

remains unclear if this early elevation in AMH contributes to the pathogenesis of hyperandrogenemia or is an early marker of PCOS. Nonetheless, these findings suggest there are early differences in the reproductive phenotype in girls with hyperandrogenemia, even before the onset of puberty.

## Reproductive Endocrinology

### ANDROGENS ACROSS SEX, GENDER AND THE LIFESPAN

#### *Erythrocytosis in a Large Cohort of Trans Men Using Testosterone: A Long Term Follow up Study on Prevalence, Determinants, and the Effect of Years of Exposure.*

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**Background:** Erythrocytosis is a known side effect of testosterone therapy in hypogonadal men and can increase the risk of thromboembolic events. Erythrocytosis is also seen in trans men (birth-assigned female, male gender identity) receiving testosterone therapy. Currently there are no clinical guidelines for the management of this problem in trans men. **Specific aims:** 1. To study the prevalence and determinants in the development of erythrocytosis in trans men using testosterone. 2. To study the association between duration of testosterone treatment and hematocrit levels. **Methods:** A 20 year follow-up study in adult trans men who started testosterone, and had monitoring of hematocrit levels at our center (n=1073). **Results:** Erythrocytosis (defined as hematocrit levels of >0.50 l/l twice) occurred in 11% of trans men. Multilevel analyses showed former or current smoking (OR 2.2, 95%CI 1.6-3.3), testosterone administration as long-acting intramuscular injection (OR 2.9, 95% CI 1.7-5.0), a higher age at initiation of hormone therapy (up to OR 5.9, 95% CI 2.8-12.3) for people above 40 compared to <18), higher BMI (>30 g/m<sup>2</sup> compared to 18.5-25 kg/m<sup>2</sup>) (OR 3.7, 95% CI 2.2-6.2) and a medical history for chronic pulmonary diseases, sleep apnea or polycythemia vera (OR 2.5, 95% CI 1.4-4.4) as determinants that increased the risk of high hematocrit levels. In the first year of testosterone therapy hematocrit levels increased most: from 0.39 l/l at baseline to 0.45 l/l after 1 year. Although there was only a slight continuation of this increase in the following 20 years (0.45 at 1 year and 0.46 at 20 years), the probability of developing erythrocytosis still increased (10% after 1 year, 38% after 20 years). **Conclusion:** Erythrocytosis frequently occurs in trans men using testosterone. The biggest increase in hematocrit was seen in the first year, but also after the first years there is a substantial number of people that present with hematocrit >0.50. Because smoking, obesity and use of injection as dosage form are associated with a higher risk for erythrocytosis, a reasonable first step in the care for transmen with erythrocytosis while on testosterone is to advise them to quit smoking and to switch to a transdermal administration type and if BMI is high, to lose weight.

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### ANDROGENS ACROSS SEX, GENDER AND THE LIFESPAN

#### *Recovery of Male Reproductive Endocrine Function Following Prolonged Injectable Testosterone Undecanoate Treatment*

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**Background:** Exogenous androgen treatment suppresses the hypothalamo-pituitary testicular (HPT) axis causing reduced serum LH, FSH and testosterone (T). Recovery of male reproductive endocrine function in past androgen abusers takes 9-18 months with persistent mild lowering of serum T. The natural history of recovery of HPT axis following prolonged injectable testosterone undecanoate (TU) treatment at standard dose is not known. Therefore, the Runoff Study investigated the rate and extent of reproductive hormone recovery over 12 months following cessation of 2 years of TU treatment in the Testosterone for Diabetes Mellitus (T4DM) Study, while men remain blinded to treatment allocation. **Methods:** T4DM participants without pathological hypogonadism (n=1007) were randomised to TU or Placebo (P) injections every 3 months for 2 years with 303 subsequently volunteering to enter the Runoff study at 12 weeks after last injection. Before T4DM study unblinding, they provided blood samples and validated sexual function questionnaires (PDQ, IIEF-15) at entry (3 months after last injection), 6, 12, 18, 24, 40 and 52 weeks later. Serum steroid profile (T, DHT, E<sub>2</sub>, E<sub>1</sub>) was measured batchwise by LCMS and serum LH, FSH and SHBG by immunoassays. **Results:** Runoff study participants in both groups were similar and did not differ from all T4DM participants. As expected, at entry to Runoff serum T was higher in TU-treated men but at all timepoints from 12 weeks onwards serum T and SHBG remained consistently 11% and 13%, respectively, lower in TU-treated than in P-treated men. Similarly, at entry sexual function scores were higher in TU-treated men but subsequently no different from P-treated men. Serum LH and FSH recovered slowly with the median time to reach their own pre-treatment baseline of serum LH was 51.1 weeks [95% CI 50.4 – 53.0 weeks] and for serum FSH was 52.7 weeks [51.0 – 60.9 weeks]. **Conclusion:** After stopping 2 years of standard dose injectable TU treatment in men without pathological hypogonadism, recovery of testicular