Growth hormone deficiency (GHD) in adults leads to disturbances in lipids and carbohydrate metabolism. The aim of the study was to assess the effects of low-dose GH therapy on lipid profile and glucose metabolism.

The analysis comprised 9 patients (4 men), age 20.1±2.1 years (mean±SD) with multiple pituitary hormone deficiency, including permanent severe GHD (PSGHD), confirmed by severely decreased GH peak (<1.0 ng/mL) in insulin tolerance test after completion of growth-promoting GH therapy. In all the patients their hormonal substitution was administered when necessary. Growth hormone therapy was renewed after at least one year from cessation of growth promotion, with a fixed daily dose 0.3 mg and continued during one year under control of IGF-I and IGFBP-3 concentrations. Body mass index (BMI), total cholesterol (TCh), LDL- and HDL-cholesterol, triglycerides (TG), as well as glucose and insulin levels in oral glucose tolerance test (OGTT) were assessed and insulin-resistance indices: HOMA-IR and IRI (according as well as glucose and insulin levels in oral glucose tolerance test (OGTT) were assessed and insulin-resistance indices: HOMA-IR and IRI (according to Belfiore) were calculated. Comparisons were made by Wilcoxon’s Signed Rank Test. Results are shown in the table. Significant (p<0.05) differences are marked with *.

<table>
<thead>
<tr>
<th></th>
<th>Before GH therapy</th>
<th>After 1 year of therapy</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI [kg/m²]</td>
<td>23.1±3.1</td>
<td>23.7±3.8</td>
<td>0.317</td>
</tr>
<tr>
<td>IGF-I [ng/mL]</td>
<td>51.3±22.3</td>
<td>186.9±80.6</td>
<td>0.008*</td>
</tr>
<tr>
<td>IGFBP-3 [μg/mL]</td>
<td>3.2±0.9</td>
<td>4.0±0.8</td>
<td>0.028*</td>
</tr>
<tr>
<td>TCh [mg/dL]</td>
<td>184±43</td>
<td>172±40</td>
<td>0.155</td>
</tr>
<tr>
<td>HDL [mg/dL]</td>
<td>58±15</td>
<td>55±17</td>
<td>0.086</td>
</tr>
<tr>
<td>LDL [mg/dL]</td>
<td>114±40</td>
<td>99±34</td>
<td>0.038*</td>
</tr>
<tr>
<td>TG [mg/dL]</td>
<td>83±43</td>
<td>87±24</td>
<td>0.477</td>
</tr>
<tr>
<td>Fasting glucose [mg/dL]</td>
<td>73±7</td>
<td>73±9</td>
<td>0.441</td>
</tr>
<tr>
<td>Fasting insulin [μU/mL]</td>
<td>2.8±1.4</td>
<td>4.4±2.8</td>
<td>0.173</td>
</tr>
<tr>
<td>HbA1c [%]</td>
<td>4.9±0.3</td>
<td>5.1±0.3</td>
<td>0.345</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>4.88±2.65</td>
<td>8.26±6.05</td>
<td>0.116</td>
</tr>
<tr>
<td>IRI-Belfiore</td>
<td>0.50±0.26</td>
<td>0.92±0.32</td>
<td>0.036*</td>
</tr>
</tbody>
</table>

Improvement of lipid profile speaks for legitimacy of low-dose GH therapy in young adults with PSGHD after completion of growth promotion. An increase of insulin resistance should be taken into account during GH administration. It seems that OGTT with calculation of IRI-Belfiore allows earlier detection of worsening of the insulin resistance than assessment of fasting glucose and insulin levels only.

The study was supported by funds from Ministry of Science and Informatisation, Project 2P05E 113 28.

Poster Presentations

**P2-d1-348 GH Treatment 1**
Effects of one year of growth hormone (GH) therapy with low-dose on lipid profile and carbohydrate metabolism in young adults with childhood-onset severe GH deficiency confirmed after completion of growth promotion
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**P2-d1-349 GH Treatment 1**
Is GH secretion stimulatory test response an adequate criterion to indicate GH therapy (in prepubertal patients with chronic growth delay without nutritional, kidney or metabolic disorders and normal thyroid function)?
Antonio Carrascosa1; Laura Audí2; Mónica Fernández-Cancio3; Anna Fabregas4; Marc Tobería4; Joan Bel5; C del Pozo5; Maria José Gaspar1; José María Gómez1; Jordi Messi6; Ramón Nosa1; L Perisé7; M Rabanal7; María Angeles Albusi7; Vicky Borras1; J Bosch7; Nuria Cabrinety7; Gemma Carreras7; Maria Clemente7; À Feliú7; A Fonollola7; Anna Guarro8; Miquel Gussinyé1; EJ. Herrero8; Gilda Hollenberg9; Raquel Monné9; M. Roqueta9; M. Torribas9; Diego Yeste10
1Hospital Vall d’Hebron, Generalitat Catalunya, Pediatric Endocrinology. Advisory Committee, Barcelona, Spain; 2Children’s Hospital Vall d’Hebron, Pediatric Service and Endocrinology Unit, Barcelona, Spain; 3Generalitat de Catalunya, Catalan GH Therapy Advisory Committee, Barcelona, Spain

In patients with chronic growth delay in whom hypothyroidism, nutritional, kidney and metabolic disorders have been ruled out, peak GH responses to two stimulatory tests are generally used to classify them as GH-deficient (GH<10 ng/ml) or GH normosecretors (GHNS) (GH¡Ý10 ng/ml). Our objective was to compare growth response to 2 years of GH therapy in 213 prepubertal children (4-11 y) classified as GHD or GHNS depending on peak GH responses to 2 stimulatory tests. The study was promoted by the Catalan GH Therapy Advisory Committee. Patients were first classified as GHSD (n=130; CA<7; 1±1.9 y; GH dose 32.0±3.7 μg/kg/d) or GHNS (n=83; CA=7±1.9 y; GH dose 32.7±3.7 μg/kg/d). No statistically-significant differences were observed in anthropometric data, at baseline (height-SDS: -3.3±0.7 and -3.4±0.8; GV: 4.5±1.0 and 4.4±0.9 cm/y; GV-SDS: -1.8±1.0 and -1.6±1.0) or during 2 years of GH therapy: first year (height-SDS: -2.4±0.8 and -2.6±0.8; GV: 8.6±1.5 and 8.7±1.4; GV-SDS: 3.5±1.6 and 3.5±1.5); second year (height-SDS: -2.0±0.7 and -2.2±0.7; GV: 6.9±1.1 and 6.8±1.1; GV-SDS: 1.6±1.1 and 1.7±1.2); height-SDS gain after 2 years (1.3±0.5 and 1.2±0.5). Among the 213 patients, 73 had been SGA; of these, 41 were GH and 32 GHNS. Among the 140 non-SGA patients, 89 were GH and 51 GHNS. Again, no statistically-significant differences were observed among the different subgroups. Patients were also classified in 3 groups: severe GH (2 tests < 5 ng/ml; n=33), moderate GHD (1 or 2 tests between 5 and 10 ng/ml; n=97) and GHNS (1 or 2 tests > 10 ng/ml; n=83). Again, no statistically-significant differences were observed among them. In conclusion, classification of prepubertal children according to peak GH responses does not predict the growth response to GH therapy in the first 2 years. These data question the need for GH secretion stimulatory tests to indicate GH therapy and emphasise the role of auxologic criteria.

**P2-d1-350 GH Treatment 1**
A boy with clinical characteristics of aphyxiating thoracic dystrophy (Jeune syndrome) and Panhypopituitarism: Growth in a boy before and during GH and thyroxine replacement therapy
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1Klinikum Bremen Nord, Klinik für Kinder- und Jugendmedizin, Bremen, Germany; 2Praxis für Humangenetik, Praxis für Humangenetik, Bremen, Germany

A boy with clinical characteristics of Jeune Syndrome characterised by dysplasia of limbs and thorax resulting in short stature. Pituitary dysfunction has not been reported yet. Here we described the case of a boy with a clinical picture of Jeune syndrome, his pituitary function and the results of consecutive treatment. The boy was born in the 32nd week with normal length and body weight. Postnatally, he had respiratory problems due to a thorax dysplasia. His proximal limbs were short, but also ulna and metacarpals and fingers. Due to the clinical findings a Jeune syndrome was assumed. After postnatal phase growth was severely and mental development was mildly retarded. He passed several episodes of bronchitis. Due to a height SDS of -7,7 at the age of 4,7y the boy was presented in our clinic for further evaluation. We performed pituitary function test and
The study was partially supported by funds from Ministry of Science and
Informatisation, Project 2PO5E 030 028.

P2-d1-352 GH Treatment 1
Long-term treatment with Omnitrope 3.3 mg/ml
ready-to-use solution of short children with GH
deficiency: 7 years follow-up
Tomasz Romet1; Ferenc Peter2; Brygida Koehler1; Renata Wasikowa1;
Mieczyslaw Walczak2; Eugeniusz Komara2; Jerzy Starzyk2;
Alexander Berghout3; Alexander Berghoud1; Paul Saenger1
1Children’s Memorial Health Institute, Endocrinology, Warsaw, Poland;
2BUDA Children’s Hospital, Endocrinology, Budapest, Hungary;
3University Hospital, Paediatric Endocrinology & Diabetology,
Katowice, Poland; Paediatric Hospital, Paediatric Endocrinology,
Wroclaw, Poland; Pomeranian Medical University, Paediatrics,
Szczecin, Poland; Paediatric Institute, Paediatric Endocrinology,
Poznan, Poland; Polish-American Hospital CMUJ, Paediatric
Endocrinology, Krakow, Poland; Sandoz Biopharmaceutical
Development, Clinical Research, Oberhaching, Germany;
Albert Einstein College of Medicine, Pediatrics, New York, United States

We report the follow-up of 84 months GH treatment with Omnitrope of GH-
deficient children with short stature. To evaluate long-term safety and efficacy
of Omnitrope. 89 previously untreated, prepubertal children (HSDS -3.0
± 0.8, height velocity (HV)SDS -2.3 ± 1.1) with GH deficiency (peak < 10
ng/ml, in 2 tests) were treated with Omnitrope 5 mg/ml Powder 0.03 mg/
kg /day (Group A) and compared to daily treatment with Genotropin (same
dose, Group B). After 9 months the increase in HSVD, HVSDS was signifi-
cant when compared to baseline and identical in both groups. Genotropin-
treated patients were switched to Omnitrope 3.3 mg/ml ready-to-use solution.
Treatment of patients in group A was continued with Omnitrope Powder for
6 additional months and then switched to Omnitrope 3.3 mg/ml ready-to-use
solution. Growth was maintained during long-term Omnitrope treatment in both
groups. The change in bone age relative to the change in calendar age
during 84 months GH treatment indicates a sustained growth potential. IGF-1
levels increased in both treatment groups to mean levels in the upper nor-
mal range. Anti-GH antibodies developed transiently in 3 patients during 69
months of treatment of the Omnitrope solution, were acceptably low and of no
clinical significance. The follow-up data show maintenance of growth during
long-term treatment with Omnitrope 3.3 mg/ml solution.

P2-d1-353 GH Treatment 1
Patient with bioactive growth hormone (GH):
short response at the 1st year of GH therapy
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1Maadi Hospital, Department of Pediatrics, Cairo, Egypt; Department of
Pediatrics, University of Pavia, Pavia, Italy

Introduction: Patients with short stature due to reduced GH biological activity
are characterized by normal or high circulating GH levels despite low basal
IGF-1 values increasing significantly after short-term GH administration and
linear growth catch-up during GH substitutive treatment. Patient A with
short stature born to non consanguineous parents was reported. The height
of father and mother were 174 and 164 cm, respectively (MHP 162.75 cm).
Chronological age was 3.9 years at presentation, height 93 cm (-3.18 SD)
and bone age 3.2 years; no dysmorphic features, karyotype was normal (46XX)
Investigation: IGF-1 generation test: basal IGF-1 was 42.9 ng/ml (<2 SD)
and the peak at day 8 is 167 ng/ml (+0.5 SD) Serum GH peak was 17.8 and
14.8 ng /ml following insulin and clonidine administration, respectively. Ce-
liac disease was excluded; no polymorphisms in GH and GH receptor genes.
Management: One year of GH therapy (0.07 IU/kg daily) led to an increase of
height velocity (9.6 cm/year).

Insulin-like growth factor-I (IGF-I) and its binding protein-3 (IGFBP-3) ge-
neration test (IGF-GT) is a standard procedure in diagnosing GH insensitivity.
IGF-I/IGFBP-3 molar ratio is considered an index of IGF-I bioavailability.
The aim of the study was to assess, if the result of IGF-GT may be a progno-
sis factor of recombinant human GH (rGH) therapy effectiveness in short
children with decreased basal IGF-I secretion despite normal GH peak in stimu-
lating tests (stimGH).

The analysis comprised 48 short children (41 boys), age 13.0±2.1 years
(mean±SD) with slow height velocity (HV), normal stimGH (16.1±7.1 ng/
ml) and decreased IGF-1 concentration. In 23 cases neurosecretory dysfunc-
tion (NSD), in 9 – decreased activity of endogenous GH (GHinact), in 16 –
GH deficiency (GHD) after repeated assessment of stimGH was found. IGF-
GT was performed with rGH administration in a daily dose 0.1 IU/kg for 7
days, leading to an increase of IGF-I secretion ranging from 57% to 347%
of basal value, with normalisation of IGF-I concentration. Next, rGH therapy in
a dose 0.60±0.07 IU/kg/week was administered and HV together with IGF-1
and IGF-3FBP concentrations were assessed after 1 year. Control group con-
sisted of 24 age and sex matched children with isolated partial GH deficiency
with the same dose of rGH.

Results:

<table>
<thead>
<tr>
<th>Results</th>
<th>IGF-I SDS after 7 days of GH therapy</th>
<th>IGF-I SDS after 1 year of GH therapy</th>
<th>IGF-I SDS after 7 days of GH therapy</th>
<th>IGF-I SDS after 1 year of GH therapy</th>
<th>IGF-I SDS after 7 days of GH therapy</th>
<th>IGF-I SDS after 1 year of GH therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>±0.12</td>
<td>±0.18</td>
<td>±0.50</td>
<td>±0.19</td>
<td>±0.40</td>
<td>±0.45</td>
</tr>
<tr>
<td>-NSD</td>
<td>±1.44</td>
<td>±2.26</td>
<td>±0.61</td>
<td>±0.20</td>
<td>±0.40</td>
<td>±0.48</td>
</tr>
<tr>
<td>-GHD</td>
<td>±1.85</td>
<td>±0.37</td>
<td>±0.58</td>
<td>±0.19</td>
<td>±0.37</td>
<td>±0.45</td>
</tr>
<tr>
<td>-GHinact</td>
<td>±0.45</td>
<td>±0.69</td>
<td>±0.76</td>
<td>±0.07</td>
<td>±0.17</td>
<td>±0.16</td>
</tr>
<tr>
<td>Controls</td>
<td>±0.08</td>
<td>±0.58</td>
<td>±0.53</td>
<td>±0.12</td>
<td>±0.48</td>
<td>±0.47</td>
</tr>
</tbody>
</table>

In all the subgroups, significant (p<0.05) increase of IGF-I SDS and IGF-
I/IGFBP-3 molar ratio during IGF-GT together with their further (insigni-
ficant) increase and significant HV improvement in the first year of therapy,
was observed. All the differences between the studied and comparative group
and among the subgroups of patients (except for GHinact) in particular time
points presented insignificant.

An increase of IGF-I secretion and its bioavailability during IGF-GT seems
to be a good prognostic factor of GH therapy effectiveness in short children
with normal stimGH, however further observations up to final height seem
necessary.

Efficacy Results

<table>
<thead>
<tr>
<th>Group</th>
<th>BASELINE</th>
<th>BASELINE</th>
<th>84 MONTHS</th>
<th>84 MONTHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>±0.17</td>
<td>±0.14</td>
<td>±0.15</td>
<td>±0.15</td>
</tr>
<tr>
<td>Group B</td>
<td>±0.60</td>
<td>±0.90</td>
<td>±0.90</td>
<td>±0.90</td>
</tr>
</tbody>
</table>

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Horm Res 2008;70(suppl 1) 105

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Discussion: we hypothesize that our patient has a particular type of molecular GH variant that is less biologically active and lead to low IGF-I levels. Treatment with rhGH is capable to restore normal linear growth.

**P2-d1-354** GH Treatment 1

Response to GH treatment and final height in adolescents and young adults with GHD chronological age TH-start > 16 years

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Caucasus Growth Centre, Clinic for Diabetes, Endocrinology and Nutrition, Tbilisi, Georgia; Tbilisi State University, Department of Endocrinology, Tbilisi, Georgia

Background: In Georgia, growth hormone treatment for growth hormone deficiency (GHD) patients has only been available since 1999. Some patients were over 16 years of age when GH treatment was started. We collected and estimated 3-year results of growth hormone therapy in these patients.

Objective and methods: 19 adolescents and young adults with GHD (12 male, 7 female, 17 primary GHD, 2 secondary GHD) aged 16-30 years were over 16 years of age when GH treatment was started. We collected and estimated 3-year results of growth hormone therapy in these patients.

Conclusions: GH therapy increased height by 21.0±6.5 cm (2.8 SDS) in male and 13.6±2.7 cm (2.1 SDS) in female patients after 3 years. The late start of puberty starting age was 22.5 years in males, and 17.8 years in females.

**P2-d1-355** GH Treatment 1

Effect of growth hormone therapy in children and adolescents with growth hormone deficiency after stem cell transplantation

Carl Philipp Schwarze; Gerhard Binder; Hans Scheel-Walter; Peter Lang; Rupert Handgretinger; Michael Ranki

University Children’s Hospital, Paediatric Haematology/Endocrinology, Tübingen, Germany; University Children’s Hospital, Paediatric Endocrinology, Tübingen, Germany

Effect of GH therapy in patients after stem cell transplantation (SCT) with growth hormone deficiency (GHD) and neurosecretory dysfunction (NSD). 9 patients (27±7m) were treated with SCT for cALL (2x), TBI (1x) and local irradiation (LJH) (1x), 4 patients had a previous SCT. Conditioning for SCT (7x allo/2x auto) was CT(3x), CT/TBI(4x), CT/CUTB/TBI(1x) and CT/LI(1x). HT was reduced at SCT at -1.6 SDS (-1.1 to -3.3), vs. target HT at 0.0 SDS (-1.4 to +1.1). Growth failure 1.8 to 5.1 yrs after SCT resulted in a HT reduction at -0.6 to -4.3 SDS with a loss of -1.0 SDS (-0.3 to 1.2). IGF-I was very low in all patients at -1.9 to -5.2 SDS. IGFBP-3 was very low in 7 patients at -2.5 to -5.5 SDS and normal in 2 patients at -1.3 and -0.9 SDS. ASTs showed GH peaks of 4.8 ng/ml (1.2 to 14.1), ITTs of 4.5/5.8/7.2 ng/ml and GH secretion of 1.6/1.7/2.5/7.9 ng/ml in patients with GHD (cut-off at 8.0 ng/ml). In the patient with NSD, GH peaks were 16.3/15.2 ng/ml/2 ASTs). IGF-I and IGFBP-3 increased in the generation test (0.033/mg/kg/day) from -3.4 to -0.3 and -5.5 to -1.3 SDS. GH doses used for therapy were 0.030/mg/kg/day (0.025 to 0.043), HT velocity before GH therapy was reduced at -1.1 to -3.2 SDS, 2.1 to 5.2 cm/y, and increased during GH therapy to -1.2 to 6.3 SDS, 4.6 to 8.6 cm/y. IGF-I normalised after GH therapy -0.8 to +1.5 SDS and -1.9 to +0.7 SDS. At the last visit up to 11 yrs after SCT, HT SDS had increased in 5 patients by 0.4 to 1.4 SDS, HT SDS remained unchanged in 2 patients and HT SDS decreased further in 2 patients due to a chronic GvHD/severe dystrophy and failure to respond to GH therapy in spite of normal IGF-I levels.

GHD may be the cause of progressive growth failure after SCT in patients receiving CT/TBI but also CT only. GH normalises growth and induces catch-up growth.

**P2-d1-356** Growth 1

Association of cartilage hair hypoplasia and growth hormone deficiency

Dorothee Schmidt; Verena Wagner; Olaf Hört

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Cartilage- hair hypoplasia (CHH) is a rare autosomal recessive disorder characterized by metaphyseal chondrodysplasia with severe growth retardation and occasionally impaired immunity. Typical clinical signs are short- limb short stature and hypoplastic hair. The responsible gene for CHH has been identified to be ribonuclease of mitochondrial RNA- processing (RMRP) gene. Growth hormone deficiency is not the underlying cause of growth retardation and patients with CHH are generally believed not to benefit from GH.
Subjects with congenital GHD and pituitary anatomical abnormalities often present variable phenotypes and different degree of hypopituitarism. We present clinical and genetic data of 54 pts with congenital hypopituitarism.

We also analyzed response to GH therapy of the 17 pts currently treated (7 mg/m²/wk).

Patients: Inclusion criteria were GHD and MR abnormality of the sellar area or GHD plus another hormonal deficiency. 45 cases had posterior pituitary ectopia (PPE), 9 anterior lobe hypoplasia. HESX1 gene was analyzed in all pts with PPE, PROP-1 in all pts without PPE and Pit-1 in the 4 cases with GHR-PRL-TSH deficiency. Besides GHD (isolated in 18 cases, 26 presented also TSH, 25 LH/FSH, 22 ACTH and 6 PRL deficiency.

Genotype: we found 2 new HESX1 mutations in one case (compound heterozygosity) and one already described PROP-1 homozigous mutation.

**Phenotype at Diagnosis:** mean ht SDS was -2.4±1.2 SDS, but in 9 cases it was > -2 SDS, associated with impaired ht velocity (HV) or hypoglycemia (4 pts); GHD was usually severe (<3 µg/L in 43 cases) but in the remaining 11 cases peaks were 3-8 µg/L; mean IGF-1 SDS was low (<2.5±1.6), but in 2/17 pts it was 0.3 and -0.5 SDS. Follow-up in recently treated group: mean 1st year HV SDS after GH was 5.3±1.8 but ranged from 1.6 to 7.9; mean prepubertal IGF-1 SDS was 0.2±1.3 but ranged from -1.7 to 3.5. No differences were found in clinical data and response to therapy between the subjects with PPE and those without it.

**Correlations:** IGF-1 at diagnosis did not correlate with GH peak. 12th month IGF-1 SDS correlated with height SDS at diagnosis (p=0.03), IGF-1 at diagnosis (p=0.008), but not with 12 month HV.

**Conclusions:** Despite PPE represents the most common pituitary anatomical abnormality, congenital hypopituitarism is a heterogeneous syndrome with variable degree of pituitary insufficiency. The genetic defect is rarely due to mutations in HESX-1, PROP-1 and Pit-1 genes. Growth response to GH therapy is usually excellent, but a fixed GH dose elicits mean-high IGF-1 levels with a high subject-to-subject variability.

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**P2-d1-359**  
**Septo-Optic Dysplasia (SOD): Clinical, endocrinological and neuroradiological evaluation. Follow-up in 46 pediatric patients**  
**Monica Warnan**; Maria Isabel Di Palma; Elisa Vaiani; Mariana Costanzo; Roberto Ruggieri; Ricardo Ceriosoimo; Marta Ciaccio; Marco A. Rivarola; Alicia Belgorosky

1Hospital de Pediatría Garrahan, Endocrine Service, Buenos Aires, Argentina; 2Hospital de Pediatría Garrahan, Neurology Service, Buenos Aires, Argentina

SOD is defined by the combination of optic nerve hypoplasia (ONH), midline malformation of the forebrain, aplasia/hypoplasia of the septum pellucidum (ASSP) and/or corpus callosum; and/or hypothalamic-pituitary insufficiency (HPI). We have followed 46 patients with SOD. All patients had ONH confirmed by ophthalmological examination and neuroradiological studies. Pituitary hormone deficiency was documented using standard endocrine tests. Patients were subdivided in Gr1 (n=27) with HPI, and Gr2 (n=19), no HPI. Groups were similar in age and time of follow-up. GH (GHD) and TSH (TSHD) deficiencies were found in 81.5% of the patients, 48.1% had ACTH deficiency (ACTHD) and 14.8% had Diabetes Insipidus (DI). All patients with ACTHD and/or DI had both GHD and TSHD. Patients developed additional pituitary hormone deficiencies over time (36% TSHD, 50% GHD). Height SDS at diagnosis in Gr1 was significantly lower than in Gr2, p<0.01. The most common midline CNS abnormality was ASP (Gr1 63%, Gr2 48%; p< NS). However cortical brain dysplasia and heterotopias in Gr2 (57%) were significantly higher than in Gr1 (19%), p<0.01. Hypoglycemia, jaundice and/or seizures were present in all patients of Gr1 (p<0.05). Brain MRI in Gr1 showed pituitary anomalies in 45% of the patients. In Gr1, 13 patients were treated with rGH, improving 1.5 Height-SDS without adverse effects. In conclusion the variable association within HPI and the neuroradiological studies suggest that SOD is a multifactorial or polygenic disorder. Physicians should be aware of hormonal deficiencies that might be present at birth or appear during follow-up.

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**P2-d1-358**  
**Genotypic and phenotypic variability in 54 subjects with congenital hypopituitarism**  
Stefano Zucchi; Lilia Baldazzi; Piero Pirazzoli; Soara Menabò; Veronica Conti; Giorgio Sponza; Margherita Costa; Citognani Almiganda; S.Orsola-Malpighi Hospital, University of Bologna, Department of Pediatrics, Bologna, Italy

Subjects with congenital GHD and pituitary anatomical abnormalities often present variable phenotypes and different degree of hypopituitarism. We present clinical and genetic data of 54 pts with congenital hypopituitarism.

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**P2-d1-357**  
**Novel de novo SOX2 mutations in patients with severe eye defects and associated developmental abnormalities**  
Marie-Pierre Vie-Lutton; Marie-Laure Sobrier; Claire de Baracè; Eva Feigtová; Sophie Rose; Idres Nourredine; Sylvie Odent; Maîté Tauber; Serge Amsterdam

1Inserm, U654, Paris, France; 2Centre Hospitalier de Saint Brieuc, Pédiatrie, Saint Brieuc, France; 3Hôpital des Enfants, Endocrinologie, Toulouse, France; 4CHU de Rennes, Génétique Médicale, Rennes, France

SOX2 is a transcription factor involved in the regulation of embryonic development and cell fate determination. Although mice carrying a targeted disruption of Sox2 in the heterozygous state have abnormal anterior pituitary development with reduced levels of Gh, Lh and Tsh, and no eye defect, the few heterozygous SOX2 mutations identified in humans can cause bilateral anophthalmia-microphthalmia, and/or developmental delay, defects of the corpus callosum, esophageal atresia, sensorineural hearing loss. Here, we investigated two independent patients with severe eye defects; the first one had right anophthalmia and left optic nerve hypoplasia, while the second, who was born to a consanguineous union, had bilateral anophthalmia associated with hypogonadotropic hypogonadism and short stature. Brain magnetic resonance imaging revealed a thin corpus callosum in the first patient, and, in the second patient, a cyst of the septum pellucidum, whereas pituitary morphology was normal. The two patients were found to carry novel de novo SOX2 mutations in the heterozygous state: patient #1 bears a missense mutation (p.W51R) involving a residue located in the HMG domain of the protein and that is highly conserved throughout evolution. A single base deletion (c.540delC) in the heterozygous state has abnormal anterior pituitary development and cell fate determination. Although mice carrying a targeted disruption of Sox2 in the heterozygous state have abnormal anterior pituitary development with reduced levels of Gh, Lh and Tsh, and no eye defect, the few heterozygous SOX2 mutations identified in humans can cause bilateral anophthalmia-microphthalmia, and/or developmental delay, defects of the corpus callosum, esophageal atresia, sensorineural hearing loss. Here, we investigated two independent patients with severe eye defects; the first one had right anophthalmia and left optic nerve hypoplasia, while the second, who was born to a consanguineous union, had bilateral anophthalmia associated with hypogonadotropic hypogonadism and short stature. Brain magnetic resonance imaging revealed a thin corpus callosum in the first patient, and, in the second patient, a cyst of the septum pellucidum, whereas pituitary morphology was normal. The two patients were found to carry novel de novo SOX2 mutations in the heterozygous state: patient #1 bears a missense mutation (p.W51R) involving a residue located in the HMG domain of the protein and that is highly conserved throughout evolution. A single base deletion (c.540delC) was identified in patient #2; this latter defect would result in a frameshift that introduces 21 novel amino acids before a premature stop codon at position 202, thereby leading to a truncated protein. Additional studies are underway to assess the functional consequences of these two novel SOX2 defects.
Our objective was to determine the prevalence and clinical significance of pituitary dysfunction following moderate/severe childhood traumatic brain injury (TBI). We recruited 16 survivors of childhood TBI (14 males). Age at study was 9-18y (median 14y). Median time since TBI: 4.5y (2.4-6.7y). Subjects provided an early morning urine sample for osmolality and underwent basal hormone evaluation at 0800-1000h, followed by a GnRH test and either insulin tolerance test (ITT, n=11) or glucagon test (in those with previous seizures, n=5). Sex-hormone priming was not performed. Median (range) SDS for height, weight and BMI were 0.64 (-1.57 to +1.89), 0.57 (-0.98 to +2.65) and 0.56 (-0.93 to +2.75). No subject had diabetes insipidus. Thyroid function tests, IGF-I, oestradiol/testosterone, baseline and GnRH-stimulated LH/FSH were all appropriate for age/sex/pubertal stage. One child had isolated prolactin deficiency (<50 mU/L). Peak GH response to stimulation was 28.4 (7.47.3) mU/L. Two subjects had peak GH <15 mU/L: both were tall (SDS +1.3 and +1.39) and peri-pubertal. Basal morning cortisol was 282 (146-722) nmol/L. Cortisol response to ITT was 507 (367-717) nmol/L; six of 11 subjects had sub-optimal cortisol responses based on local evidence-based age-related cut-offs, none low enough to warrant routine glucocorticoid replacement. In two, steroid cover was recommended for moderate/severe illness/injury. In four, repeat testing was advised in one or two years. Four subjects had adequate cortisol responses to glucagon; the fifth had high basal levels (722 nmol/L). Contrary to previous reports, GH deficiency was not observed in this cohort, 2.4-6.7y after injury. No unequivocal clinically significant endocrinopathies were found, although the hypothalamic-pituitary-adrenal axis may be vulnerable. Further work is relating these findings to the degree of primary injury and secondary brain insult in a larger cohort.

Background: In our previous work anterior pituitary function was revealed in children with history of hospitalization due to mild to severe head trauma. The most common pituitary dysfunctions caused by TBI were growth hormone (GHD), and cortisol deficiency. These endocrine sequelae are potentially serious, but treatable complications of TBI.

Objective: The aim of this study was to determine the decrease of growth rate in those of our cases where GHD due to TBI was detected. Methods: In our previous work 26 children (17 boys) aged 11.40±0.75 years were investigated 30.6±1.7 months after TBI (all data presented are means±SEM). Eleven of them (8 boys) had abnormally low GH levels in two GH tests. 25/26 children were followed through further 3 years, divided in two groups (group 1: 11 GHD TBI patients not treated with GH, group 2: 14 non-GHD TBI patients). In March 2007 calculated height SDS and body mass index (BMI) were compared within the groups to their 3-years earlier data (Feb 2004).Height SDS and growth velocity rate (GV) were compared between the groups.

Results: Height SDS decreased significantly from -0.15±0.25 to -0.99±0.22 (p<0.01) in group 1, whereas there was no significant change in group 2 (0.13±0.15 vs. 0.21±0.24, NS). Height SDS was significantly lower (p<0.05) in group 1 than group 2 on 2005 visit, but not in 2004, indicating a growth retardation in GHD group. BMI has not changed significantly in either group (group 1: 19.04±0.91 vs. 20.47±0.72, NS; and group 2: 18.11±0.72 vs. 20.47±0.02 NS). Growth velocity rate in group 1 (3.07±0.64 cm/y) and group 2 (3.64±0.60 cm/y) did not differ significantly.

Conclusions: Approximately six years after TBI significant decreases in height SDS were demonstrated in patients suffering from GHD due to head injury. Therefore regular endocrine investigations are suggested in children with TBI to diagnose endocrine abnormalities. Early GH treatment could be beneficial to avoid growth retardation in TBI children.

Introduction: Renin is a protein cleaving enzyme secreted by the juxtaglomerular apparatus. The effect of renin secretion is an increase in arterial blood pressure. A positive correlation of the blood concentration of renin and sleep quality was found in adults only in non-REM sleep, but no studies have been performed in children so far. In addition, the possible relationships of the secretion of renin with other hormones like IGF, DHEA, melatonin and sleep quality have not been studied too.

Aim: Measurement and analysis of 12 hours overnight secretion profiles of renin, IGF, DHEA, melatonin, and sleep quality by polysomnography in children affected by short stature.

Materials and Methods We studied the nocturnal blood secretion over 12 hours of renin (IRMA, DSL), DHEA (EIA, DSL), hGH (ELISA, DSL) and melatonin (RIA, DSL) by sampling every 30 minutes using a Conflow Pump and performing polysomnography in parallel in 17 children aged 6 to 21 years affected by short stature with and without growth hormone deficiency. The programs PULSAR and AnCoPuls were used for secretion analysis, SPSS for statistical analysis, ALICE for automatic analysis of polysomnography. The sleep staging and efficiency were determined according to Rechtschaffen and Kales, 1968. The nocturnal EEG-profiles were visually analyzed to synchronize results from polysomnography and blood parameter measurements.

Results First results show interdependency between renin-concentration and sleep quality over 12 hours. Patients with diseases like Prader-Willi-Syndrome and pituitary tumors show totally different relationships, as do renin to melatonin, DHEA und hGH to a lesser extent. Further investigations need to identify the existence of a system regulating hormonal secretion, sleep quality and blood-pressure in children and adolescents.

We evaluated long-term intellectual and neuro-endocrine outcomes in 35 cranially irradiated adults (22.5±4.08 years), 15 years after PFT diagnosis, neurosurgeons, 30-35 Gy neuraxial irradiation and 20Gy PFT boost (9-chemo-therapy). Those (N17) diagnosed ‘young’, (<7 years) were of comparable age to those (N18) diagnosed ‘older’ (p<0.05) at testing with shortened WAIS-R
and Anxiety/Depression scale and MRI assessment of ventricular index. Years of education, support, occupational and endocrine status were recorded. Age at diagnosis directly influenced IQ measures (r=0.5 < p<0.05). Ventricular Index significantly (p<0.05) increased with time and decreased with age at diagnosis (r = -0.48, and negatively influenced PIQ and FSIQ (r = -0.46 & r = -0.43, p<0.05). Patients had a mean education of 14.65 ± 2.04 years, 31.4% supported by a financial provision (statement). Most were not anxious (80%) or depressed (85%) and were educated (46%) or employed (37%). However, 17% were unemployed, and 15-20% reported mood disturbance. GH deficiency was isolated in all but one, and the 2 females with thyroid and/or ovarian failure had received chemotherapy with spinal irradiation. 2 patients had motor deficits, 3 required anticonvulsants one had mild auditory impairment and none had visual impairment. Radiation-based therapies for PFT in childhood impair general intelligence in the adult 9 to 27 years later, especially if diagnosed before age 7 years. This effect increases with time. Nevertheless, patients accomplish educational and occupational achievement with minimal neuroendocrine and rehabilitative support and without overt mental health problems. Significant pituitary dysfunction other than GH deficiency is uncommon, even at long (16yr) follow-up, though. chemotherapy increases glandular, sensory and motor late effects. Such comprehensive assessment on transition to young adult services especially aimed at those diagnosed young-est, with increased VI or mood disturbance, may direct targeted neurorehabilitative strategies and further increase independence rates.

P2-d1-364 Growth 1
Pituitary Dysfunction after traumatic brain injury in pediatric population: A preliminary prospective study

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Traumatic brain injury (TBI) has been associated with increased risk for developing pituitary dysfunction. Although this association has been extensively described in adults, little is known in the pediatric population, where pituitary function is critical for growth. Our goal was to prospectively evaluate pituitary function in hospitalized patients with 1) moderate or severe TBI and 2) mild TBI that additionally present with VI or mood disturbance, may direct targeted neurorehabilitative strategies and further increase independence rates.

Growth, pubertal development and endocrine function were assessed 3 months after TBI: n=11 patients, median age 11.95 years (range 6-19.9 years), 8/11 prepubertal o pubertal and median Gap GH (GCS): 11 (range 3-15). Severity of TBI was classified according to: GCS, Radiological imagine and Cerebral perfusion pressure. Pituitary function was assessed by a combination of basal (free-tirexine, TSH, GH, 8 a.m. cortisol and urinary osmolality) and dynamic tests (glucagon stimulation for assessment of somatotrophic and corticotrophic axes; and TRH, LHRH, and L-DOPA stimulation for assessment of thyrotrophic, prolactin, gonadotrophic and somatotropic axes). Abnormal results were considered: Basal: results compared with reference ranges for age,sex and pubertal stage. Dynamic test: GH peak less than 10 ng/ml, TSH surge < 2 mUL/L above basal, cortisol < 21 ng/ml pubertal LH/FSH response: LH > 10 U/l.

Three months after TBI, 64% (7/11) patients had a low GH response to either test and 3 of them showed an abnormal response to both tests. No other hormonal deficiencies were demonstrated. There was no correlation between GH response and trauma severity. At 3 months we observed an unexpected high prevalence in the pediatric population with TBI of GH abnormal response. Complete study will finish at 12 months in order to confirm the pituitary dysfunction and to assess its clinical impact. We suggest that pediatric endocrinologists should follow-up pituitary function after traumatic brain injury.

P2-d1-366 Growth 1
DNA analysis of patients with growth hormone deficiency within the French GeNeSIS program

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Growth hormone deficiency (GHD) is a rare condition that may be isolated (IGHD) or combined with other pituitary hormone deficiencies (CPhD). The identification of the underlying molecular defects is essential for genetic counselling and, in several cases, is of particular help to manage these disorders. Six candidate genes have been investigated within the framework of the Genetics and Neuroendocrinology of Short Stature International Study (GeNeSIS). We report here the French contribution to this international study. 67 patients (pts) from 53 independent families have been included with either IGHD (n=42) or CPHD (n=25). Magnetic resonance imaging (MRI) of the pituitary region showed an ectopic posterior pituitary (EPP) in 19 pts. 17 pts had extra-pituitary morphological anomalies. 26 pts from 12 families had a family history of GHD. The choice of the candidate genes to be analyzed (GH1, GHRHR, POUF1, PROP-1, HESX-1 and/or LHX-3) was determined according to the nature of the hormonal deficiencies, the MRI and the extra-pituitary phenotype. Mutations were identified in 4 families: three mutations in GH1, GHRHR, and/or HESX-1 and one mutation in PROP-1 (p.R73C). The GH-1 deletion and the PROP-1 mutation were identified in the homzygous state, in keeping with the consanguinity documented in these two families. The low percentage of molecular defects identified in this study (9.5% of independent families) further supports the need to screen other candidate genes. To this end, LHX-4, SOX-3 and SOX-2 are now included in the French GeNeSIS genetic analysis program. SOX-3 is analyzed in male patients with hypoplastic or aplastic infundibulum, and SOX-2 in patients with developmental eye defects combined with hypogonatrophic hypogonadism. In addition, HESX-1, which was previously screened only in patients with septo-optic dysplasia, is now analyzed in all IGHD or CPHD patients with EPP.

P2-d1-365 Growth 1
Placental IGFs and micronutrients correlated with infant birth weight

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Perinatal growth disorders are a vast problem globally, affecting more than 30 million pregnancies each year. Our aim was to correlate infant birth weight with maternal and infant biometric data, including the expression of placental IGF-I and IGF-II at birth and levels of serum zinc and ferritin. The data consisted of observations from eighty-nine women from Karachi, Pakistan. Placental and cord blood samples were taken immediately following delivery and were subsequently divided into two groups, small and large for gestational age (SGA & LGA). The mean birth weight was 2.79 kg; the prevalence of SGA babies being 13.4% (2SD = 2.108). Placental IGF-I and IGF-II mRNA expression was greater in the LGA group (p<0.05). Furthermore, a significant correlation was noted between infant birth weight and maternal anthropometric parameters (p<0.01). Cord zinc levels were also significantly higher in the LGA group (p<0.05). Maternal anthropometry, along with placental IGF-I and IGF-II mRNA levels, correlated significantly with infant birth weight suggesting the importance of these growth factors in birth weight outcomes. The higher zinc levels in the LGA group also suggests the importance of this micronutrient in newborn growth. Our results suggest that growth problems have a multi-factorial aetiology arising from within the infant rather than due to maternal constraint alone.
Several bone age methods are in use today: The Greulich Pyle (GP) method, the Tanner Whitehouse (TW) method and the recently introduced automated BoneXpert method. One can define transformations of one method to predict another, but an SD of typically 0.5-0.8 years remains, and it is difficult to decide which method is best. The aim of this work is to introduce a framework that assesses the effectiveness of a bone age method by its ability to predict the final adult height. The framework is grounded in the work of Bayley and Pinneau: For children where the final adult height (ah) is known, one defines the growth potential gp when the child has height h as gp = (ah - h) / ah. The study used images of 232 children from the First Zurich Longitudinal Study, which recorded X-rays close to the children’s anniversaries. The data were divided into groups of the same sex and chronological age CA, and in each group one estimated a model that predicted gp as a function of the bone age of the method under study. The prediction SD of this model was taken as a measure of the effectiveness of the bone age method and this SD was averaged over the age range 10-18 years for boys and 8-16 years for girls to obtain the average growth potential prediction error (GPE). The original manual TW ratings (which were used as basis for the famous TW3 formula for adult height prediction) yielded GPE = 1.32% [1.28; 1.36] 95% conf., but were surprisingly significantly outperformed by the original manual GP ratings with GPE = 1.26% [1.22; 1.30] 95% conf. BoneXpert obtained GPE = 1.23%, and omitting radius and ulna yielded GPE = 1.22%; these were not significantly better than GPE for manual GP method. We conclude that manual TW ratings (which were used as basis for the famous TW3 formula) are significantly better than GPE for manual GP method. One can define transformations of one method to predict another. The BoneXpert method worked as well as the manual GP rating, also when presumable because the GP method assigns a smaller weight to radius and ulna. The BoneXpert method worked as well as the manual GP rating, also when omitting radius and ulna.

Small for Gestational Age, (SGA), children account for an increasing proportion of patients referred for short stature. We describe 2 SGA siblings with a previously undescribed short stature syndrome. Two siblings, a 3 year old boy and a 7 year old girl from a highly consanguineous Pakistani family presented with short stature. Both siblings were born SGA with birth weight SDS -2.63 and -2.3 respectively. At presentation they were extremely short with height SDS of -3.0 and -4.5 respectively. Expected midparental target height SDS was -1.0. Clinical examination of the girl revealed a broad forehead with preserved head circumference, pointed chin, pectus excavatum and proximal interphalangeal joint fusion. Skeletal survey showed an unusual form of bony fusion in both feet. She has been diagnosed with deletion 18p11.2-q11.2. Neither child had evidence of hypoglycaemia. Karyotype analyses were normal. Homozygosity mapping using Affymetrix 10K SNP chips revealed a large region of homozygosity on Chromosome 18 (18p11.21-q21.2), common to both affected children but not seen in either parent or a healthy sibling. Part of this region on chromosome 18 (18p11.31-q11.2) has been described as a possible locus for a Seckel-like syndrome but neither child showed any Seckel features. There are no obvious candidate genes at this locus. Sequencing of 2 genes in this region including Rab12 and Rab1BP has revealed no mutations. In conclusion, we describe a possible new short stature syndrome associated with SGA, bony abnormalities and elevated IGF2 levels. A candidate locus on Chromosome 18 has been identified.
difference TH-FH was significantly closer than TH-iH (1.8±1.1 vs -3.1±1.2, p=0.001) while in Cgr it was significantly wider (-2.9±1.5 vs -2.4±1, p=0.03). Initial CrCl was significantly greater than final CrCl in both groups (GHGr 76±9 vs 66±14, p=0.008 and Cgr 72.5±19 vs 56±9, p=0.02). In a best subject regression test, the best model to predict FH included iH and initial CD, being iH the only significant predicting variable (p<0.01). Conclusion: rhGH was effective in improving FH in RTx patients without affecting renal function. Growth response to rhGH is significantly associated with iH.

**P2-d1-371 Growth 1**

Is glucagon provocation a truly safe and efficient test of pituitary function?

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Although the Insulin tolerance test (ITT) is the gold standard for assessing Growth Hormone (GH) and ACTH reserve, it relies on inducing and safely reversing potentially dangerous but controlled hypoglycaemia. Glucagon provocation, thought to avoid this hazard, is considered a safer alternative. It is recommended when ITT is contraindicated (eg in epilepsy) and has now replaced the ITT in many paediatric nurse-led daycare units despite its limitations in assessing cortisol reserve. We retrospectively assessed the safety and efficiency of glucagon provocation in 33 adolescents aged 11-19year (M21: F12) presenting consecutively to our metabolic day unit for dynamic pituitary function (of GH and ACTH reserve). All patients were administered glucagon (100 mcg/kg IM) after an overnight fast, with blood samples taken at half-hourly intervals for 3 hours. 16/33 (48.4 %) patients exhibited normal GH (>20mU/l) peaks, and 17/33 (51.5%) normal cortisol (>500nmol/l) reserve to glucagon. Of the 14 (42.4 %) patients with suboptimal cortisol responses, 6/14 (46%) subsequently demonstrated normal spontaneous or ACTH-stimulated cortisol peaks (>500nmol/l to 500 ng/l.73 m2 ACTH). On average serial blood glucose rose to a peak at 60mins and reached a nadir at 120mins. In 2 (6%) patients the nadir occurred after 120mins (fig 1a) and in a further 2 (6%) was significant (<2.5mmol/l). 12/33 (36%) had glucose levels <3mmol/l and experienced side effects (vomiting and nausea dizziness) sufficient to require polycal resuscitation. 12/33 (36%). A further 2 patients required IV cortisol and/or IV dextrose resuscitation. All required close glucose monitoring, one third of whom needed urgent medical review. The unpredictability, potential severity (6%) and frequency (36%) of hypoglycaemic symptoms together with the need for resuscitation in a significant proportion belie the assumption that Glucagon is a safer test than ITT. The requirement for close medical supervision and/or readmission for further adrenal testing do not suggest it is a simpler or more cost-efficient alternative either.

**P2-d1-372 Growth 1**

Characteristics of septo-optic dysplasia (SOD) without pituitary dysfunction

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In 65 children with septo-optic dysplasia (SOD), pituitary dysfunction was present in 44 (67%). We have compared birth-related features between SOD children with and without pituitary dysfunction and also compared them to isolated optic nerve hypoplasia (ONH). We have also compared auxological parameters: height, weight and body mass index (BMI) in these 3 groups. Data is shown as median (range).

**Results:** Males were in excess in all groups. Although most were born at term, those in the two SOD groups were lighter at birth, and born to younger mothers. Neonatal hypoglycaemia, but not jaundice, was commoner in children with SOD with pituitary dysfunction. 1st trimester bleeding, maternal drug and alcohol consumption were more common in the ONH group (data not shown). Children with SOD but no pituitary dysfunction, as with the ONH group were of more normal weight and BMI, in comparison with those with SOD and pituitary dysfunction.
Conclusions: Patients with SOD but without pituitary dysfunction much more closely resemble those with SOD with pituitary dysfunction in terms of their birth characteristics, but ONH patients in terms of their subsequent auxology.

**P2-d1-373 Growth 1**

**Panhypopituitarism with gigantism case report**
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Male prepubertal patient who presented at the age of 18 9/12 years complaining of enlargement of feet to the point that he could not find shoes that would fit. His height was 176.3 cm [+0.25 SDS], and had acromegalic facies (prominent supra orbital ridges, long face, prognathism and large ears). Fig 1. Size of both hands and feet was above the 97th percentile. He had normal body proportions (US/LS 0.9). His weight was 72.5 kg (0.9 SDS) and his BMI was 22.5 29.7 kg/m2 (0.3 SDS). No abnormality was noted on physical examination except for mild scoliosis. His mentality was normal. He was delivered by breech after a full term pregnancy. His weight was 2.5 kg and he developed Erb’s palsy. Surprisingly, MRI scan revealed hypoplastic anterior pituitary with ectopic posterior pituitary. Fig 2. Hormonal profile was done and confirmed panhypopituitarism. Table 1. His GH was extremely low but was biologically active. Very low IGF1 and IGFBP3 and low ALS and IGF2 were found. Table 2. By electrophoresis, big IGF2 and IGF1 were absent. Other pituitary hormones: ACTH, TSH, LH and FSH were low and hypogonadotropic hypogonadism was confirmed by LHRH analogue testing. His karyotype was normal (46, XY) and DNA analysis done to look for a cause for his overgrowth revealed no centromeric (KCNQ1OT1) or telomeric mutations (H19/IGF2) in the chromosomal region 11p15. Also, there was no paternal isodisomy or an imprinting error. Analyses of the NSD1 gene are pending. Now, at the age of 21 6/12 years his height is 186.1 cm, 2SD above his target height of 173.8 cm. We present a case where overgrowth occurred despite the absence of GH, low IGF1, IGFBP3, ALS and IGF2 with normal prolactin and leptin. This case proves that growth can occur without GH. Other still undefined growth hormones: ACTH, TSH, LH and FSH were low and hypogonadotropic hypogonadism was confirmed by LHRH analogue testing. His karyotype was normal (46, XY) and DNA analysis done to look for a cause for his overgrowth revealed no centromeric (KCNQ1OT1) or telomeric mutations (H19/IGF2) in the chromosomal region 11p15. Also, there was no paternal isodisomy or an imprinting error. Analyses of the NSD1 gene are pending. Now, at the age of 21 6/12 years his height is 186.1 cm, 2SD above his target height of 173.8 cm. We present a case where overgrowth occurred despite the absence of GH, low IGF1, IGFBP3, ALS and IGF2 with normal prolactin and leptin. This case proves that growth can occur without GH. Other still undefined growth factors might have a role.

**Table 2.**

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<td>Peak GH (GHRH + arginine)</td>
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<td>Peak cortisol (ITT)</td>
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<td>522 ng/ml (808 +/- 113 ng/ml)</td>
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<td>6.8 ng/ml (0.7-5.3 ng/ml)</td>
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</tbody>
</table>

In previous publications we reported the linear growth and growth rate of the head circumference and foot length in untreated and IGF-1 treated patients with Laron Syndrome (LS- primary GH insensitivity). The aim of this investigation was to assess the size and growth of the hands in LS patients from early childhood to adult age. Ten IGF-1 treated children with LS (4M, 6F) and 24 untreated patients (10M, 14F) were studied. Using a sensitive caliper, hand size was measured from the soft tissue tip of the 3rd finger to the soft tissue line of the palm base from standardized X rays for bone-age determination. Mean ±SD of hand size SDS was calculated using the norms of Gerver & Bruin (1996). Hand SDS in untreated LS patients decreased with age, from -2.8 ± 0.7 (age 1-3 y) to -7.3 ± 0.8 (13-15 y) and to -9.0 ± 3.9 (40-50 y), compared with height SDS of -6.3 ± 0.8 (1-3 y) and -7.3 ± 2.0 (40-50 y). During 5 y of IGF-1 administration, the hand size deficit SDS did not improve: at start of treatment the hand size was -4.0±1.4 and after 5 y treatment -4.5±1.4; concurrently the height SDS improved from -6.2±1.2 to -4.3±0.7. It is concluded that congenital IGF-1 deficiency profoundly affects the size and growth of the hand as part of its growth retardation characteristics. In early childhood the hand size in LS patients is less retarded than the linear height and foot length (not shown); with advancing age and even during IGF-1 treatment, the hand growth rate lags behind that of the body and feet.

**P2-d1-374 Growth 1**

**Hand size and growth in untreated and IGF-1 treated patients with Laron syndrome**
Osnat Keren$^{1}$; Awita Silbergard$^{2}$; Liora Korreich$^{1}$; Zvi Laron$^{2}$

$^{1}$Schneider Children’s Med. Ctr. & Tel Aviv Univ., Imaging Department, Petah Tikva, Israel; $^{2}$Schneider Children’s Med. Ctr. & Tel Aviv Univ., Endocrinology and Diabetes Research Unit, Petah Tikva, Israel

In previous publications we reported the linear growth and growth rate of the head circumference and foot length in untreated and IGF-1 treated patients with Laron Syndrome (LS- primary GH insensitivity). The aim of this investigation was to assess the size and growth of the hands in LS patients from early childhood to adult age. Ten IGF-1 treated children with LS (4M, 6F) and 24 untreated patients (10M, 14F) were studied. Using a sensitive caliper, hand size was measured from the soft tissue tip of the 3rd finger to the soft tissue line of the palm base from standardized X rays for bone-age determination. Mean ±SD of hand size SDS was calculated using the norms of Gerver & Bruin (1996). Hand SDS in untreated LS patients decreased with age, from -2.8 ± 0.7 (age 1-3 y) to -7.3 ± 0.8 (13-15 y) and to -9.0 ± 3.9 (40-50 y), compared with height SDS of -6.3 ± 0.8 (1-3 y) and -7.3 ± 2.0 (40-50 y). During 5 y of IGF-1 administration, the hand size deficit SDS did not improve: at start of treatment the hand size was -4.0±1.4 and after 5 y treatment -4.5±1.4; concurrently the height SDS improved from -6.2±1.2 to -4.3±0.7. It is concluded that congenital IGF-1 deficiency profoundly affects the size and growth of the hand as part of its growth retardation characteristics. In early childhood the hand size in LS patients is less retarded than the linear height and foot length (not shown); with advancing age and even during IGF-1 treatment, the hand growth rate lags behind that of the body and feet.

**P2-d1-375 Growth 1**

**Insulin like growth factor-I (IGF-I) concentrations in infancy are nutritionally regulated and predict subsequent longitudinal growth**
Ken Ong$^{1}$; Markus Langkamp$^{2}$; Michael Ranke$^{3}$; David Dunger$^{4}$

$^{1}$Medical Research Council Epidemiology Unit, Institute of Metabolic Science, Cambridge, United Kingdom; $^{2}$University Children’s Hospital, Paediatric Endocrinology Section, Tuebingen, Germany; $^{3}$University of Cambridge, Department of Paediatrics, Cambridge, United Kingdom

IGF-I is a major childhood growth factor and may also regulate the partitioning of weight gain into lean versus fat body mass. We aimed to identify the determinants of IGF-I concentrations in healthy infants, and in turn to assess the influence of IGF-I concentrations on subsequent growth. In a prospective birth cohort study, IGF-I concentrations were measured in 886 capillary blood samples from 565 infants at ages 3, 12 and 18 months. Weight, length, and skinfold thicknesses were measured at 0, 3, 12 and 18 months. Overall, IGF-I concentrations at ages 3, 12 and 18 months were positively associated with current body weight, length, BMI and skinfolds (P<0.001 for all); were inversely associated with current body fat mass (P=0.001); and were inversely
Adenotonsillar hypertrophy may play a role rather than a cause for the lower levels lead to decreased appetite, and also swallowing difficulties in increasing hunger and food intake, and its levels increase before the meals. This study is planned to investigate the ghrelin and IGF-1 levels in normal controls.

Methods: This study included 29 male prepubertal children between the ages of 6.5-10 years (Mean 8.8±2.5 years) with obstructive adenotonsillar hypertrophy and 20 normal male controls aged between 5.7-10.8 years (Mean 8.2±2.9 years). In both groups serum IGF-1 and fasting plasma ghrelin levels were measured at 08.30, in the morning. Results: In children with adenotonsillar hypertrophy the mean serum IGF-1 levels (203±150 ng/ml) and the mean plasma ghrelin levels (175±66 pg/ml) were lower than those of the children in the control group (354±242 ng/ml and 243±93 pg/ml respectively) and the differences were significant (p<0.05). Height and weight of children with adenotonsillar hypertrophy were significantly below those of their healthy peers (p<0.05).

Conclusions: Male children with adenotonsillar hypertrophy had lower serum IGF-1, plasma ghrelin levels than the normal male controls. Since ghrelin increases hunger and food intake, and its levels increase before the meals, lower levels lead to decreased appetite, and also swallowing difficulties in children with adenotonsillar hypertrophy may lead to suboptimal nutrition. Adenotonsillar hypertrophy may play a role rather than a cause for the lower IGF-1 and ghrelin levels.

In conclusion, IGF-1 concentrations are at least partly nutritionally regulated in infancy, as concentrations were positively related to concurrent gains adiposity and formula-milk feeding. In turn, infants who generate higher IGF-1 concentrations show subsequent greater gains in body length and lesser gains in adiposity.

**P2-d1-376 Growth 1**

**Do children with adenotonsillar hypertrophy have lower IGF-1 and ghrelin levels than the normal children**

**Tolga Sari**; **Abdullah Ayçiçek**

1Afyon Kocatepe University, Pediatric Endocrinology, Afyonkarahisar, Turkey; 2Afyon Kocatepe University, Otorhinolaryngology, Afyonkarahisar, Turkey

**Aim:** Adenotonsillar hypertrophy is associated with growth interruption during childhood. Interruption of growth hormone-IGF-1 axis resulting from abnormal nocturnal growth hormone secretion is among the postulated causes. Ghrelin is a potent GH secretagogue that also plays an important role in appetite and weight regulation which has the highest levels just before the meals. This study is planned to investigate the ghrelin and IGF-1 levels in children with adenotonsillar hypertrophy and in normal controls.

**Methods:** This study included 29 male prepubertal children between the ages of 6.5-10 years (Mean 8.8±2.5 years) with obstructive adenotonsillar hypertrophy and 20 normal male controls aged between 5.7-10.8 years (Mean 8.2±2.9 years). In both groups serum IGF-1 and fasting plasma ghrelin levels were measured at 08.30, in the morning. Results: In children with adenotonsillar hypertrophy the mean serum IGF-1 levels (203±150 ng/ml) and the mean plasma ghrelin levels (175±66 pg/ml) were lower than those of the children in the control group (354±242 ng/ml and 243±93 pg/ml respectively) and the differences were significant (p<0.05). Height and weight of children with adenotonsillar hypertrophy were significantly below those of their healthy peers (p<0.05).

**Conclusions:** Male children with adenotonsillar hypertrophy had lower serum IGF-1, plasma ghrelin levels than the normal male controls. Since ghrelin increases hunger and food intake, and its levels increase before the meals, lower levels lead to decreased appetite, and also swallowing difficulties in children with adenotonsillar hypertrophy may lead to suboptimal nutrition. Adenotonsillar hypertrophy may play a role rather than a cause for the lower IGF-1 and ghrelin levels.

**P2-d1-377 Growth 1**

**Efficacy and safety of bilateral epiphysiodesis performed in extremely tall girls and boys**

**Maria Børner; Henrik Wehle; Lars Sävendahl**

Karolinska Institutet, Department of Woman and Child Health, Stockholm, Sweden

Extreme tall stature is most often caused by genetic factors. The treatment options have been limited to treatment with high doses of sex steroids aiming to cause premature growth plate fusion and thereby reduced final height (FH). This treatment has been linked to multiple undesired side effects such as acne and aggressive behaviour in boys and weight gain, hypertension and thrombosis in girls. Premature growth plate fusion can also be induced surgically by performing bilateral epiphysiodesis around the knee, a method that could be applied in most extremely tall patients as they often have relatively long legs. So far the experience of this treatment to reduce FH is very limited. We recruited 8 girls and 7 boys predicted to have at least 8cm remaining growth and finally heights exceeding 185cm and 200cm respectively. Height, weight, sitting height (SH) and armspan were monitored yearly until FH (growth less than 0.5 cm/year). Before surgery, bone age assessment (Greulich-Pyle) and FH prediction (Bailey-Pinneau) were performed by two blinded observers. Radiological leg length and hip-knee-ankle angle measurements were performed before surgery and at FH. When compared to the initial prediction, FH was significantly reduced in operated girls (4.6cm or 36.1% reduction of predicted remaining growth; p<0.001) and boys (6.5cm or 36.6% reduction; p<0.001). The mean post-treatment leg growth was 0.5cm in girls and 0.7cm in boys confirming the effectiveness of the procedure. Relative SH increased, in girls from 50.0% at surgery to 51.9% at FH and in boys from 50.7% to 52.7%. We conclude that bilateral epiphysiodesis is an effective method to limit growth in extremely tall girls and boys. No serious side effects, as leg length difference, abnormal body proportions, angular leg deformities or infection, were reported. Expanding the study to more patients is necessary to verify the long-term safety of this treatment.

**P2-d1-378 Growth 1**

**Association between head circumference and body size**

**Erica Geraedts**; **Paula van Dommelen**; **Janina Caliebe**; **Michael B. Ranke**; **Stef van Buuren**; **Jan Maarten Wilf**; **Wilma Oostdijk**

1Leiden University Medical Center, Department of Paediatric Endocrinology, Leiden, Netherlands; 2TNO Quality of Life, Department of Statistics, Leiden, Netherlands; 3University Hospital for Children and Adolescents, Department of Paediatric Endocrinology, Tubingen, Germany

Head circumference (HC) is generally measured in clinical practice, and abnormalities of HC are associated with various syndromes (e.g. microcephaly in IGF-1 and IGF1R defects, macrocephaly in Sotos syndrome). So far, conflicting data are available on the correlation between HC and height or weight. The aim of this study was to study the correlation between HC versus height or weight in a reference population and to compare data from children with idiopathic short stature (ISS) or small for gestational age (SGA) with these reference data. Growth data from a large nation-wide growth study (14,500 children), and data at birth and in childhood from 152 ISS and 67 SGA children were expressed as standard deviation scores (SDS) for age and sex. From the reference population correlations between HC vs. height and weight were calculated. ISS and SGA data were plotted on graphs showing the reference regression equations +/- 2 SDS. HC was significantly correlated with height, with the highest correlation (r) in the first 2 months of life (r=0.519). Thereafter correlations fluctuated between 0.324-0.469, with a tendency of a higher r in adolescence (r=0.453). Correlations between HC and weight followed the same pattern as between HC and height, although all correlations were higher: r=0.628 in the first two months, 0.401-0.569 thereafter before surgery and at FH. Multiple regression analysis confirmed that weight was a stronger predictor of HC than height. In the first two months: $HC_{SDS} = 0.518weight_{SDS} + 0.129height_{SDS} (R^2=0.401)$, thereafter $HC_{SDS} = 0.408weight_{SDS} + 0.093height_{SDS} (R^2=0.224)$. For clinical purposes a nomogram of $HC_{SDS}$ vs. $height_{SDS}$ is most suitable. More than 95% of the data from ISS and SGA patients was found within the reference regression line +/- 2 SDS. We conclude that HC is associated with both weight and height, and that for the interpretation of HC its association with body size is useful.
**P2-d1-379 Growth 1**

The correlation between being born short at term and height, weight and blood pressure at age 17

Alon Farfel1; Amon Afek1; Estella Derazne1; Paul Marlob1; Nehama Linder1; Zvi Larson1

1Schneider Children’s Med Ctr and IDF, Endocrinology and Diabetes Research Unit, Petah Tikva, Israel; 2Israel Defense Forces & Beilinson Med. Ctr, Newborn Ward, Petah Tikva, Israel; 2Israel Defense Forces, Medical Corps, Tel Aviv, Israel; 2Beilinson Medical Center & Tel Aviv Univ, Newborn Ward, Petah Tikva, Israel; 2Schneider Children’s Med Ctr and Tel Aviv Univ, Endocrinology and Diabetes Research Unit, Petah Tikva, Israel

In contrast to follow-up studies of subjects being born overweight for gestational age (SGA-wt), studies on subjects born short (SGA-length) are scant. 385 fullterm newborns measuring <48 cm (SGA-L) and 585 fullterm newborns measuring >48 cm (AGA-L) born at the Beilinson Medical Center were included. Using the Israel Army computerized system: 234 SGA-L (138 Males, 106 Females) and 359 AGA-L (243 Males, 116 Females) of the above were identified at age 17. The main comparative findings (m±SD) are shown in the table.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Parameter</th>
<th>SGA-length</th>
<th>AGA-length</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Height (cm)</td>
<td>158.9 ± 7.6</td>
<td>164.2 ± 6.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Weight (kg)</td>
<td>53.8 ± 9.6</td>
<td>58.4 ± 11</td>
<td>&gt;0.001</td>
</tr>
<tr>
<td>Females</td>
<td>BMI 30</td>
<td>1.9%</td>
<td>5.4%</td>
<td>0.42</td>
</tr>
<tr>
<td></td>
<td>Weight (kg)</td>
<td>61±11.8</td>
<td>66±13</td>
<td>0.001</td>
</tr>
<tr>
<td>Males</td>
<td>BMIz</td>
<td>3.3%</td>
<td>4.4%</td>
<td>0.91</td>
</tr>
</tbody>
</table>

One subject in the SGA group and 2 in the AGA group had hypertension. One subject in the SGA group had hyperlipidemia. It is evident that children born short for gestational age become short adults and have a decreased tendency for obesity than children with a normal birth length. It is not known whether early initiation of hGH treatment will change adult height, and whether the insulin and IP(a) stimulation by hGH will have late adverse effects.

**P2-d1-380 Growth 1**

Growth of children with Down syndrome and heart malformations

Eva Stierkorb; Stephanie Lehmann-Kannt; Christine Seebald; Gormn Ludwing; Rohrer Tilman

University of Saarland, Pediatrics, Homburg, Germany

Down syndrome (DS) is the most common chromosomal aberration. The syndrome is caused by trisomy of chromosome 21. DS is associated with congenital malformations of which heart malformation are the most frequent (40–60 % of DS patients). The predominant heart malformation is an atrioventricular septal defect (40–70%). We analysed 7823 growth data from 1032 children with Down syndrome (53.5 % male). In a retrospective cohort study data was collected from German Down Syndrome children via standardized questionnaire. The frequency of heart malformation in this cohort was 53.5 %. We investigated the effect of heart malformations on growth and weight. For statistical analyses a linear model test was used. We considered values of p<0.05 to be statistically significant. In the first year of life the appearance of heart malformations has significant influence on growth (p<0.05) and weight (p<0.001). Between the ages of 2 to 5 years height was not statistically lower in children with heart malformation (p>0.004) but they still had lower weight (p<0.05). Between the 6th and 10th year of life height was also not different for children with heart malformation (p=0.584) and the weight was still lower (p<0.01). Children with Down Syndrome and heart malformation show significantly lower height and weight in the first year of life. After the malformation has been corrected, usually during the first year of life, children show a catch-up-growth, but the weight remains lower.

**P2-d1-381 Growth 1**

Plasma catecholamine responses to hypoglycemia in insulin test in children with short stature

Robert Piekarski1; Leszek Szweczyk; Teresa Jaklinska; Urszula Biadun

Medical University of Lublin, Pediatric Endocrinology and Neurology, Lublin, Poland

Background: Catecholaminergic activity in children with short stature based on literature data and former own studies is usually decreased, particularly regarding noradrenaline release. The insulin test is frequently used in diagnosis of growth hormone (GH) deficiency. It is well known that stimulation of GH secretion during insulin test is in the aftermath of hypoglycemia. The aim of the study was to estimate the plasma adrenaline (A) and noradrenaline (NA) values during diagnostic insulin test in children with short stature.

Materials and methods: 52 children with short stature (35 males and 17 females) aged 5-15.5 years at diagnosis participated in the study. The level of catecholamines (A and NA) was measured two-times by HPLC method: before and 30 min after insulin administration (an intravenous insulin bolus of 0.1 U/kg). GH and plasma glucose levels were during insulin test concurrently evaluated.

Results: The mean adrenaline value before insulin administration was 60.48 pg/ml while 30 min after insulin administration was statistically significantly higher (mean value 340.75 pg/ml). The mean noradrenaline value was 231.90 pg/ml before insulin administration and 318.96 pg/ml 30 min after insulin administration. The noradrenaline postinsulin value was slightly higher in only 67% children. In other children by contrast tendency to decrease value was observed.

Conclusions: During insulin test manifold increase of adrenaline value in children with short stature was observed. Our results indicate the intensive adrenergic response after postinsulin hypoglycemia which may have direct influence for stimulation of GH secretion.

**P2-d1-382 Growth 1**

One year treatment response in growth hormone deficient (GHD) children is best in children with an early age at start of treatment.

Data from the NordiNet® International Outcome Study (IOS)

Annette Grüters1; Oliver Blankenstein; Birgitte Tennes Pedersen; Viatcheslav Rakov3

1Charité-Universitätsmedizin, Institute for Experiment. Paediatric Endocrinology, Berlin, Germany; 2Novo Nordisk A/S, Global Development, Bagsværd, Denmark; 3Novo Nordisk Health Care AG, IM, Zurich, Switzerland

Previous analyses from Nordinet® have shown that baseline characteristics of GHD children differ from country to country. In particular this concerns age at treatment start, dose of GH and baseline height SDS (HtSDS). The aim of this investigation was to analyse one year GH treatment response (delta Ht SDS) in GHD children dependent on their age at treatment start. All children were treated with Norditropin®. They were stratified in 3 subgroups: early start - <6 y. in boys; late start -6 y. to 8 y. in girls and 10 y. to 11 y. in boys. Older children were excluded to avoid the influence of puberty. Multivariate analyses were applied to analyse the effect of age and some other characteristics on treatment response. 594 GHD children were identified for this analysis. After one year of GH treatment, changes in HtSDS significantly differed between the 3 groups dependent on the age at GH treatment start in GHD, especially between treatment start < 6 years and the two other groups of patients (table 1). Multivariate analysis also demonstrated that baseline HtSDS and cumulative dose of GH significantly influenced the change in HtSDS after one year of treatment (p<0.0001, p<0.0003 respectively). The improved treatment response (change of HtSDS) in children < 6 years and with more increased HtSDS at start of treatment most likely indicates that the diagnosis of GHD in these children is more precise than in the older children. Table 1. Changes in HtSDS after one year of GH treatment.
The purpose of this study was to determine ocular protrusion reference values of 6-18 years old children and adolescents producing sex specific percentiles for each age. The degree of ocular protrusion was measured in 1986 (1086 male and 900 female) 6-18 years old children who had no history of orbital trauma or affected diseases. A cross-sectional study for Turkish children was designed and ocular protrusion was measured using a Hertel prism exophthalmometer. We did not observe a statistically significant difference in ocular protrusion between boys and girls for both right and left eyes (Z=0.734 and p=0.463, Z=0.583 and p=0.560 for right and left eyes respectively). The mean and standard deviation (SD) of normal protrusion values of right eye was 14.62(1.61) for boys and 15.05(1.63) for girls in pubertal period. The mean and standard deviation of normal protrusion values of left eye was 14.55(1.60) for boys and 14.88(1.60) for girls in pubertal period. The difference in ocular protrusion both in prepubertal and postpubertal period for girls and boys. No subject had more than 1.5 mm of asymmetry between eyes. In pubertal period ocular protrusion of girls is significantly greater than boys. Ocular protrusion greater than 2 SD may be an indicator of disorder. Own references for each population is needed for this procedure.

### Table 1. Comparison of right and left eye protrusion for each sex in different pubertal periods.

<table>
<thead>
<tr>
<th>Periods</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male Mean (SD)</td>
<td>Female Mean (SD)</td>
</tr>
<tr>
<td>Prepubertal</td>
<td>14.17 (1.61)</td>
<td>13.99 (1.67)</td>
</tr>
<tr>
<td>Pubertal</td>
<td>14.62 (1.61)</td>
<td>15.05 (1.63)</td>
</tr>
<tr>
<td>Postpubertal</td>
<td>14.72 (1.60)</td>
<td>14.81 (1.68)</td>
</tr>
</tbody>
</table>

Image 1. Ocular protrusion in right and left eye of 7-17 years old children

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**P2-d1-384 Growth 1**

**Causes of short stature in outpatient children: A comparison after 20 years**

Jan-Hendrik Ruef; Kerstin Herberth; Michael Weiss; Eckhard Korsch

Children’s Hospital of Cologne, Department of Pediatrics, Cologne, Germany

Short stature is the most common complaint for which children are referred to a paediatric endocrinologist and can be the manifestation of several diseases. The Objective of this study was to compile the various causes in children presenting with short stature. We reviewed all charts of children seen for evaluation of short stature at the endocrine outpatient department at the Children’s Hospital of Cologne during 1977-1986 and during 1997-2006. Detailed medical history, clinical examination, relevant growth characteristics and various radiological and laboratory investigations were assessed. Referrals between 1977 and 1986 included 306 children (70% boys) with short stature with an average age of 10.0 years. Among these children normal variation of growth was the most frequent diagnosis (68.4 %) followed by intrauterine growth retardation (IUGR, 9.8 %), syndromes / genetic disorders (8.8 %), growth hormone deficiency (GHD, 3.9 %), chronic diseases (3.6 %) and others (5.6 %). Between 1997 and 2006 a total of 517 children (60% boys) with short stature were evaluated with an average age of 9.1 years. Normal variation of growth (61.0 %) was also the most common cause of short stature and there was no significant change in the frequency of IUGR / prematurity (13.2 %), syndromes / genetic disorders (7.2 %), chronic diseases (5.2 %), GHD (3.7 %) and other causes (9.7 %). But there is a marked increase in prematurity, atopic diseases and nonorganic diseases (malnutrition, psychosocial short stature). Etiological causes of short stature did not substantially change over the past 20 years. Children were younger and there were more girls referred. Atopic diseases, prematurity and nonorganic diseases seem to become increasingly relevant.

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**P2-d1-385 Growth 1**

**Short stature and GnRH agonist treatment in a girl with Tricho-Rhino-Phalangeal Syndrome (TRPS) type 1 due to a de novo 5 base pair insertion in the TRPS1 gene**

Hetty J van der Kamp; Arie van Haeringen

1Leiden University Medical Center, Paediatrics, Leiden, Netherlands; 2Leiden University Medical Center, Genetics, Leiden, Netherlands

Mutations in the TRPS1 gene on chromosome 8q24 cause tricho-rhino-phalangeal syndrome type 1 (OMIM 190350). TRPS type 1 is highly expressed in cartilage, developing joints, hair follicles and in the nasal region. In mice with a disrupted TRPS1 gene, diminished chondrocyte proliferation and survival was shown. In humans, radiological findings of cone-shaped epiphyses and premature closure of the growth plate were reported. Bone age (BA) lags behind the chronological age (CA) until puberty and then typically accelerates. Growth retardation is considered to occur postnatally as a progressive process. Reported mean (sd) adult height in patients with TRPS type 1 (n=28) was -1.68 sds ±1.29. A girl with a new mutation in the TRPS1 gene will be presented. Furthermore this girl was treated with a GnRH agonist to improve final height. She was born at term with a birth weight of 3750 gr. She had a head circumference of 2 sds, sparse slow growing hair, protruding ears, frontal bossing, a bulbous tip of the nose with notched alae nasi, a long philtrum and thin upper lip. Her development was slightly delayed. Clinically, TRPS was suspected but no deletion was found at that time. Eight years later, a de novo insertion of 5 base pairs in exon 4 of the TRPS1 gene was found, resulting in a premature translation stop at codon 352 of the protein. Her Height, Sitting Height and Bone Age (BA) are shown below. Her Target Height is 168,2 cm (-0.32 sds).

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Height (cm)</th>
<th>Height (sds)</th>
<th>Sitting Height (cm)</th>
<th>SH/H ratio (sds)</th>
<th>Tanner Stage</th>
<th>BM1 (sds)</th>
<th>Bone Age yrs (G&amp;P)</th>
<th>BA-CA yrs (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0</td>
<td>96.4</td>
<td>-3.41</td>
<td>M1, P1, A1</td>
<td>0.44</td>
<td>3.0</td>
<td>2.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.4</td>
<td>116.4</td>
<td>-3.72</td>
<td>M1, P1, A1</td>
<td>0.70</td>
<td>5.0</td>
<td>4.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.5</td>
<td>122.7</td>
<td>-3.56</td>
<td>M1, P1, A1</td>
<td>2.87</td>
<td>10.1</td>
<td>4.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.1</td>
<td>125.7</td>
<td>-3.59</td>
<td>M3, P2, A2</td>
<td>0.29</td>
<td>6.8</td>
<td>4.3</td>
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</tr>
<tr>
<td>12.1</td>
<td>128.8</td>
<td>-3.96</td>
<td>M3, P3, A1</td>
<td>0.49</td>
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<td>4.6</td>
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<tr>
<td>13.1</td>
<td>133.8</td>
<td>-4.07</td>
<td>M3, P3, A1</td>
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<td>13.7</td>
<td>135.2</td>
<td>-4.22</td>
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<td>0.70</td>
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</tr>
</tbody>
</table>

Image 1. Ocular protrusion in right and left eye of 7-17 years old children

47th Annual Meeting of the ESPE

Horm Res 2008;70(suppl 1) 115
The collected data were analyzed with chi-square test, ANOVA and Pearson correlation coefficient used with SPSS (ver. 12.0).

Results: 1) 39.2% of boys and 46.6% of girls were aware of, and satisfied with their actual height, 51.2% of boys and 42.7% of girls were with their actual weight.
2) There were no significant differences of their self-esteem, sociality, and problematic behaviors according to their actual height and weight.
3) There were significant differences of their self-esteem and problematic behaviors according to their perception and satisfaction of their height (P<0.01).
4) The levels of their perception and satisfaction of weight were well correllated with those of their self-esteem (P<0.01).

Conclusion: The children who considered themselves have short stature or obesity had problematic behaviors or bad self-esteem. Therefore, children should be educated to have the appropriate perception of their own body image.

Poor growth in children with CP has been described in literature. The purpose of this study is to describe growth of children with CP attending a Centre for treatment/rehabilitation compared to healthy children living in the same area. Assessment of 83 subjects with CP fed by mouth compared to a group of 81 healthy subjects. Outcomes included anthropometric measures of weight(W), height(Ht), head circumference(HC), body mass index(BMI), and target height (HT). National reference growth charts for healthy children were used. All measurements were performed by the same experienced paediatrician using equipment of great accuracy (Wunder electronic scales with seat mode, SECA 210 measuring mat, SECA 202 stadiometer). Mean age of CP children was 3.3 years old (range 0.19-15.3); 46(55.4%) were males. In the control group mean age was 3.9 years old (0.18-13.6); 35(43.2%) were males.

In the group mean Wt, Ht, HC, BMI, and TH for boys were 12.7kg (5.4-39), 85.8cm (55-139), 46cm (33.5-55.6), 16.3(3.3-22.5), 183 cm (173.1-192) respectively. For girls with CP the same parameters were 13.3kg (9.5-38), 88.7cm (53-153.1), 45.5cm (37.5-54.3), 15.5(11.9-24.8), and 166.5cm (158.7-178.5) respectively. In the control group mean Wt, Ht, HC, BMI, and TH for boys were 18.5kg (4.3-40.4), 104.2cm (55-162.8), 49.7cm (38.4-57), 15.9 (12.7-21.8), and 183 cm (171.5-192) respectively. For the girls in the control group they were 16.4kg (6.2-42.7), 96.5cm (64-147), 48.3cm (41.2-55), 16.3 (13.6-21.8), and 167.8cm (154-178) respectively. Children with CP compared to matched healthy subjects are at lower centiles for all growth indices but TH. Children with CP have poor growth probably due to communication difficulties that inhibit requests for food, impaired expression of hunger or food preferences, lack for self-feeding skills, and oral-motor dysfunction. The feeding problems of a child with CP limit calorie intake, the diminished intake in turn limits the child’s growth. Identification of risk factors associated with undernutrition is important for its early detection, treatment, and prevention of later consequences for behaviour and health.
visit. Use of growth-altering medications is excluded. Data from 87 subjects (55 male, 32 female) show a mean age of 9.3 ± 4.2 years, mean height SDS of -2.6 ± 0.6 and mean birth weight SDS of -0.5 ± 1.7. Mean bone age delay was 1.3 ± 1.0 years. BMI SDS was greater than HT-SDS (mean difference = 2.0 ± 1.3, p<0.001). Measured parental height z-scores (-0.34 ± 0.8, n=82) suggest slight parental short stature; the mean difference between subject HT-SDS and mean parental HT-SDS (-2.2 ± 1.0) suggests etiologies other than genetic shortness. Height velocity over a mean of 10.3 ± 3.5 months (minimum of 5 months) was inversely related to age (p=0.014) and directly related to initial IGF-1 SDS (p=0.042). Serum IGF-1 levels tended to be low (mean SDS -1.1 ± 0.9) and mean maximal stimulated GH (GHMax) was normal in 53 subjects (16 ± 7 ng/mL). There was no correlation between GHMax and IGF-1 levels or age. Subject characterization by GHMax and IGF-1 SDS suggests that 25% of subjects have low IGF-1 and normal GH (Primary IGFD) while 74% have no IGF-1 or GH deficiency (Table 1).

<table>
<thead>
<tr>
<th>GHMax &lt; 7 ng/mL</th>
<th>GHMax ≥ 7 ng/mL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGF-1 SDS &lt; -2</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>IGF-1 SDS ≥ -2</td>
<td>2</td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>51</td>
</tr>
</tbody>
</table>

These initial results suggest that about 23% of contemporary children with short stature who return untreated for an endocrine follow-up visit have low IGF-1 and normal GH (Primary IGFD). These subjects also have normal weight for height, delayed skeletal maturation and lower than average birth weights. For these subjects, IGF-1 deficiency is suggested as an etiologic factor by the tendency of IGF-1 levels to be lowest among children with lowest growth velocities.

**P2-d1-390**

Endocrine sequelae after autologous hematopoietic stem cell transplantation for solid tumors without TBI in childhood

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High dose chemotherapy (HDC) and hematopoietic stem cell transplantation (HSCT) has been increasingly used during the past 20 years and more children now survive with a long follow-up. There are several reports on late endocrine effects after total body irradiation (TBI) for allogeneic HSCT for hematologic diseases in children, however reports after autologous HSCT without TBI for solid tumors in children are sparse. 88 children (43 boys, 45 girls), who underwent HDC without TBI and autologous HSCT for solid tumors at a mean age of 6.4 ± 4 yrs, were studied at a current mean age of 16.5 ± 7 yrs. Many regimens of HDC were used but 57% of children received Busulfan-containing HDC. Height and weight measurements were compared for each patient at diagnosis of tumor, at HSCT and at this study. The mean height delta-SDS value was -0.96 SDS and the mean weight delta-SDS value was -0.26 SDS. Final height was less than -2 SDS in 17/76 (22%) of cases. This loss in height was not correlated with the use of Busulfan, but with radiotherapy. Most of the boys (87%) progressed through puberty normally but 89% of them showed tubular damage (elevated FSH serum levels > 14 UI/l in 62%, small testicular volume <10 ml in 86%). Only 2 boys had overt Leydig cell dysfunction after testicular radiotherapy, but serum LH levels higher than 8 UI/l was documented in 22% of boys. 66% of girls experienced ovarian failure whose incidence was associated with Busulfan, age and pubertal status at HSCT. 86% of children had normal thyroid function and examination. Thyroid abnormalities were only found after cervical radiotherapy or treatment for a neuroblastoma: increased serum TSH levels >6 mUI/l in 7 patients (8%), benign thyroid nodules in 6 patients (8%).

**Conclusions:**

1/ Ovarian failure and male germ cell damage are the main endocrine late effects of HDC with an equivalent rate as TBI containing regimens.
2/ Growth is less severely impaired after HDC than after TBI.
3/ Cervical radiotherapy and neuroblastoma are the main risk factors for developing thyroid dysfunction in this population.

**P2-d1-391**

A novel mutation in a large Chinese family with X-linked Spondyloepiphyseal dysplasia tarda

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X-linked spondyloepiphyseal dysplasia tarda (SEDT) is a relatively rare osteochondrodysplasia that is characterized by a disproportionately short-trunked short stature, barrel-shaped chest, radiological signs of mild to moderate epiphyseal dysplasia and hump-shaped vertebral bodies as well as an X-linked recessive mode of inheritance caused by the SEDL gene. Here we describe a rather special and very interesting novel mutation (IVS+1A>G) exactly at the rare non-canonical splicing-cut-point, which caused a series of retrievals from a rare non-canonical splice junction with AT/AC consensus to an ordinary canonical pattern with GT/AG consensus and other rarer nonstandard splice junctions with AT/AT. The error transcripts were confirmed by sequencing of RT-PCR products and re-sequencing of cDNA clones, and all the practical splice donors/ acceptors were further assessed using FSPVICE 1.0, SPL and SLM Programs to predict potential splice sites in genomic DNA. Subsequently, the expression levels of SEDL among the affected subjects, carriers and normal controls were estimated using Real-time quantitative PCR. The single nucleotide mutation activated some cryptic splice sites and provoked a total of 7 kinds of error splicing isoforms. Expression analyses showed that the expression levels in patients and carriers were both decreased. These results provide evidence that the mutation created some strong cryptic splice sites that may compete with the constitutively used splice site pairs and may impair exon definition. The identification of the IVS+1A>G presents a useful mutation in the consensus splice donor. These splicing patterns suggest a very promising area for future study on splicing mechanisms. Keywords: canonical splice site; mutation analysis; non-canonical splice site; SEDL; splicing mechanism.

**P2-d1-392**

Obesity and Fat 1

A case of PRES (posterior reversible encephalopathy syndrome) in a patient with Prader Willy syndrome

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A 7 years-old-boy, with Prader Willy Syndrome(PWS), was admitted to Emergency Room for asthenia and a headache. When the patient was three years old, since he had growth hormone deficiency, started therapy with GH. After 5 months a echocardiogram disclosed the presence of a dilatative cardiomyopathy, with mitral-aortic insufficiency and arterious hypertension, so he stopped GH therapy and started antihypertensive therapy. For the worsening of his headache with severe hypertension, ultrasound evaluation of the urinary tract showed a left kidney smaller than normal with a scarce differentiation between renal cortex and medulla. An URO-MR showed renal medulla’s cystic dysplasia; the urethra-cistograph didn’t find neither bladder-urethral reflux nor alterations in the bladder’s wall. Then a brain MR was performed and showed hypointensity, involving both of the cerebral hemispheres. Abnormal signal of brain periventricular white matter and brainstem. The diagnosis of PRES was confirmed with a posterior reversible encephalopathy syndrome (PRES) with a good response to treatment with GH.

**Keywords:** diastolic dysfunction, kidney’s cystic dysplasia, PRES
manifestations reversibility confirmed the diagnosis of PRES secondary to acute high blood pressure. This is the first case of PRES in a patient with PWS. The hypertrophic-dilatative cardiomyopathy, the arterial hypertension and the renal cystic dysplasia strongly suggested this hypothesis, confirmed by reversible characteristic MR findings.

**P2-d1-393 Obesity and Fat 1**

**Severely obese children with low birth weight demonstrate impaired cardiovascular fitness and insulin resistance compared to severely obese children with normal birth weight**

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Low birth weight (LBW) has been associated with an increased risk of insulin resistance (IR) and later in adulthood cardiovascular disease. It is also known that IR is associated with poor cardiovascular fitness in obese patients. Therefore we investigated the cardiovascular fitness and IR in obese children in regard of their birth weight. We included 163 obese children with a mean age of 11.62 ± 3.16 years and mean BMI 30.73 ± 5.3 kg/m² in this study and divided them into three subgroups according to their birth weight using Italian birth weight standards. QUICKI, ISI and HOMA-IR were calculated from a standardized OGTT. Fat distribution was determined by dual energy X-ray absorptiometry. Cardiovascular fitness was evaluated using a treadmill protocol and maximal oxygen consumption (mL/kg/min) was calculated. Twenty-four of the obese children were born with LBW, 41 were born with increased birth weight (HBW) and 98 were eutrophic. The LBW obese children had slightly lower lean body mass (%) and were slightly shorter compared to eutrophic obese children. The maximal oxygen consumption (mL/kg/min) and maximal treadmill time (min) was lower and the fasting insulin and HOMA-IR were higher in LBW obese children compared to eutrophic obese children. Also in HBW obese children fasting insulin and HOMA-IR were higher compared to eutrophic obese children. Unadjusted correlation revealed in LBW maximal treadmill time negatively related to fasting insulin (r = -0.225, P<0.05), HOMA-IR (r = -0.202, P<0.05) and fat body mass (r = -0.459, P< 0.05). In LBW and HBW obese children IR was slightly more frequent compared to eutrophic obese children. Cardiovascular fitness and IR were independently related in LBW obese children, suggesting that reduced cardiovascular fitness might be an early indicator for metabolic impairment.

**P2-d1-394 Obesity and Fat 1**

**ROHHADNET, a new syndrome with early obesity and misleading endocrine manifestations**

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ROHHAD (rapid-onset obesity with hyperventilation, hypothyroidism and autonomic dysregulation) is a newly described syndrome (Ize-Ludlow et al, Pediatrics. 2007) first reported in 1965 (Fishman, Am J Dis Child. 1965) which can cause cardiopulmonary arrests and death. We renamed the syndrome ROHHADNET to incorporate neural tumors in the acronym. This syndrome mimics several genetic obesity syndromes as well as various endocrine disorders. Endocrine studies were performed in 6 patients admitted at our clinic from 1988 to 2006 for early-onset obesity associated with growth failure in 5. The six patients later showed distinctive features of the ROHHADNET syndrome, which was recognized only after several years of evolution in 5/6. Abnormalities of the pituitary adrenal axis ranged from a true Cushing-like profile (1/6), to glucocorticoid deficiency with normal ACTH (2/6). Complete GH deficiency with low IGF1 was observed in 4/6 patients, hypogonadotropic hypogonadism in 4/6, hyperprolactinemia in 5/6, and various degrees of T3/T4 abnormalities (5/5). All had hyperammonia without diabetes insipidus. Five children had unilateral macroscopic adrenal ganglioneuroma, another source of diagnostic errors. Two patients died of cardiorespiratory arrest at 8.5 and 12 yrs of age. Given its severe prognosis, ROHHADNET should be known by pediatric endocrinologists and its diagnosis considered in cases of rapid early-onset obesity if there any added respiratory, hypothalamic, or endocrine manifestation.

**P2-d1-395 Obesity and Fat 1**

**The influence of insulin resistance on weight loss in obese prepubertal children**

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Paediatric obesity has escalated to epidemic proportions and is associated with several metabolic and cardiovascular complications. The obesity-related insulin resistance (IR) has been shown to be the main cause for the development of these complications already in youth. The aim of our study was to evaluate whether the degree of IR influences weight loss during a weight management program. We recruited 65 prepubertal Caucasian children (age mean±SD: 8.7±1.9yrs), affected by severe obesity (BMI>97th percentile). At baseline (T0), all children underwent anthropometric measurements, assessment of blood pressure, plasma lipids and fasting insulin and glucose. Homeostasis model assessment of IR (HOMA-IR) was calculated and patients were divided into two groups: group A HOMA-IR>97th percentile (n=38) and group B HOMA-IR<97th percentile (n=27). Children were encouraged to follow a hypocaloric diet for the subsequent 6 months (T6) and were assessed again at the end of this period. Differences between and within groups were analysed by unpaired or paired t-tests respectively. Associations between variables were assessed by Pearson correlation. A significant correlation was found between HOMA-IR at baseline and the change in BMI between T6 and T0 (r=0.56; p<0.0001). This change in BMI was significant different between group A and group B (-0.2±0.88 vs -1.15±1.0; p=0.003). In particular, whereas in group A there was not significant change in BMI between T6 and T0 (28.3±4.4 vs 28.5±4.0 kg/m²; p=0.1), a significant improvement in BMI was found in group B (26.5±2.5 vs 27.6±2.8 kg/m²; p<0.001). In conclusion, this study showed that a higher degree of IR is associated with a resistance in weight loss, thus suggesting that obese insulin-resistant children might need a more intensive weight management program to obtain effective results.

**P2-d1-396 Obesity and Fat 1**

**Thyroid function and metabolic syndrome in obese children and adolescents**

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An association between thyroid function and components of the metabolic syndrome in euthyroid subjects has been reported recently. The aim of the study was to evaluate the prevalence of thyroid function abnormalities in obese children and adolescents and examine the possibility of an association between them and components of metabolic syndrome. T3, T4, TSH and antithyroid antibodies were determined in 380 obese children and adolescents (154 boys), aged 3.0 to 15.5 years and in 150 healthy children of normal weight matched for age and sex. All obese children had blood pressure measurements and plasma glucose, insulin cholesterol, triglyceride and HDL determinations, while 260 of them underwent an OGTT as well. Median values of T3 and TSH of obese children were significantly higher than those of normal weight children. A positive correlation was observed between thyroid hormone concentrations and BMI z-scores of obese children. After adjustment for age, gender, sex and BMI z-scores, no significant correlation was found between T3, T4, TSH levels and HDL, cholesterol, or BP z-scores. However, an association was observed between TSH and HOMA-IR(r=0.22, p=0.01). In the group of 260 children who underwent OGTT, 20 (7.7%) were identified as having metabolic syndrome according to the WHO modified criteria. These children had also significantly higher TSH levels (p<0.05) compared to the rest of obese children. In conclusion, our findings suggested an association between thyroid function and at least two of the components of metabolic syndrome (obesity and insulin resistance) in obese children and adolescents, which needs further investigation.
Endothelial function (EF) is impaired in diseases associate with vascular complications, such as diabetes and familial hypercholesterolemia (FH). The impairment of EF assessed as flow mediated dilation (FMD) of brachial artery can predict future cardiovascular disease. To assess the alteration of EF, we longitudinally evaluate FMD in prepubertal children with genetically confirmed FH. Twelve children (7 M, 5 F; 8.19±2.90 yr) with FH and 20 control subjects entered the study. Subjects with diabetes, obesity or other metabolic disorders were excluded. In all FH patients lipid values and FMD were determined at the beginning of the study and after 32.8±9.55 mo. of diet low in saturated fat and cholesterol. FMD function was assessed by measurement of endothelium-dependent vasodilatation of the brachial artery using an ultrasound system. FMD was expressed as percentage change of diameter following reactive hyperemia from baseline. The lower FMD values obtained in our control patients were 7% so we considered it as cut-off. The baseline evaluation showed that FMD in FH children was not significantly different than control peers (20.9±23.3 vs 12.5±7.28%; p=0.143). According to sex, M were significantly older than F and had a longer follow up (38.1±7.52 vs 25.5±7.09 mo.; p = 0.015). At the end of the study, despite T-CH, LDL, HDL, and TG levels were unmodified, FMD values significantly decreased (20.9±23.3 vs 27.5±9.07%; p=0.034) resulting significantly lower than in normal subjects (p=0.002). The impairment was shown in 75% vs. 25% of children found at the start. No correlation was demonstrated between FMD and lipid levels, age and duration of the follow-up. Our data show that after few years patients with FH have a decrease of FMD values not apparently related to lipid control or to duration of diet. This difference, more evident in males, suggests that further studies are needed to better understand which factors are involved in functional changes of endothelial dysfunction.

Obesity in children is an increasingly public health problem. Effectiveness of prevention programs is not well established. Objective: To evaluate efficacy of a school-based obesity preventive program in over weight and obese children. Study design: Cross-sectional, intervention and follow-up study. Subjects and methods: 138 boys and girls aged 6 to 12 years old from a public primary school. Anthropometrical measurements and self-administered questionnaires to estimate physical activity and eating habits (KIDMED) were made at the beginning of two consecutive school years. Overweight and obesity prevalence were defined according to the International Obesity Task Force age and sex specific body mass index cut-off points. Statistical analysis: Student’s T and McNemar tests. Intervention: Global cardiovascular risk prevention program focused on obesity prevention applied over a whole school-year. The program included informative speeches and training sessions for teachers, parents and schoolchildren, and written information focused on improving eating habits, increasing physical activity and decreasing sedentary activities. Information was given and informed consent obtained. Results: 113 schoolchildren (59 boys) participated in the whole study. A slight decrease in obesity prevalence (15.9 % in 2006 vs 15% in 2007; p<0.05) and an increase in overweight (27.4% vs 35.4 %; p>0.05) were observed. There was an increase in KIDMED score (from 7.46 to 7.8). Time spent on physical activities (from 0.98 to 1.5 hours in sport activity; from 0.21 to 0.63 hours sharing daily family activities) showed a significant increase although an increase in computer time was also observed (from 0.5 to 1 hour; p<0.0001) Conclusion: This school-based intervention program failed to reach a decrease in obesity and overweight prevalence. Nevertheless, behavioural changes observed in relation to healthy eating and physical activity could be a starting point for the prevention of childhood obesity. Sources of Support: Foundation ESV-2006 grant. School program prizewinner of national NAOS strategy 2007.
Objective: To investigate the effects of a 12-week lifestyle plus exercise intervention in the school setting on metabolic syndrome markers in 7th grade children.

Methods: 104 healthy students were divided into 2 groups as follows: group 1 were controls (N = 46; Age = 12.1 +/- 0.5 yrs; Boys = 23); & group 2 (LE group) received life style & exercise intervention (N = 58; Age = 12.1 +/- 0.6 yrs; Boys = 22). The LE group alone, was further divided as <85th percentile (Lean group; N = 28), 85th -95th percentile (overweight; N = 7) or >95th percentile (Obese group; N = 22). Due to the small number of overweight children, they were not used for comparison. Detailed behavioral questionnaires & biochemical parameters were measured at baseline and post-intervention. Intervention was conducted for 12 weeks & included dance/triathlon training during and after school apart from weekly health education.

Results: Both groups were similar at baseline. After intervention both groups showed a significant decrease in waist circumference (WC) and blood pressure. In LE group, AIR, BMI increased and body fat decreased as compared to controls. Similarly, Adiponectin & IGFBP1 decreased and GDI increased, but not in control group. Among the LE subgroups, the lean subgroup had a lower percentage body fat, WC, systolic blood pressure, fasting insulin & AIR, while a higher adiponectin than the obese group at baseline & post-intervention. Both subgroups showed an increase in BMI & decreased blood pressure after intervention. The lean subgroup showed a decrease percentage in body fat, body pressure, increased IGFBP1, AIR & GDI, as compared to the obese group who showed only a decrease in blood pressure.

Conclusion: Obese children, especially with signs of metabolic syndrome, require more intensive intervention compared to lean children to achieve the same changes. Improvement in biochemical parameters can occur even before changes in BMI.

P2-d1-401 Obesity and Fat 1
Number of circulating endothelial progenitor cells is decreased in children with obesity

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Circulating endothelial progenitor cells (EPCs) are thought to preserve the integrity of the vascular endothelium and to play a role in the pathogenesis of cardiovascular disease. In this study we compared the number and functional characteristics of EPCs between obese and lean children and assessed the potential association with insulin sensitivity and endothelial dysfunction. We recruited 27 obese children (age: 12±3y, BMI-SDS: 2.3±0.52) and 33 healthy lean controls (age: 12±3y, BMI-SDS: -0.35±0.77). EPC numbers from peripheral blood were determined as CD34+/KDR+ cells in flow cytometry. Functional capacity was assessed via migration assay along an SDF-1 gradient and incorporation into a layer of human endothelial cells. Endothelial function was determined by finger plethysmography and as intima media thickness (IMT). Insulin sensitivity was evaluated by oral glucose tolerance test. The number of EPCs was significantly reduced in obese children (73±6 vs. 121±13 cells/ml blood, P<0.005) and correlated inversely with BMI SDS (r=-0.26, P<0.05). Migration of EPCs appeared mildly reduced in obese children but this difference did not reach statistical significance (16710±2579 vs. 21280±2419 cells/300mm2). Incorporation into endothelial structures was not different between EPCs of obese and lean children. Clinically, endothelial function was significantly impaired in obese subjects (RHI 1.6±0.04 vs. 1.8±0.12, P<0.001) and IMT was increased (0.04±0.01 vs. 0.03±0.001 mm, P<0.0001) and was significantly associated with 24h-blood pressure (r=0.48, P=0.0004). There was, however, no correlation between EPC number and endothelial dysfunction. The significantly impaired insulin sensitivity in obese children compared to lean controls was also not associated with EPC number or functional parameters. In summary, children with obesity already show reductions in circulating EPCs, insulin resistance and endothelial dysfunction, which are strong indicators of cardiovascular sequelae of obesity.

P2-d1-402 Obesity and Fat 1
Modelling strategies to address childhood overweight and obesity in the UK: An exploratory cost-utility analysis

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Objectives: Following a systematic review and economic analysis which demonstrated that screening for the detection of growth-related disorders and other potentially treatable conditions missed by other routes is cost-effective, in this study we explored the cost-utility of screening strategies to address the long-term effects of childhood overweight and obesity.

Research Methods and Procedures: Economic modelling was based on a systematic review from the perspective of the UK NHS. Three strategies were compared with a do nothing alternative: 1) primary prevention of overweight and obesity using a school-based programme, without screening; 2) primary prevention of overweight and obesity using a school-based programme with screening of body mass index (BMI); 3) BMI screening and treatment for children found to be above a pre-defined threshold. The model’s output was the incremental cost per quality-adjusted life year (QALY). Probabilistic sensitivity analyses were performed to assess uncertainty in the model’s parameters.

Results: The baseline result for primary prevention without screening was £290 per additional QALY. Screen and treat compared with the do nothing option is marginally cost-effective at £37900 per QALY gained. The sensitivity analyses revealed considerable uncertainty in the model’s estimates. Primary prevention alone has a probability of one of being cost-effective at a willingness to pay value of only £3000, while screen and treat compared with the do nothing option can produce an ICER of £150000 per additional QALY in some scenarios.

Discussion: Primary prevention for childhood overweight potentially has very promising cost-effectiveness. However, the clinical evidence underpinning this study has considerable uncertainty which means that the results need to be treated with caution. This study, however, lays a useful platform for future work in assessing strategies to deal with childhood overweight and obesity.

P2-d1-403 Obesity and Fat 1
Prevalence of insulin resistance and metabolic syndrome in obese children and adolescents as to migration background

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Insulin resistance is known as an important risk factor for the occurrence of the metabolic syndrome. Ethnic subgroups are high risk groups for R-HOMA-elevation and metabolic syndrome as compared to white population. We investigated if children with other than German background should be seen as high risk groups regarding R-HOMA-levels and metabolic syndrome. In the paediatric obesity centre at the Charité Children’s hospital data about migration background and R-HOMA levels were available in 922 patients (50.1% Germans, 26.4 % Turkish , 23.5 % other countries). We used R-HOMA reference values by Allard (2003), Metabolic syndrome was defined by WHO-definition. BMI-SDS was based on reference values by Kromeyer-Hauschild (2001). We used CHI² and Mann-Whitney-U-Test and multiple logistic regression models for multivariate statistic analysis. The Turkish patient group significantly more often shows a pathological elevation of R-HOMA as compared to Germans (p<0.05) and others (p<0.05). After stratification for BMI-SDS we found significantly higher R-HOMA-values for Turkish patients.
who are overweight (BMI-SDS <2) or obese (BMI-SDS 2-2.5). In extreme-
ly obese German, Turkish and other patients (BMI-SDS > 2.5) we do not see
any difference in their R-HOMA-values. In a multiple logistic regression
model the target variable “metabolic syndrome” is explained by age (OR 1.1
(CI: 1.02-1.14)) and migration background Turkish vs. German (OR 1.7 (CI:
1.13-2.68)). Turkish patients are more likely to have pathological R-HOMA-
levels and metabolic syndrome. Overweight and obese patients with Turkish
background have significantly higher R-HOMA levels. Extremely obese pa-
tients have a high risk for R-HOMA-elevation independent of their migration
background. Therefore, preventive strategies should turn their special effort
to patients with Turkish migration background as a high risk group before
getting extremely obese and suffering from metabolic syndrome.

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**P2-d1-404 Obesity and Fat 1**

Role of valproic acid in the development of insulin resistance in non obese pre-pubertal children.

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Valproic acid (VPA) is an effective treatment for epilepsy, but its use has been shown to be associated with increased body weight and metabolic changes, including insulin resistance (IR). However, it is not clear whether the development of IR is related to the treatment itself or to the associated weight gain. The aim of the present study was to evaluate whether VPA therapy could determine IR and alterations in glycaemic control in non obese pre-pubertal children treated with VPA. Eight children (5 boys; age(mean±SD):7.3±1.7years) in treatment with VPA for at least 1 year (VPA+) and 7 children (4 boys; age:8.7±2.7years) off VPA therapy for at least 6 months (VPA-) were compared with 12 healthy controls (6 boys; age:7.7±2.7years). All children underwent anthropometric measurements and an oral glucose tolerance test (OGTT), and IR indices (HOMA-IR, WBISI, QUICKI) were calculated. Differences in variables between the three groups were analysed by Kruskall-Wallis test with Mann-Whitney test for post-hoc comparisons. No significant difference was found in terms of BMI among the three groups (VPA+:18.5±4.0; VPA-:16.6±1.0; controls:15.8±2.0kg/m²; p=0.06). Fat mass was significantly higher in VPA+ children when compared to controls (27.5±7.71 vs 20.18±4.82kg/m²; p=0.04), whereas no difference was found between the two VPA groups and between VPA- children and controls. None of the children showed carbohydrate intolerance or hyperinsulinemia. This was associated with no significant difference in IR indices across the three groups (p>0.05). In conclusion, this study showed that IR was not present in children in and off treatment with VPA who did not develop obesity, even though an increased fat mass was found in those still on therapy. This suggests that the described IR in obese children in therapy with VPA might be a conse-
quence of obesity, and later amplified by treatment itself.

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**P2-d1-405 Obesity and Fat 1**

Increasing prevalence of iron deficiency in overweight and obese children and adolescents

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Background: The prevalence of childhood obesity is increasing worldwide. Since obesity is associated with increased morbidity and mortality, the World Health Organization has compared the marked increased to a global epidemic. Recent studies have reported thyroid function derangement in obese subjects, both adults and children, but the pathophysiologic mechanism is not well understood. The goal of our study is to investigate the relationship between thyroid hormones and adiposity and to determine if there is an association between sub-clinical hypothyroidism and metabolic risk factors in a sample of Iranian obese children.

Methods: 250 obese children (111 girls, 104 boys; BMI z-score 2-2.5) were evaluated. Serum glucose, insulin, triglyceride, HDL cholesterol, TSH, FT4, anti-tyroglobulin and anti-per-
oxidase antibodies were determined and blood pressure and waist circumfe-
rence were measured. Sub-clinical hypothyroidism was diagnosed (TSH was higher than 4.5 micrU/ml, with normal FT3 and FT4 and no signs or symp-
toms of hypothyroidism) in 48 patients (8.8%), 11/48 had positive antibodies and have been excluded from the analysis; in total 55/540 (10.1%) had positive auto-antibodies and were excluded from the analysis. There was a positive correlation between TSH and BMI z-score (p=0.0045) and FT3 BMI z-score (p=0.0034) and no correlation with any parameter, including between TSH and FT3 and FT4. In a multiple regression analysis adjusted for gender, age, the increase in TSH and insulin resistance index (HOMA), there was no correlation between TSH and HDL, triglycerides, blood pressure as well as between FT3 or FT4 and all the mentioned parameters. Children with TSH>4.5 micrU/ml did not differ significantly in any of the evaluated parameters from those with TSH in the normal range (table 1).

We limited our measurement to overweight and obese students (n=700) and 420 normal weight students matched for age and sex.

Results: The mean body mass index was 21.47 ± 3.5 Kg/m². In the total study population 17.9% were overweight (BMI ≥ 85th and <95th percentile) and 7.1% were obese (BMI ≥ 95th percentile). Iron deficiency was most pre-
valent among 13 to 15 years old children (6.4%) followed by 16 to 17 years old children (5.5%) and then 11 to 12 years old subjects (2.9%). Overall, the prevalence of iron deficiency increased as BMI increased from normal weight to overweight to obese (2.5%, 5.3%, and 6.9% respectively) and 13 to 15 years old adolescents demonstrated the highest prevalence of iron deficiency, which similarly increased as weight status increased (3.3%, 6.7%, and 9.2% respectively). Logistic regression analysis showed children who were overweight and obese were at least approximately twice more likely to be iron deficient as those who had normal weight.

Conclusion: With respect to increasing numbers of overweight children and the known morbidities of iron deficiency, these findings inaccordance with other studies suggest that physicians should be aware of this propable asso-
ciation, and screening for iron deficiency should be justified in children and adolescents with elevated BMI in particular female subjects.

Keywords: Iron deficiency, Obesity, Children, Adolescents

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**P2-d1-406 Obesity and Fat 1**

Thyroid function derangement and sub-clinical hypothyroidism in obese children

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Recently several studies have reported thyroid function derangement in obe-
se subjects, both adults and children, but the pathophysiologic mechanism is not well understood. The aim of our study is to investigate the relationship between thyroid hormones and adiposity and to determine if there is any asso-
ociation between sub-clinical hypothyroidism and metabolic risk factors in a sample of Italian obese children. We examined 540 obese children (269 females, BMI z-score 2.9±0.8, age 9.9±2.5 years). Serum glucose, insulin, triglyceride, HDL cholesterol, TSH, FT3, FT4, anti-tyroglobulin and anti-per-
oxidase antibodies were determined and blood pressure and waist circumfe-
rence were measured.

Sub-clinical hypothyroidism was diagnosed (TSH was higher than 4.5 micrU/ml, with normal FT3 and FT4 and no signs or symp-
toms of hypothyroidism) in 48 patients (8.8%), 11/48 had positive antibodies and have been excluded from the analysis; in total 55/540 (10.1%) had positive auto-antibodies and were excluded from the analysis. There was a positive correlation between TSH and BMI z-score (p=0.0045) and FT3 BMI z-score (p=0.0034) and no correlation with any parameter, including between TSH and FT3 and FT4. In a multiple regression analysis adjusted for age, gender, degree of overweight and insulin resistance index (HOMA), there was no correlation between TSH and HDL, triglycerides, blood pressure as well as between FT3 or FT4 and all the mentioned parameters. Children with TSH>4.5 micrU/ml did not differ significantly in any of the evaluated parameters from those with TSH in the normal range (table 1).

Results: The mean body mass index was 21.47 ± 3.5 Kg/m². In the total study population 17.9% were overweight (BMI ≥ 85th and <95th percentile) and 7.1% were obese (BMI ≥ 95th percentile). Iron deficiency was most pre-
valent among 13 to 15 years old subjects (6.4%) followed by 16 to 17 years old children (5.5%) and then 11 to 12 years old subjects (2.9%). Overall, the prevalence of iron deficiency increased as BMI increased from normal weight to overweight to obese (2.5%, 5.3%, and 6.9% respectively) and 13 to 15 years old adolescents demonstrated the highest prevalence of iron deficiency, which similarly increased as weight status increased (3.3%, 6.7%, and 9.2% respectively). Logistic regression analysis showed children who were overweight and obese were at least approximately twice more likely to be iron deficient as those who had normal weight.

Conclusion: With respect to increasing numbers of overweight children and the known morbidities of iron deficiency, these findings inaccordance with other studies suggest that physicians should be aware of this propable asso-
ciation, and screening for iron deficiency should be justified in children and adolescents with elevated BMI in particular female subjects.

Keywords: Iron deficiency, Obesity, Children, Adolescents
The prevalence of obesity continues to increase in most populations worldwide. Excess body weight is a risk factor for the development of severe chronic diseases (e.g. cardiovascular, diabetes mellitus, cancer). Socioeconomic status is an important factor associated with obesity. Aim of the study was to examine the secular trend of Body Mass Index (BMI) and the prevalence of overweight and obesity in young Greek men. This cross-sectional study was performed from May 2006 to August 2007 and was based on anthropometric data collected from 4196 conscripts of the Greek Army, aged 18-26 years. BMI was correlated to socio-demographic characteristics, i.e. the level of education, determined by the years of schooling (≤ 9, 10-12, ≥ 13), and the place of residence (metropolitan cities, urban, semi-urban and rural) of the subjects. Overweight and obesity were defined according to the WHO classification. The results of this study were compared with similar studies that were performed in Greek conscripts in the years 1969 and 1990. Mean BMI (±SD) of the conscripts of the present study was 25.1 (4.9), whereas in the year 1969 it was 23.8 (±1.8) kg/m², p<0.0001 and in 1990 it was 23.8 (±2.9) kg/m², p<0.0001. Prevalence of overweight in the present study was 30% whereas that of obesity was 12%. Overweight and obesity were not correlated with the place of residence, however there was a significant positive correlation between overweight and higher education (p<0.01), and a negative correlation between obesity and low educational level (p<0.01). Our data show a significant increase in the BMI in Greek conscripts in the last 18 years, as well as an alarmingly high prevalence of overweight and obesity in young Greek men. Overweight was correlated positively with a higher educational level, whereas obesity was correlated positively with a low educational level.

The secular trend of Body Mass Index (BMI) and the prevalence of overweight and obesity in young Greek men

**Conclusions:** A negative energy balance together with maintained physical exercise induces changes in body composition in ballet dancers. 2. Lower leptin levels and higher adiponectin levels seem to be more related with BFM than BMI.

**P2-d1-409 Obesity and Fat 1**

**Prevalence of the metabolic syndrome according to the IDF criteria in children and adolescents with overweight or obesity**

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The International Diabetes Federation has recently published a consensus on the definition of the metabolic syndrome (MS) in children (<10yrs) and adolescents. MS was defined as a waist circumference (WC) ≥90 or two or more of the following: fasting glucose ≥5.6mmol/L, triglycerides (TG) ≥1.7mmol/L, HDL-cholesterol (HDL) <0.9mmol/L, systolic blood pressure (SBP) ≥130mmHg or diastolic blood pressure (DBP) ≥85mmHg. The above mentioned definition of MS was used to assess the prevalence of MS in Dutch children/adolescents with overweight (OW) or obesity (OB) according to international criteria. Subjects were included if WC measurement were available, aged >10yrs and referred to a paediatrician. Data of 115 subjects met these criteria (OW/OB:17/98; M/F:44/71; age:13.0±2.1yrs; WC:98.1±12.4cm; Body Mass Index standard deviation score (BMI-SDS): 2.0±0.5). None of the OW met the criteria for MS, 16 had WC ≥P90 with none or one other criterium (6 criteria (OW/OB:17/98; M/F:44/71; age:13.0±2.1yrs; WC:98.1±12.4cm; Body Mass Index standard deviation score (BMI-SDS): 2.0±0.5). None of the OW met the criteria for MS, 16 had WC ≥P90 with none or one other criterium (6
hypertension; 2 increased fasting glucose; 1 increased TG; 1 decreased HDL). The prevalence of MS in OB subjects was 18.4% (18/98). The OB with the MS compared to the OB without had significantly higher WC (103.9±13.8cm), BMI-SDS (3.5±0.9), SBP (134.4±14.1mmHg) and DBP (71.5±9.6mmHg), fasting glucose (5.5±0.8mmol/L), and lower HDL (1.1±0.3mmol/L). There was no significant difference in gender, age or TG between the OB with and without MS. In OB with MS hypertension was seen most frequently (77.8%, 14/18), followed by decreased HDL (61.1%, 11/18), and increased TG and fasting glucose (both 38.9%, 7/18). In conclusion, none of the OW met the criteria for MS, although most of them showed a WC ≥90. In the OB the prevalence of MS was 18.4%. Hypertension and decreased HDL, indicating vascular implications, seemed to be the most frequent accompanying early signs of MS in this population. Therefore measurements of WC and blood pressure are the most important clinical parameters in evaluating OW and OB children/adolescents.

**P2-d1-411 Obesity and Fat 1**

**Relationship of metabolic syndrome according to the IDF criteria with fasting insulin and C-peptide levels in obese children and adolescents**

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The International Diabetes Federation (IDF) published criteria for metabolic syndrome (MS) in children age>10yrs in 2007. MS is defined as waist circumference (WC) ≥90 and 2 or more of the following parameters; fasting glucose (FG) ≥5.6mmol/L, triglycerides (TG) ≥1.7mmol/L, HDL-cholesterol (HDL)<1.03mmol/L, systolic blood pressure (SBP) ≥130mmHg or diastolic blood pressure (DBP) ≥85mmHg. However, diagnosis of MS in children does not yet represent a clinical affliction for developing cardiovascular disease or diabetes later in life. We evaluated the diagnosis of MS in relation to fasting insulin (FI) and fasting C-peptide (FCP), indicative of early signs of diabet, in obese children referred for family-based multidisciplinary cognitive behavioural treatment. Data were included of 43 obese subjects (M/F:17/26; age:13.0±2.1yrs; WC:90.4±9.5cm; BMI-SDS:3.0±0.8; FI:19.7±12.1mU/L; FCP:1.05±0.35nmol/L). Prevalence of MS was 25.6% (11/43) and subjects with MS (OBMS+) had significantly higher WC (96.7±7.6cm), BMI-SDS (3.5±0.6), FI (30.6±12.8mU/L), and FCP (1.37±0.28nmol/L) compared to subjects without MS (OBMS-). Increased FG levels (≥5.6mmol/L) were seen in 36.4% (4/11) of the OBMS+ subjects. Unexpectedly increased FCP (>0.630mmol/L) levels were already present in 84.4% (23/32) of OBMS- subjects with normal mean FI levels of 15.2±7.7mU/L (n=23). A positive family history for diabetes (pHFD) was present in 90.9% (10/11) of OBMS+ compared to 87.5% (28/32) of OBMS- No significant gender or age difference existed between OBMS+ and OBMS- subjects. MS in obese children is positively related to increased FCP and FI levels, indicative of early signs of type 2 diabetes mellitus. In OBMS- subjects increased FCP levels may precede increased FI levels. Therefore, when evaluating the obese child with a positive FHD we recommend measurement of not only fasting glucose, but also fasting insulin and C-peptide.

**P2-d1-412 Obesity and Fat 1**

**Assessment of metabolic syndrome incidence in obese children and adolescents, residents of Uzbekistan, by new IDF (2007) criteria**

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**Aim:** to assess metabolic syndrome (MS) incidence in children and adolescents with exogenous constitutional obesity (ECO).

**Materials and Methods:** 144 children and adolescents were examined (57 with ECO, 84 constituting control group). MS was diagnosed in compliance with the international criteria for children and adolescents. The examinees were divided into two groups: 6-10 years and 10-16. BMI, waist circumference (WC), lipid profile were measured, glucose tolerance test (GTT) being performed with assessment of insulin secretion and HOMA (Homeostasis model assessment) index.

**Results and Discussion:** WC had confident difference in both age groups (79.3±2.6 and 94.7±1.9cm) as compared with the control (57.4±1.1 and 64.4±0.8cm). Hypertriglyceridemia was observed in 60% of the 1st age group examinees and in 65% of those in the 2nd one, the levels of high density lipoproteins (HDL) lower than the proposed criteria in the 1st and 2nd groups were observed in 40% and 30%, respectively. In fasting obese examinees hyperinsulinemia was observed in both age groups, HOMA index being 2.9±0.7 and 3.8±0.6 in the groups to be significantly higher than in the controls (0.8±0.1, P<0.05, and 1.0±0.1, P<0.05, respectively). In obese patients of the 1st age group not more than two MS components were observed, WC ≥90 percentile being found in 87%, triglycerides 60% and HDL 40% with HOMA index ≥95 percentile being 62.5%. There were three and more MS components in the 2nd age group. WC ≥90 percentile being found in 83%, triglycerides in 74% and HDL in 30%. Arterial hypertension was registered in 11%, HOMA index ≥90 percentile in 64.5%, fasting glucose ≥5.6 mmol/L being observed in 2.1%.

**Conclusions:** in compliance with new diagnosis criteria in children and adolescents (IDF, 2007) in the 6-10 year age group MS was unobserved, in 12% of patients with ECO in the 10-16 year age group the diagnosis was established.

**P2-d1-413 Obesity and Fat 1**

**Prevalence of metabolic syndrome in obese schoolchildren according to a new definition**

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Recently, in 2007, the IDF published the definition of metabolic syndrome for children. We evaluated prevalence of metabolic syndrome (MS) in obese children according to the IDF definition. 336 children (161 girls), aged 6-16 y.o. with obesity (BMI criteria, T.J. Cole et al., 2000) were involved, among them - 109 children 6-10 y.o.. Height, weight, waist circumference (WC) at the umbilicus level, upper body fat mass (BIA), BP, serum cholesterol, triglycerides, lipoproteins, blood glucose levels were measured. Almost all children (97.9%) presented WC > 90 percentile cut-point level for age and gender (Regional references, 2004-2006). Metabolic syndrome was revealed in 33.9% of boys and 27.9% girls 10-16 y.o.. As there are no IDF recommended cut-off values of lipids and BP for children under 10 y.o., we used the same for HDL-C and 1.3 mmol/l for triglycerides, SBP and/or DBP > 90 percentile for age and gender, adopted to height percentile. The prevalence of MS in 6-10 age group was 27% in boys and 23.7% in girls. The prevalence of MS increased significantly with the degree of obesity in both age groups. Upper body fat mass % (UFM%) - the marker of visceral fat closely correlated with BMI and WC in girls, and there was only slight correlation with BMI in boys, while strong positive correlation of UFM% and waist-to-height ratio (WHR) was registered in both. UFM% and WHR closely correlated with BP, LDL-C, and inversely so with HDL-C. Conclusions: In addition to BMI standard, WC > 90 percentile cut-point may be the marker of obesity in children. However, waist-to-height ratio seems to be better standard to define “abdominal obesity” in children. Almost quarter of prepubertal obese schoolchildren present MS, and it demands new universal risk factors criteria for this age group, suitable for follow-up and evaluation of intervention effect.

**P2-d1-414 Obesity and Fat 1**

**A new device for measuring resting energy expenditure (REE) in severely obese children and adolescents with and without non-alcoholic fatty liver disease (NAFLD)**

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Obesity is a result of an energy imbalance. Lifestyle change targeted towards increasing daily energy expenditure is one of the cornerstones of obesity.
Serum Visfatin levels cannot represent the degree of obesity and insulin resistance in children and adolescents

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Visfatin is an adipocytokine secreted from the visceral fat, which the cDNA resembles the pre-B cell colony enhancing factor. In vivo tests with mice demonstrated a insulin-mimicking effect, which is caused by up-regulating intracellular insulin receptors. In our study, we focused on whether there were differences in serum Visfatin level between obese and non-obese population, and insulin resistant and non-resistant population. Also correlations between serum Visfatin levels and height, weight, BMI, AST/ALT, lipid profiles, insulin and glucose were obtained. 22 obese children and adolescents who had a BMI over 95 percentile of their age and sex and 26 healthy controls were selected and serum Visfatin and AST, ALT, lipid profiles, insulin and glucose were obtained. Significant differences were observed in serum ALT and HOMA-IR (p<0.05) but serum Visfatin showed no significant differences between the obese group and controls. Serum Visfatin showed no significant correlations between anthropometric data, AST, ALT, glucose, insulin, lipid profile and HOMA-IR in the obese group. All 48 study participants were divided into 2 groups by insulin resistance (HOMA-IR values more than 3, or less). Comparison of serum Visfatin between both groups showed a slightly increased level but statistically no significance (Insulin resistant 32, 37.33%± 15.68ng/ml vs. control 16, 35.78%± 9.75ng/ml, p=0.72). The only significant difference in mean was observed in serum triglyceride. No significant correlation between serum Visfatin and other variables were observed in the insulin resistant population. There were no direct correlations with serum Visfatin and variables regarding obesity (BMI) and insulin resistance(HOMA-IR) in children and adolescents. This might suggest that serum level of Visfatin might not represent the actual activity of this molecule in intracellular receptors. Further studies with OGTT and other variables regarding insulin resistance and obesity should be obtained to confirm our current conclusions.

Tumor necrosis factor alpha (TNFα) gene G-308A polymorphism is not associated with incidence of the metabolic syndrome in children with obesity

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We investigated whether the polymorphism of TNFα gene can predict the incidence of metabolic syndrome in children with obesity.

Material and Methods: the data came from a group of 124 children with obesity: 72 girls and 52 boys. In the control group (56 non-obese; 36 girls and 20 boys) only genetic tests was taken. The anthropometric parameters included: body height and weight, waist and hip circumferences, the thickness of 3 and 10 skinfolds. BMI, WHR and total fat by Slaughter were calculated. Each child’s blood pressure was measured. Biochemical tests consisted of: triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, leptin. The oral glucose tolerance test with measurements of glucose and insulin levels was performed. Insulin sensitivity and insulin resistance indices were calculated. Results: there were more frequent carries the A allele in the study group than in the control group (in the study group: G/G=48%, A/G=45,5%, A/A=6,5%, in control group: G/G=66%, A/G=30,4%, A/A=3,58%). In group study and control group for genotype (A/A+G/G) odds ratio [OR]=2,29, 95% confidence interval [CI],1,84-5,44, Chi²=2,62, p<0,05, for genotype AA OR=1,88, 95% CI 0,39-9,15 Chi²=2,67, p<0,05. Lower levels of HOMA index (3,04 +/- 1,51 vs 3,68 +/- 1,98, p<0,05). A comparison of the frequencies of appearance of the metabolic syndrome factors in the group with an unfavorable genotype and in the group of wild homozygous did not show any differences. AA+AG vs GG OR=0,62, 95% CI 0,14-2,73, Chi²=2,09 NS. Our data indicate that TNFα polymorphism in obese children seem not to be associated with the insulin resistance and the incidence of metabolic syndrome.
Association of osteoprotegerin and RANKL levels with insulin resistance in pubertal obese children
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Recent studies on the biology of bone have provided major advancements and suggested that activation and regulation of osteoclasts is controlled through locally active factors synthesized by osteoblasts or stromal cells. It has been also found that intercellular connections and osteoclastogenesis are regulated by osteoprotegerin (OPG)/RANK/RANKL system. OPG suppresses differentiation and activation of osteoclasts; whereas major effect of RANKL is inhibition of osteoclast apoptosis through activation and stimulation of osteoclast differentiation. OPG/RANK/RANKL system plays an important role in the reorganization of bone. Additionally, studies on adults have suggested that OPG may be related with vascular injury and atherosclerosis and have some effect on angiogenesis. Considering these information, we aimed to detect the levels of OPG and RANKL, particularly in obese children in the pubertal period and to investigate whether these parameters are correlated with insulin resistance in childhood. Study included 66 obese children with the age ranging from 9.1 to 18 years and 22 non-obese children with the age ranging from 10.5 to 18 years. Blood glucose, insulin, total cholesterol, HDL cholesterol, LDL cholesterol were measured and HOMA-IR, QUICKI and othergenic index were calculated. Serum OPG and RANKL levels were measured by ELISA method. OPG and RANKL levels did not show any difference between obese and non-obese children (p>0.05). No difference of these two parameters was observed among the children with and without insulin resistance (p>0.05). No correlation could be established between OPG and HOMA-IR, QUICKI, or othergenic index. BMD did not show correlation with OPG or RANKL. A negative correlation was observed between BMI and the QUICKI. Association of OPG levels with hyperinsulinism and insulin resistance indexes among adults has been reported in the literature and lack of this association in our study can be explained by realization of the effect of obesity and insulin resistance in the later period of life to become able to change some of the parameters.

Relationship between the K121Q polymorphism of ectonucleotide pyrophosphatase/phosphodiesterase 1 and obesity in children and adolescent
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Background: Obesity is considered to be a multifactorial trait resulting from the combined influence of genetic and environmental determinants. Nucleotide pyrophosphatase/phosphodiesterase (ENPP1) is an inhibitor of insulin-induced activation of the insulin receptor. Clinical studies have demonstrated the K121Q variant in the 4 exon of the ENPP1 gene might be associated with the obesity and insulin resistance in western children.

Objective: To study the relationship between K121Q variant and insulin resistance in obese children and adolescents among Chinese Han populations.

Method: 464 obese/overweight and 223 normal children and adolescents were recruited. The k121Q variant of the ENPP1 was genotyped by Taqman-MGB technology; their Body mass index (BMI), fasting insulin level, total cholesterol, triglyceride, and plasma glucose were determined. HOMA-beta and HOMA-IR were calculated.

Result: 1) The frequencies of K allele is the 0.894, Q allele is the 0.106 in the obese group, 0.907 and 0.093 in the overweight group, 0.879 and 0.121 in the normal group, respectively. There were no significant statistic differences in obesity/overweight group and normal group with different genotypes (OR=0.48, P=0.452). 2) Logistic regression analysis showed that the K121Q variant of the ENPP1 gene was not associated with the fasting insulin, glucose and lipid. 3) No association was found between the k121Q variants of ENPP1 and HOMA-beta(0.28) or HOMA-IR(0.94). No significant association existed between the different sex with HOMA-beta or HOMA-IR.

Conclusions: We find no evidence that the ENPP1 K121Q genotype is associated with obesity and insulin resistance in Chinese children and adolescents.
The aims of this study were to compare the effects of weight—loss diets of different macronutrient compositions on weight and Health—related quality of life (HRQOL), and to exa—mine the relationship changes in HRQOL parameters and weight—loss during weight loss programs in obese adolescents. 71 adolescents (12—18y, BMI >95th percentile) were randomly assigned to one of three 12—week diets regimens: low—carbohydrate high—fat (LCHF), low—carbohydrate low—fat (HCLF) and low—carbohydrate low—fat (LCLF). Weights, height and fat—mass percentage were measured, and the PedsQL 4.0 questionnaires were administered at the participants at baseline and at the end of the intervention. Significant similar reductions in BMI, BMI—SDS, and fat—mass percentage occurred in all 3 groups. A significant improvement in HRQOL was found only in the LCLF group. For the entire sample, significant positive correlations were found between emotional and psychosocial functioning at baseline and HRQOL parameters and weight—loss during weight loss programs in obese adolescents.

Poster Presentations

**P2-d1-422 Obesity and Fat 1**

**Influence of weight loss diets with different macronutrient compositions on health related quality of life in obese youth**

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The childhood obesity epidemic attacks the autochthonous as well as the al—lochthonous population. However, the eating habits are different. Many al—lochthonous children still eat the traditional food from the country of origin. We compared the dietary intake of in Belgium living Turkish obese children with that of native Belgian obese children, and determined how they deviate from the HGR—norms (N). The dietary intake of 15 in Belgium living Turkish obese children (group T; 10 girls; mean±SD age: 12.2±2.3 yrs; BMI: 23.2±3.6) and of 15 native obese children (group B; 10 girls; age: 12.3±2.6 yrs; BMI: 2.4±0.6 SDS) was studied by the 7—d record method. Data were analyzed with the Becl Institute Nutrition Software. The energy intake was comparable in both groups (T: 2520±285 Kcal/day; B: 2438±283 Kcal/day) and higher (p<0.001) than the recommendation (T: 118±12%; B: 115±11%; N: 100%). Macronutrient intake (expressed as % of daily energy intake) also was similar: carbohydrates: T: 49.8±4.4%, B: 48.4±3.8% (N: 55%); proteins: T: 13.1±1.3%, B: 13.9±1.5% (N: 12%); fat: T: 37.0±3.5%, B: 37.7±3.4% (N: 32%). Protein and fat intake was higher than the norm (p<0.001); carbohydrate intake was lower (p<0.001). Macronutrient subgroups were different. Polyunsaturated fats intake was lower in group T (29.2±3.4% vs 27.7±3.5%; p<0.05). In group T intake of saturated fat (14.0±1.6% vs 15.6±1.5%; p<0.01) and monounsaturated fat (5.7±1.1% vs 6.5±0.8%; p<0.05) was lower, whereas monounsaturated fat intake was higher (13.6±1% vs 11.9±2.1%; p<0.05). The vitamin D3 intake was lower in group T (1.8±1.0 µg/day vs 3.0±1.1 µg/day; p<0.005). We conclude that although the macronutrient intake was comparable between Turkish and Belgian obese children, the macronutrient composition was different reflecting cultural differences in eating habits. The target of nutritional intervention should be the same in both groups, namely lowering the intake of energy and saturated fat, and stimulating the use of fruits, vegetables and fish. The recommendations must be adapted to the tra—ditional eating habits.

**P2-d1-423 Obesity and Fat 1**

**Differences in nutrient intake between Turkish obese children living in Belgium and native Belgian obese children**

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Virga Jesseezehnhausi, Paediatric Endocrinology, Hasselt, Belgium

The childhood obesity epidemic attacks the autochthonous as well as the al—lochthonous population. However, the eating habits are different. Many al—lochthonous children still eat the traditional food from the country of origin. We compared the dietary intake of in Belgium living Turkish obese children with that of native Belgian obese children, and determined how they deviate from the HGR—norms (N). The dietary intake of 15 in Belgium living Turkish obese children (group T; 10 girls; mean±SD age: 12.2±2.3 yrs; BMI: 23.2±3.6) and of 15 native obese children (group B; 10 girls; age: 12.3±2.6 yrs; BMI: 2.4±0.6 SDS) was studied by the 7—d record method. Data were analyzed with the Becl Institute Nutrition Software. The energy intake was comparable in both groups (T: 2520±285 Kcal/day; B: 2438±283 Kcal/day) and higher (p<0.001) than the recommendation (T: 118±12%; B: 115±11%; N: 100%). Macronutrient intake (expressed as % of daily energy intake) also was similar: carbohydrates: T: 49.8±4.4%, B: 48.4±3.8% (N: 55%); proteins: T: 13.1±1.3%, B: 13.9±1.5% (N: 12%); fat: T: 37.0±3.5%, B: 37.7±3.4% (N: 32%). Protein and fat intake was higher than the norm (p<0.001); carbohydrate intake was lower (p<0.001). Macronutrient subgroups were different. Polyunsaturated fats intake was lower in group T (29.2±3.4% vs 27.7±3.5%; p<0.05). In group T intake of saturated fat (14.0±1.6% vs 15.6±1.5%; p<0.01) and monounsaturated fat (5.7±1.1% vs 6.5±0.8%; p<0.05) was lower, whereas monounsaturated fat intake was higher (13.6±1% vs 11.9±2.1%; p<0.05). The vitamin D3 intake was lower in group T (1.8±1.0 µg/day vs 3.0±1.1 µg/day; p<0.005). We conclude that although the macronutrient intake was comparable between Turkish and Belgian obese children, the macronutrient composition was different reflecting cultural differences in eating habits. The target of nutritional intervention should be the same in both groups, namely lowering the intake of energy and saturated fat, and stimulating the use of fruits, vegetables and fish. The recommendations must be adapted to the tra—ditional eating habits.

**P2-d1-424 Obesity and Fat 1**

**A common Gly972Arg polymorphism in insulin receptor substrate-1 gene is not associated with insulin resistance and metabolic syndrome in children with obesity**

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Medical University, Pediatric and Endocrinology, Warsaw, Poland

We investigated whether the Gly972Arg polymorphism in the insulin receptor substrate-1 can leads to insulin resistance and incidence of metabolic syndrome. Material and methods: the study group consisted of 112 children with obesity (62 girls and 50 boys), the control group of 56 non-obese children (36 girls and 20 boys) In control group only genetic tests was taken. The anthropometric parameters included: body height and weight, waist and hip circumferences, the thickness of 3 and 10 skinfolds. BMI, WHR and total fat by Slaughter were calculated. Each child’s blood pressure was measured. Biochemical tests consisted of: triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, lepitin. The oral glucose tolerance test with measurements of glucose and insulin levels was performed. Insulin sensitivity and insulin resistance indices were calculated. On basis the modified ATP III criteria by Ferranti, the Polish cut points were used to evaluate the incidence of the metabolic syndrome. Results: in study and in control group there were not evidences of homozygos AA. There were more frequent carries the A allele in the study group than in the control group (in study: A/C - 8.94% in control; A/C - 5.36%). The incidence of wild variant in study group was C/C - 91.06%, in control C/C - 94.65%. In study group vs control group A/C odds ratio OR=1.74, 95% confidence interval [CI] 0.46-6.48, Chi=2=0.73, NS. Comparative analyses assessing the influence of polymorphism in insulin sensitivity, resistance indices, lipids and blood pressure did not showed statistical differences. A comparison of the frequencies of appearance of the metabolic syndrom factors in the group with an unfavorable genotype and in the group of wild homoyzogo re did not show any differences. A/C vs C/C OR=2.39, 95% CI 0.14-2.73 Chi=2=1.76 NS. Our data indicate that Gly972Arg polymorphism in the insulin receptor substrate-1 in obese children seem not to be associated with the insulin resistance and the incidence of metabolic syndrome.
Insulin resistance (IR) in prepubertal obese children is postulated to be an initial condition for further metabolic disturbances. Adipose tissue distribution and the adipokine profile may influence the development of IR in childhood obesity. We compared body composition, as well as circulating levels of adipokines, resistin, IL-6, TNF-α, leptin and its soluble receptor (sOBr), between obese children with or without IR. Seventy Caucasian obese children (Tanner I, 48 males and 22 females) were studied. An OGTT (1.75 g/kg, maximum 75g) and DEXA scan (Hologic QDR4500W) were performed. Se-

Correlations: BMI correlates positively with TG/HDL in high TG/HDL group (R=0.54, p<0.05). sOB-R correlates positively with adiponectin in severe IR group (R=0.59, p<0.05) and with TG/HDL in high TG/HDL group (R=0.54, p<0.05). sOB-R correlates positively with adiponectin in normal TG/HDL group (R=0.54, p<0.05) and negatively with weight, height and age both in severe and non-severe IR patients.

Conclusions: Insulin resistance was common in presented group. 70 % (according to Homa ratio). Leptin correlates positively with degree of obesity and TG/HDL ratio in high TG/HDL group. Adiponectin and sOB-R concentrations were lower in obese children with abnormal TG/HDL. It seems that in obese children decreased adiponectin, similarly sOB-R concentrations, could be considered as determinants of higher risk of developing insulin resistance.

**P2-d1-428 Obesity and Fat 1**
Carotid artery intima-media thickness in obese children

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**Background:** Obesity has long been recognized as an independent risk factor of cardiovascular disease. Vascular changes seem to start early in obese patients. We evaluated the carotid artery intima-media thickness (IMT) and investigated their relation to cardiovascular risk factors in obese children.

**Methods:** Ultrasonographic measurements were made in 90 obese children, aged 3 to 17, versus 39 control subjects. Blood pressure, echocardiography (left ventricular parameters, LV) and fasting blood samples were obtained (glucose, insulin, lipid profile, inflammatory biomarkers - CRP, IL-6, TNFα, pappa- and adiponectin) from the obese children. The obese patients were divided into three age groups: 3-7 years old, 8-12 years old, 13-17 years old. We evaluated the relation between IMT and selected variables: age, BMI, LV, glucose, HOMA, lipid profiles, inflammatory biomarkers and adiponectin.

**Results:** Carotid artery intima-media thickness in obese and control children:

<table>
<thead>
<tr>
<th>IMT (mm)</th>
<th>Obeses (n=90)</th>
<th>Controls (n=39)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-7 years</td>
<td>0.50</td>
<td>0.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>8-12 years</td>
<td>0.50</td>
<td>0.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>13-17 years</td>
<td>0.57</td>
<td>0.37</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The IMT was no different between the hypertensive and the normotensive obese children.

**Correlations:** We found a significant positive correlation between IMT and age in the control group. In the obese children there was no significant corre-
Prader-Willi syndrome (PWS) is the most common recognised genetic form of obesity. Adult patients with PWS die prematurely from complications conventionally related to obesity, such as type 2 diabetes mellitus (DM2) and cardiovascular disease (CVD). The metabolic syndrome (MetS) is a strong risk factor for DM2 and atherothrombotic CVD. There is evidence that the development of MetS has its origin in children an adolescents, suggesting that early identification and treatment of MetS may be helpful to improve morbidity and mortality of PWS adults. The objective of this study was to estimate the prevalence of MetS among children and adolescents with PWS. Thirty-nine subjects with genetically confirmed PWS, 15 males and 24 females, aged 2.4-17.6 yr, were studied. Height and weight were measured by using standardized equipment. Growth Analyser 3 was adopted to calculate BMI-SDS values. Blood pressure (BP) was measured in each subject at least three times at 5-min intervals, and the mean values of three tests were used in analyses. Biochemical testing included measurements of fasting glucose, triglycerides, HDL cholesterol levels as well as glucose levels after Oral Glucose Tolerance Test. According to Reaven et al. (J Clin Invest 1988) and WHO criteria (Int Arch Occup Environ Health 1999), we define MetS as having at least 3 of the following: BMI-SDS>2, high systolic BP or diastolic BP, high triglycerides, low HDL and impaired glucose tolerance. The MetS component cut-points were developed with data from Italian Consensus on Childhood and Adolescence Obesity (2006). In our sample, 69.2% of subjects (n=27) had 1 or more abnormalities of the MetS, whereas 33.3% (n=13) had 2 or more. The overall prevalence of the MetS was 10.2% (n=4). The distribution of each element of the MetS was the following: obesity 56.4%, elevated BP 30.7%, high triglycerides 20.5%, low HDL 0%, IGT/DMS 7.7%. Our findings demonstrate that cardiovascular risk factors are common in young PWS subjects, suggesting a relationship with the decreased life expectancy observed during adulthood.

**P2-d1-429 Obesity and Fat 1**

**Metabolic syndrome in children and adolescents with Prader-Willi syndrome:**

**Preliminary results**

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1Istituto Auxologico Italiano Foundation, Division of Auxology, Verbania, Italy; 2Bambino Gesù Children’s Hospital, Department of Paediatric Endocrinology, Rome, Italy; 3Regina Margherita Hospital, Department of Paediatric Endocrinology, Turin, Italy; 4Bambino Gesù Children’s Hospital, Paediatric and Autoimmune Endocrine Diseases Unit, Palladio-Rome, Italy; 5Civic Hospital, Department of Paediatrics, Treviso (BG), Italy; 6University of Modena and Reggio Emilia, Department of Paediatrics, Modena, Italy; 7Oasi Maria S.S., Research Institute, Department of Paediatric Endocrinology, Troina (EN), Italy; 8University of Insubria, Department of Paediatrics, Varese, Italy; 9ASL Provincia di Milano 2, Paediatrician, Milan, Italy

Insulin resistance (IR) is a common feature of childhood obesity and a key component of the Metabolic Syndrome (MS). As in obese children IR is also strongly associated with non-alcoholic fatty liver disease (NAFLD), the latter could be considered the hepatic manifestation of the MS. The aim of this study was to evaluate the prevalence of MS among obese prepubertal children, by using two different definitions. We recruited 64 obese prepubertal children (29 boys; age median[range] 8.1[6-9]years). All children underwent anthropometric measurements, an oral glucose tolerance test, a hepatic ultrasound scan, assessment of blood pressure, plasma lipids and alanine aminotransferase (ALT). Homeostasis model assessment of IR was calculated. MS was diagnosed according to a classical definition (Weiss’s criteria): presence of 3 or more of the following criteria: BMI>2 SDS; triglycerides>95th percentile (p), HDL-cholesterol<5th p; blood pressure>95th p; impaired glucose tolerance (IGT). Then, the presence of steatosis associated with elevated ALT (>40 U/L) was included as an additional criterium to this definition. MS was found in 10 children (16.6%) according to Weiss’s criteria and in 15 children (23.4%) when NAFLD was also considered. The prevalence of MS was equally distributed between the two sexes, but increased across tertiles of HOMA-IR (p<0.01). In this group of obese children, the prevalence of the single components of the MS was as follows: hypertriglyceridaemia 32.8%, low HDL-cholesterol 3.1%, hypertension 29.7%, IGT 6.3%, high ALT 28.1%, steatosis 56%. In conclusion, this study showed that a high prevalence of the MS is already present among prepubertal obese children, particularly when NAFLD is included among the diagnostic criteria. Therefore, screening for the MS should be performed already in the prepubertal age-group and, given the association between NAFLD, IR and IGT already in children, NAFLD should be considered as an additional criterium in the diagnosis of the MS.

**P2-d1-431 Obesity and Fat 1**

**Prevalence of metabolic syndrome and insulin-resistance syndrome in overweight and obese children in Franche-Comté, France**

Marie Nicolet1; Veronique Negre2; Brigitte Mignot3; Claire Ballot1; Anne-Marie Bertrand1; 
1RePPOP-FC, Paediatrie, Besancon, France; 2CHU, Paediatry, Besancon, France

**Objective:** To ascertain the prevalence of the metabolic syndrome (MS) and insulin-resistance syndrome (IRS) in an overweight and obese paediatric population and determine whether the degree of obesity and age are related to MS and IRS.

**Patients and Methods:** 80 children were examined (42 girls, 38 boys), 25 were overweight, 55 obese. Mean BMI standard deviation score (BMI SDS) was 3.45, mean age 11.54 (from 6 to 17 years). We assessed BMI and blood pressure. HDL cholesterol, triglycerides, glyceremia and insulin levels were measured. ATP III criteria, modified for the paediatric population, were applied for MS. Reaven and WHO criteria were applied for IRS.

**Results:** High blood pressure prevalence was 28%, hypertriglyceridaemia 52%, low-HDL cholesterol 15.5% and insulin-resistance 78%. Prevalence was 16.2% for MS and 46.7% for IRS. Significant differences were observed when stratified to BMI SDS (p<0.05) and age (p<0.05). Similar results have been previously shown by Claire Levy Marchal et al., in pediatric populations from other areas of France.

<table>
<thead>
<tr>
<th></th>
<th>OVERWEIGHT (n=25)</th>
<th>OBSE (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High blood pressure</td>
<td>3 (12%)</td>
<td>15 (27%)</td>
</tr>
<tr>
<td>Hypertaglyceridaemia</td>
<td>3 (12%)</td>
<td>23 (42%)</td>
</tr>
<tr>
<td>Low HDL cholesterol</td>
<td>5 (20%)</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>17 (63%)</td>
<td>43 (81%)</td>
</tr>
<tr>
<td>Insulin resistance syndrome</td>
<td>11 (40%)</td>
<td>25 (50%)</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>1 (4%)</td>
<td>12 (22%)</td>
</tr>
</tbody>
</table>

**Conclusion:** Half of overweight and obese children presented an IRS and a quarter presented a MS. Age and degree of obesity appear to influence this prevalence. However these metabolic abnormalities may already be observed in children only affected by overweight.
**P2-d1-432** Obesity and Fat 1

**Natural history of progression of metabolic risk factors in uncomplicated obesity in urban, inner city children with diet and exercise recommendations alone**

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**Background:** Childhood obesity is a worldwide problem that has reached epidemic proportions. With obesity, the first line treatment is modification of dietary and exercise habits.

**Objective:** To evaluate the natural progression of obesity with Dietary/Exercise therapy alone on BMI, lipid profile, BP, and insulin sensitivity in children from an urban, inner city population without biochemical complications at baseline.

**Design/Methods:** This is a retrospective study of 32 obese children 11.1 +/- 3.4 yrs (22 boys, 11.7 +/- 3.4 yrs, BMI 32.3 +/- 5.4 kg/m2 and 10 girls, 9.8 +/- 3.2 yrs, BMI 27.3 +/- 7.3 kg/m2), who underwent dietary/lifestyle therapy alone. Weight, height, BMI, blood pressure (BP), HbA1c, lipid profile, liver function, fasting insulin and glucose were measured at first visit and at subsequent follow up visits. Dietary/Exercise therapy was discussed with the family at several follow up visits. Their natural progression was evaluated 18 months later.

**Results:** BMI, systolic blood pressure (SBP), fasting insulin increased significantly in the boys group and in the total group (p < 0.05), but not in the girls group. HDL significantly decreased in boys and in the total group (p < 0.05), but not in girls. There were no changes in diastolic BP, cholesterol, triglycerides, LDL, glucose, HbA1c, ALT, and AST levels.

**Conclusions:** Dietary/Exercise therapy alone did not improve HDL, insulin, BMI, and SBP. Natural history, even of uncomplicated obesity, revealed a negative progression of cardiovascular risk factors such as HDL, insulin, BMI and SBP. More intensive intervention is indicated in early childhood to prevent the formation of metabolic syndrome in early adolescence. The girls' group did not reveal statistically significant changes, only the same tendency as a whole group. This can be explained by the younger age of the studied girls and the protective effect of estrogens.

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**P2-d1-433** Obesity and Fat 1

**A treatment programme based on cognitive behaviour therapy assists weight loss in children with obesity:**

Hetty J van der Kemp; Dick Meijer; Sanne I de Vries; Matty R Crone

1Leiden University Medical Center, Paediatrics, Leiden, Netherlands; 2Cardia, Psychology, Leiden, Netherlands; 3TNO, Quality of Life, Leiden, Netherlands

The prevalence of childhood overweight is increasing. The effects of childhood overweight are serious. The objective of this study was to assess the effect of a treatment programme on weight indices and behaviour of overweight children. Overweight and obese children aged 6 - 18 years referred to the paediatrician participated in this study. Participating children and parents were asked to complete a questionnaire and the children received a medical examination at start, at the end of the first year programme and after 2 years. The questionnaire included questions on eating behaviour, physical (in)activity, interaction between parents and child and quality of life. After the baseline measurement, the children were randomly assigned to the intervention or control group. The intervention group (children and parents) was referred to a treatment programme of 1 year, based on cognitive behaviour therapy consisting of 20 sessions of 2 hours each. 32 children were included in the intervention group and 35 children in the control group (see Table 1).

Just after the programme, BMI SDS decreased in the intervention group (2.9 to 2.6) and remained the same in the control group (2.7 to 2.8). Parents in the intervention group also reported that their child was significantly less often bullied and laughed at than in the control group (often being bullied decreased in this group from 22% to 8%). More intervention children ate vegetables and fruit, were member of a sport club, and played outside after the programme: these changes were, however, not significantly different from the control group. The first results indicate that in 1 year period the programme seems to have a significant positive effect on weight in children with obesity and on perceived bullying. Additional data on weight indices, behaviour, quality of life, and interaction with parents will be presented during the meeting.

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**P2-d1-434** Obesity and Fat 1

**The C-174G polymorphism in the promoter of IL-6 gene is not associated with lipid abnormalities and incidence of metabolic syndrome in children with obesity**

Beata Pyrzak; Alicja Wisniewska; Barbara Rymkiewicz-Kluczymiska; Anna Majcher

Medical University, Pediatric and Endocrinology, Warsaw, Poland

We aimed to study whether the C-174G polymorphism IL-6 gene leads to degree of overweight, lipids abnormalities and incidence of metabolic syndrome.

**Materials and Methods:** We investigated 124 children with obesity: 72 girls and 52 boys. In the control group consisted of 56 non-obese children (36 girls and 20 boys) only genetic tests was taken. The anthropometric parameters included: body height and weight, waist and hip circumferences, the thickness of 3 and 10 skinfolds. BMI, WHR and total fat by Slaughter were calculated. Each child’s blood pressure was measured. Biochemical tests consisted of: triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, leptin. The oral glucose tolerance test with measurements of glucose and insulin levels was performed. Insulin sensitivity and insulin resistance indices were calculated. On basis the modified ATP III criteria by Ferranti, the Polish cut points were used to evaluate the incidence of the metabolic syndrome.

**Results:** There were more frequent carries the C allele in the study group than in the control group (in study group: G/G=31%, C/C=52%, C/C=16%, in control group G/G=53,6%, C/C=41%, C/C=5,4), in study group vs control group CC odds ratio [OR] 3,57, 95% confidence interval [CI] 1,01 - 12,56, Chi-2=5,02,p<0,05, for genotype C/C+G/G OR=2,56, 95% CI 1,33-4,91, Chi-2=8,04, p<0,01. Carries of CC vs GG showed a tendency for higher concentrations of HDL (50,47+/- 12,69 vs 43,97+/-10,75, p<0,05). Carries of CC vs GG showed a tendency for higher concentrations of HDL (50,47+/- 12,69 vs 43,97+/-10,75, p<0,05). Carries of CC vs GG showed a tendency for higher concentrations of HDL (50,47+/- 12,69 vs 43,97+/-10,75, p<0,05). Carries of CC vs GG showed a tendency for higher concentrations of HDL (50,47+/- 12,69 vs 43,97+/-10,75, p<0,05).