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**149**

HPLC DETECTION OF FREE CORTISOL (F) AND METABOLITES IN THE URINE OF NEWBORNS AND CHILDREN

F metabolism in newborns (Nb, age 5 days) and children (C1:1 month-6 years, C2;7-15 years) was studied by reversed phase HPLC with UV-detection[1] of urinary excretion of F, cortisone (E),6ß-hydroxycortisol (6OHF), a main F metabolite in newborns and an index of enzyme induction, and 20α-dihydrocortisol (DHFA), which recently has been shown to be a marker of altered F metabolism in adults [1]. For the detection of changes in age dependent steroid-metabolism we calculated the metabolite/F ratios and the results are only given as nmol/l (median, range).

| Group | n | F | E | DHFA | 6OHF |
|---|---|---|---|---|---|
| Nb | 46 | 19 (15- 40) | 81 (29-190) | 32 (15-155) | 211 ( 34- 962) |
| C1 | 16 | 19 (15-116) | 177 (50-300) | 107 (25-630) | 394 (136- 982) |
| C2 | 15 | 77 (15-185) | 167 (70-305) | 193 (30-800) | 936 (156-3080) |

Steroid excretion is lowest in the Nb, corresponding to their small body surface. They excrete 6OHF in relatively large amounts (6OHF/F=14.1); this ratio decreases until puberty (C2: 6OHF/F= 11.5). 6OHF was further stimulated in 8 Nb treated with phenobarbital to 2692 (899-4213). Nb excreted lower amounts of other glucocorticoids, yet more E than F (E/F=4.6); E excretion in relation to F decreases in children (C2: E/F=2.4). DHFA correlates well to F in Nb (r=0.9, DHFA/F=1.3) and increases with age more than F (C2: DHFA/F=2.5). Conclusion: In contrast to 6OHF, DHFA is not a major degradation product of F metabolism in newborns.

[1]M. Schöneshöfer et al., Clin. Chem. 32: 808, 1986

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**150**

LONGITUDINAL STUDY OF ADRENOCORTICAL STEROIDS IN LARGE FOR GESTATIONAL AGE (LGA) INFANTS AT BIRTH AND DURING NEONATAL PERIOD.

Neonatal maladaptation is frequent in LGA infants.To evaluate adrenocortical function in LGAś at birth and during postnatal adaptation,plasma aldosterone (Aldo),11-deoxycorticosterone (DOC) corticosterone (B),progesterone,17-hydroxyprogesterone,11-deoxycortisol,cortisol (F) and cortisone (E) were simultaneously followed in 9 term vaginally delivered LGA (>97.perc.) by multisteroid analysis by specific RIAs after Sephadex LH-20 chromatography in 250 µl samples.12 appropriate for gest.age (AGA) infants served as controls.All mothers were healthy with no diabetes or gestosis, no primiparae.Relevant results (LGA/AGA mean values in ng/ml):

| *p<.05 | Umb.Art. | 2 h | 12 h | 24 h | 4 d |
|---|---|---|---|---|---|
| DOC | 3.62/4.10 | 1.52/3.60* | 0.87/1.18 | 0.43/1.16* | 0.14/0.13 |
| Aldo | 0.49/0.35 | 0.58/0.17* | 0.43/0.20* | 0.51/0.17* | 0.34/0.15 |
| B | 15.7/8.52* | 6.91/9.28 | 10.7/5.23 | 4.91/0.83* | 3.23/1.85 |
| F | 173/103 * | 83.4/104 | 83.7/76.4 | 54.3/27.2* | 71.3/57.0 |
| E | 153/107 * | 55.4/83.1 | 38.8/56.8 | 22.3/41.1* | 25.2/22.6 |

Obviously,LGA infants are maintaining high Aldo levels,whereas DOC levels were lower than in AGA.High fetal glucocorticoids (B, F,E) in LGA reflect either increased fetal stress and/or placental transfer of high maternal steroids. Additionally,elevated glucocorticoids (B,F) from 12 h to 7 d point to a more stressful postnatal adaptation in LGA newborns.

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**151**

NON CLASSICAL 21 HYDROXYLASE DEFICIENCY IN CHILDREN.

Six girls and two boys presented at ages 3 to 9 years with mild clinical symptoms [pubic hair (n=7), axillary hair (n=2), mild hirsutism (n=1), clitoromegaly (n=1)]. Height Age to Chronological Age ratios and Bone Age to Height Age ratios were 1.08 ± .2 and 1.08 ± .08 (m ± SD) respectively. *Prestimulated* values of 17-Hydroxyprogesterone (17OHP) and 21 Deoxycortisol (21DF) moderately exceeded those of controls (C) in 5/8 and 6/8 cases, respectively, Testostérone and δ4-Adrostenedione in 1/2 and DHA in 1/4. *After short-acting Synacthen stimulation* (250 µg IM), 21 DF rised to values [10 ng/ml(3--33)]* significantly (p<.001) higher than those of (C) [.3(.2-.9)]* and Heterozygotes (HZ) [2(.6-7)]* in spite of some overlap with the later group. 17OHP stimulated levels [30 ng/ml(11-83)] were definitely higher than (C) [1.4(.5-4)]* and (HZ) [3(1-8)]*. These hormonal patterns closely reproduce Non Classical 21 OH-Deficiency in adults. Treatment schedules were managed according mainly to growth and bone maturation. [Geometrical mean (95% Confidence limits)]*.

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**152**

FOUR CASES OF CONGENITAL LIPOID ADRENAL HYPERPLASIA (CLAH) (20-22 DESMOLASE DEFICIENCY)

CLAH is a rare and often fatal disease due to a defect in the conversion of cholesterol to pregnenolone. We report on 4 individuals with a female phenotype, 3 of whom had a 46,XY karyotype, while 1 had a 46,XX karyotype. All patients presented with signs of adrenal insufficiency during the first months of life, and one of them died 11 weeks of age. Of the surviving patients, 2 were sisters, while their parents as well as the parents of the fourth individual were first cousins. These 3 latter patients have developed normally on glucocorticoid and mineralocorticoid replacement (observation time 14, 6, and 4 years). The diagnosis of the surviving individuals were based on extensive hormonal analyses including urinary and serum levels of C19 and C21 steroids and their metabolites, serum levels of ACTH, plasma renin activity, and ACTH and hCG stimulation tests. The diagnosis of the fatal case was based on microscopy of the adrenal glands showing changes typical for CLAH. The results suggest 1) that a recessive mode of inheritance might be involved, 2) that the patients may develop satisfactorily on glucocorticoid and mineralocorticoid replacement, and confirm 3) that the disease may affect 46,XX individuals.

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**153**

RESPONSE TO TREATMENT IN CONGENITAL ADRENAL HYPERPLASIA (CAH) DURING EARLY INFANCY.

The diagnosis of CAH and treatment response, based on plasma steroid measurements, was reviewed in 9 infants (5M, 4F) in relation to hydrocortisone (HC) dose and growth velocity in the first 3 years. Two siblings had 11β-OH deficiency; the remainder had salt-losing 21OH deficiency. Mean pre-treatment 17OH-progesterone (17P) and 11-deoxycortisol levels were 367 and 2000 nmol/l respectively in the relevant groups. Plasma 17P levels fluctuated widely during the day (31-4130 nmol/l) with no diurnal pattern. Testosterone (T) levels (mean 13.2, range 1.5 - 26 nmol/l) were increased to adult male levels, but no male was virilized. Maintenance HC (mean 25.7 mg/m$^2$/day) in 3 divided doses (and fludrocortisone 0.1-0.15 mg/day) normalized 17P levels by 3 months (median 33, 75th centile 90 nmol/L); mean T levels fell to 1.1 nmol/l (range 0.4 - 2.7) by 3 months in females, whereas similar levels in males were delayed until 6 months due to testicular T production. A mean HC dose falling to 15.3 mg/m$^2$/day by 3 yr maintained normal 17P and T levels; growth velocity SDS was -0.91 ± 1.3 (mean ± SD) at 9 months and remained normal thereafter.

Maintenance HC doses at the onset of treatment in CAH results in satisfactory control by 3 months (including the T surge in male infants) and ensure a rapid growth velocity characteristic of early infancy.

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**154**

IS THERE A ROLE FOR ANGIOTENSIN II (AT II) IN MONITORING OF THERAPY IN CONGENITAL ADRENAL HYPERPLASIA (CAH)?

16 patients with CAH were studied at home.Blood was collected fasting at bed rest between 7-8 AM and 3 hrs. after normal activity.Specimens were immediately centrifuged on ice and frozen.24-hour urine and 3-hourly saliva samples during daytime were obtained from 12 noon on the previous day.17-OH-progesterone (17-OHP) was measured in plasma and saliva;testosterone,aldosterone,renin activity (PRA) and AT II in plasma only and 17-ketosteroids,pregnanetriol (P'triol) and sodium in the urine. No values were normally distributed.Statistical evaluation used the Wilcoxon rank test and discriminant analysis.

Results: highly significant correlations existed between plasma and saliva 17-OHP at 8 AM, PRA and AT II at 8 and 11 AM,and 8 AM 17-OHP and P'triol e.g. When patients were divided into well and poorly suppressed groups according to their 8 AM 17-OHP- and P'triol-values to find additional useful monitoring parameters,saliva 17-OHP proved highly discriminating,while the probability of error was 18% for AT II and 26% for PRA. Discriminant analysis showed correct classification e.g. by saliva 17-OHP in 77%,but none by PRA or AT II.

Conclusion:AT II has no value in monitoring CAH-therapy