Title: PULMONARY HEMODYNAMICS AFTER ONE LUNG INHALATION INJURY IN SHEEP

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Introduction. The inhalation of cotton smoke causes both tracheobronchial and parenchymal damage to the lung.[1,2] We have postulated that the tracheobronchial injury results in airway obstruction and subsequent hypoxic pulmonary vasoconstriction. This may lead to entrapment of polymorphonuclear cells (PMN) in the pulmonary microvascular areas and their subsequent release of O_2 free radicals, proteases and eicosanoids. The present study tests the hypothesis that pulmonary vasoconstriction occurs in response to inhalation injury.

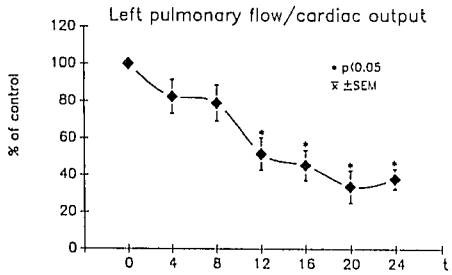
Methods and Materials. Under general halothane anesthesia nine adult range ewes, weighing between 38-47 kg, were chronically instrumented with femoral arterial, venous and thermodilution pulmonary arterial catheters. Through a left thoracotomy a 12 mm ultrasonic transit time flow probe was positioned around the left pulmonary artery and a left atrial catheter was placed. One week following the surgical procedure, baseline control data were collected in the awake state. Under general anesthesia using halothane six sheep were intubated with a modified Carlen's tube, allowing separate ventilation of the right and left lung. Smoke from smoldering cotton toweling was insufflated into the left lung by a modified bee smoker. The amount of smoke delivered to each animal was adjusted to achieve a carboxyhemoglobin level of 50%. After the smoking procedure, all sheep were awakened, extubated and studied for 24 hours while breathing room air (sea level) with free access to water and food. The sheep were sacrificed and lungs collected for histological analysis and gravimetric determinations (blood-free wet weight-to-dry weight ratio, W1/D1). Three additional sheep were anesthetized with halothane (1.4 vol% insp.) and intubated as descibed above. The left lungs were ventilated with N_2 for 10 min and hemodynamic variables and blood gases were measured.

Results. Table 1 shows the detailed results:

t (h)	0	4	8	12	16	20	24
CI	6.3	6.2	5.6	5.5	5.1	4.6*	4.4*
±SEM	0.7	0.6	0.6	0.4	0.4	0.3	0.1
PAP	19	22	24	24	26	26	27*
±SEM	1	1	2	2	1	1	2
PaO2	105	97	86*	92*	87*	83*	71*
±SEM	5	5	5	6	4	2	4
PVR	162	193	212*	235*	284*	297*	327*
±SEM	42	42	33	55	50	46	54
1PVR	100	144*	211*	408*	561*	672*	560*
±SEM		18	53	145	168	216	182

Tab.1: $\bar{x}$ ±SEM; Cardiac index (CI)(l/min/m^2); Mean pulmonary artery pressure (PAP) (mmHg); PaO2 (mmHg); pulmonary vascular resistance (PVR)(dynes sec cm^{-5}); pulmonary vascular resistance of the left lung (1PVR) (% of control)
* Student's t-test for unpaired data, comparison to control (0h), p<0.05

After inhalation injury, the left pulmonary arterial blood flow when analyzed as a fraction of CI decreased by 63% at 24 hrs (Fig.1). As the majority of CI was diverted to the uninjured right lung, the PaO_2 decreased only to 71 mmHg at 24 hrs. PAP increased progressively from a control value of 19 mmHg to 27 mmHg at 24 hrs. CI was significantly decreased at 20 and 24 hrs. 1PVR showed a 6 fold increase but when calculated for both lungs (PVR), only doubled. Histological analysis of the smoked lungs showed a severe inhalation injury consisting of deepithelization of the bronchi and cast formation in the airways. The exudative material contained large numbers of PMN, proteolytic enzymes and the stable metabolite of the potent smooth muscle constrictor thromboxane A_2. PMN averaged 163 cells/mm^2 in the smoked lungs against 62 cells/mm^2 in the non smoked lungs. Gravimetric analysis 24 h after smoke injury showed that W1/D1 of the smoke-exposed lungs (mean 9.25 + SD 1.2) was significantly higher when compared with the contralateral lungs (mean 3.9 + SD 0.35). Inducing alveolar hypoxia by insufflating the left lung with 100% N_2 resulted in a maximal reduction of 40% in blood flow through the left pulmonary artery.



Discussion. These results indicate that the reduction in pulmonary blood flow after inhalation injury are not entirely due to hypoxic pulmonary vasoconstriction since this produces a 40% decrease in blood flow against a 63% decrease with smoke. We postulate that the response of the pulmonary vasculature to smoke is a two phase phenomena. In the first phase, vasoconstriction occurs in an effort to overcome the smoke-induced ventilation-perfusion mismatch. This diversion of blood from the injured to the uninjured ventilated areas maintains the PaO_2 within a normal range. This reduction in pulmonary blood flow, however, causes an increased entrapment of activated PMN's in the pulmonary circulation, where they subsequently induce damage. In this phase mechanical obstruction and the further release of vasoconstrictive and inflammatory mediators leads to a progressive obstruction of the pulmonary microvasculature.

References.
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2. Kimura R, Traber LD, Herndon DN, Linares HA, Lubbesmeyer HJ and Traber DL: Increasing duration of smoke exposure induces more severe lung injury in sheep. J Appl Physiol 64(3):1107-1113, 1988
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