1828 EFFECTS OF CYCLOOXYGENASE INHIBITORS ON LUNG MICROVASCULAR INJURY FOLLOWING PULMONARY INTRAVASCULAR COAGULATION (PIC). Marc Perlman, Jeffrey Cooper, and Asrar Malik (spon. Bernard Pollara). Albany Medical College, Depts. of Pediatrics and Physiology, Albany, N.Y.

We compared the effects of cyclooxygenase inhibitors, meclofenamate (MEC) and ibuprofen (IBU) on the development of lung microvascular injury after PIC induced by i.v. thrombin (T) infusion (80 U/kg). Studies were made in awake (n=10) sheep with lung lymph fistulas. The animals were pretreated with either MEC or IBU. Lung lymph flow (Q_{lym}) lymph-to-plasma protein concentration ratio (L/P), and transvascular protein clearance (L/P x Q_{lym}) were determined. MEC and IBU prevented the increases in the cyclooxygenase end-products, thromboxane B₂ and 6-keto-PGF_{1α} after T. T resulted in 6-fold increases in Q_{lym} and protein clearance, indicating lung microvascular injury. MEC attenuated the initial rises in Q_{lym} and protein clearance after T, while IBU prevented both initial and steady-state responses. IBU but not MEC reduced the increases in pulmonary arterial pressure and PVR after T. In another group (n=11), lung PMN uptake after T was determined by infusing homologous 111-Indium oxine labeled PMN and measuring lung activity with a gamma camera. PMN uptake increased by 11% over baseline after T in controls, compared to 4.1% in MEC group and none in IBU group. **Conclusion:** IBU has a greater protective effect in preventing thrombin-induced lung vascular injury than MEC. The protective effect is independent of inhibition of cyclooxygenase but may be related to inhibition of neutrophil margination. (HL-17355 and HL-26551)

1829 POOR VENTILATORY RESPONSE TO CO₂ IN INFANTS WITH BRONCHOPULMONARY DYSPLASIA (BPD). T.F. Yeh, H. Patel, R. Jain, A. Mora, R.S. Pildes. Cook County Hospital, Univ. of Ill., Dept. of Pediatrics, Chicago, Ill.

Vent. response to CO₂ was studied in 4 infants with BPD (Gr.I) (mean±S.D. B.W. 2070±501 gms; G.A. 31.6±2.3 wks), 3 infants shortly recovered from BPD (Gr.II) (normal blood gases and X-ray) (B.W. 1920±550 gms; G.A. 30.6±2 wks) and 4 normal control (Gr. III) (1901±20 gms; G.A. 31.5±2.2 wks). To avoid hypoxia, all infants were given 70% O₂ during the study. Tidal volume (V_T), R.R., dynamic compliance (C_D), minutes ventilation (V_{min}), T_CPCO₂ were all measured while the infant was breathing 0.03%, 1%, 2%, 3% and 3.5% CO₂ for 2 min. There was no sign. difference in RR, C_D, V_T, P_{O2}, PCO₂ between Gr.II and Gr.III prior to study (RR: 59±12 vs 57±8; C_D 2.9±0.4 vs 3.7±0.8 ml/cmH₂O/Kg; V_T 8.7±1.1 vs 9.5±1.9 ml/Kg; P_{O2} 38±4 vs 42±3 mmHg; PCO₂ 44±3 vs 40±2 mmHg) but infants in Gr.I had higher RR (74±15) and PCO₂ (58±7 mmHg) and lower C_D (1.7±0.6) and V_T (6.5±1.8) as compared to Gr.II and III. (p<.05). Compared with base line values within the group, infants in Gr. III had sign. increase in V_T and V_{min} following breathing 2%, 3%, 3.5% CO₂; this was not seen in Gr.I and Gr.II. The RR and C_D remained unchanged in all groups during study. This study suggests that infants with BPD have less vent. response to CO₂ as compared to normal infants.

1830 ARE SURFACTANT PHOSPHOLIPID SYNTHESIS AND SECRETION LINKED IN THE FETAL TYPE II CELL? Martin Post, Arpy Barsoumian and Barry T. Smith, Harvard Medical School Department of Pediatrics, Boston.

Fetal type II cells synthesize and secrete surfactant associated saturated phosphatidylcholine (PC). In order to determine if synthesis and secretion are independently regulated processes, fetal rat type II cells were prelabelled for 20 hr with [³H]choline. A second incubation of up to 6 hr with [¹⁴C]choline in the presence or absence of centrophenoxine (an inhibitor of PC synthesis) or colchicine (an inhibitor of secretion) was carried out. Under baseline conditions, synthesis was directly linked with secretion as indicated by a constant ratio of ³H/¹⁴C in saturated PC released into the medium. Centrophenoxine (250 μM) completely inhibited synthesis (¹⁴C-saturated PC formation) but had no effect on secretion (release of ³H-saturated PC). In contrast, colchicine (10 μM) inhibited secretion by 35%, but had no effect on synthesis. These results suggest that, while under baseline conditions surfactant phospholipid synthesis and secretion are quantitatively linked, the two processes can be dissociated under specific conditions.

This approach will allow study of the putative dissociation of surfactant synthesis and secretion prior to birth.

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1831 FIBROBLAST-PNEUMOCYTE FACTOR PURIFIED WITH THE AID OF MONOCLONAL ANTIBODIES STIMULATES CHOLINEPHOSPHATE CYTIDYLTRANSFERASE ACTIVITY IN FETAL TYPE II CELLS Martin Post and Barry T. Smith, Harvard Medical School, Department of Pediatrics, Boston.

Fibroblast-pneumocyte factor (FPF) was purified from corticosteroid-treated fetal lung fibroblast conditioned medium by gel filtration and affinity chromatography. Based on bioactivity (choline incorporation into saturated phosphatidylcholine (SPC) by fetal type II cells), a 3,000-fold purification was obtained. Maximal stimulation by FPF was observed after 60 min of incubation. This finding suggests that the effect of FPF on SPC formation by fetal type II cells is not due to new protein synthesis but rather to an activation of enzymes involved in SPC production. A pulse-chase study on the metabolism of choline in fetal type II cells revealed that the presence of FPF in the chase medium increased the rate of disappearance of label from choline-phosphate and the rate of appearance in phosphatidylcholine. The radioactivity in CDPcholine was not significantly affected. This result indicates that FPF stimulates the activity of choline-phosphate cytidyltransferase, the rate-controlling enzyme in the formation of phosphatidylcholine by fetal type II cells.

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1832 PULMONARY TOXICITY OF MONOCROTALINE DIFFERS IN NEONATAL, YOUNG AND ADULT RATS Livia Todd, Michelle Mullen, Peter Olley, Marlene Rabinovitch University of Toronto The Hospital for Sick Children Dept. of Cardiology, Toronto, Ontario.

We hypothesized that the toxic effect of a single monocrotaline (M) injection (60mg/kg) would result in pulmonary vascular abnormalities of different severity in neonatal-3day(N), infant-8day(I) and adult-8 week(A) rats and might affect lung growth. Mixed Sprague-Dawley litters and A rats were used; ½ injected with M, and ½ with saline-controls(C). Two and 4 weeks after injection, rats were killed, right and left ventricles (RV, LV) weighed and lungs injected and fixed inflated for lung volumes (Vol), and morphometric analysis of alveoli/mm², arteries per 100 alveoli (A:100a), medial wall thickness of muscular arteries (%WT) and extension of muscle into peripheral arteries (%Ext). NM rats died 2-3 wks post injection. Pulmonary vascular changes and lung Vol. were similar to IM rats but alveolar multiplication was impaired (alv/mm²=129±24 vs 198±29 in NC, p<0.05). IM rats had normal lung growth, vascular changes at 2 wks similar to AM rats but at 4 wks 'adapted' ie. medial hypertrophy did not occur, and %Ext and RV:LV were less.

Group	wgt/g	RV:LV	A:100a	%WT	%Ext
NM/C-2wk	24/33**	.309/.257	3/5**	6.0/3.6	40/12**
IM/C-2wk	39/56*	.435/.330	3/3	8.5/7.2	65/17**
AM/C-2wk	297/328**	.279/.295	3/5*	5.9/4.6*	94/0**
IM/C-4wk	109/136*	.434/.292*	4/5**	4.3/4.2	74/37*
AM/C-4wk	335/351*	.453/.270**	4/6**	8.6/4.8**	96/3**

Mean values given; p<0.05* p<0.01**

Thus young lungs may respond to toxic agents more adversely during early critical periods of growth, more adaptively later.

1833 ALTERATION OF THEOPHYLLINE PHARMACOKINETICS DUE TO R.S.V. INFECTION. M. Rao, M. Ames, M. Mitchell and P. Steiner. (Spon. by L. Finberg). Downstate Medical Center, SUNY, Dept. of Peds, Brooklyn, NY.

Kraemer et al. (1982) reported on the altered theophylline clearance in 11 children during an Influenza B outbreak. In 5 children with R.S.V. infection we studied the theophylline pharmacokinetics (same dosage) during the acute illness and later at 5 weeks. None had cardiac or hepatic problems.

	Acute illness		4-5 wks post-illness	
	Serum level (mg/ml)	t _{1/2} (hrs)	Serum level (mg/ml)	t _{1/2} (hrs)
1. S.C. 11 mos.* Bronchiolitis	25.2	30.2	14	10.8
2. S.R. 16 wks Bronchiolitis	17.8	20.0	10	11
3. B.L. 20 mos.* Bronchiolitis	28.5	19.0	17	8.7
4. R.A. 3 yrs.* Ac. asthma	40.0	23.5	16	9
5. D.L. 3 mos. Bronchiolitis	20.5	19	9	10

*Developed toxic symptoms

As the above table shows, all our patients had considerably higher serum theophylline levels and significant protraction of clearance during the acute illness. We conclude that the data highlight the importance of adjusting the dose and the monitoring of serum levels of theophylline in children with severe R.S.V. infection.