25 DEVELOPMENTAL PATTERN OF α SUBUNIT IN THE PREPUBERTAL AND PUBERTAL CHILD AND IN HYPERGONADOTROPIC HYPOGONADISM. S.L. Kaplan, D.M. Styne*, F.A. Conte*, and M.M. Grumbach, Dept. of Pediatrics, Univ. of California San Francisco, San Francisco, Ca. 94143.

Glycoprotein hormones share a common α subunit but each has a β subunit which confers biologic and immunologic specificity. α glycoprotein hormone subunit (α)is present in the adult pituitary in concentrations greater than intact LH or βLH; LRF and TRF can increase α secretion. Basal and peak concentrations of plasma α were measured following IV LRF (100 µg) in 6 prepubertal (PRE), 25 pubertal (PUB), 6 with precocious puberty (PP) and 11 with hypergonadotropic hypogonadism (HH). In addition, 7 girls with HH were tested before and during 9 months of 0.3 mg/day of oral conjugated estrogens. Mean basal and mean peak rise in ng/ml (±SE) after LRF were respectively: in PRE non-detectable; in PUB 1.0±.2, 3.5±.3; in PP 0.9±.7; 2.9±.3; and in HH 4.2, 18.9. Estradiol Rx in HH decreased α to 1.3 and 5.1 respectively. In conclusion: 1) Increasing sensitivity of pituitary to LRF at puberty is characterized by an increase in both α and LH; 2) Basal and LRF stimulated α are significantly higher in GD than normal girls but low dose estrogen therapy lowers α levels to normal; 3) Estrogen lowers basal LH and FSH in GD-RX and decreases the gonadotropin hyperresponse to LRF.

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The role of Inhibin in the control of the prepubertal hypothalamic-pituitary testicular-axis.

Testicular function was studied in 9 men (18-32 years) who had received irradiation for Wilm's tumour during childhood. The dose of (scattered) irradiation to the testes ranged from 500-900 rads. 7 subjects had oligo or azoo-spermia (0-5.6 million/ml), 6 of whom had an elevated serum FSH level. One subject showed evidence of Leydig cell dysfunction (raised plasma LH and low testosterone concentration). These results were compared to those in 8 prepubertal boys who several years earlier had received irradiation for abdominal or testicular tumours (dose to the testes 500-3000 rads). In all 8 the serum FSH, LH and testosterone were within the normal prepubertal range. Thus irradiation-induced damage to the germinal epthelium in prepubertal boys produces raised FSH levels after puberty but not before it.

We conclude, therefore, that Inhibin has a negligible role in the control of the prepubertal hypothalamic-pituitary-testicular axis and that gonadal control of gonadotrophin secretion changes with sexual maturation.

27 Guest Lecture

H.S. Jacobs (St Mary's Hospital Medical School, London)

The control of FSH secretion in men and boys

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Serum somatomedin A in healthy children and children with growth disorders.

Somatomedin A has been measured in serum by a radioreceptor assay utilizing placental membranes. At birth the concentration is about 40 % of that in the adult. During childhood there is a continuous increase in somatomedin A concentration and adult levels will not be achieved until puberty. In patients with hypopituitarism and Laron's dwarfism the levels were significantly below the normal range but no patient was found to have a complete lack of somatomedin A. In children with immunopathies and stunted growth levels were found around the lower normal border. Following hGH administration serum somatomedin A concentration increased in the hypopituitary but not in the immunopathic patients. Among children with Crohn's disease the values varied considerably and were in some cases far below the normal range. Girls with Turner's syndrome had normal levels in spite of retarded growth rate as had children that were on steroid treatment. In tall girls the levels decreased during oestrogen treatment.

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Misleading aspects of serum growth hormone (GH) levels and serum somatomedin activity (S.S.A.) in growth failure from coeliac disease.

Serum GH levels and SSA (incorporation of 35S in rat cartilage) were studied in 3 children age 7, 8, 11 yrs, with isolated growth failure and bone age retardation (-2.6 to -5SD). Low SSA were consistently found : 0.20 to 0.34 (N 0.50). Thyroid and adrenal status were normal. In 2 cases responses of GH levels to arginine-insuline stimulation were normal (15 and 40 ng/ml) as well as early sleep GH peaks ; in 1 case low GH levels were found on 3 successive tests (2 to 5 ng/ml). In 1 case serum SSA did not increase under HGH stimulation test (2 x 2 mg/day/48 h) ; an increase from 0.21 to 0.51 was observed in an other. In this latter child GH therapy was instituted from 15 months with unconvincing results and persistantly low SSA. In the 3 cases coeliac disease was finally diagnosed by jejunal boipsy and catch-up of growth under gluten-free diet. In 1 child a marked increase in SSA was seen within 6 weeks of diet (0.34 to 0.72).

Conclusions : SSA is low in coeliac disease ; it is not related to the GH secretion pattern but rather to the metabolic abnormality of the disease ; it constitutes another misleading aspect of growth failure from coeliac disease.

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Plasma GH and somatomedin activity (SMA) in relation to growth retardation and weight changes in anorexia nervosa (AN).

In 3 prepubertal children with AN a severe growth retardation with low SMA was observed. This lead us to investigate the GH-SMA relationship in 13 severly underweight cases, 7 of which were aged 8-14 yr and presented low growth rates (0-3.5 cm/yr). A decreased SMA was found in 10/12 cases. By contrast GH secretion after AITT was normal in 9 cases. Plasma SMA could not be stimulated by hGH administered acutely in 2 cases (8 mg/m2/d x 4d) or during 5 months in one case (6 mg/wk). On follow-up of 6 cases, weight gain was accompanied by increased SMA values. In 2 of these, normal SMA values were observed, in spite of low GH response to AITT and in the absence of hyperinsulinism. In conclusion 1) growth retardation in AN is better correlated with SMA than GH response to AITT, 2) there is a state of resistance to endogenous and exogenous GH, 3) adequate weight gain with increased SMA may be necessary for catch-up growth in early affected children.