mice at 7 and 2 days prior to euthanasia to label bones. Decalcified tibiae were embedded in paraffin for histological analysis. Undecalcified tibiae were embedded in plastic for dynamic histomorphometry. Micro-computed tomography (μCT) was used to access bone microarchitecture of femurs and vertebrae followed by biomechanical testing of bone strength. The μCT data of distal femurs show that cPTH treatment increased bone volume in female KO mice (6.864 ± 2.318 vs 4.690 ± 1.555 %; P= 0.0328; n=9 per group) and maintained bone in male KO mice (13.37 ± 2.860 vs 13.38 ± 3.135; P= 0.9968, n= 10) compared to control. Histological analysis show higher osteoclastic activity in both sexes and genotypes when treated with cPTH, suggesting that the anabolic response may be at the level of osteoblasts and osteocytes. These promising results support our hypothesis that arrestin-mediated PTH receptor downregulation plays an important role in bone weakness associated with hyperparathyroidism. These studies are important for understanding the clinical phenotype of PHPT patients and suggest that inhibition of β-arr2 in PHPT could be a path for drug therapy.

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Adipose Tissue, Appetite, and Obesity
RARE CAUSES AND CONDITIONS OF OBESITY: PRADER WILLI SYNDROME, LIPODYSTROPHY

Weight Loss After Glucagon-Like Peptide-1 Receptor Agonist Treatment in Childhood Obesity with Diabetes and Cirrhosis Associated with a Homozygous MC4R Mutation
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SUN-602
Background
Mutations in the melanocortin-4 receptor (MC4R) represent the most common cause of monogenic obesity. Treatment options are limited but glucagon-like peptide-1 receptor agonists (GLP-1 RA) may be of use to induce weight loss.

Methods
Exome of the patient was captured using the Agilent SureSelect QXT Human All Exon V5 kit and sequenced on Illumina.

Clinical findings and results
We report obesity-associated diabetes and cirrhosis in a 13-year girl born from consanguineous parents of Afghan origin. Past medical history revealed mild mental retardation and excessive weight gain since infancy. Linear growth was normal. Her father was obese and no diabetes was found in the family. The girl was initially investigated for hoarseness and found to have pulmonary hypertension, later accepted to be secondary to cirrhosis and portal hypertension. Physical examination revealed obesity (BMI 34.9kg/m2) and acanthosis nigricans. Blood exams showed leucopenia and thrombocytopenia without anemia, compatible with portal hypertension. Chest CT revealed important dilatation of the pulmonary arteries, a nodular liver and splenomegaly. Liver biopsy confirmed cirrhosis.

An extensive workup including whole exome sequencing identified a homozygous MC4R variant [NM_005912.2 (MC4R): c.63_64del, p.(Tyr21*)], classified as pathogenic according to the ACMG guidelines. Both parents were heterozygous for this variant. An endocrinological workup showed insulin resistance with a HOMA-IR index of 7.27 and diabetes with peak blood glucose of 11.5mmol/l. HbA1c was 5.1% (32mmol/mol). Thyroid tests, lepto, proinsulin levels (3.5pmol/l, n<11.0pmol/l) were normal.

The mutation being homozygous with a predicted complete loss of function (https://www.mc4r.org.uk/), no treatment with a MC4R agonist was tried. At the age of 15 years (BMI 36.0kg/m2), the patient underwent liver transplantation because of progressive portal hypertension and to halt the progression of pulmonary hypertension. At the age of 16 years (BMI 33.2kg/m2, HbA1c 4.9% (30.0 mmol/mol), HOMA-IR 5.3) a treatment with GLP-1 RA (liraglutide) was started at a dosage of 0.6mg and progressively increased to 3mg, in an attempt to induce weight loss, avoid the accumulation of liver fat and to protect the graft. GLP-1 RA is supposed to exerts its effects on appetite independently of the MC4R pathway. 2 months after liraglutide introduction, no side effects, a weight loss of 4kg and a decrease of appetite were observed (BMI 31.6kg/m2, HbA1c 4.5% (26mmol/mol), HOMA-IR 3.14).

Conclusion
Obesity-associated MC4R mutations, in homozygous state, may lead to diabetes, liver cirrhosis and porto-pulmonary hypertension. Treatment options are scarce, but GLP-1 RA seem to have a rapid, positive effect on weight and metabolic control. Would earlier treatment have prevented progression to end-stage-liver disease and need for liver transplantation?

Diabetes Mellitus and Glucose Metabolism
DIABETES COMPLICATIONS II
Euglycemic Diabetic Ketoacidosis Associated with SGLT-2 Inhibitors- an Under-recognized Diagnosis
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MON-690
Euglycemic Diabetic Ketoacidosis Associated With SGLT-2 Inhibitors - An Under-recognized Diagnosis
Background
Sodium glucose cotransporter-2 inhibitors (SGLT-2i) are a promising class of oral anti-hyperglycemic agents with mounting evidence of reduced cardiovascular risk and renal failure, in patients with type 2 diabetes mellitus. Recent increase in their use has led to identification of hitherto unknown side effects of these drugs. Euglycemic Diabetic Ketoacidosis (eDKA), found to be associated with SGLT-2i use, is a life-threatening condition and commonly goes unrecognized due to absence of the cardinal sign of hyperglycemia.

Clinical Case
We describe a 47 year old male with history of coronary artery disease and recently diagnosed type 2 diabetes mellitus who presented to our hospital with one week history of nausea, lethargy, progressive fatigue, and shortness of breath. He was diagnosed with type 2 diabetes three weeks prior, with HBA1c of 12%. His regimen included basal insulin and recent transition to empagliflozin due to severe GI intolerance with metformin use.

On arrival he was noted to be tachycardic with a heart rate of 113/min, afibrile and normotensive. Physical exam was mostly unremarkable except for dry oral mucous membranes. Serum chemistry was consistent with high anion gap metabolic acidosis with bicarbonate of 6.9 mmol/L (21-32 mmol/L), anion gap of 29 mmol/L (10-20 mmol/L), mildly elevated blood glucose of 132 mg/dl (74-106 mg/dl), acute kidney injury with creatinine of 1.47 mg/dl (0.7-1.3 mg/dl), and a beta hydroxybutyrate level of 82.7 mg/dl (0.20- 5.63 mg/dl). Urine analysis showed ketonuria. This was consistent with a clinical and biochemical diagnosis of eDKA. He was treated with IV D5%NS-20mEq/L KCL and an insulin drip. Upon resolution of his acidosis and normalization of the anion gap he was switched to subcutaneous Insulin Glargine and Lispro. Empagliflozin was held as it was thought to be contributing to the diagnosis of eDKA.

Conclusion
Our case yet again illustrates the importance of recognition of eDKA to aid prompt management, especially with the rising popularity of SGLT-2 inhibitors. It is also important to educate patients about this condition, mostly notable in the first two months of starting the medication, to recognize the concerning symptoms and precipitating factors like dehydration, improper insulin dosing, low calorie diet, alcohol, infection, surgery. An acceptable alternative to SGLT-2i can be glucagon like peptide receptor (GLP-1) agonists, also associated with good cardiovascular outcomes.

Pediatric Endocrinology

PEDIATRIC PUBERTY, TRANSGENDER HEALTH, AND GENERAL ENDOCRINE

Prenatal Sex Steroid Serum Concentrations in Relation to Sex-Typical Play Behavior at 4 Years of Age

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SUN-066
ABSTRACT
INTRODUCTION: Sex differences in play behavior have been seen in rodents, primates and humans with literature showing some associations with maternal sex steroids. The PreSchool Activities Inventory (PSAI) is a validated tool to assess sexually-dimorphic play behavior. We assessed the associations between prenatal maternal estradiol (E2), free testosterone (fT) and total testosterone (T) and children’s PSAI scores at age 4.

METHODS: Data were collected in The Infant Development and the Environment Study (TIDES), a US-based multi-center pregnancy cohort. The analysis included 399 pregnant women with complete data on sex steroids, PSAI and covariates. Early pregnancy E2 and T were analyzed by liquid chromatography tandem mass spectrometry and fT by equilibrium dialysis using labeled testosterone. PSAI scores (masculine, feminine and composite) were calculated from questionnaires completed by mothers when child was approximately 4 years old. Covariates included: maternal age and education, child age at questionnaire completion, number of older brothers and sisters, infant race and parental attitudes towards sex-atypical play behavior. After demonstrating nonlinear associations between PSAI scores and sex steroids, we used multivariable sex-stratified quadratic regression to model these relationships.

RESULTS: The analysis included 192 boys and 207 girls (mean age: 4.5 years). Sex steroids in serum collected at 6-20 weeks’ gestation (mean: 11 weeks) were similar in mothers of boys and girls. In girls, E2 showed a quadratic relationship with the masculine score (beta (E2) = 0.003, p = 0.002, beta (E22) = -7.3E-7, p <0.001). Masculine scores were lower among girls whose mothers had E2 above the 75th percentile (2160 pg/ml). In boys, we observed a positive linear association of borderline significance (beta (fT) = 9.11, p = 0.06) and a significant negative association for the quadratic term (beta (fT2) = -7.44, p = 0.04). PSAI measures were not associated with E2 in mothers of boys, fT in mothers of girls, or T in either sex.

DISCUSSION: This study did not replicate previously reported associations between T and masculine scores in girls. However, we found that, while most maternal E2 levels were not associated with play behavior in either sex, levels above the 75th percentile were associated with reduced masculine scores in girls at age 4. Our data also suggest a somewhat reduced feminine scores in boys born to mothers with fT above the 75th percentile. These results, based on a small sample using a maternal assessment of play behavior, should be examined in a larger sample using an objective measure of play.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Severe, Symptomatic Hypocalcemia Due to Denosumab and Vitamin D Deficiency in an Osteopenic Post-Menopausal Female

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SAT-365
Background: Denosumab is a monoclonal antibody used in the treatment of osteoporosis to prevent bony injuries by increasing bone density. It has a very rare side effect of severe hypocalcemia (1) and a patient should take supplemental Vitamin D and calcium for prevention. There is debate among experts on when denosumab should be discontinued and if so, whether an alternative therapy should be started (2).