1195 STUDIES OF OXYGEN-INDUCED LUNG TOXICITY IN ANIMALS TREATED WITH PLASMANATE ®. Lee Frank, John Yam, and Robert J. Roberts, The University of Iowa, Depts. of Pediatrics and Pharmacology, Iowa City, Iowa.

Superoxide dismutase (SOD) is an enzyme thought to provide protection against superoxide anion, believed to be a prime agent of O_2 pulmonary toxicity. We have previously shown that whereas immature animals can respond to hyperoxia with an increase in lung SOD activity, adults seem incapable of this protective enzyme response (J. Peds., in press). Also, all neonatal rats (1-7 days old) survived a 3 day exposure to 96-98% O_2, but only 26% (21/80) of adult rats survived and all had evidence of marked lung edema. Treatment of adult rats with daily i.p. injections of a plasma protein fraction (Plasmanate ®) resulted in an increase in lung SOD activity (51 ± 6%) and, concomitantly, in 93% survival (39/42) after 3 days of O_2 exposure. There was no gross evidence of pulmonary edema in 37 of the 39 survivors. Subsequent to these studies, the Plasmanate ® used was found to be contaminated with bacteria (S. epidermidis and Pseudomonas species). Experiments using Millipore filtrates of this contaminated Plasmanate ® and contaminated Plasmanate ® with added gentamycin to kill the bacteria both afforded 100% survival to treated animals, while injections of the isolated living organisms in saline (18% survival) or of noncontaminated Plasmanate ® (29%) afforded no protective effect compared to untreated adult rats (26%). The mechanism(s) responsible for this markedly increased tolerance of treated animals to O_2-induced lung injury are being investigated. (Supported by GM 12675 and NIH 1F32 HL05415).

1196 ESSENTIAL FATTY ACIDS (EFA), PROSTAGLANDINS (PGS) AND HYALINE MEMBRANE DISEASE (HMD). Zvi Friedman, Lawrence Demers (Spon. by Nicholas M. Nelson). Penn State Univ Coll Med, M S Hershey Med Ctr, Dept Ped and Path, Hershey, Pa.

PGE and F exert physiological effect on the smooth muscle of blood vessels and the tracheobronchial tree; PGE dilates and F constricts. The lungs are a major site for synthesis, release and degradation of PGS. Altered PGS functions may thus contribute to the pathophysiology of HMD. 8 infants with HMD and 6 controls were studied by analyzing their plasma for PGS by radioimmunoassay, and precursor EFA by TLC and GLC. Gestational age and birth weight of sick infants were similar to controls; 31.4± 4.1 vs 33.0±3.2 weeks and 1738±708 vs 1830±204 gms, respectively. Dihomo-γ-linoleic and arachidonic acids were similar in both groups. The following PGS results (mean±SD) were obtained (pg/ml).

	PGE	PGF	PGE:F RATIO
Controls	120±15.6	79.2±17.9	1.52
Peak HMD (2-3 days)	225±105	301.7±127	0.75
Recovery from HMD	237±56	155±64	1.53
2 patients with patent ductus arteriosus (PDA)	369±99	126±18	2.92

The study demonstrated: (1) plasma PGE and F are elevated in HMD as compared with controls and the ratio PGE:F is decreased; (2) upon recovery from HMD, PGE and F are elevated as compared with controls but PGE:F ratio is increased and similar to controls; (3) increased PGE level and high PGE:F ratio may contribute to the PDA.

1197 STATIC COMPLIANCE IN INFANTS WITH HMD. EFFECTS OF DIFFERENT LEVELS OF PEEP. Tilo Gerhardt, Eduardo Bancalari, University of Miami, School of Medicine, Department of Pediatrics, Miami, Florida

The measurement of lung compliance is useful in establishing the optimal PEEP in the treatment of adult RDS. This study was conducted to assess the value of this determination in infants with HMD. Six newborns (B.W. 1340 gm, Gest. age 31 weeks) who required mechanical ventilation because of severe HMD were studied. Airway pressure, tidal volume and esophageal pressure were recorded at different levels of PEEP and peak pressure (PIP) while the infant's respiration was controlled using a prolonged inspiration, so that tidal volume and airway pressure reached a plateau. The values of static compliance (ml/cm H_2O) were:

PIP (cmH_2O)		35	30	25	20	15	10	5
PEEP	0	0.50	0.56	0.62	0.72	0.80	0.78	0.68
(cmH_2O)	+5	0.43	0.47	0.52	0.56	0.60	0.63	0.68
	+10		0.35	0.38	0.40	0.42	0.44	0.48

Lung compliance decreased as PEEP or PIP were increased, suggesting that no significant alveolar recruitment occurred. The pressure/volume curve did not show a linear part, but became progressively flatter as the PIP increased. The use of PEEP moved the tidal volume into this flatter part of the curve. The only exception to this was the decrease in C_L seen at 0 PEEP and PIP of 10 cm H_2O or less, indicating alveolar collapse. In conclusion, increasing PEEP produces a progressive decrease in C_L and therefore this measurement is of no value in determining the optimal PEEP in infants with HMD.

1198 THE FETAL LUNG PROFILE: BEYOND THE L/S RATIO. Louis Gluck, Marie V. Kulovich and Mikko Hallman. Univ. of Calif., San Diego, Dept. of Pediatrics, La Jolla.

Progressive expiratory atelectasis of RDS is attributed to deficient surfactant phospholipids. Fetal lung biosynthesis of the principal ones, lecithin (phosphatidyl choline, PC) the most abundant, and phosphatidyl inositol (PI) and phosphatidyl glycerol (PG), the acidic phospholipids, are determined developmentally during gestation. They appear in amniotic fluid and are used to monitor maturity of fetal lung and optimal time for delivery by means of a LUNG PROFILE, utilizing 2-dimensional thin layer chromatography of the extracted amniotic fluid lipids, comparing on a gestational scale L/S ratio, % disaturated PC, % PI and % PG with level of maturity. The lecithin/sphingomyelin (L/S) ratio relates concentrations of PC to sphingomyelin acting as an "Internal standard". With lung maturation PC increases and there is increasing disaturation of its fatty acid esters, measured as acetone precipitable fraction of PC. PI and PG are essential to the stability of PC; PI increases parallel to PC to 35-36 weeks, then declines. At 36-37 weeks, PG appears and increases; by term and in mature surfactant it is the 2d most abundant surfactant phospholipid. RDS is never seen once PG is present. On recovery from RDS increasing PI is seen; PG may not appear until near 36 gest wks. In infants with retained lung fluid, PG is not present in amniotic fluid but appears after birth in tracheal secretions as symptoms disappear. The lung profile greatly enhances both accuracy of prediction and understanding of lung development and eliminates non-diagnostic intermediate values.

1199 HISTAMINE RECEPTORS IN THE NEWBORN'S PULMONARY CIRCULATION. B. Goetzman and J. Milstein, Department of Pediatrics, University of California, Davis, Sacramento Medical Center (sponsored by R. Wennberg).

Histamine causes pulmonary vasoconstriction, mediated by histamine H_1-receptors, in adult animals, including sheep. In contrast, histamine is a pulmonary vasodilator in fetal sheep. However, there is little information on the transition from the fetal to adult response and the involvement of histamine H_1 and H_2-receptors. We have investigated pulmonary vascular histamine receptor antagonists, diphenhydramine and metiamide, respectively. Lambs were anesthetized with chloralose and instrumented for measurement of pulmonary blood flow and aortic, pulmonary arterial, and left atrial blood pressures. In 10 normoxemic animals, histamine (1μg/kg) transiently decreased mean pulmonary vascular resistance by 49 ± 28%. H_1-receptor blockade with diphenhydramine did not alter this response. H_2- receptor blockade with metiamide had a variable and incomplete attenuation of this response. In a 9 day old lamb, histamine (1μg/kg) increased pulmonary vascular resistance by 100% (adult type response) and after H_1-blockade, decreased the resistance by 72% (newborn type response). We conclude that in the pulmonary circulation of newborn lambs, 1) histamine H_1-receptor activity is absent, and 2) the action of histamine is probably due to stimulation of H_2 or previously undescribed H_3-receptors. The rapid transition to the adult response appears to be due to development of H_1-receptor activity.

1200 AMINOPHYLLINE STIMULATES PHOSPHOLIPID SYNTHESIS BY FETAL RAT LUNG IN ORGAN CULTURE. Ian Gross and Seamus A. Rooney (Spon. by J.B. Warshaw), Yale Univ. School of Medicine,Dept. Pediatrics, New Haven, Conn.

The administration of aminophylline to fetal rabbits has been shown to stimulate lung phospholipid synthesis. We have examined the influence of aminophylline on phosphatidylcholine (PC) and sphingomyelin (SPH) synthesis in fetal rat lung in organ culture. Control cultures were grown in F12 medium without added serum.As indicated below, exposure to 1.0 mM aminophylline for 48 hours resulted in a significant increase in the incorporation of choline into both PC and SPH in explants of 19 day lung. Activity is expressed as pmoles incorporated/mg protein/hour.

	Control	Aminophylline	Aminoph/Control	p
PC	1813	3257	1.88	<0.01
SPH	58.2	106.1	1.95	<0.001

Less stimulation was observed when explants from 20 or 21 day fetuses were used (term is 22 days). Exposure to 0.2mM dibutyryl cyclic AMP also resulted in an increase in both PC and SPH synthesis suggesting that the aminophylline effect was mediated by cyclic AMP.There was no change in the degree of saturation of the PC synthesized. The activities of choline kinase (1125 pmole/mg/min) and cholinephosphotransferase (1319 pmole/mg/min) were not significantly changed by aminophylline. Since exposure to aminophylline results in increased synthesis of both PC and SPH, it appears that aminophylline induces a nonspecific stimulation of phospholipid synthesis in fetal rat lung. Supported by USPHS grant no. HL 19752.