301

SERIAL CALCITONIN SERUM CONCENTRATIONS IN PREMATURE INFANTS DURING THE FIRST 12 WEEKS OF LIFE. Laura S. Hillman, Nancy Hoff, Eduardo Slatopolsky and John G. Haddad (Spon. by R.E. Hillman), Washington Univ. School of Med., St. Louis Children's Hosp., Dept. of Peds., Barnes Hosp. and Jewish Hosp. of St. Louis, Depts. of Med., St. Louis, MO

Serum human calcitonin (HCT) is highest within the first 48 hrs. of life. In term infants, HCT decreased to a mean ± S.E. of 151 ± 22 pg/ml at 1 week of age. Premature infants, however, had 225 ± 40 pg/ml. Twelve small premature infants were followed for 3 months to see if elevations of HCT persisted. Birth weight and gestation were 1123 ± 218 gm (760-1600 gm) and 30 ± 2.5 weeks (27-34 wks.). As shown below, moderate to severe osteopenia was present at 6 weeks of age. Hypocalcemia, elevations in serum alkaline phosphatase, and elevations in serum PTH with amino aciduria were frequent during the first 9 weeks. Serum HCT slowly fell, but remained elevated in 9/12 infants at 3 months. HCT may play an important role in the mineralization of infant bone and elevated serum HCT persists in the premature. The stimulus to HCT secretion during this period is presently unknown.

	Adult	1-2 wk.	3-4 wk.	6 wk.	9 wk.	12 wk.
HCT pg/ml	71±6	364±52	291±36	254±40	236±37	220±77
Calcium mg%	9.7±.06	8.3±.27	8.9±.23	8.7±.33	9.1±.30	9.6±.35
Alk.Phos.I.U.	<400(infant)	---	373±41	409±49	506±71	447±116
PTH µl Eq/ml	7 ± 1.8	20 ± 3	20 ± 5	14 ± 5	9 ± 2	12 ± 3
25-OHD ng/ml	24±1.5	18 ± 2	21 ± 3	22 ± 2	21 ± 3	26 ± 4
# infants with moderate osteopenia		---	3/12	11/12	4/12	2/12

302

PROVOCATIVE AND INTEGRATED CONCENTRATIONS OF GROWTH HORMONE (GH) IN DIVERSE GROWTH DISORDERS. N.J. Hopwood, R.P. Kelch, W.B. Zipf, M.L. Spencer and G.E. Bacon. Univ. of Michigan, Department of Peds., Ann Arbor, MI 48109.

Since provocative tests for GH release may not reflect normal GH secretory patterns, we studied 18 children with diverse growth disorders, age 7-18 yrs, by two standard stimuli (L-Dopa, arginine, insulin-induced hypoglycemia) and by continuous blood withdrawal (collected hourly) for 12 and 24 hr integrated GH concentrations (ICGH). Tests were started at 0800 hr; 12 hr ICGH was calculated for 1800-0600 hrs. Six patients with normal stimulation tests (peak $>$10 ng/ml) had 12 hr ICGH = 5.2 ± 2.6 ng/ml (mean ± S.D.; range 2.5-9.1); two boys with delayed adolescence had no hourly peak $>$ 10 ng/ml. Five patients with borderline stimulation tests (peak GH 7-10 ng/ml) had 12 hr ICGH 4.0 ± 2.3 (range 1.5-6.7); in 3/5, the peak integrated hourly levels were low: 4.5, 4.7, 8.7. Seven patients with low stimulation tests (peak $<$ 7 ng/ml) had 12 hr ICGH 0.75 ± 0.6 ng/ml (range 0.18-1.96); all had hourly peak ICGH $<$ 3.5 ng/ml and 6/7 had clinical evidence of GH deficiency. Patients with delayed puberty had borderline or normal provocative GH; however, 4/5 had low 12 hr ICGH and hourly peaks.

There were highly significant correlations between ICGH peak, 12 hr ICGH and peak provocative GH ($p < 0.001$). In all groups, 12 hr ICGH correlated with 24 hr ICGH ($p < 0.001$). With the exception of one child with obesity, growth velocities correlated more closely with ICGH than with provocative GH. Constant withdrawal may be helpful particularly in patients with borderline provocative tests and/or sexual immaturity.

303

THE ROLE OF RENIN AND ANGIOTENSIN IN SALT-LOSING CAH. James M. Horner and Raymond L. Hintz (Spon. by S.David Holtzman) Dept. of Pediatrics, Stanford Medical Center, Stanford, California.

Seven children with salt-losing CAH who had been off mineralocorticoid for several years were studied. 9 children with non-salt-losing CAH were controls. The 7 subjects showed clinical evidence of poor control despite suppressive doses of hydrocortisone; most showed coincidental signs of glucocorticoid excess. Chemical assessment of control included serum 17-OHP, PRA, and ACTH and 24-hour urine 17-KS and PT. The salt-losers were then placed on Florinef, 0.1 mg bid with improvement in all measured parameters (see table), decreased fatigue and salt craving, and in some, a decreased cortisol requirement without hypertension.

Group	n	HCmg/m²/d	17KS mg/d	PT mg/d	17OHP ng/dl	PRA ng/l/min
NSL	9	19.9±3.8	3.1±0.5	2.5±0.7	1030± 383	40± 6
SL	7	22.8±3.2	22.0±2.9	41.1±6.7	19134±2639	361±75
SL+Fx1m	7	22.8±3.2	12.5±3.5	15.2±4.8	4117±1814	108±34
SL+Fx3m	6	20.3±2.3	9.3±1.8	6.7±1.3	240± 49	42±14

Values=mean±SEM NSL=non-salt-loser SL=salt-loser F=Florinef HC=hydrocortisone 17KS=17-ketosteroids PT=pregnanetriol 17OHP=17-OH-progesterone PRA=plasma renin activity

We thus conclude: 1)the renin-angiotensin system can stimulate all zones of the adrenal cortex, and elevated PRA can lead to poor control in salt-losing CAH just as can inadequate suppression of ACTH; 2)salt-losers need mineralocorticoid as well as glucocorticoid replacement for optimal control; and 3)salt-losers should be maintained on mineralocorticoid for life.

304

HORMONE STUDIES IN PREADOLESCENT 47,XXY BOYS. Michael J. Hudson, Jeremy S.D. Winter, Arthur Robinson. University of Colorado School of Medicine, Department of Biophysics and Genetics; National Jewish Hospital and Research Center, Denver; University of Manitoba, Department of Pediatrics, Manitoba.

Sixteen 47,XXY boys have been followed prospectively from birth and are being recalled for endocrine studies. To date 6 boys (6yr-13yr) have been studied and available results are presented. LHRH stimulation test (10µg/Kg IV bolus) and HCG stimulation (2,000 IV 1M X 3 days) were given and analyzed for LH, FSH, testosterone & estradiol.

CA (yr-mo)	12-6	11-4	10-3	9-6
Pubic/Genital Rating	P1G2	P1G2	P1G1	P1G1
Bone Age (yr-mo)	10-9	10-4	10-0	9-0
Testicular size (cm)	2.5	2.7	1.25	1.2
Basal FSH (µg/dl)	---	6.1	12.7	14.3
Post LHRH FSH (µg/dl)	---	10.3	34.0	28.0
Basal LH (µg/dl)	---	3.3	2.1	3.0
Post LHRH LH (µg/dl)	---	19.3	4.8	3.8
Basal testosterone (ng/dl)	135	41	10	12
Post HCG testosterone (ng/dl)	914	676	54	85
Basal estradiol (ng/dl)	6.5	1.1	---	2.8
Post HCG estradiol (ng/dl)	3.4	1.2	---	1.9

We interpret these data to indicate 1) normal pituitary function, 2) the elevated estradiol, which is associated with hypergonadotrophic hypogonadism in 47,XXY adults with Klinefelter's syndrome starts to manifest itself before puberty and may be an early indication of later hypogonadism.

305

AMNIOTIC FLUID TRIIODOTHYRONINE AND CORTISOL CORRELATIONS FROM 10 TO 43 WEEKS GESTATION. A.H. Klein, B.E.P. Murphy, T.H. Oddie, R. Artal and D.A. Fisher. Fetal-Maternal Research Laboratories, UCLA-Harbor General Hosp., Torrance, CA and McGill University, Dept. of Medicine, Montreal General Hosp., Montreal, Canada.

Thyroxine (T4), triiodothyronine (T3) and reverse T3 (rT3), concentrations by RIA and cortisol (C) by radiotransinassay were measured in amniotic fluid (AF) samples from human pregnancies between 10 and 43 weeks gestation. T4 increased with gestational age (GA) between 10 and 30 weeks ($r = +0.54$, $p<0.01$) reaching a mean of 1.2 µg/dl (95% confidence limits [CL] 0.81 to 1.8 µg/dl) between 25 and 30 weeks. T4 decreased with GA between 20 and 43 weeks ($r = -0.34$, $p<0.01$) to a mean term level of 0.61 µg/dl (CL 0.33 to 1.13 µg/dl). rT3 increased with GA between 10 and 20 weeks ($r = +0.66$, $p<0.001$) to a mean level of 474 ng/dl. After 20 weeks, rT3 decreased with GA ($r = -0.77$, $p<0.001$) to a mean concentration of 62 ng/dl at term. Mean T3 increased from 5.4 ng/dl at 16-20 weeks to 12.1 ng/dl at 39-42 weeks. Mean C in AF increased between 30 and 43 weeks (13.5 ng/ml to 27.8 ng/ml). AF-C correlated directly with T3 ($r = +0.51$, $p<0.01$) and indirectly with rT3 ($r = -0.43$, $p<0.01$) between 10 and 43 weeks. Although the source of the AF iodothyronines is unknown, the high rT3 and low T3 concentrations reflect fetal serum levels more than maternal. The significant correlation between T3 and C are consistant with recent data indicating cortisol dependent increases in serum T3 concentrations and in vitro tissue conversion of T4 to T3 prior to the onset of labor in fetal sheep.

306

ONTOGENESIS OF IODOTHYRONINE PRODUCTION AND CLEARANCE IN SHEEP. A.H. Klein, D. Padgett, P. Castagna, G. Calvario, T.H. Oddie and D.A. Fisher. Fetal-Maternal Research Laboratories, UCLA-Harbor Gen. Hospital, Torrance, CA.

Production rates (PR, µg/M²/d) and metabolic clearance rates (MCR, L/M²/d) for thyroxine (T4), triiodothyronine (T3), and reverse T3 (rT3) were measured in 4 newborn sheep 7 to 14 days of age using single injection non-compartmental methods. Results were related to data in fetal and adult sheep. Thyroid secretion of T3 and rT3 were calculated from T3/T4 and rT3/T4 ratios measured in adult and fetal thyroid glands:

	Fetus MCR	Fetus PR	From Thyroid	Newborn MCR	Newborn PR	From Thyroid	Adult MCR	Adult PR	From Thyroid
T4	3.9	335		7.3	511		2.5	146	
T3	80	<27	<27	40	96	52	42	28	14
rT3	19	102	3	28	28	5	74	38	1

Newborn T4 MCR>fetal ($p<.05$) and adult ($p<.01$); newborn T4 PR>fetal ($p<.05$) and adult ($p<.01$). Fetal T3 MCR>newborn ($p<.01$) = adult; newborn T3 PR>fetal ($p<.01$)>adult ($p<.001$). Fetal rT3 MCR = newborn<adult ($p<.05$); fetal rT3 PR>newborn ($p<.01$) = adult. The T3 secreted from the thyroid is minimal in fetus, approximates 54% in newborn, and 51% in adult animals. Percent rT3 secretion approximates 3% in fetus, 18% in newborn, and 3% in adult animals. Conclusions: In the newborn a) T4 secretion is increased; b) T3 production is increased as a result of increased secretion and augmented T4-T3 conversion; c) rT3 production from T4 is decreased, and rT3 secretion is minimal; d) thyroid sensitivity to TSH or pituitary-thyroid feedback appears to be altered during this period.