FAMILIAL MALE PSEUDOHERMAPHRODITISM WITHOUT GYNECOMASTIA DUE TO DEFICIENT 17-KETOSTEROID REDUCTASE ACTIVITY James R. Givens, Robert L. Summitt, Winfred L. Wiser, Irwin J. Kerber, Richard N. Andersen, Univ. of Tennessee Coll. of Med., Depts. of Ob-Gyn. and Ped., Memphis.

Two sibs, reared as females, were recently evaluated at 18 (DC) and 17 (TC) years of age. Each had primary amenorrhea, excessive facial and body hair, male body habitus with no breast development, phallic enlargement, separate urethral and vaginal orifices, inguinal masses, shallow vaginal vault but no cervix or uterus. Each had a 46,XY karyotype. Urinary 17-KS were high (22-33 mg/24 hr) but pregnanetriol was normal. Plasma Δ^4 androstenedione (A) was 10X normal (1600-2600 ng%) and plasma testosterone was low to low normal for males (330-540 ng%). Plasma LH was 5X normal. Plasma estrone (E_1) was high and estradiol (E_2) was 3.4 ng% in TC. Plasma A and T were not significantly changed by dexamethasone, and 5000 units/day HCG for 4 days increased A and T minimally in DC. Pelvic exploration revealed testes, epididymes and vasa deferentia but no Müllerian derivitives. Histological examination of testes revealed marked Leydig cell hyperplasia. Spermatic venous plasma A and T were 178,000 ng% and 38,000 ng%, and E_1 and E_2 were 1600 ng% and 70 ng%. Findings suggest deficient testicular 17-ketoreductase enzyme activity. This defect in testosterone synthesis prevented in utero masculinization but did not interfere with Müllerian regression. Findings also suggest that gynecomastia is not invariably present in this condition despite plasma E_1 elevation.

CORRECTION BY PROLACTIN OF ELEVATED LEVEL OF ADRENAL 5α-REDUCTASE IN THE ANDROGEN INSENSITIVE (tfm) RAT PSEUDOHERMAPHRODITES (Ps). Allen S. Goldman and Bernard H. Shapiro, Children's Hospital of Phila. Philadelphia.

We have reported that Ps have a postpubertal elevation in adrenal steroid 5α-reductase activity characteristic of males castrated neonatally. In males the castration-induced defect can be corrected by testosterone, which requires the presence of the pituitary or by prolactin or growth hormone (Witorsch and Kitay, Endocrinol. 91:764, 1972). Radioimmunoassayed pituitary prolactin contents in the adults were significantly elevated over those of littermate males, but Ps serum levels of prolactin were not different. Prolactin (400 μG) was administered daily from 29-60 d of age to Ps and littermate males and females, and for 10 d to 5 mo. old Ps. Activity was determined as the total 5α-reduced labelled products from androstenedione and testosterone in adrenals taken from immature and adult animals. Prolactin significantly reduced 5α-reductase in Ps and males at all ages. The Ps may have a defect in the regulation of adrenal steroid synthesis by prolactin. This defect may be due to its insensitivity to the neonatal differentiating action of testosterone on the hypothalamic centers controlling prolactin.

HYPERTENSIVE VIRILIZING ADRENAL HYPERPLASIA WITH MINIMAL IMPAIRMENT OF SYNTHETIC ROUTE TO CORTISOL. Tania Gregory and Lytt I. Gardner. State Univ. of New York, Upstate Med. Ctr., Dept. of Ped., Syracuse, New York

One of the first described cases of hypertensive virilizing adrenal hyperplasia (VAH) (Pediatrics 8:805, 1951) has been followed from age 2 1/2 until age 26. Blood pressure as an infant was 150/90, and at age 25 was 220/160. During childhood patient was lost to follow-up for prolonged periods, and received no therapy from age 20 to 25. At this time 24 hr. urinary excretion of 17-KS was 89 mg.; tetrahydro 11-deoxycortisol (tetrahydro S), 47 mg. and pregnanetriol 5.7 mg. Hourly measurements of several plasma steroids by competitive protein binding were made during 24 hrs; concentration ranges were as follows (μg./100 ml): 11-deoxycortisol 6-26; cortisol 3-25; total corticoids 16.5-$>$40. Urinary cyclic AMP per 24 hrs. ranged from 5.3-11.6 nmoles/mg. creatinine before therapy, and was 1.9 nmoles after therapy. The results suggest either the formation of an alternate pathway to cortisol synthesis, or the existence of a form of VAH with 2 independent 11-B hydroxylating systems, exhibiting only minimal impairment of the synthetic route to cortisol. The latter would support the presence of 2 independent 11-B hydroxylating systems in the normal human adrenal. This has been suggested by Zachmann et al (JCE 33:501, 1971) to be true in infancy. Our observations on an adult indicate that these 2 systems may not be transitory, but persist into adulthood.

SOMATOMEDIN AND GROWTH HORMONE IN THE NEWBORN Raymond L. Hintz, John M. Seeds, and Roger E. Johnsonbaugh
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(introduced by Martha Lepow)

Somatomedin (SM) was measured by porcine cartilage bioassay and growth hormone (GH) by radioimmunoassay in 52 full term cord plasmas and 28 maternal plasmas. The SM in cord plasma ranged from 0.22 U/ml to 0.94 U/ml with a mean of 0.50 ± 0.19 U/ml (m ± S.D.) compared to an adult standard plasma pool of 1.0 U/ml. This was not statistically different from the SM of the maternal samples, 0.41 ± 0.20 U/ml with a range of 0.19 U/ml to 1.00 U/ml. The cord GH levels of 41.7 ± 36 mμg/ml were significantly higher than the maternal GH levels, 8.3 ± 4.7 mμg/ml, $p \leq 0.01$. The low relative value of SM in the cord plasma is consistent with that found during early childhood, and may reflect a physiologically lower level of requirement. The high neonatal GH levels are hypothesized to be a compensatory increase to overcome factors suppressing SM production. Estrogens are known to be one factor preventing the stimulation of SM by GH. Estradiol (E2) was measured by competitive protein binding in 20 cord plasmas and was markedly elevated in all, ranging from 1.05 to >5 mμg/ml. In addition, it is possible that the production mechanism for SM is not fully mature in fetal life. These observations are consistent with the hypothesis that SM is involved in the feedback control of GH and that the high newborn GH levels reflect the competence of this mechanism, not immaturity.

CRETINISM IN LAMBS:AN EXPERIMENTAL INTRAUTERINE MODEL. D.R. Hollingsworth and R.P. Belin, (Intro. by C.C. Mabry) Univ. Kentucky Col. Med., Depts. Ped. and Surg., Lexington.

Intrauterine deprivation of thyroxine in lambs causes developmental changes analagous to human congenital cretinism. Intrauterine fetal thyroidectomies were performed at 56-80 days gestation. Thyroidectomized neonatal lambs showed gross evidence of cretinism with immature wool coats, wobbly gaits, inability to suck, weak bleats and radiologic evidence of markedly delayed bone ages. In three twin pairs with one fetus thyroidectomized, the differences between normal and cretin lambs were striking. Amniotic fluid thyroxine by column (T_4/Col) was measured at thyroidectomy and at delivery by Cesarean section. T_4/Col was measured throughout pregnancy in ewes, shortly after birth in lambs and thereafter. Average T_4/Col in pregnant ewes was 2.8μg% (1.4-6.0). Average amniotic fluid at surgery (19 animals) was 1.7μg% (.5-3.6). In twin pairs with one fetus thyroidectomized, normal fetus T_4/Col average was 4.8μg% (3.5-5.6) while cretin values were 0.7-1.6μg%. In these twin pairs at Cesarean section average amniotic fluid T_4/Col was 0.96μg% for both normal control and cretin animals.

Conclusions: (1) Intrauterine fetal lamb thyroidectomy with subsequent thyroxine deprivation in utero produced morphologic, behavioral and chemical changes analagous to human athyrotic cretinism. (2) Amniotic fluid T_4/Col did not reflect fetal thyroid status, thus precluding the monitoring of amniotic fluid T_4/Col levels prenatally as an effective early detection method for cretins.

QUANTIFICATION OF PLASMA CORTISOL AND URINARY 6β-HYDROXYCORTISOL IN MOTHER-INFANT PAIRS. Marjorie G. Horning, Serrine S. Lau, Amelia Hung, Wanda G. Stillwell and Reba M. Hill, (Intr. by Louis L. Hill). Inst. for Lipid Research and Dept. of Ped., Baylor Col. of Med., Houston, Texas.

A simple rapid procedure for the quantitative extraction of plasma cortisol and urinary 6β-hydroxycortisol using an ammonium carbonate-ethyl acetate extraction procedure has been developed; 1-2 ml of plasma and 20 ml of urine were used. The extracted steroids were converted to methoxime-trimethylsilyl ether derivatives and quantified by selective ion detection using a gas chromatograph-mass spectrometer-computer system. By means of this technique cortisol and 6β-hydroxycortisol can be detected in nanogram quantities. In one mother-infant pair the concentration of cortisol was 725 ng/ml in maternal plasma, 130 ng/ml in neonatal plasma (29 hr after birth) and 190 ng/ml in placental venous plasma. The concentration of 6β-hydroxycortisol in the neonatal urine dropped from 32 μg/24 hr on day 2 to 3 μg/24 hr on day 15; the concentration in a sample of maternal urine collected at delivery was 7 μg/ml. Comparable results were obtained with other mother-infant pairs.