240 THYROTROPIN RELEASING HORMONE (TRH) AND OVINE FETAL LUNG (L) MATURATION. Allen Erenberg, U. of Iowa Coll. Med., Dept. Ped., Iowa City.

The role of TRH on ovine fetal L maturation was studied in 12 euthyroid fetuses (F). Beginning at 127 days, 6 F received 3 daily bolus IV injections (I) of 50 ug TRH and 6 control F received saline (S). All were sacrificed at 130 days. The mean body weight and weight of selected organs were similar. Initially, the mean serum thyroxine ($[T_4]$), triiodothyronine ($[T_3]$) and reverse T_3 ($[rT_3]$) levels were similar in both groups. In the S group, mean serum iodothyronine levels were similar throughout the study period. In the TRH group, mean ($\pm$ SEM) $[T_4]$ significantly increased from 12.4 $\pm$ 2.0 ug/dl to 20.9 $\pm$ 2.9 ug/dl ($p<0.01$) 8 hours (h) later returning to 12.8 $\pm$ 2.0 ug/dl at 24 h. Although there was no significant change in the mean $[T_3]$, the mean $[rT_3]$ increased from 345 $\pm$ 36 ng/dl to 568 $\pm$ 109 ng/dl ($p<0.05$) at 8 h, returning to 379 $\pm$ 56 ng/dl at 24 h. Similar changes were seen after the 2nd TRH I but no significant changes were seen following the 3rd I. There was no significant change in the mean serum cortisol level throughout the study period in any S F and 5 of 6 TRH F. The mean L tissue protein, DNA and whole L homogenate PAPase levels, protein/DNA and tracheal fluid L/S were similar in both groups. Histologically, the S group L showed areas of mature L and areas compatible with the canalicular stage of development. The TRH L was homogeneous in its mature state of development. Conclusions: TRH given directly to the euthyroid ovine F during the 3rd trimester 1) appears to affect the mesenchymal portion of the L and accelerates alveolarization; 2) increases serum $[T_4]$ and $[rT_3]$ but not $[T_3]$.

241 ADIPOSE TISSUE DEVELOPMENT IN OFFSPRING OF DIABETIC MOTHERS. Fredda Ginsberg-Fellner, Janet U. Gorkin, Jerome L. Knittle, Marcie S. Bregman and Gary J. Bergman, Mt. Sinai School of Medicine, Dept. of Pediatrics, New York.

Macrosomia and increased adiposity are well-recognized sequelae in newborn infants of diabetic mothers. However, the long-term consequences of such alterations remain controversial. In order to prospectively evaluate these factors, 23 infants of gestational diabetic mothers, IGDMs,(mean birthweight 3.6kg.), 8 infants of Class B and C insulin-dependent diabetic mothers, IDMS, (mean birthweight 3.2kg.) and 11 control infants (mean birthweight 3.1kg.) have been studied sequentially over the past 9-10 years. Increased numbers of adipose tissue cells were found in the IGDMs as early as age one (mean 6.2×10^9 total adipocytes) and have persisted to date with mean values of 19.8×10^9 adipocytes, 52% greater than normal, at age 6.8 years and 28.4×10^9 at age 9.4 years. Concomitantly, obesity (greater than 130% ideal body weight for height and age) was found in only 3 infants at age one but in 19 IGDMs by ages 6-9. In the IDM group at age one, no infants were obese, but by age 7, six had become obese having a mean of 18.6×10^9 total adipocytes. Adipose cell size was increased above 0.50 ug lipid/cell in both IGDMs and IDMs by age 6. Normal weight children were born only to mothers of normal weight prior to pregnancy. In vitro studies of adipocyte metabolism revealed blunting of epinephrine-stimulated lipolysis beginning as early as age one month and persisting to date in all obese children. The data indicate the importance of in utero factors in the development of childhood obesity.

242 EFFECT OF CAFFEINE ON THE MATURATION OF A TYPE II PNEUMOCYTE-LIKE CELL CULTURE LINE. Jacob N. Finkelstein, William M. Maniscalco, Donald L. Shapiro, Sandy H. Reuter and Christina M. Kramer. Univ. of Rochester School of Medicine, Strong Memorial Hospital, Dept. of Peds., Roch., NY

The A549 cell line is derived from a human lung adenocarcinoma and has retained many characteristics of the type II cell. Studies on the lipid composition of these cells as a function of time after culture (inoculum-$3x10^4$ cells/cm^2) show progressive changes in content and in ability to synthesize cell specific lipids. Phosphatidylglycerol (PG), a component of pulmonary surfactant, is absent early in culture but appears after 21 days in culture. By 28 days, this lipid accounts for 6.1% of total phospholipid. Choline incorporation into phosphatidylcholine (PC), decreases initially; at cell confluence it increases, going from 1.4 nmoles/hr/mg at day 14 to 2.5 nmole/hr/mg at day 21. Cell number, as measured by DNA content, remains constant. A549 cells grown in caffeine (10^{-4}M) grow at a slower rate than matched controls. Protein content in caffeine treated cultures is 25-33% lower throughout the culture period. Choline incorporation does not show the initial decline characteristic of untreated cultures, but remains high throughout the culture period. Morphologically, caffeine treated cells develop lamellar inclusions earlier. This is reflected in the lipid composition, as PG also appears significantly earlier. These results suggest that caffeine causes accelerated maturation of this type II pneumocyte-like cell culture line.

243 ONTOGENY OF SUGAR TRANSPORT IN DOG ISOLATED RENAL CORTEX TUBULES. John Foreman, Hanna Wald, Louise Pepe and Stanton Segal. The Children's Hosp. of Philadelphia, Dept. of Pediatrics, Philadelphia, Pa.

Functional immaturity of the proximal tubule as reflected in a decreased maximal tubular reabsorptive capacity for many substrates, such as glucose (TmG), has been demonstrated in infants when compared to older children and adults. But when these measurements are factored by GFR, values comparable to those found in adults are obtained suggesting that the lower TmG in infants is related to the diminished GFR. To explore the nature of sugar handling by the developing kidney independent of GFR,we examined the uptake of the model sugar, α-methylglucoside (αMG), by isolated renal cortical tubule fragments from dogs over the age range of 5 days to adulthood. In tubules from pups less than 1 week old,concentrative uptake of 2mM ^{14}C-αMG occurred by 1 min of incubation and reached a steady-state by 60 min with a distribution ratio of concentration (D.R.) of 8.4. With dogs 3 months old, the initial uptake was more rapid than the newborn pups reaching steady-state by 15 min, but the steady-state D.R. was lower(6.3). The kinetic parameters of initial uptake were for the 1 week old dog K_m=4.87,V_{max}=22.68mmoles/l intracellular fluid/5 min; the 3 month old K_m=8.05,V_{max}=54.17; and the adult K_m=7.42, Vmax=44.19. A sugar transport system is present in immature animals which resembles the adult system. With maturation there is a marked increase in the V_{max} but only a small change in the K_m. In the dog, the decreased TmG in immature animals appears to be related, in part, to a decreased number of carriers mediating sugar uptake into the renal tubule cell.

244 EFFECTS OF INCREASED UMBILICAL VENOUS (UV) OXYGENATION ON FETAL SHUNTS. Boyd W. Goetzman, Joseph Itskovitz, Abraham M. Rudolph. Univ. Calif., CVRI, San Francisco

We used the microsphere method to assess the effect of increasing UV blood O_2 on fetal cardiac output (CO) and vascular shunts by giving the ewe 100% inspired oxygen (MO_2). Two groups of fetal lambs with normal pH were studied; 5 had normal aortic PO_2 (20.4±2.4) and 5 were spontaneously hypoxemic (12.0±2.0). Although magnitude of shunts differed in the two groups, they changed in similar direction so the two groups were analyzed together. UV Hgb O_2 saturation increased from 61.6±20.7 to 85.5±15.8% ($p<0.005$) during MO_2. CO and umbilical blood flow (UBF) did not change from control values of 537±82 and 208±30 ml/min/kg. 59.7±6.6% of UV blood passed through the ductus venosus (DV); this did not change with MO_2. The percent DV blood crossing the foramen ovale to enter the upper body decreased from 38.5±8.7 to 23.5±5.5% ($p<0.001$) and the percent DV blood returning to the placenta without perfusing the fetal body increased from 32.1±5.8 to 37.9±8.0% ($p<0.05$). Lung blood flow as percent of CO increased from 4.9±3.6 to 13.8±6.4 ($p<0.005$) during MO_2. Thus, increasing UV O_2 modifies shunting of DV blood through the foramen ovale and to the placenta; this probably results from the decrease of pulmonary vascular resistance.

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245 MATERNAL ADMINISTRATION OF OXYGEN (MO_2) REVERSES CARDIOVASCULAR EFFECTS OF SPONTANEOUS FETAL HYPOXEMIA Boyd W. Goetzman, Joseph Itskovitz, Abraham Rudolph, Univ. California, Cardiovascular Research Institute, San Francisco

We measured cardiac output (CO) and its distribution using the microsphere method in 10 chronically catheterized fetal lambs (122-126 d), 5 of which were spontaneously hypoxemic (H) before and during MO_2. Mean (±SD) umbilical venous (UV) Hbg O_2 saturation was 45.3±13.8% in the H fetuses and 77.9±10.6% in the normoxic (N) fetuses ($p<0.005$) and following MO_2 increased to 76.9±17.7% and 94.2±7.9% ($p<0.005$) in the H and N fetuses, respectively. CO was 586±66 in the H and 488±70 ml/min/kg in the N fetuses ($p<0.06$) and was unchanged by MO_2. Placental blood flows were similar and not affected by MO_2. In the H as compared with the N fetuses, the % CO distributed to organs was greater for the brain, heart, and carcass ($p<0.005$, $p<0.05$, $p<0.05$), lower in the lungs ($p<0.005$), and not different in the gut and kidneys. In the H fetuses, O_2 delivery was increased to the heart($p<0.005$), decreased to the lungs ($p<0.005$) and kidneys ($p<0.05$), and similar in the brain, gut, and carcass. During MO_2, the % distribution of CO and the organ O_2 deliveries of the H fetuses achieved values that were not statistically different from the control values of the normally oxygenated fetuses. Except for increases in the lung blood flow and O_2 delivery, no significant changes were noted in the N fetuses during MO_2. This study shows that circulatory adaptations to spontaneous H differ from those previously described for acute H (Am J Obstet Gynecol 120:817, 1974) and that MO_2 reverses these changes.