355 OPTIMAL THERAPY FOR CONGENITAL ADRENAL HYPERPLASIA (CAH). Avtar K. Razdan, Stephen Bickel & Robert L. Rosenfield, Univ. of Chicago, Dept. of Ped., Chicago

Different treatment regimens based on current knowledge about ACTH rhythms were evaluated for controlling CAH. Circhoral patterns of plasma progestins (progesterone [P], 17-OH-P [17P]) and androgens (androstenedione, testosterone, dehydroepiandrosterone-SO_4)were analyzed.

Spacing cortisone (E) or cortisol(F)in 3 equal doses about q 8 h was found to bring plasma androgen levels to or below normal in the 4 cases studied. Progestins were not so well controlled, even by E doses large enough to cause evidence of overdosage in 1 patient. This treatment regimen was associated with a phase-shift of maximum adrenal secretion to 0700-1120 hr. Therefore, two other replacement protocols were attempted in two cases: giving 40% of the daily E or F dose upon arising and/or at bedtime. Both regimens were biochemically very inadequate. One patient could not be controlled until a subclinical Na-losing state was controlled by Florinef. Long-acting glucocorticoid (dexamethasone=dex) administration in one or two, low, daily doses proved to be the only form of treatment which could normalize plasma 17P in two girls. With normalization of progestins, menses began or resumed in these cases.

We conclude: 1) control of progestin levels, particularly 17P, is impossible on standard forms of therapy in some cases of CAH, 2) this is occasionally due to occult mineralocorticoid deficiency, 3) low-dose dex is the best available therapy for some cases, and 4) elevation of progestins may be more important than that of androgens in the oligomenorrhea of CAH.

356 MATURATION OF THE REPRODUCTIVE ENDOCRINE SYSTEM IN CYSTIC FIBROSIS (CF). E. Reiter, R. Stern, C. Doershuk, and A. Root. Depts. Ped., Univ. So. Fla., Tampa, and Case Western Reserve, Cleveland.

Prolonged survival has magnified the clinical problem of delayed sexual maturation in CF. Cross-sectional evaluation of 19 prepubertal and 66 pubertal CF patients revealed ($\bar{X}$ ± SEM):

	LH(mIU/ml)	T(ng/dl)*	DHT(ng/dl)*	E_1(pg/ml)†	E_2(pg/ml)†
Prepub	1.5±0.3	4.4±0.6	2.3±0.3	16.1±4.4	7.3±1.4
Pubert	5.6±1.0	193 ±30	11.2±2.1	26.4±4.2	20.9±7.2

The data are within the normal range for stage of maturation. When expressed on an age-related basis, however, the data reflect the delayed sexual development of these patients. Between 10 and 20 yr, levels of the adrenal androgen, DHAS, were significantly ($p<.01$) lower than in normal children. 23 CF patients underwent a 3 hr infusion of 100 ug synthetic LHRH ($\bar{X}$ ± SEM):

	LH-Basal	LH-Inf.	Peak LH	ΔT*	ΔE_2†
Prepub	1.8±0.4	4.6±1.7	7.7±2.8	4±.7→6.6±2.1	--
Pubert	4.8±2.1	37 ±3.2	63 ±21	71±4→153 ±43	13±3→32±8

These data do not differ from normals in our clinic. Within the group of pubertal CF, the mean ($r=.673$) and peak($r=.676$) LH response correlated significantly ($p<.01$) with the aggregate CF assessment score, as well as with each of its components. These data suggest: 1) Hormonal studies in CF reflect the degree of sexual maturation, as in normal children; 2) Adrenal androgenesis, a sensitive indicator of early pubescence, is diminished throughout the 10 to 20 yr period in CF; and 3) Delayed sexual development in CF seems related to overall clinical status, as well as to the degree of nutritional debilitation. *males †females

357 ACTION OF HUMAN GROWTH HORMONE (hGH) ON T_3 METABOLISM Iraj Rezvani, Angelo M. DiGeorge, Steven A. Dowshen, Carlos J. Bourdony. Temple Univ. Sch. of Med., Dept. of Ped., St. Christopher's Hospital for Children, Philadelphia

Although hGH has been shown to suppress the release of TSH, its action on the metabolism of thyroid hormones remains unknown. We examined the effect of hGH on a loading dose of T_3 in 11 hypopituitary children (3 to 18 years). Six patients were on oral L-thyroxine because of TSH deficiency. Before and after one month of hGH therapy (2U three times weekly), a single dose of T_3 (50 to 100 ug) was administered orally; serum levels of T_3 and T_4 were measured at 0,4,6,12,18 and 24 hours. Both before and after hGH therapy, serum levels of T_3 peaked at 4 hours and returned to normal by 24 hours. After hGH therapy, significantly higher levels of T_3 were achieved at 0,4,6,18 and 24 hours (p values from 0.003 to 0.03). In contrast, following T_3 ingestion, serum levels of T_4 decreased and reached a nadir at 18 hours. The decrease in serum levels of T_4 were of similar magnitude whether the patients were or were not receiving replacement therapy with L-thyroxine. Therefore, these changes could not be explained by T_3 induced suppression of thyroid gland. The decrease in serum levels of T_4 was not influenced by hGH therapy. In conclusion, hGH causes an increase in the basal level of serum T_3 and an augmentation of T_3 levels following a loading dose of T_3; mechanisms for these changes are not known. The decrease in serum levels of T_4 following a T_3 load, although not altered by hGH, is of special interest. This effect seems to be due to changes in extrathyroidal metabolism of T_4.

358 SEXUAL PRECOCITY CAUSED BY OVARIAN FOLLICULAR CYSTS: SPONTANEOUS REGRESSION AND RECURRENCE WITH PREPUBERTAL GONADOTROPIN LEVELS. Gail E. Richards, Selna L. Kaplan, and Melvin M. Grumbach. Univ. California San Francisco, Department of Pediatrics, San Francisco, California 94143.

Although small follicular ovarian cysts are common in asymptomatic prepubertal girls, larger ones may be associated with sexual precocity which can regress after cyst removal. We report 1 patient with recurrent functional ovarian cysts and another who had a presumptive single episode of cyst formation that regressed spontaneously. Patient 1 developed breasts at 3 years and vaginal bleeding at 4-10/12. Plasma estradiol (E_2) was 180 pg/ml and LRF response was prepubertal (LH 0.4-0.8 ng/ml LER-960). E_2 levels fell within 6 weeks to <10 pg/ml and remained low until 5-3/12 when bleeding recurred with E_2 796 pg/ml. A 4x3 cm ovarian follicular cyst with partial luteinization was removed from the left ovary. Cyst fluid contained 70,300 pg/ml E_2; 21,600 pg/ml E_1. Post-op the LRF test remained prepubertal when E_2 was <10 pg/ml. At 5-5/12 E_2 was 500 pg/ml and vaginal bleeding recurred. Treatment was begun with medroxyprogesterone acetate; during 20 months of therapy E_2 has gradually fallen to <10 pg/ml and gonadotropin response to LRF remains prepubertal (LH 0.7-1.8 ng/ml). Patient 2 presented at 3-11/12 with breast development and E_2 279 pg/ml. E_2 fell to <10 pg/ml within 1 month and remained low for 2 years. At 6 years (BA 7-10/12) E_2 was 13 pg/ml and the LRF test was pubertal. In sum 1) Markedly elevated E_2 levels can occur in functional ovarian cysts as well as tumors. 2) Sporadic ovarian cyst formation may underlie some instances of premature thelarche or arrested sexual precocity.

359 REPLACEMENT THERAPY WITH HUMAN GROWTH HORMONE (hGH); CONSERVATION VIA LOW DOSAGE AND ROUTINE THYROID (T) REPLACEMENT. Arlan L. Rosenbloom, Michael L. Netzloff, Adolfo D. Garnica, and F. Thomas Weber (Spon. by Owen M. Rennert). University of Florida College of Medicine, Department of Pediatrics, Gainesville, Florida.

Single weekly injections of 2.5mg hGH have been given for greater than one year to 15 children with hypopituitarism who had been growing 2.8cm/yr(±1.2SD). Six were receiving T, two of whom also received low dose Cortisol (C). One C-treated and one who developed hypothyroidism (HT) failed to respond to hGH the first year. The other 13 pts grew 8.2cm(±1.5) the 1st yr and 4 of them grew 7.2cm(±1.9) during yr 2 on 2.5mg/wk. The two who failed to respond the 1st yr did respond to 2.5mg 2x/wk but T therapy in one and stopping C in the other with only 2.5mg/wk produced greater growth (3.5 - 8.2 - 11.8cm/yr). Three others had 2nd yr failure due to acquired HT (2cm/yr±.2) with marked improvement on T (9±.2). Two without cryptic HT responded poorly to 2.5/wk after 1 yr and better to 2.5mg twice weekly. Twenty-two full treatment yrs at 2.5mg/wk without HT or C suppression included 13 1st yr, 4 2nd yr and 5 3rd yr periods with average growth 8.6cm/yr(±1.6). This exceeds 1st yr rates for the U.S. Collaborative Study (7.0cm/yr) using 2mg 3x/wk or the Tanner series with 4x our dose (7.3cm/yr the 1st yr - $p<.025$). Four of 9 without HT at the outset developed resistance to hGH from acquired HT. Single weekly injections of 2.5mg hGH are adequate for growth in most cases and should be accompanied by routine T therapy and minimal C replacement.

360 CIRCADIAN PLASMA GH CONCENTRATIONS IN CHILDREN WITH PHENYLKETONURIA (PKU), HYPERPHENYLALANINEMIA (H), CYSTINOSIS (C) AND HOMOCYSTINURIA (HU). H. Schedewie, Ch. Lipinski, H. Schmidt (Spon: J.Elders) Dept. Pediat, UAMS, Little Rock,AR & Univ. Children's Hosp., Heidelberg, Germany.

Inborn errors of amino acid metabolism are frequently associated with growth disorders, the pathogenesis of which is unknown. We have performed arginine-insulin tolerance tests and measurements of circadian hormone secretion in patients with PKU (n=2), H (1), C (1), HU (4) and normal control children (4). Integrated mean GH, insulin and blood sugar levels were obtained using the Sigmamotor ML-6 constant withdrawal pump. Blood was collected over ice and divided into hourly portions (n=24) to permit detection of possible pulse secretion of GH and correlations to the patients' sleep-wake activity as recorded by EEG. Two patients with HU, whose plasma and urine aminograms were normalized by diet and vitamin B_6, were re-investigated after treatment had been discontinued for > 5 weeks. Summary of findings: (1) GH concentrations in HU were markedly elevated in patients out of metabolic control as compared to subjects with near normal aminograms. (2) GH concentrations were within the normal range in H and one patient with PKU, but increased in another girl with PKU and tall stature. (3) The lowest GH concentration among all subjects was observed in a 5-year old boy with C who was also severely dwarfed.- Supported by German Research Foundation, Grant Sche. 119/1