● 445 ISOLATION OF AN IMMUNOREACTIVE SUBSTANCE IN PATIENTS WITH DEXAMETHASONE-SUPPRESSIBLE HYPERALDOSTERONISM (DSH).

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We have isolated a substance immunoreactive (IR) with the aldosterone (aldo) antibody in patients with DSH. Substantial data exists that an unidentified steroid with mineralocorticoid properties plays an important role in the etiology of the hypertension in patients with DSH. This IR substance is more polar than 18-oxocortisol by paper chromatography. It is also more polar than aldo, facilitating separation from aldo utilizing high-pressure liquid chromatography. This substance was detected in both the free (930 pg IR/ml urine) extracts of urine in patients with DSH and was not detected in non-hypertensive controls. In addition, this IR substance was not detected in an adrenalectomized patient and was not detected in two patients with 11β-hydroxylase deficiency with and without hypertension. In patients with DSH, the IR substance increased substantially after a 6 hr infusion of ACTH (3400 pg IR/ml urine). In normal controls, no appreciable amount of immunoreactivity was detected in the baseline state. After ACTH stimulation a small amount was detected. Dexamethasone administration results in suppression of aldosterone and suppression of the IR substance in patients with DSH. With the techniques we have developed, we are now able to isolate a sufficient amount of purified material to submit for mass spectrometry analysis.

† 446 TREATMENT OF ANDROGEN EXCESS IN ADOLESCENT PATIENTS.

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Fourteen hirsute girls, ages 12-22 yrs (M±SD 17.3±2.7 yrs), in whom 21OH deficiency was excluded by 1 h° IV bolus Cortrosyn test in 1981 were evaluated by a dexamethasone (dex) suppression test (0.5 mg QID) with measurement of serum androgens on d5 and then treated with a bedtime dose of dex (0.5 mg in 10, 0.25 mg in 4) for 7-41 mos (mean 15.7 mos) with visits q3 mos. Baseline free testosterone (FT) was ↑ in 14/14 (19-57 pg/ml); DHAS > 350 ug/dl in 10/14; DHA > 790 ng/dl in 8/14; Δ_4 > 300 ng/dl in 5/14; urinary 17KS > 15 mg/24 h in 8/14. With the dex test DHAS↓> 50% in all (mean 70%), FT < 15 pg/ml in 8/14. With dex treatment DHAS ↓21-92% (mean 51%), FT was < 15 pg/ml in only 4 patients. Hirsutism did not change in 9, ↓ in 4, and ↑ in 1 with dex therapy. Of 9 patients with irregular menses, only 3 became regular on dex. Side effects (striae, weight gain and acne) occurred in 6 on 0.5 mg dex but not on 0.25 mg. The 2 patients with the most striking clinical response to dex did not recur 14 mos and 28 mos off dex. All others off treatment showed ↑ serum androgens. 7/14 (5 with ↑ DS) not responding well to adrenal suppression responded to oral contraceptive therapy with ↓ FT 0.4-6 pg/ml and improved control of hirsutism. The data suggest that single dose dex is satisfactory in patients who maintain FT <15 pg/ml without side effects. In others with adequate suppression by dex test, other schedules or glucocorticoids may be necessary. In hirsute adolescents without adequate suppression of FT, ovarian therapy is required.

447 THE EFFECT OF POST-NATAL AGE ON THE RESPONSE OF THE PITUTITARY-THYROID AXIS TO THYROTROPIN RELEASING HORMONE.

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Transient hypothyroxinemia is a common problem in the preterm infant. The response of the pituitary-thyroid (P-T) axis to exogenous thyrotropin releasing hormone (TRH) infusion has been used to confirm the euthyroid state of these preterm infants. The purpose of this study was to define the effect of post-natal age on the response of the P-T to TRH infusion. Eight preterm infants with RDS (Group I) and 10 preterm infants without RDS (Group II) received 20 mcg/kg TRH IV on days 3 and 14 of life. The mean birth weights, gestational age and Apgar scores were similar in both groups. The pattern of the serum thyroid stimulating hormone (TSH) response to TRH was similar in both groups on both days. In each group, the mean serum TSH level prior to TRH infusion was similar at day 3 and day 14. The mean serum TSH level was significantly elevated by 30 minutes (m) and declining by 180 m. At 30 and 180 m, the mean serum TSH level was significantly higher at day 3 compared to day 14. Compared to pre-infusion of TRH values, the mean serum thyroxine (T_4) and triiodothyronine (T_3) levels were significantly increased on day 3 at 180 m in both groups. There were no other significant differences in mean serum T_4 and T_3 levels in either group at any other time. Conclusions: 1) In the preterm infant with or without RDS, the serum TSH response following infusion of TRH is significantly different at day 3 compared to day 14 of life; 2) the thyroid gland response is similar at 3 and 14 days.

† 448 TREATMENT OF PERSISTENT PUBERTAL GYNECOMASTIA WITH DEHYDROTESTOSTERONE HEPTANOATE (DHT-hp).

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Four pubertal boys ages 14-16 yrs. with gynecomastia for 16 mo. - 2 yrs. were treated with DHT-hp 200-400 mg IM at 2-4 wk. intervals for 4 mo. Initially, breast diameters ranged 3.8 to 7.5 cm with area of breast base (A.B.) 11.0 to 44.2 cm^2. Plasma testosterone (T), estradiol (E_2), LH, FSH and A.B. were measured weekly for 4 weeks and at 3-4 week intervals thereafter. The table shows the mean values (± S.E.) for the four boys at selected intervals.

	Initial	2 wks.	4 wks.	13-16 wks.
A.B. (cm^2)	24.3 ± 4.1		19.8 ± 3.1*	7.2 ± 1.5†
T (ng/dl)	283.8 ± 87.5	29.5 ± 3.3*	168.0 ± 63.2	40.4 ± 4.0*
E_2 (pg/ml)	23.8 ± 3.2	10.8 ± 0.8*	25.3 ± 4.3	12.8 ± 1.6*
LH (ng/ml)	15.5 ± 3.3	< 11	14.5 ± 3.5	< 11
FSH (ng/ml)	190.5 ± 50.7	58.8 ± 18.5*	137.8 ± 12.3	53.0 ± 12.8

*p < .05 †p < .001

Maximal suppression of T, E_2 and FSH occurred at 2 wks. followed by rebound at 4 wks. The injection frequency was increased to every 2-3 wks. On this schedule suppression of T, E_2 and FSH was maintained and clinical response improved. The two boys with initial T < 200 were relatively resistant to suppression of FSH and E_2 by DHT-hp. All four boys responded, had a 63 to 78% reduction in breast size and an acceptable cosmetic result. DHT-hp is a promising agent for the treatment of significant persistent gynecomastia.

449 SENSITIZATION TO PARATHYROID HORMONE (PTH) EFFECT IN KIDNEY AFTER GROWTH HORMONE (GH) REPLACEMENT THERAPY IN GH DEFICIENT CHILDREN.

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GH has been shown to sensitize the adrenal glands to ACTH, probably by increasing the activity of the mitochondrial 11-hydroxylase. In kidney cell culture, stimulation of 1↙-hydroxylase, another mitochondrial enzyme, could be induced by GH. We are presenting the long term effect (6 months) of GH replacement (0.1u/k IM three times per week) on 25 (OH) Vit D and 1,25 $(OH)_2$Vit D levels in 12 GH-deficient children (table).

	Before $\bar{X} \pm$ SD	After $\bar{X} \pm$ SD
25 (OH) D_3 (ng/ml)	22.8 ± 11.0	29.3 ± 5.7
1,25 $(OH)_2D_3$ (pg/ml)	23.8 ± 18.4	57.4 ± 23.1

The acute responsiveness (3h) of the same metabolites to the PTH administration (250u IV) was also evaluated before and after GH therapy in three children. There was not significant increase of 1,25 $(OH)_2D_3$ before GH. However, 6 months after GH therapy the PTH administration induced a 3-fold increase in the 1,25 $(OH)_2D_3$ levels, suggesting that GH exerts its effect predominantly in the kidney mitochondria by increasing the sensitivity of the 1↙-hydroxylase to PTH.

450 ASSOCIATION OF CUSHING'S SYNDROME CAUSED BY PRIMARY ADRENOCORTICAL NODULAR DYSPLASIA WITH ATRIAL MYXOMA.

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Association of Cushing's syndrome caused by primary adrenocortical nodular dysplasia (PAND) with atrial myxoma was recently reported by Schweizer-Cagianut, Salomon and Hedinger in a Swiss family. We have recently studied a female who presented at age 13 with clinical signs of Cushing's syndrome. Serum cortisol was markedly elevated, and there was no suppression with low and high doses of dexamethasone. Arteriogram indicated an enlarged left adrenal gland. On surgical removal of the left adrenal, PAND was found. After a one year remission Cushing's syndrome recurred, and the other adrenal was excised, also revealing PAND. Three years later a systolic ejection murmur with a mid-systolic click was detected. Echocardiogram revealed a large right atrial mass. Serum hyaluronic acid level was 30.8 μg/ml (normal 0-5). Two myxomas, one attached to the RA septum and the other to the septal leaflet of the tricuspid valve, were removed, with recovery of the patient. A genetic basis for the association of PAND with atrial myxoma is postulated. Determination of serum hyaluronic acid levels is helpful in the diagnosis of atrial myxomas.