

Nocturnal polyuria in patients with anterior hypopituitarism

Defects in water excretion and urinary dilution have been well known in patients with hypopituitarism and adrenal insufficiency, but there are few reports of nocturnal polyuria in these patients. Serial studies were done in 8 children (aged 5-13) with pituitary dwarfism and ACTH deficiency (A), 4 of them had enuresis, 5 with pituitary dwarfism and no ACTH deficiency (aged 2-10) and 14 constitutional dwarfs (aged 3-15) as controls. Daily urine volumes of these patients with A were 0.8-1.8l/day with highly concentrated urine ($>500\text{mOsm/l}$) at day-time (D) and diluted urine ($<400\text{mOsm/l}$) at night (N). The ratio of 12 hour urine volume of D/N were 0.65-1.0 in these patients with A and 1.3-4.9 in children without A. The patients with A excreted 40% of the ingested water (20ml/kg) within 4 hours in the morning and it was corrected by steroid administration. In the evening they could excrete normally 80% of the water. After an over-night fast, they could not concentrate their urine maximally, but it was also corrected by steroid administration. Their 6-hourly urine samples showed low 17 KGS without circadian rhythm. Our results suggest that they may not be able to excrete ingested water in the morning in the absence of appropriately elevated levels of glucocorticoids and excrete water late at night. We are now investigating serum levels of ADH and our results seem to support that the elevated levels of circulating ADH are involved in the impaired water diuresis in the patients.

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HLA-AB antigens and islet cell antibodies, (ICA) in insulin dependent diabetics (IDD) of Greek origin.

HLA-AB antigens, ICA and other autoantibodies were looked for in 110 IDD and in 100 controls (C). The following were found: The frequency of HLA-B8 antigen was higher in IDD than in C (32% versus 9.5%). The frequency of HLA-A1, -B15, -B7, and -B18 was comparable in the two groups. ICA was found in 62% of cases with disease duration (DD) of less than 1 month, 42% with DD of up to 1 year and 18% with DD of 1 to 5 years. There was a slightly higher frequency of other autoantibodies (PCA, ANA) in IDD than in C. No positive correlation was found between HLA-B8 antigen and the presence of ICA. The data on ICA and HLA B8 are analogous to those in other caucasian populations. However the different frequency found in certain of the HLA antigens confirms the existence of HLA heterogeneity in IDD groups.

Studies of the exercise test for growth hormone release.

The exercise test is frequently used as an initial stimulus to growth hormone release. In order to improve the reliability of this test we have studied it in young adult male volunteers, exercised on a bicycle ergometer.

The work load during each test was expressed as a percentage of that subject's maximum work capacity and was measured by continuous oxygen uptake.

The mean peak growth hormone and mean rise in growth hormone increased at different levels of exercise in 6 subjects.

An exercise test in 5 subjects which produced a growth hormone level of $>20\text{ mIU/L}$. in each inhibited response to further exercise tests 1 and 2 hours later.

Growth hormone levels after exercise were low in 5 subjects tested half an hour after breakfast and an unusual pattern of growth hormone response was found even 2½ hours after breakfast.

The value of exercise as a screening test for growth hormone deficiency could be improved by its being preceded by a period of rest and food restriction.

Assessment of ACTH deficiency in children with hypothalamic-pituitary dysfunction.

Insulin hypoglycemia (IH) is one of the most valuable procedures to test the pituitary ACTH reserve - especially as part of the combined test of hypothalamic-pituitary function. The ACTH response to IH is a steep increase from the time of maximal hypoglycemia (30 min. after insulin) to a peak value around 40 min. and lower values at 60 min. Reference values in 54 children studied for short stature and/or delayed puberty were 0 min: 11-82 pg/ml - 40 min: 50-300 pg/ml (very few in the "border line area" 50-70 pg/ml). Using these reference values and a peak plasma cortisol value of 400 nmol/l normal response were found in 29 of 39 children with hypothalamic-pituitary dysfunction (10 with tumour) - 11 of which had "border line" response. In 10 children ACTH deficiency was demonstrated. From a clinical point of view 8 children (with low or border line response) were considered to have adrenocortical insufficiency and were treated with cortisone. In the individual patients the correlation between ACTH and cortisol response is good, $R = 0.67$ ($p < 0.001$).

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High incidence of identifiable pathology in girls referred for evaluation of short stature

In published series of boys referred for evaluation of short stature the vast majority, 90-95%, are found not to have treatable pathology and carry the final diagnosis of constitutional delay of puberty or constitutional short stature. There are little published data on girls referred for decreased growth rate. We did a prospective study (looking for endocrine chromosomal or other medical pathology) on girls referred over a 2 year period for height $<3\%$. Work-up included history, P.E., karyotype, T4, TSH, IH, FSH and growth hormone (GH) dynamics. Of 33 girls studied, 5 were found to be XO Turner's and 4 were sex chromosome mosaics. Of these 9 girls, 3 had no stigmata of Turner's except for short stature. Three patients were found to have GH deficiency; in one this was secondary to a suprasellar germinoma and in the other 2 it was idiopathic. Three other girls were found to have non-endocrine systemic disease: neurofibromatosis, tracheoesophageal fistula and congenital microcephaly. The girl with neurofibromatosis had no discernable endocrine abnormalities and had a normal GH response to exercise tolerance test. Thus of those girls referred for short stature evaluation 45% had identifiable pathology, in marked contrast to much lower incidence of pathology seen in short boys. This underlines the need for careful evaluation of short girls.

6 β -hydroxycortisol: a marker for hepatic enzyme inhibition by lead.

Lead (Pb) ion is known to inhibit cytochrome P-450 dependent hepatic microsomal activity. To measure inhibitory effects of Pb on hepatic enzyme activity 6 β OHF excretion was determined in 11 children (age 2-9 yrs) with mild to moderate Pb intoxication (nl renal function) prior to chelation therapy. 6 β OHF is formed by the hepatic cytochrome P-450 dependent mixed function oxidase system. Correlations were examined between 6 β OHF and blood Pb, erythrocyte protoporphyrin (EP) and urinary Pb excretion after a CaNa₂ EDTA provocative test. The CaNa₂ EDTA provocative test provides an accurate "chemical biopsy" of chelatable lead stores. 6 β OHF excretion in normal controls was $0.28 \pm 0.03\text{ mg/m}^2/24\text{h}$. Excretion in Pb burdened children was reduced to $0.17 \pm 0.02\text{ mg/m}^2/24\text{h}$; ($p < .01$). There was a highly significant correlation between 6 β OHF and EP, ($r = -0.7$, $p < .01$) and 6 β OHF and urinary Pb ($r = -0.74$, $p < .01$) but none between blood Pb and 6 β OHF. 17OH corticosteroid and free cortisol excretion were not different from normal controls and correlations between these cortisol metabolites and EP or urinary Pb were not significant. **Conclusions:** Children with undue Pb absorption may have decreased 6 β OHF excretion. Since adrenal function is not impaired, reduced 6 β OHF excretion may be secondary to inhibitory action of Pb ion on microsomal enzyme systems. 6 β OHF measurements provide a sensitive probe when evaluating inhibitory effects of foreign compounds on hepatic enzyme activity.