1159 DIAGNOSIS, TREATMENT AND FOLLOW UP OF NEONATAL ARGININOSUCCINIC ACIDEMIA. Reuben Matalon, Kimberlee Michals, Steven Gross, Mark L. Batshaw and Saul W. Brusilow. Depts. of Pediatrics, Univ. of Ill. Chicago, Ill., and Johns Hopkins School of Medicine, Baltimore, Md.

Argininosuccinic acidemia is an autosomal recessive disorder of the urea cycle caused by argininosuccinase deficiency. A 2 day old male developed seizures and respiratory distress, EEG showed status epilepticus pattern, and at 4 days of age he lapsed into coma. Blood amonia was 1800 µg/dl (normal 10-150), blood amino acids revealed argininosuccinic acid (ASA) 196.98 µmol/dl and anhydro ASA 174.12 µmol/dl. Urine ASA was 34.7 Gm/Gm creatinine and anhydro ASA was 39.5 Gm/Gm creatinine. A micro assay for argininosuccinase was developed, which showed no dectable activity in patient's RBC's while a control sample released 2.77 µmol (± 0.63) of ornithine/h/ml of whole blood. Treatment with exchange transuflons and peritoneal dialysis reduced blood ammonia only slightly to 1100 µg/dl. Dramatic reduction of ammonia to 300 µg/dl occurred 24 h after intravenous therapy with 4 mM/Kg/day of arginine hydrochloride and 250 mg/Kg/day of sodium benzoate. The baby improved and his EEG became normal. At 9 months, the baby's height, weight, and head circumference are within the 50th percentile. Frequent developmental assesments have been within the normal range. Currently the baby is on 1.7 Gm/Kg of protein with arginine supplementation of 1 mM to 4 mM/Kg/day depending on the blood arginine levels. A biochemical and enzymic diagnosis of argininosuccinic acidemia can be made in the newborn period. Arginine therapy is superior to other forms of treatment in preventing hyperammonemia and neurological damage.

1160 TREATMENT OF NONKETOTIC HYPERGLYCINEMIA WITH DIAZEPAM, CHOLINE AND FOLIC ACID. Reuben Matalon, Kimberlee Michals and Sakkubai Naidu. Depts. of Pediatrics, Univ. of Ill., Chicago, Ill, and Loyola Univ. Chicago, Ill.

Nonketotic hyperglycinemia (NKH) is a disorder of glycine metabolism characterized by severe mental retardation, seizures and early death. A female presented on the 3rd day of life with hypotonia, seizures and respiratory distress was treated with phenobarbital and Dilantin with poor response. At 8 months evaluation revealed a severely delayed, hypotonic female with random eye movements, lack of head control and no interaction with her surrounding. Repeated EEG's revealed a status epilepticus pattern Plasma glycine was 72.1 µmol/dl (normal 5.6-30.8), urine glycine was 2850 mg/Gm creatinine (normal 200-250) and CSF glycine 29.2 µmol/dl (normal 3.0-6.0). No organic aciduria was present. Treatment with diazepam as a glycine antagonist and choline with folic acid for one-carbon unit transfer was adopted. Diazepam 1.5 mg/Kg with 4 Gm of choline and 2 mg of folic acid were given daily. Adequate caloric intake with 1.5 Gm of protein/Kg/day was given with sodium benzoate 150 mg/Kg/day. Three months after treatment plasma and urine glycine remained elevated, 65.4 µmol/dl and 4590 mg/Gm creatinine, respectively; however, CSF glycine dropped markedly to 8 µmol/dl. The patient improved dramatically: has had no seizures, has become alert and aware of her environment, has been smiling and has been able to hold her head. Repeated EEG showed definite improvement with fewer discharges. This new method of treatment suggests that diazepam with choline resulted in better seizure control and improvement of tone and development in NKH.

●1161 NORMALIZATION OF SEROTONIN UPTAKE IN DOWN'S SYNDROME PLATELETS. ROLE OF K^+. Ernest E. McCoy and Louise Enns, Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada.

Down's syndrome (D.S.) platelets have a decreased content and rate of uptake of serotonin (5HT) compared to normal platelets. The purpose of the present study was to determine whether 5HT uptake could be normalized in D.S. platelets. The initial rate of 5HT uptake into D.S. is 3.65±0.50 compared to normal uptake of 8.89±1.03 nmoles/hr/10^9 pl ($p<.001$). In D.S. platelets Na^+ content is increased, K^+ content is decreased and the rates of inward and outward transport of K^+ and the efflux of Na^+ are also decreased. As 5HT uptake is linked to the outward movement of K^+, the effect of normalizing K^+ content of D.S. platelets was studied. Normal and D.S. platelets were incubated in 30 mM KCl buffer for 20 min. The K^+ content of D.S. platelets after incubation (19.2±1.0 µg/10^9 pl) was the same as normal (18.0± 2.3 µg/10^9 pl ($p<.4$). While K^+ content was normalized, 5HT uptake as well as K^+ efflux rates were determined in D.S. platelets. 5HT uptake increased to 7.63±0.62 nmoles/hr/10^9 pl and K^+ efflux increased from 0.53±0.06 to 1.04±0.08 compared to normal efflux of 1.14±0.13 µmoles/hr/10^9 pl. These results indicate that the rate of 5HT efflux is linked to K^+ content and K^+ efflux. This is the first demonstration of a correctable biochemical defect in D.S. If alterations in Na^+ and K^+ content occurred in D.S. synaptosomes, they could affect amine uptake and content of these organelles concerned with neurotransmission.

1162 LIPOPROTEIN LIPASE IN PRETERM HUMAN MILK. Nitin R. Mehta, Jay B. Jones and Margit Hamosh (Spon. by P.L. Calcagno). Georgetown University Medical Center, Washington, D.C.

Lipoprotein lipase (LPL) is present in milk of several species, including term human milk. LPL, assumed to leak into milk from mammary cells damaged during suckling, has been implicated in the development of breast milk jaundice. Since increasing numbers of preterm infants are fed their own mother's milk, we have measured LPL (hydrolysis of serum-activated tri-^3H olein, 1 unit (U)=1 nmol free fatty acid (FFA) released/ml milk/min) in milk collected for 3 months from 47 women with deliveries at 26-36 wks pregnancy. The data show that:

Pregnancy		Lactation (wks)				
(wks)	N	0.2	1	3	6	12
		Lipoprotein lipase (U/ml milk/min)				
25-30	19	12±3	20±4	33±9	102±13	101±58
31-36	28	25±6	50±11	57±10	128±40	-
37-40	6	17±9	63±15	270±80	106±50	102±60

1. LPL increases with length of gestation and lactation. 2. "Drip" milk had twice the LPL activity of milk pumped simultaneously from the other breast, irrespective of duration of pregnancy or lactation, suggesting no relationship between cell damage and enzyme release. 3. Feeding of milk with very high LPL (>500) did not cause neonatal jaundice. We suggest that the level of LPL in milk might be related to its level in the mammary gland and that it could be an indicator of the latter's functional capacity. (Support NIH grant HD 10823 and AM 26641)

1163 FETAL AND NEONATAL METABOLIC RESPONSE TO EXTENDED MATERNAL CANINE STARVATION(MCS) E-L.Miettinen, R.Kliegman, K-Y.Tserng, S.Kalhan and P.Adam* CWRU,Cleveland Metro General Hospital, Division of Ped. Metab., Cleveland, OH

Circulating fuels and glucose and lactate turnover rates among fasted newborn pups of 6 control and eight 5-day starved pregnant dogs were studied between 0 and 24 hrs of age. MCS caused a 23% weight loss in pups. Fetal ketone body concentration (3.33 mM)+ paralleled the maternal ketonemia (5.78 mM) in the MCS group. Following birth, there was a rapid decline in the ketone levels. Starvation caused a significant decline in maternal blood glucose (3.22 vs 4.14 mM) while the fetal blood glucose was not significantly different. By 3 hrs of age MCS caused a significant lowering of blood glucose (2.79 vs 5.77 mM), plasma free fatty acids (FFA)(0.505 vs 0.701) and glycerol levels (0.146 vs 0.247). By 6 hrs, glucose and FFA became equivalent to controls, while glycerol values remained depressed at 6 and 9 hrs. Blood alanine concentration was increased at 3,6 and 24 hrs in the MCS pups. Glucose production rate (GPR) was similar in both groups at 3,6 and 9 hrs. However glucose metabolic clearance rate was significantly increased (8.92 vs 5.63 ml/Kg.min) at 3 hrs. GPR and glucose clearance were also elevated at 24 hrs in the MCS group. Lactate turnover and lactate carbon incorporation into glucose were not significantly different between the 2 groups. CONCLUSION: The immediate neonatal adaptive responses to fetal nutrient deprivation as a result of MCS consists of unchanged glucose turnover,gluconeogenesis from lactate and augmented muscle release or decreased hepatic utilization of alanine.*Deceased +Mean

1164 EFFECT OF EXTENDED MATERNAL STARVATION ON THE INTRAHEPATIC REGULATION OF METABOLISM IN NEWBORN DOGS E-L. Miettinen, R. Kliegman, S. Kalhan and P. Adam*. CWRU, Cleve. Metropolitan Gen. Hosp., Div. of Ped. Metab., Cleveland OH

Hepatic metabolic intermediates from fasted newborn pups of 6 control and eight 5-day starved pregnant mothers (MCS) were studied between 0 and 24 hrs of age. In the MCS fetus, glycogen concentrations were significantly reduced (416vs526 µ mol/g)+and uridinediphosphate glucose levels increased (0.196vs0.135) suggesting diminished fetal glycogen synthesis. After birth glycogen levels diminished at the same rate in the 2 groups being 197 and 304 at 24 hrs. Hepatic glucose concentrations were reduced in the MCS pups at 3 hrs (2.90vs5.97) reaching control levels at 6 and 9 hrs, again declining at 24 hrs (3.09vs5.29). Glucose-6-phosphate and fructose-6-phosphate concentrations after MCS were low in the fetus and throughout the 24 hrs. Tricarboxylic acid cycle (TCA) intermediates tended to be low after 6 hrs in the MCS group; α-ketoglutarate levels being significantly reduced at 6 and 9 hrs, malate at 9 and 24 hrs, and citrate at 24 hrs. After birth, MCS resulted in significant lowering of hepatic ATP levels while energy charge was low only at 6 and 9 hrs. In addition the cytoplasmic NAD/NADH ratio was significantly more oxidized at 3 hrs in the MCS pups. Intrahepatic ammonia concentrations were significantly elevated at 0,6,9 and 24 hrs. CONCLUSION: Extended MCS results in 1)reduced fetal glycogen synthesis or augmented fetal glycogenolysis and 2)diminished hepatic energy production after birth in spite of enhanced net hepatic glycolytic flux as a result of phosphofructokinase activation by low levels of ATP, citrate and NADH. *Deceased +Mean