Ultrasound-guided biopsy of the submental area showed cytomorphologic features of a colloid nodule with cystic degeneration (Bethesda Category II). The patient was started on levothyroxine and remained biochemically euthyroid afterwards. The submental neck mass reduced in size.
Conclusion: Dual ectopic thyroid with normally located (eutopic) thyroid gland could present with subclinical hypothyroidism. There is no single diagnostic modality that would best identify dual ectopic thyroid; thus, thyroid scan, ultrasonography, CT scan and biopsy are recommended to be used complementarily. For patients with dual ectopic thyroid and hypothyroidism, levothyroxine replacement is recommended to reduce the size of ectopic thyroid and render the patient euthyroid.

Pediatric Endocrinology

PEDIATRIC PUBERTY, TRANSGENDER HEALTH, AND GENERAL ENDOCRINE

Steroid Hormone Profile Differentiates Gynecomastia and Pseudo- Gynecomastia in Pubertal Boys

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SUN-060
Background: Gynecomastia (defined by breast tissue) and pseudogynecomastia (defined by adipose tissue) is frequent in pubertal boys. However, the underlying pathomechanisms are not fully understood so far. An association to growth hormone axis- IGF-1 axis and sex hormones has been discussed. **Methods:** We analyzed serum steroid hormones (progesterone, estradiol [E2], estriol, estrone, cortisol, cortisone, testosterone [T], dihydrotestosterone [DHT]) by liquid chromatography-tandem mass spectrometry, as well as gonadotropins, prolactin, IGF-1 and IGFBP-3 in 124 pubertal boys with breast swelling (mean age 14 +/-2 years). The steroid hormones were compared to those of 84 healthy pubertal boys (mean age 14 +/-2 years) without breast swelling. The differential diagnosis of either gynecomastia or pseudogynecomastia was determined by ultrasound. Puberty was defined by testes volumes > 3ml on each side. **Results:** A total of 86 boys suffered from gynecomastia and 38 from pseudogynecomastia. In boys with gynecomastia the ratio E2/T (median 22, interquartile range [IQR] 8–75) was significantly ($p<0.05$) higher compared to boys with pseudogynecomastia (median 12 IQR 5–21) or healthy boys without breast swelling (median 18 IQR 6–44). DHT concentrations were significantly ($p<0.001$) lower in boys with gynecomastia (median 0.13 IQR 0.02–0.38 nM/L) or pseudogynecomastia (median 0.18 IQR 0.05–0.32 nM/L) compared to healthy boys (median 0.41 IQR 0.22–0.66 nM/L). T concentrations were significantly ($p<0.05$) lower in boys with gynecomastia (median 1.8 IQR 0.7–4.2 nM/L) compared to boys with pseudogynecomastia (median 4.3 IQR 1.4–6.9 nM/L) or healthy boys without breast swelling (median 3.1 IQR 0.6–7.6 nM/L). The ratio DHT/T was significantly ($p<0.001$) lower in boys with gynecomastia (median 0.09 IQR 0.02–0.17) or pseudogynecomastia (median 0.04 IQR 0.02–0.16) compared to healthy Boys without breast swelling (median 0.13 IQR 0.05–0.28). Boys with gynecomastia did not differ from boys with pseudogynecomastia according to the other steroid hormones, prolactin, IGF-1, or IGFBP-3 concentrations. **Conclusions:** Gynecomastia is characterized by a higher E2 to T ratio compared to healthy boys without breast swelling due to a relative T deficiency in the presence of similar E2 levels. The lower DHT/T ratio in gynecomastia and pseudogynecomastia compared to healthy boys without breast swelling points towards a functional 5 alpha reductase deficiency.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING II

Transcriptome Profiling in Postnatal Pituitary Gland Identifies Cell Type-Driven Sex-Specific Changes

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MON-725
The pituitary gland is integral to the regulation of growth, metabolism, puberty, reproduction, and stress responses. Previously, we found that many genes associated with age-at-menarche in genome-wide association studies (GWAS) displayed increasingly sex-biased expression across the pubertal transition in the mouse pituitary. However, whether this trend exists beyond puberty-related genes was not known. In addition, the regulatory mechanisms underlying these gene expression changes remained to be explored. To answer these questions, we profiled the transcriptome, including microRNAs, of mouse pituitary in both sexes across pubertal transition in an unbiased manner and leveraged a recently published pituitary single cell transcriptome to explore cellular composition changes. We found that the most dynamic temporal changes in both mRNA and miRNA expression occur prior to puberty, underscoring a role for regulation of early pituitary postnatal development. We also observed ~900 genes displaying sex-biased expression patterns, arising during early development and becoming increasingly biased across puberty, including known sex-biased genes such as *Fshb* and *Lhb*. However, sex differences in miRNA expression are less pronounced, only 13 miRNAs were found to be sex-biased, suggesting lesser contribution of miRNAs to sex-biased gene expression relative to other forms of regulation. To assess whether pituitary cellular composition could underlie changes in gene expression across pubertal transition, we performed single cell deconvolution of our bulk pituitary gland gene expression. Interestingly, we found that sex differences in cell proportions were estimated to emerge across puberty: a greater proportion of lactotropes was found among females, and greater proportions of gonadotropes and somatotropes were found among males. We observed sex-biased expression patterns of marker genes for these cell types, including *Prl*, *Fshb*, and *Gh*. This finding suggests that cell proportion

differences between sexes likely contribute to whole pituitary transcriptome changes we observed, however, to what extent remains to be studied. Together our study indicates that miRNAs play a substantial role in regulation of pituitary postnatal development but that differences in cellular composition may contribute more robustly to sex-biased gene expression.

Adipose Tissue, Appetite, and Obesity

OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Single-Dose Effects of Anti-Obesity Drugs on Human Basal Metabolic Rate

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MON-593

Design and rationale: Obesity results from energy intake exceeding energy expenditure (EE) over a prolonged period. Many anti-obesity drugs are designed to decrease energy intake. However, their potential impact on EE is not well documented. We designed a placebo-controlled, double-blind, randomized cross-over study to determine the acute effects of several FDA-approved anti-obesity drugs on basal metabolic rate (BMR) under well-controlled conditions.

Protocol and inclusion criteria: This ongoing study is limited to healthy males of all ethnicities aged 18–35 years with a BMI of 18.5 to 25.0 kg/m^2. Following an overnight stay in the Metabolic Clinical Research Unit, fasting subjects were measured from 8:00am to 12:00pm in a whole-room indirect calorimeter, which was maintained at a thermoneutral temperature (26.7±0.9°C) to prevent non-shivering thermogenesis. The six treatments include placebo, caffeine as the positive control (300 mg), phentermine (37.5 mg), topiramate (200 mg), Qsymia (phentermine 15 mg / topiramate 92 mg), and naltrexone (100 mg), with a 1-week outpatient washout period after each treatment. Drug-naïve subjects received a single dose of each drug to minimize potential metabolic adaptations that may occur with weight-loss or chronic use. The prespecified primary outcome was a ≥5% increase in BMR vs. placebo for each drug. This difference can be detected for 16 subjects with 0.83 power at α=0.05 allowing for ≤25% dropout. Secondary outcomes include respiratory quotient (RQ), heart rate (HR), mean arterial pressure (MAP), and self-reported hunger.

Preliminary data: To date, 7 subjects were recruited and 6 have completed the study (26.1±4.3 years, BMI 23.1±1.4 kg/m^2, body fat percentage 18.4±4.1%). Interim analysis using paired t-tests shows, compared to placebo, caffeine trended towards increasing EE (1.17±0.07 vs. 1.27±0.12 kcal/min; p=0.07) and increased MAP by 5.5±4.2% (88±2 vs. 93±4; p<0.05), but did not change heart rate (59±10 vs. 61±13 bpm). Naltrexone increased EE by 5.9±4.3% (p<0.05). No treatments altered resting RQ compared to placebo (0.83±0.05). Phentermine increased resting HR, both alone (15.7±7.9%, p<0.01) and in Qsymia (9.2±3.6%, p<0.05), compared to placebo. Of the five drug-treatments, only Qsymia reduced self-reported hunger scores compared to placebo.

Summary and future directions: Anti-obesity drugs may increase energy expenditure by upregulating sympathetic nervous system activity. Combined with appetite suppression, the impact on energy balance can lead to weight loss. We aim to complete our study to determine whether these drugs can acutely increase EE with minimal cardiovascular side-effects and compare our findings with long-term interventions.

Cardiovascular Endocrinology

PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE

Genetic Variants Related to Familial Hypercholesterolemia in Clusters from Minas Gerais - a Southeast State of Brazil

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SUN-561

Familial Hypercholesterolemia (FH) is an autosomal dominant genetic disease, characterized by high levels of the cholesterol fraction present in low density lipoprotein (LDLc). FH is associated to early atherosclerotic coronary disease, which can result in acute myocardial infarction and angina pectoris. Clinical diagnosis of FH in adults is based on elevated LDLc levels ≥ 4,9 mmol/L and total cholesterol (TC) ≥ 7,5 mmol/L; in untreated children and adolescents LDLc ≥ 4,0 mmol/L and TC ≥ 6,7 mmol/L, associated or not with physical signs (xanthomas, corneal arch). In Brazil, it is estimated that there are from 402,000 to 607,000 cases of FH. This study aimed to evaluate the genetic variants related to FH in a small region from Minas Gerais, a southeast state in Brazil. Fifteen index cases (IC) were selected in two cities (Bom Despacho and Moema), that comprise 1.416 km^2 in that region. Family members (n=69) were also selected, when possible, for genetic analysis, which was carried out by the NGS (Next Generation Sequencing) method, using Illumina® technology. Six different genetic variants were identified: 1) Pathogenic variants in LDLR gene - Asp224Asn in 74 individuals (10 IC); Cys34Arg in 1 individual (1 IC); Asp601His in 2 individuals (1 IC); and Ser854Gly in 2 individuals (1 IC); 2) Variant of uncertain significance (VUS) in APOB gene - Met499Val in 1 individual (1 IC); and 3) VUS in PCSK9 gene - Arg237TRP in 4 individuals (1 IC). All variants were identified in heterozygosis. The data suggest that the high