deficiency potentiates the effect of hyperoxia on serotonin clearance.

From these results, we conclude that depression of pulmonary clearance of serotonin occurs in rats due to hyperoxia and is potentiated by vitamin E deficiency. This represents an early alteration of lung function due to high partial pressures of O₂. The mechanism for this hyperoxia depression of serotonin clearance is not known. However, in view of recent evidence that serotonin is removed in transit through isolated perfused rat lungs by an energy-requiring process that occurs predominantly by endothelial cells, it is possible that the depression of serotonin clearance reported here is due to damage to the pulmonary endothelium. As such, serotonin clearance may prove to be a sensitive method by which to detect and evaluate damage to pulmonary endothelium.

Since serotonin is a potent vasconstrictor, interference with its clearance may have major consequences for vascular function. Loss or depression of this "protective" clearing function of the lung might result in elevated levels of serotonin in the pulmonary venous and systemic circulations. This may in part account for the pulmonary edema and systemic hypertension that commonly occurs in O₂ toxicity in the experimental animal.³

REFERENCES

Selective Inhibition of Functions of Alveolar Epithelial Cells from an Amphibian

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The excised short-circuited bullfrog lung secretes C₂, other halides and thiocyanate into the lumen and net CCl₄. Bow accounts for the short-circuit current (Gaty-D, Am J Physiol 228:1162, 1975). Direct and indirect evidence indicates that this transport mechanism is located in the alveolar epithelial lining. The epithelium is comprised of at least 3 cell types (squamoid, cuboidal and ciliated), but it is not clear which of these participate in halide anion secretion. Dose-effect relationships for the actions of selected heavy metals and other agents on ciliary motility and on functions of the entire epithelium may help answer the question.

When HgCl₂ was added to a Ringer solution that contained disaggregated alveolar epithelial cells, ciliary motility was reduced progressively to zero as the concentration was increased from 10⁻⁷ to 10⁻⁴ M/L (Fig 1). Exposure of the luminal surface of the excised lung to the same range of metal concentrations induced a parallel inhibition of short-circuit current (Fig 2). A similar pattern of response was observed when lungs or epithelial cells were exposed to dilutions of an aqueous extract of the smoke from a high nicotine and tar cigarette (ACSE). In contrast, CdCl₂, or NiCl₂, blocked ciliary motility completely without affecting short-circuit current. Inhalation of cilia by nicotine sulfate was accompanied by a slight increase in the bioelectric current. In addition, cilia of cells that were disaggregated from the excised preparation after exposure to CdCl₂, in only the luminal bathing solution were also inhibited. These results eliminate the possibility that the apparent selective action of agents on cilia results from the exposure of a greater area of cell surface by the disaggregation procedure. The effects of CdCl₂ could be reversed by washing the cells with a dimercaprol-Ringer solution, but not with Ringer solution alone. In addition, sulphydryl agents partially reversed the inhibition of ciliary motility but not the decrease in short-circuit current that was induced by HgCl₂. Finally, NaCN reduced short-circuit current but did not affect ciliary motility.

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Removal of Circulating Vasactive Hormones by the Lung* 
Effect of Cardiopulmonary Bypass, Pulmonary Hypertension, Hemorrhagic Shock

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It is well established that the biogenic amines, 5-hydroxytryptamine (5-HT) and norepinephrine (NE), as well as prostaglandins (PG) of the E and F series are removed during passage through a variety of animal lungs.1-4 We have also determined pulmonary removal of these hormones, after their bolus IV administration to patients undergoing cardiac surgery, by measuring differences in the content of each in blood sampled simultaneously at the pulmonary artery (PA) and left atrium (LA).

Total 3H-PGE, removal, taken as the difference between unchanged PGE, sampled at the PA and LA before cardiopulmonary (CP) bypass, was over 90% in a single pass through the lung. This reflected largely metabolism, since less than 15% of the radioactivity in LA blood was associated with unchanged PGE. Total removal of PGE, was unchanged after varying times on CP bypass. In similar studies, 20% and 65% of bolus injections of 3H-NE and 14C-5-HT, respectively, were removed during a single pass in patients with normal PA pressures. In contrast to PGE, however, removal of these amines was due mainly to uptake from the vascular space, for most (> 90%) of radioactivity of blood drawn from the LA was in the form of unchanged NE or 5-HT. Amine removal also differed from that of PGE, in that it was significantly (P < 0.02) increased after CP bypass to 49% for NE and 78% in the case of 5-HT.

Total amine removal prior to CP bypass was significantly greater (NE = 59%; 5-HT = 78%) in patients with preoperative pulmonary hypertension (mean PA pressure < 22 mm Hg)* and fell after surgical alleviation of the hypertensive state, to values anticipated for the normotensive group of patients.*

Since pulmonary hypertension is also a feature of blood reinfusion after periods of hemorrhagic shock, it was of interest to compare 5-HT removal in dogs, at various times during this state, with that observed in pulmonary hypertensive patients. We found that during the hypertensive phase after controlled hypovolemia, 5-HT removal by dog lung was increased as compared with control values (80% vs. 59%). Following reinfusion of blood (ie, post-resuscitation) marked pulmonary hypertension occurred in association with significant hypoxemia and a return to normal systemic blood pressure. At this time 5-HT removal fell to less than 20%, the lowest value we have observed in any studies with experimental animal or human lung.

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