21 THE EFFECTS OF CRANIAL IRRADIATION ON GROWTH HORMONE SECRETION.

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Children with radiation-induced damage to the hypothalamic-pituitary axis have been described in whom the GH response to a pharmacological test is normal but 24 hour GH production is diminished. Therefore we have studied GH secretion under physiological conditions and in response to standard pharmacological stimuli in 14 children (9-17 years), who had received cranial irradiation between two and 14 years earlier. All 14 showed a blunted GH response to an ITT (1-14 mU/l) and, in 12, the GH response to arginine stimulation was also subnormal (1.4-19 mU/l). Physiological GH secretion was studied by measuring integrated GH concentrations in 30 minute blood samples collected over a 24 hour period by a continuous withdrawal pump. Compared to normal controls (n=5), the irradiated patients showed a significant reduction in the mean integrated GH concentration (2.2 : 8.8 mU/l; $p < 0.002$), median total 24 hour GH output (89.6 : 340.7; $p < 0.002$) and the median GH output during the first six hours of sleep (32.7 : 210; $p < 0.002$). There was no significant correlation between the maximum peak GH response to either pharmacological test and the total 24 hour GH output. All 14 children showed a blunted GH response to an ITT as well as a reduced total 24 hour GH output. Therefore we would suggest that in children suspected of radiation-induced GH deficiency pharmacological tests of GH secretion remain useful, the ITT being the test of choice because of the marked radiation sensitivity of the hypoglycaemic stimulus.

22 GROWTH IMPAIRMENT ASSOCIATED WITH HYPERCORTISOLISM: RESPONSE TO GROWTH HORMONE THERAPY.

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Hypercortisolism decreases responsiveness to GH, leading to impairment of growth. The 24-h integrated concentration of cortisol (IC-F) proved to be an accurate diagnostic procedure for hypercortisolism. In children aged 7-18 yr (n=26) of normal stature, the IC-F, mean ±1SD, was 5.9±1.6 µg/dl. In Cushing's disease, the IC-F was 20.2±4.7 µg/dl (n=13)(JCEM 54:1072,1982).

We have identified 5 children (ages 10-14 yr) who presented with short stature (less than 5% for age), slow growth (less than 4.5 cm/yr) and bone age delay (greater than 2 SD for age). All were euthyroid and their stimulated GH and 24-h IC-GH were normal. None of the patients were obese, had striae, or other classical physical findings of Cushing's syndrome. However, their IC-F ranged from 13.2-17.2 µg/dl, clearly in the range of patients with Cushing's syndrome. Two of the children were treated for 8 months with GH (0.2 U/kg three times per week) and had increased growth rate of 10.6 and 8 cm/yr respectively. A third child who was treated with less GH (0.1 U/kg three times per week) increased her growth rate from 4.5 to 5.7 cm/yr.

Conclusion: 1/Poor growth associated with hypercortisolism may occur in children who do not look Cushingoid. 2/Such children are responsive to GH therapy.

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How to predict the growth outcome of Growth Hormone treatment in short children?

33 wellnutritioned, healthy children of short stature(<-2SD) with retarded bone age were after extensive investigation put on Growth Hormone (GH) treatment (Crescormone 0,1 IU/kg and day sc) for one year. The prediction value of different parameters were evaluated against the effect of GH-treatment on growth velocity. 24 children remained prepubertal and were statistically analyzed.

Results: Growth velocity increased from 4,0 ± 0,9 to 7,2 ± 1,4 cm/year (-3,1 to -2,6 SD). Boneage was not accelerated. This increase in growth rate correlated to an increase from day 0 to day 5-10 in serumlevels of IGF I/SMA (r=0,8 p <0,001), in IGF II/s (r=0,7; p <0,01), in procollagen-III/s (r=0,7; p <0,001) and the levels of alkaline phosphatase/s . No correlation was found to the area under the curve or the max value of GH after provocative tests as insulin-arginin, Catapressan, sleep or exercise.Neither with the total amount of secreted GH over 24 h or with the secretory pattern of 24-h-GH. However, the children were selected to treatment only if they had lower amount of 24-h-GH than fast growing children.

Conclusion: These short children, with low amount of 24-h-GH but normal increase of GH after provocative tests, nearly doubled their growth rate on GH-treatment for one year. IGF I/SMA,IGF II, procollagen and ALP showed predicting value. How to best combine them as diagnostic tools is now under evaluation. However, increased final height remains to be seen.

24 GROWTH RESPONSE TO GROWTH HORMONE(GH) THERAPY IN PREPUBERTAL CHILDREN WITH PARTIAL AND TOTAL GH DEFICIENCY

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According to GH-peak values in provocation tests, GH deficiency (GHD) has been subdivided into a "total" (GH peak <8mU/l) and a "partial" (GH peak 8-15 mU/l) form by various investigators. Conflicting data on the response to hGH therapy have been reported. We studied growth acceleration in the 1st and 2nd year of GH therapy in prepubertal children with various forms of GHD. Group I: partial GHD (PGHD): at least one GH peak between 8-15 mU/l (n=14), 10 without (Ia) and 4 with TSH deficiency (Ib). Group II: isolated total GHD (n=9). Group III: total GH- and TSH-deficiency (n=8). Group IV: multiple pituitary deficiency (n=11). All patients received 4 IU twice a week i.m. The results are shown in the table (mean ±SD).

Group		Ia	Ib	II	III	IV
Age (years)		11.7±2.5	8.9±4.6	8.7±2.8	7.6±3.0	10.7±2.8
Acceleration	1st yr	4.0±1.0	3.1±1.3	3.6±1.5	7.2±3.2	3.2±1.9
(cm/yr/yr)	2nd yr	1.9±0.9	2.1±0.2	1.0±1.0	2.8±2.3	1.8±1.7

There was no difference between the growth response of total and partial GH-deficiency. Group III showed the greatest acceleration. In group I and II combined, stepwise multiple regression analysis showed that 1st year growth acceleration did not show any significant correlation with a number of clinical parameters. 2nd year growth acceleration was most closely related to pre-treatment growth velocity (r=0.71), but addition of height (SDS) and skinfold (SDS) increased the correlation coefficient to 0.92.

25 FINAL HEIGHT OF PATIENTS WITH IDIOPATHIC PITUITARY GROWTH FAILURE. CORRELATION WITH 5 ADULT HEIGHT PREDICTION METHODS AT THE ONSET AND AFTER ONE YEAR OF TREATMENT.

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The availabilty of hGH allows successful treatment of idiopathic pituitary growth failure (GH deficiency). Final height (FH) is correlated with mid parent height, bone age (BA) deficit and the increase in height velocity. Adult height prediction (AHP) methods are based either on parental height or on clinical data. Therefore AHP may be useful to predict FH early in the course of the treatment of GH deficiency. Twenty one of our patients have already reached FH. 11 (8 M, 3 F) were classified as GH and gonadotrophin deficient (CD), 10 (9 M, 1 F) as isolated GH deficiency (ID). Five different AHP methods were used on retrospective data : Tanner's Target Height (TTH), CMP NANCY Target Height (NTH) (local population analysis) (*), Bayley-Pinneau (BP), Tanner-Whitehouse 1975 (TW), Tanner 1983 (TL). The calculations were done at the onset (0) and after 1 year of treatment (± 6 weeks) (+1) using a specific software running on a APPLE IIe 64K (*). FH was significantly correlated with all calculated predictions. The results (FH=AHPxA+B) are as follow:

Meth	Nb	A	B	r	p	Meth	Nb	A	B	r	p
TTH	20	0.556	64	0.486	<0.05	NTH	20	0.667	43	0.499	<0.05
BP 0	17	0.564	69	0.797	<0.001	BP+1	20	0.445	85	0.739	<0.001
TW 0	21	0.660	55	0.653	<0.01	TW+1	21	0.818	29	0.809	<0.001
TL 0	21	0.741	41	0.739	<0.001	TL+1	21	0.859	22	0.852	<0.001

The TL+1 AHP is the most closely correlated with FH (A=0.910, B=14, r=0.804, $p < 0.01$) for the ID subgroup. HP is less closely correlated with FH for the CD subgroup. This report supports the usefulness of TL method to predict FH in GH deficiency allowing a better follow-up of the growth response.

(*) Available on request.

26 PUBERTAL GROWTH AND FINAL HEIGHT IN HYPOPITUITARY BOYS ARE NOT RELATED TO BONE AGE AT ONSET OF PUBERTY.

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Hypopituitary boys (n=29) treated with hGH (18 to 24 IU/week) were studied before and during spontaneous puberty (SP, n=9) or puberty induced with testosterone enanthate, 100 mg/month (TIP, n=20). At onset of puberty, bone age (BA, TW2) varied between 11.2 and 15.4 yrs. Total height gain during puberty (mean : 17.2 cm) was not significantly related (r=-0.38) to BA ot onset of puberty. In contrast, BA increment (ΔBA) during puberty was negatively related (r=-0.92) to BA at onset of puberty. Final height (FH) was attained in 21 out of 29 patients. Mean FH was 157.2 cm after SP and 165.5 cm after TIP. FH was a direct function of parent's height (r=0.61). After allowing for parent's height, FH was found to be significantly related to height at onset of puberty (r=0.71) and adult height predicted (TW mark II) at onset of puberty (r=0.81). In contrast, FH did not change in relation to BA at onset of puberty (r=0.28). At the end of growth, a decreased height velocity (HV) can be expected from previous HV (r=0.57) and from height achieved as a percentage of predicted FH (r=-0.56) but not from BA at that time.

We conclude that, in hypopituitary boys with SP and TIP, 1.BA at onset of puberty does not primarily influence HV during puberty and FH, 2. at onset of puberty, FH may be predicted although somewhat underestimated, 3. besides parent's height, the major factor influencing FH is patient's height at onset of puberty.