271 INDUCED FETAL-MATERNAL WATER TRANSFER IS INDEPENDENT OF FETAL PROLACTIN LEVELS. Rosemary D. Leake, Michael G. Ross, Max G. Ervin, and Delbert A. Fisher, Depts. of Pediatrics & Obstetrics, UCLA School of Medicine, Harbor/UCLA Medical Center, Torrance, CA.

Prolactin (PRL) has been shown to inhibit water transfer in vitro when placed on the surface of the human fetal chorioamnion. We have shown previously that water flow from amniotic fluid (AF) to the maternal circulation (following maternal mannitol infusion to the ewe) is diminished when AF PRL levels are increased. To examine the effect of PRL on transplacental water flow, we infused mannitol (500 ml in a 20% solution) over 10 minutes into 5 chronically catheterized ewes (121-134 days' gestation). Fetal and maternal blood gases, pH and osmolality (OSM) were measured at -6, -3 and 0 minutes before and at 10 minute intervals for 1 hour after the mannitol. One day before or after, an identical amount of mannitol was infused into the same ewe during the second hour of a 2 hour infusion of PRL (40 ± 2.2 µg/hr) into the fetal circulation, with similar q 10 minute sampling. Maternal mannitol infused without PRL evoked a rise in mean (± SEM) fetal OSM (baseline 294 ± 2.4 mOsm/kg vs post-mannitol 307 ± 2.0 mOsm/kg) similar to that following maternal mannitol during fetal PRL infusion (298 ± 2.2 vs 309 ± 2.2 mOsm/kg). Fetal blood gases and pH did not change during the studies.

Thus, PRL appears to affect water permeability at the chorioamnion but not across the ovine placenta.

272 CHRONIC RESERPINATION OF SUCKLING RATS DOES NOT INTERFERE WITH THE DEVELOPMENTAL ACCUMULATION OF PANCREATIC ENZYMES. Ping C. Lee, Ki S. Chung, Emanuel Lebenthal. Pediatrics Department, Children's Hospital, SUNY at Buffalo, Buffalo, NY.

We tested whether chronic reserpine treatment disturbed the exocrine pancreatic development of suckling rats. Rat pups (4 days old) were given reserpine (R) (50 µg/kg i.p.) or vehicle (C) daily until sacrifice at 14 or 21 days of age. R pups showed significant decreases in body weights (wt). The decreases in pancreatic wt were proportionally less than the decrease in body wt as the pancreatic wt/100 g body wt were larger in R pups. At 14 days of age, pancreatic contents of amylase, trypsinogen, and lipase were not different between R and C pups, but the enzyme contents/100 g body wt in the R pups were higher. At 21 days of age (weaning), pancreatic contents of all 3 enzymes in the R pups were less than those of C pups but the characteristic pattern of enzyme accumulation was retained. Hydrocortisol treatment at 14 days of age precociously increased pancreatic enzymes in both R and C pups. A decrease in pancreatic secretion in the R pups was evident in vivo as they have intestinal contents of pancreatic enzymes lower than in the C pups. In vitro studies usinig dispersed pancreatic acini also showed a 50% reduction in the release of amylase in the R group as stimulated by carbachol and octapeptide of cholecystokinin. These results suggest that chronic reserpine treatment of suckling rats did not cause significant disturbance in the developmental accumulation of pancreatic exocrine enzymes other than a slight delay. A definite reduction in stimulated pancreatic secretion was demonstrated.

● **273** **HEPARIN INHIBITS THE PROLIFERATION OF DIVIDING AORTIC AND PULMONARY ARTERIAL SMOOTH MUSCLE CELLS IN VITRO** Daniel S. Lessler, William E. Benitz and Merton Bernfield Stanford University School of Medicine, Department of Pediatrics, Stanford, CA

The decrease in pulmonary artery smooth muscle mass which normally occurs after birth does not occur in persistent pulmonary hypertension of the newborn (Murphy et al, J Pediatr 98:962, 1981). Heparin inhibits the proliferative effect of serum on quiescent adult rat aortic (Ao) (Hoover et al, Circulation Res 51:280, 1982) and fetal calf pulmonary artery (PA) (Coulson et al, Pediatr Res 16:110A, 1982) smooth muscle cells (SMC) in vitro. However, SMC in the developing PA are not quiescent. Therefore, we studied the effect of heparin on exponentially growing fetal calf PA and Ao SMC. Heparin inhibits the proliferation of these PA and Ao SMC in a reversible and dose-dependent manner: final cell densities (8 days of culture) were 100%, 66%, 46%, and 24% of that of control cultures (no heparin) at added heparin concentrations of 1, 10, 100 and 1000 ug/ml, respectively ($p<0.005$). The dose-response curves for PA and Ao SMC were not different. PA SMC proliferation was also inhibited by dextran sulfate, but not by the physiologic glycosaminoglycans, dermatan sulfate, chondroitin-4- or -6-sulfate, or hyaluronic acid. We conclude that heparin inhibits proliferation of expanding, as well as quiescent, populations of fetal PA and Ao SMC. Therefore, heparin-like molecules, which are ubiquitous on cell surfaces, may be regulators of the changes in PA SMC mass which occur in the perinatal period. (Supported by NIH Grant HD06763 and a Cystic Fibrosis Foundation Medical Student Traineeship.)

274 **ONTOGENY OF PARIETAL CELL FUNCTION: RESPONSE TO PGE_2,** L.R. Marino, A.I. Vinik (sponsored by W.J. Byrne), University of Michigan, C.S. Mott Children's Hospital, Department of Pediatrics, Ann Arbor, Michigan

PGE_2 decreases H^+ production by the parietal cells of mature animals & humans. To study the ontogeny of this effect, the guinea pig mucosal model was used & dose response curves (DRC) to PGE_2 in 1, 3, 7, 10 & 14d old animals were established. $CoSO_4$ staining, as an index of OH^- production (HIP) & H^+ secretion, was used to quantitate cellular response. In 3d old animals PGE_2 was a potent inhibitor of HIP over a range of concentrations from 10^{-11}-10^{-6}M; Dmax 10^{-8}M. The DRC for 1d was shifted to the right of 3d. Dmax could not be calculated but at 10^{-6}m there was a 30% decrease in HIP. The DRC of the 14d animal was parallel to the 3d, Dmax-10^{-8}M, % decrease HIP, 15% vs 30% for the 3d. In the 7 & 10d old animals PGE_2 increased HIP; Dmax 10^{-9}M; % increase 30 & 20 respectively. HIP was suppressed in all age groups by PGE_2 (10^{-6}M); most effectively in 1d with 30% decrease in the others by 10%. In summary, the response of the parietal cell to PGE_2 is age dependent & the development of this response is biphasic. Ontogenically PGE_2 may play an important role in up and down regulation of acid secretion.

275 **THE ONTOGENY OF PARIETAL CELL RESPONSE TO ACID SECRETAGOGUES,** L.R. Marino, A.I. Vinik, (sponsored by W.J. Byrne), University of Michigan, C.S. Mott Children's Hospital, Department of Pediatrics, Ann Arbor, Michigan

In vivo acid secretion by immature animals is less than that of the mature. To evaluate the ontogeny of parietal cell responsiveness to secretagogues, a guinea pig gastric mucosal model was used. Dose response curves (DRC) to Gastrin (G), Histamine (H), & Carbachol (C) were established. $CoSO_4$ staining for OH^- production (HIP) & H^+ secretion was used to quantitate mucosal response. Animals 3, 7, 10d and mature (M) were studied. Responsiveness to H (3d) developed prior to C (7d) & G (10d). The DRC of H in 7d & 10d was shifted to the left of the M. The DRC of C was similar for 7d, 10d & M. G was the most potent secretagogue in M, but the DRC was nearly flat at 3 & 7d and blunted at 10d. The Dmax (molar dose) of each secretagogue is shown below. The # in ( ) is the ratio of immature to M, HIP.

	3d	7d	10d	M
H	10^{-14}(.93)	10^{-16}(1.1)	10^{-18}(1.2)	10^{-14}
C	10^{-7}(.81)	10^{-9}(1.0)	10^{-9}(1.0)	10^{-9}
G	10^{-10}(.72)	10^{-13}(.75)	10^{-13}(.91)	10^{-12}

In summary the parietal cell of the immature animal can increase H^+ secretion in response to secretagogues, however responsiveness to G, H, & C develops independently with age. Unlike the M animal, H not G is the most potent secretagogue & the development of H's response is biphasic.

276 INFLUENCE OF VENOUS PRESSURE (VP) ON CEREBRAL BLOOD FLOW (CBF) IN NEWBORN DOGS Andrew J. McPhee, Uma R. Kotagal, Leonard I. Kleinman, Department of Pediatrics, University of Cincinnati.

Marked increases in VP occur frequently in premature newborns with RDS. Since VP affects cerebral perfusion pressure (CPP) (CPP=Mean arterial pressure (MAP)-VP) it may alter CBF or its autoregulation. To examine this we studied CBF under conditions of normal and elevated VP in 7 anesthetized, paralyzed, ventilated newborn dogs, 4-12d. MAP and sagittal sinus pressure (an estimate of cerebral VP) were measured continuously. CBF, cerebellar-brainstem blood flow (CBrBF) and cardiac output (CO) were measured using microspheres; cerebral vascular resistance was calculated. VP was elevated by a snare-ligature placed about the intrathoracic SVC after ligation of the azygos vein. In each animal, 2 measurements were made with VP normal, and 2 with VP elevated and their order was randomized. PaO_2 was > 100 torr. Results as mean ± SEM; * $p < 0.01$, t-test.

Results	VP Normal n=13	VP Elevated n=14
VP mmHg	4.5 ± 0.2	15.6 ± 1.3*
CPP mmHg	41.0 ± 2.0	27.0 ± 1.6*
pCO_2 torr	43.0 ± 0.6	43.0 ± 0.7
CO ml/kg/min	141 ± 6	70 ± 4.6*
CBF ml/100gm/min	24.3 ± 0.9	26.1 ± 2.8
CBrBF ml/100gm/min	39.3 ± 1.7	42.9 ± 4.0
CVR mmHg/ml/100gm/min	1.66 ± 0.08	1.17 ± 0.11*

Thus with moderate elevation of VP, CBF and CBrBF remain independent of CPP, demonstrating autoregulation.