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TWO GH DOSES IN THE TREATMENT OF TURNER'S SYNDROME (TS) PATIENTS: THE HIGHER DOSE INCREASED THE GROWTH VELOCITY ONLY IN PATIENTS OVER 7 YEARS OLD.
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Fifty girls with Turner's Syndrome (67I-45X, 33% other karyotypes) aged 3.0 - 9.9 years treated with biosynthetic GH at dose of 20 or 40 IU/m body surface per week in 7 subcutaneous injections.
The patients were assigned into 25 pairs according to their chronological age (CA), degree of bone retardation (BA) as compared with their chronological age, average parental height and degree of growth deficiency of the child in terms of mean parental height. In each pair, doses of 20 IU/m /week (Group A) or 40 IU/m ./week (Group B) were randomly assigned.
Analysis of the first year of treatment was carried out on two age groups: 3.0-6.9 years (20 patients) and 7.0-9.9 years (30 patients).

Age of inclusion (years)	Group A GVSDS		Group B GVSDS	
	pre	1 year	pre	1 year
3.0 - 6.9	- 1.11*	+ 3.51*	- 0.80	+ 4.98*
7.0 - 9.9	- 1.18	+ 2.69**	- 1.24	+ 5.61**

* NS   ** p < 0.001

We did not find significant differences among the children in Group A and B in the younger age category. We did not find any differences between Groups A and B in bone age advancement over the 1 year period of treatment regardless of the patient's age. We also did not observe any side-effects during treatment or differences in fasting glucose or insulin levels among Groups A and B.

We believe that doses of GH exceeding 20 IU/m. body surface per week should not be administered to TS patients under the age of 7 years.

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LINEAR GROWTH AND FINAL HEIGHT OF CHILDREN TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) WITH CHEMOTHERAPY (CT) ALONE.

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Little information is available on the influence of CT alone on linear growth in children with ALL, and both normal and impaired growth have been reported. We present growth data on 41 children (23 ♀ and 18 ♂) in 1st continuous remission after treatment for ALL. All were treated with combination CT (VCR, asparaginase, 6-MP, MTX and intrathecal MTX) and glucocorticoids. 15 patients received additional anthracyclines. None had CNS irradiation. Median age at diagnosis was 4.0 yrs (range 0.55-14.9). CT was discontinued after 3 yrs at a median age of 7.0 yrs (3.7-18.1). Median age at last observation was 14.9 (4.2-24.5). Median interval between cessation of therapy and last follow-up was 7.0 yrs (1.9-17.6). Height was measured at regular intervals from diagnosis until last follow-up. Median height-SDS (HSDS) for chronological age was calculated.

HSDS	Whole Group median (range)	♀ < 9, ♂ < 10 yrs at cessation of CT median (range)
At diagnosis	0.012 (-1.9 to 2.8) (n=39)	0.11 (-1.9 to 2.8) (n=29)
At cessation of CT	-0.24 (-2.6 to 2.6) (n=38)	-0.31 (-2.6 to 2.6) (n=30)
At last follow-up	0.14 (-2.1 to 2.7) (n=41)	0.32 (-2.1 to 2.7) (n=30)
At final height	0.057 (-1.0 to 1.1) (n=16)	-0.075 (-0.95 to 1.1) (n=7)

From diagnosis to last observation we observed at change in HSDS (p=0.0052)(Friedman test). The change was caused by a decrease in HSDS from diagnosis to cessation of CT (p=0.046) and catch-up growth from end of CT to last follow up (p=0.0094). Same significant observation was seen in children who finished CT before puberty. Conclusion: Long term growth prognosis seems to be favourable in children treated for ALL without radiotherapy.

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THE IGF-I/IGFBP-3 RATIO INCREASES DURING NORMAL AND PRECOCIOUS PUBERTY: AN INDEX OF FREE IGF-I?

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Serum IGF-I and IGFBP-3 are stimulated by the increase of pulsatile GH secretion and GH levels during puberty with a subsequent fall in adulthood. In children with chronic renal failure, changes in the IGF-I/IGFBP-3 ratio correlated to their growth retardation. However, the individual IGF-I/IGFBP-3 ratio has not previously been described in healthy children during puberty and in patients with central precocious puberty (CPP). Materials and methods: 926 healthy children (0-20 years) and 23 girls with CPP (2-9 years) before and after 2 years of treatment with GnRH analogue and cyproterone acetate participated. Serum IGF-I and IGFBP-3 were analyzed with specific RIA's. Results: In healthy children serum IGF-I and IGFBP-3 increased significantly with age and pubertal maturation. When age and puberty was taken into account, no significant sex difference was detectable. The IGF-I/IGFBP-3 ratio increased with age and puberty from a prepubertal mean (+/-SD) of 0.065 (+/-0.025) to a maximum of 0.107 (+/-0.022) (p<0.0001) in Tanner stage IV. Compared to healthy children of the same age, girls with CPP had an increased IGF-I/BP-3 ratio of 0.095 (+/-0.026). After treatment IGF-I/IGFBP-3 ratio Standard Deviation Score (SDS) for CA decreased significantly, but did not normalize.

(SDS)	IGF-I (CA)	IGFBP-3 (CA)	IGF-I/BP-3 (CA)	IGF-I/BP-3 (BA)
before	+3.2	+1.9	+2.1	+0.9
after	+1.9	+0.3	+1.8	-0.01

Conclusion: The IGF-I/IGFBP-3 ratio increases in normal and precocious puberty concomitant with increased growth velocity. Gonadal suppression in CPP reduced height velocity which was reflected by a decrease in the IGF-I/IGFBP-3 ratio. Thus, we suggest that the individual IGF-I/IGFBP3 ratio may be an index of biologically active free IGF-I.

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DECREASED SWEATING IN LARON'S DWARFISM.

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It has recently been shown that sweat secretion rate (SSR),measured by pilocarpin iontophoresis,is reduced in patients with GH insufficiency and increases during GH treatment.Thus,GH seems to exert a metabolic influence on sweat gland function which may be mediated through IGF-1.We measured SSR in 7 untreated patients with Laron's syndrome,patient 1 was then treated with IGF-1 for 22 weeks.The results were compared to SSR in 254 puberty- and sex matched healthy children. Results: SSR was significantly reduced in Laron's syndrome to subnormal values in 4 and very low values in 3 patients (p<0.00001),independently on the presence or absence of detectable serum IGF-1. Treatment with IGF-1 did not increase SSR. Table: Sex /Age Tanner SSR mg/30min (normal range)

m / 22.0	3	23.6	(49.3-202.4)
m / 13.9	1	33.7	(46.3-159.7)
f / 16.1	2	16.3	(21.4-105.8)
f / 12.2	3	28.6	(35.7-157.7)
f / 9.3	1	23.9	(18.8-122.6)
f / 13.2	4	35.7	(34.9-237.6)
f / 6.9	1	33.5	(18.8-122.6)

The results support the hypothesis that the effect of GH on sweat gland function is mediated through IGF-1,probably by a paracrine mechanism.The effect of long-term IGF-1 treatment on sweating in Laron's syndrome remains to be evaluated.

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FAT AND FAT FREE MASS IN NORMAL, DANISH CHILDREN AGED 6 TO 16 YEARS. A BIOELECTRICAL IMPEDANCE STUDY.

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Interest in the estimation of body fat mass (BF) and fat free mass (FFM) has increased in recent years due to its relationship to endocrine function, in particular growth hormone (GH) status and its change after exogenous GH therapy. Bioelectrical impedance is a reliable and non-invasive method for the assessment of body composition, in which the amount of fat and fat free mass is calculated by measuring the resistance of the body to an electric current. The aim of the present study was to determine the changes in body composition during childhood and puberty in normal Danish schoolchildren using the bioelectrical impedance method. We examined bioelectrical impedance (Holtain BCA, UK), height, weight and pubertal stage (Tanner) in 388 children, aged 6 to 16 years.

Pubertal stage	Girls BF%	SD	n	Boys BF%	SD	n
1	21.1	7.0	100	17,7	7,3	104
2	21.4	8.9	34	19.5	8.2	25
3	21.3	5.7	25	17.6	8.4	24
4	23.9	7.7	30	12.0	4.8	5
5	27.3	6.8	31	13.2	5.3	10

In girls, we found a significant increase in body fat percent (BF%) with age and pubertal maturation (p < 0.01). In boys, there was no significant change with age or pubertal maturation, although there seemed to be a fall in BF% at the end of puberty (Tanner stages 4 & 5). There was no effect of age on BF% within the pubertal stages. There was for all age groups and pubertal stages a significant difference between girls and boys, with the girls having the highest values. FFM showed reciprocal values. The differences according to sex and age found in this study are consistent with previous studies on BF using conventional methods and can be used as reference material in the study of children with disorders of growth and puberty.

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GROWTH RETARDATION AND URINARY LOSS OF GROWTH HORMONE IN CYSTINOSIS.

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Cystinosis is characterized by intracellular accumulation of cystine, which causes nephropathy and severe growth retardation. We report on two prepubertal patients, adequately treated with oral administration of cystamine. We performed a 24 hour growth hormone (GH) profile and measured serum IGF-1 and urinary GH. One patient (#1) was subsequently placed on GH therapy (2 IU/m²/day).

	Pt. #1	Pt. #2
Age (sex)	8 (F)	4.8 (M)
Height SD Score	-2.91	-3.99
Height velocity SDS	-1.6	-0.8
Height velocity SDS after 1 yr of GH	+3.9	N.D.
IGF-1 SDS	-2.6	-1.4
Urinary GH production (ng/24 h; Nl, 1-4)	4500-12000	6800-9900
24-h GH profile:		
Mean GH conc. (µg/L; Nl >2)	0.74	0.65
Average peak height (µg/L; Nl, >2)	2.00	1.80
Area under curve (AUC$_b$) (µg/24h; Nl, >14)	7.0	7.7

We found very high levels of urinary GH and low values of IGF-1. The 24h GH profiles showed a normal number of peaks and values of mean concentration and AUC$_b$ which were low compared to those of normal prepubertal children. We suggest that the growth retardation seen in cystinosis could be partly due to the excessive loss of GH in the urine, amounting to nearly 15% of the daily production and urinary filtration of GH. This loss may contribute to the low AUC$_b$ of the GH profiles. Treatment with GH increases growth velocity but the effect on final height is yet to be determined.