319 ELEVATED CIRCULATING IMMUNOREACTIVE PARATHYROID HORMONE (iPTH) IN PREMATURE INFANTS. Hans C. Dirksen and Constantine S. Anast, Harry S. Truman Memorial Veterans Hospital and Dept. of Child Health, University of Missouri, Columbia.

Serum iPTH was measured in 160 AGA full-term and premature normocalcemic and hypocalcemic infants during the first 96 hours of life. In normal full-term infants, iPTH was low in cord blood and remained low during the first 12 hours of life as serum Ca declined. Thereafter the serum iPTH rose to the mid-normal range. Consistent with our previous studies, in only 20% of serum samples from hypocalcemic full-term infants was iPTH elevated; in the remainder, iPTH was inappropriately low, though usually in the normal detectible range. By contrast, serum iPTH was elevated in 75% of samples of hypocalcemic prematures. Moreover, elevated iPTH was found in approximately 15% and 35% serum samples of normocalcemic full-term and premature infants, respectively. At any given Ca level the serum iPTH appeared to vary inversely with gestational age. The results suggest 1) That parathyroid responsiveness is greater in premature than full-term infants, possibly related to lesser period of exposure to hypercalcemia in utero and 2) That a factor(s) other than parathyroid insufficiency acts in the newborn to reduce plasma Ca; in some infants, compensatory increases in parathyroid activity may be sufficient to maintain normocalcemia, while in others there is either no compensatory increase or the increase is insufficient and hypocalcemia results. It is possible that metabolic clearance of iPTH varies with gestation and accounts, in part, for our findings.

320 ONTOGENESIS OF THYROID HORMONE PRODUCTION IN THE NEONATAL RAT. J.D. Dubois and J.H. Dussault, Département d'Endocrinologie-Métabolisme, CHUL, Québec, P.Q.

This study was undertaken to examine the ontogenesis of thyroid hormone production in the neonatal rat (from 5 days to adulthood) by measuring [^{125}I]-T_4 and [^{125}I]-T_3 kinetic parameters by single-compartmental analysis. T_4 and T_3 serum concentrations were measured by specific radioimmunoassay. The volume of distribution (VD) and the metabolic clearance rate (MCR) of T_4, high at 5 days, increase to a peak at 22-26 days and decline to adult values. The T_4 production rate (PR) low at 5 days, increases to peak values at 14 to 32 days and declines toward adult values. The T_4 fractional removal rate (K) is similar from birth to adulthood. No difference is observed for K, VD and MCR of T_3 during the life of the rat. The T_3 PR from minimal values at 5 days attains adult values at 22 days. There is therefore a delay of about 8 days between the peak of T_4 PR and the attainment of the adult T_3 PR. The T_4/T_3 PR ratio decreases from a maximal value at 5 days to values approaching those seen in the adult at 12 days. There is a significant rise at 14 days due to the marked rise in the T_4 PR before the ratio returns to adult values by 26 days as a result of the increase in the T_3 PR. The increasing T_3 PR following the peak in the T_4 PR probably represents increasing peripheral T_4-T_3 monodeiodination may be analogous to the marked rise in T_3 following birth in the sheep or human. Therefore these data confirm that the ontogenesis of thyroid hormone secretion occurs after birth in the rat and suggest that the first 20 days of life in the rat may correspond to the last trimester of gestation of the human fetus.

321 TRANSSPHENOIDAL REMOVAL OF PITUITARY MICROADENOMAS IN THE TREATMENT OF CHILDHOOD CUSHING'S DISEASE. Nives Dumbovic, Matthew H. Connors* and Lynne L. Levitsky. (Spon. by Samuel P. Gotoff). Pritzker Sch. Med., Univ. Chicago, Michael Reese Hosp. Med. Ctr., Dept. Peds., Chicago, and Univ. Calif. Sch. Med., Dept. Peds., Davis.*

The morbidity of adrenalectomy and high incidence of post-adrenalectomy Nelson's syndrome in children with Cushing's disease suggests that alternative methods of treatment would be especially useful in childhood. Two boys (patient 1, 6 9/12; patient 2, 15 yrs) with classic Cushing's disease and no evidence of pituitary adenoma on skull x-ray or pneumoencephalogram failed to respond to cyproheptadine (0.25-0.5 mg/kg). Transsphenoidal pituitary exploration and removal of a pituitary microadenoma induced complete clinical resolution in both patients. Fasting plasma cortisol levels were low (3.8, 6.2 µg/dl), and the response to insulin-induced hypoglycemia was poor (10.4, 7.1 µg/dl) 2-4 months post-operatively. GH response to insulin-induced hypoglycemia returned to normal (pre-1.3 vs. post-26.8 ng/ml), and ACTH levels rose appropriately during hypoglycemia in patient 1. Patient 2 displayed a nocturnal rise in growth hormone (pre-3.6 vs. post-6.7 ng/ml), normal prolactin (13.5 ng/ml) and increased gonadotropins (pre FSH 2.8 LH 2.3 vs. post FSH 12.8 LH 13.2 mIU/ml) associated with progressive sexual maturation. T-4 and T-3 were normal in both patients postoperatively, as were other tests of pituitary function. We suggest that transsphenoidal pituitary exploration should be the initial therapy of choice in childhood Cushing's disease.

322 THE EFFECT OF CHRONIC PTU AND LOW IODINE DIET (LID) TREATMENT ON THE DEVELOPMENT OF THE HYPOTHALAMO-PITUITARY-THYROID AXIS IN THE NEONATAL RAT. J.H. Dussault and P. Walker, CHUL, Québec, Canada.

Pregnant and neonatal rats received 0.05% PTU in their drinking water or LID (deiodinated water + Remington LID). Hypothalamic TRH, pituitary and serum TSH, and serum T_4 and T_3 were measured by specific radioimmunoassay. Both PTU and LID treated animals had low hypothalamic TRH concentrations at 1 day (0.761 ± 0.266 pg/µg protein and 0.82 ± 0.14 pg/µg protein respectively) similar to that observed in normals (Endocrinology 97: 1321, 1975) with a rapid increase to peak concentrations of 2.37 ± 0.371 pg/µg protein between 12 and 24 days for PTU-treated and 3.22 ± 0.35 pg/µg protein between 12 and 18 days for the LID group; approximately 50% of normals. Pituitary and serum TSH concentrations were significantly elevated in both groups. The PTU group were hypothyroid (undetectable serum T_4 and low T_3 concentrations). In the LID group serum T_4 was normal and peak serum T_3 concentrations were in the hyperthyroid range (157.0 ± 6.98 ng/dl at 32 days). These data indicate 1) exposure to PTU or LID results in a marked aberration of the maturation of the hypothalamo-pituitary thyroid axis in the neonatal rat 2) the decreased hypothalamic TRH concentration is compatible with an increased turnover of TRH and 3) the normal thyroid hormone concentrations in the LID group suggest that TSH may play a predominant role in negative feedback at the hypothalamic level.

323 THE EFFECT OF PERINATAL FACTORS ON CORD THYROXINE (T_4) CONCENTRATION. Allen Erenberg, (Spon. Robert G. Thompson). University of Iowa College of Medicine, Department of Pediatrics, Iowa City, Iowa.

To evaluate the effect of various perinatal factors, 4,068 cord samples were assayed for T_4 concentration, and each chart reviewed for the following factors: Cesarean section (CS), prolonged rupture of membranes (PROM), asphyxia (A), meconium stained amniotic fluid (MS), maternal diabetes mellitus (IDM), and twinning (T). The neonate was evaluated for respiratory distress (RDS) and low (SGA) and high (LGA) birth weight for gestational age. The infants were grouped by gestational age (GA) and compared to normal values (N).

GA	N	CS	PROM	A	MS	IDM	RDS	SGA	LGA	T
28-31 wks	10.7 ±0.8			10.6 ±1.4			8.6 ±1.0			
32-35 wks	11.0 ±0.5	12.6 ±1.1	10.6 ±0.8	11.1 ±0.4			10.8 ±0.5			11.9 ±0.8
36-40 wks	13.0 ±0.1	13.0 ±0.2	13.2 ±0.4	13.4 ±0.3	12.8 ±0.3	13.5 ±0.6	13.6 ±1.0	11.9 ±0.4	13.5 ±0.5	11.9 ±0.7

Value = µg% ± SEM

Only the SGA infant had a significantly lower mean cord T_4 level ($p<.01$). Conclusions: 1) Within a given GA group, perinatal factors do not affect the mean cord T_4 level. 2) The mean cord T_4 level increases with GA.

324 THE EFFECT OF FETAL THYROIDECTOMY ON OVINE FETAL LUNG MATURATION. Allen Erenberg, Mitchell L. Rhodes, Mary M. Weinstein, and Roland L. Kennedy (Spon. by Robert G. Thompson). University of Iowa College of Medicine, Department of Pediatrics, Iowa City, Iowa.

Previous studies have shown that thyroxine is one of the factors which influences fetal lung maturation. To further delineate the role of the thyroid hormones, ovine fetuses were surgically thyroidectomized at 95-99 days gestation (term gestation = 145-150 days). The thyroidectomized (Tx) and control (C) fetuses were sacrificed at 140 days. The mean serum thyroxine concentration was significantly decreased in the Tx (<1 µg%) as compared to the C (14.2 µg%). The combined heart and lung weights were significantly reduced in the Tx. Compared to the C lung, light and electron microscopic examination of the Tx lung revealed hypercellular, thickened alveolar septae and interstitium. The Tx lung alveolar lining consisted of cuboidal cells without the characteristic lamellar bodies and the tracheal fluid lecithin/sphingomyelin ratio was decreased, indicative of delayed surfactant synthesis. The DNA content was increased and protein/DNA ratio reduced per gram wet weight lung tissue in the Tx, indicating that compared to the C, there was a larger number of smaller sized cells. Thus, it appears that thyroidectomy in the ovine fetus during the second trimester significantly delays lung maturation and surfactant synthesis. Further studies are needed to define the role of the human fetal and neonatal hypothalamic-pituitary-thyroid axis in the idiopathic respiratory distress syndrome.