1135 PLASMA, LEUKOCYTE AND FIBROBLAST AMINO ACID LEVELS IN CYSTIC FIBROSIS (CF). V.S. Hubbard, D. Towne, and J.D. Schulman, NIAMDD and NICHD, NIH, Bethesda, MD

We are unaware of quantitative data on amino acid (AA) levels in CF plasma, leukocytes, and cultured cells, although alterations in methionine metabolism have been suggested in CF. Plasma samples and washed leukocyte pellets obtained after overnight fasting from clinically stable CF patients, obligate heterozygotes, and normal (NL) subjects, ages 16-30, were processed for AA analysis by standard methods. CF and NL fibroblasts matched for age and passage # were cultured in 3 different media (alpha, Eagle's MEM, and MEM + non-essential AA), harvested at confluency, and intracellular AA measured. Methionine content of all CF samples was similar to NL. Compared to NL (n=6), CF plasmas (11) had an ↑ mean level of glycine (CF 298 nmol/ml ± 12.4 [SEM], NL 231 ± 15.1, p <.005) and marginally altered citrulline and phenylalanine; for these AA, heterozygote means fell between CF and NL. CF and NL ranges for all plasma AA overlapped. CF leukocytes (5) compared to NL (3) had reduced leucine (CF 2.54 ± .46, NL 5.00 ± .29), isoleucine (CF 1.01 ± .30, NL 2.51 ± .12), valine (CF 1.52 ± .13, NL 2.94 ± .39), and phenylalanine (CF 0.86 ± .17, NL 1.95 ± .20) (all p <0.02) expressed as % of total AA; CF and NL ranges did not overlap and heterozygotes had decreases like CF for these four AA. The CF and NL fibroblasts (2 lines each) had similar AA content in all 3 media. The alterations noted in CF AA are relatively small, and have no obvious relationship to the major clinical or biochemical features of CF.

1136 URINARY EXCRETION OF GAMMA-HYDROXYBUTYRIC ACID IN A PATIENT WITH NEUROLOGICAL ABNORMALITIES: A NEW INBORN ERROR OF AMINO ACID METABOLISM? Cornelis Jakobs, Monika Bojasch, Eberhard Mönch, Dietz Rating, Hartmut Siemes, and Folker Hanefeld (Spon. by Jerry A. Schneider) Free University of Berlin, Department of Pediatrics, West-Berlin.

A 20 year old male of consanguinous Turkish parents presented with mental and physical retardation, ataxia, hypotonia, and EEG-abnormalities. Gas chromatographic-mass spectrometric studies of urinary organic acids identified two hitherto unobserved metabolites: γ-hydroxybutyric acid (GHB), 1728 µmol/l, and succinic semialdehyde (SSA), 47 µmol/l. GHB could also be detected in serum, 943 µmol/l and spinal fluid, 596 µmol/l. A new metabolic block is postulated, due to a deficiency of SSA-dehydrogenase, which converts SSA to succinic acid in the γ-aminobutyric acid (GABA) catabolic pathway. SSA degradated from GABA cannot enter the Krebs cycle and may be hydrogenated to GHB. GHB was previously used as an anesthetic drug until its neuropharmalogical and neurophysiological side effects became obvious. At present however we cannot definitely conclude that a connection between the GHB elevation in body fluids and the clinical status of this child exists. As some anticonvulsants prevent and reverse the GHB induced EEG-abnormalities we have been prompted to initiate a clinical trial with ethosuximide and sodium valproate. In the meantime we have discovered a pair of siblings presenting with mental retardation, behavioral problems, and ataxia who show the same organic acid profile. This finding supports the hypothesis that this pattern reflects a new inherited disorder.

1137 ALTERED GLUCOSE REGULATION ACCOMPANYING ASPHYXIA AT BIRTH IN THE RAT. Robert Jansen & Edward Ogata (Spon by Carl Hunt), Northwestern University Medical School Prentice Women's Hospital, Dept. of Pediatrics-OB/Gyn, Chicago.

Birth asphyxia is a major cause of neonatal morbidity and mortality and produces dysfunction in many organ systems. To study effects on glucose metabolism, we developed an animal model of asphyxia at birth. Rat pups, delivered by hysterotomy at term and maintained in humidified chambers at 36°C, were subjected to hypoxia (H) FiO_2 3-5% for 20 minutes immediately upon delivery then allowed to recover in room air. Blood sampling from consecutive litter mates was done at birth, 10,20,40,60,120,240,360 minutes. H pups were compared with control (C) animals not subjected to hypoxia. H pups showed severe asphyxia by arteriovenous blood gas tensions and pH at 20 minutes of age (PO_2 16.4 PCO_2 87.4mm Hg, pH 6.76) with elevated lactate and low pyruvate concentrations. These returned to control levels by 3 hours. Plasma epinephrine (E) and norepinephrine (NE) concentrations were elevated at birth and increased in the H pups to 16,872 pg/ml E and 11,187 pg/ml NE at 20 minutes, returning to control levels by 1 hour. The H pups were relatively hyperglycemic the first hour of life and their plasma insulin was also elevated and paralleled glucose values. Glucose and insulin concentrations returned to control levels by 2 hours. These data suggest that catecholamine release during asphyxia may be a dominant mediator of fuel availability. We speculate that during H, insulin is elevated in response to either hyperglycemia or to the insulin releasing effects of E taking precedence over NE.

1138 CARRIER DETECTION AND PRENATAL DIAGNOSIS IN TAY-SACHS DISEASE (TSD): SUMMARY EXPERIENCE OF THE FIRST DECADE. Michael Kaback, Susan Greenwald and Rick Brossman. Harbor-UCLA Medical Center, Torrance, California 90509.

Just over one decade ago the metabolic error in TSD was identified - deficient activity of lysosomal hexosaminidase A. Further advances made the prenatal Dx of TSD and heterozygote identification for this recessive trait possible. Since 1970, programs for community education, voluntary carrier screening, and genetic counseling (with prenatal Dx) have been initiated on 5 continents. Through the establishment of an international center for assay standardization, quality control, and program surveillance,* the experiences of 102 centers in 16 countries have been surveyed.

As of June 1980, 312,214 young Jewish adults have been screened. Nearly 13,000 heterozygotes have been identified and, importantly, 268 couples were identified as being "at-risk" for this condition in their offspring. An heterozygote frequency in the American Jewish population of 0.034 (1 in 29.7) has been determined. Of 814 pregnancies monitored by amniocentesis, 175 fetuses were identified with TSD. 636 unaffected infants were born as predicted. One child with TSD was misdiagnosed as unaffected in utero.

Data concerning new cases of TSD in the North American Jewish population indicate that the aforementioned efforts have contributed to a 70-85% decrease in the prevalence of this fatal neurodegenerative disorder in this population.

*Sponsored by National TSD and Allied Disorders Association

1139 PARATHYROID (PTH) AND ANTIDIURETIC HORMONE (ADH) IN REYE-JOHNSON SYNDROME (RJS). Ellen S. Kang, Genaro M. A. Palmieri, Kathryn S. Schwenzer, Hershel P. Wall, Robert Shade, Joan Crofton, and Leonard Share. Univ. TN. Ctr. Hlth. Sci., Depts. of Peds., Med., and Physiology, Memphis, TN. (spon. by John F. Griffith)

From the metabolic standpoint, several features of RJS implicate a role for cAMP in the pathophysiology of this disease. ↑ plasma cAMP is found in RJS to corroborate this possibility. In the presence of a normal degrading system, cAMP should not be expected to be ↑ in the urine. However, 25% of cases have ↑ cAMP excretion. Since PTH and ADH are both known to ↑ cAMP production by the cells of the renal tubules, these hormones were measured in plasma, retrospectively, in untreated RJS patients. ↑ ADH and PTH levels were found which correlated with the severity of the disease. In two patients, a rapid decline in the PTH levels was seen in 3-5 hours. No significant changes in serum Ca, Mg, PO_4, and osmolality were noted. These findings add two more hormones in addition to insulin, glucagon, ACTH, cortisol, GH, prolactin, and the catecholamines which are increased in the complexity of findings in RJS. A model which could accommodate some of these findings and lend insight to a possible mechanism involving Ca translocation whereby an underlying membrane lesion might be further aggravated by these abnormalities is proposed.

This work was supported in part by a grant from the USPHS, NIH HD 11657.

1140 THE EFFECT OF FATTY ACID CHAIN LENGTH IN DIETARY TRIGLYCERIDE ON ADIPOSE TISSUE METABOLISM IN HUMAN SUBJECTS. David P. Katz, Kim I. Timmers, and Jerome L. Knittle, Mount Sinai School of Medicine, New York, N.Y.

We have previously demonstrated that the enzymes phosphofructokinase (PFK) and citrate cleavage enzyme (CCE) increase in activity in response to 600 kcal diets in adipose tissue of obese humans while decreasing in lean controls. We have now examined the possible role of different dietary fats since others have shown a decrease in adipose tissue lipogenesis in vivo in rats fed medium chain triglyceride (MCT) when compared to long chain triglyceride (LCT). We compared the effect of dietary LCT and MCT in obese adolescents (n=13) before (weight maintenance;I), during (600 kcals;II), and after (1100 kcals;III) weight reduction. The diets contained 20% of calories as protein, 40% as carbohydrate, and 40% as fat (either 40% LCT or 20% LCT & 20% MCT). Fat samples were obtained weekly and analyzed for PFK, CCE, malic enzyme (ME), and glucose-6-phosphate dehydrogenase (G6PD). During period I there was no difference in enzyme activities when LCT was compared to MCT. During period II CCE was lower on MCT than LCT (3.7 ±2, 12.7±9;p<.05). During period III MCT significantly decreased the activities of PFK (26.0±11, 43.4±10;p<.03) and ME (17.7±7, 32.2±15;p<.04) while increasing the activity of G6PD (33.1±12, 16.0±11;p<.04). The lower activities of ME, CCE, and PFK during MCT diets suggests a dampening effect of the oil on glycolysis and fatty acid synthesis. MCT may be a useful adjunct to weight reduction therapy, especially during the post weight-reduction period when most diets fail.