lumbar spine of 6.2 ± 8.4%, at the total hip of 3.2 ± 6.0%, and at the femoral neck of 2.5 ± 8.0%
19 patients were considered to have (+) BMD responses, based on consistent increases in BMD and/or t-scores across all spine and hip sites. 4 patients had (-) BMD responses, based on decreased BMD and/or t-scores across all sites. 6 patients had mixed responses and 2 did not have comparative BMD data. Baseline urine calcium did not seem to correlate with clinical responses. Those patients with longer duration of thiazide and/or denosumab use had higher likelihood of (+) BMD responses. However, during the course of follow-up, 4 subjects suffered 7 fragility fractures while treated with denosumab: 3 with (+) and 1 with (-) BMD responses.
**Conclusion**: Denosumab can effectively increase BMD in a cohort of osteoporosis patients with IHC, the majority of whom also received thiazide. However, increased BMD response did not necessarily predict lower risks of fragility fractures. Further research needs to evaluate the role of denosumab therapy in such high-risk patients.

# Steroid Hormones and Receptors

## STEROID BIOLOGY AND ACTION

### *Lower Serum Estradiol Levels in Assigned Female at Birth Transgender People with Initiation of Testosterone Therapy: Results from the European Network for the Investigation of Gender Incongruence (ENIGI).*

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**SAT-745**
Introduction: Aromatization of exogenous testosterone might result in increased estradiol levels. Concerns have been raised about undesired estrogenic effects in assigned female at birth (AFAB) transgender people. How serum estradiol levels change after initiation of testosterone therapy and if these levels should be monitored, remains unclear. Methods: This prospective cohort study was part of the European Network for the Investigation of Gender Incongruence (ENIGI). Serum levels of sex steroids were assessed in 746 AFAB transgender people during a three-year follow-up period, starting at the initiation of hormone treatment. Results: Estradiol levels decreased from median [P25-P75] 45.5[24.0-102.2]pg/mL to 36.5[25.0-46.2] pg/mL over three years (P<0.001), a change was already noticeable during the first three months (mean - 17.1 pg/mL, 95% CI -23.8 - -10.6, P<0.001). Serum estradiol levels were lower in people without endogenous estradiol production (contraceptive users or post gonadectomy) at baseline and after three months, compared to people with endogenous estradiol production. Using long acting testosterone undecanoate injections resulted in a more prominent decrease in serum estradiol values over twelve months, compared to short acting mixed testosterone esters (P<0.001) or testosterone gel (P=0.001). Changes in serum estradiol were positively correlated to changes in LH (ρ = 0.107, P<0.001) and negatively correlated to changes in FSH levels (ρ=-0.167, P<0.001) and body mass index (ρ=-0.082, P<0.001). Conclusion: Testosterone administration in AFAB transgender people results in decreasing serum estradiol levels. Although an underlying mechanism for the observed decrease in serum estradiol levels remains difficult to fathom, our results suggest that testosterone administration suppresses endogenous estradiol production. The exception found in people without endogenous estradiol production may be attributed to aromatization of exogenous testosterone.

# Adrenal

## ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

### *Cyclical Cushing's Syndrome in 12 Patients with Ectopic ACTH Secretion*

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**MON-178**
Cyclical Cushing's Syndrome in 12 patients with Ectopic ACTH Secretion
**Background:** Cyclical Cushing's syndrome (CCS) is characterized by alternating periods of endogenous hypercortisolism and eucortisolism. A literature survey of 60 adult patients with CCS found 15 to have ectopic ACTH secretion (EAS) (1). The duration and frequency of hypercortisolemia are unpredictable, creating a diagnostic challenge.
**Objective:** Describe biochemical and clinical characteristics of patients with CCS due to occult or histologically proven ectopic ACTH-secreting neuroendocrine tumor (NET).
**Methods:** We conducted a retrospective medical record review of 12 adults with EAS admitted to our institution. Inclusion required 1) evidence of ectopic ACTH tumor from biochemical testing (CRH stimulation, 8 mg dexamethasone suppression [DST], and/or inferior petrosal sinus sampling [IPSS]) or pathology results and 2) cycles of hypercortisolism (Hi-F) to eucortisolism (Eu-F) off medical treatment.
**Results:** Average age on admission was 61 (46-79) years; 58% were women. All 12 had biochemical evidence of ACTH-dependent Hi-F. IPSS results suggested EAS in 9 patients, 8 of whom had Hi-F for more than two months, and 1 whose cycles occurred every 5 - 7 days. IPSS was consistent with Cushing's disease (CD) in 2 patients after Hi-F of only 6 -7 weeks and one with Eu-F on admission, estimated duration < 4 weeks. DST suggested EAS in 9 patients, and CD in the one with recent Eu-F. CRH was consistent with EAS in 10 patients, but suggested CD in 2 with marginal increases in ACTH (34.5%, 38%) but not cortisol. 7 patients had ACTH-secreting tumor on pathology (5 pulmonary, 1 pancreas, 1 appendix NET), and 5 had occult presumed EAS. Time from one Hi-F episode to the next