## A224

TITLE: EFFECT OF THROMBOXANE RECEPTOR BLOCKADE FOLLOWING INHALATION INJURY IN SHEEP

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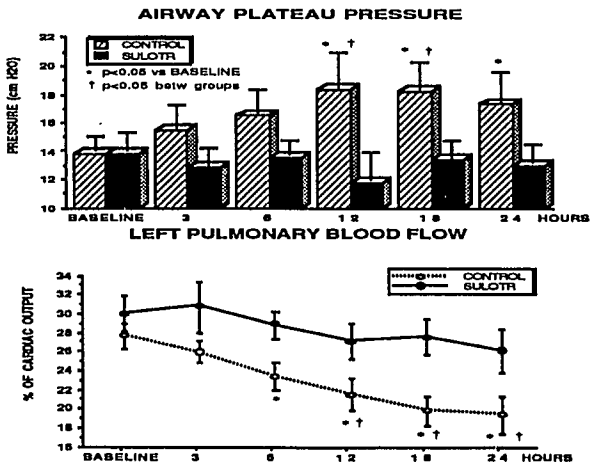
Smoke inhalation causes pulmonary vasoconstriction that is associated with bronchoconstriction and cast formation in the airways[1]. Since we have found the potent smooth muscle constrictor thromboxane(TX) $A_2$ to be elevated in the airway following inhalation injury, we determined the relative role of this agent in the pathogenesis by using the specific TX antagonist BM 13,177 (sulotroban). The left lung of chronically instrumented sheep (n=13) was insufflated with smoke. The animals were placed on a ventilator, which was connected to a lung mechanics calculator. Left pulmonary artery blood flow (LPAB) was measured by an ultrasonic transit time flow probe. Six of the studied animals received BM 13,177 (S-GR) as a bolus (0.5 mg/kg) 10 min. prior to the smoke and subsequently as a continuous infusion during the 24 hour study period (0.5 mg/kg/min). The other seven sheep served as controls (C-GR). The lungs of all animals were harvested after a 24 hour study period for determination of wet/dry ratio. Data are mean±SE and analyzed by a two way analysis of variance.

Smoke inhalation caused an increase in airway pressure and a decrease in LPAB, calculated as a percentage in cardiac output. (FIGURE). BM 13,177 treatment completely abolished the increase in airway pressure and markedly restricted the changes in LPAB. Left pulmonary vascular resistance (LPVI) rose from 0.8±0.06 to 1.8±0.08 $10^3$ dynes•cm$^{-5}$•m$^2$ in C-GR and from 0.07±0.08 to 1.5±0.16 $10^3$ dynes•cm$^{-5}$•m$^2$ in the S-GR. LPVI was significantly lower in S-GR in the late phase of the study period. Systemic vascular resistance rose to the same extent in both groups at 24 hours (from 1.6±0.1 to 2.1±0.1 $10^3$ dynes•cm$^{-5}$•m$^2$ in C-GR, 1.6±0.1 to 2.0±0.1 $10^3$ dynes•cm$^{-5}$•m$^2$ in S-GR). Arterial TX level did not increase over time in either group. Wet/dry ratio was significantly elevated in the smoked lungs of both groups (5.5±0.2 in C-GR, 5.2±0.2 in S-GR), compared to the air insufflated lungs (4.6±0.1 in C-GR, 4.3±0.1 in S-GR). No difference was found between the groups.

Thromboxane seems to be a causative mediator for bronchoconstriction and pulmonary vasoconstriction seen after smoke injury. However, increased pulmonary edema after smoke cannot be prevented by TX receptor blockade, suggesting only a little effect of thromboxane on permeability changes. Likewise thromboxane probably does not play a major role for systemic hemodynamic changes seen after inhalation injury. (GM33324)

**Reference:** 1. Intensive Care Med. 14: 25-29, 1988




## A225

TITLE: ENDOTOXEMIA: REPERFUSION INJURY TO THE AIRWAYS ?

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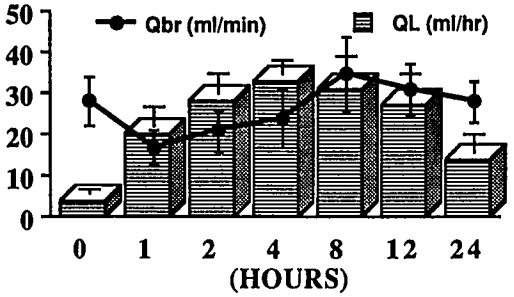
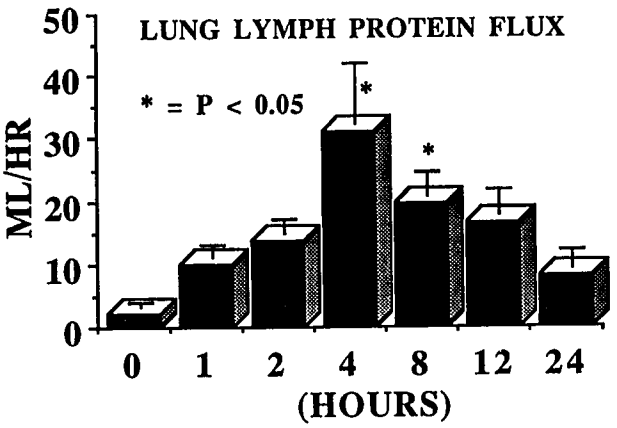
**INTRODUCTION:** The hemodynamic changes associated with endotoxemia (LPS) in sheep is well documented (1,2). Its effect on the pulmonary system is characterized by hypoxemia and lung edema. The purpose of this study was to determine if there is a possible reperfusion injury to the airways during the course of endotoxemia.

**METHODS:** Eight sheep were chronically instrumented with cardiopulmonary and lung lymph catheters. An ultrasonic transit time flow probe was placed around the bronchial artery. After a recovery period of a week, baseline data were recorded, and LPS was given at a dose of 1.5 µg/kg over 30 min. The changes in the bronchial blood flow (Qbr) as well as lung lymph flow (QL) were recorded for 24 hrs.

**RESULTS:** The results of this study are shown in the figures.




The decrease in the bronchial blood flow was associated with an increase in the bronchial vascular resistance which increased by 212%, 30 minutes after endotoxin infusion. Moreover, the PaO2 decreased by 21% whereas the the lung lymph protein flux increased by 81% at this time point.

**CONCLUSION:** The bronchial blood flow, the systemic blood supply to the airways, was markedly reduced in phase-one (pulmonary hypertension-phase). It gradually increased during the hypodynamic phase which was associated with marked elevation in lung lymph flow as well as lung lymph protein flux. This suggests that reperfusion injury to the airways might contribute to alterations in lung fluid balance during endotoxemia.

**REFERENCES:** 1. Am. J. Physiol. 254: H558-569, 1988
2. Circ. Shock 17: 103-108, 1985