presenting for investigation or follow-up of HPP from 7/1/2014 to 1/7/2020. Urine was sent to the Children's Hospital in Colorado for PEA testing. Patients were diagnosed with HPP if they had ALP levels persistently below the age-adjusted reference interval, were positive for an ALPL gene mutation/had a family history of HPP and had musculoskeletal/dental symptoms consistent with the disease. Patients were negative for HPP if ALP was not persistently low, vitamin B6 levels were normal without supplementation, negative ALPL genetic testing results (when available) and no musculoskeletal/dental symptoms. PEA levels were not considered for diagnosis. The following was collected from the EMR: PEA results, diagnosis, and ERT status. PEA levels were higher in patients with HPP not on ERT (median=117.0, N=39) vs. those negative for HPP (median=24.0, N=15, p<0.0001). The receiver operator curve for PEA in diagnosing HPP had an AUC of 0.94 (SE=0.03, p<0.0001). Specificity was 100% at PEA levels >53.5 ng/ml (sensitivity=79.5%) with an NPV of 65.2% and PPV of 100%. Initial PEA values in patients with HPP and not on ERT were higher (median 117.0, N=39) than patients on ERT (median 65.0, N=16, p=0.004). Patients who began ERT had a decline in PEA levels after treatment (mean decrease 68.1%). PEA is a specific diagnostic marker for HPP in patients undergoing investigation for HPP and may be used as a surrogate marker to monitor ERT compliance. Future studies are necessary to evaluate the association between PEA levels and functional performance.

Bone and Mineral Metabolism

PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

Relationship Between LC-MS/MS Measurements of PTHrP and Calcium in Patients With Compromised Renal Function

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SAT-LB70

Elevated concentrations of parathyroid hormone related peptide (PTHrP) may indicate hypercalcemia of malignancy and can prompt investigation into potential malignancy. Early studies using PTHrP radioimmunoassays suggested that PTHrP concentrations in normocalcemic renal failure patients were elevated due to assay cross-reactivity with C-terminal fragments present in this population [1]. At our institution, we developed a liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay for PTHrP targeting a peptide in the middle of the PTHrP sequence (to avoid measuring terminal fragments). Given the high specificity of LC-MS/MS, our objective was to revisit the earlier observation that PTHrP concentrations are elevated in renal failure patients. We used retrospective chart review to investigate 1) whether PTHrP concentrations differed between adult patients with and without renal impairment and 2) how PTHrP and calcium concentrations were related in these patients. We excluded patients with cancer; the participants (n=93, 20-90y, 56% female) were categorized based on eGFR using the 2009 CKD-EPI equation following KDIGO guidelines. We focused on patients with healthy kidney function (n=21, 20-73y, 43% female), stage 4 kidney disease (n=40, 23-90y, 63% female), and end stage renal disease (ESRD, n=19, 27-81y, 58% female), 7 of whom were on hemodialysis. When measured by LC-MS/MS, we observed higher PTHrP concentrations in ESRD and stage 4 patients compared to those with healthy kidney function (p<0.0001 for both). Overall, there was a strong negative correlation between eGFR and PTHrP (ρ=-0.768, p<0.0001). In contrast to the previous study documenting elevated C-terminal fragments of PTHrP in normocalcemic patients, we observed that 80% of patients with elevated PTHrP had hypercalcemia, in agreement with the positive association between concentrations of PTHrP and calcium (ρ=0.295, p=0.0178). No statistically significant difference was observed between distributions of PTHrP concentrations in stage 4 and ESRD patients with and without hypercalcemia. Among ESRD patients, higher PTHrP concentrations occurred in patients on dialysis compared to those not on dialysis (p=0.003). Our data suggest that elevated PTHrP concentrations are not solely due to decreased glomerular filtration; otherwise, patients on hemodialysis would have decreased PTHrP concentrations due to clearance. Considering the specificity of the LC-MS/MS method for the central portion of PTHrP, we conclude that elevated PTHrP concentrations may occur in patients with severe renal dysfunction; PTHrP elevations correlate with hypercalcemia in the majority of these patients. Clinicians should be cognizant of the method used to measure PTHrP when evaluating hypercalcemia, particularly in patients with renal insufficiency.

1) Orloff et al., Kidney International. 1993;43:1371-76.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Novel Hormonal and Metabolic Markers of Recovery From Overtraining Syndrome Unveiled by the Longitudinal ARM of the Eros Study - the Eros-Longitudinal Study.

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SAT-LB4

Background: Overtraining Syndrome (OTS) is an unexplained underperformance syndrome triggered by excessive training, insufficient caloric intake, inadequate sleep, and excessive cognitive and social demands. Investigations of markers of the challenging recovery from OTS have not been reported to date. The objective of the present study is to describe novel markers, and biochemical and clinical behaviors during the restoration process of OTS.Design: A 12-week interventional protocol in 12 athletes affected by OTS was conducted, including increased food intake, transitory interruption of the trainings, improvement of sleep quality, and management of stress.Methods: We assessed 50 parameters, including hormonal responses to an insulin tolerance test (ITT), basal hormonal and non-hormonal biochemical markers, body metabolism and composition. Results: In response to an ITT, early cortisol (p = 0.026),

early GH (p = 0.004), and late GH (p = 0.037) improved significantly. Basal estradiol (p = 0.0002) and nocturnal urinary catecholamines, (p = 0.043) reduced, while testosterone (p = 0.014), testosterone:estradiol (T:E) ratio (p = 0.0005), freeT3 (p = 0.043), IGF-1 (p = 0.003), and cortisol awakening response (CAR) (p = 0.001) increased significantly. All basal parameters and early responses to ITT normalized, when compared to healthy athletes. Basal metabolic rate, fat oxidation, body fat, muscle mass, and hydration status had partial but non-significant improvements. Conclusion: After 12 weeks, athletes affected by actual OTS demonstrated substantial improvements, remarkably IGF-1, freeT3, CAR, testosterone, estradiol testosterone:estradiol ratio, CK and catecholamines, and early cortisol, early prolactin, and overall GH responses to stimulations.

Adipose Tissue, Appetite, and Obesity

OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Novel Paradoxical Markers of Weight Loss: Is the Worse Actually the Better? a Retrospectiveanalysisof 1,567 Patientswith Obesity With Successful Clinical Weight-Loss Approaches.

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MON-LB100

Background: Obesity is a chronic, multi-factorial, and relapsing disorder that has been reported to be a risk factor to more than 200 diseases, among which the majority is direct- or indirectly triggered by the metabolic abnormalities induced by excessive body fat. Indeed, patients with obesity tend to disclose multiple alterations of metabolic markers, which tend to improve with weight loss. Despite the multiple dysfunctions extensively in this population, only mandatory biochemical exams are usually ordered, likely due to limitations in cost and lack of cost-effectiveness, since the majority of the parameters typically altered in obesity does not drive therapeutic choices or influence in an individual-based evaluation.We developed a protocol for obesity treatment that includes a thorough analysis and follow up of the biochemical parameters of patients with obesity, including more than 50 parameters, for more precise diagnosis and response to treatments. Among these parameters, we identified unexpected changes, including some that would initially be related to increased cardiovascular risk or worse prognosis when in an usual context, but which could peculiarly indicate successfulness of weight loss, since these parameters tend to return to normal levels after a period in the new body weight. Our objective is to identify whether these paradoxical changes in biomarkers are linearly correlated with body weight loss, fat loss, mass loss, or whether they were related to the use of any anti-obesity drug. **Methods:** In a retrospective cohort of 1,567 patients that underwent a clinical weight loss treatment for obesity in a obesity center (Corpometria Institute, Brasília, DF, Brazil), we performed a linear association analysis between body weight and body fat (air displacement pletismography - Bod Pod, CosMed, USA) and 65 parameters, including hormonal, metabolic, inflammatory, and immunologic parameters. We also adjusted for the use of anti-obesity drugs. **Results:** Homocysteine and triglycerides were identified to increase linearly according to the amount of weight loss (r = -0.77) and fat loss (r = -0.85), but not due to the use of any drug. Folic acid decrease was directly related to fat loss (r = 0.81). Additional findings include more significant decrease of ApoB, compared to LDLc, decreases of GGT, ALT, CRP, ESR, neutrophils, ferritin, fibrinogen, PTH, free T3, uric acid, a and temporary decrease of ApoA and HDLc, all related with body fat loss. **Conclusions:** Increase of homocysteine resulted from decreased folic acid metabolism, and increased triglycerides may be indirect markers of lipolysis, as no other plausible mechanism could explain these findings.

Reproductive Endocrinology

REPRODUCTIVE ENDOCRINOLOGY: REPRODUCTIVE FUNCTION AND DYSFUNCTION ON DEVELOPMENT

Cyclic Progesterone Therapy for Androgenic Polycystic Ovary Syndrome (PCOS) - A Systematic Review of the Literature

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MON-LB010

Women living with androgenic PCOS (WLWP) experience unpredictable oligomenorrhea[1] and are at increased risk for endometrial cancer[2]. Oral micronized progesterone (OMP) given cyclically (14 days/cycle or 4 weeks, Cyclic OMP), in luteal phase doses[3] (300 mg at bedtime) as a "luteal phase replacement" therapy would be likely to effectively treat both. In addition, evidence suggests PCOS is causally related to rapid pulsing of GnRH and LH [4]; OMP normalizes LH pulsatility if androgen levels are not elevated [4]. Previous searches did not find progesterone therapy
for PCOS [5]. Our research question: Does the peer-reviewed literature provide evidence for prescribing cyclic progesterone therapy in PCOS? Literature search methods used Medline (Ovid) and PubMed for published articles. Our search terms were: "polycystic ovary syndrome", "androgenic PCOS", and, "micronized progesterone." We sought publications with eligible women participants having androgenic PCOS, drug exposures (cyclic
OMP, vaginal progesterone, and in varying doses and durations) and specific outcomes (biochemical or patient-reported data or both) in all languages. We excluded reviews and practice guidelines but searched bibliographies for missed citations. Results discovered 18 articles in combined Medline (n=6) and PubMed (12) searches. After excluding duplicates, articles on estradiol (E2) alone E2 with OMP therapy, five eligible articles remained. We read all in full detail.
Progesterone therapy was beneficial for WLWP as, even in sub-therapeutic doses (<300 mg at bedtime) and in cycles of too short durations (<14 days), it decreased luteinizing hormone (LH) [6,7] and total testosterone [7] levels. Vaginal progesterone (200 mg, b.i.d for 2 to 12 weeks) added to letrozole ovulation induction increased the pregnancy rate from 0 to 21% [8]. Although present data suggest Cyclic