

Collapsibility of the Upper Airway during Anesthesia with Isoflurane

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Background: The unprotected upper airway tends to obstruct during general anesthesia, yet its mechanical properties have not been studied in detail during this condition.

Methods: To study its collapsibility, pressure-flow relationships of the upper airway were obtained at three levels of anesthesia (end-tidal isoflurane = 1.2%, 0.8%, and 0.4%) in 16 subjects while supine and spontaneously breathing on nasal continuous positive airway pressure. At each level of anesthesia, mask pressure was transiently reduced from a pressure sufficient to abolish inspiratory flow limitation (11.8 ± 2.7 cm H₂O) to pressures resulting in variable degrees of flow limitation. The relation between mask pressure and maximal inspiratory flow was determined, and the critical pressure at which the airway occluded was recorded. The site of collapse was determined from simultaneous measurements of nasopharyngeal, oropharyngeal, and hypopharyngeal and esophageal pressures.

Results: The airway remained hypotonic (minimal or absent intramuscular genioglossus electromyogram activity) throughout each study. During flow-limited breaths, inspiratory flow decreased linearly with decreasing mask pressure ($r^2 = 0.86 \pm 0.17$), consistent with Starling resistor behavior. At end-tidal isoflurane of 1.2%, critical pressure was 1.1 ± 3.5 cm H₂O; at 0.4% it decreased to -0.2 ± 3.6 cm H₂O ($P < 0.05$), indicating decreased airway collapsibility. This decrease was associated with a decrease in end-expiratory esophageal pressure of 0.6 ± 0.9 cm H₂O ($P < 0.05$), suggesting an increased lung volume. Collapse occurred in the retropalatal region in 14 subjects and in the retrolingual region in 2 subjects, and did not change with anesthetic depth.

Conclusions: Isoflurane anesthesia is associated with decreased muscle activity and increased collapsibility of the upper airway. In this state it adopts the behavior of a Starling resistor. The decreased collapsibility observed with decreasing anesthetic depth was not a consequence of neuromuscular activity,

which was unchanged. Rather, it may be related to increased lung volume and its effect on airway wall longitudinal tension. The predominant site of collapse is the soft palate.

WHILE collapse of the unprotected upper airway is common during anesthesia, its mechanical properties during inhalational anesthesia have not been studied in detail. Anesthesia-induced loss of pharyngeal patency occurs because of a state-related preferential inhibition of upper airway neural and muscle activity.¹⁻³ The effect of this change is to alter the balance between dilating and collapsing forces in the upper airways toward collapse.⁴ During emergence from general anesthesia, a graded return of upper airway muscle activity is thought to be the primary mechanism responsible for the gradual return of upper airway patency. Studies in animals support this notion, showing a dose-dependent increase in genioglossus muscle activity⁵ and hypoglossal nerve activity² with decreasing anesthetic depth. Whether similar responses occur in anesthetized humans is unknown, as this has not been formally examined. It is notable, however, that Drummond⁵ failed to demonstrate any relation between genioglossus activity and airway patency in anesthetized human subjects. In the current study we measured the collapsibility of the upper airway in spontaneously breathing humans during inhalational anesthesia with isoflurane. Our purpose was to examine the site and mechanism of collapse and the influence on them of anesthetic depth.

Materials and Methods

Subject Selection

Sixteen subjects were recruited from those undergoing minor surgical procedures not involving the head or neck and suitable for general anesthesia administered *via* a facemask. Recruitment was independent of any known vulnerability to upper airway collapse (*e.g.*, obesity, snoring). Informed consent was obtained in writing from each subject prior to participating in the study, which was approved by the Hospital's Research Institutional Ethics Committee.

Lung Function Testing

Between 2 and 5 weeks after surgery, measurements were obtained of total lung capacity (body plethysmograph; Collins Inc., Braintree, MA), forced expiratory volume in 1 s (digital pneumotachograph, model 400VR; Hewlett Packard, Waltham, MA), and carbon monoxide diffusing capacity (model 1182; P.K. Morgan Ltd., Gillingham, United Kingdom).

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Subject Preparation

No premedication was administered. Standard monitoring was applied, and a vein was cannulated. Anesthesia was induced with intravenous propofol (1.5–2.0 mg/kg) and fentanyl (0.25 μ g/kg) maintained with isoflurane and nitrous oxide (66%) in oxygen, administered *via* a face-mask. After attaining a surgical depth of anesthesia, and once surgery had commenced, a four-sensor pressure transducer catheter (2.0-mm external diameter) was passed into the esophagus *via* the nares (Gaeltec CTO-4; Dunvegan, Isle of Skye, Scotland). The catheter was positioned to permit simultaneous measurement of pressure changes in the esophagus, hypopharynx, oropharynx, and nasopharynx. The oropharyngeal pressure (P_{op}) transducer was visualized through the mouth and positioned just below the soft palate. A transducer 5 cm above the P_{op} transducer measured nasopharyngeal pressure while transducers 5 and 20 cm below the P_{op} transducer measured hypopharyngeal and esophageal pressure (P_{es}), respectively. A second catheter was passed *via* the nares into the oropharynx for continuous monitoring of end-tidal carbon dioxide and end-tidal isoflurane (PetISO) levels (model 602, POET II; Criticare Systems, Waukesha, WI). Prior to each study, the transducers were calibrated simultaneously with five known pressures. Carbon dioxide and isoflurane were calibrated with three gases of known concentrations.

During surgery, intramuscular electrodes were inserted percutaneously to measure genioglossus electromyogram (EMGgg).⁶ Two 25-gauge needles, each containing two sterile 50- μ m nylon-coated, stainless steel, fine-wire electrodes (Stablohm 800B; California Fine Wire Company, Grover Beach, CA), were inserted midway between the symphysis menti and the hyoid bone to a depth of approximately 25 mm. Each needle was inserted approximately 0.5 cm lateral to the midline, angled slightly ventrally toward the mandible so as to position the recording electrodes close to the origin of the genioglossus. The two pairs of electrodes were referenced to a common ground, placed on the forehead. In addition, one wire from each pair was referenced to the common ground, thereby providing a third electromyogram signal. Each EMGgg signal was amplified, band-pass filtered (10–3,000 Hz, model 7P3; Grass Instruments, West Warwick, RI), full-wave rectified, and processed with leaky integrators with a time constant of 100 ms.

On completion of surgery, the facemask was removed, the mouth was occluded by adhesive tape, the head was carefully placed in a neutral position with lower cervical flexion and upper cervical extension (using a Shea headrest), and the patient was fitted with a chin strap and a tight-fitting nasal mask, *via* which anesthesia was maintained using isoflurane in oxygen delivered with a Bain circuit (fresh gas flow rate \geq 14 l/min). Connected in series to this circuit was an expiratory port (Whisper Swivel; Respironics, Murrysville, PA) and a bilevel pos-

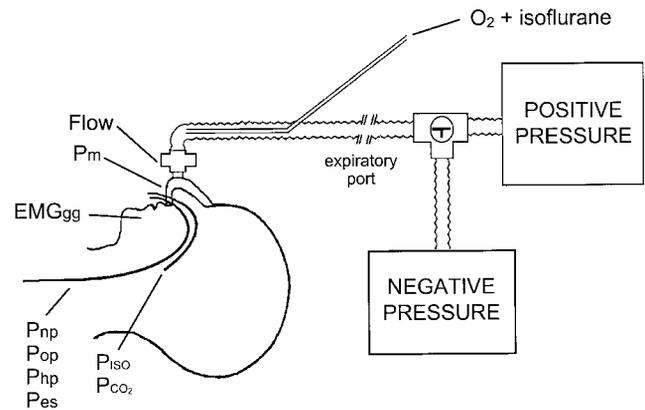


Fig. 1. Schematic representation of the experimental setup. Negative or positive pressures could be rapidly applied to the nasal mask of the anesthetized subject. P_m = mask pressure; P_{np} = nasopharyngeal pressure; P_{op} = oropharyngeal pressure; P_{hp} = hypopharyngeal pressure; P_{es} = esophageal pressure; P_{iso} = isoflurane concentration; P_{CO_2} = carbon dioxide concentration; EMGgg = genioglossus electromyogram.

itive pressure source (BiPAP; Respironics). This permitted a constant continuous positive airway pressure to be maintained using the ventilator's inspiratory positive airway pressure mode. It could also be abruptly reduced to a preset lower pressure by switching to the ventilator's expiratory positive airway pressure mode (fig. 1). Alternatively, a preset subatmospheric pressure could be rapidly applied by switching to a regulated vacuum source (model VFC204P; Fuji Electric Co., Tokyo, Japan). Air-flow was monitored with a pneumotachograph (Hewlett Packard 47303A; Waltham, MA) that had been calibrated with four known flows. Nasal mask pressure (P_m) was measured *via* a port in the mask by a pressure transducer (model 143PC, Micro Switch; Honeywell, Morristown, NJ) that had been calibrated simultaneously with the catheter-based pressure transducers.

Assessment of Upper Airway Function during General Anesthesia

Once the nasal mask had been fitted, a maintenance continuous positive airway pressure level was applied that was sufficient to abolish inspiratory flow limitation,^{7,8} and inspired isoflurane was adjusted to a PetISO of 1.2% in 100% oxygen. Once this level had been maintained for several minutes, airway pressure was rapidly changed (during early expiration) from the maintenance level to a lower pressure for five successive breaths before being changed back to the maintenance level (immediately following the fifth inspiratory effort; fig. 2). Following a recovery period, this procedure was repeated at a range of positive or negative airway pressures, including a pressure sufficient to cause complete airway collapse. The order of application of pressures was randomized. Once a sufficient number of measurements had been obtained at a stable level of PetISO, a square-wave negative pressure of 30 cm H₂O was ap-

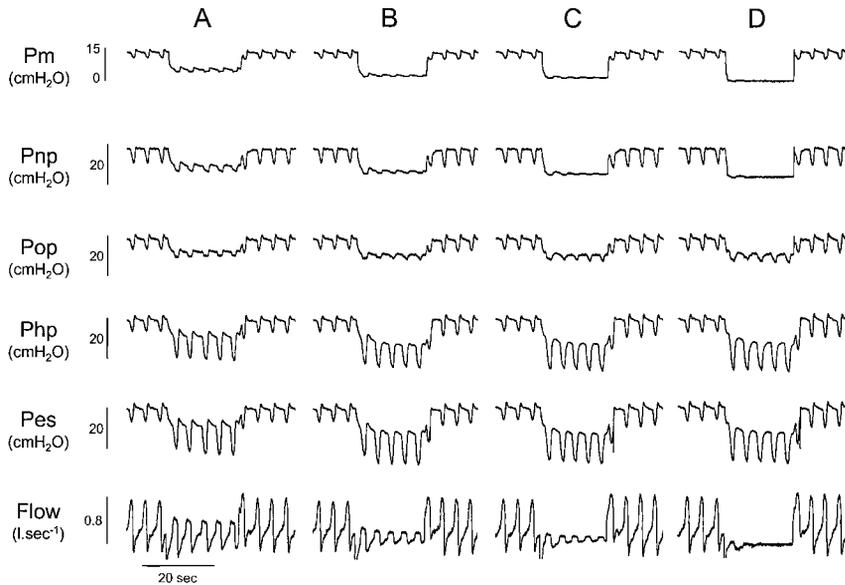


Fig. 2. Polygraph record in one subject at a stable plane of general anesthesia showing the responses when mask pressure was rapidly reduced from a maintenance pressure (approximately 14 cm H₂O) for five breaths and then returned to the maintenance pressure. This procedure was repeated at a range of positive or negative airway pressures, causing varying degrees of inspiratory flow limitation (a plateau in inspiratory flow while esophageal pressure decreased progressively, A–C; see also fig. 3), including a pressure sufficient to cause complete airway collapse (no inspiratory flow despite a changing esophageal pressure; D)). P_m = mask pressure; P_{np} = nasopharyngeal pressure; P_{op} = oropharyngeal pressure; P_{hp} = hypopharyngeal pressure; P_{es} = esophageal pressure.

plied to the airway during early expiration and maintained for a single inspiratory effort, following which airway pressure was returned to the maintenance level. All measurements, including the square-wave negative pressure, were performed at PetISO of 1.2%, 0.8%, and 0.4%. Immediately following measurements at PetISO of 0.4%, isoflurane administration was ceased, and the subject was allowed to emerge from anesthesia while breathing oxygen *via* the nasal mask at the maintenance pressure. The nasal mask and catheters were removed once the patient was sufficiently awake. EMGgg electrodes were maintained in place until the subject was able to voluntarily protrude the tongue and swallow.

All signals were digitally recorded continuously at 1,000 Hz on a Powerlab data acquisition and analysis system (model 16s; ADInstruments, Sydney, Australia).

Data Collection and Analysis

At each level of anesthesia, upper airway pressure-flow relations were derived as previously described for sleeping subjects.^{7–10} Briefly, with each reduction in P_m, the relation between inspiratory flow (Vi) and P_{es} was analyzed for each of the five consecutive breaths. When Vi reached a maximum level (Vi_{max}) and plateaued as P_{es} continued to decrease, flow limitation was considered to be present (fig. 3). For these flow-limited inspirations, Vi_{max} and P_m were averaged over breaths three to five of each sequence at each of the three levels of anesthesia. The relation between Vi_{max} and P_m was examined, and the least-squares linear regression equation was computed at each level of anesthesia. The regression equation was then solved for the P_m at which Vi_{max} became zero (P_{crit}). Measurements of peak inspiratory and expiratory amplitudes of the moving-time-averaged EMGgg signal, relative to electrical zero, were obtained during breaths at the maintenance pressure, during breaths

when P_m was reduced from the maintenance pressure, during application of the square-wave negative pressure, and during voluntary tongue protrusions and swallows. All measurements were expressed as percent change from baseline EMGgg value, which was defined as the average expiratory activity during breaths at the maintenance pressure at PetISO of 1.2%.

The region of upper airway collapse was determined from pressure changes measured during sequences in which P_m was decreased to a level sufficient to abolish Vi. Collapse of the velopharyngeal-retropalatal segment was indicated when P_{es} changes were transmitted to hypopharyngeal pressure and P_{op} but not nasopharyngeal pressure. Collapse of the oropharyngeal-retrolingual segment was indicated when P_{es} changes were transmitted to the hypopharyngeal pressure but not P_{op}.

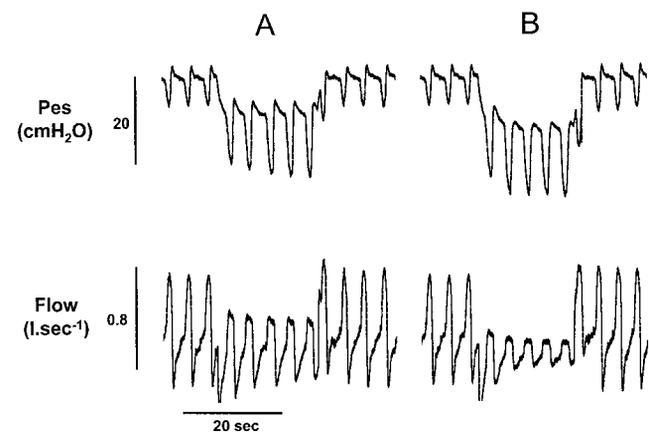


Fig. 3. Enlargement of polygraph record in figs. 2A and B demonstrating the phenomenon of inspiratory flow limitation (a plateau in inspiratory flow with continuing decrease in esophageal pressure). P_{es} = esophageal pressure.

Table 1. Anthropometric Data and Lung Function Tests

Subject	Sex	Age (yr)	Height (m)	Weight (kg)	BMI (kg/m ²)	TLC (% predicted)	FEV ₁ (% predicted)	D _L CO (% predicted)
1	M	35	1.72	82.8	27.9	108	119	106
2	F	40	1.67	63.6	22.7	110	125	107
3	F	50	1.71	110.0	37.4	99	108	88
4	M	52	1.66	78.0	28.3	109	106	116
5	M	51	1.68	74.9	26.6	121	128	129
6	M	36	1.78	84.5	26.7	96	98	92
7	M	54	1.71	77.3	26.5	112	105	120
8	M	50	1.85	81.0	23.7	135	128	131
9	M	30	1.74	91.0	29.9	120	96	119
10	M	45	1.90	131.0	36.5	124	105	122
11	M	47	1.89	94.6	26.6	85	99	98
12	M	64	1.80	88.8	27.3	78	82	87
13	M	37	1.68	77.6	27.3	100	97	100
14	M	32	1.77	74.0	23.5	106	114	100
15	M	56	1.76	106.0	34.4	78	87	84
16	M	36	1.69	78.5	27.6	96	108	98
Mean		45	1.75	87.1	28.3	105	107	106
SD		10	0.08	16.7	4.3	16	14	15

BMI = body mass index (weight/height²); TLC = total lung capacity; FEV₁ = forced expiratory volume in 1 s; D_LCO = carbon monoxide diffusing capacity.

Statistical Analysis

Comparison of each variable at each level of anesthesia was undertaken using a one-way repeated measures analysis of variance. Where significant differences were detected, a Bonferroni *post hoc* test was applied. $P < 0.05$ was considered significant. All results are reported as mean \pm SD.

Results

A total of 16 subjects, 14 males and 2 females, participated in the study. Lung volumes, spirometry, and carbon monoxide diffusing capacity were within normal predicted ranges for all subjects (table 1). Measurements of upper airway collapsibility were obtained at three levels of anesthesia in each subject. The depth of general anesthesia, as estimated from measurements of PetISO, was maintained very close to the three target levels ($1.18 \pm 0.08\%$, $0.78 \pm 0.06\%$, and $0.40 \pm 0.03\%$) and remained stable at each level of PetISO throughout any given series of measurements (coefficient of variation, $5.9 \pm 4.1\%$). The total time taken to complete the protocol was 33 ± 10 min. This included a period of 4 ± 2 min between each level of anesthesia, during which no measurements were made to allow for equilibration of PetISO. Once measurements were obtained at PetISO of 0.4%, anesthesia was discontinued and subjects were allowed to emerge breathing 100% oxygen. The time to first arousal from this point was 6 ± 4 min, at which time PetISO was $0.22 \pm 0.08\%$.

Upper Airway Behavior

For the group overall, a P_m of 11.8 ± 2.7 cm H₂O was sufficient to maintain airway patency and abolish inspiratory flow limitation. Figure 2 shows typical responses to

changes in P_m during general anesthesia in one subject. The degree of inspiratory flow limitation varied with upstream (mask) pressure (figs. 2A–C) when P_m was reduced sufficiently below the maintenance pressure. When P_m was reduced to equal or less than P_{crit} , complete upper airway obstruction occurred (fig. 2D).

On each occasion that P_m was reduced to a level sufficient to cause inspiratory flow limitation for five successive breaths, $V_{i,max}$ progressively decreased over the first two breaths before stabilizing between breaths three, four, and five (fig. 3). This pattern of change of $V_{i,max}$ was seen in all subjects during all sequences of flow-limited breaths. The averaged values from breaths three to five of each sequence were used in determining the relation of P_m to $V_{i,max}$ over the range of flow-limited breaths and thereby P_{crit} (see Methods).

At each level of anesthesia, $V_{i,max}$ was linearly related to P_m for flow-limited breaths (mean r^2 for all subjects = 0.86 ± 0.17 ; $P < 0.05$). This relation is shown for one subject in figure 4. Figure 5 shows the effect of anesthetic depth on the pressure at which flow became zero (P_{crit}) for all subjects. P_{crit} progressively decreased with decreasing depth of anesthesia (1.1 ± 3.5 , 0.8 ± 3.2 , and -0.2 ± 3.6 cm H₂O at PetISO of 1.2%, 0.8%, and 0.4%, respectively; $P < 0.05$), indicating a less collapsible upper airway. Relative to values at PetISO of 1.2%, end-expiratory P_{es} decreased by 0.4 ± 0.5 cm H₂O and 0.6 ± 0.9 cm H₂O at PetISO of 0.8% and 0.4%, respectively ($P < 0.05$).

Respiration-related phasic changes in EMGgg activity were not observed in any subject at PetISO of 1.2%. Minimal phasic EMGgg activity ($2.1 \pm 0.8\%$ of the activity recorded during tongue protrusion) was evident at PetISO of 0.8% and 0.4% in two subjects and at 0.4% only in another two subjects. When noted, the magnitude of

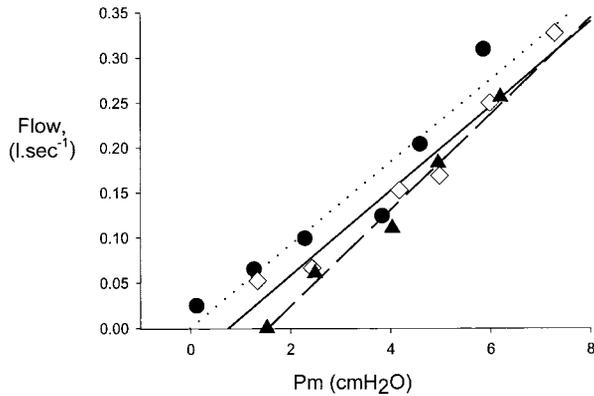


Fig. 4. Representative data from one subject showing the relation between maximal inspiratory airflow during flow-limited breaths and mask pressure (P_m) at each of the three levels of general anesthesia. Each point represents the average from breaths three to five of each reduction in P_m . As the depth of general anesthesia decreased (from an end-tidal isoflurane concentration of 1.2% to 0.8% to 0.4%), the critical pressure required to collapse the airway (P_{crit}) decreased from 1.55 to 0.75 to 0.02 cm H₂O, respectively. Dashed line and triangles = 1.2%; solid line and squares = 0.8%; dotted line and circles = 0.4%.

this phasic activity did not change with alterations in P_m . Tonic electromyogram activity was also markedly diminished during anesthesia. The example from one subject in figure 6 shows minimal EMGgg activity (fig. 6A), which was unchanged during any sequence of flow-limited breaths (fig. 6B), or by upper airway collapse induced by decreasing P_m to or below P_{crit} (fig. 6C), or by application of a 30-cm H₂O square wave of negative pressure to the mask for a single respiratory cycle (fig. 6D). On arousal from anesthesia, baseline EMGgg activity

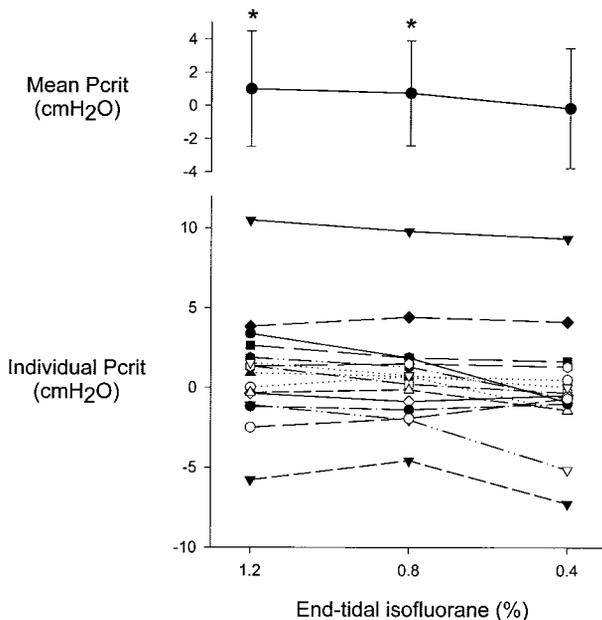


Fig. 5. Mean and individual data ($n = 16$) of the changes in critical pressure required to collapse the airway (P_{crit}) at three levels of inhalational anesthesia * $P < 0.05$ versus 0.4%; error bars \pm SD.

increased (fig. 6E), and a robust EMGgg response was observed when subjects were asked to protrude their tongue or to swallow (fig. 6F). We noted this pattern in all subjects. None demonstrated any EMG response to decreases in airway pressure, and all showed these marked increases in amplitude on arousal. Depth of anesthesia had no influence on EMGgg activity (fig. 7).

Site of Upper Airway Collapse

In 14 of the 16 subjects, when P_m was reduced to a level sufficient to collapse the airway and abolish inspiratory flow, P_{es} changes were also observed in the hypopharynx and oropharynx but not in the nasopharynx (fig. 2D), indicating airway collapse at the level of the soft palate. In the other two subjects, P_{es} changes were transmitted to the hypopharynx but not the oropharynx or nasopharynx, indicating retroglossal collapse. In any given subject, the site of collapse was similar at each depth of anesthesia.

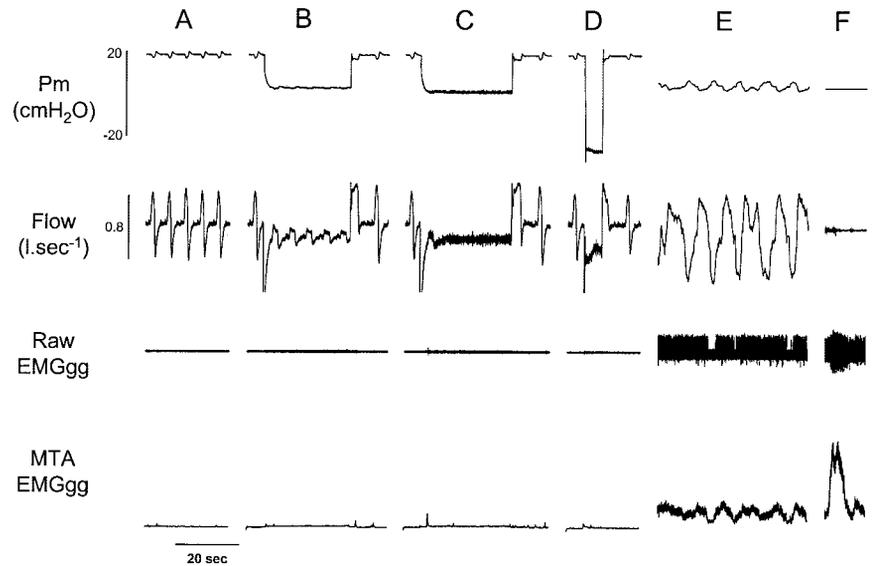
Discussion

This study examined the mechanical behavior of the upper airway during different levels of inhalational anesthesia with isoflurane. The major findings were that (1) at each level of anesthesia the mean P_{crit} for the group exceeded or was close to atmospheric pressure, implying that the pharynx is vulnerable to collapse during anesthesia, consistent with common clinical experience; (2) the upper airway of the anesthetized spontaneously breathing human behaved as a Starling resistor during flow-limited breaths; (3) while progressively more negative pressure was required to collapse the upper airway as depth of anesthesia decreased, this greater stability was not a result of increased neuromuscular activity of the upper airway, which remained hypotonic and non-responsive at all levels of anesthesia; and (4) in the majority of subjects, the upper airway collapsed at the level of the soft palate, and the site of collapse was unchanged by anesthetic depth.

Measurement of Upper Airway Collapsibility

To study upper airway collapsibility during general anesthesia, we repeatedly reduced airway pressure to levels sufficient to produce varying degrees of inspiratory flow limitation and then examined the relation between $V_{i_{max}}$ and P_m . In each subject, at each level of anesthesia, $V_{i_{max}}$ decreased linearly with P_m for flow-limited breaths. During these breaths, $V_{i_{max}}$ was not influenced by the magnitude of inspiratory P_{es} . These observations provide the first evidence that the upper airway of an anesthetized spontaneously breathing human behaves as a Starling resistor. In this condition, as airflow limitation develops, flow becomes independent of downstream pressure (and therefore respiratory ef-

Fig. 6. Polygraph record in one subject at a stable plane of general anesthesia (A–D) and during recovery (E and F), showing raw and moving-time-averaged (MTA) genioglossus electromyogram (EMG_{gg}) responses while breathing at the maintenance pressure (A), during a decrease in mask pressure (P_m) sufficient to cause flow-limitation (B) or upper airway collapse (C), during application of a 30-cm H₂O square wave of negative pressure (D), during quiet breathing on arousal from anesthesia (E), and when asked to voluntarily protrude the tongue (F).



fort), being limited to a maximum value dependent only on the upstream pressure (P_m) and on the pressure surrounding the collapsible segment.⁷

During each series of flow-limited breaths, upstream pressure was maintained constant, yet we consistently observed that V_{i,max} decreased over the initial few breaths before reaching a constant value over the final three breaths of any five-breath sequence. Boudewyns *et al.*¹¹ recently reported similar findings in obese patients with severe sleep apnea. According to the Starling resistor model, this implies a breath-by-breath change in upper airway collapsibility. Indeed, analysis of P_{crit} on a breath-by-breath basis showed that it systematically in-

creased over the initial three breaths (-2.8 ± 0.9 , -0.2 ± 0.8 , and 0.4 ± 0.8 cm H₂O, respectively; $P < 0.05$, one-way repeated-measures analysis of variance) indicating increased collapsibility, whereas breaths three to five were not statistically different (0.4 ± 0.8 , 0.9 ± 0.7 , and 1.0 ± 0.7 cm H₂O, respectively). Schwartz *et al.*¹⁰ have also observed a progressive increase in collapsibility over three successive breaths in the hypotonic upper airway during sleep, despite an increase in genioglossus muscle activity. Our results extend these findings by showing that the breath-by-breath changes in collapsibility stabilize by the third breath and that they occur in the absence of reflex changes in genioglossus activity. It is possible that they are a consequence of the effect of breath-by-breath decreases in end-expiratory lung volume (caused by greater obstruction in inspiration than expiration) decreasing longitudinal tension in the airway wall (see Mechanical Influences on Collapsibility).

As anesthetic depth decreased from a PetISO of 1.2% to 0.4%, P_{crit} decreased by 1.2 ± 1.6 cm H₂O, indicating decreased pharyngeal airway collapsibility. We recently reported that the tendency of the upper airway to obstruct during inhalational anesthesia (P_{crit}) is related to its tendency to do so during sleep.¹² It was notable, however, that despite the fact that our subjects were not selected on the basis of known vulnerability to upper airway collapse (*e.g.*, obesity, snoring), their mean P_{crit} exceeded atmospheric pressure except at PetISO of 0.4%. This demonstrates that vulnerability to collapse of the passive upper airway is remarkably common.

Neuromuscular Influences on Collapsibility

Neuromuscular activity of the upper airway muscles was inferred from electromyogram activity of the genioglossus muscle. The genioglossus was chosen because it is considered the major dilator muscle of the upper airway and is easily accessible *via* a percutaneous approach

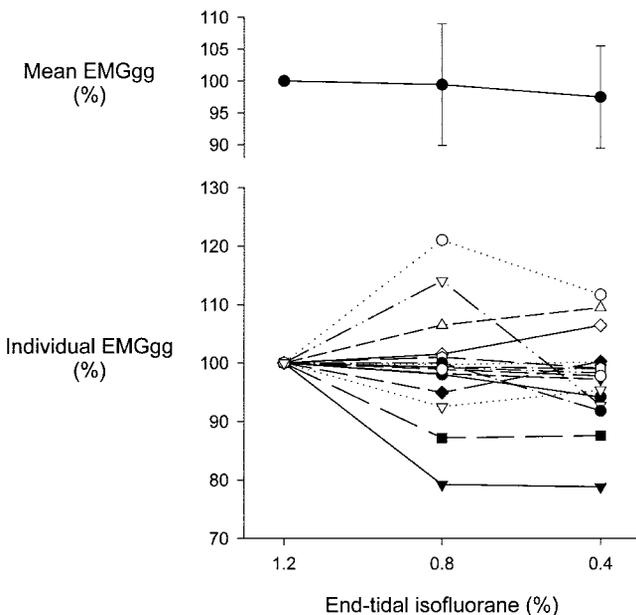


Fig. 7. Mean and individual data (n = 16) of the changes in genioglossus electromyogram (EMG_{gg}) at three levels of inhalational anesthesia. Values for EMG_{gg} are given relative to those at end-tidal isoflurane of 1.2%. Error bars \pm SD.

during general anesthesia. Whether its activity can be considered representative of other dilator muscles in the pharynx during volatile anesthesia in humans is yet to be defined, but this appears to be the case in anesthetized animals.^{13,14} Genioglossus activity was measured using three separate bipolar intramuscular electrodes positioned while the subject was anesthetized. The use of three electrode pairs was adopted to ensure an adequate electromyogram as maneuvers such as tongue protrusions or swallows, which are commonly used to validate electrode position,¹⁵ could not be performed until the subject had regained consciousness. Once conscious, a robust electromyogram response to these voluntary maneuvers was observed in all subjects, confirming that the electrodes were correctly placed.

Relative to the background level of activity during consciousness, baseline tonic genioglossus activity was markedly diminished during general anesthesia and did not change during reductions in P_m (even of sufficient magnitude to cause upper airway collapse) or during application of a square wave of -30 cm H_2O to the upper airway. The latter stimulus is known to cause powerful reflex activation of the genioglossus and other upper airway dilator muscles during wakefulness and sleep^{16,17} and is thought to be mediated by activation of pressure-sensitive mechanoreceptors in the upper airway.¹⁸ The lack of response of the genioglossus to any of these stimuli is consistent with studies in dogs, which show a strong inhibitory effect of isoflurane on upper airway mechanoreceptor activity.^{19,20} These observations suggest that the minimal phasic activity observed in the four subjects at lighter depths of anesthesia is likely to be a manifestation of central drive rather than an effect mediated by upper airway reflexes. Minimal as it was, it did not appear to affect collapsibility as behavior of these 4 subjects did not differ from that of the other 12 subjects.

Isoflurane has also been shown to decrease central respiratory drive.²¹ While it is likely that respiratory drive was depressed in the current study, it was notable that during a sequence of breaths against a collapsed or flow-limited airway, P_{es} swings became progressively greater (fig. 2), indicating that the respiratory pump muscles were able to increase their level of activity, possibly in response to increased chemoreceptor activity or by activation of mechanoreceptors in the lung or chest wall.^{22,23} Changes in genioglossus activity were not observed during these breaths, suggesting that the upper airway muscles were nonresponsive to chemical as well as mechanical stimuli. Such differential effects on the respiratory pump relative to upper airway muscles have been previously documented in animals in response to anesthetic, sedative, and analgesic drugs.^{1-3,24}

The abolition of neuromuscular activity of the pharyngeal muscles by general anesthesia allows study of the biomechanical behavior of the passive human upper

airway. Previous studies have attempted to do so during sleep or anesthesia with neuromuscular blockade. Application of nasal continuous positive airway pressure during sleep has been shown to cause relative upper airway muscle hypotonia²⁵ that persists for the breath following a reduction in nasal pressure.^{26,27} However, succeeding breaths are accompanied by a progressive return of neuromuscular drive to the upper airway muscles,¹⁰ limiting this technique to study of the first breath only, an important limitation given the breath-by-breath changes in collapsibility that we and other investigators^{10,11} have observed during flow-limited breaths. Furthermore, studies in sleeping subjects are commonly complicated by intermittent arousal and changes in sleep state. Study of the passive upper airway during complete neuromuscular blockade during general anesthesia²⁸ is also limited as this technique abolishes respiratory as well as pharyngeal muscle activity, requiring the institution of mechanical ventilatory support using positive pressure ventilation. The protocol used in the current study is advantageous as it permits examination of the properties of the passive pharynx over many breaths in the presence of decreases in intrapharyngeal pressures generated by spontaneous inspiratory muscle activity and without the occurrence of state changes.

Mechanical Influences on Collapsibility

Head and neck position,²⁹ degree of mouth opening,³⁰ body position,^{11,31} and lung volume^{29,32-34} have all been shown to influence upper airway collapsibility. In the current study all of these variables but lung volume were controlled: the mouth was sealed, subjects were supine, and the head was maintained in a neutral position throughout each study by means of a Shea headrest. The potential effect of lung volume on upper airway collapsibility was first described in anesthetized cats, where rostral tracheal displacement associated with decreased lung volume resulted in increased upper airway resistance.³² Since then other studies, mainly in animal preparations, have shown that caudal traction of the upper airway decreases its collapsibility, an effect that has been attributed to changes in airway length and longitudinal tension within the airway wall.^{29,34} In the current study, end-expiratory P_{es} , measured at the maintenance pressure, decreased by 0.6 ± 0.9 cm H_2O from an PetISO of 1.2% to 0.4% ($P < 0.05$). This implies a systematic increase in end-expiratory lung volume and therefore an increase in caudal traction on the upper airway with decreasing anesthetic depth, acting to stabilize the upper airway.

Such a mechanism could also explain the increased collapsibility we observed during breaths one to three of each sequence of flow-limited breaths. It is likely that these breaths were accompanied by a progressive decrease in end-expiratory lung volume as a consequence of greater impedance to flow in inspiration than expira-

tion, resulting in a progressive decrease in caudal traction on the upper airway.

Site of Collapse

During isoflurane-induced general anesthesia, collapse was most common at the level of the soft palate, with 14 of 16 subjects showing such a pattern. The principal site of collapse was unaffected by depth of anesthesia. These findings contrast with those of earlier studies attributing upper airway obstruction during general anesthesia to a retrolingual obstruction,^{35,36} but are consistent with more recent radiologic³⁷ and magnetic resonance imaging studies³⁸ that also show the soft palate to be the primary site of occlusion. The vulnerability of the upper airway to collapse at the region of the soft palate is likely to reflect the observation made by other investigators that it is the most compliant structure in the upper airway, both in normal subjects and in those with obstructive sleep apnea.^{26,28} It is notable that this region of the airway also appears to be the primary site of occlusion during sleep in the majority of patients with sleep apnea.²⁷

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