Date : April 10, 1980

Title : HALOTHANE REVERSIBLY INHIBITS SYNTHESIS OF LUNG PROTEINS

Authors : C. A. Watkins, Ph.D., R. Christopherson, Ph.D., S. A. Wartell, Ph.D., J. A. Hammer, B.S., and D. E. Rannels, Ph.D.

Affiliation: Departments of Physiology and Anesthesia, The Milton S. Hershey Medical Center, The Pennsylvania State University, Hershey, Pennsylvania 17033

Introduction. Although the lungs are the primary site of exposure to volatile anesthetics, little information is available regarding the effects of these agents on lung metabolism. Similarly, the effects of anesthetics on protein metabolism have received little attention. Thus, earlier observations (1) which suggested that exposure of the lungs to halothane inhibited protein synthesis were further investigated.

Methods. Ventilated rat lungs were perfused in situ (2) with recirculating Krebs-Henseleit bicarbonate buffer containing 4.5% bovine serum albumin, 5.6 mM glucose, plasma levels of 19 amino acids and 690 μM [^{14}C]phenylalanine. The gas phase was 20% O_2: 75% N_2:5% CO_2 ± halothane. Rabbit pulmonary macrophages, obtained by tracheal lavage, were incubated in a similar medium with 2% albumin (3). A mixed rat lung cell population for culture in Dulbecco's MEM plus 10% fetal bovine serum was obtained by enzymatic digestion of lung tissue, as described elsewhere (3). Protein synthesis was calculated based on the incorporation of [^{14}C]phenylalanine using the specific radioactivity of extracellular phenylalanine, as detailed earlier (4).

Results. In perfused lungs, protein synthesis was rapidly inhibited upon exposure to halothane (Fig. 1). The extent of inhibition was linearly related to dose (0-4%), with a 41% decrease in protein synthesis during the first 60 min of exposure to 4% halothane. The effect of halothane was rapidly reversible: protein synthesis returned to control rates within the first 15 min after halothane delivery was stopped (Fig. 1). The inhibitory effect was not associated with non-specific changes in membrane permeability or with ATP depletion, although evidence of altered endothelial cell function was observed (1). Both the inhibition of protein synthesis and its reversal were observed in the presence of actinomycin-D. A similar reversible inhibition of protein synthesis, which was rapid in onset and dose-dependent, was evident in primary cultures of mixed lung cells and in rabbit pulmonary alveolar macrophages. These effects were not associated with a change in the ability of the cells to exclude erythrocin-B or with increased release of lactate dehydrogenase from macrophages, indicating no effect of halothane on cell viability.

Discussion. Halothane rapidly inhibited synthesis of proteins by intact perfused rat lungs in a dose-dependent and reversible manner. Studies with isolated lung cells indicated that the effect of the anesthetic did not involve altered distribution of pulmonary flow but was exerted directly at the cellular level. Other experiments suggested that the inhibition was not due to non-specific cell damage and involved alterations in translation. Further studies are required to elucidate the mechanism by which halothane inhibits protein synthesis in the lung.

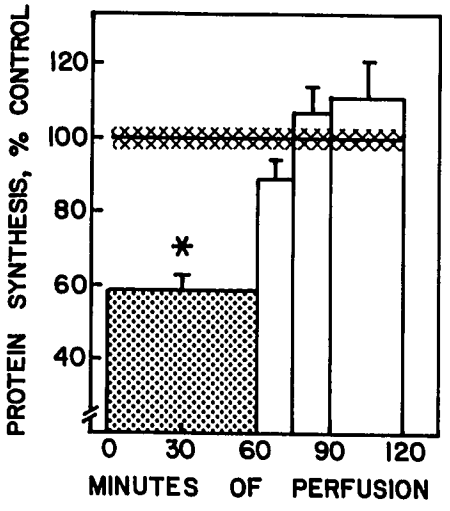

Figure 1. After exposure of perfused lungs to 4% halothane for 60 min. (shaded bar), halothane delivery was stopped and recovery of protein synthesis was monitored in the same lungs (open bars). Data (mean ± S.E.M.) are expressed as percent of the control rate of synthesis (1.76 ± 0.05 nmol phe/mg protein·hr; hatched area).

* = $p < .01$ vs control

References.
1. Rannels DE, Watkins CA and Biebuyck JF: Effect of halothane on uptake and metabolism of 5-hydroxytryptamine by rat lungs perfused in situ. Anesthesiology 51: S251, 1979.
2. Watkins CA, Rannels DE: In situ perfusion of rat lungs: stability and effects of oxygen tension. J. Appl. Physiol. 47: 325-329, 1979.
3. Manuscript in preparation.
4. Watkins CA, Rannels DE: Measurement of protein synthesis in rat lungs perfused in situ. Biochem. J. 188: 269-278, 1980.

Supported by HL-20344, HL-19190, HL-00294 and The Parker B. Francis Foundation.

Downloaded from http://pubs.asahq.org/anesthesiology/article-pdf/53/3 Suppl/S247/627210/0000542-198009001-00247.pdf by guest on 08 November 2024