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Mucociliary Flow in the Trachea during Anesthesia with Enflurane, Ether, Nitrous Oxide, and Morphine

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Tracheal mucociliary flow rates in dogs were measured with a radioactive droplet technique during thiopental anesthesia, and subsequently during enflurane, ether, and nitrous oxide–morphine anesthesia on different occasions. Enflurane, at 0.6, 1.2, 1.8 MAC, produced a dose-dependent, reversible depression of mucociliary flow equal to that previously reported for halothane. Nitrous oxide–halothane and nitrous oxide–morphine depressed mucociliary flow to the same extent as halothane at equivalent MAC levels. Ether did not depress mucociliary flow significantly from the thiopental control at any MAC level. (Key words: Lung, trachea, cilia; Lung, trachea, mucus; Anesthetics, volatile, halothane; Anesthetics, volatile, diethyl ether; Anesthetics, volatile, enflurane; Anesthetics, gases, nitrous oxide; Anesthetics, intravenous, morphine.)

HALOTHANE produces a dose-dependent reversible depression of tracheal mucociliary flow.[1] This report contains our findings of the effects of enflurane, ether, nitrous oxide, and morphine on tracheal mucociliary flow.

Method

We measured tracheal mucociliary flow in six healthy hounds by a radioactive droplet method previously described.[1] The conditions of the present study were identical to those of the prior study except for the anesthetic drugs investigated. After three control measurements had been obtained during thiopental anesthesia, 1.2 MAC end-tidal anesthetic concentration was established, and flow measured. Anesthetic dose was changed sequentially to 1.8, 2.4, 1.2, and 0.6 MAC, and flow measured at each level after 15 minutes. This sequence was followed on separate occasions in each dog for enflurane and ether. Anesthetic concentrations were measured with an infrared analyzer. On a further occasion, after measuring flow at 1.2 MAC end-tidal halothane, 0.4 MAC nitrous oxide (75 per cent) was substituted for nitrogen, 75 per cent, giving 1.6 MAC total, and flows measured. Then the halothane dose was decreased to 0.8 MAC to maintain 1.2 MAC total. Finally, halothane was discontinued, 0.5 MAC morphine (6 mg/kg) was administered intravenously, and flows were measured after 30 minutes of ventilation with nitrous oxide, 0.4 MAC, giving a total of 0.9 MAC. Inspired oxygen concentration throughout was 25 per cent.

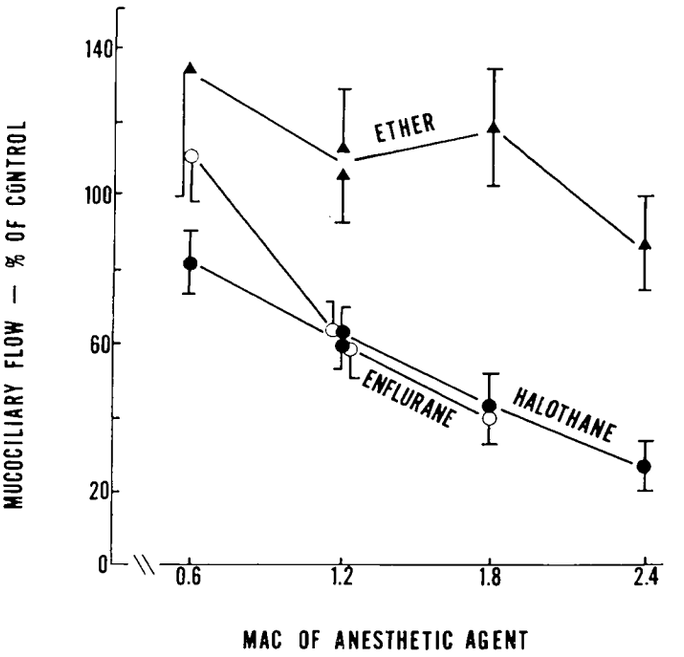

FIG 1. Effects of various MAC levels of halothane, enflurane, and ether on mucociliary flow rates in dog tracheas. Each value is a mean ± SE expressed as a percentage of the thiopental control.

Results

Mucociliary flow rates ranged from 16 to 29.9 mm/min during thiopental anesthesia, with a mean of 22.4 ± 0.8 mm/min. This is comparable to the 23.8 mm/min found previously in these dogs.[1] The coefficient of variation of the triplicate measurements was 22 per cent. All subsequent flows are normalized to a percentage of the control thiopental value for each dog on each occasion. Mean flow slowed from 59 to 40 per cent of control as end-tidal enflurane increased from 1.2 to 1.8 MAC (table 1). Cardiovascular depression did not permit study at 2.4 MAC enflurane. At 1.2 MAC, flow returned to 63 per cent of control, not significantly different from the previous value.

Flow rates during ether anesthesia were not different from control at any level. Comparison by Studentized Range Test revealed no differences

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TABLE 1. Tracheal Mucociliary Flow Rates with Ether and Enflurane as Percentages of Thiopental Controls*

	1.2 MAC		1.8 MAC		2.4 MAC		1.2 MAC		0.6 MAC	
	Ether	Enflurane	Ether	Enflurane	Ether	Enflurane	Ether	Enflurane	Ether	Enflurane
Dog 1	102.6	65.6	86.9	60.1	78.8	—	138.9	70.8	—	119.8
Dog 2	81.2	23.0	89.2	8.1	52.1	—	63.9	31.2	97.2	—
Dog 3	108.1	55.9	113.2	38.2	51.1	—	99.2	58.4	98.7	—
Dog 4	163.5	82.0	190.9	47.9	145.2	—	182.2	83.9	210.1	126.4
Dog 5	85.0	47.4	121.7	45.1	91.3	—	94.6	49.8	—	88.8
Dog 6	89.4	79.0	102.8	42.3	94.5	—	92.9	85.5	—	—
MEAN	105.0	58.8	117.5	40.3	85.5	—	112.0	63.3	135.3	111.7
SD	30.5	22.0	38.4	17.4	34.7	—	41.9	21.0	64.8	20.0
SE	12.5	9.0	15.7	7.1	14.2	—	17.1	8.6	37.4	11.6

* Each rate is the mean of three values.

between flows during enflurane and those previously reported for halothane at any MAC level, but a difference between each and ether at every level. Regression analysis of mucociliary flow as percentage of control versus MAC level showed a correlation coefficient of 0.73 for enflurane, significant at $P < 0.01$. The regression line was not significantly different from that of halothane in slope or elevation (fig. 1). Ether dose did not correlate with mucociliary flow. The flow of 62 ± 9 per cent of control produced by addition of 0.4 MAC nitrous oxide to 1.2 MAC halothane was not significantly different from the 77 ± 14 per cent produced by 1.2 MAC halothane alone. The combination of 0.8 MAC halothane and 0.4 MAC nitrous oxide gave flows of 84 ± 10 per cent of control, again not significantly different from 1.2 MAC halothane values. The addition of morphine, 0.5 MAC, to nitrous oxide, 0.4 MAC, gave flows of 70 ± 17 per cent of control, equal to the effect of 1.2 MAC halothane, but the effect varied among individual dogs (table 2).

Discussion

Mucociliary flow rates in the dog and in man during barbiturate anesthesia are comparable. Measured by the same bronchofiberscopic technique, mean tracheal mucous velocity is 7.7 mm/min in patients anesthetized with thiopental,[2] and 7.0 mm/min in dogs anesthetized with pentobarbital or thiamylal.[3] However, mean tracheal mucous velocity is 20 mm/min in awake man.[4] Thus, our control values in the dog during thiopental anesthesia should represent a decrease from the awake state.

TABLE 2. Tracheal Mucociliary Flow Rates with Halothane, Nitrous Oxide, and Morphine as Percentages of Thiopental Controls*

	1.2 MAC Halothane	1.2 MAC Halothane 0.8 Nitrous Oxide 0.4	1.6 MAC Halothane 1.2 Nitrous Oxide 0.4	0.9 MAC Morphine 0.5 Nitrous Oxide 0.4
Dog 1	78.6	60.5	33.1	39.8
Dog 2	77.9	68.6	60.5	44.2
Dog 3	73.1	118.1	63.8	108.1
Dog 4	87.4	61.0	55.4	46.3
Dog 5	52.3	92.3	60.0	136.6
Dog 6	92.6	105.4	98.5	42.6
MEAN	77.0	84.3	61.9	69.6
SD	14.0	24.5	21.0	41.9
SE	5.7	10.0	8.6	17.1

* Each rate is the mean of three values.

Why should ether depress mucociliary flow less than halothane and enflurane? Flow may be decreased by a decrease in mucous production, an increase or decrease in viscosity, or a slowing of ciliary beat.[5] These may be affected separately or in combination. The effects of anesthetic agents on secretion and viscosity of mucus are unknown. In a study of patients anesthetized with halothane, Lichtiger and colleagues found "excessive" secretions in the trachea in the presence of decreased flow, suggesting continuing production in the face of ineffective removal.[2] This would argue for a reduction in ciliary beat. The higher flows with ether could be explained by a stimulatory effect on secretion in the face of maintained or enhanced ciliary beat. Although in the protozoan the effect of ether is to depress ciliary beat,[6] this could be balanced in animals by sympathetic stimulation. In the dog, ether anesthesia induces a dose-dependent increase in circulating epinephrine,[7] whereas halothane does not.[8] In man, an increase in plasma norepinephrine rather than epinephrine occurs during ether anesthesia.[9] β- and β_2-adrenergic agents have been shown in animals and in man to increase production of mucus, ciliary beat rate, and flow of mucus.[10–14] Morphine slows mucociliary clearance in cats at a minimum dose of 0.5 mg/kg, subcutaneously.[15] The mechanism is unknown. The dose of 6 mg/kg (0.5 MAC) in this study is equivalent to about 1.2 mg/kg in man.‡

The clinical implications of this work depend on the balance of secretion production and removal. An impaired removal during halothane or enflurane anesthesia might not be a disadvantage if it were

‡ Fraioli RL: Unpublished observation.

paralleled by a decrease in production of mucus. On the other hand, if secretion production is maintained or increased, this could lead to plugging of distal airways, and subsequent atelectasis. The maintenance of mucous flow at a higher MAC level with ether suggests an advantage for ether, unless it is accompanied by a disproportionate stimulation of mucous production.

The reversibility of depression of mucous flow during halothane or enflurane anesthesia suggests that mucous clearance would be restored postoperatively unless other factors supervened. This is borne out by a pilot study of mucociliary lung clearance postoperatively in man.[16] In patients undergoing peripheral surgical operations, clearance of radiopaque tantalum powder from the airways was complete in 48 hours, whereas in 14 of 18 patients after abdominal operations clearance was delayed as long as six days. An initial delay in clearance and pooling of tantalum at six hours was followed at 18 hours by radiologically obvious atelectasis. Perhaps impaired mucous clearance, in association with the loss in lung volume seen after abdominal operations, led to the observed atelectasis.

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