

## Ventilatory Compensation for Continuous Inspiratory Resistive and Elastic Loads during Halothane Anesthesia in Humans

Carol A. Moote, M.D., F.R.C.P.(C),\* Richard L. Knill, M.D., F.R.C.P.(C),† Jane Clement, R.N.‡

Inspiratory mechanical loads were applied to the airway continuously for 5 min in healthy young adult volunteers maintained in a near steady-state of halothane anesthesia 1.1 MAC. The loads, both flow resistive and elastic in nature, had been selected to reduce the first loaded tidal volume approximately 10, 30, or 50%—these being designated “small,” “medium,” and “large” loads, respectively. The actual magnitudes of resistive load were  $8 \pm 1$ ,  $21 \pm 3$ , and  $48 \pm 6$   $\text{cmH}_2\text{O} \cdot \text{l}^{-1} \cdot \text{s}$ , and of elastic load  $6 \pm 1$ ,  $18 \pm 1$ , and  $41 \pm 5$   $\text{cmH}_2\text{O} \cdot \text{l}^{-1}$  (means  $\pm$  SEM). All loads caused an immediate reduction of ventilation proportional to the size of the load. This was followed by a gradual recovery of ventilation toward control values over approximately 2 min and then nearly stable ventilation for the rest of the loading period. Respiratory frequency was unchanged throughout. At 5 min of loading, ventilation and  $\text{Pa}_{\text{CO}_2}$  had been nearly steady for 3 min and  $\text{O}_2$  uptake and  $\text{CO}_2$  output at the airway were unchanged from control, suggesting the establishment of a near steady respiratory state. With the small and medium loads of both types, ventilation and  $\text{Pa}_{\text{CO}_2}$  in this near steady-state were not detectably different from control. With the large loads, however, ventilation was significantly reduced and  $\text{Pa}_{\text{CO}_2}$  slightly increased. The end-expiratory position of the chest wall and the relative contributions of the rib cage and abdomen–diaphragm to ventilation, as estimated by anteroposterior chest wall magnetometers, were not consistently altered by any load. The small elastic loads reduced the “effective” intrinsic elastance at the end of the loading period. Loading did not increase the ratio of dead space to tidal volume ( $V_D/V_T$ ) or the alveolar–arterial oxygen tension difference ( $P(A-a)_{\text{O}_2}$ ). It is concluded that in healthy young humans anesthetized with halothane, steady-state compensation for inspiratory flow-resistive loads up to about  $21 \text{ cmH}_2\text{O} \cdot \text{l}^{-1} \cdot \text{s}$  and inspiratory elastic loads up to  $18 \text{ cmH}_2\text{O} \cdot \text{l}^{-1}$  is virtually complete. Ventilatory compensation for these loads is due to nonchemical mechanisms, which in the case of small elastic loads reduce intrinsic elastance and thereby improve the performance of the ventilatory pump. (Key words: Anesthetics, volatile: halothane. Measurement techniques: magnetometer. Ventilation: pattern; resistance.)

ADDED MECHANICAL IMPEDANCES to breathing, ventilatory loads, occur frequently during clinical anesthesia. Common examples are soft-tissue obstruction of the upper airway, a kinked or narrow endotracheal tube, and the weight of the abdominal contents in the Trendelenburg

position. Studies of responses to experimental loads added to the airway of anesthetized humans suggest that the first loaded breath is better defended than in the awake state,<sup>1,2</sup> but that the subsequent restoration of ventilation toward control values is less,<sup>1,3</sup> with the overall response often incomplete.<sup>3,4</sup> However, these studies were conducted without control of anesthetic depth and surgical stimulation during continuous applications of loads and without ascertaining reestablishment of the steady respiratory state. In addition, the effects on arterial carbon dioxide and oxygen tensions were not determined.

The purpose of this study was to describe the steady-state ventilatory and gas exchange responses to a range of inspiratory resistive and elastic loads during a near-constant level of halothane anesthesia in healthy humans. A secondary purpose was to examine the roles of chemical stimuli and ventilatory pump performance in the responses to such loads. The roles of these factors were investigated by monitoring arterial blood gases and chest-wall motion during periods of loading and by determining the “effective” intrinsic elastance of the respiratory system at the beginning and end of applications of elastic loads.

The subjects were studied during anesthesia alone, in the absence of awake controls, because the effects of mechanical loads on respiratory function are clearly different during anesthesia,<sup>1,4</sup> and our purpose was to further characterize the particular responses of the anesthetized state.

### Methods

The protocol was approved by the Health Sciences Standing Committee on Human Research of the University of Western Ontario. Informed, written consent was obtained from all volunteers.

We studied 25 healthy unpremedicated subjects in the supine position. Anesthesia was induced with halothane in oxygen, in three cases supplemented with intravenous thiopental in a dose not exceeding 100 mg. The trachea was intubated with an 8.5-mm I.D. cuffed tube. Anesthesia was then maintained with halothane alone, the inspired concentration being adjusted to maintain the end-tidal concentration close to 1.1 MAC corrected for age.<sup>5</sup> Fifteen min or more were allowed for equilibration of tissues to this end-tidal concentration. Before testing, we ensured stability of ventilation and end-tidal  $\text{CO}_2$  concentration ( $\pm 0.2\%$ ) for at least 2 min.

\* Lecturer, Department of Anesthesia, University Hospital and University of Western Ontario, London, Canada.

† Professor, Department of Anesthesia, University Hospital and University of Western Ontario, London, Canada.

‡ Research Assistant.

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Address reprint requests to Dr. Moote: Department of Anesthesia, University Hospital, P.O. Box 5339, Postal Station A, London, Ontario, Canada N6A 5A5.

Before and throughout the tests, the subjects inhaled from a nonrebreathing circuit incorporating a Rudolph® No. 1400 nonrebreathing valve. The inspiratory resistance of the circuit was  $3.0 \text{ cmH}_2\text{O} \cdot \text{l}^{-1} \cdot \text{s}$  measured at an oxygen flow rate of  $30 \text{ l} \cdot \text{min}^{-1}$ . The fractional inspired  $\text{O}_2$  concentration ( $\text{FI}_{\text{O}_2}$ ) was kept greater than 0.95. No surgery was performed.

The resistive loads or resistors consisted of plastic tubes of various sizes, most of which contained spongy foam rubber. The flow resistance of each was nearly constant between flow rates of 5 and  $60 \text{ l} \cdot \text{min}^{-1}$ . For testing, each resistive load was incorporated in the inspiratory limb of the anesthetic circuit in parallel with open tubing that acted as a "bypass." To apply the load, the "bypass" was occluded with a clamp (fig. 1).

The elastic loads were rigid cylinders and drums of various sizes. Each was connected with the inspiratory limb of the anesthetic circuit by a short piece of wide-bore rigid tubing. To apply these loads, the circuit was obstructed just upstream to the load connection with a "loading valve" (fig. 1). For continuous application, the valve was closed throughout each inspiration and opened briefly during expiration in order to replenish the load with fresh gas and maintain the load constant from breath to breath. Closing and opening of the valve was effected by a solenoid triggered by the flow signal of the pneumotachograph.

We tested the response of each subject to one flow-resistive and one elastic load, each of which had been selected to reduce the first loaded tidal volume of that subject approximately 10%, 30%, or 50%. These sizes of load were designated "small," "medium," and "large," respectively. The loads were selected for initial effect rather than for absolute magnitude in an attempt to standardize the sizes of load for individual variation in intrinsic resistance and elastance. §

The actual magnitude of each load was determined from measurements made on the first loaded breath. The magnitude of each added resistive load was the measured

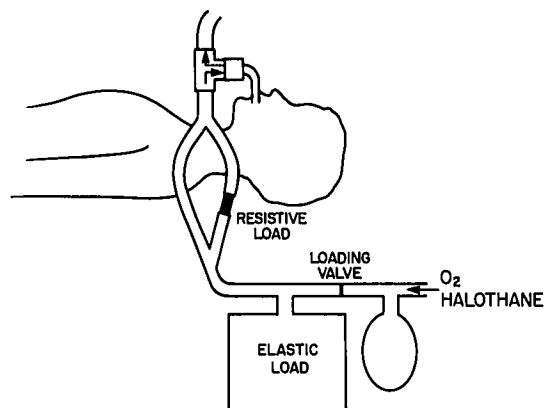


FIG. 1. Experimental set-up showing the anesthetic circuit and loads. The resistive load was situated in the inspiratory limb in parallel with a "bypass." The elastic load was connected to the inspiratory limb downstream from a "loading valve." The resistive load was applied by clamping the "bypass," the elastic load by closing the "loading valve" during the inspiratory portion of each breath.

pressure difference across the resistor at the peak inspiratory flow rate of the first loaded breath divided by that flow rate. The size of each added elastic load was the reduction of pressure within the cylinder or drum at the end of the first loaded inspiration divided by the volume of that breath.

Each load was applied at the end of an expiration and maintained throughout inspirations continuously for at least 5 min. This period of time was one that initial tests had indicated would be sufficient for the reestablishment of the steady respiratory state. To maintain a near-constant level of anesthesia on application of each load, we purged each loading device with an appropriate concentration of halothane just before its application. To maintain a constant level of anesthesia throughout the loading period, we adjusted the inspired halothane concentration as necessary to keep end-tidal halothane near control. To check on the anesthetic depth before and at the end of the loading period, we measured the arterial halothane tension. To check on the respiratory state at the same times, we measured the rates of oxygen uptake and  $\text{CO}_2$  output.

The responses to loads were assessed in several ways. Inspired ventilation, airway pressure, and end-tidal  $\text{CO}_2$  were measured and recorded continuously on a Hewlett-Packard® 7758B recorder. Arterial blood gases were determined for the control period and for 1, 2, and 5 min of loading. Rib cage and abdomen-diaphragm contributions to ventilation were estimated by chest wall magnetometry in the control period at the beginning and end of the loading period and immediately after load removal. Intrinsic elastance was derived from measurements of airway pressure and tidal volume on application and removal of each elastic load. In addition, the ratio of dead

§ With application of an elastic load, the initial loaded tidal volume depends on the intrinsic elastance.<sup>6</sup> Expressed as per cent of the control tidal volume, this initial loaded volume is given by  $\frac{E}{E + \Delta E} \times 100$ ,

where E represents intrinsic elastance of the respiratory system and  $\Delta E$  the added elastic load. If among individual subjects loads are selected such that the initial tidal volume is a constant proportion of the control tidal volume, then  $\Delta E$  will be a fixed proportion of E and the added load will bear a constant relationship with the intrinsic elastance. With application of a resistive load, the initial loaded tidal volume depends primarily on intrinsic resistance (and resistance of the experimental circuit) in a similar fashion but, in addition, on the respiratory flow pattern and the intrinsic elastance.<sup>6</sup> To the extent that these latter factors determine the initial loaded tidal volume and vary among individuals, the relationship of resistive load to intrinsic resistance would be less consistent.

space to tidal volume ( $V_D/V_T$ ) and the alveolar-arterial oxygen tension difference ( $P(A-a)O_2$ ) were calculated for the control period and 5 min of loading.

Ventilation was measured with a Fleisch pneumotachograph head (#2) incorporated in the inspiratory limb of the anesthetic circuit and calibrated as in our previous studies.<sup>7</sup> Accuracy of the pneumotachograph in the presence of our loads was confirmed in tests in which a calibrated Harvard animal ventilator or a calibrated syringe produced known flows and volumes through the loads. Values of ventilation for the control period were calculated from measurements of 30-s periods, values for the first loaded breath and first breath after removal of each load from measurements of those breaths alone and values at other times from measurements of at least three consecutive breaths. Ventilatory volumes were corrected for body surface area and expressed at body temperature and ambient pressure and saturated.

Airway pressure was measured through a side port of the endotracheal tube connector with a calibrated Vali-dyne® pressure transducer.

Inhaled and exhaled gases were sampled close to the nonbreathing valve; mixed exhaled gas, from a mixing bag added to the expiratory limb of the circuit. The oxygen, carbon dioxide, and halothane concentrations were measured with a Perkin-Elmer® 1100 mass spectrometer, calibrated, and converted to tensions as before.<sup>7</sup> Oxygen uptake and  $CO_2$  output were derived from the measurements of inspired and mixed exhaled gas concentrations, together with ventilation recorded over a 1-min period. These values were expressed at standard temperature and pressure, dry.

Arterial blood gases were measured with a Radiometer® Copenhagen BMS III system calibrated with specialty gases. Arterial halothane was determined by a multiple gas phase equilibrium technique as previously described.<sup>8</sup>

To assess the position and motion of the rib cage and abdomen-diaphragm and estimate their volume contributions to ventilation, we placed pairs of magnetometer coils anteroposteriorly across the rib cage and abdomen at the level of the nipples and just above the umbilicus. The signals, denoting AP diameters, were calibrated to represent volume change of the rib cage and abdomen-diaphragm, with the use of the Konno and Mead isovolume maneuver technique.<sup>9</sup> Isovolume maneuvers were achieved at different lung volumes by allowing the subjects to make spontaneous ventilatory efforts against an airway occlusion at functional residual capacity (FRC) and at two known increments of volume above FRC. These increments of volume were produced with a large calibrated syringe. Individual tidal volumes of interest were then partitioned into their rib cage and abdomen-diaphragm portions by finding the volumes represented by differ-

ences in the end-expiratory and end-inspiratory magnetometer signals of each chest-wall part. Magnetometer loops of simultaneous rib cage and abdominal movement throughout a single breath were recorded on a Hewlett-Packard® 7045A X-Y recorder.

The "effective" intrinsic elastance<sup>6</sup> was estimated to gain further insight into pump characteristics and performance during the applications of elastic loads. Intrinsic elastance is a measure of the stiffness of the respiratory system during active inspiration and thus the efficiency with which inspiratory neuromuscular drive is transformed to inspired volume. It is estimated from the negative slope of the linear relationship between end-inspiratory airway pressure and inspired volume ( $\Delta P/\Delta V$ ) observed when airway pressure and tidal volume are varied by applying inspiratory elastic loads at a constant inspiratory drive. In this study, it was calculated for the beginning of the loading period from the differences in pressure and volume observed between a control breath and the subsequent first loaded breath, and for the end of the loading period, from the differences observed between the last loaded breath and the subsequent first unloaded breath. It was also determined for the control period, with the use of the airway pressures and tidal volumes of a control breath and a complete airway occlusion.

The  $V_D/V_T$  was derived with the use of the Riley modification of the Bohr equation. The alveolar oxygen tension needed for determining the alveolar to arterial oxygen difference was estimated with the use of the conventional Benzinger equation.<sup>10</sup>

The data were assessed statistically with a computerized analysis of the variance with the use of Tukey's honestly significant test for multiple comparisons.<sup>11</sup> A *P* value of 0.05 or less was considered significant.

## Results

The studies of six subjects were excluded from analysis because of incomplete application of the load ( $n = 2$ ), inadequate anesthesia during loading ( $n = 2$ ), mishandling of arterial blood ( $n = 1$ ), or potentially relevant neuromuscular disease (Kearn's-Sayre Syndrome) diagnosed subsequently ( $n = 1$ ). The studies of the remaining 19 subjects were accepted. They were eight men and 11 women with ages, heights, and weights of  $24 \pm 5$  yr,  $171 \pm 10$  cm, and  $70 \pm 15$  kg, respectively (means  $\pm$  SD).

The ventilatory effects of mechanical loads were due to changes in tidal volume. Respiratory frequency remained constant throughout. On the addition of each load, tidal volume decreased immediately in proportion to the size of the load (table 1). Ventilation then increased slowly and progressively over about 2 min to a level that remained nearly steady for the remainder of the loading

TABLE 1. Size of Load and Initial Effect

	Resistive Loads			Elastic Loads		
	n	Size (cmH <sub>2</sub> O · l <sup>-1</sup> · s)	Reduction of First Loaded V <sub>T</sub> (%)	n	Size (cmH <sub>2</sub> O · l <sup>-1</sup> )	Reduction of First Loaded V <sub>T</sub> (%)
Small	6	8 ± 1	11 ± 1	6	6 ± 1	13 ± 2
Medium	6	21 ± 3	26 ± 2	6	18 ± 1	36 ± 3
Large	7	48 ± 6	53 ± 2	6	41 ± 5	53 ± 3

Values are means ± SEM.

period (fig. 2). The removal of each load resulted in an immediate overshoot of ventilation (fig. 2), the magnitude of which related to the size of the load. Except in the case of large loads, the PaCO<sub>2</sub> values during loading were not detectably different from the control value (fig. 2). The patterns of response to flow-resistive and elastic loads were similar.

By 5 min of loading, ventilation and PaCO<sub>2</sub> had been nearly stable for 3 min. The O<sub>2</sub> uptake, CO<sub>2</sub> output, and arterial halothane tension were all similar to the control values (table 2). In the presence of the small and medium loads, ventilation and PaCO<sub>2</sub> at 5 min of loading were not detectably different from control values (table 3). In the presence of large loads, however, ventilation was decreased and PaCO<sub>2</sub> values increased.

The tidal volumes (both control and loaded) determined from the sums of magnetometer measurements of rib cage and abdomen-diaphragm contributions only approximated the pneumotachograph values of tidal volume (y = 0.89x + 24, n = 320, r = 0.89, SD from regression 35 ml, V<sub>T</sub> range 82 to 640 ml), suggesting the magnetometer measurements of chest-wall volume contributions

were not exact. The rib-cage ventilation, assessed by magnetometers, varied considerably among individuals and overall was not detectably altered by any load (fig. 3). Frequently, in the presence of a load, the rib-cage signal indicated inward retraction of the rib cage during early and mid-inspiration but then outward movement towards end-inspiration. However, at other times with added loads, the rib-cage signal suggested rib cage expansion throughout inspiration. The end-expiratory configuration of the chest wall, as reflected by the magnetometer signals, was not altered by any load.

The values of intrinsic elastance found on application of the elastic loads (table 4) were nearly identical to those found in the control period with the use of airway occlusion (34 ± 3 cmH<sub>2</sub>O · l<sup>-1</sup>). On removal of the small elastic loads, intrinsic elastance was reduced (table 4). With all loads considered, the magnitude of loading induced reduction of intrinsic elastance correlated inversely with the size of the load (r = -0.998 from the correlation of the proportionate reduction of elastance at the end of the loading period with the reduction of the first loaded tidal volume).

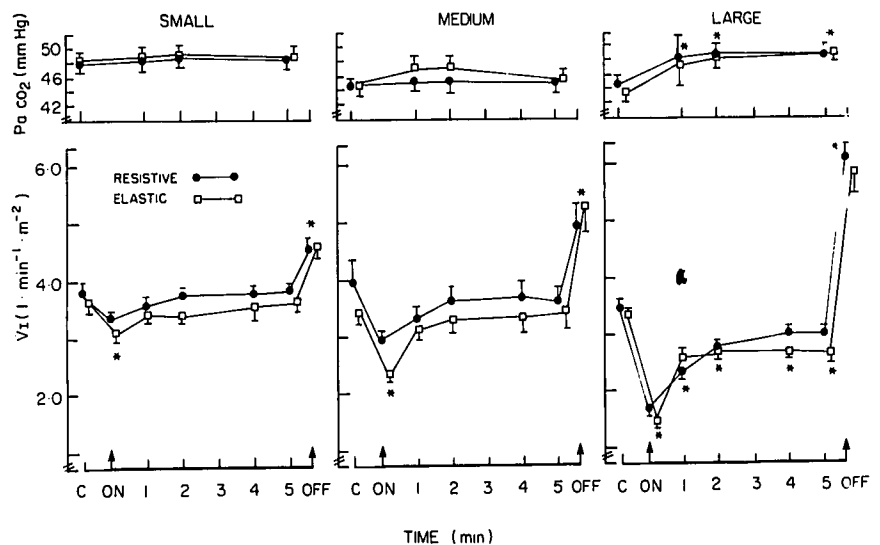


FIG. 2. Respiratory effects of small, medium, and large resistive and elastic loads. Values of PaCO<sub>2</sub> are shown for the control period and for three times during loading. Values of ventilation are depicted for the control period, for the first loaded and first unloaded breaths (ON and OFF), and three other times during the loading test. All values are means ± SEM. \* indicates significant difference from control for both types of load (P < 0.05).

TABLE 2. Steady-state Halothane Tension ( $P_{A_{HAl}}$ ),  $O_2$  Uptake ( $\dot{V}_{O_2}$ ), and  $CO_2$  Output ( $\dot{V}_{CO_2}$ )

	Resistive Loads				Elastic Loads			
	n	$P_{A_{HAl}}$ (mmHg)	$\dot{V}_{O_2}$ ( $l \cdot \text{min}^{-1}$ )	$\dot{V}_{CO_2}$ ( $l \cdot \text{min}^{-1}$ )	n	$P_{A_{HAl}}$ (mmHg)	$\dot{V}_{O_2}$ ( $l \cdot \text{min}^{-1}$ )	$\dot{V}_{CO_2}$ ( $l \cdot \text{min}^{-1}$ )
Small Control	6	$6.3 \pm 0.2$	$0.19 \pm 0.12$	$0.18 \pm 0.02$	6	$6.1 \pm 0.1$	$0.18 \pm 0.01$	$0.18 \pm 0.01$
Loaded		$6.1 \pm 0.3$	$0.18 \pm 0.02$	$0.18 \pm 0.02$		$6.1 \pm 0.3$	$0.20 \pm 0.02$	$0.18 \pm 0.01$
Medium Control	6	$6.2 \pm 0.2$	$0.21 \pm 0.03$	$0.20 \pm 0.01$	6	$6.2 \pm 0.2$	$0.17 \pm 0.01$	$0.18 \pm 0.01$
Loaded		$6.2 \pm 0.1$	$0.18 \pm 0.01$	$0.19 \pm 0.02$		$6.0 \pm 0.2$	$0.20 \pm 0.02$	$0.18 \pm 0.01$
Large Control	7	$6.2 \pm 0.2$	$0.19 \pm 0.02$	$0.15 \pm 0.02$	6	$6.4 \pm 0.2$	$0.22 \pm 0.06$	$0.13 \pm 0.02$
Loaded		$6.0 \pm 0.3$	$0.21 \pm 0.03$	$0.13 \pm 0.01$		$6.2 \pm 0.2$	$0.23 \pm 0.03$	$0.13 \pm 0.01$

Values are means  $\pm$  SEM.

The  $V_D/V_T$  and the  $P(A-a)_{O_2}$  difference were not detectably affected by any load, except for a small reduction in the  $V_D/V_T$  in the presence of the medium elastic loads (table 5).

### Discussion

In 1950, Beecher considered the adequacy of ventilation in anesthetized surgical patients breathing through smaller-than-usual endotracheal tubes that are, in essence, resistive loads.<sup>12</sup> He found that a tube of 7 mm I.D. did not increase  $P_{aCO_2}$  when compared with an unintubated upper airway. Later, Nunn and Ezi-Ashi studied the ventilatory responses of anesthetized patients exposed to a variety of experimental threshold and flow-resistive loads applied to inspiration and/or expiration for 2–7 min.<sup>3</sup> The responses to these loads generally developed slowly over 90 s and failed to restore ventilation completely to control values. Freedman and Campbell subsequently compared the ability of awake volunteers and of anesthe-

tized patients to tolerate a series of inspiratory resistive and elastic loads, each load being maintained for a 2-min period.<sup>4</sup> Overall, the results suggest that load compensation was poorer during anesthesia. More recently, Margaria *et al.*<sup>1</sup> studied the immediate ventilatory response to a series of inspiratory elastic loads in volunteers while awake and then anesthetized with thiopental. The reduction of ventilation on the first loaded breath was proportionately less during anesthesia, suggesting that the immediate compensation for added loads is better in the anesthetized state.

The primary purpose of the current study was to extend these observations by determining ventilatory and gas-exchange adjustments to both resistive and elastic inspiratory loads applied continuously until reestablishment of the steady respiratory state. To minimize experimental variables, all volunteers were young and healthy and all studies were conducted at a near-constant level of halothane anesthesia in the absence of surgical stimulation.

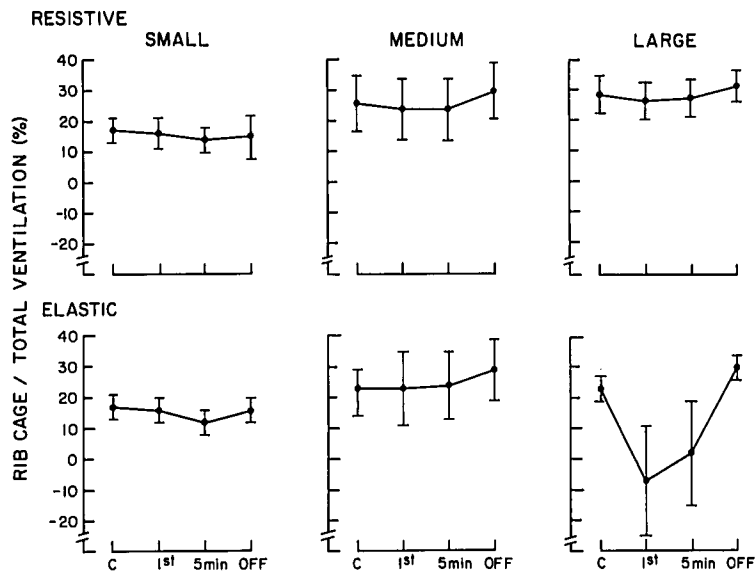
TABLE 3. Steady-state Ventilation and Arterial Carbon Dioxide Tension ( $P_{aCO_2}$ )

	Resistive Loads			Elastic Loads		
	n	Ventilation ( $l \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ )	$P_{aCO_2}$ (mmHg)	n	Ventilation ( $l \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ )	$P_{aCO_2}$ (mmHg)
Small Control	6	$3.8 \pm 0.2$	$48 \pm 1$	6	$3.8 \pm 0.2$	$48 \pm 2$
Loaded		$3.8 \pm 0.2$	$48 \pm 1$		$3.6 \pm 0.2$	$48 \pm 2$
Medium Control	6	$3.8 \pm 0.4$	$44 \pm 2$	6	$3.5 \pm 0.2$	$45 \pm 2$
Loaded		$3.6 \pm 0.2$	$45 \pm 2$		$3.4 \pm 0.3$	$45 \pm 2$
Large Control	7	$3.5 \pm 0.2$	$44 \pm 1$	6	$3.3 \pm 0.1$	$43 \pm 2$
Loaded		$3.0 \pm 0.1^*$	$48 \pm 1^*$		$2.6 \pm 0.1^*$	$48 \pm 1^*$

Values are means  $\pm$  SEM.

\* Significantly different from control ( $P < 0.05$ ).

FIG. 3. Rib-cage ventilation estimated by chest-wall magnetometers and expressed as a percentage of total chest-wall ventilation in the presence of loads. Values are depicted for the control period (C), the first loaded breath, 5 min of loading, and the breath immediately following load removal (OFF). All values are mean  $\pm$  SEM. Negative values represent paradoxical motion of the rib cage.



An attempt was made to standardize added loads for individual variation in intrinsic resistance and elastance by selecting sizes of load that produced similar reductions of tidal volume on the first loaded breath. $\S$

In keeping with previous findings, we observed that the immediate effect of an added inspiratory resistive or elastic load during anesthesia was less than what is found in the awake state (table 1).<sup>1,2</sup> The subsequent recovery of ventilation was comparatively slow, requiring about 2 min to reach a near steady level (fig. 2).<sup>3</sup> By 5 min of loading, ventilation and PaCO<sub>2</sub> had been nearly stable for 3 min (fig. 2), and oxygen uptake and CO<sub>2</sub> output were not detectably different from control (table 2), suggesting the establishment of a near steady respiratory state in the presence of loads.<sup>10,¶</sup> The major new observations relate to compensation in this steady state.

Steady-state compensation for both resistive and elastic inspiratory loads at 5 min of loading was related to the initial effect. For loads causing about a 30% reduction in the first loaded tidal volume (table 1), steady-state compensation was virtually complete, in that ventilation and PaCO<sub>2</sub> were not detectably different from the control values (table 3). For loads causing a 50% or more reduction of the first loaded tidal volume, compensation was clearly incomplete. The maximal tolerable loads in this

study corresponded to added resistances of about 21 cmH<sub>2</sub>O · l<sup>-1</sup> · s and added elastances of 18 cmH<sub>2</sub>O · l<sup>-1</sup>. Although these limits for short-term complete compensation are considerably less than those observed in awake humans,<sup>4</sup> they are nonetheless surprisingly good.

Our findings yield some insight into the mechanisms of this steady-state compensation during anesthesia. In general, mechanisms that defend ventilation in the face of mechanical loads can be classified into two types: those that act to stabilize the first loaded breath and those that act to progressively increase the inspiratory effort or the efficiency of the inspiratory effort on subsequent breaths.<sup>6,13</sup> Potential mechanisms operating on the first loaded breath are the passive elastance and resistance of the respiratory system together with the elastance-like and resistance-like effects of shortening respiratory muscles and of distortions of the respiratory system from its passive configuration. These factors can be quantified and considered together in terms of "effective" intrinsic elastance and resistance. The greater the values of "effective" elastance and resistance, the less the immediate effects of an inspiratory load. Potential mechanisms effecting compensation on subsequent breaths are: 1) increments in

¶ It might be expected that the added work of breathing associated with loads would increase oxygen uptake and CO<sub>2</sub> output above control values. However, the resting work of breathing during anesthesia has been estimated to consume only about 3% of the overall oxygen uptake and to generate a similar proportion of the CO<sub>2</sub> output.<sup>5</sup> Although the largest loads of this study may have doubled this percentage value, it is unlikely that such a magnitude of change would be detected by our measurement techniques.

TABLE 4. Intrinsic Elastance Determined with Elastic Loads (cmH<sub>2</sub>O · l<sup>-1</sup>)

	Load Application	Load Removal
Small	33 $\pm$ 6	20 $\pm$ 3*
Medium	36 $\pm$ 6	28 $\pm$ 7
Large	35 $\pm$ 4	33 $\pm$ 3

Values are means  $\pm$  SEM.

\* Significantly different from control ( $P < 0.05$ ).

TABLE 5. Steady-state Indices of Intrapulmonary Gas Exchange

	Resistive Loads			Elastic Loads		
	n	$V_D/V_T$ *	P(A-a) $O_2$ (mmHg)	n	$V_D/V_T$ *	P(A-a) $O_2$ (mmHg)
Small	6			6		
Control		$0.52 \pm 0.02$	$231 \pm 46$		$0.52 \pm 0.02$	$245 \pm 50$
Loaded		$0.51 \pm 0.01$	$239 \pm 48$		$0.50 \pm 0.02$	$256 \pm 43$
Medium	6			6		
Control		$0.45 \pm 0.02$	$230 \pm 31$		$0.47 \pm 0.02$	$239 \pm 36$
Loaded		$0.45 \pm 0.01$	$222 \pm 38$		$0.44 \pm 0.02$ †	$228 \pm 35$
Large	7			6		
Control		$0.53 \pm 0.05$	$243 \pm 28$		$0.55 \pm 0.06$	$233 \pm 11$
Loaded		$0.55 \pm 0.05$	$249 \pm 19$		$0.53 \pm 0.04$	$238 \pm 11$

Values are means  $\pm$  SEM.

$V_D/V_T$  = ratio of dead space to tidal volume; P(A-a) $O_2$  = alveolar-arterial oxygen tension difference.

\* Includes apparatus dead-space of 25 ml.

† Significantly different from control ( $P < 0.05$ ).

inspiratory drive secondary to behavioral, chemical, or mechanical stimuli, and 2) improvements in the transformation of inspiratory drive to ventilatory volume as a result of favorable changes in the operating characteristics of the ventilatory pump.

In our anesthetized volunteers, the calculated "effective" intrinsic elastance averaged  $34 \text{ cmH}_2\text{O} \cdot \text{l}^{-1}$ , in keeping with previous reports.<sup>1,2</sup> The "effective" intrinsic resistance, estimated only indirectly,\*\* averaged  $30 \text{ cmH}_2\text{O} \cdot \text{l}^{-1} \cdot \text{s}$ . These values are two or more times those reported for awake humans,<sup>1,6</sup> presumably because of the added passive elastance and resistance of the anesthetized state and perhaps also the added distortions of the active respiratory system during anesthesia.<sup>14</sup> These added impedances account for the greater stability of the first loaded breath during anesthesia.<sup>1,2</sup>

Among mechanisms that may have acted to increase inspiratory drive after the first loaded breath in our subjects, behavioral factors can be excluded because they obviously do not play a role during anesthesia. The only chemical stimulus that is effective in increasing inspiratory drive and thus could be acting in load compensation during halothane anesthesia is added  $\text{CO}_2$ .<sup>7</sup> In the early course of progressive compensation for small and medium loads, small and transient increases of  $\text{PaCO}_2$  may have played a role in increasing inspiratory drive, but this factor did not appear to contribute to the steady-state response (table 3). Steady-state compensation for these loads was

achieved without a detectable increase of  $\text{PaCO}_2$ , and removal of these loads resulted in an immediate overshoot of ventilation above control values despite  $\text{PaCO}_2$  values being unchanged from control values. In the presence of large loads, there was a modest increase of  $\text{PaCO}_2$  that persisted to the steady-state, suggesting a contribution of added  $\text{CO}_2$  to this response. However, steady-state compensation for the smaller loads must have involved some other load-compensating mechanism(s).

Another mechanism is suggested by our observation that small elastic loads substantially reduced intrinsic elastance by the end of the loading period. Medium elastic loads showed a trend toward doing the same (table 4).†† Because inspiratory times remained the same during all these measurements, this observation means that in relation to inspiratory neuromuscular drive, a larger tidal volume was obtained at the end of the loading period than at the outset. This implies that continuous loading with the smaller elastic loads caused an improvement in the performance of the ventilatory pump such that ventilatory pressures were more efficiently transformed to tidal volume. The time course of this improvement and the extent to which it contributed to compensation cannot be ascertained from our data.

The physiologic basis of such a mechanism of compensation is unclear. It could reflect a loading-induced progressive increase in intercostal muscle activity<sup>15</sup> acting to stabilize the rib cage against the potential distorting effects

\*\* Each value of intrinsic resistance was estimated from the proportionate reduction of tidal volume produced by each added resistance, the value of that resistance, the respiratory frequency, and an assumed value of effective elastance of  $34 \text{ cmH}_2\text{O} \cdot \text{l}^{-1}$ , using a general expression for quantifying loading responses.<sup>6</sup> This approach makes several simplifying assumptions including that of a regular sinusoidal pattern of ventilatory pressures. The value of anesthetic circuit, endotracheal tube, and connector resistance was subtracted.

†† The beneficial effect of a reduced intrinsic elastance at the end of the loading period might seem incompatible with the benefit of a high elastance on load application. However, a high elastance only reduces the relative effect of an added load on the first loaded breath. Because it is costly in terms of energy expended by ventilatory muscles, it is detrimental to subsequent increases in tidal volume produced by added inspiratory effort.

of loading<sup>16</sup> and of anesthesia itself.<sup>14</sup> Alternatively or in addition, it could represent a favorable change in the operating (force-length and force-velocity) characteristics of inspiratory muscles.<sup>6,13</sup> Our failure to detect with AP chest-wall magnetometers a loading-induced change in the relative rib cage contribution to ventilation (fig. 3) or a loading-related change in end-expiratory position of the chest wall does not necessarily exclude or support either possibility. Changes in configuration or motion of the chest wall or operating characteristics of inspiratory muscles could have occurred without being detected by this technique. Of interest was the finding that the magnitude of reduction of elastance produced during loading correlated inversely with the size of the load. This suggests an underlying mechanism whose activation is reduced or expression-impaired with increasing size of load.

Overall, the data indicate that in the presence of inspiratory loads of modest magnitude, compensation is achieved initially by virtue of high intrinsic resistance or elastance, and in the steady respiratory state by a mechanism or mechanisms that appear to operate independent of chemical stimuli. The nature of these latter mechanisms is unclear. However, in the case of elastic loads, they would seem to act, at least in part, by reducing intrinsic elastance and thus by improving the performance of the ventilatory pump. In the presence of larger loads, these mechanisms cannot and/or do not participate to the same relative extent, and as a result,  $P_{aCO_2}$  values increase and play a role in the steady-state response.

Before loading, values of  $P(A-a)O_2$  and  $V_D/V_T$  were typical of healthy subjects anesthetized with halothane.<sup>17,18</sup> During the steady-state of loading, there was no detectable difference in either variable, except for a small reduction in the  $V_D/V_T$  in the presence of medium elastic loads (table 5). We conclude that inspiratory loads of the magnitude and for the duration studied do not impair intrapulmonary gas exchange during light halothane anesthesia. Thus, whatever the mechanisms of the increased  $V_D/V_T$  and  $P(A-a)O_2$  associated with anesthesia itself, they appear to be insensitive to the effects of such loads.

Acute loads applied to the airway can be considered to simulate to some extent the mechanical effects of certain acute loads commonly encountered in clinical practice, such as those associated with soft-tissue obstruction of the upper airway or a narrow endotracheal tube. The ability of our subjects to compensate fully for inspiratory flow resistances up to  $21 \text{ cmH}_2\text{O} \cdot \text{l}^{-1} \cdot \text{s}$  supports the suggestion of Beecher and Nunn that the resistances of endotracheal tubes having 5–7 mm I. D. (approximately 18 and  $4 \text{ cmH}_2\text{O} \cdot \text{l}^{-1} \cdot \text{s}$ , respectively, measured at flow rates of  $30 \text{ l} \cdot \text{min}^{-1}$ ) should be well tolerated by spontaneously breathing anesthetized adults.<sup>3,12</sup> Nevertheless, it must be emphasized that our subjects were healthy young adults, anesthetized with halothane alone and exposed to

experimental loads for only 5 min. Extrapolation of these observations to other conditions may not be warranted.

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