Objective: We sought to identify risk factors associated with detection of pituitary pathology among hypogonadal men with mild hyperprolactinemia and aimed to improve selection of those indicated for pitMRI.
Methods: A retrospective, case-control study was performed. Men under 75 presenting with clinical hypogonadism and mild hyperprolactinemia (15-50 ng/dL) who underwent pitMRI at a single tertiary care center were included. Individuals presenting with clinical symptoms strongly suggestive of a pituitary mass (e.g. visual change, headache, panhypopituitarism) were excluded, as were patients who had been previously evaluated for hyperprolactinemia. Age, body mass index (BMI), presenting symptoms, prescription history, and pitMRI findings were abstracted from the electronic medical record.
Results: 141 men met inclusion criteria. A minority exhibited pituitary pathology (n=40, 28%) with adenoma being the most common finding (n=35, 88%). Empty sella variants and non-neoplastic cysts comprised the remainder of pathologies (n=5, 12%). Mean PRL was higher in men with pituitary pathology than in controls (27.2 vs. 23.3 ng/mL; p=0.0106), while mean T levels were lower (190 vs 287 ng/dL; p=0.0001). Mean PRL/T ratio values were greater in cases (0.34 vs. 0.08; p<0.0001), as were median values (0.15 vs. 0.09). PRL/T outperformed PRL or T in predicting positive pitMRI findings (AUC: 0.75 vs. 0.64 vs. 0.71, respectively). A PRL/T ratio >0.08 was 90% sensitive, detecting 36/40 lesions, and 42% specific, excluding 42/101 patients with normal anatomy (p=0.0003). If applied to the study cohort, this cutoff would have reduced pitMRI burden by 30%. Ordering pitMRI when the PRL/T ratio >0.08 or when PRL >25 increases sensitivity (98%, 39/40 lesions detected) at the cost of decreased specificity (32%, 32/101 controls excluded). Presenting symptoms including fatigue, decreased libido, erectile dysfunction, and gynecomastia did not vary between cases and controls. Though patients with pituitary lesions were more likely to receive dopamine agonists than controls (40% vs. 23%; p=0.0392), they were not more likely to be prescribed testosterone, antipsychotics, or antidepressants.
Conclusions: The PRL/T ratio is superior to PRL or T alone in identifying pituitary pathology in hypogonadal men with mild hyperprolactinemia. Ordering pitMRI when the PRL/T >0.08 is sensitive for detecting pituitary lesions and may reduce pitMRI burden in this population by 30%.

Pediatric Endocrinology

PEDIATRIC ENDOCRINE CASE REPORTS I

Pulmonary Hypertension in a Patient with Neonatal Graves Disease

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INTRODUCTION
Neonatal hyperthyroidism is a transient disorder seen in neonates born to mothers with current or past history of Graves' disease. We present a rare case of a Neonatal Graves' disease with pulmonary hypertension (PH) which completely resolved with treatment of hyperthyroidism.

CLINICAL CASE
Baby B was a 3200 g term male born to a 40-year-old hypothyroid mother. He was prenatally diagnosed with Trisomy 21 and coarctation of the aorta (CoA). He developed respiratory distress soon after birth and was admitted to the NICU. His echocardiogram (echo) showed a large patent ductus arteriosus (PDA) and increased tortuosity of juxtaductal aorta with no significant gradient. Near-systemic pulmonary artery pressure was noted in the absence of any evidence of left heart failure. Cardiology determined his CoA to be hemodynamically insignificant and not the cause of his PH. Successive trials of 100% FiO2, Nitric Oxide (NO), and Sildenafil resulted in only minimal improvement of his PH. Thyroid function tests (TFT) obtained on day of life (DOL) 8 showed serum TSH of 0.01 uIU/ml [0.87 - 6.43] and FT4 of 3.5 ng/dl [0.9 - 1.5]. Further interaction with the mother revealed that she had a history of Graves' disease treated with radioactive iodine (RAI) and resultant hypothyroidism. Baby B's TSH receptor antibody (TRAb) and thyroid stimulating immunoglobulin levels were elevated at 7.38 IU/l [0-1.75] and 3.38 IU/l [0-0.55], respectively.
He was thus diagnosed with Neonatal Graves' disease and was started on Methimazole (MTZ) 1 mg/kg/day on DOL 8. Subsequently, potassium iodide was added. FT4 showed gradual normalization by DOL 15. Beta blockers were not added due to absence of hypertension or significant tachycardia. Serial echo showed improvement of PH, consistent with the decline in FT4 levels. Sildenafil and FiO2 were slowly weaned and discontinued by DOL 30. MTZ was then tapered and discontinued. A final echo showed complete resolution of PH, unobstructed aortic arch and persistent PDA.

DISCUSSION
Neonatal hyperthyroidism occurs due to transplacental transfer of TRAb from mother to fetus, stimulating the fetal thyroid to make excessive thyroid hormones. Risk correlates with TRAb titers in the mother. Our patient had pulmonary hypertension which did not resolve with FiO2, NO and Sildenafil. However, it showed complete resolution with normalization of FT4 levels by antithyroid drugs. Hyperthyroidism commonly presents with systemic HTN, but we found 3 neonatal cases in the literature presenting with PH that resolved with treatment of hyperthyroidism. The mechanism is unclear, but hypotheses include increased clearance of pulmonary vasodilators and decreased clearance of pulmonary vasoconstrictor and decreased surfactant production/function(1).

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Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID II

Thyroid Stimulating Hormone Levels Amongst Reproductive Age Latinas: Findings from the ELLAS Study

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Background: National population data on thyroid disease in women comes largely from NHANES. Prior research utilizing data from NHANES 1999-2002 indicated a 3.1% prevalence of hypothyroidism and 0.6% prevalence of hyperthyroidism among reproductive aged women. In this dataset, Mexican Americans had a similar risk of hypothyroidism but a slightly higher rate of hyperthyroidism when compared to non-Hispanic whites. We present data from a prospective cohort study of reproductive aged Hispanic women residing in the United States (US) in order to examine thyroid disease prevalence in this population.

Methods: The Environment, Leiomyomas, Latinas and Adiposity Study (ELLAS) is a prospective NIMHD funded longitudinal cohort study of reproductive age Latinas/Latinx females in Southeast Michigan. Demographic and health data were collected via bilingual interviewers. Height, weight, and body composition were measured by trained staff using a Tanita MC780U scale. Fasting morning venipuncture was performed and samples were collected in a serum separating tube and sent to a commercial lab (Labcorp – Burlington, NC) for TSH electrochemiluminescence immunoassay [normal reference range 0.45-4.5 mIU/L]. The data were analyzed using SAS version 9.4 (Cary, NC).

Results: 516 patients have enrolled in ELLAS and 450 of these have completed the first study visit. Mean age, BMI, and body fat % were 37.7 ± 7.0 years, 29.9 ± 6.8 kg/m^2, 36.3% ± 6.6% (mean ± SD) respectively. Reported countries of birth were Mexico (76.2%), US (9.8%), Central America (6.7%), South America (5.6%), and the Caribbean Islands (0.7%). 34 (7.6%) participants reported a pre-existing thyroid condition. Of those, 28 reported they had been treated for a thyroid condition in the past, and 14 were currently taking prescription medication for thyroid disease. TSH levels were available on 418 women. Of those with a known thyroid condition, 6.5% had TSH values < 0.45 and 16.1% had elevated TSH values (> 4.5) at the time of their study visit, compared to 1.7% and 7.4% overall. 0.2% had TSH > 10. Among those without a known history of thyroid disease, 1.3% had TSH < 0.45 and 6.7% had TSH > 4.5 at their visit. BMI, body fat %, and country of birth were not associated with TSH levels, but there was a small yet significant effect of age on TSH (p=0.009).

Conclusion: In this US cohort of Hispanic women of reproductive age, we observed a high prevalence of thyroid dysfunction in those without pre-existing disease. In women with a known thyroid condition, the prevalence of abnormal TSH values was also high, representing both under- and over-treatment with thyroid hormone. Screening for thyroid disease in this population is important and presents a potential opportunity for intervention in an often underserved population.

Neuroendocrinology and Pituitary

CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY

Pituitary Hyperplasia Due to Severe Primary Hypothyroidism: An Uncommon Manifestation of a Common Disease

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Background Pituitary hyperplasia (PH) is a non-neoplastic increase in one or more cell subtype of the adenohypophysis. It is physiologically seen in pregnancy from resultant lactotroph hyperplasia and pathologically in organ dysfunctions that lead to loss of negative feedback on hypothalamus like primary hypothyroidism and primary adrenal insufficiency. Although primary hypothyroidism is common, PH is an under-recognized consequence of long-standing hypothyroidism. **Case Description** A 26-year-old female with class 3 obesity, type 2 diabetes mellitus, and primary hypothyroidism on replacement presented for evaluation of secondary amenorrhea. Two months prior to presentation, she underwent a brain MRI for new-onset headache which revealed diffusely enhancing homogenous pituitary tissue measuring 2.3 cm with upward lifting of the optic chiasm. Serum prolactin was elevated at 86.2 ng/ml (2.8-26 ng/ml). This was presumed to be secondary to a prolactinoma and cabergoline was started by the referring provider. Subsequent workup revealed elevated thyroid-stimulating hormone (TSH) at 494.11 mU/L (0.30- 4.00 mU/L) and a low free thyroxine (FT4) of 0.2 ng/dl (0.8-1.7 ng/dl). Other pituitary hormones were within normal limits. The visual field examination was normal. It was noted she had a persistently elevated TSH over the past five years. On further questioning, the patient ran out of levothyroxine replacement 6 months ago and had been generally non-adherent to therapy for years due to nausea. Improved medication adherence resulted in the normalization of prolactin and reduction in TSH level. Repeat MRI 2 months later revealed a reduction in her pituitary hyperplasia to 2.1 cm. **Discussion** In severe primary hypothyroidism, there is loss of negative feedback to the hypothalamus due to low circulating FT4 and triiodothyronine (T3) concentrations. As a result, there is stimulation of thyrotropin-releasing hormone (TRH) which promotes thyrotroph hyperplasia. A strong correlation exists between TSH concentration and the degree of pituitary hyperplasia. The typical MRI finding is a diffusely enhancing homogenous pituitary mass. Despite optic chiasm contact, physiologic pituitary hyperplasia rarely causes visual field defects. High concentrations of TRH stimulates prolactin release with resultant mild hyperprolactinemia. Although PH is reversible with therapy, rare cases with subsequent development of panhypopituitarism while on therapy have been reported in the setting of longstanding hypothyroidism. Very rarely, chronically untreated primary hypothyroidism