

Mucociliary Clearance in the Canine Lung during and after General Anesthesia

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Central and peripheral pulmonary mucociliary clearance was assessed by tantalum bronchography and serial chest roentgenograms in dogs. Thiopental, 25 mg/kg, did not change clearance from awake values. Halothane, 1.2 MAC, for six hours, delayed both central and peripheral clearance by at least three hours. After halothane or diethyl ether, 1.2 MAC, for two hours, recovery of mucociliary clearance was delayed for approximately three and a half hours. (Key words: Airway: cilia. Anesthetics, intravenous: thiopental. Anesthetics, volatile: diethyl ether; halothane. Lung: mucus.)

IMPAIRED MUCOCILIARY CLEARANCE after general anesthesia may predispose patients to atelectasis, particularly following major abdominal operations.¹ The influence of anesthetic agents on overall pulmonary mucociliary clearance is not known, although studies indicate that anesthetics may significantly impair tracheal mucociliary flow.^{2,3} Halothane, enflurane, nitrous oxide and morphine depress mucociliary flow in the dog trachea, whereas diethyl ether does not.² In this study we measured clearances of tantalum from the trachea, mainstem bronchi and peripheral airways during halothane anesthesia compared with the awake state. We also compared clearance rates during recovery from thiopental, halothane, and ether anesthesia.

Methods

Mucociliary clearance from the lung during anesthesia was examined by tantalum bronchography in healthy hounds, previously demonstrated to have good mucociliary flow,² under four conditions: thiopental 25 mg/kg; halothane, 1.2 MAC (1.2 per cent end-tidal), for six hours; halothane, 1.2 MAC, for two hours, and recovery for six hours; diethyl ether, 1.2 MAC (3.7 per cent end-tidal), for two hours and recovery for six hours. There were six dogs, each weighing 22-25 kg, in each group, except that only five dogs received diethyl ether.

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Received from the University of California, San Francisco, San Francisco, California. Accepted for publication April 20, 1978. Supported by the Medical Research Service of the Veterans Administration. Presented at the Annual Meeting of the American Society of Anesthesiologists, October 1977.

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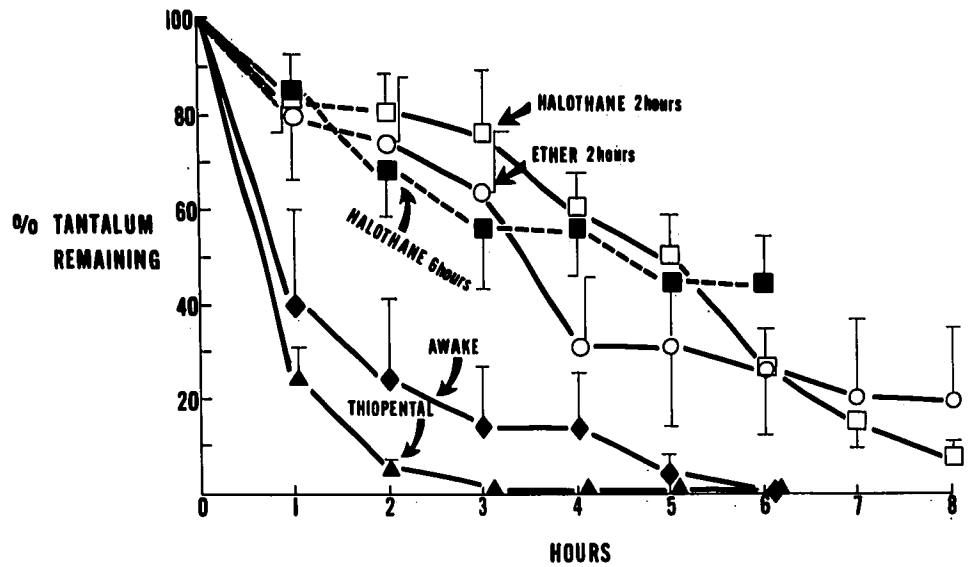
Each dog was studied on four occasions, several weeks apart. On each occasion anesthesia was induced with thiopental, 25 mg/kg, the trachea was intubated, and the lungs were ventilated with air. Tantalum was insufflated with the dog supine before the animal was placed prone for roentgenography. In the first study, after induction with thiopental, the endotracheal tube was removed, and roentgenograms were repeated for six hours as the dog recovered. In the second study, anesthesia was continued for six hours with halothane, 1.2 per cent end-tidal, measured with an infrared analyzer. Controlled ventilation was maintained with oxygen, 25 per cent, in nitrogen, humidified to more than 90 per cent relative humidity at 32-35 C. Tidal volume was 30 ml/kg at 6-10 breaths/min to maintain peripheral venous carbon dioxide tension at 30-40 torr. Roentgenograms were taken hourly during anesthesia. In the third study, halothane, 1.2 per cent end-tidal, was maintained for two hours, then discontinued. The endotracheal tube was removed and the dog allowed to recover while roentgenograms were taken for six hours. In the fourth study anesthesia was maintained with diethyl ether, 3.7 per cent end-tidal, for two hours, and roentgenograms repeated for the next six hours.

Awake studies were performed in an additional three healthy hounds with chronic tracheal stomas. The stomas were healed and covered by loosely opposed skin folds, so that mouth breathing was preserved but access to the trachea could be obtained. In the awake dog the tracheal stoma and tracheo-bronchial tree were anesthetized with 6 ml of 2 per cent lidocaine prior to tantalum insufflation.

For tantalum insufflation, a radiopaque catheter 2 mm in diameter was passed into the origin of each mainstem bronchus in turn, and tantalum powder of mass median diameter 2.5 μ m insufflated from a DeVilbiss powder blower until airways 2 to 5 mm in diameter were outlined on fluoroscopic examination. The trachea was then outlined as the catheter was withdrawn. Approximately 1 ml, or 16 g, of powder was needed per dog. With the animal prone, a posteroanterior chest roentgenogram was taken after tantalum insufflation. The roentgenogram was repeated hourly, using the same exposure at end-inspiration while the animal lay prone in a plastic foam cradle.

Roentgenograms were assessed as follows. Each author, unaware of the timing or sequence of films,

FIG. 1. The rates of central mucociliary clearance in awake dogs and dogs anesthetized with thiopental were more rapid than those seen with halothane for six hours, halothane for two hours, or ether for two hours. Clearance is assessed as percentage tantalum remaining on serial radiographs. The dotted line indicates the duration of anesthetic administration.



ranked them according to the amount of tantalum remaining. Then, by comparison with standard bronchograms, and referring to the radio-opacity of tantalum on the initial film as 100 per cent tantalum dose, he independently scored each film according to the percentage of tantalum remaining.⁴ The percentage of tantalum was assessed in 10 per cent increments. We scored each film separately for central and peripheral airways. Central airways were defined as trachea and mainstem bronchus to upper lobe origin. Peripheral airways were defined as those beyond the upper lobe origin. Times to 20 and 50 per cent clearance both centrally and peripherally were compared by analysis of variance and the Student-Newman-Keuls test. *P* values less than 0.05 were considered significant.

Results

There was excellent correlation in clearance values between observers. For each film the value assigned by one author was plotted against the value assigned by the other to give a linear regression of $y = 2 + 0.97x$ ($r = 0.98$).

Clearances of tantalum for all groups are shown in figure 1 for central airways and in figure 2 for peripheral airways.

There was no difference in times to 20 per cent clearance of central airways among the groups (table 1). However, the times to 50 per cent central airway clearance were 42 min for the group receiving thiopental and 75 min for the awake group, both significantly different from 273 min for the group receiving

FIG. 2. As in figure 1, the rates of peripheral mucociliary clearance in awake dogs and dogs anesthetized with thiopental were more rapid than those seen with halothane for six hours, halothane for two hours, or ether for two hours. The dotted line indicates the duration of anesthetic administration.

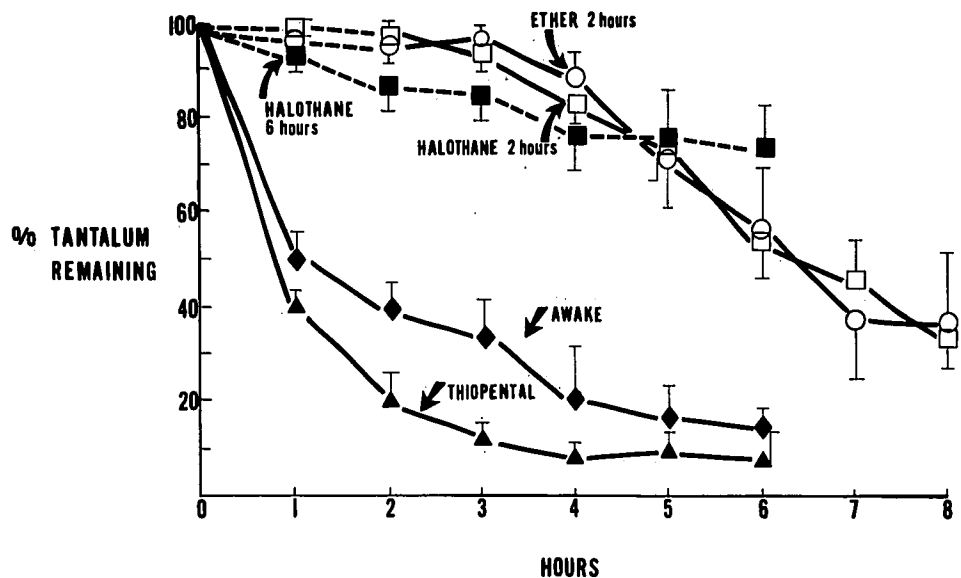


TABLE 1. Times Taken to Achieve 20 Per Cent and 50 Per Cent Clearance of Tantalum from Central and Peripheral Airways of the Dog

	Central Clearance					Peripheral Clearance				
	Awake	Thiopental	Halothane 6 Hours	Halothane 2 Hours	Ether 2 Hours	Awake	Thiopental	Halothane 6 Hours	Halothane 2 Hours	Ether 2 Hours
Time to 20 per cent clearance										
Mean (min)	30.1	19.4	99.0	133.0	184*	24.7	22.4	218.3†	228.3	278.0
SE	15.0	2.5	31.1	38.7	78.2	2.9	2.5	56.5	25.6	57.9
Number	3	6	6	6	4	3	6	4	6	5
Time to 50 per cent clearance										
Mean (min)	75.4	41.5	273.0	246.7	238.0	76.7	56.7	‡	390.7	368.0
SE	37.4	5.8	46.9	43.2	70.3	21.9	9.2		24.8	31.9
Number	3	6	6	6	5	3	6		6	5

There was no difference among the groups with respect to 20 per cent central clearance, but at 50 per cent central clearance, and 20 or 50 per cent peripheral clearance, clearances in the awake and thiopental-treated groups were significantly faster than those in the halothane-treated and ether-treated groups. At 50 per cent central clearance, the significance of the difference was $P < 0.05$;

at 20 or 50 per cent peripheral clearance, $P < 0.001$ level.

* One dog did not achieve clearance by the end of the study.

† Two dogs did not achieve clearance by the end of the study.

‡ Only one dog achieved 50 per cent clearance by the end of the study.

halothane for six hours, and from 238 min for the group receiving diethyl ether for two hours. Times to 20 per cent peripheral clearance were 22 min and 25 min for the thiopental-treated and awake groups, significantly different from 218 min for the group receiving halothane for six hours, 228 min for the group receiving halothane for two hours, and 278 min for the group receiving ether for two hours. Finally, times to 50 per cent peripheral clearance were 77 min for the awake group and 57 min for the thiopental-treated group, significantly different from 368 min for the group receiving ether for two hours or 391 min for the group receiving halothane for two hours. Times to 50 per cent peripheral clearance could not be assessed for the group that received halothane for six hours, since only 30 per cent clearance had been achieved by six hours. Clearances for the awake group and the thiopental-treated group were comparable at each time, and those for the groups receiving halothane and ether were comparable at each time except that 50 per cent peripheral clearance was not achieved in the group receiving halothane for six hours.

Discussion

Tantalum bronchography was chosen to assess the effects of various anesthetics on overall mucociliary clearance from the lung because of our belief that tantalum provided advantages not present with radioactive particles. With tantalum the inert metal particles adhere to the airway mucus and are cleared by the ciliary apparatus. The sites of deposition can be visualized and differentiated, which cannot be done

with radioactive particles. Serial comparisons may be made of the same areas or airways, and airways may be separated from alveolar contamination. The disadvantage of the tantalum approach is the semiquantitative assessment of clearance by visual perception. However, the close agreement between observers in this study and in others⁴ attests to the reproducibility of the method. The tantalum was well tolerated by the animals, with the exception of throat clearing of sputum and tantalum arriving at the vocal cords. Persistent coughing in one dog and vomiting in another necessitated repeated studies.

Central clearance in this study was linked to peripheral clearance, in that material cleared from the distal bronchi would be seen in the trachea. Hence, clearance time from the trachea is shorter when tantalum is not also distributed to the smaller bronchi.⁴ Time to 50 per cent clearance of radioisotopes from the trachea of awake man is 30 min,^{7,8} followed by a second peak of radioactivity at two to three hours, attributed to particles moving into the trachea from the bronchial tree.⁹ Thus, bronchial clearance should have contributed to the slow phase of central clearance seen at two hours in the awake and thiopental-treated groups in this study (fig. 1). Since, in the dogs receiving diethyl ether or halothane for two hours, less than 10 per cent of the distal tantalum had cleared at the time that 50 per cent central clearance had occurred, we postulate that the prolonged 50 per cent clearance time represented a true depression of central clearance.

Hence, halothane and diethyl ether depress both central and peripheral mucociliary clearance during

and after anesthesia, while an induction dose of thiopental does not. Why should ether and halothane delay postanesthetic clearance? One possible explanation is that since the depressant effects of volatile anesthetic agents on cilia⁸ and on tracheal flow are readily reversible,² perhaps stagnant mucus changes in viscosity or depth. Assuming the effect is dependent on the duration of exposure, recovery of clearance should be slowed after administration of thiopental for two hours.

This study was designed to allow optimum conditions for mucociliary flow. Atropine, dry gases, and a sealed endotracheal tube cuff were avoided. These factors, in combination with halothane, stop tracheal mucous flow in surgical patients.⁹ Postoperative impairment of mucociliary clearance of tantalum has been shown to precede pulmonary atelectasis in patients undergoing abdominal operations. We postulate that the delay in peripheral mucociliary clearance after halothane or ether anesthesia, in conjunction with a loss of lung volume and impaired pulmonary mechanics, leads to retention of mucus and subsequent atelectasis.

The authors thank Henry Fuhs for his excellent technical assistance, and E. I. Eger, II, for his constructive criticism of the manuscript.

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