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83 PREVALENCE AND AETIOLOGY OF ENDOCRINE DISORDERS FOLLOWING TREATMENT OF BRAIN TUMOURS.

116 children (51F,65M) treated for brain tumours remote from the hypothalamus or pituitary and clinically disease free at the time of study were assessed. All had received cranial irradiation, 76 spinal irradiation and 34 adjuvant chemotherapy. Mean age at treatment was 6.7 years (1-15) and follow up 8.5 years (1-23).

112 children had abnormalities of growth and/or GH secretion.

Primary thyroid dysfunction was identified in 36% of all children treated with craniospinal irradiation, with or without chemotherapy. Of 30 children treated with craniospinal irradiation and chemotherapy, 66% had primary hypothyroidism. The contribution of chemotherapy to primary thyroid dysfunction was highly significant ($p<0.001$). Secondary thyroid dysfunction occurred in 6 of 116 children.

Primary gonadal dysfunction was present in 64% of girls treated with craniospinal irradiation, with or without chemotherapy. Chemotherapy did not affect the incidence. No girls treated with cranial irradiation alone were affected. 4 of the boys who had received chemotherapy (36%) had primary testicular dysfunction. Hypogonadotrophic hypogonadism was found in 6% of children.

ACTH deficiency was found in 4 of 85 children assessed.

Data from this large series indicate the extent of endocrine damage and the contributions of radiotherapy and chemotherapy in its aetiology.

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84 GROWTH AND PITUITARY FUNCTION IN CHILDREN TREATED FOR ACUTE LYMPHATIC LEUKEMIA (ALL).

52 children in continuous complete remission from ALL and off all drugs for 2 years were studied. 39 had received cranial irradiation with 2400 cGy (group I) and 13 with 1800 cGy (group II). Height was measured at diagnosis, at end of treatment and then after 6,12,24 months. Hypothalamic-pituitary function was investigated with an arginine, L-Dopa, LHRH and TRH test. Basal T3, T4, fT3, fT4, ACTH and cortisol were also assayed. Results were compared with those of short normal subjects of the same age. A significant reduction of height SDS compared to that at diagnosis was still present two years after therapy withdrawal only in group I ($p < 0.05$). In group I 71.4% showed a normal GH response (>8ng/ml) in at least one test (vs 100% in controls, $p < 0.01$) and 22.8% a negative response to both GH tests (vs 0% in controls, $p < 0.01$). In group II these figures were respectively 91.6% and 0%. A normal response to arginine was evident in 60.6% of group I vs 54.5% of group II and to L-Dopa in 54.2% of group I vs 100% of group II ($p < 0.005$; $p < 0.05$ vs controls). No differences were evident between the two groups as regards gonadotropins and pituitary-thyroidal or pituitary-adrenal axis. Group I however showed significant higher PRL values. These data suggest that perturbation of growth and of pituitary function is more frequent after 2400 cGy cranial radiation and support the hypothesis that the mechanism which controls the GH response to L-Dopa is more vulnerable to cranial radiation than that which controls the GH response to arginine.

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85 FINAL STATURE AFTER GROWTH HORMONE (GH) THERAPY IN RADIATION-INDUCED GH DEFICIENCY

31 children, rendered GH deficient by cranial (C,n=12) or craniospinal (CS,n=19) irradiation, received GH, and their growth response was compared to that of 14 GH treated idiopathic GH deficient patients (I). 7C, 8CS, and all I patients have completed growth. All groups grew poorly before therapy, but all showed significant increments in velocity on GH, maintained over 3 years (over first year, 4.2 C,3.3 CS,5.2cm/yr I). Irradiated children entered puberty at an early bone age (BA 10.4 ±1.6yrs),irrespective of sex or tumour diagnosis. I patients entered at a "normal" BA (12.4 ±1.4yrs). Mean pubertal duration for chronological age was similar (I 2.8yrs, all irradiated 2.7yrs), but the mean change in BA was 3.7yrs for I and 4.8yrs for the irradiated ($p<0.01$). The change in "height age" for BA ($\Delta HA/\Delta BA$) was 1.03 (range 0.48-2.46) for I and 0.69 (range 0.37-1.23) for C and CS,($p<0.05$). The latter complete growth early and show a poor gain in height for each yearly increment of BA.

The final height SD scores were -2 (C) and -2.6 (CS), with no change in SD score, and -2.6 (I), with catch-up growth of +2.1. On GH, the irradiated children had maintained their centile position but had not exhibited catch-up growth due to their rapid progression through puberty. Thus GH therapy benefits irradiated GH deficient children, but endeavours to limit pubertal progression may improve their height prognosis further.

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86 LONG-TERM STATUS OF HYPOPITUITARY DWARFS.

The psychosocial consequences of GH deficiency and of its treatment with growth hormone (hGH) have been evaluated from 44 answers to a questionnaire mailed to 50 patients aged 18 to 36 years (m 21.7 ± 3.4 yrs), treated with hGH for at least 3 years (m 5.6 ± 2.8 yrs), 22 idiopathic and 22 with detectable cause, 15 with isolated GH deficiency and 29 with multiple deficiencies. Final height was -2.9 ± 0.9 SD below the average. The results (%) were the following :

	Fair	Medium	Poor
Self-evaluation of height	57	34	9
Appreciation of the treatment	68	25	7
Self-evaluation of scholarship	41	39	20
Professional or educational level	27	48	25
Sexual relations	14	25	61
Relations with family and friends	82	3	15

	yes	no
Self-evaluation of handicap in the past	88	12
Self-evaluation of handicap at present	20	80
Employment or academic studies	68	32

From these results the final score among 43 patients may be considered as excellent in 9, good in 10, medium in 15, insufficient in 8, very bad in 6, in spite of appropriate medical and psychosocial support. Earlier care and perhaps some increase of doses of hGH could improve these results in the future.

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87 PSYCHOLOGICAL ASPECTS IN CHILDREN AND ADOLESCENTS WITH HYPOPITUITARISM.

Reports on psychological aspects in dwarfed children have demonstrated inconsistent results. This was partly due to heterogeneity of samples or use of non standardized test procedures. We have therefore evaluated patients with proven hypopituitarism using a selection of age related tests. The patients were submitted to a well defined and standardized protocol testing in particular intelligence, social behavior, emotional stability, anxiety and behavior in social stress situations. 48 patients, 33m, 16f, aged 6 to 26 yrs with isolated growth hormone deficiency (n=22) and multiple pituitary deficiencies (n=26) were evaluated. Up to the time of testing duration of therapy was 0.3 to 16 yrs, height was -2.7±1.9 SDS (mean±SD). For adequate evaluation the sample was divided into two age groups (6.8-15.6 yrs, n=23; 15.9-26.1 yrs, n=25). Results: General intelligence was in the average range. Despite these findings a high percentage of children had delayed schooling or had to repeat a class. When patients with additional thyrotropic disorders were considered separately (n=14) the test result was in the lower normal range. In contrast to previous reports visual motor abilities were better than average. Unexpectedly, patients were normal regarding emotional stability, frustration tolerance and did not show any tendency towards depression or psychosomatic disorders. Social behavior was characterized by an infantile attitude towards personal environment. In case of frustrating situations children demonstrated a tendency to avoid aggressiveness which might be due to good repressing mechanisms.

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88 THE LONGTERM EFFECTS OF GROWTH HORMONE THERAPY

The growth of 73 patients treated continuously with growth hormone (GH) for up to 5 years has been analysed. Catch-up growth in the sense of an improvement in height velocity SDS was induced in all patients regardless of age and pubertal status at start of treatment. There was improvement in height SDS for BA over the first year of therapy but overall, there was no change in height SDS for CA or BA compared to the start of treatment indicating that the deficit induced by poor growth velocity at any age is irrecoverable.

Data from 58 patients who commenced treatment before puberty (mean CA 7.9, range 2.2-13.5, mean BA 6.3, 0.8-9.9) was contrasted with those from 15 patients commenced on treatment during puberty (mean CA 14.2, range 11.8-16.1, mean BA 11.9, range, 7.8-15.3). There was no significant differences in response. The notion, widely promulgated, that GH is ineffective in older patients is plainly incorrect.

These data accord with the demonstration that mid childhood and pubertal growth is GH pulse amplitude mediated and that children of any stature will respond to GH given in adequate dose. Standard criteria used to define sufficiency or insufficiency did not add to pretreatment height velocity in predicting the magnitidude of the response to GH therapy.