895 FREE C-PEPTIDE LEVELS IN INFANTS OF DIABETIC MOTHERS: RELATIONSHIP TO HYPOGLYCEMIA, MACROSOMIA, AND HYALINE MEMBRANE DISEASE. I. Sosenko, J. Kitzmiller, S. Loo, K. Gabbay, P. Blix, A. Rubenstein (Spon. by H.W. Taeusch). Departments of Pediatrics and Obstetrics, Harvard Medical School and University of Chicago, Boston, MA. and Chicago, ILL.

Hyperinsulinism is postulated to be related to three major abnormalities in the infant of the diabetic mother (IDM): postnatal hypoglycemia, macrosomia, and hyaline membrane disease (HMD). To test these associations we measured free C-peptide in cord serum of infants of gestational and insulin-requiring diabetics. Free C-peptide levels measure endogenous insulin secretion independent of interfering antibodies. No significant correlation was found between free C-peptide and gestational age in IDM's. IDM's who developed hypoglycemia (serum glucose<30 mg/dl in the first 6 postnatal hours) had significantly ($p<0.025$) higher cord free C-peptide levels as compared to those without hypoglycemia (7.37±1.23 ng/ml, n=37 vs. 3.91±0.69, n=35, mean±SEM). IDM's with birth weight above the 90th %-ile for gestational age had significantly ($p<0.05$) higher cord free C-peptide levels as compared to those with birthweight below the 90th %-ile (7.51±1.46, n=31 vs. 4.18±0.60, n=43). 7 IDM's who developed HMD did not have significantly elevated cord free C-peptide levels as compared to 71 IDM's without HMD. The lower than expected incidence of HMD in this series precludes a definitive evaluation of the relationship of hyperinsulinism to HMD in the IDM. We conclude that hyperinsulinism in the IDM, as reflected by free C-peptide level, is directly related to macrosomia and to postnatal hypoglycemia.

896 SYMPATHETIC CONTROL OF THE FETAL ENDOCRINE PANCREAS: A KEY TO NEONATAL ADAPTATION. Mark A. Sperling, Ronald A. Christensen, Supriya Ganguli, Rajen Anand. UCLA - Harbor General Hospital, Department of Pediatrics, Torrance, CA

Adrenergic (ADR) agonists, with or without α (phentolamine) or β (propranolol-P) blockers were infused to the chronically cannulated sheep fetus in the third trimester, in order to test the hypothesis that ADR mechanisms are responsible for the characteristic surge in glucagon (IRG), fall in insulin (IRI) and stabilization of blood glucose (G) following birth. 5 to 7 animals comprised each series. With epinephrine (EPI) 6 μg/min, IRG rose from 75±8 pg/ml to 219±45 pg/ml at 60 min ($p<0.01$), IRI fell from 23±2 uU/ml to 13±3 uU/ml ($p<0.05$) and G rose from 14±4 mg/dl to 42±10 mg/dl ($p<0.02$). P alone for 45 min did not alter basal IRG or G, but IRI fell from 20±3 to 11±4 uU/ml. However, P markedly inhibited the response to EPI; peak IRG was 96±8, peak G 24±2 while IRI fell to 8±3. Qualitatively similar but markedly attenuated changes in IRG, G and IRI occurred with EPI 0.1 μg/Kg/min. With NOR-EPI 2 μg/min, IRG was unchanged, IRI fell by 12±4 uU/ml, ($p<0.02$) and G rose by 8±2 mg/dl ($p<0.02$). Phentolamine alone augmented IRI from 18±3 to 38±5 uU/ml ($p<0.02$), without a change in IRG or G; with addition of NOR-EPI the rise in G was prevented and no further change in IRI or IRG was seen. Conclusions: 1) Appropriate ADR modulation of IRG, IRI, and G responses are established in the third trimester; 2) spontaneously occurring patterns in IRG, IRI, and G after birth can be simulated by EPI in utero; 3) spontaneous EPI secretion may be a key signal for neonatal energy adaptations that involve pancreatic hormones.

897 BIOCHEMICAL CHANGES DURING ANESTHESIA IN CHILDREN. A. Stanec, R. W. Lent, D. Duncalf, (Spon. by L. Finberg), Albert Einstein College of Medicine, Montefiore Hospital and Medical Center, Departments of Anesthesiology and Laboratory Medicine, Bronx, NY.

This investigation explored the effect of anesthesia on serum electrolytes and enzymes in relation to the etiology of malignant hyperthermia (MH). Forty children undergoing elective surgical procedures under halothane anesthesia were studied. Control blood samples were taken 5 minutes after induction of anesthesia and repeated in 3, 6, 15, 30, 60 minutes after a single 1 mg/kg IV dose of succinylcholine chloride (Sch). The results demonstrated: a)a mean fall in ionized serum calcium of 0.75 mEq/L at 3-6 minutes; b)a mean rise in creatine phosphokinase (CPK) activity of 150 U/L; c)a mean rise in serum potassium of 0.2 mEq/L and a mean fall in serum sodium of 6 mEq/L.

The finding of a fall in serum calcium ion with a corresponding rise in CPK activity, supports the hypothesis that a preexisting defect in permeability of many membranes exists in MH patients, and is further exaggerated by the passive transfer of calcium ions during the state of membrane depolarization. Thus the rapid rise of intracellular calcium in precipitating the MH crisis after exposure to triggering agents may be potentiated.

898 HYPERINSULINISM (HI) IN INFANCY: EFFECT OF SOMATOSTATIN (SS) ADMINISTRATION AND ALTERATIONS IN INSULIN BINDING (IB) TO MONOCYTES. W.Tamborlane, V.Soman, R.Sherwin and M.Genel, Depts. of Pediat. & Med., Yale Univ. Sch. of Med., New Haven, CT (Sponsored by Joseph B. Warshaw).

SS, an inhibitor of insulin (I) secretion, has been reported to reduce glucose requirements and thus facilitate the treatment of hypoglycemia associated with HI in infancy. In addition, while I levels have been shown to affect IB and IB is an important determinant of I action, the effect of HI on IB in infants has not been determined. We therefore examined the effect of varying doses of SS on glucose regulation and IB before and after chronic I suppression in a 15 mo. old boy with HI. Low dose SS (2 μg/kg/min) promptly reduced plasma I (30-35%) and increased plasma glucose (22 to 80 mg%) but failed to maintain euglycemia without glucose administration. When SS was increased (8 μg/kg/min), normal plasma glucose was maintained despite withdrawal of exogenous glucose. IB to monocytes was determined before and 4 wks following suppression of excessive I secretion with diazoxide. Pre-Rx IB was markedly reduced (1.2%) as compared to normal control children (7.0 ± 0.3%, N=6). Post-Rx IB increased 300% in association with a reduction of basal I from 38 to 7 μU/ml. These data provide further evidence for the potential therapeutic efficacy of SS in HI but emphasizes the need for individualization of dosage. Furthermore, IB was inversely related to I levels in our patient as seen in other hyperinsulinemic states in adults. These changes in IB may serve as a protective compensatory response and could prove useful in the diagnosis of HI.

899 HYPOPARATHYROIDISM (hPTH) ASSOCIATED WITH NEPHROGENIC DIABETES INSIPIDUS & INCOMPLETE RENAL TUBULAR ACIDOSIS. Chandra M. Tiwary, Timothy A. Anderson, and Norman D. Proyor. (Spon. by James W. Bass) Dept of Pediatrics, Walter Reed Army Medical Center, Wash, DC, and Portsmouth Naval Hospital, VA.

A male infant of healthy parents (birth weight 3374 gm) developed tetany at 6 days of age. hPTH was diagnosed based on hypercalcemia (6.9 mg/dl), hyperphosphatemia (9.0 mg/dl), hypercalcemic and phosphaturic response to paratharmone with clinical and biochemical response to vitamin D (25000 units). Hyposthenuria was noted at 6 mos. The child was reevaluated at 12 yrs of age for polyuria unaffected by water restriction. Creatinine clearance, ACTH stimulation test, skeletal x-rays and IVP were normal but nephrocalcinosis was noted. Water deprivation (20 hrs) resulted in 4.4% weight loss, fixed low urine osmolality (Osm) and fixed urine flow. The final urine Osm was 379 mOsm/kg, urine flow 55 ml/hr, and serum Osm 287 mOsm/kg. One and two hours after 5 units of aqueous vasopressin (VP) injection the urine osmolality remained 378 and 377 mOsm/kg. Lowest urine pH during 5 hr NH_4Cl test was 5.95. Three day NH_4Cl test: baseline titrable acidity (TA) was 12.9 mEq/l, serum CO_2 24 mEq/l, serum Cl^- 103 mEq/l. Values after NH_4Cl ingestion were 21.5, 18, & 112, respectively. Normally, in urine there is a rise of ≥ 36 mEq/TA per 24 hrs. The absence of renal response to VP and impairment of urine acidification on acid load may be a vitamin D effect. The presence of hyposthenuria in early infancy with later development of nephrocalcinosis suggest a true association with hPTH; previously unreported.

900 HYPOAMMONEMIA IN GYRATE ATROPHY OF CHOROID AND RETINA. David Valle, Saul W. Brusilow, Mackenzie Walser, Muriel I. Kaiser-Kupfer. Johns Hopkins University School of Medicine, Departments of Pediatrics and Pharmacology, Baltimore, and National Eye Institute, Clinical Branch, Bethesda.

Gyrate atrophy (GA) is an inherited chorioretinal degeneration associated with hyperornithinemia. The enzyme defect is a deficiency of ornithine-δ-aminotransferase (OAT) (Valle et al Proc. Natl. Acad. Sci. 74:5159, 1977). In 4 GA patients we have noted abnormalities in the components of the labile nitrogen pool in plasma. Most impressive was a reduction in plasma ammonium concentration (GA range 0-13 μM; normal mean ± 1SD is 27±6 μM). Plasma glutamate (GA 5-22 μM; normal 43±14 μM), aspartate (GA 6-15 μM; normal 15±5 μM), and glutamine (GA 367-557 μM; normal 654±64 μM) were also reduced. Alpha-ketoglutarate was normal. No other amino acids were subnormal except lysine (owing to lysinuria). Arshiraff et al. (Clin. Res. 25:321A, 1977) reported low blood glutamates in GA and suggested that this resulted from decreased formation of glutamate in the OAT reaction. We suggest alternatively that high ornithine concentrations in GA stimulate the urea cycle, producing a new balance between the rate of urea formation and the levels of urea precursors. The rate of urea formation in GA is normal (SUN 10-17 mg/dl, urea N excretion 10 g/day). Hence urea precursors are all lowered. The corollary, that arginine (and therefore ornithine) deficiency results in hyperammonemia has been well established in animal species that require arginine. The subnormal levels of urea precursors, particularly glutamate, could play a role in retinal degeneration