1688 NALOXONE ENHANCES RESPIRATORY OUTPUT IN PIGLETS THROUGH FOUR WEEKS OF AGE. Walker A. Long & Edward E. Lawson (Spon. by H.S. Harned), University of North Carolina, Department of Pediatrics, Chapel Hill.

Endorphins, endogenous neurotransmitters with opiate-like properties, are suspected to modify respiratory drive. Naloxone, a specific opiate antagonist, has been shown to enhance respiratory output (RO) in adult cats (Lawson, JAP 47:1105, 1979) and spontaneously breathing rabbits ≤4 days but not in rabbits ≥5 days (Hazinsky, Ped Res 14:643, 1980). To further investigate the central response to naloxone in young animals without confounding blood gas changes, 5 young piglets (<7 days) and 5 older piglets (≥21 days) were anesthetized, vagotomized, paralyzed and ventilated (FIO_2=1.0). End tidal CO_2 was kept constant by a servo-controller (mean end tidal CO_2=31.5mmHg). RO was quantified by moving average of the phrenic neurogram. Breath-by-breath frequency, neural tidal volume, inspiratory rate of rise, T_I and T_E were calculated by an on-line computer. A baseline period of RO was recorded following which naloxone (.4 mg/kg) was given intravenously. RO 5 minutes after naloxone was compared to baseline. In young piglets RO increased to 192±27% (±SEM) of baseline. RO of older piglets increased to 141±7% of the baseline value. In both young and older piglets the increase in RO was due to increased neural tidal volume (185±21% and 137±5% respectively) which resulted from enhanced inspiratory rate of rise (218±31% and 147±16% respectively). T_I was slightly shortened in 8/10 animals. T_E remained effectively unchanged. We conclude that 1) naloxone enhances the RO in both younger and older piglets; and 2) the increase in RO is due to increased central respiratory drive.

1689 REGULATION OF FATTY ACID SYNTHESIS IN DEVELOPING RAT LUNG. William M. Maniscalco and Jacob N. Finkelstein (Spon. by Donald L. Shapiro) Univ. of Roch. School of Medicine, Strong Memorial Hospital, Dept. of Peds., Rochester, NY

Fatty acids are integral components of both pulmonary surfactant and cell membranes. De novo fatty acid synthesis in adult tissues is regulated by the interplay of nutrition and hormones on the content of rate limiting enzymes, their state of phosphorylation and the concentration of allosteric effectors. To determine if de novo fatty acid synthesis in developing lung is regulated by similar factors, we measured the activity of the rate limiting enzyme acetyl-CoA carboxylase and its in vitro regulatory characteristics in fetal, newborn and adult rat lung. In fetal lung, acetyl-CoA carboxylase activity, measured in 100,000xg cell supernatant, increased from 1.01 nmoles/min/mg protein at 19 days gestation to 3.15 nmoles/min/mg protein by term (22 days). By one day after birth, activity fell to 30% of the peak fetal value. Activity remained low at 1, 2 and 3 weeks of age and in adult lung. In vitro activity of enzyme from fetal lung was greatly influenced by allosteric effectors: 2.0 mM citrate increased activity 5 fold while 25μM palmitoyl-CoA decreased activity by 75%. Pre-incubation in dephosphorylating conditions (10mM Mg++) resulted in a 50% increase in activity while phosphorylating conditions (2mM Mg++ - 4mM ATP) decreased activity 86%. These data demonstrate that acetyl-CoA carboxylase is very active in fetal lung, and the activity falls to low levels in the newborn period. In addition, in vitro regulation of the enzyme in fetal lung was qualitatively similar to that reported for adult liver, suggesting that fetal lung enzyme activity is modulated by similar mechanisms.

1690 EFFECTS OF EXOGENOUS PALMITATE ON DE NOVO FATTY ACID SYNTHESIS IN FETAL LUNG EXPLANTS. William M. Maniscalco and Anita R. Parkhurst (Spon. by Donald L. Shapiro) University of Rochester School of Medicine, Strong Memorial Hospital, Department of Pediatrics, Rochester, NY.

De novo fatty acid synthesis in fetal lung is probably an important source of the long chain fatty acid constituents of pulmonary surfactant and membrane phospholipids. In some tissues, de novo fatty acid synthesis is regulated, in part, by the availability of exogenous fatty acids. Utilizing fetal rat lung explants, we measured de novo fatty acid synthesis by determining the rate of ^3H_2O incorporation in saponifiable lipids. During a 48 hr. incubation in synthetic medium, ^3H_2O incorporation in explants from 19 day fetal rat lung increased from 15.1 nmoles/mg protein/hr to 34.2 nmoles/mg protein/hr. Incorporation into glycerides increased from 5.81 nmoles/mg protein/hr to 8.58 nmoles/mg protein/hr. ^{14}C-glucose incorporation into fatty acids also increased 2 fold during this time. Addition of 2.5mM palmitic acid to the incubation medium for 24 hrs. resulted in a 45% decrease in ^3H_2O and ^{14}C-glucose incorporation into fatty acids. There was, however, a 2.5 fold increase in ^3H_2O incorporation into glycerides. After 48 hrs. of culture in palmitate, ^3H_2O incorporation into fatty acids was not different from the control explants, while incorporation into glycerides by the explants cultured in palmitate continued to be 2.5 fold greater than controls. These data suggest that de novo fatty acid synthesis in fetal lung explants is regulated in the short term by the availability of exogenous fatty acid. In addition, exogenous fatty acid results in an increase in the incorporation at ^3H_2O into the glyceride moiety.

1691 APNEA FROM LARYNGEAL CHEMOREFLEX (LCR) STIMULATION DURING SLEEP IN THE NEWBORN LAMB. Francois Marchal, Barry C. Corke, Hakan Sundell. Vanderbilt University, Dpt of Pediatrics and Anesthesiology, Nashville, TN.

In order to evaluate the effects of different activity states (AS): wakefulness (W), Rapid Eye Movement (REM), and Quiet Sleep (QS), on the recovery from LCR induced apnea, we studied 4 premature newborn lambs chronically instrumented with tracheostomy, EEG and EOG leads for 1 to 5 weeks. During each AS, the LCR was stimulated with water for 5 s. The response was evaluated as the % decrease in ventilation from the baseline period for 30 s after the onset of stimulation (ΔV). ΔV was greater during REM (85.9±17.8)+and QS (82.4±17.3) than during W (55.9±21.5)*, but there was no difference between REM and QS. Following arousal, which occured in 1/4 of the tests during sleep, the response was markedly reduced (ΔV=53.7±28.6). However, one lamb needed frequent resuscitation after stimulation during either REM or QS. Respiratory drive for each AS was evaluated during the baseline period by measuring mean inspiratory flow (Tidal Volume/Inspiratory Time: Vt/Ti), assuming no variations in lung resistance among different AS. Vt/Ti was lower during either QS (55.7±19.7) or REM (50.4±14.5) as compared to W (70.5±33.5)*.

During both REM and QS, if arousal does not occur, the newborn lamb is more vulnerable to LCR stimulation induced apnea which can be fatal. A more sustained apnea during sleep may be related to a decreased respiratory drive and/or a decreased sensitivity to hypoxemia. It is postulated that, although the importance of such reflex apnea in the human infant is unknown, the impaired recovery observed during sleep may reproduce the sequence of events occuring in SIDS.

* $p<0.05$ + values are Mean ± SD.

1692 IDENTIFICATION OF A MAJOR HEPARIN-BINDING SERUM PROTEIN AND ITS RELATIONSHIP TO CYSTIC FIBROSIS (CF). Rita T. Margolies, Bruce Gray, and Thomas F. Boat, Case Western Reserve University, Rainbow Babies and Childrens Hospital, Department of Pediatrics, Cleveland, Ohio.

Heparin binding to serum proteins and their subsequent precipitation is increased in CF (Pearson and Lubin, Ped. Res., 13, 834 (1978). To investigate the molecular basis for this effect, sera from CF patients and age-matched controls were precipitated with 50 mg% heparin at pH 5.57. Resolubilized pellets were fractionated on DEAE-Sephadex and analyzed by double immunodiffusion, SDS-PAGE, immunoelectrophoresis, and radial immunodiffusion. Most of the protein eluted as IgG. The table presents our data concerning amounts of IgG and precipitated protein per ml serum.

	Age	n	Protein ppt. mg (+ S.D.)		IgG, mg (+ S.D.)	
CF	>12	19	20.52 ± 4.82		13.46 ± 4.25	
N	>12	19	12.27 ± 3.28	$p<0.001$	10.56 ± 2.94	$p<0.05$
CF	<12	8	9.20 ± 3.03		8.13 ± 3.66	
N	<12	8	11.02 ± 0.02	NS	7.66 ± 2.04	NS

When serum from all sources was fractionated by StaphA-Sepharose into IgG and non-IgG fractions, 85-88% of heparin precipitable material was in the IgG fraction. We propose that increased levels of precipitable proteins are related to elevated concentrations of serum IgG. This conclusion is supported by our finding that the normal levels of IgG in the serum of young CF patients result in normal amounts of precipitate. Our data do not support the hypothesis of Pearson and Lubin that a generalized defect in serum protein glycosylation is the basis of the heparin effect.

1693 LABOR STIMULATES SURFACTANT SECRETION IN NEWBORN RABBIT LUNG SLICES. Pamela A. Marino and Seamus A. Rooney. Yale Univ., Dept. of Pediatrics, New Haven, CT.

We previously reported that labor increased the amount of surfactant phospholipid in newborn rabbit lung lavage but it was unclear if the effect was on synthesis or secretion. We have now examined the effect of labor on secretion in a slice model. Newborn rabbits are injected i.p. with ^3H-choline and killed 4 h later. Slices from the blood-free lungs are incubated in buffer for 2.5 h. Initially the lipids secreted are similar to those of lung tissue but after 3 changes of buffer the lipids secreted are very similar to those of lung lavage. We measure the rate of secretion of ^3H-phosphatidylcholine (PC) during this period. At 31 days gestation the rate of secretion increased from 198±18 cpm/h/mg tissue protein in 16 litters delivered before labor to 281±21 in 31 litters delivered after oxytocin-induced labor ($P<0.02$). Spontaneous labor was also stimulatory while oxytocin without labor was not. We attempted to mimic and abolish the effect of labor on PC secretion by incubating the slices with various agents. $10^{-5}M$ prostaglandin E_2 and $10^{-4}M$ terbutaline stimulated secretion in slices from animals delivered prior to labor by 20% and 33%, respectively. Pilocarpine had no effect. $2x10^{-4}M$ indomethacin and $10^{-4}M$ propranolol inhibited secretion in slices from animals delivered after labor by 49% and 42%, respectively. Atropine had no effect. These data show that labor stimulates surfactant secretion and thus may be an important factor in the prevention of RDS. The effect of labor may be mediated, at least in part, by prostaglandins and catecholamines both of which increase during labor and birth. (Supported by HD-11018).