have with an inhaled anesthetic, a possible hypothesis to explain the increased incidence of pneumonia would be a direct, anesthesia-induced depression of lung defenses. Thus, we investigated the effects of a commonly used general anesthetic agent, halothane, on pulmonary antibacterial activity and ciliary activity.

**Materials and Methods**

**Pulmonary Bactericidal Studies**

Mice were anesthetized with halothane concentrations for a period of four hours. They were then allowed to recover and one hour later were challenged for 30 minutes with aerosolized P. aeruginosa radiolabeled Staphylococcus aureus. Immediately after aerosol challenge and again four hours later, equal numbers of previously anesthetized and control mice were killed by exsanguination. The lungs were aseptically removed, homogenized, serially diluted and cultured quantitatively in triplicate on petriplates.

These plates were incubated and the colonies counted. Radioactivity was measured by transferring a separate aliquot of lung homogenate into scintillation vials. The radioactivity was assayed in a liquid scintillation counter and expressed as counts per minute per ml of the material assayed. Intrapulmonary antibacterial activity was determined in individual animals by comparing four-hour bacterial count/isotope ratio counts to a similar ratio determined immediately after the aerosol exposure.

**Ciliary Activity Studies**

Under strict sterile conditions, the trachea of a ferret was dissected from below the vocal cords to the carina by blunt, bloodless dissection, then removed, and complete rings prepared by cutting transversely between tracheal cartilages. The rings of trachea were carefully transferred to sterile screw-top tubes containing 1 ml of Leibowitz-15 medium and rolled on a tissue rotator in a 33°C incubator. The use of L-15 medium and rolling the screw-top tubes prolonged the survival of the ciliated epithelium beyond that obtained using other standard media.

Under strict sterile conditions, halothane concentrations were bubbled through the medium and the ciliary activity was determined. Room air was bubbled through the control tubes.

Groups of tubes were exposed to halothane concentrations, 1.0, 2.0, 3.0, 4.0, and 5.0 percent and ciliary activity was determined on a daily basis for five days. All tubes were read blindly by a single observer (BRM) and data expressed as percentage of cilia beating. To determine the recovery of ciliary activity, another group of culture tubes was exposed to 4 percent halothane. Every 24 hours a set of culture tubes was exposed to air and the recovery of ciliary activity recorded.

**Results**

Intrapulmonary bactericidal activity was depressed in both groups of anesthetized animals. At four hours, the mice that had been anesthetized had a significantly greater percentage of viable bacteria remaining (41.8 ± 4.1 percent with one MAC halothane and 43.1 ± 3.4 percent with two MAC halothane) when compared to controls (29.3 ± 2.3 percent; P < .02 with one MAC halothane and 18.5 ± 1.3 percent, P < .005 with two MAC halothane). These studies demonstrated that the alveolar macrophage function is adversely affected after...
exposure to halothane. The ciliary activity after exposure to increasing concentrations of halothane showed that at 1 percent and 2 percent halothane there was no impairment, while 3 percent halothane caused some ciliostasis. Dramatic reduction in the ciliary activity occurred at halothane concentrations of 4 percent and 5 percent. Results of recovery of ciliary activity of tracheal rings exposed to 4 percent halothane concentrations showed that there was immediate and complete recovery for as long as three days after the removal of the anesthetic. After four days of exposure, recovery was incomplete, and after one week no recovery of ciliary activity was noted with death of respiratory epithelial cells.

**DISCUSSION**

Pulmonary alveolar macrophages (PAM) play a key role in the antibacterial defenses of the lung. Their activity is modulated by both humoral and cellular immunity. Phagocytosis and intracellular killing of bacteria by the PAM is an active energy-utilizing process, dependent entirely on aerobic oxidation. Halothane is an agent known to depress oxidative phosphorylation. Also, the microtubular structures of cells are distorted by halothane and their integrity is essential for phagocytosis. Therefore, it could be argued from a theoretic point of view that halothane will depress pulmonary macrophage function.

However, a previous study by Goldstein et al. concluded that halothane failed to depress PAM, whereas methoxyflurane and cyclopropane did depress their activity. Our results are at variance with these data, and suggest halothane does cause significant depression of lung antibacterial activity. This finding is consistent with the anesthetic action of halothane and methoxyflurane at a sub-cellular level.

The in vitro organ culture model of tracheal rings has the advantage of assessing the effects of prolonged exposure to halothane on ciliary activity. Our studies showed that halothane concentrations of 4 percent or more impaired ciliary activity and prolonged exposure was cytotoxic after several days. Halothane exposure of less than four days was followed by complete recovery of ciliary activity. Since in clinical practice 4.0 percent halothane concentrations are rarely used, and then only briefly for induction, we conclude that at the usual concentrations of halothane there is minimal depression of ciliary activity, which is reversible after termination of the exposure.

**REFERENCES**


**IMMUNOLOGY OF THE LUNG**

**DISCUSSION**

**Dr. Rylander:** Have you considered that the effect of anesthesia on the incidence of pneumonia may be caused by the inhalation of mucus? There were some papers about 15 years ago which showed that instillation of pure mucus down into the alveolar region very severely depressed bacterial action.

**Dr. Manawadu:** I do not know whether anyone has done any work on the effects of anesthetic agents on the mucus.

**Dr. Repine:** Does halothane or its products remain in the lung and later the multiplication rate of the bacteria independently of host defense mechanisms?

**Dr. Manawadu:** Yes, it might have an effect because halothane per se inhibits bacterial multiplication.

**Question:** I'd like to make a comment on Dr. Manawadu's paper and then to ask him a question. Dr. Manawadu, you found that 4 percent halothane was required to inhibit the ciliary activity and Dr. Forbes found that lower percentages inhibited mucociliary clearance in dogs. The premise for your study is that ciliary beating is a major determinant of mucociliary clearance. I'd like to put forward an alternative hypothesis that the consistency and the depth of the periciliary fluid could affect the ability of the cilia to sweep the gel up to the mouth. At the concentrations used, did the cilia stop beating or was their activity only impaired?

**Dr. Manawadu:** The cilia were either beating or not beating. It's a very dramatic change. The difference between our system and Dr. Forbes' is in the mucociliary clearance. He is looking at 3 factors: 1) in the ciliary activity, 2) in the mucus, and 3) in the coordination of the ciliary activity. In our study we were only looking at the ciliary activity.

**Impairment of Human Alveolar Macrophage Oxygen Consumption, and Superoxide Anion Production by Local Anesthetics Used in Bronchoscopy**

**John R. Hoidal, M.D.; James G. White, M.D.; and John E. Repine, M.D.**

Bronchoscopic subsegmental lavage is used extensively to obtain human alveolar macrophages (AM) for

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