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The Cardiovascular Effects of Nitrous Oxide–Halothane Anesthesia in Man

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The cardiovascular effects of nitrous oxide–halothane–oxygen anesthesia were studied in eight unpremedicated healthy male volunteers and the results compared with those obtained in previous studies in which only halothane–oxygen anesthesia was used. Adding nitrous oxide to halothane–oxygen anesthesia resulted in less depression of the cardiovascular system than comparable levels of halothane–oxygen anesthesia. The differences were greatest at light levels of anesthesia and early in the anesthetic course. Most of the differences between the nitrous oxide and non-nitrous oxide groups were abolished at deeper levels of halothane anesthesia or after five hours of anesthesia had elapsed. Body temperature increased an average of 0.3 C with increasing depth of halothane anesthesia when nitrous oxide was present. The effect of discontinuing nitrous oxide for 15 minutes was also compared with data from a previous study in which nitrous oxide was added to halothane–oxygen anesthesia. The results seem to confirm a sympathetic stimulating action of nitrous oxide. (Key words: Halothane; Nitrous oxide; Circulation; Circulatory effects of anesthesia.)

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RECENTLY, Eger and colleagues studied the cardiovascular effects of halothane in young healthy male volunteers under conditions of constant carbon dioxide tension and body temperature.[1] They examined not only the effect of varying alveolar concentration, but also the effect of time. They found that halothane causes an initial depression of cardiovascular function which is directly related to the alveolar concentration, and which lessens with duration of exposure. Halothane, however, is often given with nitrous oxide, and the addition of nitrous oxide enables a reduction in the amount of halothane needed for anesthesia.[2] Furthermore, recent evidence suggests that nitrous oxide may have cardiovascular effects which antagonize those of halothane. Smith and colleagues[3] found that addition of nitrous oxide to halothane–oxygen anesthesia for 15 minutes late in the anesthetic course produced signs of alpha sympathetic activation, with increased mean arterial pressure, right atrial pressure, systemic vascular resistance, etc. Although the nitrous oxide was given for only a short time in Smith's study, his findings did suggest that at equivalent anesthetic levels (MAC) nitrous oxide–halothane–oxygen anesthesia might be less depressing to the circulation than halothane–oxygen alone. Therefore, we determined the cardiovascular effects of nitrous oxide–halothane–oxygen anesthesia and compared them with those of halothane–oxygen anesthesia.

Materials and Methods

We studied eight unpremedicated fasting healthy 22 ± 1 (SE)-year-old male volunteers after informed consent had been obtained.

TABLE 1. Awake Control Values (Mean ± SE)

	Halothane[1]	Halothane–Nitrous Oxide
Number of subjects	15	8
Age (years)	23 ± 1	22 ± 1
Height (cm)	183 ± 2	184 ± 1
Weight (kg)	78 ± 2	82 ± 3
Hemoglobin (g/100 ml)	16 ± 0.2	14.5 ± 0.3*
Hematocrit (per cent)	48 ± 0.7	43.8 ± 0.9*
Core temperature (C)	36.8 ± 0.1	36.7 ± 0.1
Cardiac output (l/min)	6.3 ± 0.2	5.3 ± 0.4*
Mean right atrial pressure (torr)	1.8 ± 0.4	4.6 ± 0.4*
Mean arterial pressure (torr)	95 ± 2	92 ± 4
Total peripheral resistance (ohms)	1221 ± 67	1388 ± 149
Heart rate (beats/min)	77 ± 3	63 ± 4*
Stroke volume (ml)	83 ± 4	86 ± 8
Pa_{O_2} torr)	503 ± 8	116 ± 8*
Pa_{CO_2} torr)	35.2 ± 0.9	38.1 ± 1.0
Base excess (mEq/l)	−2.2 ± 0.06	−2.1 ± 0.57
Forearm (muscle) blood flow (ml/100 ml/min)	3.5 ± 0.7 (n = 10)	2.9 ± 0.5
Forearm venous compliance (ml/100 ml torr)	0.09 ± 0.01 (n = 11)	0.09 ± 0.02 (n = 6)
Left ventricular minute work (kg-meters/min)	8.13 ± 0.32	6.58 ± 0.45*
Left ventricular stroke work (kg-meters)	0.103 ± 0.007	0.108 ± 0.010
Ejection time index (msec)	405 ± 6.0 (n = 9)	410 ± 4.5
Mean rate of ventricular ejection (ml/sec)	281 ± 10 (n = 9)	279 ± 23
Oxygen consumption (ml/min)	236 ± 19 (n = 11)	235 ± 18 (n = 7)
Ratio of cardiac output to oxygen consumption	27.2 ± 2.0 (n = 11)	22.6 ± 1.1 (n = 7)

* $P < 0.05$.

We measured arterial pressure, right atrial pressure, cardiac output, venous and arterial blood gases, end-tidal carbon dioxide, electrocardiogram, skin and esophageal temperatures, heart sounds, IJ-wave amplitude of the ultra-low-frequency ballistocardiogram, which is believed to vary directly with myocardial contractility,[4] and forearm (muscle) and finger (skin) blood flows. We have described the methods and calculations used to make these determinations.[3, 5]

During the awake control period, controlled ventilation (using an Airshields ventilator) with 30 per cent oxygen in nitrogen was used, keeping Pa_{CO_2} between 30 and 40 torr. Then, with the subject breathing spontaneously from a mask through a conventional circle system, anesthesia was induced with nitrous oxide, halothane, and oxygen. Following intubation of the trachea without the use of muscle relaxants, controlled respiration was instituted sufficient to maintain Pa_{CO_2} between 30 and 40 torr throughout the study. Care was taken throughout the study to keep inspiratory time shorter than expiratory time to minimize the cardiovascular effects of positive intrathoracic pressure.

The next circulatory measurements were made 40 ± 3 (SE) minutes after induction at an end-tidal halothane concentration of ½ per cent and a nitrous oxide concentration of 70 per cent. These measurements were repeated at 1 and 1½ per cent halothane with 70 per cent nitrous oxide, allowing approximately 15 minutes for stabilization at each new anesthetic level. Nitrous oxide was determined as the difference in inspired oxygen concentration from 100 per cent.

End-tidal halothane was then held constant at 1 per cent for 239 ± 17 minutes, after which the nitrous oxide was eliminated by using 100 per cent oxygen. After 15 ± 1 min-

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utes, measurements were taken, and then the 70 per cent nitrous oxide was restored. Last, after 374 ± 15 minutes, the end-tidal halothane concentration was once again changed to ½, then to 1, to 1½, and finally to 2 per cent—all with a background of 70 per cent nitrous oxide. Blood volume was determined by dye dilution[6] at three periods in each study: preanesthesia, early anesthesia, and late anesthesia. Intravenous fluids were restricted to less than 2,600 ml per study. On the average, duplicate cardiac output values differed by less than 7 per cent.

The data were compared with the results of Eger's previous study, in which only halothane–oxygen was used.[1] Comparisons were made at equipotent anesthetic concentrations or multiples of these concentrations, using the concept of minimum alveolar concentration (MAC)[7] and using Student's *t* test with a significance level of less than 5 per cent. The data of Saidman and Eger[2] suggested that 70 per cent nitrous oxide is equivalent in anesthetic potency to 0.45 per cent halothane, which was added to the halothane concentration in our group and the sum divided by 0.84 per cent (MAC for halothane in this age group[8]) to give the MAC multiple of the nitrous oxide–halothane–oxygen group. The same calculations were used for the halothane–oxygen group except that no addition for nitrous oxide was necessary.

Results

The same pattern of cardiovascular response reported by Eger for halothane alone was found in our nitrous oxide–halothane group. For example, cardiac output, left ventricular work, left ventricular stroke work, and IJ-wave amplitude decreased while heart rate and mean right atrial pressure increased with increasing depth of anesthesia. Also, with increasing duration of anesthesia (five hours), cardiac output, heart rate, left ventricular work, left ventricular stroke work, and IJ-wave amplitude increased while total peripheral resistance and mean right atrial pressure decreased in our group.

More important, however, is the comparison between our nitrous oxide–halothane group and Eger's halothane group at equal MAC levels. The control (awake) values for the two groups were similar in most respects (table 1). The nitrous oxide–halothane group, however, had significantly lower values for hemoglobin, hematocrit, cardiac output, heart rate, and left ventricular minute work, and a significantly higher value for mean right atrial pressure. Compared with halothane alone, during the first hour of anesthesia 1.2 MAC nitrous oxide–halothane caused significantly less depression of cardiac output, mean arterial pressure, stroke volume, left ventricular minute work, left ventricular stroke work, mean rate of ventricular ejection, IJ-wave amplitude, and muscle blood flow (table 2). Late in anesthesia, at 1.2 MAC, the differences between the two groups ceased to exist except for less depression of left ventricular minute work in our nitrous oxide group. At 1.8 MAC or more, no differences were evident except smaller reductions in mean arterial pressure and IJ-wave amplitude early at 2.4 MAC and in left ventricular minute work, mean arterial pressure, and IJ-wave amplitude late in anesthesia at 1.2, 1.8, and 2.4 MAC, respectively, in the group receiving nitrous oxide. Nitrous oxide caused mean right atrial pressure to be significantly higher both early at 2.4 MAC and late at 3.0 MAC. The changes in these variables are graphed in figures 1–3.

Body temperatures did not vary significantly from those reported for the halothane series, but tended to increase with increasing MAC levels of halothane plus nitrous oxide. In the nitrous oxide group, body temperature increased from 36.6 ± 0.1 (SE) C to 36.9 ± 0.1 C early and from 36.8 ± 0.1 C to 37.1 ± 0.1 C late, while skin temperature decreased from 34.7 ± 0.2 C to 34.4 ± 0.4 C early and from 34.7 ± 0.2 C to 34.4 ± 0.3 C late as depth of anesthesia was increased from 1.2 to 2.4 MAC early and from 1.2 to 3.0 MAC late in the anesthetic course. Skin blood flow tended to decrease concomitantly. These changes took place over a few minutes despite constant environmental conditions (temperature, drafts, light, etc.).

Changes in cardiovascular function 15 minutes after discontinuation of nitrous oxide at a stable (more than 3 hours) 1 per cent end-tidal halothane–nitrous oxide concentration were compared directly with results found when the opposite situation was studied—that

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TABLE 2. Comparison of Halothane with Halothane–Nitrous Oxide Anesthesia
(Per Cent of Control unless Otherwise Indicated)

	Early Anesthesia			Late Anesthesia			
	MAC 1.2	MAC 1.8	MAC 2.4	MAC 1.2	MAC 1.8	MAC 2.4	MAC 3.0
Number of subjects							
Halothane	15	6	9	12	14	11	7
Halothane–N_2O	8	8	6	8	8	8	7
Time of anesthesia (min from induction)							
Halothane	31 ± 1	52 ± 2	58 ± 4	310 ± 11	303 ± 13	321 ± 23	385 ± 32
Halothane–N_2O	40 ± 3*	62 ± 4	79 ± 6*	374 ± 15*	399 ± 13*	423 ± 14*	450 ± 15
Halothane concentration (end-tidal, per cent)							
Halothane	1.01 ± 0.03	1.55 ± 0.02	2.00 ± 0	0.95 ± 0.03	1.58 ± 0.01	2.00 ± 0	2.44 ± 0.02
Halothane–N_2O + 0.45	0.94 ± 0.01*	1.48 ± 0.01*	1.97 ± 0.02	0.95 ± 0.02	1.48 ± 0.02*	1.93 ± 0.01*	2.40 ± 0.02
Cardiac output							
Halothane	78 ± 2	98 ± 4	99 ± 5	107 ± 9	91 ± 4	78 ± 7	78 ± 8
Halothane–N_2O	98 ± 6*	99 ± 5	98 ± 3	109 ± 11	97 ± 6	90 ± 4	86 ± 6
Total peripheral resistance							
Halothane	92 ± 4	92 ± 7	91 ± 9	74 ± 3	97 ± 3	70 ± 2	77 ± 3
Halothane–N_2O	86 ± 7	90 ± 9	99 ± 10	80 ± 8	81 ± 9	77 ± 10	76 ± 8
Heart rate							
Halothane	102 ± 3	101 ± 4	102 ± 5	109 ± 3	115 ± 3	115 ± 5	122 ± 8
Halothane–N_2O	99 ± 3	103 ± 6	108 ± 9	110 ± 7	125 ± 9	127 ± 11	132 ± 12
Mean arterial pressure							
Halothane	76 ± 2	97 ± 4	99 ± 5	79 ± 3	93 ± 3	90 ± 5	93 ± 5
Halothane–N_2O	86 ± 4*	72 ± 6	98 ± 5*	89 ± 4	81 ± 5*	76 ± 7	77 ± 8
Mean right atrial pressure (torr change)							
Halothane	2.5 ± 0.6	3.7 ± 1.3	4.7 ± 0.7	0.7 ± 0.5	1.7 ± 0.4	3.9 ± 0.6	3.5 ± 0.9
Halothane–N_2O	3.0 ± 0.2	5.3 ± 0.4	6.7 ± 0.5*	0 ± 0.7	3.1 ± 0.8	5.7 ± 0.9	8.8 ± 1.2*
Stroke volume							
Halothane	78 ± 2	98 ± 5	97 ± 4	91 ± 4	89 ± 3	69 ± 7	64 ± 7
Halothane–N_2O	98 ± 4*	97 ± 4	93 ± 4	91 ± 6	89 ± 5	75 ± 5	67 ± 7
Left ventricular minute work							
Halothane	64 ± 3	94 ± 4	98 ± 5	98 ± 4	93 ± 5	52 ± 8	58 ± 10
Halothane–N_2O	84 ± 6*	89 ± 5	98 ± 4	90 ± 10*	78 ± 7	69 ± 8	68 ± 10
Left ventricular stroke work							
Halothane	63 ± 3	94 ± 5	92 ± 5	93 ± 4	93 ± 5	45 ± 7	47 ± 8
Halothane–N_2O	84 ± 5*	91 ± 5	97 ± 5	75 ± 6	94 ± 5	55 ± 6	53 ± 9

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TABLE 2. (*Continued*)

	Early Anesthesia			Late Anesthesia			
	MAC 1.2	MAC 1.8	MAC 2.4	MAC 1.2	MAC 1.8	MAC 2.4	MAC 3.0
Ejection time index							
Halothane	101 ± 2 (n = 9)	101 ± 2	107 ± 4 (n = 6)	93 ± 12 (n = 9)	106 ± 3 (n = 8)	107 ± 2 (n = 8)	79 ± 22 (n = 3)
Halothane-N_2O	102 ± 1	97 ± 1	93 ± 1*	90 ± 10	89 ± 10	89 ± 10	99 ± 3
Mean rate of ventricular ejection							
Halothane	77 ± 2 (n = 9)	66 ± 5	46 ± 7 (n = 6)	77 ± 11 (n = 9)	75 ± 6 (n = 8)	62 ± 9 (n = 8)	50 ± 27 (n = 3)
Halothane-N_2O	95 ± 5*	70 ± 4	59 ± 3	94 ± 6 (n = 7)	87 ± 5 (n = 7)	82 ± 3 (n = 7)	76 ± 7
IJ wave amplitude							
Halothane	70 ± 3 (n = 14)	57 ± 6	39 ± 4	84 ± 4	70 ± 4	46 ± 6	55 ± 5 (n = 5)
Halothane-N_2O	81 ± 5*	65 ± 7	54 ± 5*	97 ± 7	85 ± 8	75 ± 9*	65 ± 11
Muscle blood flow							
Halothane	100 ± 10 (n = 10)	88 ± 14 (n = 6)	59 ± 9 (n = 7)	140 ± 28 (n = 9)	153 ± 41 (n = 8)	92 ± 19 (n = 8)	73 ± 23 (n = 4)
Halothane-N_2O	181 ± 38*	113 ± 22	76 ± 18	229 ± 49	173 ± 36	125 ± 32	103 ± 42
Skin blood flow							
Halothane	215 ± 20 (n = 4)	169 ± 25 (n = 3)	75 ± 38 (n = 2)	137 ± 80 (n = 3)	56 ± 26 (n = 3)	63 ± 44 (n = 2)	
Halothane-N_2O	731 ± 433	362 ± 183	242 ± 109	1054 ± 812	602 ± 457	590 ± 418	603 ± 507
Venous compliance							
Halothane	78 ± 8 (n = 12)	93 ± 15 (n = 5)	85 ± 14 (n = 6)	101 ± 28 (n = 11)	75 ± 13 (n = 9)	68 ± 10 (n = 8)	73 ± 14 (n = 4)
Halothane-N_2O	111 ± 12 (n = 6)	113 ± 12 (n = 6)	88 ± 22 (n = 5)	133 ± 26 (n = 6)	110 ± 14 (n = 6)	106 ± 19 (n = 6)	100 ± 30 (n = 5)
Body temperature (C)							
Halothane	36.8 ± 0.1		36.8 ± 0.1 (n = 13)	37.0 ± 0.3		36.8 ± 0.1 (n = 12)	
Halothane-N_2O	36.6 ± 0.1	36.7 ± 0.1	36.9 ± 0.1	36.8 ± 0.1	36.9 ± 0.1	37.0 ± 0.1	37.1 ± 0.1
Skin temperature (C)							
Halothane							
Halothane-N_2O	34.7 ± 0.2	34.6 ± 0.2	34.4 ± 0.4	34.7 ± 0.2	34.8 ± 0.2	34.6 ± 0.2	34.4 ± 0.3

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TABLE 2. (*Continued*)

	Early Anesthesia			Late Anesthesia			
	MAC 1.2	MAC 1.8	MAC 2.1	MAC 1.2	MAC 1.8	MAC 2.4	MAC 3.0
P_{O_2} (torr)							
Halothane	466 ± 17		480 ± 17 (n = 13)	465 ± 20		462 ± 19 (n = 12)	
Halothane–N_2O	128 ± 4*	125 ± 3	125 ± 4*	129 ± 5*	133 ± 5	132 ± 5* (n = 7)	136 ± 5
P_{CO_2} (torr)							
Halothane	38.5 ± 1.2		41.0 ± 1.1 (n = 13)	38.2 ± 0.8		38.4 ± 1.4 (n = 12)	
Halothane–N_2O	39.3 ± 0.5	39.2 ± 1.0 (n = 7)	42.0 ± 0.5	39.1 ± 1.1	39.6 ± 0.9	40.7 ± 1.1	41.2 ± 0.6
pH							
Halothane	7.37 ± 0.01		7.34 ± 0.01 (n = 13)	7.35 ± 0.01		7.35 ± 0.01 (n = 12)	
Halothane–N_2O	7.36 ± 0.01	7.37 ± 0.01	7.34 ± 0.01	7.35 ± 0	7.35 ± 0.01	7.34 ± 0.01	7.32 ± 0
Base excess (mEq/L change)							
Halothane	−0.4 ± 0.5		−1.5 ± 0.4 (n = 13)	−1.7 ± 0.7		−1.8 ± 0.7	
Halothane–N_2O	−1.0 ± 0.5	−0.8 ± 0.3	−1.4 ± 0.2	−1.6 ± 0.3	−1.3 ± 0.6	−1.5 ± 0.4	−2.5 ± 0.7
Oxygen consumption							
Halothane	76 ± 5 (n = 11)		66 ± 8 (n = 8)	88 ± 8 (n = 10)		76 ± 8 (n = 7)	
Halothane–N_2O	85 ± 6 (n = 7)	66 ± 7 (n = 7)	68 ± 5 (n = 5)	80 ± 13 (n = 7)	81 ± 6 (n = 7)	89 ± 9 (n = 6)	77 ± 6 (n = 6)
Ratio of cardiac output to oxygen consumption							
Halothane	110 ± 10 (n = 11)		80 ± 18 (n = 7)	118 ± 11 (n = 9)		105 ± 12 (n = 6)	
Halothane–N_2O	115 ± 4 (n = 7)	105 ± 6 (n = 7)	82 ± 6 (n = 6)	139 ± 12 (n = 7)	119 ± 3 (n = 7)	115 ± 10 (n = 6)	110 ± 13 (n = 6)

* $P < 0.05$.

Mean ± (SE)

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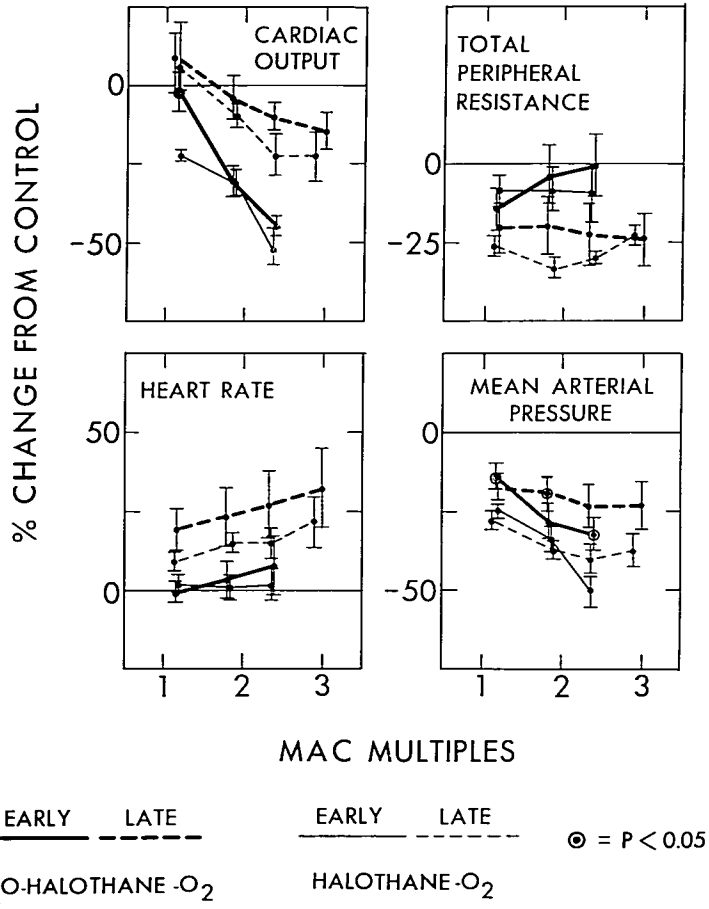

FIG. 1. Comparison of N_2O–halothane (bold lines) anesthesia with halothane–oxygen (fine lines) anesthesia[2] at equal MAC levels. The solid lines represent early anesthesia and the dashed lines, late anesthesia. The horizontal axis is in multiples of MAC (see text for method of calculation) and the vertical axis is in per cent change from control.

is, 70 per cent nitrous oxide was added for 15 minutes after a stable 1 per cent end-tidal halothane concentration had been attained[3] (table 3). In contrast to the halothane group (to which nitrous oxide was added for 15 minutes), mean right atrial pressure, forearm vascular resistance, and forearm venous pressure decreased, and forearm blood flow in-

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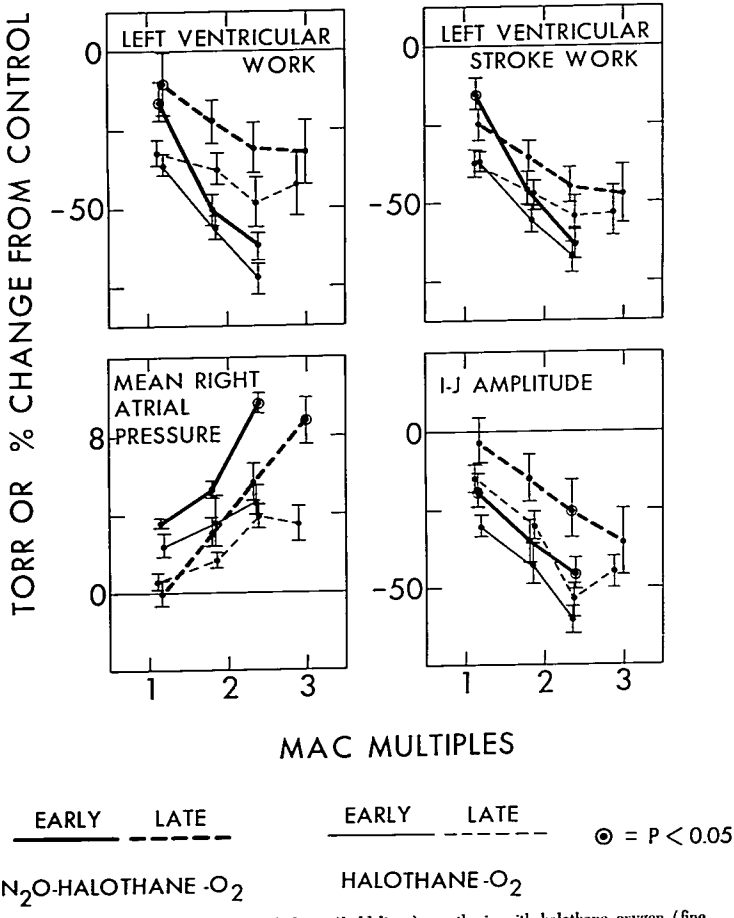

FIG. 2. Comparison of N_2O–halothane (bold lines) anesthesia with halothane–oxygen (fine lines) anesthesia[4] at equal MAC levels. The solid lines represent early anesthesia and the dashed lines, late anesthesia. The horizontal axis is in multiples of MAC (see text for method of calculation) and the vertical axis is in per cent change from control, except for mean right atrial pressure, which is torr change from control.

creased. Blood volumes and hematocrits were unchanged throughout the studies. Preanesthesia blood volume was 6.81 ± 0.45 (SE) liters and preanesthesia hematocrit was 43.8 ± 0.9 per cent. Early anesthesia values were 6.79 ± 0.56 liters and 43.0 ± 0.9 per cent.

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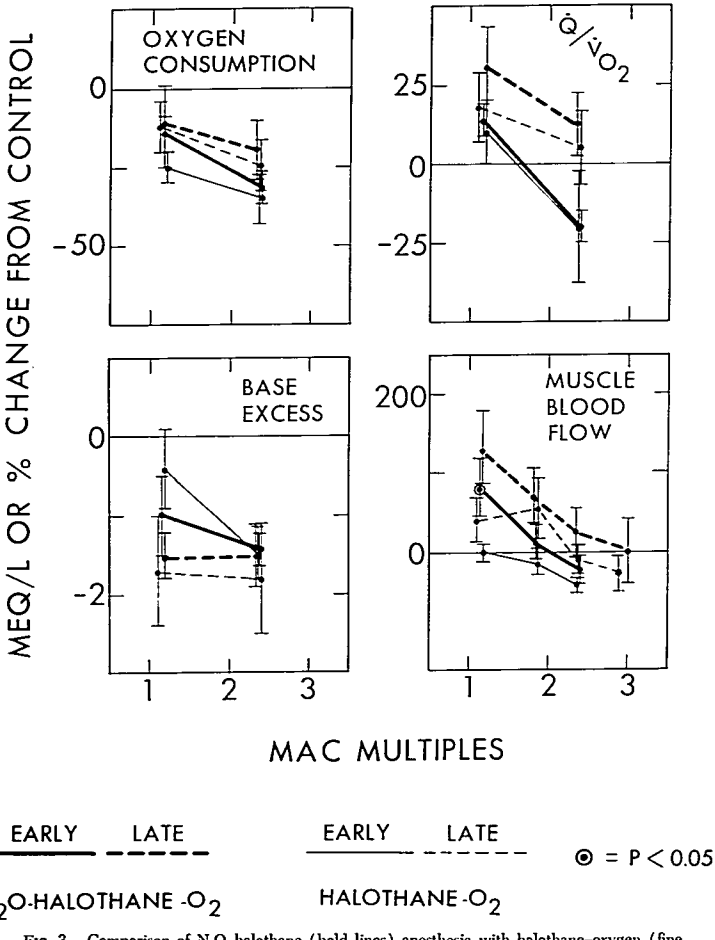

FIG. 3. Comparison of N_2O–halothane (bold lines) anesthesia with halothane–oxygen (fine lines) anesthesia[4] at equal MAC levels. The solid lines represent early anesthesia and the dashed lines, late anesthesia. The horizonal axis is in multiples of MAC (see text for method of calculation) and the vertical axis is in per cent change from control, except for base excess, which is mEq/l change from control.

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TABLE 3. Cardiovascular Effects 15 Minutes after Changing the Background Mixture Late in Anesthesia*

	Halothane–O_2 to Halothane–N_2O (from Smith *et al.*[3])			Halothane–N_2O to Halothane–O_2		
	Per Cent Change	SD	Significance of Change	Per Cent Change	SD	Significance of Change
Cardiac output	−2.98	13.32	NS	1.75	21.72	NS
Heart rate	2.65	5.00	NS	3.00	11.22	NS
Mean arterial pressure	5.70	13.92	NS	0.12	14.28	NS
Mean right atrial pressure (torr)	1.77	0.85	$P < 0.001$	−2.28	0.96	$P < 0.001$
Stroke volume	−5.74	10.44	NS	−0.75	23.79	NS
Systemic vascular resistance	12.63	14.10	$P < 0.02$	3.50	9.38	NS
"Central" blood volume (catheter-to-catheter)	4.16	10.49	NS	3.38 (n = 6)	16.13	NS
Left ventricular minute work	2.77	22.27	NS	4.87	38.52	NS
Left ventricular stroke work	0.06	18.93	NS	4.01	38.24	NS
Left ventricular stroke power	0.80	18.36	NS	−8.63 (n = 7)	24.17	NS
IJ-wave amplitude	2.30	19.37	NS	9.98	40.12	NS
Ejection time index	1.54	5.08	NS	1.14	1.86	NS
Mean rate left ventricular ejection	−6.28	13.00	NS	−7.00 (n = 7)	16.11	NS
Tension–time index	6.43	9.06	$P < 0.05$	−2.43	12.29	NS
Forearm blood flow	−21.20	21.02	$P < 0.01$	37.25	28.24	$P < 0.01$
Forearm venous pressure	−12.18	33.51	NS	−13.94 (n = 7)	12.48	$P < 0.05$
Forearm vascular resistance	41.89	41.43	$P < 0.01$	−18.25	24.59	NS
Forearm venous compliance	3.79	35.97	NS	10.18 (n = 6)	14.40	NS

* This table compares the late anesthesia changes in Smith's study 15 minutes after nitrous oxide was added to constant halothane–oxygen anesthesia[3] with those in this study 15 minutes after nitrous oxide was eliminated from constant nitrous oxide–halothane anesthesia. The values are expressed as per cent change from the steady state prior to the change (unless otherwise indicated).

Late in anesthesia the values were 6.87 ± 0.60 liters and 42.9 ± 1.0 per cent, respectively.

Discussion

The two groups compared in this paper were very similar. The control values of hemoglobin, hematocrit, cardiac output, heart rate, and left ventricular minute work were lower and the mean right atrial pressure higher in the group that received nitrous oxide, but these differences were small and should not affect the comparison. A possible explanation for these differences is that the volunteers given nitrous oxide were perhaps more relaxed and closer to a basal control level, and thus would show less depression under anesthesia. However, the similarity of oxygen consumption values relative to age, height, and weight in the two groups appeared to exclude this possibility. Other differences between the groups were compensated for by the choice of controls. For example, inhalation of high concentrations of oxygen has been known to decrease cardiac output and heart rate. However, in a recent study (Smith *et al.*[3]) we found that changing from 100 per cent oxygen and halothane to 25 per cent oxygen plus nitrogen and halothane affected only

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the heart rate, which increased slightly but significantly. Our control measurements were taken with the subjects breathing 30 per cent oxygen. During anesthesia, there were also some differences in the comparable times of anesthesia, as well as the halothane concentrations, but these also were small.

Our data taken from the first hour of anesthesia showed more cardiovascular depression with nitrous oxide–halothane anesthesia than that found by Hornbein and colleagues.[9] There are several possible explanations for these differences. In Hornbein's study, the subjects were allowed to breath spontaneously and, as a consequence, the stimulatory effects of elevated Pa_{CO_2} (46–60 torr) was present. In addition, the analysis of end-tidal halothane concentration may have been in error in Hornbein's study because of the lower ventilation and tidal volumes associated with spontaneous ventilation. This would lead to an overestimation of the alveolar concentration. Finally, Hornbein's data collection began 1½ hours following induction of anesthesia. By this time some degree of circulatory recovery, which is temporally related, may have become manifest.[1]

The data obtained upon removal and then reinstitution of nitrous oxide with halothane–oxygen anesthesia also suggest, but do not prove, that nitrous oxide may cause alpha sympathetic stimulation, as previously reported by Smith and associates[3, 10] (table 3). Millar's finding that the addition of nitrous oxide to halothane anesthesia in cats produced an increase in preganglionic cervical sympathetic discharge supports the conclusion that nitrous oxide causes sympathetic stimulation.[11]

That body temperature increased, skin temperature decreased, and skin blood flow tended to decrease with increasing depth of anesthesia agrees with previous observations on the effect of depth of halothane anesthesia on heat retention[1] and suggests that deeper levels of halothane anesthesia may cause hyperthermia. This is presumably secondary to decreased heat loss from the skin.

The partial recovery of cardiovascular function with time is seen with nitrous oxide–halothane anesthesia, as it is with halothane[1, 12] and other anesthetics.[5, 13, 14] Five hours of anesthesia increased cardiac output, heart rate, mean arterial pressure, left ventricular minute work, left ventricular stroke work, and the ratio of cardiac output to oxygen consumption from the measurements made in the first hour. Mean right atrial pressure decreased with time. These findings of stimulation are consonant with a time-dependent increase in beta sympathetic activity or sensitivity, as suggested by Price and colleagues.[15] Blood volume and hematocrit remained constant during the study, ruling out changes in these as a mechanism for the stimulation.

Base excess changed in a manner similar to that found with halothane alone. It decreased slightly with duration of anesthesia. The ratio of cardiac output to oxygen consumption also increased with time, but at any given time decreased with deeper anesthesia. These changes were the same as those found with halothane alone, and indicated that perfusion and oxygenation with increasing depth were probably adequate even though cardiac output decreased more than oxygen consumption.

Although the differences shown in this study were statistically significant, they were small. The elderly or debilitated patient, or the patient receiving sympatholytic medication, may react far differently from our young, healthy volunteers. In such patients the sympathetic stimulating properties of nitrous oxide may not be manifest, and the small benefit accruing from the combination of nitrous oxide with halothane would thus disappear.

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Blood Transfusion

COMMERCIAL BLOODBANKING There is no national blood donor program in the U. S. The American Red Cross collects about half, community and hospital banks about a fourth, and commercial banks the remaining fourth of the blood dispensed. Commercial banks pay $4 to $10 per pint to prisoners, hippies, addicts, and Skid Row residents, and this blood is the source of 90 per cent of the cases of serum hepatitis. The hepatitis rate following transfusion is 0.3 per cent for vounteer donors, 3.0 per cent for commercial donors. Tests for the Australia antigen can detect less than half of the blood capable of causing hepatitis. Because commercial donors sell blood cheaply, less effort is made to recruit volunteers; the commercial blood banks are increasing their share of the 7,000,000-unit annual need. Statistics regarding blood use and results are unreliable because banks that operate within state boundaries are not subject to Federal inspection. Blood from commercial sources should be labeled "high-risk" and avoided, if possible. (*Allen, J. G.: Commercial Blood in Our National Blood Program, Arch. Surg. 102: 122–126, 1971.*)

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