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Effect of dehydroepiandrosterone (DHA) and androstenedione (Δ) on gonadotropin release and testosterone secretion in male rats.

The data of Ducharme et al (JCEM 42: 484, 1976) suggest that DHA and Δ may play a role in activating the hypothalamic-pituitary gonadal axis at puberty in man. In order to verify the capacity of these steroids to trigger gonadotropin release, urethane anesthetized 250-300 gm Sprague-Dawley male rats were injected with 100 to 1600 ng of DHA or Δ through a jugular catheter and heparinized blood obtained at -10, 5, 10, 30 and 60 min for LH measurement by RIA. Control rats received only vehicle. In another series of experiments, unanesthetized rats received the same treatment by the intra peritoneal (I.P.) route and plasma was obtained by decapitation at 1, 2, 4, 8 and 24 hours for plasma LH, FSH and T determination by specific RIA. The reactivity of the hypothalamic-pituitary axis was assessed by the response to LH-RH. All animals tested responded to LH-RH but no significant increase in plasma LH, FSH or T was observed within 1 h of administration of any I.V. dose of DHA or Δ used. In contrast, despite individual variations, LH release was induced 24 h post 100 and 200 ng of DHA and Δ I.P. with concomitant rise in T. These data suggest that in young pubertal male rats, some steroids mainly of adrenal origin, namely DHA and Δ , are effective in triggering the hypothalamic-pituitary gonadal axis. The specificity of this action and their role in the elevation of the gonadostatic threshold at puberty remain to be determined.

36 G.J. BRUINING*, J. SMITH*, G.B. FORBES*, E.W. BERGINK* and J.L. WITTLIFF* (Intr. by H.K.A. Visser). Sophia Children's Hospital, Rotterdam, and University of Rochester, U.S.A. Alterations in plasma testosterone and sex hormone binding globulin during puberty.

Others have reported a decrease in sex hormone binding capacity during male puberty and higher values for adult females than for males. We have examined the relationship of the total serum testosterone (T) to total sex hormone binding globulin (SHBG) (T:SHBG ratio) as an index of biologically active T during the pubertal development of both sexes. We estimated SHBG by polyacrylamide gel electrophoresis (J.Clin.Endo.Metab., in press) and T by immunoassay in 33 boys and 30 girls aged 9-19 years (CA) and compared the T:SHBG ratio with clinical parameters of pubertal development. Informed consent was obtained from the parents and the study was approved by our human experimentation committee. Tanner staging, bone age (BA) and lean body mass (LBM) by K-40 counting were estimated. In boys plasma T rose and SHBG fell as puberty advanced. The T:SHBG ratio appears to be positively correlated with the difference between BA and CA, and the correlation with the LBM/Ht ratio was 0.76. In contrast the girls showed little change in either T or T:SHBG ratio during puberty and no relationships with the clinical parameters were found. The T:SHBG ratio may be useful as a parameter of male pubertal development.

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37 J.L. CHAUSSAIN, A. GUILHAUME*, M. ROGER*, P.E. GARNIER*, P. CANLORBE and J.C. JOB. Hosp. St-Vincent de Paul, Paris, France. The hypothalamo-pituitary-gonadal axis (HGPA) in children with precocious puberty.

36 children with true precocious puberty (25 girls aged 2 to 8 years, and 11 boys aged 1 to 9 years) were studied. The study included plasma testosterone (T) or estradiol (E2) assay, LH and FSH measurement before and after LHRH (0.1 mg/m²), and determination of nycthemeral variations of plasma LH in 9 subjects, sleep being monitored by polygraphic recorder. In the girls a parallel increase of E2 and LH was observed, correlated to the clinical degree of sexual maturation. A sleep-induced rise of plasma LH was present in 3 girls at stage P3 and in 1 girl at stage P4, absent in a P2 girl. 2 boys exhibited a parallel increase of T, LH and FSH. In the 9 other boys a contrast was noted between pubertal levels of T (2.5 to 5.8 ng/ml) and prepubertal levels of LH and FSH after LHRH. In 4 of them T response to HCG (3 x 1500) was in the upper range of adult values. In 4 of them no sleep-induced peak of LH was detected. It appears that in precocious puberty of girls the whole maturation of the HGPA is similar to that of normal, while in boys the early increase of the testicular sensitivity to LH may be concomitant with an incomplete pubertal maturation of the hypothalamus.

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Neonatal Diagnosis of Familial Type II Hyperlipoproteinemia.

In recent publications^x we have shown that the diagnosis of familial type II hyperlipoproteinemia can be made at birth by simple biochemical methods, suitable for screening programs. The concentration of cord serum very low density and low density lipoprotein was estimated in 1000 newborn infants, using three different methods: electroimmunodiffusion, turbidimetry and Heparin-CaCl₂ precipitation. The serum cholesterol was estimated in both parents. An incidence of familial hyperlipoproteinemia of 0.7% was found. Early diagnosis is important, since treatment from early life seems beneficial in this disease, which is characterized by severe hypercholesterolemia and risk of premature ischemic heart disease in males.

^xPediatrics, 1976, 57: 214
Clin. Chim. Acta, 1976, 66: 29

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Antibody production of the mammary gland in mothers after oral colonization of their infants with E. coli 083.

Twenty breast-fed infants were colonized by oral administration with a non-enteropathogenic E. coli strain 083. The antibody and secretory IgA response in the mammary gland was followed from birth during the time of breast feeding. Four infants and 14 single milk samples were used as controls. At the same time the serum antibody response in 13 artificially fed, colonized infants were examined.

Mothers of colonized breast-fed infants had significantly higher antibody levels in milk than controls. Secretory IgA was twice as high in milk of mothers whose infants were colonized, when compared with controls. There was no serum antibody response in breast-fed infants after colonization, but high serum antibody titers were found in artificially fed colonized ones.

The E. coli strain evoked local antibody response in the mammary gland in mothers of colonized infants, but had no systemic immunizing influence because of the inhibitory effect of antibodies in the mothers milk.

43 J. PITT* and B. BARLOW* (Intr. by Dr. V. terMeulen). Department of Pediatrics and Surgery Columbia College of Physicians and Surgeons, New York. Effect of stress and of formula feeding on the acquisition of intestinal flora in newborn rats.

In a rat model of neonatal necrotizing enterocolitis, breast milk, and most specifically milk macrophages have been shown to be protective to the susceptible stressed rat. Moreover, it was found that the affected animals died with enterobacterial septicemia. (Ped. Res. 1974, V. 8, p. 110). In order to better define the role of the gastrointestinal flora in this disorder, the kinetics of their establishment in the stressed and unstressed newborn rat were determined as a function of feeding. Newborn rats were fed whole breast milk, frozen breast milk, formula and formula with peritoneal macrophages. They were studied on days 1, 3, and 7 following birth. The gut was divided into duodenum-jejunum, ileum-cecum, and colon. These portions of gut were homogenized and quantitative cultures of aerobic and anaerobic flora were performed. Stress alone appeared to favor the establishment of enterobacterial flora, this effect being most dramatic in the duodenum-jejunum. Sterile milk formula and frozen rat milk fed rats had a greater level of enterobacterial colonization than nursed rats or rats fed the formula plus peritoneal macrophages. Thus these leukocytes, which can be demonstrated to be viable in the stomach and jejunum, protect against colonization with enteric bacteria *in vivo*. Whether they protect through their demonstrated bactericidal activity or through other mechanisms remains to be determined.