95 M. ROGER*, J.-E. TOUBLANC*, K. NAHOUL* and P. CANLORBE. Fondation de Recherche en Hormonologie et Hôpital Saint-Vincent-de-Paul, Paris, France. Gonadal secretory responses to hCG in prepubertal and pubertal girls.

The ovarian responsiveness to hCG was studied in 7 girls at pubertal stage I, 7 girls at pubertal stage II and 8 subjects with complete Turner syndrome aged 15 to 20. hCG was injected IM, 3 x 1500 IU every other day after informed consent of parents. Plasma testosterone (T), androstenedione (A), progesterone (P), 17-hydroxyprogesterone (17-OHP), estradiol (E2) and cortisol (F) were measured before and after hCG by radioimmunoassays with chromatographic step. In Turner subjects the ranges of basal values were: T: 0.13-0.33 ng/ml, A: 0.27 - 1.44 ng/ml, P: Non Detectable(ND) - 0.26 ng/ml, 17-OHP: 0.27 - 1.48 ng/ml. There was no significant increase after hCG. In group I, the ranges of basal values were: T: 0.06 - 0.17 ng/ml, A: 0.08 - 0.41 ng/ml, P: ND - 0.38 ng/ml, 17-OHP: 0.15 - 2.60 ng/ml, E2: ND - 25 pg/ml, F: 45 - 120 ng/ml. Except for F, there were significant increases after hCG ($p < 0.025$) The ranges of increments were: T: 0.01 - 0.16 ng/ml, A: 0.08 -0.48 ng/ml, P: 0 - 1.62 ng/ml, 17-OHP: 0 - 1,61, E2: 0 - 18 pg/ml, F: -35 - +75 ng/ml. In group II, the ranges of basal values were: T: 0.05 - 0.19 ng/ml, A: 0.10 - 0.62 ng/ml, P: ND - 0.20 ng/ml, 17-OHP: 0.14 - 1.35 ng/ml, E2: 4 - 30 pg/ml and F: 45 - 129 ng/ml. Again there were significant increases ($p < 0.025$), except for F. The ranges of increments were: T: 0.09 - 0.33 ng/ml, A: 0.14 -1.84 ng/ml, P: 0 - 0.15 ng/ml, 17-OHP: -0.85 - 2.04 ng/ml, E2: 8 - 16 pg/ml, F: -69 - +83 ng/ml.These data give evidence that prepubertal ovary, like prepubertal testis, is easily responsive to hCG.

96 LONGITUDINAL STUDY OF THE GONADOTROPHIN RESPONSE TO LUTEINISING HORMONE RELEASING HORMONE IN CHILDREN WITH PRECOCIOUS PUBERTY TREATED WITH CYPROTERONE ACETATE

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To assess the effect of cyproterone acetate (150-200 mgm/m^2 daily) on gonadotrophin secretion 7 children (1♂,6♀) with precocious puberty received 100 µg of synthetic luteinising hormone releasing hormone (LHRH) at diagnosis and at regular intervals during treatment. The response of luteinising hormone (LH), follicle stimulating hormone (FSH) and gonadal steroids were assessed by radioimmunoassay. Plasma LH and FSH after LHRH injection were analyzed by the peak response and the area circumscribed by the 2 hr. curve of gonadotrophin concentration. The initial LH response was greater than or equal to that seen in normal puberty. Though the LH response decreased with treatment it remained in the pubertal range in 6 children and in only one did it fall to prepubertal values. After 6-9 months therapy the LH response in 4 children increased but did not reach the levels found before treatment. The initial FSH response was variable but was consistently lowered by therapy in 6 children. Gonadal steroids fell during the early months of treatment often to prepubertal levels but later rose in those children in whom the LH response had increased. It is concluded that cyproterone acetate has an antigonadotrophic effect but, at the dosage used, does not substantially nor persistently decrease the amount of readily releasable LH in precocious puberty.

97 Z. LARON., Z. DICKERMAN* and R. PRAGER-LEWIN*. Institute of Pediatric and Adolescent Endocrinology, Beilinson Hosp. Petah Tikva & Sackler Med. School, Tel Aviv University, Israel.

Effect of Prolonged Clomiphene Citrate Administration to Boys with Retarded Sexual Development.

Clomiphene citrate, 50mg/day was given for 30-90 days to 16 boys with retarded sexual development aged 15-19 years (BA 12½-15 years). 11 of the patients underwent a standard LRH test (50µg/m^2 i.v.) prior and after treatment with clomiphene. The boys,mainly those at pubertal stage P_{3-4} showed definite acceleration of their pubertal process, as judged from the evaluation of pubic hair, testicular volume, penile length and growth velocity. The most consistent laboratory finding was the rise of plasma testosterone levels (mean +307.8%). The effect on the plasma gonadotrophins was variable. The LH levels rose in 6 boys and the FSH in 5. There was no correlation between these changes and the testosterone rise and increase in testicular volume; we therefore assume also a direct clomiphene effect on the testes or plasma androgen binding globulin. It seems that clomiphene citrate may be a useful drug to accelerate delayed puberty at stages P_{3-4} (Tanner)or P_2 (Laron-Dickerman).

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97a HUMAN PROLACTIN DURING PUBERTY : A LONGITUDINAL STUDY. Ch. SULTAN, B. DESCOMPS, A. CRASTES de PAULET and R. JEAN (Intr. by : J. BERTRAND) - Laboratoire de Biochimie C et Clinique des Maladies des Enfants CHU St-Charles 34000 MONTPELLIER (France).

Longitudinal studies are very adequate to detect small individual and significant variations of plasmatic hormons. Thus we performed prolactin determination (PRL) in 12 boys and 9 girls who were patients, in the pediatric department of CHU St-Charles for non-endocrine chronic diseases. PRL determinations were done according to Reuter et al. (1975, Path. Biol. 23, 761-767) using commercial Kits (IRE-Fleury, Belgium) tested in our laboratory for specificity and reproductibility with NIH and MRC standards. In our hands, the "intra-assay" error was 5 %, the "inter-assay" error 10 % and the equivalence was found to be 40 µI.U.= 1 ng NIH, VLS-1. In boys (n = 12) the mean PRL values as a function of Tanner's puberal stages were found to be (ng/ml) : stage I : 4.4±0.2 ; stage II : 3.3 ±0.2 ; stage III : 2.7±0.2 ; stage IV : 2.2±0.3 ; stage V : 4.8±0.2 Between stages II and IV, an important decrease of PRL was observed which was followed by an increase at the end of puberty, PRL becoming slightly higher than at stage I. This pattern could not be detected by a non-longitudinal study. In girls, PRL levels (ng/ml) increase progressively throughout puberty : stage I : 3.0±0.3 ; stage II : 3.7±0.2 ; stage III : 3.9±0.2 ; stage IV : 4.6±0.3 ; stage V : 6.0±0.4. These results agree with PRL levels observed in groups of prepuberal and postpuberal girls. Thus PRL variations during puberty are made obvious by longitudinal studies but their eventual implication in the maturation process of the hypothalamo-pituitary gonadal axis is still to be determined.

98 H.L. LENKO*, J. PERHEENTUPA, L. VUORENKOSKI* and V. VUORENKOSKI*. University Children's Hospital, Helsinki, and Central Hospital, Kokkola, Finland. Voice frequency during normal and retarded growth, and during androgen treatment.

We have measured basal, lowest and highest voice frequency (BF, LF,HF), using a simple method, in (1) 372 normal subjects: children and adolescents at ages 6, 8 and 10 years and at the different pubic hair stages (PH), and adults; (2) 71 children with different types of growth failure, and (3) 48 boys with delayed growth and maturation and 31 girls with Turner's syndrome, during fluoxymesterone treatment. BF fell in boys between ages 8 and 10 years (from 259 to 247Hz), but not in girls (253Hz). LF fell between ages 6 and 10 years in boys (from 234 to 203Hz) and girls (from 230 to 218 Hz), and a sex difference appeared. In puberty, a gradual fall of BF and LF occurred parallel to PH development, both in boys (to 100, 90Hz) and girls (to 213, 180Hz). An abnormally high BF was observed in 3 of 12 hyposomatotropic children, 4 of 7 children with Mulibrey nanism, and 2 of 9 children with other prenatal growth failure. Boys with delayed maturation had subnormal BF at PH 1 prior to treatment. At PH 2, fluoxymesterone (0.135mg/kg/day) treated boys had lower BF than untreated boys. Girls with Turner's syndrome also had slightly subnormal BF for PH after fluoxymesterone (0.10mg/kg/day). The voice effect was individually variable. In some cases androgen was discontinued because of voice change and a recovery was observed. The method is useful in the clinical characterization of growth failure and stage of puberty. It is particularly recommended for voice monitoring during androgen treatment when a change is undesirable.

99 J. MÄENPÄÄ*, H.L.LENKO* and J. PERHEENTUPA. University Children's Hospital, SF-00290 Helsinki 29, Finland. Evaluation of fluoxymesterone treatment of slow growth and maturation.

56 boys, aged 9.2 - 17.8 years, with height deviation for age (HD) (mean±SD) -2.6 ± 0.8 SD, lag in Greulich-Pyle bone age (BA) 2.7 ± 0.9 years, and height deviation for BA corrected according to a longitudinal Finnish study (IPH, index of potential height) -0.9 ± 0.8 SD, were given fluoxymesterone 0.13 ± 0.05 mg/kg daily (dose increasing with BA) for 1.0 ± 0.4 years, minimum 0.4 years. Growth velocity during treatment was greater ($p<0.001$) both in boys with initial BA =10 years (group I, N=16, 7.5 ± 0.8 cm/year) and in boys with initial BA >10 years (group II, N=40, 9.0 ± 1.3 cm/year) compared with similar control groups (N=15 and 36, velocity 4.1 ± 1.4 and 6.1 ± 2.1 cm/year, respectively). ΔHD was 0.4 ± 0.3 SD during treatment against 0.1 ± 0.4 SD in controls ($p<0.01$). ΔIPH for group I was -0.4 ± 0.6 SD against -0.4 ± 0.6 SD in controls, and for group II 0.2 ± 0.3 SD against 0.0 ± 0.3 SD in controls ($p<0.02$). 8 boys of group I and 21 boys of group II had a follow-up >0.4 years after treatment and their total ΔIPH was -0.7 ± 1.4 SD and 0.2 ± 0.3 SD, respectively. The size of testes clearly increased during treatment in 2/3 of the boys. Of plasma gonadotrophins FSH decreased from pretreatment levels after 4 - 6 months treatment, LH showed no significant change. 3 boys of group I had frequent erections or appearance of pubic hair. Our mode of treatment brings about an acceleration of growth and maturation. In boys with BA >10 years its mean effect on final height is a slight increase. In younger boys this effect is uncertain and it may not be wise to treat boys prior to BA 10 years.