†1765 THE EFFECTS OF INDOMETHACIN ON THE HYPOXIC VASOPRESSOR RESPONSE IN ISOLATED LUNGS OF NEWBORN LAMBS.

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Previous studies suggest that pulmonary prostaglandin metabolism and action change during the newborn period. Indomethacin, a cyclo-oxygenase inhibitor, increases pulmonary artery pressure (Ppa) in perinatal animals. However, indomethacin has no effect on hypoxic and normoxic Ppa in the isolated perfused lungs of 2-3 month old lambs. This study examined the effects of indomethacin on the steady state pulmonary vascular response to graded hypoxia in isolated perfused lungs of 2-4 day old lambs. Lungs were randomly exposed to 3 levels of hypoxia and returned to an inspired 0_2 tension (PiO_2) of 200 torr after each hypoxic stimulus. The mean Ppa +/- SE (torr) at flow = 50 ml/kg.min for control (C) and indomethacin (I) groups were:

PiO_2 (torr)	200	50	30	0
C (n=5)	12.7+/-1.4	15.5+/-2.6	22.1+/-3.0	11.4+/-0.6
I (n=6)	17.0+/-2.3	27.5+/-3.3	26.8+/-2.7	13.8+/-2.1

In both groups hypoxia (50 and 30) caused an increase in Ppa and vasodilation occurred at 0. Indomethacin enhanced the pressor response ($P<.05$). Moreover we noted that, in the C group after a first hypoxic exposure, subsequent hypoxic responses were blunted in comparison with the I group ($p<.05$). These results suggest that, in isolated lungs of 2-4 day old lambs, an initial hypoxic pressor response caused the release of a dilator prostaglandin which attenuated subsequent responses.

†1766 EFFECTS OF 17β ESTRADIOL ON THE PULMONARY CIRCULATION.

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Prior studies have shown that 1) mature ewes have an attenuated hypoxic pulmonary vasoconstrictor response (HPVR), 2) 17β estradiol (E_2) administered 2-4 days prior to study of juvenile ewes reduces their HPVR to adult ewe levels, 3) E_2 enhances prostaglandin production by systemic vessels. This study examined the effects of indomethacin (I) on the steady state pulmonary vascular response to graded hypoxia in isolated perfused lungs of 3 groups of juvenile ewes - controls (C and CI), E_2 treated 36-60 hours before study (E_2S, E_2SI) and E_2 treated 72-110 hours before study (E_2L, E_2LI). Mean pulmonary artery pressure (Ppa) at flow = 50 ml/kg.min for 3 levels of inspired 0_2 (PiO_2) for each group (n) were: (* = less than C, $p<.05$).

PiO_2	C(6)	CI(5)	ES(6)	ESI(6)	EL(7)	ELI(5)
200	17.4	15.8	14.8	15.4	17.0	11.0*
30	28.8	30.2	24.3	29.5	19.8*	22.9*
0	12.0	12.5	11.7	13.0	9.6*	8.3*

In all groups the peak response is seen at 30 torr. There was a time dependent attenuation of the HPVR caused by E_2. While indomethacin had no effect on the HPVR in any group, it did return responsivity (Δ in Ppa 200-30) in E_2L to C values ($p<.05$). These results suggest that although E_2 may increase pulmonary prostaglandin synthesis, there is also an apparent time-dependent reduction in vascular resistance caused by non-prostaglandin dependent mechanisms.

●1767 INCREASED NASAL POTENTIAL DIFFERENCE AND AMILORIDE SENSITIVITY IN NEONATES WITH CYSTIC FIBROSIS.

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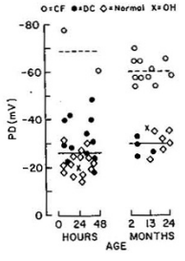
Cystic fibrosis (CF) patients have an increased nasal transepithelial potential difference (PD) which reflects an increased Na^+ absorption across a relatively Cl^- impermeable membrane. To evaluate respiratory epithelial function in CF neonates, the maximal PD and the voltage response to superfusion of 10^{-5}M amiloride (Am), an inhibitor of Na^+ transport, were recorded between a Ringer perfused bridge on the nasal mucosa and a reference electrode in the subcutaneous space. We studied two term CF neonates presenting with meconium ileus (MI) and compared the results to 15 term healthy neonates including 1 obligate heterozygote (OH) for CF, and 12 term disease control (DC) neonates including 2 with ileal atresia, 2 with meconium aspiration, 1 with pneumonia, and 7 with Transient Tachypnea of the Newborn. Both neonates with MI had raised sweat Cl values (x̄ = 110meq/l) at 2 mo. The CF neonates had higher PDs than normal or disease controls (fig). Superfusion with Am induced a 72% reduction in PD in the CF neonates as compared to healthy (40.0±3.7%) and disease (41.0±2.6%) neonates. Also the neonatal PDs are comparable to values in older infants (2-24mo) where a similar PD pattern is present (fig). Moreover, the PD and Am response in CF neonates are similar to older (>6yr) CF children and adults (-64.9±9.3mV; 77.7±1.8%, n=51). These results suggest that: (1) nasal epithelial dysfunction is present in CF patients shortly after birth, and (2) the nasal PD may be a diagnostic adjunct to the sweat test in the early diagnosis of CF.



1768 THE EFFECT OF INHALED DRUGS UPON CILIA MOTILITY.

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Cilia are essential for the proper maintenance of the respiratory tract. Inhaled drugs are frequently used in the treatment of respiratory disorders and have been shown not to alter ciliary structure. Their effect on ciliary motility has not been adequately studied. In the present study, the effect of various inhaled drugs on the duration of cilia motility was examined using specimens of rabbit trachea. All specimens were studied at room temperature via light microscopy with control samples analyzed concurrently. One drop of the specified drug was placed on the trachea and the duration of ciliary beat was monitored. The following results were obtained:

DRUG	N	pH	Cessation Time(min) mean	range
Nasalcrom	57	6.87	20.8	3-60
Nasalide	45	5.88	4.2	0.02-15
Afrin 0.05%	12	7.21	33.0	17-90
Alupent 5%	12	3.41	19.1	5.2-44.4
Mucomyst 10%	12	6.49	1.4	0.65-2.0
Mucomyst 20%	12	6.70	0.04	0.02-0.07
Neosynephrine 0.25%	12	6.58	20.2	8-35
Ocean	13	8.71	22.3	13.7-35
Amiloride 10^{-4}M	4	7.00	314.0	247-342
Amil + Mucomyst 10% (1:1)	4	--	0.03	0.02-0.05
Amil + Mucomyst 20% (1:1)	4	--	0.03	0.02-0.08
Control (Hanks B.S.S.)	-	7.00	120.0	90-150

All drug effects were reversible with washings of normal saline. The wide ranges of cessation time were thought to be due to tissue variation or to mucus on the tissue specimen causing decreased drug penetration. Mucomyst most rapidly effected the cilia. Nasalcrom increased the initial gross frequency of motility to greater than that of matched controls; however, early cessation was still evident. Correlations will be made with electron micrographic findings and in vivo functional studies. These effects should be kept in mind when prescribing inhaled drugs for patients.

1769 THE EFFECT OF FUROSEMIDE ON COMPLIANCE (CDYN) IN ACUTE AND CHRONIC PULMONARY FAILURE.

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Furosemide was effective in improving Cdyn in a group of preterm infants suffering from respiratory distress syndrome (RDS) during the first week of life, but had no effect on another group with bronchopulmonary dysplasia (BPD) studied at a later age. Eight infants (BW 1530+/-500g, GA 32+/-2wks) with RDS were studies at 2+/-1 day of age, and eight (BW 840+/-390g, GA 29+/-3 wks) with BPD at 35+/-25 days. Cdyn and PO2 were measured immediately prior to the intravenous infusion of furosemide 1mg/kg and again 20 minutes post infusion. Eight infants (BW 1570+/-520g, GA 32+/-2wks) served as RDS controls, evaluated on day 3+/-2 without furosemide. The results are noted below:

	Cdyn(ml/cm H2O) Pre	Post	PO2(mmHg) Pre	Post
RDS	0.7+/-0.4	0.9+/-0.4	51+/-4	78+/-29
Cont.	0.9+/-0.3	0.9+/-0.3	57+/-14	60+/-19
BPD	0.7+/-0.4	0.6+/-0.4	74+/-32	69+/-35

The rise in Cdyn in the RDS group was significantly greater than the responses in both control and BPD infants. In this group of infants furosemide was effective in improving compliance in infants with respiratory failure in the early course of RDS but was ineffective in the later complication of BPD.

†1770 PULMONARY ENDOTHELIAL PERMEABILITY IN ASTHMA.

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The hypothesis that pulmonary endothelial permeability (PEP) is increased in asthma was tested in a guinea pig model. Animals were sensitized to ovalbumin by subcutaneous injection two weeks prior to testing (asthmatic group). Normal animals did not receive the sensitizing ovalbumin. A third group of animals was desensitized by repeated exposure to nebulized ovalbumin, with epinephrine rescue, over a 4-6 week period (desensitized group). Pulmonary function was assessed by plethysmography in each group during a control period and after challenge with nebulized ovalbumin. PEP was assessed by the rate of appearance of the albumin tag, Evan's blue, in the lung, and systemic endothelial permeability (SEP) by the rate of decline of serum concentrations of Evan's blue. All groups had comparable pulmonary function during the control period. Ovalbumin inhalation produced a decrease in dynamic lung compliance and an increase in airway resistance only in the asthmatic group. PEP was increased in the asthmatic animals, while SEP was comparable in all groups. Pulmonary edema occurred in both the asthmatic and desensitized groups.

Group (N)	compliance % control	resistance % control	lung weight % normal	PEP ug/g/30min
Normal (7)	124±36	103±61	100±9	18.2±7.4
Asthmatic (7)	39±26*	293±103*	131±16#	31.6±10.2#
Desensitized (7)	89±60	155±103	136±9#	14.2±3.4

Values=means±SD *P<.01 vs control period; #P<.05 vs normal group

Pulmonary dysfunction in asthma is accompanied by increased PEP. Pulmonary edema, alone, does not explain these changes.