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GROWTH AND GROWTH HORMONE IN CHILDREN AFTER ALLOGENEIC BONE MARROW TRANSPLANTATION.

All children surviving bone marrow transplantation (BMT) 1980-84 have been followed every year regarding their growth. There are 21 long time survivors age 1-14 at the time of BMT, 3 had severe aplastic anemia (SAA), 18 had leukemia. All patients were conditioned with cyklophosphamide, leukemic children also had 10 GY of total body irradiation (TBI) delivered by a linear accelerator at a mean dose rate <0,05 GY/min.
The children who suffered from SAA have all grown normally after BMT. The remaining 18 show a poor growth during the first year after BMT, 7/18 deviated -1 SD or more. Growth hormone (GH) stimulation tests with insulin and arginine were performed every year. Though growth was poor the first year, 19/20 had a normal GH response. At year three, however, 10/18 failed to respond normally. To further investigate physiological GH secretion, 24 hour profiles were done in 13 cases. In 5 of these, there was not one significant GH-peak (>8 ug/l). 4 children had one peak and 4 children had 3-5 peaks. Also when calculating the area over baseline, 7/10 had obvious pathological profiles. So far, 6 children had injection therapy of GH for more than 6 months, 4 show increment of growth velocity.

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TESTICULAR IRRADIATION (TI) FOR ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) : LONG TERM FOLLOW-UP OF LEYDIG CELL FUNCTION AND PUBERTAL DEVELOPMENT.

Leydig cell insufficiency is a frequent complication of bilateral TI with 24 gy (NEJM 1983). To describe the long term follow-up and the testosterone (T) deficiency we studied, with an interval time since TI >2yrs, 28 boys irradiated with 12X2Gy at 4.8 to 16.9 yrs, before (24) or during (4) puberty. All but 4 received also cranial prophylactic irradiation. All but the 2 olders at TI had leydig cell insufficiency manifested by a low T response to hCG (7X1500U) and/or by increased basal plasma LH (>5mIU/ml) when bone age (BA) >12yrs (n=21). The 8 patients with normal (2) or compensated (6) T secretion had normal spontaneous virilisation with T between 4.3 and 8 ng/ml. This group included all the boys irradiated during puberty. Age at TI and T/hCG were highly correlated (n=21, r=0.62, p<0.001). In 6 cases, a 2nd hCG test performed at intervals from 0.6 to 5.5yrs, showed a response identical to the 1st test (r=0.99). Similarly in 8 cases having a 2nd evaluation after >2yrs, when BA>12yrs and LH>5mIU/ml, a correlation was found between basal T and prepubertal T response to hCG (r=0.79, p<0.01).
In conclusion 1) The severity of leydig cell insufficiency is highly related to age at testicular irradiation. 2) No significant change from the initial evaluation was observed on follow-up. 3) Spontaneous pubertal virilisation may occur and was usually permitted by compensated T insufficiency.

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ICHTHYOSIS(I) AND HYPOGONADISM(H) IN TWO BROTHERS WITH DELETION OF THE SHORT ARM OF THE X-CHROMOSOME.

Two brothers aged 9.5(N) and 17 years(J) respectively, underwent bilateral orcheopexy at the age of 4 years and were recently examined for H. They were healthy,tall,of normal intelligence and they presented skin lesions of I. The testes were small (1ml in N bilaterally, and in J R:1ml, L:3-4ml). J. had received testosterone for 1 year and had Tanner III pubic hair. There was no response of serum testosterone to HCG and no appreciable response of LH and FSH to IV LHRH. Serum DHEAS values were 518 in N and 3700ng/ml in J. STS activity in WBC was 0 pmols/hr/mg protein in both subjects (control:24.9). Flow cytometry showed the X chromosome to be 2-3% smaller than normal, indicating a large deletion of about 5 million base pairs. No hybridization to the probe GMGX9 (DXS 237) was found, indicating steroid sulfatase (STS) gene deletion. There was hybridization to the probe dic 56 (DXS 143), which is proximal to STS. This puts a proximal limit on the extent of the deletion. They were heterozygous for the probe p19b at the MIC2X locus which puts a distal limit on the deletion. Hence, in these two brothers with I and H, a large deletion of the short arm of the X chromosome was disclosed which included the STS locus, the closely linked locus DXS 237 and the gene for hypogonadism, findings which offer the opportunity for speculations on the locus of control of normal testicular development and function.

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3 INJECTIONS OF HCG ARE AS EFFECTIVE AS 10 INJECTIONS IN THE TREATMENT OF CRYPTORCHIDISM

Treatment of cryptorchidism with GnRH preparations has some disadvantages-it requires daily applications over 4 weeks and involves the uncertainty of parents' cooperation.HCG therapy (i.m.) is safer but 10 injections according to the IHF schedule can no longer be accepted.That's why in an alternative study which included 309 boys with cryptorchidism (158 unilateral, 151 bilateral), a HCG schedule (I)with 3 HCG i.m. injections (1-3 yrs=3x1000IU,3-6 yrs=3x1500IU, 6-10 yrs =3x3000IU, 10-13=3x5000IU; intervals=7-10days, n=146) and the IHF schedule (II) with 10 inj. in age-dependent dosages (n=146) were compared. Complete descent was seen in 46/151 (30.5%) testes (abdominal, inguinal retention and prescrotal testes) under I and 80/203 testes (39.4%) under II (p=n.s.) Partial descent occured in 41% of the cases under I and 40.4% under II. In patients with abdominal and inguinal retention the positive results were comparable in the age groups 1-3 (n=124) and 3-6yrs (n=101), but in the age group 6-13yrs (n=93) 10 inj. were more effective ($p < 0.05$). Follow-up results 2-9 months after therapy were nearly identically. Concl.:HCGtherapy with 3 HCG inject. is a safe alternative procedure to the GnRH therapy.

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CRYPTORCHIDISM : COMPARISON OF 2 PROTOCOLS OF TREATMENT BY HUMAN CHORIONIC GONADOTROPIN (hCG).

It is believed that the positive action of hCG on cryptorchidism is mediated by the rise in endogenous testosterone (T). Previous studies have shown that plasma T rises steadily for 4-5 days (d.) after a single hCG injection (inj.). This study was undertaken to test the hypothesis that it is unnecessary to repeat inj. before that peak. The proposed protocol (Rx) (I) consisted of 4 IM inj. of 100 IU/kg of hCG at 4 (n = 16) or 5 d. intervals (n = 79). Results, being similar, are given in the total group (I) (n = 95) and compared to that of a previous Rx (II) using 7 inj. of 1500 IU of hCG every 48 h (group II, n = 440). The % of unilateral (UC; 60%) and bilateral cryptorchidism (BC; 40%) was identical in both groups. Success (complete descent) was recorded in 50.9% of UC and 50% of BC in group I, and 40.7% of UC and 36.7% of BC in group II. Rate of relapse (at 1-4 yrs) was similar in group I (9%) and II (10%). Plasma T was measured respectively 4 and 1 d. after the last inj. in Rx I and II. Mean (±SD) T levels (ng/dl) were not different whether Rx was successful or not, either with Rx I (392 ± 207 and 430 ± 207) or II (495 ± 247 and 541 ± 304). In total groups, T levels were lower ($p = 0.003$) with Rx I (410 ± 207) than with Rx II (516 ± 273), possibly due to a relatively late time of sampling in Rx I. Finally, T values were normally distributed in Rx I but not in Rx II (median being respectively 384 and 443). In conclusion, a Rx using hCG at doses related to body size and inj. at only 4-5 day intervals appears as efficient, or even more, as Rx using frequent hCG injections in the treatment of undescended testis.

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C-PEPTIDE LEVELS IN NEWLY DIAGNOSED IDDM AS AN INDICATOR FOR THE ADJUSTMENT OF THE INSULIN DOSE.

Repeated plasma basal and glucagon stimulated C-peptide (CP) levels were determined at diagnosis, 1 mo. & 3-mos. intervals for 2 yrs in 72 newly diagnosed IDDM (38 M, 34 F)with a mean age of 12.1 ± 2.7 yrs. An analysis was performed of the correlation between basal and peak CP levels, HbA1 and daily insulin (I) dose at each period. According to basal and peak CP at 3 and 12 mos., three groups were differentiated:

Gr.	n		Basal CP (pM/ml)	Peak CP	I U/kg/d	HbA1%
A	18	3 mos	0.22±0.08	0.38±0.17	0.33±0.16	7.4±1.0
		12 mos	0.20±0.15	0.31±0.16	0.49±0.23	8.9±1.9
B	35	3 mos	0.17±0.09	0.27±0.12	0.63±0.20	8.6±1.7
		12 mos	0.12±0.08	0.19±0.14	0.77±0.21	10.1±2.0
C	14	3 mos	0.07±0.05	0.13±0.07	0.82±0.29	11.8±1.5
		12 mos	0.04±0.03	0.04±0.04	0.85±0.19	10.0±1.1

The following predictive factors for future insulin needs were found: a) basal CP levels at diagnosis of 0.15 pM/ml or more (Gr. A) are predictive for a long remission; b) a ratio of peak CP/I (exogenous) of less than 0.5 at 1 month (Gr. C) indicates no chance of remission and calls for progressive increase of insulin dose.