278 BREATHING RESPONSE TO HYPOXIA IN RELATION TO MEASURED PLASMA NEUROMODULATORS DURING POSTNATAL DEVELOPMENT. Immanuela R. Moss, Michael Runold, Ingrid Dahlin, Yuji Yamamoto, Bertil B. Fredholm, Fred Nyberg and Hugo Lagercrantz. University of Texas Health Science Center at Dallas, Department of Pediatrics, Dallas, Texas; Karolinska Institutet, Nobel Institute for Neurophysiology and Departments of Pediatrics and Pharmacology, Stockholm, Sweden; University of Uppsala, Department of Pharmacology, Uppsala, Sweden.

Breathing response to 12 and 6% O_2 in N_2 (in isocapnia) was measured in 1-5 and 19-25 day old acute, anesthetized piglets before and after 3 mg/kg i.v. naltrexone. The degree of interaction between the anesthetic and naltrexone was assessed. At the end of each hypoxic trial, arterial blood was sampled for measurements of pH and gas tensions, (Met)enkephalin-Arg^6-Phe^7, adenosine, noradrenaline and adrenaline. Results show that, as compared to older animals, young piglets (1) have greater degree of ventilatory depression in response to increasing severity of hypoxia; (2) have greater ventilatory responses with naltrexone than without the drug, and (3) demonstrate amelioration or reversal of the biphasic hypoxic response with naltrexone. Furthermore, enkephalin, adenosine, noradrenaline and adrenaline tend to increase during hypoxia in the younger animals. We conclude that, while the central role of catecholamines in respiration is uncertain at present, this study provides further evidence for the possible role of opioid peptides and adenosine in early postnatal hypoxic depression. (Supported in part by the Swedish Medical Research Council and by NIH grant HL36939 (IRM)).

●279 REDUCED TRANSFER OF CALCIUM ACROSS THE IN SITU PERFUSED PLACENTAE OF INTRAUTERINE GROWTH RETARDED (IUGR) RAT FETUSES. Zulf Mughal, Richardus Ross & Reginald C. Tsang. U. Cincinnati, Cincinnati, OH.

Neonatal rickets has been associated with IUGR secondary to conditions of reduced utero-placental blood flow during pregnancy, e.g., toxemia. There are no studies of calcium transport in IUGR. To test the hypothesis that chronic reduction in utero-placental blood flow impairs materno-fetal calcium transfer, placental calcium transfer was studied using an in situ placental perfusion technique (Mughal et al, 1986, J Physiol 377, 5 P) in rats where IUGR was induced by bilateral uterine artery ligation on day 17 of gestation, & in control animals. On day 20 of gestation (term=22 days), animals were anesthetised with intraperitoneal sodium thiobutabarbitol & fetal circulation of one of the placentas (Pl) was perfused via an umbilical artery cannula with Kreb's Ringer solution. ^{45}Ca & ^{51}Cr-EDTA (diffusional marker) were injected into the mother, & their steady state clearance (Cl) from maternal circulation to perfusate was calculated from samples collected from a cannula in the umbilical vein. (mean ± SEM)

	IUGR (n=6)	CONTROL (n=6)	P
Fetal weight (g)	2.3 ± 0.2	4.1 ± 0.2	<0.0001
Total fetal Ca (mg)	5.4 ± 0.4	8.5 ± 0.3	<0.0001
Total fetal Ca/F wt.($mg.g^{-1}$)	2.3 ± 0.1	2.1 ± 0.1	0.07
$Cl^{45}Ca$($\mu l.min.^{-1} mg\ Pl^{-1}$)	35.2 ± 2.0	93.1 ± 12.2	0.001
$Cl^{51}Cr$-EDTA($\mu l.min.^{-1} mg\ Pl^{-1}$)	5.6 ± 1.0	4.7 ± 0.5	0.45

Thus, the total fetal calcium is reduced in IUGR fetuses; the reduction was proportionate to body weight reduction. The steady state materno-perfusate transfer of calcium, but not the diffusional marker, is markedly reduced across placenta of growth retarded fetuses, presumably due to diminished active placental transfer of calcium.

▲280 EFFECTS OF MATERNAL DIABETES ON INSULIN RECEPTOR mRNA LEVELS IN FETAL RABBIT LIVER Naomi D. Neufeld, Ira D. Goldfine. University of California, Cedars-Sinai Medical Center and Mt. Zion Hospital Medical Center, Depts. of Pediatrics, Medicine and Physiology, Los Angeles and San Francisco, CA.

Maternal diabetes is associated with marked increases in insulin receptor (IR) numbers on fetal tissue plasma membranes. We examined the effects of alloxan-induced diabetes in pregnant New Zealand rabbits on IR mRNA levels in fetal rabbit liver at 31 d. gestation.

Group	Glucose mg/dl	R_0 ng/100 ug	IR mRNA O.D. Units	IR/actin ratio
Control	89+3	15.2	100%	5.4+0.4
Diabetic	340+5**	68.7	74%	5.1+0.5

*p <0.005, **p<0.001, vs controls

Total IR increased 4 fold in offspring of diabetics. Fetal rabbit liver Poly A+ RNA was subjected to gel electrophoresis, hydridization to a radiolabelled rat IR cDNA probe and autoradiographs analyzed by densitometry. Data were expressed as a percent of maximum intensity compared to a constitutive standard,(actin mRNA). Ratios of IR to actin mRNA were also calculated for each specimen from slot blot analyses. There was no change in IR m RNA levels in fetal liver from offspring of diabetic pregancies. CONCLUSIONS: Increases in IR number in fetal tissues of diabetic pregnancies is not due to an increase in receptor mRNA levels, but possibly may be explained by either post-transcriptional or translational changes, or by differences in membrane environment (i.e., fluidity) which alters receptor exposure.

●281 β-ADRENERGIC AGONISTS AND cAMP ANALOGUES MARKEDLY INCREASE THE LEVELS OF SURFACTANT APOPROTEIN AND ITS mRNA AND INDUCE DRAMATIC MORPHOLOGIC CHANGES IN HUMAN FETAL LUNG IN VITRO. Janelle Odom, Jeanne M. Snyder, Vijayakumar Boggaram and Carole R. Mendelson (Spon. by C.R. Rosenfeld), Cecil H & Ida Green Ctr Reprod Biol Sci, UTHSCD, Dallas, TX 75235.

The use of β-adrenergic agonists for treatment of preterm labor is associated with a decreased incidence of RDS in premature newborns. In the present study, antibodies and a cDNA probe specific for the major surfactant apoprotein were used to evaluate the effects of Bt_2cAMP and the β-agonist, terbutaline, on the levels of surfactant apoprotein and its mRNA in human fetal lung in organ culture, using Western and Northern blotting. A marked stimulatory effect of Bt_2cAMP on the levels of surfactant apoprotein and mRNA in the fetal lung tissue was observed within 48 h of its addition to the medium. Terbutaline caused a dose-dependent increase in surfactant apoprotein and mRNA to levels comparable to those observed after treatment with Bt_2cAMP. Using light and electron microscopy, we found that after 48 h incubation with Bt_2cAMP, a significantly greater proportion of the ductular epithelium of the fetal lung explants was comprised of type II cells; these ducts were enlarged greatly and the interalveolar connective tissue reduced as compared to control explants. Abundant secretory material (lamellar bodies and tubular myelin) was observed within the ducts of the Bt_2cAMP-treated tissue; little secretory material was observed in control tissues. Thus, catecholamines acting through β-adrenergic receptors and cAMP, may serve an important role in surfactant apoprotein gene expression and in morphologic development of the human fetal lung.

●282 HYPEROXIA CAUSES DISEQUILIBRIUM IN THE REGULATORS OF FIBRINOLYSIS IN THE LUNG. Lance Parton, David Warburton, C. Michael Bowman, Clarence Lloyd, Walter Laug; Dev. Lung Biol. Res. Ctr. Divs. Neonatology & Ped. Pulm. & Hem-Onc, Childrens Hospital of L.A., USC School of Medicine.

Fibrin deposition occurs in acute and chronic pulmonary injury: in the alveoli-with hyaline membrane disease (HMD); and in the interstitium-with chronic inflammatory conditions such as idiopathic pulmonary fibrosis (IPF). The mechanism underlying fibrin deposition in the lung is unknown, but may involve a disequilibrium of the protease-anti-protease balance in the fibrinolytic pathway. We have isolated and partially characterized a 50 kDA protein from multiple components of developing lungs-fetal bronchoalveolar lavage (BAL), fetal primary type II cells in culture and fetal lung fibroblasts (WI38, IMR90) in culture-which is a plasminogen activator inhibitor (PAI) as demonstrated by reverse fibrin autography (RFA). We have also isolated a 57 kDA protein from these same sources that is a plasminogen activator (PA). We investigated the PA/PAI balance during hyperoxia both in vivo-in BAL from newborn rabbit pups exposed to F_IO_2 85%; and in vitro-in serum-free conditioned media collected from fetal lung fibroblasts (WI-38) exposed to oxygen concentrations from 21 to 95%. BAL after hyperoxia demonstrates a predominance of PA with little PAI detectable. In contrast, fetal lung fibroblasts exposed to oxygen concentrations for 24, 48 or 72 hours produced primarily a PAI. We conclude that hyperoxia alters the balance of PA and PAI in the lung. We speculate that the predominance of PAI may favor fibrin deposition in the interstitital component.

283 CELLULAR AND IMMUNOGLOBULIN CONTENT OF NEONATAL MILK. William Pittard, Kitty Geddes, Samuel Pepkowitz and Randal Carr. Department of Pediatrics, Medical University of South Carolina, Charleston, South Carolina. The cellular and immunoglobulin content of neonatal breast secretions from 12 full term infants less than 10 days post delivery was studied. Precision pipettes were used to aspirate the mammary gland secretion directly from the neonates cleaned nipple/areola skin surface. Cleaning was performed with sterile cotton and water and air dried. For measurement of the immunoglobulin concentration, direct innoculation of the neonatal milk into radial Immunodiffusion plates, using the kallestad low level IgA, IgM, and IgG kit was performed. Cell viability was assessed using the trypan blue exclusion technique and the differential cell count was performed on a cytocentrifuged preparation following Wrights staining. Although cell viability was greater than 90 percent, fewer cells per ml of fluid were found in neonatal milk than are reported in mother's milk. The predomonant cell types observed were lymphocytes and macrophages. The immunoglobulin content was predominantly IgG with minimal concentration of IgA, and no IgM detected. These data suggest similar but different cellular and immunoglobulin regulatory mechanisms in neonatal breast secretions as compared to mothers' milk and indicate a need for further study to determine the clinical significance of these observations.