257 CEREBRAL METABOLISM IN THE PUP OF A CANINE DIABETIC MOTHER (IDM) R. Kliegman, E-L.Miettinen, S.Kalhan and P. Adam* CWRU,Clev Met Gen Hosp,Div Ped Met.,Cleve.OH

Term pups from 6 insulin diabetic dogs were compared to controls from 6 litters after 0,3,6,9 and 24 hrs of neonatal fasting. Fetal cerebral glucose (CG) levels were elevated in IDMs (N=8) (5.45±0.98 vs 1.87±0.28 μmol/g)+ but equalized by 3 hrs as IDM levels declined and controls increased. Cerebral glycogen(Gly) was increased in fetal IDMs (3.45±0.61 vs 1.66±0.16). Gly was equivalent to controls at 3,6 and 9 hrs and was lower than controls at 24 hrs (1.54±0.21 vs 2.46±0.24). Cerebral glucose-6-phosphate, fructose-6-phosphate, phosphoenolpyruvate, pyruvate and lactate (L) were similar during the day except L was elevated in IDMs at 24 hrs. Cytoplasmic NAD/NADH ratios were unaffected, as were citrate, α-ketoglutarate and malate. IDM calculated oxaloacetate levels were elevated at 0,3 and 9 hrs. ATP, ADP, AMP and phosphocreatine levels were equivalent at all times. Cerebral glutamate and aspartate were higher among IDMs throughout the study while alanine was elevated only after birth. Glutamine was higher in the IDMs at 6 and 24 hrs. Cerebral ammonia levels were not affected. Though gamma aminobutyrate was elevated in fetal IDMs (1.26±0.14 vs 0.915±0.15) this did not persist. These data suggest that maternal canine diabetes 1) ↑fetal cerebral Gly stores, and 2) ↑fetal and neonatal cerebral amino acid pools. As CG is an important precursor of cerebral amino acids, ↑fetal CG provision may result in augmented cerebral amino acid pools. Alternately, ample G supply may spare cerebral amino acid utilization. Nonetheless, fetal cerebral substrate stores are enhanced.

*Deceased +Mean±SE

258 HEPATIC METABOLISM FOLLOWING NEONATAL CARBOHYDRATE ALIMENTATION IN DOGS. R. Kliegman, E-L. Miettinen, S. Kalhan and P. Adam* CWRU, Cleveland Metro Gen Hosp, Division of Pediatric Metabolism, Cleveland, Ohio.

Following birth pups were divided into 3 groups. As glucose(G) and galactose (Gal) are important monosaccharides for neonates, pups received an enteric feed of 0.625gm/Kg of either G (N=7) or Gal (N=7) at 6 hrs of age. The third group was fasted from birth. At 9 hrs, blood G levels were equivalent in fasted and G fed pups. Compared to fasting pups, those fed Gal had higher circulating G levels (7.1±0.9 vs 5.2±0.7 mM p<.05).+ Plasma free fatty acids were lower in the alimented pups (301±33 vs 880±10 μM p<.001). Hepatic G levels were not different however, glycogen(Gly) content was elevated following G (664±33 μmol/g p<.01) and Gal (588±50 p<.05) compared to fasted controls (430±55). Glucose-6-phosphate and fructose-6-phosphate were equivalent among all pups. In contrast fructose-1,6 diphosphate was elevated following G (0.022±0.002) and Gal (0.029±0.009 vs 0.012±0.002). In addition phosphoenolpyruvate was higher after G (0.135±0.02) or Gal (0.134 ±.03 vs 0.074±0.01) feeding. Nevertheless hepatic pyruvate and lactate levels were unaltered, as was the cytoplasmic NAD/NADH ratio. Enteric G or Gal resulted in higher levels of ATP (1.64± .11(G) 1.78±.18(Gal) vs 1.25±.09). ADP and AMP values were not altered. In conclusion, neonatal canine carbohydrate alimentation results in: 1) ↑hepatic Gly content; 2) ↑hepatic glycolytic flux through phosphofructokinase or diminished gluconeogenic flux through fructose diphosphatase; and 3) ↑hepatic ATP production or ↓utilization.

*Deceased +Mean±SE

259 REGULATION OF HEPATIC METABOLISM IN THE PUP OF A CANINE DIABETIC MOTHER (IDM). R. Kliegman, E-L.Miettinen, S. Kalhan and P. Adam* CWRU, Clev Metro General Hosp., Division of Pediatric Metabolism, Cleveland, Ohio

Six insulin dependent diabetic dogs were mated and delivered at term. Pups were compared to those from 6 control litters and studied after 0,3,6,9 and 24 hrs of neonatal fasting. The fetal hepatic metabolic environment in the IDM (N=8) was characterized by elevated hepatic glucose (G)(7.85±.76vs4.74±.45 μ mol/g) glycogen (Gly)(759±70vs519±18), pyruvate (py)(.201±.017vs.123±.012), citrate (.298±.027vs.179±.025), aspartate(Asp)(.995±.117vs.608± .529) concentrations and augmented energy charge (.745±.014vs.697 ±.010). Fetal fructose-1,6 diphosphate (FDP)(.0084±.0012vs.019± .003) and AMP(.198±.01vs.283±.033) were lower in IDMs. Fetal Gly synthase activity was not affected however active Gly phosphorylase was decreased. Hepatic G levels became equivalent to controls at 3,6,9 and 24 hrs. Gly content remained elevated at 3 and 6 hrs becoming equivalent to controls at 9 and 24 hrs. Gly content declined to 304±50 in controls and to 466±110 in IDMs by 24 hrs. At 3 hrs the cytoplasmic NAD/NADH ratio and at 3,6 and 9 hrs Py levels were elevated in IDMs. At 3,9 and 24 hrs, IDM FDP and ADP levels remained lower. Hepatic alanine and Asp levels were increased in IDMs by 6,9 and 24 hrs. These data suggests that maternal canine diabetes 1) ↑fetal substrate stores without attenuating neonatal glycogenolysis, and 2) during the fetal period inhibition of phosphofructokinase by ↑citrate and ↑AMP values and inhibition of pyruvate dehydrogenase by ↑citrate may explain the alterations of FDP and Py respectively at these times.*Deceased.

260 DISSOCIATION OF THYROID HORMONE STIMULATED RESPIRATION AND Na/K ATPase ACTIVITY IN BROWN ADIPOSE TISSUE (BAT) AND LIVER IN THE NEWBORN RABBIT. Alan H. Klein, Jennifer Jenkins, Anita Reviczky and Delbert A. Fisher, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance.

The effects of triiodothyronine (T3) on oxygen consumption (QO_2), Na/K ATPase activity and mitochondrial alpha glycerophosphate dehydrogenase (αGPD) activity in BAT and liver were studied in newborn rabbits. Each of seven 5 day old litters was divided in half, and the newborns injected with either T3 (20 μg/100 g BW /day, SC) or vehicle for 3 days. Basal QO_2 with and without ouabain was determined on isolated BAT cells or chopped liver. αGPD and Na/K ATPase were measured on tissue from individual animals. T3 stimulated BAT QO_2, mean (±SEM)=119±18 vs 65±4 μl $O_2/10^6$ cells ·hr in controls, p<0.005; there was no effect of ouabain in either group. BAT αGPD increased in response to T3 (1850±119 ΔOD x 10^3/mg protein·min vs 1266±121 in controls, p<0.005), but Na/K ATPase was unchanged. Hepatic QO_2 was similar in T3 treated and control animals; ouabain suppressed respiration by ∿30% in both groups. Hepatic αGPD showed no response to T3, while Na/K ATPase was significantly increased (0.307±.025 μMPi/mg protein·hr vs 0.202±.021 in controls, p<0.003). Conclusions: 1) BAT respiration and mitochondrial αGPD but not Na/K ATPase are thyroid sensitive in the newborn rabbit. 2) Hepatic Na/K-ATPase activity is responsive to T3 but αGPD and respiration are not. 3) T3 stimulation of respiration is dissociated from changes in Na/K ATPase activity in liver and BAT.

261 EFFECT OF INTRALIPID ON RESPIRATORY CALORIMETRY IN PRETERM INFANTS. Melinda S. Kwong, Katherine C. King, Satish C. Kalhan, Eeva-Liisa Miettinen, & Kou-Yi Tserng, Case Western Res. Univ. at Cleve. Metro. Gen. Hosp., Cleve. Ohio.

The purpose of this study was to determine, 1) whether intralipid (IL) infusion in preterm infants leads to decrease in transcutaneous oxygen tension ($TcPO_2$) and apnea, 2) whether change in $TcPO_2$ is due to decreased pulmonary diffusion or increased oxygen utilization. $TcPO_2$, oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), respiratory quotient (RQ), respiratory rate, serum triglyceride (TG) & free fatty acid (FFA) were serially measured in 5 preterm AGA infants (B.W. 980-2430 gm) before and during a 4 hr IL infusion with peripheral parenteral alimentation. Total caloric intake ranged from 80-110 Kcal/kg.d. Infants remained in room air at constant environmental temperatures throughout the study.

*(Mean±SD)	$\dot{V}O_2$ cc/kg·min	$\dot{V}CO_2$ cc/kg·min	RQ	$TcPO_2$ Torr	TG mg/dl	FFA μM/L
Pre IL	5.5±.5*	7.0±.5	1.25±.10	55±11	27±8	294±79
During IL	5.7±.7	6.7±.6	1.17±.05	50±14	171±7	2160±1384

No significant change in skin temperature occurred. Only one infant developed apnea during IL infusion with a simultaneous decrease in $TcPO_2$. One additional infant had a decrease in $TcPO_2$ during IL. A decrease in RQ occurred consistently in all 5 infants and 4/5 infants had an increase in $\dot{V}O_2$. Concl. 1) Apnea & change in $TcPO_2$ were not consistently observed during IL infusion, 2) RQ values greater than 1.0 suggest the anabolic state of the infants, 3) Preterm infants are capable of adapting to changes in the available nutrients for oxidative metabolism.

262 ARGININE VASOTOCIN INHIBITS OVINE FETAL/MATERNAL WATER TRANSFER. Rosemary D.Leake,Sue Palmer,Gary K.Oakes, Henry Artman, Ann Marie Morris and Delbert A. Fisher. Dept. of Peds. & Obstet.,Harbor-UCLA Med.Center, Torrance, Ca.

Arginine vasotocin (AVT) is found in the mammalian fetal pineal and was previously shown to decrease water flow across guinea pig placental membranes in vitro. To examine this effect in vivo we infused mannitol (Osmitrol 500 ml in a 20% solution) into 6 chronically catheterized ewes (129-144 days gestation). Fetal and maternal blood gases, pH, blood pressure (BP), heart rate (HR), hematocrit (Hct), and osmolality (Osm) were measured at eight 10 minute intervals before and after the mannitol. One day later an identical amount of mannitol was infused into the ewe during a 2hr infusion of AVT into the fetal circulation,with similar blood sampling. In 4 control ewes 500 ml normal saline (NS) was infused in place of the mannitol.

Maternal mannitol infused without fetal AVT evoked a greater rise in mean (±SEM) fetal osm (baseline 291 ± 2.1 mOsm/kg vs post mannitol 313 ± 6.1 mOsm/kg) than did maternal mannitol during fetal AVT infusion (289 ± 1 vs 297 ± 3.1 mOsm/kg; p<.05).During the AVT infusion fetal HR, pH and pO_2 remained unchanged; fetal pCO_2 increased from 30 ± 2 to 37 ± 4 (p<.05). Fetal BP increased from 64 ± 3 to 75 ± 2 mmHg (p<0.01). NS infusion produced no change in any parameter.

Thus: 1)AVT in the fetal circulation diminishes water transfer from fetus to mother in response to a maternal osmolar stimulus; 2)This effect may be mediated by decreased fetal/placental blood flow or by a direct AVT effect on placental water transfer.