Cushingoid features, and biopsy-proven Candida esophagitis. Initial testing was consistent with ACTH-dependent Cushing syndrome: elevated 24 hour urinary cortisol excretion (1,310.54 mcg/24h; n <50 mcg/24h), abnormal 1 mg dexamethasone suppression test (68.3 ug/dL), and elevated ACTH level (200 pg/mL; n: 7.2–63.3 pg/mL). MRI was negative for a pituitary lesion but abdominal CT revealed an 8.8 cm liver mass with biopsy consistent with a well-differentiated neuroendocrine tumor, WHO Grade 2. Subsequent ^{68}Ga-DOTATATE-PET/CT noted DOTATATE uptake in the liver lesion, a 0.9 cm right pulmonary nodule, and the pancreatic tail without CT correlate. Initially, the patient was prescribed mifepristone and spironolactone for hypokalemia. Given her NET of unknown primary, metastatic disease, and immunocompromised state due to hypercortisolism, the patient was not a candidate for surgical resection of her NET but was instead referred for bilateral adrenalectomy. However, she rapidly decompensated from complications of her hypercortisolism prior to surgery. Her weakness progressed to immobility, and she developed acute psychosis manifested as agitation and mutism. The patient was immediately admitted to the hospital where she developed new-onset atrial flutter and myelosuppression requiring multiple transfusions. She underwent urgent bilateral adrenalectomy, but despite surgery, her postoperative course was complicated by hypoxemic respiratory failure and shock. The patient shortly thereafter expired from pulseless electrical activity arrest.

Conclusion: This atypical case of an ectopic ACTH-secreting NET highlights the life-threatening complications associated with severe hypercortisolism, including: opportunistic infection, severe metabolic abnormalities, psychosis, myopathy, and critical illness that can incite myelosuppression and unstable arrhythmias. These patients can quickly deteriorate and are at high risk for mortality. Early diagnosis and swift reversal of their hypercortisolism with bilateral adrenalectomy are oftentimes needed to prevent these potentially fatal complications.

Pediatric Endocrinology

PEDIATRIC SEXUAL DIFFERENTIATION, PUBERTY, AND BONE BIOLOGY

Effect of Pubertal Induction with Gonadotropins and GnRH Therapy in Male Hypogonadotropic Hypogonadism: Meta-Analysis

Swashti Agarwal, MBBS, Paul Austin, MD, Alexis C. Wood, PhD, Lefkothea P. Karaviti, PHD, MD.
Baylor College of Medicine, Houston, TX, USA.

SUN-092

Background: The use of gonadotropins is a recent strategy for inducing puberty in adolescent males with hypogonadotropic hypogonadism (HH). Testosterone use has been discouraged in patients who desire to preserve fertility. Human chorionic gonadotropin (hCG) has been recommended for inducing puberty in HH; however, several clinicians administer hCG in combination with other gonadotropins. The benefits of using combination gonadotropin therapies (hCG+) over hCG monotherapy in prepubertal adolescent males with HH has not been clearly established. We performed a meta-analysis to assess the outcomes of hCG compared to hCG+ in terms of virilizing effects and testicular growth in peripubertal boys with HH.

Methods: We evaluated for heterogeneity among studies. We calculated pooled means for the post-treatment mean testicular volume (MTV), testosterone (T) level, and penile length for the hCG monotherapy and hCG+ treatment groups. We performed a meta-regression analysis to examine the contribution of various factors to post-treatment outcomes including baseline T level, age, treatment duration, and study quality.

Results: The meta-analysis included seven studies. All participants were prepubertal (age range: 13.3–25.9 years), with weighted mean treatment durations of 10.95 months for hCG monotherapy and 28.2 months for hCG. There was significant heterogeneity in baseline age ($Q = 121.71$; $df = 1$; $P < 0.001$) and T levels ($Q = 436.74$; $df = 1$; $P < 0.001$) between the two treatment groups. The hCG+ group had a larger post-treatment MTV, but it was not significantly different between the two groups (6.60 mL [95% CI, 3.18–10.02] for hCG monotherapy vs. 10.02 mL [95% CI, 8.30–11.75] for hCG+; $P = 0.079$). Post-treatment T levels differed significantly between the two groups (101.89 ng/dL [95% CI, 50.7–153.08] for hCG monotherapy vs. 424.10 ng/dL [95% CI, 304.59–543.62] for hCG+; $P < 0.0001$). A meta-regression analysis of post-treatment T levels showed that baseline age, baseline T level, and study grade did not contribute significantly to the difference between treatment groups. Treatment duration explained 3.04% of the difference between the two groups ($P < 0.0001$). After adjusting for treatment duration, the post-treatment T level remained significantly higher in the hCG+ group compared to the hCG monotherapy group. The hCG+ was also associated with better outcomes for post-treatment penile length, although these findings relied on data from only three studies.

Conclusion: Our study indicates that hCG+ therapies provide potential benefits over hCG monotherapy for pubertal induction in males with HH, regarding T levels and penile growth, with no difference in testicular growth between treatments. Prospective pediatric studies are needed to assess the benefits of these therapies in patients with HH and, ultimately, to establish guidelines for gonadotropin therapy in the adolescent population.

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I

Quality of Life Following Treatment for Graves' Disease: A Comparison of Radioactive Iodine Ablation and Surgery

Christopher W. Rowe, BSC, MBBS, FRACP, Nicholas D. Blefari, MBBS, Natalie Rutherford, MBBS, FRACP, Cino Bendinelli, MBBS, FRACS, Chris O'Neill, MBBS, MS, FRACS.
John Hunter Hospital, New Lambton Heights, Australia.

SAT-427

Introduction: Quality of Life (QoL) is reduced in patients with Graves' disease, however the impact of treatment modality is unclear, with conflicting evidence from recent studies (1–3). We hypothesized that surgery would have a greater impact than radioiodine on QoL in Graves' disease, especially with regard to the physical-symptom subdomain.

Methods: Patients treated with thyroid surgery for benign disease (n=425) or radioactive iodine for hyperthyroidism (n=1637) at a single tertiary institution between 2000 and 2017 were invited to complete a validated thyroid-specific QoL instrument (City of Hope), reporting scores 0–10, where higher scores are associated with greater QoL. Responses were received from 307 patients, of whom 114 (37%) had Graves' disease, treated with total thyroidectomy (n=23) or doses of 15mCi (550MBq) radioiodine (n=91, including 19 patients receiving 2 or more doses). The results of patients with Graves' disease are reported here. Medians [interquartile ranges] are compared with the Mann-Whitney test (alpha 0.05).
Results: 85% of respondents were female, with no difference in gender between groups (p=0.11). Thyroidectomy patients were more likely to be younger (36 [31–49] vs 50 [39–59] years, p=0.004); and have a shorter duration between treatment and survey (5.9 [2.4–9.6] vs 7.6 [4.9–11.6] years, p=0.04). No overall QoL deficit was seen in patients treated with surgery compared to radioiodine (6.8 [5.2–7.3] vs 7.0 [5.8–8.1], p=0.08). However, patients treated with surgery reported reduce QoL in psychological (6.6 [4.7–7.5] vs 7.0 [5.9–8.2] p=0.05) and social (7.9 [6.4 – 8.9] vs 8.9 [7.4–9.8] p=0.01) subdomains compared to radioiodine-only treated patients. Within the social subdomain, the QoL detriment was driven by lower scores relating to questions regarding impact on personal and family relationships, support, and isolation (p<0.001), and not by impact on activities of daily living or employment concerns. Interestingly, there was no between group difference in the physical symptom subdomain (p=0.16). QoL differences between treatment modalities were preserved when patients receiving multiple doses of radioiodine were excluded.
Discussion In this non-randomised cross-sectional study from a tertiary-hospital population in Australia, a QoL deficit was demonstrable in subdomain scores for patients with Graves' disease treated with surgery compared to radioiodine, although the overall result was not significantly different. Better understanding of patient experiences is required to guide treatment strategies and appropriately counsel patients.
References (1) Torring et al. Thyroid. 2019;29(3):322–31. (2) Abraham-Nordling et al. Thyroid. 2005;15(11):1279–86. (3) Ljunggren et al. Thyroid. 1998;8(8):653–9.

Neuroendocrinology and Pituitary

HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

TSH/TSHR Signaling Deficiency Impairs Spatial Learning and Memory

Sisi Luan, PhD, He Zhao, PhD, Jiajun Zhao, MD, PHD.
Shandong Provincial Hospital affiliated to Shandong University, Jinan, China.

SAT-285

Background: Subclinical hyperthyroidism is associated with cognitive impairment, but the mechanism has remained unclear. As subclinical hyperthyroidism is characterized by significantly decreased TSH levels, this study aimed to investigate whether TSH regulates cognitive function. **Methods:** The correlation between TSH and cognitive impairment was investigated in a cross-sectional population study. The role of TSH/TSH receptor (TSHR) signaling in spatial learning and memory was further examined by behavior tests in *Tshr*$^{-/-}$ mice. Dendritic spine, synaptic density and structure of hippocampal CA1 pyramidal neurons were detected by Golgi's method and electron microscopy. The mRNA and protein expression levels of learning and memory-related genes were assessed by RNA sequencing, real-time PCR, immunoblotting and immunofluorescence approaches. **Results:** Serum TSH level correlated negatively with cognitive impairment in the current population. Consistently, *Tshr* deletion in mice led to significantly compromised performance in hippocampus-dependent tasks, reduced dendritic spine density and excitatory synaptic density as well as altered synaptic structure in CA1 subfield of the hippocampus. Furthermore, the mRNA levels of learning and memory-related genes were altered, and protein levels of CREB-regulated genes were downregulated in the hippocampus of *Tshr*$^{-/-}$ mice. **Conclusions:** These findings reveal that TSH/TSHR signaling ablation impairs spatial learning and memory, indicating a decline in TSH level might contribute to the increased prevalence of cognitive impairment in subclinical hyperthyroidism patients.

Bone and Mineral Metabolism

BONE DISEASE FROM BENCH TO BEDSIDE

Neonatal Severe Hyperparathyroidism: Extreme Hypercalcemia as a Robust Marker for Homozygous Dosage of Pathogenic CASR Variants

Stephen J. Marx, MD, MD[1], Ninet Sinaii, Dr., PhD[2].
[1]NIH - NICHD, South Palm Beach, FL, USA, [2]NIH - NICHD, Bethesa, MD, USA.

SUN-366

Context: Neonatal severe hyperparathyroidism (NSHPT) is a rare and life-threatening emergency. It includes generalized hyperparathyroid bone disease and respiratory distress from combinations among a narrowed thorax, rib fractures, hypotonia, and biochemical disturbances. Successful therapy is compatible with long life and a healthy prognosis. However, neuromotor retardation may persist after otherwise successful therapy. The time and amplitude of hypercalcemia likely correlate with irreversible neuromotor retardation; thus, early intervention seems critical in many cases. NSHPT is usually caused by homozygous or heterozygous pathogenic variant(s) of the *CASR*; a heterozygous variant of this gene is also the usual cause of familial hypocalciuric hypercalcemia (FHH or FHH1). Homozygotes and heterozygotes with NSHPT are often not distinguished in the current literature. In theory, their management should differ. Optimum treatment in homozygotes is early total parathyroidectomy with induction of postoperative hypoparathyroidism. Optimal management of heterozygotes is more complex. It consists in temporizing measures and varies from careful observation without surgery, to bisphosphonates and/or calcimimetics, and to subtotal parathyroidectomy. The heterozygotes can then develop into healthy babies with asymptomatic FHH1. Evidence Acquisition: Each case met strict criteria for "severe" and neonatal disease. We analyzed the core