

IS THE INCIDENCE OF CHILDHOOD THYROID CARCINOMA DECLINING?

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In the last 15 years 32 children aged 6 to 19 have been referred to Massachusetts Gen. Hosp. with solitary thyroid nodules. Excisional biopsy revealed carcinoma in 5 (15%), adenoma in 18 (56%), and miscellaneous diagnoses in 9 (28%). Patients with carcinoma, ages 7-15, gave no history of x-ray exposure in infancy, and all were euthyroid. Lymph node metastases were present in all at the time of diagnosis. Treatment included thyroidectomy, modified radical node dissection, and mediastinal explorations, and postoperative full replacement thyroid therapy. Two patients were treated with I131 additionally. One of these died of lung metastases; the other was lost to follow-up. The remainder, followed for 4-8 years, were disease free when last seen.

Benign thyroid tumors were present in 4 boys and 14 girls, ages 6 to 19, with a mean age of 14. All were euthyroid; 8/18 had technetium scans showing 6 "warm" and 2 "cold" nodules. At surgery there were 15 follicular adenomas, 2 fetal adenomas, and a Hurthle cell adenoma.

Miscellaneous conditions seen in the remaining patients included ectopic normal thyroid tissue and agenesis of the left thyroid lobe. In the past, 50% of nodules in childhood were malignant (1). Our series, born since knowledge of the danger of irradiation induced malignancies became widespread, suggests the incidence of childhood thyroid carcinoma may be declining.

(1) Hayles, A. B., et al., Amer. J. Surg. 106: 735, 1963.

EFFECT OF LUTEINIZING HORMONE RELEASING HORMONE (LH-RH) UPON THE SECRETION OF LH IN NEWBORN RATS. B. Shapiro, A. Root, A. Goldman and G. Duckett, Depts. of Pediatrics, Univ. of Penna. Sch. of Med., Phila., and Univ. of South Florida Col. of Med., Tampa.

One µg of synthetic LH-RH (Beckman) in 5 µl of normal saline was administered subcutaneously to male (N=14) and female (N=9) rat pups between 10 and 20 hrs. after birth. Control animals (males, N=13; females, N=9) received normal saline. Twenty min. after injection the animals were sacrificed by decapitation. LH levels were determined in serum and whole pituitary glands by radioimmunoassay. LH data are expressed in terms of NIAMDD-Rat LH-RP-1. In males pituitary LH content was similar in control (0.595±.364 (SD) µg/pituitary) and LH-RH injected animals (0.518±.135 µg). In females pituitary LH content was lower in LH-RH treated rats than in control animals (0.527±.110 µg, 0.725±.184 µg, p<0.02).

Serum LH concentrations (ng/ml) in female control pups were significantly higher than in male control pups (p<0.01). Serum LH concentrations were significantly higher in male and female pups who had received LH-RH than in animals injected with saline:

	Males	Females
Control	25.7 ± 18.3	62.0 ± 14.6
LH-RH	98.4 ± 23.3	132.6 ± 14.8
p	<0.01	<0.01

These data indicate that LH-RH stimulates the secretion of LH in male and female newborn rat pups.

PATHOGENESIS OF DIABETES MELLITUS (DM): CAPILLARY BASEMENT MEMBRANE THICKNESS (BMT), GLUCOSE DISPOSAL RATE (K), PLASMA INSULIN (I), AND GROWTH HORMONE (GH) IN CHILDREN. Bagher M. Sheikholislam, Hung-Jung Lin, Stephen R. Stephenson, Gregory E. Peterson, Dennis F. Devereux, and Thomas L. Volk (Intr. by Charles F. Abildgaard). Univ. Calif. at Davis, Sch. Med., Depts. of Ped., Path.

Children (ages 3-16) with expected low incidence of vascular disease should be ideal subjects for studying the relationship between carbohydrate (CHO) intolerance and vascular abnormalities in the pathogenesis of DM. 56 K values were determined by IV glucose tolerance test (IVGTT) in 17 diabetic and 31 control (C) children (most C had a family history of DM). BMT was measured in 17 diabetics and 17 controls.

K values for diabetics were 0.82±0.50 (mean±SD) and for C group 1.84±0.70 P<0.001. BMT in the diabetics (1844±320Å) did not differ significantly from that in C (1581±495Å) but in both groups increased BMT was associated with evidence of CHO intolerance. Of 11 patients with BMT >1800Å, 10 had K <1.2, and all had high (>110mg%) 60' plasma glucose (60PG). 60PG may be a sensitive index of CHO intolerance, as suggested by the following; (a) 3 C with high 60PG and no DM in the family consented to oral GTT; all were markedly abnormal, (b) 11 IVGTT on 4 C born of conjugal diabetics yielded high 60PG although K were always >1.2.

Plasma I and GH response to IVGTT and duration of DM did not correlate with BMT. 5 patients with DM had normal BMT, which suggests that CHO abnormalities precede increased BMT.

A Model for the Circadian-Episodic Secretion of Cortisol, W.R. Slaunwhite, Jr., T. Aceto, Jr., W.J. Jusko, S.B. Keenan, and C. Siefert, Children's Hosp. and Schools of Dentistry, Medicine and Pharmacy, State Univ. of N.Y., Buffalo, N.Y.

Cortisol measurements were made on plasma obtained every 30 min. for 25 hrs. In a model using a catenary system consisting of adrenals and a body compartment, a cosine function was assumed to reflect the circadian variation in adrenal synthesis of cortisol, a switch function to describe its episodic release and first order kinetics to describe plasma clearance. Data was subjected to computer non-linear regression analysis to obtain least square estimates of model parameters. A correlation coefficient of 0.94 was obtained. Results (mean ± 1 S.D.) on 7/8 normal children (5-17 yrs.) are as follows. Adrenal secretory rate (SR) was 312 ± 84 µg/hr/m² (or 7.5 ± 2.0 mg/d/m²) with an amplitude of 255 ± 57 µg/hr/m² giving a mean maximum and minimum SR of 567 and 57 µg/hr/m², respectively. Adrenal was maximally on 22% of the day and slowly secreting 54%. The results indicate that troughs of plasma cortisol concentration are caused by diminished secretion rather than lack of secretion. Maximal secretion occurred at 7.9 ± 1.9 hrs. A.M. Plasma clearance of cortisol was 104 ± 24 l/d/m² corresponding to a half-life of 58 ± 11 min. Apparent adrenal content of cortisol equivalents was 337 ± 199 µg/m² (4.5% SR). This method has great potential for assessing adrenocortical metabolism during stress or during glucocorticoid therapy.

PLASMA TSH AND PROLACTIN IN VARIOUS FORMS OF HYPOTHYROIDISM. S.N. Suter, M.L. Aubert, S.L. Kaplan, and M.M. Grumbach, Dept. Ped., Univ. Calif. San Francisco, San Francisco, California.

Previous studies showed that thyrotropin releasing factor (TRF) stimulates thyrotropin (TSH) and prolactin (PRL) secretion. We compared plasma TSH and PRL in various forms of thyroid dysfunction. Plasma TSH and PRL were measured in 32 normal short children, in 19 patients with untreated primary hypothyroidism (PHT), none of whom had galactorrhea (age range: 11 wks-14 yrs), in 18 patients with idiopathic hypopituitarism (IHP) with TSH deficiency and in 14 children with hypopituitarism with a mass lesion (HPML).

	Prolactin (ng/ml)	TSH (µU/ml)
Normals n=32	5.7±0.75 (1-22)	4.5±1
PHT n=19	24.8±5.1 (4.8-79)	902±382
IHP n=18	9.8±1.9 (0-24)	< 2.5
HPML n=13	11.5±2.1 (2.6-26)	< 2.5
	mean ± SE range	mean ± SE

In PHT, irrespective of etiology, plasma TSH levels were all strikingly elevated, the response to TRF was augmented, and prolactin levels were significantly higher than in normal children, in idiopathic hypopituitarism and in hypopituitarism with a mass lesion. Eight of 19 patients with PHT had PRL levels markedly above the upper range of normal. The elevated levels fell to normal with treatment. These data suggest that the elevated plasma prolactin levels may be a consequence of increased TRF secretion or an increased sensitivity of the pituitary to TRF.

COMPARISON OF HUMAN GROWTH HORMONE (hGH) AND OXANDROLONE AS GROWTH STIMULATING AGENTS IN PATIENTS WITH GROWTH HORMONE DEFICIENCY. Diana S. Tattoni and Vincent C. Kelley, Univ. Wash., Dept. Pediat., Seattle.

21 patients with growth retardation secondary to Growth Hormone deficiency have been studied prospectively during a control period of 6 months and 3 six-month therapy periods during which they received in random order Oxandrolone (Anavar®) alone, .25mg/Kg/day; hGH alone, 2 IU-3x per week; or a combination of these two drugs in the doses mentioned. Careful height measurements and bone-age determinations were made at the beginning and end of each of the four study periods.

The patients studied included 10 with idiopathic panhypopituitarism (Group I), 6 with panhypopituitarism secondary to craniopharyngioma (Group II), and 5 with isolated growth hormone deficiency associated with other primary non-endocrine pathology. Patients with thyroid and/or adrenal insufficiency were maintained on appropriate substitution therapy throughout all four study periods.

Results indicate that in Groups I and II Oxandrolone was effective in stimulating growth, hGH was more effective, and the combination of the two drugs was even more effective. In Group III, none of the therapy regimens was significantly effective. In all groups and study periods advancement in bone age was quite similar to that in height age, thus providing no substantiation for concern over compromising eventual adult height attainment.