175 THE EFFECTS OF INTRAUTERINE GROWTH RETARDATION (IUGR) ON FETAL LUNG CHOLINE KINASE ACTIVITY. Barbara L. Chrzanowska, Rodney E. Ulane, Laura L. Stephenson, Menachem Nitzan, Joseph D. Schulman, NICHD, Bethesda, MD 20014.

The effect of decreased uterine blood supply on one aspect of pulmonary phospholipid metabolism, the developmental pattern of choline kinase (CK), was studied in rats from 17 through 21 days gestation. Spraque-Dawley rats were operated on at the 17th day of pregnancy by ligation of the uterine artery of one horn as described by Wigglesworth (J. Path. Bact. 88:1, 1964) with the opposite horn left untouched (control). On days 18, 19, 20 and 21, fetuses were delivered by C-section and immediately decapitated. The frequency of IUGR fetuses (weighing less than 80% of mean control horn fetuses) in the ligated horn was approximately 50%. The lung wet weight to body weight ratios in the IUGR fetuses were consistently lower than the control litter mates at days 18, 19 and 20. The specific activities of CK were approximately 20% higher in the IUGR fetal lungs on days 20 and 21. No significant differences in CK specific activities were found between sham operated and non-operated controls and lungs from fetuses in the control horns. We conclude that decreased blood supply to the pregnant rat uterus results in a slightly increased activity per mg protein in the lung of the first enzyme of phosphatidylcholine biosynthesis. This increase was not observed in livers from the same fetuses. IUGR fetuses have been reported to show increased amounts of pulmonary phosphatidylcholine and accelerated pulmonary development. Our findings suggest that alterations in CK activity may be involved in this phenomenon.

176 FETAL SHEEP PLASMA INSULIN CONCENTRATION AND UMBILICAL LACTATE UPTAKE. Sharon S. Crandell, Frank H. Morriss, Eugene W. Adcock, Robert N. Marshall, and Cherylann Tuchman. (Spon. by R. R. Howell). Univ. of Texas Medical School at Houston, Dept. of Pediatrics, Houston.

To determine the relationship between fetal and maternal plasma insulin concentrations (I_f, I_m) and umbilical uptake of glucose (Q_g) and lactate (Q_l) in sheep, 6 ewes of 120-130 days gestation were prepared with indwelling catheters in the umbilical vein, fetal pedal artery and vein, and maternal uterine and femoral arteries. Fed state Q_g, Q_l, I_f, and I_m were determined at intervals from the 2nd to the 11th postoperative day (POD). Q_g and Q_l were determined by the Fick principle employing steady state diffusion of antipyrine to determine umbilical blood flow. Studies were performed before (control n=15) and after (n=15) the perfusion of the uterine artery with ovine insulin 7.5 mU/kg ewe/30 min. Insulin was measured by radioimmunoassay.

Results: Control I_f and I_m in μ U/ml increased with increasing POD as described by the following regression equations: $I_f = 0.76$ POD + 3.74, (F ratio, $p < .025$), and $I_m = 1.86$ POD + 8.61, ($p < .05$). Uterine artery insulin infusion increased I_m but did not affect I_f or Q_l. The postoperative increase in I_f from 5.5-16.0 μ U/ml was associated with a decrease in Q_l in mM/min/kg fetus: $Q_l = -0.004\ I_f + 0.072$ ($p < .025$). Q_g was unrelated to POD, Q_l, or I_f.

Conclusions: These studies (1) confirm the lack of ovine insulin transfer across the ovine placenta in vivo, (2) demonstrate increasing I_m and I_f for as long as 11 days after surgery and resumption of maternal nutrition, and (3) show that umbilical lactate uptake is inversely related to fetal plasma insulin concentration, but is independent of umbilical glucose uptake and of maternal plasma insulin concentration.

177 PARADOXICAL EFFECT OF PROTEIN-BINDING ON PLACENTAL TRANSFER OF STEROIDS. Joseph Dancis, Valerie Jansen, Mortimer Levitz. NYU School of Med. Dept. Ped. and Obstet. & Gynecol., New York City.

The relation of protein-binding to the transfer rates of a series of polar and non-polar steroids has been studied in an in vitro perfusion system of human placenta. The clearance indices (C.I. = clearance substrate:clearance antipyrine) for the polar steroids (dexamethasone, betamethasone, prednisolone, cortisol, estriol) from buffer solutions ranged from 0.36 to 0.74. The addition of serum albumin, lg/dl, to maternal and fetal perfusates had relatively little effect (C.I. 0.25 - 0.51). The C.I. of the non-polar steroids (ethynilestradiol, progesterone, estrone, diethylstilbesterol) from buffer solutions ranged from 0.11 to 0.26. The addition of lg/dl of serum albumin to the perfusates caused a sharp increase in C.I. (0.52 - 0.83).

Percent binding to serum albumin measured by equilibrium dialysis for the polar steroids were 35 to 60; for the non-polar steroids, 89 to 94. Binding to 20% placental homogenate were 12 to 31 and 60 to 96, respectively.

The transfer of lipid-soluble materials between maternal and fetal plasma is best understood as a series of equilibria in which binding to placenta plays a pivotal role.

178 VARIATIONS OF BLOOD OXYGEN AFFINITY AND CONTENT ON CARDIAC OUTPUT (C.O.) AND OXYGEN TRANSPORT TO THE TISSUES IN NEWBORN LAMBS. Maria Delivoria-Papadopoulos, Endla K. Anday, Evan Lipton, James D. Ferguson, Univ. of Pennsylvania. Philadelphia, Pa.

Four groups of two week old lambs were exchange transfused (E.T.) after chronic catheterization. Five lambs, Group I, served as controls; 4 lambs, Group II, received fresh, settled maternal blood; 4 lambs, Group III, received fresh, packed maternal blood and 6 lambs, Group IV, received fresh, packed fetal blood. Cardiac output (C.O.), arterial and venous PO_2, hematocrit (Hct) and P_{50} were measured before and two hours after E.T. No significant changes were noted in Group I for all parameters. Mean values for C.O. decreased in all groups following the E.T. (Gr. II by 57% ($p < 0.01$); Gr. III by 14% ($p < 0.05$); Gr. IV by 34% ($p < 0.025$). There were no changes in mean PaO_2 in any of the groups; however, mean P_vO_2 increased in Gr. II by 13% ($p < 0.05$), and decreased in Gr. IV by 7% ($p < 0.025$). Mean Hct increased in Gr. II, III and IV by 10%, 48% and 36% ($p < 0.0025$) and mean P_{50} increased in Gr. II and III by 59 and 43%. These data indicate that with no change in P_{50} but increased Hct the resulting decreased P_vO_2 is in response to a decreased C.O., theoretically compromising O_2 transport to the tissues. With an increased Hct, the decreased C.O. results in no change in P_vO_2 presumably counteracted by the increased P_{50}. In contrast, increased P_{50} and moderate increased Hct (10%) results in increased P_vO_2, presumably facilitating O_2 transport to the tissues, while maintaining a decreased C.O., thus reducing circulatory demands.

179 FETAL LAMB ARGININE VASOPRESSIN (AVP) RESPONSE TO A SINGLE HEMORRHAGE. W.H. Drummond, A.M. Rudolph, L.C. Keil, M.A. Heymann. Department of Pediatrics, University of California, San Francisco and NASA-Ames Research Center, Moffett Field, California.

Hemorrhage (H) has been reported to stimulate AVP release in the fetal lamb. To examine the determinants and time course of the fetal response to H, 7 chronically catheterized fetuses of 92-116 days gestation were hemorrhaged 15-20% of blood volume at a rate of 2%/min. Heart rate, arterial PO_2, PCO_2 and pH did not change. Serum AVP, osmolality and hematocrit were drawn at 10 min intervals for 60 min. Blood volume sampled was replaced immediately with fetal blood. AVP was measured by radioimmunoassay. Assay cross reactivity with arginine vasotocin and angiotensin II was negligible. During H, mean systemic arterial pressure (SAP) fell 24% from 40±1 to 30±2 torr ($p<.01$). Serum osmolality did not change H, but rose from 293±1.2 to 298±1.9 mOs ($p<.05$) by 30 min. Serum AVP levels showed a biphasic response. The base line AVP value of 1.6±.20 pg/ml rose to 27.9±14.9 ($p<.01$) by the end of H (10 min), then declined to 16.6±4.8 pg/ml at 20 min before rising again to 34.2±12.8 pg/ml by 30 min. Immediately after H, serum AVP correlated inversely with SAP change ($r=.58$), and not with serum osmolality ($r=.12$). By 30 min AVP correlation with SAP change was non-existent ($r=.05$) while a strong positive correlation between osmolality and serum AVP was found ($r=.87$). We conclude that the biphasic shape of the fetal AVP response curve to a single H represents a dual response, the first phase triggered mainly by falling SAP and the second phase by increased serum osmolality.

180 THE RELATIVE ROLE OF ANAEROBIC AND LOWERED METABOLISM IN NEONATAL ANOXIA TOLERANCE. Rolf R. Engel. Dept. of Pediatrics, University of Minnesota, Minneapolis.

The energy metabolism of newborn dogs subjected to anoxia was investigated by simultaneous direct and indirect calorimetry before, during and after anoxic episodes. In all 12 experiments the decrease in rectal temperature, heat loss, calculated heat production and post anoxic oxygen consumption provided incontrovertable evidence for a significant decrease in the rate of energy turnover during anoxia. With 9 or more minutes of anoxia at 29°C ambient temperature there was at least a 50% decrease in the rate of heat production. During longer anoxic intervals of 16 minutes at 20°C, heat production decreased to 80% of control values, and yet complete recovery occurred.

The concept of an anoxic oxygen debt was extended to encompass situations with changing rates of heat production by defining an oxygen debt in terms of the difference between direct and indirect calorimetry. The oxygen debt incurred (anoxic heat production ranged from 250 to 770 cal/kg) and the oxygen debt paid back (excess of indirect calorimetry over direct calorimetry) during the recovery period agreed within 12% ($r=0.7$). Identical studies on newborn kittens, rabbits and rats confirmed that in neonatal anoxia a progressive decrease in the metabolic rate of more than 70% is compatible with survival.