● 440 ARGININE VASOPRESSIN (AVP): A MECHANISM FOR "STRESS-INDUCED" ACTH SECRETION IN THE FETUS. Daniel J. Faucher, John C. Porter, Charles R. Rosenfeld, Depts. Pediat., Ob-Gyn, Physiol., Univ. Texas, Southwestern Med. Sch., Dallas, TX.

The "stress" hormone AVP has been shown in vivo and in vitro to directly stimulate ACTH secretion and to potentiate the effects of corticotropin releasing factor (CRF) in adult animals. A similar role for AVP in fetal secretion of ACTH during "stress" is unclear; therefore, we have studied the effect of continuous 30min infusions of AVP (12mU/min) on the secretion of ACTH in chronically instrumented late gestation fetal sheep (n=10, 130-141d) while continuously monitoring heart rate (HR) and mean arterial pressure (MAP). Arterial blood samples were obtained prior to, 15 and 30min during, and 60min postinfusion for measurements of PO_2, PCO_2, pH, hematocrit (Hct), AVP, and ACTH. As expected, at 30min HR fell from 167±6 (X̄±SE) to 115±7bpm* and MAP rose from 52±2 to 66±3mmHg*, both returning to control levels 30min postinfusion. PaO_2, pHa, and Hct were unchanged; $PaCO_2$ fell from 42±1.0 to 37±1.3mmHg*. Plasma levels of AVP rose from 2.3±0.2 to 85±7.5* and 89±11* pg/ml at 15 and 30min, respectively, while plasma levels of ACTH rose from 18±2.4 to 28±3.7 and 43±8.0*pg/ml, respectively, an increase of 150±45% at 30min; both returned to control levels at 60min postinfusion. Neither the preinfusion values nor the AVP-induced rise in plasma ACTH at 30min were significantly related to changing gestational age; however, there was a trend for the 30min %ΔACTH to fall. As in adult animals, AVP acts as a CRF, thereby suggesting an important role for this peptide hormone in modulating and coordinating the cardiovascular and hormonal responses observed during fetal "stress." *p<0.05.

● 441 ADAPTATION OF THE HYPOTHALAMIC-PITUITARY-ADRENAL AXIS IN LATE-ONSET CONGENITAL ADRENAL HYPERPLASIA. Penelope Feuillan, Peter Avgerinos, Thomas Schürmeyer, George Chrousos. Developmental Endocrinology Branch, NICHD, NIH, Bethesda, MD.

Patients with late-onset congenital adrenal hyperplasia(LOCAH)due to partial 21-hydroxylase deficiency have no clinical evidence of hypocortisolism, unlike patients with classical forms of CAH, who have elevated plasma ACTH and low serum cortisol levels. In order to study the interactions of the various components of the hypothalamic-pituitary-adrenal axis in LOCAH,we administered ovine corticotropin releasing hormone(oCRH),1 ug/kg,at 20:00h to 10 untreated patients with LOCAH (8 females, 2 males, ages 7-35y). Baseline(basal,B) and oCRH-stimulated(peak, P) ACTH and cortisol responses did not differ from normal and the integrated ACTH:cortisol response ratio was also normal. Stimulated serum 17-hydroxyprogesterone responses were significantly greater than normal ($p<0.005$). Stimulated serum Δ 4-androstenedione responses in 5 postpubertal female patients moderately exceeded those of 5 age-matched control females(p=NS). [Data shown as mean +SEM]

	ACTH,pg/ml		CORTISOL,ug/dl		17 OHP,ng/dl		ADIONE,ng/dl	
	B	P	B	P	B	P	B	P
Pts:	9.5 2	24±4	5±1	18±2	159±50	1135±197	98±5	256+48
Nls:	7.5±1	26±2	4±1	15±1	49±23	88±15	87±17	162±26

We conclude that patients with LOCAH compensate for the cortisol biosynthetic defect at the expense of a moderate increase in adrenal androgen secretion. The normal ACTH and cortisol responses to oCRH suggest that a new equilibium has been established between the pituitary and the adrenal gland.

442 THE NON-HORMONAL IODINE STATUS OF MOTHERS OF HYPOTHYROID INFANTS. Fort,P.,Marks-Katz,M. and Lifshitz,F. Dept. of Peds., Cornell University Medical College,New York, NY 11021 and Dept. of Peds., North Shore University Hospital, Manhasset,NY 11030.

Excessive intake of iodine by mothers can result in congenital hypothyroidism (CH) in their offspring. To assess such a possibility in a group of 17 newborns with CH, we evaluated the iodine status of their mothers by assessing iodine intake during pregnancy (by dietary recall) and by measuring maternal serum protein bound iodine (PBI) levels 3 weeks after delivery.In 7 out of 17,24 hr urinary excretion of iodine (UEI) was also measured. Thyroid disfunctions in newborns (low serum T4 levels with elevated TSH) were detected at 3 days of age by the N.Y. State Screening Program for CH and confirmed,usually at 2 weeks of age.Eight infants had goitrous hypothyroidism,5 ectopic thyroid gland and 4 thyroid agenesis.The dietary recall revealed that none of the mothers was consuming an excessive amount of iodine during pregnancy.The mean +SD serum PBI levels in all mothers were normal (6.24±1.0ug/dl).The mean±SD PBI levels of mothers of infants with goitrous hypothyroidism were the same as those with other types of CH (5.96±0.8ug/dl).The mean±SD 24 hr UEI was 10.7±6.7 ug/dl.None of the mothers was found to have any abnormalities of the thyroid function,and did not have anti-thyroid antibodies.An excessive intake of iodine during pregnancy appears to be a rather infrequent event and thus an unlikely cause of CH in newborns.Nor a lack of iodine in the mothers' diet appears to be a cause of CH.

443 ROLE OF GROWTH HORMONE ON PLASMA EPIDERMAL GROWTH FACTOR CONCENTRATIONS. Joseph P. Frindik, Stephen F. Kemp, M. Joycelyn Elders. University of Arkansas for Medical Sciences, Pediatric Dept. Little Rock, AR.

Epidermal growth factor (EGF) is known to accelerate proliferation and differentiation of multiple cell types. We previously reported that growth hormone deficient (GHD) children have decreased urinary EGF excretion compared to normal children and the excretion of EGF increases with growth hormone (GH) administration. We developed a heterologous, double antibody radioimmunoassay (RIA) based on mEGF to estimate plasma concentrations of EGF in humans. The detection limit of the assay was 0.10 ng/ml. Using this method, mean concentration of EGF in plasma from adults was 4.8±1.7 ng/ml and the mean concentration in normal children was 8.4±0.3 ng/ml. Plasma and urinary EGF in GHD children before and during treatment (0.08 U GH/kg t.i.w.) are shown in the table below:

Time	No.	Plasma EGF ng/ml	No.	Urinary EGF ug/gm/cr
Before	10	7.4±1.5	10	21.4±4.2
2 mo.	3	5.3±0.5	8	47.3±4.1
4 mo.	6	6.0±1.3	-	-
6 mo.	6	8.4±2.2	6	43.1±5.3
12 mo.	9	5.6±2.5	5	42.0±5.9
18 mo.	6	7.2±3.1	-	-

These data suggest that the plasma concentrations of EGF do not change with GH treatment of GHD children despite increases in urinary excretion. We conclude that the increased urinary excretion of EGF could reflect increased urinary clearance of this factor rather than increased production.

444 LEYDIG CELL TUMOR PRESENTING AS CONGENITAL ADRENAL HYPERPLASIA (CAH). Martin A. Goldsmith, Sharyn B. Solish, Raimo Voutilainen and Walter L. Miller, Valley Children's Hospital, Fresno, CA and Dept. of Pediatrics, Univ. of California, San Francisco.

Sexual precocity and a testicular mass can result from a Leydig cell tumor or from simple virilizing CAH with adrenal rests in the testes. These diagnoses are usually distinguished by very high plasma 17-hydroxyprogesterone (17OHP) in CAH. However, 17OHP from adrenal rests may not be suppressible with glucocorticoids, and these entities may not be distinguishable pathologically. A 3 6/12 y.o. boy had a 2-3 month history of rapid growth and phallic enlargement. The left testis was 1.0 cm and the right was about 1.7 cm long, obscured by a hydrocele. Bone age was 7 yr, testosterone (T) 498 ng/dl, and 17OHP 3340 ng/dl, suggesting CAH. Glucocorticoid treatment failed to suppress 17OHP and T, and virilization progressed. At 3 9/12 y.o. the 17OHP was 7409, the T was 548, and the right testis had grown to about 2.7 cm. An LRF test was prepubertal and an ACTH test showed no significant rise in the elevated basal 17OHP, androstenedione or 21-deoxycortisol. Ultrasonography and magnetic resonance scanning revealed a mass replacing the right testis, shown at surgery to be a 2.0 cm Leydig cell tumor. The tumor contained mRNA for P450scc (the cholesterol side-chain cleavage enzyme) and P450c17 (17 α-hydroxylase/17,20 lyase), but no detectable mRNA for P450c21 (21-hydroxylase), as is typical of testicular tissue but not adrenal tissue. The post-op 17OHP and T were normal before and after ACTH. This case illustrates that Leydig cell tumors and non-suppressible adrenal rests in CAH may be hormonally indistinguishable preoperatively.

445 COMPARISON OF HYPOTHALAMUS PITUITARY ADRENAL AXIS SUPPRESSION (HPAS) FROM TOPICAL STEROIDS BY STANDARD ENDOCRINE FUNCTION TESTING AND GAS CHROMATOGRAPHY MASS SPECTROMETRY(GCMS). Ronald W. Gotlin, Paul V. Fennessey, Joseph Morelli, Lois Huff, W.L. Weston, University of Colorado, Sch. of Medicine, Dept. of Ped. & Derm., Denver, CO

We compared GCMS with plasma and urinary free cortisol concentrations to determine indices of HPAS in urine samples obtained from subjects treated with topical steroids. The subjects were 37 males requiring treatment for severe psoriasis valgaris. Two topical ointments betamethasone diproprionate (A) and Clobetasol 17-proprionate (B) were studied employing a double blind, randomized, parallel matrix. Over a 12 weeks we compared standard endocrine function tests (plasma and urinary free cortisol) with GCMS. Twenty-four hour urines and a.m. plasma were obtained prior to, during and after the treatment; treatment efficacy was evaluated by one of the investigators in each phase.

A dramatic and similar treatment response was observed with both agents and laboratory indices of HPAS were correlated with clinical response. While no difference in treatment response between the ointments was seen, HPAS was more marked with agent B (84%) than A (22%) and persisted longer.

	Agent A (n=18)		Agent B (n=19)	
Suppression	4	22%	16	84%
Inc. or no chg.	14	78%	3	16%

GCMS provided a sensitive index of HPAS and revealed evidence of adrenal adrogen as well as glucocorticoid suppression. We found that plasma cortisol though less sensitive than GCMS does provide a rapid and practical estimate of cutaneous absorption of topical steroids and HPAS.