Global Fatigue Score decreased from 5.6 (2.5) at BL to 3.5 (3.0) at W48, and to 3.8 (2.2) at W144 (both p<0.01). All 3 domains of the Brief Pain Inventory decreased with burosumab (W144 Pain Severity and Pain Interference p=0.05), indicating reduced pain. The SF-36 mean (SD) physical component summary score increased from 33 (10) at BL to 39 (10) at W48 (p<0.05) and to 41 (12) at W144 (p<0.01), indicating improved physical functioning. The mean (SD) number of sit-to-stand repetitions, an assessment of proximal muscle function, increased from 6.7 (4.2) at BL to 8.5 (4.2) at W48 (n=10; p=0.01). All subjects had ≥1 adverse event (AE). Two subjects discontinued: 1 to undergo chemotherapy to treat an AE of neoplasm progression and 1 failed to meet serum phosphorus dosing criteria and therefore received minimal burosumab dosing. There were 16 serious AEs in 7 subjects, all unrelated to drug. Of the 6 subjects with a serious AE of tumor progression/compression, 5 had a history of tumor progression prior to enrollment. There was 1 death, considered unrelated to treatment. In adults with TIO Syndrome, burosumab was associated with improvements in phosphate metabolism, osteomalacia, skeletal metabolism/fracture healing, physical functioning, fatigue, pain, and quality of life.

**Cardiovascular Endocrinology**

**PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE**

**Elevation of Serum Kisspeptin in Hypertensive Women**

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**SUN-568**

Kisspeptin and leptin have been shown to have an effect on the cardiovascular system. This study aimed to compare serum kisspeptin and leptin levels between the non-hypertensive (non-HT) and the hypertensive (HT) groups with or without body mass index matching, and determine correlations between systolic blood pressure or diastolic blood pressure with serum kisspeptin and leptin levels as well as clinical and adipocyte parameters. 30 female patients who underwent abdominal surgery were recruited. Blood samples, anthropometric data, and tissue samples of visceral and subcutaneous fat were obtained. Serum kisspeptin levels (ng/ml) (non-HT=1.01±0.1 vs. HT=1.53±0.19), body weight (kg) (non-HT=55.45±2.37 vs. HT=63.69±2.42), waist circumference (cm) (non-HT=78.01±2.49 vs. HT=84.89±2.40), hip circumference (cm) (non-HT=92.94±2.18 vs. HT=99.43±1.85), plasma glucose (mg/dl) (non-HT=55.45±2.37 vs. HT=63.69±2.42), plasma insulin (μM/ml) (non-HT=4.64±0.92 vs. HT=7.13±0.85), the homeostatic model assessment for insulin resistance (HOMA-IR) (non-HT=0.94±0.20 vs. HT=1.72±0.22), and height of visceral adipocytes (μm) (non-HT=72.64±6.75 vs. HT=90.25±4.52) were significantly higher but the quantitative insulin sensitivity check index (QUICKI) (non-HT=0.41±0.01 vs. HT=0.36±0.01) was significantly lower in hypertensive compared to non-hypertensive subjects (p<0.05 all). Systolic blood pressure had significantly positive correlations with diastolic blood pressure (R=0.568, glucose (R=0.526), the HOMA-IR (R=0.387), and serum kisspeptin (R=0.569), but has a significantly negative correlation with the QUICKI (R=-0.414). Diastolic blood pressure had positive correlations with body weight (R=0.477), waist circumference (R=0.517), hip circumference (R=0.578), glucose (R=0.533), the HOMA-IR (R=0.415), and width (R=0.436) and height (R=0.439) of visceral adipocytes, but has a negative correlation with the QUICKI (R= -0.464). In conclusion, kisspeptin, obesity especially visceral adiposity, and insulin resistance might contribute to increased blood pressure in hypertensive subjects.

**Thyroid**

**THYROID DISORDERS CASE REPORTS I**

**A Case of T3 Thyrotoxicosis**

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Clinical vignette ENDOCRINE SOCIETY 2020

Title: A case of T3 thyrotoxicosis induced by a dietary supplement.

A 24 yo man consulted for a 2 weeks history of diaphoresis, fatigue, insomnia, palpitations and headache associated with a 20 pounds lost. The patient didn’t have a goiter or any signs of orbitopathy. The results revealed a free T3 level of 45.8 pmol/L upon arrival (normal (N) 3.4-6.8 pmol/L), free T4 level of 6.4 pmol/L (N 11.0–22.0 pmol/L) and TSH level less than 0.005 mUI/L (N: 0.35 to 3.50 mUI/L). Facing those results, a complete review of the patient medication and natural product consumption was done. The patient revealed that he was using, since a month, a vegetable extracts nutritional supplement that didn’t included iodine. He was asked to stop the nutritional supplement and propranolol 10 mg twice daily was prescribed. Thyroid function tests were done 3 days after. The results demonstrate a fT3 level of 4.6 pmol/L, a fT4 level of 5.6 pmol/L and a TSH that still suppressed. A thyroid scintigraphy was performed 7 days later and showed a homogeneous uptake of 18.5% (N 7.0% – 35.0%). We saw the patient 2 weeks later and we ordered another thyroid function test with TSH receptor antibodies, TPO antibodies and thyroglobulin. The results were the following: fT3 of 5.1 pmol/L, fT4 of 12.1 pmol/L, TSH of 2.31 mUI/L, thyroglobulin of 19.8 μg/L (N: 1.4 – 78) and normal levels of antibodies against TPO and TSH receptors. To confirm the contamination of the nutritional supplement by fT3 we used a plasma pool of normal patients in which we measured thyroid function tests at baseline and after we have added the nutritional supplement powder to reflect the dose suggested by the manufacturer. The results showed that fT3 level increased by 36.5%, fT4 by 11.2% and TSH didn't changed. The powder was then analyzed by an external laboratory that wasn’t able to demonstrate the presence of fT3 nor fT4. The two diagnostic possibility facing those results were that the powder induced an interference
with immunoassay used to measure fT3 and fT4 but not TSH or thyrotoxicosis induced by the nutritional supplement with limitation in the technique that tried to identify fT3 in the powder. Given the presentation of the patient, we are convinced that this case represents a thyrotoxicosis induced by a nutritional supplement.

In conclusion, Graves’ disease is responsible for 60–80% of the cases of hyperthyroidism. However, there are few cases reports of thyrotoxicosis induced by nutritional supplement but some studies demonstrate the presence of thyroid hormone in significant amounts in some commercially available health supplements. This case highlights the importance of verifying exposition to medications and natural products when confronted to cases of thyrotoxicosis.

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**Thyroid**

**THYROID NEOPLASIA AND CANCER**

*Physician Management of Thyroid Cancer Patients’ Worry: Is It “Good” Enough?*

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**Introduction:** Despite the excellent prognosis of most thyroid cancer patients, cancer-related worry is common. Additionally, patients report that being told by physicians that they have a “good cancer” invalidates their fears of having cancer and creates mixed and confusing emotions. However, it is not known what proportion of physicians try to reassure patients with the description “good cancer”.

**Methods:** Patients diagnosed with differentiated thyroid cancer in 2014–2015 from the Surveillance, Epidemiology and End Results Program (SEER) registries of Georgia and Los Angeles County were asked to identify endocrinologists and surgeons involved in managing their thyroid cancer. Physicians were surveyed using the modified Diliman method. They were asked to describe their thyroid cancer patients’ worry at time of diagnosis and what they tell them if worried. A multivariable logistic regression was conducted to identify physician characteristics associated with reporting thyroid cancer as a “good cancer”.

**Results:** Response rate was 69% (448/654). Overall, 40% were endocrinologists, 30% were general surgeons and 30% were otolaryngologists. A total of 8% of physicians reported that their patients are not worried or are a little worried at diagnosis, 27% that they are somewhat worried and 65% that they are quite or very worried. Ninety-one percent of physicians reported providing details on prognosis including information on death and recurrence to worried patients, 61% tell them their physicians are experienced in managing thyroid cancer, and 50% tell them that thyroid cancer is a “good cancer”. Factors associated with report of telling patients they have a “good cancer” included endocrinology specialty (odds ratio (OR) 1.84, 95% confidence interval (CI) 1.07–3.17, compared to endocrinology), private practice setting (OR 2.57, 95% CI 1.42–4.75, compared to academic setting) and Los Angeles site (OR 2.23, 95% CI 1.46–3.45, compared to Georgia site). Physicians who perceived that their patients were quite or very worried at time of diagnosis were less likely to use this terminology (OR 0.55, 95% CI 0.35–0.84) and more likely to encourage patients to seek help outside of the physician-patient relationship (OR 1.82, 95% CI 0.35–0.84), compared to patients not to somewhat worried.

**Conclusion:** Most physicians in our sample from two diverse geographic areas report perceiving patient worry as common at time of thyroid cancer diagnosis. They report addressing this worry with different strategies, including telling patients they have a “good cancer”. The benefit of such strategies on patient outcomes still needs further investigation.

**Neuroendocrinology and Pituitary**

**ADVANCES IN NEUROENDOCRINOLOGY**

*GABA Receptor-Dependent Inhibition and Excitation of GnRH Neuron Dendrons near the Median Eminence in Mice*

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**SUN-247**

The gonadotrophin-releasing hormone (GnRH) neuron cell bodies are scattered throughout the basal forebrain but funnel their projections to the median eminence to control fertility in all mammals. In mice, these long projections, termed “dendrons”, have characteristics of both dendrites and axons and are found to receive large numbers of synaptic inputs just prior to entering the median eminence. While the effects of many neurotransmitters have been documented at the GnRH neuron cell body, very little is known about the neural control of the distal dendron.

To examine the role of amino acid neurotransmitters in the regulation of the thin GnRH neuron distal dendrons, we used confocal microscopy in combination with real-time GCaMP6 calcium imaging in acute horizontal brain slices. Adult male and female GnRH-Cre mice were given stereotaxic injections of a Cre-dependent AAV expressing GCaMP6s and, > 3 weeks later, the brain removed and a single thick horizontal brain slice prepared that included the base of the brain and median eminence. The intracellular calcium levels of multiple dendrons were monitored simultaneously while puffs of amino acid receptor agonists were applied. Surprisingly, GABA exhibited a dual action on calcium concentrations with an initial transient increase followed by a prolonged decrease and subsequent rebound. The administration of GABAA and GABAB receptor agonist and antagonists revealed that the transient increase resulted from a quickly desensitizing activation of GABAA receptors while the decrease and subsequent rebound was dependent upon the slower kinetics of the GABAB receptor. Kisspeptin exerts a potent long-lasting elevation of calcium levels in GnRH dendrons and this was robustly inhibited by subsequent GABAB receptor activation. In contrast to