105 ADRENARCHE AND URINARY EXCRETION OF ANDROGEN METABOLITES IN GONADAL DYSGENESIS (GD)

Janos HOMOKI, Stefan WUDY and Walter M. TELLER, University of Ulm, Dept. of Pediatrics, Ulm, F.R.G.

To examine the suggestion that adrenarche is independent from gonadarche we determined the 24h urinary excretion of 5 androgen metabolites by 14 patients with karyotypes 45,XO (group A) and by 8 patients with chromosomal mosaics or structural X abnormalities (group B) compared to 21 healthy girls (group C). Chronological ages: (median, range); A: 13.6, 2.9-18.1, B: 12.3, 9.2-20.7, C: 10.4, 5.6-15.1 years, respectively. Pubic hair: (median, range); A: 1, 1-3, B: 1-2, 1-4, C: 2, 1-5 stages, respectively. The method used consisted of Sep-pak extraction, enzymatic hydrolysis, derivative formation and capillary column gas chromatography. Statistics were done by multiple linear regression and Wilcoxon test. Results: (mg/24h, median, max)

	Group A	B	C
DHEA	0.1;1.5*	0.1;0.5*	0;0.2
16α OH-DHEA	0.2;0.9*	0.2;0.3	0;0.2
16β OH-DHEA	0.1;1.2	0.1;0.1	0;0.2

*($p < 0.03$)

In contrast to An and Et the excretion of DHEA and its metabolites was significantly higher in A and B compared to C. Conclusion: The adrenarche in GD is comparable to healthy girls. In GD the elevated excretion of DHEA and its metabolites may be due to adrenal stimulation by an as yet unknown adrenal androgen stimulating hormone. Supported by DFG (Ho-471).

106 SCHWANGERSCHAFTSPROTEIN (SP1): IN VITRO DELIVERY INTO MATERNAL AND FETAL CIRCULATION

Ivo Henrichs, Reiner Benz, Alfred S. Wolf and Walter M. Teller. University of Ulm, Centers of Pediatrics and Obstetrics, D-7900 Ulm, F.R.G.

The pregnancy-specific β_1-glycoprotein or schwangerschaftsprotein (SP1) exists in two forms: SP1ß is of trophoblastic origin and a glycoprotein with a molecular weight of 90,000 daltons. Together with a second protein which is not produced by the placenta it occurs in its second form SP1 . It is accepted that the rising concentration of SP1 during pregnancy reflects the growth of the placenta. - Is there a detectable release of SP1 also into the fetal circulation? To study this question, 9 human term placentae were investigated for 90 to 120 min by an in vitro perfused open placental lobule preparation. A radioimmunoassay measured SP1ß and SP1α simultaneously. The sensitivity of determination was $\leq$ 2,5 ng/ml. Results:

1. In the serum free fetal venous outflow, the concentrations of SP1 in all placentae were between 2,2 - 11,75 ng/ml.- The calculated release was 3,43 ng/min/g placenta (median; range 2,38 - 4,67).
2. The maternal venous concentrations of SP1 were between 175 - 862 ng/ml.- The calculated release was 830,4 ng/min/g placenta (median; range 621 - 1175,4).

Conclusion: The in vitro measurements show evidence for the release of SP1 into fetal circulation. With regards to fetal and maternal blood volume, there could exist different half-life times in mother and neonate.

107 MICROFILTER PAPER METHOD FOR CORTISOL RADIOIMMUNOASSAY AND ITS APPLICATION TO MASS SCREENING FOR CONGENITAL ADRENAL HYPERPLASIA (C.A.H.)

Kenji Fujieda, Nobuo Matsuura, Masaru Fukushi and Nobuo Takasugi, Department of Pediatrics, Hokkaido University School of Medicine and Sapporo Institute of Public Health, Sapporo, Japan

Since 1982, City of Sapporo has been conducting regional screening program for C.A.H. In this program, four out of 63000 newborns have been found to be C.A.H. At the cut-off point of 5ng/ml 17-OH progesterone, recall rate is about 1%. Prematurity and perinatal complication of neonates contribute this high recall rate. Therefore, in order to make recall rate smaller, cortisol level was determined from filter paper. ϕ 5mm filter paper disc was extracted with dichloromethane and then cortisol was assayed using specific antiserum and ^3H cortisol as a tracer. Data were expressed as ratio of 17-OHP/cortisol (M±S.D.). Results obtained are as follows.

	C.A.H. before Rx	False positive	Premature	Normal Newborn
N	9	12	13	20
17OHP/Cortisol	2.1±0.8	0.03±0.01	0.05±0.04	0.03±0.03

These results suggest that cortisol determination from filter paper in addition to 17OHP determination can remarkably reduce the recall rate of C.A.H. at risk.

108 A NEONATAL MASS-SCREENING FOR CONGENITAL ADRENAL HYPERPLASIA (CAH) BY FLUORESCENCE ENZYME IMMUNOASSAY (EIA) METHODS.

K.Shimozawa, J.Yata, T.Kitagawa, M.Murata, Y.Tsuchiya, A.Kawauchi, M.Matsumoto, K.Okada & Y.Watanabe. Dept. of Pediatr. Tokyo Med.& Dent. Univ., Dept. of Pediatr. Surugadai Hosp. Nippon Univ, Dept. of Pediatr. the 2nd Hosp. Tokyo Woman's Med.Colla, Dept. of Pediatr. Kiyose Children's Hosp, Tokyo Assoc. of Health Service & Tokyo Branch of Jap. Assoc. for Maternal Welf.

We have carried out a pilot neonatal mass-screening for CAH due to 21-hydroxylase deficiency (21-OHD) since Jan. 1984 in Tokyo, Japan, using two fluorescence EIA methods for "Disc-17-hydroxyprogesterone (17-OHP)" measurement, which are a direct EIA by ß-galactosidase (ß-gal method) and an extractive EIA by peroxidase (POD method). During a period of 11-months, 25,546 neonates were examined and the mean±SD values by ß-gal and POD methods were 18.1± 12.4 and 1.78±1.58 ng/ml, respectively. We decided the 99th-percentile value in ß-gal method and the 99th-percentile value and/or 5ng/ml in POD method as re-sampling points, resulting 0.8% (213/25,546) were candidates for re-sampling. If neonates might show high "Disc-17-OHP" concentration beyond 20ng/ml, we recalled them immediately for detailed evaluations. As a result, 4 infants proved to have 21-OHD and the incidence of 21-OHD was calculated to be 1/6,387. Although there were many low-birth weight infants (47.3%) in the candidates for re-sampling, their absolute "Disc-17-OHP" values were much lower than those in the detected patients.

The present study demonstrates that the fluorescence EIA methods for "Disc-17-OHP" measurement are well applicable for neonatal mass-screening for CAH and indicates that the incidence of 21-OHD is much greater than that previously reported by case-assessment.

109 CONGENITAL ADRENAL HYPERPLASIA (CAH) - 2 UNUSUAL CASES WITH ADRENAL INSUFFICIENCY AND COMPLEX URINARY METABOLITE PATTERN.

M. Damkjær Nielsen, K.E. Petersen, I. Winsløw and N. Hobolth. University of Copenhagen, dep. of Clinical physiology, Glostrup Hospital and dep. of pediatrics, Hvidovre Hospital. Dep. of Pediatrics, Kolding Hospital, DENMARK.

Among a large group of CAH, 21 hydroxylase deficiency (21 OH-def) studied - 2 atypical cases were observed. (Plasma values are given in nmol/l and urinary excretion in mg/24h). PLH, a girl born virilized in 1969, had elevated excretion of 17 KS (3), she was a salt loser and is HLA A3B47 homozygous. During subsequent years of control 17 OH-progesterone (17 OHP), androstenedione (Adione) and pregnanetriol (Ptriol) never was elevated and aldosterone secretion allways subnormal. The pt. was reevaluated at the age of 13 years and during cortisone therapy. ACTH stimulation (60 min) showed no increase in 17 OHP (1.2) or cortisol (F) (405-279). ACTH stimulation (3 days) showed a non-significant rise in F-metabolites (10.7-12.8), 17 KS (1.3-1.5) and a moderate increase in Ptriol (0-3.6). Presumably the patient has 21 OH-def in adrenals with insufficient steroid production. - MLA, a girl born virilized in 1981 had very high values of 17 OHP (238) and Adione (>35). There was a subnormal response in F (60 min) after ACTH (300). The urinary steroid metabolite pattern was very peculiar for a case with 21 OH-def. During ACTH stimulation (3 days) there was only a slight rise in different metabolites: F-metabolites (0.17-1.1), 17 KS (0.03-0.08), Ptriol (0.07 -0.26), 16 OH-pregnenolone (0.1-0.6) and 16 OH-DHA (0-0.1). Furthermore many unknown steroids were found.

110 CURRENT MANAGEMENT OF CONGENITAL ADRENAL HYPERPLASIA (CAH): A SURVEY OF THE LAWSON WILKINS PEDIATRIC ENDOCRINE SOCIETY (LWPES).

Penelope P.Feuillan, Gordon B. Cutler, D.Lynn Loriaux & George P. Chrousos. NIH, NICHHD, Developmental Endocrinology Branch, Bethesda, Md.

Most studies have shown that patients with virilizing CAH are ultimately shorter than their peers. Although great progress has been made in the treatment of CAH, standard criteria for the management of this condition have not been developed. To assess current treatment practice for children with CAH with respect to drug, dose, dose schedule and criteria for dose adjustment, we polled by questionnaire all members of the LWPES. This summary is based on a response of 35%.

Most respondents use hydrocortisone (76%). Some prefer cortisone acetate (17%) and a few use prednisone (7%). Of those using hydrocortisone, 1% give 5-10 mg/m^2/day, 63% give 10-20 and 36% give 20-30 mg/m^2/day. Treatment is given on a tid schedule by the majority (66%), the rest use a bid schedule. None give hydrocortisone or cortisone once daily. Many distribute drug evenly over the day (52%), while others prefer a larger pm dose (30%) or a larger am dose (18%). The main indications for using Florinef are an elevated PRA and salt-wasting. Some, (15%) give it to all non-hypertensive patients.

Most respondents adjusted the dose of glucocorticoid on the basis of plasma (17-OH P &/or delta-4 A) and urine (17KS &/or P triol) measures together with growth and maturation rates. Some however, rely only on serum levels (10%) or on urine measurements (5%). A few prefer to depend solely on rates of growth and maturation.

This survey supports the hypothesis that regimens used to treat CAH vary widely, particularly with regard to scheduling of medication. Thus, studies comparing different approaches to management with objective measures of outcome, such as growth rates and ultimate stature, seem indicated.