283 NEONATAL HYPOGLYCEMIA ASSOCIATED WITH ANTERIOR HYPOPITUITARISM. David R. Brown and David B. Klain. Children's Health Center and Dept. of Peds. University of Minnesota, Minneapolis. (spon. by Robert A. Ulstrom.)

We have observed the association of profound hypoglycemia and anterior hypopituitarism in four newborns. All presented with hypoglycemia during the first 30 hours of life, which reached levels less than 10 mg.%. Rates of 20-30 mg./kg./min. of 20% dextrose were required to maintain glucose levels above 30 mg.%. All infants were products of complicated pregnancies and deliveries and had APGAR scores of five or less at one and five minutes.

Measurements of anterior pituitary function including serum TSH, T_4, ACTH, cortisol and growth hormone, in addition to metapyrone and cosyntropin stimulation, revealed anterior panhypopituitarism in three infants and isolated ACTH deficiency in the other. Posterior pituitary function was normal in all cases. Unresponsiveness of TSH to intravenous thyrotropin releasing hormone (TRH) and normal serum prolactin levels further support anterior pituitary dysfunction in contrast to a hypothalamic etiology. Autopsy on one infant revealed no anterior pituitary tissue. The three surviving patients are all doing well on appropriate hormone replacement. Micropenis was present in the one male and all infants showed a widening of the midfacies.

This unappreciated cause of early neonatal hypoglycemia may be related to birth hypoxia or anatomic malformation of the anterior pituitary and its rudiments. These may be more susceptible to events at birth than previously appreciated and consequently this system should be more agressively evaluated in newborns.

284 ANTIBODIES TO LUTEINIZING HORMONE IN A PATIENT TREATED WITH GROWTH HORMONE. S. Burstein, F.A. Conte, S.L. Kaplan, and M.M. Grumbach. Dept. Pediatrics, Univ. of California San Francisco, San Francisco, Ca.

Many clinical grade preparations of hGH (human growth hormone) are contaminated with hLH and hFSH. However, no evidence of a clinical effect of such contamination has been described. We report the development of antibodies to hLH in a patient treated with hGH for isolated GH deficiency.

J.C. was first investigated for short stature at 7-11/12 years and GH therapy was begun at 8-9/12 years for a diagnosis of isolated GH deficiency. On LRF (luteinizing hormone releasing factor) testing, the LH rose from 0.8 to 1.2 ng/ml (LER 960); FSH response also was normal. At 11-11/12 years the patient was still prepubertal with undetectable testosterone levels. A repeat LRF test revealed an "apparent" basal plasma LH of 25.4 ng/ml. Further studies indicated that his serum had antibodies to hLH which have persisted for over 2-1/2 years on growth hormone therapy without the development of significant GH antibodies. ^{125}I-hLH was bound to his serum in a displacable fashion; hFSH and hTSH displaced this tracer only at doses compatible with contamination of these standards by hLH. Radioiodinated hFSH, hTSH and hLH-α were not bound; the antibody is directed against the LH-β subunit. The binding capacity of the serum and the equilibrium constant for the binding reaction are sufficiently great to be physiologically significant.

285 A Virilizing Adrenocortical Tumor in a Female Infant: Steroidogenesis In Vivo and In Vitro. Lucienne A. Cahen, Dorothy B. Villee, M. Linda Powers, and John F. Crigler, Jr., Harvard Med. Sch., Children's Hosp. Med. Cen., Endocrine Division, Boston, Mass.

Normal adrenal and adrenal tumor cells from a female infant with a virilizing adrenal tumor were grown in tissue culture for a period of 7 weeks with and without ACTH (0.1 unit/ml). The cells grew well and continued to produce steroid hormones, as measured by radioimmunoassay of individual steroids in the culture medium. Compared to normal cells, tumor cells with no ACTH added produced equivalent amounts of cortisol, 18OH corticosterone, and 18OH deoxycorticosterone, but lesser amounts of dehydroepiandosterone (DHA), androstenedione (A), testosterone (T) and progesterone. Normal cells exposed to ACTH showed an increase in all steroids measured whereas ACTH-exposed tumor cells showed an increase principally in DHA, consistent with a deficiency in 3β-hydroxysteroid dehydrogenase. Concentrations of DHA, A and T in the patient's serum were elevated before the adrenal tumor was removed. The relative concentration of the three androgens in media of tumor cells in vitro resembled that in patient's serum in vivo. These studies demonstrate that both normal and tumor cells of adrenal can be maintained for a long time in vitro, that they retain their ability to respond to ACTH and that they produce their characteristic steroids. The tumor cells appear to have a 3β-hydroxysteroid dehydrogenase deficiency.

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286 STUDIES OF PLASMA CALCITONIN IN HYPOPITUITARISM AND HYPOTHYROIDISM. Dennis E. Carey, Kenneth Lee Jones, Jacqueline G. Parthemore, and Leonard J. Deftos. University of California San Diego School of Medicine and San Diego VA Hospital. Departments of Pediatrics and Medicine. La Jolla, California 92093

The secretion of calcitonin (CT) was studied in 17 children, 10 with hypopituitarism and 7 with agoitrous hypothyroidism. Plasma CT levels were measured by radioimmunoassay in the basal state and following infusion of pentagastrin (0.5 μg/kg) and 10 minute infusions of calcium (2.3 mg/kg Ca^{++} as $CaCl_2$). Of the 10 children who have hypopituitarism, 5 were studied before and after one year of human growth hormone (HGH) therapy and 5 were studied before treatment only. Basal and peak response CT levels were essentially unchanged by HGH. In the patients with hypopituitarism, CT levels increased from 41.9 ± 5.1 pg/ml to a peak of 67.4 ± 10 pg/ml after pentagastrin and from 38.8 ± 5.2 pg/ml to a peak of 107 ± 14.9 pg/ml after calcium infusion. In the cretins, CT levels increased from 33.8 ± 6.5 pg/ml to 35.8 ± 7 pg/ml following pentagastrin and from 31.4 ± 5.9 pg/ml to 40 ± 4.9 pg/ml following calcium. Although basal levels of CT seemed to be lower in cretins, these values could not be rigorously validated. The patients with hypopituitarism had greater CT responses than the cretins, especially to calcium infusion. These studies suggest that children with hypopituitarism have a greater CT response to calcium infusion than do normal adults and that CT secretion is abnormal in patients with athyreotic cretinism.

287 EFFECTS OF ANDROGENS IN SICKLE CELL DISEASE WITH SEVERE GROWTH RETARDATION S. Castells, A. Brown, N. Solomon, E. Dunn, and N. Muthukrishnan. Depts. of Pediatrics and Radiology, SUNY, Downstate Med. Ctr., B'klyn, N.Y.

Eight sickle cell patients, 9-15 yr., with severe growth retardation, retarded bone age and delayed puberty had normal serum concentrations of T_4,T_3,PRL after chlorpromazine stimulation, and normal adrenal functions measured by circadian variation of plasma cortisol, plasma cortisol during hypoglycemia, ACTH and metyrapone tests. hGH response to insulin-induced hypoglycemia was abnormally low in 4/8. Four males and 3 females had elevated plasma concentrations of LH and FSH; 4 males had low plasma testosterone and 3 females had low plasma estradiol. The severe growth retardation seems to result from a primary gonadal hypofunction associated in some cases with hGH deficiency.

Ethylestrenol, a synthetic androgen, was administered for one year at 2 to 4 mg daily. Range of growth rate before therapy was 1.2-4.9 cm/yr; during therapy was 3.6-15.6 cm/yr. There was no acceleration in bone age. No significant changes in Hgb., Hct., reticulocyte count and fetal Hgb occurred. A striking finding was a consistent increase in red cell mass measured by ^{51}Cr tagging of the RBC. There was a tendency towards a further shortening of an already short ^{51}Cr RBC survival in 4/6. There were no consistent changes in an already very low plasma ^{59}Fe disappearance rate. Ethylestrenol, was found to stimulate growth without accelerating bone maturation, and to increase red cell mass without prolonging red cell survival.

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288 THE EFFECT OF HYPOXIA ON PERIPHERAL METABOLISM OF THYROXINE. B.Chance, M.Kaplan, T.Moshang,Jr., R.Utiger and O.Takahashi, Dept. of Ped., Hahnemann Med.Coll. and Dept. of Med., Univ. of Pa., Phila., Pa.

The peripheral metabolism of T_4 has been noted to be altered in a number of non-thyroidal illnesses. The known relationship of thyroid hormones and oxygen consumption led to these studies investigating the effects of hypoxia on peripheral metabolism of T_4. T_4,T_3, rT_3 and TSH levels were determined in patients with status asthmaticus and cyanotic heart disease, none of whom were cachectic or malnourished. Mean results(±SEM)are tabulated below.

	PO_2 mmHg	T_4 μg/dl	T_3 ng/dl	rT_3 ng/dl	TSH uU/ml
Controls		8.25±0.5	104.8±4.7	21.6±1.20	4.0±0.3
Chronic Hypoxia	47	6.35±0.8	72.6±7.5	34.3±4.03	5.45±1.2
Acute Hypoxia	66	7.48±1.1	92.7±6.1	37.7±6.1	1.77±.46

There was a significant decrease in T_3 levels with a significant increase in rT_3 in the patients with chronic hypoxia. Even hypoxia of short duration caused a significant increase in rT_3. T_4 levels were also lower in the chronic hypoxic group. These data are similar to the findings obtained during catabolic non-thyroidal illnesses. These alterations in thyroid function tests may reflect an adaptive phenomenon at the cellular level, i.e.,a protective mechanism which can divert T_4 to rT_3, or conversely, as during cold exposure, can increase production of T_3. In light of these data correlating hypoxia and thyroid hormones, the suggestions that the low thyroid function levels in RDS infants may be etiologically related to RDS may need to be reevaluated.