

Performance of Lungs and Bronchi During Inhalation Anesthesia

Frank J. Colgan, M.D.*

The influence of five inhalation anesthetics on lung function and bronchial caliber was determined in dogs during undisturbed spontaneous respiration. Both changes in transpulmonary pressure and changes in smooth muscle tone induced by anesthetics affected the performance of lungs and bronchi.

Dynamic lung compliance and bronchial distensibility increased significantly during halothane anesthesia without appreciable alteration of the transpulmonary pressure gradient, indicating that halothane reduces bronchomotor tone. Bronchi were less distensible and lung compliance fell during cyclopropane anesthesia suggesting an increase in bronchomotor tone. Changes in lung compliance and bronchial distensibility were minor during ether, methoxyflurane and trichlorethylene anesthesia.

Alterations in lung compliance reverted spontaneously during emergence from all anesthetics. With the exception of ether, a positive correlation existed between lung compliance and bronchial distensibility during anesthesia. Deep ether and cyclopropane anesthesia were found to afford some protection against bronchoconstriction and the decrease in lung compliance following intravenous histamine.

THIS study was undertaken to determine the effect of inhalation anesthetics on lung function and bronchial caliber during undisturbed spontaneous respiration in the dog. Respiratory parameters known to influence the mechanical behavior of the lung including respiratory flow rates, airway resistance, tidal

volume and transpulmonary pressure gradients were measured throughout the anesthetic experience. Dynamic lung compliance measurements allowed undisturbed breathing, and changes in bronchial caliber were recorded by direct measurements with an intrabronchial probe.

The effects of ether, cyclopropane, halothane, trichlorethylene and methoxyflurane were determined on the above parameters. In addition, intravenous histamine, a potent bronchoconstrictor, was given before, during anesthesia and during emergence to determine if any anesthetic agent alters the effect of histamine on compliance and bronchial caliber.

Method

Thirty-four unmedicated dogs, weighing 15 to 25 kg. were lightly anesthetized with 20 mg./kg. of intravenous pentobarbital and placed in the supine position. A double lumen bronchial catheter with a cylindrically-shaped recording probe was passed through a no. 9 Jackson bronchoscope under direct vision into a secondary bronchus of the right lower lobe (fig. 1). The catheter was attached to a Grass PT-5 pressure transducer which is particularly suited for recording changes in gas volume.¹ When the probe was snugged into a bronchus, the thin rubber sleeve comprising the circumference of the cylinder became responsive to changes in bronchial transmural pressure. Alterations in caliber of the bronchus which occur during respiration cause changes in the volume of the recording probe. The larger volume of the transducer reservoir compared to the volume of gas rhythmically displaced from the bronchial probe during a single respiratory cycle, effectively produced an adiabatic and isothermal system during the periods of changing gas compression.² This system was not isothermal, however, for longer pe-

* Associate Professor of Anesthesiology, University of Rochester School of Medicine and Dentistry and Senior Associate Anesthesiologist, Strong Memorial Hospital, Rochester, New York.

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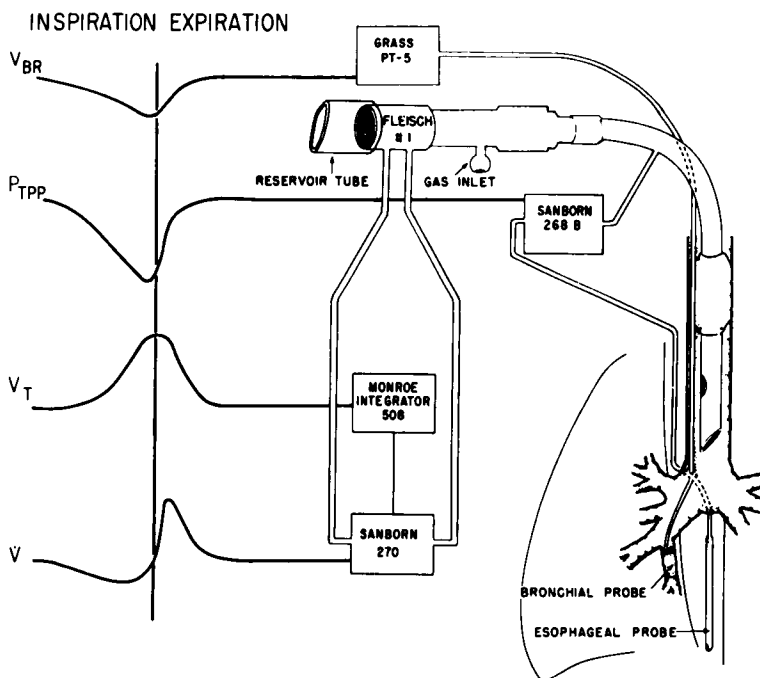


FIG. 1. Schematic diagram of recording method. V_{BR} , volume of isolated bronchial segment; P_{TPP} , transpulmonary pressure.

riods, since small changes in temperature around the transducer occurred during the course of a prolonged anesthetic—changing the temperature of the gas within the reservoir and affecting the base line of the tracing. Changes in bronchomotor tone were evident as changes in the base line of the tracing at end-expiration over short periods of time, as following the intravenous injection of a drug. An esophageal balloon was placed in the lower third of the esophagus and balanced against airway pressure to record transpulmonary pressure. A Fleish no. 1 pneumotachometer was attached to an endotracheal tube to measure air flow and the signal then integrated electrically to record tidal volume. Oxygen, which acted as a carrier gas for anesthetic gases, was admitted at twice the minute volume between the endotracheal tube and the pneumotachometer.

Continuous tracings of bronchial caliber, transpulmonary pressure, tidal volume and flow rate were made with a Sanborn four-channel recorder and computations made from tracings taken at a speed of 50 mm./second during spontaneous respiration.

All efforts were directed toward achieving as near normal spontaneous respiration as pos-

sible so as not to mechanically interfere with the response of the lung. An endotracheal tube of as large bore as possible was used as well as the Ayres T-piece technique for administering anesthesia so as to minimize airway resistance. Dynamic lung compliance measurements were expressed as the ratio of inspired volume to the difference between transpulmonary pressure at the beginning of inspiration (no flow), and expressed as liters per centimeter of water ($\Delta V/\Delta P_2$ in figure 2).

Mean airway resistance was expressed as a ratio of the change in transpulmonary pressure to the change in air flow occurring between points of equal lung volume during inspiration and expiration (fig. 2). Measurements were made when the inspiratory flow rate reached 0.15 liter/second.

Bronchial distensibility was determined as the ratio of the change in cross-sectional area of the isolated segment of bronchus to the original cross-sectional area per unit change in transpulmonary pressure ($\Delta A/A \times 100/\text{cm. of water}$). The change in volume of the isolated segment was measured during a centimeter of water increase in the transpulmonary pressure gradient (fig. 2). Since the length of the

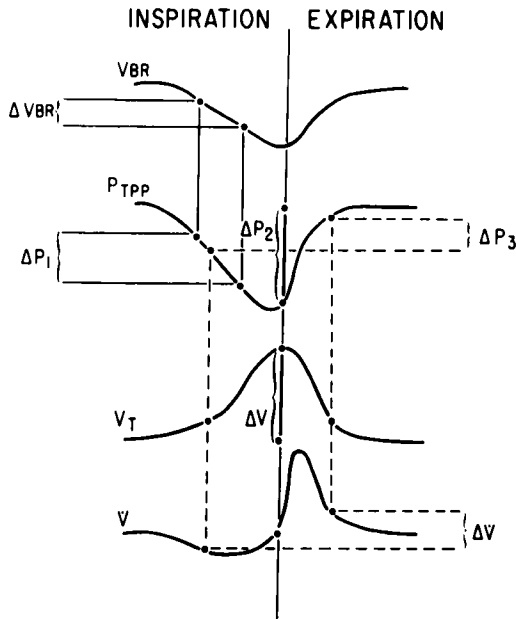


FIG. 2. Ratio used in computing bronchial distensibility: $\Delta V_{BR}/\Delta P_1$, dynamic lung compliance: $\Delta V/\Delta P_2$, and mean airway resistance: $\Delta P_3/\Delta V$.

isolated bronchial segment does not change, any change in volume of the segment may be considered a change in the cross-sectional area. Details of computing change in bronchial volume and calibration of the probe are described elsewhere.³ Since bronchial distensibility decreases at pressures further from the resting transpulmonary pressure, all measurements of bronchial volume changes during the course of an anesthetic were made over the same absolute pressure gradient.

Recordings of bronchial caliber, transpulmonary pressure, tidal volume and respiratory flow rate were made during the light pentobarbital anesthesia. Histamine (0.015 mg./kg.) was then given intravenously to produce bronchoconstriction and the decrease in bronchial caliber and lung compliance determined. After return of all parameters to a steady state, an anesthetic gas was added to the inspired oxygen. Response to histamine was again evaluated during deep anesthesia and during emergence. Dogs receiving cyclopropane were maintained at end-expiratory cyclopropane

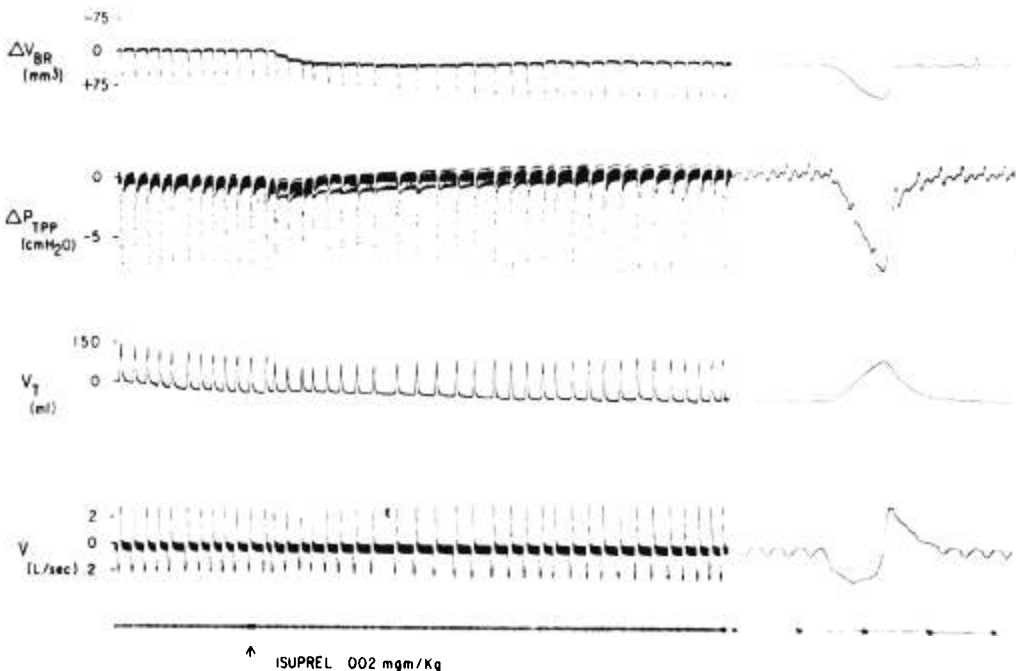


FIG. 3. Bronchodilation and changes in transpulmonary pressure, tidal volume and air flow resulting from intravenous isoproterenol (Isuprel).

TABLE 1. Respiratory Parameters Before (A), During Deep Anesthesia (B), and Emergence (C) (Mean Values)

		V _T (ml.)	Resp. Rate (per min.)	Peak $\dot{V}_{insp.}$ (l./sec.)	Peak $\dot{V}_{exp.}$ (l./sec.)	Duration Insp. (sec.)	Duration Exp. (sec.)	Resistance Mean (cm. H ₂ O/l./sec.)
Ether	A	180	9	0.30	0.51	1.1	0.8	2.4
	B	84	22	0.16	0.27	0.8	0.6	2.7
	C	155	22	0.25	0.44	1.1	0.6	2.3
Halothane	A	247	7	0.23	0.57	1.6	1.0	3.0
	B	234	5	0.20	0.49	1.5	0.9	2.6
	C	280	6	0.25	0.65	1.8	1.0	2.5
Cyclopropane	A	252	10	0.34	0.58	1.2	1.0	2.2
	B	195	6	0.20	0.48	1.4	0.8	2.5
	C	251	18	0.32	0.61	1.1	0.9	2.6
Methoxyflurane	A	285	7	0.32	0.60	1.3	1.2	4.5
	B	210	6	0.27	0.27	1.2	0.9	4.6
	C	278	8	0.27	0.31	1.4	1.4	4.4
Trichlorethylene	A	230	7	0.22	0.49	1.5	0.9	4.9
	B	101	14	0.18	0.26	0.9	0.6	4.5
	C	185	11	0.21	0.44	1.2	0.8	3.9

levels of 17–33 mg. per cent determined with the Scholander "quick" analyzer described by Linde and Price.⁴ Ether was given until electroencephalographic level 4 was achieved. Trichlorethylene or 2.5 per cent halothane was given for a minimum of 30 minutes and methoxyflurane via a fully-opened Ohio no. 8 vaporizer for one hour before measurements were taken. Isoproterenol (0.002 mg./kg.) was given at the end of each experiment to confirm the capability of the bronchus under study to dilate (fig. 3).

Results

The effects of inhalation anesthetics on the mechanical profile of respiration are summarized in table 1. All anesthetics produced a decrease in tidal volume during deep anesthesia. The respiratory rate doubled with both ether and trichlorethylene, but slowed with halothane, cyclopropane, and methoxyflurane. No significant change in mean airway resistance occurred during the administration of any anesthetic when measured at the same flow rate, yet peak inspiratory flow rates were reduced during deep anesthesia with all agents.

The ratio of the duration or time of inspiration to expiration (T_i/T_e) for all agents

ranged from 1.00 to 1.75. Measurements were made from levels of light pentobarbital anesthesia to deep levels of inhalation anesthesia. In spite of the doubling of the respiratory rate with ether and trichlorethylene, the ratio of inspiration to expiration remained essentially unchanged. Deep halothane anesthesia also produced no change in the ratio. The ratio rose from 1.20 to 1.75 during deep cyclopropane, and from 1.08 to 1.33 during deep methoxyflurane anesthesia.

Compliance and Bronchial Distensibility. During halothane anesthesia bronchial distensibility increased 4 per cent per cm. of water, and was associated with a 30 per cent increase in lung compliance (table 2). During emergence, these values returned toward pre-anesthetic levels. Bronchial distensibility decreased in the group of dogs receiving ether anesthesia, but in spite of the markedly decreased mean tidal volume and increase in respiratory rate, lung compliance changed little during anesthesia but increased 10 per cent during emergence. Bronchi were less distensible during inhalation of cyclopropane and lung compliance decreased 14 per cent during deep anesthesia, in spite of only a modest decrease in tidal exchange. During trichlor-

TABLE 2. Bronchial Distensibility and Lung Compliance Before (A), During Deep Anesthesia (B), and Emergence (C) Mean values

		Bronchial Distensibility (ΔA/A × 100/cm. H ₂ O)	Lung Compliance (l./cm. H ₂ O)	Control Compliance (%)
Ether 6 dogs	A	9	0.056	
	B	5	0.059	+ 4.7
	C	5	0.062	+10.2
Halothane 7 dogs	A	6	0.059	
	B	10	0.077	+30.1*
	C	8	0.058	- 1.6
Cyclopropane 9 dogs	A	10	0.057	
	B	6	0.049	-14.0*
	C	7	0.052	- 8.2
Methoxyflurane 6 dogs	A	6	0.066	
	B	5	0.062	- 6.7
	C	5	0.065	- 0.8
Trichlorethylene 6 dogs	A	4	0.049	
	B	5	0.054	+10.2
	C	5	0.048	- 2.9

* P < 0.01.

ethylene anesthesia, compliance increased 10 per cent without an appreciable change in bronchial distensibility. Methoxyflurane produced no significant changes in either bronchial caliber or lung compliance.

A positive correlation was apparent between bronchial distensibility and dynamic lung compliance, except during ether anesthesia. Changes in lung compliance during deep anesthesia, whether an increase or decrease, reverted toward preanesthetic values upon withdrawal of the anesthetic, with the exception of ether. Compliance continued to increase upon withdrawing ether.

Transpulmonary Pressure. Mean values of end-expiratory transpulmonary pressure during anesthesia were essentially unchanged from control values (fig. 4). During emergence from ether, methoxyflurane, and trichlorethylene, however, a slightly more negative resting transpulmonary pressure was maintained. Only during the emergence from ether anesthesia was the transpulmonary pressure gradient consistently more negative both at the resting and peak inspiratory levels.

Effect of Histamine During Anesthesia. Under light pentobarbital anesthesia, before inhalation agents were administered, histamine produced mean decreases in lung compliance of 27 to 38 per cent and decreases in bronchial caliber of 13 to 21 per cent in the five groups of dogs tested (fig. 5). During deep ether, histamine reduced compliance by only 6 per cent, and bronchial caliber was reduced 9 per cent. A significant attenuation was also noted during cyclopropane anesthesia. Decreases in compliance and bronchial caliber exceeded control values following histamine given during deep trichlorethylene anesthesia. Little or no change from control values occurred during halothane or methoxyflurane anesthesia.

Discussion

Bronchial Caliber and Distensibility During Anesthesia. Bronchial caliber and distensibility responded to both changes in transmural pressure and bronchial smooth muscle tone during anesthesia. A marked decrease in bronchial caliber was noted with cyclopropane, ether, and trichlorethylene whenever the induction was "crowded" with too high a concentration. Most of the decrease in caliber could be accounted for by the less negative resting transpulmonary and bronchial transmural pressure gradients, effecting a reduction in caliber. Bucking, tachypnea and a reduced tidal exchange accompanied the reduction in caliber producing a situation similar to the so-called tight-chest syndrome. These gross changes in caliber did not recur when high blood levels of anesthetic agents were gradually reached. No shift in the resting transpulmonary pressure or transpulmonary gradient occurred during deep anesthesia, with any agent and observed changes in bronchial distensibility were presumed to be due to alteration of bronchomotor tone.

Anesthetics are known to exert a direct action on bronchial⁵ smooth muscle. When exposed to ether, bronchial smooth muscle slices dilate and ether in dogs produces significant increases in plasma epinephrine and norepinephrine,^{6,7} the former being a potent bronchodilator. The observed increases in plasma catecholamines exceeded concentrations which *in vitro* are known to influence smooth muscle

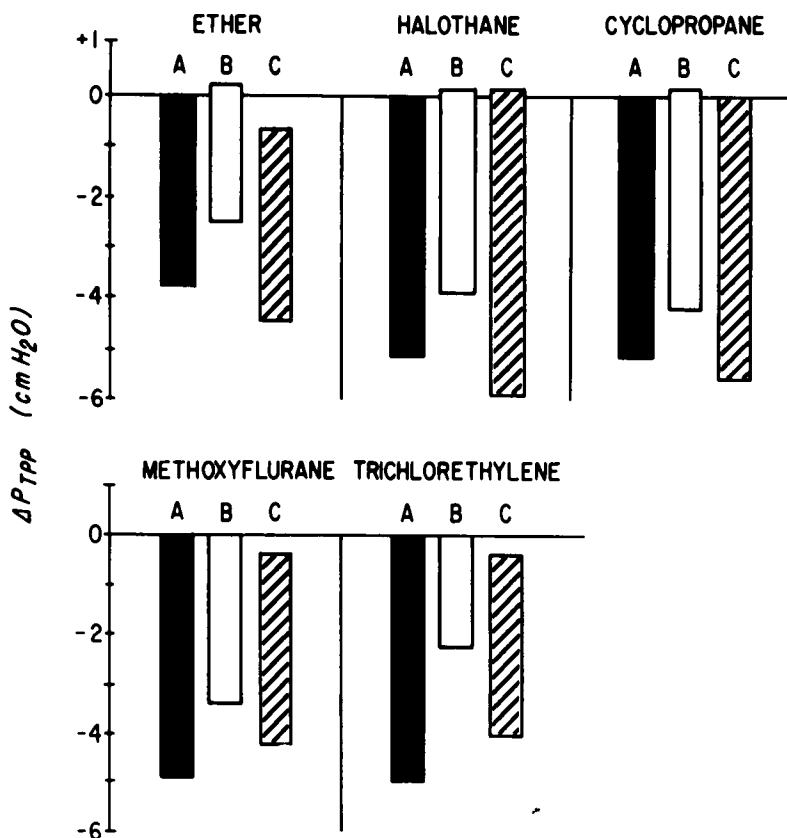


FIG. 4. Mean inspiratory transpulmonary pressure ranges before (A), during (B), and after (C) anesthesia.

tone.⁸ Thus ether has been shown to have a direct relaxing effect on bronchial smooth muscle and to increase sympathetic excitation of which bronchial relaxation is a component.

During deep ether anesthesia, our dogs showed a reduction in bronchial distensibility which was an unexpected finding. It is believed that the markedly reduced tidal volume

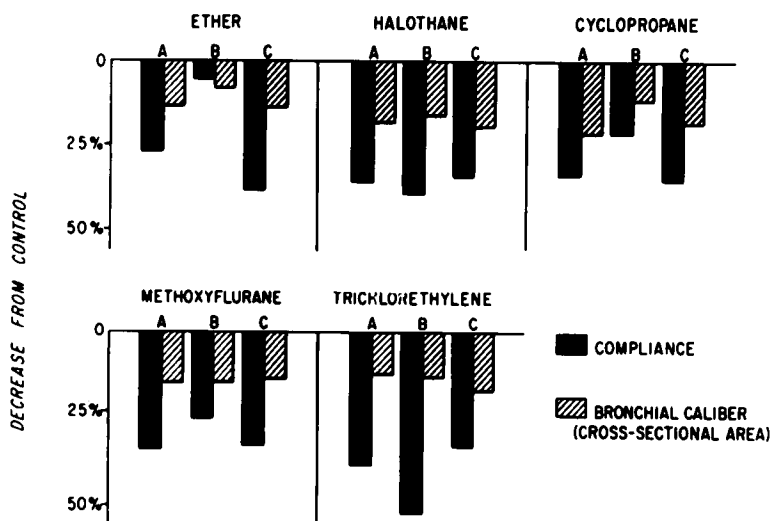


FIG. 5. Effect of histamine (0.015 mg./kg.) on compliance and bronchial caliber, before (A), during (B), and after (C) anesthesia.

associated with a respiratory rate of 22 per minute, may have dampened the response of the catheter-transducer system and accounted for some of the apparent decrease in distensibility. During emergence from ether, however, the transpulmonary pressure gradient was consistently more negative both at the resting and peak inspiratory levels. This shift in the transpulmonary pressure gradient toward more negative values promotes an overall increase in bronchial caliber, FRC and lung compliance. Since bronchial distensibility decreases with increase in the FRC,^{9, 10} the observed decrease in bronchial distensibility following ether anesthesia may in part be due to this. Changes in compliance during deep ether were negligible, but a small increase occurred during emergence. Thus, in spite of both experimental and clinical evidence to the contrary, no evidence of a reduction in bronchomotor tone occurred during deep ether anesthesia; the slight increase in compliance during emergence is explainable on a more negative shift in the transpulmonary pressure gradient favoring an increase in the FRC.

Neither trichlorethylene or methoxyflurane anesthesia had any significant effect on bronchial distensibility or lung compliance.

Cyclopropane, unlike ether, produces only a slight increase in plasma epinephrine in the dog; and sympathoadrenal activation is not considered an essential homeostatic mechanism in the dog.⁶ In addition, cyclopropane causes bronchoconstriction when applied directly to bronchial slices.⁵ Our dogs showed a significant fall in lung compliance and bronchial distensibility during deep cyclopropane anesthesia, adding evidence to the clinical impression that cyclopropane increases bronchomotor tone.

Although the direct effect of halothane on bronchial smooth muscle is not known, clinical experience has proved it to be a valuable anesthetic for patients with bronchospastic disease.¹¹ Our experience with halothane in dogs supports this impression since halothane produced a highly significant increase in compliance and bronchial distensibility during anesthesia, suggesting that a significant decrease in bronchomotor tone occurs. A decrease in bronchomotor tone allows the lung to be more easily distracted during inspiration favoring

spontaneous recruitment of functional lung tissue.³

Lung Compliance During Anesthesia. With the exception of ether, a positive correlation exists between bronchial distensibility and dynamic lung compliance. Our data indicate that a progressive fall in compliance does not necessarily occur during the anesthetic period. Rather it suggests that compliance of the lung increases or decreases in a characteristic way with each anesthetic agent, reflecting constantly the changes in airway smooth muscle tone. Tracheal caliber is known to change with changes in smooth muscle tone,¹² while constriction of both the larger airways³ and alveolar duct sphincters¹³ are associated with a reduction in lung compliance. Kahn has even suggested that smooth muscle tone within alveolar walls also plays a significant role in altering lung compliance.¹⁴

Whether decreases in lung compliance following increases in smooth muscle tone may also represent closure of areas of functioning lung tissue or coincide with a reduction of the FRC without closure of air spaces has not been determined. Yet changes in compliance in the dog,³ or vital capacity in man,^{15, 16} following changes in bronchomotor tone are quite readily reversed spontaneously. In the present study when compliance was reduced during anesthesia, return toward preanesthetic values occurred promptly with spontaneous respiration alone suggesting that atelectasis would be an unlikely cause of the decrease in compliance during anesthesia.

Effect of Histamine During Anesthesia. The data indicate that deep ether attenuates the bronchoconstrictive effect of histamine, exerting a protective effect on the lungs and bronchi and is in keeping with the experimental findings of others. Waugh and Greene found that deep ether anesthesia offers significant protection against anaphylactic shock and believed that catecholamine release associated with ether was an important factor in producing protection.¹⁷

Deep cyclopropane anesthesia in our dogs also attenuated the effect of histamine but to a lesser degree than ether. Both of these agents are known to be associated with rising levels of serum catecholamines in the dog.^{9, 7} Small amounts of epinephrine are known to

reduce the effect of histamine on bronchi both in man^{15, 16} and dogs.¹⁸ We believe that the presence of elevated plasma catecholamines in the blood caused by ether and cyclopropane may be responsible for reducing the response to histamine during anesthesia. In contrast, halothane did not attenuate the response to histamine and this agent characteristically does not elevate serum catecholamine.⁶

Summary and Conclusions

The effects of five inhalation anesthetics on lung function and bronchial distensibility were determined on 34 dogs. The behavior of lungs and bronchi during anesthesia reflect physically-induced changes in pressure across the lungs as well as alterations in autonomic function.

Halothane reduced bronchial smooth muscle tone as evidenced by an increase in bronchial distensibility and dynamic lung compliance during anesthesia. Deep cyclopropane anesthesia made bronchi less distensible and significantly reduced lung compliance. Bronchi were also less distensible during ether anesthesia but no significant change in compliance was noted. Methoxyflurane and trichlorethylene had little effect on bronchi and lung compliance.

Changes in compliance occurring during deep anesthesia were spontaneously reversible during emergence; no evidence of a progressive fall in compliance during anesthesia was obtained.

The characteristic decreases in lung compliance and bronchial caliber resulting from intravenous histamine is attenuated only during deep ether and cyclopropane anesthesia. It is suggested that elevated catecholamines in the blood produced by these agents may counter the action of histamine.

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