106 L. DAVID, E. de PERETTI and R. FRANCOIS. Service de Pédiatrie, S bis, Hôpital Edouard Herriot and Unité INSERM U 34, Lyon, France. Abnormal adrenal dehydroepiandrosterone (DHA) production : a frequent, curable cause of hirsutism in childhood and adolescence ?

The case of a 13 years old pubere girl with severe hirsutism and irregular menses is presented. The hirsutism was noted since infancy ; puberty had started at the age of 9. She had no sign of virilism. Important hirsutism was also present in the mother. Markedly elevated plasma DHA level was found (934 ng/100ml) ; plasma testosterone (T) level was 34 ng/100ml. Urinary corticosteroids and plasma cortisol, 17 OH progesterone, ACTH, LH and FSH levels were normal. Under synacthen administration (1mg/day/3days) plasma DHA rose to 1 556 ng/100ml and plasma T to 51,9 ng/100ml, with a normal response of plasma cortisol (8 to 26 µg/100ml) and urinary 17 hydroxycoticosteroids (5,56 to 70,9 mg/24 h). Fluoxymesterone (20 mg/day/4days) did not induce any significant change in plasma DHA : 976 ng/100ml. By contrast low dosage of dexamethasone (DXM) (0,50 mg/ day/ 3 days) induced a major decrease in plasma DHA : 117 ng/100ml ; there was no further decrease under high dosage of DXM (8mg/day/3 days) : 126 ng/100 ml. Long term treatment (15 months) with DXM (0,25 mg/day) was followed by a complete disappearance of the hirsutism and a normalisation of menstruations with plasma DHA level of 100 ng/100ml and plasma T level of 10,4 ng/100ml. Following this observation we have studied 4 similar cases of DHA dependant hirsutism without evidence of enzymatic defect : 3 adolescents 16 to 17 years old in whom hirsutism started at puberty and a 8 years old girl with a hirsutism present since infancy.

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Effect of aminoglutethimide (AG) on urinary cortisol and metabolites in patients with Cushing's syndrome (CS).

The effect of AG (4x 250 mg, 670 mg/m^2 daily) on the excretion of cortisol (RIA) and its metabolites (gas chromatography on capillary column) was studied monthly during 2 to 5 months in 4 patients with CS not due to an adenoma. Basal cortisol metabolites were moderately (total 10.9 ± 1.3 (SEM), THE 5.2 ± 0.8, THF-alloTHF 3.5 ± 0.6, cortolone 1.5 ± 0.5, β-cortolone 0.7 ± 0.2 mg/m^2/day) and free cortisol was markedly (803 ± 282 µg/m^2/day) increased. Under AG, all compounds were reduced (minimum total 1.45 ± 0.7, THE 0.73 ± 0.3, THF-alloTHF 0.41 ± 0.3, cortolone 0.13 ± 0.05, β-cortolone 0.07 ± 0.06 mg/m^2/day, free cortisol 267 ± 38 µg/m^2/day) and a non-steroidal peak appeared on the chromatogram. The reduction was most significant for the total metabolites ($p < 0.001$), followed by THE, THF-alloTHF (< 0.01), cortolone and β-cortolone (< 0.05) but not significant for free cortisol. With continued treatment, a rebound was noted after 3 to 5 months (total 4.62 ± 1.6, THE 2.82 ± 0.2, THF-alloTHF 2.45 ± 0.8, cortolone 0.63 ± 0.02, β-cortolone 0.28 ± 0.05). It is concluded that 1) AG reduces cortisol synthesis in man only temporarily as in animals, 2) paradoxic steroid increments in the early phase of treatment as reported from colorimetric analysis are non-specific, and 3) AG possibly modifies steroid catabolizing liver enzymes (inhibition of 5β-reductase and stimulation of 20α- and 20β-dehydrogenase).

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VISUAL EVOKED RESPONSES IN CONGENITAL HYPOTHYREOIDISM.

Visual evoked responses (VER) were studied in 10 children with hypothyreoidism. The age when the disease was discovered varied from 1 week to 1½ years. Five infants were younger than 3 months, three between 3 - 6 months. The diagnosis was in all cases verified by the finding of low levels of T3, T4 or PBJ and markedly increased levels of TSH in blood. Nine childrenwere examined repeatedly, 7 younger infants were followed up during several months. In all of them EEG responses to photostimulation were recorded. In 4 infants also somatosensory evoked responses (SER) were examined. Before treatment prolonged latencies and/or less mature patterns of VERs were observed. Most increased latencies were found in infants during the first months of age. During hormonal therapy latencies decreased to the normal level (or below it) and followed then the normal developmental curve. Also the response pattern became normal. Photic driving improved very rapidly, SERs if recorded, behaved in the same way as VERs. The results show, that VERs are useful for assesment of the degree of the delay in the development of the brain and effectivity of the treatment in congenital hypothyreoidism.

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Blood volume in growth hormone deficiency (GHD).

It has been shown that panhypopituitarism or GHD is associated with decreased red cell volume (RCV), blood (BV) and plasma volume (PV) (Rodriguez and Shahidi, NEJM 285: 479, 1971). No data regarding the effect of growth hormone supplementation on BV in children with GHD have been reported. We have studied BV (Evans blue) in 24 growth-retarded children without endocrine abnormalities (I), 14 untreated (II) and 23 HGH-treated children (III) with GHD of similar age (5 to 18 years). The results were as follows:

I: BV 75.9±8.1; PV 49.8±5.4; RCV 26.1±3.8 (SD)ml/kg
II: BV 67.6±8.6; PV 45.2±5.6; RCV 22.4±3.5 (SD)ml/kg
III: BV 73.7±9.1; PV 48.8±6.4; RCV 24.9±3.6 (SD)ml/kg

No significant sex differences were found in any group. In 10 patients with GHD studies were performed before and 3 to 6 months after onset of therapy. Mean weight related BV, PV and RCV increased significantly (paired t-test; p 0,001) by 15.2, 14.7, and 17.1%, respectively, to normal values. These observations of low BV in GHD and its restoration to normal values by HGH substitution provide evidence that HGH interferes with the regulation of BV.

Informed consent of patients and/or parents was obtained in all cases.- Supported by DFG (SFB 147)

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TSH and PRL response to TRH: correlation with age, sex, and gonadal activity.

TRH (200 µg/1.73 m^2, i.v.) was given to 89 normal subjects (43 males and 46 females; ages: 2.5-81 yrs.), 7 Klinefelter's (K.s.) and 11 Turner's (T.s.) syndromes. TSH and PRL response were evaluated using Δ as well as the incretory area: results were fairly similar with both methods. TSH response decreases with age (the difference is significant between children and aged subjects in both sexes); its behaviour is similar in males and females; T.s. and K.s. behave as normal subjects of the same age. As for PRL, its correlation with sex is evident; higher values in females than in males and, among the former, higher in adult than in prepuberal subjects. Moreover, PRL levels in T.s. are lower and in K.s. higher than those of adult subjects of corresponding sex. In conclusion: after TRH i.v., PRL response seems to be influenced by gonadal activity (oestrogens dependent?); while TSH shows no correlation with varying oestrogens levels, such as is found in physiological or in (tested) pathological conditions.

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Studies on a hypothalamic islet-stimulating factor in childhood obesity.

The ventrolateral hypothalamus secretes a factor that in experimental animals stimulates insulin secretion both in vitro and in vivo. This hypothalamic humoral factor is also demonstrable in serum (Martin et al.: J. Endocrinol. 1973:58:681). We studied the activity of this factor in sera of obese children. Urea treated serum was fractionated through Amicon membranes and the serum fractions between 1,000-10,000 Daltons were tested for islet-stimulating activity by measuring insulin released by isolated rat islets exposed to 5.5. mM glucose plus the test fraction. So far we have analysed sera of 12 obese children. In two cases a significant stimulation of the islets has been found. The same children presented hyperinsulinemia at OGTT. One of these patients had become obese after operation of a hypothalamic tumor. The preliminary results indicate that a hypothalamic humoral factor may play a role in the etiology of some forms of childhood obesity

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