contrast to our hypothesis, Vit D deficiency was not associated with a higher rate of thyroid irAEs. In fact our data suggest that patients who are vitamin D sufficient at the time of starting ICI therapy may be at greater risk of developing thyroid irAEs. Our study is limited by small numbers and the retrospective nature of the study. Prospective studies should be performed to determine the significance of Vit D levels on ICI related thyroid disease.

Adrenal

ADRENAL CASE REPORTS II

Delayed Diagnosis of Cushings Syndrome: Hiding in Plain Sight!

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SUN-157

Background: Endogenous Cushing's syndrome (CS) is rare, with an incidence of 0.7-2.4/million people/year.[1] It should be considered in individuals with diabetes (DM), hypertension (HTN), osteoporosis or electrolyte abnormalities.[2] We present a patient with DM2 and persistent hypokalemia for 10 years found to have ACTH-independent Cushing's disease as the cause of metabolic syndrome. **Case:** 62 y.o. M admitted with abdominal pain, a history of DM2 (2012) on Metformin 500 mg BID, HTN (2010) and on ramipril 10 mg qd, with chronic lymphedema on furosemide 20 mg qd. He reported 3-inch height loss. On exam, had facial plethora, moon facies, supraclavicular fullness, thick violaceous abdominal striae and kyphosis. Past history was significant for abdominal/leg cellulitis, muscle weakness, difficult to heal wounds, easy bruising and recurrent hospitalizations for hypokalemia, despite being on KCl up to 80 mEq/d for 10 years. Labs showed AM cortisol at 22.6 ug/dL, ACTH <5 pg/mL, 24-hour urine free cortisol of 523 ug/d (normal < 60 ug/d). AM cortisol after 1 mg overnight dexamethasone suppression was 36.8 g/dL, ACTH <5 pg/mL. CT abdomen showed right adrenal nodule, 4.0 x 3.5 cm with density of 22 HU. MRI showed lipid-poor adenoma measuring 3.9 x 3.5 cm, raising concern for adrenocortical malignancy. Patient underwent right adrenalectomy. Pathology was consistent with benign adenoma showing no nuclear pleomorphism, lipid rich cells containing eosnophillic cytoplasm. Mib-1 stain <1% cells and positive inhibin. He was maintained on steroids post op due to concern about adrenal insufficiency. Hypokalemia, DM and lymphedema resolved completely 4 months post op with weight loss of ~30 pounds. HbA1c improved to 5.1%, metformin was stopped and he was maintained on Carvedilol 6.125 mg BID for HTN. He was diagnosed with osteoporosis with T score -4.0 at mean femoral neck, -2.9 for mean total hip with non-diagnostic spine. He had multi-level chronic compression fractures of the mid-thoracic spine. **Conclusion:** Delayed diagnosis of CS, as occurred in our patient, can result in detrimental consequences such as life threatening electrolyte abnormalities, cardiovascular events, fractures and premature death.[1] Identifying CS can be challenging as clinical presentation is variable. [2,3] Early recognition, diagnosis and control of CS is crucial to decrease morbidity and mortality. Our patient demonstrated rapid resolution of DM, hypokalemia and lymphedema after surgery; however, prolonged exposure to endogenous cortisol resulted in compression fractures and osteoporosis requiring follow up treatment. **References:** 1. Ille I et al, The Multifarious Cushings. Acta Endocrinol.2019 15(2):261-269 2. Reimondo G et al, Lab differentiation of Cushings syndrome. Clin Chim Acta. 2008;388(1-2):5-14 3. Fan L et al, Association of hypokalemia with cortisol and ACTH levels in Cushings disease. Ann N Y Acad Sci. 2019

Steroid Hormones and Receptors

STEROID BIOLOGY AND ACTION

A Prospective Non-surgical Treatment for Inguinal Hernias

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SAT-747

Background: Inguinal hernias are a widespread public health issue and typically diagnosed in one-fourth of all men. Despite hernia repair being the most commonly performed surgery in the US, the mechanisms causing this disease are currently unknown. We previously developed a mouse model that expresses the human aromatase gene (*Arom*^{hum}) wherein all male mice develop inguinal hernias. We further showed that high production of estradiol by aromatase in the lower abdominal muscle (LAM) via binding to estrogen receptor caused increased fibroblast proliferation and muscle atrophy which leads to inguinal hernia formation (1).

Hypothesis: Disruption of estrogen signaling via ablation of estrogen production using an aromatase inhibitor or inhibition of estrogen receptor by an estradiol antagonist can prevent or reverse the formation of inguinal hernias.

Results: We previously demonstrated that aromatase inhibitor, letrozole, completely prevented the formation of inguinal hernias in *Arom*^{hum} mice (1). Here we show that ER-dependent estradiol antagonist fulvestrant can also prevent LAM tissue fibrosis, muscle atrophy and hernia formation in *Arom*^{hum} mice (n=4, p=0.0007). WT littermates did not show hernia formation with or without fulvestrant treatment (n=4). Furthermore, we demonstrate that aromatase inhibitor letrozole can reverse mild to moderate size of hernia (150-160 mm^2), while placebo-treated mice had progressively enlarged hernias (n=7, p=0.04). We subsequently show a reduction in muscle fibrosis and a restoration of myocyte size in *Arom*^{hum} mice with letrozole treatment.

Conclusion: Estrogen produced as a result of aromatase expression in estrogen-sensitive LAM tissue stimulates the proliferation of estrogen receptor-expressing fibroblasts, fibrosis, muscle atrophy, and hernia formation. Ablation of estrogen production or its signaling not only completely prevents this phenotype but also reverses mild to moderate-sized hernias. Our findings pave the pathway for developing the first potential preventive and therapeutic pharmacological approach for combating recurrent inguinal hernias in elderly men through modulation of estrogen signaling in abdominal muscle tissue.

Reference: (1) Zhao H, et al.,PNAS. 2018 Oct 30;115(44):E10427-36.

Healthcare Delivery and Education

EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

Incorporating Transgender Competent Care into the Medical School Curriculum

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MON-134

Abstract: Incorporating Transgender Competent Care into the Medical School Curriculum

Background: According to recent estimates, the US transgender population has doubled in the last decade. Incorporating transgender competent care into medical education is a growing need, and a focus of the AAMC. Care of the transgender individual is multifaceted, and medical school curriculae on transgender care are limited and lack standardization. Similarly, strategies for measuring effectiveness and impact of these curriculae remain limited.

Methods: Over 3 years, the use of a transgender clinical correlation in the endocrine section of the second-year medical student pre-clerkship curriculum progressed to the use of a triple modality intervention. This included (1) a self-directed written handout with terminology and the basic tenants of medical transition therapy with an optional podcast, (2) a traditional presentation covering social, ethical and multi-disciplinary transgender care, and (3) an interactive session with a transfemale and transmale patient. An anonymous 8 question pre-and post-intervention survey using an electronic clicker system was performed. Questions included interest level, comfort level with various aspects of transgender-competent care and resource awareness.

Results: Prior to the intervention, 74% of students were interested in learning more about transgender competent care. After the learning intervention, in all questions focusing on knowledge and skills of transgender care, students reported a significant increase in their comfort level (Figure 1, $p<0.5$, all). This included reporting now higher comfort levels regarding goals of hormone therapy (8 to 63%), use of transgender affirming medications (19 to 44%), barriers to care (30 to 79%), and long term and multidisciplinary care (8 to 63% and 13 to 71%, pre- and post-intervention respectively). At the end of the intervention, students felt they had more resources to access information about transgender-competent care (pre-23% to post-94% $p=<0.05$).

Conclusion: Knowledge and skills in the care of transgender individuals is poor in the pre-clerkship medical school years. The interest to learn about transgender care is positive. This multi-modality intervention was successful in increasing medical student comfort and knowledge about comprehensive transgender care, and increased student awareness of available resources. Introduction of transgender care should be implemented early in medical student training.

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Figure 1. Change in student comfort across transgender competent care.

* $p < 0.05$

Adrenal

ADRENAL PHYSIOLOGY AND DISEASE

Electron Transport Chain Complex 2 in Mitochondrial Pregnenolone Synthesis

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SUN-219

The mitochondrial P450 family of enzymes (SCC), which require the electron transport chain (ETC) complexes III, IV and V, initiate steroidogenesis by cleaving the sidechain of cholesterol to synthesize steroid hormones, an essential component for mammalian survival. SCC is required for full-term gestation, and aberrant expression may cause pseudohermaphroditism, breast cancer or polycystic ovary syndrome. Complex II or succinate dehydrogenase (quinone) is shared with the TCA cycle and has no proton pumping capacity and no known role in steroid synthesis. We now show that succinate is an intermediate metabolite in the TCA cycle and plays a central role physiologically. Specifically, complex II is required for SCC activation, where the proton pump facilitates an active intermediate state conformation at the matrix, so that in the presence of succinate, ATP can add phosphate. A longer intermediate equilibrium state generates a transient stabilization to enhance the binding of phosphate anions in the presence of succinate anions, resulting in higher enthalpy and activity. An inhibition of the processing at the intermediate state stops phosphate addition and activity. We further describe that phosphate circulation brings the molten globule, an intermediate, to an active folded state. This is the first report showing that an intermediate state activated by succinate facilitates ETC complex II interaction with complexes III and IV for metabolism.

Pediatric Endocrinology

PEDIATRIC GROWTH AND ADRENAL DISORDERS

First Report of Disease-Specific Patient-Reported Outcomes from a Randomized Phase 2 Trial of Once-Weekly Somapacitan vs Daily GH in Children with GHD

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