## 161 THE STEROID BINDING GLOBULINS CBG AND SHBG IN MATERNAL AND FETAL BLOOD AND IN AMNIOTIC FLUID DURING THE PERINATAL PERIOD

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To investigate the regulation and physiological significance of the steroid binding globulins in fetal life, we measured the distribution of CBG and SHBG in maternal and fetal blood and in amniotic fluid. In spite of high circulating estrogens a highly consistent transplacental gradient was found between mother and fetus: CBG 20.1 ± 3.4 (SD) µg/ml (n=32) versus 82.6 ± 12.8 µg/ml and SHBG 3.0 ± 1.0 (SD) µg/ml (n=62) versus 40.1 ± 9.2 µg/ml. The concentration of both proteins in amniotic fluid was variable at a significant lower level: CBG 3.8 ± 2.1 (SD) µg/ml and SHBG 1.1 ± 0.6 µg/ml (n=27), respectively. During the first puerperal week maternal CBG and SHBG concentrations fell markedly, while the CBG-levels in the newborns remained unchanged (17.5 ± 5.8 µg/ml) and, in spite of a sharp estrogen decrease, the SHBG-levels increased significantly: (5.6 ± 1.8 µg/ml). These findings suggest, that fetal and maternal CBG- and SHBG-levels are independently regulated. While maternal steroid binding globulins are highly estrogen dependent, the regulation in fetuses and newborns seems to be controlled by other mechanisms. These may be related to an autonomous process which may regulate the steroid hormone activity during this period.

## 162 ANDROGEN RECEPTORS IN "TRANSITORY ANDROGEN INSENSITIVITY SYNDROME" OF THE NEWBORN

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Androgen receptor analyses of scrotal tissue from a boy with congenital growth hormone (GH) deficiency associated with micropenis, done at age1 and 3yrs, revealed a decreased cytosolic binding for testosterone(T) and dihydrotestosterone(DHT), compared to controls or similar age* (patient vs controls, age1 and 3yrs, respectively; Nmax for T: 28 and 30 vs 150±30 and 130±28 fmol/mg protein, M±SD; Nmax for DHT: 30 and 114 vs 205±98 and 480±135). Nuclear T receptor was not detectable at age1, but showed abnormal high binding at age 3yrs (90 vs 22±5). Nuclear DHT receptor was within normal limits at age1 and 3yrs (117 and 180 vs 91±28 and 181±26). Tissue specific 5α reductase (A5R) activity was found to be 3.2 pmol/h/mg protein (age1) and 16.1 (age3)(controls*: 15.8±1.9, M±SD).
HCG stimulation resulted in a 3-fold rise of plasma T (0.15 to 0.46 ng/ml) at age1 and a 6-fold rise (0.18 to 1.09) at age 3yrs, without change of DHT. Strechted penile length was 1.1 cm (≤3.centile) at age1 and increased up to 3.2cm (>25.centile) at age3.

The receptor and A5R data indicate a catch-up growth and normalization of the external genital status. We postulate a "transitory androgen insensitivity syndrome" in this patient.

*K Herkner et al. J steroid Biochem.24 (1986) 239-243

## 163 URINARY ANDROSTANEDIOLS CHARACTERIZE THE GENITAL STATUS OF THE NEWBORN WITH TRANSITORY ANDROGEN INSENSITIVITY SYNDROME (TAIS)

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Urinary excretion of 5α-androstane-3α,17ß-diol (5α-diol) and 5ß-androstane-3α,17ß-diol (5ß-diol) was evaluated by capillary gas chromatography as biochemical markers for the development of the external genitalia in an infant with micropenis and cryptorchidism secondary to TAIS*. Plasma testosterone (T) and dihydrotestosterone (DHT) as well as excretion of their urinary metabolites 5α-diol and 5ß-diol were analyzed prior to and after short HCG stimulus.
A 3-fold rise of T was noted at age 1yr (0.15 to 0.46 ng/ml) and a 6-fold rise at age 3yrs (0.19 to 1.09).DHT raised slightly at both ages. Urinary 5ß-diol was below detection limit (2ug/24hrs) at 1yr, only detectable on day 3 of the HCG stimulus at age 3yrs (6), but normal at age 4yrs (112). In contrast, normal values were observed for 5α-diol at ages 1yr (51.4), 3yrs (65.9) and 4yrs (84.2), respectively. Controls of similar age*, n=3 5α-diol 72.5±27.1, 5ß-diol 128.7±35.1 (M±SD). Stretched penile length was 1.1cm (<P3) at age 1yr, 3.2cm (P25) at age 3yrs and 4.1cm (P50) at age 4yrs.

We postulate, that low urinary 5ß-diol excretion in early infancy reflects insufficient development of the androgen dependent tissue. Moreover, when combined with normal 5α-diol excretion, a physiologic male sexual development can be expected.

*A Lischka et al. Ped Res 19, 1087 (1985).

## 164 REDUCED NEPHROTOXICITY OF CISPLATINUM BY USE OF AMILORIDE

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High-dose (100 mg/m$^2$ body surface) cisplatinum (CPL) for treatment of osteogenic sarcoma causes a considerable degree of nephrotoxicity. We studied 18 patients receiving high-dose CPL 37 times. In 17 treatment episodes amiloride, a diuretic agent, was given (dosage about 0.15 mg/kg body weight). Renal function was monitored by endogenous creatinine clearance (CC), serum β2-microglobulin (β2-M), urinary β2-M and alanin-aminopeptidase (AAP) urinary excretion. In response to CPL administration urinary β2-M and AAP rose tremendously with a peak level about 25 times and a 24 hours excretion about ten-fold higher than before CPL treatment. Serum β2-M and CC were less alterated. After additional use of amiloride urinary β2-M showed a peak level below 30 per cent and a 24 hours excretion below 45 per cent compared to the treatment episodes without amiloride. The AAP excretion did not change significantly. The different effect of amiloride on β2-M and AAP may give a hint to its way of action, since these two substances indicate tubular damage of different localization.

## 165 CEREBROSPINAL FLUID CERULOPLASMIN IN CHILDREN AFFECTED BY ACUTE LYMPHOBLASTIC LEUKEMIA.

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Ceruloplasmin(CPN)in 57 cerebrospinal fluid(CSF)samples from 30 children affected by acute lymphoblastic leukemia(ALL)undergoing central nervous system(CNS)prophylaxis with intrathecal methotrexate(MTX)+prednisone(PD)+cytosine arabinoside(Group I)or MTX+PD(Group II),and from patients off therapy for at least 1 year(Group III) was studied by an immune nephelometric method.Controls were CSFs from adults undergoing myelography for diagnosis of discal hernia.All samples contained less than 6 cells/µl and less than 600 mg/l protein.

| CSFs | n | CPN(mg/l) mean | (range) | P |
|---|---|---|---|---|
| Group I | 15 | 0.438 | 0-1.06 | <0.002* |
| Group II | 24 | 0.614 | 0-1.73 | 0.005* |
| Group III | 17 | 0.777 | 0-2.88 | >0.05 * |
| Controls | 16 | 1.326 | 0.4-4.5 | |

*determined vs controls by Wilcoxon test

Whether the decrease of CPN reflects an impaired turnover or an alteration of its immunologic reactivity,remains to be elucitated.A defect in this powerful antioxidant may expose patients to CNS damage by $O_2$ radicals.

## 166 THE RELATIONSHIP BETWEEN DISTURBED LIVER FUNCTION, IRON AND MARKERS OF HEPATITIS B VIRUS INFECTION IN BRITISH CHILDREN WITH BETA THALASSAEMIA.

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Although chronic liver dysfunction in β Thalassaemia major has been associated with transfusion induced iron overload, Chronic Hepatitis B virus (HBV) infection has also recently been implicated. We, therefore, studied 16 children (8 male, 8 female) aged 1-14 years, to assess the influence of iron overload measured by serum ferritin and the volume of transfused blood, and the presence of markers of HBV infection (HBs Ag, HBc Ab, HBs Ab) on liver dysfunction. Thirteen children had elevated serum transaminases; 6 of these had received > 100 units of blood and had had serum ferritin levels of > 6,000mcg/L. All 16 received chelation therapy with a fall in serum ferritin levels from a maximum of 1280-13,900mcg/L to a minimum of 370-5,450mcg/L. Concommitant improvement in liver function occured in 10. Although 11 patients had visited HBV endemic areas and 6 had been transfused there, only 2 developed markers of HBV infection. Both had clinical, biochemical and serological evidence of acute HBV infection; they had abnormal liver function prior to the HBV infection, and transaminases returned to these levels after the acute HBV infection.

Thus in children, iron overload rather than HBV infection is the major cause of chronic liver dysfunction. However, active immunisation against HBV is necessary to protect these children who commonly receive transfusion whilst in endemic areas.