† 1831 VASCULAR-PULMONARY DYSPLASIA (VPD) ASSOCIATED WITH NEONATAL RAT HYPEROXIA. Stanley G. Shaffer, Donald W. Thibeault, Diane H. O'Neill, Frederick K. Hall, Sandra K. Bowen. University of Missouri at Kansas City School of Medicine, Children's Mercy Hospital, Kansas City, Missouri.

The chronic sequelae of neonatal hyperoxia was studied in male rats exposed to 100% O_2 for the first 8 days of life. Dams were rotated between 41 oxygen treated (O_2) rats and 29 room air controls. Following O_2, rats had standard care until 60 days of age. Survival rate was 97%. Body weights at 60 days were similar. In vivo right ventricular pressure was measured percutaneously under anesthesia and was increased in the O_2 group (30.5 ± 4.3 vs 22.7 ± 3.3 mm Hg p <.0005). Hearts and lungs were excised at 63 days. Organ weights were similar between groups, however, right to left ventricular weight ratios were increased in the O_2 group (.316 ± .028 vs .259 ± .022 p <.0005). Air pressure-volume curves were similar but in the O_2 rats fluid deflation curves were shifted left and maximum fluid lung volumes were greater (14.05 ± 1.25 vs 12.03 ± .71 ml p <.0006). Pulmonary arteries were perfused at 100 cm H_2O with a barium-gel mixture and lungs fixed at 25 cm H_2O with formalin. Morphometric studies showed that the O_2 rats had an increased volume proportion of parenchyma (.865 ± .014 vs .820 ± 2.8 p <.05), increased mean linear intercept (111.5 μ ± 17.6 vs 75.3 μ ± 4.7 p <.005), decreased alveoli and ducts per mm^2 (78.4 ± 5.2 vs 127.9 ± 8.4 p <.0005) and fewer small arteries (20-200 μ) per mm^2 (2.9 ± .41 vs. 4.3 ± .57 p <.0005). The number of small arteries/100 alveoli were similar. We conclude that neonatal hyperoxia is associated with VPD as indicated by a decrease in the number of arteries, cor pulmonale and emphysematous changes in the air spaces.

1832 THE EFFECTS OF INHALATIONAL ANESTHETICS AND QUINACRINE ON ARACHIDONIC ACID-INDUCED PULMONARY VASOCONSTRICTION Jay R. Shayevitz, Richard J. Traystman, Gail H. Gurtner (Spon. by Mark C. Rogers). The Johns Hopkins Medical School, The Johns Hopkins Medical Institutions, Departments of Anesthesiology/Critical Care Medicine, and Medicine, Baltimore. Using the isolated perfused rabbit lung, we have shown that anesthetic agents augment pulmonary vasoconstriction (dPpa) in response to t-butyl-hydroperoxide by generating thromboxane A_2 (TxA_2). Quinacrine (Q) has been described as an inhibitor of phospholipase A_2 (PLA_2). Arachidonic acid (AA) also causes dPpa and bypasses the PLA_2-mediated step in eicosanoid metabolism. AA-stimulated pressor response should not be augmented in the presence of anesthetic agents and should not be inhibited by Q. We tested these hypotheses in 5 isolated rabbit lungs perfused in a non-recirculating manner with Krebs-Henseleit (KH) solution. AA, 10-20 ug, was delivered into the inflow tubing over 1 min. The lungs were then ventilated with 2 MAC cyclopropane (C_3H_6) for 10 min and rechallenged with AA. Perfusion was begun with Q at 0.1mM (pH adjusted to 7.35-7.45) and a third AA challenge was delivered. C_3H_6 was discontinued, the lungs ventilated with air, and then given a fourth dose of AA. For air+AA, dPpa=20.8±10.9 (mean±SD); for C_3H_6+AA, dPpa=30.5±17.8; for air+Q+AA, dPpa=2.3±2.4; for C_3H_6+Q+AA, dPpa=30.5±5.2 torr. By 1-way ANOVA the effects of C_3H_6 and Q were significant (P<0.001). By the Newmann-Keuls test, C_3H_6 did not have a significant effect on dPpa after AA, but Q inhibited the response to AA with and without C_3H_6 (P<0.05). Thus Q is not a specific PLA_2 inhibitor in our model.

†1833 QUINACRINE INHIBITS ARACHIDONIC-ACID INDUCED PULMONARY VASOCONSTRICTION. Jay R. Shayevitz, Richard J. Traystman, and Gail H. Gurtner (spon. by Mark C. Rogers). The Johns Hopkins Medical School, The Johns Hopkins Medical Institutions, Departments of Anesthesiology/Critical Care Medicine, and Medicine, Baltimore.

Quinacrine (Q) has been described as an inhibitor of phospholipase A_2 (PLA_2). We have used quinacrine to inhibit arachidonic acid (AA)-induced pulmonary vasoconstriction in the isolated perfused rabbit lung. The lungs of five New Zealand White rabbits were isolated and pefused in a non-recirculating manner in situ with Krebs-Henseleit (KH) solution. AA was delivered into the inflow tubing at a dose of either 10 or 20 ug, depending on which dose produced a pulmonary vasopressor response (dPpa) of 10 torr or greater over baseline. The lungs were then perfused with Q-containing KH solution at a concentration of 0.1mM (pH adjusted to 7.35-7.45) and rechallenged with arachidonic acid. Q was then washed out with plain KH solution for approximately 20 min and the lungs were bolused with a third dose of AA. Before Q perfusion dPpa=12.7±4.4 (mean±SD); after Q, dPpa=2.7±2; and after washout dPpa=10.2±6.5 torr. By 2-way ANOVA the effect of quinacrine was significant at P=0.002. By Least Significant Difference the pre-quinacrine and post-washout values for dPpa are not different. In our model, therefore, quinacrine is not a selective inhibitor of PLA_2, and the inhibitory effect is reversible. These results suggest that quinacrine is an inhibitor of the smooth muscle contractile response, by acting as a calcium channel blocker or as a calmodulin inhibitor.

1834 ANESTHETIC AGENTS DECREASE PULMONARY VASCULAR FLUID FLUX AFTER OXIDANT CHALLENGE. Jay R. Shayevitz, Richard J. Traystman, Gail H. Gurtner (Spon. by Mark C. Rogers). The Johns Hopkins Medical Institutions, Departments of Anesthesiology/Critical Care Medicine, and Medicine, Baltimore.

In the isolated perfused rabbit lung tert-butyl-hydroperoxide (t-bu-OOH) produces a pulmonary vasopressor response by generating thromboxane A_2 (TxA_2). Inhalation anesthetics augment both the pressor response to t-bu-OOH and the production of TxA_2. We investigated the effect of cyclopropane (C_3H_6) on lung fluid flux in isolated rabbit lungs perfused with Krebs-Henseleit (KH) solution with recirculation. We continuously recorded pulmonary artery pressure (Ppa) and left atrial reservoir weight (dw). Ten preparations were given 2 t-bu-OOH challenges of 200 uM over 1 min while being ventilated with air, separated by 10 min, followed by ventilation serially with C_3H_6 at 0.5 and 2MAC each for 10 min with 200uM t-bu-OOH challenges at each anesthetic dose separated by 10 min. Four preparations, used as controls, were treated similarly, but were ventilated only with air. Results are below, expressed as flux in $mL \cdot min^{-1}$:

Challenge	1	2	3	4
CONTROL (mean±SD)	0.13±.12	0.13±.06	0.20±.12	0.46±.50
C_3H_6 (mean±SD)	0.19±.12	0.21±.10	0.01±.16	0.04±.14

By 2-way ANOVA and Least Significant Difference, fluxes with both doses of C_3H_6 are significantly less (P<0.02) than flux with air ventilation alone. This study demonstrates that, although anesthetics augment eicosanoid production after oxidant challenge in the isolated lung, they decrease fluid flux. Cyclooxygenase products thus contribute little to lung fluid leak.

† 1835 HYPEROXIA AND PHAGOCYTIC FUNCTION IN NEONATAL LUNG. Michael P. Sherman (Spon. by C.T. Barrett) UCLA Medical Center, Dept. of Pediatrics, Los Angeles

Hyperoxia and its effects on lung phagocyte function were tested by exposing rabbits to a FiO_2-0.95+ or 0.21 for 2, 4, and 7 days after birth. In vitro oxidative metabolism of lung phagocytes, obtained by lavage, was studied by polarographic measurement of O_2 consumption±1mM cyanide. In vivo pulmonary clearance was ascertained by comparing the numbers of viable Staphylococcus aureus in the left lung at 0 and 6 hours after aerosol infection, and bacterial ingestion was measured by histologic examination of the right lung. Lavage effluents contained >94% alveolar macrophages (AM) through 4 days of exposure. After 7 days, the mean number of granulocytes in lavages of O_2-exposed animals rose to 77% and the group's cumulative mortality increased to 20% vs 4% in control litters. The mean clearance of S. aureus by control was 63, 60, and 72% at 2, 4, and 7 days vs O_2-exposed newborns which killed 64, 19 and 26% of the inhaled bacteria at those ages(p<0.02 O_2 vs control at 4 days). Impaired killing was not due solely to decreased ingestion because the mean numbers of intracellular bacteria exceeded 60% at 6 hr after infection in every O_2 and control group. At 4 days, O_2-exposed AM had lower basal and stimulated mitochondrial O_2 consumption (0.8±0.2 and 1.6±0.3 nmol O_2 consumed/10^6AM/min, X±SEM, n = 6) vs control AM (1.7±0.2 and 2.9±0.3, n = 6, p<0.02). Hyperoxia alters phagocytic killing of inhaled S. aureus by neonatal AM and is associated with diminished mitochondrial O_2 consumption. Granulocytes become a secondary lung defense after hyperoxia induces bactericidal dysfunction in the newborn AM.

†1836 FREE WATER CLEARANCE DURING STATUS ASTHMATICUS (SA). Rosalyn Singleton, Donald I. Moel, and Richard A. Cohn (spon. by L. Pachman). Northwestern University Medical School, Children's Memorial Hospital, Department of Pediatrics, Chicago, Illinois.

Patients in SA often have elevated plasma antidiuretic hormone levels. To determine if children in SA have impaired water excretion and increased risk of developing hyponatremia when given a fluid challenge (FC), 5 consecutive patients with moderate asthmatic symptoms after 2 doses of epinephrine were given 20 ml/kg of D_5 0.2% N.S. i.v. over 30 minutes. Urine was collected at 20 minute intervals for free water clearance (CH_2O). This protocol was repeated 24-48 hours later after clinical improvement (CI). Values of serum Na (S_{Na}, mEq/L), serum osmolality (S_{osm}, mOsm/kg H_2O), minimal urine osmolality (min U_{osm}, mOsm/kg H_2O), and CH_2O (ml/min) after acute FC in patients during SA and after CI; ()= change in S_{Na} or S_{osm} after FC. *p<.05, SA vs CI for paired data.

PT.	AGE	S_{Na}		S_{osm}		MINIMAL U_{osm}		CH_2O	
	yr	SA	CI	SA	CI	SA	CI	SA	CI*
1	15	145(+6)	141(-4)	268(- 4)	300(-24)	123	89	5.4	13.0
2	10	134(-4)	133(+3)	275(+ 2)	266(+ 2)	62	86	8.5	9.3
3	7	131(-5)	135(+4)	274(- 4)	277(+ 3)	156	66	1.0	11.4
4	5	134(-4)	136(+3)	259(-13)	255(+ 1)	43	2	2.5	6.3
5	9	131(-4)	134(+2)	258(-12)	259(+ 1)	55	39	3.8	6.3

There was no difference in S_{Na} or S_{osm} after FC during SA vs after CI; 4/5 patients in SA had lower S_{Na} and S_{osm} after FC and 4/5 after CI had higher S_{Na} and S_{osm} after FC. Minimal U_{osm} achieved after FC tended to be lower after CI but the differences were not significant. However, CH_2O was significantly lower during SA vs CI. Despite the small risk of hyponatremia, pediatricians infusing hypotonic fluids to children in SA should be aware of temporary impaired water excretion.