Halothane Depresses Mucociliary Flow in the Trachea

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Tracheal mucociliary flow rates in dogs were measured with a radioactive droplet technique during thiopental anesthesia, and subsequently during halothane anesthesia. Body temperature and inspired gas temperature and humidity were held constant. Ventilation was controlled with 25 per cent oxygen in nitrogen to produce PaO₂ 30 torr. Mucociliary flow rate remained constant when halothane concentration was held constant at 1.2 MAC halothane. Mucociliary flow rates at 0.6 MAC halothane were comparable to those after thiopental, 25 mg/kg. Increases in concentration from 0.6 to 1.2 to 1.8 to 2.4 MAC halothane progressively depressed mucociliary flow. Flow at 2.4 MAC halothane was 27 per cent of the control (thiopental) value. Flow returned to previous values as end-tidal halothane concentration was reduced. The depression produced by halothane may represent impairment of an important pulmonary defense mechanism. (Key words: Lung, trachea, efflux; Lung, trachea, mucus; Anesthetics, volatile, halothane.)

The mucociliary apparatus removes inhaled debris and organisms from the lung. Impairment of this mechanism by anesthesia could contribute to postoperative atelectasis and bronchopneumonia. Pentobarbital or thiopental anesthesia reduces mucociliary flow by 35 per cent from awake values in sheep,1 but there is disagreement about the effects of changing depths of anesthesia and barbiturates. Bridger and Proctor observed that mucociliary flow in the nose ceased during deep barbiturate anesthesia,2 whereas Marin and Morrow found no change in flow in the trachea with increments of barbiturate.3 The effects of different concentrations of inhalational anesthetic agents have not been studied. This paper reports a dose-dependent, reversible depression by halothane of tracheal mucociliary flow rate.

Method

Six healthy hounds, on a normal fluid intake and free of upper respiratory tract infection, were anesthetized with thiopental, 25 mg/kg. Each was placed in the supine position with the trachea horizontal. The trachea was intubated and the lungs ventilated with 25 per cent oxygen in nitrogen to an end-tidal carbon dioxide concentration of 4 per cent. Resulting arterial carbon dioxide tensions, measured every two hours, were 27–33 torr. Oxygen tensions were 90–110 torr. Inspired gas was maintained at 32–35°C with relative humidity >90 per cent using a Bennett Cascade humidifier. I have found that these conditions do not impair mucous flow.1,3 Temperature and humidity were measured at the top of the endotracheal tube with rapid-response wet and dry thermocouples.4 Rectal temperature was maintained at 37–38°C with a heating blanket. The endotracheal tube cuff was deliberately underinflated to allow a gas leak during inspiration. This prevented damming of mucus at the cuff. I have shown that endotracheal intubation does not alter mucociliary flow from pre-intubation values under these conditions.5

Mucociliary flow was measured as follows. Two sodium iodide (NaI) scintillation counters were positioned externally in series over the long axis of the trachea. Each counter was collimated to a narrow slit transverse to the long axis. The distance between the counters was 5.5 cm for a point of technetium (Te⁹⁹m) 3 cm below the collimators. Via a fine cannula passed down the

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endotracheal tube a 15-μl droplet of radioactive pertechnetate in saline solution was deposited on the tracheal mucosa distal to the counters. As the pertechnetate, moving towards the larynx, passed under each counter in turn, a peak of radioactivity was recorded on a constant-speed chart recorder (fig. 1). Assuming that the pertechnetate in saline solution binds to mucus so that its rate of movement reflects that of the mucus, its comparative mucous flow rates can be calculated. Mucociliary flow rate was calculated from the time from 50 per cent of peak radioactivity under the distal counter to 50 per cent of peak radioactivity under the proximal counter (fig. 1). As can be seen in figure 1, 50 per cent of peak radioactivity is a more precise point than peak radioactivity itself.

All mucociliary flow measurements were made in triplicate, as areas of no-flow may exist adjacent to moving streams of mucus, and a single determination may give a spurious value. Variation of all measurements about the means quoted in table 1 was 14.7 per cent. After three control measurements made during thioental anesthesia, 1.2 per cent (1.2 MAC) end-tidal halothane was achieved and maintained for 5 hours. Halothane concentrations were measured with an ultraviolet analyzer. During this time mucociliary flow was measured repeatedly. These studies were done to rule out a temporal effect of halothane. The end-tidal halothane concentration then was changed sequentially to 1.8, 2.4, 1.2, and 0.6 per cent. At each concentration, mucociliary flow was measured in triplicate after 15 minutes at a constant end-tidal concentration.

**Results**

As expected, mucociliary flow rates varied among dogs anesthetized with thiopental. In accord with values reported for barbiturate

| Table 1. Mucociliary Flow Rates (mm³/min) in Tracheae of Dogs Anesthetized with Thiopental, and with Various Concentrations of Halothane* |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Thiopental      | Halothane       |                 |                 |                 |
|                 | 1.2 Per Cent    | 1.8 Per Cent    | 2.4 Per Cent    | 1.2 Per Cent    | 0.6 Per Cent    |
| Dog 1           | 30.7            | 22.3 (72.6)†    | 19.3 (62.9)     | 14.7 (47.9)     | 20.7 (67.4)     | 24 (78.2)       |
| Dog 2           | 37.7            | 20.0 (74.3)     | 21.3 (56.5)     | 12.0 (31.8)     | 22.7 (60.2)     | 27.5 (72.9)     |
| Dog 3           | 25.7            | 4.9 (19.1)      | 2.7 (10.5)      | 2.0 (7.8)       | 11.3 (44.0)     | 16.7 (63.0)     |
| Dog 4           | 29.3            | 20.3 (69.3)     | 10.3 (35.2)     | 4.9 (16.7)      | 9.2 (31.4)      | 18.3 (62.5)     |
| Dog 5           | 9.3             | 6.6 (69.5)      | 3.5 (36.8)      | 2.2 (23.2)      | 9.9 (104.2)     | 10.7 (112.6)    |
| Dog 6           | 9.8             | 6.6 (67.3)      | 6.2 (63.3)      | 3.2 (32.7)      | 5.7 (38.2)      | 9.6 (95.0)      |
| **MEAN**        | 23.8            | 14.8 (62.0)     | 10.6 (44.2)     | 6.5 (26.7)      | 13.9 (60.9)     | 17.8 (81.5)     |
| SD              | 11.6            | 9.9 (21.2)      | 8.0 (20.7)      | 5.5 (14.0)      | 6.8 (24.8)      | 7.1 (19.8)      |
| SE              | 4.7             | 4.1 (8.6)       | 3.3 (8.4)       | 2.2 (5.7)       | 2.8 (10.1)      | 2.9 (8.1)       |

* Each rate represents a mean of three values.
† The numbers in brackets represent flow rates as percentages of the thiopental value in the same dog.
Fig. 2. Effects of time on mucociliary flow in six dog tracheas at 1.2 per cent end-tidal halothane. Each triangle represents a mean of three measured values. Each line connects values for one dog.

Discussion

Mucus is produced by tracheobronchial goblet cells and mucous glands and swept by cilia up to the larynx, where it is swal-
lowed or coughed up. This process clears inhaled organisms and particles from the lungs. The mucus consists of a surface gel layer, underneath which is a more liquid sol layer in which the cilia beat. The tips of the cilia propel the gel layer upwards during the forward stroke. As the mucus streams upward, the total cross-sectional area of the Airways diminishes, and absorption takes place from the sol layer to maintain a constant depth of 5 μm. Clearance can be impaired by increase or reduction in the volume or viscosity of secretions, or by reduction in ciliary beat, or both.

Since hydration, body temperature, inspired oxygen or carbon dioxide, inspired temperature, and humidity, and inflation of an endotracheal tube cuff affect mucociliary flow, each was controlled during this study. Water deprivation reduces mucociliary flow by increasing the viscosity of secretions. Mucociliary flow varies directly with body or mucosal temperature over a range of 32–42°C. Since high concentrations of oxygen in the inhaled air reduce flow, inspired oxygen was maintained at 25% per cent in nitrogen. To avoid impairment of flow produced by high carbon dioxide concentrations, arterial carbon dioxide was maintained at 30 torr. Inhalation of dry gas slows mucous flow4,9 by thickening mucus and eventually stopping ciliary beat. Inhaled water vapor was delivered at more than 30 mg/kg, and at temperatures between 32 and 35°C. Over this range mucous flow does not vary.10 The presence of an inflated endotracheal tube cuff slows tracheal flow in dogs over a 1–2 hour period.12 This effect is not seen with an uncuffed tube,13 nor with the partially deflated cuff used in this study.

In women undergoing gynecologic surgery, ventilation with clinical concentrations of halothane from a circle absorber circuit has been found to stop mucociliary flow in the trachea in 90 minutes.14 However, the patients reported in this study received antisialogogue premedication, a cuffed endotracheal tube was used, and inspired water vapor content would have been 16.6 mg/kg at the top of the endotracheal tube. In contrast, the present study shows that when the above-mentioned factors are controlled, halothane reversibly slows but does not stop mucous flow.

Mucous flow can be reduced by an alteration in mucous viscosity or volume, by a reduction in ciliary beat frequency or efficiency, or by both mechanisms. The effect of anesthesia on sputum viscosity or volume has not been determined. A reduction in sputum volume seems unlikely, in that secretions are seen in the trachea during general anesthesia with halothane,15 and secretions continued to be swept into the pharynx and endotracheal tube in this study. Excessive secretions could overload the ciliary apparatus and reduce clearance. A more likely explanation for the observed decrease in mucociliary flow is depression of ciliary beat by halothane. Xinn and co-workers found a dose-dependent reversible depression of ciliary beat in the protozoan Tetrahymena pyriformis by inhalation anesthetics, including halothane,14 in doses comparable to those used in the present study. Cilia are morphologically the same throughout the animal kingdom.

If depression of mucociliary clearance in the trachea reflects slow clearance distally in the lungs, a correlation between depressed clearance during general anesthesia and postoperative atelectasis and bronchopneumonia could be expected, due to retention of mucus and organisms in distal airways. This would apply especially to the patient with chronic bronchitis in whom excessive secretions and organisms are already present. No such correlation has been proven. Previous studies have confirmed the importance of pre-existing respiratory disease in the etiology of postoperative respiratory complications, but have shown no difference in incidence between patients given general and those given spinal anesthesia.16,17 However, a recent study has shown 5% per cent mortality from respiratory failure in patients who had chronic pulmonary disease after general anesthesia, compared with no death in those given spinal or epidural anesthesia, who had comparable surgical procedures.18

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References

Obstetrical Anesthesia

PLACENTAL BARRIER TO NEUROMUSCULAR BLOCKERS The authors report data obtained in 18 women undergoing elective cesarean section at term. Anesthesia was accomplished by the administration of thiopental followed by succinylcholine, tracheal intubation, and ventilation with 50 per cent nitrous oxide-oxygen. Tagged 14C-dimethylulbocurarine (14C-dime) was injected intravenously 2, 4, 6, and 10 minutes before clamping of the umbilical cord at delivery. Maternal and umbilical blood samples were obtained for determination of total 14C activity. The highest concentration in maternal-vein blood was found in 2 minutes; by 4 minutes, this concentration had decreased by 50 per cent. The highest concentration in umbilical-vein blood was seen at 6 minutes, and corresponded to 12 per cent of the maternal venous concentration at that time. The authors suggest that "these results strengthen further the assumption that the human placental barrier is not absolute for the passage of the non-depolarizing neuromuscular blocking agents." They also state that it might be wise to omit this drug prior to delivery if fetal distress is suspected. (Kivalo I, Saarikoski S: Placental transfer of 14C-dimethylulbocurarine during cesarean section. Br J Anaesth 48:239–242, 1976.)