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VENTILATION INDUCED RELEASE OF PULMONARY SURFACTANT IN IMMATURE FETAL GOATS. Edmund A. Egan, Robert M. Nelson, Bruce MacIntyre, Depts. of Peds., Children's Hospital, SUNYAB, Buffalo, NY & Univ. of Fla., Gainesville.

Eighteen immature fetal goats were exteriorized by hysterotomy with the placental circulation intact. The trachea was canulated and 5ml of fetal lung liquid removed. No pulmonary surfactant was detectable in lung liquid or amniotic fluid in any animal by the bubble stability test (BST). Animals were ventilated with O_2 for 1 hour at a tidal volume of 9 ml/kg (range 6-11), a rate of 20/min, an end expiratory pressure of 0. At 1 hour carotid blood gases were sampled, residual lung fluid was sampled, the animals sacrificed and static pressure volume measured in situ with the thorax open. Results are grouped by BST results on residual lung liquid at 1 hour of age.

BST @ 1 hr	N	Gest.Age(d.)	FRC/TLC(x100)	PaO_2	$PaCO_2$
0	4	117(115-120)	0	18(15-23)	84(67-107)
1:1-1:4	7	125(120-130)	7 (0-14)%	81(32-192)	51(28-65)
1:4	7	134(130-140)	19 (10-33)%	206(74-267)	30(21-40)

All values are mean (range). All means different p .05.

Pulmonary surfactant, undetectable in lung fluid before ventilation, was released in all but the most immature animals. Efficiency of ventilation, oxygenation, and development of FRC were related to the amount of surfactant present. Ventilation dependent release of surfactant would explain the initial compensation of immature infants who develop progressive respiratory failure after a few hours.

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VENTILATOR MANAGEMENT AND PNEUMOTHORAX IN NEONATES WITH RDS. Stephen C. Engelke, Robert T. Stein, Joanne Nicks, Marcia Sosnowski, Lee Walder, and Dietrich W. Roloff, Univ. of Michigan Sch. of Med., Dept. of Ped., Ann Arbor, Michigan (Spon. by William F. Howatt).

An apparent doubling of the incidence of pneumothorax in premature neonates mechanically ventilated for RDS prompted a comparison of ventilator therapy in these patients, past and present. In 1973-75, 16 of 86 infants treated for RDS developed pneumothorax/pneumomediastinum/pneumopericardium (PN) after intermittent mandatory ventilation using a Baby Bird respirator, while in 1976-77 the frequency of PN increased to 28 of 54 patients ventilated ($p < 0.03$). Record review demonstrated no differences in birth weight, severity of disease, age at intubation, interval from intubation to PN or mortality. Ventilator settings immediately prior to clinical evidence of PN showed similar peak pressures, PEEP, and FiO_2. However, there were significant differences ($p < 0.01$) in ventilator rates and flow rates:

	Vent Rate/min			Flow Rate (L/min)	
	≤ 20	> 20		≤ 8	> 8
1973-75	7	8	1973-75	7	8
1976-77	25	3	1976-77	25	3

Between these periods a change in ventilator policy to using longer inspiratory times occurred. The association between lower flow and ventilatory rates and a higher incidence of PN suggests that either variable alone or in combination with longer inspiratory times may increase the risk for alveolar rupture and development of pneumothorax.

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PULMONARY SUPEROXIDE DISMUTASE (PSOD) ACTIVITY IN THE EUTHYROID (E) AND ATHYROTIC (Tx) OVINE FETUS. Allen Erenberg, Lee Frank, Robert J. Roberts and Mitchell L. Rhodes, U. of Iowa Coll. Med., Dept. Ped., Iowa City and U. of Indiana Coll. Med., Dept. Int. Med., Indianapolis, In.

Animal studies have shown that the development of pulmonary oxygen toxicity is enhanced in the hyperthyroid and delayed in the hypothyroid state. PSOD activity was studied in 5 E at 130 and 5 E at 140 days (d) gestation and compared to 5 Tx at 130 and 5 Tx at 140 d gestation. All Tx were surgically thyroidectomized at 95 to 99 d gestation. Values = Mean ± SEM

	Heart&Lung (L) wt. (gm)	DNA (mg/gm L)	Protein DNA	SOD (units/gm L)	SOD DNA
A. 140 d E	200±14	7.4±0.3	8.1±0.3	217±22	28.8±4.0
B. 140 d Tx	130±23	9.2±0.5	6.7±0.2	325±24	36.8±5.1
C. 130 d E	143±18	8.0±0.7	8.7±0.4	365±29	46.7±4.2
D. 130 d Tx	102±07	9.9±0.6	7.6±0.4	287±35	29.2±3.5
A vs C	<0.025	NS	NS	<0.005	<0.01
B vs D	NS	NS	NS	NS	NS
A vs B	<0.025	<0.01	<0.005	<0.005	NS
C vs D	<0.05	<0.05	<0.05	NS	<0.005

Although the Tx lung contained an increase number of smaller sized cells compared to E, there was no change in cell number or size within the Tx or E groups from 130 to 140 d. The PSOD activity per cell was decreased in E from 130 to 140 d, but tended to increase in Tx. Thus, in E, PSOD activity per cell decreases with increasing gestational age. Hypothyroidism in the ovine fetus during the last trimester retards fetal lung growth and alters PSOD activity.

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ECHOCARDIOGRAPHIC EVALUATION OF RIGHT VENTRICULAR FUNCTION IN PATIENTS WITH CYSTIC FIBROSIS

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Non-invasive evaluation of right ventricular (RV) function has been difficult in patients with cystic fibrosis (CF). Echographic recording of the pulmonary valve permits measurement of the phases of RV systole, and the ratio of the RV pre-ejection period to the RV ejection time (RPEP/RVET) correlates well with pulmonary artery pressure. RPEP/RVET and other echographic measurements including RV wall (RVW) and dimension (RVD) were compared with pulmonary function tests and clinical scores in 28 CF patients ranging in age from 4-35 years. RPEP/RVET correlated well with percent vital capacity (%VCA) r=-0.74, residual volume (%RVol) r=0.72, and clinical score r=-0.77. RVW and RVD correlated poorly ($r<0.50$) with %VCA, %RVol, and clinical score. Multilinear regression of RPEP/RVET and RVD improved correlations significantly for %RVol (r=0.82 and clinical score (r=0.84). Patients in right heart failure (RHF) exhibit significantly higher RPEP/RVET (mean 0.43) than those without RHF (mean=0.33) indicating higher pulmonary artery pressure or diminished RV contractility in patients with RHF. The use of digoxin did not significantly change this value. At the conclusion of the study satisfactory pulmonary valve echograms could be obtained in 2/3 of patients tested and success was independent of the severity of the pulmonary disease.

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OXYGEN TOXICITY IN NEONATAL AND ADULT ANIMALS OF VARIOUS SPECIES. Lee Frank, John R. Bucher, Robert J. Roberts. Univ. of Iowa School of Medicine, Departments of Pediatrics & Pharmacology, Iowa City, IA. 52242.

Immature animals have been considered to be more resistant to O_2 lung toxicity than adults. A biochemical explanation for exceptions to this generalization was the basis for this study. Neonatal and adult animals of 5 species were exposed to 95+% O_2 for 24 hrs and their lungs analyzed for changes in antioxidant enzyme activity (superoxide dismutase(SOD), catalase(CAT), glutathione peroxidase(GP)). Animals were also continuously exposed to 95+% O_2 to determine survival times. The results follow:

SPECIES	ADULT:SURVIVAL,ENZYME△		NEONATE:SURVIVAL,ENZYME△	
Guinea pig	4-5 days	(NC)	4-5 days	(NC)
Hamster	5-6 days	(NC)	5 days	(NC)
Rat	3 days	(NC)	»7 days	(↑SOD,CAT,GP)
Mouse	5 days	(NC)	»7 days	(↑SOD,GP)
Rabbit	4-5 days	(NC)	»7 days	(↑SOD,CAT,GP)

(NC=no change;↑=significantly increased vs. air control,$p<.05$)

Neonatal rats,mice, and rabbits exhibit relative tolerance to O_2 lung toxicity(based on survival and lung histology) compared to the respective adults. These neonates also demonstrate rapid increases in lung antioxidant enzymes, whereas the O_2-susceptible adults lack this protective response. No lung enzyme response to O_2 challenge and equal susceptibility to hyperoxia was observed in neonatal and adult guinea pigs and hamsters. The findings support a lung biochemical basis for the resistance of neonatal animals of certain species to O_2 lung injury. (NIH #GM 12675).

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BACTERIAL ENDOTOXIN PROTECTION FROM PULMONARY OXYGEN TOXICITY. Lee Frank and Robert J. Roberts. Univ. of Iowa College of Medicine, Departments of Pediatrics and Pharmacology, Iowa City, IA. 52242.

We have discovered that treatment with small doses of bacterial lipopolysaccharide (endotoxin)(approx. 1/100th LD_{50}) affords marked protection against O_2-induced lung damage and lethality in adult rats exposed to hyperoxia. Whereas the untreated adult rat normally succumbs to 95+% O_2 exposure after 72 hours(66/201=30% survival) with survivors showing evidence of severe lung injury(pulmonary edema and/or hemorrhage), rats treated with daily i.p. doses of endotoxin exhibit tolerance to O_2 lethality(265/274=97% survival) and lung damage (approx. 85% without evidence of pulmonary edema or hemorrhage). In addition to investigating possible mechanisms to explain the marked protective action of endotoxin treatment (↑lung antioxidant enzyme activity, $p<.05$; ↓number of potentially detrimental alveolar macrophages, $p<.05$), preliminary attempts have been made to determine if endotoxin will offer similar protection from O_2 toxicity in other species and other age animals. To date, endotoxin treatment appears to be protective only in the adult rat and rabbit(75% vs. 0% survival in 95+% O_2). Initial experiments have been done in neonatal guinea pigs(55% vs. 13% survival, but only 18% free of lung pathology); neonatal hamsters(21% vs. 17% survival); and, adult mice(57% vs. 50% survival). Whether there is a true species(and/or age) specificity for endotoxin protection, or whether ideal dosage schedules in the other species have not yet been determined, remains to be resolved. (NIH# 1F 32 HL05415, GM 12675).