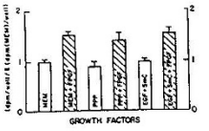
● 301 SOMATOMEDIN-C (SM-C) LEVELS IN FETAL SHEEP ARE INDEPENDENT OF SERUM PLACENTAL LACTOGEN LEVELS. D.H. Polk, R.W. Lam, J.P. Newnham, C.J. Hobel and D.A. Fisher, UCLA School of Medicine, Harbor-UCLA Medical Center, Dept. of Pediatrics, Torrance, CA and Cedars-Sinai Medical Center Los Angeles, Dept. of Pediatrics and Obstetrics, Los Angeles.

The factor(s) regulating fetal growth remain obscure and classic hormones appear not to be involved. Fetal size correlates with fetal SM-C levels; however, fetal growth hormone appears to have no effect either on fetal SM-C or fetal growth. Placental lactogen has been suggested as a modulator of fetal somatomedins. To assess this possibility in the sheep model, time-dated pregnant ewes with singleton fetuses (n=7) underwent fetal arterial catheterization at 111±3 d of gestation (term=150 d). Daily blood samples were obtained from each fetus until parturition or death. (Mean survival=20 d). Serum samples were assayed for both placental lactogen and SM-C. There was no correlation between placental lactogen and SM-C during the study period (r=.03, n=82). A second group of fetuses (n=5) underwent single umbilical artery ligation at 111±3 d of gestation. This procedure results in markedly elevated levels of placental lactogen in the fetus. Chronically catheterized animals were sampled daily and samples were assayed for both placental lactogen and SM-C. Despite the increased plasma placental lactogen levels in these single umbilical artery ligated fetuses, there was no demonstrable correlation between plasma placental lactogen and SM-C concentrations (r=.03, n=66). Conclusion: Somatomedin-C levels in fetal sheep are independent of serum placental lactogen levels during the third trimester.

● 302 Fetal Lung Cells: A Paracrine Competence Growth Factor Active on Type II Cells. M. Post, A.D. Stiles and B.T. Smith, Department of Pediatrics, Harvard Medical School, Boston, MA.

During the process of organogenesis lung mesenchyme affects the differentiation of the epithelium in an organ-specific fashion. In the present study we examined whether mesenchymal-epithelial interactions also play an important role in epithelial cell growth. We found that the mesenchyme elaborates a factor which stimulates the proliferation of fetal Type II cells. The production of the factor by the mesenchyme was organ-specific, age-dependent but inhibited by glucocorticosteroids. Incubation of quiescent Type II cells with competence (PDGF) and progression (EGF + SMC, platelet poor plasma) factors in the presence or absence of fibroblast derived mitogen revealed that fetal lung fibroblasts produce a competence growth factor (FPGF: Fibroblast



Pneumonocyte Growth Factor) which is capable of acting on adjacent epithelial Type II cells. These results indicate that cellular interactions within the lung influence its growth as well as its differentiation during fetal life.

This study supported by grants from the ALA and NIH-HL-33069.

303 A NEW METHOD FOR COMPUTER PROCESSING OF FETAL BREATHING ACTIVITY (FBA) BY EPOCH ANALYSIS. Henry R. Rey, Raymond I. Stark, Coll. of P&S, Columbia U., Depts. of Pediatr. & Ob. & Gyn., Presb. Med. Ctr., NYC.

Current analytic methods including time and frequency domain approaches are often inadequate to fully characterize FBA. Because of its episodic nature and changing character with gestation, FBA does not lend itself to rigorous statistical analysis. To overcome this problem, we have developed an analytic approach which assumes that the activity occurs quasi-randomly during most of gestation, identifies episodes of activity (breathing) and non-activity (apnea) and characterizes the data within these epochs in a straightforward manner.

Using a minicomputer, coded human ultrasonic or baboon tracheal fluid pressure data are digitized, pre-processed for removal of artefacts and breath detection. The distribution of detected breaths is used to identify epochs of FBA and to characterize each epoch with appropriate parameters, including duration, # of breaths, mean fetal breathing rate (FBR), FBR variability and mean breathing amplitude. Tabular and graphical outputs provide epoch by epoch results and summary statistics for a complete study.

This approach offers several advantages: 1) data dependence making no assumptions about periodicities or character of breath-activity, 2) focus on the activities of interest while filtering out inherent variability and 3) systematic data reduction and application of standard statistical techniques to multiple recordings from any number of subjects.

= 304 REGULATION OF SURFACTANT SECRETION FROM ISOLATED TYPE II CELLS BY LOW MOLECULAR WEIGHT POLYCATIONS. Ward R. Rice, Fannie M. Singleton (Spon. by J. Whitsett). University of Cincinnati Medical Center, Cincinnati, Ohio

Polycations are potent mediators of cellular secretion in a variety of cell systems through interaction with neuropeptide binding sites (e.g., substance P). We tested whether compound 48/80 or other polycations alter surfactant release from Type II cells. ^{3}H-Choline was used to label phosphatidylcholine pools and release of ^{3}H-phosphatidylcholine (^{3}H-PC) assessed in purified rat Type II cells. 48/80 and polymyxin B (PB) were potent inhibitors of terbutaline-stimulated and basal ^{3}H-PC release. IC_{50} was 1-2µg/ml for 48/80 and 5µg/ml for PB. Control release of ^{3}H-PC was 1.17±0.17% and decreased to -0.23±0.09% in the presence of 48/80 (10µg/ml) or to 0.40±0.09% in presence of PB (5µg/ml, $p<0.05$ for both agents). Control release of ^{3}H-PC from terbutaline-stimulated cells was 6.45±0.49% decreasing to 2.25±0.61% in the presence of 48/80 (10µg/ml, $p<0.001$). PB (5µg/ml), also inhibited terbutaline-stimulated ^{3}H-PC release (control=3.32±0.47% and PB=1.67±0.33%, $p<0.05$). Neither polycation was cytotoxic as judged by lactate dehydrogenase release. This inhibition was readily reversed by washing cells after exposure to either agent. Larger polycations, polyarginine, polyornithine and polylysine had no significant effect on ^{3}H-PC release at concentrations ≤5µg/ml and were cytotoxic at concentrations ≥5µg/ml. Inhibition of ^{3}H-PC release by 48/80 and PB appears to be site specific since polylysine, polyarginine and polyornithine did not alter ^{3}H-PC release. These data support existence of a counter-regulatory system mediating surfactant secretion from Type II cells, possibly mediated by neuropeptide binding sites. Supported by American Lung Association, NIH HL 28623 and HD 11725.

= 305 REGULATION OF SURFACTANT SECRETION FROM TYPE II CELLS: MECHANISM OF TUMOR PROMOTER ACTION. Ward R. Rice, Fannie M. Singleton, Deborah A. Lorow (Sponsored by J. Whitsett) University of Cincinnati Medical Center, Cincinnati, Ohio.

Tumor promoter 12-O-tetradecanoylphorbol 13-acetate (TPA) is a potent secretagogue for surfactant release from lung: its mechanism of action remains unknown. Since TPA activates a Ca^{2+}, phospholipid (PL) C-kinase in other cells we tested whether TPA alters surfactant release from isolated Type II cells in a Ca^{2+} dependent fashion and whether polymixin B, a known inhibitor of C-kinase, blocks effects of TPA. TPA caused a dose dependent release of ^{3}H-choline labelled phosphatidylcholine (^{3}H-PC) from purified rat Type II cells in primary culture:

[TPA, nM] mean ± SEM for 3 experiments ($p<0.001$)

	0	.01	.1	1	10	50	100
%^{3}H-PC Released	1.79± 0.44	1.39± 0.17	1.54± 0.28	3.03± 0.85	3.61± 0.60	6.24± 0.92	5.50± 0.76

TPA was not toxic as monitored by lactate dehydrogenase release. Since C-kinase is a Ca^{2+} PL dependent enzyme, effects of calcium ionophore A23187 and TPA together on surfactant release were studied. TPA-induced (100nM) ^{3}H-PC release was significantly potentiated by A23187 (10nM): Control 1.40±0.23%; A23187 1.61±.24%; TPA 3.30±0.40%; A23187+TPA 5.63±0.39% ($p<0.001$ for A23187+TPA vs. control; $p<0.05$ for TPA vs. control). Polymixin B, a known inhibitor of Ca^{2+}-PL kinase, partially blocked TPA-induced ^{3}H-PC release: Control 1.17±0.17%; polymixin B 0.40±0.08%; TPA 4.07±0.34%; TPA+polymixin B 2.43±0.29% ($p<0.05$ for TPA vs. control and TPA+polymixin B vs. polymixin B alone). These data provide support for C-kinase involvement in regulation of TPA-induced surfactant secretion. Supported by the American Lung Association, NIH-HL-28623 and HD-11725.

= 306 CEREBRAL BLOOD FLOW AND O_2 METABOLISM AFTER ASPHYXIA IN NEONATAL LAMBS. Adam A. Rosenberg (Spon. by John W. Sparks). University of Colorado School of Medicine, Department of Pediatrics, Denver.

A neonatal lamb model was developed to examine the regulation of cerebral blood flow (CBF) and metabolism during the critical period after an asphyxial insult. 7 newborn lambs were studied. Control measurements were made of blood gases, brachiocephalic artery (CaO_2) and sagittal sinus (CvO_2) O_2 contents, CBF (microsphere technique), cerebral O_2 consumption ($CMRO_2$), cerebral O_2 delivery (OD=CBF x CaO_2), and cerebral fractional O_2 extraction (CaO_2-CvO_2/CaO_2). After an episode of severe asphyxia, measurements were repeated at timed intervals. Immediately after asphyxia (5-20'), there was a marked increase in CBF compared to control [86 ± 9 $ml \cdot 100g^{-1} \cdot min^{-1}$ (±SEM) to 263 ± 45; $p<.01$]. OD increased from 13.6 ± 1.4 $ml \cdot 100g^{-1} \cdot min^{-1}$ to 37.7 ± 4.3 ($p<.001$) and $CMRO_2$ fell 5.67 ± 0.5 $ml \cdot 100g^{-1} \cdot min^{-1}$ to 4.15 ± 0.55 ($p<.01$). Cerebral fractional O_2 extraction, the relationship between oxygen uptake and delivery, fell from 0.42 ± 0.02 to 0.11 ± 0.01 ($p<.001$). This reactive hyperemia was followed in all animals by a period of hypoperfusion (30'-4 hr) in which CBF = 53 ± 5 ($p<.05$ from control), $CMRO_2$ = 3.55 ± 0.33 ($p<.001$ from control), OD = 7.84 ± 0.3 ($p<.005$ from control). By 24 hours (n=3), all parameters had returned to baseline. These data demonstrate an uncoupling of blood flow and oxygen metabolism immediately after asphyxia with a decrease in $CMRO_2$ despite a marked increase in OD. This is followed by a period in which both $CMRO_2$ and OD are depressed. These changes in CBF and cerebral O_2 metabolism may be important in the pathogenesis of asphyxial brain injury.