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Combined test for hypothalamic/pituitary function in growth retarded children, treated with human growth hormone (HGH).

Among 23 growth retarded children, 9 showed a lack of growth hormone (GH) response and 14 an intermediary response to insulin tolerance test (ITT). After HGH treatment for 42 months (mean) all were retested with a combined pituitary stimulation test (ITT + TRH + LHRH) with estimation of GH, somatomedin (SM), ACTH, TSH, prolactin (PRL), LH and FSH.

The 9 formerly GH-non responders showed a permanent GH deficiency (group I), while 10 of the previously GH-intermediary responders now had a normal GH response (group II) and 4 still had intermediary response (group III).

In group I SM was low, the ACTH response subnormal, the TSH and PRL response prolonged and in prepubertal children deficient LH and FSH response was found, whereas these parameters with few exceptions all were normal in group II and III.

This indicates: 1) Lack of GH response is a persistent condition often accompanied by hypothalamic dysfunction with abnormal secretion of other anterior pituitary hormones. 2) Intermediary GH response may be transient and associated with normal secretion of anterior pituitary hormones.

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Some aspects of hypothalamic pituitary function in anorexia nervosa.

In 7 girls age 13-18 yrs. with anorexia nervosa and secondary amenorrhea the gonadotropines (LH and FSH), thyroid stimulating hormone (TSH), prolactin (PRL) and growth hormone (GH) were evaluated by stimulation tests; in addition estradiol (E_2) and progesterone (P) were determined. The basal values of LH and FSH were low compared to controls. After luteinizing releasing hormone (LHRH) stimulation (100 µg iv bolus) the LH peak levels were decreased as well, whereas FSH showed exaggerated responses. E_2 was significantly decreased in all cases. P levels were in the upper range of the normal controls. The basal TSH and PRL levels were in the normal range. After thyrotropin releasing hormone (TRH) stimulation (200 µg iv) the responses of both TSH and PRL were normal as well. GH response was determined after insulin tolerance test (ITT) and after LHRH: the initial GH-values in both stimulation tests were elevated in 3 of the 7 patients; however, the following value was much lower. In the ITT one of the 7 girls had an insufficient GH response, after LHRH there was no GH response with one exception. In conclusion LH and FSH responses in anorexia nervosa showed prepubertal patterns. TSH and PRL responses were normal. The increased initial GH levels might be interpreted as reaction to venipuncture and not as increased basal levels. - Informed consent was obtained from all patients.

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Modified response to single-dose metyrapone (M) in delayed adolescence (DA)

23 males with DA (mean chronologic 15.7 ± 2.0 , bone age 12.4 ± 2.1 yrs, SD) and excluded growth hormone (GH), gonadotropin (Gn) deficiency or hypothyroidism were studied. Cortisol response to insulin was normal (16.7 ± 2.6 to 30.8 ± 2.5 µg/dl, SEM, n=16). After oral M (500 mg/m²), 1 to 3 consecutive 12h urine samples were collected for analysis of THS (gas chromatography, normal >300 µg/m²/12h and maximum in 1st sample). 37 tests with 37 1st, 21 2nd and 11 3rd samples were carried out. The results could be divided into 2 main groups: 25 tests (group A) were subnormal in the 1st sample 12 of them with very weak (39 ± 8 µg/m²/12 h) and 13 with insufficient (191 ± 16 µg/m²/12 h) THS response. Values in the 2nd and 3rd sample were higher (delayed response). In 12 other tests (group B), the results were normal (1016 ± 143 µg/m²/12h) in the first and lower in the 2nd and 3rd samples. In 3 patients with repeated tests there was improvement with increasing bone age. The THS responses to M did not correlate with those of GH, Gn and TSH to stimuli. It is concluded that the THS response to single-dose M may be temporarily insufficient or delayed in DA. We interpret this finding not as ACTH deficiency, but rather as a transiently reduced or slow hypothalamic responsiveness.

Supported by the Swiss National Science Foundation (Grant No. 3.883.077).

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W.v.PETRYKOWSKI*, R.BECKMANN*, N.BÖHM*, U.P.KE-TELSEN*, H.H.ROPERS* and M.SAUER*(Intr. by W. Teller). Childrens Hospital, Dept. Pediatric Muscle Diseases, Institutes of Pathology and of Human Genetics, University of Freiburg, West Germany. Adrenal insufficiency, myopathic hypotonia, severe psychomotor retardation, failure to thrive, fatty liver, megalocornea, chronic constipation and terminal bladder ectasia in 2 brothers.

The above problems were observed in 2 of 5 siblings from early infancy until death at ages 3.25 and 1.6 years. Both were the product of uneventful pregnancies and had normal weight at term. First admissions were at 3 resp. 9 weeks of age because of severe emaciation with hyponatremia and hyperkalemia. Adrenal insufficiency developed gradually during the first year of life, as documented with insulin- and Synacthen-tests. Neither child learned to sit and both were markedly autistic. Failure to thrive could only partially be improved by cortisol substitution. Floppiness was a leading symptom throughout. Muscle enzyme activities were strongly elevated. Electromyography showed a myopathic pattern. Muscle-biopsy revealed dystrophic changes in light- and electron-microscopy. Progressive bladder ectasia (1000 ml) finally appeared. At autopsy brain and spinal cord findings were normal, lipid analysis however suggested demyelination. No similar cases could be found in the literature.

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Sensitivity to exogenous insulin and endogenous insulin release in hypopituitary non-hypoglycemic children treated with HGH.

35 hypopituitary patients treated with HGH, 5 hypopituitary subjects before the start of HGH treatment and 15 short-normal children were studied. Informed consent of the parents was obtained. In all the subjects an OGTT and a continuous IGTT were performed. Of the 35 subjects, 16 showing a normal OGTT were submitted to an insulin-induced hypoglycemia test during therapy and 1 month after suspension. All the short-normal and hypopituitary subjects not under treatment showed a normal OGTT, 4 of the treated patients had an abnormal OGTT. In the subjects treated with HGH the insulin secretion was significantly lower than that of the normal children ($p < 0.01$) but not significantly different from that of the non-treated hypopituitary children. A weekly significant difference ($p < 0.05$) was evident between the minimum blood glucose reached during treatment and that found after treatment suspension.

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Maturation of pituitary-hypothalamic function by exogenous testosterone enanthate.

The response to exogenous testosterone enanthate (TE) (200mg IM once each month for three months) was evaluated in 10 males, age 16 ± 0.8 years (mean ± 1 S.D.) diagnosed as constitutional delay of puberty (CD). Prior to the onset of therapy, the following were measured: serum LH and GH every 30 min. for 24 hrs; FSH-LH conc. following a single 100 µg bolus of Gonadotropin Releasing Hormone (GnRH); the GH conc. following sequential arginine-insulin stimulation. Two months after the last injection of TE, the same series of tests were performed. Patients have been followed 1 - 2-1/2 yrs. All 7 patients who were Tanner Stage I had a significant increase ($p < .01$) in both the mean 24 hr concentration of LH and GH, a significantly increased LH conc. following GnRH, $p < .01$, and a significantly increased plasma testosterone conc. ($p < .001$), although the last dose of TE was 60 days earlier. All patients have continued their pubertal progression as evidenced by continued increase in plasma testosterone, progression in secondary sex characteristics and normal osseous maturation without compromise in predicted height. These results may be compatible with a testosterone induced maturation of hypothalamic pituitary function.