419 MECHANISMS OF SODIUM (Na) CONSERVATION IN SALT-LOSING CONGENITAL ADRENAL HYPERPLASIA (SL CAH). Bruce S. Keenan, Don P. Wilson, John H. Holcombe, Raghu Nath and George W. Clayton. Dept. of Pediatrics, Baylor College of Medicine, Houston, Texas.

Na balance and fractional sodium excretion (FeNa) were measured in 10 infants with SLCAH, treated with subcutaneous pellets of 11-deoxycorticosterone acetate (DOCA). On 2mEqNa/Kg/d intake, Na balance was +.56 ± .30mEq/Kg/d (s.d.) n=10 and on 1 mEq/Kg/d + 0.05 ± .31 (n=18). On 1 mEqNa/Kg/d, FeNa decreased from 0.49 percent ± .08 (s.e.) to .23 ± .02. Inexplicably, each infant showed an increase in plasma DOC on the 1mEq/Kg diet: 170 + 18 (s.e.) ng/dl to 321 + 32 (P<.005). The correlation between changes in FeNa and DOC (r=-.155) was not significant and there was no significant change in blood pressure or creatinine clearance. Weight decreased 2.1 percent ± 0.6 (s.e.), but change in weight did not correlate with change in FeNa, DOC or plasma renin (PRA). Although PRA was elevated in many of these studies, there was no correlation between initial PRA and sodium excretion on day 3 of either diet. Maintaining Na balance on 1mEq/Kg Na despite elevated initial PRA suggested that a compensation had been made to less than adequate DOC levels. One infant with congenital absence of adrenal function showed decrease in FeNa without a change in plasma DOC. Clearly DOCA therapy is necessary for sodium homeostasis in these mineralocorticoid deficient subjects. However, these data indicate that nonsteroidal mechanisms play a major role in the renal adjustment to acute Na restriction. (This work supported in part by USDA/ SEA 58-7B30-9-60)

420 DISRUPTED OVARIAN FUNCTION IN RHESUS MONKEYS WITH EXPERIMENTALLY INDUCED INSULIN INSUFFICIENCY. Joseph W. Kemnitz, Stephen G. Eisele, Michael J. Engle, Robert H. Perelman, Guenther Scheffler, and Philip M. Farrell. University of Wisconsin-Madison, Regional Primate Research Center and UW Hospital and Clinics, Department of Pediatrics.

We are utilizing a nonhuman primate model to elucidate the mechanisms of abnormal fetal lung development in pregnancies complicated by maternal hyperglycemia. Healthy adult female Macaca mulatta were made severely diabetic by infusion of the pancreatic B-cell toxin streptozotocin (STZ, 47.5 mg/kg). These animals have impaired reproductive function as evidenced by daily ratings of coloration of sexual skin and incidence of menstruation. Prior to receiving insulin therapy, diabetic animals (n=6) exhibited only 26% of the expected number of apparently ovulatory menstrual cycles (1 cycle/30 days, 321-408 days of observation/animal) compared to 89% for control animals (n=7, 114-304 days/animal; t= 5.17, p<.01). Diabetic animals receiving insulin therapy (n=6, 62-436 days/animal) also exhibited fewer than expected normal cycles compared to controls (51%, t=2.45, p<.05). Radioimmunoassay revealed serum concentrations of estradiol and progesterone in amenorrheal diabetic monkeys to be comparable to those seen in ovariectomized monkeys. Three of 4 control pregnancies were maintained into the third trimester, while 1 of 1 untreated diabetic and 2 of 4 treated diabetic pregnancies were maintained. Additional monkeys treated recently with a lower dose of STZ (30mg/kg) have exhibited milder glucose intolerance and less disruption of ovarian function. (Support: NIH HD11429 and RR00167 and JDF 79R263.)

● **421** ACUTE SOMATOMEDIN RESPONSE TO GROWTH HORMONE THERAPY. Stephen F. Kemp, Ron G. Rosenfeld, and Raymond L. Hintz. (Spon. by R.M. Suskind). Stanford University School of Medicine, Department of Pediatrics, Stanford, CA and University of South Alabama, Department of Pediatrics, Mobile, AL.

We have examined the acute somatomedin (SM) response to growth hormone (GH) therapy in 21 GH deficient children using a placental membrane radioreceptor assay (RRA), which measures a variety of SMs, and a radioimmunoassay (RIA) specific for SM-C and insulin-like growth factor I (IGF-I). RRA and RIA SM determinations were performed on the same acid-chromatographed samples, obtained before initiation of therapy and 13 hr after each of 4 daily injections of GH (0.1 U/kg). The 4 days of GH therapy resulted in an increase in SM levels from 0.39±0.24(SD)U/ml to 1.18±0.62(SD) U/ml determined by RRA and 0.19±0.14(SD)U/ml to 0.82±0.51(SD)U/ml determined by RIA. A single injection of GH resulted in a significant rise in plasma SM levels measured by either RRA or RIA (p<0.001). Subjects who responded poorly to 2 injections of GH also had low SM levels after 4 days and even after 6 weeks of GH therapy.

The RRA resulted in consistently higher values than the RIA, particularly when compared to a pure IGF-I/SM-C standard. SM peptide content determined by RRA and RIA were strongly correlated for individual subjects as well as for the whole group. However, the RRA/RIA ratio among individual subjects varied from 0.85 to 2.50. The marked difference in SM peptide content measured by RRA and RIA and the variability in the RRA/RIA ratio among individual subjects suggests that the IGF-I/SM-C RIA measures only one of a number of GH dependent SM peptides.

● **422** 1,25 DIHYDROXYVITAMIN D(1,25 D) AMELIORATES PREDNISONE INDUCED GROWTH RETARDATION IN LONG EVANS RATS. Lyndon Key, Patricia Baker, Marc Drezner, and Stephen Osofsky (Spon. by Constantine Anast), Dept. of Pediatrics, Harvard Medical School, Boston, Mass., Depts. of Medicine and Pediatrics, Duke Univ. Med. Center, Durham, N.C.

High-dose prednisone therapy in rapidly growing children is complicated by decreased linear growth. Alterations in Vitamin D metabolism are proposed as a factor contributing to this. To test this hypothesis, 50ng of 1,25 D were administered to weanling Long Evans rats, in addition to 1.0mg of prednisone, from days 21-45. This 21 day period represents the period of most rapid growth for the weaned rats. The mean increments of growth (cm ± SD) for the prednisone treatment and control groups are as follows:

CONTROLS		TREATMENT	
Sham-fed(10)	1,25 D(10)	Prednisone(8)	1,25 D+Prednisone(9)
6.4±1.6cm	5.9±1.6cm	4.4±1.1cm	5.5±0.8cm

The mean increment of growth for rats treated with prednisone is significantly less than the sham-fed group and the group treated with 1,25 D($p<0.01$)*. Notably, rats supplemented with 1,25 D during treatment with prednisone have a growth rate that is superior to that of rats on prednisone alone ($p<0.05$)*, but not significantly different from either control group ($p>0.2$)*. Thus, 1,25 D supplementation improves growth when administered to rats receiving high-dose prednisone therapy. This supports the hypothesis that decreased 1,25 D contributes to reduced growth during high-dose prednisone therapy.

*analysis by single-tailed t test.

423 THE EFFECT OF GROWTH HORMONE (hGH) ON THE GONADAL RESPONSE TO CHORIONIC GONADOTROPIN (hCG) IN HYPOPITUITARISM. Howard Kulin, Eugeniusz Samojlik, Steven Santner, Richard Santen, and Laurence Demers, PA State U., Coll. Med.,M.S. Hershey Med. Ctr.,Depts. Ped.,Med. & Path.,Hershey, PA.

Data from rodent studies and the presence of phallic underdevelopment in some boys with isolated hGH deficiency suggest a role for somatotropin in gonadal sex steroid production. To assess this possibility, testosterone (T), estrone (E_1), and estradiol (E_2) were measured following 2 days of hCG before, during and after 1 yr of treatment with hGH in 14 patients with hGH deficiency. Gonadotropin excretion remained normal for prepubertal children in all individuals throughout the protocol. Four boys exhibited consistently poor T responses to hCG (poor responders) while the data in 5 patients (responders) reflect either the effect of repeated short courses of hCG or a synergistic action of hGH at testicular level. In 5 girls, only small E_2 increments were elicited by hCG but E_1 levels increased significantly and revealed an hGH-mediated effect. The $\bar{X}$ ± SEM for T (ng/dl) in boys and E_1 (pg/ml) in girls at 72 hr post hCG is shown below. An asterisk indicates significance ($p<.05$) compared to basal tests.

Group	basal	6 mo hGH	12 mo hGH	6 mo off hGH
Poor responders(T)	46±18	49±5	62±12	64±21
Responders (T)	169±46	296±79*	265±46	274±43*
Girls (E_1)	29±9	31±7	56±9*	39±15

Conclusion: hGH may increase gonadal responsivity to hCG in man but it does not promote increased T in those hypopituitary boys (with normal gonadotropins) who have reduced Leydig cell reserve.

424 THE CLINICAL SPECTRUM OF OPTIC NERVE HYPOPLASIA, HYPOPITUITARISM, AND ABSENT SEPTUM PELLUCIDUM. Stephen H. LaFranchi, Cheryl E. Hanna (Intro. by Neil R. M. Buist). University of Oregon School of Medicine, Department of Pediatrics, Portland.

Of 17 patients with optic nerve hypoplasia, hypopituitarism (HP), or absent septum pellucidum (SP), 11 presented with features of HP, 5 with eye signs, and 1 with microcephaly. Of the 11 with signs of HP, 9 had neonatal problems: 7 with hypoglycemia, 3 with diabetes insipidus, and 1 with microgenitalia. All 5 with eye signs presented with decreased vision in infancy. The infant with microcephaly underwent a CT scan which demonstrated an absent SP and corpus callosum. The disorder did not appear to be heritable in any case, although there was a female preponderance (12 female, 5 male); 6 of 17 mothers were teenagers at conception. Pituitary hormone deficiencies and CT scan findings are shown below:

		Hypo-	Pituitary Hormone Deficiencies					CT Scan	
Presentation	N	plastic Discs	HGH	TSH	ACTH	FSH/LH*	DI	Normal	Absent SP
Hypopituitarism	11	11	10	10	7	1	3	7	2
Eye signs	5	5	1	1	1	0	0	2	1
Absent SP	1	0	0	0	0	0	0	0	1
Totals	17	16	11	11	8	1	3	9	4

(*Only 2 patients have reached adolescence)

This experience demonstrates the need for an awareness of eye problems in neonates with HP and of HP in infants with optic nerve dysplasia. Whether this clinical triad represents one entity or several remains to be seen.