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Comparison between NPH and PZI insulin in the treatment of diabetic children.

The purpose of this study was to compare the difference in the control in children treated with 1 injection of NPH or PZI. 16 children first treated with NPH + regular insulin (RI) were shifted to PZI + RI (Leo). The doses (U/Kg) were NPH + RI = 1.0± 0.2 & PZI + RI = 1.1±0.2. The control of the diabetes was estimated before the shift and after 1 year on PZI using an index which consists of the percentage of daily urinary sugar estimations (Clinitest Ames) which are under 1%. There was no difference in the afternoon, evening & total indices but the morning indices were significantly better with PZI + RI than with NPH + RI 58%±19 vs 38%±23 ($p < 0.01$). The morning index in 6 children on NPH only was 29%±19, which is very poor. As PZI insulin Leo was found to be a better preparation for the control of night glycemia, the use of 1 injection of NPH insulin has to be reevaluated. For adequate control 2 daily injections of NPH or a good PZI preparation (action not longer than 24 hrs and non antigenic) are recommended.

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ANDROGEN AROMATIZATION IN GYNECOMASTIA: IN VITRO STUDIES

The etiology of durable pubertal gynecomastia remains unexplained. Hormonal studies are controversial and receptor measurements inconclusive. A local conversion of androgens has been suggested. We have studied glandular and adipose fractions obtained from mastectomy of 3 adolescent boys. Microsomal suspension of the tissues was incubated with ^{14}C testosterone or ^{3}H-Δ4-androstenedione. Aromatization activity was measured by tritiated water formed during the incubation. Placental microsomes served as control. The identification of estrogen products was performed as follows: sodium partition, filtration on isomerase column, elution of the radioactivity corresponding to estrogens (E_3) and finally gel chromatography of that extract. In placental microsomes, aromatase activity was: 0.66 pmoles/mg protein/min; in adipose tissues: 0.14 fmoles/mg protein/min; in glandular tissues: 0.13 fmoles/mg protein/min. We conclude that in vitro gynecomastic glandular tissue transforms androgen to the same extent as adipose tissue. An exaggerated local estrogen formation can most likely be excluded.

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Progress in testing for heterozygosity in congenital adrenal hyperplasia (C A H).

In order to obtain an improved differentiation between heterozygotes and normals, the increase of 17-OHP in plasma of CAH parents (n=30) and of controls (n=31) was measured after ACTH (Synacthen) stimulation i.v. at 60' under standardised basal conditions. The ACTH stimulation was performed after suppression of the adrenal cortex with 1.5 mg dexamethasone (Dex.) given the previous evening. Females were tested between days 3 and 8 of the menstrual cycle. Plasma 17-OHP was measured by a specific RIA. The mean increase of 17-OHP was significantly higher in heterozygotes than in normals ($p=0.0005$). In the control group, 100% of the males and 89% of the females showed an increase below 200 ng/dl. Assuming an increase of 200 ng/dl as the dividing line for the differentiation, 54% of the CAH fathers and 100% of the CAH mothers were found to be heterozygotes. Because of the unsatisfactory differentiation of CAH fathers, we now carry out our former test without Dex. administration in males. However, for the detection of female heterozygotes, the test described here is a marked improvement.

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Further studies on the physiological role of dehydroepiandrosterone sulfate (DHAS) : lack of effect on growth in patients with short stature and delayed adrenarche.

A girl and 5 boys 10→16 yr old with severe idiopathic short stature were studied. The 2 older boys had also thalassemia major. All were prepubertal. None had received a previous hormonal therapy. Endocrine studies were normal except for extremely-low-for-age levels of DHAS and DHA. 5 mg per day of DHAS was given per os for 6-12 months. Velocity of growth was unchanged. Bone maturation was not accelerated. DHAS, DHA, testosterone (T), Δ^4-androstenedione (Δ^4), 17OH progesterone (OHP) and cortisol (F) levels and their diurnal variations were measured before and under therapy : DHAS rose 5→10 fold, DHA rose 2→8 fold during treatment, but they only reached levels normal or subnormal for age. T and Δ^4 increased slightly or not. OHP and F levels and their diurnal rhythms were unchanged. In conclusion 1) several months of DHAS substitutive therapy even restituting normal or subnormal levels of DHAS and DHA were ineffective to change the velocity of growth in short patients with delayed adrenarche. 2) A more prolonged therapy might be of interest ; higher doses seem needed in some cases to reach physiological levels of adrenal androgens.

105 F.HASCHKE* and L.HOHENAUER* (intr. by W.Swoboda).Childrens Hospital, Linz, Austria. Endocrine studies in 4 patients with Prader-Willi-Labhart-Syndrom (PWL-S) during early infancy and childhood.

We have studied blood glucose and insulin response to oral glucose load(OGTT) in 2 girls and 2 boys, in whom PWL-S was discovered at birth(3x) and at 4 months(1x) respectively.At the age of 6 months, 3 patients showed an abnormal OGTT,2 with delayed insulin response and the third with hypoinsulinaemia.The third patient changed to hyperinsulinaemic response in an abnormal OGTT at the age of 3 years.In 2 boys with cryptorchidism LHRH tests were carried out at the age of 2and 3years; both showed low basal LH values and a diminished response to 25µgLHRH iv.Four weeks treatment by synthetic LHRH(HOE 471) intranasally led to an improved position but no complete descensus of the testicles and a normalisation of LHRH test in only one boy.3 months after the end of LHRH therapy a biopsy of testicles in the responsive boy showed seminiferous tubules with an average diameter of 55µ and 4 spermatogonia,whereas the non-responsive boy showed almost no spermatogonia and an average diameter of 4o µ.

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Treatment of idiopathic growth hormone deficiency:Comparison of growth hormone alone with growth hormone plus thyroxine.

From a series of 36 children with idiopathic hypopituitarism 12 had isolated growth hormone deficiency (IGHD) and 24 multiple pituitary deficiencies (MPHD).9 patients with IGHD on long term treatment with hGH alone (12.5 U/m^2 weekly were compared with 16 MPHD patients receiving T4 substitution (150 µg/m^{2}daily) in addition.
I) Before therapy: a)IGHD: age 7.2,height(SDS): -3.66;BA (TW-RUS) (SDS):-2.8;height prediction (TW-RUS age based)(SDS):-2.67;b)MPHD: age 9.6, height(SDS):-4.04;BA(SDS):-3.8;height prediction (SDS):-2.6.II)Duration of therapy: IGHD:4.8;MPHD: 4.5.III)Height velocities(cm/yr): 1st: IGHD:8.54; MPHD.7.54;2nd: IGHB 6.59;MPHD 6.96; 3rd: IGHD: 5.68;MPHD:6.89.IV) Bone age progression during total treatment (yr/yr):IGHD 0.95; MPHD:1.09.
V) At the end of therapy: a)IGHD:height (SDS): -2.57;prognosis:-1.78,b)MPHD:-2.21,prognosis:-1.44. These results strongly support T4 medication if additional hypothyroidism is suggestive.