● 476 EVOKED POTENTIALS IN NEWBORNS WITH CONGENITAL HYPOTHYROIDISM. Gail E. Richards, Karyl A. Norcross and Anita Cavallo, (Sponsored by Bruce S. Keenan) Department of Pediatrics and Neurology, University of Texas Medical Branch, Galveston, Texas.

To evaluate the effect of congenital hypothyroidism (CH) on nervous system development, we performed evoked potential studies on 6 infants at 3-8 weeks of age with CH before any therapy was given. All infants were screened at the time of hospital discharge and again at about 2 weeks by filter paper determination of T4 and TSH. A serum specimen confirmed the abnormal filter paper values at the time of study. The infants participating in this study all had serum TSH concentrations > 100 μU/ml (normal <7). Serum T4 range was 4.1-8.5 μg/dl at the time of study. All had thyroid tissue on ^{99}Tc scan. 4 had ectopic thyroid tissue and 2 had a thyroid gland in the normal location.

Brainstem auditory evoked potentials (BAEP) were abnormal in 4 of 6 infants and showed prolonged I-III and I-V interpeak latencies in all (> 2.5 S.D. above lab mean for age). Visual evoked potentials (VEP) were abnormal in 3 of 6 subjects and all showed a pattern of immaturity. Somatosensory evoked potentials (SSEP) were normal. These BAEP results indicate selective caudal brainstem dysfunction in these infants with CH that is not consistent with immaturity alone and differs from BAEP abnormalitites in older children who had been treated for CH for many years (Pediatr Res 20:570,1986).

We conclude that infants with relatively mild CH (serum T4 values > 4 μg/dl at 3-8 weeks of age) have evidence of abnormal caudal brainstem development, and that normal T4 production is necessary to assure normal brain development at a time before diagnosis of CH can be made by neonatal screening.

● 477 LONG TERM GROWTH IN JUVENILE ACQUIRED HYPOTHYROIDISM. Scott A. Rivkees, John D. Crawford, Hans H. Bode, Pediatric Endocrine Unit, Massachusetts General Hospital, Shriners Burns Institute and Harvard Medical School, Boston, MA 02114

Long term growth was assessed in 17 girls (F) and 6 boys (M) presenting with hypothyroidism at ages 11.4±2.6 (m±SD) and 10.2±4.7 yrs. Bone ages (F 6.2±3 and M 6.1±2.7 yrs, Greulich-Pyle) and growth pattern suggested duration of hypothyroidism >3 yrs. Pre-illness heights were 0.27±.12(7F) and 0.39±.15 (4M) SD scores (SDS) above average. At diagnosis height SDS had fallen to -4.04±.5 (F) and -4.15±.5 (M) (height ages 7 and 7.1 yrs) but predicted heights (Bailey-Pinneau) were normal (F 155±7.5 and M 177±7.7 cm). Serum T_4 was 1.1±0.3 ug/dl and TSH 570±255 mIU/ml at diagnosis. On T_4 therapy (3.4±.3 ug/kg/day) serum T_4 averaged 9.6±2.5 ug/dl and TSH 2.9±3.9 mIU/ml. Concomitant with onset or progression of puberty during the first 18 mos of therapy change in skeletal maturation (ΔBA) exceeded that of height age (ΔHA) resulting in loss of predicted mature height;ΔBA/ΔHA ratio 1.73±3.5 (F) and 2.1±.46 (M). This loss was proportional to duration of hypothyroidism. Adult height SDS were lower than pre-illness SDS (7F=-2.62±.16 and 4 M=-1.9±.19) and mature heights were also lower than predicted height at diagnosis. Adult females stood 149±5 cm (HA 11.6 yrs) and males 168±5.1 cm (HA 14.7yrs). Conclusion: Prolonged juvenile hypothyroidism results in permanent height deficit. This loss is proportional to duration of illness and is not due to excessive T_4 therapy. The data tempt speculation that delay of puberty might ameliorate the height deficit.

478 GONADOTROPIN SURGE IN INFANTS OF MEN WITH KALLMANN'S SYNDROME. Susan R. Rose, Fernando Cassorla, Richard J. Sherins, Devel. Endocrinol. NICHD, NIH, Bethesda

We hypothesized that some infants of men with Kallmann's syndrome (genetically transmitted condition) would show deficiency of the neonatal gonadotropin and sex steroid surge demonstrated in normal infants. Most affected individuals are not identified until the onset of puberty is delayed. Accordingly, we evaluated seven infants fathered by men who became fertile after hormonal treatment for Kallmann's syndrome. Midline facial features and genital anatomy were normal in all. Blood was sampled through an indwelling line every 20 minutes from midnight to 2 AM for LH, FSH, and either estradiol (E2) and testosterone (T), prior to an LHRH test (100 mcg IV).

sex	age (days)	E2 (pg/ml)	T (ng/dl)	highest basal LH(mIU/ml)	FSH	LHRH peak LH	FSH
M	56	-	234	11	1	46	5
M	81	-	65	17	8	80	26
M	85	-	183	13	5	40	8
M	92	-	273	11	6	-	-
F	46	86	-	10	14	16	26
F	99	<10	-	4	3	20	35
F	113	15	-	<4	4	26	37

These data indicate that infants of Kallmann's fathers have the gonadotropin and sex steroid surge shown for normal infants. We conclude that either our infants do not have Kallmann's syndrome, or the neonatal surge remains intact despite protential later loss of gonadotropin release.

479 NOCTURNAL THYROTROPIN SURGE IN NORMAL CHILDREN. Susan R. Rose, Mark H. Zweig, Bruce C. Nisula (Spon. by George Chrousos) Developmental Endocrinology NICHD, NIH, Bethesda, MD 20892

A nocturnal surge in serum thyrotropin (TSH) occurs in adults between late afternoon and midnight. To determine if a similar TSH surge occurs in children, we studied 32 children, ages 4 to 18 years, who were normal in height and weight. Samples for TSH were drawn through an indwelling catheter hourly for 24 hours in older children or 1500 to 0400 in smaller children. Serum TSH was measured by a 3-site mouse monoclonal IRMA(Serono Diagnostics, Inc.), which has a sensitivity less than 0.3 μU/ml. The nocturnal TSH surge was calculated as the percent increase in the nighttime TSH (3 consecutive values with highest mean) over the daytime TSH (3 consecutive values with lowest mean). The time of peak was the mid-time point of the highest 3 values at night.

Age (yr)	N	Day TSH (μU/ml)	Night TSH (μU/ml)	p value	Nocturnal TSH Surge (%)	Time of Peak
4-8	6	2.0±.4	3.9±.5	<.01	121±32	2230±40
9-11	9	1.7±.2	3.8±.6	<.01	122± 9	2320±20
12-13	10	1.8±.3	4.1±.6	<.01	160±34	0010±30
14-18	7	1.7±.2	3.5±.2	<.01	93±27	0130±50*

Values shown are mean ± SE; * p <.001, compared with age 4-8.

All the children demonstrated a significant nocturnal TSH surge. The timing of the surge differed with age. Younger children had their surge significantly earlier in the night than did adolescents. We conclude that normal children as young as 4 years of age have a nocturnal surge of TSH.

● 480 MOSAICISM OF SKIN 1,25 DIHYDROXYVITAMIN D_3 (1,25) RECEPTORS IN THE ADULT AND NEONATAL SHEEP? INCREASED RECEPTOR DENSITY IN WOOLY SKIN. Richardus Ross, Jane Florer (Spon. by R.C. Tsang) U. of Cincinnati Med. Ctr., Dept. Pediatrics, Cincinnati, OH.

Autoradiographic studies in rats have demonstrated specific localization of 1,25 in hair follicle basal cells, whereas, in humans, the absence of 1,25 nuclear binding is associated with alopecia. These observations suggest a role of 1,25 in the regulation of the epidermal cells responsible for hair growth and/or differentiation. We hypothesized that in a species which demonstrates a mosaicism of hair growth, such as the sheep, there would be a similar mosaicism of 1,25 receptor concentrations. We tested this hypothesis in nuclear receptors prepared by high salt extraction of a low salt crude nuclear fraction of wooly, flank skin (W) versus non-wooly, groin skin (NW). 3H-1,25-Receptor complexes exhibit a 3.5S binding component that co-sedimented with the sheep intestinal receptor, bound to DNA-cellulose and eluted with 0.16M KCl. Scatchard analysis revealed the following equilibrium binding data:

	Wooly skin (n=7)	Non-wooly skin (n=7)	
Kd (nM)	0.36 ± 0.09	0.23 ± 0.07	NS
Nmax (fm/mg prot)	102 ± 18	20 ± 7	p<0.005

Preliminary studies of neonatal skin indicate a similar mosaicism though receptor concentrations are generally twice that in the adult. These data represent the first demonstration of a cutaneous mosaicism of 1,25 receptors in an animal species. The finding of increased 1,25 receptor density in areas of wool production provides further evidence for a role of 1,25 in the regulation of hair growth and/or differentiation.

● 481 FETAL AND NEONATAL PARATHYROID GLAND FUNCTION: USE OF THE CYTOCHEMICAL BIOASSAY TO DETERMINE CIRCULATING LEVELS OF BIOLOGICALLY ACTIVE PTH (bioPTH) IN NORMAL AND HYPOCALCEMIC NEONATES. Lewis P. Rubin, James T. Posillico, Allison I. Caplan, Edward M. Brown, Constantine S. Anast, Departments of Pediatrics and Medicine, Harvard Medical School, Boston, MA

Elevated fetal plasma total calcium (Ca), ionized calcium (Ca_i) and inorganic phosphorus (P) decline during the first 2-3 days of life. 1/3 to 1/2 of preterm infants will exhibit an exaggerated early neonatal hypocalcemia (ENH). Previous studies of immunoreactive PTH (iPTH) in ENH have yielded inconclusive results since some antisera are directed against biologically inactive forms of hormone. We used a sensitive cytochemical bioassay to measure circulating levels of bioPTH as well as iPTH. Assays were carried out in umbilical cord plasma (n=60) and plasma from normo- and hypocalcemic neonates from 25-42 weeks gestation (n=10). The bioassay is based on PTH mediated stimulation of glucose 6-phosphate dehydrogenase activity in distal convoluted tubules of guinea pig kidney. Cord plasma bioPTH was elevated (30.7±10.1 (SEM) pg/ml) compared to normal adults (9.2 ±1.0 pg/ml). Addition of antihuman PTH antibody to plasma extinguished bioactivity. Postnatal decline in Ca (7.2±0.2 mg/dl) and Ca_i (1.05±0.05 mM/l), even in extremely preterm infants, resulted in increased bioPTH levels (61.8±11.3 pg/ml). When Ca increased after day 3, bioPTH was suppressed to levels below those obtained from paired cord samples. iPTH also rose and fell inversely with Ca. Biologically active PTH is produced by the fetus and newborn infant, and circulating levels of hormone respond to physiological changes in Ca and Ca_i.