426 PITUITARY APLASIA IN AN 11 YEAR OLD GIRL: BIOCHEMICAL AND RADIOLOGICAL EVALUATION. M. De Vroede, M.J. Nelson, G.B. Cutler, and D.L. Loriaux. (Spon by J. Sidbury) DEB, NICHD, Bethesda, Maryland 20205.

An 11 year old girl presented with short stature. Panhypopituitarism was diagnosed and replacement therapy was started with thyroxine, cortisol, and growth hormone treatment, which resulted in catch-up growth. We obtained the following hormonal data: 1) undetectable growth hormone secretion after arginine-insulin (<0.8 ng/ml), 2) no prolactin rise after TRF and chlorpromazine (<2 ng/ml); 3) no TSH rise after TRF (<1.0 μIU/ml), 4) no LH, FSH rise after LRF. When LRF was given 0.025 ug/kg IV every 2 hours for 5 days (Valk, JCEM 53, 184, 1981) LH remained <3.5 mIU/ml and FSH was undetectable. A 5-d ACTH infusion caused a modest rise of plasma cortisol (<0.2 to 8.8 ug/dl), consistent with secondary adrenal insufficiency. Posterior pituitary function and adrenomedullary function were normal. The thyroid responded normally to exogenous TSH. Aldosterone secretion increased upon upright posture and on a low salt diet. Skull radiography showed a shallow sella turcica. Cerebral computed tomography did not identify the pituitary gland and suggested hypoplasia of the right carotid artery. This was confirmed by a a technetium scan of the brain, which showed asymmetric cerebral blood flow. In conclusion, this patient had biochemical and radiological evidence of absence of the pituitary gland. Thus, although she survived without treatment until age 11, she appears to have the syndrome of congenital pituitary aplasia described by Blizzard (J. Ped. 48, 782, 1956). Pituitary vascular insufficiency is a possible cause of this patient's pituitary aplasia.

427 **ADRENAL SONOGRAPHY AND COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF CLASSICAL AND NONCLASSICAL 21-HYDROXYLASE DEFICIENCY CONGENITAL ADRENAL HYPERPLASIA,** IA Engel, S Pang, MI New, Depts of Pediatrics and Radiology, The New York Hospital-Cornell Medical Center, New York, NY 10021

Adrenal sonogram and computed tomography (CT) studies were carried out as a part of the diagnostic workup either for evaluation of the cause of elevated androgen levels or to look for autonomously functioning adenomatous adrenal lesions in patients with proven classical or nonclassical steroid 21-hydroxylase deficiency (21-OH def) congenital adrenal hyperplasia (CAH). Sonograms revealed unequivocally hyperplastic adrenal glands in 2 neonates with female pseudohermaphroditism due to classical CAH and in 1 inadequately treated 9-year-old child with classical CAH.

Adrenal CT was performed in 12 patients. These CT studies revealed massively macronodular, hyperplastic adrenals in a 30-year-old patient with untreated classical CAH and markedly enlarged adrenals in 4 patients with poorly treated classical CAH, while mildly hyperplastic adrenals were seen in 4 of 7 patients with nonclassical (mild) CAH.

Thus, sonographic and CT examination of the adrenal glands exhibited unequivocal evidence of bilateral adrenal hyperplasia in classical 21-OH def CAH, indicating the usefulness of these studies in expediting the diagnosis of classical CAH. However, the CT evaluation in the nonclassical form of CAH is not consistently useful in imaging adrenal hyperplasia.

428 PRODUCTION OF INSULIN-LIKE GROWTH FACTOR-I (IGF-I) BY HUMAN PLACENTAL TISSUE. Michael Fant, Alan Moses, and Hamish Munro. (Spon. by Barry T. Smith) Depts. of Pediatrics and Medicine, Harvard Medical School and USDA Human Nutrition Research Center, Boston, Mass., and Dept. of Nutrition and Food Science, Mass. Inst. of Tech., Cambridge, Mass.

Previous data revealed that a variety of mouse fetal tissues, with the exception of the placenta, are capable of producing IGF-I that may act locally to regulate fetal growth (D'Ercole, et al.,Dev. Biol. 75: 315, 1980). Although the placenta is essential for normal fetal development, little is known regarding the mechanisms controlling placental growth. Human placental explants were examined at various stages of gestation for the ability to produce IGF-I in organ culture. The placental explants were washed extensively and incubated in serum-free media. The media was acidified and chromatographed over a Sephadex G-50 column to separate the IGF-I from specific binding proteins. IGF-I was measured by specific radioimmunoassay (RIA). Placental tissue from all gestational ages secreted immunoreactive IGF-I, 2.19±.35 ng./mg. prot./48 hrs. (Mean± S.D.). There was no difference in IGF-I production between pre-term (9-19wk.) and term placentae under these conditions. The activity was reduced >60% by 50 uM cyclohexamide, suggesting that most of the activity was the result of de novo protein synthesis. The similarity of this material to authentic human IGF-I is supported by parallel displacement in the RIA and co-elution on a Sephadex G-50 column. The human placenta contains specific IGF receptors. These data demonstrate that the human placenta is also capable of producing IGF-I, that may act locally to regulate placental growth.

● 429 MECHANISM OF PRECOCIOUS PUBERTY IN GIRLS WITH McCUNE-ALBRIGHT SYNDROME (MAS). Carol M. Foster, Ora H. Pescovitz, Thomas H. Shawker, Judith L. Ross, Gordon B. Cutler, D. Lynn Loriaux and Florence Comite (Spon. by Daniel W. Nebert). NICHD and Diagnostic Radiology, NIH, Bethesda, MD 20205

We studied 7 girls, ages 1.3 to 10 yrs., with precocious puberty associated with MAS. In 6 of the 7 girls, basal and LHRH-stimulated gonadotropins and bioactive LH were prepubertal. In one girl, gonadotropins and bioactive LH were in the pubertal range. Ovarian volumes (mean 6.4, range 1.4 - 12.9 ml) were increased in all 7 girls compared to prepubertal girls (nl < 0.9 ml - Radiology 125:477(1977)). The girls with MAS had greater asymmetry in ovarian volume than did girls with true precocious puberty (TPP) (R to L difference 5.9 ± 1.9 ml vs. 1.5 ± 0.2 ml in TPP; $p < 0.05$). The logarithm of plasma estradiol correlated significantly with ovarian volume ($p < 0.05$). Ovarian volumes and plasma estradiol fluctuated markedly over time. LHRH-analog treatment, given to 6 of the 7 girls, failed to suppress menses, ovarian cyst volume, or estradiol levels in the five girls who had low gonadotropins. The girl who had true puberty responded to LHRH-analog treatment. She had a bone age of 13.5 years, which is within the range when puberty normally occurs. Thus, we cannot exclude the possibility that her gonadotropins were also low when secondary sex characteristics first appeared. We conclude that the mechanism of precocious puberty in the majority of girls with MAS is intermittent ovarian estrogen secretion independent of pubertal hypothalamic-pituitary activation.

● 430 ACCELERATION OF LINEAR GROWTH AFTER REPEATED DOSES OF GROWTH HORMONE-RELEASING FACTOR (GRF). Marie Gelato, Judith Levine Ross, Ora Pescovitz, Fernando Cassorla, Marilyn Skerda, Penelope Feuillan, D. Lynn Loriaux, and George R. Merriam. (Spon. by David Nelson). DEB, NICHD, Bethesda.

GRF's are potent stimulators of GH secretion in man. We administered 1 μg/kg GRF 1-44 NH_2 to 15 children with documented GH deficiency, ages 4-20 years. 12/15 had a measurable GH response. Following discontinuation of GH therapy for at least 2 months, 2 responders and 1 nonresponder then received 1 μg/kg GRF IV q 3 h for 10-12 d. Short-term growth was assessed by the lower leg measurement technique of Valk et al. (Growth 47:53, 1983). GH was measured q 20 min for 12 h on the 1st, and 5th or 7th days of multiple-dose therapy and for the first 12 hours off GRF. Somatomedin-C (SmC) levels were drawn daily. Baseline GH levels were <0.7 ng/ml. In the 2 responders, mean peak GH response to GRF increased, SmC rose, and lower leg growth velocity (GV) accelerated (Table). GH levels returned to baseline after GRF was stopped. The third patient had no hormonal or growth response.

			Single Dose	---------Multiple Doses----------			
Pt.	CA yrs	BA yrs	Peak GH ng/ml	Peak GH, ng/ml Day 1	Day 5/7	SmC, U/ml Basal→Rx	ΔGV mm/3wks
1	10 2/12	7 6/12	9.3	9.2	13.9	0.18→0.71	3.3
2	13 6/12	12.6/12	2.2	4.2	14.3	0.46→2.0	1.2
3	20 8/12	11	1.1	<0.7	<0.7	<0.1 →<0.1	0

Thus most children with GH deficiency respond to GRF, and multiple doses of GRF can accelerate short-term linear growth. GRF may form the basis for an alternative treatment of GH deficiency.

● 431 RENEWED CATCH-UP GROWTH ON INCREASING GROWTH HORMONE (GH) DOSAGE DURING GH REPLACEMENT THERAPY J. Gertner, S. Cianfredi, W. Tamborlane, Yale U. School of Med.

Sustained accelerated growth is necessary for GH-deficient patients to achieve normal mature heights. However, the catch-up growth seen during the initial 12-18 mos of standard GH replacement Rx (0.3 U/kg/wk) does not persist and few GH-treated children attain their full potential height. Previous studies of the dose/growth-response relationship have been confined to the initial phase of Rx. To assess the efficacy and safety of higher doses, given when catch-up growth had ceased, we gave GH for 8 months at 0.9U/kg/week to 8 GH-deficient children (7-12 yrs) earlier treated for 2-8 yrs with GH at 0.3 U/kg/wk. Mean growth velocity (GV) increased from 5.5±1.2 to 9.7±2.5 cm/yr ($p < .01$). GV corrected for bone age was, as expected, normal on standard Rx and increased to over 5 standard deviations above the mean on the higher dose. This acceleration represents a renewal of true catch-up growth. Mean somatomedin C levels rose from 0.32±0.3 to 0.95±0.9 U/ml ($p < .05$) as GV increased. Glucose tolerance was barely affected by the dose increase, while the area under the insulin curve increased slightly (1.3±.5 to 2.2±.2 mU/ml.min; p=.17). Serum lipid levels were not adversely affected, fasting triglycerides falling from 67±34 to 64±21 mg/dl, while cholesterol, rose from 158±31 to 166±22 mg/dl. There was no change in the need for thyroid replacement, two patients had modest elevations in anti-GH antibody titers during high dose Rx. Improved supplies of GH may permit an upward revision in dose recommendations for replacement Rx.