Frailty score was inversely correlated with cFT (p<0.001, R^2=0.058), TT (p=0.041, R^2=0.014) and SHBG (p=0.003, R^2=0.029). However, after adjustment for age and duration of HIV-infection, cFT, TT and SHBG were excluded from the regression model.

CONCLUSIONS: Low cFT and TT levels are associated with multimorbidity and poor health status in HIV infected men. The bidirectional nature of this relationship leads to the figuration of an intriguing vicious circle where T deficiency triggers the onset of comorbidities or, vice versa, poor health status induces hypogonadism. At the same time, notwithstanding the inverse relation between FT and frailty, it seems that other stronger predictive factors, and in particular the duration of infection, are involved in determining the health outcome in this clinical setting.

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Adrenal

ADRENAL CASE REPORTS I

Treatment-Resistant Hypertension in a Post-Transplant Patient with Cystic Fibrosis: A Rare Case of Pheochromocytoma

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SAT-209

Background: Pheochromocytoma is a rare catecholamine-producing tumor with an estimated incidence of less than 0.1% in the global population. We present the case of a pheochromocytoma in a 25-year-old man with a background history of a double-lung transplant for Cystic Fibrosis, carried out 5 years earlier. **Clinical Case:** A 25 year old, with a background history of Cystic Fibrosis and a Double Lung transplant in 2012 presented to the emergency department with crampy abdominal pain, nausea and vomiting. He was diagnosed with Distal Intestinal Obstruction syndrome (DIOS) for which he was admitted for rehydration and laxatives. Contrast-enhanced computed tomography (CT) imaging of the abdomen and pelvis which showed a 3.4 cm right adrenal lesion, which was confirmed by a subsequent MRI Adrenals and an Endocrinology review was requested. On review, the patient was noted to be hypertensive with a blood pressure averaging 170/90 despite treatment with 3 different anti-hypertensive medications - namely amlodipine, telmisartan and doxazosin. On review of his medical notes, it was clear that he had been persistently hypertensive over the last 3 years. On further questioning, he noted increasingly frequent sweating episodes over the last number of months but denied any palpitations, headache or back pain. Laboratory analysis showed an elevated plasma normetanephrines (NMN) of 3167 pmol/L (182-867) as well as elevated metanephrines (MN) of 793 pmol/L (61-377) and high 3-MT of 257 pmol/L (<185). His MIBG scan showed only a mild increase in the uptake of tracer to the right adrenal gland compared to the left. The case was discussed at a multidisciplinary meeting and given the suggestive laboratory and radiologic findings, a presumptive diagnosis of pheochromocytoma was made. After controlling blood pressure with an alpha-blocker and beta-blocker for a week, the patient was hydrated and scheduled for an elective right adrenalectomy. The histopathology of the excised adrenal gland was consistent with a 3cm pheochromocytoma with none of the adverse features associated with malignant potential. The patient recovered well post-op, his blood pressure normalised and he was discharged home well for follow-up at the Endocrine and Transplant clinics. **Conclusion:** We describe a rare case of a right adrenal pheochromocytoma in a young man with multiple co-morbidities, who completely recovered after tumor resection. This case highlights the crucial importance of investigating secondary causes of hypertension, especially in younger patients. This is the first documented case in the literature of a case of pheochromocytoma in a post-transplant patient with Cystic Fibrosis. ***References:*** 1. Farrugia FA, Marikos G et al. Pheochromocytoma, diagnosis and treatment: Review of the literature. Endocrine Regulation, Volume 51, Issue 3, 30th August 2017.

Adrenal

PROGRESS IN ADRENAL CORTEX AND MEDULLA RESEARCH

NAD+ Availability Modulates 11β-HSD1-Mediated Glucocorticoid Regeneration in Mouse Skeletal Muscle

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OR03-06

11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) is an NADPH-dependant reductase located in the sarcoplasmic reticulum (SR) lumen of skeletal muscle. It generates active glucocorticoids to regulate permissive and adaptive metabolism and contributes to the development of the Cushing's syndrome phenotype in mice receiving oral corticosterone. The SR enzyme hexose-6-phosphate dehydrogenase (H6PDH) generates NADPH which supports 11β-HSD1 activity. H6PDH depletion disrupts the SR NADPH/NADP ratio leading 11β-HSD1 to assume glucocorticoid-inactivating dehydrogenase activity. Little is understood regarding routes to NAD(P)(H) biosynthesis and metabolism in the SR. Here we asked whether modulating cellular nicotinamide adenine dinucleotide (NAD+) availability (the parent molecule of NAD(P)(H)) would influence muscle 11β-HSD1 activity given its sensitivity to the SR

NADPH/NADP ratio. We used FK866 to inhibit nicotinamide phospho-ribosyltransferase (NAMPT, rate-limiting enzyme in NAD+ biosynthesis) to deplete NAD(P)(H) in wild type mouse primary myotubes. FK866 treatment for 48h impaired cellular energetic status, reducing NAD+ (>90%), NADP+ (>50%) and ATP (>30%) without limiting cell viability. 11β-HSD1 reductase activity was decreased to 30% that of untreated cells (152±18 vs. 512±44 pmol/mg protein/h respectively, p<0.005). Employing H6PD knockout myotubes, NADP+-dependent 11β-HSD1 dehydrogenase activity was also impaired following NAMPT inhibition. The NAD+ precursor nicotinamide riboside (NR, 0.5mM), which bypasses NAMPT inhibition through the NR kinase pathway restored NAD+ levels and rapidly rescued 11β-HSD1 reductase activity in wild type and dehydrogenase activity in H6PD knockout myotubes. To assess this *in vivo*, we examined 11β-HSD1 reductase activity in muscle explants of inducible muscle-specific NAMPT knockout mice in which NAD+ levels are reduced by 90%, and show 40% lower activity compared to wild type explants (114±14 vs. 67±10 pmol/mg protein/h, p=0.04). These data suggest a novel level of redox-regulated 11β-HSD1-mediated glucocorticoid metabolism in skeletal muscle. These data also imply a pathway by which NAD+ status is communicated between the cytosol and the SR, which is contrary to the current belief that the pyridine nucleotide pool in these compartments is separate. NAMPT inhibition is being studied as a potential anti-cancer therapy and these data reveal hitherto unanticipated effects this therapy may have in a range of tissues.

Bone and Mineral Metabolism

OSTEOPOROSIS: DIAGNOSIS AND CLINICAL ASPECTS

Addressing the Burden of Hip Fracture in Older Men

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SUN-373

INTRODUCTION: Men have a lower incidence of hip fracture compared to women. However, hip fractures comprise a greater proportion of overall fractures in men and result in greater morbidity and mortality. In 2015, a new high-risk fracture prevention program was implemented in our medical group, targeting men aged 70-85y with hip, pelvic, humerus, wrist or vertebral fracture for osteoporosis treatment within 6 months of the fracture event. In this study, we examined patient characteristics, site of hip fracture, treatment initiation and time to treatment initiation in men who experienced a hip fracture before and after implementation of this new fracture prevention program.

METHODS: This study examines data from 1114 men age 70-85y (81% white race) who experienced a hip fracture during 2013-2014 (N=527) and 2015-2016 (N = 587), based on a principal hospital discharge diagnosis, excluding men who had received osteoporosis treatment in the prior year. Initiation of osteoporosis treatment within 6 months following the hip fracture and time to initiation of osteoporosis treatment (bisphosphonate, teriparatide, denosumab) were examined. The following covariates were ascertained using data from electronic health records and databases: age, race/ethnicity, smoking status, body mass index (BMI), and history of diabetes mellitus with diabetes pharmacotherapy. A Charlson Comorbidity Index was derived using health record data form the prior year. The site of hip fracture was classified as femoral neck or pertrochanter. Subgroups were compared using the Chi-square test.

RESULTS: Among the 1114 men with hip fracture (mean age 79 ± 4 years), half (54%) experienced a fracture in the femoral neck and the remainder (46%) in the pertrochanter. Nearly 1 in 5 (17%) men were current smokers, 13% were obese (BMI ≥30 kg/m2), 25% had diabetes mellitus, and 42% had a comorbidity index ≥3. One fourth (24%) had a clinical fracture diagnosed in the past 2 years. Osteoporosis treatment initiation post-hip fracture increased from 16% in 2013-2014 to 29% in 2015-2016 with implementation of the high-risk program targeting men (p<0.01). Time to treatment examination of 2013-2014 vs 2015-2016 revealed that the largest increase in treatment initiation was seen at 2-4 months (4% vs 12%, p<0.01) whereas non-significant differences were seen at ≤2 (7% vs 10%) and 4-6 (4% vs 7%) months following hip fracture.

CONCLUSION: Implementing targeted post-hip fracture intervention in men dramatically increased osteoporosis treatment following fracture, with the largest intervention seen 2-4 months after fracture. The high burden of prevalent fractures, smoking, and diabetes highlights the need for post-fracture intervention and counseling for modifiable risk factors.

Genetics and Development (including Gene Regulation)

G PROTEIN-COUPLED RECEPTOR SIGNALING IN ENDOCRINE SYSTEMS: NOVEL MECHANISMS IN HEALTH AND DISEASE

Mutational Study of the GPR119 Receptor Binding Site

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OR24-01

The GPR119 receptor, a class A G-protein coupled receptor located in the pancreatic β cells, induces insulin production when activated. Due to its specific activity, the pharmaceutical industry has identified GPR119 as a target for the treatment for type 2 diabetes. The lack of a GRP119 crystal structure has hindered the study of the receptor so our laboratory developed GPR119 active and inactive homology models. Docking studies with the inactive receptor model indicated that two leucine residues facing the binding pocket, L5.43(169) and L6.52(242), may be involved in ligand activation. Additionally, a serine at the extracellular end of the pocket, S1.32(4), may help orient of the ligand in the binding pocket via hydrogen bonding. To gain further insight into the role of these residues and