195 PROGNOSTIC SIGNS IN THE EVOLUTION OF PREMATURE THELARCHE (PT). Alfred Tenore, Teresa Quattrin, Patrizia Lubrano, Maria L. Sandomenico, Adriana Franzese, Angela Mariano. II Faculty Medicine, Dept Pediatrics and IV Patologia Generale, Naples, Italy.

Since PT can be a first sign of precoc. puberty(PP), the aim of our study was to identify simple items in the first 6 mos of follow-up(F/U) that could predict if PT would evolve to PP.

30 girls with PT were studied. First evaluation included bone age(BA) basal E_2,FSH,LH and Prl. GnRH was done in 12 and F/U BA in 22. Based on clinical outcome after F/U of 2±1y(m±sd), patients were divided into 2 groups(G): 1)invaried, decreased or regressed 2)Progressed to PP. Age at onset in G2(60±34mos) differed from those in G1(16±20mos;p <0.005). LH was higher in G2(7±3uUI/ml vs 2.9±1.6;p <0.001). FSH, although elevated, did not differ between G1 and 2. FSH/LH areas after GnRH and basal E_2 did not differ. Initial BA was advanced(>2sd) in G2 but also in 21% of G1. In F/U an acceleration of BA and growth velocity was seen only in G2.

The following points may help in an early prediction of the evolution of PT:a)age of onset less than 3y is typical of PT, b) LH is increased only in those who progress to PP, c)advanced BA is typical of PP but since it may also be found in other cases(21%), an abnormally increasing BA during a short term F/U(6mos) is indication of an evolution to PP.

196 DANAZOL TREATMENT IN PUBERTAL GYNECOMASTIA Wolf Beck, Peter Stubbe. University of Göttingen, Department of Pediatrics, Göttingen, FRG

The aim of the study was to provide a treatment alternative to mastectomy in pubertal boys with excessive breast enlargement.

Patients and treatment: 16 boys with pubertal gynecomastia between 9 x 7 and 3 x 3 cm in diameter and Tanner stage 3 - 4 were treated with Danazol 200 mg daily for 6 months.

Results: The antigonadotropic action of Danazol was documented by inhibition of basal gonadotropin secretion, by disappearence of normally sleep dependent gonadotropin rhythms as well as by diminished pituitary response to LHRH stimulation. Simultaneously, plasma testosterone secretion was suppressed to levels according stage Tanner 2 without reduction of testicular volumes. After 6 months of therapy without any side effects pubertal gynecomastia was reduced in size to 2 x 2 cm in diameter in 15 patients. There was one treatment failure where mastectomy was performed after 3 months on Danazol. In all responding patients, the hypothalamo-pituitary-gonadal axis normalized within 6 months after termination of drug therapy and no relapse was observed over a control period up to 44 months.

In conclusion: The continuing regression of breast development during Danazol treatment emphasizes the effectiveness of this drug in excessive pubertal gynecomastia as an alternative regimen to surgical intervention.

197 GROWTH HORMONE SECRETION IN CONSTITUTIONAL DELAY OF GROWTH AND DEVELOPMENT (CD).

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Recently growth hormone (GH) treatment of patients with CD has been advocated because of insufficient GH secretion during sleep. We intended to prove these findings by comparing GH secretion during spontaneous sleep between 8 p.m. and 2 a.m. every 30 min and EEG controlled sleep during the first slow wave sleep (SWS) at night every 10 min.

Patients: Sleep studies were performed in 13 boys with CD aged 11 to 16.8 years and heights below 2 SD for age. Bone age retardation was 1.5 to 5 years, pubertal development Tanner 1 to 2. Five healthy controlls with comparable age and pubertal development served as controlls. Informed consent was obtained from all parents.

Results: 13 patients with CD secreted 2025 ng x min x ml^{-1} GH (696 - 4175) during spontaneous sleep and 9 pts 550 ng x min x ml^{-1} GH (351 - 2215) during SWS. Four controlls showed 1715 (618 - 2480) during spontaneous sleep and 5 controlls 693 (435 - 868) during SWS respectively. All values are given as median and range in brackets. Median of GH peak was 20.5 and 20.9 during SWS and 28.1 and 20.5 ng/ml during spontaneous sleep in patients and controlls respectively.

Conclusion: Since there was no evidence of insufficient GH secretion during sleep in patients with CD, GH treatment of these patients cannot be based on insufficient GH secretion during sleep in these children.

198 SALIVARY (SP) AND PLASMA PROGESTERONE (PP) IN FEMALE ADOLESCENTS. Wolfgang Sorgo*,Guido Saur*,Milo Zachmann,Walter M.Teller, Depts. of Pediatrics,University of Ulm,FRG, and University of Zurich,Switzerland.

A significant correlation between simultaneously determined SP and PP was found in 69 healthy adolescent girls (r=o.562, p<o.ool). 29 were still premenarchal (chronologic age -CA- lo.5-15, bone age -BA- lo-13.5 years -yrs-). 8 had anovulatory cycles (CA 12.8-21, BA 13-18, gynecologic age -GA- o.1-6.7 yrs) and 4 presented primary and secondary amenorrhea (CA 12-18.8, BA lo-18 yrs). 17 with ovulatory cycles (CA 13-21.4, BA 13-18, GA o.3-7 yrs) provided progesterone values during the follicular phase (FP) and 11 during the luteal phase (LP). SP and PP concentrations during FP did not differ from premenarchal girls or those with cyclic abnormalities. With respect to FP the coefficient of correlation between SP and PP was r=o.432 (n=58, p<o.ool). The correlation between SP and PP during LP was r=o.783 (n=11, p<o.ol). The regression equation of the log normally distributed values was y=3.49863+1.14611x (y=PP,x=SP). Provisional normal ranges for SP and PP during ovulatory cycles were established. During FP SP and PP ranged from 7o-28o and 5oo-24oo pM/L, while the highest SP and PP levels during LP were 8oo and 39ooo pM/L. The Wilcoxon test was significant between progesterone during FP and LP both for SP (p<o.o5) and PP (p<o.ool).

Conclusion: Serial analyses of SP are suited to characterize phase and type of a cycle. Because of the high correlation it is possible to calculate PP during LP based on SP.

199 Use of Pelvic Ultrasound for the Assessment of Gonadotrophin Secretion in Disorders of Female Puberty

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We have used pulsatile administration of gonadotrophin releasing hormone to induce puberty in 12 girls with hypogonadotrophic hypogonadism and have been able to mimic the clinical, endocrine and ultrasound changes of normal puberty. By following gonadotrophin profiles and matching them with ultrasound examination, we have been able to define the morphological (multicystic progressing to dominant follicle) appearances of the ovary that are characteristic of increasing pulsatile gonadotrophin secretion. We have established normative ultrasound data in 40 control subjects.

In our hands, pelvic ultrasound has become a non-invasive method of assessing gonadotrophin pulsatility and, using measurements of ovarian volume and of uterine size together with ovarian morphology, we can reliably distinguish simple delay of puberty from hypogonadotrophic hypogonadism and central precocious puberty from isolated premature thelarche during a single consultation. This technique offers substantial advantages for paediatric endocrine practice; it can also be used longitudinally to document response to therapeutic regimens, again without recourse to detailed endocrine studies.

200 MODULATION OF BASAL AND GRF-STIMULATED GH SECRETION BY MELATONIN AND VICE VERSA IN MALE RATS

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In humans,release of GH due to insulin induced hypoglycemia was noted to inhibit the basal level of the pineal hormone melatonin(MEL)(Gupta et al,1983)and viceversa(Smythe and Lazarus, 1974).In order to study the interaction between stimulated GH and and MEL in adult male rats,the following studies were carried out:1.Effect of GH stimulation with GRF(1µg/bw,iv),l-dopa(5µg iv) and insulin hypoglycemia(4IE iv) on circulating MEL. 2.Effect of MEL(50µg sc for 4 days) on basal GH levels and effect of GH(50µg sc for 4 days) on circulating MEL concentrations. 3.Effect of MEL(50µg sc at -60 and -30 min) on GH release due to GRF,l-dopa and insulin. A significant(p<0.01) increment in GH level(188±7 ng/ml,x±SEM) due to GRF decreased MEL concentrations while peaking of the former was synchronized with the nadir of the latter.The other two GH stimulators,although less effective,also suppressed MEL levels significantly(p<0.05).MEL pretreatment suppressed significantly GH levels from the control(1.7±1 vs 16.7± 8,p<0.05).Similarly,GH treated animals showed significantly suppressed MEL levels in relation to the controls(3.1±2 vs 70.9±8 pg/ml,p<0.001).When GRF,l-dopa or insulin was administered to stimulate GH in the MEL pretreated animals,the peak was entirely abolished.The fact that the GRF induced GH release suppressed MEL and pretreatment with MEL suppressed the GH response to GRF indicates a possible interaction at the pituitary level.

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