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# Abstracts

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## In Search of Candidate Genes Genotype Phenotype Correlation: Role of Klotho Polymorphisms and Vitamin D Receptor in Bone Mineral Density in Mexican Children and Adolescents with Turner Syndrome

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**Objective:** To describe the distribution of the polymorphism rs7975232 of the vitamin D receptor (VDR) and rs9536282 of the Klotho gene and its association with bone mineral density (BMD) in Mexican girls with Turner syndrome (TS).

**Material and Methods:** Observational transversal analytic study. Patients with TS, who were determined BMD of three regions by DEXA (dual-energy X-ray absorptiometry), DNA was extracted by Qiagen, with analysis of 74 samples of controls 46XX. SNP rs7975232 of the VDR gene and rs9536282 of the Klotho gene was detected through the KASP method. The effects of polymorphism and karyotype were analyzed by general linear model, and the project was authorized by the Research and Ethics Committees of the INP.

**Results:** We present 45 patients with TS, 27 45X and 18 with other cytogenetic findings. The patients with 45X tend to have lower bone mineral content (p = 0.072). The genomic distribution of the polymorphism was different from the controls: AA homozygous polymorphism of the VDR predominated (18% vs 9%, p = 0.07) and the heterozygous polymorphism of Klotho in patient with TS (20% vs 10.7%, p = 0.07); was associated with mayor prevalence of low bone reserve in the three regions, with lower TBMD (p = 0.01) and TBMDz (p = 0.04), and marginally with BMD (p = 0.08). The patients heterozygous to both polymorphisms had mayor prevalence of low bone reserve in the three regions compared with heterozygous to a single polymorphism. Patients heterozygous of the Klotho gene have lower BMD, TBMDz (p = 0.008), while patients heterozygous of the VDR gene have lower BMD (p = 0.03). The polymorphism VDR impacts on the bone health, the patients AA homozygous have lower TBMD (p = 0.03) and the CC homozygous patients tend to have more DMOL1L4 (0.11).

**Conclusions:** This pioneer study shows the possible association of the polymorphism rs7975232 of the VDR and rs9536282 of the Klotho gene to explain the variability of bone health in TS.

## YAP1 Inhibition Impairs Cell Proliferation and Reduces Beta-Catenin Expression in Adrenal Cells

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**Background:** YAP1, effector of HIPPO pathway, plays a crucial role in the maintenance of postnatal adrenal cortex and Regulates cell proliferation and apoptosis in Several tissues. Recently, we Showed association of the overexpression of YAP1 in pediatric adrenocortical tumors (PACT) with worse prognosis.

**Aims:** To Evaluate the role of YAP1 on cell proliferation and Its Interaction with beta-catenin in adrenocortical cells. To analyze the Involvement of YAP1 expression in pACT.

**Methods:** NCI-H295 tumor cells adrenocortical Were Treated with verteporfin (10 uM), a drug for FDA-approved macular degeneration age-related that Present acts inhibiting YAP1/TAED complex. Using qPCR we evaluated mRNA expression of the HIPPO pathway genes (LATS2, STK3, STK4), ITS targets (CTGF), TEAD4, CTNNB1 (beta-catenin) and cell cycle markers (CCND1, CKD2 and CCNE1). In Addition, YAP1, phosphoYAP1 (Ser127) and Beta-catenin protein expression by Western blot Were Analyzed (WB). Cell proliferation (MTS) was measured after 96 h treatment until. YAP1 mRNA expression in pACT was analyzed using data available in the Gene Expression Omnibus database (GSE76019, pACT = 34).

**Results:** In silico analysis Showed that YAP1 higher mRNA was associated disease free survival with lower in pACT. Verteporfin antitumor effect on adrenal tumor cells was shown by reduced cell proliferation after 48 h (–28.29%, p = 0.0001) and 96 h (–43.2%, p = 0.001) reduced mRNA expression of CTGF and TEAD4 (p = 0.0001), CTNNB1 (p = 0.05) and CCND1, CDK2 and CCNE1 (p = 0.005) and mRNA expression of core Increased kinase genes (LATS2, STK3 and STK4; p = 0.05). Showed WB reduced protein expression of YAP1 (–88.5%, p = 0.0005) and phosphoYAP1 (–94.6%, p = 0.0005) and Beta-catenin (–50.4%, p = 0.001).

**Conclusions:** Overexpression of the YAP1 oncogene has a role on ACT progression and associates with poor outcome in patients with pACT. Inhibition of the YAP1-Hippo pathway has antitumor effects in adrenal cells by downregulating CCND1/Beta-catenin. YAP1 is a novel prognostic marker in pACT and YAP1 inhibition is a novel potential adjuvant therapy for patients with ACT.





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## Tri Ponderal Mass Index a Good Anthropometric Index to Evaluate Adiposity in Children and Adolescents

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**Objective:** To evaluate-different anthropometric methods to estimate body fat content by DXA (bfDXA) in Children and Adolescents.

**Methods:** We conducted a cross-sectional study. We included 1,513 participants Between 5 to 18 years old. We measure weight, height and waist circumference (WC) by standardized methods and we Calculated body mass index (BMI), tri-weight index (TMI [weight/height3]) and waist-to-height ratio (WHtR). The body fat content was less EVALUATED by whole body DXA head with GE Lunar iDXA equipment. A linear regression analysis was performed of each anthropometric parameter to estimate bfDXA. We Also Analyzed ROC curves for the detection of overweight/obesity (≥bfDXA p85) and we Identified the optimal cut-off value for TMI in our population at Youden's point where the index is maximum. We compare the diagnostic performance of BMI z-score (ZBMI), WC, WHtR and TMI.

**Results:** We Identified R2 Between 0.28 to 0.76 with the different anthropometric methods in males and 0.51 to 0.66 in females. The WC Had the lowest values of R2 while TMI, BMIZ and WHtR Explained a higher variance of bfDXA. The areas under the curve to detect overweight/obesity Were found Between 0.92 and 0.95 for IMT, BMIZ and WHtR in Both Genders, without significant Differences Between them. We TMI Identified ≥15.2 kg/m$^3$ in an optimal Both genders as cut-off value (Youden index 0.75, 95% CI 0.70 to 0.79), less than previously reported almost cut-off ≥16.0 kg/m$^3$ in boys and ≥16.8 kg/m$^3$ in girls (Youden index 0.65, 95% CI 0.58 to 0.71). The diagnostic performance to detect overweight/obesity for each measure are shown in anthropometric Table 1.

**Conclusion:** TMI is an easy and acceptable tool to estimate body fat content in children and adolescents, and does not require interpretation ITS percentiles or Z-scores. TMI has a better diagnostic performance for an adequate classification of adiposity in comparison of BMIZ and WHtR.

## Genetic Causes of Short Stature in Patients with Previously Diagnosed as Idiopathic Prenatal Short Stature

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**Objective:** To perform a genetic-molecular investigation of a group of non-syndromic small for gestational age (SGA) Patients without catch-up growth.

**Methods:** We selected 55 Patients born SGA [birth weight and/or length standard deviation score (SDS) ≤–2 for gestational age] with persistent short stature at the age of 2 or above [height SDS ≤–2] without any cause of short stature Known, Such as maternal, placental or fetal causes. They Were screened by exome (WES) or targeted sequencing panel, ACCORDING TO Disponibility. Patients with negative result in the target panel submitted to WES Were.

**Results:** We Identified nine (16.4%) being found pathogenic variants in genes associated with growth disorders Already: IHH (n = 2); NPR2 (n = 2); PTPN11 (n = 2); SHOX (n = 1); ACAN (n = 1) and NF1 (n = 1). All Identified single nucleotide variants are extremely rare or absent in public database, Were Predicted to be deleterious, and segregated with the phenotype.

**Conclusion:** Analyzing SGA Patients with persistent short stature in the absence of other additional features is a challenge. After excluding maternal, placental, and fetal factors associated to fetal growth impaired, about 40% of them are diagnosed as idiopathic short stature prenatal. The new genomic Approaches are effective to diagnose a larger number of Previously undiagnosed patients. Among the Patients in the present study diagnosed, most of them HAD short stature due to cartilage disorders, indicating mild forms of skeletal that dysplasia must be a common cause of growth disorders in this group.



**Table 1.** Diagnostic performance to detect overweight/obesity

| | Evils | | | | | Females | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Sen | Spe | AC | PPV | NPV | Sen | Spe | AC | PPV | NPV |
| BMIZ | 96 | 73 | 76 | 38 | 99 | 96 | 71 | 75 | 37 | 99 |
| WHtR | 99 | 73 | 76 | 38 | 100 | 97 | 57 | 63 | 27 | 99 |
| IMT cut-off previously reported* | 74 | 93 | 91 | 66 | 96 | 65 | 93 | 89 | 62 | 94 |
| IMT (≥15.0 kg/m$^3$) | 87 | 89 | 88 | 57 | 98 | 93 | 80 | 82 | 45 | 99 |

* >16.0 kg/m$^3$ in males and >16.8 kg/m$^3$ in females.

Sen: sensibility, Spe: specificity, AC: adequate classification, PPV: positive predictive value; NPV: negative predictive value.

## Determinants of New Onset Metabolically Obese Normal Weight Phenotype In children

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**Objective:** To identify determinants for the development of new onset metabolically-obese-normal-weight (MONW) phenotype among previously healthy normal-weight children as they enter puberty.

**Methods:** The QUALITY cohort comprises 630 Caucasian youth, aged 8–10 years at baseline, with a parental history of obesity. Of these, children with normal-weight and no metabolic risk factors were identified and reassessed 2 years later (n = 193). Children were classified as MONW at follow up if they remained normal-weight and developed at least one of the following metabolic risk-factors: triglycerides >110 mg/dL, fasting glucose >110 mg/dL, HDL-cholesterol <40 mg/dL, blood pressure (BP) >90th percentile for age, sex and height, or a waist circumference >90th percentile for age and sex. They were classified as metabolically healthy normal-weight if they remained normal-weight and without any metabolic risk-factors. We used multivariable logistic regression models to determine whether adiposity (anthropometrics and DXA, baseline and change over 2 years), lifestyle habits (moderate-to-vigorous physical activity measured by accelerometer, self-reported screen time and dietary intake measured by 24-hr recalls) and family history of cardiometabolic disease (obtained from parent questionnaires) were associated with incident MONW.

**Results:** Of the 193 children who were normal-weight and metabolically healthy at baseline, 45 (23%) became MONW two years later. While baseline adiposity did not predict incident MONW status, changes over the 2 years in body mass index (BMI) or waist-to-height ratio (WHR) did. Indeed, children who increased their BMI z-score (OR = 2.76; 95% CI = 1.36; 5.61) or their WHR (OR = 2.17; 95% CI = 1.07; 4.40) were at increased risk of developing MONW status compared to those who remained stable or decreased their BMI or WHR. Lifestyle habits and family history of cardiometabolic disease were not associated with incident MONW status.

**Conclusions:** Clinicians should consider screening for metabolic risk-factors children who present an increase in BMI or WHR as they enter puberty, despite being normal-weight.

## IGF 1R Overexpression and Nuclear Localization in Glioblastoma Cells: In Vitro & In Vivo Studies

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**Background:** CNS tumors are the most frequent solid tumors in children. In pediatric gliomas, IGF-1R nuclear localization was significantly associated with both high-grade tumors and increased risk of death, suggesting that nuclear IGF-1R localization may contribute to an aggressive phenotype.

**Aim:** To characterize the impact of IGF-1R overexpression and nuclear localization in glioma cells.

**Methods:** U87Mg glioblastoma cells were transfected with pEGFP-IGF1R to generate stably transfected cells. Lys1025-1100-1120 were targeted by mutagenesis to avoid IGF-1R nuclear translocation. Proliferation assays were carried out during 5 days, and wounding assay for 18 h with/without IGF-1. Protein extracts were obtained from whole lysates or after subcellular fractionation and processed by western blot (WB). Gene expression was quantified by rqPCR. IGF-1R/IR inhibitor OSI906 was used at 0.5 uM. Male nude mice were injected for in vivo experiments (1,5e6cells/flank/mice).

**Results:** Stably transfected cells with 5(B4U87) or 50(B2U87) times basal expression of IGF-1R showed higher tumor incidence and shorter latency time compared to parental cells when injected in nude mice. In vitro, an increase in pAKT, pERK and pMAPK38 was observed after IGF-1 stimulation. Nuclear localization of IGF-1R was verified by IF and WB (8 h IGF-1 stimulation). These effects were blocked by 1 h preincubation with OSI906. Although CyclinD1 levels were slightly increased in B2U87 and B4U87 cells in response to 24 h IGF-1 stimulation, proliferation and apoptosis were not different from parental cells. Wounding assay showed an increased motility in both B2U87 and B4U87 compared to parental cells. Moreover, GLUT-1 expression showed a two-fold increase after 24 h IGF-1 stimulation that was abrogated by OSI906. Cells expressing GFP-IGF-1R1025x-1100x-1120x showed no IGF-1R nuclear localization and a lower increase in GLUT-1 expression upon IGF-1 stimulation.

**Conclusion:** IGF-1R overexpression and nuclear localization may contribute to an aggressive phenotype of glioblastoma by increasing motility and metabolism of tumor cells rather than increasing its proliferation.

## The Usefulness of Combined Analysis of Serum and Salivary Cortisol Response to Maximum Low Dose Acth Test to Define the Requirement of Hormone Replacement Treatment

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**Introduction:** The low-dose synacthen test (LDT) is widely used to assess central adrenal insufficiency (CAI); however, the total serum cortisol (C) cut-off value is controversial. A correct diagnosis of CAI is required, but overdiagnosis may lead to unnecessary hormone replacement therapy. Salivary cortisol (SC) reflects the levels of free serum cortisol and is a noninvasive alternative.

**Objective:** To define a new cut-off value of serum cortisol in pediatric patients evaluated for suspected CAI considering SC of normal responders.

**Patients and Methods:** 145 pediatric patients (88 males) with suspected of CAI were included in the study. Mean age (SD) was 11.3 years (4.88). All patients underwent LDT with intravenous injection of 1 μg/$m^2$ of tetracosactide (Synacthen 1-24). Serum C and SC levels were measured at baseline and after 30 and 60 minutes. The highest value of the tested parameters, at either 30 or 60 minutes, was regarded as the maximum response value. Reference cut-off value ≥18 μg /dl of serum cortisol levels were considered as a sufficient response (CAS).

**Results:** A significant positive correlation between maximum C and SC response was found (r = 0.90, p = 0.001). Patients were divided according to serum cortisol response into the following groups (Gr): CASGr: n = 72, (median (interquartile range) C and SC, 21.3 μg/dl (19.8–35.2) and 1.14 μg/dl (0.77–1.58), respectively, and CAIGr: n = 73 (median (interquartile range) C and SC, 14.5 μg/dl (12.2–16.4) and 0.58 μg/dl (0.36–1.04), respectively. ROC curve analysis established a SC cut off level of <0.61 μg/dl for CAI diagnosis (specificity and sensitivity of 84% and 56.3%, respectively).

Considering the lower quartile SC of CASGr (SC ≥0.77 μg/ dl), an intermediate (I) Gr (ICAIGr) was established within the CAIGr. ICAIGr: n = 28/73 (median (interquartile range) C and CS, 16.35 μg/dl (14.25–16.87) and 1.16 μg/dl (0.88–1.29), respectively. The remaining 45 patients were considered real (R) CAI, median (interquartile range) C and SC 13.2 μg/dl (11.3–15.3) and 0.41 μg/dl (0.32–0.55), respectively. Significant differences in maximum serum C level responses were found among CASGr, ICAIGr, and RCAIGr (p < 0.001).

**Conclusion:** A maximum response of serum C <16.35 and SC response of <0.77 g/dl May be Appropriate cut-off values to define RCAI. Recognition of an ICAIGr Allows Avoiding unnecessary hormone replacement therapy; However, rigorous patient follow-up is required.

## CYP21A2 Gene Deletions: High Frequency of Undiagnosed Ehlers-Danlos Syndrome in Congenital Adrenal Hyperplasia Patients

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**Introduction:** The contiguous gene deletion syndrome, CAH-X, was reported almost 8.5% in an Congenital Adrenal Hyperplasia of (CAH) Patients with a TNXA/TNXB chimera (Morissette et al 2015). This results in deletions of CYP21A2 gene, encoding 21-hydroxylase Necessary for cortisol biosynthesis, and TNXB, encoding the extracellular matrix glycoprotein tenascin-X (TNX). There are three TNXA/TNXB chimeras (CHI, CH2, CH3) That Differ in the junction site, resulting in TNXB haploinsufficiency or dominant negative effect Ehlers Danlos Syndrome and an (EDS) phenotype. Recently, it has been described to biallelic form of CAH-X syndrome.

The aim of study was to analyze esta copy number variations (CNV) and genetic status of TNXB gene in 58 CAH due to CYP21A2 Patients deletion to determine the frequency of TNXB Alterations in our population.

A Total of 58 unrelated carriers of CAH Patients CYP21A2 gene deletion (65 alleles) Were screened for TNXB defects. All the Patients Were Analyzed for the presence of CH1 by MLPA technique evidenced by 120 bp deletion in exon 35 and TNXB Were screened for other TNXB Alterations CH2 and CH3 related to by exon 40, 41 and 43 Sanger sequencing.

The presence of TNXB due to CH1 deletion was found in 28/65 (43%) alleles of CYP21A2 gene deletion carriers, while chimeras (CH1, CH2, CH3) Were found in 47/65 (75%) alleles. Of 58 Patients EVALUATED for CNVs, haploinsufficiency of TNXB was found in 39 Patients and Patients presented to four biallelic form.

High frequency of TNXB Alterations in CYP21A2 was found in our deletion alleles carrier population. Sanger sequencing and MLPA Resulted useful to TNXB characterize deletion. Genotype-phenotype correlation accurate remains to be elucidated In This cohort. Nevertheless, based on the results of esta study, we recommend to Evaluate TNXB status in These Patients, warranting assessment of connective tissue dysplasia Including cardiologic alterations in positive cases.

**Table 1.**

| | Basal | GH | DHT0.1 | GH + DHT0.1 | DHT0.25 | GH + 0.25 DHT |
|---|---|---|---|---|---|---|
| pJAK2/JAK2 | 0.53±0.06 | 0.93±0.24* | 0.43±0.07 | 0.74±0.15 | 0.59±0.16 | 0.89±0.23 |
| C-pSTAT5/STAT5 | 0.40±0.03 | 0.91±0.04* | 0.56±0.2 | 0.78±0.07 | 0.53±0.08 | 0.82±0.11 |
| N-pSTAT5/STAT5 | 0.38±0.05 | 0.95±0.035* | 0.33±0.12 | 0.67±0.13 | 0.46±0.19 | 0.74±0.2 |
| IGF-I | 0.23±0.02 | 0.63±0.03* | 0.33±0.01 | 0.59±0.08 | 0.29±0.03 | 0.55±0.1 |

* $P < 0.05$ vs Basal GH; n = 5.

## Androgen Effects Over Cellular Sensitivity to GH Do Not Appear to Be Direct, But Through May Be Mediated Aromatization to Estrogen

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**Introduction:** Previously we reported (Joint Meeting-Washington DC 2017) that relatively low concentrations of estradiol (E2: 20 pg/mL) and high concentrations of testosterone (T: 10 ng/mL), potentiate the JAK2/STAT5 signaling pathway induced by GH in the HEPG2 cell line. Our results suggest that critical concentrations of steroids may modulate GH sensitivity, but it is unknown whether these androgens effects are direct or mediated through aromatization to estrogen.

**Objective:** To evaluate the effects of dihydrotestosterone (DHT), a not aromatizable androgen to E2, on the activation of JAK2/STAT5 and IGF-I gene expression induced by GH in HEPG2 cells.

**Methods:** HEPG2 cells were grown in a steroid-free medium. At 80% confluence, cells were treated with or without DHT at different concentrations (0, 0.1, 0.25 ng/mL) for 24 h, and were subsequently stimulated with rhGH 40 ng/mL for 15 min. Cytoplasmic JAK2 and STAT5 and nuclear STAT5 were analyzed by Western-immunoblotting. IGF-I expression was studied by qRT-PCR after 24 h incubation with DHT, which was followed by 24 h co-stimulation with the sex hormone and GH. The data were analyzed by Kruskal Wallis Test and expressed as mean ± SEM. $P < 0.05$ was considered significant.

**Results:** GH significantly stimulated the phosphorylation and the expression of IGF-I in HEPG2 cells. Cells stimulated with different concentrations of DHT showed similar pJAK2 and pSTAT5 compared to basal levels. In cells preincubated with DHT, GH showed an increase in cytoplasmic pJAK2 and pSTAT5, but these levels were similar to those observed after stimulation with GH alone. In addition, nuclear pSTAT5 was also similar to that observed after GH alone. Expression of IGF-I was maintained when DHT and GH stimulation were combined.

**Conclusions:** The GH signaling pathway is not enhanced when HEPG2 cells are stimulated with relatively low or high concentrations of dihydrotestosterone, indicating that DHT does not appear to modulate GH sensitivity in HEPG2 cells. These data suggest that androgens may enhance the cellular sensitivity to GH through its aromatization to estrogen rather than by a direct effect.

## Circulating Klotho and FGF21 Leves in Children with Type 1 Diabetes During an 18-Months Follow-Up Study

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**Introduction:** Klotho has been identified as a putative aging-suppressor gene and co-receptor for FGF 21. The deficiency of Klotho has been associated with type 2 diabetes (T2D), and morbidity frequently observed in aging subjects. Recent studies showed that Klotho ameliorates β-cell damage in T2D. On the other hand, FGF21, a co-receptor of Klotho, is a critical regulator of long-term energy balance and metabolism. There is a lack of previous studies evaluating Klotho and FGF21 serum levels in type 1 diabetes (T1D).

**Aim:** To assess the serum concentration of Klotho and FGF21 in patients with T1D during an 18 months period, and determine the correlation of these hormones with duration of diabetes, HbA1c, and insulin dose.

**Methods:** Children with T1D (n:24, girls: 11) were studied. Klotho and FGF21 levels were determined at baseline and the end of the follow-up period by commercial ELISA. Mann-Whitney's U and Wilcoxon test and Spearman's correlation were used. Results are expressed as mean ± SEM.

**Results (Table):** Lower FGF21 levels were observed in T1D boys compared with T1D girls. A decrease at of FGF21 levels at follow-up compared to baseline was observed only in T1D boys. A negative correlation between Klotho levels and T1D duration at baseline was observed ($r = -0.397$, $p = 0.045$), but no association was present with HbA1c nor insulin dose. No correlation was observed between Klotho and FGF21 serum levels.

**Conclusions:** These data suggest that T1D boys exhibit lower FGF21 levels compared to T1D girls, and decreasing levels of this hormone are observed over time in the male gender; Klotho correlated negatively with increasing duration of this condition. This is the first longitudinal assessment of Klotho and FGF21 levels in T1D children. Future studies should evaluate the mechanisms explaining why girls with T1D exhibit elevated FGF21 levels and the decreasing Klotho levels with advancing duration of the disease. (FONDECYT:1170895).

**Table 1.**

| | Baseline | | | Follow-up | | |
|---|---|---|---|---|---|---|
| | All (24) | Girls (11) | Boys (13) | All (24) | Girls (11) | Boys (13) |
| Age (years) | 12.2±0.6 | 13.2±0.9 | 11.3±0.6 | 13.9±0.5 | 14.8±0.8 | 13.1±0.7 |
| Klotho (ng/ml) | 215±28 | 223±49 | 208±34 | 203±29 | 201±46 | 202±40 |
| FGF21 (pg/ml) | 264±58 | 366±93 | 187±31* | 218±546 | 332±86 | 121±26*, & |

* P < 0.05 vs. T1D girls T1D boys; & P < 0.05 T1D boys at follow-up vs. baseline.

## Parental History of Premature Ischemic Heart Disease Is Associated with Lipoprotein a Levels Apo a Isoforms and Carotid Intima Media Thickness in Mexican Adolescents

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**Objective:** To analyze the association of parental history of premature ischemic heart disease (PHPHD) with Lp (a) levels, apo (a) isoforms and carotid intima media thickness (CIMT) in adolescents.

**Methods:** In a cross-sectional study, we included 100 adolescents aged 14 to 18 years, 50 and 50 without PHPHD with, Both groups matched by age Were, sex and BMI. All participants completed cardiovascular risk factors standardized questionnaires. There Were Measured anthropometric indexes, blood pressure, serum fasting blood glucose, C-reactive protein, lipid profile, Apo A1, Apo B, Lp (a), apo (a) isoforms, LDL particle size, oxidation susceptibility of LDL and ITTC by B. Small mode ultrasound in apo (a) isoforms was low molecular weight defined with <22 KIV repeats.

**Results:** The antropometric, clinical and metabolic variables as well as Apo A1, Apo B, LDL particle size, LDL oxidation susceptibility of like were among with and without PHPHD adolescents. On the other hand, subjects PHPHD ADH with Increased ITTC (0.53 ± 0.04 mm vs. 0.47 ± 0.02 mm, p = 0.001), higher Lp (a) Concentrations [9.6 mg/dL (3.7–24.1) vs 6.1 mg/dL (2.2–16.0) p = 0.01] and higher prevalence of small apo (a) isoforms, 20% vs. 4%, p = 0.014) Compared When PHPHD Those without. Total Cholesterol, LDL-C, Apo B, blood pressure and PHPHD had a positive and significant association with the ITTC. Stepwise regression analysis Showed that systolic blood pressure and PHPHD independent predictors of CIMT Were.

**Conclusion:** Adolescents with Increased ADH PHPHD ITTA, Lp (a) Concentrations and Frequency of small isoforms. Systolic blood pressure and PHPHD Were Independently ssociated with CIMT. This is the first study to Evaluate the association of PHPHD with Lp (a) levels, apo (a) isoforms and CIMT in Mexican adolescents. Lp (a) levels and apo (a) isoforms are genetically determinated and there are not modifiable cardiovascular risk factors, so the appropiate identification will intervene in the early Allows risk factors in adolescent with proven PHPHD.

## Height Sitting Height and Lower Limbs Growth Velocity During Puberty in Hypophosphatemic Rickets

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Familial Hyphophosphatemic Rickets (HR) is the most frequent cause of hereditable rickets.

**Objective:** To report the growth velocity and biological parameters during puberty in children with HR.

**Methods:** Out of 96 children with HR, treated in our multidisciplinary team, between 1992 and 2018, 18 patients, 8 males and 10 females, provided sufficient data to analyze growth during puberty. All children received treatment with phosphorus and calcitriol. Growth data was collected from mid-childhood until adult height. Height and sitting height were measured with Harpenden instruments; Leg length was obtained by substracting sitting height from height. Individual growth curves were estimated by fitting the Preece Baines model 1 to each individual's data. Pubertal development was scored on Tanner scale. To analyzed growth curves, patients were divided in 2 groups: patients with good or poor compliance to treatment. Good compliance to treatment was defined if the patient had more than 80% of appointment and months per year of treatment according to local guidelines for HR.

**Results:** In males, the mean ± SD adult height was 158.65 ± 5.39 cm (–2.03 SDS) and 142.2 ± 1.98 cm c(–4.41 SDS) for those with good and poor compliance to treatment respectively. In the good compliance male's group, chronological age (CA) and maximal growth velocity were 13.30 ± 0.84 yr and 7.84 ± 0.63 cm/yr respectively. Total adolescent growth was 33.6 ± 6.08 cm. Mean CA at testis volume 4 and 20 cc, were 11.07 ± 1.22 and 14.69 ± 1.49 yr respectively. In females, the mean adult height was 147.23 ± 5.08 cm (–2.22 SDS) and 136.94 ± 7.42 cm (–3.92 SDS) for those with good and poor compliance to treatment respectively. In the good compliance female's group, CA and maximal growth velocity were 11.46 ± 0.63 yr and 6.95 ± 0.69 cm/yr respectively. Total adolescent growth was 28.27 ± 8.09 cm. Mean CA at Tanner breast 2 and menarche were 10.86 ± 0.9 and 12.71 ± 0.42 yr respectively. Mean CA at maximal growth velocity for height, sitting height and lower limbs of 4 males with good compliance were 13.2 ± 0.96, 13.64 ± 0.41 and 13.1 ± 1.16 yr, respectively. Mean maximal growth velocity were 7.58 ± 0.7, 4.33 ± 1.09 and 3.06 ± 0.29 cm/yr for height, sitting height and lower limbs respectively.

**Conclusions:** Height growth spurt was higher better in the good compliance to conventional treatment group. In males lower limbs growth spurt was less of magnitude than that of the sitting height.

## Novel EPAS1 HIF2A Mutation Associated with Paraganglioma and Polycythemia Case Report

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**Background:** A new syndrome of paraganglioma-polycythemia with or without Accompanying somatostatinomas has-been recently described, or mosaic Caused by somatic mutations of gain of function EPAS1, the gene encoding for the hypoxia-inducible factor (HIF2A). Paragangliomas and somatostatinomas are catecholamine and somatostatin producing neuroendocrine tumors.

**Case Report:** We describe the clinical Characteristics and the molecular findings of a patient WHO presented polycythemia and malignant paraganglioma with. She presented with polycythemia at 3 years of age and at 8 years old had a stroke due to a hypertensive crisis. A unilateral adrenal pheochromocytoma was diagnosed. Furthermore, she developed multiple abdominal surgeries paragangliomas which Several required. The patient has no evidence of somatostatinomas, but maintained high hematocrit.

**Methods:** Obtained DNA from blood, buccal cells and archival materials from two separate paragangliomas was Analyzed for SDHB, SDHD and EPAS1 encoding gene mutations. Results: A HIF2A/EPAS1 mutation (c.1592C>T, p.P531L) was found in the two separate paragangliomas, with approximately 20% and 15% of variant allele frequency (VAF). The mutation was detected in blood at Present <5% VAF and buccal cell DNA (~10% VAF), consistent with mosaicism. The mutation was absent in blood from Both parents, excluding germline transmission. No mutation was detected in SDHB or SDHD. The syndrome of paraganglioma-polycythemia results from activating mosaic EPAS1/HIF2A mutation leads to constitutive which stability of HIF2A and upregulation hypoxia-related genes, and genes Involved Including EPO in angiogenesis and metabolism.

**Conclusions:** This patient underscores the Importance of performing genetic screening in Children with pheochromocytoma/paraganglioma due to the high frequency of genetic mutations. The patient requires follow up and screening Continuing for somatostatinomas. Moreover, diagnosis of the syndrome have clinical value east since the identification of the Pathways Involved in Its pathogenesis May Have Implications therapeutic potential.

## Preimplantation Genetic Testing (PGT) for Carrier of SHOX – Related Haploinsufficiency

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Leri Weill dyschrondosteosis (LWD) is characterized by short stature, mesomelia and Madelung deformity. It is caused by haploinsufficiency of SHOX gene located in the pseudoautosome region of Xp22.3 and Yp 11.3. Most of the patients have deletions between 90 KB and 2.5 MB. A minority of them present point mutations. LWD is a genetic disorder that is transmitted by a pseudodominant pattern.

We report the request of a young couple with an increased genetic risk for having an affected children with LWD because the woman is carrier of this syndrome. MLPA analysis detected a deletion of 1.28 MB from X-000.436939 to X-001712090 (Hg18loc). According to the knowledge of the risk of transmission for their descendence is 50%, the couple decides to perform a PGT to avoid having affected babies. PGT consists of an in vitro fertilization procedure with genetic study of pre-embryos prior to being transferred to the uterus.

Prior accessing to the procedure a basic fertility studies on the couple were performed, which were normal. We had also to find the haplotype informative using several STRs linked to the deleted and flanking region. The STRs tested were: DXYS10093, DXYS10137, DXYS10138, DYS290, DXS1068, DXS1055 and DYS393. The STRs selected as informative to the study of the blastocysts were: DXYS10137, DXYS10093, DXS1055 and DYS393. The pre-embryos in the lab were obtained performing a standard IVF/ICSI procedure, except that on day 4 of the in vitro development, a drilling of the pellucide zone was carried out to favour the hatching on the fifth day and thus facilitate the biopsy of the trophoblast cells. Twelve metaphase II oocytes were aspirated, of which 9 fertilized normally and 5 of them reached the blastocyst stage on day 5 and 1 in day 6 post ICSI. After the biopsy the blastocyst were vitrified. The removed cells were intubated and frozen at −20 °c until lysis and amplification by QF-PCR with a mixture of the 4 informative STRs achieved. Of the 6 analyzed, three resulted with two copies of SHOX and three with haploinsufficiency. The woman was transferred three times, after preparing the endometrium with estrogens and progesterone. In the third transfer she achieved an evolutionary pregnancy that culminated with the birth of a normal and healthy baby. Based on the literature, it is the first time that a PGT is recorded in an homogeneous SHOX-related haploinsufficiency carrier.

## GH Reference Values in Serum and Whole Blood Spots on Filter Paper in Newborn by Electrochemiluminescence (ECLIA)

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Congenital Growth Hormone deficiency (GHD) in newborn is a rare disease, which can cause threat to life due to hypoglycemia that Begins in the first week of life. Reviews and consensus papers on the diagnosis of GHD in childhood Provide no evidence-based approach to the diagnosis of GHD in the neonatal period.

Few data Have Been Reported About the GH measurements in serum and dried blood spots on filter paper samples in healthy neonates born Appropriate for gestational age (AGA).

**Aims:** To establish GH reference values in serum and whole blood spots samples on filter paper in newborn and to compare the GH concentrations obtained.

**Subjects and Methods:** We analyzed 181 serum (F: 89, M: 92) and 216 whole blood spots (F: 109, M: 107) samples obtained from AGA neonates between 2–15 days of life.

GH concentrations were measured by ECLIA Roche C600, which is calibrated against the 2nd International Standard Code 98/574 in serum as well as eluted from filter paper samples. The 2.5–97.5 percentiles were calculated. The comparison of the GH measurements based on serum or filter paper was performed by Spearman correlation coefficient.

**Results:** The 2.5 and 97.5 percentiles results are shown in the table.

The Spearman correlation coefficient between the GH concentration obtained in serum and on whole blood spots samples was 0.88 ($p < 0.0001$).

**Conclusions:** The neonatal period is characterized by physiological high GH levels due to immature feedback mechanisms. GHD diagnosis can be realized only in the presence of an accurate GH reference values.

Human GH secretion is pulsatile from the very beginning, however, newborn screening card spotted with blood during the first week of life, when neonatal hypersomatotropism is present, provides such high levels that, even at the nadir of GH pulsatility determination of a basal values could contribute to detect GHD accurately.

**Table 1.**

| | Sample gender | n | 2.5th percentile GH (ng/mL) | 97.5th percentile GH (ng/mL) |
|---|---|---|---|---|
| F | Serum | 89 | 3.89 | 44.98 |
| M | Serum | 92 | 2.91 | 45.10 |
| F | Blood spots | 109 | 2.44 | 41.32 |
| M | Blood spots | 107 | 3.25 | 50.00 |

## Social Network-Based Social Support and Weight Status Among Adolescents: A Pilot Study

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**Objective:** We examined the cross-sectional relation between social network-based social support (SS) and weight-related outcomes among adolescents in a pilot study within the QUALITY cohort, a longitudinal study investigating the natural history of obesity in youth.

**Methods:** Participants (egos) completed a social network questionnaire, in which they nominated up to 10 people (alters) with whom they discussed important matters in the past year. Participants reported their own and each alters' age, sex, body shape, lifestyle behaviors (frequency being active, web surfing, eating healthfully), relationship (family, friend), frequency alter exercises with ego, and frequency alter encourages ego to exercise. We created a motivational SS score based on these two latter items, and a role-modeling SS score based on alters' body shape and lifestyle behaviors. Scores above the overall median were categorized as supportive. Outcomes were body mass index z-score (zBMI) and accelerometer-measured minutes of moderate-to-vigorous physical activity (MVPA). Multiple linear regressions adjusted for age and stratified by sex were conducted.

**Results:** 45 participants were included (29 boys); mean age was 16.4 years, zBMI ranged from –1.2 to 3.9, mean MVPA was 22.4 minutes/day. Participants nominated a mean of 6.6 alters (38% family and 62% friends). The motivational SS score was significantly associated with zBMI, positively in girls (+0.19 zBMI for a 10% increase in the proportion of supportive alters) and negatively in boys (–0.14 zBMI for a 10% increase in the proportion of supportive alters). Motivational SS was not associated with MVPA. Role-modelling SS was not associated with either outcome.

**Conclusion:** Our study suggests that the relation between perceived motivational SS and weight status differs between adolescent boys and girls. These preliminary findings suggest that leveraging social support to enhance lifestyle interventions needs to be sensitive to gender-based beliefs.

## A Novel Iodide Transport Defect-Causing NA+/I-Symporter (NIS) Carboxy-Terminus Mutant Uncovers a Critical Tryptophan-Acid Motif Plasma Membrane Transport Required for

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**Introduction:** I-transport defect (ITD) is an autosomal recessive disorder is the inability Whose hallmark of the thyroid follicular cell to mediate active I- accumulation. ITD is an uncommon cause of congenital hypothyroidism dyshormonogenetic due to loss-of-function mutations in the Na +/I- Symporter (NIS) -coding gene slc5a5. Here, we Aimed to determine Whether a pediatric patient with a clinical phenotype of an inactivating mutation ITD harbors in the slc5a5 gene, and if so, to ascertain the Molecular Mechanisms of the effect of the mutation on NIS function.

**Methods:** The whole coding region of the gene was PCR-slc5a5 amplified and subjected to Sanger sequencing, and in silico and in vitro functional computational studies of a newly Identified NIS mutation Were performed.

**Results:** We report a novel homozygous missense and loss-of-function mutation in the gene slc5a5 as a cause of congenital hypothyroidism dyshormonogenic. The proband Carries a G>A transition at position 1682 in exon 14 RESULTING in a Gly to Glu substitution at residue 561 (G561E) intracellularly located in the carboxy-terminus facing NIS. We show you reduce markedly I-that G561E When the protein uptake is heterologously Expressed in MDCK-II cells, the transport of G561E Because NIS to the plasma membrane is severely impaired. Significantly, G561Q NIS, like G561E, is severely retained in the endoplasmic reticulum. Bioinformatics fully reveal conserved tryptophan-acidic (WD) Whose motif disruption (W565A/D566A NIS) leads to NIS retention in the endoplasmic reticulum. Computational and biochemical analysis Indicates that G561E impair the recognition of the adjacent WD motif by the kinesin light chain (KLC) 2, just thus impairing mutant NIS exit from the endoplasmic reticulum. Moreover, short-hairpin RNA-mediated knockdown KLC2 in FRTL-5 cells you reduce NIS expression at the plasma membrane, and consequently minimal I- NIS-mediated accumulation.

**Conclusions:** Altogether, our data G561E Indicate that shifts the equilibrium of the Unstructured WD motif towards a more structured and rigid conformation.

Unable to Interact with KLC2, THUS Severely Affecting NIS maturation beyond the endoplasmic reticulum and reducing I- accumulation in the thyroid follicular cell.

## Effects of Cola Drinks and Nonnutritive with Nutritive Sweeteners on Glucose and Pancreatic Response. Crossover Trial in with Adolescents Obesity, Type 2 Diabetes and Eutrophics

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**Objective:** To Evaluate the glucose and pancreatic response after the intake of soft drinks and nonnutritive with nutritive sweeteners in adolescents with obesity, type 2 diabetes (T2D) and eutrophics.

**Methods:** We crossover trial to Conducted in adolescents (10 with obesity, 10 and 10 eutrophics with T2D). We Measured serum levels of glucose, insulin and glucagon at 0, 30, 60, 90 and 120 min after drinking 355 ml of the following beverages: Drink with sucrose cola, with aspartame/acesulfame-K, with sucrose/Stevia, and sparkling water. The washout period Between the beverages consumption was 1 week. In every occasion, the participants HAD 8 hours. They fasted, and any other uses They didn't meal through the two hours after consumption of each beverage. We Analyzed the Differences in different periods of time and in the area under curve.

**Results:** As expected, we Observed an Increase in glucose at 30 min after the consumption of glue Drink with sucrose, with higher levels in participants with T2D (~60 mg/dL), followed by eutrophics (~46 mg/dL) and lowest in participants with obesity (~27 mg/ dL), $p = 0.05$. These changes in glucose proportional to Were an insulin levels (~900, ~1240 and ~2200 pg/mL respectively, $p = 0.05$). DESPITE of sucrose content of the tail Drink with Stevia, we Observed Increase of a lightly glucose levels at 30 min in the three groups of participants (11–27 mg/dL) and to decrease at 60 min, with the lowest levels in comparison with the other three participants with beverages in obesity and eutrophics (~4–9 mg/dL), but not in Patients with T2D ($p = 0.05$). Although the glucose levels Between Were like sparkling water and soda with the aspartame/acesulfame-K.

**Conclusion:** The serum glucose levels are similarly after the intake of cola drinks with aspartame/acesulfame K and sparkling water. However, cola drinks with nonnutritive sweeteners are not inert, and They Could Affect the pancreatic hormone response.

## Depression Screening in the Pediatric Diabetes Clinic: Integrating a Clinician-Administered, Patient Health Questionnaire

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**Background:** Depression is under-recognized in children with type 1 diabetes. We administer the Patient Health Questionnaire-2 (PHQ-2), a validated, two-question depression screening tool, in our routine diabetes clinic visits for all children over 12 years of age. The aim of this study was to determine if PHQ-2 screening identifies patients who may benefit from behavioral health inter-

vention. We also studied the demographics and resource utilization of children who screened positive using this test.

**Methods:** We assessed children aged ≥12 years attending the diabetes clinic at the Children's Hospital of Philadelphia from July 1, 2016 to May 1, 2017 in a retrospective chart review. Results of those who screened positive on this test (Score ≥3) were compared to those screened negative using chi-squared and student's t-test for categorical and continuous variables, respectively.

**Results:** Of the 1539 eligible children, 236 (15%) scored >0 and 62 (3.9%) screened positive. Of these, 19 (31%) were referred to behavioral health for initial assessment, while 11 (18%) had previously been evaluated. Females were more likely to screen positive (5.3% vs 2.7%, $p < 0.001$) as were black versus white patients (8% vs 2.8%, $p < 0.001$). Those with positive screens had higher mean HbA1c (10 vs 8.5%, $p < 0.001$), number of emergency department visits (0.27 vs 0.08, $p = 0.03$), hospital admissions (0.45 vs 0.1, $p = 0.01$), and missed outpatient appointments (1 vs 0.6, $p < 0.001$) over the previous year. Mean patient ages (16.9 vs 16.5 years, $p = 0.13$) and durations of diabetes (6.5 vs 7.3 years, $p = 0.17$) were similar in both groups.

**Conclusion:** Depression screening using the PHQ-2 can be conducted in the context of routine outpatient diabetes visits. This tool identified children with previously unrecognized depressive symptoms who demonstrated disparities from the overall clinic population with regard to gender, race, glycemic control, hospital resource utilization.

## Genetic Evaluation of Syndromic Short Stature Children Born Small for Gestational Age

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**Objectives:** To perform a clinical and genetic-molecular investigation of a group of syndromic SGA Patients without catch-up growth.

**Methods:** The initial cohort of 118 Patients Consist born SGA [birth weight and/or length standard deviation score (SDS) ≤–2 for gestational age] without catch-up growth at the age of 2 or above [height SDS ≤–2] and dysmorphic features, developmental delay and/or intellectual disability. These Patients Were EVALUATED clinically, laboratory and radiologically. They Were classified as Known (n = 53) or unknown (n = 65) syndromic short stature, According to the establishment of the clinical diagnosis by routine exams and clinical evaluation. We selected to the study Patients with only unknown syndromic short stature patients. They Were submitted for molecular karyotyping (aCGH/SNPA) and/or whole exome sequencing (WES).

**Results:** Sixty-five Patients Were classified as unknown syndromic short stature based on the clinical data. Forty-three underwent aCGH/SNPA screening and 12 (27.9%) Patients HAD pathogenic CNVs. Twenty-six Patients Were submitted to WES and 13 (50%) pathogenic ADH/possibly pathogenic variants in genes associated with growth disturbance Already: ANKRD11 (n = 3); COL2A1 (n = 2); SRCAP (n = 2); BRCA1; POC1A; IGF1R; PTPN11; KIF11 and PCNA (each one, n = 1). These genes associated were with rare syndromic conditions associated with growth impairment. All are extremely rare SNVs identified or absent in public database, were predicted to be deleterious and segregated with the phenotype.

**Conclusion:** The rarity, variability and clinical heterogeneity of syndromic short stature to clinical diagnosis Makes Establishing difficult. Our genetic evaluation protocol established the definitive diagnosis in 38.4% (25/65) of a group of Patients with syndromic short stature unknown. A clinical diagnostic paradigm with a systematic evaluation phenotype, molecular karyotyping, and exome sequencing Increases the diagnostic rate of unknown syndromic short stature patients.

## Central Precocious Puberty in a Girl with Unusual Presentation of Schimmelpenning-Feurstein-Mims Syndrome a Case Report

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**Introduction:** Craniopharyngiomas the most commonly found are hypothalamic pituitary tumor in childhood isolated. At diagnosis, Most Patients present with Pain and endocrine symptoms related to the rupture of the hypothalamic-pituitary axis function.

In all, the manifestations are associated to hypopituitarism, but less Frequently, precocious puberty May Occur. Although the tumors of the central nervous system are common childhood neoplasms Relatively, the association with early puberty is uncommon. Sometimes, even the distant tumors of the central nervous system due to GnRH can Stimulate the hypothalamic pituitary compression of cases of region in hydrocephalus. We report a case of a child with precocious puberty Associated with giant craniopharyngioma. Currently, the endocrinological comorbidi-ties are under control.

**Case Report:** LSS, 5.4 years, from São Paulo. Birth through vaginal delivery, 34 weeks gestational age of.

At 15 months, she developed speech difficulty, visual loss and strabismus. A Magnetic Resonance Imaging was performed, with the image of an extensive and calcified craniopharyngioma. At 3 years of age she underwent surgery to cystic drainage, without success and an Ommaya chamber was inserted for future intrathecal chemotherapy. Six months later, she presented loss movement in the right side of the body due to tumor compression. At the age of 4.3 years the patient received intralesional. The therapy was not able to slow the progress of the tumor. At 4.6 years, to surgical resection was performed. The chamber and 90% of the craniopharyngioma was removed, peritoneal shunt valve was inserted for hydrocephalus treatment. A month after the surgery, the patient was admitted to our hospital, for Central Hypothyroidism monitoring, which was diagnosed prior to resection. At the occasion, Tanner stage was B1P1 her and she was receiving Levothy-roxine 25 mcg./day. At the same time, she started breasts development.

Puberty Rapidly evolved, with progression from Tanner B1P1 to B3P1 in 3 months. At 4.9 years, the patient presented a bone age of 6.8 years. In the same year a new surgical approach was performed peritoneal with bypass valve reinsertion due to a local complication. She is currently being treated with Leuprolide Acetate 7.5 mg every 28 days, Levothyroxine, Baclofen and Valproic Acid, Tanner stage of Maintaining B3P1.

**Conclusion:** Although rare, early puberty May be Associated with craniopharyngioma. Probably Caused by high intracranial pressure, but May Also be a consequence of surgical resection, since the patient presented the symptoms 2 months after treatment definitive.

## Deterioration of B-Cell Function from Adolescence to Emerging Adulthood Is Associated with BMI Trajectory Since Early Childhood

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**Background:** The prevalence of type-2 diabetes (T2DM) has tripled in the last 20 years in young populations associated to the obesity epidemic. Early adiposity rebound (EAR) is a strong determinant of deterioration in β-cell function. We explored the association of BMI trajectory from infancy to adolescence with insulin sensitivity and β-cell function in adolescence and emerging adulthood.

**Methods:** Observational prospective study in n = 532, 22 year-olds (51% males) from a Chilean infancy cohort. BMI was measured from birth to 22 y. Adiponectin, Glucose (Gli) and insulin were measured at 16 y and 22 y. HOMA-IR, HOMA-%β, HOMA-%S, Disposition Index and HOMA-AD were calculated.

Four groups were defined: participants who were never obese (NOB); participants with obesity only at 16 y (recent-onset obese, ROB); participants who were obese at 5 y but not at 10 and 16 y (formerly obese, FOB); and participants who were obese since the age of 5 (persistently obese, POB). Associations were tested using the Kruskal-Wallis test and the Wilcoxon signed-rank test.

**Result:** At 16 y and 22 y, ROB and POB participants had significantly higher values of Gli, insulin, HOMA-IR, HOMA-%β, and HOMA-AD, and lower values of HOMA-S and DI, compared to NOBs and FOBs. No differences were found between NOBs and FOBs and between ROBs and POBs. All groups had a significant variation of HOMA-IR, HOMA-%β, HOMA-%S and HOMA-AD from 16 y to 22 y, but only the POB group had a significant increase in Gli and a significant decrease in DI over this period.

**Conclusion:** Current and persistent obesity were associated with impaired insulin sensitivity and impaired β-cell function in adolescence and emerging adulthood. Participants with EAR who transitioned to normal weight had similar insulin sensitivity and β-cell function compared to participants who were never obese. Attacking EAR might be an effective strategy to prevent early onset of T2DM. Funding: NHLBI-HL088530, CONICYT-PAI79140003.

## Clinical and Molecular Characterization of Pediatric and Young Patients with Pituitary Adenomas

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**Objective:** Pituitary tumors in pediatric and young patients comprise a rare pathology. They present particular clinical and molecular characteristics, and often associate genetic variations,

**Table 1.**

| Patient | Age (Years) | Gender | Tumor type | MRI (mm) | Gene |
|---|---|---|---|---|---|
| 1 | 14.1 | M | GH-secreting | 15 | AIP |
| 2 | 19.0 | F | PRL-secreting | 10 | CDKN1B |
| 3 | 10.3 | M | GH-secreting | 40 | AIP |
| 4 | 15.9 | F | PRL-secreting | 18 | SDHB |
| 5 | 23.0 | M | PRL-secreting | 10 | AIP |
| 6 | 15.9 | F | PRL-secreting | 13 | MEN1 |
| 7 | 16.5 | F | PRL-secreting | 18 | SDHD |
| 8 | 13.9 | F | ACTH-secreting | 55 | AIP |
| 9 | 10.8 | F | Non-secreting | 12 | PRKAR1A |
| 10 | 28 | F | GH-secreting | 8 | MEN1, SDHD |
| 11 | 12.9 | M | PRL-secreting | 24 | AIP, SDHD, PRKAR1A |
| 12 | 13.1 | F | PRL-secreting | 24 | SDHD |
| 13 | 13 | M | PRL-secreting | 13 | SDHD |
| 14 | 11.1 | F | PRL-secreting | 26 | PRKAR1A |
| 15 | 9.9 | F | PRL-secreting | 5 | SDHD |

mostly in the AIP gene and less frequently in MEN1, GNAS, CDKN1B and PRKAR1A.

The aim of this study is the clinical characterization of children, adolescents and young adults diagnosed with familial or sporadic pituitary adenoma, and the molecular study by next generation sequencing (NGS).

**Methodology:** Clinical characteristics at diagnosis of patients under 30 years presenting a pituitary adenoma were collected and genetic characterization was performed in germline using a targeted gene panel by NGS. In silico analysis were done and PCR and Sanger sequencing was used for variant confirmation and to study parents and affected family members.

**Results:** We included 91 patients under 30 years old, 57% corresponding to pediatric individuals. The most frequent type of adenomas is prolactinoma (44%), followed by non-functioning (21%). Alterations in heterozygosis have been identified in 15 patients.

**Conclusions:** A genetic alteration was observed in 16.5% of the studied patients. These subjects tend to be younger at diagnosis and PRL-secreting.

The p.Arg271Trp mutation in the AIP gene is the most frequent among the sporadic cases of gigantism.

## Advances in Treatment and Molecular Studies of Pediatric Pheochromocytoma (PCC) and Paraganglioma (PGL): A Large Single Center Cohort

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Pheochromocytoma and paraganglioma are rare Tumors that causes 0.5–2% of hypertension in pediatric Patients and Constitute a treatable cause of surgically arterial hypertension. These Tumors are inherited in as much as 80% in pediatric cases, and all Patients with Mutations Should be followed closely for the risk of recurrence and malignancy. Advances in surgical treatment and molecular studies Have improved the management of These patients.

**Aim:** To report a large series of pediatric pheochromocytoma and paraganglioma Patients with seen at a single center since 2005 to 2017.

**Results:** Patients seventeen (12 ills) were included surgical procedures and 20 Were performed. All Patients HAD catecholamines elevated levels. Eleven Patients HAD unilateral PCC (4 recurrence), bilateral PCC 3 3 2 ADH PGL and simultaneous PGL and PCC. 16/20 In laparoscopic surgeries was performed, One of These ended in an open surgery. In all of them intra arterial surgical Control of hypertension was adequate. Four surgeries Were made with the traditional technique due to the complexity of tumor location. Mean time for laparoscopic surgical approach was 134 ± 66 vs 173 ± 92 minutes for open surgical approach (p = 0.22). Time of hospitalization was lower in Patients Significantly WHO underwent open surgery laparoscopic vs (66.8 ± 13.8 vs 105.6 ± 36 hours, respectively, p = 0.04). In all studies Patients genetic Were performed. Ten Patients ADH gene mutations in vhl and 4 in SDHB gene. One patient probably had a pathogenic variant in the SDHD gene and a probably benign variant in the SDHB gene. In conclusion, we highlight that Pediatric Patients with PCC and PGL can be Treated with a minimally invasive surgical procedure Minimizing the risk of hypertensive crises and lowering days of hospitalization. In Addition, molecular genetics is mandatory In These Patients in order to improve increase follow-up.

## Neonatal Screening for Congenital Adrenal Hyperplasia CAH Comparison of Methods and Gestational Age Obtaining GA Related Cutoff Values

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**Introduction:** CAH screening is mandatory in Argentina since 2007. Neonatal screening in the Argentine public health system is organized as a network of jurisdictional laboratories (provincial/regional), supplied by the National Ministry of Health. The adoption of a new analytical system (Quantase, BioRad) for the Determined national network need to reevaluate the cut-off values and compare Their performance with a Previously Known methodology (DELFIA, PerkinElmer).

**Objective:** To compare methods and to Obtain Both cutoff values based on gestational age corrected (CGA).

**Materials and Methods:** In 779 samples from newborns dried blood, 17OHP was Analyzed using two competitive immunoassays: Method A: Quantase 17OHP Neonatal Screening (Evolys TwinPlus equipment) and Method B: DELFIA Neonatal α-17OHP (VICTOR fluorometer). Statistical analyzes Were performed using MedCalcV13.1.2 software. Linear regression Between Both analytical systems was performed. CDC 17OHP QC materials (Atlanta, USA) was EVALUATED at low, medium and high levels (Target Values: 37.1; 68.7; 131.0 nmol/L blood) and Were used to evaluate-accuracy (Recovery%) and interassay precision (CV%). Bland Altman (diferencia and plots ratio) Were Analyzes performed to compare metodologías. To cut off values defined samples Were divided into groups CGA (weeks) was 17OHP Whose

**Table 1.**

| | Low-A | Medium-A | High-A | Low-B | Medium-B | High-B |
|---|---|---|---|---|---|---|
| Recovery, % | 93.7 | 85.9 | 87.2 | 89.9 | 111.6 | 113.3 |
| CV, % | 14.1 | 13.1 | 19.3 | 12.5 | 17.7 | 15.6 |

**Table 2.** Statistical parameters

| | 17OHP nmol/L Mean blood– | SD | Median | 97.5th percentile | 99th percentile |
|---|---|---|---|---|---|
| GR1 | 35.8 | 36.7 | 25.5 | 151.2 | 188.6 |
| GR2 | 22.2 | 16.2 | 17.0 | 67.6 | 78.5 |
| Gr3 | 10.6 | 7.3 | 8.8 | 30.7 | 41.3 |

mean statistically different (F-ratio 102.7; p = 0.001; Scheffe test for all pairwise comparisons): Gr1: <34 (n = 53); Gr2: 34–36 (n = 95); Gr3: >36 (n = 525). For each group, population parameters (mean, SD, median) and 97.5 and 99 percentiles were evaluated.

**Results:** Regression analysis was: y = 4.6298 + 1.0277x (95% CI: 3.9145< b <5.3451 and 0.9817< a <1.0737) (p = 0.0001). See Table 1.

Limits of agreement from Bland and Altman difference plots ratio: Mean (± 1.96DS): –4.9 (–20.6 to 10.6) and 0.7 (–0.4 to 1.8). See Table 2.

**Conclusions:** Quantase Screening Neonatal 17-OHP Demonstrated good agreement and analytical performance Compared to DELFIA. It was able to Obtain preliminary cut-off values adjusted for CGA.

## A 260 kb Deletion Mapping 420 kb Upstream to SOX9 Identified in a 46, XY Female Without Campomelic Dysplasia and in Her Mother with Premature Ovarian Failure and 46, XX Karyotype

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SOX9 acts as a transcription factor testis-activating downstream of SRY, playing a critical role in Sertoli cell differentiation with testis cord formation and subsequent differentiation chondrocytes. Due to mutations or deletions in 17q24.3 genomic, SOX9 haploinsufficiency causes campomelic dysplasia (CD) in combination with male-to-female sex-reversal In about 70% of 46, XY Individuals. SOX9 expression is regulated by Several long-distance Enhancers/cis regulatory elements, Extending 1.5 Mb upstream and downstream of the coding sequence, Whose disruption causes disorders of sex development and phenotypic variability with bone disease. We report to deletion of SOX9 present in 46, XY female with delayed puberty. The same deletion was found in her 46, XX mother with premature ovarian failure.

**Case Report:** A 14.5 yr-old girl was incomplete pubertal development Referred for. Familial background: mother 36 yr-old with polycystic ovaries and amenorrhea since 33 yrs of age, maternal cousin with menopause at 36 yrs, and Grandmother with delayed puberty. At clinical examination: Were height and weight at 3rd–10th centiles respectively, pubertal development BI/III, PH II and external female genitalia standard. No skeletal malformations Were Observed. Lumbar Spine densitometry Showed low bone mineral density. Pelvic ultrasound detected a small uterus (29x7x14 mm) and two images Corresponding to small gonads (18 and 16 mm).

**Laboratory Results:** LH 44 IU/L; FSH 128 IU/L; E2 10 pg/mL; T 41 ng/dL. High levels of gonadotrophins (Repeated one month apart), and low AMH (<1.2 pmol/L) gonadal dysgenesis confirmed complete. Karyotype: 46, XY. Both parents Have Normal karyotypes. Prophylactic gonadectomy was performed, histological analysis Showed bilateral streak without germ cells.

**Molecular Studies:** Direct sequencing of mutation analysis of causative genes for Known 46, XY DSD: SRY and NR5A1 did not reveal mutations. Copy-number Alterations Were analysed CYTOSNP using 850K (Illumina) and Karyoarray®8x60K (based Agilent CGH) in the patient and her parents. We identified by CMA to heterzygous we at 17q24.3 deletion upstream position, encompassing 32.5 kb sex-reversal region of SOX9. The deletion, present in the patient an her mother, was in physical length 260 kb and 420 kb started at a position upstream to the codon star SOX9. ACCORDING to the databases Follows the patient's karyotype was rewritten as: 46, XY. arr [hg19] 17q24.3 (69436041-69696519) x1. Our results detected a new case of 46, XY gonadal dysgenesis complete without campomelic dysplasia, and support the notion that the 32.5 kb DNA XYSR contains elements essential for testicular development. We suggest for the first time an association Between a deletion in the SOX9 regulatory sequences and premature ovarian failure in 46, XX female.

## Disease Monitoring Program (DMP) In X-Linked Hypophosphatemia (XLH): A Long-Term, in Longitudinal Outcomes Study Patients with XLH

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X linked hypophosphatemia (XLH) is a chronically debilitating disorder caused by inactivating mutations of the PHEX gene, resulting in excess FGF23 and defects in renal phosphate reabsorption. The resulting hypophosphatemia impairs bone mineralization and musculoskeletal function. Given that XLH is a rare disease, there is a lack of long-term longitudinal information on the XLH disease state.

The XLH Disease Monitoring Program (XLH-DMP) is a prospective, multinational, longitudinal outcomes study to systematically describe the clinical, radiographic and biochemical manifestations and progression of XLH in children and adults. Furthermore, the XLH-DMP will collect real-world information on long-term safety and effectiveness of burosumab, a fully human monoclonal antibody that inhibits excess FGF23, recently ap-

proved in the US and EU for the treatment of XLH. The XLH-DMP will enroll ≥500 patients with confirmed clinical diagnosis of XLH, of which ≥200 will be pediatric patients (age <18 years), in the US, Canada, and Latin America. The XLH-DMP will include patients who may or may not be treated with burosumab during the 10-year course of the study. All patients who previously participated in burosumab clinical trials will be invited to participate. The XLH-DMP will follow Good Clinical Practice standards.

All patients will be assessed at scheduled in-clinic visits at study entry, and at Years 1, 3, 5, 7, and 10, with additional visits at Years 2, 4, and 6 for pediatric patients from burosumab clinical trials. Key laboratory assessments will include serum phosphorus concentration. Renal monitoring will include assessment of serum and urine creatinine, urine protein-to-creatinine ratio, and nephrocalcinosis by renal ultrasound. Scheduled radiographs will be included to assess rickets and lower leg deformities in children, and presence and healing of fractures/pseudofractures in adults from burosumab clinical trials. Age-appropriate patient-reported outcomes will assess pain and physical function. In addition, all serious adverse events (AEs) and burosumab-related AEs, prior/current concomitant medications, work/school and disability status, XLH treatment satisfaction, and healthcare resource utilization will be collected every 6 months, by phone or in-clinic. The XLH-DMP will establish a comprehensive dataset that will lead to improved understanding of the natural history of the disease, and provide further insight into the long-term safety and effectiveness of burosumab treatment in patients with XLH. Our dedicated approach to monitor patients longitudinally in a real-world setting may overcome issues encountered with patient registries and may provide more useful outcomes for rare diseases like XLH.

## Ectopic Thymus Intrathyroidal in the Differential Diagnosis of Thyroid Nodules: An Experience in 147 Pediatric Patients

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**Introduction:** Ectopic intrathyroidal thymus is a rare benign condition caused by migration of the thymus during embryogenesis. The disorder is asymptomatic, in the majority of cases it is incidentally diagnosed as a thyroid nodule.

**Objective:** The aim of this study was to report the intrathyroidal location of ectopic thymic tissue and to describe the sonographic findings in children to alert physicians on the benign nature of this condition in order to avoid invasive imaging studies and/or unnecessary surgeries.

**Methods:** A retrospective descriptive study was conducted consisting of a review of the clinical charts and thyroid ultrasonography studies by a single specialist, from January 2010 to August 2017 with nodular images in the thyroid gland. Ectopic intrathyroidal thymus was defined as hypoechoic intrathyroidal lesions with punctuate, bright internal echoes "spiculated" features that do not change during follow-up.

**Results:** Of a total of 147 patients with thyroid nodules we identified 12 children with lesions suggestive of an intrathyroidal thymus (8.1%). Mean age at diagnosis: 4.25 years.

The intrathyroidal thymus was an incidental finding in all cases. Images were unilateral in eight and bilateral in four patient. All lesions were located in the mid and/or posterior portion of the gland. Mean size was 0.64 x 0.6 cm. On ultrasonography in all cases the lesions were hypoechoic with punctuate, bright internal echoes and without significant vascularization.

A watch-and wait-attitude with sonographic follow-up (mean 1.62 years) was adopted in all patients except a 7-year-old boy who presented with uncertain findings. In this case, surgical resection was performed and pathological examination confirmed intrathyroidal thymus tissue.

**Conclusions:** Thymic inclusions in the thyroid gland are a rare but increasingly common finding, possibly related to the use of ultrasonographic Increased studies. Pediatricians and Radiologists Should be aware of esta entity to differentiate it from other thyroid lesions Avoiding unnecessary studies and treatment in These patients.

## Biomarkers for the Failure of Beta Cells in Mexican Children Diagnosed Type 1 Diabetes Mellitus With: IAPP Cytotoxic Oligomers

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**Objective:** To detect cytotoxic oligomers hIAPP (CO) In Patients diagnosed with one type diabetes mellitus (T1DM) and Their chronic complications.

**Methods:** Transversal analytical, observational, ambispective, blind study. The hIAAP CO Were produced in vitro in order to obtener rabbit polyclonal antibodies. An indirect ELISA and Western blot Were developed to Identify them blindly. Demographic, clinical and metabolic control variables Were registered. Analysis: General linear model with significance p = 0.05. Pela Investigation and Ethics Committees of the IMSS and INP.

**Results:** We presented 53 Patients with T1DM. Average age of 13 ± 3.5 years, 47.5 evolution (42.4) suffering from bad months and metabolic control (HbA1c 10.1 ± 2.2%).

The complications associated non-linearly with the number of oligomers (R2 = 008, p = 0.27) Were metabolic syndrome in Accordance to IDF, dyslipidaemia, hypertension and ALT elevation. Number of chronic complications presented: none 56% 18.8% one, two 7%, 15.1% and 1.9% three four.

**Conclusions:** This study shows that pioneering the hIAPP COs are biomarkers for the damage of β cells in Patients with T1DM and are associated with chronic complications.

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## An Intensive 12-Month Multidisciplinary Program For Children With Newly Diagnosed Type 1 Diabetes Improves Glycemic Control Through 2 Years

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**Background:** The diagnosis of type 1 diabetes (T1D) in a child brings significant medical, psychosocial and educational challenges for the child, parents and medical team. We developed a structured multidisciplinary program that spanned this first year with the goal of supporting families as they moved along the continuum from novice to expert in managing T1D, and assessed the durable effect of this program on glycemic control in children with newly diagnosed T1D.

**Methods:** The Type 1 Year 1 (T1Y1) program included assigning a diabetes educator who tailored the program of diabetes education to the family lifestyle and their readiness to take on more independence. Coaching was provided via telephone, electronic communication, structured 2-hour one-on-one education appointments, and group classes. Structured social work and nutrition appointments were also provided, and multidisciplinary T1Y1 team meetings with patient reviews were implemented. We identified all patients diagnosed with T1D in the two years before (7/1/12 to 6/30/14: Controls) and after (7/1/14 to 6/30/16: T1Y1 Group) the start of the T1Y1 program. A clinical diagnosis of T1D and at least one positive diabetes autoantibody (anti-GAD, anti-insulin, anti-ICA512 or anti-ZnT8) was required for inclusion in an intention-to-treat analysis. Baseline demographics and hemoglobin A1c (HbA1c) measurements at baseline, 6, 12, 18 and 24 months from diagnosis were recorded.

**Results:** There Were 331 Patients in the Control group and 418 in the intervention group. The distribution of age, sex and severity of ketoacidosis at diagnosis were similar between groups, but there

**Table 1.**

| | Pre-T1Y1 | Post-T1Y1 | p |
|---|---|---|---|
| Number | 331 | 418 | |
| Male, n (%) | 184 (55.6) | 233 (55.7) | 0.97 |
| Age, years | 10.3 (4.3) | 10.4 (4.5) | 0.9 |
| *Insurance* | | | |
| Commercial | 254 (76.7%) | 289 (69.1%) | 0.047 |
| Medicaid | 66 (19.9%) | 107 (25.6%) | |
| Insulin pump in first year | 75 (22.7%) | 120 (28.7%) | 0.06 |
| CGM in first year | 21 (6.3%) | 61 (14.6%) | <0.001 |
| Attended AHM Class | 200 (47.8%) | | |

**Table 2.**

| | Pre-T1Y1 | Post-T1Y1 | P |
|---|---|---|---|
| All Patients | | | |
| 6 months | 7.16 (6, 7.5), n = 280 | 6.6 (6, 7.5), n = 388 | <0.001 |
| 12 months | 7.7 (6.9, 8.5), n = 277 | 7.3 (6.5, 8.2), n = 375 | 0.001 |
| 18 months | 7.9 (7, 8.8), n = 267 | 7.6 (6.8, 8.5), n = 308 | 0.043 |
| 24 months | 8.1 (7.1, 9), n = 266 | 7.8 (7, 8.7), n = 204 | 0.096 |
| ≤5 years | | | |
| 6 months | 7.85 (7.3, 9), n = 38 | 7.7 (7.1, 8.5), n = 58 | 0.15 |
| 12 months | 7.5 (7.5, 8.6), n = 37 | 7.8 (7.2, 8.6), n = 57 | 0.66 |
| 18 months | 7.8 (7.15, 8.7), n = 37 | 8.05 (7.4, 8.63), n = 46 | 0.7 |
| 24 months | 7.6 (7, 8.35), n = 37 | 7.7 (7.2, 8.63), n = 32 | 0.6 |
| 5.1–11.9 years | | | |
| 6 months | 7.2 (6.7, 7.9), n = 138 | 6.7 (6.1, 7.4), n = 172 | <0.001 |
| 12 months | 7.85 (7.3, 8.5), n = 134 | 7.3 (6.7, 8.1), n = 170 | <0.001 |
| 18 months | 8.1 (7.2, 8.8), n = 131 | 7.7 (6.9, 8.4), n = 134 | 0.03 |
| 24 months | 8.2 (7.3, 8.95), n = 129 | 7.95 (7, 8.7), n = 92 | 0.3 |
| ≥12 years | | | |
| 6 months | 6.6 (6, 7.6), n = 103 | 6.4 (5.7, 7), n = 158 | 0.02 |
| 12 months | 7.35 (6.3, 8.6), n = 106 | 6.9 (6.2, 7.9), n = 148 | 0.14 |
| 18 months | 7.4 (6.6, 8.8), n = 99 | 7.4 (6.4, 8.7), n = 128 | 0.3 |
| 24 months | 8.1 (6.75, 9.4), n = 100 | 7.5 (6.7, 9), n = 80 | 0.12 |
| ≥12 years Female | | | |
| 6 months | 6.6 (6.1, 7.7), n = 38 | 6.6 (6, 7.1), n = 60 | 0.5 |
| 12 months | 7 (6.4, 7.7), n = 39 | 7 (6.4, 7.7), n = 60 | 0.6 |
| 18 months | 7.3 (6.4, 8.5), n = 37 | 7.5 (6.8, 8.5), n = 50 | 0.4 |
| 24 months | 7.7 (6.6, 8.5), n = 34 | 7.6 (6.9, 8.8), n = 29 | 0.8 |
| ≥12 years Male | | | |
| 6 months | 6.7 (5.9, 7.6), n = 65 | 6.3 (5.6, 7), n = 98 | <0.01 |
| 12 months | 7.5 (6.6, 8.7), n = 67 | 6.8 (6, 8.2), n = 88 | 0.043 |
| 18 months | 7.9 (6.6, 9), n = 62 | 7.3 (6.2, 8.9), n = 78 | 0.07 |
| 24 months | 8.2 (6.9, 9.9), n = 66 | 7.3 (6.6, 9.1), n = 51 | 0.048 |

was a higher proportion of patients without private medical insurance (a surrogate marker for lower socioeconomic status) in the T1Y1 group (25.6 vs 19.9%, p = 0.047). Median HbA1c was lower in the T1Y1 group at 6 (6.6 vs 7.2%, p < 0.001), 12 (7.3 vs 7.7%, p = 0.001), and 18 (7.6 vs 7.9%, p = 0.043) months. The A1c difference was similar, but failed to reach statistical significance at 24 months from diagnosis (7.8 vs 8.1%, p = 0.09). The greatest augmentation of outcomes was observed among 5 to 12-year-olds, and in teenage male patients.

**Conclusion:** An intensive, multidisciplinary diabetes management program which Provides active coaching to families of children with new-onset T1D Contributes to a sustained improvement in glycemic control. As the effect size Appears to Wane outside of the intervention period, our next step will be to Develop a less-intensive, but sustainable program to run beyond the first year. Further analysis of our data May lead to a better understanding of the Differences in efficacy of This Program amongst different demographic groups.

**Included:** Positive for one or more of anti-insulin, -GAD65, -ICA512 or -ZnT8 antibodies. within 3 months of A1c 6-, 12-, 18- and 24-months. If more than one available, the closest to the date was used. All children included in analysis, program Regardless of Compliance with (intention to treat).

## Novel LRP5 to Osteoporosis Associated Variant Syndrome Pseudoglioma

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**Background:** Osteoporosis is a complex disorder, influenced by environmental and genetic factors. Primary osteoporosis is a rare early onset disorder with high morbidity and mortality. Wnt signaling pathway is involved in bone remodeling regulation.

**Case Report:** Boy born from consanguineous parents with history of retinal detachment in the maternal line. Delivered at term, AGA with microcephaly. Bilateral congenital retinal folds caused him progressive irreversible vision loss and microophthalmy. Since 5 y he developed two vertebral and four low trauma long bone fractures. Referred at 8.6 y, he presented normal weight, height and growth velocity, Tanner stage I, microcephaly and bulky vision. White sclera, normal teeth, absence of hyperlaxity, slight kyphosis and adequate neurodevelopment were observed. DEXA demonstrated low bone mineral density (BMD): L2-L4 0.370 g/m$^2$ (Zscore –3.9 SDS); bone metabolism markers within normal range (calcium 10.3 mg/dL; phosphate 4.9 mg/dL; magnesium 1.9 mg/dL; ALP 195 IU/L; bone-ALP 61.5 ng/L; PTH 54 pg/ml; 25OHvitamin D 24 ng/ml; CTX 1231 pg/ml; Calcium/Creatinine 0.2; PTR 91%). Secondary causes of osteoporosis were ruled out. After two years of Zoledronic acid every six months and specific exercises, his BMD has improved to –2.2 SDS,

**Conclusions:** LRP5 is a single-span transmembrane protein required for Wnt/βcatenin signaling pathway, relevant for fetal and postnatal osteogenesis. We identified a novel homozygous LRP5 loss-of-function mutation in this patient, which causes autosomal recessive Osteoporosis-pseudoglioma syndrome (OPPG, OMIM 259770). Scarce information exists regarding osteoporosis treatment in children. Understanding the molecular mechanisms underlying primary osteoporosis is important for improving screening of comorbidities, genetic counselling and development of novel therapies. Affected vertebras slightly reshaped without fractures recurrence. SNP-array showed loss of heterozygosity in 11p15.1-11q13.3, containing the low-density lipoprotein receptor-related protein-5 gene (LRP5), a gene expressed in fetal ocular macrophages and osteoblasts. A novel homozygous nonsense variant (NM_002335.3:c.441G>A, p.Trp147Ter) was identified in LRP5 using a skeletal dysplasia NGS panel. Parents, heterozygous for this variant, have normal BMD.

## Follow Up in a Pediatric Cohort with Differentiated Thyroid Cancer (DTC): Response to Initial Therapy at 2 Years

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**Background:** DTC in childhood has a more aggressive presentation but no overall increase in mortality compared to adults. Objective: to describe the initial postoperative ATA risk classification of a cohort of pediatric patients with DTC treated uniformly and to evaluate the response to initial therapy at 2 years based on the modified ATA dynamic risk stratification (DRS) for adults.

**Patients and Methods:** We retrospectively analyzed a cohort of 17 pediatric patients diagnosed with papillary DTC between 2008 and 2015 treated initially with total thyroidectomy and radioactive thyroid ablation. Median age at diagnosis was 13.8 years (range 5.2–18) and 11/17 were pubertal. Initial ATA risk was classified in low, intermediate and high risk according to TNM, thyroglobulin (TG) and images. Clinical outcome at 2 years was assessed by DRS into 4 categories: excellent response (non-evidence of disease [NED]), indeterminate response, biochemical incomplete response and structural incomplete response according to stimulated TG and imaging findings.

**Results:** Postoperative ATA risk classification showed 18%, 18% and 64% patients with low, intermediate and high risk. DRS at 2 years revealed 47%, 18%, 6% and 29% of patients with excellent, indeterminate, biochemical incomplete and structural incomplete response respectively. At 2 years all low risk patients remained NED while 33% of the intermediate and 36% of the high risk group achieved NED status.

**Conclusions:** The aggressiveness of pediatric DTC at presentation assessed by the pediatric ATA risk classification was confirmed in our cohort. Dynamic DRS at 2 years of follow-up showed

a marked change compared to admission. Although preliminary, our results suggest that DRS is a good and useful response to therapy categorization for the surveillance of pediatric DTC patients. Its use would allow a more accurate treatment decision according to changes in biochemical and structural findings.

## Relation Between High Levels of IGFBP3 AND Recurrence of Craniopharyngioma in Pediatric Patients at National Institute of Pediatrics from 2013 to 2018

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**Objective:** To determine the association Between levels of insulin-like growth factor-1 (IGF1), IGFBP3 and the recurrence of craniopharyngioma in Children with mild high at onset of the disease.

**Material and Method:** We conducted an observational, descriptive, retrospective, cross-sectional study. A total of 42 pediatric patients with clinical and radiological diagnosis of craniopharyngioma were evaluated. Serum levels of IGF1 and basal IGFBP3 were determined and correlated with tumor recurrence.

**Results:** 42 patients with craniopharyngioma are presented, of which 52% are male, 48% female. 67% of these sample presented recurrence during its evolution. The levels of IGFBP3 were determined at the onset they were percentylated according to age and sex. The leves of IGFBP3 were between +1 and +2 SD in 5% and between +2 and +3 SD in other 5% of the sample. The relationship between high levels of IGFBP3 and recurrence was researched. X2 = 1.615 and p = 0.204 were calculated and it was found that patients with higher levels did not present tumor recurrence in this sample.

**Conclusions:** IGF1 and IGFBP3 are important in normal brain development the overexpression might be positively associated with risk of brain tumor development like gliomas, in this study we evaluated patients treated at the National Institute of Pediatrics with diagnosis of craniopharyngioma in the last 5 years. The tumor recurrence and the high levels of IGFBP3 was not significant, reason for which it is concluded that there is no direct relationship between both factors.

## Gonadotropin-Dependent Pubertal Disorders are Common in Patients with Virilizing Adrenocortical Tumors in Childhood

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**Objective:** To investigate the impact of early exposure to androgen excess on gonadotropin-dependent puberty (GDP) and on final height (FH) of patients with childhood adrenocortical tumors (ACT).

**Methods:** This is a retrospective cohort study of 63 patients (69.8%: female) with virilizing ACT during childhood, followed in a single institution from September 1975 until September 2017. Epidemiological, clinical, anthropometrical, hormonal, histopathological and molecular data were collected from medical records. The occurrence of GDP and the achievement of FH were evaluated. Central precocious puberty (CPP) and early fast puberty (EFP) were considered pubertal disorders. Data between patients with normal puberty and pubertal disorders were compared.

**Results:** At diagnosis of ACT, median age was 25.8 months and duration of signs, 6 months; stature SDS was 0.5 (–3.6–3.9) and bone age advancement was 14.7 months (–27.9–85.4). To date, 58.7% of the patients developed GDP: 26 had normal puberty, 7 had CPP, and 3 had EFP. Gonadotropin-releasing hormone analogues effectively treated CPP and EFP. Tall stature and older age at diagnosis of ACT were associated with risk of CPP alone [RR 4.17 (95% CI 1.17–14.80)] and of pubertal disorders [RR 3.0 (95% CI 1.04–8.65)], respectively. Recurrence/metastasis during follow-up was associated with risk of CPP alone [RR 4.17 (95% CI 1.17–14.80)] and of pubertal disorders [RR 3.0 (95% CI 1.12–8.02)]. Among the 19 patients that reached FH, stature SDS dropped from 1.4 to –0.02 since diagnosis of ACT (p = 0.01). Seventeen of them achieved normal FH. There was no difference in FH SDS between patients with normal puberty and pubertal disorders (p = 0.75).

**Conclusions:** This study shows that gonadotropin-dependent pubertal disorders are more common than previously expected in patients with childhood virilizing ACT. Additionally, it confirms that FH is usually not impaired, reiterating the good prognosis for FH in these patients. At last, the study reinforces the importance of close and prolonged endocrinology follow-up after surgery, not only to detect ACT-related complications, but also to promptly identify and treat the consequences of early exposure to androgen excess.

## Effects of Severe Hypothyroidism on Sertoli Cell Anti-Mullerian Hormone (AMH) Production

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**Background:** The FSH receptor, a member of the G-protein-coupled receptor family, is highly homologous to other glycoprotein hormone receptors, like TSH receptor. Signaling of both receptors involves activation of adenylyl cyclase and cAMP production. Clinical and experimental evidence suggests that promiscuous activation of the FSH receptor may exist when TSH concentration is extremely elevated in patients with hypothyroidism. FSH induces Sertoli cell proliferation and AMH gene transcription, however, there is no information about AMH production in patients with long-lasting high TSH.

**Case Presentation:** A male patient was referred at 4 years of age for evaluation of short stature. Patient's height was 92.1 cm (–2.16 SD) and mid-parental height was –0.52 SD. Bone age was 2 years, coinciding with the start of growth retardation. Physical exam revealed dry skin with no goiter. He was prepubertal: genital stage 1 and pubic hair 1. Testicular volume was 3 ml. Stretched phallus length was 3 cm.

**Table 1.**

| | At diagnosis | 3 m | 12 m | 28 m | Normal range |
|---|---|---|---|---|---|
| TSH, mUI/ml | >1000 | 680 | 43 | 20 | 0.5–6.5 |
| AMH, pmol/L | 4700 | 2013 | 1390 | 1436 | 300–1800 |

At diagnosis he had a severe autoimmune hypothyroidism with TSH >1000 μUI/ml, T4 <0.5 μg/dl, FT4 <0.4 ng/dl and positive thyroid antibodies. Gonadal axis was prepubertal (LH 0.3 mUI/ml, FSH 2.9 mUI/ml, Testosterone <10 ng/dl and Prolactin 13.6 ng/ml), AMH was abnormally high at 4700 pmol/L. Given the insufficient response to treatment with levothyroxine, he was diagnosed with celiac disease and started a gluten-free diet. Levothyroxine dose was tritiated to normalize his TSH level. The concentration of AMH gradually decreased as TSH levels normalized (Table). He had an appropriate catch up growth.

In summary, we report the association of high AMH levels in a patient with long-lasting high TSH and AMH normalization after successful treatment of hypothyroidism, which provides a proof-of-concept of the ability of high levels of TSH to stimulate FSH receptor and induce AMH production.

## Assessment of Beliefs and Behaviors Related to Reproductive Health in Adolescent and Young Women with Type 1 Diabetes in Chile

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**Objective:** With adolescents and young women are at risk for T1D reproductive-health problem. The aim of the study was to describe beliefs and behaviors in sexual and reproductive-health of adolescent and young Women with T1D in Chile.

**Methods:** Young Women with T1D (N: 46; age 14–26 years) Were recruited at to free educational camp in Chile. Reproductive beliefs and behaviors Were evaluated with a standardized written questionnaire. The questionnaire was translated into Spanish and validated by experts in Chile. Each question ADH a Likert-like format (scores: 1 to 7; higher score being more likely). The questionnaire EVALUATED seven different aspects: perceived susceptibility and severity About Health Risks and unwanted pregnancy; intentionality of professional help and contraception; perceived benefits, barriers, and self-efficacy Regarding sexuality, contraception, pregnancy and preconception Control. Results are Shown as median. Likewise, perceptions of risk of unwanted pregnancy and risk of mother and child health evaluated as Were Percentages. All participants/parents signed consent assent and.

**Results:** Highly susceptible subjects felt (score: 7) with high severity (score: 6.1) Toward unwanted pregnancy and Health Risks. High benefits (score: 6.8) self-efficacy (score: 6.5), and low barriers (score: 1.6) to support reproductive Accessing Were Reported. Intentionality of aid was low (score: 2.8), and moderate for contraception (score 4.1). A moderate perception of risk of pregnancy (% ± sd ± 26.66) and health risk of the mother (± 22.62) and child (± 27.62) were observed.

**Conclusions:** Young Women with T1D In This study Know the Risks Associated with sexual behavior and benefits of preconception counseling (PC), but do not plan to seek help, DESPITE reporting low barriers. These data confirm that Should begin at puberty PC to Prevent unplanned pregnancies. (FONDECYT Grant 1170895).

## Schaaf Yang Syndrome with Multiple Pituitary Hormone Deficiency a Case Report

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**Case Report:** A 210/12 years old male patient consults for growth evaluation. I HAD some dysmorphias delayed psychomotor development Associated with and arthrogryposis. Full exome sequencing was Requested. An heterozygous, of pathological novo variant at MAGE-LIKE 2 (MAGEL2; OMIM * 615547) was found diagnosing Schaaf-Yang syndrome (SHFYNG). History and physical exam neonatal revealed hypotonia, development delay/intellectual disability, feeding problems, cryptorchidism with bilateral orchiopexy, chronic constipation, dysmorphic facial features, strabismus, Vices of Refraction, hypotonia at time of exam, small hands, small feet and short stature with deceleration of growth rate (5 cm/year). Laboratory exams Showed Repeated low IGF-1 (31.9 and 39 ng/ml); ACTH stimulating test: basal cortisol 10.4 ug/dl and 60 min 10.2 ug/dl; TSH 2.87 mIU/ml, 145 prolactin. 9 ng/ml (91% recovery). Magnetic resonance of the Sellar Region hipoplasic Informed pituitary. Multiple pituitary hormone deficiency was diagnosed with adrenal insufficiency, growth hormone deficiency and hyperprolactinemia.

**Results:** *Review of Literature:* Schaaf-Yang syndrome is a rare illness due to truncating mutations in the maternally imprinted, paternally MAGEL2 Expressed gene, which is located in the Prader-Willi critical region 15q11-13. It is Characterized by developmental delay/intellectual disability, hypotonia, feeding Difficulties, contractures of the small finger joints and autism spectrum disorder. Also sleep apnea, gastroesophageal reflux, and fetal movement Decreased Frequently are Reported. Endocrinological pathologies are associated low stature and hypogonadism. NEVERTHELESS endocrinological a systematic assessment of Individuals with SHFYNG has not Been Reported to date.

**Conclusions:** It Seems that Important Patients with Schaaf-Yang syndrome needs to be EVALUATED by endocrinologist. Panhypopituitarism has not Been Described in Cases Previously published. A complete study of pituitary hormones Should be performed in cases to see if Already Described multiple pituitary hormone deficiency is part of the syndrome.

## Clinical and Molecular Study of Patients with Hypercalcemia or Hypocalcemia and Alterations in the Calcium Sensor Receiver

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**Objective:** We carried out a complete clinical and genetic characterization of our cohort of 87 individuals from 37 families presenting with serum calcium and PTH anomalies, one of the largest series described. Molecular diagnosis is a useful diagnostic tool in calcium metabolism disorders. The calcium-sensing receptor (CaSR) is known to play a central role in the regulation of extracellular calcium homeostasis.

**Methods:** The CASR was screened for mutations by polymerase chain reaction followed by direct Sanger sequencing.

**Results:** 70 patients from 29 families presented presumable CASR inactivating mutations. Those patients presented hypercalcemia (mean 11.5 mg/dL) but normal or inappropriately increased intact PTH concentration (mean 68.8 pg/ml). On the other hand, 17 patients from 8 families presented presumable CASR activating mutations. Those patients presented with serum calcium mean level of 7.1 mg/dL and hypoparathyroidism (mean PTH 15.7 pg/mL). Specifically, we found 33 different mutations.

**Conclusions:** Our study confirms the association of hypocalciuric hypercalcemia and hypercalciuric hypocalcemia with alterations in the calcium sensor receptor. Patients with mutations of the CASR gene may not present such a pure picture of hypercalcemia with hypocalciuria or hypocalcemia with hypercalciuria. Molecular studies are important for confirming the diagnosis and distinguish it from other entities. Our genetic analysis confirmed the diagnosis of CaSR disorders in 87 patients of the study cohort.

## Histopathological Assessment of Gonads in Testicular and Ovotesticular 46 XX Disorders of Sex Development

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Disorders of sex development (DSD) are congenital conditions in which development of chromosomal, gonadal or anatomical sex is atypical. The aim of study was to characterize esta Histology of the 46,XX DSD prepubertal gonads.

We studied 25 gonads of fourteen 46,XX DSD patients. The age of biopsy/gonadectomy was 1.17 (0.08–4.17) years (median and range). Molecular studies confirmed the absence of SRY in blood samples of all patients and in 8 patients DNA gonads. Gonadal histology was assessed on H&E stained sections by two double blinded specialists and the findings were classified as testicular, ovarian or ovotesticular parenchyma, undifferentiated gonadal tissue (UGT) and gonadoblastoma (GB). Immunohistochemical (IHC) analysis identified Sertoli cells (SOX9), ovarian follicular cells (FOXL2), somatic cells (inhibin B), pluripotent germ cells (OCT3/4) and steroidogenic cells (HSD3B2 and CY-P17A1).

Twenty one gonads (12 patients) Were classified as ovotesticular and 4 (2 patients) as testicular. Dysgenetic testicular parenchyma was found in all Cases.

Regarding the patients with ovotestis, in 2/12 the first biopsy showed only testicular tissue and a second biopsy revealed ovarian tissue as well. Moreover, 3 cases presented UGT and in 2 other patients GB was found.

IHC analysis of SOX9 and FOXL2 confirmed the presence of testicular/ovarian parenchyma, even in apparently undifferentiated structures. OCT3/4 was positive in 6 gonads (3 patients): 4 with UGT features (2 patients) and 2 with GB (1 patient). HSD3B2 and CYP17A1 revealed the presence of active steroidogenic cells. Expression of inhibin B, SOX9 and FOXL2 in UGT and GB was found.

Interestingly, in all cases signs of dysgenesis were only found in testicular parenchyma. It is noteworthy that a second biopsy in 2 former testicular cases revealed the presence of ovarian parenchyma. Considering the histopathological findings in early childhood, a close clinical follow up of patients with a specialized DSD team is suggested.

## Analysis of PHEX Mutations in 21 Families with Hereditary Hypophosphatemic Rickets Hereditary in a Single Tertiary Center

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Hereditary Hypophosphatemic Rickets (HHR) is a group of inherited disorders characterized by hypophosphatemia due to renal-phosphate wasting and a defective vitamin D metabolism, rickets and disproportioned short stature. Different genetic defects are known to cause HHR, although they share similar clinical and biochemical features. Dominant-X-linked HR (XLHR) is the most frequent form, with an incidence of 1 in 20.000 live births, although dominant and recessive autosomal forms are also described. XLHR is caused by inactivating mutations in the PHEX gene (phosphate-regulating gene with homologies to endopeptidases on the X chromosome), which includes 22 exons encoding a 749 amino acid transmembrane endopeptidase.

**Aim:** To characterize by molecular analysis PHEXdeleterious mutations in a cohort of pediatric patients with HHR.

**Methods:** Genomic DNA from 25 patients (and 6 symptomatic parents) belonging to 21 unrelated families with HHR were screened by Sanger sequencing looking for mutations in PHEX gene. All patients were treated by our multidisciplinary team at one single institution.

**Results:** Fourteen different PHEX mutations were identified in 18 patients from 14 unrelated families (in 8/15 sporadic cases and in 6/6 familial cases).

Five were novel mutations: one missense, c.1404G>T (p.Lys468Asn); one nonsense, c.1996C>T (p.Gln666Ter); two

frameshift, c.293delT (p.Met98Ser fs Ter10) and c.2044_2048delinsATAACTCAG (p.Gln682Ile fsTer36); and one splice donor site mutation, c.2070+5G>A.

Missense mutation resulted to be deleterious by in silico prediction tools. Nine previously reported mutations were also found.

**Conclusions:** Our study showed that 14/21 unrelated families with HHR carried mutations in the PHEX gene, which accounted for 67%. This result is consistent with the percentage of detected mutations reported in published cohort studies, which ranged from 45% to 87% for PHEX. Moreover, in familiar HHR cases screen PHEX mutations is highly recommended.

## Possible Partial Ectopic Posterior Pituitary: Imaging Clinical and Endocrinological Manifestations a Case Series

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**Objective:** To describe six cases of possible partial ectopic posterior pituitary gland (PEPP) seen on head magnetic resonance imaging (MRI) and their associated clinical and endocrinological manifestations.

**Methods:** This is a single-center case series, from a tertiary public university health center in Montreal, Canada. Cases of children with possible PEPP were selected prospectively from 2005 to 2017, based on head MRI findings. History, exam findings and hormonal evaluation were extracted from the medical record, and images were reviewed and interpreted by an experienced pediatric neuro-radiologist.

**Results:** All the cases, two boys and four girls between 8 days and 14 years old, were characterized by the presence of two midline bright spots on the thin focused T1 weighted sequences obtained with fat suppression technique. While one bright spot was located at the normal expected site of the neurohypophysis in the posterior sella, another was in the midline median eminence or along the normal appearing pituitary stalk above the sella, most likely corresponding to a partial presentation of the ectopic posterior pituitary gland. The possible PEEP was associated with different clinical phenotypes. One patient had isolated growth hormone deficiency, another had combined thyroid stimulating hormone and growth hormone deficiency, while the others had intact pituitary function. Of the remaining four patients, one had CHARGE syndrome, another one had motor developmental delay and one had septo-optic dysplasia without evidence of endocrinopathies to date.

**Conclusions:** Evaluation of pituitary function may be needed when PEPP is possibly found in the MRI. Long-term follow-up may provide additional information on others pituitary hormone deficiencies.

## Short Stature Associated to Partial Growth Hormone Insensitivity (GHI) Due to a Digenic Disorder with a Hypomorphic Variant in IGFALS Combined to a Novel Heterozygous STAT5B Missense Variant

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**Background:** GHI is characterized by growth failure, elevated GH, and low IGF-I and IGFBP-3 serum levels. GHI has been associated to monogenic defects in several genes including GHR, STAT5B, IGF1, IGFALS.

**Aim:** To characterize the molecular defect in a patient with the short stature and GHI.

**Case:** The boy was born at term AGA from non-consanguineous parents. His parents and siblings had normal height. At 2.1 years, patient's height was 73.5 cm (–3.23 SD), weight 8.28 kg (–2.5 SD), and head circumference 48.5 cm (0 SD). He presented proportionate short stature, wide forehead and normal mental development.

**Results:** Biochemical and endocrinological evaluation were normal, including stimulated GH peak (7.8 ng/ml), with undetectable IGF-I and low IGFBP3 levels (1.34 μg/ml; –2.01 SD). IGF-I generation test (rhGH 33 μg/kg/day for 7 days) showed a poor response (IGF-I <25 to 40 ng/ml; IGFBP3 0.85 to 2.15 μg/ml; ALS 269 to 671 mU/ml). The patient improved 1 SD in height after a 2-year period of rhGH treatment. An already described heterozygous variant in IGFALS (c.1642C>T, p.Arg548Trp) and a novel heterozygous missense variant in STAT5b (c.1896G>T, p.Lys632Asn) were found by candidate gene approach and WES, respectively. In vitro transfected CHO cells secreted significantly less R548W-ALS compared to WT-ALS [1]. Studies using K632N-STAT5b transfected into HEK293-T cells showed impaired STAT5b phosphorylation upon GH stimulation. Also, its transcriptional activity determined by luciferase reporter assay, was diminished under basal and GH-stimulated conditions. Co-transfection of K632N- and WT-STAT5b resulted in decreased transcriptional activity compared to WT-STAT5b, suggesting a dominant negative effect for K632N-STAT5b. Interestingly, this effect was reversed under GH stimulation (200 ng/ml).

**Conclusion:** The combined effect of a hypomorphic ALS variant (p.Arg548Trp) and a novel heterozygous STAT5b variant (p.Lys632Asn) with dominant-negative properties could be responsible for the patient's partial GHI phenotype.

*Reference*

1 Martucci et al. Mol Cell Endocrinol 2016;429:19–28.

## Craniosynostosis Secondary to Hypophosphatemic Rickets Experience in a Single Tertiary Center

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Familial Hypophosphatemic (FHR) Rickets is the most frequent cause of heritable rickets. The features vary widely: short stature, bone pain, bowed legs and premature fusion of the skull bones, however, there are few reports of craniosynostosis in this condition.

**Objective:** To describe the clinical, auxological characteristics and treatment of patients with craniosynostosis associated with FHR. All children received conventional treatment with phosphorous supplement and calcitriol.

**Methods:** Clinical notes and cranial images were retrospective analyzed by a multidisciplinary team. Out of 96 children (29 male/67 female) with hipophosphatemic rickets attended in our multidisciplinary clinic, between 1992 and 2018, 50 had cranial images.

**Results:** Out of 50, 24 (48%) had craniosynostosis diagnosis: 13 male/11 female.

Nineteen (79.1%) out of 24 had dolicocephaly and 5 (20.8%) had normal head shape. None of them had microcephaly and head circumference growth was normal in all of them. The most commonly affected suture was sagittal in 70%. Four patients had undergone-at least 1 cranial remodeling surgery- for: 1) sagittal craniosynostosis and severe scaphocephaly, 2) pansynostosis and indirect sign of endocranial hypertension, 3) coronal synostosis and facial asymmetry and 4) the surgery was undergone before the 1st appointment to our clinic. Three patient with craniosynostosis presented Chiari Type I malformation association.

**Conclusion:** We report a large cohort of pediatric patients with FHR associated to Craniosynostosis. It is important to consider this association, for early diagnosis and eventual surgery.

## Non-Alcoholic Fatty Liver Disease Is Associated with Deterioration of B Cell Function from Adolescence to Emerging Adulthood

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**Background:** Fatty liver disease (NAFLD) is frequently associated with obesity, insulin resistance, glucose intolerance and type 2 diabetes (T2DM). Epidemiological evidence support a close association between T2DM and NAFLD in young populations. We aimed to study the association of NAFLD at 22 y with the variation of insulin sensitivity and β-cell function from adolescence and emerging adulthood.

**Methods:** Observational prospective study in n = 473 22 year-olds (49.7% males) from a Chilean infancy cohort. NAFLD was measured with abdominal ultrasound validated with MRI. BMI, adiponectin, glucose (Gli) and insulin were measured at 16 y and 22 y. HOMA-IR, HOMA-%β, HOMA-%S, disposition index (DI) and HOMA-AD were calculated. The Wilcoxon-Mann-Whitney test was used to compare participants with and without NAFLD and the Wilcoxon signed-rank test was used to find differences within the groups.

**Results:** In the sample, 27% of participants had NAFLD. At 16y and 22 y, participants with NAFLD have significantly higher values of BMI, insulin, HOMA-IR, HOMA-%β and HOMA-AD and significantly lower values of HOMA-%S and DI compared to participants without NAFLD. Although both groups show a significant change of HOMA-IR, HOMA-%β, HOMA-%S and HOMA-AD from 16 y to 22 y, only the participants having NAFLD had a significant decrease in DI.

**Conclusion**: NAFLD in emerging adulthood is associated with reduced insulin sensitivity and decreased β-cell function in adolescence and emerging adulthood. Likewise, NFLD was associated with a significant deterioration of the β-cell function from adolescence to emerging adulthood.

## Mody Case Series in Bucaramanga Colombia

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**Introduction:** Maturity onset diabetes of the young (MODY), a monogenic form of diabetes, is Estimated to account for Between 1% and 2% of all cases of diabetes.

**Material and Methods:** This is a series of 22 case studies that Were Carried out in the endocrinology, emergency or genetics services, Involving four health centers, in which Patients between 2 and 18 years of age Were included all of Whom complied with the ADA criteria for MODY diagnosis, presenting clinical and laboratory Characteristics symptomatic of MODY.

**Results:** We describe the characteristics found: Were variables demographic (sex, age at the moment of recruitment and the diagnosis of MODY, clinical (Personal history of breastfeeding, ketoacidosis episodes, insulin use, family Members with DM, and anthropometric measurements at the moment of diagnosis) and laboratory glycemia, glycosuria, antibodies and glycosylated hemoglobin at the moment of diagnosis.

**Discussion:** The presence of a family history of first-degree diabetes, age at diagnosis, absence of ketoacidosis, the need for insulin During the first 5 years after diagnosis, glycosylated hemoglobin and C-peptide value are Characteristics that Should be evaluated in MODY in the pediatric patient.

## Growth in Children with Congenital Adrenal Hyperplasia Classical Diagnosed by Neonatal Screening

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Hospital Sor Maria Ludovica

**Introduction:** Linear growth Allows monitoring metabolic Control in Children with congenital adrenal hyperplasia classical (SCF).

**Aims:** To analyze linear growth and puberty in a group of children with SCF detected by neonatal screening.

**Method:** Patients Thirty-two (F: 15, M: 17) Were with SCF EVALUATED at start of treatment, 6 and 12 months of age, and Annually. We analized age at start of treatment, z-height, z-BMI, hydrocortisone dose (hCd), bone age (BA) and 17-OHP blood levels up to the age of five (Table) and age of onset of puberty. Final height was Compared with mid parental height (MPH). Statistical analysis: Anova test-Spearman correlation.

**Results:** Median age at start of treatment was 18 (10; 22) days. See Table 1.

Six boys and girls started four standard puberty at 11 ± 0.9 and 9.5 ± 0.21 years, respectively. Final height in seven of them (F 2; F: 5) was –1.17 ± 0.6 SDS, at –0.75 ± 0.79 SDS below MPH.

Six boys and five girls presented at 6.4 ± precocious puberty 1.85 and 6.72 ± 0.35 years, respectively.

**Conclusions:** Height in the first 6 months of treatment Showed to decline, Recovering afterwards. Up to the age of five, Showed an Increase Normal BMI and BA was. Final height was standard, but slightly lower than mid parental height, in Children with Normal puberty.

Precocious puberty was frequent in this group, suggesting other factors like compliance that Could influence growth.

## Length Estimation Based on Clinical and Anthropometric Measures in Newborns

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**Backgrounds and Aims:** Nutritional assessment is a crucial part of the inpatient care of newborns. For the above, anthropometric measurements: such as weight and length are required; however, invasive procedures in neonatal care units Preventative correct measurement. As an alternative, estimations are used anthropometric by Means of formulas that use the measurement of body segments, which Have Been developed in older age groups and Their Application in neonates is not exact and accurate. The aim of study is to identify identity esta clinical and anthropometric variables that Explain the variability of length in newborns.

**Methods:** We Conducted a cross-sectional study in term and preterm 46 which newborns of Both sexes Were included. Were Recruited participants from public and private hospitals in Mexico City. Sociodemographic background and perinatal data Were Collected. Measurements of weight, length, head circumference and body segments (arm span, length ulna, tibia length and lower leg length) Were performed with standardized techniques. These data included in regression models Were to estimate the crown-heel length Obtained with an infantometer (gold standard). The equation Obtained was Compared with Stevenson and Gauld formulas.

**Results:** The variables that had a greater correlation with length Were: gestational age (r = 0.720, p = 0.05), birth weight (r = 0.760, p = 0.05), head circumference (r = 0.784, p = 0.01), lower leg length (r = 0.821, p = 0.01) and weight (r = 0.868, p = 0.01). ACCORDING to the linear regression analysis, the best Identified formulated to estimate the crown-heel length of newborns includes lower leg length, head circumference and sex (R2 = 0.86). No significant difference was Identified Between the Estimated length with This formulation and the length measurement made with the infantometer (47.62 ± 2.09 vs 47.62 cm ± 2.25 cm, p = 0.997). Our linear regression model was better as the formulas Previously Reported. We Identified an average difference of –8.6 to –9.7 cm with Stevenson's formylated and of –14.9 to 24.3 cm with Gauld's (p = 0.0001) in comparison with the infantometer measure.

**Table 1.**

| | Start (a) | 6 month (b) | 1st year (c) | 2nd year (d) | 3rd year (e) | 4th year (f) | 5th year (g) |
|---|---|---|---|---|---|---|---|
| Mean height (SDS) | –0.92±1.50* | –1.83±1.85* ab | –1.61±1.67 | –1.15±1.27 | 0.71±1.13 | 0.47±1.23 | 0.11±1.28* ag |
| Mean BMI (SDS)** | –1.46±1.21** | 0.24±1.27** ab | 0.67±1.42** ac | 0.68±0.91** ad | 0.89±0.96** ae | 0.97±1.23** ag | 1.33±1.40** ag |
| HCd Median (mg/m$^2$/day) | 36.00 (32.80; 43.55) | 20.84 (19.12; 22.09) | 17.94 (16.12; 19.52) | 16.00 (14.44; 19.20) | 15.13 (13.00; 19.91) | 14.52 (11.83; 16.83) | 14.00 (10.79; 18.09) |
| Mean BA (SDS) | | | 0.87±0.33 | 1.89±0.85 | 1.03±2.59 | 3.88±1.33 | 5.36±2.43 |
| Median 17-OHP (Ng/ml) | 45.00 (22.50; 50.00) | 2.13 (1.11; 10.70) | 1.30 (0.54; 8.95) | 1.10 (0.48; 3.90) | 0.82 (0.48; 6.00) | 1.37 (0.46; 14.20) | 2.40 (0.46; 20.00) |

*, ** $p < 0.0001$.

Negative correlation was found Between HCd and height (r = –0.27, $p < 0.0001$).

**Conclusions:** Our linear regression model is more accurate to estimate the Crown-heel length of newborns as Previously Reported methods. This makes Could be a great tool to ASSESS the nutritional status of hospitalized newborns in Whom it is not possible to measure the length with the gold standard.

## Neonatal Hyperglycaemia Due to Subcutaneous Fat Necrosis Successfully Treated with Pamidronate

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**Introduction:** Subcutaneous fat necrosis (SCFN) can cause severe neonatal hypercalcemia. SCFN can develop in patients with hypoxic ischemic encephalopathy (HIE) that require treatment with head cooling. It has been previously suggested that pamidronate may be the first line of treatment for SCFN induced hypercalcemia. We report a case of neonatal hypercalcemia due to presumptive SCFN, successfully treated with pamidronate.

**Case Report:** A term female infant was born by emergency cesarean section due to fetal distress, body cord was noted during delivery. Bradycardia and apnea prompted intubation and resuscitation. Active cooling initiated due to HIE. Patient required extracorporeal membrane oxygenation (ECMO) for 3 days due to respiratory failure. Severe anasarca was noted on the third week of life. At 4 weeks of age, patient was noted to have hypercalcemia of 14.9 mg/dL (7.3–11.9 mg/dL). Patient's generalized edema made it impossible to evaluate for the presence of SCFN. Work up for causes of hypercalcemia was negative (significantly and appropriately suppressed PTH of <4.0 pg/mL (8.0–85.0 pg/mL), normal 25-hydroxy vitamin D of 19 ng/mL (30–80 ng/mL), normal phosphorous of 6.4 mg/dL (4.0–7.0 mg/dL) and normal alkaline phosphatase of 216 U/L (80–250 U/L). Hyperhydration and furosemide were started.

Despite aggressive treatment, hypercalcemia persisted. Pamidronate was started at day of life 32 at 0.25 mg/kg per dose. Calcium worsened after initial dose. Second dose of pamidronate was given at 0.5 mg/kg and calcium levels improved. A 3rd dose of 0.5 mg/kg was then given and calcium continued to decrease. Calcium levels measured 24 hours after the last dose were normal at 9.4 mg/dL. Calcium remains normal after 3 months of being followed. As the patient's clinical course got better, and anasarca improved, erythematous nodule was noted on patient's cheek, compatible with SCFN.

**Discussion:** Successful treatment of hypercalcemia secondary to SCFN with pamidronate has previously been noted.

SCFN is positively associated with infant history of HIE treated with therapeutic hypothermia. Exact mechanism remains unclear. First line of treatment for hypercalcemia due to SCFN is the same as for other causes, hyperhydration followed by calcium wasting diuretics. Corticosteroid therapy can be used as well. Pamidronate induces osteoclast apoptosis and improves hypercalcemia. From literature three to four doses of pamidronate 0.25–0.5 mg/kg is sufficient to normalize calcium and is well tolerated. Effect is usually seen within 24 hours of infusion. Our case is unique as pamidronate was started with just the clinical suspicion of SCFN. SCFN was suspected due to history of HIE, requiring head cooling and timing of hypercalcemia.

## Novel Homozygous IGF1 Gene Mutation in a Child with Severe Pre and Postnatal Growth Retardation

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**Objective:** Human IGF1 gene defects have been reported in seven cases. We describe a patient with severe short stature presenting a novel homozygous IGF1 gene mutation and its functional characterization.

**Case:** Patient born from consanguineous parents at 40 weeks of gestational age with IUGR. His birth weight was 1910 g (–3.06 SD), length 38 cm (–6.3 SD), and head circumference 34 cm (–0.4 SD). His mother and father were born with low weight (1900 g and 2500 g, respectively) and had short adult height (–1.92 SD and –2.6 SD, respectively).

**Results:** At 3.2 years of age, the patient's height was 74 cm (–6.15 SD), weight 6.1 kg (–5.1 SD), head circumference 41 cm (–6.05 SD). Physical examination revealed proportionate short stature, microcephaly, and facial dysmorphism (frontal bossing, triangular face, bulbous nose, full lips and retrognathia). He also presented bilateral sensorineural deafness, mild global developmental delay, and hyperactivity behavior. Basal levels of GH and IGF-I were variable (GH: 1.9 to 29 ng/ml; IGF-I: 47 to 206 ng/ml), and IGFBP-3 levels were normal-high (2.3 to 5.3 μg/ml). Karyotype was normal (46, XY). SNP array showed multiple chromosomal homozygosity regions, including 12q23.2 where IGF1 maps. The patient was homozygous and his parents heterozygous for a novel missense variant (NM_001111285.2: c.322T>C, p.Tyr108His). The change of a highly conserved Tyr residue (Tyr60 in the mature IGF-I peptide), was predicted as pathogenic by multiple bioinformatic tools. Tyr60 has been described to be critical for IGF-I interaction with type 1 IGF receptor. In vitro studies using patient's serum to stimulate HEK293T cells, showed a marked reduction of IGF-1R phosphorylation compared to control serum.

**Conclusion:** In summary, we report a novel IGF1 variant associated with familial short stature. Our preliminary functional studies suggest that this mutation may result in a diminished IGF-1 bioactivity, explaining the observed clinical condition.

## Oral Glucose Disposition Index in Pediatric Patients and Its Relationship with Methodological Variability of Insulin Measurement

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**Introduction:** It is Widely accepted impaired insulin secretion that and systemic insulin sensitivity are found in Type 2 Diabetes Mellitus. Numerous indexes Have Been Described Characteristics to Evaluate Both. The hyperbolic relation Between indexes of insulin secretion and sensitivity Obtained from IVGTT've Been replicated by using Also indexes derived from OGTT surrogate. The oral glucose disposition index (DI-oral) derived from the OGTT Seems to be an accurate indicator to describe Both aspects. It is like in Individuals with the same degree of glucose tolerance. However, due to the methodological variability for measuring insulin, it is difficult to interpret These indexes.

**Objective:** To Evaluate the hyperbolic relationship Between insulin secretion and insulin sensitivity of oral-DI, the variability of Its determination and Its behavior in pediatrics.

**Materials and Methods:** 132 Overweight/Obese Patients (5–13 year old) Were Studied. The OGTT was performed in These Patients, glucose and insulin Were Measured. Insulin was Determined by two methods in Sixty Patients (IMMULITE 2000 Siemens, Roche Cobas e-411).

**Results:** The hyperbolic relationship between the different indexes of insulin secretion (Insulinogenic, Stumvoll-1PH and AUCI/G ratio) and insulin sensitivity (HOMA-S and Matsuda) was analyzed. The pair AUCI/G-WBISI was found to be the one that fits the hyperbola best (r2=0.855). Patients were categorized into three groups according to the glycemic level (<0.90, 0.91–0.99, >1.0 g/l). An oral-DI decrease was observed in groups with the highest blood glucose level. Unlike the other indexes evaluated, no significant differences were found in the values of oral-DI calculated with the two insulin methods ($p = 0.52$).

**Conclusion:** Oral-DI Could be a robust tool to Evaluate insulin secretion/sensitivity in Pediatric Patients since it is not Affected by the method used. Due to the relationship of insulin secretion with the degree of insulin sensitivity, This index Showed the best correlation with glycemic status.

## Hypophosphatasia: A Novel Mutation in a Mild Childhood Form

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**Introduction:** Hypophosphatasia is an inborn error of metabolism that features low serum alkaline phosphatase (ALP) activity caused by loss-of-function mutation (s) of the gene that encodes the tissue-nonespecific isoenzyme of ALP (TNSALP) that regulates skeletal and dental mineralization. There are different forms of hypophosphatasia with a wide variation in severity, ranging from high-mortality neonatal to mild forms in adults associated with fragility fractures and osteomalacia.

**Objective:** Report a novel mutation.

**Clinical Case:** A seven-year-old boy with short stature, postnatal growth retardation, development delay and learning disabilities. Background: normal delivery, BW: 2860 g, BL: 47 cm. GA: 39 weeks. Mother with short stature (143 cm –2.9 SDS), bone pain and ALP: 26 UI/L (NR: 40–150) PLP (Pyridoxal 5′phosphate): 40 µg/L (NR: 5–50). Physical exam: Weight: 15.3 kg (–2.64 SDS), Height: 100.5 cm (–3.99 SDS), Head circumference: 49.0 cm (–2 SDS), upper segment: 56.2 cm (pc 25). Target Height: 162.2 cm (–1.55 SDS). Cleft palate, micrognathia, low set ears, wide spaced nipples, mild hyperlaxity, short and wide fingers, clinodactyly of the 5th finger. Tanner stage I. Laboratory tests showed low serum ALP: 62 UI/L (NR: 135–537 for age and sex), PLP/vitamin B6: 41 µg/L (NR: 5–50), 4 Piridoxic acid: <3 µg/L (NR: 3–30). Radiological imaging: Hypomineralization in proximal ulna, radious and distal humerous, widening of the first metacarpals with radioluscent zones in all metacarpals and widened metaphyses in lower long bones. Analysis ALPL gene: exon 5 heterozygous variation c.317A>Gp. (Gln106Arg), sequencing Sanger. None ALPL gene deletion or duplication was found. Mother carries the same mutation.

**Conclusions:** This is a novel mutation, probably an heterozygous mutation with dominant effect that generates a mild form of hypophosphatasia.

## Insulin Sensitivity and Cardiovascular and Anthropometric Profile in Adolescence as Predictors of Non Alcoholic Fatty Liver Disease in Early Adulthood Results from the Longitudinal Study Santiago

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**Background:** The prevalence of nonalcoholic fatty liver disease (NAFLD) has increased among the youth as physical inactivity and unhealthy diets have grown. Imaging procedures to diagnose NAFLD are expensive and they are not always available for preventive purposes. We tested whether selected insulin sensitivity, cardiovascular and anthropometric biomarkers in adolescence predict the onset of NAFLD in early adulthood.

**Methods:** Observational study inn = 473 22 year-olds (50% males). At 16 y, BMI, waist circumference (WC), systolic and diastolic blood pressures (SBP and DBP) were measured. Total fat mass (TFM) was estimated (DXA). Fasting lipid profile (TC, TG, HDL), glucose, and insulin were measured. HOMA-IR HOMA-S, and SPISE Index were estimated. NAFLD at 22 y was diagnosed using ultrasound (Hamaguchi score for echogenicity ≥4). Logistic regression models were ran separately for males and females to test the association between these markers (predictors) and the odds of having NAFLD (outcome). BMI variation at 16–22 y was used as a control variable.

**Results:** NAFLD prevalence was 26% and 28% in males and females, respectively. In males, after adjusting for BMI variation from 16 y to 22 y, we found that insulin, HOMA-IR, SBP, TG, WC, TFM and BMI significantly increased the risk of NAFLD. Con-

versely, HOMA-S, SPISE, and HDL significantly reduced the odds of having the disease at 22 y. Notably, a one-unit increase in HOMA-IR increased by 45% (OR. 1.45, 95% CI: 1.15–1.84) the odds of NALD at 22 y. In females, only insulin, HOMA-IR, BMI and TFM were related to higher risk of NAFL at 22 y.

**Conclusion:** Among males, we found an association between insulin sensitivity, cardiovascular and anthropometric biomarkers in adolescence with NAFLD in early adulthood. These relationships are less clear among females. Insulin sensitivity, cardiovascular and anthropometric biomarkers in adolescence might be used to predict NAFLD in males but not always in females.

## Reproductive Hormone Levels in Patients with Cryptorchidism and RAS MAPK Pathway Variants Associated to Rasopathies

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Cryptorchidism is a frequent finding in Patients with RASopathies, which are Caused by derangements in RAS/MAPK genes. Recently, we reported almost the first molecular study of RAS/MAPK pathway variants in a cohort of Patients with cryptorchidism isolated genes. We detected nucleotide substitutions associated to 2.9% RASopathies in Patients with isolated cryptorchidism.

**Aim:** To compare reproductive hormone levels in cryptorchid Patients with and without RAS/MAPK pathway variants associated to RASopathies.

**Methodology:** Six Patients with RAS/MAPK pathway variants (RAS +) Were classified by Tanner stage and laterality (unilateral or bilateral cryptochidism). These Were matched Patients Patients with 104 without RAS/MAPK pathway variants (RAS-). Serum levels of Testosterone; Luteinizing hormone (LH); Follicle-stimulating hormone (FSH); Anti-Müllerian hormone (AMH) and Inhibin B Were Determined in all Patients (110).

**Results:** In the RAS + Group Four Patients Were Tanner I (unilateral); One Tanner II (unilateral) and one Tanner IV (bilateral). In the group RAS- 80 Patients Were Tanner I (unilateral); 20 Tanner II (unilateral) and 4 Tanner IV (bilateral). For Patients in Tanner I no hormonal Differences Were detected. For Tanner II, however, a lower level of Inhibin B was Observed in the RAS + patient [60.3 vs. 120.4 ± 52.1 pg/ml]. In Addition, in the Tanner stage IV to relativamente AMH level was low in the RAS + Observed patient [10.2 vs. 33.2 ± 24.9 ng/ml].

**Conclusions:** Patients with isolated cryptorchidism that exhibit RAS/MAPK pathway variants associated RASopathies with lower levels of relative Have Inhibin B (Tanner II) and AMH (Tanner IV) than without Patients RAS/MAPK pathway variants. Interestingly, similar lower levels pubertal Have Been Reported for Patients with Noonan Syndrome. If This difference is confirmed in a larger number of Patients, reproductive hormonal criteria May be useful to study RAS/MAPK gene variants in Patients with isolated cryptorchidism. (Fondecyt 1140450).

## Translational Medicine Copy Number Variants CNV in the Regulatory Region of SHOX Gene and Bone Modeling in Girls with Turner Syndrome 45X TS45X Preliminary Results

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**Research Objective:** To ASSESS the association of bone modeling and CNV in the regulatory region of SHOX gene in Mexican girls with TS45X.

**Material and Methods:** We Studied Patients with TS45X 58 and 20 controls with 46, XX karyotype (95% CI). Extracted DNA was using Qiagen kits, and high density (Affymetrix) microarrays performed. We Analyzed CNV in the regulatory region of SHOX gene with ChAS3.1 software. We Calculated height z-score at different moments During follow up and z-score of bone mineral density (BMD) of three regions Obtained by dual-energy X-ray absorptiometry (DEXA). Genomic effects through generalized linear Were Analyzed model. This project was authorized by the Research Committee of INP.

**Results:** 24 Patients with TS45X Have Been Analyzed so far. The distribution of CNV in the regulatory region of SHOX gene of cases with TS45X was different from controls; 100% of controls and 4.3% of cases ADH CNV = 2 Patients with TS45X Were found to Have CNV = 1 in 82.6% NVC = 3 in 4.2% and CNV = 4 in 8.3%. CNV = 1 was associated with z-score of higher Estimated target height ($p = 0.051$) and birth length ($p = 0.25$), but lower height z-score at last medical visit Their [(−3.23 ± 1.20 vs. −2.96 ± 0.59, $p = 0.66$], even though 9 girls (vs 1 non treated) milk received growth hormone analogues and 8 ADH induced puberty. The z-scores of BMD of lumbar spine ($p = 0.11$) and overall body ($p = 0.10$) tend to be higher in Patients with CNV = 1.

**Conclusions:** 1. There are Differences Between the number of CNV in the regulatory region of SHOX gene in Mexican girls with TS45X Compared with healthy controls. 2. The presence of CNV = 1 Tends to be associated with z-score higher length at birth, but lower height z-score at the beginning of growth hormone treatment, puberty onset and last medical visit.

## X Linked Dominant Chondrodysplasia Punctata-2 (CDPX2): Novel Mutation c.541delC (p.His181Thrfs 12) in the EBP Gene

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**Introduction:** Chondrodysplasia punctata is a heterogeneous group of skeletal dysplasias with particular clinical and genetic characteristics. X-linked dominant chondrodysplasia punctata-2 (CDPX2) also known as Conradi-Hünermann-Happle Syndrome [OMIM 302960] is a disease caused by mutations in the gene EBP (emopamil-binding protein) is located in Xp11.22 – p11.23. This gene encodes the enzyme 3-beta-hydroxysteroid-delta(8),delta (7)-isomerase (cholestenol Delta-isomerase) (E.C 5.3.3.5), which intervenes in the metabolism of cholesterol. This disorder that is characterized by ichthyosis, chondrodysplasia punctata, cataracts and short stature. The disease occurs almost exclusively in females.

**Case Report:** We report a case of a patient 7-year-old girl who is a full term baby born by Caesarian, to non-consanguineous parents, she was healthy at birth with no neonatal problems. At the age of six months she developed short stature and loss of weight, was valued several times without establishing a diagnosis. At the age of four years was remitted. Examination showed disproportionately short stature, macrocephaly, frontal bossing, hypoplasia of midface, depressed nasal ridge, high-arched palate, scoliosis, asymmetric limb shortening, lines of Blaschko, ichthyosis, sparse hair, patchy areas of alopecia, postaxial polydactyly (resected), radiological features include shortening of long bones with metaphyseal flare; short, broad femoral neck; and squared, shortened ilia. DNA was extracted from whole blood, sequencing for EBP gene showed that the patient has c.541delC (p.His181Thrfs*12) mutation.

**Discussion:** X-linked dominant chondrodysplasia punctata-2 (CDPX2) is not common, which should considered in patient with disproportionately short stature associated skin alteration described. We compared the clinical characteristic and radiological with cases report. The mutation identified in the presented case has not been reported previously.

## First Case of Hypoparathyroidism, Deafness, and Renal Dysplasia (HDR) Syndrome Due to a Novel Mutation in GATA3 with Gene Amastia and Athelia

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The combination of Hypoparathyroidism, Deafness, and Renal dysplasia (HDR syndrome) is a rare autosomal dominant condition primarily caused by haploinsufficiency of GATA3 gene. GATA3 is a zinc finger transcriptor factor, member of a family of transcriptional activators (GATA) that participates in early development. GATA3 is essential in the embryonic development of the parathyroids, auditory system and kidneys, and other tissues and, like other GATA family members, may be involved in the etiology of human conditions. Patients with HDR syndrome may present absent or hypoplastic parathyroid glands, alterations of inner ear morphology and urinary tract abnormalities such as renal dysplasia, unilateral kidney agenesis, or vesicoureteral reflux.

We report a female infant case of HDR syndrome. She was admitted to our Hospital at 7-years of age because of dehydration and chronic renal failure secondary to vesicoureteral reflux. The patient was a known case of seizure disorder since 8 months of age. She also presented postnatal growth retardation and neurological maturational delay. Bilateral sensorineural hearing loss with hearing aid requirements was diagnosed at 4 years of age. Interestingly, on physical examination amastia and athelia were found. During the initial endocrine evaluation, low levels of serum calcium were detected and Hypoparathyroidism was diagnosed. GATA3 exons and intron boundaries were direct sequenced in genomic DNA isolated from peripheral blood lymphocytes of the patient. A novel nonsense mutation p.Gln363* in exon 5 in heterozygous state was found.

To our knowledge, this is the first case of HDR syndrome with amastia and athelia.

In summary, the present study provides further evidence that GATA3 haploinsufficiency is the major cause of HDR syndrome and expands the phenotypic spectrum.

## Biochemical Hyperthyroidism in a Newborn Due to Biotin Immunoassay Interference

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**Introduction:** Neonatal hyperthyroidism is an infrequent condition. Most cases are due to placental transferal of thyroid-stimulating hormone (TSH) receptor autoantibodies (TRAb), from Grave's disease with mothers to Their fetuses. Even rarer causes are sporadic disease and genomic Grave's activating mutations in the TSH receptor of the neonate.

DESPITE the clinical thyrotoxicosis of the patient, thyroid function tests are Important tools in diagnosing hyperthyroidism. The results of the tests are normally easy to interpret. There are, however, some caveats in the measurement and judgment, one of which less commonly considered, is the interference with the assay used in the analyzes. Biotin is a small molecule found in every cell. Streptavidin is a much larger protein Biotin that Binds with a very high affinity. When These two molecules are present in the same solution, they bind in an Inevitably They Essentially irreversible way. This fact is used in a growing number of immunoassays for measuring multiple hormones.

**Objective:** With newborn to describe biochemical interaction assay Caused by hyperthyroidism from biotin intake.

**Case Report:** Male born at 39 weeks of gestation after an uncomplicated pregnancy. Weight: 3180 g, length: 50 cm. Apgar score: 8/9. I was the first child of healthy parents. There was no family history of thyroid disease. Twenty four hours after birth

have presented seizures and I was ADMITTED at the Neonatal Department. Were Routine chemistries normal electroencephalogram was altered with the normal brain CT. Neurologist recommended levetirazetam, carnitine, pyridoxine and biotin, with a favorable clinical evolution. Neonatal screening was performed in serum at 5 days of life and Showed TSH: 0.01 uUI/ml (0.80–8.29 RV). Complementary thyroid function test (TFTs) Were performed: T4: 24.9 ug/dl (7.4–19.1 RV), fT4: 7.7 ng/dl (1.26–2.8 RV), T3: 650 ng/dL (RV 137–321), TPOAb >600 IU/ml (RV <35), TGAb: 385 IU/ml (RV <40), TRAb >40 IU/L (RV <1.6) (Cobas Roche® ECLIA 8000). His mother TFTs were measured in standard. The newborn was clinically euthyroid goiter without, in discordance with the biochemical result. New TFTs after 48 hours were performed using CLIA Siemens® IMMULITE 2000 systems: TSH: 1.66 mIU/ml, T4: 17.2 ug/dl, fT4: 1.64 ng/dl, TPOAb 7 IU/ml, TGAb: 10 IU/ml.

**Conclusion:** This case highlights important issues to be critical worked in clinical practice: between considered clinical and biochemical consistency data. It is important that clinicians be aware of the potential for interference by biotin immunoassay in order to avoid misdiagnosis and patient harm due to inappropriate treatment.

## Hypoparathyroidism Deafness Renal Dysplasia Syndrome HDR Report of a Family Case

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**Background:** Hypoparathyroidism is infrequent in pediatrics patients. The causes are congenital or acquired. Among the genetic etiologies, the HDR syndrome is a rare autosomal dominant condition and is caused by a GATA3 gene mutations. This gene encodes a zinc finger transcription factor essential in the embryonic development of parathyroid glands, auditory and renal systems.

**Aim:** Report a family with HDR syndrome GATA3 with a new molecular genetic variant.

**Case Description:** The proband, a 4 year old hispanic female was admited to the hospital due to hypocalcemic tetany. A low PTH level was detected. Her mother, sister, and maternal uncle have neurosensorial hipoacusia. The mother had myoclonic epilepsy in her youth and hypocalcemia, hypoparathyroidism and basal ganglia calcifications were reported by then but no diagnosis or appropriate treatment were made at that time. Her older sister has similar metabolic alterations and both have unilateral palpebral ptosis. The proband has language delay with normal hearing, mild hypertonia, Chvostek sign and tiptoe walking. A cerebral CT scan showed parenchymal calcifications in both hemispheres. She and her sister have renal hypoplasia detected by renal ultrasound with normal renal function.

**Comment:** Barakat et al. described 4 children with hypoparathyroidism and sensorineural deafness who died due to progressive renal failure (HDR). Since then family cases have been described with phenotypic variations. Van Esch et al. defined a critical 200-kb region on chromosome 10p15.1-p14 that contains the GATA3 gene. This gene belongs to a family of zinc finger transcription factors that are involved in vertebrate embryonic development.

Its haploinsufficiency is the underlying mechanism of HDR syndrome. A new genetic heterozygous variant of GATA3, pTyr225Ter was detected in these 3 patients. The appearance of a premature codon stop predicts the presence of a truncated protein and the possible affectation of its biological activity.

**Conclusions:** Hypoparathyroidism is infrequent in pediatrics patients and we must search other signs that point towards genetic causes. The patient and her family have typical characteristics of this unusual syndrome. Beside the usual management of hypoparathyroidism they will require a nephrological monitoring since the prognosis depends on the renal disease. In addition, genetic counseling should be granted, as it is an autosomal dominant pattern of variable penetrance.

## Insulin Resistance Parameters in Children Who Were Born Very Preterm and Adequate for Gestational Age

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**Background:** Very preterm neonates are at risk for metabolic syndrome later in life. Our objective was to compare anthropometric measures and insulin resistance variables between children who were born very preterm (VPT, <32 gestational weeks) and term (T, >37 gestational weeks), and adequate for gestational age (AGA).

**Methods:** In this cross-sectional cohort study we recruited 113 children 5.0 to 8.5 years old from the preterm clinic of our institutions: 72 VPT (gestational age = 29 ± 2 weeks) and 41 T (gestational age 39 ± 1 weeks) with a similar socio-economical background. All children presented a Birth Weight Standard Deviation Score (BW-SDS) higher than 2, as calculated using INTERGROWTH21. We measured height, weight and abdominal circumference, and calculated body mass index (BMI) percentiles using WHO references. After overnight fasting, glycemia, insulin, triglycerides and HDL-Cholesterol were determined. We determined the homeostasis model assessment insulin resistance (HOMA-IR) index, the quantitative insulin-sensitivity check index (QUICKI), and the triglyceride to HDL-C ratio (TG/HDL-C).

**Results:** Were comparable VPT and T in chronological age (6.6 ± 0.9 vs. 6.7 ± 1.0 years; p = 0.535) and anthropometrics variables: height SDS (–0.19 ± 0.86 vs. 0.10 ± 1.03; p = 0.903), abdominal circumferences (58.5 ± 7.4 vs. 58.50 ± 7.1 cm; P = 0.982), BMI-percentile (59.0 ± 32.0 vs. 64.0 ± 29.0th; p = 0.476), and BW-SDS (0.40 ± 1.03 vs. 0.52 ± 0.72; p = 0.512). Insulin-resistance parameters are presented in the Table.

As expected there is a positive correlation BMI and TG/HDL-C ratio (r = 0.281; p = 0.003).

**Conclusion:** At this age, insulin-resistance parameters in children who were born very preterm and adequate for gestational age

**Table 1.**

| | VPT (n = 72) | T (n = 41) | Total (n = 113) | p value |
|---|---|---|---|---|
| Glycemia (mg/dL) | 84.54±6.52 | 83.10±7.19 | 84.02±6.77 | 0.278 |
| Insulin (uU/mL) | 5.79±3.39 | 5.36±2.56 | 5.63±3.11 | 0.485 |
| HOMA-IR | 1.23±0.75 | 1.12±0.56 | 1.19±0.69 | 0.425 |
| Quicki | 0.17±0.02 | 0.17±0.04 | 0.17±0.03 | 0.269 |
| TG/HDL-C | 1.44±1.03 | 1.01±0.46 | 1.28±0.89 | 0.014 |

were not different compared to children born at term. Nevertheless, TG/HDL-C ratios were higher in VPT which could suggest a potential metabolic risk; therefore, it is essential to follow this group during their lifespan. Fondecyt 1160836.

## Epidemiology and Clinical Characteristics of Cystic Fibrosis Related Diabetes in Pediatric Patients Treated at a Single Institution

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**Objectives:** Clinical and epidemiological characterization of patients with cystic fibrosis related diabetes (CFRD) treated at Pediatric Hospital Roberto del Río, Santiago, Chile, during 2017.

**Methods:** We reviewed clinical history of 34 patients treated at Cystic Fibrosis (CF) Outpatient Clinic. Data regarding epidemiological and antropometric features, screening with oral glucose tolerance test (OGTT) and prescence or abscense of hyperglicemia in acute exacerbation and/or glucocorticoid therapy, was collected. The study was approved by local ethics committee.

**Conclusions:** The prevalence of CFRD in our patients is similar as reported in literature. Screening is performed in few patients. Abnormalities in glucose metabolism are present without overt diabetes. More CF patients should undergo screening for glucose abnormalities to allow early interventions and improve their outcome.

**Results:** Thirty four patients were enrolled. 18 were boys, median age 9.3 years (1–21 yr). 76% were eutrophic. Three patients had CFRD (9%), all of them boys. Of all patients without CFRD, OTGG was done in 7 (21%) and was abnormal in 2 (29%). Hyperglicemia in acute exacerbation was present in 5 patients with CF and without CFRD (16%). Genetic study was performed in patients with CF and CFRD. Results are shown in table 1.

**Table 1.** Genetic study of CFTR variants in CF and CFRD Patients

| CFTR genotype | Patients with CF, n (%) | Patients with CFRD, n (%) |
|---|---|---|
| F508del homozygous variant | 6 (18%) | 0 |
| Heterozygous F508del variant | 18 (53%) | 3 (100%) |
| Other CFTR genetic variants or non determined variants | 10 (29%) | 0 |
| Total, n | 34 (100%) | 3 (100%) |

## Pitfalls of Bone Age Determination by Ultrasound Baus

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**Objective:** Aiming to compare Greulich-Pyle with Baus (GP) radiographic method of bone age determination (Barx).

**Method:** We evaluated 494 Control health students (F: 250; M: 244), and BMI age range 6–17 y Between ± 2 SDS. Baus was performed Employing the SonicBone Medical device and barx was done using a portable device Rx. Barx was established after reading of 3 experienced Investigators (2 pediatric endocrinolo-gists and 1 radiologist).

**Results:** A significant Correlation between Baus and barx was Identified Both in girls (r = 0.92; p = 0.001) and boys (r = 0.91; p = 0.001). A significant correlation was Also Between detected chronological age (CA) and BA methods (Baus: r = 0.95 and barx: r = 0.94, p = 0.001). Differences Between Were Both methods detected in the predominantly upper age limits. Unexpectedly, a predominant influence was Identified for CA and Stature When a multiple regression analyzes Were performed. In order to test esta finding, we select one single Baus single Undergoing Repeated reading, modifying one by one the following variables: CA: ± 2 y; and Stature: ±1 SDS. The Baus results were different in each tested Significantly condition. Therefore, unexpected Differences of Baus reading Were Obtained in the same single by changing CA or height. It Seems that only 20% of Baus is Determined by the sonographic variables.

**Conclusions:** Determination Baus presents adequate adjustment in the normal population with average GP-barx. But, the inclusion of CA and stature in ITS algorithm to offer potential source of imprecision When analyzing of Patients with BA pathological conditions with short/tall stature or in conditions in which bone age delay/advancement is expected. THEREFORE, we expect serious limitations in Baus use in clinical conditions Several pathological.

## Pediatric Adrenocortical Tumors a Single Tertiary Center Experience Clinical Biological and Pathological Characteristics Analysis

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**Objective:** To Evaluate the clinical, biochemical, staging (ST ACCORDING TO COG system), and pathologic (Wieneke index) Characteristics of ACT in a single pediatric tertiary center.

**Subjects and Methods:** 28 Patients with pediatric ACT (CA <18 years) Treated between1987–2017.

**Results:** Mean CA at diagnosis was 4.6 and F/M ratio 2.5/1. Median follow-up was of 3.64 and (range 0–12 y). Initial clinical signs hormone overproduction Were: 57.1%, abdominal mass/pain: 35.7%, and hypertensive encephalopathy: 7.1%. In clinically predominant virilizing (n = 16) mean ± SD Height-SDS (1.03 ± 1.29) and∆BA-CA Were Significantly higher, while BMI-SDS (0.79 ± 0.8) was lower than in clinically Significantly predominant Cushing (n = 10) (p = 0.05). Limited disease (ST I/II) was Observed in 13 (46.4%), advanced disease ST III in 10 (35.7%) and ST IV 5 Patients (17.8%). Accordingly to hormonal production Were Analyzed: Gr1 (n = 14) co-secretion of androgens and cortisol, Gr2 (n = 8) isolated androgen secretion, and Gr3 (n = 2) cortisol secretion (4 Patients Could not be Assessed). High serum DHEAS levels in Gr1 Gr2 and (X ± SD 18603 ± 16419 ng/ml) Were detected. Serum DHEAS levels in Were Significantly higher IV vs ST ST I (p = 0.03). Total adrenalectomy was performed in 26/28 patients. Eight Patients (ST III-IV) received adjuvant chemotherapy (AChemo) with cisplatin, etoposide and doxoru-bicin. Disease free survival (DFS) and overall survival (OS) was both100% for ST III, and 46.7% and 53.3% for Stage III-IV respectively (mean follow-up of 8.4 and 8.6 y). A tendency of higher DFS on AChemo (75%, n = 8) vs without AChemo (29%, n = 7) was found (OR = 0.13, 95% CI 0.01–1.31). Tumor staging correlated positively and significatively with tumor weight and Wieneke criteria (p = 0.01). Conclusions: Height and BMI mirror ACT hormonal secretion. High serum DHEAS levels Might be used as a biological marker of tumor stage. ST I/II Were associated with best outcomes. Long term follow-up is needed to draw valid conclusions of using AChemo. Tumor staging correlated positively and significatively with tumor weight and Wieneke criteria (p = 0.01). Conclusions: Height and BMI mirror ACT hormonal secretion. High serum DHEAS levels Might be used as a biological marker of tumor stage. ST I/II Were associated with best outcomes. Long term follow-up is needed to draw valid conclusions of using AChemo. Tumor staging correlated positively and significatively with tumor weight and Wieneke criteria (p = 0.01).

**Conclusions:** Height and BMI mirror ACT hormonal secretion. High serum DHEAS levels Might be used as a biological marker of tumor stage. ST I/II Were associated with best outcomes. Long term follow-up is needed to draw valid conclusions of using AChemo.

## Stimulating TSH Receptor Autoantibodies Measurement in Children with Hyperthyroidism. Analytical and Clinical Performance of an Automated Chemiluminescence Immunoassay

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**Introduction:** The most common cause of hyperthyroidism (HT) in children is Graves' disease (GD), caused by antibodies that stimulate the thyroid gland. GD is confirmed by testing TSH receptor autoantibodies (TRAbs). Stimulating TSH receptor autoantibodies (TSI) are pathognomonic, and are present in 98% of patients with GD. The immunoassays show high analytical and clinical sensitivity but do not allow detection of TSI only. Recently, the first automated method to test the TSI level has become available.

**Objective:** To study the clinical performance of an automated immunoassay for TSI determination in children with HT, and to analyze the correlation with a current method for TRAbs quantification.

**Material and Methods:** Be of 74 subjects were divided into two groups: the group with HT n = 47, age mean±SD (13.2 ± 3.39), subjects were selected based on clinical and laboratory results. Patients with thyrotoxicosis without HT were excluded. The control group n = 27, age (11.6 ± 5.23), was selected from patients with craniopharyngioma in whom thyroid function was tested. Thyroid function and TRAbs were assessed with chemiluminescent immunoassays and manual RIA, respectively, and TSI using chemiluminescent immunoassay from Siemens-Immulite 2000 ROC plot, Kruskall-Wallis, and correlation were used for statistical analysis.

**Results:** TSI were positive in all HT subjects (cut-off >0.55 IU/L) and not detectable (<0.1 IU/L) in control subjects (p < 0.0001). There were no false positive or false negative results. Performance of the assay was good (CV% 1.2 and 14.2). ROC plot analysis showed excellent sensitivity and specificity (100% each) AUC = 1. Inter-assay correlation was good (r = 0.85 p < 0.0001) in the HT group. All but one TRAb positive HT patient were positive for TSI as well.

**Conclusions:** The TSI study method showed good accuracy with high sensitivity and specificity. The cut-off suggested by the manufacturer is adequate for children as well; indeed, a lower cut-off could be used in our groups.

## Clinical and C Peptide Plasma Concentration Differences in Patients Between 2 and 18 Years of Age with Diabetes Mellitus and Who May Present with Pancreatic Autoantibodies. A Case-Control Study

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**Objective:** Establish clinical and laboratory criteria that allow the medical doctors to diagnostic suspicion of MODY and determine which patients require confirmatory tests.

**Methods:** Case control study, in patients with diagnosis of diabetes between 2 and 18 years, with or without autoantibodies, in five institutions in Bucaramanga, Colombia. Measurement of fasting plasma C peptide (RV: 0.7–1.9 ng/ml) and autoantibodies (GAD and IA2) was performed on all patients by ELISA technique. The clinical and laboratory characteristics of each group were compared. This study was funded by Colciencias, external code: 110265741650.

**Results:** See Table 1.

**Conclusion:** MODY should be suspected in patients with negative antibodies, with onset of illness at an older age, who have a family history of DM diagnosed before age 30, who usually do not have ketoacidosis or glycosuria, with glycosylated hemoglobin levels lower, use oral antihyperglycemic drugs as part of management and need insulin after 5 years of diagnosis.

## A 60-Minute LH Diagnostic of Central Precocious Puberty

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**Introduction**: Managing (PP) has-been a challenge due to varied clinical presentation and the lack of standardization in definition and hormonal parameters for Assessing outcomes.

**Objective:** To describe clinical and hormonal features of children Who Had undergone GnRH Stimulation Test as part as the diagnosis of PP.

**Methodology:** Chronological age, weight, height, bone age, LH, FSH, estradiol/testosterone were analyzed in 145 children (130 females and 15 males) with clinical evidences of early pubertal development and GnRH Stimulation Test performed between 2003 and 2017 at Children's Hospital in New Orleans, LA. Leuprolide Acetate: 20 mcg/kg/dose max 400 mcg SQ was used as protocol. LH and FSH were measured at 0, 30, 60, 90 and 120 minutes post-injection; Estradiol/Testosterone at 0 and 120 minutes post-injection. LH ≥5 mlU/mL and/or LH/FSH ratio >1 was considered a positive (pubertal) response.

**Results:** 81 subjects (55.9%) showed positive response and 64 (44.1%) negative response after GnRH. The mean chronological age was 5.81 ± 2.52 in the negative group and 7.37 ± 2.07 in the positive group (p = 0.000). Weight, height and bone age were higher in the positive group (p = 0.002, p = 0.001, p = 0.000). Basal LH and estradiol, peak LH, peak LH/FSH ratio were also higher in the positive response group (p = 0.000, p = 0.002, p = 0.000 respectively). 25 subjects (30.9%) with pubertal response showed basal LH <0.3 mIU/mL. In the positive response group, the LH peak was at 60 min in 22 patients (27.16%) and 120 min in 43 patients (53.09%). A LH ≥5 mlU/mL was achieved in 72 patients (88.9%) at 30 min; and in the remaining 9 (11.1%) at 60 min.

**Table 1.** Characteristics at diagnosis of DM between patients with and without autoantibodies

| Characteristic | Antibodies | | P value |
|---|---|---|---|
| | Positive (n = 58) | Negative (n = 45) | |
| Female | 35 (55.17%) | 26 (57.78%) | 0.791 |
| EB for 6 months | 20 (34.48%) | 22 (48.49%) | 0.140 |
| Age at Diagnosis (years)* | 7 (4 a 10) | 8 (4 a 11) | 0.036 |
| DM in relatives | 35 (58.62%) | 32 (71.11%) | 0.327 |
| Relatives with DM and diagnosis <30 years | 8 (13 79%) | 15 (33.33%) | 0.025 |
| Ketoacidosis | 39 (67.24%) | 17 (37 78%) | 0.003 |
| Glycosuria at diagnosis | 44 (75.86%) | 16 (35.56%) | <0.001 |
| Glucose at diagnosis* (mg/dl) | 459.5 (360–583) | 250.0 (135–499) | 0.164 |
| HbA1C at diagnosis (%)* | 9 (7.4–10.9) | 8 (6 5–9.4) | 0.034 |
| Current use of oral hypoglycemic | 1 (1.72%) | 10 (22 22%) | 0.001 |
| Clinical diagnosis | | | |
| DMT1 | 58 (100%) | 23 (51.11%) | <0.001 |
| MODY | – | 22 (48.89%) | |

*Median and IOR.
DM: Diabetes mellitus; EB: Exclusive breastfeeding.

**Conclusions:** GnRH Stimulation Test is still essential for the management of PP. Samples drawn at 30 and 60 minutes Could be sufficient for the diagnosis.

## Central Precocious Puberty After Surgical Resection of Giant Craniopharyngioma in a Girl

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**Introduction:** Craniopharyngiomas are the most commonly found hypothalamic pituitary isolated tumor in childhood. At diagnosis, most patients present with pain and endocrine symptoms related to the rupture of the hypothalamic-pituitary axis function. In general, the manifestations are associated to hypopituitarism, but less frequently, precocious puberty may occur. Although tumors of the central nervous system are relatively common childhood neoplasms, the association with early puberty is uncommon. Sometimes, even distant tumors of the central nervous system can stimulate GnRH due to compression of the hypothalamic pituitary region in cases of hydrocephalus. We report a case of a child with precocious puberty associated with giant craniopharyngioma. Currently, the endocrinological comorbidities are under control.

**Case Report:** LSS, 5.4 years, from São Paulo. Birth through vaginal delivery, 34 weeks of gestational age. At 15 months, she developed speech difficulty, visual loss and strabismus. A Magnetic Resonance imaging was performed, with the image of an extensive and calcified craniopharyngioma. At 3 years of age she underwent a cystic drainage surgery, without success and an Ommaya chamber was inserted for future intrathecal chemotherapy. Six months later, she presented movement loss in the right side of the body due to tumor compression.

At the age of 4.3 years the patient received intralesional. The therapy was not able to slow the progress of the tumor. At 4.6 years, a surgical resection was performed. The chamber and 90% of the craniopharyngioma was removed, a peritoneal shunt valve was inserted for hydrocephalus treatment. A month after the surgery, the patient was admitted to our hospital, for central hypothyroidism monitoring, which was diagnosed prior to resection. At the occasion, her Tanner stage was B1P1 and she was receiving Levothyroxine 25 mcg/day. At the same time, she started breasts development. Puberty evolved rapidly, with progression from Tanner B1P1 to B3P1 in 3 months. At 4.9 years, the patient presented a bone age of 6.8 years. In the same year a new surgical approach was performed with peritoneal bypass valve reinsertion due to a local complication. She is currently being treated with Leuprolide Acetate 7.5 mg every 28 days, Levothyroxine, Baclofen and Valproic Acid, maintaining a Tanner stage of B3P1.

**Discussion/Conclusion:** Although rare, early puberty may be associated with craniopharyngioma. Probably caused by high intracranial pressure, but also may be a consequence of surgical resection, since the patient presented the symptoms 2 months after definitive treatment.

## Evaluation of Four Direct Immunoassays for Measuring Estradiol Impact in Pediatrics

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**Introduction:** The determination of serum estradiol is used in pediatrics for the evaluation of several pathologies. The reference method is Isotope-Dilution Gas Chromatography-Mass Spectrometry. However automated immunoassays are the most widely used due to their simplicity and practicality, although these methods do not present good sensitivity at low levels. As a result, it is difficult to interpret the results for clinical decisions in pediatric population due to the differences found in the immunoassays.

**Objective:** Evaluation of four direct immunoassays for the determination of estradiol in pediatric patients and their clinical applications.

**Subjects and Methods:** 96 girls will be from (0.9 to 15 years) Were Analyzed by four automated tests for the determination of estradiol: Immulite 2000 (IMM), Advia Centaur CP (AC), Architect (AR), Cobas E411 (CB). Fifty-four patients were classified into groups according to Tanner stages. The limit of quantification was calculated.

**Results:** Significant differences were observed among all methodologies. The Pasing-Bablok analysis showed correlation only between CB and AR. The dispersion between the methods increased at low values and were higher in IMM. The values between Tanner stages I, II and III were similar for all platforms, however CB was able to differentiate stage I from III.

**Conclusions:** It was observed low reproducibility between the platforms and high dispersion of values at low levels of estradiol. This has an impact on the usefulness of these methods for clinical decisions, making it difficult to evaluate patients with levels of estradiol within this range. Cut-off values should be established for the beginning of pubertal development for each methodology, since those proposed in the literature can not be extrapolated. The determination of estradiol is not a useful tool for the evaluation of precocious puberty in girls in the initial stages, since it would not allow to differentiate populations with stages I, II and III of pubertal development.

## Randomized Study of Vitamin D Supplementation for the Prevention of Acute Respiratory Infections Aris of Chile in Preschools

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Vitamin D (VD) would be a potential agent to Prevent ARIs due to multiple effects on the immune system. Systemic reviews Suggest a benefit of VD in the prevention of ARIs. In Chile, previ-

ous studies in children show high rates of VD deficiency (DVD) in Santiago (S), Talcahuano (T) and Punta Arenas (PA), probably associated with low solar radiation and lack of fortification of food with VD.

**Objective:** To Evaluate the effectiveness and safety of supplementation with the VD to reduce incidence of ARIs.

**Methods:** Multicenter, randomized, controlled, double-blind study in children from 1.5 to 3.5 years of age in S, T and PA, WHO Were Assigned to receive placebo, VD3 5,600 IU/week or 11,200 IU/week for 6 months. The primary result was number of IRAs; Secondary outcomes included number of hospitalizations, variation of serum levels of 25 (OH) VD and LL37 (cathelicidin).

**Results:** Were Recruited subjects 303 (101 in S, 103 in T and 99 in PA), average age of 26 ± 6 months, 45% female. Baseline Characteristics: Children of T HAD longer breastfeeding (BF), lower percentage fortified milk used formulates with VD (>250 UI/l) and had a lower level of 25 (OH) VD. The percentage of DVD was 13% in S; 32% and 21% in T in PA. Children with less use of DVD ADH fortified milk with VD Compared with children without DVD (19% vs 36%, p = 0.012). There was no correlation Between age, sex, birth weight, height at birth, gestational age, z-score weight/height, excess weight or obesity with basal DVD. There Were no Differences Between groups in baseline demographic or clinical variables. After six months of intervention, there was no difference Between the number of hospitalizations or ARIs Among the three arms, nor in the subgroup that Initiated with the DVD study (p = 0.47). Were there no significant variation Differences in serum LL37 Among the three arms (p = 0.36). There was a significant difference in longitudinal change of 25 (OH) VD Between the arms 3, Achieving a greater Increase in serum 25 (OH) VD in group VD3 11,200 IU/week. In the placebo group, only 6% of the children ADH VD at the end of sufficiency winter, Compared with 56% in the group VD3 5,600 IU/week and 64% in the group VD3 11,200 IU/week (p = 0.001).

**Conclusions:** This study shows weekly VD3 with that supplementation in doses equivalent to 800 IU and 1600 IU/day is safe and effective to reduce rates in Chilean DVD pre-school children, but did not change the number of Significantly in This population IRAs.

## Hyperthyroidism Beyond the Thyroid

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Pediatric Hospital Foundation Mercy

**Background:** Thyrotropin-secreting pituitary adenomas (TSHomas) are a rare cause of Hyperthyroidism. Represents TSHomas About 0.7 to 0.84% of all cases of hypophyseal adenomas. The majority of the cases are diagnosed in middle aged Patients, but there are some Reported in the range of 11–84 years of age. A 14-year-old man presented visual acuity with headaches and loss for the last month. Past medical history was significant sub-clinic family in a maternal aunt Hyperthyroidism Treated with radioactive iodine ablation. The clinical examination revealed bitemporal hemianopia, tanner stage 3 without other abnormalities Blood TSH test Reported: 6.5 μU/ml (0.4–4), and serum-free thyroxine (Free T4) of 3.07 ng/dL (0.98 to 1.63 ng/dl). Demonstrated to solid MRI lesion on the seal-suprasellar region and floor of third ventricle that Measured 30 x 21 x 24 mm and the optic chiasm displaced. Blood test Were Repeated: TSH: 9.4 μU/ml (0.4–4), Free T4: 2.3 ng/dl (0.98 to 1.63 ng/dl), am cortisol 9.6 ug/dl (8–10 ug/ dl), prolactine: 18.98 ng/ml (4–15 ng/ml) and FSH: 3.04 – LH: 2.51. Thyroid ultrasonography revealed heterogenous echogenicity and goiter with small Colloid cysts. An altered auditory evoked potentials retinal-cortical pathway bilaterally. The patient underwent surgery. Pathology Demonstrated tumor cells positive for TSH and negative for prolactine, ACTH, LH, FSH, GH and FSH. A low Ki67 proliferative index was reported almost (Ki67 <5%) which confirmed the diagnosis of a TSHoma. Post surgical blood tests hormone normally were. At this moment the normal thyroid function patient has.

**Conclusions:** TSHoma is a rare tumor in the pediatric population with an unpredictable prognosis. They are an infrequent cause of hyperthyroidism and Should be suspected on Patients with subclinical hyperthyroidism.

## Characterization of Endocrinopathies in Patients with 22q11 Deletion Syndrome

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**Introduction:** The 22q11 deletion syndrome is a multisystemic genetic alteration, which presents a high variability in its phenotype, it is cataloged as the most common microdeletion syndrome with a prevalence of 1 per 4,000 live newborns. Its main manifestations are congenital heart disease, immunodeficiency, hypoparathyroidism, alterations in the palate, problems with feeding and genitourinary anomalies. Additionally, other associated endocrinopathies such as hypo or hyperthyroidism and growth hormone deficiency can be found.

**Objectives:** Characterize the endocrinopathies related to the 22q11 deletion syndrome in a cohort of patients attending a children's hospital in the city of Medellín during the period from January 2011 to December 2017.

**Methods:** Retrospective descriptive observational study of a group of children diagnosed with a 22q11 deletion syndrome attending a children's hospital in the city of Medellín from January 2011 to December 2017.

**Results:** Thirty-seven patients with a confirmed diagnosis of 22q11 deletion syndrome were included. 37.8% had some endocrinopathy, the most frequent being hypoparathyroidism (21.6%), followed by hypothyroidism (13.5%), hyperthyroidism (2.7%) and GH deficiency (2.7%). There was wide heterogeneity in the clinical presentation, with late onset of severe hypocalcemia associated with seizure or precipitated in the postoperative cardiac surgery, which highlights the importance of continuous follow-up as indicated by the guidelines. The short stature is mainly related to nutritional factors. Auxological monitoring is required with the use of syndrome-specific tables and carefully monitor the growth rate.

**Conclusions:** It is essential to carry out an adequate multidisciplinary follow-up, based on the specific clinical guidelines, to avoid serious complications such as convulsions due to hypocalcaemia. It is important to track size with the specific curves of the syndrome and analyze the growth rate.

## Effect of Growth Hormone Replacement in the Vascular System of Adult Hypopituitarism Patients with Childhood Onset

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**Objective:** To Evaluate the recombinant human growth hormone (rhGH) replacement in the metabolic parameters and vascular system in adult Patients with hypopituitarism childhood onset.

**Patients and Methods:** Fifty-one adult hypopituitarism childhood onset Patients with Were selected for a transverse study. They Were divided into two groups: 1- Under GH replacement: 13 male, 14 female with age 33.2 years median, under GH replacement in adult life with 7.38 years median time; 2- Off GH replacement: 13 male, 11 female with age 36.9 years median and without GH replacement in adult life of 10.4 years median time. Anthropometric parameters, dual energy X-ray absorptiometry-(DEXA), lipid and glycemic profile, and structural and functional parameters of the blood vessels (carotid intima media thickness, arterial stiffness and flow mediated dilation) Were EVALUATED.

**Results and Conclusions:** The diagnosis of obesity and overweight was higher in Patients without rhGH replacement. Among the anthropometric Characteristics, the waist-to-height ratio and diastolic blood pressure higher Were In Patients without replacement ($p = 0.03$ and $p = 0.019$, respectively). There Were no statistical Differences Between groups lipid profile and metabolic Regarding. In the evaluation of DEXA body composition through, the Fat Mass Index Among Patients under rhGH was Significantly lower than replacement in Patients without rhGH ($p = 0.029$). Although no statistical difference in the vascular parameters Between Patients with and without rhGH replacement, was Observed a trend towards higher arterial stiffness in the group without replacement ($p = 0.051$). In the group of Patients without rhGH use, arterial stiffness had a significant and positive correlation with the use rhGH time without ($p = 0.038$). These data Suggest that the replacement of rhGH in Adults with childhood onset hypopituitarism May Have effects on cardiovascular system protective. We can close up commercial that hypopituitarism diagnosed in the childhood is Important to be followed along adult life.

## Reference Values of Automated Bone Age and Bone Health Index for Mexican Children and Adolescents

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**Background:** BoneXpert is a software for automated measurement of bone age and bone health index (by radiogrammetry). The accuracy error (repeatablility) of the software for bone age is much smaller than measure the human rating errors and the accuracy relative to the human routine ratings is 0.70–0.80 years. Differences in skeletal maturation Have Been Reported Between ethnicities, so it is Important to Have the specific references for the local population.

**Objective:** To present bone age and bone health index reference curves for Mexican children and adolescents.

**Methods:** We Conducted a prospective, cross-sectional study. We included 722 healthy children Between 5 and 18 years old of Mexico city's metropolitan area 2018. Between 2017 and hand AP radiography was taken and BoneXpert Analyzed using automated software to determine bone age and bone health index. We constructed the reference values for bone age curves and bone health index.

**Results:** We Observed a bone age similar to the Greulich and Pyle scale up to age 10 and approximately 0.9 years ahead Then at the end of puberty. An Increase in the bone health index was Observed ACCORDING TO the Increase in skeletal maturation; however, the values at the end of puberty are lower than in Caucasian Populations Reported that at the same bone age, in particularly for boys (mean 5.5 ± 0.46 in boys and girls in mean ± 5.3).

**Conclusions:** Mexican Have children an acceleration in bone age that causes an advance of about 1 year at the end of puberty.

This Could have an effect on the end lower adult height Observed in the Mexican population in comparison with Caucasian Populations. Additionally, the bone health index in Mexican children is lower than in Caucasian Populations at the end of puberty. Future studies are required to Evaluate the Clinical Implications of esta observation.

## Follow-Up on Bone Health in Children with Acute Lymphoblastic Leukemia (ALL)

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**Background:** Acute lymphoblastic leukemia (ALL) is the MOST common pediatric cancer. Skeletal Morbidity Has Been Recognized as a complication of ALL and STI treatment, occurring at diagnosis, During Chemotherapy and/or years later.

**Aim:** To describe the effect on bone health adversely, in terms of vertebral fractures (VF) and bone mineral density (BMD) in the follow-up of Children with ALL.

**Design, Patients and Methods:** Descriptive and retrospective study. Children with ALL Were selected from the Endocrinology Division of Children's Hospital Ricardo Gutierrez. Clinical and auxological characteristic Were recorded. VF and BMD which Were Assessed by thoracolumbar spine lateral radiographs (According to the method Genant) and dual-energy x-ray absorptiometry (DXA, Hologic or using Either Lunar Prodigy), respectively. Estimates (in months) of the presence of VF or abnormal BMD Were EVALUATED since diagnosis.

**Results:** 29 Children with ALL Were included (age at diagnosis: 5.38 ± 3.16 years). The follow up time was 46.21 ± 42.10 months. Twenty-two Were Assessed with lateral spine radiograph and 26 with DXA. Only children under chemotherapy HAD 7/29 VF 5 within the first 12 months of treatment and 2 During the second year of treatment. Were not detected along VF further follow-up. A low BMD was Identified in Patients 5/26, 2 of them During the first year of treatment (Lunar DXA Z score = –4.0, and DXA Hologic Z score = –3.9) and ADH VF Both Present in the second year. The other three children developed low BMD on follow up (84.33 ± 74.54 months): DXA Hologic Z score = –2.1 (n = 1) and DXA Z

Score = –3.05 ± Lunar 1.3 (n = 2). All patients improve their BMD. However, only 2/5 their normalized values. Back pain was not a constant symptom associated with VF and only Appeared in Children with VF 2/7.

**Conclusion:** VF are common in children with All and is more prevalent along the first year of treatment. Usually are asymptomatic, therefore remain might undetected if routine surveillance is not performed. The BMD can be AFFECTED too, so an early diagnosis and intervention Should be Considered in order to Prevent compromise of future bone mass peak.

## Phosphocalcic Metabolism in Intestinal Insufficiency: Cross-Sectional Analysis

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**Introduction:** Bone health is an important challenge in pediatric patients with intestinal insufficiency. Individualizing nutrition and supplementation helps to optimize metabolic parameters. Maintaining appropriate levels of vitamin D (Vit-D) may improve bone quality.

**Objectives:** To analyze phosphocalcic metabolism in patients with intestinal insufficiency and to establish metabolic parameters to maintain bone health.

**Material and Methods:** Clinical records of 80 patients undergoing follow-up in the intestinal rehabilitation clinic of a University Hospital were analysed; 32 were excluded (7 died, 6 incomplete records and 19 lost follow-up). Data of 48 patients (32 boys) were finally analyzed; 41 met inclusion criteria: currently in follow-up and phosphocalcic assessment during previous year. Diagnosis was made in neonatal period in 85.1%, range 0–13 years; 72.3% had structural pathology. Time between diagnosis and evaluation was 5.1 years (0.4–17.1). Anthropometric assessment showed weight (mean Z score +SD) –0.98 +1.44, height –1.58 +1.5; weight/height 100.2 +13.2%. Intestinal function was categorized according to anatomical conditions: 8% ileostomized, 39% with colon without ileocecal valve and 52% with colon and ileocecal valve. Four patients received intestinal transplantation and 40% underwent intestinal elongation surgery. Patients were under enteral nutrition (63%), parenteral nutrition (6.5%) or combined enteral-parenteral nutrition (30.5%); 61% were on Vit-D supplementation. Vit-D sufficiency was considered when value was >20 ng/ml. Patients were divided in 2 groups according to Vit-D status: group 1, insufficient (n = 22); group 2, sufficient (n = 19); and in 3 groups according to skeletal radiological findings (Rx): R1, normal (n = 12); R2, abnormal (n = 17); R0, not available (n = 12).

**Results:** No significant differences in anthropometric and biochemical variables were found between D1 and D2. Parathormone levels (pg/ml) and Vit-D supplementation (IU/day) (mean +SD) were 35 +23 and 5500 in D1; 31.6 +17 and 5047 in D2 (p ns). Rx were available in 29 patients, 17 of 22 in D1 (59% abnormal); 12 of 19 in D2 (33% abnormal). Vit-D levels were different between R1 and R2 (25.1 +8.5 vs. 16 +7.3 ng/ml) (p 0.007). Vit-D doses were 3.625 vs. 9.291 UI/day (p ns).

**Conclusion:** Patients with normal Rx had better levels of Vit-D, despite receiving lower dosis. Vit-D supplementation must be individualized in order to get values >20 ng/ml.

## Advanced Medullary Thyroid Carcinoma in an 11-Year Old Boy: Treatment with Vandetanib

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Children's Hospital "Ricardo Gutiérrez"

**Case Report:** An 11 year old boy with a longstanding history of hypotonia and diarrhea starting at 3 months of age Consulted at our center Because of a multinodular goiter (MNG) with multiple adenomegalies detected on a spinal MRI and CNS. Physical exam Showed to read boy (BMI: 12.5), with average stature and mar-fanoid phenotype, thick lips and eyelids and multiple small whitish nodules on His tongue. Cervical examination revealed cervical MNG with adenomegalies. TSH was 25.8 mU/I Normal thyroid hormones with, negative thyroid antibodies, circulating calcitonin 58085 pg/ml (RV: 0–46) and the normal urinary catecholamines. Cervical ultrasound Showed a left dominant heterogeneous nodule with Increased vascularization center and right small microcalcifications and 2 nodules with microcalcifications and abnormal cervical multiple lymphadenopathies. FNAB was positive for medullary carcinoma (MTC) with wash out positive for calcitonin. Bone scan was negative but multiple pulmonary metastases Were found on CT. Proto-oncogene RET mutation c.2753T>CpM918T was found in exon 16 confirming MEN 2B Syndrome. Partial resection of the thyroid tumor and neck dissection was left Decided to reduce tumor mass and adjacent tissue compression. In the presence of a locally and distant metastatic MTC with vandetanib treatment was started. After the first month Decreased by 90% calcitonin. Currently after 22 months of treatment His serum calcitonin is 1400 pg/ml. Dramatically improved gastrointestinal symptoms and allowed school reinsertion. Photosensitivity was the only adverse event and was managed with Local treatment. His illness has stabilized vandetanib and allowed a better quality of life.

## Disorders of Sex Development in Mexican Child: Experience of Interdisciplinary Approach in 10 Years

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**Objective:** Describe the prevalence, clinical characteristics and treatment of the types of Disorder of Sex Development Disorders (DSD) according to the current classification among Mexican Children.

**Methods:** Retrospective, descriptive study of all cases DSD in Hospital Regional de Alta Especialidad del Bajío from 2007 to 2017.

**Results:** A total of 123 patients were included and classified according to karyotype in:

– DSD 46,XX 23.6% (n = 29): Congenital Adrenal Hyperplasia (CAH) (n = 25, 86%), Ovotesticular DSD (n = 2, 6.9%), XX testicular DSD (n = 1) and MURCS association (n = 1).

– DSD 46,XY 29.3% (n = 36): Disorder in androgen synthesis or action of androgen (n = 20, 55.5%) (5 α reductase deficiency (n = 4), testosterone deficiency (n = 5), androgen insensitivity syndrome n = 11), DSD testicular regression (n = 1) and others (n = 15) that included hypospadias, cryptorchidism and micropenis.

– Sex chromosome DSD 47.1% (n = 58): Klinefelter Syndrome (n = 3, 5.2%), Turner Syndrome (TS) or variants (n = 47, 81%); 3 patients had 3 positive Y sequences, DSD 45,X/46,XY (n = 2, 3.4%); one with mixed gonadal dysgenesis and one with ovotesticular DSD), and DSD with other alterations (n = 6).

We improved diagnostic and treatment with simultaneous surgical procedures including laparoscopic surgery and cystoscopy. The interdisciplinary group evaluated biological, social and psychological information and them we recommend the assignment of social sex.

Two cases of ovotesticular DSD, MURCS and the CAH were assigned as female. All DSD 46,XY were assigned male. TS with positive SRY was assigned male. Mixed gonadal dysgenesis (45,X/46,XY) was assigned female by own decision.

**Conclusion:** Frequency of the types of DSD showed predominance of DSD 46, XY over DDS 46,XX like to some global studies. The interdisciplinary work, the incorporation of new techniques and the decision of the patient must be taken into account for the assignment.

## Androgens Throughout Puberty in Girls with Premature Biochemical Adrénarche

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Premature adrenarche (PA) has been identified as a risk factor for PCOS. This May Depend on risk factors: such as ethnicity, birth weight and weight gain in childhood. In the GOCS cohort (Cohort Growth and obesity) followed from 2006 (born in 2002–2003), PA was defined by DHEAS (RIA) >75th percentile for sex (High DHEAS (HD) >420 ng/ml at age 7.0 yr.

**Aim:** To determine androgens During puberty in girls with HD and standard DHEAS (ND) EVALUATED by RIA and by LCMS/MS During puberty.

**Methods:** 242 girls (60 HD) with annual clinical examination Including breast Tanner (B) assessment Until 1 yr postmenarche (PM) and fasting blood sample for DHEAS, DHEA Androstenedione (A2), testosterone (T) and 17-Hydroxiprogesterone (17OHP) (RIAs and LC-MS/MS). Mann-Whitney test was used to compare Difference between high DHEAS and DHEAS regular groups.

**Results:** Are summarized in the table as mean ± SEM; *=p < 0.05 was considered significant. Girls with HD presented earlier breast and pubic hair (9.3 vs 9.8 yr) developmental and menarche (11.7 vs. 12 yr). Time between B2 and menarche was similar between groups.

At B2 HD group showed persistent mild hyperandrogenism (T: 0.078 ± 0.006 vs 0.066 ± 0.003 ng/ml and A2: 0.31 ± 0.1 vs 0.27 ± 0.01 ng/ml; p < 0.05) compared with ND. No further differences were observed.

**Table 1.**

| | ND (182) | HD (60) |
|---|---|---|
| DHEAS 1 (RIA) | 245±64 | 613±24 |
| DHEAS T2 (RIA) | 519±17 | 939±41 |
| DHEAS T2 (LCMS) | 331±13 | 649±32 |
| DHEA T2 | 1.12±0.05 | 1.73±0.11 |
| DHEAS T4 (RIA) | 774±42 | 1260±95 |
| DHEAS T4 (LCMS) | 429±19 | 814±60 |
| DHEA T4 | 1.77±0.09 | 2.76±0.16 |
| DHEAS PM | 756±29 | 1233±89 |
| DHEA PM | 3.81±0.14 | 4.75±0.28 |

1= 7 years; T2: Breast Tanner 2; T4: Breast Tanner 4; PM: 1 year after menarche.

**Conclusion:** In Chilean adolescents, PA is associated with earlier breast, pubic hair and menarche and persistent higher DHEAS and DHEA throughout puberty. We believe our findings support that adrenarche is not a benign process and continuous follow-up of this cohort is a unique opportunity to address prospectively the interrelationships of PA, early growth and adiposity as determinants of ovarian function and metabolic risks. In addition, measurements of steroids performed by mass spectrometry yield lower values with respect to RIA measurements, which makes it necessary to establish reference values for this new methodology.

## A Novel Mutation in GATA3 in a Patient with Bakarat Syndrome

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**Introduction:** Barakat syndrome is an autosomal dominant disorder characterized by the triad of hypoparathyroidism, sensorineural deafness and renal malformations caused by mutation in GATA3 gene located on chromosome 10p15.

**Objective:** To report the case of a patient with Barakat syndrome with an unreported mutation in GATA3 gene contributing to a better compression of this syndrome.

**Clinical Case:** A 9 years old girl was referred to our department because of hypocalcemia that caused seizures. Hypoparathyroidism was diagnosed with the following workup: PTH: 8.95 pg/ml, calcium: 7.42 mg/dl, phosphorus: 8.11 mg/dl, ionic calcium: 0.96 mmol/ l.

As a remarkable antecedent she had moderate mental development delay and bilateral hearing loss. She had no renal alterations and the brain MRI revealed basal ganglia calcifications. Calcium and calcitriol was indicated with good outcome. During the fol-

low-up, bicornuate utero was found by MRI, with metrorrhagia that is still under treatment with progesterone.

GATA3 exons and intron boundaries were direct sequenced in genomic DNA isolated from peripheral blood lymphocytes of the patient. A novel missense variant p.Cys267Ser in exon 3 in heterozygous state was found. All in silicoprediction tools determined that this substitution is deleterious or pathogenic.

**Conclusion:** We report a novel mutation in GATA3 gene in a patient with hypoparathyroidism and hypoacusia. Even though Barakat syndrome has a triad of hypoparathyroidism, hypoacusia and renal alterations as the usual presentation, literature identifies cases with different phenotypes in patients with GATA3 defects, evidencing the heterogeneity of this syndrome. This patient also has uterus malformation that was previously described in other reports, and may be associated to the effect of GATA3 in the miometrium development.

## Thyroid Profile Findings in Children and Adolescents After Cancer Treatment

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**Objective:** Endocrinology dysfunctions are frequent findings in children and adolescents after cancer treatments. This is tethered to chemotherapy, irradiation, invasive procedures and/or the tumor itself. Our objective is to report thyroid abnormalities from neoplasia survivor patients.

**Methods:** 173 neoplasia survivor patients were retrospectively studied in our endocrinology clinic. Serum levels of T3, total and free T4, TSH and thyroid antibodies were analyzed.

**Results:** 91 of 173 presented with alteration in their thyroid profile. Of these, 52 were male and median age referral to endocrinology was 11.4 years. The most prevalent thyroid dysfunction was a moderate elevation of TSH (<10 μIU/ML) seen in 32.9% of the patients, followed by 37.5% and 28.5% of primary and central hypothyroidism, respectively. Six patients had TSH <10 μIU/ ML and needed treatment due to hypothyrodism symptoms albeit two had their TSH values normalized without medication. Altogether, 73.6% of patients with thyroid profile abnormalities received levothyroxine. The average first TSH level in patients diagnosed with primary hypothyroidism was 43.7 μIU/ML. Twenty-six patients presented with central hypothyroidism: 24 of them due to tumor in the central nervous system (CNS), 1 due to cranial tumor histology located outside the CNS and 1 owing cranial radiation as part of the treatment for Hodgkin's lymphoma. Six patients developed hypothyroidism as a consequence of partial or total thyroidectomy. These patients had surgical procedures to control: 4 papillary carcinoma as second tumor (3 prior Hodgkin lymphomas and 1 hepatoblastoma without prior cervical radiation), 1 adenoma post ALL and 1 adenomatous goiter after Hodgkin's lymphoma.

**Conclusion:** As a consequence of the high prevalence of thyroid abnormalities in neoplasia survivor patients, it's recommended to monitor the thyroid function to identify and provide an early approach by the pediatric endocrinologist.

## Clinical and Molecular Characteristics of Patients with Congenital Hyperinsulinism

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**Objective:** To describe the evolution and molecular study of infants with Hypoglycemia due to Congenital hyperinsulinism (HCH).

**Method:** Retrospective, ABCC8, KCNJ11, GLUD, GCK and HNF4A genes were studied at the Wellcome Wolfson Medical Research Centre, University of Exeter Medical School, UK.

**Results:** 17 children, 41% injury, birth weight SDS 0.74 ± 2.36, 12% small and 18% large for gestational age. Age at onset was <24 h in 59% Intervalor 4 to 8 months and 29% Between 1.2 to 1.8 years 12%. Diagnosis was based on 36.1 ± 8.52 mg hypoglycemia/dl (range 19–48) with detectable insulin 12.8 ± 19.60 mUI/ml (range 1.3 to 57), absence of ketones and positive response to glucagon test (>30 mg/dl). First line therapy was diazoxide (DZX) in 100%, Accompanied by Hydrochlorothiazide in 65% and in Those Patients with No DZX response (n = 11) we used 12% Octeotride (n = 2), 6% (n = 1) LAR Octeotride and 12% (n = 2) needed near Total pancreatectomy. A molecular study was performed in twelve children which was positive in 6 patients (50%).

Six Children with genetic defects:

– ABCC8 gene mutation was found in three patients: a) 1 heterozygous missense mutation p.Val204Met gene, PET/CT examination with Ga68-DOTATE ruled out a focal lesion, diazoxide was discontinued after 1 year; b) homozygous mutation, p.Ala670fs and p.Thr1043fs. A 18F-DOPA-PET/CT, showed diffuse uptake, the child responded to therapy with diazoxide + hydrochlorothiazide; c) two new mutations [L1171R;V1174M]. He required pancreatectomy after 3 years of diazoxide + octeotride treatment.

• GLUD1 gene heterozygous mutation p.Arg322His. The child remains under diazoxide + hydrochlorothiazide therapy.

• KCNJ11 gene heterozygous mutation, p.leu147pro was found in two patients. One was studied with a PET/CT with Ga68-DOTATE which did not show focal images, and it still being treated with diazoxide. The other infant (12 months) needed octreotrideLAR with good response.

Six Children with average molecular study:

• Three did not require further treatment after 3–5 years.

• Three Have Remained under therapy for 6–11 years.

Five children without molecular study (debut at time with no available molecular study):

• One required pancreatectomy at age 6 months.

• Four discontinued diazoxide after 9–13 weeks of life and two were SGA.

Currently eight patients are euglycemic and free of treatment (age 8.1 ± 4.4), seven patients remain under therapy (age 5.3 ± 4.3), two children required pancreatectomy with secondary diabetes, and two children have developed neurocognitive impairment.

**Conclusion:** HCH Patients exhibit an heterogeneous clinical course. The genetic study is important to define their clinical course and and to select appropriate therapy.

## Congenital Lipoid Adrenal Hyperplasia Star Gene Splicing Mutation in a Colombian Intron 1 in 46XY Patient Case Report and Review of Latin-American Cases

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**Introduction:** Congenital Lipoid Adrenal Hyperplasia (CLAH) Classic form is a severe and potential lethal presentation of Primary Adrenal Insufficiency and DSD in a 46XY patient in the neonatal period due to deficiency of steroidogenic Acute Regulatory Protein (StAR) responsible of the fast pathway of steroid synthesis. CLAH is common in Japanese, Korean Arabic and Chinese Populations and only 5 cases in Latin-Americans Have Been with no relations to describe the common Populations. StAR gene has seven exons located in chromosome 8p11.23 StAR and encodes 285 amino acid protein. 67 mutations Have Been Reported in Patients with CLAH. 16% are splicing mutations and three published Latin-Americans Patients are in this group.

**Objective:** To describe a first case report in Colombia of a female patient karyotype 46XY with, and CLAH and review of the literature.

**Methods:** Medical History Molecular analysis and review by automatic DNA sequencing of exons and introns all regions of StAR gene from DNA of peripheral leucocytes.

**Results:** WHO Patient presented with hypoglycemia, hyponatremia, hyperkalemia mild transitory congenital cardiac anomalies in the neonatal period as Primary Treated Adrenal Insufficiency DESPITE elevated serum cortisol normal 17OHProgesterone, external female genitalia, 46 XY karyotype, on follow-on she started seizures, and HCG test negative an end diagnosis of CLAH at the age of 5 years with molecular analysis, homozygous G to T mutation within the splice site of intron 1 (IVS1 + 1G>T). Her mother is heterozygous. No information available of the father. The same splicing mutation has-been described only in a Chilean and Mexican patient.

**Conclusions:** CLAH is a rare Autosomic Recessive Disorder that Should be rule out in all neonates with hyponatremia, hyperkalemia and hypoglycemia and female genitalia apparent Normal Normal cortisol. The remains unexplained. This unique splicing mutation in intron 1 Suggests a founder effect in Latin-Americans.

## Satisfaction of the Experience Lived by the Health Care Professionals Volunteers in Three Educational Camps for Type 1 Diabetes and Adolescents in Chile Children

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**Objective:** To Evaluate the satisfaction of the experience of the volunteers health care professionals (HCPs) in three educational camps of the Juvenile Diabetes Foundation of Chile for Children and Adolescents with Type 1 diabetes (T1D).

**Methods:** A descriptive, quantitative study and transectional was made. A Likert survey was created, with scores from 1 to 5, the higher the agreement with the statement. The instrument was reviewed by a committee of experts and volunteers applied to all Regular workers outside the HCP, diabetes During three consecutive camps in 2017 and 2018. Conducted by the same institution. The instrument EVALUATED the perception of five aspects linked to professional practice (contribution to professional performance and curriculum approach to the patient with T1D, interdisciplinary teamwork and self-confidence) and to 2 aspects related to the training received During the camps (contribution to the performance at camp and for the professional life).

**Results:** 93 surveys were completed. 39 by different HCPs 26 physicians (general practitioners, residents, specialists and subspecialists), 8 nutritionists and 5 nurses. 54 students responded: 4 from medicine, 33 and 17 from nursing from nutrition. The median of the score for each question was 5 of 5. No difference was found between different HCPs or professionals and students.

**Conclusions:** Have studies the impact of diabetes Measured educational camps on adherence and glycemic Control in the assistants. However, studies that measure the benefits for HCP After their participation in activity These are lacking. We Reported that the perceived satisfaction is high. Both professionals and Consider students as an educational diabetes camps effective tool to Increase Their knowledge, confidence and professional performance Regarding the Management of Patients with T1D. Studies that measure the real impact of educational esta instance on knowledge, skills and aptitudes on HCPs are still needed.

## Monogenic Diabetes and Congenital Hyperinsulinism Due to Dominant Mutations at the ATP-Dependent Potassium Channel SUR1 Subunit (ABCC8 Gene)

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**Introduction:** Congenital hyperinsulinism (HI) is the most frequent cause of persistent hypoglycemia in childhood. It is a heterogeneous disease with an important genetic component. The most frequent causes are recessive or dominant inactivating mutations in the ABCC8 gene encoding the SUR1 subunits of the ATP-dependent potassium channel. There is controversy over if these mutations can be associated with diabetes in adulthood.

**Objective:** Clinical and genetic characterization of families with dominant mutations in ABCC8 gene causing HI in the proband, with the purpose of investigate the presence of diabetes in the family carriers.

**Methods:** The phenotype and genetics of 7 families with dominant ABCC8 mutations were studied. Genetic studies were carried out by NGS custom panel and/or conventional Sanger sequencing (ABCC8-RefSeq:NM_001287174.1).

**Results:** Six different heterozygous missense dominant mutations in the ABCC8 gene were identified in seven probands. All probands presented a mild and diazoxide responsive HI. All mutations found were located in the intracellular domains of SUR1; four of them are clustered within NBD2 domain, a previously described hotspot for ABCC8 dominant acting mutations.

Two patients inherited the mutations from their asymptomatic parents. One case had a de novo mutation, presented transient hypoglycemia that has progressed to diabetes later in childhood. Three cases inherited the mutation from the mother with:

1) diabetes; 2) hypoglycemia at 13 months, hypoglycemia of unknown-etiology and gestational diabetes in the adulthood, 3) gestational diabetes and currently sporadic hypoglycemia. Other carrier relatives also had diabetes.

Another interesting case with ABCC8 dominant mutation is a 56-year-old woman with recurrent episodes of hypoglycemia and epileptic seizures and her son, who presented hypoglycemia in childhood, diabetes and obesity in adolescence and currently sporadic hypoglycemia.

**Conclusions:** Carriers of dominant mutations in ABCC8 gene have a variable phenotype, ranging from persistent/transient mild hyperinsulinism which can progress to diabetes, to gestational diabetes and/or diabetes in adulthood.

## Risky Sexual Behaviors and Reproductive Knowledge in Adolescents and Young Women with Type 1 Diabetes

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**Objective:** To evaluate risky sexual behaviors and reproductive knowledge in adolescents and young women with type 1 diabetes mellitus (T1D) in Chile.

**Methods:** Adolescents and young women with T1D were studied during 2018. Two standardized written questionnaires were translated into Spanish (Charron-Prochownik et al., 2006). The first instrument evaluated age of initiation of sexual activity, use of contraception and sexual behaviors associated with the risk of unplanned pregnancy. The second questionnaire measured knowledge (% correct) about diabetes and pregnancy, contraception, sex; general family planning; and diabetes pre-conception education. Data are shown as mean±SD.

**Results:** 51 young women were studied. They had age and T1D duration of 19 ± 4.1 and 9.2 ± 5.9 years, respectively (age range: 15–30 years). Previous sexual activity was reported in 55% of the subjects, and the age of initiation was 16.9 ± 2.1 years. Most patients (89%) reported that their parents knew about their sexual activity, and 64% of the women reported having used some contraceptive during their first sexual intercourse.

The type of contraceptive that was used in the first intercourse were condoms (50%) and combined oral hormonal contraception (32%). The reasons for choosing these types of contraception were safety, ease of use and access, and prevention of sexually transmitted diseases.

The proportion of subjects that reported ever using methods with a low rate of pregnancy prevention rate were the following: coitus interruptus (59%), emergency contraception (34%), rhythm method (19%) and vaginal shower (11%). More than half of the patients reported having had unprotected sex (56%) at least once. The mean knowledge scores that were correctly answered by the patients were pregnancy: 70 ± 19%, contraception: 85 ± 13%, sex: 79 ± 10%, family planning: 85 ± 11% and pre-conceptional counseling: 55 ± 64%. The main sources of information for adolescents were school sexual education classes, parents, and friends.

**Conclusions:** These results suggest that risky behaviors related to unprotected sex and risk of unplanned pregnancy are prevalent in adolescent and young women with T1D. Enhancing pregnancy outcomes and knowledge of the risks associated with these behaviors and could be beneficial (FONDECYT grant 1170895).

## ABCC8 Mutation as a Cause of Congenital Hyperinsulinism: A Case Report

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**Introduction:** Congenital Hyperinsulinism (CH) is the main cause of serious and persistence hypoglycemia in the neonatal period and it is secondary To inadequate insulin secretion despite hypoglycemia as the result of a genetic alteration of the sulfonylurea receptor of the beta cell. More than 150 mutations of the ABCC8 and 25 in KCNJ11 gene have been reported incidence is 1 in 5000 a live newborn babies, Higth metabolic fluxes, diazoxide, octreotide and even subtotal pancreatectomy are required.

**Objective:** To describe a case of CH to make people aware of its diagnosis and treatment.

**Materials and Methods:** We reviewed the clinical chart of a neonate with difficult to control hyperinsulinism. The propositus was a male burn at 36 week of gestation in no consanguineons parents. Weight 3.920 grams, height 52 cm. Patient presented at 13 hours of life, with a blood glucose of 3 mg/ dl, insulin of 99.1 Uu/ ml and a serum cortisol of 3.65 ug/dl. A subtotal pancreatectomy was performed because of no response to metabolic flow including diozoxide, octeotride and hydrocortisone. Pathology described as generalized nesidioblastosis. Hypoglycemia and hyperinsulinemia persisted following surgery pancreatectomy subtotal. Genetic studies revealed a heterozygous ABCC8 gene, missense, variant p (Gly 228 Asp) wite paternal inheritance suggesting uniparental disomy. This mutation has not be.

**Conclusion:** Knowledge of the genetic alteration allows better management and parental counselling of this condition.

## Pediatric Graves Disease Experience with Institutional Definitive Treatment

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Children's Hospital "Ricardo Gutiérrez"

**Background:** In pediatric Graves' disease (PGD), long term antithyroid treatment with drugs (DTAs) is the first line choice but a second alternative Often as radioiodine or thyroidectomy Such has to be considered.

**Objective:** To describe the outcome of PGD related to the therapeutic choice.

**Methods:** Medical records of the Patients diagnosed with PGD (2007–2015) in our center Were retrospectively reviewed. Demographics, treatment indication and evolution Were retrieved. In Those In Whom a second alternative treatment was indicated, the cause of esta switch, median time (MT) to indication and adverse effects (AE) Were registered.

**Results:** 66 records were reviewed (50 girls, median age 11.9 years (range (r): 1.5–17.1) received INITIALLY ATDs 65 and one was Treated with 131I. 24% (n: 16) Were lost to follow up after 2.6 years (r: 0.1–6.9), 28% (n: 18) continued on clinical follow up and in 32 (48.5%) was Indicated another option treatment: 18 received 131I and 14 underwent surgery. 9/18 Patients under DTAs remitted (hypothyroidism or euthyroidism) at a MT of 3 years (r: 1–6.3) and 9 are still Treated (median follow up: 3.7 years (r: 0.1–6.7)). 18 patients received 131I (16 girls, MT to indication 1.1 years (r: 0–4.9). 1 for autoimmune hepatitis, 4 for ATDs AE and 13 for poor compliance 14 (78%) after one dose remitted (median 10 mCi (r: 0.5–16)) and four required 2 doses rendered hypothyroid All Patients in a MT of 0.2 years (r: 0.1–0.8). No complications or AE Were registered. 14 Patients (10 girls) at a MT underwent thyroidectomy since diagnosis of 1.8 years (r: 0.1–6.8): 3 for ATDs AE, 6 for poor compliance (1 with severe ophthalmopathy, one with big goiter) and 5 for thyroid nodules. 10 (71.4%) presented postsurgical complications: such as 1 hungry bone, 6 transient hypoparathyroidism and 1 sepsis. Two Patients (14.3%) ADH definitive hypoparathyroidism. Transient and postsurgical complications definitive were significantly higher than those for 131I ($p = 0.01$).

**Conclusion:** Long term follow up in PGD is difficult and poorly Achieved. 131I treatment was safe without adverse outcomes correctly, Although surgery while the risk of Indicated entails transient and definitive complications.

## Consumptive Hypothyroidism: Case Report

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**Introduction:** Hemangioendothelioma (HHE) is a vascular lesion more frequent in the first year of life. The term includes a spectrum of vascular lesions ranging from benign and self-limiting to aggressive and life-threatening. The hepatic form of HHE is a rare tumor in infancy Typically presenting. The Natural course of HHE is Characterized by a proliferation phase and plateau phases followed by involution. Hypothyroidism in Patients of this group is Attributed to expression of type 3 iodothyronine deiodin-ase (D3) by the tumor tissue. The Increased activity leads to rapid enzyme degradation of thyroid hormones, RESULTING in severe hypothyroidism, thyroid hormone When inactivation by D3 Exceeds the synthetic capacity of the thyroid gland. Less than 100 Patients with This entity Have Been published in the literature.

**Objective:** To report The Importance of checking thyroid function in Children with neonatal massive hemangiomatosis.

**Case Report:** A 5 month-old male was derived by progressive hepatomegaly of 2 months of evolution. No Relevant perinatal and neonatal history Normal screening. Physical examination Showed rough facies, broad nasal bridge, puffy eyes, Hypotonia, tachycardia, hepatosplenomegaly with regular stools, and delay in neurocognitive milestone. Abdominal ultrasound Showed enlarged liver due to multiple solid hypoechoic lesions. Abdominal angio computed tomography confirmed multiple hypervascularized solid liver lesions Compatible with HHE. Propranolol treatment was indicated. With clinical suspicion of hypothyroidism, thyroid function test (TFT) Were Requested. Laboratory values Were: hemoglobin 9 g/dl, 500,800 platelets/$mm^3$, hepatogram elevated with gammaglutamyltranspeptidase 80 IU/L, 186.4 TSH mIU/m, T4 8.2 ug/dl, fT4 0.8 ng/dl, T3 0.3 ng/ml. Levothyroxine (LT4) (50 ug/d) treatment was started. At 17 months, I have presents adecuate neu-

romadurative growth and development, normalization of TFT and hepatic lesions in resolution under LT4 and propranolol treatment.

**Conclusions:** A high index of suspicion for consumptive lead to hypothyroidism Should Evaluate thyroid function in HHE. T3 low value is indicative of esta condition.

## Successful Treatment of Goiter in Utero Fetal Case Report

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Congenital goiter can result in fetal (polyhydramnios, esophageal obstruction and delivery dystocia due to cervical hyperextension) or neonatal (tracheal obstruction, respiratory distress) complications. The diagnosis is made by ultrasound (US). Occasionally, clinical history and US findings May lead to the presumptive diagnosis of fetal hyper or hypothyroidism. Although, the dosage of thyroid hormones in fetal blood exceptionally May be Necessary. DESPITE early treatment, congenital hypothyroidism Patients with Decreased can show performance in neurocognitive tests.

**Objective:** To describe the diagnostic and therapeutic process in a patient fetal goiter and hypothyroidism with.

**Patients and Methods:** A 35 year old woman, first pregnancy, multiple pituitary insufficiency secondary to pituitary adenoma, on treatment levothyroxine with 75 ug/d and hydrocortisone 10 mg/d, WHO required inductive treatment of ovulation, was derived by detection of fetal goiter; at 31st week US Showed: single female fetus, estimated weight 1740 g (p72), fetal cardiac frequency (FCF) 136 beats per minute (low), cervical mass Compatible with tracheal compression with goiter, polyhydramnios. At 32nd weeks chordocentesis (TSH 191.4 uU/mL, T4 1.9 ug/dl, fT4 <0.4 ng/dl, T3 0.4 ng/ml, thyroglobulin 8674 ng/ml) and amniocentesis (TSH 1.1, 1.2 T4, fT4 <0.4, 0.7 T3) Were performed. A dose of 400 ug of LT4 was administered by amnioinfusion.

At 33rd week cord blood values Were: 11.6 TSH, T4 6, fT4 1 T3 0.5, TG 3835; US Showed Increased Decreased goiter and FCF. She received 5 weekly infusions of 400 ug LT4.

**Results:** Delivery was by elective caesarean section at 38 weeks. A vigorous newborn, bIrth weight 2940 g, with standard physical exam and not palpable thyroid. Thyroid US Showed left lobe 31 x 7 x 10 mm; right lobe: 24x 7.7 x 13 mm. Were cord blood TSH values 10.4, FT4 1.1, 8.6 T4, T3 0.72. Hypoplasia of distal femur nucleus was evidenced on Rx. She Began with LT4 treatment at 48 hours of life with periodic Adjustments to weight and biochemical ACCORDING data. At 15 months, she presented weight and height in the 50th percentile, absence of goiter normal neuromaduratives milestones under LT4 4.7 ug/kg/d. Results of molecular studies are pending.

**Conclusions:** With intraamniotic LT4 treatment of goiter reduction allowed and probably preserved neuromadurative potential.

## Neonatal Diabetes Monogenic in the National Institute of Child Health. Importance of Genetic Diagnosis in the Therapeutic Attitude

*Marianella Pinto*[1], *Carlos Del Aguila*[1,2], *Oswaldo Nuñez*[1,2], *Manuela Chavez*[1], *Oscar Espinoza*[1], *Martha Quispe*[1], *Miguel De Los Santos*[1]

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The neonatal monogenic diabetes is a condition must be taken into that account in neonates and infants with sustained hyperglycemia. The present paper AIMS to report four cases of monogenic diabetes diagnosed at the National Institute of Child Health (ISN) analyzing the clinical presentation, diagnostic criteria and treatment. The four cases are male children WHO before the disease Began Their year of age, shortness of breath with presenting, in one case fever and diarrhea and vomiting, simulating septic illness. At admission, all had blood glucose levels above 600 mg/dl, with glycosylated hemoglobin >6.5% and urine tests with glucosuria and ketone bodies present. All Were Treated Initially as ketoacidosis and diabetic Were intensive insulin therapy with discharged. Subsequently, genetic studies Were Carried out to define the diagnosis Given the early onset of presentation. In one of the Patients, the genetic diagnosis was made only at 7 years, Given the irregularity of the Consultations. In the first, second and fourth cases Were mutations found in the KCNJ11 gene, which codes for the Kir6.2 subunit of the ATP-sensitive potassium channel. In the third case, a missense heterozygous mutation of the insulin gene (INS) was found. With These results, in the first, second and fourth cases the transfer to sulphonylureas with good evolution Began. In the third case, being a mutation in the insulin gene, the patient continued intensive insulin therapy with. It is Concluded that persistent hyperglycemia in infants with the differential diagnosis within esta Should be suspected entity, being of great Importance the identification of the genetic mutation, will determine the esta since treatment of the patient, Improving glycemic response and quality of life.

## Vitamin D Dependent Rickets Type 1A Case Report

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The dependent rickets vitamin D type 1 is an autosomal rare disorder in which very low concentrations of calcitriol not increase with the administration of PTH, caused by a defect in the alpha-hydroxylase renal (CYP27B1 gene) that converts 25 OH vitamin D calcitriol. We present a male patient one year and five months old, previously healthy, who begins his disease at 10 months of life by refusing to remain standing. It has pain and irritability when the mother puts him in that position, and dropped into a sitting position. It was previously handled as developmental dysplasia of the hip. A valuation of Orthopedics, Genetics and Endocrinology, presents stunting, delayed tooth eruption, hypotonia of the lower limbs, skeletal abnormalities of the lower limbs, psychomotor re-

tardation. Radiographs has widened epiphyseal and frayed with marked osteopenia. Laboratories metabolism of calcium and phosphorus are requested, finding hypocalcemia, hypophosphatemia, major elevated alkaline phosphatase and PTH, with levels of 25-OH vitamin D in failure and very low levels of vitamin D. 1,25 OH 1alpha hydroxylase deficiency is suspected, treatment is initiated with supplementation of calcium and phosphorus, and calcitriol.

After a month of treatment, levels of calcium and phosphorus levels returned to normal, alkaline phosphatase and PTH decreased, and the patient improved clinically significantly. study of CYP27B1 gene complete sequencing is performed, a state of compound heterozygotes by the presence of two pathogenic variants in the CYP27B1 gene is reported. During his subsequent evaluations, the patient gained weight and height appropriately. He began ambulation and pain disappeared. Continues with supplementation of calcium, phosphorus and calcitriol, and given genetic counseling because it is an autosomal recessive disorder.

## Treatment with Growth Hormone in Renal Transplant Patients Response to the First Year as a Predictor of End Height

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**Introduction:** Short stature is a problem in Children with kidney diseases. The effectiveness of GH in These Patients Has Been Widely Demonstrated.

**Objectives:** 1. To analyze our experience in Transplanted Kidney Patients (RT) Treated with GH. 2. To Establish predictors of response.

**Material and Methods:** Retrospective analysis of medical records of RT WHO received GH in a University Hospital. Twenty five RT inclusion criteria received GH fulfilling (short stature, low growth velocity (GV) and normal renal function); 22 (18 boys) Were included. Patients were divided in height according to increment during first-year treatment. Good responders (G1: increment >0.5 SDS) (n = 10) and bad responders (G2: increment <0.5 SDS) (n = 12). Age at RT was (mean + SD) 7.2 +3.4 years; G1: 6.1 +3.5; G2: 8.1 +3.1 (p ns). Height at RT was −2.42 +1.43 SDS; G1: −2.73 +1.27; G2: −2.14 +1.57 (p ns). GH treatment was Initiated at +3.19 10.8 years; 3.68+2.35 years after transplantation.

**Results:** Were there no Differences in chronological age (CA) and bone age (BA) between groups. Height at beginning of GH was −2.59 +1.02 SDS; G1: −2.74 +0.93; G2: −2.47 +1.1 (p ns). With target height difference was 2.79 +1.29; G1: 3.11 +1.5; G2: 2.37 +0.91. (P ns). height gain (HG) after first-year of treatment was +0.45 +0.48 SDS; G1: +0.14 +0.9; G2: +0.05 +0.27 (p = 0.0001). Were there no Differences Between groups in renal function. Patients Reached an adult Thirteen height of −2.58 +1.1 SDS; G1 (n = 6) −1.81 +0.53; G2 (n = 7) −3.23 +1.06 (p 0.01). Total G1 HG was +1.04 +1.14 SDS; G2, −0.54 +1.2(P 0.03). Patients Who Did not received hemodialysis preRT (N = 6) Showed better response at first year of treatment and the total height gain (0.83 +0.21 SDS); vs. Those Who Were submitted to hemodialysis (0.3 +0.48 SDS)(P 0.01). Also adult height was different (−1.66 vs. −2.99 +0.61 +1.04 SDS) (p 0.03).

**Conclusions:** With treatment GH in RT can improve increase height. Growth response at first-year of treatment, as well as not Having Been subjected to hemodialysis are predictors of good response.

## Adiponectin as a Marker of Peripheral Insulin Resistance in Adolescents with Polycystic Ovarian Syndrome (PCOS) and as a Tool to Suspect Insulin Receptor Defects

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**Background:** Decreased serum adiponectin levels are associated with obesity and peripheral insulin resistance (IR). PCOS is Characterized by anovulation and hyperandrogenism and chronic faq frequently is associated to IR. Some defects of Insulin Receptor Have Been Proposed as Mechanisms to Explain ovarian hyperandrogenism in PCOS.

**Objectives:** To explore adiponectin levels in PCOS adolescents and to Evaluate if adiponectin would Identify potential Patients with hyperandrogenism associated to defects in the insulin receptor or intracellular signal pathway ITS.

**Patients and Methods:** Prospective cross-sectional study. Twenty PCOS adolescents (16.4 ± 2 years) diagnosed ACCORDING TO AES standard criteria and 10 healthy adolescents cycling (16.0 ± 1.5 years) Were Studied. Fasting glucose, insulin, adiponectin, androgens (total and free testosterone, androstenedione) Were Measured. HOMA-IR >2.5 was used a surrogate of IR.

**Results:** 11/20 (55%) Patients Showed PCOS IR (4 with Normal BMI and 7 with high BMI). Adiponectin levels in PCOS Patients with Increased BMI and insulin resistance lower than in Were Both PCOS and controls with a normal BMI (ANOVA way on p = 0.05). Significant correlations Between inverse adiponectin, BMI (r = −0.79, p = 0.001) and HOMA-IR (r = −0.53, p = 0.02) Were Observed In Patients with PCOS. Two Patients with high adiponectin levels Were excluded from the regression model bivariant as outliers. Both unexpectedly high levels of ADH In Spite of adiponectin Having the highest values of HOMA-IR. In one of them, a novel missense heterozygous variant in the domain of INSR tyrosine kinase was Identified (NM_000208.3 (INSR): c.3449T>C (p.Leu1150Pro)) and classified as likely pathogenic Applying ACMG guidelines. Molecular study of insulin receptor gene from the other patient is under process.

**Conclusions:** Adiponectin levels are negatively associated with BMI and the severity of peripheral insulin resistance, while serum androgens do not seem to be related to them. Unexpectedly high levels of Adiponectin in Patients with PCOS exhibit insulin resistance WHO Should lead towards molecular studies to rule out insulin receptor defects.

## Adiponectin and Cardiometabolic Parameters in Obese Children According To Their Physical Activity Level

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**Methods:** We studied 64 patients (31 with morbid obesity, 20 obese and 13 overweight) aged 5–16 years. We registered: IMC-SDS, Trunk-Index (waist + neck circumference/height), blood pressure and sedentarism score. We obtained DXA Trunk-Fat Mass Index (T-FMI), Appendicular-Lean Mass Index (A-LMI), Appendicular Lean/ Fat Tissue ratio (A-L/F). We determined fasting and 2-hour glycemia, insulinemia, HOMA-IR, Triglycerides/ HDL-Cholesterol ratio, Matsuda's whole body insulin sensitivity index (WBISI), 30-minutes Insulinogenic Index (30-InsIndex) and oral-Disposition Index (o-GDI) from an OGTT.

**Results:** Active patients had lower Trunk-Index (0.58 ± 0.07 vs 0.65 ± 0.06; $p < 0.001$), lower systolic blood pressure (96 ± 11 vs 103 ± 9 mmHg; $p < 0.05$), lower Triglycerides/HDL-Cholesterol (1.8 IC-95% 1.3–2.5 vs 2.5 IC-95% 1.9–3.1; log-transformation $p < 0.05$), lower T-FMI (7.4 ± 2.4 vs 8.9 ± 2.2; $p < 0.05$) lower A-LMI (3.2 ± 0.9 vs 4.0 ± 1.5; $p < 0.05$) and higher A-LMI (1.2 IC-95% 1.1–1.4 vs 1.1 IC-95% 1.0–1.2; Mann-Whitney's $p < 0.05$). Patients who performed >10 hour/week of physical activity had higher adiponectin (<5 h: 23033 ± 10085, 5–10 h: 28635 ± 15968, >10 h: 35922 ± 15711 ng/mL; Anova $p < 0.05$) and a better metabolic profile, with lower fasting glucose (<5 h: 98 ± 6, 5–10 h: 95 ± 4, >10 h: 93 ± 5 mg/dL; Anova $p < 0.05$) 2-hour-glucose (<5 h: 124 IC-95% 113–131, 5–10 h: 106 IC-95% 99–114, >10 h: 102 IC-95% 96–113 mg/dL; log-transformation Anova $p < 0.05$), lower HOMA-IR (2.4 ± 1.5 vs 3.9 ± 2.2; $p < 0.01$), higher WBISI (<5 h: 2.3 IC-95% 1.6–3.6, 5–10 h: 2.6 IC-95% 1.8–4.0, >10 h: 4.0 IC-95% 3.4–5.1 1/[mg/dL.mcU/mL]; log-transformation Anova $p < 0.01$), lower 30-InsIndex (1.9 ± 1.2 vs 2.8 ± 2.1; $p < 0.05$) and higher o-GDI (<5 h: 4.92 IC-95% 3.71–6.53, 5–10 h: 7.57 IC-95% 4.03–8.35, >10 h: 6.84 IC-95% 4.85–10.21 1/mcU/mL2; Mann-Whitney's test $p < 0.05$ 15 vs 5 h).

**Conclusion:** Obese children and adolescents with a family history of metabolic syndrome and increased trunk fat mass who performed more physical activity had a better body composition and a favourable effect on their metabolic profile, with a higher seric adiponectin and a higher oral glucose disposition index. On the contrary, sedentary patients were predisposed to the early development of type 2 diabetes, with a lower oral disposition index and a higher 2-hour glycemia. We hypothesized that their higher absolute appendicular lean mass was the expression of the effect of their higher insulin level promoting overall growth and an increased intramyocellular fat deposition.

## Growth Velocity in Period After Post Menarcheal Chilean Girls

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**Background:** Menarche is one of the last stages of pubertal development, which coincides, with the completion of longitudinal growth. However, the factors that Affect esta Latter process are unknown.

**Objective:** To ASSESS growth velocity (GV) During post menarcheal period in a group of Chilean girls and clinical variables to evaluate-proposed to be associated to this growth.

**Methods:** This study is nested in the Growth & Obesity Chilean Cohort Study (GOCS), which is a longitudinal follow-up of 540 girls since age 4 from middle-low socioeconomic level 2003. Since born in year 2009, clinical evaluation with anthropometry was Assessed every six months Together with the registration of date at menarche. In a prospective fashion healthy girls attending GOCS Were followed 4 years. The height and weight SDS Were Calculated ACCORDING TO NCHS curves. The evolution of post-menarcheal growth (in cm gain) in girls was EVALUATED through a mixed model.

**Results:** The mean age at menarche of time for the cohort was 11.9 ± 1 years. Were 312 girls followed for 3 years and 178 girls for 4 years. After 2 years post menarche, the girls Reached a growth plateau (<0.5 cm difference) and the average height was 5.3 ± 3.4 gain cm. This gain was associated age at menarche with the. There was an inverse correlation Between the age of menarche and cm of height gain in four years after Reached of follow-up. ($R = -0.14$, $p = 0.001$). There Were statistically significant for the growth Differences Between the age Studied groups (Table 1).

**Conclusions:** Post menarcheal growth ends 2 years post-event and GV is inversely correlated to the age at menarche. Table 1: Delta Height menarche post.

## Metabolic Control in Children with Diabetes Mellitus Type 1 Users of Insulin Infusion Pump with Predictive Insulin Suspension

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**Objective:** Evaluation of the metabolic control in children with Diabetes type 1 who use insulin continuous infusion pump with predictive insulin at 6 months.

**Methos:** Follow-up study in children with Diabetes Mellitus type 1 users of Medtronic minimized 640G smart guard technology, which includes the function of predictive suspension of insulin. The values of glycosylated hemoglobin (Hba1c), total insulin dose per kilogram of body weight (DDT) before the start of insulin bursting and at 6 months after use were compared; analyzed the difference between the first month and the sixth month of pump use in the average of exposure to hyperglycemia (AUC >140 mg/dl); average exposure to hypoglycemia (AUC <70 mg/dl).

**Results:** Sixteen children were followed up, 68% male, average age 7.4 years ± 2.3; time with diabetes 3 years 5 months ± 1.3 years, the indication for the use of pump 66% of the cases was by microdoses of insulin, the rest by hypoglycemia. The Hba1c prior to the pump was 7.6 ± 0.51 and at 6 months 7.1 ± 0.76 (p = 0.02), the DDT per kilo of weight prior to pump use was 0.72 ± 0.04 and the 6 months 0.74 ± 0.16 (p = NS), AUC >140 mg/dl at the first month was 44.13 ± 18.9 vs at 6 months 31.85 ± 12.4 (p = 0.02); AUC <70 mg/dl first month was 0.20 ± 0.03 and at 6 months 0.52 ± 0.22 (p = 0.01).

**Conclusion**: In this follow-up, a continuous infusion pump with predictive insulin suspension was found to improve metabolic control of patients at 6 months of follow-up, measured both in Hb A1c and a decrease in time in hyperglycemia >140 mg/dl. Being a safe treatment and with a low level of hypoglycemia.

## Buschke-Olllendorff Syndrome. A Case Report With Disproportionate Short Stature

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**Case Report:** A seven-year-old female patient with short stature. Non-consanguineous parents, borned at 40 weeks with intrauterine growth restriction; normal dentition and neurodevelopment. Healthy parents and brethren. TH 156 cm (SD –1.28), brothers with normal height. Her stature is 106 cm (SD –3), BMI 12.72 kg/m$^2$ (SD –2.4), breadth 99.2 cm, lower segment 49 cm, upper segment 57 cm, US/LS: 1.16; prominent forehead, mediofacial hypoplasia, high palate and mesomelia. Indurated not painful nodules on the back of second metacarpal of the right hand at about 1 cm of diameter, and interglute region, non-mobile; hipopigmented macule located on dermatome T7-T8 of right hemi-body; normal external genitalia. Calcium, phosphorus, alkaline phosphatase, electrolytes serum levels, venous gases, globular sedimentation velocity, IGF1 and GH test, were all normal. Four years and six months of bone age. Spine, hips, upper and lower limbs radiographic images shows numerous rounded radiopacities in scapula, humerus, radius, acetabular roof, femur, metacarpals and carpus.

**Discussion/Conclusion:** BOS also known as "osteopathy condensans" or "spotty bone disease", is characterized by innumerable osteosclerotic lesions, which are usually an incidental finding in radiographic images. and are usually located in long bones (epiphysis and metaphysis). BOS, is caused by a mutation in LEMD3 gene (also called MAN1) located in 12q14.3 We present a patient with disproportionate short stature, not neurodevelopment alterations were found and genetic tests have not been possible to apply yet; diabetes mellitus, precocious puberty have been described.

## Growth Hormone Treatment Adherence in Latin American Patients: Real-World Data from the Easypod™ Connect eHealth platform

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**Introduction**: The easypod™ electromechanical injection device electronically transmits adherence data for patients receiving recombinant human growth hormone (r-hGH; Saizen®) to treat growth disorders. The device works with the eHealth platform easypod™ Connect, to allow healthcare professionals to access adherence data. The aim of this analysis was to evaluate real-world adherence to r-hGH therapy administered via easypod™ over 1, 3, 6 and 12 months in Latin American (LATAM) patients.

**Methods:** Data were downloaded on 3rd February 2018 from 2,727 patients transmitting their r-hGH data to easypod™ Connect in nine LATAM countries (Argentina, Brazil, Chile, Colombia, El Salvador, Guatemala, Mexico, Nicaragua and Peru). The period of recorded data varied, according to individual's treatment length. Patient adherence (categorised as high [≥85%], intermediate [>56%–84%] or low [≤56%]) was calculated as mg Saizenâ injected vs mg Saizenâ prescribed. Only data after the 10th injection registered on easypod™ were analysed, to exclude test/training injections. Puberty cut-off points were 10 years for girls and 12 years for boys.

**Results:** In total, 2,727 patients recorded >10 injections. Overall, there were 1,734 patients (63.6%) in the high-adherence category, 764 (28.0%) in the intermediate and 229 (8.4%) in the low-adherence category. There was a decrease in the proportion of patients in the high adherence category over time at the different time points; however, 66.6% of patients were still in the high adherence category after 12 months (compared with 84.5% at month one). The LATAM data were consistent with the global data: 1, 2 overall, a higher proportion of younger patients were in the high-adherence category than older patients (670 [69.4%] vs 1,064 [60.42%]) and a higher proportion of females were in the high-adherence category than males (754 [64.4%] vs 980 [62.9%]). The patients in the high and intermediate-adherence categories had the highest mean number of data transmissions (4.75 [SD 9.16] and 4.37 [SD 9.25] respectively) compared with the low adherence category (2.15 [2.37]).

**Conclusions:** This is the first analysis of adherence exclusively in LATAM patients in a real-world clinical setting using easypod-TM Connect. Overall, the majority of patients were in the high-adherence category. Adherence was higher in younger than older patients and was slightly higher in females than males. LATAM data follow the same trend as that of the global population. Patient/caregiver engagement via data transmission should be considered important for maintaining high adherence levels.

## Final Results of NordiNet® International Outcome Study: Key Outcomes in Pediatric Patients

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**Objective:** NordiNet® International Outcome Study ([IOS]; NCT00960128), to non-interventional study (2006–2016) Assessed the effectiveness and safety of with Real-world Norditropin® treatment. Were Outcomes Assessed in children with growth hormone deficiency (GHD), born small for gestational age (SGA), Turner syndrome (TS), renal chronic disease (CRD), idiopathic short stature (ISS), Noonan syndrome (NS) and Prader Willi syndrome (PWS).

**Method:** Patient information was using a web Entered-based system. 17,995 Pediatric Patients Enrolled: 17.711 included in the full analysis set (FAS) (safety evaluation); 11,967 in the effectiveness analysis set (EAS). Endpoints included change from baseline in height standard deviation scores (ΔHSDS) and near-adult height (NAH) SDS (height at age >16 [boys]/>15 [girls] and height velocity <2 cm/year, or height at >18 years). Non-serious adverse reactions (NSARs), and serious adverse events SARs (SAEs) Were recorded. Data are mean (standard deviation).

**Results:** Patient numbers by indication Were FAS/EAS: GHD, 9967/7141; SGA, 4274/3200; TS, 1374/936; CRD, 290/200; ISS, 485/317; NS, 154/106; PWS, 132/67. At start treatment, Patients with PWS (4.7 [5.00] years) Were the youngest: GHD, 9.1 (4.1); SGA, 7.9 (3.4); TS, 08.07 (03.08); CRD, 8.3 (4.4); ISS, 10.1 (3.5); NS, 8.9 (3.8). Patients born SGA Were Shortest (HSDS) at baseline (–2.97 [0.91]): GHD, –2.55 (1.10); TS, –2.66 (0.93); CRD,–2.74 (1.17); ISS, –2.82 (0.99); NS, –2.83 (1.13); PWS, –1.94 (1.48). GH Average dose (mg/kg/day) was lower for PWS (0026 [0008]) versus GHD (0032 [0008]); SGA, 0038 (0009); TS, 0044 (0009); CRD, 0041 (0011); ISS, 0038 (0014); NS, 0.040 (0.009). Follow-up treatment (years) was longest for Patients with TS (4.3 [2.8]): GHD, 3.8 (2.9); SGA, 3.6 (2.8); CRD, 2.8 (2.6); ISS, 3.3 (2.4); NS, 3.4 (2.9); PWS, 4.0 (3.5). ΔHSDS was greatest in year 1: GHD, 0.69 (0.56); SGA, 0.65 (0.44); TS, 0.54 (0.36); CRD, 0.61 (1.19); ISS, 0.52 (0.38); NS, 0.51 (0.38); PWS, 0.85 (0.90). Proportion (%) of Patients with HSDS >–2 was (baseline/year 3): GHD, 26.2/79.3; SGA, 9.3/64.4; TS, 22.1/63.5; CRD, 23.5/59.4; ISS, 18.3/56.8; NS, 17.9/67.5; PWS, 59.7/89.3. NAH SDS was: GHD, –1.16 (1.22) (n = 943); SGA, –1.97 (0.95) (n = 190); TS, –2.08 (0.84) (n = 189); small numbers of Patients Achieved NAH During the observation period in other Indications. Safety: no new signals Were Observed. Number of events/number of Patients Were: NSARs, 288/249; SARs, 133/90; SAEs, 352/224.

**Conclusions:** In Pediatric Patients, growth hormone was associated with Increased HSDS and Increased proportion with HSDS >–2. No new safety signals Were revealed.

## Adrenoleukodystrophy Linked to X: Presentation of Three Cases

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The X-linked adrenoleukodystrophy (X-ALD) is a progressive neurodegenerative disease, due to an alteration in the gene located on chromosome ABCD1 Xq28 that produces ALDP deficiency, peroxisomal which alters β-oxidation and produces an accumulation of long chain fatty acids Very (LCFA) in serum, the adrenal cortex and white matter of the Central nervous system.

**Case 1:** A 7-year-old male, 10 Months with strabismus, brain magnetic resonance was performed: shown signs of leukodystrophy. Asymptomatic, LCFA study: elevated. Healthy parents and sister. ACTH 387 pg/ml (1.1–3.8), Renin activity 3.10 ng/mL/hr (1.1–3.8), basal cortisol 12.7 ug/dl (3–15.4) and post ACTH 14.1 ug/dL. Hydrocortisone was started, it remains stable for two years. However, I have had a progressive neurological compromise: do not hold the head, spasticity and cortical blindness at 16 years.

**Case 2:** Male, two years and three months, healthy, first pregnancy, healthy parents with a family history of adrenoleukodystrophy with two maternal uncles. A study is performed, and it confirms a diagnosis of presymptomatic Adrenoleukodystrophy, confirmed by LCFA and mutation c.1175T>C (p.Leu392Pro) in the ABCD1 gene. Renin activity 2.41 ng/mL/hr (1.0–6.5), cortisol 17.6 ug/dl (3–15.4) and 22.2 minutes post ACTH 30 ug/dL. Currently, five years three months asymptomatic.

**Case 3:** Male, nine years and ten months old, progressive right hemiparesis presents, magnetic resonance brain lesions shown leukodystrophy. The LCFA concentration was high, concordant with clinical suspicious. Patient with progressive neurological deterioration evolves and adrenal insufficiency.

X-ALD is a progressive disease that has an asymptomatic phase, which Evolves with neurological compromise and adrenal insufficiency. At present, there is no curative treatment available, and the transplantation of hematopoietic stem cells has-been Studied that achieves stabilization of the disease. Looking for adrenal insufficiency and genetic counseling is essential.

## Binge Eating Disorder Diagnosis Among Obese Pediatric Population

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Binge Eating Disorder (BED) can be defined as a severe and treatable disorder characterized by recurrent episodes of eating large amounts of food. Data about this issue among pediatric population is scarce since its recent official recognition by DSM-5 in

2013. Due to identify BED, a binge eating scale (BES) questionnaire, with properly validated portuguese translation, was used with obese children and adolescents regularly evaluated at Santa Casa de Misericórdia de São Paulo.

The studied group comprehend individuals under 18 years old, with obesity defined by World Health Organization Body Mass Index z-score (WHO BMI z-score) over 2 and whose weight gain could only be explained by dietary calorie excess. Patients with endocrine pathologies such as hypothyroidism, hypercortisolism, hypothalamic disorders and monogenetic obesity were not evaluated.

54 children were included, 27 girls and 27 boys, with a mean age of 12.1 years old (±2.6). 29 individuals (57%) scored BES enough to be characterized as BED, 16 boys (59.2%) and 13 girls (48.1%). It was found a correlation between BMI SDS and BES results ($r = 0.279$; $p = 0.04$). We divided all patients in two groups: with and without BED and we compared both groups in relation to cholesterol and triglycerides levels, fasting insulin and glycemia, gender and chronological age. There were no differences between groups of any of these variables.

The present evaluation shows that BED has a high prevalence at the investigated group. Although results did not associate such eating disorder with worsen lipid levels, nor higher insulin and glycemia, it can be understood ad a factor of weight gain and maintenance. Once diagnosed, BED treatment may be a factor of better outcomes among obese children. More studies are needed to better understand and treat BED.

## Outlook on Understanding and Communication in DSD According to the Mothers Perspectives

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Communication in DSD is complex: it Involves diagnosis and treatment aspects, psychological status of the families and the cultural context. An adequate understanding by parents is essential for approach and communication in DSD.

**Objective:** Evaluating the DSD care setting in order to identify the doubts and the barriers to the adequate understanding and optimal communication. Still in progress, specific questionnaires are being applied to mothers. The mean age of mothers was 35 yrs (95% CI 32–35, SD:7.8). 70% lived in urban areas and 40% didn't finish high school. The median age of the children was 71 months. 40% of them had CAH. The mean follow-up was 87 months. 70% of the mothers were initially informed by obstetricians and pediatricians still in the maternity hospital. However, almost 20% of children had their diagnosis suspected after leaving the hospital, due to lack of knowledge of the delivery assistance. Additionally,56% of the mothers were indifferent/unsatisfied dissatisfied with the way in which they were initially informed due to lack of competence of the health professionals in dealing with the condition. Regarding the degree of the understanding about their children condition, although 54% were satisfied/very-satisfied, 56% didn't even know the name and characteristics of the conditions, 75% didn't understand why the condition happened and 65% still had doubts.

The doubts were mainly related to the genitália appearance; diagnostic elucidation; continuous treatment; genetic counseling; future sexual activity, fertility and the condition influence on the child's behavior. Regarding communication, 76% reported difficulty in communicating to relatives, 68% were very uncomfortable about what people think or talk about their children. In truth, 65% of the mothers have already been victims of negative comments related to their children condition. For their children, 68% of mothers think they should know about their conditions during childhood, gradually, with the help of doctors and psychologists. In relation to the term used to name such conditions, genital malformation was considered the most appropriate (59.5%) and disorders of sexual development and disease were considered the least adequate (each with 38.9%). related to lack of knowledge of the condition and fear of the associated stigma. The data above show that there is still a lack of knowledge by health professionals, mothers and society, which worsens the stigma and make communication about the theme more difficult. Improving knowledge in DSD among parents, patients, and society will favor communication related to the topic and the well-being of these patients.

## Use of Insulin Infusion for Severe Hypertriglyceridemia in Children

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**Objective:** To describe the cases of severe hypertriglyceridemia Where was the initial insulin infusion therapy to lower triglycerides.

**Material and Methods:** We retrospectively reviewed the case files of 29 mexican children hospitalized for severe hypertriglyceridemia in the last 4 years, who were managed with insulin infusion as an initial therapy.

**Results:** From the 29 cases reviewed 58.6% were male and 41.4% female. The mean triglycerides value was 1,962.48 mg/dl. Acute pancreatitis was found in 27.6% of the patients as a complication of severe hypertriglyceridemia. The average days of insulin infusion was 4. The infusion rate began at a minimum dose of 0.028 U/kg/hr and a maximum of 0.096 U/kg/hr. We analyzed the values of triglycerides before and after treatment by Wilcoxon test obtaining a z-4.46 which was statistically significant $p < 0.001$. Hypoglycemia was presented in 20.7% of the patients secondary to the use of insulin infusion.

**Conclusions:** The risk of pancreatitis is far more worrisome once triglyceride concentrations exceed 1,000 mg/dl, which was demonstrated in our study were 27.6% of the patients complicated with acute pancreatitis. There are no established guidelines for the management of severe hypertriglyceridemia in children, but with our study we demonstrated that using insulin infusion at dose range 0.02 U/kg/hr to 0.09 U/kg/hr, lowered the triglycerides.

## Hyperinsulinemic Hypoglicycemia of Infancy Multicentric Study in Three Hospitals in Lima, Peru

*Nataly Miranda[1,2], Julissa Angulo[3], Karen Sotil[1], Ana Bonilla[2], Lilia Rojas[2], Gaudi Lozano[2], Sandra Orihuela[5], Karen Ramos[2], Sheyla Pariona[5], Ruth Bindels[1], Jyp Payano[1], Patricia Rondon[6], L. Loidi[7], Lidia Castro[8], Flanagan Sarah[9], Ellard Sian[10], Houghton Jayne[11]*

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**Introduction:** Persistent hyperinsulinemic hypoglycemia of infancy (PHHI) is the leading cause of persistent hypoglycemia in infants and is an Important factor of neurological damage for survivors.

**Methodology:** The aim of this study was to describe the diagnosis and evolution of patients diagnosed with PHHI. The medical records of patients diagnosed in the last eight years (2010–2018) were reviewed, collecting information related to age, symptoms, laboratory tests, anatomopathological study and genetic, therapeutic and evolution.

**Results:** We found a total of 11 cases. The most common symptom was convulsion associated with hypoglycemia. The age of presentation in most cases was during the first month. Hyperinsulinemia was demonstrated in all patients. All received medical treatment initially with octreotide or diazoxide. 6 of them responded to the drugs. 5 patients had an unfavorable response, therefore, they underwent pancreatectomy, in 3 patients subtotal resection (80–95% pancreas), in 2 patients nearly complete resection (98% pancreas). The pathology reported nesidioblastosis. The genetic study was carried out on patients and their parents: 7 patients with mutation of the ABCC8 gene (homozygous, heterozygous, missense), 1 patient with mutation of the KCNJ11 gene, 1 patient with homozygous mutation of the HADH gene, 1 patient no one genetic mutation was found in blood, but in pancreatic tissue was found partial segmental loss of the maternal allele in the region of chromosome 11 that encompasses the KCNJ11 and ABCC8 genes and 1 patient without mutation ABCC8 or KCNJ11. Their evolution was: 1 had hyperglycemia after surgery, required insulin, currently euglycemic, 4 in treatment with diazoxide, 5 in treatment with octreotide, and 1 died post -second pancreatectomy. 8 patients have delay psychomotor development.

**Conclusions:** The evolution observed in our patients is similar to that described in other studies, highlighting the importance of genetic testing in the management. It is necessary to do an early diagnostic and treatment to minimize the development of neurological sequelae.

## Neonatal Hyperglycaemia

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**Introduction:** Neonatal diabetes may present with nonspecific signs and symptoms shared with other pathologies. It can be transient (TND) or permanent (PND). The most frequent cause of PND is the mutation of the genes encoding the potassium channel. It may also be a part of another disease such as the IPEX Syndrome.

**Objective:** To present two patients with permanent neonatal diabetes of different origin.

**Material and Methods:** Case 1: 3 months old boy who is admitted with bronchiolitis due to respiratory syncytial virus. Glycemia was 300 mg/dl and glycated haemoglobin 11%. Neonatal diabetes was suspected. Insulin therapy was indicated until 10 months of age when mutation of Kir 6.2 subunit encoding gene was confirmed. He was transferred to glibenclamide therapy with an excellent response. Case 2: 11 days newborn admitted to the neonatal intensive care unit (NICU) for hypovolemic shock and metabolic acidosis with glycemia 580 mg/dl. During his stay at the NICU, secretory diarrhea, very high IgE and primary hypothyroidism without antibodies were detected. IPEX syndrome was suspected and confirmed by mutation of the gene encoding FOXP3.

**Results:** The patient with Kir 6.2 mutation had a very good response to glibenclamide. Last HbA1c was 6.5%. He did not have severe hypoglycaemia. The patient with IPEX syndrome is under insulin therapy by microinfusion. He also takes levothyroxine. Initially he required parenteral nutrition but now he is receiving oral nutrition. At present, his glycemic control is poor. Last HbA1c was 8.8%. He is now waiting for a bone marrow transplant.

**Conclusion:** In a patient with permanent neonatal diabetes it is important to evaluate the presence of other associated signs and symptoms to diagnose other causes than the most frequent mutations. The importance of molecular biology is highlighted, which allowed a diagnosis of certainty and a specific treatment for each patient.

## Pituitary Duplication and Precocious Puberty Case Report

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**Introduction:** Duplication of the pituitary gland (DPG) is a very rare developmental anomaly that is often associated with other abnormalities – the DPG-plus syndrome and occurs during blastogenesis. Associated abnormalities include hypertelorism, cleft palate, mouth and tongue dysmorphism, persistence of the craniopharyngeal canal, midline clival defects, choanal atresia, and ectopic adenohypophyseal or hamartomatous pharyngeal masses. Its association with true precocious puberty has been described. The exact mechanism responsible for this is still unknown, but may be related to the well-documented association with hypothalamic hamartomas.

**Objective:** To describe the case of a girl with pituitary duplication and precocious puberty.

**Case Report:** A 7.9 years old girl was referred because of precocious thelarche. She had the antecedent of surgery for partial craniofacial duplication, oral teratoma and cleft palate. At physical examination her height and weight were in the 75 percentile. Pubertal development with breast Tanner stage 3–4 and Pubic hair tanner 3. She had mental retardation, hypertelorism, mandibular duplication and flattened midface. Lab Workout showed ganadotropines in puberal range and uterine longitudinal diameter of 40 mm with ovarian size of 2.8 and 3 cc. In MRI it was observed total duplication of the pituitary gland, and an image described as pseudohamartoma was informed. After that the rest of hypothalamic pituitary axes were evaluated being in normal values. Treatment with GnRH analogue was started with good response, she showed regression of pubertal signs.

**Conclusions:** Pituitary duplication should be considered in patients with obvious all facial midline anomalies, and to be done in MRI should these patients.

## When an Adrenal Tumor Repeats a Case Report

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**Introduction:** Adrenocortical carcinoma (ACC) has an annual incidence of 0.7 to 2 per million. In Southern Brazil, the incidence during childhood is 2.9 to 4.2 per million This is mainly attributed to the high prevalence of the p.R337H low-penetrance allele of TP53. A contralateral adrenal tumor can be found in 5% of patients.

**Case Report:** Female with history of clitoromegaly and pubarche at 18 months when was diagnosed with right Adrenocortical carcinoma; metastases were rule out and she underwent surgery. At 6 years of age, patient again presented clitoromegaly, thelarche, adult type body odor, deep voice change and pubarche. Physical examination revealed weight: 22 kg, p64, Z0.365, height 118 cm P58, Z0.21 BMI, 15.8 P62 Z0.31, Tanner M2, VP3, and clitoral length of 4 cm. Blood test showed Estradiol 15 PG/ML, luteinizing hormone (LH) 0.16 MUI/ML, total testosterone 0.72 NG/ML, androstenedione levels 2.5 NG/ ML, urine cortisol levels 13.74 UG/24 h, AM Cortisol 6.3 UG/DL, PM Cortisol 3.88 UG/DL, DHEAS 524.1 UG/DL, Plasma Free metanephrines 11.7 PG/ML (<90 PG/ML), urinary fractionated metanephrines 26.2 MCG/24 h. Abdominal MRI revealed a 8.8x9.3x7.4 cm left adrenal mass, 320 ml volume, with heterogeneous intensity: low intensity tumor on T1 and high intensity on T2 images. Bone age was 10 years and 6 months. Metastases were ruled out. The patient underwent left adrenalectomy. Histopathological studies revealed ACC, Ki67 proliferation index was 25%. Molecular analysis revealed TP53 Germline Mutation: c.838A>G (p.Arg280Gly). Li-Fraumeni syndrome was confirmed. Currently the patient is in bi-monthly follow-up by pediatric oncology and endocrinology. Last DHEAS is 0.31 mcg/dl.

**Conclusions:** The patients mutation is described as infrequent and It could have relationship with this unusual bilateral presentation, taking into account that the other side suprarenal compromise occurred 5 years after the primary diagnosis.

## Adherence in Mexican Children with Growth Hormone Deficiency and Small for Gestational Age Treated with r-hGH and the Easypod™ Device

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**Background:** Adherence to recombinant human growth hormone (r-hGH) May influence achievement therapeutic goals. The easypod™ auto-injector is a comfortable and easy way to Provide daily administration of r-hGH.

**Objective:** To describe r-hGH delivered by adherence easypod-™ in children with growth hormone Mexican deficiency (GHD) for gestational age or small (SGA).

**Methods:** The Easypod™ Connect Observational Study (ECOS) is an international, five-year, longitudinal, observational study, Aimed to ASSESS country-specific adherence to r-hGH therapy via the easypod™. Secondary goals Were height velocity, height velocity standard deviation scores (SDS), height, height SDS and IGF-1 Concentrations. Data Were Obtained from medical records and the easypod™ electronic database. Adherence is Expressed as percent and it was Calculated as the number of Days with injections received divided by the number of days of injections planned. Spearman's product-moment correlation was used to ASSESS the association of adherence with growth outcomes.

**Results:** Among 193 Mexican children (mean height at baseline: 124.88 ± 18.95 cm), 147 (76.16%) were easypodTM-naïve, with 105 (71.4%) GH-naïve. In all, 118 patients were GHD, 24 SGA and 5 had Turner syndrome. Mean age was 9.96 ± 3.41 years, 56.8% were boys. Overall adherence was >90% at 1-year and >80% at 4-year follow-up. Therapy adherence was similar according to r-hGH indication or experience with r-hGH. Mean height gain was 8.78 ± 2.20 cm at 1-year follow-up.

Mean height velocity was 8.80 ± 1.94 cm per year. Normal IGF-1 concentrations were attained in 84.7% children at 1-year follow-up. Adherence was associated with change in height ($r = 0.254$, $p = 0.003$), change in height SDS ($r = 0.239$, $p = 0.005$), height velocity ($r = 0.183$, $p = 0.03$) and height velocity SDS ($r = 0.194$, $p = 0.03$).

**Conclusion:** A high and sustained adherence to r-hGH is observed with the easypodTM device in Mexican children with GHD and SGA. The present analysis suggests an influence of adherence on growth outcomes; nevertheless, this hypothesis should be confirmed in future research.

## Frequency of Overweight and Obesity in Congenital Adrenal Hyperplasia Patients with by Adjusting the Body Mass Index According to Age for Height, Parental Age for Mid-Geight and Bone Age

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**Objective:** To estímate the frecuencia of overweight and obesity in congenital adrenal hyperplasia Patients with (CAH) by adjusting the body mass index (BMI) to Height for age; age for parental Mid-Height (MPH) and bone age, in order to evaluate-nutritional status in Children with adrenal pathology.

**Material and Methods:** Cross-sectional study of 39 children (24 female and 15 male, age 2 to 10 years) CAH with Treated Between 2015 and 2018. BMI percentiles (LMIC) Were Calculated ACCORDING TO chronological age, height for age, age and biological age for MPH.

**Results:** The overall frequency of overweight and obesity was 33%. We Observed an Increase of 39% in overweight and obesity When adjusting the BMI to Height/age. The correction of BMI for age ACCORDING TO MPH and bone age reduced the frequency of obesity from 15% to 8%. The frequency of Decreased only overweight BMI When adjusting to bone age (15% to 8%); in the other the overweight Increased Adjustments.

**Conclusions:** The use of BMI and chronological age ACCORDING TO height/age is not the best option to detect cases of overweight and obesity in Patients with CAH. We Observed a reduction of overweight and obesity by the BMI adjusting for bone age and Mid-parental height. Suggest the single generic esta skeletum potential and the maturation Should be Considered When esta diagnosis obesity in patients. It Should be Considered that there are other factors influence the metabolic that status and growth of Patients with CAH.

## Physical Growth of Children with Salt Wasting Congenital Adrenal Hyperplasia During the First Two Years of Age in the Child Health's Institute During the Period 2000–2016

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**Background:** Congenital Adrenal Hyperplasia is an autosomal recessive disease caused by loss or severe decrease in activity in steroidogenic enzymes involved in cortisol biosynthesis, thus inadequate replacement with glucocorticoids does not suppress the excess of adrenal androgens causing alterations in the linear growth pattern with low final height; while the excess results in a decrease in the rate of growth.

**Methods:** It is an observational, descriptive and retrospective study, we collected data on weight and length at birth, age at diagnosis, hydrocortisone and fludrocortisone doses, weight and length every 6 months, and calculated of the growth rate at the first and second year of age.

**Results:** We analyzed 55 patients (34 women and 21 men) with salt-wasting form of CAH with increased 17OHP concentrations (median: 50 ng/ml), the diagnosis being earlier in women (median: 21 days) than in men (median: 52 days) with initial maintenance hydrocortisone dose of 18.8+6.1 mg/m$^2$/d and fludrocortisone of 158.3+58.6 mcg/m$^2$/d. The patients had average length of 0.07+0.75 SD at birth, while they had –1.67+1.33 SD with greater affectation in males (–2.29+1.18 SD) ($p = 0.022$) at 6 months, they had average length of –1.84+1.27 SD at 12 months and it was – 1.51+1.10 SD at 24 months. The calculation of the growth rate in the first year was –1.03+1.62 SD while in the second year of –0.89+1.06 SD.

**Conclusions:** Decreased growth rate was Demonstrated in salt-wasting form of CAH Patients reaching the shortest length at 6 months of age, received the highest that period hydrocortisone deuces with a recovery at 24 months.

## Rare Association Between Imperfecta and Osteogenesis Combined Pituitary Hormone Deficiency the Role of Bone Age

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University of São Paulo

**Objective:** Describe patient with severe osteogenesis imperfecta (OI) and combined pituitary hormone deficiency (CPHD).

**Case Report:** A 13-years-old female has-been followed at our service since the first year of life with the diagnosis of type III OI. She Had Several fractures in the first year of life and have evolved with deformities of upper and lower limbs and severe short stature (height Z-score: –7.6). She Has Been Treated with pamidronate since the diagnosis of OI. During the following We were surprised with the severe bone age (BA) delay (BA of 6.83 years When She Was 10.75-years-old) as it is not expected in Patients with OI. The laboratory evaluation was CPHD Compatible with: free T4: 0.64 ng/dL (normal range (NR): 0.93–1.7), TSH: 2.87 UI/mL (NR: 0.27–4.20), IGF-1: <20 ng/mL (NR: 115.9–533.4), IGFBP-3: 1.1 mg/L (NR: 2.52–6.29), Cortisol: 2.2 µg/dL (NR: 6.7–22.6). Hypophysis of computed tomography was average. The patient and Has Been Treated with hydrocortisone acetate (10 mg/m$^2$/day), levothyroxine (50 mcg/day) and somatropin (0.1 u/kg/day).

**Conclusion:** In this patient type III OI with the unexpected finding of severe delay of BA was the first clue for the diagnosis of CPHD.

## Association Between the Use of Antenatal Steroids for Lung Maturation and Hypoglycemia in Newborns Between 26 and 34 6/7 Weeks of Gestation

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**Objective:** The aim of this study was to evaluate the difference between the incidence of hypoglycemia in those preterm newborns who were exposed to steroids and those who were not.

**Methodology:** This is a prospective cohort study of preterm infants born between 2017 and 2018 at a gestational age of 26 to 34 6/7 weeks in the Hospital Universitario de Santander-HUS-in Bucaramanga, Colombia.

**Results:** 128 preterm infants were evaluated. 111 (86.7%) had been exposed to antenatal steroids. The median maternal age was between 23 and 24 years of age for both those who were exposed and those who were not (p = 0.190). The exposed vs unexposed maternal comorbidities were: preterm labor (70.6% vs. 52.3; p = 0.157), premature rupture of membranes (29.4% vs. 27.9%; p = 0.921) gestational diabetes (5.9% vs 7.2%; p = 0.842), urinary tract infection (29.4% vs 18.0; p = 0.270) and chorioamnionitis (11.8% vs 9.0%; p = 0.717). Female sex patients were 47.1% vs 45.1% (p = 0.927) respectively. The median gestational age was 33 weeks for both groups (p = 0.216) and birth weight was 1640 vs 1945 g (p = 0.190) respectively. The proportion of Apgar scores under seven at 5 minutes was 11.8% vs 5.4% (p = 313). Median metabolic flux was similar among the two groups (6.17 vs 6.19 mg/kg/min, p = 0.365). The incidence proportion of hypoglycemia during the first 48 hours of life was 29.4% in unexposed vs 24.3% in exposed (RR 0.827, IC95% 0.371–1.851; p = 0.652), while incidence density of hypoglycemia was 8.80 and 6.30 cases per 1000 person-hour (HR 8,859 m IC95% 0.380–1.912; p = 0.468), respectively.

**Conclusion:** There was no significant difference in the incidence of hypoglycemia among those who were exposed to antenatal corticosteroid for lung maturity and those who were not.

## Growth Characterization in a Cohort of Renal Allograft Recipients in Bogota Colombia

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Pediatric Nephrology Foundation Cardioinfantil

**Objective:** This study describes AIMS to growth, prevalence of short stature before renal transplant (RTX), catch up growth after RTx and associated factors in a cohort of renal allograft recipients.

**Methods:** We retrospectively reviewed 72 renal allograft recipients underwent WHO RTx at Fundacion Cardioinfantil Between January 2008 and April 2017 with Regular follow-up afterwords for 5 yrs. Pre-Rtx Height was Analyzed by height Z scores (Ht_Z) and Demographic Characteristics Where Compared Between Children with Normal and short stature. Post-RTX growth was Analyzed by Ht_Z at 1, 2 yrs after RTx end and adult height. It was Considered catch-up growth in the z-score Increase ≥0.5 per year. Where possible factors associated Compared Between presenting children catch up growth without vs Those it.

**Results:** Age was 11.0 ± RTx at 3.64 yrs. 56.9% (41/72) evils. Mean Ht_Z before RTx was –3.08 ± 1.66. Before RTx 69.4% (50/72) and the short stature ADH 52.8% of Those (38/50) severe short stature. RTx pre-dialysis duration was associated to pre RTx Short stature (p = 0.02). 2 yrs post RTx growth analysis was possible in 42/72. 42.9% (18/42) Showed catch-up after 1 yr of RTx and 23.8% (10/42) after 2 yrs. Pre-RTx Height and GFR at 1 yr after RTx Where the only factors associated (p = 0.03 ± 0.02 respectively). 22.2% (16/72) Have end height attained mean ± 1.85–2.58 Ht_Z.

**Conclusions:** This is a 17-year-old female, with medical history of Acute lymphoblastic leukemia in 2016. Patient relapsed in 2017. The patient received salvage therapy with ALL-REZ BFM 90. While on treatment with dexamethasone patient presents fasting and postprandial hyperglycemia.

## Two Types of Diabetes Occurring Simultaneously and First Report of Novel Mody Diabetes Mutation in Colombia

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**Introduction:** MODY accounts for 2 to 5% of diabetes cases. Many patients are missclassified as having either type 1 or 2 diabetes. Mutations in hepatocyte nuclear factor-1-alpha and the glucokinase gene are most commonly identified, occurring in 52% to 65% and 15% to 32% of MODY cases, respectively. The wide clinical spectrum and subtle clinical manifestations can make type MODY diabetes an unrecognized diagnosis. Many times, the diagnosis is made because of other evident causes of diabetes such as during glucocorticoid therapy, obesity, and pregnancy.

**Case Report:** This is a 17-year-old female, with medical history of acute lymphoblastic leukemia in 2016. Patient Relapsed in 2017. The patient received salvage therapy with All-REZ BFM 90. While on treatment with dexamethasone patient and postprandial hyper-Physical exam without findings of obesity, no insulin resistance signs. Blood test revealed: C-peptide 4.49 ng/ml, HbA1c 5.3% and fasting insulin 8.65 UUI/ML. Metformin and insulin were prescribed while on treatment with steroids, achieving adequate control. After steroid suspension diabetes treatment was suspended too, but soon after, fasting hyperglycemia recurred with range between 100–120 mg/dl and metformin was reinitiated.

The only positive finding was diabetes on father and paternal grandfather, classified as diabetes type 2 without usual phenotype. MODY 2 diabetes was suspected because of fasting hyperglycemia. Molecular studies reported mutation in heterozygosis, in the GCK gene: (c.1322C>G, p.Ser441Trp). This mutation is not registered on any data base in Colombia. At this moment patient is under treatment with low sugar diet and aerobic exercise.

**Conclusions:** An adequate classification diabetes can avoid unnecessary treatments. Family history is always of great Importance to help to suspect another type of diabetes.

## 18F Dihydroxyphenyl Alanine Positron Emission Tomography Imaging 18F DOPA PET CT in a Patient with Congenital Hyperinsulinism and a Suspicion of Disease Following Focal Molecular Genetic Testing

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**Introduction:** Congenital hyperinsulinism (HI) results for an insulin secretion mainly Inappropriate Caused by mutations in the ABCC8/KCNJ11 which genes encode for the pancreatic β-cells-ATP-sensitive potassium channel-(KATP) SUR1 and Kir6.2 subunits. The diagnosis is based on the evidence of plasma insulin detected During hypoglycemia. Diffuse/focal pancreatic disease can be Differentiated by 18F-dopa PET imaging. Lesionectomy can cure hypoglycemia in focal disease, in Patients with Diffuse Whereas WHO disease do not respond to diazoxide treatment pancreatectomies are extensive Frequently required. Focal and diffuse disease Have different genetic Mechanisms. Diffuse disease is Often Caused by the recessive inheritance of two focal KATP channel mutations Whilst disease Develops When an Individual Inherits a single recessively-acting KATP channel mutation on the paternal chromosome which is unmasked by paternal uniparental disomy within the pancreas. Monoallelic recessively-acting ABCC8/KCNJ11 mutations predict disease focal with ~97% sensitivity.

**Objective:** To present a patient with HI, with an apparent diffuse Involvement of the pancreas by 18F-DOPA-PET-CT evaluation with a novel variant recessively-acting ABCC8. Case report: A 1-day-old female presented with seizures associated with hypoglycemia. She was born at term after an uneventful pregnancy with regular weight, length. No dysmorphic features Were noticed. Maximum glucose infusion rate required to Maintain Normal blood glucose was 12 mg/kg/min.

**Results:** During hypoglycemia Laboratory: Glucose: 40 mg/dl (>55), Insulin 19.3 mIU/l (NV <1) βhydroxybutyrate: 0.07 mmol/l (0.03 to 0.35), NEFA 0.2 mmol/l (0 to 0.9), ammonia 35 umol/l (64–107). High insulin level allowed diagnosis of hypoglycemia During HI.

The 18F-DOPA PET-CT evaluation Demonstrated diffuse pancreatic disease. Genetic testing Identified a novel heterozygous missense variant ABCC8 (p.V802D, c.2405T>A) inherited from her father unaffected. The SIFT and PolyPhen bioinformatics programs to predict pathological Causing a deleterious effect substitution on protein function. The absence of response to diazoxide and octreotide lead to a near-complete pancreatectomy Control of hypoglycemia Achieving sufficient under frequent feeding.

**Conclusions:** The finding of a monoallelic recessively-acting variant did not predict ABCC8 to focal disease in our patient, the presence of a, Although focal lesion giant not be excluded can Because loss of heterozygosity studies using DNA was pancreatic not performed.

## Recombinant Growth Hormone in Children and Adolescents Wit h Turner Syndrome

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**Objectives:** The Turner Syndrome Consensus Group recommend recombinant Growth Hormone (rhGH) therapy Should start around 4 years old. However, in Brazil, you have-been established diagnosis in older ages in MOST Cases. We report the outcome of rhGH therapy after three years and one in growth of 40 Turner Syndrome (TS) girls, correlating the response to Their karyotype.

**Material and Methods:** We performed an observational retrospective study, data collecting medical records of 40 girls diagnosed by karyotype with TS, which Were received rhGH therapy and followed in the Pediatric Endocrinology Outpatient Clinic of Universidade de São Paulo, Brazil. They Were Assigned into two groups ACCORDING TO karyotype: group A (45, X) and group B (other karyotypes). Height z-score was in the beginning of Calculated treatment, one and three years after.

**Results:** Group A contained 25 Patients (62.5%). Diagnosis was established at 4.5 and 6.5 at therapy started years old. Group B contained 15 Patients (37.5%), diagnosed at 6.6 years and 8.2 years at therapy started. Mean height z-score –2.6 Were ± 1.2 and –3.2 ± 0.8, respectively, at the admission. Treatment duration was 5.9 ± 3.8 years and the dose was 0.3 mg/kg per week. After 1 and 3 years, height z-score was –2.4 ± 1.1 and –2.3 ± 1.2 in Group A, and –2.4 ± 1.1, –2.6 ± 0.6 and in Group B. Final height was EVALUATED in 24 Patients (15 in Group A and 9 in Group B) and more than Both groups Achieved 90% of the target height. In Addition to short stature, Patients in the sample ADH: thyroid diseases (n = 17), cardiopathies (n = 16), Alterations kidney (n = 14) and diabetes (n = 2).

**Conclusion:** Recombinant human growth hormone height Increased in Both groups, as described in other studies. Also, a better response was Observed in Patients with other karyotypes rather than in 45, X.

## Adherence to rhGH Treatment from Electronic Monitoring in Children with Growth Disorders: Italian Real-World Data Descriptive Analysis

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**Introduction:** Adherence to growth hormone (GH) therapy is poor Often in Patients with growth disorders, as well end Affecting growth as other clinical outcomes. Adherence've Always Been difficult to monitor, but nowadays the introduction of the easypod™ electromechanical auto-injector Enables device an automatic Real-time record of adherence data (date, time and dose injected for each patient administration) accessible to heathcare professional via the eHealth easypod™ Connect Platform (EPC).

**Purpose:** The aim of esta analysis was to Evaluate Real-world adherence to GH therapy in the Italian patients' cohort adminis-

tered via easypod™ (and registered on EPC) at different time points.

**Materials and Methods:** The records of 755 Patients prescribed r-hGH (Saizen™) using the easypod™ autoinjector and transmitting data to the easypod Their Connect™ platform in Italy Were Analyzed. In order to exclude test/training injections only after the 10th registered data registered Were Analyzed. Adherence was Calculated as mg of r-hGH injected vs mg prescribed. Adherence ACCORDING TO age (pre-pubertal/pubertal; puberty cut-off points 10 years of age for girls and 12 years for boys) and gender was Assessed at five time interval up to month 24 (M1, M3, M6, M12, M24). Were Patients categorized as high (≥85%), intermediate (>56%–84%) or low adherent (≤56%). Reasons for privacy, a minimum of 10 is required to disclose Patients the number of transmitting Patients, THUS the analyasis was performed the two extreme cases Assuming (ie 0 and 10 Patients on the category) and results are presented as range (min-max).

**Results:** Considering all available data, the distribution of Patients is 76.2%–72.3%, 19.1%–20.6%, 4.8%–7.0% in the high, medium and low adherence categories, respectively. At M1 and M3, 741–801 Patients Were still transmitting data, with ≤10 Patients in the low adherence category and proportionally more Patients in the high adherence category (667, 91.3%–84.5%). At M6, M12 and M24, the analysis Showed 600–660 (M6), 457–517 (M12), 213–273 (M24) Patients transmitting data, with 86.7%–78.8% (M6), 83.8%–74.0% (M12) and 77.9%–60.8% (M24) in the high-adherence group. Adherence was not different Between prepubertal/pubertal groups and male/female groups.

**Conclusions:** These data show that administration of GH via easypod™ is associated with high adherence to treatment over time. Analysis of real-world data Provides a unique opportunity to Understand patients' adherence to treatment in real life, and the dynamics of adherence changes, allowing to design Appropriate management strategies.

## Endocrine Abnormalities in Mexican with 22Q11.2 Microdeletion Syndrome

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**Objective:** To determine the frequency of endocrine disorders in patients with 22q11.2 microdeletion syndrome.

**Material and Methods:** Cross-sectional descriptive study of 22 mexican children with 22q11.2 microdeletion syndrome, were evaluated to characterize their growth patterns, presence of hypoparathyroidism and thyroid dysfunction.

**Results:** The mean age at diagnosis was 3 years and 8 months (range from 1 month to 17 years old), 12 female and 10 Were Were male, mean birth weight and length was –1.08 SD and –0.92 SD respectively. During follow-up average weight in children under 2 years was –2.30 SD and –1.96 SD was average height Compared with WHO standard values. From 2 to 5 years of age was –1.93 SD average weight, height was –2.07 SD Compared with Normal values CDC. The most frequent endocrine manifestation was hypoparathyroidism (27%) diagnosed at an average of 4 years of age (range 1 to 10 years), followed by short stature (13.6%) and thyroid disfunction (4.5%), all of them Manifested as primary hypothyroidism diagnosed.

**Conclusions:** Patients with 22q11.2 microdeletion syndrome frequently have endocrine manifestations. Our findings highlight the importance of careful endocrine evaluation and follow-up of these patients.

## Novel FOXP3 Mutation in a Patient with Early Onset IPEX Syndrome

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**Background:** Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome is a monogenic autoinmune disease characterized by early-onset life-threatening multisystemic autoimmunity. This rare hereditary disorder is caused by loss-of-function mutations in the gene encoding the forkhead box P3 (FOXP3) transcription factor, which plays a key role in the differentiation and function of CD4+ CD25+ natural regulatory T cells, essential for the establishment and maintenance of natural tolerance.

**Objective:** To report clinical and genetic findings in a male patient affected by the classical triad of enteropathy, neonatal diabetes and eczema, with a novel FOXP3 gene mutation.

**Method:** IPEX syndrome was diagnosed based on clinical features and biochemical examination on a 5 weeks old boy. Genomic DNAs were extracted from peripheral blood leukocytes of our patient and his parents with their informed consent for genetic studies. Sanger sequencing was performed. A FOXP3 mutation on exon 12 was confirmed.

**Results:** Patient born at term, birth weight 3,050 kg. He presented vomit and dehydration on admission with glycemia 5.11 g/L and acidosis, diabetic ketoacidosis. HbA1c 4%. He received insulin infusion. Glycemic control was variable, with frecuent hyperglicemia and hypoglicemia. Few days after admission he developed severe and persistent diarrhea. Enteropathy was confirmed by endoscopy and byopsia. He required parenteral nutrition for a long period. Eczema was also diagnosed. He showed autoimmune cytopenias. Sequence analysis of the FOXP3 gene was undertaken. Our patient was hemizygous for a FOXP3 frameshift variant resulting in loss of the stop codon, p.(Thr428fs). Current evidence suggest that this novel variant is likely to be pathogenic, consistent with a diagnosis of IPEX syndrome. His mother is heterozygous for the mentioned variant, and she is therefore a carrier of IPEX syndrome.

**Conclusion:** We reported a classical case of IPEX syndrome with early onset of diabetes and enteropathy. The identification of the mutation confirmed the diagnosis which helped to make decisions as regards treatment, was important to predict prognosis and future risk for new offsprings.

## Differentiated Thyroid Carcinoma (DTC) with an Adolescent in Lung Metastases: The Importance of a Multidisciplinary Approach

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Despite the good prognosis of DTC, in cases of advanced and progressive disease, therapeutic options are limited.

**Objective:** To report the case of a Patient with Advanced DTC WHO developed thyrotoxicosis from lung metastases (Mets). Seventeen-year-old male neck with enlargement of 4 years' duration, hard stony goiter of 60 g and right lymph node conglomerate of 10 cm; TSH <0.02 mIU/L. Neck CT: multiple nodules on the right lateral region (from angle to supraclavicular region maxillary); thyroid enlargement displacing the trachea. FNA thyroid and lymph nodes: papillary carcinoma (PC); Thyroglobulin (Tg) in lymph node aspirate >300 ng/ml. Total thyroidectomy with lymph node dissection: papillary carcinoma Differentiated well (classic, solid and follicular variant) 5.5x1.2 cm in size, Angiolymphatic emboli, Involvement of the thyroid capsule, perithyroid tissue, muscle and resection margin. Neck CT: multiple lymph nodes in the right lateral cervical chain. Chest CT: Multiple reticulonodular bilateral lung lesions. T3N1bM1, HIGH risk of recurrence. Therapeutic dose (TD) of $^{131}$I was planned. TSH: 0.04 mIU/L, Tg: >300 ng/ml, ATG: 312 IU/ml. Suspected thyrotoxicosis secondary to lung mets Functioning. Methimazole was Initiated to Increase TSH and as pretreatment for $^{131}$I therapy. TD 200 mCi was administered (under corticoids). Whole body scan post TD (+): Both thyroid bed and lungs. Sorafenib was Initiated. Hand-foot syndrome (Sorafenib was discontinued for 4 months). Spirometry: severe obstruction and restriction. Corticoid therapy was Initiated. Ultrasound: suspicious lymph node images for mets. FNA (+) for PC mets and FNA-Tg >3000 ng/ml. Lymphadenectomy: 4 lymph nodes (+) for PC. Second TD of $^{131}$I: 109 mCi (previous dosime-try). CT: reticular opacities in lungs. Tg: 164 ng/ml (on T4). Spirometry: ventilator restrictive impairment. CO diffusion capacity test: Severely Decreased (absolute and hemoglobin-adjusted values). Scintigraphy: normal perfusion. SPECT/CT: parenchymal abnormalities, predominantly in the middle lobe. Five years after His first visit, the patient has lost 5 kg, with Tg 110 ng/mL (on T4).

**Conclusions:** With adolescents DTC with distant mets require a multidisciplinary management. Options are limited and the benefit/risk of treatment available each Should be Assessed, Given the high risk of recurrence.

## Hypophosphatemic Hypercalciuric Rickets 3 Brothers Dent's with Disease

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**Brother 1:** 7 years old boy, with right genu valgum and short stature (–2.11 DS); X ray shows features rickets. Plasmatic Calcium 9.3 mg/dl; phosphate 2.5 mg/dl; Alkaline phosphatasas 460 U/L -Parathyroid hormone 83 pg/ml – 25OH Vitamin D 24 ng/ml. Urine calcium 159 mg/24 h (9.2 mg/k/day) – Urine phosphatus 870 mg/24 h – Tmp/GFR 2.6 (3.8–5.0 NV) – urine protein 100 mg/ dl.

**Brother 2:** 4 year old boy. Genu valgum from 3 years old. Short Stature (–3.08 DS). Rachitic rosary and wide metaphysis. Normal calcium; Phosphate 2.8 mg/dl; Alkaline phosphatasas 742 U/L -Parathyroid hormone 155 pg/ml – 25OH Vitamin D 5.4 ng/ml. Urine calcium 210 mg/24 h (17 mg/k/day) – Urine phosphatus 670 mg/24 h – Tmp/GFR 1.9 (3.8–5.0 NV) – urine protein 110 mg/dl. With nephrocalcinosis Renal ultrasound.

**Brother 3:** Healthy boy Until 10 I start When genu valgum. I have mild hypophophatemia and hypercalciuria. They receive phosphate and citrate salts and thiazide diuretics; Increased plasma Phosphate. Genu valgum partially improved. They had good renal function. The genetic study Identified the mutation. P [S244L]; [=] in the CLCN5 gene in the three siblings. The carrier is mother and father does not present mutation.

Dent's Disease is a X-linked inherited renal tubular disorder Characterized by manifestation of proximal tubular dysfunction: proteinuria, hypercalciuria, nephrolitiasis, nephrocalcinosis and renal failure progressive. Rickets Occur in a minority of patients. The disease is found in males and female carriers are asyntomatic or show a very mild phenotype. Caused by mutations in It's Either CLCN5 (Dent's disease1) or OCRL1 (Dent's Disease2) genes located on chromosome Xq25 and Xp11.22 respectively. Treatment is supportive. Thyazides diuretics are used to treat hypercalciuria. In rickets must use phosphate and Vitamin D suplements with caution since it May Increase hypercalciuria. High citrate diets seem to delay of renal disease.

## WFS1 Double Mutation in Siblings with Wolfram Syndrome

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**Introduction:** Wolfram syndrome is an autosomic recessive disorder in which early onset diabetes mellitus, optic atrophy, sensorineural deafness, central diabetes insipidus and neurodegeneration are seen. It is associated with mutation in WFS1 and CISD (WFS2) genes. WFS1 codified a protein localized in the endoplasmic reticulum attached to cell membrane, which mutation causes calcium homeostatic Alterations on cascades and apoptosis.

**Objectives:** To describe clinical Characteristics associated with a double mutation WFS1 in a couple of siblings.

**Methods:** Case report.

Patient 1: second son with diabetes mellitus since the age of 3 years, sensorineural deafness and optic atrophy at 10 years old, bladder disfunction Associated with, and diabetes insipidus at 12 years. Later in adolescence, nervous conduction velocity was impaired and psychiatric symptoms started. Gene Sequence Analysis Showed WFS1 two different homozygous mutations: c 315 + 1G>A and c 589G>Ap.val197met3.

2. Patient First is, WHO started with diabetes at the age of 3 years, sensorineural deafness at 16 years and later optic atrophy. He is not presenting diabetes insipidus neither, nor bladder disfunction or neuropsychiatric symptoms.

Gene Sequence Demonstrated the same double mutation Previously Described in His Brother.

**Conclusion:** Wolfram syndrome is an infrequent genetic cause of diabetes mellitus is associated with sequential which affectation of Several systems. Even in Patients with the same mutation, the clinical and progression May be variable.

## Neonatal Familial Hypercholesterolemia Neonatal Case Report

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**Introduction:** Familial Hypercholesterolemia (FH) is an autosomal dominant genetic condition characterized by very high total and LDL cholesterol leading to eruptive xanthomatosis and coronary disease causing suddon death. Phenotypes translate into homozygous and heterozygous, the latter being more common with a frequency of 1 in 1000.000 homozygous presentation is more serious and usually shows antecedent of consanguinity. Gene mutations of the LDL receptor are reported l in 85–95% of cases and that of apolipoprotein B in 5–15%.

**Objective:** To describe a patient with neonatal familial hypercholesterolemia and her family and the causative mutation.

**Methods and Materials:** Revision of clinical history of two sisters with familial Hypercholesterolemia and consanguinions parents in whom genetic studies were performed. Newborn of 37 gestational weeks with a cholesterol of 2900 mg/dl and her four years old sister with a cholesterol of 390 mg/dl treated with atorvastatin.

Genetic studies in mother and daughters revealed heterozygous for p.Pro105_gly314 delins Arg of the LDL receptor gene and homozygous C.13369 G>A, P (Asp 4457 Asn) of the Apo B gene with Clinical Significance is uncertain.

**Conclusion:** It is suggested to perform genetic studies in all patients with hypercholesterolemia at early age to ascertain their genetic origen and evaluate optimal treatment.

## Other Cause of Short Stature Hypophosphatasia Report of a Case

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**Introduction:** The diagnostic approach of the child with short stature is challenging. In Latin America malnourishment is the main cause but rare diseases must be considered. Hypophosphatasia, an inborn errors of metabolism Characterized by defective bone mineralization and deficient activity of the tissue-nonspecific isoenzyme of alkaline phosphatase can cause short stature.

**Objective:** To present a case of short stature due to hypophosphatasia.

**Methodology:** Report of the diagnostic approach of a case.

**Case Report:**

• 3009-2016: Boy, age: 3 years and 10 months. Because of short stature Referred not Relevant medical history was Reported. Physical exam: height below –2SD (CDC 2000). No other Relevant findings. Studies Were ordered.

• 0810-2016: Bone age 2 years, 4 years chronological age. TSH: 2.68 μIU/ml FT4: 1.8 ng/dl IGF1: 69 ng/ml, observation and nutritional indications were prescribed.

• 1407-2017: In my consult, Mother: 154.4 cm, Father: 182.5 cm, Mid-parental height: 174.9 cm (Z –0.26), Patient: height: 92 cm (Z –2.16), weight: 13 Kg (Z –2.39), BMI: 13.5 (Z –1.47), 20 primary teeth with multiple damage, slight hyperflexibility in the upper extremities and an "unusual" pattern of ossification was Reported in the carpogram. Skeletal dysplasia, hypophosphatasia mutations in collagen or Were Proposed to phospho-calcic complete metabolic panel and referral to genetics Were ordered.

• 0109-2017: Patient is seen by another pediatric endocrinologist and a geneticist, both standard as the laboratory report, diagnose constitutional delay of growth indications and give nutrition.

• 0705-2018: The patient returned to my consult, 5 years 6 Months: height: 101.7 cm (Z –2.14) Weight: 14 Kg (Z –2.96) BMI: 13.5 (Z –2.02), Growth Velocity: 4.3 cm/Year (p = 3%), laboratory results: 01/08/2017: 24 hs Calciuria: 1.5 mg/kg/day, tubular reabsorption phosphate 94%, PTH: 24.07 pg/ml, 25OH-Vitamin D: 53.24 ng/mL Alkaline phosphatase: 153.8 U/L (normal 156–369). 04/07/2018 Bone age: 3 years. Due to physical exam, impaired growth and laboratory findings, hypophosphatasia was diagnosed and confirmation laboratory and molecular analysis of gene ALPL Were Requested.

• 0106-2018: Alkaline phosphatase: 116.66 U/L (normal 156–369), gene sequencing ALPL (Sponsored by Alexion laboratories): c.892G>A p. (Glu298Lys) in heterozygous state, this mutation Has Been Previously Reported as Causing pathogenic hypophosphatasia. Levels of alkaline phosphatase: Father: 122 u/L (normal range 40–150) Mother: 41 U/L (normal range 40150).

**Results and Conclusions:** This case was misdiagnosed in different settings During the approach of short stature, but an exhaustive physical examination was the key to an Appropriate differential diagnosis. Hypophosphatasia in Its clinical spectrum includes short stature, teeth loss and/or cavities that May be the clue for diagnosis.

## Epidemiological Profile in Patients with Suprarenal Carcinoma – Child Cancer Hospital in Sorocaba SP/ Brazil

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**Introduction:** Adrenal carcinoma is a rare disease, accounting for 0.02% of neoplasms worldwide. The estimated incidence in children in the South and Southeast of Brazil is 10–15 times greater than around the world (0.21 cases/million), with approximately 3.4 cases/million affecting children under age 14. The concentration of cases in Paraná and São Paulo, seems to be related to p53

gene mutation. It mainly affects children under age 5(65%), and adults between 40–50 years old, with female predominance. The conjecture arises from the hormonal excess, with 60% tumors being active. There may be palpable abdominal mass, precocious pubarch and growth acceleration. It is present in the virilizing form, Cushing's syndrome and mixed. Treatment is complete resection, associated with chemotherapy deficiency. Tumor capsule removal increases the risk of local reoccurrence.

**Goal:** epidemiological profile study of adrenal carcinoma at the Child Cancer Hospital in Sorocaba (state of São Paulo), serving up to – 1,500,000 inhabitants.

**Methodology:** Data from 12 patients, during 2000–2017 interval, at an approximate incidence of 0.45 cases per million children, analyzed at diagnosis: sex, age, main signs and symptoms, hormone suggestive dosage of malignancy and tumor size.

**Results:** From the 12 patients, 4 (33.3%) were boys and 8 (66.6%) were girls; at diagnosis: 11 (91.65) were less than 5 years old; hair and acnes were present in 11 (91.6%) children; 6 (50%) had palpable abdominal mass; and 6 (50%) had cushing disease. Preoperative dehydroepiandrosterone sulfate (DHEA-S) greater than 1000 ug/dL (suggestive of malignancy) was found in 4(33.3%) patients; and in 2 cases (16.6%) the tumor weight was over 1000 grams.

**Conclusion:** Adrenal carcinomas are rare, aggressive, and rapidly progressive with higher incidence in Parana and Sao Paulo. The presence of hair and acnes in children under age 5 strongly suggests adrenal carcinoma and it requires a rigorous investigation for its diagnosis and future treatment.

## Evaluation of Cardiovascular Risk Factors in Obese Children

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**Introduction:** Cardiovascular Risk Indicators Were Analyzed in a pediatric population.

**Material and Methods:** 101 children analyzed: triglycerides (TGC) divided: 2 to 9 years and ≥9 years, and low risk (2–9 years: <75 mg/dl, ≥9 years: <90 mg/dl), moderate (2–9 years: 75–99 mg/dl, ≥9 years: 90–129 mg/dl) and high (2–9 years: ≥100 mg/dl, ≥9 years: ≥130 mg/dl), total cholesterol (<170 mg/dl and ≥170 mg/dl), HDL cholesterol (<45 mg/dl, ≥45 mg/dl), non-HDL cholesterol, risk level: low <120 mg/dl, moderate 120–144 mg/dl and high ≥145 mg/dl; and LDL cholesterol (low risk: <110 mg/dl, moderate: 110–129 mg/dl and high: ≥130 mg/dl); TGC/HDL index (cut-off level: ≥2.05), TGC/Glucose index (≥8.15), insulinemia (≥20 mg/dL). The classifications were extracted from the last Children`s Hospital Association Consensus Statements for Comorbidities of Childhood Obesity.

**Results:** Regarding triglycerides, the age group of 2 to 9 years (both sexes) had a higher % risk of severe, and on the contrary, in the ≥9 years, the highest % occurred in those with a slight risk. LDL-cholesterol was a poor marker of cardiovascular risk, only 6.93% had severe risk levels (>% in girls 8.93% vs boys 4.45%). The 56.43% presented HDL <45 mg/dl. In 24.75%, total cholesterol ≥170 mg/dl was found (approximately 30% of children vs 20% of girls). Non-HDL cholesterol was also a poor risk marker, only 11.88% presented severe risk. The TGC/glucose index was the highest indicator: 62.37% of the children, and the TGC/HDL index was elevated by 51.48%. Only 34.65% of the population had insulinemia values ≥20 mg/dL. The girls had lower levels of HDL, the boys % higher TCG/glucose index, TGC/HDL and insulinemia.

**Conclusions:** The TGC/glucose index was the indicator with the highest percentage of high values (62.37%). This together with low HDL (56.43%) and the TGC/HDL index (51.48%) were the 3 indicators that showed higher than 50% of children. It is important to analyze these indicators in children with obesity (and not only triglycerides, LDL-cholesterol and non-HDL cholesterol, since these were poor indicators of risk).

## Method Validation and Clinical Utility of Leptin Determination by Elisa Prepubertal in Children

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**Introduction:** Eventhough leptin assay is available for more than twenty years, genetic engineering allowed us to obtain standars from recombinant DNA technology (97/594 NIBSC), as well methodology that does not use radioisotopes, as ELISA. Clinical use of leptin determination ranges from very low concentrations (lipodistrophies) to high concentrations (obesity).

**Objective:** To verify an ELISA leptin assay by EP15 A3 at low concentrations (TEa1 ng/ml); to calculate functional sensibility (FS) and to evaluate clinical utility of this assay in lipodistrophy diagnosis.

**Methods:** An ELISA leptin assay was used, calibrated with NIBSC 1st IS 97/594. Calibration range was 0.45–60 ng/ml. Detection limit was 0.04 ng/ml.

Controls provided by manufacturer at concentrations of 0.75, 1.5 and 2.45 ng/ml were used to verify the performance of the method. Functional sensibility was determined as the lowest con-

**Table 1.**

| | | n | Median leptin (ng/ml) | 5–95% percentile |
|---|---|---|---|---|
| The normal weight and overweight | Girls | 22 | 1.67 | 1.67-3.13 |
| Obese | Girls | 18 | 9.01 | 9.01-17.94 |
| The normal weight and overweight | Boys | 25 | 0.61 | 0.61-2.04 |
| Obese | Boys | 16 | 6.51 | 6.51-12.56 |

**Table 2.**

| Patient | Age | Diagnosis | Leptin, ng/ml |
|---|---|---|---|
| 1 | 8 | Generalized Lipodistrophy | 1.46 |
| 2 | 0.83 | Generalized Lipodistrophy | 1.31 |
| 3 | 6 | partial Lipodistrophy | 1.85 |

**Table 3.**

| Leptin (ng/ml) | % CVr | % CVwl | SIGMA |
|---|---|---|---|
| 0.75 | 12.3 | 13.1 | 6.0 |
| 1.5 | 10.5 | 10.5 | 4.4 |
| 2.45 | 7.0 | 9.8 | 3.7 |

centration with an interassay variability of 20%, under experimental conditions established at our laboratory. Leptin levels of 3 patients with lipodistrophy (2 general and 1 partial) were determined and compared with a previously reported sample of normal weight and obese prepubertal patients (Tables 1 and 2).

**Results:** Method performance by EP15 A3 is shown in table 3. Functional Sensibility was 0.61 ng/ml.

**Conclusions:** Method performance was verified with a TEa of 1 ng/ml and FS of 0.61 ng/ml. From the comparison between patients with lipodistrophy and normal weight prepubertal controls we may conclude that this method is not useful in the diagnostic procedure of lipodistrophy, as there is an overlap between patients and controls. It would be of utility to evaluate if leptin levels at high concentration could be used as a marker of metabolic syndrome in obese patients.

## Vitamin D Serum Levels and Associated Factors in a Healthy Child Population

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**Objectives:** Different epidemiological studies confirm a state of vitamin D deficiency worldwide. Its measurement is due to the resurgence Important of classical pathology and Its Involvement in carcinogenic, infectious, cardiovascular and autoimmune processes. The objective of esta study is to know the levels of vitamin D in the healthy child population of a region of province of Spain.

**Methods:** 281 healthy children were recruited. Average age 9.0 years (3.9–14.9) attended in Primary Care, for a full year. Demographic, anthropometric, nutritional and serum measurement data of 25(OH) D were obtained. 25(OH) D was classified as sufficient (>20 ng/ml), mild deficit (between 10 and 20 ng/ml) and severe deficit (<10 ng/ml). The nutritional data were evaluated according to the 24-hour dietary survey. Measurement of 25(OH) D: immunochemiluminscence. Statistical analysis: usual tests (Chi-square-t Student).

**Results:** The prevalence of vitamin D deficiency D is 18.1% (25(OH) D <20 ng/ml). Being 1.4% of severe deficit (25(OH) D <10 ng/ml). A deficit of 54% was observed in non-Caucasian ethnic groups. In relation to seasonality, it is observed that in summer-autumn there is a 10% deficit and in spring-winter it is around 30%. There is a significant difference with the ethnicity, the season of the year, skin photo type and the time of sun exposure. The association with factors such as the Tanner stage, age, BMI, sports activity, use of protector was lower. A low intake of calcium, potassium, vitamin D, vitamin E and folic acid was observed, as well as high protein, calories and fat.

**Conclusions:** Just as at the international level, our child population has a high prevalence of vitamin D deficiency. Ethnicity, seasonality, skin photo type and time of sun exposure are risk factors for vitamin D deficiency.

## Abdominal Perimeter (PC) and Waist Circumference Index (ICT) vs Body Mass Index (BMI) as Diagnostic Alternatives for Overweight and Obesity in Children Aged 3 to 14 Years

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In the face of the continuous growth and constant change of the child's body composition. The diagnosis of obesity becomes difficult. It is known that the body mass index (BMI) can not distinguish between the increase of adipose tissue and the growth of other tissues. Hence, identifying an anthropometric index that helps us easily diagnose children with overweight and obesity is necessary.

**Objective:** To evaluate the correlation of the abdominal perimeter and the waist circumference index (iCT) with the BMI, to identify obesity and overweight in the pediatric population that attended the Endocrinology office of the Central Military Hospital from June to December 2017.

**Patients and Method:** Cross-sectional study in 380 children, between 8 to 14 years. 186 (48.95%) males and 194 (51.05%) females. Obesity was diagnosed with a body mass index (BMI) >95th percentile and overweight ≥85th percentile to 95th percentile. For the statistical analysis Spearman's correlation index was used, sensitivity, specificity was determined and areas under the curve were measured to establish the best cutting point of the iCT and PC that discriminates obesity and overweight.

**Results:** In the 380 children studied, 70 (18.42%) were overweight, 159 (41.84%) were obese. The PC and BMI in both men and women have a very strong positive linear correlation, that is, the higher the PC the higher the BMI and the sensitivity in both males 87.3% versus 81.7 and the PPV 80.5% versus 79.5%, as in women sensitivity 90.9% against 89.8% and PPV 76.2% against 81.4% is higher in obesity.

**Conclusion:** The iCT is an alternative to diagnose obesity in children older than 8 years.

## Macroadenoma Pituitary Growth Hormone Producing a Teenager

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H. Universitario Dr. José E. González

**Introduction:** Pituitary gigantism is the exceptional condition in pediatrics, most pediatric endocrinologists are on average 1 to 2 patients in his career. 95% of pituitary adenomas are producing GH, the hypersecretion causes increased IGF-1.

**Methods:** 14 year old female who started his condition by presenting increased weight and height, intermittent frontal headache with no predominance of schedule. He added decreased vision, visual acuity 20/200. MRI tumor supraselar 3 cm x 3.3 cm x 3.1 cm, expansion of the sella turcica, involucre both cavernous sinuses and upper displacement contact and the optic chiasm. Apparent age more than chronological, coarse facies. With prognathism, macroglossia, protrusion of the frontal bone, widening lips, nose and ears. Large hands and feet. Female genital phenotype tanner 3. bitemporal hemianopia and acanthosis nigricans skin on the neck, armpits, popliteal crease, cubital fossa and knuckles. Somatomedin C at 1072 ng/ml. Glucose suppression test >40 ng/ml. Hypopituitarism presents.

**Results:** Treatment was started with cabergoline and hormone replacement. Passes transnasal surgery, resecting 70% macroadenoma. Acutalmente the patient has improved levels of IGF-1 in following. Transsphenoidal surgery is the treatment of choice in the case of this patient.

## Adult Height in Short Children Born Small Gestational Age SGA Treated with Growth Hormone GH

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**Introduction:** GH is effective in Improving height in short children born SGA and STI treatment was approved in Europe, USA an Argentina.

**Objective:** To report the response to GH treatment in SGA children Reached adult WHO height (AH) in a University Hospital.

**Material and Methods:** Retrospective analysis of medical records of SGA children received GH treatment WHO. Inclusion criteria: birth weight (BW) and/or body length (BL) at birth <percentile 10 for gestational age (GA); height at start of treatment <–1.87 SDS pubertal onset or prediction of AH with <1.8 SDS; AH Reached all. Patients: 17 children (8 evils) with (mean + SD) 1722 + 700 gr BW, BL 41.0 + 4.9 cm, GA 35.0 + 4.0 weeks, target height SDS –0.36 + 0.7, GH treatment started Between 3.2 and 12.6 years (mean 8.34 + 2.6 years). Height was lower than the average range in 14 Patients (–1.87 to –4.41 SDS), three with Silver-Russell phenotype. Three pubertal children started treatment for poor prognosis of AH presenting Between 8.5 and 9.1 Years with height SDS Between 0 and –1.35. Initial height SDS was –2.28 + 1.09. Initial dose of GH 48 + 4 ug/kg/day.

**Results:** Height SDS During treatment was: 1.09 + –2.28 baseline; –1.71 + 0.97 1st year; pubertal start –1.13 + 0.8; AH –1.41 + 0.49 (all, p = 0.00 since start of treatment, p paired test). Increased growth velocity after 1 year of Significantly treatment from 5.3 + 1.4 to 8.4 + 1.5 cm/year (p = 0.00). During the height gain 1st year of treatment was 0.58 + 0.29 SDS (p = 0.0000 paired t test); at the end of treatment it was 0.86 + 1.1, p = 0.0064; 14 Reached anAH >–2 SDS in 12 AH and was in Their target height range. There Were no Differences inAHBetween Patients WHO Gained >0.5 SDS (n = 9) or <0.5 SDS at the 1st year of treatment; neither in thepubertal height gain Between Patients with (n = 9) or without LHRH analogue. The duration of the treatment was 6.46 + 2.8 years. There was Correlation between height gain and years of therapy r: 0.763, p = 0.001.

**Conclusion:** With treatment GH Increased AH SDS in SGA children.

## Central Adrenal Insufficiency in Pediatric Survivors

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**Introduction:** Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy. As the survival rate has improved significantly, it is necessary to monitor of long term treatment complications. The high doses of glucocorticoid as part of their treatment may lead to suppression of the hypothalamic pituitary adrenal axis. The aim of this study was to evaluate the prevalence of ACTH deficiency and the relation with the ALL treatment.

**Methodology:** We conducted a descriptive, retrospective and observational study. We analyzed the medical records of patients referred with ALL. Inclusion criteria: Patients who have ALL with follow up in endocrine service. Exclusion criteria: Patients who have ALL in therapy time. Clinical examination was performed according to the Children's Oncology Group Long-Term Follow-Up Guidelines. Statistical analysis: Categorical data were expressed as number of cases and percentage. The continuous data are expressed as median and range/mean and DS.

**Results:** The medical records of 243 patients diagnosed with leukemia were selected from May 2007 to April 2018. Of the 243 patients (55% male), the mean age at diagnosis of ALL was 6.5 ± 3.9 years, the 16% were high risk, the 89% were type B; the 21% presented relapsed. The mean cortisol values were 11.9 ± 3.4 µg/dl. 10% require ACTH low dose test. 6.2% were insufficient requiring substitutive corticoid treatment.

**Conclusions:** Corticotrophin insufficiency was diagnosed in 6.2% in paediatric leukemia survivors. The adrenal response should be determined and the hydrocortisone treatment should be considered in episodes compatible with adrenal insufficiency.

## Neonatal Screening for Congenital Hypothyroidism in Children with Down Syndrome

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Hospital Sor Maria Ludovica

**Introduction:** Down syndrome (DS) is the most common congenital cause of Mental Retardation. Prevalence is 1/625 live births in Buenos Aires Province. DS newborns have a high incidence of congenital hypothyroidism (CH) and an Increased risk of growth impairment and learning disabilities. THUS, early diagnosis of CH in These children is an Important achievement.

**Aim:** To analyze prevalence of DS in CH Patients with eutopic gland and describes the course of the Characteristics and disease. To search Differences Between DS and DS Children with no CH and eutopic gland.

**Method:** We evaluated data from each DS detected by newborn CH with neonatal screening (Group 1) (n24 M: 11, F: 13) referred to our center Between 1996 and 2017. This group was followed up to the age of 2, and it compared with DS was not permanent newborns who had CH and eutopic gland (Group 2) (N122 M: 62, F: 60). CH etiology, age at start of treatment, maternal age and cardiac diseases associated were analyzed. Weight, thyroid stimulating hormone (TSH) concentration and dose levothyroxine (LTD) were evaluated at start, one and two years. Statistical analysis: Student test, Mann-Whitney and Fisher.

**Results:** The prevalence of DS Among Patients with eutopic gland was 16.43%.

Etiology was Studied in 12 (50%) patients. Eutopic gland was found in 11 (91.6%) and in one athyreosis. Median age was 36 maternal (32.5 to 37.3) years.

Eleven (45.8%) Patients Suffered from heart conditions, 4 (16.6%) died, 7 (29.1%) discontinued follow-up and 2 (8.3%) Were Referred to another center. Mean weight was Significantly lower in group 1 ($p = 0.001$). Were found no significant Differences Between age at diagnosis acerca groups, TSH value and LTd.

**Conclusions:**

1. DS prevalence was high in CH Patients with eutopic gland.
2. Dyshormonogenesis the most frequent etiology was in These children.
3. Were LTd requirements like in DS and DS Patients with no CH and eutopic gland.

## Precocious Puberty in a Girl with Neurofibromatosis Type 1 and Optic Glioma Case Report

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**Background:** Neurofibromatosis type 1 (NF 1) is a common autosomal dominant neurocutaneous disorder associated with an increased risk of benign tumor formation. Optic nerve gliomas occur in aproximately 15% of the patients and are usually diagnosed in the first decade of life. Precocious puberty due to optic glioma is not rare in patients with NF 1, especially when the optic chiasm is involved.

**Case:** We describe an 8 year old caucasian girl with family history of NF1 (mother and brother). The patient was diagnosed with NF1 at 2 due to the presence of café-au-lait lesions, axillary and inginal freklings and Lisch nodules. To highlight she presented a bilateral optic glioma which compromise the optic chiasm. She was referred for precocious puberty. Since the age of 7 she presented progressive breast enlargement, pubic hair and menarche 1 month before the consult. At the exam she had thelarche and pubic hair stage 3 of Tanner with an advanced bone age. Her height was at 97th percentile and the projected final height was 143 cm calculated by Bayley and Pinneau method. Pelvic ultrasound had pubertal characteristics and basal luteinizing hormone shows a pubertal range greater than 0.3 mIU/mL. Given the diagnosis of precocious puberty, the short final stature and the psychosocial context we decided to start treatment with gonadotropin releasing hormone analogs.

**Discussion:** The incidence of NF1 is 1 in 3000 births and family history is described approximately in 50% of the cases. It is caused by defects in the NF1 tumor suppression gene. There is a wide clinical variability even in familiar cases. Precocious puberty is the most common endocrine disorder in children and it is usually associated with optic gliomas as described in this case.

**Conclusion:** This report illustrates the necessity of a close follow-up in children with NF1 to achieve an early diagnose and an appropriate treatment of the precocious puberty as well as other endocrine disorders.

## Central Precocious Puberty Due to Hypothalamic Hamartoma

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**Introduction:** Central precocious puberty (CPP) is caused by premature activation of the hypothalamic-gonadal axis, idiopathic CPP is the commonest cause but at younger presentation organic cause is more frequent.

**Objective:** Case report of an infant with organic due to hypothalamic precocious puberty hamartoma (HH).

**Clinical Case:** 1 year 2 months old girl, presented with 3 days of vaginal bleeding, history of blinking and facial grimaces episodes associated to progressive bilateral breast development since 4 months old. Her physical exam shows tanner III breast development, tanner II pubic hair, axillary odor and estrogenic vaginal discharge, weight in 86th percentile and height in 83th percentile with accelerated growth. Laboratory shows elevated estradiol (74.1 pg/ml) and gonadotropins (LH 4.5–57.2–35.5 uU/ml, and FSH 5.5–22.4–19.5 uU/ml, basal, 30 and 60'post LHRH injection). Pelvic US shows pubertal uterus with 3 mm echogenic endometrium, ovaries of 3.7 cc (right) and 0.9 cc (left) and bone age of 3 years old. Other hormones including TSH, freeT4, cortisol, prolactin, b-HGC, AFP, 17OH progesterone, Androstenedione and DHEAS were within normal limits. EEG was normal. Brain MRI shows a voluminous hamartoma of tuber cinerum. Neurosurgical

evaluation was done not requiring surgical treatment. Monthly gonadotropin-releasing hormone analogue (GnRHa) (Triptorelin) was initiated (113 mg/kg) and the follow up shows a decrease in growth rate and size breast and no more genital bleeding. Pelvic US after 3 months show a decrease in ovarian and uterus size.

**Discussion:** We present an infant with CPP secondary to HH which is a benign tumor that produces CPP by pulsatile GnRH secretion or by inhibiting the neuroendocrine inhibitory pathways of the gonadal axis.

**Conclusion:** Rapidly progressive CPP in infancy requires appropriate laboratory and radiologic evaluation to determine the organic cause, and treatment without delay is imperative.

## Follow-Up of Growth in the First Two Years of Live in Children with Congenital Hyperinsulinism on Octreotide Therapy

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**Objective:** The aim of this study was to evaluate the growth in the first two years of live in children with congenital hyperisulinism due to ATP sensitive potassium channel mutation managed with daily octreotide therapy.

**Methods:** Data regarding family and medical history, auxological measurements, bone age development, physical examination, molecular tests, growth factors (serum IGF-1), thyroid function, liver function tests, and hepatobiliary ultrasonography were measured.

**Results:** The median age of CHI diagnosis was 4 week (range 2–28 wk). The mean (±SD) dose of octreotide required was 16 μg/kg/d (range 8–22 μg/kg/d). The decrease growth velocity was the most prevalent side effect.

**Conclusions:** Octreotide was efficient, glycemias were maintained in the usual range, but reduced growth velocity because decreased growth factors and suppressed growth hormone production. This type of treatment should be restricted to patients who do not respond to conventional treatment. Long-term studies are required to assess the final height in this group of patients.

## Bartter Syndrome and Growth Hormone Deficiency

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**Introduction:** Classic Bartter syndrome is a salt-wasting tubulopathy caused by mutations in the CLCNKB (chloride channel Kb) gene. Short stature is one of the clinical manifestations in these children. Growth hormone deficiency has been suggested as a cause of persistent growth failure in patients with classic Bartter syndrome. In the present work, we describe the case of a patient with CLCNKB gene mutation and review the reported cases of classic Bartter syndrome associated with growth hormone deficiency.

**Case Presentation:** Classic Bartter syndrome is a salt-wasting tubulopathy caused by mutations in the CLCNKB (chloride channel Kb) gene. Short stature is one of the clinical manifestations in these children. Growth hormone deficiency has been suggested as a cause of persistent growth failure in patients with classic Bartter syndrome. In the present work, we describe the case of a patient with CLCNKB gene mutation and review the reported cases of classic Bartter syndrome associated with growth hormone deficiency.

**Conclusions:** The present case strengthens the association between classic Bartter syndrome and growth hormone deficiency. We propose that growth hormone status should be considered while treating children with classic Bartter syndrome.

## Risk Factors for Obesity with Metabolic Complications in with the Pediatric Population Daniel Alcides Carrión National Hospital 2018

*Isabel Pinedo, Magaly Flores, Denisse Alva, Alfonso Ramirez*

Hospital Nacional Daniel Alcides Carrión

**Objective:** We Assessed the risk factors for metabolic complications in obesity with the pediatric population.

**Methods:** Patients aged 2–14 years with BMI/age ≥p85 Were included, Patients with chromosomopathies, previous use of corticosteroid, insulin sensitizers, growth hormone and/or gonadotropin analogues, Were excluded. The ethical principles Were respected.

Patients with hypertransaminasemia (TGP ≥25 mg/dl), dyslipidemia, dysglycemia (glycemia ≥100 mg/dl), hepatic steatosis, high risk of NAFLD (TGP ≥25 mg/dl and steatosis hepatic), hyperinsulinism and insulin resistance Were Considered as case group. Were comparison made using Student's t test, X2 test. A significance level of 5% was accepted.

**Results:** 54 Patients (mean age 17.9 ± 3.67, 55.6% male, Morbid Obesity 22.2%) Were included. 61.1% HAD Obesity Patients with metabolic complications. The Waist-to-height ratio (WHR) was 0.61 ± 0.06 cm/m. The median basal Glucose was 94.5 mg/dl [86–98], C-LDL 119 mg/dl [113–131], TGP 39 mg/dl [22–55]. Mean basal insulin was 21.18 IU (±9.6), HDL-C 41.12 mg/dl (±9.96) Dyslipidemia (72.7%) was the most frequent metabolic complication, HOMA-IR>p90 for Age (55.5%) and Tanner (33.3%), hepatic steatosis (50%), high risk of NAFLD (44.4%) and Hyperinsulinism (38.9%). The mean time of physical activity at home was 0.59 h/day in the group with metabolic complications, and 2.21 h/day in the group without complications ($p = 0.000$); Obesity in tutor was 33.3% in the case group ($p = 0.001$). Time in front of screen, time of physical activity in the school, insulin resistance indexes and WHR were not significant.

**Conclusions:** The physical activity time at home and Obesity of the Tutor Were with obesity risk factors to metabolic complications. Dyslipidemia, insulin resistance and hepatic steatosis need to be Assessed in the first clinic evaluation.

## Cost-Effectiveness Analysis of Neonatal Screening Program for Congenital Hypothyrodism in Regional Peruvian Program

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**Objective:** To evaluate the costs and benefits of neonatal screening for Congenital Hypothyroidism, at the Hospital Nacional Docente Madre Niño San Bartolomé, during the observation period between 2015 and 2017, to show that the net benefits obtained by the prevention of mental retardation associated to untreated Congenital Hypothyroidism, justifies the allocation of resources to cover the expenses generated by this program and could even support the allocation of additional resources for the expansion of program coverage.

**Method:** The direct costs of the program for screening, diagnosis and treatment were estimated based on the costs of the procedures performed as part of the program. The benefits are the costs averted by prevention of mental retardation that would affect the individual in case of Congenital Hypothyroidism.

**Results:** The execution of the screening for Congenital Hypothyroidism program, during the observation period, provides an estimated net benefit between 218,060.00 USD and 554.329,19 USD, such values corresponding to discount rates of 10% and 4% respectively. The B/C indicator varies between 8.59 and 21.42 which indicates that the benefits obtained with the execution of the program, after covering its costs, are equivalent to at least 8.59 times the value of those costs.

**Conclusion:** The detection of Congenital Hypothyroidism through neonatal screening is economically profitable for society as a whole, because it provides benefits for individuals and their families and allows savings of marginal costs that would be incurred in case the newborn with Congenital Hypothyroidism did not receive early treatment.

## Polyostotic Fibrous Dysplasia and Precucocious Puberty Mccune Albright Syndrome a Case Report

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**Background:** Fibrous dysplasia (FD) is a benign bone lesion low frequency, congenital but not hereditary, due to a somatic mutation. They can cause pains, deformations and fractures. It Can Occur in any bone of the skeleton and be mono- or polyostotic. The Latter can be part of the McCune Albright syndrome (SMA), with extraskeletal manifestations: such as spots on cafe au lait skin or endocrinopathies like precoucious puberty.

**Case:** An 8 year-old girl that presented, after falling from her height, a transverse fracture of mid-diaphyseal displaced left femur in a bone that Settled with patological Characteristics. Osteosynthesis and biopsy of bone fragments, that inform fibrous dysplasia, Were performed. The bone scyntigraphy evidenced with polyostotic lesions predominance of the left half of body. At the exam she HAD and pubic hair telarche Tanner 3 accelerated growth velocity, and history of an isolated genitorrhagia at 6 years old. Of the paraclinical assessment, an advanced bone age and elevated estradiol suppressed gonadotrophins with stands out. The combination of polyostotic bone dysplasia and precocoious lead to the diagnosis puberty of SMA.

**Discussion:** The incidence of SMA is 1/100,000 to 1,000,000 births and it is Caused by a mutation of the GNAS-I Gene that Affects only some somatic cells. The incidence of FD is unknown, and 3–10% presented in the context of SMA. Precocious puberty is The most commonly endocrine manifestation of esta syndrome. Usually is a peripheral precocity puberty, and one central secondary May Develop Because of sex steroid withdrawal as we described in our case.

**Conclusion:** The thread of the diagnosis of SMA can be a bone fracture on a patological. A detailed anamnesis and physical examination Should be Carried out investigating other comorbidities of the syndrome for early diagnosis and timely treatment.

## To Compare the Capacity of the Waist Size Index ICT vs Body Mass Index (BMI) to Detect Metabolic Risk Factors in Children from 6 to 13 Years Old

*Jenny Cortez, Isabel Pinedo*

Central Military Hospital

It is visceral fat've Known that metabolic and inflammatory action and the body mass index (BMI) has limitation to determine the distribution of body fat. Given the constant change in the child's body composition and the presence of metabolic changes at younger and younger ages; it is Necessary to Identify specific that somatic indices help us predict metabolic risk.

**Objective:** To compare the capacity of the waist circumference index (iCT) vs body mass index (BMI) to detect metabolic risk factors.

**Patients and Method:** Cross-sectional study in 76 children, 6 to 13 Between years old. Obesity was diagnosed with a body mass index (BMI) >95 percentile, and abdominal obesity with iCT ≥0.5. The presence of fasting blood glucose ≥100 mg/dl, the total cholesterol ≥170 mg/dl, triglycerides ≥130 mg/dl in >10 years and >100 mg/dl in ≤10 years, TGP >35 mg/dl, hyperinsulinemia >12 in pre-pubertal and >15 in pubertal, the HOMA index ≥3.1 and iCT and BMI Were Compared To determine which has better diagnostic efficiency. For the statistical analysis, sensitivity, specificity and areas under the curve Were Measured to Establish the best cut-off point iCT that Discriminates metabolic risk.

**Results:** 76 children, 42 men and 34 women Were Studied. Comparing the diagnostic efficiency of the iCT against the BMI, sensitivity of 93.3 vs. 83.7% was found for hypertriglyceridemia, 83.3% against 70% for hyperinsulinemia and 85.3% against 70.6% for insulin resistance.

**Conclusion:** The iCT is a more efficient than the BMI indicator to Identify metabolic risk in children of school age.

## Impact of TSH on Metabolic Syndrome in Children Euthyroid with DM1

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[1]National Institute of Pediatrics; [2]Research Unit on Metabolic Diseases, CMXXI

**Objective:** To ASSESS serum TSH and association of metabolic syndrome (MS) in children euthyroid with DM1.

**Material and Methods:** A cross-sectional study, analytical, observational, retrospective. We reviewed, in the clinical file of the INP, Endocrinology's Service patient data Went to the WHO from 2008 to 2018 consultation; We Identified with DM1 185 subjects Who Had the first determination of FT4 and TSH with the simultaneous determination of the lipid profile and positive microalbuminuria and metabolic monitoring demographic, clinical and metabolic variables Were recorded. We used multiple linear regression analysis and logistic regression to ASSESS the impact of HRT on the lipid profile and SM. This was approved by Committees of inquiry and ethics from the National Institute of Pediatrics.

**Results:** We divided into the two groups euthyroid Patients to the level of ACCORDING TSH [low level (n = 103) 0–2 mIU/L (1.30 0.41) and high level (n = 82) 2.01 to 4.0 (2,790.53 miu/L), p = 0.000]. We defined the criteria ACCORDING TO Patients of the IDF, the prevalence of overall Obtaining dyslipidemia (71%), obesity (27%) and metabolic syndrome 6.4%. Patients with low TSH level associated Were with greater frequency of metabolic syndrome vs 13.8% 5.6%. In Patients with high TSH level, it was Significantly Associated with hypertriglyceridemia (p = 0.005), the HDL cholesterol higher (p = 0.004), and so the border with Total cholesterol (p = 0.06).

**Conclusions:** This is the first study in our environment that shows the association of Concentrations of TSH in euthyroid Patients with DM1 over the presence of SM. The high-normal TSH May exert effects on the occurrence and/or severity of the components of the SM and esta Represents a risk factor for early atherosclerosis in Patients with DM1, Representing a major expense to the possibilities of the national health system, emphasis is Placed on the Importance of modifying the model of care of the child with DM1.

## Adrenocortical Tumor Presenting as Isosexual Precocious Pseudopuberty in a 34-Month-Old Boy

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Adrenocortical tumors are rare causes of Peripheral precocious puberty in childhood, with an incidence of 0.4 per million children Annually. Mutations in the tumor suppressor gene TP53 are The most common, and it shows in an isolated way in up to 30% or Associated with other entities, Such as Li-Fraumeni syndrome (LFS) and Li-Fraumeni-like (LFL), by 70% and 20% to 40%, respectively. Almost 90% of esta tumors are highly productive of hormones, and Their clinical variability of presentation depends on the hormonal secretion.

**Case Report:** A 34-month-old child from Bolivia has an Increase in penile length from 8 months associated with pubarche. Family history: MH 154 cm, 13 years old menarche, PH 170 cm, 168.5 cm MPH (–1.4 SDS).

Physical examination: Height 92.5 cm (–1.2 SDS) Weight 16.1 kg (+0.5 SDS), BP 85/50 mm Hg. No acne. Tanner: aap2, penis length 6 cm, testicles 3 ml bilateral. Complementary tests (see table).

Alpha-fetoprotein, BHGC, nephrins and catecholamins normally were. Bone age (GreulichyPyle) 6 years old. Abdominal and testicular ultrasound Were normal. Abdominal CT: Left adrenal tumor 3x2.5x2.9 cm with Central calcifications.

After complete resection of the tumor, the histopathological study confirmed an adrenal carcinoma. Immunohistochemistry showed an overexpression for p53.- Ki67: 50%. The sequencing of the TP53 gene, revealed a germinal line mutation TP53 (17p13.1), already described in the LFS. 2 years later, in a full body MRI, a 3.3x2.6x4.2 cm left para -aortic lesion was identified in the same location of the previously described tumor with a calcified appearance. After complete removal started chemotherapy, according to protocol by the oncology service.

**Conclusion:** Li -Fraumeni syndrome Increases the risk of developing cancers Several types of from childhood to adulthood.

Given the lack of management guidelines, and the wide degree of penetrance and expression of TP53, it is Necessary to close follow up with a complete sequencing of TP53 gene.

**Table 1.**

| | Normal range | Pre surgery | Post surgery |
|---|---|---|---|
| LH, U/L | | <5.0 | 0.0 |
| FSH, U/L | | 0.2–5.0 | 0.4 |
| 17 OH Progesterone, ng/dl | 0.0–2.2 | 0.7 | 1.4 |
| DHEA-S, umol/L | 0.4–4.9 | 2.2 | 2.0 |
| Androstendione, nmol/L | 0.7–3.0 | 1.3 | 0.4 |
| Testosterone, ng/dl | <25.0 | 58 | <20 |
| Aldosterone, nmol/L | 0.1–0.9 | 1.0 | 0.1 |
| Act. Renin, ug/L.h | 1.8–2.9 | 9.4 | 2.6 |

## Liver Dysfunction and Oestrogenic Therapy in an Adolescent with Turner Syndrome

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**Introduction:** Turner syndrome results from the total or partial loss of the X chromosome. Liver involvement is frequent. The prevalence of these abnormalities range from 23% to 28% in young patients and reaches 80% in middle-aged women. The oestrogen-induced hepatotoxicity was proposed as the main cause of abnormal liver tests, however its role has not been well established, alterations in the tests and changes in hepatic architecture were observed in patients with and without oestrogen therapy.

**Objective:** We report a 15-year-old adolescent girl with Turner syndrome who presented elevation of liver enzymes with oestrogen therapy.

**Clinical Case:** Weight: (DS-2.13); Height: (DS-3.25), BMI: 20.05 kg/m$^2$ (pc25-50), Tanner Stage 1. Bone age: 15 years old. Laboratory: karyotype by banding G 45, X0; LH: 24.6 mUI/ml (2.12–10.89); FSH: 82.10 mUI/ml (3.85–8.78); Estradiol: <10 pg/ml (24–114); T4L: 0.81 ng/dl (0.65–2.0); TSH: 2.02 mUI/ml (0.49–4), ATPO: 1.0 U, ASAT: 28 UI/L, ALAT: 20 UI/L, Total cholesterol: 170 mg/dl (0–200). Celiac disease antibodies negative. Bone densitometry: lumbar spine L1-L4 Z Score –1.24; femur: Z score: –1.15. He received substitute replacement therapy. One year after treatment: ASAT: 127 UI/L (0–32), ALAT: 794 UI/L (0–33), γ glutamyl transferase: 96 U/L (0–40), CMV, HAV, HBV, HCV Antibodies negative. FAN, ASMA, ANTI LKM: negative. Abdominal ultrasound: normal. Substitute therapy was discontinued. 10 months later ASAT: 389 UI/L, ALAT: 877 UI/L. Liver biopsy: mild nonspecific inflammatory lobular alterations.

Ursodeoxycholic acid 500 mg/d was indicated and hormone replacement therapy restarted. 3 months later the transaminases values were ASAT: 34 UI/L, ALAT: 77 UI/L; γ glutamyl transferase: 27 U/L.

**Conclusions:** Oestrogen treatment suspension did not improve liver function in this patient, which supports the continuity of the same. Ursodeoxycholic acid treatment may have been beneficial.

## Discrepancy Between Tanner Stage and Testicular Volume: Key Diagnostic Clue for Sex Reversal

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**Background:** The physical examination in an adolescent check up must include the measurement of testicular volume.

**Clinical Case:** 17-year-old adolescent boy came up to His yearly check. I was 165 cm tall (–0.98 SDS) and his weight was 45.4 kg (–2.18 SDS). Tanner stage: Genitalia 5, Pubic Hair 5 and Testes of 6 cc. No gynecomastia. Initial tests Showed: FSH 30.4 mIU/ml (RV: 0.7 to 11.1 mIU/ml), 26.14 LH mIU/ml (RV: 0.8 to 7.6 mIU/ml) Testosterone: 6.1 ng/ml (RV: 3–10 ng/ml), AMH: 3.74 ng/ml (1.43–11.6 ng/ml). A karyotype (G-banding) revealed 46, XX (n: 50) leading us to the diagnosis of XX Male Sex Reversal. Molecular detection of SRY gene (+) by PCR, confirmed the diagnosis.

**Conclusion:** This case enphazises The Importance of testicular volume measurement in the usual physical examination in apparently healthy male patients.

## Metformine and Sibutramine Therapy in Children and Adolescents with Overweight and Obesity

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**Objectives:** We report the outcome of Body Mass Index (BMI) of 35 Patients That were followed in the Pediatric Endocrinology Outpatient Clinic of Universidade de São Paulo, Brazil, Regarding the use of Metformine, Metformine Associated with Sibutramine and lifestyle Modifications only.

**Methods:** We performed an observational retrospective study, collecting medical records data of 35 Patients, diagnosed overweight and obesity With, followed in the Pediatric Endocrinology Outpatient Clinic of Universidade de São Paulo, Brazil. All Patients Were Already under lifestyle for 6 months Modifications. They Were Assigned into three groups received treatment ACCORDING TO: group A (lifestyle Modifications only), group B (lifestyle Modifications and Metformine) and Group C (Modifications lifestyle, Metformine and Sibutramine). BMI z-score was Calculated at the Beginning of treatment and after 6 months.

**Results:** The mean age was 12.4 years. Group A contained 14 Patients (40%) healthy habits. They received orientation. The mean BMI z-score was +3.3 ± 1.5 in the beginning and +3.1 ± 1.1 after six months. Group B contained 16 Patients (45.7%), Which Metfomine for six months received. The mean BMI z-score was +2.5, +2.4 ± 0.5 and ± 0.6, in the beginning and after six months, respectively. Group C contained 5 Patients (14.2%), Whom received Metformine associated with Sibutramine. The mean BMI z-score was +2.8 ± 0.5 in the beginning and +2.5 ± 0.7 after six months. Treatment duration was 6 months and 4.6 months for Metformine for Sibutramine, and the mean dose was 1500 mg and 10 mg, respectively.

**Conclusion:** All groups presented a reduction of BMI after 6 months follow-up. Groups A and B presented at a similar BMI small loss. But, even though the sample in Group C was small, was associated Metformine when with Sibutramine (Group C), the BMI loss was more noteworthy.

## Spontaneous Menarche in Patients With Turner's Syndrome

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Turner's Syndrome is a very common chromosomal abnormality that affects 1:2500 to 1:4000 of female born children and is characterized by total or partial absence of an X chromosome. The phenotypic expression is diverse, being the most important: short stature, gonadal disgenesia and infertility. About 30% of the patients have spontaneous puberty, 10–20% spontaneous menarche and 1–2% of them preserve fertility.

**Case Report:** CB, 15 years old, female, referred to a pediatric endocrinology clinic due to short stature. Reports difficulty in gaining weight at birth. Adequate NPMD. Denies concomitant diseases or previous treatments. Reports menarche at age 12 with intense flux and regular cycles. Physical examination shows low implantation of hair on the nape, microretrognathia and short neck. Weight: 43 kg, height: 141.5 cm (Z score –3), target height: 159 cm (Z score –0.3). Tanner M5P5. Complementary examinations: bone age compatible with the chronological age, LH 2.41 mUI/mL (pre-pubertal <1.5), FSH 6.85 mUI/mL (pre-pubertal <4.0), estradiol 58.0 pmol/L (pre-pubertal <110), IGF-1 332 (237–996). Karyotype was requested in peripheral blood lymphocytes with a banding technique: 46, X, del (X)(p11.2)[22]. At age 16, height 145 cm, pelvic US: 78 $cm^3$ uterus, 5.5 $cm^3$ right ovary, 7.4 $cm^3$ left ovary. Initiated estrogen replacement due to menstrual irregularity.

**Discussion and Conclusion:** The early Turner's Syndrome diagnosis can improve life quality and self-esteem in adult patients. The use of GH can lead up to 8.5 cm higher growth than expected. Estrogen therapy can stimulate and preserve bone tissue, contribute to stature growth and increase the chances of gestation. Therefore, the examination of short stature in young girls should always include karyotype, even in patients without such stigmas.

## Polyostotic Fibrous Dysplasia, Case Report

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**Introduction:** Poliostic fibrous dysplasia is a rare disease in children (OMIM 174800). It is secondary to postzygotic mutation leading to a functional defect in the α subunit of the G protein, resulting in uncontrolled proliferation of bone precursor cells. Clinical manifestations are skeletal deformities, fractures and pain.

**Patient and Method:** A 7 year old male child with a history of 2 years of lameness and lower limb hypotrophy. Radiographs revealed an expansive lesion in the right femoral neck without cortical compromise, coxa vara and hypomineralization. Scintigraphy showed increased uptake in the right femur, right tibia and left fibula and a biopsy reported fibrous dysplasia. He presented two femoral fractures requiring surgical management. There were no bone disorders in his family and no consanguinity.

**Results:** At the time of evaluation, the presence of cafe au lait spots, signs of pubertal onset, hypercortisolism or hyperthyroidism were discarded. Laboratories ruled out hypophosphatemia, a condition that may be associated with polyostotic disease. Pain was controlled with NSAIDS. The beginning of bisphosphonate was deferred.

**Conclusions:** Images (radiography and scintigraphy), biopsy and molecular study are the key for diagnosing this condition. The typical image of cortical thinning without its involvement and the heterogeneous expansive lesion was decisive in making further studies. Upwards 70% of patients with polyostotic fibrous dysplasia can develop endocrine hyperfuncion, and check for this condition. Early treatment is important with bisphosphonates as zoledronic acid, pamidronate or olpadronate. Preventing fractures and pain management is necessary to improve patient functionality.

## Different Clinical Manifestations in a Family with the Same Pathogenic Variant in the Gene Coding for Steroidogenic Factor-1

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Pathogenic variation in the gene coding for NR5A1 steroidogenic factor 1 (SF1) is the second AFFECTED Most Frequently Causing Gene Disorder of Sexual Development (DSD) after the androgen receptor (AR) gene. SF1 has Also Been Involved in familial forms of premature ovarian failure (POF) and infertility. We report clinical and genetic findings in two brothers 46, XY with DSD in a non-consanguineous family.

The index case, a 46, XY DSD boy of 4 years, an external masculinization Showed score of 5.12 (= 3 labia fusion, micro-phallus = 0, urethral meatus = 0, right gonad = 1, left gonad = 1) and a pelvic ultrasonography Müllerian with Rests. His profile was concomitant hormone: testosterone <2.5 ng/mL (0.2 to 13), luteinizing hormone <0.1 mIU/mL, follicle stimulating hormone 0.8 mIU/mL, inhibin B 20.3 pg/mL (4–352) and 16.0 ng hormone antimüllerian/mL (1.4–11.6).

The second child 46, XY was born with atypical genitalia: external masculinization score 5/12 (= 3 labia fusion, micro-phallus = 0, urethral meatus = 0, right gonad = 1, left gonad = 1) and pelvic ultrasonography without Müllerian Rests. Hormonal profile at 3 days of life was: AM cortisol 19.9 mg/dL (>10), testosterone 82.2 ng/dL (75–400) and androstenedione 272 ng/dL (10–279).

Were not pathogenic variants found in the AR gene, but the analysis of a panel of 8 DSD genes, probably Showed a pathogenic variant in the gene NR5A1 (p.Arg84His) in Both brothers.

Three maternal aunts-grandmothers presented menopause than 35 years Earlier; the mother, which has not yet ovarian failure, and the eight years old sister Were Also Studied. The same pathogenic variant was Observed in all of them.

It is essential to study the genetic cause in Patients with DSD, due to the Clinical Implications for the Patients, But Also for genetic counseling to the family.

## Response to the Use of Growth Hormone in a Patient With Rothmund-Thomson Syndrome

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**Introduction:** Rothmund-Thomson syndrome is a genodermatosis characterized by poikiloderma, short stature, sparse hair, absence or scarcity of eyelashes and eyebrows, cataracts, skeletal abnormalities, premature aging and predisposition to cancer. It is caused by mutations in the RECQL4 gene.

**Objective:** The case of a patient with a confirmed diagnosis of Rothmund Thomson is reported, and the response to management received with growth hormone is also shown.

**Description:** Female patient, product of first pregnancy of consanguineous parents, course with gestational diabetes, delivery at 35 weeks, weight 1527 gr and length 39 cm. Starts follow-up by endocrinology at 2 years for short stature, at which time it was found with a size of –4.9 SD, phenotypically with sharp facies, scanty hair and eyebrows, multiple wart-like keratosic plaques, hypo and acromic skin macules. At 3 years and 11 months, a diagnosis of Rothmund Thomson type II syndrome with a mutation in the RECQL4 gene was made. Additionally, with a history of nephrocalcinosis and 2 fractures of the radius and 1 of the tibia. Currently with 9 years and 4 months, height in –2.7 SD and starting puberty. It has been managed with somatropin since 2 years. In multidisciplinary monitoring. So far by oncology orthopedics and dermatology has not been shown malignancy.

**Conclusion:** The Rothmund-Thomson syndrome is an infrequent cause of short stature, without finding reviews in the literature that show the management of these patients with growth hormone. It is shown that in this patient there is a clear improvement in height, however it is recommended to use low doses and close clinical monitoring, accompanied by a multidisciplinary group given the increased risk of cancer, mainly osteosarcoma during childhood and skin cancer in the stage adult.

## Inefficiency of Levothyroxine Suspension in a Neonate

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**Introduction:** Congenital hypothyroidism is one of the major causes of preventable mental retardation. Optimally, diagnosis should be early, hormonal replacement and normalization of thyroid function tests should happen before 2–3 weeks of life. Levothyroxine is the treatment of choice for congenital hypothyroidism. As of the moment, the tablet levothyroxine has been exclusively used over liquid formulation as liquid formulation is deemed unstable. The pills can be crushed in a spoon and dissolved in water, formula, breast milk or other liquid right before administering with a dropper or a syringe. The pills should not be mixed in a full bottle of formula or breast milk. We present a case of a congenital hypothyroidism initially responding well to tablet formulation and showed significantly increased TSH level when switched to a liquid preparation.

**Case:** Patient was born at 32 weeks of gestational age with birthweight of 1.73 kg. She was admitted to NICU for prematurity. Other than prematurity, pregnancy and delivery were uncomplicated. Initial newborn screen noted a TSH of 70.5 uIU/mL (N < 20 uIU/mL). Serum thyroid function test revealed a TSH of 215 uIU/mL and Total T4 of 0.08 ng/dL. Patient was started on levothyroxine 25 mcg tablet daily at day of life 7. Repeat TSH and Free T4 after 1 week of treatment, revealed a TSH of 0.686 and FreeT4 of 4.12 ng/ dL. Levothyroxine was discontinued. After 1 week off levothyroxine, repeat tests were done and TSH came back at 47.5 uIU/mL and FreeT4 was 0.84 ng/dL. Levothyroxine 25 mcg/ml solution was restarted day of life 21. The baby was otherwise fine with unremarkable physical exam. Patient was eventually discharged from NICU. Patient came for follow up at day of life 38 at the pediatric endocrinology clinic. Her TSH was checked at his Pediatricians office and was noted to be 120 uIU/mL. His Levothyroxine was switched to tablet and was increased to 37.5 mcg daily. Repeat tests done at DOL 50, showed a TSH that was trending down to 9.241 uIU/mL.

**Conclusion:** Levothyroxine (T4) is a synthetic hormone considered to be the standard of care for treatment of congenital hypothyroidism. Treatment is most effective if given orally as a tablet form. As of the moment, there are no liquid formulations and no compounding recipes that produce a stable concentration of levothyroxine. Efforts to create suspension especially for neonates should be avoided as this is a critical time for brain development. The case presented shows how treatment of congenital hypothyroidism can be ineffective if we use a liquid formulation for levothyroxine.

## Difficulties in the Diagnostic Process of a Patient with Turner Syndrome (TS) and Ovotesticular DSD

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Clinical variability of TS is related to the broad range of associated chromosome abnormalities and accurate karyotyping is essential for genetic counseling.

**Objective:** To describe the diagnostic process and its difficulties in a patient with TS and ambiguous genitalia at birth.

**Case Report:** Patient (2.6 yr) presenting for follow-up of Congenital Adrenal Hyperplasia (CAH), diagnosed at the age of 3 months based on clitoromegaly and 17-OHP: 7 ng/mL (normal gynecological ultrasound). Clitoroplasty at 2 years of age. Under treatment (hydrocortisone 7.5 mg/day): 17-OHP: 0.12 ng/mL, DHEAS: 330 ng/mL, Δ4: 0.1 ng/mL, Testosterone: 0.15 ng/mL. Height: 80 cm (SDS–2.5), Weight: 10.8 Kg (Pc10), BoneAge: 1.8 yr. The dose of hydrocortisone was decreased and molecular genetic testing was negative for CAH. Based on low adrenal androgen levels, growth velocity ≤p3 and phenotypic features (Turner's facial appearance, short fourth metacarpal, short neck, cubitus valgus), tapering of corticosteroid therapy continued until discontinuation. One year later: 17-OHP: 0.92 ng/mL, DHEAS: 100 ng/mL, Δ4:

0.3 ng/mL, Testosterone <0.1 ng/mL; karyotyping: 46, XY in 20 metaphases and Clonidine test (GHmax: 34.4 ng/mL). HCG test: Testosterone (B): 0.19 ng/mL, Testosterone (Post): 0.80 ng/mL. Gonadectomy (8.6 yr): both gonads with testicular parenchyma with seminiferous tubules and ovarian parenchyma with primordial follicles and scarce germ cells (Molecular testing of the gonad: SRY+). At 10.2 yr (LH: 32 mIU/mL, FSH: 85 mIU/mL): pubertal induction. Menarche 13 yr. Based on phenotype suggestive of TS and final height: 138 cm (23 yr): repeat cytogenetic testing was performed in 100 metaphases: 45, X [28]/46, XY [72]. Comorbidity assessment: normal, except for osteoporosis.

**Discussion:** Even if CAH is the most common cause of DSD in girls, if biochemical/molecular findings are negative, karyotyping should be considered as the most relevant test for early diagnosis. When there is high clinical suspicion of TS and in the absence of monosomy X, an analysis of a higher number of metaphases should be considered to rule out chromosome mosaicism. In cases as the one reported, a correct genetic diagnosis is essential for potential early therapies (e.g. GH therapy), allowing for a rational approach that may consider the situation of the patient and his/her family.

## Cerebral Edema in Diabetic Ketoacidosis Risk Factors

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**Introduction:** Diabetic ketoacidosis is the first manifestation of Type 1 diabetes mellitus (DM), 25% of cases can be usually triggered by infectious or emotional conditions. The main symptoms are: polydipsia, polyuria, nocturia, polyphagia – less noticeable in younger children. It is characterized by glycemia >200 mg/dL, metabolic acidosis (pH <7.3 and/or bicarbonate <15 mEq/dL), presence of ketonemia/ketonuria. The treatment is done with hydration, insulin therapy, replacement of potassium(K), bicarbonate and other electrolytes in individualized cases. The most serious complication is cerebral edema (approximately 1% of cases) and is associated with high morbidity and mortality (30%). It is more common in diabetic primodespensation and may appear within 24 hours after the onset of ketoacidosis.

**Case Report:** AGOC, 6 years old, arrives at our service in diabetic ketoacidosis without diagnosis of DM1. Mother refers to weight loss of 5 kg, polydipsia, polyuria and nocturia in the last month, evolving with inappetence and prostration 4 days ago. It enters into poor general state, agitated, drowsy, dehydrated, with Kussmaul respiration, capillary glycemia: 386 mg/dL, arterial blood gas-severe metabolic acidosis (pH 6.9, HCO3 3.9, pCO2 17.2 pO2 57, 3; 2ªgasometry with pCO2 12.4); urine1-ketone bodies 2+, K: 7.9. Performed intravenous hydration, continuous infusion of insulin (0.1 U/kg/h) and capillary glycemia control. After 16 hours, the patient presented nausea, vomiting, headache and worsening of drowsiness. Due to cerebral edema confirmed in cranial CT, treatment with intravenous hypertonic solution was initiated and transferred to the Intensive Care Unit. Patient evolved with clinical improvement and was discharged to Infirmary.

**Conclusion:** Studies have demonstrated risk factors associated with the development of diabetic ketoacidosis with cerebral edema. These include: severe acidosis, low pCO2 (ventricular narrowing), elevated urea and absence of previous diagnosis of DM1. We need to investigate these factors, since the early diagnosis of cerebral edema is essential for the success of the treatment.

## Nesidioblastosis in a School Age Patient

*Rosario Almanzar, Adonise Rosario, Elbi Morla*

Intec

Describes the presentation of a clinical case of nesidioblastosis in a school-age patient.

**Clinical Case:** Female of 7 years and 5 months of age, with a history of clonic seizures from-tonic 1 year of age, Treated with Oxcarbazepine. Presenting symptomatic hypoglycaemia one and a half years later, So THAT His Doctor started treatment with L-carnitine since then and Until Now. At 4 years old, anticonvulsants are suspended. Current disease Characterized by diaphoresis and dizziness; generalized tonic-clonic presents movements, ocular retroversion with loss of consciousness (on two occasions), is Transferred to a medical center Where They Demonstrate glycemia at 18–11–32–16 mg/dl respectively, dextrose solution with momentary place improvement. It remains for 9 days without complete recovery and fever Appears 3 days of evolution and is Transferred to the RRC Children's Hospital, where it is Studied and confirmed hypoglycemia, laboratory tests reveal that high counter-regulating hormones, insulin levels in 2, 700 mIU/ml, stabilizes with octreotide and it is to carry out DECIDED surgery for pancreactectomy, open laparotomy is performed. Trans-operative biopsy Reported: hyperplasia of the islet of Langerhans cells. So 95% of pancreatic tissue is removed, and treatment is hyperglycemia presents started with INSULIN ANALOGS SLIM-ACTION (0.14 units/kg/d) PANCREATIC ENZYMES 10,000 d, 15 min prior to meals, MULTIVITAMIN. One month after surgery, the patient presented signs of hypoglycemia again, insulin was discontinued and the patient was ADMITTED, hypoglycemia was verified, and second surgical intervention was performed. An excess of 5% of the pancreas and 2nd portion of the duodenum was performed with an end-to-end anastomosis. Currently responding to tx with analogous insulin. With stabilizes octreotide and it is to carry out DECIDED surgery for pancreactectomy, open laparotomy is performed. Trans-operative biopsy Reported: hyperplasia of the islet of Langerhans cells. So 95% of pancreatic tissue is removed, and treatment is hyperglycemia presents started with INSULIN ANALOGS SLIM-ACTION (0.14 units/kg/d) PANCREATIC ENZYMES 10,000 d, 15 min prior to meals, MULTIVITAMIN. One month after surgery, the patient presented signs of hypoglycemia again, insulin was discontinued and the patient was ADMITTED, hypoglycemia was verified, and second surgical intervention was performed. An excess of 5% of the pancreas and 2nd portion of the duodenum was performed with an end-to-end anastomosis. Currently responding to tx with analogous insulin. With stabilizes octreotide and it is to carry out DECIDED surgery for pancreactectomy, open laparotomy is performed. Trans-operative biopsy Reported: hyperplasia of the islet of Langerhans cells. So 95% of pancreatic tissue is removed, and treatment is hyperglycemia presents started with INSULIN ANALOGS SLIM-ACTION (0.14 units/kg/d) PANCREATIC ENZYMES 10,000 d, 15 min prior to meals, MULTIVITAMIN. One month after surgery, the patient presented signs of hypoglycemia again, insulin was discontinued and the patient was ADMITTED, hypoglycemia

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## Importance of Neonatal Screening for Suprarenal Hyperplasia in Twins and Genetic Correlation

*Liliana Mejia de Beldjenna*[1], *Audrey Matallana*[2], *Silvia Chahin*[3], *Roxana Merino*[4], *Alicia Belgorosky*[4]

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**Introduction:** Congenital adrenal Hyperplasia (CAH) is a group of genetic defects in cortisol, aldosterone and androgen synthesis leading to clinical manifestations of steroid excess and deficiency and placing patients at risk of adrenal crisis and death, changes in sexual identity, and even death if not recognized early. The programs for tamizaje for neonatal CAH, and other diseases are considered essential activities world wide for public health prevention for the early detection and identification of genetic, metabolic and endocrine disorders in newborns. Tamizaje prevents death in the affected patients, and positively impact the health f patients, families and society overall, lead to efficient use of health care resources, and thus reduce health care expenses.

**Objective:** To describe the importance of neonatal tamizaje for CAH and the impact in the diagnosis and management of patients.

**Methods:** Described 2 twins born in Argentina, to healthy Colombian parents.

Patients were diagnosed with congenital adrenal hyiperplasia at birth by tamizaje, and confirm by genetic and blood work.

**Results:** Twins of 35 weeks, #1 neonatal tamizaje of 17OHP 151 ng/dl (VN 40 ng/dl) #2 neonatal tamizaje of 17OHP 151 ng/dl (Vn 40 ng/dl). blood confirmation in both of 17OHP >2000 ng /dl(VN 200 ng/dl. Both with the mutation CYP21OH In2 homocigota o In2/ ELCONV. Treatment from the 5th day of life with hidrocortionsone and fludrocortisone.

**Conclusion:** The prognosis of CAH have improved thanks to neonatal tamizaje for 17-OHP, preventing death for adrenal crisis since it lead to ealy diagnosis specially in males, and facilitates the right sexual gender designation, improving social integration according to the genetic sexual orientation. In this case the genetic analyis confirm the sensitivity and specificity of the tamizaje.

## Growth Hormone Treatment in Short Children with X Linked Hypophosphatemic Rickets Three Cases Reports

*Mauro Borghi, Carlos Longui, Caroline Pellicciari, Jordana Padua*

Santa Casa de São Paulo

**Introduction:** Children with X-linked hypophosphatemic Rickets (XLH) are more prone to short stature DESPITE treatment and vitamin D. With phosphate objective describes the outcomes of GH therapy (50 mcg/kg/day) hypophosphatemic rickets In Patients with and short stature at diagnosis.

**Patients and Methods:** We Analyzed the retrospective data of 3 Patients from outpatient pediatric endocrinology clinic, diagnosed hypophosphatemic with ricket. The data consisted of gender, age of diagnosis of chronological rickets, height (SDS WHO) at the beginning and at last visit of GH therapy, prescribed medication to treat hypophosphatemic ricket and target height (SDS).

**Case Report:** MAOS, 13 years and 7 months, male, diagnosed as XLH at 2.5 years old. The initial therapy consisted of vitamin D (.75 mcg/d) and phosphate (1.5 g/d). I started GH treatment (50 mcg/kg/day) at age 9.4 years, height –2.17 SDS at beginning of GH therapy and underwent orthopedic surgical procedure at age 10. Final Height not yet Achieved. Current height: –1.26 SDS. Familial +0.58 SDS Target Height.

JMP 16 years and 6 months, female, diagnosed as XLH at 4 years old. The initial therapy consisted of vitamin D (.75 mcg/d) and phosphate (1.5 g/d). She started GH treatment (50 mcg/Kg/day) at age 9.7 years, height SDS at –1.41 beginning of GH therapy and underwent orthopedic surgical procedure at age 12. Final Height SDS –1.41. Familial Target Height –0.08 SDS.

ARCJ, 16 years and 5 months, male, diagnosed as XLH at 1.6 years old. The initial therapy consisted of vitamin D (.75 mcg/d) and phosphate (1.5 g/d). I have GH treatment started (50 mcg/Kg/day) at age 10.3 years, height –1.31 at beginning of GH therapy and underwent orthopedic surgical procedure at age 11. Final Height SDS –1.79. Familial Target Height –1.75 SDS.

**Conclusion:** Early treatment of rickets and Appropriate stature could improve prognosis. However, in cases of delayed treatment,

the use of GH Should be started as soon as possible to end Improve height. Further studies with early introduction of GH and follow-up of These Patients Should be performed.

## Disorder of Sex Development: 46, XY Girl

*Hana Ruminate*[1,2], *Patricia Lacourt*[2], *Javiera Basaure*[2], *Angelica García*[2], *Claudia Godoy*[1,2], *Alejandro Martínez*[1], *Javiera Hansen*[1]

[1]Pontificia Universidad Catolica de Chile; [2]Hospital Dr Sotero del Rio

Disorders of sex development (DSD) are a wide range of conditions with diverse features and pathophysiology as MOST that Often present in the newborn atypical genitalia, or in adolescence as a pathological pubertal development. A 9 y 10 m EVALUATED old girl at the Catholic University Endocrinology Unit for proportionated short stature, and with Decreased growth velocity. PHYSICAL EXAM Height 123 cm (–2.3 DS) Weight 27.6 kg, BMI 18.2 (p77%) SS/SI 1.01. The abdominal examination did not reveal any mass. Breast tanner 1 pubic and axillary hair was absent. Normal anatomy external genitalia was in not estrogenized and. Were not virilisation features noted. LABORATORY Blood cell count, cre-atinine, chemistry, lipidic profile, total IgA antibodies and Anti-transglutaminase standard. Endocrine tests Showed 1.62 mIU TSH/ml, FT4 1.39 ug/dl, IGF-1 13 ng/ml (85–306), IGFBP-3 3.7 mg/L (2.3–5.8). Bone age 7 and 10 y 4 m for chronological age. Cariotype 46, XY. LH 4.8 mUI/ml, Estradiol <5 pg/ml Testosterone <2.5 ng/dl, Inhibin B <2.6 pg/ml and Antimullerian Hormone <0.01 ng/ml. Pelvic magnetic resonance shows a prepubertal uterus (length 3.5 cm), and gonads Were not founded. Disorders of male sex development panel of genes: hemizygous variant c.380>G (p.Tyr127Cys) on SRY gene. This variant on SRY is of uncertain significance, it has-been, Although Reported in an Individual with sex reversal.

**Discussion:** SRY gene has a significant role in sex development. It spurs the development of Sertoli cells from gonadal bipotential precursors via the action of SOX9. Absent or dysfunctional SRY is found in Individuals with female phenotype and 46, XY genotype. Although evidence is available to determine the Currently Insufficient role of esta variant in disease, the study of His Father and the find of the same variant in other Patients with the same phenotype will allow more clarification of the role of esta variant in our patient.

## Mutation of the Gene Men 1 as a of Endocrine Neoplasia Multiple Family Type 1

*Liliana Mejía de Beldjenna*[1], *Juliana Llano*[2], *Jose Mejía*[3], *Maria Centeno*[4]

[1]Universidad Libre ,GRINPED,Cali, Colombia; [2]Universidad Georgetown, USA; [3]Universidad del Valle, Colombia; [4]Universidad Libre, Cali, Colombia

**Introduction:** Type 1 Multiple Endocrine Neoplasia (MEN 1) is a genetic disease caused by a germinal mutation of the MEN 1 gene. The mutation conditions loss of function and the absence of a neoplasia, suppressor protein, which facilitates their development in some endocrine glands, inheritance is autosomal dominant. There is a sporadic form without familial predisposition but with at least two of the three abnormalities: parathyroid adenomas, pancreatic tumor (gastrinomas, insulinomas) pituitary adenomas (prolactinomas, somatotropinomas). But, there is a familial for as well with known predisposition as some of the abnormalities described above. Digestive tract tumors may be also present as well as those of bronchus and thymus. Pheochromocytomas occur rarely.

**Materials and Methods:** To describe a Colombian family with type 1 MEN affecting four generations including mother and siblings, we analyze the MEN 1 gene in a mother and her son affected.

**Results:** Mother with 42 years to diagnosis with Pancreatic tumor, tumor of trachea, neuroendocrine tumor of stomach and liver and, Pituitary adenoma and are with 9 years to diagnose parathyroid adenoma and prolactinoma. Both with with Autosomal dominant mutation C482G>A/p.Gly161 Aspen of MEN 1 gene.

**Conclusion:** Investigation of the MEN I gene allows the recognition of affected members of a family even before the disease is manifested clinically and prevent associated mortalities.

## Hipophyseal Causing Central Lesions in Girls Precocious Puberty

*Liliana Mejía de Beldjenna*[1], *Mirey Siuffi*[2]

[1]Universidad Libre GRINPED, Cali, Colombia; [2]Clinica Farallones

**Introduction:** Precocious Puberty (PP) is defined as the initiation and progression of puberty before age 8 in girls and 9 in boys. It has an incidence of 1:5000 to 1:10000 subjects and a relationship of women /men of 20:1. Based on genetic studies and improved image techniques it has been possible to identify causes that were considered idiopathic in 90% of cases These include CNS lesions, those independent of GNRH and idiopathic. In girls idiopathic causes are 2.5 times more common than neurogenic lesions, including tumors.

**Objective:** To characterize 86 patients with central precocious puberty between to 2000 and 2017 seen in Pediatric Endocrine Clinics. Etiology was defined by magnetic resonance of the sella with gadolinium.

**Methods and Materials:** This was a retrospective analysis of clinical charts of girls seen at four Institutions from Cali Colombia.

**Results:** We reviewed 86 charts of a girls with precocious puberty with a median age of appearance of 84 ± 15.5 months, median consultation time of 7.5 ± 13.1 months and 44% with pelvic echographic changes. Median bone age was 10 ± 1.9 years in 33%. We found hypothalamic -pituitary lesions causing precocious puberty in 33% of patients (n = 28). Hormone hypersecretion was found only in prolactinomas: Astrocytoma 1, sellar Depression 1 Meningioma 1, Microadenomas 20, Prolactinoma 1, Hypophyseal cyst1, Pars planitis cyst1. RMN normal in 67% of patients(n = 58).

**Conclusion:** Nuclear magnetic resonance is of utmost importance for evaluating patients with precocious puberty.

## Sitosterolaemia Presentation of a Clinical Case

*Sara Hernandez*[1], *Esteban Uribe*[2]

[1]Pediatric Endocrinology; [2]Dermatology

8 year old female patient referred by the dermatology department with clinical symptoms of xantomas on elbows and knees, physical examination showed normal blood pressure, had no eyelids without lipemic xantomas corneal ring or other important findings. Initial lipid profile showed a total cholesterol 639 mg/dl and LDL (low density lipoprotein) of 571 mg/dl. Which they were confirmed 4 weeks after similar results.

Studies of his father and mother show a total cholesterol of 147 mg/dl and 252 mg/dl, respectively.

Treatment was started with atorvastatin 10 mg/day with poor response so dose was increased to 20 mg/day. After 2 months of treatment, the patient developed acute liver failure, which required hospitalization. The cause of liver failure could not be confirmed but Statin vs a naturopathic medicine the patient was receiving, which could not be identified was suspected. After the suspension of both products, liver function completely recovered.

With total cholesterol levels of 335 mg/dl and LDL 280 mg/dl, management began with ezetimibe 10 mg/day, achieving a very favorable response with reduced levels of total cholesterol to 156 mg/dl and LDL to 99 mg/dl. Besides a marked clinical improvement achieving a reduction of xanthomas by 80%.

Imaging studies were liver ultrasound within normal limits, Carotid Doppler ultrasound showed no atheroma and a normal echocardiogram.

Genetic studies reported were conducted:

1. Panel Familial Hypercholesterolemia: Sequences DNA promoters, coding regions and exon-intron junction of the LDLR, APOB, PCSK9, and STAP1 APOE genes. Result: No conclusive detected variant c.3844G>A, p (Asp1282Asn) of APOB gene (NM_000384.2) heterozygous, classified as UNCERTAIN CLINI CAL.

2. Hypercholesterolemia Autosomal Recessive: Sequences DNA promoters, coding regions and exon-intron junction of LDLRAP1 gene. Negative result.

3. Lysosomal acid lipase deficiency promoter DNA sequences, coding regions and exon-intron junction of LIPA gene. Negative result.

4. Panel Sitosterolemia: Sequencing of ABCG5 and ABCG8 genes was detected in the presence of heterozygosity pathogenic variant c.1083G>A (p.Trp361Ter) in the gene ABCG8.

Genetic studies rule out a Family Hipercolerolemia, an autosomal recessive hypercholesterolemia and lysosomal acid lipase deficiency, and siguieren the diagnosis of a sitosterolaemia.

Although this entity is an autosomal recessive disease, there are presentations made heterozygosity and there are reported cases of clinical manifestations of this disease in heterozygotes. The favorable clinical response to ezetimibe strongly supports the diagnosis of a sitosterolaemia.

# Author Index

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