

Effects of Nitrous Oxide on Volume and Pressure of Endotracheal Tube Cuffs

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The effects of nitrous oxide on endotracheal tube cuff gas volumes and pressures were determined with 50 size 32–40-Fr Foregger endotracheal tubes fitted with fluted latex rubber cuffs. The cuffs were inflated with 5, 10, or 15 ml of air and then exposed to 100, 75, 50, or 25 per cent nitrous oxide in oxygen for one to four hours. Nitrous oxide increased cuff gas volumes in a concentration- and time-related fashion. The increases were significant ($P < .001$) after one hour of exposure and often dramatic after four hours. Intracuff pressures also increased after nitrous oxide, with pressures frequently reaching 70 and occasionally 100 mm Hg. These findings demonstrate that nitrous oxide has the capacity to diffuse into latex rubber endotracheal tube cuffs in significant volumes and suggest that such diffusion may result in overexpansion of the cuffs and cause upper-airway obstruction and trauma in the intubated patient. (Key words: Anesthetics, gases; nitrous oxide; Equipment: endotracheal tube cuffs.)

UPPER-AIRWAY OBSTRUCTION in the anesthetized, intubated patient is a well-recognized complication of endotracheal intubation.¹⁻³ Endotracheal tubes may be kinked,²⁻⁴ become occluded by various foreign bodies,²⁻⁵ or become obstructed when the distal orifice rests against the carina or when the cuff is overinflated and compresses the wall of the tube or covers its tip.¹⁻⁶ An air-inflated endotracheal tube cuff within the trachea represents a gas-filled pocket in the body. Since Tenney *et al.*⁷ and Eger and

Saidman⁸ have shown that an enclosed gas-filled space in the body will expand if it contains a gas (nitrogen) which is less soluble in blood than the gas respired (nitrous oxide), one cause of upper-airway obstruction in the intubated patient may be overexpansion of the cuff, secondary to diffusion of nitrous oxide into it. This study was conducted to determine whether nitrous oxide diffuses into standard air-inflated latex endotracheal tube cuffs and, if so, to quantitate the cuff volume changes and rates at which they occur during exposure to various concentrations of nitrous oxide.

Method

Nitrous oxide diffusion was studied with 50 Foregger spiral-embedded latex rubber endotracheal tubes, ten each of sizes 32 through 40 Fr. The tubes were fitted with appropriate sizes of fluted latex rubber cuffs which, after complete deflation, were inflated with 5, 10, or 15 ml of air. The tubes were then exposed in a glass container to a continuous flow of compressed air at 4 l/min or to 100, 75, 50, or 25 per cent nitrous oxide in oxygen for one to four hours (fig. 1). At the ends of these periods the gas in the cuffs was aspirated, measured with a calibrated syringe, and analyzed for oxygen, nitrogen, and nitrous oxide on a Hewlett-Packard gas chromatograph. Nitrous oxide-nitrogen reverse diffusion was studied in ten 34-Fr tubes whose cuffs were filled with 100 per cent nitrous oxide and exposed for four hours to 100 per cent nitrogen.

The effect of prolonged exposure to nitrous oxide was also studied. In these experiments cuffs of 34-Fr tubes were filled with 10 ml of air and their volumes were measured after 8, 12, 16, 24, 36, and 48 hours of continuous exposure to 100 per cent nitrous oxide.

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Change in cuff pressure was measured in tubes exposed to 100 per cent nitrous oxide. This was done before, and one to four hours after, exposure to the gas by connecting the tips of the cuff catheters to a Statham pressure transducer and recorder.

All experiments were done at 20 C, 40–50 per cent relative humidity, and a barometric pressure of 630–644 torr in a temperature- and humidity-controlled room.

Results

There was no change in the endotracheal tube cuff gas volume of any tube exposed to air, regardless of the initial cuff volume or time of exposure. Exposure to nitrous oxide increased cuff gas volumes in a concentration- and time-dependent fashion (table 1). Volumes increased significantly ($P < .001$) after one hour of exposure, with all concentrations of nitrous oxide studied, and became greater by four hours. Continued exposure to 100 per cent nitrous oxide after four hours resulted in small but steady increases in cuff gas volumes to 12–16 hours (table 2). Following this, the volumes steadily declined, reaching by 48 hours, in those cuffs initially filled with 10 ml of air, a mean of 6.2 ± 0.4 ml. Cuffs filled with 100 per cent nitrous oxide and exposed to 100 per cent nitrogen had a rapid decline in cuff volume. No cuff in this group had a volume greater than 1 ml after four hours of exposure.

Although the largest absolute changes in volume occurred when the cuffs were inflated with 15 ml of air, the relative increases with 5 ml were significantly greater ($P < .01$, Student's *t*-test for paired data) than those with 10 or 15 ml after four hours at all concentrations of nitrous oxide (table 1). The 34-Fr tubes inflated with 5 ml sustained increases in cuff gas volumes which averaged 356, 246, 186, and 102 per cent after four hours of exposure to 100, 75, 50, and 25 per cent nitrous oxide, respectively. After exposure to the same concentrations of nitrous oxide for four hours, these tubes had increases in cuff gas volumes that averaged 272, 183, 145, and 65 per cent when inflated with 10 ml, and 286, 176, 102, and 63 per cent when inflated with 15 ml.

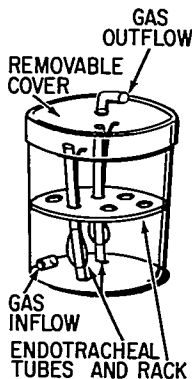


FIG. 1. Glass container used to expose endotracheal tubes to nitrous oxide.

Except for the 32-Fr tubes, with initial cuff volumes of 10 or 15 ml of air, tube size did not influence final cuff gas volumes after exposure to nitrous oxide (table 3). However, after equal periods of exposure and at all concentrations of nitrous oxide, the 32-Fr tubes had significantly greater increases in cuff gas volumes ($P < .01$) than any of the other sizes of tubes with similar initial cuff volumes. After four hours of exposure to 100 per cent nitrous oxide, these tubes sustained mean increases in cuff gas volumes of 356 and 360 per cent after 10 and 15 ml, respectively, while mean increases with the other sizes of tubes ranged from 272 to 316 per cent after 10 ml and 236 to 286 per cent after 15 ml.

After four hours of exposure to 25 per cent nitrous oxide and 75 per cent oxygen, analysis of gases in endotracheal tube cuffs demonstrated that, in addition to nitrous oxide, a small amount of oxygen had diffused into the cuffs (table 4). Since cuffs filled with 5, 10, and 15 ml of air originally contain approximately 1, 2, and 3 ml of oxygen, the amount of oxygen transferred is the difference between the calculated final cuff gas contents (table 4, column E) and the above original oxygen contents. Changes in cuff gas

TABLE 1. Effects of Nitrous Oxide on Cuff Gas Volumes (Means \pm SD) of Ten 34-Fr Latex Rubber Endotracheal Tubes*

Initial Cuff Volume	Concentration of N ₂ O (Per cent)	Final Cuff Volume (ml)			
		1 Hour	2 Hours	3 Hours	4 Hours
5 ml	100	13.0 \pm 0.8	16.8 \pm 1.0	20.0 \pm 1.7	22.8 \pm 1.5
	75	10.0 \pm 0.9	12.3 \pm 0.9	14.8 \pm 1.4	17.3 \pm 1.2
	50	9.0 \pm 0.6	10.8 \pm 1.0	11.5 \pm 1.1	14.3 \pm 1.0
	25	8.0 \pm 0.5	8.8 \pm 0.5	10.0 \pm 0.9	10.1 \pm 0.8
10 ml	100	20.0 \pm 1.2	26.8 \pm 1.3	30.2 \pm 1.5	37.2 \pm 1.3
	75	18.3 \pm 1.1	21.8 \pm 1.0	25.5 \pm 1.3	28.3 \pm 0.9
	50	16.0 \pm 0.8	18.8 \pm 0.8	20.0 \pm 1.1	24.5 \pm 1.0
	25	13.8 \pm 0.7	14.5 \pm 0.7	15.5 \pm 0.6	16.5 \pm 0.7
15 ml	100	33.5 \pm 2.1	38.5 \pm 2.3	48.8 \pm 2.5	58.0 \pm 3.1
	75	25.8 \pm 1.9	31.0 \pm 2.0	33.8 \pm 1.8	40.0 \pm 3.0
	50	21.5 \pm 1.2	25.0 \pm 2.1	28.3 \pm 2.0	30.3 \pm 2.1
	25	20.0 \pm 1.1	21.3 \pm 1.7	23.0 \pm 1.9	24.5 \pm 2.0

* All volume changes, compared with initial volumes, were significant ($P < .001$) using Student's *t* test for paired data.

TABLE 2. Effects of Prolonged Exposure to 100 Per Cent Nitrous Oxide on Cuff Gas Volumes (Means \pm SD) of Ten 34-Fr Latex Endotracheal Tubes Initially Filled with 10 ml Air

Initial Cuff Volume	Final Cuff Volume (ml)							
	4 Hours	8 Hours	12 Hours	16 Hours	20 Hours	24 Hours	36 Hours	48 Hours
10 ml	37.2 \pm 1.3	39.8 \pm 2.0	41.2 \pm 3.1	40.1 \pm 2.9	34.9 \pm 1.6	26.8 \pm 1.5	11.3 \pm 0.8	6.2 \pm 0.4

TABLE 3. Effects of 100 Per Cent Nitrous Oxide on Cuff Gas Volumes (Means \pm SD) of 50 Latex Rubber Endotracheal Tubes*

Initial Cuff Volume	Tube Size	Final Cuff Volume (ml)			
		1 Hour	2 Hours	3 Hours	4 Hours
5 ml	32	12.8 \pm 0.8	16.8 \pm 0.8	20.8 \pm .84	24.0 \pm 1.6
	34	13.0 \pm 0.8	16.8 \pm 1.0	20.0 \pm 1.7	22.8 \pm 1.5
	36	14.8 \pm 1.0	16.2 \pm 2.1	19.0 \pm 2.9	21.5 \pm 2.1
	38	12.7 \pm 1.2	17.3 \pm 1.5	21.0 \pm 1.7	23.3 \pm 2.1
	40	13.6 \pm 0.5	16.8 \pm 0.5	21.8 \pm 1.3	23.4 \pm 0.5
10 ml	32	25.2 \pm 4.0	32.0 \pm 3.5	39.6 \pm 4.0	45.6 \pm 4.8
	34	20.0 \pm 1.2	26.8 \pm 1.3	30.2 \pm 1.5	37.2 \pm 1.3
	36	20.8 \pm 1.0	21.2 \pm 1.7	32.5 \pm 2.5	38.5 \pm 3.3
	38	21.7 \pm 1.0	28.7 \pm 1.1	35.3 \pm 1.0	41.0 \pm 2.1
	40	22.2 \pm 1.2	28.9 \pm 1.3	36.8 \pm 2.2	41.6 \pm 3.4
15 ml	32	33.4 \pm 2.9	49.4 \pm 5.0	57.0 \pm 4.9	69.0 \pm 5.6
	34	33.5 \pm 2.1	38.5 \pm 2.3	48.8 \pm 2.5	58.0 \pm 3.1
	36	27.8 \pm 2.0	35.5 \pm 3.0	41.3 \pm 3.2	50.3 \pm 3.9
	38	28.7 \pm 2.2	39.0 \pm 3.1	44.3 \pm 3.3	54.3 \pm 3.5
	40	31.8 \pm 2.8	37.5 \pm 3.2	48.0 \pm 4.1	52.2 \pm 3.7

* All volume changes, compared with initial volumes, were significant ($P < .001$) using Student's *t* test for paired data.

TABLE 4. Effects of Four Hours of 100 and 25 Per Cent Nitrous Oxide in Oxygen on Cuff Gas Concentrations and Contents (Means \pm SD) of Ten 34-Fr Latex Rubber Endotracheal Tubes

Column A Nitrous Oxide	Column B Initial Cuff Volume (ml)	Column C Final Cuff Gas Concentration (Per Cent)			Column D Final Cuff Volume (ml)	Column E* Calculated Final Cuff Gas Contents (ml)		
		O ₂	N ₂	N ₂ O		O ₂	N ₂	N ₂ O
100 per cent	5	4.3 \pm 0.4	17.1 \pm 1.9	77.5 \pm 3.2	22.8 \pm 1.5	1.0	3.9	17.7
	10	5.1 \pm 0.5	21.3 \pm 2.3	73.1 \pm 4.1	37.2 \pm 1.3	1.9	7.9	26.9
	15	4.9 \pm 0.7	20.2 \pm 1.5	73.8 \pm 2.5	58.0 \pm 3.1	2.8	11.7	42.8
25 per cent	5	22.9 \pm 0.7	38.6 \pm 2.1	37.6 \pm 2.9	10.1 \pm 0.8	2.3	3.9	3.8
	10	23.1 \pm 0.9	48.5 \pm 2.6	27.2 \pm 2.2	16.5 \pm 0.7	3.8	8.0	4.5
	15	22.7 \pm 0.6	48.6 \pm 2.5	26.9 \pm 2.1	24.5 \pm 2.0	5.6	11.9	6.2

* The product of column C times column D.

volume after 100 per cent nitrous oxide were, however, almost entirely due to movement of nitrous oxide into the cuff, with little or no diffusion of oxygen or nitrogen in the opposite direction. The 34-Fr cuffs originally filled with 5, 10, and 15 ml of air still contained 1.0, 1.9, and 2.8 ml of oxygen and 3.9, 7.9 and 11.7 ml of nitrogen, respectively, after four hours of exposure to 100 per cent nitrous oxide (table 4). By 48 hours, however, analysis of gases in endotracheal tube cuffs showed no oxygen and less than 0.5 per cent nitrogen.

Cuff pressures after exposure to nitrous oxide are given in table 5. Although the smaller cuffs had higher initial cuff gas pressures and more rapid rises in pressure after exposure to nitrous oxide, all cuffs demonstrated progressive increases in cuff pressure with increases in cuff volume to mean peak pressures ranging from 63 to 76 mm Hg. Greater volumes resulted in gradual reduction in cuff pressures and then, in some, a second rise.

Discussion

In 1965, Eger and Saidman⁸ found that a gas-filled space in the body will expand if the gas within it is less soluble in blood and other body fluids than is the gas respired. They showed that nitrous oxide, a gas 34 times more soluble in blood than nitrogen, when inspired in a concentration of 75 per cent, increased intestinal gas volumes

100–200 per cent in four hours and increased gas volumes in pneumothoraces 200–300 per cent in two hours. Our study demonstrates that volume changes similar to those occurring in enclosed gas-filled spaces in the body also occur in enclosed air-filled endotracheal tube cuffs exposed to nitrous oxide. These findings suggest that endotracheal tube cuff overexpansion secondary to nitrous oxide diffusion may cause upper-airway obstruction, and possibly also glottic and subglottic trauma, in the intubated, anesthetized patient.

Both Tenney *et al.*⁷ and Eger and Saidman⁸ reported that two main factors govern the rate at which increases in volume take place in gas-enclosed spaces in the body: 1) the rate increases as solubility of the respired gas in blood increases, and 2) the rate increases when the blood flow to the space, or the blood flow/space volume ratio, increases. Other factors which influence rate of diffusion through a semipermeable membrane and might affect the rate at which nitrous oxide or any other respired gas moves into an enclosed gas-filled space include: temperature; the gram molecular weight of the respired gas; its permeability through or solubility in the tissue making up the wall of the space; the pressure differential of the respired gas across this wall. Since blood was not used in these experiments and would not be directly in contact with an inflated endotracheal tube cuff in the trachea, neither of the two factors mentioned by the above authors would appear to be important in the

TABLE 5. Effects of 100 Per Cent Nitrous Oxide on Mean Cuff Pressures of (Means \pm SD) 50 Latex Rubber Endotracheal Tubes

Tube Size	Initial Cuff Volume (ml)	Initial Cuff Pressure (mm Hg)	Final Cuff Pressure (mm Hg)			
			1 Hour	2 Hours	3 Hours	4 Hours
32	5	0	58.3 \pm 9.8	67.3 \pm 12.3	71.3 \pm 10.7	74.0 \pm 14.4
34	5	0	55.1 \pm 13.6	65.0 \pm 15.4	69.5 \pm 12.2	74.2 \pm 16.3
36	5	0	52.3 \pm 7.2	65.7 \pm 3.1	66.8 \pm 7.6	73.0 \pm 8.7
38	5	0	43.0 \pm 5.4	56.5 \pm 12.1	58.7 \pm 10.9	61.2 \pm 11.2
40	5	0	29.4 \pm 4.6	35.1 \pm 5.3	36.0 \pm 6.4	36.9 \pm 6.7
32	10	49.3 \pm 4.6	75.4 \pm 19.8	67.0 \pm 8.7	65.3 \pm 7.7	62.1 \pm 6.3
34	10	46.0 \pm 5.2	69.2 \pm 15.7	73.1 \pm 18.2	73.2 \pm 10.2	72.0 \pm 16.2
36	10	42.8 \pm 5.2	65.8 \pm 8.1	70.9 \pm 6.2	75.1 \pm 13.2	73.4 \pm 10.1
38	10	31.3 \pm 6.1	60.2 \pm 9.1	63.7 \pm 11.8	62.4 \pm 12.9	61.0 \pm 9.9
40	10	24.6 \pm 6.3	49.0 \pm 6.7	63.1 \pm 8.9	54.3 \pm 7.8	54.3 \pm 7.2
32	15	60.1 \pm 7.8	61.3 \pm 8.8	51.6 \pm 7.2	51.4 \pm 9.3	56.6 \pm 10.2
34	15	55.0 \pm 7.9	50.0 \pm 8.9	50.0 \pm 10.9	48.2 \pm 14.4	46.5 \pm 16.2
36	15	52.1 \pm 8.2	63.2 \pm 21.2	62.0 \pm 16.7	61.5 \pm 18.2	60.5 \pm 17.6
38	15	46.7 \pm 6.4	51.0 \pm 11.9	58.2 \pm 13.2	58.4 \pm 16.7	62.5 \pm 17.7
40	15	31.2 \pm 3.2	64.6 \pm 3.2	54.2 \pm 4.2	54.2 \pm 6.8	65.2 \pm 3.2

rate or extent of endotracheal tube cuff volume change after exposure to nitrous oxide. Rather, our findings suggest that cuff wall thickness, the partial pressure difference of nitrous oxide and oxygen across the cuff wall, and possibly the solubility of these gases and nitrogen in latex rubber are the most important determinants of the rate of gaseous diffusion into and out of latex rubber air-filled endotracheal tube cuffs. Tables 3 and 5 demonstrate that the most rapid increases in cuff volume and pressure at all concentrations of nitrous oxide consistently occurred in the smallest tubes studied (32 Fr). These cuffs had the smallest residual volume (3 ml) and were therefore most stretched; their wall thickness and thus their nitrous oxide diffusing distance were decreased the most by any initial volume of air. On the other hand, the more rapid increases of volume in cuffs initially filled with 5 ml of air compared with those filled with 10 or 15 ml can be explained by the larger initial and subsequent cuff pressures in both of the latter (table 5). These increased pressures must result in proportional increases in the partial pressures of all gases within the cuff. This, of course, would tend to decrease the pressure gradient across the cuff wall for any

nitrous oxide in the cuff, and increase it for nitrogen, both of which would hinder cuff volume expansion.

In all the experiments, endotracheal tube cuff volume changes were directly related to the partial pressure difference of nitrous oxide across the wall of the cuff. Although less diffusible than nitrous oxide, oxygen also contributed to an increase in endotracheal tube cuff volume when its concentration gradient across the cuff wall was high (75 per cent outside the cuff versus 20 per cent inside, table 4). When lower concentrations of oxygen were used, *i.e.*, 50 or 25 per cent, passage of oxygen into the cuffs was negligible, less than 1 ml in four hours. Nitrogen diffusion was the least of the three gases studied (table 4). This is surprising, considering nitrogen has a lower gram molecular weight than the other two gases, and the concentration gradients used (80 per cent inside the cuff versus 0 outside) during all the experiments were always favorable for its diffusion out of the cuff. Although a comparison of the diffusibilities of nitrous oxide, oxygen, and nitrogen through latex rubber has not been published, work by Stannett and Szwarc⁹ has shown that oxygen is three to four times more diffusible than nitrogen

through most polymer membranes. These authors have also demonstrated that with any given pair of gases the ratio of the permeability constants remains roughly constant for a wide variety of polymer films, even though actual values may vary by as much as several thousand times. Barrer¹⁰ has shown that the process of permeation of gas through a plastic or rubber membrane occurs as a sequence of three phenomena: 1) absorption and solution of the gas into the membrane at one surface; 2) diffusion of the gas through the body of the membrane; 3) dissolution and freeing of the gas from the membrane at the other surface. Our findings suggest that at least one of these phenomena is impaired in the diffusion of nitrogen, as compared with nitrous oxide, through standard latex rubber endotracheal tube cuffs. These data also raise the question whether a similar impairment of nitrogen diffusion through biologic membranes occurs. At the present time permeability coefficients of nitrogen through tissue membranes have not been determined, but the possibility of poor diffusibility of nitrogen through biologic membranes may be another, and possibly a more important, cause of enclosed gas expansion after exposure to nitrous oxide, than is nitrogen's insolubility in blood.

In addition to upper airway obstruction, and perhaps more important, endotracheal tube cuff overinflation secondary to nitrous oxide diffusion may be a cause of postoperative glottic and subglottic edema, and tracheal mucosal erosion. The Foregger cuffs used in this study have residual volumes between 3 and 4.5 ml and are thus classified as large-residual-volume cuffs requiring only small cuff inflation volumes and intracuff pressures to effect tracheal wall seals. Table 5 shows that with initial cuff volumes of 5 ml mean intracuff pressures increased from 0 to as high as 58 mm Hg after one hour, and to 74 mm Hg after four hours, of exposure to 100 per cent nitrous oxide. A few 32-Fr cuffs filled with 10 ml of air developed pressures of more than 100 mm Hg after similar exposures. Intracuff pressures below 100 mm Hg have not been shown to result in lateral tracheal wall pressures above normal systolic

arterial blood pressure¹¹ and therefore probably do not cause enough tracheal wall compression to produce tissue ischemia. However, some investigators have demonstrated that low-residual-volume (0-2 ml) cuffs develop intracuff pressures as high as 300 mm Hg with cuff volumes of only 4-5 ml and, when placed in the tracheas of animals, cause tracheal distortion and lateral tracheal wall pressures as high as 160 mm Hg. Local tissue necrosis, fibrosis and stricture, and tracheoesophageal fistulas have been reported with prolonged use of the tubes.¹²⁻¹⁴ Using a number of brands of polyvinyl chloride low-residual-volume cuffs, experiments in our laboratories have demonstrated that clinical concentrations of nitrous oxide (25-75 per cent) will result in enough nitrous oxide diffusion in four hours to raise intracuff pressures more than 200 mm Hg with initial cuff volumes of 2-4 ml of air and as high as 400 mm Hg with 10 ml of air or more (Stanley, unpublished data). It is therefore understandable that if the extent of nitrous oxide diffusion and development of intracuff pressure in patients are similar to those in these *in-vitro* experiments, even short periods of endotracheal intubation with polyvinyl chloride low-residual-volume cuffs may result in significant glottic or subglottic trauma.

Experiments are now being conducted in our operating rooms to determine whether nitrous oxide diffuses as readily into air-inflated endotracheal tube cuffs in the tracheas of patients as it does into cuffs *in vitro*. If the results of these studies are similar to those presented here, nitrous oxide would appear to be a better cuff-inflating gas than room air, or if room air were used, it would be important to deflate cuffs periodically in order to avoid build-up of endotracheal tube cuff volume and pressure during nitrous oxide anesthesia.

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