ENDOCRINE EFFECTS OF CHRONIC ADMINISTRATION OF Δ^9-TETRAHYDRO-CANNABINOL (Δ^9-THC) TO PREPUBERAL MALE RATS.
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Although some reports have appeared which seem to indicate that Δ^9-THC, the active principle derived from marijuana, can influence some endocrine functions, no systematic study has yet been published on the endocrine effects of its chronic administration to animals. Groups of 21-day old male Sprague-Dawley rats were injected intraperitoneally 3 times a week for a month with either 1.0 or 10.0 mg/kg of Δ^9-THC or with the vehicle. At the end of the experimental period, the animals were sacrificed by decapitation, endocrine organ weights were recorded; plasma and pituitary levels of GH, LH and FSH were measured by radioimmunoassay. Endocrine organ weights of rats treated with 1.0 mg/kg of Δ^9-THC were not significantly different from those of controls, but plasma levels of FSH were higher and pituitary levels lower than in controls (Mean ± S.E. Plasma FSH: Δ^9-THC: 512 ± 27, controls: 382 ± 41 ng/ml, $p < 0.02$; pituitary FSH: Δ^9-THC: 23.1 ± 0.8, controls: 30.3 ± 4.5 ug/mg, $p < 0.05$). Rats treated with 10.0 mg/kg of Δ^9-THC had lower ventral prostate weights (Δ^9-THC: 153 ± 7, controls: 184 ± 9 mg, $p < 0.02$) and lower plasma LH levels (Δ^9-THC: 4.0 ± 1.4, controls: 25.1 ± 5.0 ng/ml, $p < 0.001$). These results indicate that the active principle of marijuana can influence the development of the reproductive system.

INSULIN: GROWTH PROMOTING HORMONE IN CRANIOPHARINGIOMA.
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Normal or accelerated growth in the absence of growth hormone (GH) occurs in some patients following surgery for craniopharingioma. To elucidate the mechanism of growth, blood levels of prolactin (Pr) insulin (IRI) and somatomedin (Sm) activity were measured in 8 children following removal of the tumor. In all patients GH responses were subnormal following insulin-induced hypoglycemia, arginine and L-dopa. Growth rates were 3.5 to 10.8 cm/year with a mean of 6.1 ± 0.9 (SEM) cm. Serum Pr was normal in 4 patients; in 3, vasopressin antibodies interfered with the assay. Sm activity was low in one patient and normal in 6. In 7 patients with adequate growth mean peak IRI levels were 125.57 ± 26.74 (SEM) μU/ml after oral glucose (G); 71.00 ± 24.37 (SEM) μU/ml after I-V tolbutamide (T) and 91.83 ± 34.40 (SEM) μU/ml after I-V arginine (A). These values were similar to or higher than mean peak IRI in normal children [79.55± 19.73 (SEM) μU/ml after G; 56.22 ± 10.79 (SEM) μU/ml after T and 40.7 ± 7.0 (SEM) μU/ml after A] and in children with idiopathic hypopituitarism [34.00 ± 7.43 (SEM) μU/ml after G and 11.50 ± 1.73 (SEM) μU/ml after T]. One patient with suboptimal growth had normal Sm but low IRI levels (30 μU/ml after G and 25 μU/ml after T).

These data suggest that: a) insulin may be the growth promoting hormone in these patients; b) Sm may not be necessary for postoperative growth and does not appear to be generated by Pr.

PERIPHERAL ENDOCRINOPATHY CAUSING SEXUAL PRECOCITY IN ALBRIGHT'S SYNDROME.
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To elucidate the cause of sex precocity in Albright's syndrome, three girls (ages 1 10/12, 4 6/12, and 5 1/12 years) with polyostotic fibrous dysplasia and cafe-au-lait spots were studied. Periodic vaginal bleeding was present in all and skeletal maturation significantly advanced. Plasma luteinizing hormone (LH) and follicle stimulating hormone (FSH) concentrations were at or below the lowest detectable level of the assay (2.0 mIU/ml) awake and during sleep; radioimmunoassay of FSH in 24 hour urine samples showed no elevation over childhood levels. By contrast, the estrogen levels were markedly elevated; plasma estradiol ranged between 606 and 795 pg/ml and estrone between 149 and 175 pg/ml, concentrations greater than observed during normal follicular and luteal phases of adult menstrual cycles. Plasma progesterone, undetectable (< 20 pg/ml) in serial intermenstrual measurements suggested lack of ovulation. These findings suggest the precocity of all three children was due to primary ovarian dysfunction rather than being of central origin. Autonomous hyperfunction of the peripheral target glands as the pathogenetic mechanism underlying the several endocrinopathies of this syndrome is further suggested by the coexistence of nodular adrenal hyperplasia in one of the girls whose elevated plasma cortisol levels failed to suppress with dexamethasone and plasma ACTH level was low.

EVIDENCE FOR HYPOTHALAMIC-PITUITARY DYSFUNCTION IN THE PRADER-WILLI SYNDROME.
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The etiology of the Prader-Willi Syndrome is obscure. Although the clinical characteristics (obesity, mental retardation, hypotonia and hypogonadism) suggest hypothalamic dysfunction, this has not been documented. We have studied two patients (15 and 22 yr.) with this disorder in whom clinicopathologic correlation was possible. Both were severely obese (150 and 190 kg) with glucose intolerance. Cold exposure (4° C for 1 hr.) produced an abnormal decrease in body temperature in one child. Plasma growth hormone (GH) did not increase with arginine-insulin, or L-dopa stimulation. Plasma cortisol showed a diurnal variation but blunted response to hypoglycemia. Basal T4 and TSH were normal and the TSH, T4 and T3 responses to TRH were normal in both patients. Basal testosterone was low in both individuals and LH and FSH responses to LRH were blunted. Clomiphene stimulation failed to augment plasma gonadotropin levels. The pituitary glands were of decreased weight but neither the pituitary nor hypothalamus was abnormal on light microscopy. These studies indicate abnormal hypothalamic-pituitary function in both patients. Involvement of the temperature control center, absent clomiphene response, abnormal GH responsiveness and normal anatomical findings support the formulation of a functional hypothalamic abnormality.

PLASMA 17-HYDROXYPROGESTERONE, 21-DEOXYCORTISOL AND CORTISOL IN CONGENITAL ADRENAL HYPERPLASIA (CAH).
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In CAH with deficient 21-hydroxylation there is impaired cortisol (F) biosynthesis resulting in elevated plasma levels of 17-hydroxyprogesterone(17-OHP) and urinary excretion of pregnanetriol. Increased urinary excretion of 11-ketopregnanetriol also occurs, but data concerning plasma levels of the precursor 21-deoxyF are limited, and the purpose of the current study was the measurement of plasma levels of 17-OHP, 21-deoxyF and F in patients with CAH.

Plasma samples were obtained from twelve patients (3d-40yr) with CAH before and three after treatment, and from four normal controls (4d-18yrs) following ACTH administration. Steroids were isolated by Sephadex LH-20 column chromotography of plasma extracts and quantitated by RIA.

Plasma 17-OHP was 2.2-5.7 fold higher than 21-deoxyF in each patient. In all untreated patients, the levels of both steroids were elevated, without relation to age or variant of CAH, and decreased with therapy. Mean values for patients were significantly different from those for normal controls.

	17-OHP	21-deoxyF	F
CAH	337 ± 166 ng/ml	88 ± 42 ng/ml	57 ± 25 ng/ml
Controls	3.7 ± 0.9 ng/ml	ND	253 ± 81 ng/ml

Conclusion: Patients with untreated CAH have elevated plasma levels of not only 17-OHP but also 21-deoxyF, and the concentration of 17-OHP exceeds that of 21-deoxyF in individual patients of all ages.

PSEUDO-HYPOALDOSTERONISM DUE TO SWEAT GLAND DYSFUNCTION.
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1½ mo. old white female has experienced repeated spontaneous episodes of hyponatremia, hyperkalemia, dehydration and shock since birth. Serum Na has been as low as 113 mEq/L and serum K as high as 11.1 mEq/L. Physical examination, growth and development have been normal.

Balance Studies 3-5 Days after following Diets were:

	Normal Na (20 mEq/day)		High Na
	Control	with DOCA	80 mEq/day
Serum Na	122	132	135
Serum K	7.6	7.1	5.4
24 Hr Urine Na	2	4	10
24 Hr Urine K	12	3	17
Sweat Na	216	184	
Sweat K	12.6	11.8	
Plasma-Aldo ng%	>73		8
PRA ng/ml/3 hr	194		16

Urinary 17-keto, 17-OH and pregnanetriol baseline and with ACTH stimulation were normal. Renal function has been normal. Salivary Na was 70 and K 16 mEq/L. Chest X-ray and 72 hour fecal fat excretion have been normal. There is no family history of cystic fibrosis.

Aldosterone is known to control Na and K secretion by kidney, sweat and salivary glands. It is proposed that this patient presents a new syndrome of pseudo-hypoaldosteronism with the end organ defect in sweat glands instead of the kidneys.