behaviour. **Objective:** To assess the ability of a high-fat diet (HFD) versus a regular chow diet (CD), starting up to 10 weeks pre-pregnancy, to modify glucose clearance before and during pregnancy and affect maternal behaviour in the CD1 mouse. **Study Design:** Two groups of 3-4 week-old female CD1 mice were fed a HFD (fat=60 kcal%; carbohydrate=20 kcal%; protein=20 kcal%) or CD (fat=14 kcal%; carbohydrate=60 kcal%; protein=26 kcal%) and maintained on their respective diets throughout the study and weighed periodically. After at least 4 weeks of feeding on their diets, mice were allowed to breed. Glucose tolerance was tested using 2 g/kg of i.p. glucose at gestational day (GD) -1) after fasting (16 hours-overnight) as well as during pregnancy at GD16.5. An even number of pregnant and non-pregnant females were selected for each diet for maternal behaviour testing. Tests include an assessment of nest building at GD16.5-17 (use of nesting material and nest quality), and after birth pup retrieval at postpartum day (PD) 3, 4 and 5 (time of retrieval of each of the four pups within six minutes) using video capture. **Results:** The HFD led to a significant increase in weight relative to mice fed a CD. HFD impaired glucose-load clearances at GD -1 and 16.5 ($p<0.05$) compared to mice fed a CD. Mice fed on HFD performed poorly in the nest building task ($p<0.01$) as well as demonstrated a reduced completion rate on the pup retrieval test on PD3 (CD=8/10 vs. HFD 2/9 mice) but their retrieval response latency was improved by PD4 (CD=8/10 vs. HFD 8/9 mice) and PD5 (CD=7/10 vs. HFD 7/9 mice). **Conclusions:** Initial observations suggest that a HFD for at least 4 weeks before and during pregnancy results in overweight CD1 mice with impaired glucose clearance, and a negative effect on maternal behaviour as assessed by nest-building during pregnancy and pup retrieval postpartum; however, with regard to the latter, mice on the HFD show the ability to learn. Additional behavioural tests for locomotion, anxiety, risk avoidance and object recognition memory during or after pregnancy, as well as associated changes in hormonal signaling and adult neurogenesis are also currently under investigation.

# Bone and Mineral Metabolism

## BONE DISEASE FROM BENCH TO BEDSIDE

### *Enthesophytes Are a Common Feature of FGF23-Mediated Hypophosphatemia Due to Tumor-Induced Osteomalacia*

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**SUN-364**

***Background:*** Tumor-induced osteomalacia (TIO) is a rare cause of FGF23-mediated hypophosphatemia in which mesenchymal tumors produce ectopic FGF23, leading to renal phosphate wasting, decreased 1,25-dihydroxy-vitamin D and hypophosphatemia. Clinical features include muscle weakness, fractures and bone pain. Entheses are sites where tendons, ligaments, fasciae and joint capsules attach to bones. Calcifications in entheses, called enthesophytes, are frequent in adults with X-linked hypophosphatemia (XLH), the most common genetic form of FGF23-mediated hypophosphatemia. One study reported 68% of XLH patients having enthesopathies at an average of 18 different insertion sites per person (Polisson, NEJM, 1985). However, the prevalence of enthesophytes in patients with TIO is not known.

***Methods:*** Skeletal surveys of 66 patients with TIO were reviewed by a single radiologist for the presence of enthesophytes, which were then grouped into the following sites: occiput, axial, upper extremities, pelvis/femur, tibia/fibula and feet. The data presented are from the 59 patients (33 men, 26 women) for whom near-complete skeletal surveys were available; feet radiographs were not available in 9 subjects. Descriptive statistics and regression analyses were performed, including analyses of concurrent intact FGF23 and phosphate levels. Data are presented as mean ± SD.

***Results:*** At the time of the skeletal survey, the age of the subjects was 48.7 ± 14.4 years; 78% were over 40 years. The estimated duration of TIO was 6.6 ± 5.3 years. Mean phosphate level was 1.7 ± 0.5 mg/dL (normal 2.5-4.5 mg/dL) and intact FGF23 was 743 ± 1213 pg/mL (normal < 50 pg/mL). Enthesophytes were identified in 51/59 patients (86.4%) with a mean of 4.5 ± 3.7 enthesophytes per patient (range 0-14). The most frequently affected site was the feet (35/50, 70%) followed by occiput (30/59, 51%), pelvis/femur (28/59, 48%), axial (22/59, 37%), upper extremities (18/59, 31%), tibia/fibula (18/59, 17%). In many subjects, more than one enthesophyte was seen within each region - the total number of enthesophytes in the cohort were: feet – 84, pelvis/femur -74, upper extremities – 40, occiput – 30, axial – 23, tibia/fibula – 16. Multiple linear regression demonstrated a significant positive relationship between number of enthesopathies with age and duration of TIO ($p < 0.001$). Intact FGF23 and phosphate did not significantly correlate with enthesophyte number.

***Conclusions:*** Similar to XLH, these data demonstrate that enthesopathies are a common feature of tumor-induced osteomalacia, increasing with both age and duration of disease. The underlying mechanism of enthesophytes in the general population is unclear and may be related to mechanical forces and/or inflammation. The additional factors of chronic hypophosphatemia and elevated FGF23 likely contribute to this mechanism.

# Reproductive Endocrinology

## OVARIAN FUNCTION — FROM OLIGOMENORRHEA TO AMENORRHEA

### *A Randomized Controlled Trial of a Lifestyle Intervention with Longitudinal Follow up on Ovarian Dysmorphology, Hyperandrogenism, and Menstrual Irregularity in Women with Polycystic Ovary Syndrome*

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The recent International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome

(PCOS) recommended healthy lifestyle interventions (dietary, exercise, behavioral modification, or combined) as the first-line therapy to mediate favorable metabolic outcomes in PCOS. However, the relationship between lifestyle modifications and reproductive health in PCOS is less clear. Specifically, a favorable dietary composition to facilitate reproductive changes in women with PCOS remains unknown. Further, the longitudinal impacts of lifestyle change programs in women with PCOS is poorly elucidated. We hypothesized that a low glycemic index pulse-based diet containing lentils, beans, split peas, and chickpeas would be more effective than the Therapeutic Lifestyle Changes (TLC) diet at improving insulin sensitivity without an energy-restricted protocol and would improve reproductive health outcomes in women with PCOS after a 16-week intervention. Our objective was to compare the effects of a nutritionally balanced pulse-based diet with the TLC diet on ultrasonographic markers of ovarian morphology, hyperandrogenism, and menstrual irregularity. Women (n=30) randomized to the pulse-based and TLC (n=31) groups completed a 16-week intervention. All women participated in aerobic exercise (minimum 5 days/week; 45 minutes/day) and received health counseling (monthly) about PCOS and the benefits of lifestyle modification. Additionally, we evaluated the effects of the intervention on the reproductive outcomes by longitudinal follow-up of all participants. Follicle numbers per ovary (FNPO, 2-9 mm), ovarian volume (OV), free androgen index (FAI), intermenstrual intervals, and insulin sensitivity (Matsuda index and homeostasis model assessment of insulin resistance [HOMA-IR] were evaluated at baseline, 16-week post-intervention, and 6- and 12-month post-intervention follow up visits. Follicle numbers per ovary (mean change ± SD, -10 ± 15), OV (-2.7 ± 4.8 mL), FAI (-3 ± 2), intermenstrual interval (-13 ± 47 days), and body mass index (BMI, -1.6 ± 4.2 kg/m$^2$) decreased, and Matsuda index (1.1 ± 3.1) increased over time in both groups (All: $P \leq 0.01$), without group-by-time interactions (All: $P \geq 0.27$). Groups maintained reduced OV, FNPO, FAI, and menstrual cycles 6 months post-intervention, despite a propensity for weight regain as evidenced by increased BMI (1.0 ± 4.8 kg/m$^2$; $P < 0.01$). Decreased FNPO, FAI, and HOMA-IR at 16-week tended to revert to baseline levels 12 months post-intervention in both groups (All: $P \leq 0.05$). Both interventions improved ovarian dysmorphology, hyperandrogenism, and menstrual irregularity in women with PCOS. Our observations elucidate the importance of longitudinal surveillance for sustainable adherence to newly adopted healthy lifestyle behaviors and reproductive health in PCOS (ClinicalTrials.gov identifier, NCT01288638).

# Neuroendocrinology and Pituitary

## CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY

### *Lithium Induced Partial Nephrogenic Insipidus: An Unusual Presentation*

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**SUN-283**

Background: Diabetes insipidus (DI) is characterized by hypotonic polyuria and polydipsia. Nephrogenic DI is the result of an inadequate response of the kidneys to arginine vasopressin (AVP), either due to hereditary causes or acquired from various drugs, most commonly lithium. Clinical case: A 30 year old male with past medical history of Hashimoto's thyroiditis, severe mental impairment was admitted to the hospital for abdominal pain. Medical history was difficult to obtain since the patient was nonverbal. His thyroid function tests, electrolytes including sodium, potassium were all normal on admission. During the hospital course, he was made NPO for both an upper and lower GI endoscopy. He notably had a mild increase in sodium level with subsequent improvement after restitution of diet. Two days after the procedure, he was found to be drinking out of the toilet and also attempting to drink from the urine jug. Due to this odd behavior, he had to be put on physical restraints. The day after, he was found to have a serum sodium of 158 mEq/L. Hypotonic saline was started and urine output was notably ranging from 6-10 L/day with a negative balance. Desmopressin (DDAVP) test was done with a resultant urine osmolality of 170, 237, 257 and 264 mOsm/kg after 30, 60, 90 and 180 mins. Subcutaneous DDAVP was started with some improvement of serum sodium and decrease in urine output. Endocrinology service was consulted for the evaluation of hypernatremia and polyuria. Initial review of his medications did not show any potential cause of DI. Further inquiry of his prior medication history revealed that he had taken Lithium for over 10 years and stopped 4 months prior to the admission due to polyuria. After excluding other causes of polyuria, with partial improvement of urine osmolality to a level <300 mOsm/kg and a clinical history of prior Lithium therapy, a diagnosis of partial nephrogenic DI was made. Patient was started on HCTZ and given adequate water intake with subsequent improvement of his serum sodium back to normal. Conclusion: Nephrogenic DI due to Lithium use usually recovers after treatment is stopped but could be persistent for several years after. In our case, the patient compensated for his polyuria with increased water intake. When his water intake was restricted due to physical restraints, polyuria and subsequently hypernatremia became evident. A thorough medication history including past drug use is essential as it can help unravel the offending agent which was Lithium in our case. There needs to be an increased awareness that the effect of Lithium in the kidneys could be persistent even after stopping the drug for up to many years. References: Thompson CJ. Persistent nephrogenic diabetes insipidus following lithium therapy. Scott Med J 1997; 42:16-17.

# Pediatric Endocrinology

## UNDERSTANDING AND TREATING PEDIATRIC GROWTH DISORDERS

### *Phase 3 FliGHt Trial: Experience of Switching from Daily Growth Hormone Therapy to Once-Weekly TransCon HGH in Children with Growth Hormone Deficiency*

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