Regulation of insulin release at low O_2 tensions is important to hypoxic children because of their increased reliance upon carbohydrate metabolism for energy production. We have found immunoreactive insulin (IRI) release inhibited by alpha adrenergic receptor stimulation in hypoxic puppies. Since cyclic AMP mediated insulin release is thought to relate the adrenergic receptor and its physiologic response, the effects of cyclic AMP elevation on IRI levels at low O_2 tensions were studied. Hypoxic puppies were given an analogue of cyclic AMP, dibutyryl cyclic AMP (DCAMP), to test the effects of exogenous cyclic AMP elevation and theophylline, a phosphodiesterase inhibitor, to test the effects of endogenous elevation of cyclic AMP.

In air breathing puppies ($PaO_2 > 75$ mm Hg), either DCAMP or theophylline infusion resulted in sustained elevations of plasma IRI and glucose. With 75 min of hypoxia alone ($PaO_2 25-35$ mm Hg), plasma IRI remained at baseline levels despite the development of marked hyperglycemia. In contrast, puppies receiving DCAMP or theophylline after 30 min of hypoxia were found to have significantly higher IRI levels than did the hypoxic control group ($p < 0.05$). The IRI levels reached with DCAMP or theophylline appeared related to the concomitant glucose levels.

These observations suggest alpha adrenergic inhibition of insulin release in hypoxia is the result of reduced cyclic AMP levels.

- 85 *Aldosterone Metabolism in Cystic Fibrosis (CF).* ARTEMIS P. SIMOPOULOS, ALLEN LAPEY, THOMAS F. BOAT, PAUL A. DI SANT'AGNESE and FREDERICK C. BARTTER, NIH, Bethesda, Md.

CF patients show inability to retain salt through sweat leading to serious and at times, fatal complications through cardio-vascular collapse. Aldosterone-renin system metabolism has never been accurately determined in this disorder.

Five CF patients, 13 to 21 years of age, were studied on an air-conditioned metabolic unit on constant dietary regimens with 9, 109, and 240 mEq/24 h sodium intake for 8-day periods. During each 8-day period of different sodium balance, aldosterone secretion rate (ASR) and plasma renin activity were measured; the latter in both the supine and upright position.

All patients were in good sodium metabolic balance and renal electrolyte conservation was normal. On the 109 mEq sodium regimen, the mean ASR was $282 \mu\text{g}/24 \text{ h}$ (normal: 91 ± 30.4). In 4 out of 5 patients on the 240 mEq sodium regimen, the mean ASR was $205 \mu\text{g}/24 \text{ h}$ (normal: 35.9 ± 16.1); the 5th patient suppressed moderately to ASR $62 \mu\text{g}/24 \text{ h}$. On the 9 mEq sodium regimen, all 5 patients were able to increase normally to ASR $702 \mu\text{g}/24 \text{ h}$ (normal mean: 639 ± 441). Plasma renin values were somewhat elevated on the different sodium intakes, but rose normally with the upright posture.

Conclusions: In 5 CF patients, ASR and renin values were slightly elevated, but responded normally to decreased oral sodium intake and postural changes. ASR did not suppress as expected on the high sodium intake. This state of slight hyperaldosteronism secondary to increased renin release is probably due to adaptation to frequent excessive sodium losses via the sweat and consequent extracellular volume changes.

- 86 *Maturation of Hypothalamic-pituitary Control of Thyroid Function in the Human Fetus.* CALVIN J.

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The human fetal thyroid is capable of concentrating iodine and synthesizing hormone by 12 weeks. Fetal thyroxine (T_4) production is thyrotropin (TSH) dependent and the fetal pituitary contains TSH by 10-12 weeks. Little is known, however, about maturation of neuroendocrine control of fetal thyroid function. Serum T_4 , free T_4 (FT_4) and/or immunoreactive TSH were measured in paired maternal and cord blood specimens obtained at the time of therapeutic abortion or premature delivery of 35 pregnancies 11 to 34 weeks in duration and 17 pregnancies at term. Fetal pituitary were obtained when possible for determination of TSH content. Maternal T_4 and TSH did not change between 11 and 40 weeks but the mean FT_4 between 11 and 18 weeks was higher than the value at term. Fetal T_4 , FT_4 and TSH were low between 11 and 18 weeks. TSH and T_4 increased abruptly between 18 and 22 weeks and, with FT_4 , increased progressively thereafter to term. Fetal pituitary TSH content also increased abruptly between 18 and 22 weeks. There was no correlation between maternal and fetal serum T_4 , FT_4 or TSH values. The data indicate that a) the fetal pituitary thyroid system functions autonomously of the maternal system; b) rapid maturation of the fetal hypothalamic-pituitary control occurs between 18 and 22 weeks; c) fetal T_4 secretion increases progressively between 24 weeks and term.

- 87 *Short Stature and Growth Hormone Deficiency Due to Histiocytosis X.* M. E. LAHEY, F. M. KENNY and A. L. DRASH, Dept. of Ped., Univ. of Utah Med. Center and The Children's Hosp., Univ. of Pittsburgh Sch. of Med.

Diabetes insipidus (DI) is a common complication of histiocytosis X. Anterior pituitary function has not been previously systematically studied. Both anterior and posterior pituitary function has been evaluated in 11 children with histiocytosis. The following methods were used. Insulin hypoglycemia and arginine infusion for GH, serum PBI, T_4 , and ^{131}I uptake for thyroid function, and metyrapone stimulation for adrenal function. Concentrating ability was used as an index of vasopressin release. Gonadotropin was assessed by physical examination only. In 6 patients, only vasopressin and growth hormone (GH) response was studied. In 5 thyroid and adrenocortical evaluation was also obtained. Of the 11 children, 4 were of normal height for age, while 7 were below the 3rd percentile. Those children with normal height all had normal GH response. Two of them had DI with normal thyroid and adrenal function. Of the 7 children with retardation of linear growth, 6 were found to be GH deficient. The 1 child with normal GH had a strong family history of short stature. Five had DI and all were GH deficient. Thyroid studies were normal in 2 and adrenal studies in 3 of these. One child had histiocytosis of the thyroid gland with goiter and hypothyroidism. In 3 children of adolescent age with short stature, GH deficiency and DI, puberty was delayed. This study documents that histiocytosis may involve the anterior and/or posterior pituitary. An adequate clinical evaluation should include study of the anterior pituitary.

- 88 *Distribution of ^3H -acetyl Growth Hormone (^3H -HGH) in the Subcellular Fractions of Rat Liver.* VADDANAHALLY T. MADDIAH, IRAJ REZVANI,