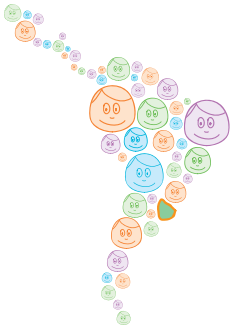
HORMONE
RESEARCH IN
PÆDIATRICS



XXIII Reunión Anual de la
Sociedad Latinoamericana de
Endocrinología Pediátrica

20 al 23 de noviembre 2012
Radisson Montevideo Victoria Plaza Hotel
Montevideo, Uruguay

ABSTRACTS

XXIII Annual Meeting of the Pediatrics Endocrinology Latinoamerican Society (SLEP)

Montevideo, Uruguay, November 20–23, 2012

Guest Editor
Carmen Susy Pisciottano Rodríguez, Montevideo, Uruguay

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Invited Speakers

Prof. Scott A. Kivkees, MD
Professor of Paediatrics
Yale Child Health Research Center – Director
Section of Developmental Endocrinology and Biology – Chief
Florida, USA

Prof. Guy Van Vliet, MD
Pediatric Endocrinologist
Chief of Endocrinology Service
CHU Sainte-Justine Research Center
Montreal, Canada

Prof. Ingrid Libman, MD, PhD
Assistant Professor
Division Pediatric Endocrinology
Department of Pediatrics
Children´s Hospital
Pittsburgh, USA

Prof. María Verónica Mericq
Profesora Asociada a la Clínica de Endocrinología Infantil
Instituto de Investigaciones Materno Infantil (IDIMI)
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Institute Affairs
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Louisiana State University Health Science Center
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Programm

November 20, Tuesday

08:00–18:00	Registration
18:30–19:30	Conference 'Thyroid Disease in Pregnancy: The Point of View of the Pediatric Endocrinologist' Dr. Scott Rivkees (USA)
19:30–20:00	Opening Ceremony
20:00–21:00	Ceremony in Honor of the 'Maestro de La Endocrinología Latinoamericana 2012, Award' Cocktail

November 21, Wednesday

08:00–09:00	Conference 'Differentiated Thyroid Cancer in Children: An Update of Treatment and Log Term Follow Up' Dr. Scott Rivkees (USA)
09:15–10:15	Oral Presentation ROOM A / ROOM B
10:15–10:45	Break
10:45–12:15	Oral Presentation ROOM A / ROOM B
12:30–13:00	Conference 'Efficacy of Aromatase Inhibitor Treatment in Pediatric Patients' Prof. Matti Hero (Finland)
13:00–13:30	SLEP Symposia 'Biochemical and Genetic Assessment of GH Insensitivity' Dr. Horacio Domené (Argentina)
13:45–15:00	Lunch/NOVO NORDISK Symposia
15:00–16:30	Poster Session ROOM C
16:30–17:00	Break

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17:00–18:00	Conference 'Is the Incidence of Congenital Hypothyroidism Really Increasing?' Prof. Guy Van Vliet (Canada)
18:15–19:00	Conference of Dr. César Bergada 'Metabolic Disorders, Bone Mineral Metabolism and Cardiovascular Risk in the Growth Hormone Deficiency Syndrome' Dr. Roberto Lanes (Venezuela)
19:15	SLEP Meeting

November 22, Thursday

08:00–09:00	Conference 'Neonatal Screening: What is the Situation in Uruguay?' Dr. Graciela Queiruga (Uruguay)
09:15–09:45	Conference 'A New Comer: Type 2 Diabetes in Childhood and Adolescence' Dr. Ingrid Libman (USA)
09:45–10:15	Break
10:15–11:45	SLEP Symposia 'Is Latin America Doomed to Follow the Steps of the USA? Obesity, Pre-Diabetes and Type 2 Diabetes in Pediatrics – Prevention and Therapy' Dr. Alfonso Vargas (USA)
11:45–13:15	Oral Presentation
13:00	Free Afternoon

November 23, Friday

08:00–09:00	Conference 'Aromatase Inhibitor in Pediatrics: Treatment Safely' Dr. Matti Hero (Finland)
09:15–10:15	Oral Presentation ROOM A/ROOM B
10:15–10:45	Break
10:45–12:15	Oral Presentation ROOM A/ROOM B
12:30–13:00	Conference 'Toward Evidence Based in Prenatal Counselling for Klinefelter Syndrome' Prof. Guy Van Vliet (Canada)
13:00–13:30	SLEP Symposia 'Fetal Intrauterine Growth and Conditions in Adulthood' Dr. Verónica Mericq (Chile)
13:45–15:00	Lunch/SANDOZ Symposia
15:00–16:30	Poster Session ROOM C
16:30–17:00	Break

17:00–18:00	Conference 'Type 1 Diabetes and Obesity in Childhood: an Undesirable Emerging Association' Dr. Ingrid Libman (USA)
18:15 – 19:15	SANOFI-AVENTIS Symposia
20:30 – 21:00	Closing Ceremony and Adwards
21:00	Gala Dinner

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Horm Res Paediatr 2012;78(suppl 2):1–67

Abstracts

Oral Presentation

1

Quantifying Adherence to Growth Hormone Treatment: The Easypod™ Connect Observational Study (ECOS)

Calzada Leon, Raul[1(*)]; Belgorosky, Alicia[2]; Davies, Peter[3]; Kim, Ho-Seong[4]; Borkenstein, Martin[5]; Du, Minlian[6]; Kirk, Jeremy; Kostalova, Ludmila[7]; Lebl, Jan[8]; Loche, Sandro[9]; Luczay, Andrea[10]; Nicolino, Marc[11]; Norgren, Svante[12]; Rodriguez Arnao, Dolores[13]; Vandermeulen, John; Gasteyger, Christoph[14]; Zieschang, Jürgen[15]; Zignani, Monia[14]

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Background: Recombinant human growth hormone (r-hGH) is indicated for pediatric patients with a variety of growth disorders. Until recently, analysis of adherence to treatment has been limited by recall bias and reliance on self-reporting. Accurate recorded data on r-hGH use can now be collected using the easypod™ auto-injector. The multinational easypod™ connect observational study (ECOS) was launched in 2010 to collect and analyze r-hGH dosing, clinical and auxological data from patients prescribed r-hGH via easypod™. Twelve countries are currently recruiting patients. **Objective:** To assess adherence in patients receiving r-hGH via easypod™. Secondary objectives include describing the impact of adherence on clinical outcomes and identifying adherence patterns. **Methods:** Data will be obtained from patients' medical notes and uploaded from auto-injectors. Auxological parameters are collected, and prescribed dosing data recorded at clinic visits as per routine clinical practice. Annual adherence will be calculated (number of days the patient administered injections divided by the expected number of injection days over 1 year, as a percentage). Dose intensity (total amount of dose received divided by planned amount of dose over 1 year, as a percentage) will be analyzed. Adherence data will be correlated with clinical outcomes. An adherence pattern will also be developed based on patients' age, sex, indication, self-injection, and time on treatment. The study will run until 2015, with yearly analyses, and will be overseen by a multinational scientific steering committee. **Conclusions:** With data from ECOS, it will be possible to accurately assess r-hGH treatment adherence in various growth disorders and explore its potential impact on growth. Ultimately, drivers of and barriers to treatment adherence will be identified, allowing appropriate support programs to be developed.

2

Physical Inactivity in Early Postnatal Stages Influences GLUT4 Gene Expression by Epigenetic Mechanisms in Rat Skeletal Muscle

Márquez, José Luis[1(*)]; Hirabara, Sandro[2]; Fiamoncini, Jarlei[3]; Hatanaka, Elaine[2]; Alba-Loureiro, Tatiana[3]; de Lima-Salgado, Thais[3]; Guzman, Neftalí[4]; Curi, Rui[3]; Salazar, Luis[5]

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Background: Type 2 diabetes (T2D) is a multifactorial disease and has been related to obesity and high levels of physical inactivity. **Objective:** To evaluate the epigenetic effects of early physical inactivity and its potential relationship with the origins of T2D. **Methods:** Forty male Wistar rats were distributed in two groups: condition standard (Std) and movement restriction (MR). Between days 23 and 70 after birth, MR group was kept in small cages that did not allow them to perform relevant motor activity. From day 70 to 103 after birth, 10 rats of each group were fed with high fat diet (HFD). Insulin-stimulated glucose uptake in incubated soleus was determined. Gene expression of GLUT4 was evaluated in this muscle. Finally, the global DNA methylation of muscle cells of soleus was evaluated and the methylation pattern in a specific region of GLUT4 gene promoter was determined. **Results:** HFD administered by 30 days during the adult life, generated an increase of the fat mass and greater weight gain in animals that remained inactive during their early postnatal development. HFD generated a diminution of glucose uptake induced by 1000 mU/mL of insulin in isolated and incubated soleus of the animals MR but not in Std. The early physical inactivity modified the GLUT4 gene expression in soleus muscle and a global DNA hypomethylation was found in MR groups. Finally, the movement restriction was associated with hypermethylation of the specific region in the GLUT4 gene promoter. **Conclusions:** Physical inactivity in early stages of development promotes an insulin resistant phenotype that can be explained by

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dysregulation of GLUT4 gene expression, mediated by epigenetic modifications that include global DNA hypomethylation and specific hypermethylation of a regulatory region in the promoter of this gene.

3

Benefits of 1yr Steroid Withdrawal (SW) are Translated into Better Longitudinal Growth, Lipid Profile and Trunk Fat in Pediatric Kidney Transplant Recipients

Mericq, Veronica[1(*)]; Salas, Paulina[2]; Pinto, Viola[2]; Cano, Francisco[3]; Reyes, Loreto[4]; Gonzalez, Magdalena[5]; Michea, Luis[5]; Delgado, Iris[6]; Delucchi, Angela[7]

[1]Institute of Maternal and Child Research, University of Chile, Santiago, Chile | (*) Chile; [2]Pediatric Nephrology Unit, Hospital Excequiel Gonzalez Cortes, Santiago, Chile; [3]Pediatric Nephrology Unit, Hospital Luis Calvo Mackenna, Santiago, Chile; [4]Pediatric Endocrinology Unit, Catholic University, Santiago, Chile; [5]Institute of biomedical Sciences, University of Chile, Santiago, Chile; [6]Department of Statistics, University of Desarrollo, Santiago, Chile; [7]3 Pediatric Nephrol Hospital Luis Calvo Mackenna, Santiago, Chile

Background: Glucocorticoids immunosuppressant in pediatric kidney transplant (Tx) recipients does not allow improving longitudinal growth post-Tx. **Objective:** To determine the effect of early (6d) steroid withdrawal (SW) in longitudinal growth, growth factors, insulin sensitivity (IS) and body composition. **Methods:** Prospective, randomized, multicenter study in first pediatric kidney recipients of low immunological risk. Physical data: height, BMI, waist, hip at: pre-Tx, monthly up to 12 months. Labs: IGF-I, IGFBP3, IS (OGTT: glycemia and Insulin every 30 min, ISI composite, TyG index) and body composition (DEXA and pQCT) pre-Tx and up to 12 months post Tx. **Results:** 30 patients: 14 SW (7M;7F), 12 in Tanner I, 2 in Tanner II and 16 with steroids (SC) (10M, 6F) 12 in Tanner I, 4 in Tanner II, (mean ± SDS) chronological age 7.8 ± 4.3 yrs., bone age 7.4 ± 4.2 yrs., height –2.3 ± 0.99 SDS, BMI –0.3 ± 1.2 SDS. After 1 yr SW showed a better height, with a gain of +1.2 ± 0.22 SDS vs.+ 0.60 ±0.13 SDS ($p<0.02$), growth velocity of 10.9±3.9 cm vs. 6.6±2.2 cm ($p<0.001$),accompanied by a lower IGFBP3 SDS ($p<0.05$), cholesterol (<0.05), and higher HDL-C (<0.05). BA /CA ratio progressed faster in SW patients (0.33 ±0.5 yr vs. –0.15 ±0.51 yr, $p<0.02$) and these patients had lower trunk fat with no differences in Insulin sensitivity. Analyzing only the prepubertal patients (n=24; SW=12), we found a lower glycemia (<0.05), VLDL-C (<0.01), triglycerides (<0.05), TyG index (<0.02). **Conclusions:** SW improved longitudinal growth, lipid profile and trunk fat in pediatric kidney transplant recipients. In prepubertal subjects the decrease in TyG suggests a better IS. Future follow-up will allow us to analyze whether these changes are maintained allowing these patients to achieve a better adult height and metabolic profile compared to SC. Supported by Fondecyt 1080166.

4

Arterial Hypertension in Children: Impact on Pro-inflammatory, Endothelial Damage, and Oxidative Stress Parameters

Campino, Carmen[1(*)]; Martinez-Aguayo, Alejandro[2]; Aglony, Marlene[2]; Garcia, Hernan[2]; Bancalari, Rodrigo[2]; Avalos, Carolina[2]; Bolte, Lilian[2]; Loureiro, Carolina[2]; Carvajal, Cristian[3]; Garcia, Lorena[4]; Lavanderos, Sergio[4]; Fardella, Carlos[3]

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Arterial hypertension affects 4% of children but its impact at the level of cardiovascular damage and upon parameters, which determine this injury, is unknown. **Objective:** To evaluate in hypertensive children the impact of this injury on pro-inflammatory, endothelial damage and oxidative stress parameters. **Patients and Methods:** 306 children (5–16 y). Group 1: Hypertensives (n=111); Group 2: normotensives with at least one hypertensive parents (n=101); Group 3: normotensives children with both parents normotensives (n= 95). hsRCP, adiponectin, IL-6, IL-8, TNF-α; PAI-I, MMP9 and MMP2 activities and malondialdehyde were measured. **Results:** (median [Q1-Q3]): The comparison between groups 1, 2 and 3 showed significant differences in levels of hsCRP (mg/L): 1.2[0.4–2.3]*,**, 0.5[0.2–1.6], 0.5 [0.2–1.3]; PAI-I (ng/ml): 22.2[13.4–31.7]*, 18.8[9.8–27.3], 14.9[8.9–23.3] and MMP-9 (number of changes respect to an internal control): 2.2[1.3–3.0]*, 1.8[1.2–2.5], 1.6 [1.2–2.3]. The others variables analyzed did not show significant differences between the groups. *$p<0.05$ group 1 vs group 3, **$p<0.05$ group 1 vs group 2. **Conclusions:** We found an increase in inflammation subclinical and endothelial damage variables. These results highlight the importance of routine blood pressure measurement in children population. This work was supported by Fondecyt 1100356, FONDEF D08I1087 and Nucleo Millenium on Immunology and Immunotherapy P07/088-F Chilean grants.

5

Clinical-laboratory Evaluation and Ovary Morphology by Ultrasound in Patients Whit P450c17 Deficiency

Carvalho, Luciane Carneiro[1(*)]; Matsunaga, Regina Martin[1]; Costa, Elaine Maria Frade[1]; Domenice, Sorahia[1]; Silva, Rosana Barbosa[1]; de Castro, Margaret[2]; Mermejo, Livia[2]; Quezado, Rosana[3]; de Castro Maia Ribeiro Teixeira, Virgínia[3]; Gonçalves, Fabrícia Torres[4]; Carrilho, Alexandre José Faria[5]; Camargo, Kenny Yelena Del Toro[6]; Finkielstain, Gabriela[7]; Bergadá, Ignácio[7]; Taboada, Giselle Fernandes[8]; Mendonça, Berenice Bilharinho[1]

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Background: Congenital adrenal hyperplasia due to P450c17 deficiency is a rare autosomal recessive. **Objective:** Report the clinical, laboratory, genetic and imaging of ovarian 46, XX patients. **Population:** We evaluated eighteen patients belonging to 12 families. **Results:** Most patients had amenorrhea primary (83%) and 89% of the patients had blood hypertension at diagnosis. We observed a high incidence of emotional disorders such as depression and anxiety (13/18). All patients showed elevated levels of LH and progesterone, and decreased androgen levels. The ultrasound assessment showed an increase of at least one of the ovaries in 75% of the patients before treatment and ovarian macrocists in 56%, three of them reported previous surgery indicated by twisting or ovarian rupture. Molecular study was performed in 14 out of 18 patients and 13 patients have inactivating mutations in the CYP17 and 1 in POR gene. The most prevalent mutation in CYP17 was p.W406R, followed by p.P428L. The patients were treated with dexamethasone, estrogen and progesterone with ovarian volume reduction. **Conclusions:** We emphasize the importance of basal progesterone assay to diagnosis and the high prevalence of ovarian macrocists with risk of twisting and psychiatric disorders, in 46,XX patients whit P450c17 deficiency.

6

Functional Characterization of Three Novel Mutations in the CYP11B1 Gene in 11b-hydroxylase Deficiency

Marino, Roxana[1(*)]; Parajes, Silvia[2]; Perez Garrido, Natalia[1]; Maceiras, Mercedes[1]; Rose, Ian T.[2]; Ramirez, Pablo[1]; Warman, Diana M.[1]; Rivarola, Marco A.[1]; Krone, Nils[2]; Belgorosky, Alicia[1]

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Context: Steroid 11b-hydroxylase deficiency (11b-OHD) is the second most common (5–8%) cause of congenital adrenal hyperplasia (CAH) and results from homozygous or compound heterozygous mutations of CYP11B1 gene. **Objective:** To detect CYP11B1 mutations in three 11b-OHD patients. To characterize clinical and endocrinological features. To analyze the functional consequences of three novel CYP11B1 mutations. **Methods:** CYP11B1 exons and intron boundaries were direct sequenced in all patients and parents. Functional studies were perfomed using a COS7 cell in vitro expression system comparing wild-type (WT) and mutant CYP11B1 activity. **Clinical Cases:** Two male and one female patients were studied. Female was born with ambiguous genitalia. In both males signs of virilization (pubic hair, penile stimulation and advanced bone age) at 3 and 7.7 years old was observed. The oldest one presented also bilateral Gynecomastia. Hormonal studies were compatible with 11b-OHD diagnosis. Treatment with oral hidrocortisone was started with good clinical and laboratory response in all of them. **Results:** All patients had CYP11B1 mutations on both alleles. Three novel mutations were identified: p.R453W and p.L407F completely abolished enzyme activity while p.R138C mutation showed partial functional impairment (9.8% of WT). **Conclusion:** Herein, we demonstrate the pathogenicity of three novel CYP11B1 mutations. It was not possible to differentiate if the p.R138C mutation, which preserved 9.8% of WT activity, is a variant that affect prenatal or earlier postnatal steroidogenesis since it was found in an affected male. It seems that this variant would be associated with an intermediate phenotype. Our study provide important information for clinical and genetic counseling in 11b-OHD.

7

Characterization of a Novel Variant (L163R) of the Von Hippel Lindau Protein (pVHL)

Matho, Cecilia[1(*)]*; Merlino, Alicia*[2]*; Sanso, Gabriela*[1]*; Coitiño, Laura*[2]*; Pennisi, Patricia*[1]

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Background: Von Hippel-Lindau (VHL) is a hereditary syndrome caused by VHL gene mutations. VHL protein (pVHL) forms a multiprotein complex that polyubiquitylates and determines the proteasomic degradation of HIF1α, a transcription factor involved in the regulation of genes implicated in angiogenesis, apoptosis and cell proliferation. **Aim:** To analyze *in silico* the structural characteristics and *in vitro* the functional properties of the novel variant L163R. **Methods:** Bioinformatic and molecular modeling tools were used to predict and compare the structure and properties under normoxia/hypoxia conditions of L163R and native pVHL, evaluating the MM-PBSA energy for complex formation. RCC786-0-VHL$^{-/-}$ cells, both parental or stably transfected with pBabe-puro-HA-VHL-L163R (obtained by site-directed mutagenesis) were used for proliferation assays. **Results:** *In silico*, the complex formed by L163R was more unstable than the one formed by the native protein. *In vitro*, the proliferation rates of RCC786-0-VHL^{L163R} and RCC786-0-VHL$^{-/-}$ were similar, which was suggestive of the expression of an inactive protein. **Conclusion:** L163R genetic variant might decrease the stability or even prevent the formation of the multiprotein complex, suggesting a possible pathogenic role for this variant. We have combined molecular modeling with *in vitro* experiments for functional characterization, to better understand the pathogenic mechanism of L163R variant.

8

Genetic Analysis in Patients with Clinical Suspicion of Von Hippel Lindau (VHL) Type 1 Disease

Mathó, Cecilia[1(*)]*; Trarbach, Ericka B.*[2]*; Barontini, Marta*[1]*; Sansó, Gabriela*[1]

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Background: VHL disease is an autosomal dominant disorder, which increases susceptibility to a variety of benign and malignant tumours. VHL type 1 is associated with large deletions or truncating/null mutations of *VHL* gene. **Aim:** to implement a complete *VHL* genetic analysis for patients with clinical suspicion of VHL type1. **Methods:** We evaluated *VHL* in 8 subjects (7 unrelated) with clinical suspicion of VHL type1 with or without family history. DNA sequencing and UPQFM-PCR (*Universal Primer Quantitative Fluorescent Multiplex* PCR) were performed for the detection of point mutations and large *VHL* deletions, respectively. Individuals with/without *VHL* deletions were included as controls, and MLPA (*Multiplex Ligation-dependent Probe Amplification*) was used to confirm the deletion identified. **Results:** We detected a deletion removing exons 2 and 3 of *VHL* in one sporadic male patient and a nonsense p.W88* in another. **Conclusions:** UPQFM-PCR technique proved to be convenient, useful, reliable and consistent with MLPA. We were able to confirm VHL type1 disease in two symptomatic patients, with no family history. The use of UPQFM-PCR for the detection of large *VHL* deletions, together with the preexistent methods in our laboratory, provided a complete genetic study for patients with clinical suspicion of VHL type1 disease.

9

Fibroblast Growth Factor 21 (FGF21) and First Yr Growth in Term and Preterm Infants

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Fibroblast growth factor 21 (FGF21) is a recently discovered metabolic and growth regulator. Interestingly, FGF21 inhibits GH-induced JAK2-STAT5 signaling in the liver, suggesting a novel negative feedback loop that prevents excessive JAK2-STAT5 signaling from the GH receptor in the liver. [FGF21] increase during fasting and in obesity (resistance?). Growth in infancy is very fast and may be related to FGF21 concentrations. Our aim was to investigate the role of FGF21 during the first yr growth in 40 infants, 20 born at term (10 AGA/10 SGA) and 20 born premature with very low birth weight (<32 Weeks/<1500 grs, 10 AGA/10 SGA). Complete anthropometric data at birth, 6 m and 12 m plus a blood sample for [FGF21], [IGF-I/II] at 6 and 12 months were analyzed. At 6 months terms had a better weight ($p<0.05$) and length ($p<0.05$), as well as 12 months a better weight ($p<0.005$) (SDS) than preterms. At 6 months [FGF21] were significantly higher in term infants compared to preterms (240.2±45.9 vs. 92.9±14 pg/ml, $p<0.01$) as well as IGF-II at 6 and 12 months (6 m: 625.6±38.6 vs. 456.1±20.7, 12 m: 614.4±38.6 vs 443.2± 21 ng/ml $p<0.001$). In term infants [FGF21] at 12 m correlated inversely with length at 6 ($p<0.05$) and 12 m ($p<0.01$) and [FGF21] at 6 m [IGF-1] at 6 months ($p<0.001$). When separated by BW correlations held only true in AGA infants. In contrast, in preterms similar inverse correlations were observed with [FGF21] at 6 m with weight at 6 ($p<0.05$) and 12 m ($p<0.001$). In Preterms [IGF-I] 6 m correlated directly with length at 6 ($p<0.05$) and 12 m ($p<0.05$). Our results suggest a different preferential role (growth inhibitor/metabolic regulator) of FGF21 in term vs. preterm infants. An increase in the sample size and exploring the relationships with insulin/leptin may help to clarify the role of FGF21 in infancy. Supported by Fondecyt 1090028 and 1110240.

10

Growth Hormone (GH) Assay Standardization: Clinical Implication on Serum GH Cut-off Value for Pharmacological Tests Used to Diagnose GH Deficiency (GHD) in Children

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Background: GH deficiency (GHD) needs to be biochemically confirmed by measurements of GH concentrations during pharmacological stimulation tests (PhT). Recently, it has been introduce a new recombinant highly purified standard (IS) for GH calibration assays by manufactures and as a consequence, cut-off of PhT should be revised. **Aims:** To evaluate the cut-off PhT value for recently modified ICMA-GH calibrated with IS-98/574 and to determine the diagnostic efficiency (DE) of the recalculated PhT cut-off. **Material and Methods:** Serum GH concentration from 157 samples (baseline and in response to arginine-clonidine stimulation tests) from 92 short children were measured concomitantly by ICMA IS-80/505 (withdrawn by Siemens) and current ICMA IS-98/574 assay from Siemens. Passing-Bablok and ratio plot analyses were used for between-assay comparisons. We calculated a new PhT cut-off in terms of IS 98/574 for fixed x value of 6.1 ng/mL (ICMA IS-80/505) using the regression curve obtained. DE of the new ICMA IS-98/574 GH cut-off to define GHD in children, was studied using other independent 43 peak GH serum samples (13/43 from GHD children, peak ICMA GH IS-80/505<6.1 ng/mL) by ROC curve analysis. **Results:** ICMA-GH IS-98/574 results were negatively biased compared to ICMA-GH IS-80/505 (GH IS-98/574=0.74xGH IS-80/505+0.26, r^2=0.979); mean ratio (IS-98/574/IS-80/505): 0.79±0.17. The calculated cut-off value for considering GH sufficient response to PhT was >4.7 ng/mL in terms of GH IS-98/574 assay. Using this cut-off of 4.7 ng/mL, all 13 GHD children were correctly diagnosed in terms of the recalibrated GH IS-98/574 assay [DE: 100%; Sensitivity: 100% (95 IC%: 88.4–100); Specificity: 100% (75.3–100%)]. **Conclusions:** We found a shift to lower GH results (in average: 20%) after the standardization of the widely used ICMA-GH assay. Regarding our results, the proposed cut-off value in terms of IS-98/574 (4.7 ng/mL) constitutes a useful diagnostic tool for GHD in pediatric patients.

11

PROP1 Overexpression in Corticotrophinomas: An Additional Evidence of its Role on Maintenance of Pituitary Cell Lineage Committed with Corticotroph Differentiation

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Background: The expression of transcription factors involved in early pituitary development, such as PROP1 and POU1F1, has been detected in pituitary adenoma tissues. **Objective:** In this study, we sought to characterize the PROP1 and POU1F1 transcriptional profile in functioning and nonfunctioning pituitary adenomas, in an attempt to identify their role in tumorigenesis and hormone hypersecretion. **Population and Methods:** RT-qPCR analyses were performed to assess transcriptional pattern of PROP1, POU1F1, TPIT and hormone-producing genes using tumoral samples from corticotrophinomas (n=10), somatotrophinomas (n=8), and nonfunctioning adenomas (n=6). **Results:** POU1F1 exhibited high expression only in somatotrophinomas (3-fold increase on average) when comparing with normal pituitary tissue. PROP1 expression was, on average, 18-fold increase in corticotrophinomas, 10-fold increase in somatotrophinomas, and 3-fold increased in nonfunctioning adenomas. TPIT transcriptional levels were, on average, 27-fold increased in corticotrophinomas. TPIT mRNA levels were positively correlated with POMC expression levels (r=0.49 p=0.014). Earlier studies showed that several patients with PROP1 loss-of-function mutations developed ACTH deficiency or progressive decline of corticotrope function. **Conclusion:** Our data demonstrate that PROP1 is overexpressed in pituitary adenomas, mainly in corticotrophinomas, supporting a role for PROP1 in the maintenance of cell lineage committed with corticotroph differentiation.

12

Cyclic AMP Reduces Aromatase Activity in Human Placenta Explants in Culture

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Background: Aromatase (Aro) is the key enzyme for estrogen biosynthesis and is encoded by Cyp19 gene. In human placenta (h-PL), Aro is expressed exclusively in syncytiotrophoblast and estrogens play a crucial role in placental physiology. We have previously described alternative splicing of the Aro coding region that would be involved in the control of Aro expression. Recently we

described a new alternative mRNA that includes intron 9 (IN9) and generates a shorter and inactive Aro protein. It has been reported that cAMP increase Aro expression in h-PL. **Objective and Hypotheses:** Evaluate cAMP regulation of aromatase mRNAs expression in human placenta explants in culture. We propose that IN9 variant is differently regulated by cAMP. **Methods:** Explants cultures of 5 term h-PL were studied. Aro activity was evaluated by measurement of estradiol production (E2) using testosterone as substrate. Aro mRNAs were evaluated by RT-Real time PCR with specific primers for total (CYP19), intron 9 (IN9) and active (Arom). β-actin was used as housekeeping gene. **Results:** We observed in the 5 cultures that cAMP (0.25uM) significantly reduces Aro activity (E2-cAMP/E2-basal:0.550±0.091,mean±SEM), paired t-test $p<0.05$. Although, under cAMP, CYP19/β-actin mRNA expression seems to increase (cAMP/basal:1.138±0.100, mean±SEM), Arom/CYP19 ratio significantly decreases (cAMP/basal:0.746±0.075, mean±SEM) paired t-test $p<0.05$. Moreover, analysis of Arom and IN9 variants showed that Arom/IN9 ratio significantly decreases (cAMP/basal:0.599±0.061, mean±SEM), paired t-test $p<0.05$, as well as the Aro activity. **Conclusions:** We describe for the first time that Aro activity is reduced by cAMP. This reduction was also observed in the Arom/IN9 mRNA ratio. As the IN9 variant is a truncated Aro mRNA translating to an inactive protein lacking the heme-binding region, we propose that the expression of this variant would be involved in the regulation of Aro activity in human term placenta.

13

Atenuation of the Growth Hormone (GH) Intracellular Signaling Pathway During the Neonatal Period

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Introduction: Linear growth during the neonatal period does not appear to depend on GH, so we postulate that tissue sensitivity to GH may be reduced during this period. **Aim:** To determine the activation of JAK2 and STAT5 and the *ALS* expression in skin fibroblasts obtained from newborns compared to prepubertal boys. **Methods:** We obtained skin fibroblasts from 12 normal newborns (Nb) and 10 normal prepubertal boys (Pp), who underwent elective surgery. The proteins were studied by Western Blot and the *ALS* expression by RT-PCR. **Results:** In the Table, the values are shown as mean ± SEM. Pp vs Nb *$P<0.05$. **Conclusion:** Our results indicate that the GH signaling pathway is attenuated in the fibroblasts of newborns compared to prepubertal boys, suggesting a decreased tissue sensitivity to GH during the neonatal period. FONDECYT 1095118.

Table 1. (for Abstract 13)

Clinical features of the subjects studied						
Subjects	Age		Height (Z-score)		Weight (Z-score)	
Nb	8.7±0.6 days		−0.09±0.20		−0.05±0.24	
Pp	6.3±0.6 years		−0.52±0.20		−0.05±0.18	
Molecular features of the subjects studied						
Subjects	JAK2 Activation "basal"	JAK2 Activation 15 GH	STAT5 Activation "basal"	STAT5 Activation GH	*ALS* Expression 16 h "basal"	*ALS* Expression 16 h GH
Nb	1.11±0.09	1.2±0.15	1.05±0.17	1.01±0.06	0.8±0.03	0.82±0.03
Pp	0.97±0.09	1.2±0.08	1.01±0.06	2.01±0.53*	0.83±0.03	1.12±0.09*

14

Klotho, FGF21 and FGF23 in Cord Blood from Small (SGA), Appropiate (AGA) and Large (LGA) for Gestational Age Newborns. Relation with IGF-I/II, IGFBP-3, ALS and Birth Weight and Length

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Introduction: Klotho is expressed in placenta, it has been associated with aging and act with FGF21/23. **Objective:** To determine the cord blood (CB) concentrations of Klotho, FGF21, FGF23, IGF-I, IGF-II, IGFBP-3 and ALS and its relationship with birth anthropometry. **Method:** We studied 50 NB-SGA, 49 NB-AGA and 43 NB-LGA. CB concentrations were determined by immunoassays. Results are shown in the table as mean ± SEM, differences were determined by ANOVA / Kruskal-Wallis and correlations by Spearman test. We found an inverse correlation between birth weight and FGF23 concentrations ($r = –0.316$), a direct relationship between CB concentrations of IGF-I with Klotho ($r = 0.274$) and inverse with FGF23 ($r = –0.38$). **Conclusion:** The lower CB concentrations of IGF-I, IGFBP-3, ALS and Klotho and higher of FGF23 found in the NB-SGA suggest that these growth factors may play a role in the development of intrauterine growth restriction.

Table 1. (for Abstract 14)

	SGA	AGA	LGA
Gestational age (weeks)	38.5±0.17	39.2±0.15	39.5±0.16
Birth weight (SDS)	−1.96±0.08*	0.24±0.13	2.49±0.12#
Birth length (SDS)	−1.39±0 15*	0.28±0.11	1.52±0.12#
IGF-I (ng/ml)	61.6±3.8*,#	74.2±4.5	90.2±4.6
IGF-II (ng/ml)	633±26*	723±22	622±44&
IGFBP-3 (mg/L)	0.79±0.06*,#	0.96±0.04	1.34±0.12
ALS (nmol/L)	39.6±3.7#	44.6±3.7	50.9±2.4
Klotho (ng/ml)	708±55*	848±62	764±56
FGF21 (pg/ml)	47.3±15.9	43.1±11.8	51.9±24.7
FG23 (pg/ml)	18.3±5.7*,#	6.9±1.7	7.9±3.0

* p < 0.05 SGA vs AGA; # SGA vs LGA; & LGA vs AGA; SEM: Mean standard error FONDECYT 111 0240.

15

Repercussions of TSH Cutoff Level to 6 mU/l in Neonatal Screening for Congenital Hypothyroidism in Santa Catarina: Preliminary Results

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Objective: This study assessed the implications of changing the cutoff level of TSH from 10 to 6 mU/l. **Methods:** The study population was constituted of 74.123 children screened for Congenital Hypothyroidism by the National Screening Program in Santa Catarina, from March 2011 to February 2012. The TSH cutoff level was 6 mU/l. If TSH was between 6 and 10 mU/l a second sample was collected. If TSH > 6 mU/l in this second sample, the child was sent for medical evaluation. **Results:** 435 children were recalled for presenting TSH between 6 and 10 mU/l in the first sampling, 28 remained TSH > 6mU/l in the second sampling. Among these, 15 were diagnosed as dyshormonogenesis or transient, two ectopic thyroid and one thyroid hypoplasia. **Conclusion:** Reduce the TSH cutoff level from 10 to 6 mU/l, reduces the number of false negatives, increasing the test sensitivity, but increases the number of false positives and recalls. Despite these negative points, reduce the cutoff level allows the diagnosis of thyroid abnormalities which require treatment, justifying its adoption.

16

Elastography for the Diagnosis of Cancer in Children

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Background: Thyroid nodules are uncommon in children before puberty (1.5%). However, the diagnostic approach should be more aggressive in children because thyroid nodules are more often malignant than in adults. Elastography is a new technique that uses ultrasound to provide an estimation of tissue stiffness by measuring the degree of distortion under the application of an external force. Stiffness is usually correlated with malignancy because benign lesions are supposed to be softer. A previous report on thyroid nodules concluded that off-line processed US elastograms may predict malignancy with 96% specificity and 82% sensitivity. We found no studies in the literature on elastography in the diagnosis of thyroid cancer in childhood, which is the purpose of our work. **Objective:** Evaluate elastography in the diagnosis of thyroid cancer in childhood. **Population and Methods:** The study included 28 patients less than 18 years of both sexes with thyroid nodule, seen from August 2011–June 2012 in the Department of Endocrinology, Santa Casa de São Paulo. We collected TSH, free T4 and calcitonin; performed USG, elastography and FNA cytology by the same operator. **Results:** Elastography stiffness was found in six cases; the histology in 4 of them was malignant (three papillary carcinomas, 1 medullary carcinoma) and in 2 was benign (1 follicular adenoma; 1 colloid). Softer was found in 22 nodules, all of them had benign lesions. In this group, we found 14.3% of thyroid cancer. **Conclusions:** US elastography has great potential for diagnosis of thyroid cancer. Larger prospective studies are needed to establish the diagnostic accuracy of this new technique in children.

17

Establishment of Reference Ranges for Thyrotropin, Thyroxine, Free Thyroxine and Triiodothyronine in Neonates and Infants

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Pediatric healthcare is critically dependent on the availability of accurate and precise reference intervals to allow appropriate clinical interpretation. **Aims:** To obtain reference intervals for TSH, T4, fT4 and T3 in a pediatric population from Córdoba, Argentina.

Table 1. (for Abstract 17)

	n	TSH (μIU/mL)			T4 (μg/dL)			fT4 (ng/dL)			T3 (ng/dL)		
		2.5 th	50 th	97.5 th	2.5 th	50 th	97.5 th	2.5 th	50 th	97.5 th	2.5 th	50 th	97.5 th
4–29 days	68	1.23	3.53	7.55	7.41	10.89	17.26	1.11	1.51	2.26	127.30	194.20	270.60
30–89 days	230	1.09	2.94	7.99	7.39	11.00	16.53	0.99	1.38	1.96	140.00	220.10	307.90
90–365 days	112	0.69	2.21	7.53	7.14	10.53	15.80	0.93	1.30	1.87	140.60	229.70	337.40

Subject and Methods: Serum samples of 410 healthy neonates and infants (age range 4 to 365 days) were analyzed using electrochemiluminescent immunoassay (cobas e 601). **Results:** No significant difference existed between the sexes. The percentile 2.5th, 50th and 97.5th were calculated for all reference groups. **Conclusion:** We report pediatric reference intervals for TSH, T4, fT4 and T3. It should assist pediatricians in interpreting these hormonal results more accurately and thereby lead to improve diagnosis of childhood thyroid diseases.

18

Analysis of Variables Influencing Intelligence Quotient in Children with Congenital Hypothyroidism Detected by Neonatal Screening

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Intelligence quotient (IQ) of children with congenital hypothyroidism (CH) could be influenced by its severity and treatment. **Aim:** to analyse the relation between IQ and variables at start and in the follow-up to the age of 3 years. **Methods:** IQ was determined (WISC III test) in 56 children with CH (F:40, M:16), age: 9.4–9.7 years, and was related with variables: etiology, birth weight, age and maternal education, number of siblings, initial TSH, T4 and Levothyroxine dose (LTd); and follow-up variables: TSH, T4 and LTd. Central values were compared (Mann-Whitney test). Multiple lineal regression models were adjusted to IQ with studied variables. **Results:** Median initial LTd was 13.1 (5.6–16.2) ug/kg/day, median IQ was 111.5 (78.0–154.0). IQ was related with: initial TSH (p=0.0001), maternal education (p=0.0467) and number of siblings (p<0.0001). It was not related with follow-up variables. During the first year of life, median LTd were: 5.00 in dyshormonogenesis, 6.42 in athyreosis, 6.10 in dysgenesis (p<0.05). **Conclusions:** 1) CH children treated according to actual recommendations had normal IQ. 2) IQ was lower in CH children with higher initial TSH, lower maternal education and greater number of siblings. 3) Variables in follow-up were not found related with IQ.

19

Diagnostic Features of Pediatric Thyroid Nodule: A 4 Year Prospective Study

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Introduction: Pediatric thyroid nodules have a greater risk of malignancy than in adults. **Objective:** To study a pediatric cohort of patients with thyroid nodules. **Material and Methods:** We prospectively studied 66 consecutive patients that came to consultation in our center between 2007 and 2011. Clinical features, thyroid function, Doppler ultrasound (US), Tc^{99m} scan, ultrasound guided FNAB cytology and histology of those patients who underwent surgery were evaluated as well as the differences between the characteristics of benign and malignant nodules. **Results:** 59 patients were analyzed (7 lost to follow up) 83% girls, median age 13.9 years. 88% pubertal. Cause of referral: palpable nodule (78%), multinodular goiter (MNG) (13.5%), goiter (5%) and ultrasound finding (3.4%). 5 % had risk factor. 86.7% were euthyroid, 8.9% hypothyroid and 4.4% hyperthyroid. 22.2% had positive antythyroid antibodies. Median ultrasound greatest nodular diameter was 21mm (r: 8–80). 63% were solid, 19.2% had central microcalcifications, 5.2% irregular limits, 22.8% central vascularization and 8.8% pathologic lymphadenopathies. 62% were cold. Malignant and suspicious for malignancy FNAB results showed a positive and negative predictive value for malignancy of 57.1% and 92.3% respectively (diagnostic efficiency 65.1%). 43 patients underwent surgery: 10 papillary carcinoma, 5 colloid cyst, 16 nodular hyperplasia, 3 MNG, 7 follicular adenoma 1 thyroglosal, 1 lymphoep-

ithelial intrathyroid cysts. Papillary carcinoma was found in 38.5% of MNG and 16.7% of solitary nodules. All carcinomas were euthyroid, solid on ultrasound ($p < 0.05$) and 50% presented pathologic lymphadenopathies ($p < 0.05$). Malignant results in FNAB were always cancer. **Conclusions:** Our findings confirm that most pediatric nodular disease is benign, however with a greater incidence of cancer than in adults. US and US guided FNAB were the most useful tools in our strategic approach.

20

Effectiveness of the Neonatal Screening for Congenital Hypothyroidism (CH) in Preterm Newborns (PTNB)

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A higher incidence of CH and delayed TSH rise were reported, both in programs based on T4 or on TSH with supplementary samples in PTNB with gestational age (GA)<32 weeks. **Objective:** To verify this trend and assess the effectiveness of supplementary sampling to detect additional cases. **Methods:** To compare a) prevalence of PTNB and b) ratios of GA<(32) and EG(32-36) in 184 CH (G1) detected in 357151 newborns, with the general population (G2: 34994 NB). In 802 PTNB (in G3: n=21078 NB) supplementary samples were counted in PTNB EG<32 sem (n380). **Results:** Table 1 In G3, from 380 samples GA(<32) 67% had ≥1 replicates. **Deaths:** 14(3.7%) and 8 CH were detected, including one PTNB GA:27 weeks (1st sample: TSH=821 uIU/ml) and a term baby (1st sample:TSH<10; 2nd sample TSH=78) who was re-evaluated during his hospitalization for heart disease. **Conclusions:** The incidence of CH and delayed TSH rise is lower in PTNB than expected according to other experiences. The strategy of getting supplementary samples has not been effective to detect additional cases.

Table 1. (for Abstract 20)

	G1 157: term NB 16: PTNB 11: GA unknown	G2	G1 vs G2 Test: Chi-square
Prevalence PTNB	9.25%; n = 16/173	7.6%; n = 2470/34994	p = ns
%PTNB GA(<32)	1.15%; n = 2	0.7%; n = 223	p = ns
%PTNB GA(32–36)	8.1%; n = 14	6.9%; n = 2247	p = ns

21

Differences in the Effects of First Year Growth on Body Composition and Resting Energy Expenditure in Preterm Children with Born Very Low Birth Weight (VLBW) Either Appropriate (AGA) or Small for Gestational Age (SGA)

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Fast growth in first 3 months of life adversely affects metabolic risks of young adults born at term. Controversy exists with regard to differences in metabolic risk in PT born SGA or AGA. **Goal:** To determine whether there are differences in BC, REE and metabolic variables between children born VLBW either AGA or SGA and whether these differences are related to a certain period of weight gain during the first year of life. 67 VLBW PT (<32weeks /<1500g), (40 AGA, 27 SGA). Followed as part of the National Program for VLBWPT infants from age 40 weeks until 7 yrs. BC by DEXA (Lunar DPX-L), REE by indirect calorimetry using the method (Deltatrac) and blood sampling at age 6.7 0.5 years. Continuous variables: mean and SD and t Student test (independent groups). Categorical variables, frequencies and proportions compared by X2 (for independent groups). To assess the relationship of the different growth periods and body composition and energy expenditure: linear regression models with body composition and REE as dependent variables and the changes of weight SDS and length SDS as independents variables, were built. All these data were analyzed by a multivariate analysis. VLBWSGA children were leaner ($p<0.05$), shorter ($p<0.01$) and had lower waist and hip circumferences ($p<0.005$), HDL Cholesterol ($p<0.05$) and higher % fat ($p<0.05$), % region of interest fat (ROI) ($p<0.04$), trunk fat ($p<0.01$) than their AGA counterpart (adjusted by age, sex and BMI). Weight gain patterns differed between SGA and AGA VLBW ($p<0.001$).The difference is observed by CA 0 and 3 months of life. After adjusting for age, gender and adequacy at birth there was a direct correlation between weight gain in the first 3 months and total fat, % total fat, % ROI,% trunk fat and inversely with REE and Fat free mass (FFM). Weight gain between 6–9 months in SGA was correlated with total and % fat mass and ROI whereas in AGA correlates only with REE and REE/FFM. Weight gain between 9–12 months in SGA was correlated with total and % fat mass and trunk fat. By age 6 yr lower BW + higher fat mass subjects had higher Insulin and leptin ($p<0.001$). In summary, there were significant differences between SGA/AGA VLBW children in anthropometry, body composition and calorimetry and these differences were correlated to early periods of growth. All periods of weight gain in SGA are correlated to fat mass whereas in AGA 6–9 months of weight gain are correlated with REE. We speculate that the difference in this period may be due to higher lean mass in AGA children.

Table 1. (for Abstract 23)

	Group 1 HC Low IGF-I n = 5	Group 2 HC Normal IGF-I n = 5	Group 3 WT Low IGF-I n = 5	ANOVA
Gender (M/F)	4/1	3/2	3/2	
Age (years)	8.66±0.80	7.86±0.96	7.48±1.42	NS
Height (SDS)	−3.09±0.12[a]	−2.66±0.08	−2.91±0.11	P = 0.04
IGF-I (SDS)	−3.43±0.40[b]	−0.54±0.43[c]	−2.63±0.18	P = 0.0003
IGFBP-3 (SDS)	−3.14±0.31[de]	−0.97±0.49	0.15±0.28	P = 0.0001
ALS (SDS)	−3.98±0.26[be]	−0.90±0.52	−0.10±0.19	P = 0.0001
TCF/Total counts %	7.6±1.2	7.6±0.44	8.8±1.5	NS
TCF+rhIGFBP-3/Total counts %	31.6±2.2[cd]	48.8±1.7	46.7±4.1	P = 0.002
ΔTCF	24.0±2.7[df]	41.1±1.7	37.8±4.0	P = 0.0032

[a] P = 0.05 vs. G2; [b] P < 0.001 vs. G2; [c] P < 0.01 vs. G3; [d] P < 0.01 vs. G2; [e] P < 0.001 vs. G3; [f] P = 0.05 vs G3.
Results are expressed as mean±SEM.

22

A Novel Heterozygous *OTX2* Deleterious Variant (p.H230L) in a Patients with Hypopituitarism and Ectopic Posterior Pituitary Without Eye Malformation

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Background: Several transcription factors are necessary for the differentiation of five hormone producing cell types in the adenohypophysis. Patients with mutations in *HESX1*, *GLI2*, *LHX3*, *LHX4*, *SOX2*, *SOX3*, *PROP1*, and *POU1F1* have been described in humans with pituitary hormone deficiencies. *OTX2* mutations can cause eye malformations (anophthalmia and microphthalmia) alone or in association with isolated GH deficiency (IGHD) or combined pituitary hormone deficiency (CPHD). Recently, two unrelated patients with CPHD associated with ectopic posterior pituitary lobe (EPP) without ocular abnormalities were found to harboring heterozygous *OTX2* mutations. **Objective:** To analyze *OTX2* in patients with IGHD or CPHD. **Patients and Methods:** We studied 142 bBrazilian patients with CPHD and 44 with IGHD. Patients' DNA samples were subjected to polymerase chain reaction using intronic primers to amplify the translated exons and intron-exon borders,than PCR products were purified and sequenced by the Sanger method. **Results:** A novel variant p.H230L in *OTX2* was found in a single patient with CPHD associated with EPP without eye malformation. This variant was not found in 400 controls alleles. The histidine at the position 230 is conserved across the species and *in silico* analysis predicts a deleterious effect of leucine substitution. Familial segregation revealed heterozygous carriers (mother and two unaffected brothers) suggesting incomplete penetrance. We are assessing the function of this variant in cell culture assays and exploring the possibility of digenic inheritance with exome sequencing in the affected patient. **Conclusion:** Our set of 186 patients with CPHD without ocular malformation is the largest population screened for mutations in *OTX2*. The detection of only one suspicious variant in 186 individuals suggests that *OTX2* is an uncommon cause of CPHD or IGHD without eyes malformation in the Brazilian population.

23

Limited Ability for in Vitro Ternary Complex Formation (TCF) in Idiopathic Short Stature (ISS) Children Heterozygous Carriers (HC) for *IGFALS* Genetic Variants Associated with Low Levels of IGF-I, IGFBP-3 and ALS

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Background: Near 10% of ISS children present *IGFALS* gene variants, 50% associated with low levels of IGF-I, IGFBP-3 and ALS. We hypothesized TCF may be involved in the reduction of IGF-I levels. **Objective:** To determine TCF in ISS children HC or wild type (WT) for *IGFALS* gene with normal or low IGF-I levels. **Methods:** Patients were divided in three groups according to *IGFALS* genotype and IGF-I levels. TCF was determined by size exclusion chromatography with and without the addition of rhIGFBP-3 (6 µg/ml). **Results:** Basal TCF levels did not differ among groups; after rhIGFBP-3 addition G1 showed significantly lower TCF and ΔTCF values. Basal TCF did not correlate with ALS (r=0.23, NS); it did after rhIGFBP-3 addition (r=0.66; P=0.0069). **Conclusion:** The limited ability for TCF in G1 suggests a cause-effect relationship between the carrier status and the IGF-I deficiency, that could be responsible for their short stature.

24

Domain Specific-mutation in *CDKN1C* is the Cause of Image Syndrome

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IMAGe Syndrome (Intrauterine growth restriction, Metaphyseal dysplasia, Adrenal hypoplasia congenita, and Genital anomalies) OMIM 300290, is an undergrowth developmental disorder with life-threatening consequences. Identity-by-descent analysis in an Argentinean family with IMAGe syndrome identified a 17.2Mb locus on 11p15 that segregated in affected family members. Targeted exon array capture of the disease locus, followed by high-throughput genomic sequencing and validated by dideoxysequencing, identified c.825T>G mutation resulting in a p.Phe276Val missense alteration in *CDKN1C* ($P57^{KIP2}$). Familial analysis demonstrated an imprinted mode of inheritance where only maternal transmission of the mutation resulted in IMAGe syndrome. *CDKN1C* inhibits cell-cycle progression and targeted expression of IMAGe-associated *CDKN1C* mutation in Drosophila caused severe eye growth defects, suggesting a gain-of-function mechanism. Furthermore, IMAGe- associated mutation clustered in the PCNA-binding domain of *CDKN1C* and resulted in loss of PCNA binding. In contrast loss-of-function mutations in the N-terminal cyclin dependent kinase domain of *CDKN1C* has been shown to result in an opposite syndrome, Beckwith-Wiedemann Syndrome, an overgrowth syndrome with adrenalomegaly. This novel mechanism for *CDKN1C* regulation revealed the undergrowth-associated IMAGe syndrome and may in the future elucidate previously unidentified mechanisms involved in cell transformation and cell cycle progression.

25

Molecular Characterization of Pseudohypoparathyroidism Type Ia and Ib

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Background: Pseudohypoparathyroidism-Ia and Ib (PHP-Ia and PHP-Ib) are characterized by hypocalcemia and hyperphosphatemia due to PTH resistance. They are caused by mutations in exons 1-13 of *GNAS* gene (PHP-Ia) or by defects in the imprinted *GNAS* locus (PHP-Ib). Patients with PHP-Ia present other hormone resistances and the so-called Albright's hereditary osteodystrophy (AHO). The same phenotype is also found in patients diagnosed with pseudopseudohypoparathyroidism (PPHP), which do not present hormone resistance. On the other hand, patients with PHP-Ib present PTH resistance with no AHO. **Objectives:** To characterize a cohort of patients with suspicion of PHP, studying the *GNAS* locus at structural and epigenetic level, trying to identify the molecular mechanisms responsible of the regulation of the methylation of the locus, and to evaluate the phenotype-genotype relationship. **Patients and Methods:** 35 patients (31 children, 4 adults) with suspicion of PHP were analyzed. The 13 codifying exons of the *GNAS* gene were studied by PCR and direct sequencing. Deletions and duplications within the locus, as well as the methylation status of the DMRs in the region were evaluated by MS-MLPA. **Results:** 29 out of 35 patients (83%) presented with molecular alterations that explain their clinical status: 16 mutations in the *GNAS* gene (46%) and 13 loss of methylation (37%): 4 in A/B exon only and 9 in A/B plus NESPas and XLas. Six patients (17%) did not present any alteration in the *GNAS* locus. **Conclusions:** There is a wide variability in the distribution and characteristics of the mutations in the *GNAS* locus. The imprinting alterations in the *GNAS* locus (loss of methylation) can be due to deletions in the imprinting regulatory elements, 20q chromosome disomy, or stochastic mechanisms. New studies are required in order to evaluate the negative cases.

26

Spine Bone Mineral Density in Children with Duchenne Muscular Dystrophy Treated with Corticosteroids

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Background: Reduced mobility and glucocorticoids (GC) as adjunctive therapy may cause osteoporosis and fractures in children with Duchenne Muscular Dystrophy (DMD). **Objective:** To assess

lumbar bone mineral density (BMD), its relation with age, time of immobilization, duration of GC therapy, and cumulative dose of GC. **Methods:** We analyzed in 26 boys (mean age ± SDS: 11.5 ±2.6y, weight Z-score: –0.05±1.18, and height Z-score: –1.62±0.9) with DMD treated with deflazacort (n=14) or methylprednisone (n=12) during 3.8±2.2 years (range: 0.4–8.8), vitamin D (300 to 2400 IU/day) and calcium supplement (0.13 to 1 g/day) with calcium intake by dairy products of 586±234 mg/day: Lumbar L2-L4 bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (Lunar, Prodigy), serum calcium (Ca), phosphate (P), alkaline phosphatase (AP), PTH and urinary calcium and D-Pyridoline/creatinine (uD-Pyr). **Results:** The cumulative GC dose was 25.8±18.2 g (range: 4.6–65.7). Mean BMD SDS was –2.1±1.4 ranging from –5.9 to 0.4. BMD SDS was < –2 in 12 (46%), and < –1 in 20 patients (77%). Mean BMD SDS was inversely correlated with age ($p<0.0001$), time of immobilization ($p<0.0001$), duration of corticosteroid therapy ($p<0.02$) and cumulative dose of corticosteroids ($p<0.0001$).Twelve patients were wheelchair-bound (mean age: 12.9 ±2.3 y, immobilization time was 2±1.9 y). Three patients had long bone fractures and 11 had vertebral crush fractures. Significantly lower BMD SDS (–3.16±1.42) in patients with in comparison with those without vertebral fractures (–1.33±0.86, $p<0.005$). The number of fractures was positively correlated with cumulative GC dose. Ca, P, AP and PTH were within the normal range. Urinary calcium and uD-Pyr were increased in 39% and 50% of the patients respectively. **Conclusion:** Long-term immobilization and treatment with high corticoids doses affect bone mineralization in children with DMD and might worsen the outcome of the disease.

27

Ovarian Reserve (OR) after Chemotherapy Due to Acute Lymphoblastic Leukemia (ALL) During Infancy. Preliminary Results

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Advances in chemotherapy increase survival of patients with leukemia but can leads to infertility and decrease in OR. Prepubertal ovaries appear to be resistant to cytotoxic agents. **Aim:** Assess the ovarian function after ALL treatment with chemotherapy in infancy in postmenarcheal girls. **Methods:** Women 15–35 years old treated for ALL according to PINDA protocol(1986–2002) at least 5 years before were recruited. Physical exam, pelvic ultrasound, FSH and Antimüllerian hormone(AMH) were determined and compared with 26 controls(Codner et al). **Results:** 29 women 21.7±0.8 years old. Age at diagnosis 5.9±3.5. Age at menarche 12.6±1.6(11–17). 20.8% had history of amenorrhea, 17.2% pregnancy attempt and gestation in 3/5. 24% are on oral contraceptives(OC). FSH 6.2±4.4 vs 5.8±0.4 uUI/ml in ALL vs controls respectively and AMH 5.5±0.5 vs 2.4±0.3 ng/ml ($p<0.001$). No differences in AMH between women on OC or not.Two have FSH≥10, one AMH between –1 to –2 SD and 1 <–2 SD (treated at 15 years old). Ovarian volume (OV) 6.7±0.8 cc and follicle number 4.8±2.5. **Discussion:** With standard doses of chemotherapy, ovarian function often is retained, FSH is a marker of ovarian function and AMH, OV and FN are emerging as a markers of OR. It is important provide information and evaluate OR to help the patients make decisions regarding to fertility.

28

Dysgenesis Signs and Atypic Expression of OCT-3/4 in Testis of Prepubertal Patients with Androgen Insensitivity Syndrome

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Background: In the human prepubertal testis (HPPT), the androgen receptor (AR) is expressed in peritubular and intestitial cells, but not in Sertoli cells. Adult patients with the complete kind of androgen insensitivity (CAIS) have dysgenetic testis. **Hypotheses:** Human prepubertal testis with androgen insensitivity might have risk of gonadoblastoma. **Objective:** To characterize the testis from PP patients with CAIS or PAIS (partial androgen insensitivity). **Population and Methods:** We have studied nine PP patients (CAIS: n=7, PAIS: n=2) gonadectomized at the range of 1.33 and 9.75 years old. To reach the diagnostic, we used the phenotypic features, the hormone studies, the absence of response of SHBG to the stimulus of testosterone (T) and the molecular study of AR gen (n=5) (4 mutations M749V, R631X, E603X, L621P and 1 deletion,del1550-1569ex1). Histology, immunoexpression of OCT-3/4 (transcription factor, specific of embryonic stem cells), AR and ERα and T secretion in primary cell culture were studied. HPPT without endocrine pathology were used as control (C, n=10). **Results:** Signs of testicular dysgenesis were found in 7/9 samples; carcinoma in situ and/or OCT-3/4 expression in 5/9; hiperplasia of Leydig cells (LC) in 4/9; atypic cytoplasmatic localization of AR in 3/9. Positive expression of ERα in hyperplasic LC, different to C (ERα negative). T secretion in vitro confirmed the presence of steroidogenic cells in cell culture of the patients. **Conclusions:** The OCT-3/4, a marker elected to predict the risk of gonadoblastoma, was found in testis of prepubertal patients with CAIS and PAIS. Therefore our results suggest that it is necessary to undergo a biopsy to define the therapeutic behaviour in prepubertal patients.

29

The Influence of Glucocorticoid Receptor Gene Variants on Glucocorticoid Sensitivity

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Introduction: Glucocorticoid (GC) sensitivity can be evaluated by the intravenous dexamethasone suppression test (IV-DST). Polimorphic GR variants are associated to increased (GRβA3669G) or decreased (GRαBclI C/G) GC sensitivity. **Aim:** To correlate GR gene variants with GC sensitivity measured by the IV-DST. **Patients and Method:** We studied 70 normal adolescents/young adults, 42males/28females, CA=19–23y, mean(SD) BMI=23(3)kg/m2. GRβ variant was detected by real time PCR, and GRα variant detected by PCR-RFLP (BclI enzyme digestion). **Results:** (see table) Glucocorticoid sensitivity is significantly higher in individuals with the GRβA3669G variant when compared with individuals with the GRαBclIC/G variant. These findings are opposite to the previously described, and are possibly ensured by the use of the IV-DST infusion. This IV infusion avoid the undesirable influence of the first liver passage observed when using oral administration.

Table 1. (for Abstract 29)

	N	% cortisol suppresion mean (SD)
Homozigous wild type	18	37.9 (17.7)
GRα (BclI C/G)	30	33.0 (18.0)
GRβ (A3669G)	16	44.7 (17.5)*
GRα+GRβ	06	31.2 (21.4)

* GRβ vs. GRα; p = 0.04; Student t-test.

30

Characterization of the Novel Misssense Mutation G250V in Type II 3beta-hydroxysteroid Dehydrogenase (3ß-HSD2) Gene Found in a 46, XX (female) Patient with Congenital Adrenal Hyperplasia (CAH)

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Background: 3βHSD2 deficiency is characterized by varying degrees of salt loss and mild virilization/normal external genitalia in females and undervirilization in males. **Objective:** To characterize a novel misssense mutation G250V in 3β-HSD2. **Methods:** A 7-month-old 46,XX girl, was referred with pubarche and postnatal clitoromegaly. Consanguinity was known. Hormonal profile showed low cortisol 4.8ug/dl and high ACTH 2888 pg/ml, DHEAS53000 ng/ml, 17OHProg141 ng/ml and plasma renin423.9 ng/ml.These data point to 3βHSD2 deficiency. Enzymatic activity was analyzed by in vitro analysis of mutant recombinant enzyme generated by site-directed mutagenesis after its transient expression in COS cells. **Results:** Enzyme activity using pregnenolone as substrate, revealed relative conversion rates of pregnenolone to progesterone of 78±4% and 21±1% by WT and G250V-3β-HSD2 enzymes respectively. Using dehydroepiandrosterone as substrate the conversion rate to androstenedione was 87±8% and 23±7% by WT and G250V-3β-HSD2 enzymes respectively. **Conclusions:** We identified a novel G250V 3βHSD2 gene mutation which causes an incomplete loss of activity. Flux via "backdoor" pathway, which convert 17OHProg to dihydrotestosterone has been implicated in human disorders of androgen excess.We hypothesized that this pathway could not be activated in 3β-HSD2 deficiency due to low intraadrenal 17OHProg substrate, explaining mild virilization or normal differentiation in females.

31

Assessment of Blood Pressure in Children and Adolescents with Congenital Adrenal Hyperplasia Due to 21OH Deficiency

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Some studies have shown a high frequency of hypertension in children with Congenital Adrenal Hyperplasia (CAH) due to 21-hydroxylase deficiency (21OHD). **Objective:** To evaluate blood pressure (BP) in children and adolescents with CAH due to 21OHD. **Patients and Methods:** 21 patients (median age 14.5y) with CAH were submitted to clinical and laboratory evaluation, with measurement of BP and Ambulatory Blood Pressure Monitoring (ABPM). **Results:** Fourteen patients had the classic form of the disease (12 had salt-wasting CAH), 71.4% were female, 19% were overweight and 28.6% were obese. Among the different types of glucocorticoid (GC), 14.3% of patients received dexamethasone, 28.6% hydrocortisone and 57.1% prednisone. Regarding the dose of GC, 28.6% of patients were using low dose, 28.6% high-dose and 42.8% received an adequate dose. 95% had normal BP and 5% had pre-hypertension. Thirteen patients were submitted to ABPM, 15.4% had normal BP, 23% had pre-hypertension and 61.5% had hypertension. No relationship was found between the type of glucocorticoid used for treatment and the occurrence of hypertension. None of the patients showed low plasma renin levels or high sodium level. **Conclusion:** ABPM identified hypertension in patients with CAH due to 21OHD, despite the normal manual blood pressure measurements.

32

Idiopathic Central Precocious Puberty (ICPP): Efficacy of GnRH Analogues (GnRHa) Treatment in 81 Girls Assisted in a Single Pediatric Endocrine Center

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ICPP is characterized by precocious sexual development and accelerated bone maturation with consequent impairment of adult height (AH). GnRHa is the treatment of choice for ICPP. **Objective:** To assess AH and to determine factors influencing AH in girls with ICPP treated with GnRHa. **Patients and Methods:** 81 girls with ICPP treated with GnRHa who had reached AH were included. Clinical features, target height (TH), bone age (BA) and predicted adult height (PAH) by G&P were assessed. Univariate and multivariate analyses of the factors potentially associated with AH were performed (Infostat 2008). Data are shown as mean ± SE. **Results:** At start of treatment Chronological age (CA) was 7.53±0.17(0.8–7.9) years. Bone age (BA) was 9.78±0.21 years and BA-CA was 2.3±0.11years. Initial height was 131.8±1.29 cm and PAH was 154±0.74 cm. Patients were treated for 2.7±0.2 years. All patients showed clinical and hormonal parameters of adequate therapeutic response. At end of treatment CA was 10.32±0.05 years, BA was 11.9±0.07, BA-CA was 1.64±0.09, height was 147.7±0.70, PHA was 159.9±0.76 cm. AH was 160.47±0.72 cm no different to TH (160.02±0.62 cm). AH-PAH at the start was 6.06±0.63 cm. Data of univariate analyses showed no correlation between BA and CA at start of treatment with AH. Multiple linear regression analysis showed a significant positive association of AH with height at end of treatment, TH and % of TH achieved at end of treatment ($p=0.0012$) Interval between CA at onset of puberty and CA at start of therapy showed significant and negative association with AH. ($p<0.05$) Postreatment linear growth showed a significant negative association with BA at end and significant positive association with the interval between CA at end of treatment and age at menarche ($p<0.0001$). **Conclusion:** Treatment with a GnRH in ICPP girls showed to be effective to reach a normal AH according to TH, independently of CA at start of treatment.

33

Apparent Mineralocorticoid Excess: Case Report and Molecular Diagnosis

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Apparent mineralocorticoid excess syndrome (AME) is an autosomal recessive disorder due to excess activation of the mineralocorticoid receptor (MR) by cortisol secondary to a defect in the enzyme 11βhydroxysteroid dehydrogenase type 2 (HSD11B2) with failure to convert cortisol to cortisone.Typical patients present with severe hypertension, hypokalemia, and undetectable aldosterone (A). **Objective:** To report a patient with typical phenotypic features of AME. This male patient from a nonconsanguineous family presented at age 10 months with low weight gain and muscular weakness. He had a low birth weight 2010 gr, two months of polyuria, polydipsia. His physical exam revealed height –2.96 SDS, weight –3.73 SDS, low lean mass. He presented with hypertension (115/77 mm Hg), low plasma renin activity < 0.2 ng/ml/h, hypokalemic 2.9 meq/L with metabolic alkalosis, suppressed A < 20 pg/ml, and bilateral nephrocalcinosis. With diagnosis of AME he began treatment with dexamethasone, with normalization of her blood pressure, PRA, and potassium. During follow-up spironolactone and hydroclorotiazide were added because of persistent hypercalciuria, failure to thrive and some registers of hypokalemia. Sequence analysis of the HSD11B2 gene revealed heterozygous mutations IVS3+14C>T, N223D (maternal allel) and R337H/ΔY338 (paternal allel). **Comment:** AME is a rare disease (only 100 cases described) and diagnosis before the age of one year is very difficult. The mutations found in this patient were already described. In *vitro* expression studies revealed very low enzymatic activity, consistent with the young age of presentation with a severe phenotype (Carvajal 2003, Mune 1995). The gene for 11βHSD2 (HSD11B2) has been cloned and localized to chromosome 16q22. More than 20 specific mutations in the HSD11B2 gene have been reported to date. The diagnosis of AME should be suspected in patients with features of low birth weight, failure to thrive, polyuria, polydipsia, and hypertension.

34

Clinical and Genetic Findings of Paraganglioma/Pheochromocytoma Syndromes Associated with SDHB and SDHD Mutations (Pgl4 and Pgl1)

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Pgl4 and Pgl1 are related to gene mutations encoding succinate dehydrogenase subunits B(SDHB) and D(SDHD). Pheochromocytomas and pgl occur in both syndromes. The genetic findings and the differences in clinical features of 19 index cases with Pgl4, (twelve youngster 8–17y and 7 adults) and 3 Pgl1 adults, with 1–12 years of follow up(median=4) are described. All Pgl4 and 2 Pgl1 presented symptoms caused by hypersecretion of catecholamines with NA and VMA increase. 5/19 Pgl4 presented adrenal and 15/19 extra-adrenal pheo, 8/19 were malignant. 1/3 Pgl1 presented adrenal pheo and all of them developed head and neck pgl. PCR followed by direct sequencing was performed to characterize *SDH* mutations. The SDHB analysis showed:5 missense mutations:#R217G(2), #S198R(1), #L65R(1), #Q235*(1), #E178*(1), 1 Frameshift:c166_170delCCTA(10), 1 Del1-2 and 2 intron variations, IVS2+33G>A and IVS2+35G>A. The SDHD mutations were: c341_2ATdel, c57_Gdel and c217dup. Five new variants(#) were considered pathogenic based on predictions tools available online.10/23 SDHB relatives studied were carriers, 3/10 had clinical disease.18/29 SDHD relatives were carriers, 6/18 had head and neck pgl. The frequency of the deletion c166_170delCCTCA was remarkably higher than reported so far, ($p<0.001$, Fisher Exact test). Age of diagnosis, phenotypes and rate of malignancy of SDHB and SDHD was different with higher incidence in youngster and risk of malignancy in Pgl4, and higher frequency of head and neck tumors in SDHD.

35

Phenotype-genotype Characterization of Congenital Hyperinsulinism in Spanish Population

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Background: Congenital hyperinsulinism (CHI) is characterised by recurrent episodes of hyperinsulinemic hypoglycemias due to an inappropriate secretion of insulin by the pancreatic ß-cells. Genetically CHI is a heterogeneous condition, caused at least by mutations in 8 different genes. **Objectives:** Elucidate the genetic of CHI in our population and explore genotype-phenotype correlations. **Methods:** 55 Spanish infants with persistent CHI belong to unrelated families were studied for alterations in *ABCC8*, *KCNJ11*, *GCK, GLUD1* and *HNF4A* genes by sequence analysis. **Results:** The onset of hypoglycemia occurred within the first hours or days of life in 27 probands, and only in 4 after one year of life. The most common symptoms at diagnosis were in order of prevalence: convulsions > hypotonia >altered level consciousness > tremor > cyanosis, while 23.6% were asymptomatic. 44 patients were treated with diazoxide and were effective in 32 of them. Mutations were identified in 45.5% (25/55) of patients. Of these, 17 in the K_{ATP} channel genes and 8 in the other genes. *ABCC8* inactivating mutations were found in 64% (16/25) of the cases, 7 were heterozygous, 4 homozygous and 3 compound heterozygous. Only one patient presented a mutation in *KCNJ11*. Pancreatectomy was performed in 11 patients, of which 7 had mutation in ABCC8. *GLUD1* was studied in those children with elevated serum ammonia levels and three different heterozygous mutations previously described were identified. A novel *HNF4A* mutation was identified in a proband with macrosomia and hyperinsulinemic hipoglycemia and in his mother who had diabetes. Missense heterozygous activating *GCK* mutations were identified in 4 patients. **Conclusion:** Mutations in *ABCC8* are the most frequent cause of the CHI in Spanish population. In a high percentage of cases the cause of their CHI is not known, therefore studies of other candidate genes would be required in order to determine the genetics cause of the disease.

36

Fractional Excretion of Sodium as a New Component of the Metabolic Syndrome in Pediatric Population

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Salt-intake affects blood pressure (BP) and metabolic syndrome (MS) components. In pediatrics patients, scare evidence exists regarding the relation between salt excretion and MS components. **Objective:** To evaluate the association between the fractional excretion of sodium (FENa-12 h), with some MS components: waist/ height ratio; insulin resistance, dyslipidemia and hypertension. **Subjects and Methods:** 291 children were studied, 49.1% females, age (median [Q1–Q3]) = 11.7[9.4–13.3] years. The systolic and diastolic blood pressure index (SBPi & DPBi) using the observed BP/50th percentile BP were calculated. 12-hour nocturnal urine (7:00 PM to 7:00 AM) were collected. Serum and urinary Na and creatinine, were measured. FENa-12 h were calculated. The associations were studied by Rho's Spearman. **Results:** Nocturnal FENa-12 h correlated positively with waist/ height ratio (Rho=0.129; P= 0.029), HOMA-IR (Rho=0.137; P=0.020) TG/ HDL-Col (Rho=0.149; P= 0.014); SBPi (Rho= 0.133; P= 0.024), DBPi (Rho=0.209; P <0.001). **Conclusions:** Nocturnal FENa-12 h was associated with MS com-

ponents. These associations observed in childhood could be relevant in the development of resistant hypertension as well as cardiovascular disease and chronic kidney disease in adulthood. Supported by Chilean grants: FONDECYT 1100356,FONDEF D08I1087 and the Millennium Nucleus on Immunology and Immunotherapy P07/088-F.

37

Molecular KCNJ11 and ABCC8 Genes in Congenital Hipoglycemia Hiperinsulinemic

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Introduction: Hypoglycemia Hiperinsulinêmica Congenital (HHC) is the gravest form of hiperinsulinism. Mutations at ABCC8 and KCNJ11 genes determine clinical form and therapeutic response. **Methods:** Samples of 43 HHC patients had annalysed KCNJ11 and ABCC8. The DNA was extracted and amplified by PCR and subsequently sequenced utilizing oligonucleotide for the region M13. The sequencies obtained were edited and compared to reference (GenBank ABCC8 NM_352.3 and KCNJ11 NM_000525) by the software SeqScape v2.6. **Results:** 258 sequencias showed variations in three points of the exon 1, two points of the exon 2 and a point of the exon 3 of the gene ABCC8, and in seven points of the gene KCNJ11, five of the thirteen variations are related in the literature as related to HHC. Only one amino acid change cause variation of the protein, whereas of the seven variations of the gene KCNJ11, six cause alteration of the protein. **Conclusion:** Punctual mutations of the genes KCNJ11 and ABCC8 are associated to the HHC of Brazilian sample. The knowledge of the mutation helps the clinical one as regards the handling proposed.

38

Serum 25-hydroxyvitamin D is Positively Associated to BMI and Serum Uric Acid in Pediatric Obese Patients

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Background: Many non-calcemic actions of active vitamin D have been described, including the reduction of the risk for metabolic syndrome (MS). On the other hand in obese patients the increased deposition of 25-hydroxyvitamin D (25OHD) in adipose tissue may reduce its bioavailability. **Objective:** This study aimed to evaluate the 25OHD status and the association between serum 25OHD (s25OHD) with BMI and the laboratory parameters of obesity and MS in obese pediatric patients. **Methods:** 95 obese patients were evaluated. The patients were considered vitamin D sufficient, insufficient or deficient if their s25OHD were respectively >30, 10–30 or <10 ng/mL. The s25OHD was correlated to BMI-SDS, PTH and to the following laboratory parameters of obesity and MS: leptin, CRP, uric acid, total cholesterol, HDL, triglycerides and HOMA-IR. The correlation was studied through Pearson's correlation coefficient. Statistical analysis was based on SPSS version 15.0. **Results:** The mean BMI-SDS was 2.2±0.43 and the mean age was 14±2.4 years. With respect to the 25OHD status 5.3%, 85.3% and 8.4% of the patients were respectively classified as vitamin D sufficient, insufficient and deficient. We found a significant positive correlation between s25OHD and BMI-SDS (r:0.21; p:0.04) and uric acid (r:0.30; p:0.02), and a significant negative correlation between s25OHD and PTH (r:–0.22; p:0.03). The other correlations were not significant. **Conclusions:** 93.7% of the obese pediatric patients studied were considered vitamin D insufficient or deficient. Unlike most previous studies, in our study serum 25OHD correlated positively with BMI-SDS and with a laboratory parameter of metabolic syndrome (serum uric acid). A causal relationship could not be established due to the cross-sectional design of this study.

39

Type 4 Retinol Binding Protein as a Marker of Hepatic Steatosis in Adolescents with Type 2 Diabetes

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Introduction: RBP4 is an adipokine that is associated with insulin resistance. In obese pediatric patients its concentrations are elevated. In adult population with type 2 diabetes mellitus (T2D) there is a positive correlation between RBP4 levels and hepatic steatosis (HS). The information about RBP4 concentrations in adolescents with T2D, and its association with HS is scare. **Objective:** To evaluate the association between RBP4 concentrations and HS in adolescents with T2D. **Material:** Cross sectional study. 34 adolescents withT2D were included. **Method:** We determined glucose, glycated hemoglobin A1c (HbA1c), lipid profile, and RBP4 levels. The degree of HS was determined by hepatic Doppler-ultrasound using Tominaga Classification. **Results:** Of the total of patients, 64.7% were female. The median age was 14.37 ± 2.27 years, BMI 26.84 ± 11.18 kgm², waist circumference 86.65 ± 12.20 cm and HbA1c 9.27 ± 3.27%. 33.3% patients did not have steatosis, 41.7% had moderate HS and 25% had severe HS. RBP4 concentrations were higher in patients with severe HS compared with those with moderate and non HS (p=0.04). **Conclusion:** In adolescents T2D, RBP4 levels are associated with the degree of HS. This adipokine could be used as an HS serum marker.

40

Renal Injury Biomarkers in Children with Type 1 Diabetes Mellitus. Preliminar Data

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Objective: To cuantificate biomarkers of renal injury, NFAT5 and HIF-1α and NGAL, in pediatric patiens with type 1 diabetes mellitus and to compare its level according to metabolic control. **Methods:** 20 children and adolescents with type 1 Diabetes Mellitus were studied, 2 groups according its average HbA1c on the last year, couple by age, sex and puberal stage were formed. Preliminar results of 8 DM-1 patiens are presented. Sex, age, time from diagnosis, HbA1c, serum creatinine, microalbuminuria and albuminuria creatininuria ratio were registered. A 5 ml of blood were collected, serum was isolated by centrifugation (4000g x 10 minutes) and supernatant (S) and exosomes (E) fraction were obtained by ultracentrifuged cell-free serum (38000gx1hr, 4° C). Each fractions, was treated with lysis buffer. NFAT5, HIF-1α and NGAL concentration were determined in 100 micrograms of S and E fractions by Western blot. Average and SD were calculated and cluster analysis was done. **Results:** Table 1 show general data and laboratory results. Renal injury biomarkers are shown in fig 1. NFAT5 was expressed equally in patients with bad and good control in both fractions studied. HIF-1α and NGAL were highly expressed in patients with bad control compared with good control group, in S and E. The abundance of each biomarker was lightly increased in the exosome fraction. Cluster análysis show that overall measured biomarkers are grouped according metabolic control en 2 groups.

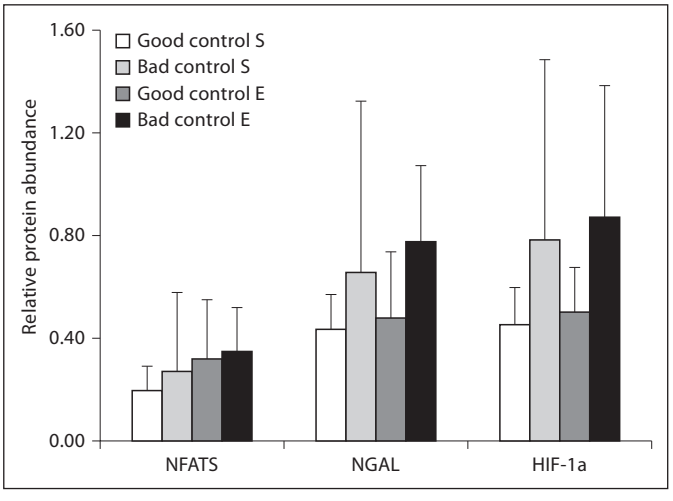

Fig. 1. NFAT5, NGAL and HIF-1a in S and E fractions by group (for Abstract 40).

Table 1. General results by group (for Abstract 40)

Group		Good Control	Bad Control
N		4	4
Male/female		3/1	3/1
HbA1c (%)		7.8 + 3.5	11 + 1
Age (years)		14.0 ± 2.7	14.4 ± 0.4
Time DM-1 (years)		6.2 + 2.4	7.5 + 3.5
NFAT5	S1	0.2 + 0.1	0.27 + 0.14
	P2	0.32 + 0.23	0.36 + 0.16
	Total	0.52 + 0.32	0.63 + 0.3
NGAL	S1	0.43 + 0.13	0.65 + 0.42
	P2	0.48 + 0.26	0.78 + 0.29
	Total	0.91 + 0.32	1.44 + 0.67
HIF-1a	S1	0.45 + 0.15	0.78 + 0.30
	P2	0.5 + 0.18	0.68 + 0.51
	Total	0.95 + 0.32	1.66 + 0.70

Conclusions: The present data suggest that the determination of these renal injury biomarkers in children with type 1 diabetes mellitus seems to be a promissory tool for precocious renal involvement in type 1 DM-1 children.

Poster Presentation

41

Diagnosis of Papillary Carcinoma in Pediatric Patients with ^{99M}TC Scan Hyperfunctioning Thyroid Nodules in a Iodine Sufficient Area

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Background: Thyroid cancer usually has reduced iodine uptake and normal thyroid function. Rarely cancer is reported within or near hyperfunctioning nodules. Higher incidence is reported in iodine deficient areas soon after introduction of iodinization. Fine needle aspiration biopsy (FNAB) of hot nodules is not routinely performed. **Objective:** We report three adolescents from a iodine sufficient area detected in 3 pediatric endocrinology centers with hyperfunctioning thyroid nodules which upon surgery, histopathology revealed a papillary carcinoma. **Results:** Case 1 (14yrs) referred due to a firm nodule in her neck, ultrasound(US) showed an heterogeneous irregular cystic-solid mass of 19x14x13 mm, it was hyperfunctioning with normal extranodular thyroid uptake. Due to suspicious US findings, family history of thyroid cancer and unsatisfactory FNAB, thyroidectomy

was performed which revealed carcinoma. Case 2 (13yrs) referred due to a firm nodule in her neck, US showed a cystic-solid nodule of 6x3.5x4 cm which was hyperfunctioning with almost total inhibition of contralateral lobe. FNAB was benign, thyroidectomy was decided because of the nodule size allowing diagnosis of carcinoma. Case 3 (15yrs) had hyperthyroidism. US showed a heterogeneous irregular solid nodule of 23x13x21 mm with micro-calcifications. It was hyperfunctioning with normal uptake in the rest of the gland. Nodulectomy led to diagnosis of papillary carcinoma within the nodule. **Conclusions:** Thyroid glands with hot nodules need to be carefully evaluated because malignance can be present. Further studies will determinate which is the best strategy for accurate diagnosis and treatment of hot nodules in pediatrics.

42

Thyroid Nodules in Children: Evaluation of the Clinical and Ultrasound Thyroid Examinations as Predictive Diagnostic Variables

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Background: In children, the incidence of thyroid nodules is 1.5%. **Objective:** To determine the incidence of benign and malignant thyroid nodules in children and to analyze predictive diagnostic variables. **Population:** A descriptive, retrospective study was conducted in 128 children with thyroid nodules. **Results:** 80% underwent surgery, FNA yielded adequate specimens in 22% (n: 28); 57.8% had thyroid cancer. A solitary thyroid nodule was found in 55%, a nodule associated with lymphadenopathy in 22.5%, and a conglomerate 22.5%. Pathological examination confirmed thyroid cancer in all conglomerate and in 91% of the cases with a nodule associated with lymphadenopathy ($p < 0.0001$). Ultrasound findings: probably malignant: 57%; probably benign: 22%; undetermined: 22%. A significant association was found with the pathological diagnosis ($p = 0.0001$). Table 1. **Conclusions:** Combined palpation and ultrasound examination was useful to predict malignancy.

Table 1. General results by group (for Abstract 42)

Indicators (n = 102)	Palpation	Ultrasonography	Combined Palpation+Ultrasonography
Sensitivity	74.6% [63.5; 85.7%]	88.1% [79.8; 96.3%]	91.5% [84.3; 98.6%]
Specificity	95.3% [89; 100%]	76.9% [64.3; 89.5%]	46.5% [31.6; 61.4%]
Positive predictive value	95.7%	89.7%	96.3%
Negative predictive value	73.2%	90.9%	87.1%
False positive results	4.3%	10.3%	12.9%
False negative results	26.8%	9.1%	4.8%

43

Blood Spot TSH in Chilean Neonates: Is a Cut-off Value of 15 mU/L Appropriate?

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Introduction: The selection of an appropriate blood spot thyrotropin (ns-TSH) threshold value for the screening of congenital hypothyroidism is still under discussion. In Chile, a cut-off value of 15 mU/L for ns-TSH is currently recommended when using the DELFIA system. **Objective:** To describe ns-TSH values in Chilean neonates **Subjects and methods:** We analyzed data from 2356 neonates, born in the Pontificia Universidad Católica de Chile hospital between July 2010 and April 2011. We did not exclude newborns presenting comorbidities or admitted to intensive care unit. ns-TSH levels were determined with the DELFIA system, and results are expressed as median, 3rd and 97th centiles. **Results:** The median ns-TSH was 2.97 mU/L [0.58 and 10.95 mU/L]. The percentage of neonates with ns-TSH levels >15 mU/L was 0.59 %, and 3.23% presented ns-TSH between 10 and 15 mU/L. Also, 0.33% had ns-TSH =0.10 mU/L. **Conclusion:** Regarding these results, and published experiences, we recommend the follow up newborns with ns-TSH between 10 and 15 mU/L and to evaluate costs and benefits of lowering the cut-off of 15 to 10 mU/L. Also, neonates with TSH < 0.58 mU/L should be evaluated.

44

Papillary Carcinoma of the Thyroglossal Duct Cyst: Case Report in a 12 Year Old Girl

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Thyroglossal duct cysts (TGDC) are the most common thyroid developmental anomalies accounting for 75% of midline neck tumors in children and 7% in adults. Carcinoma of the TGDC has been reported in less than 1% in adults. **Objective:** Describe the case of a pediatric papillary carcinoma of the TGDC. **Case Report:** A 12 year old girl presented with an asymptomatic fast growing neck mass noticed 7 months previous to consultation. Her past medical history was unremarkable. US revealed a 21x13 mm cystic-solid mass with microcalcifications and a normal eutopic thyroid gland. With a presumptive diagnosis of TGDC a Sistrunk procedure was performed. Histological evaluation revealed a papillary carcinoma of 12x6mm in the wall of a 35x25x25 mm TGDC. The patient was referred to our Unit for follow up. Physical examination revealed a euthyroid pubertal girl with a non palpable thyroid gland without palpable cervical nodes. Neck and chest CT scan were normal. In order to complete treatment she underwent a total thyroidectomy. Histologic examination revealed no tumor. Postoperatively, ablative ^{131} I was administered, WBS performed on day 5 revealed focal radioiodine uptake confined to the inferior cervical region. Cervical US showed a right yugular adenopathy of 15x7 mm with a heterogeneous vascularized rounded area. FNAB cytology was positive for papillary carcinoma and washout TG positive. Surgical excision was performed with histologic diagnosis of papillary metastatic infiltration. **Conclusions:** Although exceptional in pediatrics, rapid growth of TGDC in absence of infection with US signs suggestive of malignancy should alert of the possibility of TGDC carcinoma. The lack of thyroid involvement does not rule out the presence of metastasis and follow up should be the same as for differentiated thyroid cancer.

45

Hyperthyroidism in Children and Adolescents

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Hyperthyroidism (HT) has a prevalence of 0,1/100000 in children and 1/100000 in adolescents, the most frequent etiology is Graves disease (GD). **Objective:** To review clinical presentation, etiology and management of hyperthyroidism in children and adolescentes. **Method:** Retrospective review of clinical records of hyperthyroid children, under 15 years, who consultes between april 2004 to july 2012 in our unit. HT diagnosis was done by suppressed TSH and elevated thyroid hormones. Etiological study with TRAb, AbTPO, ATG; Thyroid ultrasound and I131 uptake were done. **Results:** 22 patients; 54.5% female. Age at diagnosis: 10.12 ± 3.28 years (range 2 a 14.8). Clinical presentation was characterized for goiter (95%), tachicardia (86%) and exoftalmus (73%). Etiology: GD was diagnosis in 72.7% and Hashitoxicosis in 27.3%. Management: 100% were treated with antithyroid drugs (DAT) as first option; 27% begin treatment with Propiltyouracilo and since 2007 with Tiamazol. 68.1% became euthyroid at 7.67 months. 36.4% presentes hypothyroidism at 6.5 ± 4.3 months from DAT treatment, LT4 treatment was indicated and 31.8% has used it intermittently. I131 was used in 1 girl with persistent positive TRAb after 8 years of treatment. Thyroidectomy was indicated in one patient with persistent positive TRAb at 7.25 years of DAT treatment. 91% recieved propanolol for adrenergic symtoms manegement (3.14 ± 2.42 months). Adverse reactions for DAT were transitory poliarthralgia, transient granulocitopenia and 1 patiend died for sepsis of oral focus and haemathophagocitic syndrome of uncertain etiology. **Conclusions:** Goiter is the most frequent symptom in pediatric HT; Grave Disease the most frequent etiolog and; DAT have allowed to control HT in the majority of patients without adverse effects. Radioiodine therapy and thyroidectomy are sporadic alternatives for HT treatment in pediatric patients.

46

Multiple Endocrine Neoplasia Type 2B (MEN 2B)-Case Report

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Background: MEN 2B is a rare autosomal dominant syndrome including medullary thyroid carcinoma, pheochromocytoma, gastrointestinal disorders, marphanoid face, and mucosal multiple ganglioneuromas. Medullary thyroid cancer is present in 100% of cases, is the major cause of mortality and often appears during the first decade of life. RET proto-oncogene germline activing mutations are causative for MEN 2B. The 95% of MEN 2B patients are associated with a point mutation in exon 16 (M918/T). **Objective:** Present a case diagnosed with medullary thyroid carcinoma and MEN 2B, approaching the diagnosis of MEN 2B and its treatment. **Methods:** This is a case report of a male child, 13 years and 4 months old, with a palpable thyroid nodule. Conducted nodule evaluation with laboratory tests (TSH, free T4, calcitonin), thyroid ultrasound, fine-needle biopsy (FNA). After diagnosis of medullary thyroid carcinoma was

evaluated RET gene mutation in the patient and family, and investigation of other features of MEN 2B. **Results:** The investigation of the nodule demonstrated by FNA lesions suggestive of medullary carcinoma, laboratory tests were normal except calcitonin: 3770 pg/ml. The search for mutations of the RET gene was positive for the patient with a mutation at codon 918 and negative for both parents and sister. Assessing its history, the patient had reported constipation and diarrhea and the clinical examination showed neuromas of the oral mucosa, and hyperextension of joints. The investigation of pheochromocytoma was negative. Performed total thyroidectomy and removal of lymph nodes. **Conclusions:** The rarity of this syndrome can cause delayed diagnosis. Patients with gastrointestinal disorders and mucosal neuromas should be investigated for MEN 2B, because early diagnosis and treatment are essential to their survival.

47

Multiple Follicular Adenomas in a Girl with Congenital Hypothyroidism Due to a Thyroid Peroxidase (TPO) Gene Mutation

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Congenital primary hypothyroidism occurs in 1/3000 neonates. Defects in thyroid hormonogenesis (dyshormonogenesis) represent about one-fifth of the cases. Few patients have been reported to date with thyroid tumors. **Objective:** Report the case of a girl with congenital hypothyroidism due to an organification defect that developed multiple follicular adenomas. **Case report:** A 16 year old girl with a thyroperoxidase defect (compound heterozygous c.215del A p.Q72fsX86 mutation in exon 4 and c.2422T>C p.C808R mutation in exon 14) diagnosed at birth by neonatal screening with a TSH >200 mIU/L, TG 314 µg/L and goiter. She was reevaluated at age 6 with a perchlorate discharge of 77%. Early treated with poor compliance since age 4, presented at age 16 with multinodular goiter. Due to persistence of thyroid nodules and suspicious US signs total thyroidectomy was performed. Histopathological examination diagnosed five follicular adenomas. **Conclusions:** Congenital hypothyroidism due to dyshormonogenesis may develop thyroid tumors. Although inadequate thyroid hormone treatment compliance may be the cause of thyroid enlargement, the potential tumorigenetic effects of the mutations found in this patient are unknown underscoring the importance of a careful and regular follow-up.

48

Identification of a *De Novo* Mutation in the Thyroid Hormone Receptor ß Gene (TRß) in a Colombian Family with RTH

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Introduction: Resistance to thyroid hormone (THR) is an autosomal dominant disorder which affects 1: 40,000 births. It is characterized by a decreased response of target organs to thyroid hormones leading to an increase in serum thyrosina (T4) and triiodothyronine (T3) with lack of inhibition of the secretion of thyrotropin (TSH), due to mutations in the thyroid hormone receptor β gene (TRβ). **Objective:** To describe a mutation of novo in the thyroid hormone receptor β gene (TRβ) in un patient baby. **Material and Methods:** We present a clinical case incluiding genetic analisis of TRB. **Results:** Male with 15 months age, craneostenosis, psychomotor retardation, hypoacusia, decreased visual acuity and sweating without palpitations. With: total T4 >30 µg /dl (v.n. <12 µg /dl), free T4 >12 ng /dl(v.n <2ng /dl), total T3 >8, TSH 2.7 µIU /ml. Thyroid scan thyroid enlargement with normal uptake. He harbors a new mutation in exon 10 of the TRβ gene, which consists of a deletion of a cytosine at nucleotide 1318 and results in a frameshift that produces a stop codon at position 442. Unique in her family. **Conclusion:** Baby with resistance to thyroid hormones caused by a mutations de novo of the subunit TRB of the thyroid hormone receptor. It is noteworthy that mutations found in Colombia are unique to our country.

49

Congenital Hypothyroidism 5 Years of Experience

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Introduction: In our country the screening for congenital hypothyroidism (CH) is mandatory and is performed dosing in cord blood TSH (CB). It is also mandatory screening for Phenylketonuria, Congenital Adrenal Hyperplasia and Cystic Fibrosis on heel blood (HB) samples on filter paper. **Objective:** Evaluate the impact of CH in the period 2007–2011 and show the benefits of having the HB sample to corroborate the elevated TSH CB in a set range. **Materials and Methods:** We analyzed TSH 144787 CB 68924 on filter paper, cut-off 15 uUI/mL and 75863 serum CB, cut-off 25 mUI/mL. Was confirmed in HB, cut-off 10 uUI/mL of TSH in serum CB was worth between 25 and 50 uUI/mL and filter paper between 15 and 25 uUI/mL.

Results: From 144787 CB 2.8% were higher than the cut-off value, being 60 CH. During 2007–2009 were cited 100% of these samples and between 2010–2011 only 15% when using the HB sample to check TSH CB. **Conclusions:** Using the HB as a second sample we reduced the percentage of citations as indicated for Neonatal Research Program.

50

Thyroid Nodule – Primary Thyroid Tuberculosis

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Primary thyroid tuberculosis is a rare disease, its clinical features are not specific; may resemble a thyroid carcinoma, a cold abscess, multinodular goiter or manifest as a common thyroid nodule. To diagnose it, histological examination is necessary. A case of a thirteen-year-old girl was treated for presenting nodule in right thyroid lobe, wich demonstrated no lymphadenopathy. Complementary exams: Normal hemogram, elevated globular sedimentation velocity, normal values of TSH, free T4, T4 and T3. Thyroid peroxidase antibodies and thyroglobulin antibodies were negative. Ultrasound: Hypoechoic and heterogeneous nodule of 3.2 x 2.4 cm in right lobe. Fine needle aspiration: Central caseous necrosis, peripheral lymphocyte infiltration and Langhans giant cells. With Ziehl Neelsen technique is demonstrated acid alcohol resistant bacillus. PPD skin test was negative, chest radiography was normal, as well as abdominal ultrasound and CT vertebral; sputum culture, negative. She was treated with antitubercular drugs, the nodule involuted. The possibility of primary thyroid tuberculosis should be considered in populations where tuberculosis is endemic, including those without clinical signs of systemic tuberculosis.

51

Toxic Effects of the Propylthiouracil

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Background, Objective: The propylthiouracil (PTU) is indicated for the treatment of hyperthyroidism. The FDA reported it as a risk of clinically serious complications. **Materials, Methods, Case Report:** women of 15 years old, treated 14 months with PTU 300 mg/day. Presents injury in oral cavity, dysphagia, vomits, diarrhea, fever and headache. The physical exam: dehydrated, pale, conjuctival hyperemia, heart frecuency: 120/min, exophthalmos, 2 cm ulcerative lesions in high palate and inferior arcade, sialorrhea, increased thyroid size, outlying tremor, purpuric lesions in pelvis and inferior members. **Results:** TSH 0.001 uUI/L, T4L 2.5 ng/dL T3 354 ng/dL, GB 700, platelets 164.000/uL, Hb 11.2 g/dl. PCR 4.8, EGO: bleed (++) ketones (+) proteins (+), negative cultivations. Thyroid Echography: increase homogeneous size. Antibodies antireceptor TSH 20.9 UI/L. EKG: Sinus tachycardia. Antibodie ANCA-MPO 57.4 U/ml. skin Biopsy: Nonnecrotizing lymphocytic vasculitis of small surface capillaries and venules. Treatment: Suspension of PTU, use of antibiotics, fluconazole, propanolol, prednisone and filgastrin. Favorable evolution. Day 13: Radio-active Iodo. **Conclusions:** The severe complications associated to the PTU are related with vasculitis ANCA-MPO positive. Clinical manifestations such as: renal commitment, skin changes, breathing tract, fever, arthralgia, myalgia, scleritis and leukopenia. The patogenia of the vasculitis is uncertain yet, but it is related to mieloperoxidasa.

52

Thyroid Storm Associated to H1N1 Infection

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Thyroid storm is a rare initial presentation of Graves' disease, may be associated with certain infections, such as precipitating events. It is described the case of a 14-year-old teenager who was treated for fever, headache, sore throat, productive cough, dyspnea, palpitations, nervousness, tremor in their hands and myoarthralgias. Physical exam: Fever (39.1 °C), tachycardia (180 beats/minute), hypertension (160/85 mmHg), tachypnea (36 breaths/minute). Auscultation: Crackles in both lungs. Diffuse goiter was palpable. Chest X-ray: Hilar congestion and peribronchial cuffing. Lab: Leukopenia (3100/uL) with lymphocytosis (54%). Electrocardiogram: Sinus tachycardia. By clinical findings were requested thyroid hormones, showing decreased TSH, 0.01 mU/L (normal 0.3–4 mU/L) and elevated T3, 23.5 pmol/L (normal 2.5–5.7 pmol/L) and free T4, 38.8 pmol/L (normal 9–24 pmol/L); thyroid peroxidase antibodies and thyroglobulin antibodies were positive. Nasopharyngeal swab: Positive for H1N1 virus. Treatment: Prophylthiouracil, propanolol, Lugol's solution and supportive therapy. After a week thyroid hormones decreased and vital signs normalized. It is important to examine the thyroid gland in patients with respiratory infection (such as H1N1 infection) and cardiovascular instability, as thyroid storm may be part of differential diagnosis in these cases.

53

Accelerated Growth in Hyperthyroidism Graves Basedow is not Related to Increased Responsiveness to Stimulation of GH

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Acceleration of the growth speed (VC) is frequent in pediatric patients hyperthyroid, but little is known about when begins or if the Thyroid Hormones (HT) act directly on GH or its receptor, or IGF-1. It is considered the GHBP reflects the abundance of the GH receptor.

Objective: Determine whether there are changes in the VC in children with Disease Graves Basedow Hyperthyroidism (HEGB) before and after treatment with antithyroid and if those changes are mediated by increased responsiveness to GH stimulation, or its receptors. **Population:** 3 boys and 5 girls from 9 to 16 years of age with HEGB presenting T4 between 15 and 37 ug/dl and TSH < 0.1 uUI/ml with Anti TrAb + and Ab anti TPO +, with typical manifestations (diffuse goiter, exophthalmos, decreased weight, intolerance to heat, Hyperhidrosis, psychoemotional alterations, tremor, tachycardia.), highlighting the phenotype lanky and size between 50 and 95 PC. According to the anamnesis clinic was insidious onset between 3 to 10 months earlier. The growth curve that could be obtained in 5 patients, revealed that the VC had accelerated from a year to six months earlier, from 40–50 PC to 70–90 PC. Size epigenetics in 5 cases corresponded to a PC that was lower than that of the patient. Size was measured bi-monthly and GH, GHBP and GH stimulation with clonidine, before and after 6 months of treatment. They were treated with Propylthiouracil (PTU) TID 75 to 300 mg/day according to requirement to normalize the thyroid profile. **Results:** Before and after 6 months of treatment GH, GHBP and GH post clonidine test were within normal range and showed no significant variations. On the other hand the VC declined to PC 50–60. **Conclusion:** The acceleration of the VC is an early manifestation of HEGB. The invariability of GH post clonidine test, as well as GHBP and GH before and post treatment suggests that VC in HEGB changes are not mediated by the interaction of GH and its Receptor.

54

Familial Papillary Thyroid Carcinoma: Description of 4 Cases

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Introduction: Familial papillary thyroid carcinoma (FPTC) is clinically defined by 2 or more first degree relatives with this tumor, without components of any genetic syndrome. It represents 5 % of all Papilar Thyroid carcinomas, an autosomal dominant inheritance with incomplete penetrance and variable expressivity, it is more common in women 2–3:1, diagnose is at earlier age than sporadic carcinoma. It is suspected in a multifocal, multinodular or bilateral lesion and in children and males cases. It is associated with benign thyroid disease (36–57%), increased risk of another neoplasia, more frequency of local invasion (32%), recurrence (20–50%) and lymph node metastases (57%). **Clinical Cases:** 4 index cases and their clinical features are describe in the annexed table. **Conclusions:** FPTC has a worse prognosis than sporadic carcinoma and a high suspect index at the families affected is necessary for a precocious diagnoses and treatment.

Table 1. (for Abstract 54)

Case	Gender Male or Female	Familial background (n)		Association with benign thyroid disease	Age of diagnoses	Histology	Multifocal Multinodular Bilateral	Local invasion/ Vascular invasion/ Lymph metastases	Recurrence	Follow up (time)
		FPTC	Benign thyroid disease							
1	F	3	5	Autoimmune thyroiditis	10 years	Usual variety	No	No	No	8 months
2	F	1	2	No	13 years	Diffuse Sclerosant variety	Bilateral	Local and vascular invasion, lymph metastases.	Yes	7 months
3	F	2	4	Autoimmune thyroiditis	13 years 4 months	Usual variety	Multinodular	Local invasion	No	4 years
4	M	2	1	No	14 years 6 months	Usual variety	No	Lymph metastases	No	4 years 6 months

55

Short Treatment of Subclinical Hypothyroidism Enables Diagnostic Confirmation

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Introduction: Subclinical hypothyroidism (HS) can be underdiagnosed because poorly defined clinical and hormonal levels. Consumption of iodized salt could increase HS prevalence. We observed symptoms and signs so far little related to HS and patients who discontinued treatment had hormonal changes clarifying the diagnosis. **Objective:** Study the thyroid profile changes and symptoms so far little related HS, post treatment for six months, determining its diagnostic utility. **Methods:** 8 boys and 15 girls between 7 and 12 years of age, consumers of iodized salt, with T4 borderline normal and TSH between 5 and 10 uUI/ml, repeated, with Ac Anti TPO + in 2, presenting frequent redness and burning of ears in 5, anxiety and irritability in 14, depressive trend in 3, slow growth (VC) (PC < 20 p/age) 15, sloth and drowsiness in 12, decreased

Table 1. Clinical features and MRI findings of 30 patients with IGHD (for Abstract 56)

Gender		Consanguinity	Familial cases	Anterior pituitary hypoplasia	*Abnormal posterior pituitary	**Abnormal stalk
Male	Female					
17	13	4	10	23	23	18

* Includes ectopic or non visualized posterior pituitary; ** Includes transection or absent stalk.

physical performance in school at 16 and 11 overweight in 10, hypercholesterolemia in 5, were treated for six months with levothyroxine at low doses (from 1 to 3 ug/kg day) as it was required to normalize TSH. Two months after discontinuation of the treatment was measured thyroid profile. **Results:** After six months of treatment, all clinically improved: less redness and burning ears, best character, less irritable, anxious or depressive, accelerated to 50 PC VC, improved activity and performance, decreased weight, 4 normalized BMI and 5 their cholesterol. Two months after the treatment, in 17 patients TSH was clearly high, above 10 uUI/ml with low T4, normalized in 5 and remained the same in 1. **Conclusion:** Hormonal values in HS are better defined after treatment with levothyroxine, suggesting awareness tissue, useful to clarify the diagnosis. Clinical improvement confirms the symptoms observed are related with the hormonal deficit. Studies on vegetative nervous system could clarify the pathophysiology of discomfort in the ears.

56

Absence of *NEUROD4* Mutations in Patients with Congenital Isolated Growth Hormone Deficiency

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Background: The incidence of Isolated Growth Hormone Deficiency (IGHD) is estimated to be 1:4000–1:10000. Mutations in *GH1* and *GHRHR* are known causes of IGHD but a large number of patients remain without molecular diagnosis. The study of *Neurod4* knockout mice showed that this gene is critical for maturation and expansion of somatrotropes by regulating the expression of *GHRHR*. We hypothesized that *NEUROD4* loss-of-function mutations could underlie some cases of IGHD. **Objective:** To screen *NEUROD4* for mutations in patients with IGHD. **Methods:** Mutations in *GH1* and *GHRHR* were ruled out in all patients. All patients met the diagnostic criteria of the Brazilian centre. The entire coding region of *NEUROD4* was evaluated in 30 patients (17 males) by Sanger Method using automatic sequencing. **Results:** Ten patients presented a heterozygous allelic variant HGVS NM_021191.2: c.31 C>T previously described as polymorphism rs2656804. It is not conserved among species. The other 20 patients presented the most common allele C/C. Clinical and MRI findings are described in the table 1. **Conclusions:** Despite the role that *Neurod4* has in somatrotope development in mice, we found no loss-of-function mutations implicated in the aetiology of IGHD in a selected group of Brazilian patients.

57

Differences in the Protein Content and Basal Phosphorylation of AKT, mTOR and S6K$_{1/2}$ in Human Term Placentas of Small (SGA), Appropiate (AGA) Large (LGA) for Age Gestacional

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Introduction: We previously reported a higher protein content of IGF-I, IGF-IR and AKT in SGA vs. LGA placentas. At the moment there is no information on the activation of AKT downstream in placenta. **Objective:** To determine the protein content

Table 1. (for Abstract 57)

		SGA n = l4	AGA n = l4	LGA n = 14
Total AKT (AU)	CP	2.13±0.47$^{\&}$	1.73±0.39	0.97±0.18
	BP	2.91±1.06$^{\&}$	1.31±0.28	0.92±0.12
Total mTOR (AU)	CP	3.70±1.03*	0.70±0.15	2.82±0.86$^{\#}$
	BP	3.66±0.95*	0.88±0.21	1.85±0.51$^{\#}$
Total S6K$_{1/2}$ (AU)	CP	4.37±0.93*	1.71±0.39	4.54±1.00$^{\#}$
	BP	4 68±1.21	2.36±0.81	3.50±0.74
Phospho AKT Ser (AU)	CP	0.15±0.06	0.24±0.07	0.09±0.04$^{\#}$
	BP	0.11±0.04*	0.27±0.07	0.06±0.02
Phospho mTOR (AU)	CP	1.58±0.62$^{\&}$	1.66±0.31	0.42±0.11$^{\#}$
	BP	1.45±0.51$^{\&}$	1.43±0.33	0.35±0.07$^{\#}$
Phospho S6K$_{1/2}$ (AU)	CP	1 21±0.23*	5.95±1.94	2.00±0.67$^{\#}$
	BP	0.97±0.36*	4.61±1.02	1.76±0.54$^{\#}$

$p < 0.05$: * SGA vs AGA; $^{\&}$ SGA vs LGA; $^{\#}$ LGA vs AGA Fondecyt 111 0240.

and basal phosphorylation of AKT, mTOR, and $S6K_{1/2}$ in SGA, AGA and LGA human term placentas. **Methods:** In 42 placentas we determined the protein content and basal phosphorylation of AKT, mTOR, and $S6K_{1/2}$ by western blot in the chorionic plate (CP) and in the basal plate (BP) of the placentas. Results are shown in the table as mean ± SEM. Differences were assessed by ANOVA or Kruskal-Wallis test. **Conclusion:** The higher protein content and reduced basal phosphorylation of mTOR and $S6K_{1/2}$ in SGA and LGA placentas compared with AEG suggest that signal transduction system would be associated with IGF-IR/IR modulating fetal growth.

58

Klotho Inhibits the Phosphorylation of IGF-IR, AKT and $ERK_{1/2}$ Induced by IGF_I in Human Term Placenta

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Klotho is a transmembrane protein, associated with aging, which has been suggested to inhibit the intracellular signaling induced by IGF-I. **Objective:** To study the effect of Klotho on signaling induced by IGF-I in human placental explants. The effect of pre-incubation with different doses Klotho on the phosphorylation of IGF-IR, AKT and $ERK_{1/2}$ induced by IGF-I 10-8M was studied by western blot in explants from basal (BP) and chorionic plate (CP) from 25 placentas of AEG newborns. Results are shown in the table as fold increase over the basal condition ± SEM. Differences were assessed using the Student t test paired or Wilconson test. **Conclusion:** We described for the first time that Klotho is able to inhibit the phosphorylation of IGF-IR, AKT and $ERK_{1/2}$ induced by IGF-I in human placental explants. These results suggest that Klotho may be involved in prenatal growth by modulating the IGF-I signaling in human placentas at term.

Table 1. (for Abstract 58)

		IGF-I 10^{-8}M	IGF-I 10^{-8}M + Klotho 2×10^{-9}M
IGF-IR (fold)	CP	11.88 ± 3.37	4.42 ± 0.57*
	BP	10.61 ± 2.62	4.89 ± 0.95*
AKT-Ser (fold)	CP	17.05 ± 3.06	7.51 ± 1.25*
	BP	12.70 ± 2.80	6.56 ± 1.80*
$ERK_{1/2}$ (fold)	CP	1.63 ± 0.15	1.17 ± 0.12*
	BP	1.49 ± 0.11	1.13 ± 0.10*

* $p < 0.05$; Fondecyt 111 0240.

59

Isolated Adrenocorticotrophin (ACTH) Deficiency due to Mutations in TPIT Transcription Factor Gene: A Report of Three Cases

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Isolated ACTH deficiency is rare: characterized by adrenal insufficiency, with normal secretion of other pituitary hormones, and absence of structural pituitary anomalies. TPIT is a T-box transcription factor, important in the last step of corticotrophs differentiation in mice and humans, and part of the transcription regulatory complex assembled on the proopiomelanocortin (POMC) promoter gene. TPIT expresses exclusively in POMC positive pituitary cells. Mutations in TPIT transcription factor, account for one cause of isolated ACTH deficiency. **Objective:** We report 3 patients, all with consanguineous parents, who presented with severe hypoglycemia, with ACTH<5pg/ml and non measurable cortisol, at the time of hypoglycemia. Rest of pituitary function was normal, assessed with basal laboratory tests. All patients did well under hydrocortisone treatment. **Results:** Sequencing the TPIT gene, revealed a homozygous mutation in each patient (previously reported): exon6 R286X in two patients, and exon3 R179X in the other, leading to a premature stop codon, which results in a complete loss of function of the protein due to mARN decay. **Conclusion:** Isolated ACTH deficiency, due to mutations in TPIT transcription factor, should be considered in cases of hypoglycemia, consanguinity and previous neonatal death.

60

Two Novel IGF1R Gene Heterozygous Mutations in Unrelated Children with Pre and Postnatal Growth Retardation, and Microcephaly

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Background: Several IGF1R gene mutations have been described as a cause of growth retardation due to IGF1 insensitivity. **Objective:** To analyze mutations in the IGF1R gene in two children suspected to have IGF1 insensitivity. **Population:** Patients were born small for gestational age, microcephaly and presented developmental delay. The boy was evaluated at 18 months (P1) and the girl at 3.2 years old (P2) and both showed a mild dysmorphic phenotype. P2 showed no postnatal catch-up growth, while P1 reached a normal Height SDS at 2

years of age without changes in head circumference. **Results:** Basal and stimulated serum GH, IGF-1 and IGFBP3 levels were quite variable among them. No chromosome 15 anomalies were detected. Two novel heterozygous mutations, de novo R1256S (P1) and R1337C (P2) were detected in the exon 21 of IGF1R gene. The aminoacid substitutions were located at highly conserved aminoacid residues in the protein. These mutations were predicted to affect protein function using the sequence homology based SIFT tool, the structure-based PolyPhen approach and the Mutation Taster. The father and sister of P2, carrying the R1337C mutation, were normal. To elucidate the function of the mutated IGF1R we measured IGF-1 dependent DNA synthesis in fibroblast cell primary cultures from P1, P2 and a control subject (C) by ^{3}[H]thymidine incorporation into DNA treated with IGF-1(50ng/ml) for 16, 20 and 24 hs. We observed that IGF-1 significantly induced DNA synthesis in C at 20hs($p<0.05$). However, no significant increase was observed in P1 and P2 (P1: 2.26 SD 0.45; P2: 2.89 SD 0.23; C: 5.71 SD 0.43 fold increase; $p<0.05$ by ANOVA and Student Newman Keuls Test). **Conclusions:** We report two novel heterozygous mutations, de novo R1256S (P1) and R1337C (P2) in exon 21 of the IGF1R gene which leads to inhibition of cell proliferation induced by IGF-1. These findings strongly suggest that these mutations lead to failure of the IGF1R and causes pre and postnatal growth retardation.

61

Clinical and Molecular Characterization of Seven Families with Léri-weill Dyscondrosteosis

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Background: Lerí-Weill Dyscondrosteosis (LWD) is a condition characterized by short stature, mesomelic shortening of limbs, and a wrist deformity known as Madelung deformity. This syndrome is associated to *S*hort stature *HO*meobo*X* gene (*SHOX*) haploinsufficiency. **Objective:** To correlate clinical, radiological and molecular findings in seven families with LWD. **Methods:** Anthropometric characteristics and X-ray studies were performed in patients and theirs relatives. Multiplex Ligation-dependent Probe Amplification (MLPA) was performed to detect deletions and duplications of *SHOX* and its enhancer regions. High Resolution Melting (HRM) and sequencing was employed to screen for mutations in *SHOX* coding exons. **Results:** Clinical, radiological and molecular data are depicted in the Table. **Conclusions:** The molecular-based screening strategy applied allowed detection of five LWD-*SHOX* associated deletions and two previously unreported *SHOX* missense mutations. Molecular studies confirmed the clinical diagnosis of LWD, and therefore improved the genetic counseling offered to these affected families. Fondecyt-1095118.

62

Variable Reproductive Phenotype in Chilean Women with GnRH Deficiency (GnRHD)

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Introduction: GnRHD is a congenital or acquired disorder characterized by an absolute or relative deficiency of GnRH that involves alterations in sexual maturation and infertility. Affected women may present partial pictures from a late menarche to a primary amenorrhea with anosmia. A *5:1 male-to-female sex ratio has been reported.* Phenotypic and genotypic characteristics of GnRH deficient women have not been well described. Our aim is to describe the reproductive characteristics of Chilean women with variable forms of GnRHD. **Methods:** Descriptive study of 70 women under treatment for GnRHD. A complete health evaluation, smell test and DNA screening for genetic defects were performed. **Results:** The patients were divided in 3 groups: 29 nHH-KS (normosmic hypogonadotropic hypogonadism and Kallmann syndrome), 24 CDP (constitutional delayed puberty) and 16 with HA (hypothalamic amenorrhea). The

Table 1. (for Abstract 61)

Patients						Affected parents
Age (gender)	SHOX anomaly	Birth length (SD)	Current height (SD)	Armspan/height (ratio)*	Madelung deformity (–/+)	Height (SD)
7y 10m (M)	SHOX deletion	–0.37	–2.96	0.93	–	–2.64 (f)
7y 2m (F)	SHOX deletion	–0.12	–2.81	0.94	+	–3.66 (f)
17y 1m (F)	c.439C > A (p.R147S)	+0.28	–2.65	0.95	+	–2.04 (m)
9y 8m (F)	Partial SHOX deletion (ex4-6b)	–0.54	–3.07	0.92	+	–3.42 (m)
10y 4m (M)	SHOX deletion	–0.75	–2.52	0.96	+	–3.42 (m)
3y 6m (M)	SHOX deletion	–0.75	–1.53	0.96	–**	–3.57 (m)
3y 3m (F)	c.778G > C (p.A260P)	–0.98	–2.46	0.99	–**	–3.91 (m)

* A value < 0.96 suggests mesomelic shortening; ** Children may develop MD later in life; (F) father (M) mother.

Table 1. (for Abstract 62)

Reproductive phenotype of women with GnRH deficiency						
		nHH-KS		CDP		HA
n (%)		29 (41.4)		24 (34.3)		16 (22.8)
Age at evaluation (years)		23.3		24.6		22.8
Father or brothers "late bloomers" (n)		9		9		3
Mothers or sisters with late menarche (n)		12		12		5
Family history of delayed puberty or HH (n)	one parent	13		11		6
	both parents	4		5		1
Telarche	no	2				
	yes	27		24		16
	spontaneous	10		21		16
		at 13.9 yo		at 14.1 yo		at 12.1 yo
	induced	17		3		
		at 17.9 yo		at 15.5 yo		
Menarche	no	9		6		
	yes	20		18		16
	spontaneous	1		12		16
		at 15 yo		at 16.3 yo		at 13.1 yo
	induced	19		6		
		at 19.4 yo		at 16.3 yo		
Women seeking fertility		8		7		3
Successful pregnancies		0		17		2
Smell test results						
Smell test		nHH-KS		CDP		HA
		n	%	n	%	n	%
Normal		6	20.7	10	41.7	8	50
Mild hyposmia		9	31.0	9	37.5	6	37.5
Moderate hyposmia		4	13.8	3	12.5	1	6.3
Severe hyposmia		1	3.4	0	0.0	1	6.3
Anosmia		9	31.0	2	8.3	0	0
RSV (number of women screened)		6 (15)	40	1 (14)	7.1	1 (10)	10

age at evaluation and reproductive characteristics of the 3 groups are shown in Table. In 8 women (19.5%) rare sequence variants (RSV) were identified: one digenic (*GNRHR/PROKR2*) and 7 monogenic (*FGFR1, TAC3R, PROK2, CHD7)*. A 40% of the group nHH-KS have RSV vs. 7% of CDP and 10% of HA group. **Conclusions:** GnRHD is a disorder that can be present in females, and therefore the sex ratio *must be reevaluated. The anosmia, traditionally a concern in males, is present also in women and correlate with a more severe phenotype.* These results suggest that a attention to phenotype may induce an early suspicion and avoid a late steroidal replacement with a lower impact in bone mineral density.

63

Expression Pattern of Stem Cell Marker SOX2 Analyzes in the Pituitary of Experimental Mice with Hypopituitarism

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Background: The stem cell tissue-specific are characterized by their ability of potential differentiation and self-renewal. Pituitary stem cells is involved in cell turnover and homeostatic regulation but little is known about their pattern of expression in hypopituitarism. Spontaneous mutant mice with hypopituitarism as Ames (Prop1 mutated) and Snell (Pou1f1 mutated), presented at birth hypoplastic pituitary and dysmorphology at birth and normal appearance of the pituitary, respectively, both offspring evolved with full hypoplasia on the seventh postnatal day. Cga gene knockout mice, responsible for glycoprotein hormones alpha subunit, presented hypopituitarism and

pituitary hyperplasia. **Objective:** To analyze the SOX2 expression, stem cell marker, in animal models with hypopituitarism. **Material and Methods:** Pituitaries from Ames (Prop1), Snell (Pou1f1) and Cga gene knockout were colected at P0 (birth day), P7 (7 days post natal), 4 and 8 weeks (W) of life. SOX2 was analyzed by RT-PCR by Taqman in the pituitaries collected at 4 and 8W and subjected to RNA extraction and cDNA synthesis. P0 and P7 pituitaries were used for immunohistochemistry (IHC) **Results:** Cga knockout gene mice at 4 and 8W, showed no SOX2changes by RT-PCR. Snell Mutants (PIT1) of 4 and 8W showed SOX2 increased such as 2.8 and 2.5 fold, respectively. Ames mutant compared with normal at 8W showed 3.5-fold SOX2 increase. Normal 4W compared to 8W showed 3.8 times decreased, but no difference in the 4W mutant compared to 8W. IHC in the mutant Ames showed increased SOX2 expression at P0 and P7. **Conclusions:** The increased expression of SOX2 only in Prop1 and Pou1f1 mutated genes, factors responsible for the terminal differentiation of pituitary cell lines, suggests a possible role of SOX2 in the differentiation of stem cells in the pituitary hypopituitarism.

64

Genetic Screening in Children with Congenital Combined Pituitary Hormone Deficiency

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Mutation frequency of genes involved in Congenital multiple pituitary hormone deficiency (CMPHD) varies between populations. Genetic screening in CMPHD from Argentina. In 25 children with sporadic CMPHD genetic studies were guided by phenotypes: hormone deficiencies and MRI findings. Studied genes were *PROP1, HESX1, SOX3, PITX2, OTX2, LHX4* and *LHX3*. Mutations were found in two(8%). Heterozygous *LHX4* mutation (p.Lys242del) was found in a boy with corticotroph, somatotroph, thyrotroph and lactotroph deficiencies, pituitary hypoplasia without extrapituitary abnormalities. Heterozygous *LHX3* allele variant(p.Arg310Pro) was present in a boy with nystagmus, microcephaly, normal neck rotation; gonadotroph, corticotroph, somatotroph, thyrotroph and lactotroph deficiencies; pituitary hypoplasia, ectopic neurohypophysis and disrupted stalk. *LHX4* mutation affected a biologically critical and highly conserved residue, in favor of the pathogenic role of the variant in the observed phenotype. Functional studies of the *LHX3* mutated protein were suggestive of a rare polymorphism, thus unlikely to account for the phenotype. A genetic screening strategy, based on endocrine and neuroradiological phenotype allowed the identification of gene defects. The frequency of mutations in *LHX3* and *LHX4* in CMPHD is low. Clinical relevance of such mutations should take into account functional studies and cosegregation pattern. The etiology of most of the cases of CMPHD remains to be established.

65

Complete ALS Deficiency Associated with a Novel Leu409Phe *IGFALS* Gene Mutation

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Background: GH insensitivity has been associated to *GHR*, *STAT5B*, *IGF1* and *IGFALS* gene defects. Despite similar degrees of IGF-I deficiency only *IGFALS* gene defects result in mild growth deficit. **Objective:** To characterize the molecular defect in a short boy presenting IGF-I and IGFBP-3 deficiencies. **Methods:** The proband, a 13.8 year old prepubertal boy, born SGA at term (weight 2810 g, –1.2 SDS; height 44 cm, –3.66 SDS) from consanguineous parents (father 160 cm, –1.88 SDS; mother 157 cm, –0.60 SDS), is the fourth of nine siblings, height –2.65 SDS, BA 12.75 years for CA 13.42. Stimulated GH and IGFBP-3 levels were determined by ICMA, IGF-I by RIA, ALS by Western imm unoblot and in vitro ternary complex (TC) formation by size exclusion chromatography. **Results:** He was GH sufficient (22.0 ng/ml), had low IGF-I (–4.15 and –4.70 SDS) and undetectable IGFBP-3 and ALS levels. He was unable to form TC, even after spiking with rhIGFBP-3. *IGFALS* gene sequencing revealed a homozygous novel missense mutation (c.1225C>T; p.Leu409Phe), predicted to be probably damaging by *in silico* analysis. **Conclusions:** Mild growth retardation with pubertal delay associated to severe IGF-I and IGFBP-3 reductions led to the molecular characterization of another ALS deficient patient.

66

Aortic Dilation in a Large Cohorte of Pediatrics Patients with Turner Syndrome

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It has been described an increased risk for aortic dilation (AD) and dissection in Turner Syndrome (TS) at all ages, 24% presented before 20 years of age. Our aim was to assess aortic dimensions in a large group of girls with TS and and risk factors associated with AD.

Methods: Diameters of the ascending aorta (AA) were measured by Computed Tomography. AA was normalized to body surface area (ASI). ASI greater than 2.0 cm/m2 defined AD. **Results:** Seventy three TS patients were included. Twenty two patients (30%) had AD. Ages ranged from 3.2 to 20. 1 years. Six of them (27%) had severe AD, ASI >2.5 cm/m^2. Bicuspid aortic valve, karyotype 45X, hypertension and treatment with growth hormone were not associated with AD. Only aortic coarctation was significantly associated with severe AD. In two cases, prophylactic surgery was indicated (Age 11.4 and 9 years). Follow-up in nine girls (mean 2.55 years) showed no changes in the IA. **Conclusions:** Due to the high prevalence of AD in our pediatric population of TS, the evaluation of ASI in all TS girls is recommended. Follow up is necessary to know long time consequences of these findings.

67

Evaluation of Body Composition and Muscle Force During Transition Phase of Patients Treated with Recombinant Growth Hormone

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Growth hormone (GH) promotes linear growth and is crucial for the acquisition of bone and muscle mass peaks. **Aims:** to evaluate body composition and muscle force of males during the transition phase (T), treated with GH during childhood and early adolescence and whose final height was equal to target height. **Methods:** 18 patients were evaluated and according to peak GH on ITT and basal IGF-I, were classified as: GH deficient (GHDT, n=9) and GH sufficient (GHST, n=9). Eighteen, healthy males, of same age served as control group (CG). Bone mineral density (BMD), lean and fat mass (LM and FM) was measured by DEXA method and dynamic muscular force of knees by isocinetic dynamometer. **Results:** BMD values (total body and lumbar spine) were smaller in the GHDT in comparison to GHST and CG ($p<0.05$). LM and FM of groups GHDT and GHST were different of the values of CG ($p<0.05$). Values of muscle force of GHDT were smaller than those of CG ($p<0.05$). **Conclusion:** The schedule of treatment with GH of these patients was not able to provide body composition and muscle force values identical to those of CG.

68

Signaling Pathway by Levothyroxine (T4) in Fibroblasts of Normal Boys

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Introduction: T4 has been used to try to increase the growth velocity of children with idiopathic short stature and normal thyroid function, but it´s mechanism of action is unknown. To study whether T4 has an effect on tissue sensitivity to GH, we investigated the activation of JAK2 and STAT5 in fibroblasts from normal children, which were co-stimulated with GH and T4. **Aim:** To determine the effect of stimulation with GH alone, or in combination with T4 on JAK2 and STAT5 activation in cultured fibroblasts. **Methods:** Skin fibroblasts were obtained from 8 normal boys (6.6±0.7 years old) during elective surgery. We studied the activation of JAK2 and STAT5 after 24h stimulation with GH alone, or associated with two concentrations of T4 (250 nM and 500 nM). Nuclear and non-nuclear fractions were extracted and quantified by Western Blot. **Results:** In the Table, the values are given as mean ± SEM, *GH+T4 vs GH $P<0.05$ (n=8). **Conclusions:** Co-stimulation with GH and T4 500 nM amplifies tissue sensitivity to GH, which is demonstrated by increased nuclear STAT5 activation. These findings may help to explain the effect of T4 treatment on the growth of some children with idiopathic short stature. Supported by MERCK-SERONO.

Table 1. (for Abstract 68)

Stimuli (24 h)	Cytoplasm JAK2 Activation	Cytoplasm STAT5 Activation	Nucleus STAT5 Activation
GH (200 ng/mL)	1.2±0.3	1.1±0.2	0.95±0.2
GH+T4 (250 nM)	0.9±0.1	1.1±0.2	0.98±0.2
GH+T4 (500 nM)	1.2±0.2	1.0±0.04	2.2±0.4*

69

Idiopathic Short Stature in an Azoospermic Patient with a Terminal Y Chromosome Microdeletion and a Heterozygous Deletion of the Pseudoautosomic Regions 1 and 2

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Background: Y chromosome microdeletions (YMD) are the most prevalent cause of primary spermatogenic failure. The pseudoatosomic regions (PAR1 and PAR2) are located at the ends of the sex chromosomes and allow homologous recombination. PAR1 deletions have been associated with infertility, and recently with Y chromosome microdeletions. The function of many genes in the PARs is still unknown, but haploinsufficiency of *SHOX* in PAR1 produces short stature and Léry-Weill dyschondrosteosis. **Objective:** We studied a 20 year old man with azoospermia and a 46, XY(qh-) karyotype which prompted a YMD study. In addition, his adult height of 157 cm prompted a molecular PARs study. **Methods:** DNA from peripheral blood of the patient and his parents was used to study YMD (PCR) and PAR deletions (MLPA). **Results:** We detected YMD from the distal palindrome 4 (AZFb+c / Yqter). MLPA analysis showed haploinsufficiency of PAR1 and PAR2, and the radiological study showed curvature of radius and cubitus, consistent with *SHOX* haploinsufficiency. Molecular studies in the parents were normal. **Conclusions:** The molecular findings described in our patient are the cause of his short stature and secretory azoospermia, occurred *de novo* and appear to involve related molecular mechanisms. Fondecyt Grant No 1120176.

70

Recurrent R183H *GH1* Gene Mutation in a Patient with Autosomal Dominant Isolated Growth Hormone Deficiency (IGHD)

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Introduction: IGHD type II results from autosomal dominant (AD) *GH1* gene molecular defects. **Aim:** To characterize the molecular alteration of a short male child. **Subject and Methods:** The patient, a boy born from non consanguineous parents, presented at chronological age (CA) 5.13 years: height –3.36 SDS, prominent forehead, mild facial hypoplasia and normal neurological development. MRI showed pituitary hypoplasia. His father (height 142.5 cm, –4.46 SDS) presented typical features of IGHD, while his mother (height 152.6 cm, –1.33 SDS) was not clinically affected. GH secretion was assessed by ICMA after sequential arginine-clonidine test and IGF-I by RIA. The whole *GH1* gene was PCR amplified and automatically sequenced. **Results:** IGHD was confirmed by low stimulated GH (GHmax: 2.2 ng/ml), undetectable IGF-I levels, normal TSH response to TRH and normal PRL and cortisol levels. The patient received rhGH replacement therapy for 9.3 years with good growth response. He began puberty at 12 CA and at 15 years of age had a height of –0.88 SDS, G5, PH5, T15/15. *GH1* gene sequencing revealed a c.626G>A transition in exon 5, predicted to result in the missense mutation p.R183H. **Conclusions:** The finding of the recurrent R183H mutation, characterized in more than 40 subjects worldwide and presenting a large phenotypic variability, ranging from normal stature and GH secretion to complete GHD, could be responsible for the AD type II IGHD in this patient.

71

Williams Syndrome: One Case Diagnosed by Comparative Genomic Hybridation

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Introduction: Williams Syndrome (OMIM: # 194050) is a rare genetic multisystem disorder cause by delation in the long arm of chromosome 7. Its incidence is estimated to be 1/10000 live birth. This condition is characterized by distinctive facial features, learning disability, hypercalcaemia, short stature, supravalvular aortic stenosis, pumonic valvular stenosis among others. Diagnosis is based on clinical criteria and the detection of delation by Fluorescent In Situ Hybridization (FISH). **Case Report:** 7 year old boy, without pathological background or consanguinity. Pulmonic valvular bilateral stenosis was diagnosed when he was three months old, Later on strabismus dacrioestenosis and intellectual disability. Ionic calcium, phosphorus, and parathyroid hormone were normal. PAl exam, weight, short stature, anteverted nares, a long and flat phyltrum, thick lower lip, malocclusion dentition and conical teeth, hypotonía. FISH for the critical arm of chromosome 7q was normal. Comparative Genomic Hybridization (CGH) was performed detecting the lost of 1.4 Mb in the region 7q11.23. **Discussion and Conclusions:** This patient was clinically diagnosed with Williams Syndrome; however, the condition could not be confirmed during five years. A negative FISH increased doubts. CGH results confirm diagnosis and we were able to establish prognosis, management and counseling. This technology should be kept in mind in the evaluation of syndromes as a more exact tool.

72

Vertebral Deformities are More Frequent in Children Born SGA Independent of the use of Aromatase Inhibitors

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Deformities of the anterior vertebral body described during the use of Aromatase Inhibitors (AI) are similar to those found in patients with juvenile kyphosis – Sheuermann disease (SD). Our hypothesis is that these vertebral changes are related with birth weight and are independent of AI treatment. **Objective:** To identify the frequency of children born SGA in individuals with SD who did not use AI. **Methods:** Neonatal and anthropometric variables of the last visit were obtained from 27 patients with SD (table). There was a significantly greater proportion of SGA infants among patients with Scheuermann disease compared to that expected in the general population (p = 0.013). **Conclusion:** Born SGA should be considered as a factor associated with Scheuermann´s disease, independent of the use of AI. Therefore, before concluding that vertebral deformities are caused by AI it is necessary to correct for birth weight covariate.

Table 1. (for Abstract 72)

	SGA (n = 5)	AGA (n = 22)
Birth Weight (kg)	1.9 (1.5/2.3)	3.3 (2.2/5.0)
Gestational Age (wk)	40 (32/40)	40 (32/40)
Final Height (SDS)	–1.1 (–2.2/1.3)	–0.9 (–4.1/1.6)
BMI (SDS)	0.3 (–0.5/1.1)	–0.2 (–2.9/2.4)
Expected frequency in the general population (proportion)	3/100 (0.03)	97/100
Observed Frequency in Sheuermann D. (proportion)	5/27 (0.185)*	22/27

* p = 0.013; expected vs. observed; two proportions Z-test.

73

Evaluating the Relation between Gene Polymorphism of De GH Receptor in Response to Short-term Treatment with Growth Hormone in Children with GH Deficiency and Ectopic Neurohypophysis

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Background: GHD is associated with ectopic posterior pituitary (EPP) in approximately 40%. Previous studies suggest that the response to GH therapy may vary with the deletion of exon 3 (del3) GH receptor (GHR) gene. **Objective:** To evaluate the response after 1 year of GH therapy in GHD-EPP patients, according to GHR gene polymorphism. **Methods:** We evaluated the del3 of GHR gene in 44 patients with GHD-EPP by PCR allele-specific. The clinical data observed were: target height (SDS), height (SDS) and IGF1 (SDS) at diagnosis and after one year of GH treatment (0.1 UI /kg/d). Patients with no compensated hypothyroidism, or using GnRH analogue were excluded. **Results:** The mean (SD) chronological age (CA) of the 34 boys and 10 girls, was 6.7 (3.4) years and height SDS was –3.6 (1.2) at diagnosis. Our results showed that 9 (20.4%) patients had del3/del3 genotype, 18 (40.9%) del3/fl and 17 (38.6%) fl / fl. There was no difference of CA, height SDS at diagnosis or after one year after treatment between the three groups. There was no difference of IGF1 levels either. **Conclusions:** There is no correlation between del3 and better response to treatment in GHD patients with EPP.

74

Implicancias Clínicas De Duplicación Parcial Xp E Inactivación Al Azar De Cromosoma X

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Pure duplications of the short arm of X chromosome are relatively rare. Males present mental retardation, multiple congenital malformations and short stature. Genetic imbalance in females with dup(Xp) is compensated by preferential inactivation of their abnormal X-chromosome and are phenotypically normal. We report on a 8 years old girl with learning difficulties, few Turner Syndrome features and a mosaicism with partial duplication Xp and random X-inactivation. The physical examination showed:height: (P10–25); weight: (P75); head circumference (+1SDS). Growth velocity: 5.25 cm/year. She had personal history of frequent atypi-

cal febrile seizures and primary enuresis. Features as wide palpebral fissures, big eyes, bulbous nose, rotated ears, short neck and bad dental occlusion and short hands were found. Abdominal, cranial, column ultrasound and echocardiography were normal. Chromosome analysis was performed in lymphocytes using high resolution, GTG and RHG banding. Karyotype: 45,X/46,X, dup(X) (p11.2p22.3). Parent´s karyotype: normal. FISH analysis with whole X-chromosome painting (wcpX), Xp11.2 and Xp22.3 Live probes, demonstrated tandem Xp duplication. Replication studies showed that the normal and duplicated X-chromosomes were randomly inactivated. Therefore, in this case there is X-monosomy, functional disomy Xp11–p22.1 in the cells with an active dup(X) and duplication of Xp22.3, resulting in a phenotypically abnormal female with intellectual disability.

75

Endocrine Abnormalities in Patients with Fanconi Anemia before and bfter Hematopoietic Stem Cell Transplantation

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Fanconi Anemia (FA) is characterized by progressive bone marrow failure, congenital anomalies and predisposition to cancer. Endocrine complications are common before or after hematopoietic stem cell transplantation (HSCT). **Aims:** To evaluate endocrine disfunctions in patients with FA treated in reference service. **Methods:** 43 patients were evaluated regarding age at diagnosis and HSCT, growth, thyroid, dyslipidemia, glucose metabolism, puberty, vitamin D (VD) levels and bone mineral density (BMD). **Results:** 16 patients were evaluated before HSCT (G1), and 27 after HSCT (G2). In G1 the median age at diagnosis of FA was 3.1±3.7y. Endocrine evaluation showed: short stature (SS) 12, hypothyroidism (HT) (4), hypogonadism (1), panhypopituitarism (1) and low levels of VD (1). In G2 the median age at diagnosis was 6.5±3.3y and they were submitted to HSCT at 9.6±2.7y; 12 patients were transplanted from related donors and 15 from unrelated. Endocrine evaluation showed: SS (15), hypogonadism (8), altered glucose metabolism (6), low levels of VD (6), HT (5), hyperlipidemia (4), low levels of BMD (3), precocious puberty (1). **Conclusions:** Endocrine abnormalities are common in patients with FA. The most frequent complications were related to disorders of growth, puberty and thyroid.

76

Neuroendocrine Alterations in Obese Children: Sexual Dimorphism in Melatonin Secretion

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Objective: To evaluate 6-sulfatoxymelatonin (6-SM) concentrations in prepubertal obese children of both genders with and without Metabolic Syndrome (MetS). **Material and Methods:** We evaluated 56 obese subjects, 18 females (5–10.4 years) and 38 males (5–12.2 years); 9 females and 14 males had MetS. Urinary 6-SM was measured in nocturnal (6PM–8AM) and diurnal (8AM–6PM) samples. **Results:** TABLE 1 [a] p=0.01 vs. females without MetS, [b] p = 0.02 vs. females without MetS, [c] p=0.0037 vs. Delta females without MetS, [d] p=0.009 vs Delta/BMI females without MetS, [e] p=0.03 vs. females without MetS (Mann-Whitney) Females: nocturnal 6-SM correlated with insulin (r=0.4876, p<0.05) and glucose (r=0.6218, p<0.05)(Spearman). **Conclusions:** Females with MetS have higher nocturnal 6-SM than females without MetS. Males with and without MetS have similar 6-SM concentrations. In females, nocturnal 6-SM positively correlates with insulin and glucose; not in males. These differences would support sexual dimorphism independently of BMI.

Table 1. (for Abstract 76)

	Females without MetS	Females with MetS	Males without MetS	Males with MetS
Nocturnal 6-SM (µg)	1.86 ± 0.49	6.54± 2.38[a]	3.30 ± 0.65	3.98 ± 1.50
Nocturnal 6-SM (µg)/ BMI-SDS	0.75 ± 0.24	2.54 ± 1.05[b]	0.98 ± 0.20	1.00 ± 0.34
Diurnal 6-SM (µg)	0.76 ± 0.25	0.74 ± 0.18	0.66 ± 0.08	0.99 ± 0.52
Diurnal 6-SM (µg)/ BMI-SDS	0.31 ±0.12	0.28 ± 0.08	0.19 ± 0.02	0.25 ± 0.11
6-SM Delta (nocturnal-diurnal)	1.10 ±0.25	5.80 ± 2.29[c]	2.64 ± 0.59	3.02 ± 1.17
6-SM Delta/BMI-SDS	0.44 ±0.12	2.27 ± 1.00[d]	0.79 ± 0.18	0.79 ± 0.27
INSULIN (µIU/1)	9.0 ± 1.0	18.5 ± 4.3[e]	14.3 ± 1.99	16.5 ± 2.23

77

Rasopathies: Molecular Entities with Pediatric Endocrine Outcome?

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Introduction: The RAS / MAP responsible for signal transduction receptor membrane to the nuclear DNA activates a cascade processes involving protein synthesis and cell replication, including the MAP kinase, causal switch of "on" or "off" of cellular function. Mutations of the cascade result in gain or loss of function, producing clinical conditions such as cancer and associated congenital syndromes (Noonan syndrome, LEOPARD, Cardio Facio Cutaneous (CFCS), Costello and Legius), autosomal dominant disorders caused by mutations with gain of function. His presentation with short stature makes them a need for pediatric endocrinology consultation, which requires the best knowledge and the ability to integrate a management team. **Materials and Methods:** We report 4 cases of mutations of the RAS / MAPK: Neurofibromatosis1, Legius Syndrome, Cardio Facio Cutaneous Syndrome and Noonan Syndrome. Data are presented as clinical endocrinological evaluation for each one. **Conclusions:** Shared Alterations in NCFC syndromes are associated with mutations in genes in the same way, which explains their overlapping clinical phenotypes. It emphasizes the importance of phenotypic and genetic heterogeneity of each of the entities. Molecular diagnosis can change the prognosis and follow-up (food, cardiac and neurological therapies rate variation, GH management, susceptibility to cancer) and genetic counseling to parents and patients (prenatal diagnosis in CS, CFC, NF1 and NS and preimplantation in NF1), open the stage for new research on possible therapeutic management of postnatal growth and modulation of activity of MAPK and diminish its clinical progression. These entities should be familiar to the specialty to generate guidelines for rational and targeted approach in improving the quality of life of these patients, proposing links with international consortia in order to facilitate proper study.

78

Evaluation of the Interpretation of Magnetic Resonance Pituitary with Contrast Medium in Patients with Short Stature: Study Interobserver Agreement

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Background: Magnetic resonance imaging with contrast pituitary imaging (NMR) is used to evaluate the hypothalamic-pituitary morphology in patients with short stature and suspected growth hormone deficiency. **Objective:** Assess the degree of concordance between the interpretation of NMR pediatric endocrinologist and radiologist. **Methods:** Study of diagnostic tests, we evaluated 28 NMR of patient with short stature, interpreted by a radiologist and a pediatric endocrinologist, we determined the degree of interobserver agreement using Cohen's kappa. **Results:** Mean age 10.46 ± 2.7 years, 19 men (67.9%), Tanner M1/G1 21 patients (75%). There was significant difference in the interpretation of pituitary regard to the aspect ($p < 0.0001$), a discrepancy concavity with sunken ceiling and crescent sign ($p = 0.02$) and adenohypophysis ($p < 0.0001$).The absence of invasion in pituitary stalk and neurohypophysis contrast medium showed no difference between observers. **Conclusions:** NMR correctly interpreted is a gold standard in the approach to patients with short stature, contributing to diagnosis, prognosis and early treatment. There are no studies that assess the degree of concordance in radiological interpretation of the hypothalamic-pituitary morphology between different observers. It is important to standardize radiological criteria to assess the pituitary as its morphology has important clinical implications.

79

Case Report: Macroprolactinoma in Childhood

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Background: Prolactinomas are rare in childhood (0.1/million). They are more aggressive in this age group, with higher prevalence of macroprolactinomas. **Objective:** To report the case of macroprolactinoma in childhood. **Methods:** Female patient, 10 years old, reported the onset of headache, reduced visual field on the left, right amaurosis, and weight gain in two months. No other previous diseases. Her parents are healthy and they are not consanguineous. No history of pituitary adenomas or endocrine diseases in her family. No gestational or perinatal problems. Physical exam: weight: 43.7 kg (P75–90), height: 1.35 m (P25), BMI: 23.9 kg/m² (P>97); Tanner: M1P1. No galactorrhea. MR identified an expansive lesion, heterogeneous, cystic, in sellar and suprasellar region, with optical chiasmal compression, involving the carotid and affecting the cavernous sinus (50x40x35 mm). **Results:** Initial hypothesis: craniopharyngioma. She was submitted to decompressive surgery with drainage of necro-hemorrhagic content. The tumor tissue immunohistochemistry was positive for prolactin. Started cabergoline (1 mg/week) with reduction in the lesion size and decrease of prolactin levels: 8368 (1 month); 6650 (2 months); 1196 (3 months); 568 ng/ml (4 months). She reported improvement in headache, without change in visual acuity. **Conclusions:** The highest prevalence of craniopharyngioma in childhood and the lesion's characteristics, with cystic and hemorrhagic components, initially led to the misdiagnosis. Therefore, in patients with cystic lesion in seal and suprasellar region, the prolactinoma should be considered in differential diagnosis, because it allows specific and less aggressive therapy. Adequate control with cabergoline prevented more extensive surgery in the sellar region.

80

Assessment of Long-Term Growth in Patients Small for Gestational Age Growth Hormone-treated

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The benefits of treatment with growth hormone (GH) on height gain in children born small for gestational age (SGA) with persistent short stature have led to its approval in Europe, USA and Argentina. **Objective:** To report response to long-term treatment with GH in SGA patients of a Private Universitary Hospital. **Methods:** We analyzed retrospectively auxological data of 21 children (14 males) PEG at baseline and annually during treatment with GH. The patients presented: mean (SD) BW 1735.1 (785.9) g, BL 42.5 (4.8) cm, GA 34.8 (4.9) weeks and genetic target height –0.46 (0.86) SDS. They started GH treatment (0.33 mg/kg /w) at 6.85 ± 2.78 years with height –2.68 (0.56) SDS. **Results:** The gain in height SDS from start of treatment was significant during five years of follow up (table). Growth velocity (GV) increased 1.94 (2.1) cm / year, p = 0.000 for the first year of treatment. **Conclusion:** GH therapy was effective in increasing height SDS in SGA children.

Table 1. (for Abstract 80)

Years of treatment	N	Height (SDS)	Δ Height (SDS)	GV (cm/year)
0	21	–2.7±0.6		5.9±1.5
1	21	–2.1±0.6	0 57±0.3**	7.8±1.3
2	18	–1.9±0.8	0.89±0.5**	6.4±1.4
3	14	–1.7±0.8	1 07±0.5**	6.7±1.0
4	10	–1.3±0.8	1.43±0.7**	6.2±1.3
5	7	–1.1±0.7	1.75±0.6**	5.9±1.4
6	4	–1.0±0.7	1.72±1.1	4.7±3.0
7	2	–1.0±0.3	2.12±0.5	3.9±0.3

Height, height gain vs. baseline (Δ) and growth velocity mean±SD.
Δ height vs. baseline; **p = 0.000 (paired t test).

81

Adult Height in a Large Cohort of Turner Syndrome and the Effects of Growth Hormone Treatment

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Short stature is a cardinal finding in Turner Syndrome (TS) and different factors have been associated with response to growth hormone (rhGH) treatment in these patients.Our aim was to assess the adult height (AH), the response to treatment and related factors to outcome in children with TS. **Methods:** We studied 73 patients with TS who reached AH. 57 girls (Gr1) completed treatment with rhGH (mean duration 4.9 years) and 16 girls did not receive (Gr2). The height SDS was calculated according to our normal and ST population's reference standards (SDS and SDS-TS). **Results:** Delta AH-mid parental height SDS was different between groups (Gr1 vs. Gr2 –2.15 –3.19, p <0.005). In Gr1, a gain of 1.65 SDS-TS related to height at baseline (BH) of treatment was found (p <0.001). In a multivariate regression, AH SDS-TS was positively related to duration of treatment and BH SDS-TS and negatively to bone age at baseline. **Conclusions:** Treatment with rhGH allowed in girls with TS, improve AH in relation to the ST population of our country. The initiation of treatment before the height affectation would be mandatory to optimize the AH in these patients.

82

Hypoplasia of the Internal Carotid Artery and Hypopituitarism: An Unusual Association

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Hypoplasia of the internal carotid artery (ICA) is a rare vascular anomaly. The association with hypopituitarism is unusual, only ten cases have been reported.We report a 9.2 years old girl with 4 month evolution of polyuria and polidipsia with no history of perinatal pathology. Height: –1.62 SDS, Weight: –0.68 SDS. Central diabetes insipidus was diagnosed with no other pituitary deficiencies. Eye fundus: normal. Tumoral markers: negative. Magnetic resonance angiography: small anterior pituitary, absence of posterior pituitary, thickened stalk, hypoplasia of the left ICA. Desmopressin treatment was iniciated. A year later, growth retardation with GH deficiency was detected. MRI: no changes compared to previous. At the age of 11.2 years in Tanner II, rhGH was started with adequate response. Fifteen months later thyroid hormone was initiated (progressively low levels of T4 and FT4 with suspicion of central hypothyroidism). After 3 years (with no medical follow up taking only desmopressin) the patient went back to hospital with signs of hypothyroidism in Tanner IV, no menarche. Lab: TSH 133.3 mUI/ml, antithyroid antibodies positive (Height: +1.3 SDS, Weight: +0.29 SDS). A primary autoinmune hypothyroidism was diagnosed. **Conclusion:** Hypoplasia of the ICA may lead to pituitary hypoplasia with hypopituitarism. This is an unusual association.

83

Pituitary Stalk Tuberculosis, Difficult Diagnosis

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Introduction: Schoolgirl with hipopituitarism due to stalk tuberculosis without compromising another organ. **Case Report:** We report a female patient 6 years old, who was referred for poor growth velocity, and below target height, bone age delayed; we diagnose central hypothyroidism, diabetes insipidus and growth hormonal deficiency. A magnetic resonance MR shows hypothalamic-hypophyseal thickened; we carry out PCR and concluding stalk tuberculosis (Mycobacterium tuberculosis) without pulmonary compromise. She was treated antituberculosis therapy with successful following. **Discussion and Conclusions:** Tuberculosis infections incidence has increased all around the world and stalk pituitary compromise in pediatrics is uncommon. We should consider tuberculosis in patients showing thickened stalk and hipopituitarism.

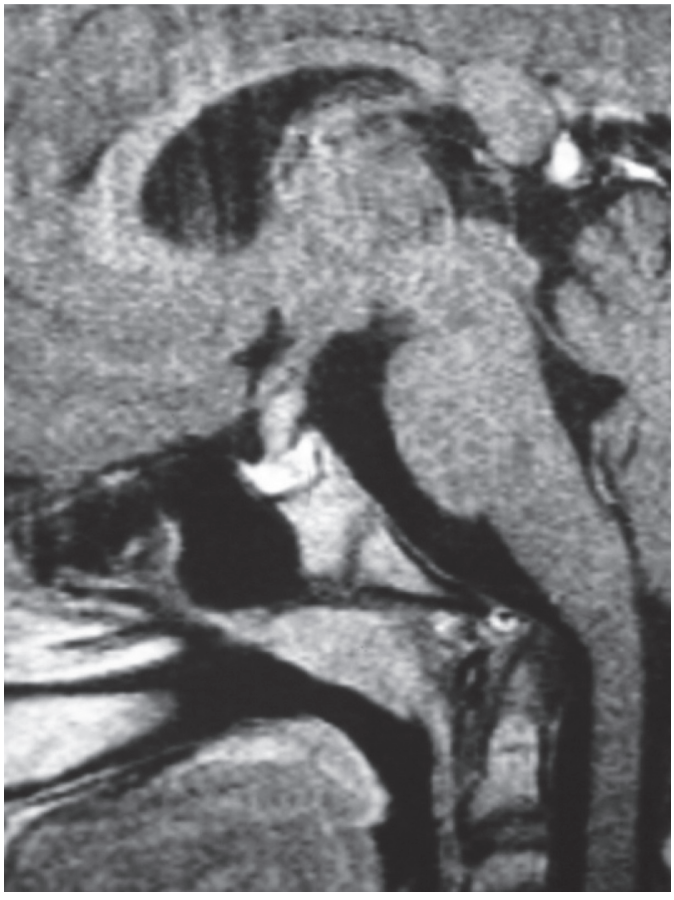

Fig. 1. (for Abstract 83)

84

Chronic Cluster-like Headache in a Patient with a Macroprolactinoma: Bromocriptine Vs. Cabergoline?

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Background: Cluster-like headaches (CH) associated with pituitary adenomas have been reported, mostly with prolactinomas. Also, measurement of prolactin (PRL) with two site monoclonal assay can result in falsely low measurement know as hook effect. **Objective:** We present a case of macroprolactinoma presenting with CH, initially with moderate hyperprolactinemia due to hook effect. **Case Report:** 18 years old, female.3-year history of evolution compatible with CH severe pain left retroorbital, intense symptoms associated with ipsilateral lacrimation, conjuntival injection and ptosis, lasting around 2 hours, with a frequency of 4–5 headaches/week, with no triggering factors and no remission periods, as assessed by a neurologist,and trated with NSAIDs and ergotamine, decreasing frequency of attacks to 1–2 times/week. Later on, she presented with, amenorrhea and galactorrhea, without neurological disorders, with the initial PRL of 125 ng/ml, with normal levels of TSH, FT4 and early morning cortisol.MRI of the brain revealed a lobulated sellar mass measuring 3x3 cm, with suprasellar, sphenoid, and left cavernous sinus invasion and optic chiasm compression. Repeated PRL levels performing a 1/100 dilution were 1320 ng/ml. Cabergoline was treated with increasing doses up to 1 mg/week, triggering headaches with similar, more severe and longer lasting. One month is changed to Bromocriptine in doses 7.5 mg/day, well tolerated. Reinstall menstrual cycles, the PRL was normal. MRI at 3 months, decreased tumor size 12x12 mm. **Conclusion:** CH may be associated with pituitary tumors; thus cluster headaches with atypical presentation should alert for close follow up, as well as warrant PRL level measurement. Also, high dose hook effect should be ruled out in the setting of large pituitary adenomas with moderate increase in prolactin levels.

85

Congenital Hypopituitarism

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Introduction: Congenital Hypopituitarism (CHP) is a rare condition with an incidence of 1/53000 newborns, a variable clinical presentation in terms of severity and time of appearance of hormone deficiencies. Early diagnosis prevents damage in cognitive function and reduces co-morbilities. **Objectives:** To evaluate the contribution of clinical signs and symptoms, hormone testing and imaging to diagnosis of CHP in children. **Materials and Methods:** Twelve

patients with diagnosis of CHP were retrospectively evaluated during the first two years of life. **Results:** Of the 12 patients, 25% were referred for suspected CHP during the neonatal period. They presented neonatal hypoglycemia (83.3%), micropenis (83.3%), seizures (58%), and cholestasis (8.3%). Deficiency in four tropins (GH-TSH- ACTH- GnRH) was observed in 50% of the patients (33% of three tropins and 17 % of two). Brain MRI showed hypoplastic adenohypophysis, absence of stalk and ectopic neurohypophysis (58%). **Conclusions:** Our observations support the fact that deficiencies in contraregulatory hormones are a cause of persistent neonatal hypoglycemia, which may be acute and early. Although the diagnosis can be made with high degree of accuracy with biochemical tests, the presence of clinical signs (hypoglucemia or micropenis) can contribute to an early diagnosis.

86

Physical Activity Regularly Increases Secretion of GH Response to the Test of Stimulus by Exercise

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Exercise stimulates the secretion of GH which has diagnostic application in exercise Test (TE). In healthy children with low PC or below the size epigenetics, wanting a non-pharmacological stimulation, can be useful to speed up the rate of growth (VC). But generally the TE has response mediocre in such children, especially if they are sedentary. In other glands endocrine it is considered possible cellular awareness to achieve better secretory response. **Objective:** Study changes in GH response to TE in normal children with stature in low percentiles after a period of two months of a program of daily physical activity. **Population:** 10 boys and 10 girls between 8 and 9 years of age, with stature in 5-25 PC, without nutritional deficiency, no pathology endocrine, parasitic or organic disorder, with steady growth in the past two years, prepuberal, BMI between 22 and 28, were subjected to the TE for GH stimulation prior to joining a supervised aerobic exercise program combining aerobics and basketball during one hour a day for a period of two months, out of which the TE was repeated. **Results:** In the TE before the program the basal GH was between 0.1 and 3 ng/ml with a peak between 2.5 and 7 ng/ml. TE was repeated after 2 months of physical activity program, and the values were higher: basal GH from 0.2 to 4 ng/ml with peak between 5 and 12 ng/ml showing a significant difference when compared to the peaks of the TE before and after the programme ($p < 0.001$). **Conclusion:** The increase in peak GH response to TE, after a period of two months of physical activity, suggests that there was an awareness of the somatotrophs to respond in greater magnitude to TE. This observation suggests that, if continue in the program of physical activity, children VC will also increase, with therapeutic applicability.

87

Endocrine Disorders after Craniopharyngioma Treatment in Children: A Retrospective Study

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Background: Craniopharyngiomas correspond to 1.2–4% of intracranial tumors in childhood. Despite being benign, they have high morbidity due to their location. Endocrine disorders may be present at diagnosis or as a result of treatment. **Objective:** To retrospectively investigate endocrine disorders in children after craniopharyngioma treatment. **Population/Methods:** Nineteen patients (11 girls) aged 5.7±3.8 years, referred between 1996–2011, whose assessments were reviewed in the first three years after treatment (surgery, radiotherapy, chemotherapy). Anthropometric data (weight, height, BMI), hormone deficiencies (IGF-1/IGFBP-3, TSH/T4L, ACTH/cortisol, LH/FSH, diabetes insipidus) and dyslipidemia (total cholesterol≥200 mg/dL, LDL≥130 mg/dL, triglycerides≥130 mg/dL) were investigated. **Results:** (Table 1.) 93% of 14 patients whose lipid profile was evaluated presented dyslipidemia. Specific hormone replacements were initiated shortly after diagnosis, except for GH therapy, introduced 1.5±0.7 years after surgery. **Conclusion:** Endocrine disturbances were found at the beginning of follow-up and continued to appear during the study period, indicating the importance of early follow-up.

Table 1. Percentage of disorders observed by year of follow up (for Abstract 87)

Follow-up			
Endocrine disorders	1st year	2nd year	3rd year
Diabetes insipidus	89	89	89
Hypocortisolism	89	89	89
Central hypothyroidism	68	89	89
Growth hormone deficiency	47	79	89
Gonadotropin deficiency	5	5	6
Short stature	37	32	33
Decreased growth velocity (<4cm/year)	42	42	44
Obesity	47	42	44
Overweight	11	21	17
Number of patients (n)	19	19	18*

* 1 patient did not completed 3 years of follow-up.

88

Nephrolithiasis and Nephrocalcinosis Screening by CT Scan in Children with X-linked Hypophosphatemic Rickets Confirmed by the Presence of *PHEX* Mutations

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Background: Patients with X-linked Hypophosphatemic Rickets (XHR) represent a group characterized by hyperphosphaturia secondary a *PHEX* inactivating mutations. Hyperphosphaturia may by itself increase the risk of stone formation by increasing urinary saturation. Moreover, nephrocalcinosis is a potential complication of XHR treatment. **Aim:** To confirm the molecular basis of XHR and to evaluate the presence of nephrolithiasis and nephrocalcinosis in XHR children. **Population and Methods:** The genetic analysis of *PHEX* was performed in seven children diagnosed with XHR. They were followed up with clinical and laboratorial evaluations. Renal ultrasound and a renal multislice CT scan were performed to search signs of nephrolithiasis and nephrocalcinosis. **Results:** All of the patients were asymptomatic and had no previous history of renal colic. Despite of hyperphosphaturia, none of them had hypercalciuria, hypocitraturia or impaired renal function measured by creatinine clearance. One ultrasound detected nephrocalcinosis, whereas CT scan showed nephrocalcinosis in four children. There were no findings of nephrolithiasis in any of the images. Six different mutations were found in *PHEX* gene. **Conclusion:** In this cohort, the occurrence of nephrocalcinosis detected by CT renal scan was elevated. Therefore this co-morbidity must be investigated in children with XHR to enable an early intervention and prevent its progression.

89

Association between Bone Mineral Density and VDR and IGF-1 Genes Polymorphisms in Patients with Congenital Adrenal Hyperplasia (CAH-21OH) Treated with Glucocorticoids

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Introduction: Patients with Congenital Adrenal Hyperplasia (CAH) with glucorticoid therapy (GC) may present bone metabolism alterations. Vitamin D receptor (VDR) and IGF-I gene polymorphisms are considered as genetic markers of bone mineral density (BMD). **Objectives:** To analyze VDR and IGF-I gene polymorphisms in CAH patients and the relationships with bone markers and BMD. **Methods:** Sixty six CAH patients treated with GC were classified in two groups according to the presence of an adequate (Acl) or inadequate (Icl) clinical and biochemical control. We evaluated BMD by DEXA, bone markers (osteocalcin and β-crosslaps), VDR gene polymorphisms (Bsm I and Fok I sites) and IGF1, by PCR-RFLP. Statistical analysis: Chi, Wilcoxon or Mann-Whitney and Krustal Wallis tests. **Results:** Patients carrying FF genotypes showed the lowest *z-score* of spine BMD (FF: –1.41; Ff: 0.13; ff: –0.10; $P<0.05$). The analysis of IGF-1 gene polymorphisms revealed that the frequency of allele 192 in the Icl group was lower *vs* controls. CAH patients with genotype 0/0 (absence of allele 192) presented higher values of β-crosslaps (0/0: 1.57 ng/mL; 0/192: 1.24 ng/mL; 192/192: 1.02 ng/mL; $P<0.05$) and lower BMDs (0/0: 0.84 gr/cm^2; 0/192: 1.10 gr/cm^2; 192/192: 1.00 gr/cm^2; $P=0.05$). **Conclusions:** CAH patients lacking allele 192 have an altered bone turnover and inadequate response to therapy. In addition, patients with genotype FF have the lowest bone mass. The evaluation of these polymorphisms may be useful to predict as predictors of low bone mass in patients with CAH.

90

Satisfaction Survey on the Use of Calcium Carbonate in the Form of Emulsion (Pluscal Mousse®) in Pediatric Patients

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Introduction: To acquire peak bone mass during childhood and adolescence, it requires an adequate calcium intake. These requirements are affected when conditions or medications that affect supply. The use of salts of calcium supplements, most often are not tolerated by pediatric patients. **Objective:** To assess tolerance and response to treatment with calcium carbonate administered as an emulsion, a survey of satisfaction in pediatric patients requiring calcium intake as part of their treatment. **Patients and Methods:** We evaluated 43 pediatric patients (18 women), mean age 11.9±4.7 years, with use of calcium supplement. 67.4% received calcium carbonate previously, in the form of tablets (mean dose: 985.4 ± 438.2 mg/day). Among those receiving calcium before starting the mousse, the average number of tablets consumed was 2.09 tablets/day = 1046±486 mg of elemental calcium/day. The mean number of scoops of mousse used was 1.78 tablespoons/day = 890±454 mg of elemental calcium/day. Blood levels of Ca, P, PTH (ECLIA, Roche), 25OHVit D (Diasorin RIA) were measured. Statistical evaluation was performed with the t test for paired samples. **Results:** 74.5% reported a good tolerance / very good / excellent, 25.5% reported poor tolerance. 83.7% preferred the emulsion, and only 16.3% preferred tablets. Thirty patients (69.8%) completed 3 months of observation, 5 (11.5%) were lost, 5 (11.5%) discontinued due to gastrointestinal intolerance, 1 (2.3%) discontinued treatment because liked, and 2 (4.7%) discontinued treatment without clarifying why. The mean calcium before starting

the emulsion: 9.0±1.2 mg/dl at 3 months: 9.3±0.8 mg/dl, p = <0.012, among those receiving tablets and moved to the emulsion, serum calcium levels were higher in the latter: 8.65±1.47 vs. 9.14±1.14 mg/dl respectively, p<0.02. The mean value of iPTH before the start of the emulsion was 74.3±153 pg/dl, at three months: 39.0±34.7 pg/dl, there was no statistically significant difference, if an improving trend PTH levels. **Conclusion:** Although the number of patients is small to draw definitive conclusions, the survey suggests that use of the emulsion in the form of mousse can raise the plasma calcium level significantly, with better tolerance, better response and adaptation to the tablets.

91

Dental Abnormalities in Children with X-linked Hypophosphatemic Rickets Confirmed by the Presence of *PHEX* Mutations

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Background: X-linked hypophosphatemic rickets (XHR) is caused by loss-of-function mutations in the *PHEX* gene. This disorder is characterized by a defect in renal phosphate transport, causing phosphate wasting, hypophosphatemia, defective bone mineralization and dental abnormalities such as taurodontism which is a condition that supports the development of dental abscesses. **Aim:** To confirm the molecular basis of XHR and to evaluate dental abnormalities in children with XHR. **Population and Methods:** Genetic analysis of *PHEX* and panoramic radiograph were performed in nine children diagnosed with XHR. **Results:** Four patients presented permanent dentition, 4 patients with mixed dentition and 1 patient with deciduous teeth. These findings matched chronological age. The presence of taurodontism was found in seven X-rays. None of the patients had dental abscesses or periapical lesions. Dental caries were found in one patient and teeth restoration found in 3 patients. These findings may indicate a good oral health despite of the anatomical condition. Six children had areas of hypomineralization, especially in the jaw. Seven mutations in *PHEX* were found. **Conclusion:** Patients with XHR are predisposed to dental abscesses and their complications. In our cohort, the adequate treatment and good oral hygiene of these children may justify the absence of these alterations.

92

Improvement of Calcifications in a Patient with Generalized Arterial Calcification of Infancy Treated with Pamidronate

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Background: In generalized arterial calcification of infancy (GACI) the low levels of ENPP1 enzyme, responsible for the synthesis of inorganic pyrophosphate, results in increased calcification of medium and large arteries. 85% of patients die within the first 6 months of life due to myocardial infarction and progressive ischaemia of vital organs. There is evidence that survival may improve with early treatment with pamidronate (PM). **Objective:** To report a patient with GACI successfully treated with PM. **Methods:** Fetal diffuse calcifications in the descending aorta (AO), aortic arch and pulmonary artery were identified at 35 weeks of gestational age through echocardiography (ECO). While cranial ultrasound and computed tomography performed in the neonatal period showed no calcifications, ECO revealed calcifications of the aortic and pulmonary valve rings, the left coronary artery (LCA) and entire AO (arch, descending, thoracic and abdominal). The mineral metabolism was characterized by hyperphosphatemia (6.2 mg/dL). ENPP1 gene mutations analysis is ongoing (negative results until the moment). The patient has been treated with endovenous PM administered as three-days cycles each two months, at a dose of 0.5 mg/kg/day. This treatment started when he was 28 days-old. **Results:** The patient is 1.8 years-old and is still being treated with PM, with good outcome. ECO performed at 5 months of age showed decreased calcifications, but still present in the LCA, ascending AO, and transverse arch. The last ECO done at the age of 1.8 years revealed marked improvement of the calcifications on LCA, aortic and pulmonary valve rings, abdominal AO and transverse arch. **Conclusions:** Although the calcifications of some patients with GACI may improve spontaneously, we believe that in our patient the treatment with PM has contributed to the remission of severe arterial calcifications. On the other hand, ECO has shown to be a sensitive tool for diagnosis and follow-up.

93

Epidermal Nevus Syndrome with Hypophosphatemic Renal Rickets

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The term epidermal nevus syndrome is used to describe the association of diffuse cutaneous nevi abnormalities with extra skin alterations that involve the central nervous, skeletal, and renal systems. Incidence is1:1000 and is probably a result of genetic mosaicism. We report a case of a patient with a history of syndrome of epidermal nevus in limbs and trunk, skeletal changes since birth and that evolved with rickets and hyperphosphaturia. **Case Report:** JU, white, female, admitted at the age of 5 with pyelonephritis. Evolved with renal exclusion. Submitted to nephrectomy and diagnosed Wilms´ tumor. Presents since birth cutaneous nevi diffuse, scoliosis, and diagnosis of cerebellar lipoma. FA: negative for diseases of bone metabolism, has a normal twin sister. Referred to the department by presenting radiographic changes and pain.Laboratory tests showed rickets with decrease in the rate of tubular reabsorption of phosphate. Ca (9.4MG /dl), FA (2.492 U/L) P (2.3MG /dl), TRF (82.3%). Introduced Vitamin D (0.5 mcg of calcitriol) and phosphate (1.25 g day) with improvement of clinical and radiographic manifestation. **Conclusion:** We emphasize the importance of the clinical diagnosis of the syndrome of epidermal nevus and the association with metabolic bone diseases.

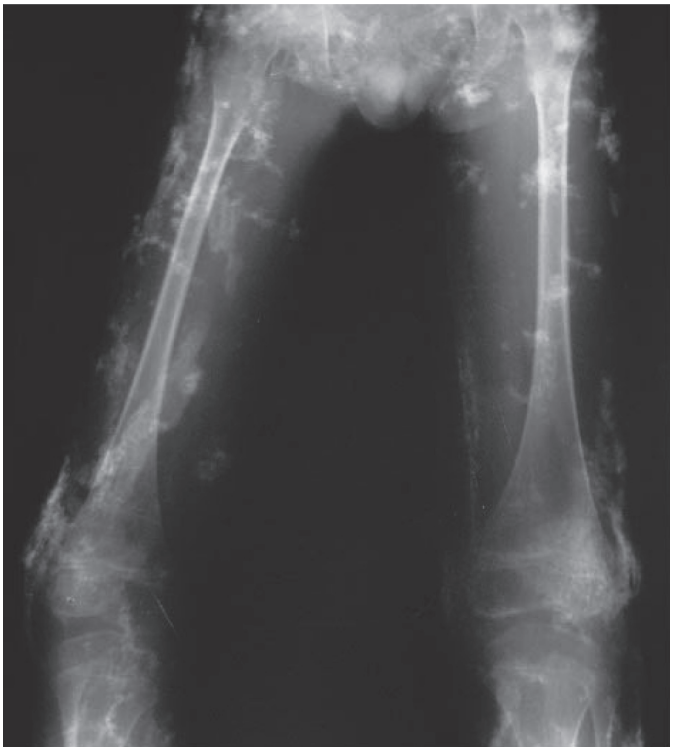

Fig. 1. Lower limbs RX at diagnosis (for Abstract 94).

94

Idiopathic Calcinosis Cutis: A Case Report

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LL male, 8 years old, only son, no memorable records. He had 4 years ago irregular, hard and painful nodules of 2–4 cm, at face, abdomen, upper and lower limbs; they start as edema progressing to soft injuries which become hard with white material. Serum calcium 11mg/dL. CBC, renal function, PTH, phosphatemia, ANA, ANCA, C3 and C4 normals. Upper and lower limbs X-R: subcutaneous lines compatible with calcium deposits (fig 1). BA 7 years. Bone densitometry z score –2.1. Lesion biopsy: calcareous concretions. We made diagnosis of Idiopathic Calcinosis cutis. He was treated with Colchicine and Ibandronate. He had clinical and imaging improvement. Calcinosis cutis is a disorder characterized for subcutaneous deposits of calcium, that can be of type dystrophic, iatrogenic, secondary and idiopathic. The treatment is with Colchicine as anti-inflammatory, biphosphonates, aluminum hydroxide, warfarin and intralesional or systemic corticosteroids and immunosuppressive therapy for advanced cases.

95

Six Year Growth Hormone Treatment in Short Children with X-linked Hypophosphatemic Rickets: Effects on Linear Growth

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Context: Children with X-linked hypophosphatemic rickets (XLH) are prone to progressive disproportionate stunting despite oral phosphate and vitamin D treatment. **Objective:** Our objective was to analyze the effects of GH treatment on stature and linear body segments in short children with XLH. Design, Settings, and **Patients:** A 6-yr controlled GH administration in short prepubertal children with XLH on phosphate and calcitriol treatment was conducted. **Results:** XLH patient presented at time of enrollment with significant impairment of stature (–2.4SDS). GH resulted in a sustained increase in linear growth (final stature –1.55SDS; Familial target height –0.08). **Conclusions:** The 6-yr GH treatment improved linear growth without progression of body disproportion in short children with XLH.

96

Evaluation of Stature Development during Childhood and Adolescence in Individuals with Familial Hypophosphatemic Rickets

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Objective: To evaluate the stature in patient with XLH. **Method:** The stature of 28 patients with XLH was accompanied between 1971 and 2011. **Results:** At diagnosis, short stature was obtained in 85.7% of the cases; the average age at diagnosis was 6 years. A correlation between the age of diagnosis and the Z score at diagnosis in patients who were submitted to the treatment, was observed. There was a significant difference between the initial stature and the final stature in six patients who were treated with vitamin d and phosphate. **Conclusion:** The evaluation of the growth stature in patients with XLH and the variables, as age at diagnosis, and the beginning of treatment, as well as Z score on the final stature, reinforce the need for an early diagnosis and confirm the importance of treatment.

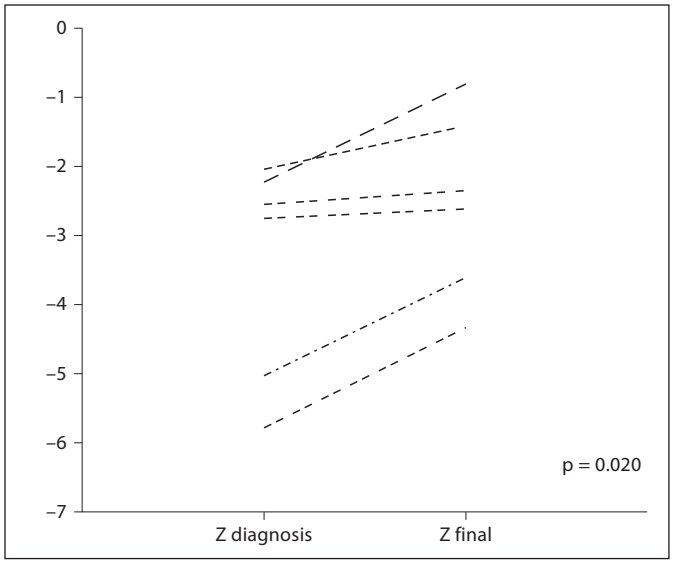

Fig. 1. Analysis patients treated medically and final height (for Abstract 96).

97

Use of Recombinant Human HCG Test (rh-HCG) in the Evaluation of Testicular Steroidogenesis

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The evaluation of prepubertal testicular function is usually done through gonadal stimulation with hCG obtained by urinary extraction, However, this type of HCG is no longer available in many countries. **Aim:** To evaluate the usefulness of rh-HCG in recognize testicular steroidogenesis. **Patients/Method:** We studied 18 prepubertal boys (CA:0.8–9.0y) with unilateral (n=15) or bilateral (n=3) cryptorchidism, without hypospadias or any other genital abnormality. We exclude patients with previous use of HCG or testosterone. Samples were obtained at baseline and 7 days after a single dose of rh-HCG (OVIDREL 250mcg), subcutaneously. **Results:** There was a significant increment in testosterone after hr-HCG (paired t-test; $p<0.001$*). We concluded that the stimulation with rh-HCG in a single subcutaneous dose is able to stimulate testicular steroidogenesis, being potentially useful in the evaluation of testicular function. A larger number of control subjects with isolated cryptorchidism should be evaluated to establish normal reference values.

Table 1. (for Abstract 97)

	Baseline	Post rh-HCG
17OHProgesterone (ng/ml)		
mean (SD)	0.5 (0.5)	0.7 (0.4)
min-max	0.1–1.9	0.2–2.1
Androstenedione (ng/ml)		
mean (SD)	0.3 (0.5)	0.3 (0.2)
min-max	0.1–2.1	0.1–0.7
Total Testosterone (ng/dl)		
mean (SD)	20 (0)	176.4 (100.7)*
min-max	20–20	29.0–442.0
HCG (mUI/ml)		
mean (SD)	nd	14.6 (9.4)
min-max		1.8–39.1

98

Defect of Sexual Development 46,XY, Complete Androgen Insensitivity: Report of a New Mutation in the Androgen Receptor

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A female infant at age 6 month was operated from bilateral inguinal hernia. Testicles were observed in both inguinal hernia sac. The familia history was unremarkable. Her karitype was a 46,XY. A ginecologic ultrasound showed a blind vagina and not uterus. Her testosterone, DHT and AMH levels were in the male range. An androgen receptor mutation E838X in exon 7 was found. It produces a stop codon and probably a biological inactive protein. This mutation has not been described before.

99

Clinical Description of Five Pediatric Patients with Rapid-onset Obesity and Clinical Signs Suggestive of ROHHADNET Syndrome

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Background: ROHHADNET is characterized by rapid-onset obesity, alveolar hypoventilation, hypothalamic and autonomic dysregulation, neural crest tumors, respiratory failure, and sudden death. As literature reports are scarce, the diagnostic criteria have not been clearly established. **Objective:** To report five girls admitted to our center between 2007 and 2011 with a follow-up ranging from 8 months to 4.16 years. **Results:** All five patients had rapid-onset obesity at the age of (X+SD) 5.24 ± 0.6 years. The following signs and symptoms were found: Central hypoventilation confirmed by polysomnography (n=2), transient obstructive apneas (n=2), autonomic dysregulation (n=5), hypothalamic-pituitary dysfunction (n=5): central hypothyroidism (n=4), hyperprolactinemia (n=3), growth hormone deficiency (n=2), precocious puberty (n=1) and adrenal insufficiency (n=1), hydrosaline balance disorders (n=3), neurobehavioral difficulties (n=2), and ganglioneuromas (n=3). Neural Tumor was diagnosed 9 months previous to the onset of obesity in one patient. One patient died at 6.64 years of age consequence of severe alveolar hypoventilation. **Conclusion:** Awareness of the syndrome, clinical suspicion, and early diagnosis may improve morbidity and mortality. ROHHADNET should be considered in cases of rapid-onset obesity associated with one or more of the above-mentioned symptoms.

100

Evaluation of Neck Circumference in Children and Adolescents from Brazil

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Introduction: The increased neck circumference (NC) is associated with a greater degree of obesity and risk of complications requiring reference to pediatric patients. **Objective:** To evaluate the use of NC as an indicator of overweight and obesity in children and adolescents. **Method:** Assessment of weight and height to calculate body mass index (BMI, CDC 2000) of children and adolescents aged 6–19 years, enrolled in schools of São Paulo, Brazil. They were divided into two groups: normal weight (BMI between 25th and 75th percentiles) and overweight/obese (BMI above the 85th percentile). NC measurement was conducted in the region of the thyroid cartilage, with a measuring tape. Statistical analysis were performed by Sigma-stat3.5. **Results:** 2804 children were evaluated, 50.1% girls and 49.9% boys. Normal weight group=1198 children and overweight/obese=837. We found a positive correlation in both groups, between NC and age, and a statistically significant difference when comparing the two groups for NC and BMI SDS. In overweight/obese group there was a correlation between NC and BMI SDS ($r=0.26$, $p<0.05$). It was possible to established normal values of NC (mean (SD) for children over 6years, of both sexes. **Conclusion:** NC measurement can be used to evaluate nutritional status of children and adolescents.

Table 1. (for Abstract 100)

Age	6 years	7 years	8 years	9 years	10 years	11 years	12 years	13 years	14 years	>15 years
Mean(SD) F	25(1.2)	25.3(1.1)	25.7(1)	26.6(1.3)	27.2(1.2)	28.5(1)	28.8(0.9)	29.1(1.2)	29.6(1.1)	30.4(1.2)
Mean(SD) M	25.6(1.1)	25.8(1.2)	26.4(1.1)	26.8(1.1)	27.7(1.2)	28.4(1.4)	29.9(1.9)	30.6(1.7)	32.2(1.8)	33.8(3.4)

F: female; M: male.

101

Obese Children have Elevated Markers of Endothelial Inflammation even in the Absence of Comorbidities

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The presence of subclinical endothelial inflammation markers (SEIM) may represent increased cardiovascular risk in obese children. It has been suggested that obese without comorbidities could be considered "uninflamed obese". **Objective:** To compare SEIM in obese children with (Ob+) and without (Ob–) comorbidities, with eutrophic children. **Methods:** we examined 161 obese children (BMI >p95 NCHS), between 5–15 years old, assessing comorbidities: Hypertension (>p90), HDL-C < 40 mg/dL, Total cholesterol >200 mg/dL, Triglycerides > 110 mg/dL and/or Hyperglycemia ≥100 mg/dL. We define (Ob+) those with 1 or more comorbidities (N = 81) and (Ob–) those without them (N = 17). All study participants gave written informed consent. It was determined: PAI-1, Total cholesterol (TC), LDL – cholesterol (LDL-C), Adiponectin, TNF-α and Interleukines 6 y 8. They were compared with a control group (N=144). **Results:** The SEIM: PAI-1, us PCR and LDL-C were significantly higher in both groups of obese vs eutrophic ($p<0.001$). There were no significant differences between Ob+ vs Ob–. The other parameters showed no differences. **Conclusion:** Obesity per se represents a state of subclinical endothelial inflammation in children. The most sensitive parameters were us PCR, PAI-1, and LDL-C. Detection of MIES before comorbidities can help establish changes in lifestyle to prevent the development of these.

102

Arterial Stiffness and Endothelial Function in Obese Children and Adolescents

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Vascular function is impaired in hypertension, diabetes, metabolic syndrome (MS) and obesity. In the pediatric population there are few studies about the endothelial function (EF) and arterial stiffness (AS). **Objective:** To determine vascular function assessing EF and AS in obese children and adolescents and its relation to cardiovascular risk factors. **Methods:** We studied obese boys (BMI ≥ percentile of 97) of the endocrinology outpatient service of the Hospital del Niño Jesús (Hosp) with no history of prior disease (n=25, age: 12.6±0.5 years). We measured anthropometric parameters, fat mass (FM), blood pressure and laboratory data. The EF was assessed by reactive hyperemia and AS by the pulse wave. Data were compared with non-obese boys from the Hosp or Avellaneda school – Monteros (n=13, 13.8±0.7 years). **Results:** The obese showed higher FM, waist circumference (WC), insulinemia and HOMA index. BMI was correlated with FM (R2: 0.5844, $p<0.01$, n=23). The hyperemic response was greater in non-obese (28.1±4.1%, n=13) than in obese (14.4±1.8%, n=25, $p<0.001$). Only in obese EF was negatively correlated with age, WC and HOMA index. The AS was significantly higher ($p<0.01$) in obese (68±2, n=23, $p<0.01$) vs. non-obese (53±4%, n=12). **Conclusions:** The obese group, even lacking MS, have insulin resistance and altered WC. The lower EF and higher AS in obese indicate that an altered vascular function is already present at early ages. The negative correlation between EF with HOMA and also with WC indicates that humoral alterations may be implicated in vascular dysfunction. These data indicated the importance of lifestyles changes in obese, even before the onset of MS.

103

Cardiovascular Risk in Chilean Adolescents: The Role of Family History of Type 2 Diabetes and Obesity. Raquel Burrows, Marcela Reyes, Valeria De Toro, Paulina Correa, Estela Blanco, Betsy Lozoff, Marcela Castillo, Sheila Gahagan. Inta. University of Chile, Rey Juan Carlos University, University of California and University of Michigan

Burrows, Raquel[1(*)]; Gahagham, Sheila[2]

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Background: T2DM family history (FHDM) and obesity raises the risk of insulin resistance (IR), Metabolic syndrome (MetS) and T2D. Dietary and western lifestyle patterns are strong determinant. In Chile, the prevalence of obesity and T2DM increased from 21.8% to 32% and 3.8% to 10.1% respectively, between 1993 and 2001. **Objective:** To study the association of FHDM and obesity with IR and MetS in a cohort of Chilean adolescents. **Design:** In 498 adolescents (16.7 years old) from a longitudinal follow-up study, BMI, waist circumference, blood pressure, triglycerides, HDL-chol, glucose, insulin, HOMA-IR, and physical activity (PA) habits, were measured. Mets was diagnosed according Cook criteria and score Mets was calculated. To measure the influence of FHDM, obesity and PA on MetS and IR, linear and logistic regressions were used. **Results:** Adolescents with FHDM had significantly higher prevalence of abdominal obesity, high diastolic pressure, fasting hyperglycemia and IR, compared to adolescents without history. FHDM significantly increases ($p<0.05$) HOMA-IR, and also did obesity ($p<0.000$) and low PA($p<0.05$). However, FHDM is not significantly associated with MetS ($p<0.11$), but if you are obesity, male sex and PA ($p<0.002$). The risk of MetS was estimated for FHDM, obesity, sex and physical activity. Obesity, male gender and low PA

were associated with highest risk of MetS (p<0.001), however, the FHDM showed no significant associations. **Conclusions:** Obesity and low physical activity are associated with a higher risk of IR and MetS risk than FHDM.

104

Familial Aggregation, Parental Transmission and Heritability of Type 2 Diabetes Mellitus in Families of Mexican Children and Adolescents

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Introduction: Diabetes mellitus type 2 (DM2) is spreading to all age groups in Mexico due to the interaction of environmental risk factors in genetically susceptible individuals, which determines patterns of transmission of the disease in relatives of affected patients. **Objective:** To estimate the familial aggregation, parental transmission and degree of heritability of type 2 diabetes in Mexican families of children and adolescents with the disease. **Methods:** This is a case-control study that included families of pediatric patients with T2DM and families of children and adolescents without diabetes. By developing pedigrees analyzed for the presence of diabetes in three generations. The data were obtained through interrogation in second degree relatives and were corroborated biochemically in the first degree (parents and siblings). Familial aggregation was assessed by comparing the prevalence of the disease between families and case-control odds ratios for individuals with varying degrees of kinship. We compared the involvement of family members between paternal and maternal line and calculated the heritability of the disease. **Results:** Were included 56 case families (n = 1026) and 48 control families (n = 826). The prevalence of the disease was 23.7 vs. 8.1% respectively. There was an increased number of women affected, but no differences among the members of paternal and maternal side counterparts. A history of first or second degree with diabetes was associated with an increased risk of T2DM. The heritability of diabetes was estimated at 0.63 (p<0.001). **Conclusions:** There is significant familial aggregation of T2DM in Mexico. The prevalence of the disease is higher in women. The 63% of the phenotypic variability in relation to type 2 diabetes in Mexican children and adolescents appears to be related to genetic susceptibility factors.

105

Frequency of Overweight and Obesity in Children with Type 1 Diabetes and Glycemic Control: Preliminary Data

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Objective: To identify the frequency of overweight and obesity in children and adolescents with type one diabetes. **Methods:** Chart review of children and adolescents with type one diabetes followed at the outpatient clinic of diabetes in a pediatric university center. Exclusion criteria were use of glucocorticoid or medications with impact on weight gain, genetic syndromes, chronic diseases, celiac disease or incomplete anthropometric information. Statistical analysis was performed with SPSS for Windows version 19. **Results:** 228 patients, 102 (44.7%) females, average age of 10.6±3.9 years, and disease duration of 5.4±3.4 years. Overweight/obesity was found in 35.5% of children, without statistically significant differences between average A1c, age, disease duration between nutritional categories. Overweight patients had significantely larger insulin dosage (insulin/kg) (p=0.004; p=0.054). Linear regression pointed disease duration (p=0.000) and insulin dosage (p=0.000) as BMI predictors. **Conclusion:** These data confirm world trends of increased frequency of overweight and obesity, including the diabetic population and point out the need for lifestyle changes also in this population.

106

Changes in the Subclinical Inflammatory Parameters by Puberty in a Healthy Pediatric Population

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Introduction: It is postulated that puberty would produce a subclinical inflammatory condition, but there is lack of good quality evidencie that proves it. **Objectives:** To evaluate if there is any difference at inflammatory parameters (IP) levels in pubescents vs prepubescents children. **Subjects y Methods:** A group of 113 chidren was checked with an average age of 10.59 DS: 2.82, 55.8% women, 58.4% pubescents. The evaluation included anthropometry,

Table 1. (for Abstract 106)

Parameter	Overall		Prepubescent		Pubescent		P value
	Percentile 50	Interquartil Range	Percentile 50	Interquartil Range	Percentile 50	Interquartil Range	
Tumoral necrosis factor (TNFα) pg/ml	17.32	(12.6–24.23)	17.32	(13.12–24.23)	17.46	(11.56–24.24)	0.74
Interleukin 6 (IL6) pg/ml	11.85	(8.33–14.6)	12.62	(8.45–15.55)	11.68	(7.96–14.51)	0.53
Interleukin 8 (IL8) pg/ml	19.45	(16.04–28.21)	18.72	(16.41–25.28)	20.14	(15.53–30.07)	0.51
Ultrasensitive PCR (PCRus) mg/l	0.29	(0.2–0.77)	0.26	(0.2–0.68)	0.34	(0.2–0.82)	0.73
Plasminogen Activator Inhibitor Factor (PA[]) ng/ml*	12.76	(7.7–19.65)	8.51	(5.56–15.68)	14.72	(10.22–22.56)	0.0006*
Adiponectin µg/ml*	13.4	(11.1–17)	14.2	(12.6–18.2)	12.65	(9.6–15.3)	0.015*

blood preasure measuring, puberal staging according Tanner. FNTα, Interleukins 6 and 8, PAI I, Adiponectine and PCRus was measured. **Statistic Analysis:** Descriptive analysis, percentils, correlation coefficient, simple linear regression and student T test for averages. **Results:** Table. **Conclusions:** Differences in adiponectine and PAI I levels between pubescentsvs prepubescents was found, suggesting that this parameters are the most specific to puberal changes. IP level of this pediatric population can be use as a reference.

107

Neck Circumference is a Good Predictor of Blood Pressure Levels in School Children

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Introduction: Hypertension is a major health problem, underdiagnosed in children. Early identification of children at risk for high blood pressure levels is important to prevent cardiovascular complications. Excess body fat, particularly central adiposity, are recognized as important predictors of hypertension. Considering that body mass index (BMI) does not adequately describe regional adiposity, other indices of body fatness have being explored. **Objectives:** To investigate the ability of different anthropometric parameters (BMI, neck circumference, waist circumference and waist to height index) in predicting blood pressure (BP) levels in school children. **Methods:** A total of 320 children aged 6 to 13 years were evaluated. Weight, height and waist and neck circumferences were measured. BP levels were measured three times and converted to standard deviation scores (SDS) adjusted for sex, age and height. Hypertension was defined following the criteria of the 2004 Task Force Report on High Blood Pressure in Children and Adolescents. **Results:** The prevalence of high BP was 6% (3% pre hypertensive and 3% hypertensive children). Among those who were obese, this prevalence increased to 11%. Systolic blood pressure (SBP) SDS were significantly related to BMI SDS ($p = 0.003$) and waist to height index (W/H-I) ($p < 0.001$). Diastolic blood pressure (DBP) SDS showed linear association with BMI SDS ($p = 0.005$), W/H-I ($p = 0.008$) and neck circumference ($p = 0.004$). The best individual predictor of SBP was the W/H-I ($R^2 = 0.037$). Neck circumference was o superior to both BMI and W/H-I in predicting DBP, explaining 2.6% of observed variability. **Conclusions:** BMI, waist to height and neck circumference are useful tools to predict BP levels in children. Neck circumference is a simple measurement which has been under-valorized, and may be used as a valuable screening method for diastolic blood pressure elevation in children.

108

Birthweight is Directly Related to Body Mass Index and Inversely Related to Blood Pressure Levels in School Children

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Introduction: Since the so-called Barker Hypothesis, which pointed to the intrauterine life environment an important determinant of metabolic conditions, much has been published about the association between birthweight, hypertension and obesity. However, few studies have explored this association during childhood, especially in developing countries. **Objectives:** To evaluate the relation among birthweight, childhood body mass index (BMI) and blood pressure (BP) levels in school-children from a medium-sized city in southeast, Brazil. **Methods:** In a sample of 175 children aged 6–13 years, weight, height and BP levels were measured three times. BMI and BP levels were converted to standard deviation scores (SDS) adjusted to sex and age (BMI) or sex, age and height (BP levels). Birthweight was accessed through parents' interviews and hospital registries (child's card). Pearson's test, One Way ANOVA and linear regressions were performed on statistics. **Results:** It was observed a positive and linear correlation between the present BMI SDS and

the birthweight SDS (p<0.001). BMI SDS got average –0.5, +0.2 and +0.7 in children classified as small, adequate or large for gestational age, respectively (p=0.009).Blood pressure levels SDS were positively influenced by the child's BMI (p=0.003 for systolic and p=0.005 for diastolic BP). By the other side, there was a negative and linear association between birthweight and systolic BP levels SDS (p=0.03). Hence, the most important predictor of BP levels was the weight gain from birth to school age, which explained 5% (p=0.019) of systolic and 4% (p<0.001) of diastolic BP variation. **Conclusion:** In this sample, the combination of low birthweight and high BMI in school age is an important predictor of increased blood pressure levels in children.

109

Components of Metabolic Syndrome and Insulin Resistance are Associated in Obese Children with Uric Acid Levels

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Background: Association of hyperuricemia with metabolic syndrome (MS) components has been described. However, this relationship is not considered criteria of MS. **Objective:** To determine the correlation between uric acid, components of MS and insulin resistance (IR) in a population of obese children. **Population and Methods:** 133 obese children with a body mass index (BMI) = 2 SDS. MS was defined according to IDF criteria and blood glucose level at minute 120. HOMA index = 3 defined IR. **Results:** The mean age of 10.28 ± 2.32 years; 56% male, and 47% pubertal with no differences in BMI by sex and pubertal stage. The IR was 32% and 6 patients had MS. Uric acid correlates with BMI (r: 0.344), waist circumference (r: 0.397), systolic pressure (r: 0.186), HDL-c (r: –0.244), triglycerides (r: 0.199), glucose (r: 0.416) and glucose 120´(r: 0.254), insulin (r: 0.315) and HOMA (r: 0.3229). **Conclusions:** 1) Uric acid correlates with the major components of MS and IR in our population. 2) Influence of uric acid to predict the presence of MS should be evaluated in a population with higher prevalence of MS. Work partially funded by the Foundation Ikertu.

110

Frequency of Diabetic Neuropathy and its Related Factors in Adolescents with Type 2 Diabetes Mellitus

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Background: Diabetic neuropathy is a common complication in adults with type 2 diabetes mellitus (T2D), which is presented to the diagnosis in 10%, and 50% at ten years of evolution. In the pediatric population has increased the incidence of T2D, but data on microvascular complications in this age group is scarce. **Objective:** To evaluate the frequency of diabetic neuropathy and associated factors in adolescents with T2D. **Methods:** Cross-sectional study. We included 50 patients with T2D. **Results:** Of all patients, 50% were female. The median age was 15.3 ± 2.3 years. Diabetic neuropathy frequency was 50%. We found that in 42% of patients motor nerve conduction velocity was altered, and was abolished in 8%. The sensory nerve conduction velocitywas altered in 20% and abolished in 2%. The factor associated with the development of neuropathy in adolescents with T2D were HbA1c (OR = 1.6 95% CI 1.1–2.3). **Conclusions:** The frequency of diabetic neuropathy in adolescents with T2D was 50%. Poor glycemic control is associated with the presence of diabetic neuropathy in adolescents with T2D.

111

Lipid Profile of Patients with Down Syndrome with Overweight or Obesity

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Introduction: Overweight is common in patients with Down syndrome (DS). Death from cardiovascular disease is not common in these patients. Information about lipid profile (LP) of patients with DS and body mass index (BMI) compatible with overweight (OW) or obesity (OB) is limited. **Aim:** To evaluate the LP of DS patients who have more than 2years(y) with OW or OB. **Methods:** Review of data from patients with DS over 2y. Were analyzed: sex, chronological age (CA), total cholesterol (TC), HDL-cholesterol, LDL-cholesterol, triglycerides (TG) of patients with OW and OB (WHO, 2007). Values were compared with reference values (t test). Patients were divided into major and minor 19anos. **Results:** 49 patients were assessed, 25 male. The mean CA was 12.26y. OW or OB was found in 30 patients (61.22%). 43 patients were under 19y, in 24/43 BMI was OW or OB. All patients older than 19y were with OW or OB. The LP abnormal / elevated in these patients was TC (p <0.05) and HDL (p <0.5). The values of LDL and TG levels were below the reference values (p <0.05).

Conclusion: The LP in DS patients with OW or OB did not indicate cardiovascular risk. The elevation of HDL in these patients could be a protective factor.

112

Lipid Profile and Pro-inflammatory Molecules in Overweight Children

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Childhood overweight is associated with overweight / obesity in adulthood and increases the risk of cardiovascular disease and type 2 diabetes. The aim of this work was to study the lipid profile and inflammation markers in a children population with overweight. Fifty overweight children who were attended at Endocrinology Service of a pediatric hospital, aged 8–12 years and 20 children with normal weight, were studied. Waist circumference (WC) and BMI (considered overweight BMI> 85th and <95th percentile for age and sex) were measured. In both groups was determined: lipid profile (total cholesterol, HDL-C, LDL-C, triglycerides, nHDL-C and Tg / HDL-C ratio), soluble E-selectin (sE-S), TNF-α, fibrinogen (Fg), high sesitivity C-reactive protein (hsCRP) and HOMA index was calculated. Data were expressed as median and interquartile range, using the Spearman coefficient for correlations between variables. Overweight subjects showed higher levels of Tg [102 (73–140) vs. 69 (61–84) mg / ml, p = 0.01] and Tg / HDL-C ratio [2.6 (1.8–4.8) vs. 1.6 (1.4 to 2.0), p = 0.001] than control group. sE-S, TNF-α, Fg, hs, CRP, insulin and HOMA values were also significantly higher in overweight group than controls. Elevated levels of Tg, Tg / HDL-C ratio, and molecules markers of a low-grade inflammatory state, suggesting an increased atherogenic risk in overweight children.

113

Predictors of Microalbuminuria in Pediatric Patients with Type 1 Diabetes Mellitus

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Nephropathy constitutes the most serious type 1 diabetes mellitus` (T1DM) complication being microalbuminuria the initial manifestation. **Objective:** To determine the role of epidemiological, clinical and biochemical factors in the development of microalbuminuria in T1DM patients. **Design:** Case and control study. **Patients:** Type 1 diabetic mellitus patients of age less than 18 years. **Intervention:** 64 T1DM patients where studied. 22 patients with microalbuminuria were the cases and 42 patients without it were the controls. Data was recorded based on epidemiological factors: age at diagnosis, time from oonset, gender, family history of diabetes, nephropathy, dyslipidemia, and/or hypertension. Clinical factors: nutritional status, pubertal stage and blood pressure. Biochemical factors: HbA1C, microalbuminuria and lipid profile. Both cases and controls were followed for one year. Statistical analysis was carried out with chi square, odds ratio and multiple logistic regression calculations. **Results:** The risk factors were high diastolic blood pressure (p=0.037), puberty (p=0.008), high HbA1C (p<0.0001), hypertriglyceridemia (p=0.007) and hypercholesterolemia (p<0.0001). **Conclusions:** The elevated HbA1c, hypercholesterolemia and puberty were the more important risk factors for the development of microalbuminuria. The main measures to prevent the development of microalbuminuria were good metabolic control and good management of dyslipidemia, especially in puberty.

114

Relationship between Metabolic Syndrome Components, Adipokines and Insulin Resistance in Obese Hildren

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Background: Several hormones and adipokines have been implicated as promoters of Insulin resistance (IR) either as protectors. **Objective:** Determine whether there was correlation between adipokines with metabolic syndrome (MS) components and IR. **Population and Methods:** 133 obese children with Body Mass Index (BMI) = 2 SDS. MS was defined according to IDF criteria and blood glucose level at minute 120. HOMA = 3 defined IR. Adiponectin, leptin, ghrelin were analysed. **Results:** Mean age 10.28 ± 2.32 years, 56% male and 47% pubertal with no differences in BMI by sex and pubertal stage. MS was diagnosed in 6 patients and IR in 32%. Correlations: R values in brackets Adiponectin: with BMI (–0.262), waist circumference (WC) (–0.193), systolic pressure (SP) (–0.275), diastolic pressure (DP): (–0.186), HDL-c (0.354), triglycerides (–0.236), insulin (–0.291) and HOMA (–0.291). Leptin:

with BMI (0.476), WC (0.374), triglycerides (0.212), insulin (0.368) and HOMA (0.362). Ghrelin: with BMI (–0.194), WC (–0.217), SP (–0.286), glucose (–0.172), HDL-c (0.206), triglycerides (–0.202), insulin (–0.361), HOMA (–0.378). HOMA with BMI (0.392), WC (0.389), triglycerides (0.377), glucose 120'(0.244). All correlations were statistically significant ($p < 0.05$). **Conclusions:** 1) Adiponectin correlated negatively with the main criteria of metabolic syndrome and HOMA 2) The HOMA index correlated positively with waist circumference.

115

Type 1 Diabetes Mellitus Therapy with Mesenchymal Stem Cells

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Introduction: The reversion of type 1 diabetes is the aim of different therapies. We have tried the infusion of mesenchymal stem cell to stop the immune reaction against B pancreatic cell. **Methods:** Four type 1 diabetic patients with less than 6 weeks of diagnosis, with no ketoacidosis and no other disease, have recieved 8 stem cell infusions. The initial clinical response and adverse efects are reported. **Results:** One boy and 3 girls with ages between 12 and 13 years have recieved 8 infusions of mesenchymal stem cell each one. Low fever and flu like symptons occurred. **Conclusion:** Initial report show to be safe the mesenchymal stem cell infusion to type 1 diabetic patients with good metabolic response.

116

Tryglicerides/HDL Index is a Likely Insulin-resistance Marker in Children and Adolescents

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Reference methods for quantifying insulin resistance (IR) are complex in healthcare activities or research with large number of subjects and subrogated indexes are used HOMA-IR (HI), QUICKI (QI). **Objective:** Determine if triglycerides/HDL ratio (TG/HDL-c) values in a simple and specific way IR in children and adolescents compared with HI, QI and blood insulin (I), leptin (L) and adiponectin (Ad). **Methods:** 125 children (Age: 14.1+4.7 ys) by BMI (overweight Pe >85 <95, obesity: Pe≥95), waist circumference (WC: central obesity Pe>95), determinations blood glucose, lipids, I (RV < 15 uU/mL), L (RV 1–15 ng/mL) and Ad (RV 5–30 ng/mL), were studied. HI (RV<2.4), QI (RV>0.33) and TG/HDL-c (RV<2.3) were calculated. Statistical analysis: summary measures and CI95%, Student's and Fisher's tests (program SPSS 15). Significance level: 5%. **Results:** There was significant for I, HI, QI, L and Ad ($p<0.01$). 70% with TG/HDL-c>2.3 had I>15 uU/ml ($p < 0.01$), 60% HI>2.4 ($p < 0.01$), 71% QI<0.33 ($p<0.01$), 58% high L ($p=0.04$) and 60% low Ad ($p=0.09$). Considering central obesity by WC: 52% of subjects had TG/HDL-c>2.3 ($p=0.07$), 52% HI>2.4 ($p=0.32$) and 52% QI <0.33 ($p=0.2$). TG/HDL-c not correlated with age, Glucose or BMI, was on the limit of significance with WC ($r=0.16$, $p=0.056$) and was significant with I ($r=0.4$, $p<0.01$), HI ($r=0.4$, $p<0.01$), QI ($r=0.36$ $p<0.01$), L ($r=0.4$ $p<0.01$) and Ad ($r= – 0.4$ $p<0.01$). TG/HDL-c sensitivity and specificity with: HI were 60% and 78%, QI 59% and 79% and I 70% and 74%, respectively. **Conclusion:** TG/HDL-c is a simple, reliable and economic index for evaluating IR in children and adolescents, with moderate sensitivity and good specificity. It is validated by comparison with HI, QI, I, L and Ad, less intensely. It also shows the activity of insulin on fats metabolism without the own insulin analysis.

117

Specialized Nutritional Interference in the Treatment of Patients with Type 1 Diabetes at the Tertiary Level

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Introduction: The treatment of children and adolescents with type 1 diabetes is based on the triad of diet, physical activity and proper insulin administration. Generally, in our service, the first guidelines are provided by doctors, but in subsequent returns we have observed that they also requires education by a nutritionist and trainer. **Objective:** To observe specialized nutritional interference on glucose control. **Method:** After an initial period of follow-up, 42 patients were systematically referred to the dietitian and received individualized guidance. Anthropometric and glucose control parameters were obtained at the beginning, at 3 and 6 months. Data were

Table 1. (for Abstract 117)

Time	Glucose mg/dL fasting	Post prandial	Frutosamine Mmol/L	HbAlc %
Initial data	190.5±101.8	277.0±157.9	441.6±106.0	9.4±22
3 month	175.6±114.0	191.9±111.8	415±11.2	9.0±2.4
6 month	195.0+89.7	223.3+168.0	414.3+105.4	9.2+2.6
ANOVA	0.116	0.318	0.974	0.874

analyzed by ANOVA. **Results:** 24 patients were females, between 4 and 20 years (median: 12), and 18 were males between 4 and 17 years (median: 11).The next table represents glucose control parameters obtained. **Discussion:** Despite the attention given to nutritional education provided by the specialist we did not find any improvement on glucose control parameters, suggesting the need for interference in other aspects of treatment.

118

Hyperinsulinemic Hypoglycemia: Experience in a Pediatric Population

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Background: Hyperinsulinemic hypoglycemia (HH) is the main cause of persistent and recurrent hypoglycemia during infancy. Diagnosis is based on hypoglycemia and detected levels of insulin. Ketonemia and fatty acids are negatives. Recommended drugs are diazoxide, octreotide and glucagon, however diazoxide is not standardized in our country. Pancreatectomy is often required. **Objective:** To describe clinical and treatment features of children with HH followed in our department from 1992 to 2011. **Population and Methods:** All patients diagnosed with HH were included in our study. The following data from medical records were extracted: gender, perinatal data, age at first hypoglycemia and diagnosis, laboratory findings, response to drug treatment and performing pancreatectomy. MedCalc program 12.3.0 was used. Data were analyzed with Pearson test. **Results:** A total of 21 patients were analyzed. Twelve were female, 17 were born in term and 13 by cesarean section, with an average weight of 3363 g (±970.5) and length 49.5 cm (±2.89) at birth. First episodes of hypoglycemia occurred approximately at 3 months-age, ranging from the first day of life (29%) up to 3 years old. Median (med) age at diagnosis was 8 months, but 33% occurred after the first year. Laboratory findings at diagnosis varied as follows: glucose from 5 to 47 (med 36.5) mg/dL; insulin from 2.5 to 112 (med 12.4) mcU/mL; mean VIG value was 7.4 (±0.52) mg/kg/min; ammonia, uric acid and lactate were normal. In diagnosis, 5 patients were treated with rhGH, 8 with glucocorticoid, 5 with octreotide and 20 with diazoxide (mean dose 11.7 mg/kg/day [±5.6]). During maintenance therapy, the dose of diazoxide was 7.4 mg/kg/day (±6.2). Pancreatectomy was necessary in 4 patients, due to response failure in clinical treatment. **Conclusions:** HH is a severe disease with high neurological morbidity that depends on the time of diagnosis and initial treatment. Early access to oral diazoxide is essential for a better prognosis.

119

Rare Case of Inborn Error of Metabolism: Hyperinsulinism Hyperammonemia Syndrome (S.HI / HA)

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The S.HI / HA is the second most common syndrome of congenital hyperinsulinism. Described missense mutations, most GLUD1 novo gene (10q23.3) encoding the glutamate Deshidrogenasa1 (GLUD1) of the mitochondrial matrix with gain of function. They have recurrent symptomatic hypoglycemia secondary to hyperinsulinemia, in several cases well controlled with diazoxide, generalized seizures, absences, even without hypoglycemia. **Case Report:** Girl of 9 months with tonic clonic seizures, neurodevelopmental delay, hypoglycemia (glucometria: 10 mg/dl), not associated with fever or other triggers, requiring high metabolic flux. Analytical determinations in the presence of hypoglycaemia and lactic acid, pyruvic, growth hormone, cortisol, ketones, amino acids in blood and urine normal, except for the presence of Hyperinsulinism and Hyperammonemia. Eco-abdominal normal. Genetic studies confirmed a unique genetic variant GLUD1 in the DNA sequence variant with unknown significance (Heterozygous GLUD1: C.1493> T), a serine was replaced by a leucine at position GLUD1 AA498 of protein, presented adequate response to diazoxide. **Conclusions:** The association of hypoglycemia and moderately elevated levels of ammonium should be suspected the existence of S.HI / HA, which should be confirmed by molecular studies. Early diagnosis is essential and appropriate management approach.

120

Complications and Associated Diseases in Children with Type 1 Diabetes Mellitus

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Background: Diabetes mellitus type 1 (DM1) is associated with numerous complications and associated diseases, which begin to develop in children and determine high morbidity and mortality. Some are related to poor metabolic control, some not. **Objective:** To determine the prevalence of complications in children with DM1. **Population and Methods:** Based on retrospective review of medical records of children suffering from DM1 assisted in the Pereira Rossell Hospital between 2000 and 2009. Complications and associated diseases were diagnosed according to international guidelines. **Results:** In the study period 185 patients were identified. The median time to disease progression was 5 years (range 0–13 years). Complications and associated diseases

Table 1. (for Abstract 120)

Complication	% affected children (n = 185)
Retinopathy	0
Nephropathy	5.5
Joint disorders	1.2
Hepatomegaly	11.7
Hepatic steatosis	5.5
Celiac disease	12.9
Hypothyroidism	30.7

are shown in the table below. **Conclusions:** The prevalence of microvascular complications was low, despite years of development of DM1. The prevalence of associated diseases is high.

121

Exercise Produce Clinical and Behavioural Improvement in Obese Adolescents with Anxious-depressive Syndrome

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Anxiety and depression are relatively frequent in obese children and adolescents, which tend to worsen the habits and causative factors of obesity and metabolic disorders. Sedentary lifestyle is a common cause of obesity related to alterations in serotonin reuptake, other chemical mediators and neuronal transmission. It has been described that exercise improves cognitive functions, behavioural, neurotransmission and stimulates the release of molecules associated with welfare. **Objective:** Assess changes in anxiety and depression in response to aerobic exercise one hour a day for three months, in obese adolescents with tendency to depression and anxiety. **Population:** 12 teenage boys obese (BMI = 31 to 39) showing clinically moderate alterations to the behavior of anxious type, as well as depressive tendencies, were valued with Hamilton Test getting a score of moderately high, between 25 and 35, characteristic of the anxious depressive syndrome. The evaluation of thyroid function was normal. Began type aerobic fitness program, one hour a day for three months, with careful control of assistance and daily stimuli, at the end of which was repeated the Hamilton test to assess possible changes in anxious depressive syndrome. **Results:** There was a modification of the score which stood between 9 and 15 at the Hamilton Test, representing a statistically significant improvement ($p < 0.001$). Everyone improved behavior showing less anxiety or depressive periods, decreased weight, BMI between 27 and 35. Also improved self-esteem and compliance with recommended diet. **Conclusion:** Aerobic exercise has a beneficial effect on obese adolescents with anxious depressive syndrome so it should be used more extensively in these patients to prevent a more severe development of the alterations, which in turn worsens the causative factors of obesity and metabolic disorders.

122

Prevalence of Overweight and Obesity and its Determinants in Children and Adolescents from a Network Private Education

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Introduction: Nowadays, in Brazil, we observed the transition from malnourish to increasing prevalence of obesity, probably related to socioeconomic and behavioral aspects. **Objective:** To determine the prevalence of overweight and obesity in children and adolescents from a network private school. **Method:** In the last year, 48.390 subjects were registered as students at the city of Uberaba, being 7.258 in 29 private schools (15%) of which we calculated a proper sample of 164 students randomly selected. Anthropometrics, demographics, socioeconomic, and lifestyle data were obtained from the subjects between 6 and 17 years. Data were analyzed by Pearson or Spearman correlation tests; $p<0.05$ was considered significant. **Results:** We evaluated 87 females and 77 males and found 7 malnourished subjects (3.2%), 99 had adequate weight (45.8%), 12 were overweighted (5.6%) and 46 had obesity (21.3%). Significant, positive correlations between nutritional status and hours of sedentary activity ($p<0.046$), economic status ($p<0.021$) were observed. **Discussion:** The increase in purchasing power as a result of economic stability in Brazil provides access to media activities and food. Young people became sedentary and assumed unhealthful dietary habits, resulting in obesity that at a long term may outcome in diabetes, hypertension, and others comorbidities.

123

Diabetic Ketoacidosis in Children Less than 15 Years

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The increasing of the knowledge and technological development should reduce theincidence of diabetic alterations however is still frequent cause of hospitalization. **Objective:** To determine the fre-

cuency, causes, historical behavior, relationship with age, sex of the diabetic ketoacidosis in children less than 15 years old. **Population and Methods:** It was elaborated an observational investigation, retrospective in a cohort of subjects with clinical debut of Diabetes Mellitus type 1 before 15 years old since January 1980 to December 2010. **Results:** 206 children, no difference between sex, 51% of all the patients initiated with diabetic ketoacidosis and 28% with severe presentation, it was more frequent in girls p 0.01 and less age 7.43 years p 0.00. Diabetic ketoacidosis as a debut decreased since 63% during the years 80th until 42% during the decade 2000. The total episodes shows tendency to drecease and since the beginning of 1977 there is notable reduction of the diabetic ketoacidosis recurrence in relationship to the previous years p 0.00. Diabetic ketoacidosis is a clinical presentation of diabetes mellitus, it is more frequent in females and small children showing tendency to decrease. Diabetic ketoacidosis recurrence may be avoided.

124

Psychological Characterization of Diabetic Scholars Type 1 through their Graph Representations

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Diabetes Mellitus type 1 affecting not only physical health but also its psychological and social function so its multidisciplinary focus is imposed. **Objective:** To characterize psychologically to the scholars type 1 through their graph. **Population and Methods:** The sample 30 scholars with Diabetes Mellitus type 1 observed through their drawing spontaneous and thematic about their family and I am equal different to my friends. The results of their drawing constitute a way of espression and reflect attention in the emotional sphere, obsession, anxiety, difficulty in the communication and physical contact with friends and family. They are feeling hyper watched, controllable and monitory. **Conclusions:** Difficulties in the capacity of resilience. The presence of social groups are constructing strength but they are not becoming in factors of protection because they do not evolve positive factors in the control of the disease, they restrain them. We suggest to the medical personnel and family to teach the increasing of the attitude through the development of adequate self esteem, the family support.

125

Epidemiological Evaluation of Patients with Diabetes Mellitus followed in a Pediatric Endocrinology Reference Service

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The most common form of Diabetes Mellitus (DM) in childhood is DM1. Etiology is multifactorial and autoimmune markers are present in 85–90%. Other autoimmune diseases such as Celiac Disease (CD) and Hashimoto's Thyroiditis (HT) are more prevalent. **Objective:** To analyze the epidemiological profile of diabetic patients followed in a reference service of Pediatric Endocrinology. **Patients and Methods:** Retrospective, observational and descriptive study of 192 patients seen during 1 year, included by convenience. Age at diagnosis, sex, type of diabetes, associated diseases, determination of anti-GAD, anti-insulin (AI) and anti-islet cell (ICA) antibodies were evaluated. **Results:** 56.2% of patients were females, mean age at diagnosis was 6.9 years (0.8–14.4 years). Diagnoses were: DM1 (184), indeterminate (3), MODY (2), secondary to cystic fibrosis (2) and DM2 (1). Associated diseases were: hypothyroidism [HT (13), other forms of hypothyroidism (4), congenital hypothyroidism (1)], asthma (6), CD (4), Fanconi's Anemia (4) and Turner Syndrome (1). ICA was positive in 11/39, AI in 6/32 and anti-GAD in 25/42. **Conclusions:** Age at diagnosis was similar to that reported in the literature; female sex was slightly predominant; positive antibodies rate was lower than expected; and the most prevalent associated disease was HT.

126

Clinical Variability in Three Patients with Suspected Short Chain Acyl Coenzyme a Dehydrogenase Deficiency

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Background: Short Chain Acyl Coenzyme A Dehydrogenase Deficiency (SCADD) is a disorder of fatty acid metabolism, which generates accumulation of C4 in blood and Ethylmalonic Acid, Butyrate and Butirilglicina in urine. The aim of this paper is to present three patients in whom this diagnosis was made, its clinical features and laboratory studies, as an example of its wide clinical variability. **Population and / or Methods:** This is a series of cases whose characteristics are shown in Table 1. **Results:** The clinical and laboratory findings are suggestive of SCADD. Only in patient

3 the *ACADS* sequencing was possible and the patient was reported as double homozygote (c.280G> A and c.625G> A in both alleles), this changes had been reported in both symptomatic and asymptomatic patients, therefore its significance is uncertain. Although the three patients are treated with dietary management only patient 3 is asymptomatic. **Conclusions:** Based on what was observed in these patients, we believe that elevated blood C4 should be considered as an alarm data that needs to be confirmed by testing enzymatic activity and gene sequencing to help explain a phenotype-genotype relationship.

127

Perinatal Factors Related to Metabolic Syndrome Risk in Pediatric Obese Patients Living in Mexico City

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Introduction: Obesity is highly prevalent in Mexican children. Metabolic syndrome (MS) prevalence in our pediatric obese population is up to 50% owing to elevated risk of diabetes mellitus and cardiovascular disease during early adulthood. **Aim:** To evaluate perinatal variables related to high risk of metabolic syndrome during childhood. **Patients and Methods:** Obese pediatric patients were recruited from the Pediatric Obesity Clinic at the General Hospital of Mexico (ages 2–17). Perinatal variables, such as Family history, pregnancy characteristics and outcome, as well as eating behaviors during the first year of life were analyzed. **Results:** 279 patients were included for analysis and 58.4% were diagnosed with MS. Bivariated and logistic regression model analysis showed that BMI, having a 1st degree relative with diabetes (1stDM), as well as had been early introduced to solid foods (EISF <6 months) were significantly associated to metabolic syndrome (p=0.001). While analyzing the interaction of both variables (1stDM and EISF) the probability of being diagnosed with MS increased up to 68%. **Conclusion:** Epidemic control of obesity must be mainly addressed to preventive strategies. Early solid food introduction seems to be a potential modifiable risk factor in our population.

128

Behavior of the Fatty Liver not Alcoholic (HGNA), in Children and Adolescent Overweight and Obese

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Background: The obesity is a syndrome nutritional multifactor, its prevail in children and adolescents he/she goes in increase. This brings I get several complications that appear from the pediatric age, one of them it is not the illness of Fatty Liver Alcoholic (HGNA). **Objectives:** To determine the frequency of presentation of the fatty liver not alcoholic (HGNA) in children and adolescents with overweight and obese and their association with biochemical variables. **Hypotheses:** The liver fatty non alcoholic is a frequent affection in children and adolescents with overweight and obese. **Methods:** He/she was carried out a prospective descriptive study in an universe of 138 children overweight and obese among 6–19 years that went to Consultation of Pediatrics in the Service of Urgency, during the period of April to October of the year 2011; the sample constituted 39 patients that were diagnosed a HGNA through the realization of the abdominal ultrasound. Age, sex, type of obesity was determined by the calculation of the IMC; severity of of liver steatosis and the total cholesterol studies, triglycerides, blood glucose, hepatic function (TGP); the data were processed by means of the statistical system of SPSS for Windows. **Results:** The frequency of HGNA was of 28.26%, with prevalence of the HGNA slight 69.23%, and in connection with the severity of the obesity the patients that presented moderate obesity (64.10%) HGNA presented and as for the relationship for age group the adolescents were represented in 58.97%, without variation in the sex. The alterations of triglycerides and cholesterol (biochemical variables) they prevailed in 58.97% and 20.51%, respectively. **Conclusions:** The HGNA was a frequent chronic affectation in children and adolescents with overweight and obese, associated to biochemical alterations of triglycerides and increased cholesterol. **Key Words:** Fatty liver not alcoholic, children, adolescents, overweight and obese.

129

Acquired Generalized Lipodystrophy (AGL) Associated with Thyroiditis and Autoimmune Hepatitis. Case Report

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Lipodystrophies are heterogeneous; genetic or acquired disorders characterized by selective loss of body fat and insulin resistance. We report a 15 years old girl, with family history of autoimmune diseases. At age 2, mother notices loss of fat mass in buttocks. At 9 physical exam showed decreased fat mass in lower limbs, plus an abnormal lipid and thyroid profile, therefore she was referred to our unit. At first evaluation she had normal leptin levels, negative mutations for inherited lipodystrophies and hypertriglyceridemia. Thyroid ultrasound showed a multinodular goiter secondary to Hashimoto thyroiditis (TSH11.3 uUI/ml anti thyroid antibodies positive). She was started on diet with higher protein and low carbohydrates, and levothyroxine. At 12, an abdominal ultrasound showed fat liver infiltration associated with hypertransaminasemia and normal prothrombin, being diagnosed as autoimmune hepatitis. At age 14, she showed a progression of fat loss to arms, legs and trunk, severe acne, acanthosis nigricans, oligomenorrhea and insulin resistance. Associated with progressive increase of hypertransaminasemia thus she was started on steroids (budesonide9 mg/day) plus Metformin (2000 mg/day). AGL is a rare entity, but involves many other autoimmune diseases. An early suspicious of this patients may help in search of the concomitant diseases and prevent serious complications.

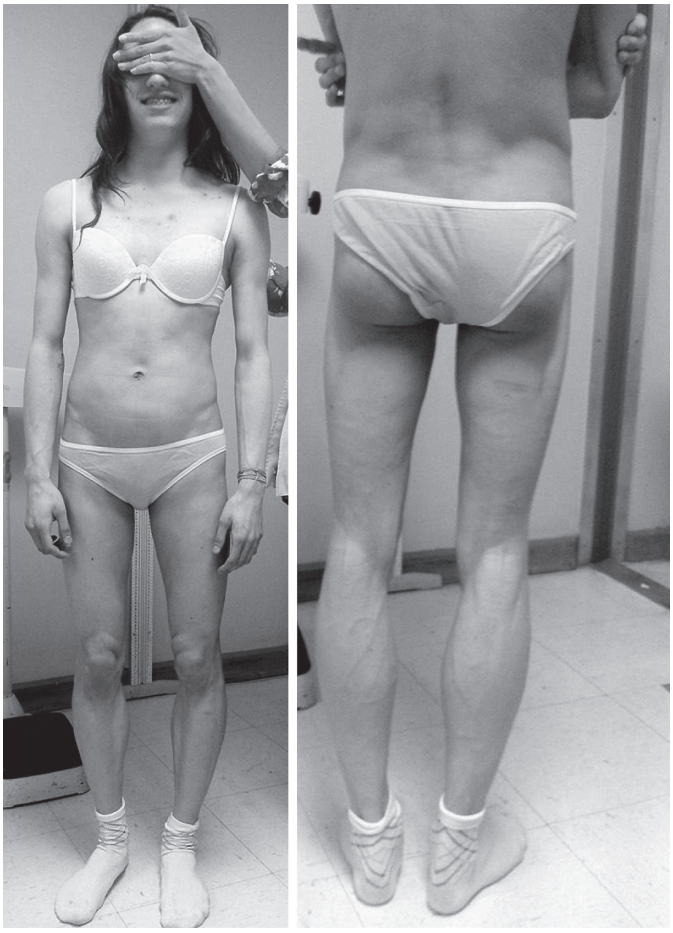

Fig. 1. (for Abstract 129).

130

Cardiovascular Risks Factors in Preschoolers at a Health Provider Institution

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Background: The presence of overweight and obesity in children increases the likelihood of presentation in adulthood with a direct association with the occurrence of cardiovascular risk. There have been identified environmental risk factors associated with the presence of overweight and obesity and the onset of metabolic and cardiovascular diseases in an increasingly early age. **Objectives:** Establish the prevalence of overweight, obesity and other known risk factors for cardiovascular and metabolic disease in preschoolers outpatients. **Materials and Methods:** This was a cross-sectional observational study, 328 patients were taken. Statistical associations was determine using chi2, Fisher, OR and confidence intervals. **Results:** The prevalence of overweight and obesity was 19.2%, 17% were breastfed for less than 4 months, 33.2% had an excessive calorie intake, only 5.9% reported suitable consumption of fruits and vegetables, 50.3% do sedentary activities. There was an association between breastfeeding <4 months and the presence of overweight and obesity OR = 2.4 p = 0.05 (CI 1.2–5.0). **Conclusions:** Breastfeeding for less than 4 months showed a significant association with the presence of overweight and obesity, so the needs of increasing longer breastfeeding time for reduce early onset of overweight and obesity it is a matter of public health.

131

More Clinical Manifestations in Adolescents with Metabolic Syndrome and Benefit of an Insulinosensitizer

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The description of alterations that are part of the metabolic syndrome are on the rise. Hypertriglyceridemia, abdominal obesity and insulinoresistencia are closely related in teens, occurring at

the same time further alterations with potential risks of which we have seen acrocordones in neck and armpits, Seborrheic Keratosis, and smell of stale grease scalp, that are not usually described in children and adolescents. Insulinosensitizers type glitazonas are useful in adults but there is little information on adolescents. **Objective:** Study the Association of hypertriglyceridemia with cervical acrocordones, Seborrheic Keratosis, and smell of stale grease in scalp and abdominal obesity in adolescents and its response to pioglitazone. **Population:** 11 male and 7 female adolescents between 15 and 19 years of age, with abdominal obesity: PC between 114 and 130 cm in males and between 97 and 110 cm in women with hypertriglyceridemia, cervical acrocordones, Seborrhea, acne, Seborrheic Keratosis, pruritus and grease smell stale on scalp, hair loss, glycemia in altered fasting or oral glucose intolerance. They were treated for 3 months with pioglitazone 50 mg day, diet-restricted sweets and alcohol, higher consumption of fish and 1 hour daily of aerobic physical activity program, including abdominal exercises. **Results:** Decreased abdominal fat men PC arriving between 110 and 125 cm and women between 95 and 105 cm. Normalized triglycerides, glucose, improved Seborrhea, acne, pruritus, Seborrheic Keratosis and stale odor on scalp. Acrocordones no more increased. **Conclusion:** Abdominal obesity is related with Seborrheic Keratosis, hypertriglyceridemia, and rancid odor in scalp in adolescents, alterations that improve with diet, exercise, and use of an insulinosensibilizador, which points to that the hyperinsulinism is the common pathophysiological mechanism.

132

Growth and Puberty in Children and Adolescents with Type 1 Diabetes Mellitus

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Inadequate treatment of Type 1 Diabetes mellitus (T1DM) may impair linear growth and sexual maturation of children and adolescents. The metabolic control in order to minimize the appearance of chronic complications and ensure normal growth with quality of life is the main goal of treatment. **Aims:** To evaluate growth and puberty in children and adolescents with T1DM. **Methods:** Ambispective study of 41 patients with T1DM, chronological age (CA) 4 to 18 years. **Results:** Twenty one patients (14 girls) were pubertal; insulin dose did not differ between pubertal and prepubertal, 83% had HbA1C>7.5%, BMI was normal in most cases, height Z score (HZS) at diagnosis (–0.01) was higher than the target height (TH,-0.31) while the current (–0.21) did not differ from TH, bone age (BA) and CA were concordant in 59%, 35% of girls and 6% of boys had BA>CA, 62% had predicted final height (PFH)≈TH, no association was found between PFH and HbA1C. IGF-I below the mean was observed in 26/37 patients, but without correlation with HZS and HbA1C. **Conclusion:** In this population, HZS and PFH did not differed from TH; HbA1C≤7.5% had no effect on growth and puberty, which were normal.

133

Mauriac's Syndrome – an Important Cause of Hepatomegaly and Transaminases Elevation in the Patient with Type 1 Diabetes Mellitus

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Universidade Federal do Triângulo Mineiro | (*) Brasil

Background: Mauriac's syndrome occurs in individuals with type 1 diabetes mellitus (T1DM) and poor long-term glycemic control, and includes hepatomegaly by glycogen loading (glycogenic hepatopathy-GH), transaminase elevation, growth retardation, delayed puberty, cushingoid features and hypercholesterolemia. **Objective:** To report an adolescent with Mauriac's syndrome. **Methods:** Review of patient records and literature. **Results:** FAA, 12 years old, T1DM diagnosed 2 years ago, Weight: 39.4 kg (SD: –0.3), Height: 153 cm (SD: +0.3), Tanner M2P3 since 2 years ago, poor glycemic control (HbA1c: 16%), hepatomegaly and cushingoid features. Biochemical testing: TGO: 107.3 U/L, TGP: 84.5 U/L, cholesterol: 282.1 mg/dL, LDLc: 183.7 mg/dL, HDLc: 58.0 mg/dL, VLDLc: 40.4 mg/dL, Triglycerides: 202 mg/dL. Liver biopsy showed cytoplasmic glycogen deposits, without fibrosis, steatosis or inflammation. **Conclusions:** As features of Mauriac's syndrome the patient had hepatomegaly, pubertal delay, cushingoid features, elevated liver enzymes, hypercholesterolemia, and liver histology compatible with GH. The differential with non-alcoholic fatty liver disease was achieved histologically by liver biopsy. Pathophysiologically, in persistently hyperglycemic patients with T1DM, insulinization results in conversion of glucose to glycogen in hepatocytes, causing hepatomegaly that resolve with proper treatment.

134

Factors of Risks Associated to the Overweight and Obese in Children and Adolescents

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Background: The obesity is considered an epidemic at the moment in increase to world scale, this phenomenon affects children and adolescents and he/she associates with the precocious appearance of other chronic affections. **Objectives:** To determine the factors associated to the overweight and the obesity in children and adolescents assisted in the Consultation of Pediatrics of the Service of Urgencies. **Hypotheses:** The precocious weaning, the family antecedents of obesity, the alimentary behavior not appropriate and the sedentary is factors of risk of infantile obesity. **Methods:** it was carried out a descriptive study, among April and October of 2011, that a sample of 138 children and adolescents that went to the Consultation of Pediatrics of the Service of Urgency. The study variables were: age, sex, weight, carves, index of corporal surface, arterial tension, personal and family antecedents of obesity, diabetes mellitus and arterial hypertension, weight when being born, time of maternal nursing and I begin of the ablactating and the consumption of such foods as: fruits, vegetables and fried foods and of little nutritional value and the physical or sedentary activity realization. The data were processed by means of the statistical system of SPSS for Windows. **Results:** The obese one was represented in 63.76% with prevalence in the masculine sex (34.05%), the feminine one was reflected in 29.71%. The overweight behaved in 36.23%, without variation in the sex, in it relates with the age the group it prevailed 5–9 years with 52.89%, followed by the 10–14 year-old group with 29.71%. The bronchial asthma the personal antecedent that was presented with more frequency in these patients with 21.73% for both groups was (RR 0.981404959). The family antecedent of obesity, diabetes mellitus (RR 9.090909091) and the arterial hypertension were present with frequencies for both groups, the same as the normal weight when being born, with 60% in the overweight and the 61.36 in the obese one. The weaning before the six months of life was of 84% in the overweight and 79.54% in the obese one and the ablactating behaved respectively in 78% and 76.13%. In cases with overweight 54% consumed fruits and vegetables and 100% of foods of poor nutritional value and with 98% of consuming fried foods; in connection with the obese ones they didn't consume fruits and vegetables 60.22% (RR 1.309288538) , 98.86% of foods of poor nutritional value and 92.04% fried foods. In connection with the physical activities it was significant the non realization for both groups in with 94% and 100% respectively, and 100% in both groups makes sedentary activities. **Conclusions:** The obesity prevailed, genetic factors of this family illness existed, they presented weaning and precocious beginning of ablactating and the studied group not presented an alimentary behavior appropriate and a level of null physical activity. **Key Words:** Obesity, overweight, children, adolescents, feeding, physical activity.

135

Epidemiological Description of Children with Type 1 Diabetes Mellitus Assisted in the Hospital Pereira Rossell between 2000 and 2009

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Background: Diabetes mellitus type 1 (DM1) is the most common chronic endocrine disease in childhood. It has been an increased incidence and decreased age of debut. Have been identified perinatal risk factors, racial differences and stressors before the debut. **Objective:** Determine the epidemiological characteristics of children with DM 1 assisted in the HPR. **Population and Methods:** A retrospective study through the analysis of medical records of patients with DM1 assisted in the HPR between 2000 and 2009. **Numerical Analysis Results: Conclusions:** In the period studied DM1 was not a highly prevalent disease. We did not identify a decrease in age of debut, difference by sex or perinatal risk factors. Most patients debuted in CAD. In a significant percentage stressors were identified prior to the debut.

Table 1. (for Abstract 135)

N = 185	
Sexo Femenino (%)	52
Edad de debut (años) Rango; Media, Mediana	1–14, 7.4; 8
Razablanca (%)	96
Debut Cetoacidosis (%)	72
Debut Hiperglicemia (%)	20
Síndrome diabético precoz (%)	34
Antecedentes Familiares Diabetes (%)	6.7
Madre > 35 años (%)	8.6
Pretérmino (%)	8.6
Preclampsia (%)	4.3
Bajopeso alnacer (%)	4.3
Infecciones previo al debut (%)	17.2
Vacunaciones previas al debut (%)	55.8

136

Hypoketotic Hypoglycemia: Case Report of Methylglutharic Aciduria

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Objective: To report a case of methylglutharic aciduria and review the causes of hypoglycemia in infants **Methods:** 18 mo. patient. Referred for an episode of hypotonia, ocular version and clonic movements of left arm with post-ictal period of 20 minutes concurrently with blood glucose of 11 mg/dl Hypoglycemic events started at 4 mo. Patient admitted to ICU for pneumonia and respiratory failure. Physical findings were normal except for midfacial hypoplasia. **Results:** Metabolic acidosis (HCO3–16.9 mmol/l), with elevated anion gap(21) was found. Mild elevation of lactate (16.7mg/dl) and ammonia 198 (10–47). ACTH (30.9:0–60 pg/ml), cortisol (1031), and insulin (<2U/ml) responses where normal. Free fatty acids, and carnitin where normal. No ketones present in urine or blood. levated 3-oh-3-metilglutarico(3976 nmol/mol crea)3 oh isovalerico (2184 nmol/mol crea)y 3metilglutaconico (7688 nmol/mol crea) methyl glutaril CoA Liase deficiency. **Conclusion:** In presence of hypoketotic hypoglycemia, the primary causes to consider should be: beta oxidation disorders, hyperinsulinism and methylglutharic aciduria. Precise diagnosis is imperative to initiate specific treatment.

137

Diabetes Mellitus Type 1: Implications of a Chronic Disease on Children's Quality of Life

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Background: Diabetes mellitus type 1 (DM1) is the second chronic disease of childhood. The treatment required and the high prevalence of complications and associated diseases determine a large impact on quality of life of the child **Objective:** Describe the impact on children's quality of life suffering from DM1 Pereira Rossell Hospital beneficiaries (HPR). **Population and Methods:** Retrospective study based on chart review of children suffering from DM1 who attended the HPR between 2000 and 2009. **Results:** In the time period 185 children were identified. The time evolution of their disease ranged between 1 and 13 years. School delay was identified in 21.5%. The same percentage showed psychiatric illness. These patients showed a mean of 5.6 hospitalizations (range 0–18), an average of 3.5 episodes of ketoacidosis (range 0–13) and a mean income of 3.3 intensive care unit (range 0–4). **Conclusions:** Children suffering from DM1 were greatly affected their quality of life, with consequences that can leave permanent sequelae. Intensive treatment is necessary to mitigate these results.

138

Obesity and Dyslipidemia in Children

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Background: Obesity is the most prevalent chronic disease at childhood, it is considered a world wide public health problem and has become the XXI century epidemic. **Objectives:** To determine the prevalence of dyslipidemia in obese children; also to describe the clinic and epidemiologic characrteristics of the patients included, kind of dyslipidemia and non alcoholic fatty liver disease associated, and evaluate the adherence to treatment. **Methods:** Descriptive, retrospective study from 2008 to 2010. Results were expressed as percents, CI 95%. We used the x2 test. **Results:** From 120 patients, 69 presented regular obesity (57.5%) and 51 severe obesity (42.5%). A total of 73% had dyslipidemia (high total cholesterol 17%, high LDL cholesterol 16%, low HDL cholesterol 51% and high tryglicerides 42%). 3 patients a had non alcoholic fatty liver disease. 30% continued clinic contols a year after. None of the patients achieved a normal weight. **Conclusions:** The prevalence of dyslipidemias un our obese children is high, we could not find an association between kind of obesity and kind of dyslipemia. Adherence to obesity`s treatment was low. Prevention is very important, promoting a healthy life style includes chidren and their families.

139

Education Program for Children and Adolescents with Diabetes

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Background: The education program, implemented in the Diabetes Unit, reflects the importance of transdisciplinary work when dealing with patients with diabetes and their families. This process started in 2008, and it has been implemented since January 2011. This practice has clearly shown the need to review the sequencing, the didactic transposition of the contents and the search of dissemination of information through different media, such as the one provided by *Plan Ceibal*, which enables universal access to the ICTs (Information and Communication Technologies). Evaluation and studies on the impact on quality of life are still pending. The team's dedication and professional growth are essential for the treatment to be successful. **Objective:** Educate children and adolescents with diabetes, democratize access to information and achieve better treatment outcomes. **Population:** Aimed at children up to age 14 with diabetes, ASSE (State Health Services Administration) beneficiaries. Approximate total number of 100 diabetics. **Methodology:** The program is made up of 2 modules. The first provides basic knowledge and starts once the child is admitted. The second module offers

a schedule of talks that seek to provide further knowledge of the disease. **Conclusion:** We achieved better adherence and better metabolic control.

140

Clinical Humoral of Diabetic Children Characterization

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Background: Diabetes mellitus is a chonic illness that constitutes a problem of health objective describing clinical humoral characteristics in diabetic type 1 method retrospective descriptive analytic observational study of 60 diabetic patients type 1 among 1 to 18 years age the analyzed were age sex weight size nutritional state clinical presentation to the debut evolution time complications glycaemia lipids glycosylated hemoglobin microalbuminuria glomerular flitration 24 hours glycosuria results prevalence among 10–14 years in the masculine sex clinical form of more frequent presentation was the hyperglycemia in the group of 5–9 years 63.3% was eutrophic 76.6% was as more frequent complication the hypoglycemia in the patients of more evolution time 98.3% did not present alterations in the eye bottom 44.3% Had HbA1C among 8–8.5 65% presented normal figures of glycaemia and lipid 31.6% with positive microalbuminuria. **Conclusions:** Prevalence of the masculine sex among 10–14 years being debut forms (hyperglycemia/ ketosis) the most frequent relation between the bad metabolic control older evolution time and microalbuminuria the evolution of time older than 10 years was related with complications.

141

Unit of Diabetes. Pediatric General Reference Policlinica Pereira Rossell Hospital

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Background: Prior to the setting up of the child with diabetes was controlled by endocrinologist, pediatric care relegated. **Objectives:** In 2010 creates the unity of diabetes: general objective to achieve the formation of an interdisciplinary team, integrating the pediatrician with a patient´s holistic approach, giving priority to their education. **Methodology:** Created encoded file, processing data in Epi: info. On admission the child is assessed by a pediatrician, licensed nurse, nutritionist, and psychologist, in each query is educated and applied education program. Supervision is done by endocrinologist on the topic. 73 patients entered the program, 30 boys and 43 girls, mean age 10 years and 7 months, Montevideo 39.5%, 60.5% of the Interior. They debuted with ketoacidosis 56%, 24% with hyperglycemia without ketosis., And 12% hyperglycemia. On admission the mean value of glycosylated hemoglobin was 9.5%. We have significant underreporting, one of the items to improve. **Conclusions:** Integration of the interdisciplinary team doctor in the Unit, his dedication to education has been the most important achievement, the challenge is to improve the quality of records and data processing.

142

Triptorelin Acetate Allergy in Patients with Central Precocious Puberty

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Introduction: Treatment of Central Precocious Puberty (CPP) with Triptorelin acetate (TA) is widely used. TA is also indicated in adults with prostatic disease, endometriosis or uterine fibroids. Some of the adverse reactions described are headaches, weight gain, emotional lability and local reactions. Severe allergic reactions (angioneurotic edema or anaphylaxis) are described less frequently and mainly in adults. **Objective:** To describe severe allergic reactions in girls with CPP attended at the Endocrinology Unit Material and **Methods:** 8 girls who were referred between 4 and 8 years of age, because of premature puberal development. At first referral all had Tanner Stage 2 to 4, starting before 8 years of age. CPP was diagnosed based on physical exam and complementary studies. All had normal MRI, and treatment with TA was initiated. Between first and fifth dose they presented angioneurotic edema of face and neck, giant urticaria, loss of function of lower limbs, paleness, hypotension and cyanosis requiring corticoid treatment, antihistaminic and adrenaline and 1 patient required admission. Except for the first patient, all were studied at the Allergy Unit, with prick-test and intradermal skin tests for TA and dextran, diagnosing TA hypersensitivity in the 7 patients and dextran hypersensitivity in 2. **Conclusion:** During the last years, at the Endocrinology Unit we observed and increment of severe allergic reactions to triptorelin, documenting allergy to TA and Dextran. Because of this, at our Department, we observed patients who received TA during the first doses and give patients alert. We think it is important to know the real incidence of this reaction as well as define the time needed for observation.

143

Adrenocortical Carcinoma in Children by Mutation of TP53 Gen: a New Endocrinological Disease in Chile?

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Case 1: A four months old girl with an increasing of body hair, skin hyperpigmentation, cushingoid face, acne on forehead and cheeks, pubic hair Tanner III and clitoromegaly (3.6 cm) as well as high levels of androgens and hypercortisolism were found (Table 1). The CT showed a 5.3 cm solid and cystic tumor in left adrenal gland which was resected and etapified in stage I. The histological analyses showed an adrenocortical carcinoma (ACT). A positive result for TP53 R158H in the patient and her mother were found by genetic studies (hereditary germ line mutation). No relapse was notified in 18 months of follow up. **Case 2:** A 10 year old girl, with 2 months of weight gain, full moon fascie with acne and coarse hair is described. The girl showed dorsal and pubic hair (T III), breast I. BMI p98, P art 124/75 (p95–99), as well as hypercortisolism and hyperandrogenism by laboratory analises. The CT showed a solid cystic left adrenal mass of 9.1 cm presenting a capsule rupture (stage III) which was completely resected. She received QT protocol as St Jude´s 2010. After one year, she presented local recurrence. It was resected newly, received local RT and started Mitotane. TP53 (+) R175H, corresponding to a novo germline mutation, since parents are (–). **Discussion:** ACT is uncommon, with incidence 0.3 / million in children, 60% is <4 years old, and 60% female. Hyperandrogenism is present in 85% and hypercortisolism in 35% of cases, 10% are non-functioning and 75% occurs in stages I and II. Overall survival is 54% at 5 years. The best prognostic factors are stage I (90% survival), age <4 years and to have only hyperandrogenism. It should be found only 1 case / year in Chile, but since 2011 have been diagnosed 5 ACT and 3 functioning adrenal adenomas. For this reason, we studied the tumor suppressor TP53 gene, whose mutation is strongly associated with ACT. The incidence of ACT is 15 times higher, due to increased prevalence of TP53 mutation (+) R337H in southern Brazil. Both patients and the mother of the first are (+) to TP53 mutation. This exposes them to a greater risk of ACT and other tumors (leukemia, sarcoma, breast cancer and of the CNS) and thus require an oncological follow for life looking for new tumors.

Table 1. (for Abstract 143)

	Case 1	Case 2	Normal values
Free cortisol/Urine great 24 h	342	435	7–25 ug/g
ACTH	5.9	<5	10–60 pg/ml
Testosterone	814	206	<10 ng/dl
DHEA-S	17.2	4.43	0.35–4.3 ug/ml
17 OH progesterone	6.1	3.9	0.3–1.5 ng/ml
Androstenedione		>10	<3 ng/ml
Aldosterone		6.4	2.5–16 ng/dl
Plasma Renine Act		1	0.9–5.2 ng/ml/h
Urine Metanephrines	7	10	52–341 ug/24 h

144

Early BMI and Height Growth and Premature Adrenarche in 7 Years Old Chilean Children

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Background: Accelerated weight and height gain in infancy have been associated with adrenarche. However, the exact temporality of these events remains unclear. **Objective:** To assess the relationship between early body mass index (BMI) and height growth and DHEAS at 7 years. **Methods:** In 975 children (46% girls) of birth weights 2500–4500 g we abstracted weight and height 0–4y from health records and measured them annually thereafter. We calculated BMI: weight/heigth^2 and defined 5 periods of interest: prenatal, 0–6, 6–24, 24–48 and after 48 months. At 7y we measured DHEAS plasmatic concentrations. We used general lineal models to test associations, adjusting for age and sex. **Results:** BMI was over the WHO standards from birth on (0.91 BMI-SDS at 7y) while height was slightly below until 4y and increased thereafter (0.18 height-SDS at 7y). At 7y, mean DHEAS was 35.2±21.8 µg/dl; 19.7% children had ≥50 µg/dl. BMI and height at birth were inversely associated with DHEAS at 7y (Table 1). BMI gains, particularly from 2–4y, increased DHEAS levels while only height gain in the 4–7y period had a positive association (Table 1). Children with DHEAS ≥50 µg/dl compared to remaining children presented

Table 1. (for Abstract 144)

BMI				Height		
Months	β	95% CI		β	95% CI	
		Inferior	Superior		Inferior	Superior
0	–0.11	–0.2	–0.03	–0.16	–0.24	–0.07
0–6	0.03	–0.05	0.11	–0.03	–0.12	0.05
6–24	0.12	0.03	0.21	0.06	–0.03	0.14
24–48	0.19	0.1	0.27	0.15	0.04	0.25
48–84	0.05	–0.04	0.13	0.21	0.12	0.31

significantly higher BMI from 4y onwards (Dif BMI-SDS at 4y: 0.35 95% CI(0.51–0.19), p<0.05) and higher height beyond 5y (Dif height-SDS at 5y: 0.18(0.32 to 0.03), p<0.05). Analyses did not differ by sex (p>0.05) **Conclusions:** In normal birthweight children, smaller size at birth, increased weight gain before 4y, and increased linear growth after 4y were associated with higher DHEAS at 7y; in premature adrenarche increased adiposity precedes and probably leads to subsequent linear growth. Supported by Fondecyt #1100206 & 1090252.

145

Evaluation of Health Related Quality of Life of Children and Adolescents with Congenital Adrenal Hyperplasia

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Studies on health related quality of life (HRQoL) of patients with Congenital Adrenal Hyperplasia (CAH) are recent and show controversial results. **Objective:** To evaluate HRQoL of children and adolescents with CAH, on both physical and psychosocial dimensions. **Patients and Methods:** 24 patients (17 females) with CAH (14 salt-wasting and 10 simple virilizing), aged between 5 and 18 years (mean 11.5 ± 3.4 years),were evaluated, together with their guardians. Two generic instruments were used: PedsQol 4.0 for patients and CHQ answered by the guardians. Higher scores indicate better HRQoL. **Results:** There was a significant (p<0.05) decrease in HRQoL scores, both on patient's and on guardian's evaluation, when compared with healthy controls (table 1). **Conclusion:** Children and adolescents with CAH showed worse HRQoL. There is need for therapeutic strategies that consider overall health of patients with CAH, observing the effect on HRQoL of these patients.

Table 1. (for Abstract 145)

PedsQol4.0 (n)	Patients (24)	Controls (180)	p value
Physical dimension	75.6 (±15.1)	95.9 (±5.8)	0.018
Psychosocial dimension	63.9 (±18.1)	85.0 (±9.6)	0.026
CHQ (n)	**Guardians (24)**	**Controls (314)**	**p value**
Physical dimension	43.5 (±8.1)	55.1 (±3.6)	0.015
Psychosocial dimension	42.0 (±9.8)	53.0 (±7.0)	0.029

146

Pediatric Reference Intervals for FSH, LH, Estradiol, Testosterone, DHEA-S and Cortisol for a Population of Cordoba, Argentina

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Introduction: The gonadotropin and steroid values obtained in various laboratories are often not comparable because of methodological differences. It is important to have normal data that are specific for the methods being used in the laboratory performing the test. **Aims:** To determine the reference values for FSH, LH, estradiol (E2), testosterone (To), DHEA-S and cortisol in our population pediatric. **Subject and Methods:** 410 healthy neonates and infants between 4 to 365 days were recruited. The blood samples were collected for establishing age and sex-stratified reference intervals for FSH, LH, E2, To, DHEA-S and cortisol using Electrochemiluminescence, Cobas e 601 analyzer. The results are shown in table 1. **Conclusion:** This reference values specific for age and sex may help in this period of life to increase the diagnostic power of this parameters for the assessment of endocrine disorders.

Table 1. (for Abstract 146)

		4–59 days n: 196		60–89 days n: 102		90–365 days n: 112	
		2.5 th	97.5 th	2.5 th	97.5 th	2.5 th	97.5 th
DHEA-S (µg/dL)	F	20.15	316.95	18.40	203.70	0.20	65.10
	M	19.69	407.83	8.50	175.40	2.60	81.10
Cortisol (µg/dL)	F	0.46	23.03	1.15	28.00	2.55	19.40
	M	0.64	18.25	1.01	19.40	1.68	26.00
To (ng/dL)	F	12.0	81.6	12.0	48.2	12.0	22.2
	M	13.4	418.0	13.4	388.0	12.0	295.0
FSH (mlU/mL)	F	1.07	22.50	1.56	11.70	0.92	16.70
	M	1.74	5.74	0.86	4.78	0.32	2.90
LH (mlU/mL)	F	0.10	2.20	0.10	1.00	0.10	1.60
	M	0.26	9.10	0.27	8.67	0.10	6.35
E2 (pg/mL)	F	12.0	80.9	12.0	78.8	12.0	78.5
	M	23.2	66.9	12.0	66.0	12.0	66.0

147

Results of Screening for Congenital Adrenal Hyperplasia

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Introduction: Screening of Congenital Adrenal Hyperplasia (CAH) is mandatory for all newborns (NB) in our country since 5 November 2007. It is performed by quantifying 17-OH-progesterone in heel blood, collected after 40 hours of life, on paper S & S 903. The determination is made by competitive enzyme immunoassay (EIA). **Objective:** Report confirmed cases from January 2008 to June 2012. **Materials and Methods:** Hormone Quantification was performed using the reagent Quantase TM Neonatal Screening 17-OHP BIO-RAD on a CODA Open Microplate System BIO-RAD with whole blood collected on filter paper, obtained by heel prick in newborn (NB). The cutoff point was adjusted for gestational age and birth weight. Screening of premature and twin were repeated after 20 days of life. **Results:** From 212,772 samples tested positive 25 cases were confirmed by endocrinologist. 60% were born weighing more than 2500 g. **Conclusions:** During the study period the incidence was 1 in 8510. 20% of the cases involve males born at term without signs of illness.

148

Congenital Adrenal Hyperplasia Due to CYP-21 Hydroxylase Deficit: Lessons from a Single Center Series Managed with a Standardized Treatment from Birth to 8 Years: Part I: Auxology

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In patients with CYP-21 CAH initial growth acceleration, excessive weight gain & rapid bone age advancement are frequently observed. 69 patients were diagnosed at birth and followed until age 8. Treatment protocol included hydrocortisone(HC), fludrocortisone and salt, high initial doses are used HC from diagnosis to 15 days, & then adjusted to the biological criteria. The data were divided into three phases: 0–3 years, 3–5 y & 5–8 y. Overtreatment is suggested during the early postnatal period with a loss of height in SD & height adjusted for parental height SD, followed by "Catch up" where growth rate is accelerated & advanced bone age. Despite good biological control a critical period between 3 and 8 is observed. Further studies are needed to distinguish between an effect due to the half-life of HC or insufficient dose. Further studies are needed to distinguish between an effect due to the half-life of HC or insufficient dose.

Table 1. (for Abstract 148)

	Mean	Boys (n)	Girls (n)	p	Group SW (n)	Group SV (n)	p
0–36 months							
HtSD	–0.5l±l.05 (571)	–0.64±1.16 (263)	–0.40±0.94 (308)	0.006*	–0.59±1.05 (409)	–0.29±0.99 (167)	0.001*
MP-Ht SD	–0.54±1.19 (540)	–0.96± 1.16 (251)	–0.17±1.08 (289)	0.00001*	–0.54±1.27 (375)	–0.5l±0.91 (161)	ns
Weight	–0.54±1.14 (575)	–0.491±1.12 (261)	–0.58±1.17 (314)	ns	–0.29±1.72 (415)	–0.691±1.16 (158)	0.008*
ΔBA/CA	0.89±0.28 (236)	0.92±0.27 (113)	0.86±0.29 (121)	ns	0.87±0.27 (158)	0.95±0.24 (74)	ns
36–60 months							
HtSD	–0.2±0.92 (215)	–0.25±0.93 (121)	–0.33±0.91 (94)	ns	–0.28±1.0 (143)	–0.32±0.64 (55)	0.01*
MP-Ht SD	–0.23±1.09 (218)	–0.60±0.94 (121)	0.22±1.11 (97)	0.00001*	–0.24±1.09 (141)	–0.15±0.88 (56)	ns
Weight	0.21±1.14 (216)	0.26±1.19 (121)	0.13±1.08 (95)	ns	0.39±1.18 (144)	–0.21±0.88 (55)	0.00007*
ΔBA/CA	1.06±0.27 (150)	1.05±0.24 (87)	1.09±0.32 (63)	ns	1.07±0.28 (89)	1.04±0.29 (47)	ns
60–96 months							
HtSD	0.2±0.88 (271)	0.24±0.91 (165)	0.13±0.84 (106)	ns	0.19±0.93 (175)	0.23±0.74 (71)	ns
MP-Ht SD	0.26±1.1 (277)	–0.04±1.06 (167)	0.73±0.98 (110)	0.00001*	0.26±1.13 (176)	0.38±0.82 (68)	ns
Weight	1.00±1.48 (275)	1.27±1.57 (172)	0.55±1.20 (103)	0.0004*	1.26±1.48 (178)	0.50±1.36 (72)	0.0002*
ΔBA/CA	1.16±0.20 (208)	1.14±0.21 (134)	1.19+0.17 (74)	ns	1.17±0.28 (127)	1.13±0.19 (58)	ns

149

Growth Velocity During Post Menarcheal Period in Chilean Girls is Influenced by Socio-economic Status, But Not by Body Mass Index. Preliminary Results

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Background: Menarche announces the last period of growth. However, the factors that affect this process are unknown. **Objective:** To assess growth velocity (GV) during post menarche period according to type of school, a proxy of socioeconomic level in Chile, and body mass index (BMI). **Methods:** Healthy girls (N=106) attending schools from low socioeconomic level (LSL; N=48) and from high socioeconomic level (HSL; N=58) were followed by 2.5±0.3 years. Height and weight were assessed every 6 months by a pediatric endocrinologist. The height and weight SDS were calculated according to NCHS curves. Mixed model and regression analysis were used to evaluate the effect of type of school and BMI on growth velocity. **Results:** GV was determined by type of school (p=0.005), but not by BMI (0.72). Regression analysis showed a decrease of height SDS in both type of schools, but higher in LSL than HSL(–0.15 vs. –0.34 SD/year, P<0.0001). The average parental height size was similar in girls from both schools. **Conclusions:** During the post menarche girls from HSL level exhibit higher GV than compared to those from LSL, even after adjustment by BMI. In order to understand better this finding, we will follow the girls until final height.

150

Prevalence of Polycystic Ovarian Syndrome (PCOS) in Adolescents with History of Idiopathic Central Precocious Puberty (ICPP)

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Introduction: PCOS in reproductive age ranges between 5 and 10%. Data about PCOS in adolescents with history of ICPP are controversial; several authors found increased incidence in patients treated with GnRH analogues (GnRHa). **Objective:** To evaluate the prevalence of PCOS in adolescents with history of ICPP and its relation with GnRHa treatment. **Subjects:** 54 girls with history of ICPP were divided into two groups. Group (GA), (n=29) treated with GnRHa, chronological age (CA) 16.3±1.7 years and group B (GB) (n=25) untreated girls, CA 14.6±2.1 years. Age at menarche (AM), Gynecological age (GyA), menstrual cycles characteristics, body mass index (BMI) and clinical hyperandrogenism at least three years after menarche were analized. Serum testosterone and androstenedione were measured by ECLIA and RIA respectively. PCOS was diagnosed according to Androgen Excess Society Consensus (AESC). Results (mean ± SD): AM in GA was 9.5±0.4 and in group B was 11.7±0.8 years (p<0.001), GyA was 4.48±1.9 in GA and 5.1±2.1 years in GB(p=ns). BMI in GA was 22.8±4.6 and 24.7±4.9 in GB (p=ns). Fourteen of 54 patients (26%) met the AESC criteria for PCOS. Prevalence of PCOS: GA 17.2% vs GB 36% (p=ns). **Conclusion:** A high prevalence of PCOS is found in girls with history of ICPP, however this is not related to treatment with GnRHa.

151

Evaluation of Bone Mineralization in Pediatric Patients with Classic Congenital Adrenal Hyperplasia

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Corticosteroid therapy reduces bone mineralization. At the Congenital Adrenal Hyperplasia (CAH), despite continuous treatment with glucocorticoid, the high levels of androgens could counteract this effect. Few studies describe bone mineral density (BMD) in children and adolescents with CAH. **Objective:** To describe BMD in pediatric patients with classical CAH form and to evaluate possible deleterious effects of corticosteroid on bone mineralization. **Patients and Methods:** One evaluated sex, current age, age at initiation of treatment, steroids in use, current dose (mg/m^2 hydrocortisone equivalent) and average time of use. The patients underwent bone densitometry (DXA) of whole body and spine (L1 – L4) and classified if normal BMD (Z score > –2) or low for age. **Results:** A total of seven girls were evaluated, four of them salt wasting and 3 simple virilizing, mean age of 9.98±3.29 years, the start of corticosteroid therapy at 2.58±0.78 months of life, and current dose average equivalent in hydrocortisone of 14.98±5.99 mg/m^2/day and average use time of 9.77±3.14 years. In all girls BMD was normal for age, with a mean of 0.92±0.1 g/cm^2 (Z –0.04±0.44) for whole body and 0.93±0.2 g/cm^2 (Z +0.7±0.69) for the column. **Conclusion:** Steroid therapy in patients examined did not affect bone mineralization.

152

Cyp-21 Hydroxylase Congenital Adrenal Hyperplasia: Lesson from a Single Center Series Managed with a Standardized Treatment from Birth to 8 Years: Part II: Biological Parameters and Treatment Balance

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In prepubertal patients with CAH found a good clinical and biological balance may favor a better outcome of height, weight and bone age in puberty. However, little has been described on the relevant elements in this age. In 69 patients with classic CAH, diagnosed by screening and followed until 8 years we determined the most relevant parameters: in the first 6 months of life "minipuberty" in males can be confusing and therefore is not recommended in this period.Correlations were made between height, bone age and biological criteria as well as between 17OHP 8 am, 12 pm and 5–7 pm and testosterone levels and renin. Values <75 percentile of testosterone at 8am, correlate well with values of 17OHP during the day and with a growth velocity <2 SD or Bone Age / Chronological <1.1. We Propose the use of percentiles for biological values as a good monitoring criteria in this age group.

153

A Patient with Primary Pseudo-hypoaldosteronism Type I with Severe Hyperkalemia

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Primary pseudo-hypoaldosteronism type I (PHA1) due to mutations in the mineralocorticoid receptor gene (NR3C2) presents as milder and transient salt-wasting syndrome caused by kidney aldosterone resistance; whereas mutations in the epithelial sodium channel (ENaC) subunits coding genes, determine a severe and persistent systemic form. **Objective:** We report a 2yrs-old boy with PHA1 kidney phenotype, who requires near surveillance because of persistent severe hyperkalemia. **Results:** A 3-week-old patient born to healthy unrelated parents was admitted with failure to thrive and dehydration. Laboratory: Na:120 mEq/l(132–145), K:7.79 mEq/l(3.6–5.9), 17-hydroxyprogesterone: 1.2 ng/ml(<4.0), cortisol: 13.9 ug/dl Aldosterone: 4300 pg/ml (50–900) and plasmatic renin activity (PRA) > 15 ngAngiotensineI/ml/h. Renal function was normal. The normal kidney ultrasound and the absent of urinary infection rule out secondary PHA1. A normal sweat test makes the systemic phenotype less probable. Karyotype was normal: 46,XY. No sequence variations were detected by direct sequencing of the NR3C2 gene. Sodium supplementation was required during 4 months, but potassium exchange resins are still required. At 8 mo levels of potassium reach 7mEq/l. **Conclusions:** Near follow up due to severe life-threatening hyperkalemia continues to be necessary. Gene dosage study will allow to known if there is an heterozygous NR3C2 deletion. The study of the ENaC gene could be of interest because patients with homozygous mutations of this gene and transient kidney phenotype were reported.

154

Central Adrenal Insufficiency could not be Confirmed by Measurement of Basal Serum Dheas Levels in Pubertal Children

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Central adrenal insufficiency (CAI) diagnosis remains challenging, particularly when the deficiency is partial. It has been proposed basal serum dehydroepiandrosterone sulfate (B-DHEAS) levels as a possible marker of adrenal function in adults patients. Our aim was to evaluate the usefulness of B-DHEAS levels to diagnose CAI in pubertal patients. **Methods:** Fifty six (26 females and 30males) pubertal patients, mean +SDS chronological age: 14.2+2.6 years) were studied. Patient diagnosis were the follow: chronic corticoid treatment (n:11), idiopathic and secondary hypopituitarysm (n:26) hystiocitosis (n:1), septo optic dysplasia (n:2), Autoimmune diseases (n:7) Prader Willi Syndrome (n:3), Others (n:6). All patients underwent 1-µg cosyntropin test (LDT). B-DHEAS levels were matched

Table 1. Auxological and hormonal levels based on testosterone levels below or above the 75th percentile (for Abstract 152)

	MP HtSD	ΔBA/CA	Testosterone	Morning 17-OHP	Noon 17-OHP	Evening 17-OHP	Renin
0–6 months							
<75th percentile	–0.05±1.1	0.72±0.3	0.8±0.5	128 ± 165	25 ± 35	14 ± 83	123 ± 312
>75th percentile	–0.55 ± 1.0	0.96 ± 0.4	3.9 ± 1.8*	240 ± 231	10 ± 39	22 ± 149	84 ± 311
Total 6–96 months							
<75th percentile	–0.39 ± 1.1	1.03 ± 0.2	0.13 ± 0.1	18 ± 86	6 ± 38	3 ± 39	23 ± 78
>75th percentile	0.14 ± 1.1**	1.12 + 0.2**	0.76 ± 0.4**	155 ± 207**	39±101**	29 ± 101**	34 ± 89*

* $p < 0.005$, ** $p < 0.001$.

for age and gender. **Results:** Normal LDT cortisol response in 30 patients (Gr1) and below the normal cut off limit in 26 (Gr2), (Mean + SDS serum cortisol levels: 0.584 +0.6 and 0.349+0.1 nmol/l respectively) were found. B-DHEAS levels were below in 8 patients (26%) in Gr1 and higher than the 2.5th in 14 patients (53.8%) in Gr2. **Conclusion:** B-DHEAS levels in pubertal children seem not to be useful either to diagnose sufficiency or insufficiency central adrenal function. Dynamic testing is necessary for assessing hypothalamic pituitary adrenal axis.

155

Hyperandrogenism in Adolescents as Frequent Expression of Non Classical Form of Congenital Adrenal Hyperplasia

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Hyperandrogenism is considered a very frequent pathology, with a very strong familiar component; however all the genes are not clear identified. **Goals:** Clinical characterization of teenagers with hyperandrogenism, identifying its etiology, recognizing the comorbidities and identifying phenotypic manifestations in first and second grade relatives that could be related to carrier states. **Material and Methods:** Girls/teenagers attending the Pediatric Endocrinology Department of the INEN during last year with hyperandrogenic symptoms of were studied. A clinical characterization of comorbidities and familiar history was investigated. **Results:** 21 teenagers were studied. Diagnosis of hyperandrogenism was made at the average age of 12.8 years. Family history of hirsutism and/or infertility was identified in 57% of first or second grade relatives. Physical examination showed acne, hirsutism, clitoromegaly, premature pubarche, acantosis nigricans in an isolated way or a combination of them in 20 patients (95%). Overweight or obesity was present in 52%. Clinically were presented in a 67% related with comorbidities, hypertension (5%), metabolic syndrome (10%), type 2 diabetes (5%) and thyroid disease (29%). From the studied group 14 (67%) corresponded to congenital adrenal hyperplasia in nonclassical form confirmed by ACTH acute stimulation. **Conclusions:** Hyperandrogenism in adolescents presented with high frequency of hirsutism, overweigh or obesity, it was mainly secondary to congenital adrenal hyperplasia. Family history of hirsutism and/or infertility were relevant in first or second grade relatives. There were heterogeneous comorbidities.

156

Growth during the First Three Years of Life in Children with Classical Congenital Adrenal Hyperplasia Diagnosed by Newborn Screening

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Linear growth allows monitoring metabolic control in classical congenital adrenal hyperplasia (CCAH). **Aims:** To analyze linear growth in children with CCAH diagnosed by newborn screening and molecular analysis, up to the age of 3years (G1), to compare height and bone age (BA) at 3years, with children diagnosed pre new newborn screening period (G2). **Method:** Age at start of treatment (AST), z-height, z-BMI, hydrocortisone dose (HCd), BA in G1 (17 children) and AST, z-height, BA at 3years in G2 (15 children) were analyzed. **Statistical Analysis:** Student, Mann-Whitney, Wilcoxon tests. **Results:** AST: G1: 14(2–22) days, G2: 45(5–821) (p=0.015). Table: **Conclusions:** 1) Children diagnosed by screening showed height decrease in the first 6 months, with later recovery and BMI increase. 2) At 3 years, they did not show differences in height or BA with children previously diagnosed despite earlier detection, but they showed lower BA dispersion.

Table 1. (for Abstract 156)

	Start		6 months	1 year	2 years	3 years	
	G1	G2	G1	G1	G1	Gl	G2
z-height x±sd	–0.81±1.46*		–1.74±1.08*	–1.60±1.19	–1.34±1.00§	–1.00±0.75§	–1.04±1.44
z-BMI	–1.34±1.02**		0.48±0.83**	0.93±0.91	0.61±0.77#	1.03±0.84#	
HCd (mg/m^2)	34.71±4.85	32.63±5.29	20.69±1.36	18.59±3.14	16.83±3.94	16.40±4.70	
BA Med (min-max)				0.8 (0.3–1.8)	1.5 (1.0–2.5)	2.5 (1.5–3.5)	2.3 (1.0–6.0)

*,§,#,**: $p < 0.05$.

157

Implications of Low Birth Weight, BMI and Pubertal Onset in Girls Importance of Expected Birth Weight Ratio [EBW] in a Group of Rapid Maturers Girls Maturers from Bogotá (colombia)

Llano, Mauricio(*)

Centro Médico de los Andes | (*) Colombia

Introduction: Recent studies related BMI in early pubertal onset at least 1/3 of girls. In girls, low birth weight followed by a spontaneous catch up has been associated with early menarche, reduced ovarian volume, diminished ovulating rates in rats, in addition to ovarian hyperandrogenism in girls with premature pubarche. **Material and Methods:** In an observational study we examined a female population in a correlation between BMI percentile and pubertal onset considering birth weight. Expected birth weight in 201 girls (25.03%) were obtained and was adjusted for maternal age, maternal weight, maternal height, parity, sex and gestational age reached. from a total of 803 girls at starting puberty, divided according to BMI centile in 4 groups, obesity (percentile> 95), Risk of Obesity (RO) (percentile 85–95), Risk of Overweight (RS) (75–95 percentile) and weight at p <75. **Results:** Analyzed the birth weight adjusted to low weight girls, compared with normal birth weight for correlation with gonadarche, adrenarche and BMI, there is a slight but not significant trend (p=0.32) of lower birth weight for girls with premature adrenarche, not significant for initial gonadarche and obesity. A direct correlation and progressive BMI percentile according to centilar location at beginning of puberty, being negative for low statural groups and reaching 17.2% and 25.4% of obesity in patients with heights above 75th centile (Risk of Obesity). Of all the girls discussed the expected birth weight seeking this inverse correlation between BMI and pubertal onset was not observed as previous data published. More data is necessary in order to clear other groups results.

158

Assessment of Serum Basal Cortisol in 120 Healthy Children

Botelho Barra, Cristina(*)*; Novato Silva, Ivani; Rodrigues, Tânia; Lane, Jovita; Colosimo, Enrico*

Universidade Federal de Minas Gerais (UFMG) | (*) Brasil

The basal cortisol measurement may reflect the hypothalamic-pituitary-adrenal axis integrity. The same reference values ??of basal cortisol have been used, in practice, for adults and children. However, results obtained from an adult population may not be suitable for pediatric patients and can negatively impact the quality of the evaluation in childhood. The objective of this study was to assess basal cortisol levels in children, following the CLSI/IFCC C28-A3 guidelines. Morning serum cortisol levels at 8:00 am were measured by ICMA in 120 healthy individuals, 4–19 years old (median=12) from a public school. We observed that baseline serum cortisol levels increased with age and pubertal maturation, but didn't change with gender. Adolescents who were 16 to 19 years old had higher serum cortisol values than younger ones and also than those with incomplete pubertal development. The basal serum cortisol reference limits (2.5 and 97.5 percentiles) for the healthy subjects were: 2.97 [90% CI (1.44, 3.69)] and 23.4 mg/dL [90% CI (16.3, 26.3)]. The cortisol values (4.46; 22.7 mg/dL) suggested as normal by the reference service were considered inappropriate for the pediatric population studied. We concluded that reference intervals for basal serum cortisol should be determined specifically to the pediatric population.

159

Prevalence of Obesity, Body Mass Index, Fasting Glucose and Lipid Profiles in Children with Central Precocious Puberty (CPP) and Early Puberty (EP) Before and During 3 Years of Treatment with a GnRH Analog (GnRHa)

Colmenares, Ana[1(*)]*; Gunczler, Peter*[2]*; Lanes, Roberto*[2]

[1]Unidad de Endocrinología Pediátrica, Instituto Venezolano del Seguro Social | (*) Venezuela; [2]Unidad de Endocrinología Pediátrica, Hospital de Clínicas Caracas

Objectives: To evaluate the rate of obesity, BMI, glucose and lipids in children with CPP and EP treated with GnRHa and in similar untreated patients. **Methods:** 49 subjects were treated with GnRHa, while 36 children were followed without treatment. Patients were divided into 3 groups (Group A: CPP + EP, Group B: CPP and Group C: EP) and 2 subgroups (1: treated and 2: untreated). CA, BMI, glucose and lipids were similar at baseline. **Obesity:** BMI above +2 SDS. **Results:** At diagnosis patients with CPP and EP had a high prevalence of obesity. While in non-treated patients it showed a decreasing trend, in GnRHa-treated patients it remained unchanged. BMI did not change. Glucose increased in group A. TC remained unchanged in groups A and B, while it decreased in C1 and increased in group C2. HDL-C increased in treated patients. LDL-C was higher in group B1. Triglycerides remained unchanged. **Conclusions:** The prevalence of obesity in CPP and EP is high. It tends to decrease in non-treated subjects and remains unchanged in treated patients. In CPP/EP glucose increased. TC decreased in treated patients with EP. HDL-C increased with treatment in all groups, while LDL-C was higher in treated patients with CPP.

Table 1. Niveles de β-hCG durante la evolución por Elisa e ICMA (for Abstract 161)

β -hCG mU/ml (0–5)	25/10/11	28/10/11	15/11/11	17/12/11	3/01/12	9/02/12	13/03/12	13/04/12	10/05/12
AxSym Elisa	4.79	2.7		5.5	5.57	10.8		12.1	10.2
Immulite ICMA		8.8	21.4	21	21.1	46	55.3		53.7

160

Atypical Presentation of an Adrenocortical Carcinoma

Finozzi Silva, María Rosa(*); Ordoqui, Rosina; Torosian, Lidia; Belzarena, Cristina

Clinica de Endocrinologia y Metabolismo Hospital de Clinicas | (*) Uruguay

Background: The Adrenocortical carcinomas (ACCs) are rare, with an approximate incidence of 1 case / million / year. 60% can produce some kind of hormone, glucocorticoids, androgens or mineralocorticoids. Usually in children the clinical presentation is with virilization (84%), and the criteria of malignancy are distant metastases and regional invasion. Its molecular pathogenesis is associated with inactivating mutations of tumor suppressor genes and overexpression of IGF-II. Surgical resection is the only curative treatment, if it is not possible it can be performed cytotoxic chemotherapy. **Objective:** We report the case of an adolescent female with virilization, whose diagnosis and evolution are exceptional. **Case Report:** 16 y.o., progressive virilization since the age of 4: hirsutism, muscle hypertrophy and clitoromegaly without thelarche or menarche. Severe hyperandrogenemia was found with an increase of total and free testosterone, DHEA-S and 17-OHP (from 10 to 25 times the ULN), secondary to a 15 cm right adrenal mass, without involvement of adjacent organs or metastasis. Tumor resection was performed, with the pathological report of an adrenal carcinoma (tumor weight 700gs), using the classification system Weiss. One year after surgery, the signs of virilization had reversed, accompanied by progressive thelarche and menarche, with normalization of androgens. The 17 OH P-ACTH stimulating test ruled out a congenital adrenal hiperpasia (HAC) **Conclusion:** ACCs are rare tumors that can be extremely aggressive. It is striking the behavior of this ACCs, which was manifested at the age of 4 with progressive virilization up to the age of 16, without regional invasion or metastasis and no evidence of having been preceded by a virilizing CAH. Despite the ACCs have been considered to have a poor prognosis, in the contemporary series the data suggests that survival may be improving.

161

Elevated Serum Total ß-hCG Outside of Pregnancy in an Adolescent Girl

Enacán, Rosa Elizabeth(*); Ballerini, María Gabriela; Arcari, Andrea; Petrobelli, Patricia; Ropelato, María Gabriela; Gryngarten, Mirta

División de Endocrinología. Hospital de Niños Ricardo Gutiérrez. | (*) Argentina

Human chorionic gonadotropin (hCG) is a glycoprotein hormone produced mainly by trophoblastic tissues. Other entities than pregnancy can also show β-hCG positive results. There are many sources of hCG and reasons for elevated levels outside pregnancy. Elevated serum β-hCG has been reported in chronic renal failure (CRF) patients under hemodyalisis. We report the case of a 15-years old, non pregnant patient with chronic renal failure, in treatment with hemodyalisis, admitted with abnormal uterine bleeding at a pediatric hospital. She had persistently elevated serum β-hCG levels measured by two different assays after ruled out the likelihood of heterophile antibodies, α-fetoprotein and free β-hCG. (Table 1) All imaging tests performed were normal excluding underling malignancies process. Patient received hormonal treatment with good response. After excluding pregnancy and tumoral causes, persistent high of β-hCG levels in a patient with CRF require a careful long term follow to exclude a hidden malignant process and to avoid inappropriate therapeutic. This finding may suggest reduced metabolism and clearance of β-hCG, or changes in β-hCG production secondary to uremia.

Author Index for Abstracts

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Erratum

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Select Oral Presentation

1

Increased Cardiovascular Risk Factors in Young Patients with 21-Hydroxylase Deficiency

Rodrigues, Tania Maria Barreto[1(*)]; Barra, Cristina Botelho[1]; Santos, Jovita Lane Soares[1]; Costa, Aline Barbara Pereira[2]; Goulart, Eugenio Marcos Andrade[1]; Ferreira, Adaliene Versiani Matos[2]; Silva, Ivani Novato[1]

[1]Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte | (*), Brasil; [2]Escola de Enfermagem, Universidade Federal de Minas Gerais, Belo Horizonte, Brasil

Recent reports pointed to increased risk of cardiovascular disease in deficient 21-hydroxylase (21-OHD) patients. **Objective:** to identify cardiovascular risk factors in those patients compared to the healthy population. **Methods:** Clinical, nutritional and laboratory assessment, and evaluation of the carotid Intima-Media Thickness (cIMT) by ultrasonography in 113 subjects: 40 with 21-OHD (5–20 years) and 73 healthy, without overweight or obesity, matched by sex and age. **Results:** Out of 40 patients, ten (25%) were overweight. Patients had higher systolic (p = 0.0186) and diastolic (p = 0.0095) blood pressure levels; also, the Z score height/age was lower (p = 0.033) and the Z BMI/age was greater (p = 0.000) compared to controls. Body composition, lipid profile, and adiponectin and leptin levels were similar between groups. The cIMT (n = 38 patients, 22 controls) was significantly higher in patients in both the right (p = 0.0240) and the left (p = 0.0003) common carotid artery. Comparisons between groups, excluding overweight 21-OHD patients, showed the same differences, suggesting changes are inherent to the disease itself. **Conclusion:** Increased cIMT, higher BMI z score and blood pressure levels in young 21-OHD patients, regardless of overweight, suggest the need for identification/early intervention to prevent cardiovascular risk.

2

The Influence of SOCS2 Polymorphism on Adult Height and Its Interactive Effect with GHR-EXON 3 and -202 A/C IGFBP3 Polymorphisms in Patients with Turner Syndrome (TS) and Growth Hormone Deficiency (GHD) after Long Term Recombinant Human Growth Hormone (RHGH) Therapy

Braz, Adriana[1(*)]; Costalonga, Everlayny[1]; Trarbach, Ericka[2]; Antonini, Sonir[3]; Guerra-Júnior, Gil[4]; Scalco, Renata[1]; Arnhold, Ivo[1]; Mendonça, Berenice[1]; Jorge, Alexander[2]

[1]Unidade de Endocrinologia do Desenvolvimento, Laboratorio de Hormonios e Genetica Molecular LIM/42 do Hospital das Clinicas, Disciplina de Endocrinologia da Faculdade de Medicina da Universidade de Sao Paulo | (*) Brasil; [2]Laboratorio de Endocrinologia Celular e Molecular LIM/25, Disciplina de Endocrinologia, Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo; [3]Departamento de Pediatria da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo; [4]Departamento de Pediatria da Faculdade de Ciencias Médicas da Universidade Estadual de Campinas, Brasil

Background: There is great interindividual variability in the response to GH therapy. Ascertaining genetic factors can improve the accuracy of growth response predictions. **Objective:** To assess the influence of *SOCS2* polymorphism (rs3782415) and its interactive effect with *GHR-exon 3* and -202 A/C *IGFBP3* (rs2854744)

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polymorphisms on adult height of patients with TS and GHD treated with rhGH. **Design and Patients:** Genotypes were correlated with adult height data of 65 TS and 47 GHD patients treated with rhGH by multiple linear and logistic regressions. **Results:** Baseline clinical data were indistinguishable among patients with different genotypes. *SOCS2* genotype has an independent influence on adult height in patients with TS and GHD treated with rhGH. Patients with at least one *SOCS2*-C allele were 0.7 SDS higher than those homozygous for *SOCS2*-T allele (95% CI 0.3–1.1, $p < 0.001$). Multiple linear regression models were used to predict adult height. *SOCS2* ($p = 0.003$), *GHR-exon 3* ($p = 0.016$) and -202 A/C *IGFBP3* ($p = 0.013$) polymorphisms together with clinical factors [short stature etiology ($p < 0.001$), height SDS at the start of treatment ($p = 0.011$) and target height SDS ($p = 0.043$)] accounted for 60% of the variability in adult height of patients with TS and GHD treated with rhGH. The same result was obtained when total height SDS gain was evaluated as dependent variable ($r^2 = 0.82$). Patients harboring any two negative genotypes in these 3 different locus (homozygosity for *SOCS2*-T allele; the *GHR-exon3* full-length allele and/or the -202C-*IGFBP3* allele) were more likely to achieve an adult height at the lower quartile (odds ratio of 13.6; 95% CI 4.7- 39.7, $p < 0.001$). **Conclusion:** Polymorphisms located in these three distinct locus have independent and interactive influence on growth outcomes of TS and GHD patients treated with rhGH. The use of these genetic markers could identify among rhGH-treated patients those who are genetic predisposed to have less favorable outcomes.

3

Elevation of C-Reactive Protein (CRP) Levels during Luteal Phase in Adolescents with TYPE 1 Diabetes (T1D)

Lopez, Patricia[1(*)]*; Merino, Paulina M.*[2]*; Martinez, Daniela*[1]*; Iñiguez, German*[1]*; Castro, Andrea*[1]*; Cassorla, Fernando*[1]*; Perez-Bravo, Francisco*[3]*; Codner, Ethel*[1]

[1]Institute of Maternal and Child Research, School of Medicine, University of Chile | (*) Chile; [2]Departments of Pediatrics, Campus Centro, School of Medicine, University of Chile; [3]Nutrigenomics Laboratory, Nutrition Department, School of Medicine, University of Chile

Introduction: Chronic complications and mortality rate are higher in females compared to males with type 1 diabetes (T1D), but the mechanisms involved in this gender differences are unknown. One possibility is the presence of detrimental inflammatory process during luteal phase (LP), which would represent a unique phenomenon in women. **Aim:** To compare CRP levels during follicular phase (FP) and LP in post-menarcheal adolescents with T1D, and to evaluate the relationship of this inflammatory marker with body mass index (BMI), IGF-1 and HbA1c levels. **Methods:** We evaluated 25 post-menarcheal adolescents with T1D and 21 healthy adolescents (C) during FP and LP. CRP was measured with usELISA kit. Ovulation was determined by a salivary progesterone level >3 ng/ml in day 21–23. Non-parametric statistics was used (paired t test and Wilcoxon). **Results:** T1D girls showed higher levels of CRP compared to C group in LP (4.7 ± 2.9 and 1.7 ± 2.3 μg/ml, respectively, $p = 0.03$). Higher CRP was observed in T1D during LP vs FP (Wilcoxon paired test, $p = 0.03$), but not in C ($p > 0.05$). Similar proportion of ovulatory cycles were observed in both groups (50% T1D and 31.8% C, $p > 0.05$). Lower IGF-1 levels were present in T1D compared to C only during the LP (284.0 ± 66.4 and 343.4 ± 38.7 ng/ml, respectively, $p < 0.0001$). Luteal CRP levels correlated with BMI, but not with HbA1c and IGF1 in T1D girls. CRP >3 ng/ml, suggestive of high cardiovascular risk, was more prevalent in T1D than C girls in FP and LP (34.5 vs. 4.3% and 55.2 vs. 8.7%, respectively, $p < 0.0001$). **Conclusions:** Higher CRP levels are present in LP with greater elevations of this inflammatory marker between both phases in adolescents with T1D than in healthy adolescents. These changes, added with the higher percentage of patients with elevated CRP may be related to the high risk of cardiovascular disease in women with T1D (Fondecyt1100123).

4

Hyperparathyroidism in Two Patients with Sclerosteosis: A Consequence of Sclerostin Deficiency?

Dias, Camila M.[(*)]*; Passone, Caroline G.B.; Menezes-Filho, Hamilton C.; Kin, Chong Ae; Kuperman, Hilton; Damiani, Durval*

Instituto da Crianca – FMUSP | (*) Brasil

Background: Sclerosteosis (Scl) is a rare autossomal recessive disease characterized by progressive osteosclerosis of skeleton. Scl is caused by inactivating mutations of the SOST gene, which encodes for sclerostin, a protein that inhibits bone formation. PTH is a negative regulator of sclerostin. **Objective:** We aimed to evaluate the bone mineral metabolism in two non related patients with Scl. **Patientes and Methods:** The bone mineral metabolism of two patients (a 1-year-old girl and a 5-year-old boy) with Scl (cG374A/pW124X mutation in homozygosis) were studied through plasma evaluation of levels of calcium (PCa), phosphorus (P), alkaline phosphatase (AP), 25-hydroxyvitamin D (25OHD) and PTH. Calciuria was determined through calcium to creatinine relation in an urinary sample (Uca/UCr). **Results:** The girl and the boy showed, respectively: a normal and a slightly reduced PCa (10.1 and 8.4 mg/dl; normal range: 8.8–10.8 mg/dl), a mild hyperphosphatemia (6.3 and 5.4 mg/dl; normal range: 2.7–4.5 mg/dl), increased AP (742U/L and 351U/L; reference value: <462 U/l and <269 U/l, respectively), 25OHD slightly reduced (26 and 21 ng/ml; normal range: 30–80 ng/ml), increased PTH (101 and 180 pg/ml; normal range: 16–87 pg/ml) and reduced UCa/UCr (0.036 and 0.014; normal range: 0.1–0.25). **Conclusion:** We believe that the hyperparathyroidism observed in these patients with Scl may be related to increased bone mineral accretion associated to excessive bone formation or may be a consequence of sclerostin deficiency. This last hypothesis suggests that in bone physiology the negative regulation of sclerostin by PTH may be counterbalanced by the negative regulation of PTH by sclerostin.

Erratum

5

Hearing Evaluation in Children with Congenital Hypothyroidism

Muñoz, Monica Barby[1](*); Dassie-Leite, Ana Paula[1]; de Lacerda, Luiz[1]; Marques-Pereira, Rosana[1]; Hamerschmidt, Rogério[2]; Nesi-França, Suzana[1]

[1]Pediatric Endocrine Unit, Department of Pediatrics, Federal University of Parana, Curitiba, PR | (*) Brasil; [2]Otorhinolaryngology Department, Federal University of Parana, Curitiba, PR

Introduction: Untreated congenital hypothyroidism (CH) can cause several changes in the auditory system, such as abnormal cochlear development, degeneration of the sensory epithelium, distortion of the tectorial membrane and dysfunction of presynaptic cells in the cochlea. There are few studies showing the true prevalence of hearing disorders in patients with CH diagnosed by neonatal screening (NS). **Aims:** To evaluate hearing in children with CH and correlate with clinical characteristics. **Methods:** 50 children (mean age 9.0 ± 2.2 years, CH diagnosis by NS in 48) under treatment since 19 ± 14 days and 28 unaffected children (control group). Pure-tone and speech audiometry, tympanometry, auditor evoked cortical potential (AECP) and interviews with the person responsible for the children were performed. **Results:** hearing complaints were reported in 16%, school difficulties in 24%. In audiometry, one patient (dyshormonogenesis with positive perchlorate discharge test) showed a dysfunction characterized as unilateral sensorineural hearing loss and descending. No change was observed in measures of acoustic impedance. In AECP no statistically significant difference between groups, nor correlation according to disease severity, etiology of HC and age at onset of treatment. **Conclusion:** CH, when treated early, does not cause hearing loss in children.

6

Profile Investigation of Patients Referred to a Specialized Service for Sex Differentiation Disorders and Their Diagnosis: What Has Changed in the Last Two Decades?

Franco-da-Graça, Felipe(*); Maciel-Guerra, Andréa Trevas; Guerra-Junior, Gil; Marques-de-Faria, Antonia Paula

Universidade Estadual de Campinas (Unicamp) | (*) Brasil

The knowledge about diagnosis, prognosis and treatment of disorders of sex differentiation (DSD) has had great advances, but the early identification and investigation of these cases is still crucial. The aim of this study was to compare the initial period of operation of the Interdisciplinary Group for the Study of Sex Determination and Differentiation from Unicamp, with the present time regarding the profile of patients referred as well as the distribution and accuracy of diagnoses. **Methodology:** Data were collected from medical records on clinical features, evaluation methods and diagnosis of the first 50 patients with genital ambiguity (from 1988) and the last 50 (until 2011). The two groups were compared using the qui-square test and Mann-Whitney test. **Results and Conclusions:** There was neither reduction in the age of referral of patients nor an increase of cases without sex assignment. Furthermore, an increase in the frequency of cases with evident genital ambiguity was noticed, indicating that there are still flaws in the recognition of the genital ambiguity by health professionals. On the other hand, there was an increased use of hormonal tests and karyotype in research, and molecular tests have become routine, resulting in a significant decrease of idiopathic cases, making it more appropriate to define the sex of rearing and the institution of therapeutic measures.

Oral Presentation

1

Genetic Characterization of Neonatal Diabetes in Spain

Martínez, Rosa(*); Rica, Itxaso; Garin, Intza; Urrutia, Inés; Aguayo, Anibal; Castaño, Luis; Grupo Español de seudohipoparatiroidismo

Endocrinology and Diabetes Research Group, Cruces Hospital, University of Basque Country, CIBERDEM, CIBERER, Barakaldo, Spain | (*) España

Background: Neonatal diabetes mellitus (NDM) is a rare but devastating metabolic disorder characterized by hyperglycemia within the first six months of life which it can be transient or permanent or be present like a clinical feature of a Syndrome. A genetic diagnose is possible for most of these patients with mutations in at least 13 different genes or alterations in the chromosome 6q24 region. **Objetives:** Describe genetically Spanish families diagnosed with NDM and evaluate the response to sulphonylureas in patients with K_{ATP} channel genes mutated. **Methods:** 48 patients of independent families were studied for alterations in *KCNJ11*, *ABCC8*, *INS*, *GCK*, and in patients who had specific clinical features: *INSR*, *IPF1*, *HNF1B*, *FOXP3*. **Results:** We have identified the genetic cause in 79% of patients (38), 20 of them were transient neonatal diabetes and 18 permanent. We found 22 heterozygous activating mutations in the genes encoding SUR1 (*ABCC8*) and Kir6.2 (*KCNJ11*) subunits of the pancreatic ATP-sensitive potassium channel. Of these, 15 patients carried previously described mutations in *KCNJ11* and 7 patients presented mutations in *ABCC8* gene, most of them with an optimal response to sulphonylureas except for one 1 of them with a novel variant who did not respond to sulphonylureas. We identified abnormalities in the 6q24 region in 9 patients, 4 of them presented loss of imprinting with hypomethylation, 3 had paternal uniparental disomy of chromosome 6 and 2 had paternal duplication of the 6q24 region. The rest of patients: 4 had mutations in INS gene, 1 patient, with leprechaunism, carried described compound heterozygous mutations in *INSR* gene, and 1 patient, with IPEX Syndrome, presented a novel hemizygous mutation (p.Leu95fs) in *FOXP3* gene. **Conclusions:** The majority of patients who develop NDM can be described genetically. Mutations in K_{ATP} channel genes are the most frequent cause in Spanish population, most of them respond satisfactory to sulphonylureas.

Erratum

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[1]Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte | (*), Brasil; [2]Escola de Enfermagem, Universidade Federal de Minas Gerais, Belo Horizonte, Brasil

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2

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Lopez, Patricia[1(*)]; Merino, Paulina M.[2]; Martinez, Daniela[1]; Iñiguez, German[1]; Castro, Andrea[1]; Cassorla, Fernando[1]; Perez-Bravo, Francisco[3]; Codner, Ethel[1]

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Introduction: Chronic complications and mortality rate are higher in females compared to males with type 1 diabetes (T1D), but the mechanisms involved in this gender differences are unknown. One possibility is the presence of detrimental inflammatory process during luteal phase (LP), which would represent a unique phenomenon in women. **Aim:** To compare CRP levels during follicular phase (FP) and LP in post-menarcheal adolescents with T1D, and to evaluate the relationship of this inflammatory marker with body mass index (BMI), IGF-1 and HbA1c levels. **Methods:** We evaluated 25 post-menarcheal adolescents with T1D and 21 healthy adolescents (C) during FP and LP. CRP was measured with usELISA kit. Ovulation was determined by a salivary progesterone level >3 ng/ml in day 21–23. Non-parametric statistics was used (paired t test and Wilcoxon). **Results:** T1D girls showed higher levels of CRP compared to C group in LP (4.7 ± 2.9 and 1.7 ± 2.3 μg/ml, respectively, $p = 0.03$). Higher CRP was observed in T1D during LP vs FP (Wilcoxon paired test, $p = 0.03$), but not in C ($p > 0.05$). Similar proportion of ovulatory cycles were observed in both groups (50% T1D and 31.8% C, $p > 0.05$). Lower IGF-1 levels were present in T1D compared to C only during the LP (284.0 ± 66.4 and 343.4 ± 38.7 ng/ml, respectively, $p < 0.0001$). Luteal CRP levels correlated with BMI, but not with HbA1c and IGF1 in T1D girls. CRP >3 ng/ml, suggestive of high cardiovascular risk, was more prevalent in T1D than C girls in FP and LP (34.5 vs. 4.3% and 55.2 vs. 8.7%, respectively, $p < 0.0001$). **Conclusions:** Higher CRP levels are present in LP with greater elevations of this inflammatory marker between both phases in adolescents with T1D than in healthy adolescents. These changes, added with the higher percentage of patients with elevated CRP may be related to the high risk of cardiovascular disease in women with T1D (Fondecyt1100123).

4

Hyperparathyroidism in Two Patients with Sclerosteosis: A Consequence of Sclerostin Deficiency?

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Background: Sclerosteosis (Scl) is a rare autossomal recessive disease characterized by progressive osteosclerosis of skeleton. Scl is caused by inactivating mutations of the SOST gene, which encodes for sclerostin, a protein that inhibits bone formation. PTH is a negative regulator of sclerostin. **Objective:** We aimed to evaluate the bone mineral metabolism in two non related patients with Scl. **Patientes and Methods:** The bone mineral metabolism of two patients (a 1-year-old girl and a 5-year-old boy) with Scl (cG374A/pW124X mutation in homozygosis) were studied through plasma evaluation of levels of calcium (PCa), phosphorus (P), alkaline phosphatase (AP), 25-hydroxyvitamin D (25OHD) and PTH. Calciuria was determined through calcium to creatinine relation in an urinary sample (Uca/UCr). **Results:** The girl and the boy showed, respectively: a normal and a slightly reduced PCa (10.1 and 8.4 mg/dl; normal range: 8.8–10.8 mg/dl), a mild hyperphosphatemia (6.3 and 5.4 mg/dl; normal range: 2.7–4.5 mg/dl), increased AP (742U/L and 351U/L; reference value: <462 U/l and <269 U/l, respectively), 25OHD slightly reduced (26 and 21 ng/ml; normal range: 30–80 ng/ml), increased PTH (101 and 180 pg/ml; normal range: 16–87 pg/ml) and reduced UCa/UCr (0.036 and 0.014; normal range: 0.1–0.25). **Conclusion:** We believe that the hyperparathyroidism observed in these patients with Scl may be related to increased bone mineral accretion associated to excessive bone formation or may be a consequence of sclerostin deficiency. This last hypothesis suggests that in bone physiology the negative regulation of sclerostin by PTH may be counterbalanced by the negative regulation of PTH by sclerostin.

5

Hearing Evaluation in Children with Congenital Hypothyroidism

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Introduction: Untreated congenital hypothyroidism (CH) can cause several changes in the auditory system, such as abnormal cochlear development, degeneration of the sensory epithelium, distortion of the tectorial membrane and dysfunction of presynaptic cells in the cochlea. There are few studies showing the true prevalence of hearing disorders in patients with CH diagnosed by neonatal screening (NS). **Aims:** To evaluate hearing in children with CH and correlate with clinical characteristics. **Methods:** 50 children (mean age 9.0 ± 2.2 years, CH diagnosis by NS in 48) under treatment since 19 ± 14 days and 28 unaffected children (control group). Pure-tone and speech audiometry, tympanometry, auditor evoked cortical potential (AECP) and interviews with the person responsible for the children were performed. **Results:** hearing complaints were reported in 16%, school difficulties in 24%. In audiometry, one patient (dyshormonogenesis with positive perchlorate discharge test) showed a dysfunction characterized as unilateral sensorineural hearing loss and descending. No change was observed in measures of acoustic impedance. In AECP no statistically significant difference between groups, nor correlation according to disease severity, etiology of HC and age at onset of treatment. **Conclusion:** CH, when treated early, does not cause hearing loss in children.

6

Profile Investigation of Patients Referred to a Specialized Service for Sex Differentiation Disorders and Their Diagnosis: What Has Changed in the Last Two Decades?

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The knowledge about diagnosis, prognosis and treatment of disorders of sex differentiation (DSD) has had great advances, but the early identification and investigation of these cases is still crucial. The aim of this study was to compare the initial period of operation of the Interdisciplinary Group for the Study of Sex Determination and Differentiation from Unicamp, with the present time regarding the profile of patients referred as well as the distribution and accuracy of diagnoses. **Methodology:** Data were collected from medical records on clinical features, evaluation methods and diagnosis of the first 50 patients with genital ambiguity (from 1988) and the last 50 (until 2011). The two groups were compared using the qui-square test and Mann-Whitney test. **Results and Conclusions:** There was neither reduction in the age of referral of patients nor an increase of cases without sex assignment. Furthermore, an increase in the frequency of cases with evident genital ambiguity was noticed, indicating that there are still flaws in the recognition of the genital ambiguity by health professionals. On the other hand, there was an increased use of hormonal tests and karyotype in research, and molecular tests have become routine, resulting in a significant decrease of idiopathic cases, making it more appropriate to define the sex of rearing and the institution of therapeutic measures.

Oral Presentation

1

Genetic Characterization of Neonatal Diabetes in Spain

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Background: Neonatal diabetes mellitus (NDM) is a rare but devastating metabolic disorder characterized by hyperglycemia within the first six months of life which it can be transient or permanent or be present like a clinical feature of a Syndrome. A genetic diagnose is possible for most of these patients with mutations in at least 13 different genes or alterations in the chromosome 6q24 region. **Objetives:** Describe genetically Spanish families diagnosed with NDM and evaluate the response to sulphonylureas in patients with K_{ATP} channel genes mutated. **Methods:** 48 patients of independent families were studied for alterations in *KCNJ11*, *ABCC8*, *INS*, *GCK*, and in patients who had specific clinical features: *INSR*, *IPF1*, *HNF1B*, *FOXP3*. **Results:** We have identified the genetic cause in 79% of patients (38), 20 of them were transient neonatal diabetes and 18 permanent. We found 22 heterozygous activating mutations in the genes encoding SUR1 (*ABCC8*) and Kir6.2 (*KCNJ11*) subunits of the pancreatic ATP-sensitive potassium channel. Of these, 15 patients carried previously described mutations in *KCNJ11* and 7 patients presented mutations in *ABCC8* gene, most of them with an optimal response to sulphonylureas except for one 1 of them with a novel variant who did not respond to sulphonylureas. We identified abnormalities in the 6q24 region in 9 patients, 4 of them presented loss of imprinting with hypomethylation, 3 had paternal uniparental disomy of chromosome 6 and 2 had paternal duplication of the 6q24 region. The rest of patients: 4 had mutations in INS gene, 1 patient, with leprechaunism, carried described compound heterozygous mutations in *INSR* gene, and 1 patient, with IPEX Syndrome, presented a novel hemizygous mutation (p.Leu95fs) in *FOXP3* gene. **Conclusions:** The majority of patients who develop NDM can be described genetically. Mutations in K_{ATP} channel genes are the most frequent cause in Spanish population, most of them respond satisfactory to sulphonylureas.