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DIAGNOSTIC USEFULNESS OF INTRAVEINOUS ACUTE SOMATOCRININE (GRF) IN SHORT CHILDREN.

Synthetic Human GRF 1-44, kindly provided by R. Guillemin[1], was given IV bolus (1 ug/kg/b.w.) to 37 children or adolescents with severe growth failure due to GH deficiency prior to GH therapy, including 9 with Idiopathic Isolated (11.), 6 with Idiopathic Panhypopituitarism (IP.), 19 with GH deficiency secondary to a brain tumor (BT.).

In II., IP. and BT. mean plasma GH peakds after GRF were 10, 8.2 and 16.1 ng/ml respectively compared to 4, 2.6 and 4.5 after glucagon propanolol. Acute IV bolus of GRF seems to discriminate with a higher efficiency GH deficiency secondary to a brain tumor from idiopathic, although overlap is observed. However in case of a "too good" GH response to acute IV bolus of GRF, possibility of brain tumor must strongly be (re)considered.

One case with severe growth retardation, marked boulimia without obesity and idiopathic isolated GH deficiency shows a dramatic GH peak at 88 ng/ml 15 mn after GRF, which suggests a primary GRF deficiency possibly due to a defect of the Arcuate Nucleus region. Such a marked GH peak was also observed in two cases of anorexia nervosa.

These data provide evidences of GRF usefulness in the diagnosis of the etiology and (or) the pathophysiology of GH deficiency. They also raise the possibility that GRF could play a role in the regulation of appetite.

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LRH administration in increasing frequency schedules in the hypogonadotropic male patient.

In search for an optimal induction of puberty, LRH was administered iv in three different consecutive schedules, each lasting for 4 weeks in three hypogonadotropic boys:

	pulse dose	pulse interval
1	20 µg	180 min.
2	20 µg	90 min.
3	20 µg	45 min.

Results: Schedule 1 elicited a clear increase of the FSH level, while LH and T (Testosterone) increased slightly.
On the presumed physiologic schedule 2 (Santen and Bardin,1973) LH, FSH and T increased into the normal adult range.Only 1 patient showed LH pulses strictly coincident with the exogenous LRH pulses. On schédule 3 gonadotropin and T levels remained high or even further increased. There was no evidence of desensitization of the gonadotrophic cells.
These data suggest that:
1.The increase of gonadotropins during early puberty (FSH first, followed by LH) may be the result of increasing LRH stimulation with a pulse frequency lower than presumed physiologic in adults.
2. Pulsatile LRH treatment with a frequency higher than "physiologic" does not result necessarily in desensitization of the gonadotrophic cells, in contrast to observations in the female rhesus monkey (Wildt et al.,1981).

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Is a decreased LH response to LHRH in prepubertal boys with cryptorchidism predictive of permanent gonadotropin deficiency?

Among more than 300 prepubertal boys with uni- or bilateral cryptorchidism, 15 with low LH response to LHRH (peak LH ug/l LER 907: 30.1 ± 7.8 SD) could be followed up to the age of 12 - 16.5 years and had at least 2 further LHRH tests (25 ug/m^2 i.v.). At that age, all had signs of spontaneous puberty (testes ≥ 3 ml and/or pubes Tanner stage ≥ 2); peak LH values were 102.3 ± 40.7 SD (difference first/last LH peak $p < 0.001$ in 14 boys). In 10 of them the rise of LH response appeared at pubes 2 - 3, in 4 at pubes 4 - 5. In one boy with testes of 20 ml and pubes 5 at the age of 14.4 years, LH peak values remained <40, comparable to patients with persistent gonadotropin deficiency. Before puberty, peak FSH values were low in half of these patients; during puberty, 13 boys had normal and 2 increased FSH values.

Our results show that LH deficiency - suggested to be a causative factor of cryptorchidism - is present in this group of patients. However, it seems to be of transient nature as demonstrated by the rise of LH response and the occurance of spontaneous puberty.

Supported by the Swiss National Foundation Grant No. 3.984.080

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Gonadotrophin release after TRH in prepubertal subjects.

In some instances, the gonadotrophins were found to be released after TRH administration in adults. Therefore, we evaluated serum gonadotrophin concentrations after separated injections of LHRH (25 µg/m2) and TRH (6 µg/kg up to 200 µg). The latter was injected 90 min after the former. The FSH and LH concentrations measured immediately before LHRH and TRH injections were considered as basal values to calculate the subsequent responses. The data were analyzed according to sex and to the prepubertal (PP) or pubertal (P) pattern of gonadotrophin responses to LHRH (JCEM, 54:733,1982). Only patients with either gonadal or hypothalamopituitary deficiency were excluded. In 9 PP boys, the mean (± SEM) FSH increment after TRH was 1.67± 0.67 mIU/ml. This represents 53% of the FSH response to LHRH in these subjects. In 17 P boys, a lower ($P < 0.05$) FSH increment after TRH was observed : 0.38 ± 0.11 mIU/ml (17% of the response to LHRH). In 16 PP girls, the mean FSH increment after TRH was 1.36± 0.37 mIU/ml (15% of the response to LHRH). In 5 P girls, it was only 0.24± 0.15 mIU/ml (3% of the response to LHRH). In PP boys and girls, the mean LH increments after TRH represented respectively 53 and 29% of the LH responses to LHRH; in contrast, they represented 6 and 0% of the responses to LHRH in P boys and girls. Since TRH might elicit a gonadotrophin release in PP subjects, we suggest that it should be administred apart from LHRH.

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Urinary excretion of androgen metabolites in Turner's syndrome (TS).

In TS controversial results are published on urinary excretion of androgen metabolites. Therefore we investigated the 24 h urinary excretion of 8 androgen metabolites (C_{19} steroids) by 8 TS patients (45,XO) (group A) compared to 17 healthy girls (group B). Bone ages (BA): (median range); A:12.1, 7.2-13.5, B:12.5, 7.2-15.9 yrs, respectively. The method used consisted of Sep-Pak extraction, enzymatic hydrolysis, derivative formation and capillary column gas chromatography. Results: The excretion of total C_{19} steroids was not different in A and B before as well after BA of 10 years. Before: A=1.5±0.2, B=1.3±0.4, after: A=2.7±1.2, B=1.7±0.9 [mg/m^2/24 h]. Also individual C_{19} steroids showed no differences between A and B before BA of 10 years. After BA of 10 years, however, in TS the urinary contents of DHA and androstenetriol-16α were significantly ($p<0.01$) higher than in healthy girls: (mean,±SD) DHA: (A=0.3±0.2, B=0.05±0.04), androstenetriol-16α: (A=0.3±0.1, B=0.09±0.08) [mg/m^2/24 h]. Conclusion: The total amount of androgen metabolite excretion by TS does not differ from healthy girls of the same bone age. In TS of bone age >10yrs the elevated excretion of DHA and androstenetriol-16α is probably due to either lack of conversion to testosterone or to increased adrenal synthesis.
Supported by DFG (Ho-471).

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No evidence for linkage between HLA and male pseudohermaphroditism due to 17,20-desmolase deficiency

A family is described with two siblings suffering from male pseudohermaphroditism due to 17,20-desmolase deficiency.A possible association of the gene for 17,20-desmolase with the major histocompatibility complex on the short arm of chromosome 6 was tested by segregation analysis of the HLA haplotypes in three generations of this family.HLA ABCDR typing was carried out with the Ninth International Histocompatibility Workshop serum set of over 800 different antisera.In addition,the polymorphisms of two other chromosome 6 markers,properdin factor B of the alternative complement pathway (BF) and of the enzyme glyoxalase I (GLO) were investigated.We found,that the two affected children were HLA genotypically different, and both differed by one haplotype from their healthy sister.We conclude from these results, that a close linkage between the HLA,BF, and GLO loci and the locus for 17,20-desmolase deficiency is unlikely.The lod score value reaches - 0.721 for a recombination fraction theta = 0.05.Unlike the gene for 21-hydroxylase deficiency,the gene locus for 17,20-desmolase is apparently not located in the major histocompatibility complex region on chromosome 6.