**23** W.G. SIPPELL*, W. MÜLLER-HOLVE*, F.BIDLINGMAIER, D.KNORR. Div. of Paediatr. Endocrinol., Children's Hospital, and 2nd Hospital for Women, University of Munich, Germany.

*Concentrations of Eight Unconjugated Steroids in Human Amniotic Fluid Throughout Gestation.**

Since corticosteroids have been shown to be essential for fetal organ maturation, knowledge of their endogeneous levels during fetal life is fundamental. Therefore, unconjugated progesterone(P) and 17α-hydroxyprogesterone(OHP), 11-deoxycorticosterone (DOC) and 11-deoxycortisol(S), corticosterone(B) and cortisol(F), aldosterone(A) and cortisone(E) were simultaneously determined by specific RIAs after automated LH-20 chromatography in 54 control samples of amniotic fluid obtained at 16 to 40 weeks of pregnancy. Whereas the progestins P and OHP increased significantly ($p<0.01$) only after 25-30 weeks from means of 17.4 and 1.8 ng/ml in early pregnancy to 28.3 and 3.3 ng/ml at term, all corticosteroids except E showed a gradual, and highly significant ($p \ll 0.001$) rise throughout gestation which was most pronounced in the biologically most active steroids F and A whose mean levels rose from 7.4 to 51 and from 0.082 to 0.471 ng/ml, respectively. E levels rose ($p<0.01$) from 9.94 ng/ml at 16 - 19 weeks to 16.8 ng/ml at 31 - 35 weeks, then dropped ($p<0.01$) to 10.8 ng/ml at term. Precursor to substrate ratios suggested a significant, rather gradual activation of fetal 21-hydroxylase (P/DOC and OHP/S), 18-hydroxylase + 18-OH-dehydrogenase (B/A) and 11β-hydrogenase(E/F) throughout gestation, whereas the 11β-hydroxylase activity (DOC/B and S/F) did not increase significantly.

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**24** M. ZACHMANN, J. GIRARD, G. DUC, R. ILLIG and A. PRADER, Depts. of Pediatrics, Universities of Zurich and Basel, Switzerland

Prenatal manifestation of isolated ACTH-deficiency.

In a 34 yr old pregnant woman, serum(S)-HPL (3.3 ug/ml, 34 weeks) and urinary (U)-HCG (19000 IU/24 h, 28 weeks) were normal, but U-estriol (5.4, 4.5, 3.5mg/24h at 32, 33 and 34 weeks) was low without any complications. A boy (48.5 cm, 2980 g) was delivered after 38 weeks with Apgar score 9/10/10. He had neonatal hypoglycemia (31 mg/dl), muscular hypotonia, transient hyperbilirubinemia, and unilateral cryptorchidism. U-16-hydroxylated steroids and THE-response to ACTH were normal excluding placental sulfatase deficiency and congenital adrenal hypoplasia, but U-THS after a single dose of metyrapone(M, 500mg/$m^2$) was <60μg/12h. At age 4 yrs, extreme fatigue, spells of daytime sleep, and aggressive behavior occurred 3 - 4 times a week. Plasma cortisol (F) responded to ACTH (4.0 - 20.3 μg/dl), but U-THS after M was extremely low (<10 μg/$m^2$/12h). With severe insulin induced hypoglycemia (14 mg/dl), S-ACTH increased insufficiently (87 to 102 pg/ml, normal maximum 216-522pg/ml). GH-response to insulin and arginine and TSH response to TRH were normal, while the LH and FSH response to LHRH was low. Treatment with F (10 mg daily) resulted in disappearance of the symptoms. It is concluded that fetal ACTH-deficiency may be a cause of low maternal U-estriol.

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**25** M.J. Dillon, J.V. Leonard*, J.M. Buckler, D. Ogilvie*, D. Lillystone*, J.W. Honour* and C.H.L. Shackleton. Hospital for Sick Children, London; Paediatric Dept. University of Leeds; Clinical Research Centre, Harrow, England.

Pseudo hypoaldosteronism (PHA). Use of plasma renin/aldosterone profile and gas chromatographic/mass spectrometric (GC/MS) analysis of urine in diagnosis.

Ten infants with PHA presented with urinary Na loss, hyperkalaemia and ostensibly normal renal and adrenocortical function. Plasma renin activity (PRA) and aldosterone concentration (PA) were markedly increased in all cases and GC/MS analysis of urine revealed characteristically increased excretion of aldosterone and its metabolites. Na supplementation was effective treatment and could, in the majority of patients, be discontinued between 1 and 2 years of age, even though the primary defect persisted. The use of the above investigative techniques allows rapid distinction between PHA and 18 oxidation defects in aldosterone biosynthesis, and may reveal the true incidence of PHA amongst children with unexplained sodium wasting disease.

**26** A. ROITMAN*, S. ASSA*, R. KAULI and Z. LARON. Institute of Pediatric and Adolescent Endocrinology, Beilinson Medical Center & Sackler School of Medicine, Tel Aviv University, Israel.

Prolactin deficiency, obesity and enlarged testes - a new syndrome?

An infant with progressive obesity and bulimia present from birth was first seen by us at the age of 1 year and has now been followed for 3 years. He grew consistently along the 90th percentile with slight bone age retardation. He had enlarged testes for age (4ml). His motor and mental development was slightly retarded. The main laboratory findings were: a) persistently low basal prolactin levels and very low response (peaks < 5 ng/ml) to TRH, metoclopropamide, 2-deoxyglucose and insulin hypoglycemia, b) low-normal serum thyroxin (4.9-6.9 μg/dl) with subnormal responses of TSH to TRH (peaks 3.6 and 7 μU/ml), c) exaggerated response of FSH to LH-RH (peaks 4.0, 4.5, 8.0 mU/ml) and exaggerated testosterone response (300 ng/dl) after HCG (1500 Ux3). CNS investigation which included a CAT-scan revealed no pathology. It is concluded that this child has a hypothalamic-pituitary disturbance not hitherto described. The endocrine findings can be explained by an oversecretion of LH-RH and PIF and lowered secretion of TRH, in addition to a stimulation of the hypothalamic appetite center.

Z. Laron - Established Investigator of the Chief Scientist's Bureau Ministry of Health.

**27** A.S.GOLDMAN* and W.BOUTWELL* (intr. by V. Stanescu). Teratology Division, Children's Hospital of Philadelphia, Philadelphia, PA.

Biochemical mechanism of corticoid-induced cleft palate in rats linked to anti-inflammatory action.

Glucocorticoids produce cleft palate in offspring of rodents in direct relation to their anti-inflammatory potency. Recently, the anti-inflammatory action of glucocorticoids has been shown to be inhibition of arachidonic acid release from membrane phospholipids in several different models of inflammation in direct relation to anti-inflammatory potency. Thus, we have determined whether the production of cleft palate in rat fetuses by dexamethasone 3.5 mg/kg on days 12 to 15 of gestation is affected by concurrent injections of arachidonic acid 300 mg/kg. This produced a marked correction of the degree of cleft palate produced by dexamethasone (59/146, 40.4% vs. 129/180, 71.7%; P=0.034 Mann-Whitney test). Pregnant rats were also treated with either dexamethasone or saline on days 12 to 14 and $^3$H-arachidonic acid on day 15. After four hours fetuses of dexamethasone-treated animals had significantly increased uptake of $^3$H vs. controls. Moreover, the increased $^3$H was incorporated chiefly into phospholipid demonstrating a reverse of release of fetal palatal arachidonic acid. Thus, the teratogenic action of corticoids appears to be due to their anti-inflammatory action.

**28** V.STANESCU, R. STANESCU* and P.MAROTEAUX*. Hôpital des Enfants-Malades, Paris, France.

Growth cartilage abnormalities in osteochondrodysplasias.

Histological histochemical, electron microscopical and microchemical studies were performed on growth cartilage in 68 cases of 19 different forms of osteochondrodysplasia. 14 "atypical" cases were also studied.

Abnormalities of proteoglycans were found in Kniest disease, pseudo-achondroplasia, spondilo-epiphyseal dysplasia (Kozlowski type) and strongly suggested in thanatophoric dwarfism. Abnormalities of collagen were found in fibrochondrogenesis and in diastrophic dwarfism. There was an accumulation of intracellular lipid in pycnodysostosis and hypochondrogenesis and of glycoproteins in several atypical cases. In a pair of twins with atypical spondilo-epiphyseal dysplasia the presence of many multinucleate chondrocytes suggested an impairment of cell division. The cytochemical and ultrastructural abnormalities found in cases of polyepiphyseal dysplasia with a probably recessive transmission were different from those observed in typical polyepiphyseal dysplasia (dominant, Fairbank type). A heterogeneous group of cartilage abnormalities was found in chondrodysplasia punctata. In several cases of chondrodysplasia prococious hip arthrosis developed ; abnormalities of articular chondrocytes were histochemically identical to those found in growth cartilage of patients with the disease.