and androgen) and clinical (e.g. delayed growth of breast bud) markers of puberty. Investigation of the mechanistic basis for these differences and their potential clinical consequences for girls with higher TBF deserves further study.

Pediatric Endocrinology

PEDIATRIC ENDOCRINOLOGY: GROWTH AND DEVELOPMENT

Self-Reported Feelings of Adult Patients With Differences of Sex Development (DSD) Regarding Genital Surgical Procedures

LIA MESQUITA LOUSADA, MD[1], SORAHIA DOMENICE, PhD[2], Elaine Maria Frade Costa, PhD[1], Tania A. Bachega, MD, PhD[3], Rafael Loch Batista, MD PhD[4], Berenice Bilharinho Mendonca, PhD[5].

[1]Hospital das Clnicas -FMUSP, São Paulo, Brazil, [2]Disciplina de Endocrinologia e Metabologia, Laboratrio de Hormnios e Gentica Molecular/LIM42, So Paulo, Brazil, [3]So Paulo University, Sao Paulo, Brazil, [4]Universidade de So Paulo, Sao Paulo SP, Brazil, [5]University Sao Paulo Fac Medical, Sao Paulo, Brazil.

Introduction: Differences of sexual development (DSD) define congenital diseases in which there is an atypical development of chromosomal, gonadal or anatomical sex, and may present varying degrees to genital atypia. There has been a discussion about the ideal time for surgical approach of atypical genitalia. S, because some non-governmental entities argue that the surgical approach should be delayed until adulthood after the patient's consent. **Objective/methodology:** To analyze the perspectives of adult DSD patients followed at a reference center in São Paulo on the surgical approach to correct atypical genitalia, through a semi-directed interview. **Results:** Thirty-seven adult patients with atypical genitalia were interviewed. Patients' mean age was 36 years. 70% of them had atypical genitalia diagnosed at birth. The patients' median age at the genitoplasty approach was 5 years (1 to 35 years). The median time interval between the beginning of the follow-up at the referral center and the surgical procedure was 1.9 years. When asked about the ideal period/age for genitoplasty, 72.2% considered the childhood, 16.7% cited when they're teenagers, 8.3% in adulthood and 2.8% did n't know. The discomfort reported by the patients related to atypical genitalia decreased after the surgical approach: from 3.8 to 2.9 $p < 0.01$ (on a scale of 1 "without discomfort' to 4 "extreme discomfort"). Insecurity about the appearance of genitalia and functionality during sexual intercourse influences negatively affective relationships. Four (10.8%) patients presented gender dysphoria, all of them with 46,XY DSD, three with partial gonadal dysgenesis (all approached surgically before being admitted to our referral service) and one with 5-alpha-reductase 2 deficiency**. Conclusion:** Most 46,XY DSD patients considered childhood the ideal time to correct their atypical genitalia. An early follow-up in a reference center and an adequate evaluation by a multidisciplinary may influence the positive results associated to the surgical approach of the atypical genitalia in childhood and the low prevalence of gender dysphoria in adulthood.

Reproductive Endocrinology

ANDROGENS ACROSS SEX, GENDER AND THE LIFESPAN

Peripubertal Anti-Mullerian Hormone Levels Are Associated With Hyperandrogenemia During Adolescence: The Avon Longitudinal Study of Parents and Children

Abigayil Dieguez, MD[1], Chen Yeh, MS[2], Laura Rasmussen-Torvik, PhD[2], Laura Christine Torchen, MD[3].

[1]Ann & Robert H Lurie Children's Hospital of Chicago, Northwestern Feinberg School of Medicine, Chicago, IL, USA, [2]Northwestern University Feinberg School of Medicine, Chicago, IL, USA, [3]Northwestern University, Chicago, IL, USA.

Polycystic ovary syndrome (PCOS) is among the most common endocrine disorders in women and is associated with negative reproductive and metabolic outcomes including subfertility, pregnancy complications, metabolic syndrome, and type 2 diabetes. The diagnosis of PCOS cannot be made until reproductive maturity, when the diagnostic criteria of hyperandrogenemia and oligomenorrhea develop. However, studies have described early metabolic and reproductive characteristics of the disorder in girls at increased risk, suggesting the pathogenesis starts much earlier. Indeed, studies in animal models suggest that exposure to excessive androgen or anti-Mullerian hormone (AMH) levels during critical developmental periods can program the offspring to develop the metabolic and reproductive features of PCOS during reproductive maturity.

We investigated early maternal or peripubertal factors associated with hyperandrogenemia during adolescence using data from the Avon Longitudinal Study of Parents and Children (ALSPAC), a United Kingdom birth cohort which has been ongoing since 1991. We performed linear regression to test for an association of testosterone levels at 15 years with peripubertal reproductive and metabolic phenotypes and with maternal measures of insulin sensitivity. Peripubertal phenotypes included AMH levels at 7, 9, and 11 years, and androstenedione, DHEAS, SHBG, IGF-1, fasting insulin, QUICKI, post-glucose insulin, leptin and adiponectin at age 8 years. Maternal phenotypes included fasting insulin levels and QUICKI at a post-partum visit. Unadjusted and adjusted analyses including the covariates pubertal stage, ethnicity, maternal and daughter BMI were performed.

Testosterone levels at age 15 years were significantly positively associated with AMH levels at ages 7(N=299), 9(N=295), and 11(N=300) years in both the adjusted and unadjusted models (Age 7 unadjusted $P<0.0001$, adjusted $P=0.01$; Age 9 unadjusted $P<0.0001$, adjusted $P=0.003$; Age 11 unadjusted $P<0.0001$, adjusted $P=0.02$). Testosterone at age 15 years was also associated with DHEAS at age 8 years using the unadjusted ($P<0.0001$) but not the adjusted model. There was no significant association between any of the other peripubertal metabolic and reproductive phenotypes or the maternal metabolic phenotypes of fasting insulin and QUICKI with testosterone level at age 15 years.

We have found a persistent and significant positive association of AMH levels at pre- or peri-pubertal ages with testosterone levels during adolescence, a developmental stage at which a clinical diagnosis of PCOS can be made. It

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.

Milou Cecilia Madsen, MD[1], Dennis van Dijk, MD[1], Chantal Wiepjes, MD[2], Elfi Conemans, MD-PhD[2], Abel Thijs, Md-PhD[1], Martin Den Heijer, MD-PhD[1].
[1]AMSTERDAM UMC, Amsterdam, Netherlands, [2]Amsterdam UMC, Amsterdam, Netherlands.

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/m2 compared to 18.5-25 kg/m2) (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.

Reproductive Endocrinology

ANDROGENS ACROSS SEX, GENDER AND THE LIFESPAN

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

Nandini Shankara-Narayana, MBBS FRACP PhD[1], Reena Desai, MSc[2], Ann Conway, MB, BS, FRACP[1], Bronwyn Gwenneth Ann Stuckey, MBBS, FRACP[3], Warrick John Inder, MBChB, MD[4], Mathis Grossmann, MD, PhD, FRACP[5], Bu Beng Yeap, MBBS, FRACP, PhD[6], Robert Ian McLachlan, MD PhD[7], Ly P. Lam, MBBS MD MPH PhD[2], Karen Bracken, PhD[8], Gary Allen Wittert, MBBch, MD, FRACP[9], David J. Handelsman, FRACP, PhD, MBBS[10].
[1]Concord Repatriation General Hospital, Sydney, Australia, [2]ANZAC Research Institute, Sydney, Australia, [3]Keogh Institute for Medical Rsrch, Nedlands, Australia, [4]Princess Alexandra Hospital, Woolloongabba QLD, Australia, [5]University of Melbourne/Austin Health, Heidelberg, VIC, Australia, [6]University of Western Australia, Crawley, Australia, [7]Hudson Institute of Medical Research, Brighton, Australia, [8]NHMRC Clinical Trials Centre, University of Sydney, Sydney, Australia, [9]University of Adelaide, Adelaide, Australia, [10]Anzac Research Institute, Sydney, Australia.

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_2, E_1) 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