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FERTILITY AND SEMEN QUALITY IN PREVIOUSLY GROWTH HORMONE TREATED MEN.

32 men aged 20-35 years (median 27.3 years) who were treated in childhood or adolescence with growth hormone participated in the study. Sixteen had isolated growth hormone deficiency and 16 panhypopituitarism with insufficiency of two or more pituitary hormones including growth hormone. All patients were adequately hormone substituted except growth hormone. They were all interviewed. Only one patient, a man aged 27 with partial growth hormone deficiency, had fathered a child. Seven of ten patients with 'complete growth hormone deficiency' (<3.0 ng/ml) were asked to deliver seminal fluid by masturbation. None had normal spermiograms. Four patients with panhypopituitarism had very low volume of seminal fluid (< 1 ml) and azoospermia, whereas three patients with isolated growth hormone deficiency showed moderate impairment of the spermiogram including abnormal motility.
Thus, the majority of men with growth hormone deficiency may have dysfunction of the reproductive system.

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GROWTH HORMONE SECRETION AFTER CLONIDINE STIMULATION TEST IN PREVIOUSLY TREATED GROWTH HORMONE DEFICIENT CHILDREN.

Thrirty-four previously growth hormone treated persons aged 17 to 35 years, diagnosed in childhood as growth hormone deficient with insulin hypoglycaemia and growth hormone peak concentrations <7 ng/ml, were re-evaluated with clonidine stimulation test.
Twelve of 13 patients with panhypopituitarism still showed severe growth hormone deficiency (<5 ng/ml peak concentration). Of the 23 isolated growth hormone deficient persons only 11 still showed severe growth hormone deficiency while 4 persons showed signs of partial growth hormone deficiency (5.4-8.6 ng/ml). Eight persons had normal growth hormone response.
In conclusion: 1) In children with panhypopituitarism the growth hormone deficiency may be more definite than in children with an isolated defect, or alternatively 2) the diagnosis of growth hormone deficiency may be more difficult to establish in patients with isolated growth hormone deficiency.

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BASAL PLASMA GHRH LEVELS AT THE DIFFERENT STAGES OF LIFE.

Basal plasma GH releasing hormone (GHRH) concentrations were measured after extraction by RIA in 240 healthy normal subjects between birth and 80 years of age: 32 full term newborns (cord blood) 53 prepubertal children of at least 6 years of age, 155 pubertal children at Tanner's stage II to V, 8 male adults, 20 old subjects of at least 70 years of age. Basal plasma GHRH was found to be respectively mean ± SEM 62 ± 4 pg/ml in newborns, 40 ± 4 pg/ml in prepubertal children, 66 ± 5 pg/ml at stage II of puberty, 123 ± 17 pg/ml at stage III, 136 ± 22 pg/ml at stage IV and 60 ± 5 pg/ml at stage V, 29 ± 4 pg/ml in adults and 20 ± 5 pg/ml in old people. This study indicates an increase in GHRH basal levels throughout puberty, stage of life where GH secretion is increased, and a progressive decrease with adult and old age, stage of life where GH secretion is lower.

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COMPARISON OF THE INTRAVENOUS GHRH TEST AND 24-HOUR HORMONE SECRETION IN CHILDREN WITH GROWTH RETARDATION

A stimulatory test with intravenous GHRH (2mcg/kg) and study of physiological GH secretion over the 24-hour period with GH sampling every 20 min (calculation of the integrated concentration (IC) and the value of the maximum nocturnal peak) was carried out in 94 children. Their mean age was 10.75±3.35yr and mean growth retardation -2.78±0.67 SD. The means of the parameters studied were : GH peak after GHRH 30.4±16.8 ng/ml, IC 3.11±1.97ng/ml/min and physiological secretory peak 26±4ng/ml. The children were divided into three subgroups according to their IC : normal IC (G1,m=4;67±2.2ng/ml/min,n=39), intermediate (G2,m=2.36±0.3ng/ml/min, n=30) and low (G3,m=1.65±0.45ng/ml/min, n=25). The mean of GH peaks after GHRH did not signiticantly differ between the three subgroups. The means were respectively : G1,32.97±2.71 ng/ml; G2,30.39±2.9 ng/ml; and G3,26.25±3.61 ng/ml. There was no significant correlation between the GH peak after GHRH on the one hand and the IC or the physiological secretory peak on the other in these three groups. The GHRH test was considered positive when the GH peak was greater than 10 ng/ml. 77 of 94 children had a positive response. 17 children did not respond to GHRH stimulation. Study of the physiological secretion showed GH deficiency in 6 of the 17 children (mean IC 1.45± 0.28), but in 11 children 24-hour secretion was normal. The GHRH test does not therefore make it possible to differentiate in testing for pituitary deficiency and cannot be considered as a diagnotic test for GH deficiency.

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THE EFFECTS OF INTRAVENOUS(IV),SUBCUTANEOUS (SC) AND INTRANASAL(IN) ADMINISTRATION OF GH-RH(1-44)NH2 ON GROWTH-HORMONE SECRETION IN NORMAL MEN:DOSE-RESPONSE RELATIONSHIPS.

To compare its effectiveness in stimulating growth-hormone (GH) release, GH-RH (1-44) NH2 was given intravenously (80 mcg; n=16), subcutaneously (2.1; 4.2; 8.4; 12.6; 16.8 and 21 mcg/kg; n=16) and intranasally (1.4; 3.6; 7; 14; 21and 28 mcg/kg; n=16) to normal male volunteers.
GH stimulation occured in a dose-responsive manner after SC and after IN routes of administration.Although the degree of GH stimulation,in terms of GH peak and GH integrated concentration,was variable among subjects,the greatest amount of stimulation occured with the highest doses. If maximal observed concentration of GH is used as an indicator of responsiveness to the various doses and routes of administration,approximatelly a 15 fold higher SC dose and a 25 fold higher IN dose were required to stimulate a comparable amount of GH secretion as compared with IV administration.
Stimulation of GH secretion occured within 30 minutes of IV and SC administration and within 45 minutes of IN GR-RH(1-44)NH2 administration.
It is concluded that optimisation of IN administration of GH-RH(1-44) NH2 is necessary before using it for long-term therapy in children with GH deficiency.

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NYCTHEMERAL GH SECRETION IN RESPONSE TO IV CONTINUOUS PERFUSION, BOLUS INJECTIONS OR SUBCUTANEOUS ADMINISTRATION OF GRF(1-29NH2) IN NORMAL MALE VOLUNTEERS.

As a preliminary step to the potential use of growth hormone releasing factor (GRF) in pituitary dwarfism, growth hormone (GH) response to the 1-29 fragment of the GRF molecule (given by Ares-Serono) was studied in 6 normal male volunteers (age 19-23yrs). According to a pre-determined dose-response curve, an iv continuous perfusion (0.1ug/kg/hr) and bolus injections (0.3ug/kg/3hr) i.e. a total dose of 2.4ug/kg, were given over 24 hours in each subject at a week interval. Furthermore, GRF was also injected subcutaneously at 8pm (1.0 or 5.0ug/kg). Plasma GH levels were measured at 20' interval and the results compared to a control period. Food intake and sleep periods were recorded. Continuous GRF perfusion produced an increase in GH pulses (7.8±1.1 vs 4.1 ±1.0 peaks/day, $p<0.001$) as well as a constant but not significant rise in peak amplitude. Bolus injections caused GH release in 44/48 injections. This release was particularly marked during night time. Given subcutaneously, GRF caused a moderate rise in GH in 3/4 subjects, using the highest dosage only. In conclusion, GRF(1-29NH2) is effective in increasing GH secretion in normal males without apparent desensitization of the pituitary and with maximal sensitivity and response during night time.