JUVENILE THYROTOXICOSIS: Vanitha Vaidya, John S. Parks, Rebecca T. Kirkland, Alfred Tenore, Alfred M. Bongiovanni. Univ. of Pa. Dept. of Pediat. The Children's Hospital of Philadelphia.

88 patients with thyrotoxicosis were seen over the past 21 yrs: the female/male ratio was 4:1. The ages ranged between 2 to 8 years. 28 patients were lost to follow-up and 60 were followed for an average of 3.9 yrs. Family history of thyroid disease was present in 23 patients and was thyrotoxicosis in 12. Of 28 patients (46%) who underwent sub-total thyroidectomy, 13 relapsed after an average of 3 years of medical treatment; 5 had hypersensitivity to Propylthiouracil; 11 showed poor cooperation. Prophylactic thyroid hormone was begun in 5 patients after surgery, and in an additional 8 because of subsequent hypothyroidism. Fourteen had permanent remission on medical treatment, three of whom may have had thyrotoxic thyroiditis. Of the series of 60, one child was referred after treatment with RAI^{131}, and another died of other causes.

Fourteen patients on Propylthiouracil continue to be followed, and the longest duration of medical treatment has been 6 years in one patient. Our experience leads us to employ medical treatment for prolonged periods when there are no complications.

THE ETIOLOGY OF PRECOCIOUS SEXUAL DEVELOPMENT IN PRIMARY HYPOTHYROIDISM. Herbert L. Vallet, Lesley S. Baldwin, Donna S. Gursky (Intr. by Richard B. Goldbloom), Dalhousie Univ., Dept. of Ped., I.W.K. Hosp. for Child., Halifax, Nova Scotia.

The etiology of precocious sexual development in this disease entity has not been identified in vivo, but has been linked (in theory) with a concept of "overflow stimulation" of the anterior pituitary gonadotrophs, and/or of the hypothalamus with resultant releasing factor effects.

We have developed a rat hemi-pituitary (pit) organ culture system. Utilizing NIAMD reagents both secreted and added rat LH was measured in medium 199 by radioimmunoassay. Pituitaries from 10 day old males secreted LH at a constant rate of 41.31 mug/hr/mg pit wet wt. ±SEM with hourly media changes. When Rat LH-RP-1 was added to the media an immediate rise in hourly LH secretion was observed (Day 1, 103.3 ± 28.9; Day 2, 190.67 ± 18.65). On Day 2 of culture a dose response was present. The LH-RP-1 contains 0.22 USP (Bovine) TSH Units/mg (McKenzie Assay) which appears to be responsible for the marked stimulation of LH secretion. Differential stimulation studies utilizing purified LH, FSH and TSH will confirm this observation.

This study suggests that high endogenous TSH secretion which occurs in primary hypothyroidism has a direct stimulative effect on the gonadotrophs, and is responsible for the precocious sexual development. The suppression of TSH by thyroxine administration and resultant remission of precocity in these patients, further support our findings.

FETAL AND NEONATAL DEVELOPMENT OF THE HYPOTHALAMIC-PITUITARY-GONADAL (HPG) AXIS. Herbert L. Vallet, Donna S. Gursky, Lesley S. Baldwin (Intr. by Richard B. Goldbloom), Dalhousie Univ., Dept. of Ped., I.W.K. Hosp. for Child., Halifax, Nova Scotia.

A male rat model was developed to study parameters which may relate to the rise in plasma testosterone (T) seen in male human neonates, and also to define the critical period of HP differentiation (male-female types) after which reversal of brain sex centers (acyclicity vs cyclicity) cannot occur.

Animals were studied from 19 days gestation (da gest) to 29 da postnatal (pn) for pituitary (pit) and testicular wt., pit and plasma LH and FSH, and ano-genital distance (A-G). LH and FSH were measured by radioimmunoassay using NIAMD reagents.

Fetal pit LH concentration remains constant at 0.20 ug/mg (wet pit wt.) ± 0.05 SEM. A peak of 11.1 ± 0.1 is reached at 9 da pn declining to 5.14 ± 0.15 at 29 day pn. Plasma LH is 80.0 mug/ml ± 0.8 to 3 da pn. A peak of 125.5 ± 12.2 is seen at the time of maximum pit LH synthesis, then the plasma level declines to 48.0 ± 7.2 at 29 da pn. This interval is interrupted by a small peak at 20 da pn. The A-G, which reflects degree of virilization shows its greatest increase between 3-12 da pn, concomitant with rapid testes maturation. Pit FSH shows a rise from birth to 29 da pn with no peaks.

This biphasic LH ontogeny may explain the neonatal and pubertal rise in human plasma T. The immediate neonatal pulse seen in early HP maturation is most likely responsible for the irreversibility of male brain sex centers with regard to cyclicity, if manipulated after this critical period.

BECKWITH'S SYNDROME AND ITS ENDOCRINOLOGIC MANIFESTATIONS. Herbert L. Vallet, Winston S. Parkhill, Kathleen A. Poon, Wai M. Cheung and Donna S. Gursky. Dalhousie Univ., Depts. of Pediatrics and Surgery, I.W.K. Hosp. for Child., Halifax, Nova Scotia (Intr. by Richard B. Goldbloom).

Numerous endocrine abnormalities have been noted in this syndrome, among which have been pituitary cell and pancreatic B-cell hyperplasia, neonatal hypoglycemia, cytomegaly of fetal adrenal cortex, increased birth wt., advanced bone age and most recently a reported suggestion of elevated plasma insulin.

A 10 wk. old male infant with this syndrome, has been studied repeatedly in regard to endocrine function for 12 mos. Studies show appropriate insulin responses to hypoglycemia and glucose loading (fast, 9.5-24.0 uU/ml; peak 24.5-35.0). Fasting growth hormone levels were normal (5.0-10.4 mug/ml) with excessive responses to hypoglycemia (26.4) and arginine (33.0) and normal levels to glucagon (14.2). The plasma cortisols to I.V. ACTH and to lysine-8-vasopressin on two occasions were normal. A blunted cortisol response was seen twice during spontaneous asymptomatic hypoglycemia. Metapirone tests show no rise on day 3; the patient required hydrocortisone during an untoward response to anesthesia. Posterior pituitary function was intact. Bone age and milestones were normal; linear growth and wt. gain excessive. A karyotype revealed a satellited member of the G Group.

This study suggests inconsistent and lack of persistent endocrine dysfunction in this syndrome. The etiologic relationship of hyperinsulinemia and hypoglycemia should not be made.

OPHTHALMIC STEROIDS, CUSHING'S SYNDROME AND PERSISTENT SUPPRESSION OF THE PITUITARY-ADRENAL AXIS. Herbert L. Vallet, Edward V. Rafuse, Kathleen A. Poon, Eleanor Grimm, Lesley S. Baldwin, Depts. of Pediatrics and Ophthalmology, I.W.K. Hosp. for Child., Halifax, Nova Scotia (Intr. by R. B. Goldbloom).

A 10 9/12 yr. old male presented with marked weakness, rapid wt. gain, atrophic skin, striae, truncal obesity, a buffalo hump, hirsutism and Cushingoid facies; these signs and symptoms developed during a short course of 3 retrobulbar injections of depo-triamcinolone (40 mg) and topical hydrocortisone (30 mg total over 6 weeks). This treatment was prescribed in conjunction with surgery performed for a perforating eye injury complicated by retinal detachment.

Intravenous ACTH administration showed normal adrenal responses as measured by serum cortisols. Low fasting serum cortisols with loss of normal diurnal rhythm were present. Oral metapirone tests gave no responses. Withdrawal of topical steroids resulted in a rapid loss of Cushingoid features over a 3 to 6 mo. period. Tests of pituitary-adrenal function did not return to normal for 2 years; symptoms of adrenal insufficiency occurred with moderate exertion.

This study outlines a new cause of iatrogenic Cushing's Syndrome with sequelae which persisted for 24 mo. It is suggested that low dose ophthalmic steroids should be used with caution; retrobulbar depo-steroids may cause prolonged pituitary suppression because of proximity to this organ.

DIFFERENT EFFECTS OF hGH AND bGH ON ELECTRON TRANSPORT COMPONENTS OF LIVER MITOCHONDRIA. Craig Weston, Vaddanahally T. Maddaiah, Platon J. Collipp, Shang Y. Chen, Viswanathan Balachandar, Jagan N. Pahuja. Dept. of Ped., Nassau County Med. Ctr. and SUNY Stony Brook Health Sciences Ctr., E. Meadow, N.Y.

Mitochondrial (mito) protein synthesis has been shown to be influenced by hypophysectomy (Hy) and GH treatment (JBC 248 4263:1973). **Cytochromes a, a_3, b, c, c_1 and flavin have now been measured by difference spectrophotometry in purified mito of rats after Hy and subsequent treatment with hGH and bGH. Concentrations were calculated independently of one another by solving simultaneous equations - mean ± SD. Hy significantly decreased (p 0.01) the concentration (nmoles/mg protein) of all cytochromes and subsequent GH treatment increased. hGH did not but bGH did decrease flavin to near normal level. This appears to be the first reported difference in the mechanism of action between the two hormones in Hy rats.**

	a	a_3	b	c	c_1	flavin
Normal	0.256	0.158	.460	.192	.268	0.993
	(.020)	(.024)	(0.044)	(.02)	(.027)	(.058)
Hy	0.218	0.130	.374	.166	.241	1.253
	(.04)	(.021)	(.043)	(.02)	(.023)	(.081)
Hy + hGH	.277	0.163	.400	.189	.260	1.292
	(.025)	(.026)	(.034)	(.02)	(.028)	(.125)
Hy + bGH	.274	0.146	.460	.185	.196	1.051
	(.008)	(.024)	(.067)	(.038)	(.076)	(.139)