µg/dl prolactina 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 diagnosis 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 treatment 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; 78/81 (96.8%) 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 18/81 (22.4%), 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 ATE. Totally, 46/81 (56.8%) pts had hypothryoidism. 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±9.9 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 AHSDS 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 39/1.4 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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2S.Orsola-Malpighi Hospital, Pediatrics, Bologna, Italy

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 DR3, 4 and DQ2, 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 (transglutaminase 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 anaemia, 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 dis-tension 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 through bowel have not been adequately investigated and lamination during brain development. Although hypothyroidism can present with functional intestinal obstruction and abdominal distress 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.

Methods: A 21 days baby girl, product of consanguineous marriage presented

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with vomiting and abdominal distension. Weight was 2.5 kg and length 48 cm. On examination, there was facial puffiness, open posterior fontanelle, dry skin, cold peripheries and prominent abdominal veins with visible peri-stasis. 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 µIU/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.
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: Craniohypopangioma 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 cerebi and diabetes insipidus. Association or coincidence?

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Vita Salute San Raffaele University, Pediatric Endocrine Unit, Milano, Italy

Background: Pseudotumor cerebi (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-year-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 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 electrolyte 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.

Methods: 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/m2. 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/m2. 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®

Judith Ross1; Peter Lee2; Robert Guth3; John Germak3

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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® (somatropin 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 AHSDS by age, gender, and pubertal status in children treated with GH.

Methods: Treatment-naive 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 AHSDS than girls after 3 years or longer treatment duration (p<0.001). When stratified by baseline age, younger patients showed greater AHSDS than older patients for both genders (Table). In addition, children with GHD who remained pre-pubertal after 5 years of treatment had the greatest AHSDS (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) AHSDS over 5 years by Age and Gender.

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<th>All Males</th>
<th>All Females</th>
<th>All</th>
<th>Female</th>
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<td>Ages &lt; 11 yrs</td>
<td>Ages &gt; 11 yrs</td>
<td>Female N</td>
<td>Ages &lt; 16 yrs</td>
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PAO-154
Role of prophylactic medical examination for early diagnosis of endocrine disorders
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Background: Considerable increasement 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 schoolchildren.

Methods: All children were splitted 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 mesuraments 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 diagnost. 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 predominated 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 predomination 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 prophylactice medical examination.

PAO-155
Rett syndrome associated with thyroid hypoplasia – a synergic association for neurological disturbances: case report
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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 stereotypes, and seizures. The patients neonatal and perinatal history were normal (BW 3100g, BH 50cm). She could play with toys with 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.

Conclusions: 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 prophylactice medical examination.

PAO-156
Central hypothyroidism secondary to maternal hyperthyroidism
Pilar Sevilla-Ramos¹; Maria Alija²; Esther Cid³; Nerea Lopez-Andres⁴; José María Jimenez-Busto⁵
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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 asymptomatific 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 bpm 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), macrogliosis. TSH 0.02 mU/L, T4L 1.31 ng/dl, T3 1.05 ng/dl, antithyroglobulin 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 T4 belongs to overweight and obesity (61% of revealed endocrinological disorders). 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 sexual development abnormalities with predomination at the age of 11-17 years.

PAO-157
Congenital chloride diarrhea with congenital hypothyroidism in two siblings: case report
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Background: Congenital chloride diarrhea (CCD) is a rare autosomal recessively inherited disorder causing watery stool and dehydration characterized by impairment of Cl⁻/HCO₃⁻ exchange.

Objective: Infrequency of CCD makes diagnostics difficult and CCD compa- nying 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 intratrheal polyhydramniosis; he was diagnosed as Bartter syndrome and indomethacin treatment was started. But all the medi- cations 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 di- agnoses of congenital hypothyroidism and Bartter syndrome.

Results: We figured out CCD in our investigation of these two siblings that

The age; small thyroid volume 1 ml (more then -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 synergistic mechanism of synaptic damage and neuronal metabolism. 3. Are necessary more sofisticate genetic analysis to solve the link between hypothyroidism and Rett syndrome.
feecal 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 literature because of the first reported cases of CCD accompanying 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/m², ± 3.53 SD). She had a tall disproportional stature (183 cm, ± 3.5 SD), only internal 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 gonadotropin 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. IGF1 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), i.sh (STS++, DXZ+, SRY). Bone age corresponded to calendar age. Ultrasound visualized a hypoplasic 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 pseudautosomal 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**

*Daniel Wikowski; Eziibia Piontek; Mieczyslaw Szalecki*

The Children’s Memorial Health Institute, Department of Endocrinology and Diabetology, Warsaw, Poland.

**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:

### PAO-160

Abstract withdrawn.

### PAO-161

**The evaluation of body composition and metabolic parameters in girls with central precocious puberty receiving GnRH agonist therapy**

*Dogus Vural1; Huseyin Demirkilek1; Didem Aydogdu2; Nazli Gonc1; Ayfer Alkaasluglu1; Alevo Ozon1; Nurgun Kandemir1*

1 Hacettepe University, Pediatric Endocrinology, Ankara, Turkey; 2 Hacettepe University, Pediatrics, Ankara, Turkey.

**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 OGGT 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.

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**Abstract withdrawn.**
Re-evaluation of metabolic parameters of obese children after 5-7 years
Gulay Demirdag1; Sibel Tulgar Kinik2; Ayse Canan Yaziç1
1'Baskent University, Pediatrics, Ankara, Turkey; 2'Baskent University, Pediatric Endocrinology, Ankara, Turkey; 3'Baskent University, Biostatistics, Ankara, Turkey

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: none

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 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.

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.

Autoantibody positivity and 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 groups. 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.
Results: FISH study confirmed the supernumerary marker chromosome is originated from the 14 or 22 chromosome and includes two copies of the autosomal p-arms; 47,XXY+mar ish idic(14;22). Array comparative genomic hybridization were performed with arr ehC 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 + 1T, Gln> stop gene mutation in factor IX gene and missense mutation of 4th exon of LDL receptor with genotype LDLR-C188 (C>V).

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, microcephaly, no hypoplasias, 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, 0.7ng/dl, and 115ng/dl respectively. As beta-CTG 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 (19.5µu/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 deficient 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: 3 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 ultrasound showed a cystic nodule of 19 x 14 x 13 mm with heterogeneous vascularized polypoid mass of irregular limits in the right lobe. The rest of the gland was normal.99mTc 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. 9.24ug/dl (6-14) free T4: 1.44 ng/dl (0.8-2.2) T3: 178 ng/dl (80-220) TSH 4.42 mUI/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 microopenis, choree, penoscrotal hypoplasia 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 invesitgation 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.

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**PAO-170**

**The difficulties of investigating and treating an endocrine patient in resource limited countries**

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Muhumbili National Hospital, Paediatric and Child Health, Dar es Salaam, Tanzania

**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 (e.g., Cushings 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, trunc obesity, hirsutism, pubarche and was hypertensive (117/67mmHg). Morning cortisol levels were increased. Adenobdominal US showed an adrenal adenoma. Computed tomography showed a mass in the right adrenal tumor. Was put on ketoconazole tablets later on was operated and the capsulated tumor was removed, currently awaiting the biopsy results.

**Conclusion:** No diagnosis has been confirmed todate, most of the investigative work is still ongoing.

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**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 the department with a diagnostical history in the context of the diagnosis of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. He was under glucocorticoid treatment in high doses administrated in acute crisis because of recurrent hypogenitalism, and the capsulated tumor was removed, currently awaiting the biopsy results.

**Results:** From history we found that he frequently present hypotension, hypoglycemia, nausea and vomiting crisis, reported to be refractory to cortisone treatment.

**Discussion:** On September 2008 he was given growth hormone (GH) 0.03 u/kg/day, patient height was 92.8 cm. +2.5 SD, height velocity 6.048 cm/year. On February height is 92.8 cm. +2.5 SD, height velocity 6.048 cm/year.

**Conclusion:** Patients with congenital adrenal hyperplasia with GH resistance may benefit from GH at a dose range from 0.09a/kg/day to 0.12a/kg/day to maintain an appropriate height velocity.

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**PAO-172**

**Achondroplasia in a girl with G 1138 A mutation, response to growth hormone therapy, two and half years follow up**

Sameh Tawfeik; Mona Alfar; Heba Hassan; Solal Mohamed

1; Maadi, Pediatrics, Cairo, Egypt; 2; Cairo University, Pediatrics, Cairo, Egypt; 3; Ain Shams, Pediatrics, Cairo, Egypt; 4; Ain Shams, Genetics, Cairo, Egypt

**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 53 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 (FGFR3) gene.

**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.

**Conclusion:** 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 0.09a/kg/day to 0.12a/kg/day to maintain an appropriate height velocity.
In our study GnRHa treatment did not allow reaching TH but
Conclusions:

Background: GnRH analogues have been used for treatment of precocious
growth for almost 30 years. However, it is still discussed whether this treat-
ment is optionally delayed growth of the final height in 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 100μg/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: GnRHa 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).

Conclusions: In our study GnRHa 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-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 improves 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 100μg/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. Group 2 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: GnRHa 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).

Conclusions: In our study GnRHa 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-176**
Retrospective study of 215 patients admitted in a pediatric intensive care unit for diabetic ketoacidosis between 1998 and 2008
Frederique Tixier1; Aline Guevart1; Cecilia Heng Yong1; Jean Claude Berthier2; Philippe Klee3; Frederic Valla4; Marc Nicolino4
1Hopital Femme Mère Enfant, Division of Pediatric Endocrinology, Lyon Bron, France; 2Hospital Femme Mère Enfant, Pediatric Intensive Care Unit, Lyon Bron, France

Objective and hypotheses: To investigate the relationships of physical activity (PA) and sedentary behaviours (television 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±1.2 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 “abnormally 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-175**
Physical activity and sedentary behaviours among obese prepubertal children
Sonya Galcheva1; Violeta Iotova2; Mina Lateva2; Yoto Yotov2
1Varna Medical University, Department of Pediatrics, Varna, Bulgaria; 2Varna Medical University, Department of Internal Medicine, Varna, Bulgaria

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 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±1.2 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 “abnormally 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.
Follow-up of girls with complete androgen insensitivity syndrome (CAIS) and gonads in situ during and after puberty – two case reports

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 MT4/5 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 clinic 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 had shown no 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 unsuspicuous 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.

Final height after treatment for acute lymphoblastic leukemia

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 form 1972 to 2001 who reached final height. The median age at diagnosis was 5 years (range 0-14), 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.

Secondary transient pseudohypoaldosteronism – a report of two cases

Background: Secondary pseudohypoaldosteronism (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 mmo/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-OHFP 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, aldosteron 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.

Invasive pituitary adenoma secreting growth hormone, TSH, prolactin and α-subunit in a 12-year-old girl

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. Ophtalmological 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 α-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 pe.
and dehydration. She has been referred for persistent hyponatremia and sub-

Introduction:

Background: Intracranial germinoma is a rare malignant tumor, only consti-

Objective: We present a patient with coincidence of germinoma and lympho-

development of Cushing disease, only one described in children. The patient was 5-6 years old, with no history of endocrine disease. A careful physical examination revealed central obesity, hirsutism, plethora, hypertension, weight gain, growth arrest and symptoms of premature adrenarche. Clinical examination revealed paleness, vital findings were normal. Dehydration

Conclusions: The diagnosis of central diabetes insipidus with thickened pituitary lobe and 5 mm pineal cyst. During 2,5-year observation growth velocity decreased to 3,5 cm/year. Stimilation tests confirmed growth hormone defi-

Result: StAR protein deficiency is the most severe and rare form of steroid biosynthesis disorder. 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. Cate
tory analysis and advanced investigations if needed should be performed.

PAO-182

Introduction: Lipoid congenital adrenal hyperplasia is an autosomal reces-
sive disease due to deficiency of StAR protein that transports cholesterol into the mitochondria for adrenal steroid synthesis. StAR is also essential for the

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 sub-
sequently 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 hypoglycematation 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/l , K: 6.4 mEq/l, 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. Cate
tory type was 46 XY, t(4;9)(p16.6;p13.3) and a paternal translocation was determined.

Laparoscopic investigation showed intra-abdominal located testes, any Mul-

cularian structure was not found. There was no increase in testosterone during three days of stimulation with hCG 1500 U/dose and gonadectomy was per-
formed. She is still receiving hydrocortisone (14mg/m2/day) and fludrocorti-
sone (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. Cate
tory analysis and advanced investigations if needed should be performed.

PAO-183

A rare case of early onset of Cushing disease

Background: Cushing disease is the most common cause of hypercortisola-

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-

cal examination revealed central obesity, hirsutism, plethora, hypertension, psychological disturbances, puberty stage: A2, P2, testes 3 ml. Laboratory findings showed hypercortisolaemia (54,3 µg/dl in the morning, 39,2 µg/dl at midnight), hyperandrogenaemia, high level of ACTH (162, 375 pg/ml). CRH stimulation and Dexamethasone suppression tests were performed, confir-
mingle 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 eno-
lase and chromogranin A were normal. Inferior petrolas 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 hy-
percortisolaemia, on the basis of the results of hormonal tests, a neurosurgi-
cal treatment was planned. The patient started pharmacological therapy with
ketocanazole and hydrocortisone replacement as a preparation for the neuro-
surgical procedure. Transphenoideal pituitary exploration showed a microad-

doma and adenosyn 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)
Sandra Barth; Stefan A. Wudy
Justus Liebig University, Division of Paediatric Endocrinology and Diabetology, Center of Child and Adolescent Medicine, Giessen, Germany

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 <5µg/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 (15 males, 2 females, mean age 5.71 yr) 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.

<table>
<thead>
<tr>
<th>Age in yr (delay in %)</th>
<th>Chronological age Mean in yr</th>
<th>PH Mean in yr (delay in %)</th>
<th>MC Mean in yr (delay in %)</th>
<th>CP Mean in yr (delay in %)</th>
<th>RU Mean in yr (delay in %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with CDG</td>
<td>10.2</td>
<td>8.1 (21%)</td>
<td>7.4 (27%)</td>
<td>8.2 (20%)</td>
<td>8.5 (17%)</td>
</tr>
<tr>
<td>Patients with GHD</td>
<td>5.7</td>
<td>4.8 (16%)</td>
<td>4.4 (23%)</td>
<td>3.5 (39%)</td>
<td>4.0 (29%)</td>
</tr>
</tbody>
</table>

PAO-185

Abstract withdrawn.

PAO-186

Transsexualism in an African setting; case report
Olumide Jarrett1; Oluymori Esan2; Omolola Ayoola2
1University College Hospital, Paediatrics, Ibadan, Nigeria; 2Royal Manchester Children’s Hospital, Endocrine Science Research Group, Manchester, United Kingdom

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 inappropriate 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 I for breast and a well developed normal male external genitalia with a solitary right testis. Hormonal profile revealed normal testosterone (31.2nmol/L, normal values 15 – 40nmol/l) and low estradiol levels (0.0nmol/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-year-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 hyperphosphatemia. Serum parathormone level was found high (512 pg/ml N:4.5-36). Parathyroid scintigraphy suggested parathyroid adenoma. Parathyroidectomy was performed and the diagnosis of parathyroid adenoma was confirmed histopathologically. The family history was negative for multiple endocrine neoplasim 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 tendinopathies.

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
Minyong Zhan1; Feihong Luo2; Shuxian Shen3; Hong Xia4; Yuechen Tu5; Fengxia Guo1; Tingting Huang1; Dijing Zh1; Zhuhui Zhao1; Rong Ye1; Ruqiang Cheng1; Xiaojing Li1
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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), 0.57-2.55cm (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:X2 = 139.73, p<0.01; 2008:X2 = 289.2)

Printed Abstracts Only
Population: We report 3 cases of ovotestis DSD from Mauritania, raised as males. They have different degrees of penile curvature and microprosopon, proximal hipoplasia, bifid scrotum or unilateral or bilateral cryptorchidism. In 2 of them a gonad was palpable. No uterus was found. 170H-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).

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penis (cm)</td>
<td>2.9</td>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>Palpable gonad</td>
<td>Right</td>
<td>Left</td>
<td>No</td>
</tr>
<tr>
<td>Right gonad</td>
<td>Ovotestis</td>
<td>Ovotestis</td>
<td>Ovary</td>
</tr>
<tr>
<td>Left gonad</td>
<td>Ovary</td>
<td>Ovotestis</td>
<td>Ovotestis</td>
</tr>
</tbody>
</table>

Penil curvature correction was performed with penoscrotal transposition and testis/ovotestis orchidopexy, with removal of ovary and internal female genitalia (Case 1). Subsequently, stage-two 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-192

Generalised arterial calcification of infancy - a novel mutation of the ENPP-1 gene
Vishal Mehta1; Sanjay Gupta1; Rupal Patel1; David Horton1; Eamonn Sheridan1; Frank Ruth2
1Hull Royal Infirmary, Paediatrics, Hull, United Kingdom; 2St James’ University Hospital, Department of Clinical Genetics, Leeds, United Kingdom; Munster University Children’s Hospital, Paediatrics, Munster, Germany

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 to 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 idopathic 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. A64AfsX11) 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. Rare 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.

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-193

Gonad function in patients with classic galactosemia
Milva Orquidea Bal; Sara Monti; Ilaria Bettocchi; Federico Baronio; Alessandra Castici; Alessandro Cicognani
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Background: Classic galactosemia is an inherited inborn error of the major galactose assimilation pathway, caused by gactose 1-phosphate uridyltransferase (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 galactitol.

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, genotopically 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.

Conclusions: 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; 1 M) 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 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 abnormalities 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 (GnRHa). 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 advanced with respect to 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.

<table>
<thead>
<tr>
<th>BA/CA</th>
<th>advanced</th>
<th>normal</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>age before GnRHa [years]</td>
<td>7.4±2.2</td>
<td>9.3±1.7</td>
<td>0.001</td>
</tr>
<tr>
<td>hSDS before GnRHa</td>
<td>1.84±1.14</td>
<td>0.87±1.22</td>
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<tr>
<td>PAH SDS before GnRHa</td>
<td>-0.95±1.35</td>
<td>0.14±1.18</td>
<td>0.005</td>
</tr>
<tr>
<td>therapy duration [years]</td>
<td>3.7±2.2</td>
<td>2.8±1.90</td>
<td>0.066</td>
</tr>
<tr>
<td>hSDS after GnRHa</td>
<td>1.02±1.34</td>
<td>0.48±1.21</td>
<td>0.156</td>
</tr>
<tr>
<td>PAH SDS after GnRHa</td>
<td>-0.42±1.15</td>
<td>-0.31±1.23</td>
<td>0.806</td>
</tr>
<tr>
<td>ΔPAH SDS</td>
<td>0.53±0.99</td>
<td>-0.44±0.86</td>
<td>0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BA/HA</th>
<th>advanced</th>
<th>normal</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>age before GnRHa [years]</td>
<td>7.8±2.5</td>
<td>8.7±1.6</td>
<td>0.265</td>
</tr>
<tr>
<td>hSDS before GnRHa</td>
<td>0.97±1.15</td>
<td>2.03±1.16</td>
<td>0.001</td>
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<tr>
<td>PAH SDS before GnRHa</td>
<td>-1.40±0.93</td>
<td>0.60±0.97</td>
<td>0.001</td>
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<tr>
<td>therapy duration [years]</td>
<td>3.7±2.3</td>
<td>2.8±1.7</td>
<td>0.094</td>
</tr>
<tr>
<td>hSDS after GnRHa</td>
<td>0.32±1.17</td>
<td>1.41±1.23</td>
<td>0.001</td>
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<tr>
<td>PAH SDS after GnRHa</td>
<td>-0.96±0.93</td>
<td>0.31±1.05</td>
<td>0.001</td>
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<tr>
<td>ΔPAH SDS</td>
<td>0.42±0.94</td>
<td>-0.28±1.05</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Conclusions: The therapy with GnRHa proved to be effective in improving height prognosis only in children with advanced BA.

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 pursued 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 al 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.

Conclusions: The therapy with GnRHa proved to be effective in improving height prognosis only in children with advanced BA.
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 TIDM).

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 13.3y 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, adiposi, diabetes mellitus (DM), hyperlipidemia, growth hormone deficiency (GHD), hashimoto thyroiditis, epilepsy. Case 2, A 16.5y female patient, karyotype was 45,NO, height 134cm (−4.76SD), weight 40.5kg, short neck, micrognathia, 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: 14y, Ultrasound: small uterus and ovaries could not be detected, fatty Liver; MRI: pituitary gland dysplasia, partial empty sella turcica. She also suffered epilepsy since 6 months-old. Diagnosis: TS, MS, adiposi, diabetes mellitus (DM), hyperlipidemia, GHD.

Conclusions: It appears that β 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 ≥ 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 ± 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 data. 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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1IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Department of Pediatrics, Endocrine Unit, Milan, Italy; 2IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, ENT Department, Milan, Italy

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 snorinopathy 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, hemorraghes, respiratory complications requiring reintubation and/or supplemental oxygen administration.

Material and methods: Eighty-one children underwent a complete orohi-notolaryngological 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 pre-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 increase(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) compared(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(0.2,0.43)p(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 NF1 and hamartoma.

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 stimulation (LH:2.0 mIU/ml), 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 desease, hypothyroidism, growth hormone deficiency were excluded. Bone age was correspondent to chrono-

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 deregulation 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 hyperglycemia 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 u/mL, c-peptid:26.5 ng/L. Blood glucose levels were elevated more than 30 mg/dl with IV glucose. 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 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 an 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

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among patients affected by OI and the possible correlation with the severity of the underlying 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 found 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

Myxedematosus 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 cranioopharyngioma 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 petibial, 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/l). 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 case 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-
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; Candiobaryngioma (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/m2. Patients with CP and LCH required higher doses (375.85mcg/m2 [mean age=9.6years] and 341.04mcg/m2 [7.41years] respectively) whilst patients with SOD and HPE required lower doses (141.24mcg/m2 [mean age=3.1years]; 70.78mcg/m2 [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+ concentration (N=26) was 138.4 (131 – 155) mmol/l. 20 patients had paired urine and plasma osmolalities checked during these periods, insulin did not change during these periods. The first group received 30 ml/M2 of the solution and the other groups received 15 mL/M2 compared by paired T test on these two periods (SPSS 12). . The first group had no chronic complication of diabetes or concomitant disorder. Distillate of Urtica dioica leaves was prepared in the laboratory. Patients were divided into the following groups: 1) Control, 2) Group received 15 ml/M2, 3) medium obesity while 25 cases were severely obese. Neither one pre- seced 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. Conclusion: 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 to 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 bleeds and post-operative complications.
Objective and hypotheses: Androgens are known to enhance erythropoiesis. Some androgens are converted to more potent androgen receptor agonists in peripheral tissues.

Results: We studied 8 patients aged 22.1 years (15-33). Their BMI was 20.5 322 by mean values and ranges.

Methods: 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). Oligoamenorrhea was found in 2 cases (number 5 and 6). We detected an impaired lung function (FEV1 <80%) in 3 cases (number 3, 5 and 6). One case presented CF-related diabetes (number 7) and impaired fasting glucose in 3 cases (number 4, 6 and 7) with HOMA score.

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). Oligoamenorrhea was found in 2 cases (number 5 and 6). We detected an impaired lung function (FEV1 <80%) in 3 cases (number 3, 5 and 6). One case presented CF-related diabetes (number 7) and impaired fasting glucose in 3 cases (number 4, 6 and 7) with HOMA score.

Conclusions: None of the children 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.

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 signs) of adrenarche and serum DHEAS ≥1 µmol/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 leucocyte count. In the entire study population, erythrocyte count was positively correlated with DHEAS, IGf-1 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.

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 prepubertal children.

Conclusion: In obese children change in lifestyle has to begin before onset of puberty. Performance of OGTT is important to detected insulin resistance as major risk factor to develop Type 2 Diabetes. Insulin und glucose results of non obese children differ from obese children.

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, dietic 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 ± 2.71 kg. During the 21-day hospitalisation, the average BMI was reduced by -2.12 ± 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 ± 0.08 of fat was considerably lower, (p < 0.05) in all examinees -1.65 ± 0.23, the waist circumference was reduced by -7.85 ± 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, retractive testis and orchidopexy 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 types 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 and 14 years. The frequency of palpation was 2.5% for those of between 3 and 6 years, retractive testis was 5.2%, there were no cases of orchidopexy 0.75% at the age between 7-10 years; orchidopexy was 0.35% and retractive testes was 0.15%; the frequency of pure cryptorchidism drops more than 3.3 times and retractive testes does 7 times to the puberty age.

**Conclusion:** The prevalence of cryptorchism and the mean age of orchiopexy are high among schoolchildren aged 10-12. The prevalence of cryptorchism differs significantly from the prevalence reported fifteen years ago. It is now show 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 tumours 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 cliteromegaly. Serum assays confirmed hypercortisolism with loss of diurnal variation for cortisolsecretion (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<15μg/dl (5-57))

**Results:** She had no cliteromegaly. Serum -testosterone [<0.1ng/ml (0.1-1.3)] was 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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Alder Hey Children’s Hospital, Paediatric Endocrinology, Liverpool, United Kingdom

**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 (IGHD) 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 those who had 2 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 (ΔHt 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 ΔHt SDS for patients at the three time points during treatment with GH.

**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-
term 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±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, hyperuricemia 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.
Conclusions: β-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 β-hCG may be useful. β-hCG value was also an accurate indicator of the response to therapy.

Conclusions: Virilization occur of external genitalia, in absence of appreciable gonads and with genital feminization, 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.

Conclusions: 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.

Conclusions: We retrospectively compared growth data of girls with CPP (n=14, small for gestational age (SGA) improve their prospective adult height?

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).

Methods: We retrospectively compared growth data of girls with CPP (n=14, small for gestational age (SGA) improve their prospective adult height?.
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=2, 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. 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-
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

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Girls prepubertal period (16,7%)</th>
<th>Girls pubertal period (83,3%)</th>
<th>Boys prepubertal period (30%)</th>
<th>Boys pubertal period (70%)</th>
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<tr>
<td>Energy value (%)</td>
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<tr>
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<tr>
<td>Magnesium (%)</td>
<td>100</td>
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<td>73,3</td>
<td>42,9</td>
</tr>
</tbody>
</table>

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.

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 HbA1C 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 ad 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 dietary or insulin treatment may be effective in protection of fetuses of diabetic mother from the negative effects of gestational diabetes.

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.
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 53.5% 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 dietary 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-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 unre Markable. No vitamin D taken by mother during pregnancy or child after birth. On physical examination at 6 months of age length was 70cm (1.45D) 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 (8.6-10.5mg/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/L), free thyroxin: 0.69 ng/dl (0.8-1.8ng/dl), cortisol: 2.65 ug/dl (4.2-7ug/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: 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 cou pled 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 alfalcacidol 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 gladiun. 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 found. 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-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 prolong 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.

Conclusion: 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: 12 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 high for 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/ann) 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, IAA 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 β-cell function and subsequent options of treatment by repaglinide, a short acting insulin secretagogue (maximum plasma concentration within 0.5 – 1h, half life 1h) which also stimulates early insulin secretion and is thus suitable to be combined with a β-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 time.

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-
glide responsive diabetes in whom traditional tests couldn’t clarify the etiology 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 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-2010 and distributed by sex: 44.3% females and 55.6% males. The annual incidence peak was found in the 10 to 14 years age-group.

**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 24 bolus (n:73) HbA1c: 7.52+/−0.8; p<0.001]. In our country, children have 4-5 meals/d, with midnight 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 lunch. 21 patients were included. Mean age +/- DS: 15.14 +/- 4.19 years (range 9-17). Diabetes evolution: 7.52 +/- 4.19 years (1-16). 11 males (52.4%), 10 females (47.6%), 2 prepubertal (9.5%), 19 pubertal (90.5%).

**Results:**

<table>
<thead>
<tr>
<th>Insulin requirements (U/Kg/d)</th>
<th>Before change</th>
<th>After change</th>
<th>Mean of differences</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>Before change</td>
<td>After change</td>
<td>Mean of differences</td>
<td>p</td>
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<td></td>
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<tr>
<td></td>
<td>1.12 ± 0.23</td>
<td>1.11 ± 0.27</td>
<td>-0.01 ± 0.19</td>
<td>NS</td>
</tr>
</tbody>
</table>

Premixed insulin administered at breakfast in 33% of the patients, at lunch in 43,9%, 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.

 printed Abstracts Only
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 (250%), financial constraints in investigations (4100%), lack of diagnostic tools (375%), and unwillingness to continue follow up (250%).

Conclusions: There is still delay in diagnosis of children with ambiguous external genitalia in our environment. Lack of diagnostic facilities, belief in religious practices and fear of managing diabetes continues to be the main problem.

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 a screening test. Besides, it is not routine to discriminate between secondary or tertiary CCH using the TRH test. Pituitary CH is due to TSHB and TRH 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 from 30, 60, 120 and 180 min. and FreeT4 and TotalT3 at 0 and 180 min. We evaluated 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), hyperpermia and reduced TSH related to her FT4 (TSH 1.2 mU/L, FT4 0.92 ng/dl). 2. A 12 year old boy with hypothyrominaemia (TSH 5.4-8 mU/L) and 3. An 11 year old boy with hyperthyrominaemia (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-246

A case of short stature due to phosphatediabetes

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Methods: 397 children from 0 to 18 years of age with diagnose DM1 were participating in the study. Particularities of DM1 according to gender, date of birth, onset of disease and complications.

Results: The diagnosis of phosphatediabetes 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. Child's 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); serum phosphate remains below target height. Biochemical monitoring performed regularly under the treatment, serum phosphate concentration (TmP/GFR) 0,25mmol/l. Genetic tests results not available yet.

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.
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 fever.

**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.

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**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.