Hemodynamic effects of nitrous oxide in isoflurane-anesthetized cats

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Objective—To determine the hemodynamic effects of nitrous oxide in isoflurane-anesthetized cats.

Animals—12 healthy adult domestic shorthair cats.

Procedure—Cats were anesthetized by administration of isoflurane in oxygen. After instruments were inserted, end-tidal isoflurane concentration was set at 1.25 times the individual minimum alveolar concentration, and nitrous oxide was administered in a Latin-square design at 0, 30, 50, and 70%. Each concentration was administered for 25 minutes before measurements were obtained to allow for stabilization. Heart rate; systemic and pulmonary arterial pressures; central venous pressure; pulmonary artery occlusion pressure; cardiac output; body temperature; arterial and mixed-venous pH, P_{CO_2}, P_{O_2}, and hemoglobin concentrations; PCV; and total protein and lactate concentrations were measured before and during noxious stimulation for each nitrous oxide concentration. Arterial and mixed-venous bicarbonate concentrations and oxygen saturation, cardiac index, stroke index, rate-pressure product, systemic and pulmonary vascular resistance indices, left and right ventricular stroke work indices, arterial and mixed-venous oxygen contents, oxygen delivery, oxygen consumption, oxygen extraction ratio, alveolar-to-arterial oxygen difference, and venous admixture were calculated.

Results—Arterial pressure, central venous pressure, pulmonary arterial pressure, rate-pressure product, systemic and pulmonary vascular resistance indices, arterial P_{CO_2}, and PCV increased during administration of 70% nitrous oxide. Arterial and mixed-venous pH, mixed-venous P_{O_2}, and alveolar-to-arterial oxygen difference decreased during administration of 70% nitrous oxide. Results before and during noxious stimulation were similar.

Conclusions and Clinical Relevance—Administration of 70% nitrous oxide to isoflurane-anesthetized cats resulted in improved arterial pressure, which was related to a vasoconstrictive effect. (*Am J Vet Res* 2003;64:273–278)

Cats apparently are particularly sensitive to the cardiovascular depressant effects of potent inhalation anesthetics, compared with the sensitivity of other species. Cardiac output is more depressed at similar planes of anesthesia in cats than in dogs and humans, and hypotension is common in anesthetized cats.[1-4]

Although the **minimum alveolar concentration (MAC)** of nitrous oxide is high in cats (estimated by use of extrapolation as being 255%), this agent can be combined with more potent anesthetics in an attempt to reduce the dose of the latter, provide some analgesia, and limit anesthetic-induced cardiovascular depression.[5] In contrast to more potent inhalation anesthetics, nitrous oxide reportedly does not depress and may stimulate the cardiovascular system in various species including dogs and humans.[6-11]

Nitrous oxide is commonly used as an anesthetic adjunct in cats during inhalation anesthesia; however, cardiovascular effects of nitrous oxide have not been reported in this species. The study reported here was conducted to determine the hemodynamic effects of nitrous oxide in cats anesthetized with isoflurane. We hypothesized that nitrous oxide would stimulate, in a dose-dependent manner, the cardiovascular system and result in an increase in variables such as **heart rate (HR)**, arterial pressure, and cardiac output. Moreover, to mimic clinical conditions, we applied a noxious stimulus and repeated the measurements.

Materials and Methods

Animals—Twelve healthy adult domestic shorthair cats that weighed (mean ± SEM) 5.42 ± 0.44 kg were used in the study. The MAC of isoflurane had been determined in each cat in another study[a] by use of the tail-clamp technique. Food was withheld from the cats for 12 hours before the experiments were performed. The study was approved by an institutional animal care and use committee.

Insertion of instruments—Anesthesia was induced with isoflurane in oxygen by use of an induction box and a facemask. The trachea was then intubated with a cuffed endotracheal tube, and anesthesia was maintained by administration of isoflurane in oxygen via a Bain circuit with an oxygen flow rate of 500 mL/kg/min. A catheter was passed through the lumen of the endotracheal tube so that its distal tip was positioned at the end of the endotracheal tube. This catheter was used to sample end-tidal gases. A 22-gauge, 2.5-cm catheter[b] was inserted in a cephalic vein, and lactated Ringer's solution was administered at the rate of 3 mL/kg/h. A 5-F, 7.5-cm introducer[c] was placed in a jugular vein. A 4-F, 75-cm thermodilution catheter[d] was inserted through the introducer, and fluoroscopic observation was used to position the distal port and thermistor in the pulmonary artery to enable us to monitor cardiac output, pulmonary artery pressure, **pulmonary artery occlusion pressure (PAOP)**, central venous pressure, and core body temperature as well as to collect mixed-venous blood (pulmonary artery) samples. A 24-gauge, 9-cm catheter[e] was inserted in the femoral artery by use of the Seldinger technique for arterial pressure measurement and collection of arterial blood samples.

Monitoring of hemodynamic variables—Each cat was placed in right lateral recumbency. An ECG (lead II), HR,

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systolic arterial pressure (SAP), **diastolic arterial pressure (DAP)**, **mean arterial pressure (MAP)**, **mean pulmonary arterial pressure (PAP)**, and **central venous pressure (CVP)** were continuously monitored and recorded by use of a physiograph[f] and acquisition software.[g] All pressure transducers were calibrated against a mercury manometer before each experiment, and the 0 value was designated at the level of the sternum. Inspired and expired oxygen, carbon dioxide, isoflurane, and nitrous oxide were continuously monitored by use of a Raman spectrometer[h] calibrated with 6 calibration gases of known concentrations (0.5,[i] 1.5,[j] and 2.5%[k] isoflurane and 25,[l] 50,[m] and 75%[n] nitrous oxide). Calibrations were repeated at 80-minute intervals, which corresponded to the internal calibration interval of the spectrometer. Manually collected samples of expired gases were analyzed in triplicate by use of the spectrometer, and mean values were calculated. Arterial and mixed-venous pH, P_{CO_2}, and P_{O_2} were measured, and bicarbonate concentration and **oxygen saturation** (S_{O_2}) were calculated by use of a blood gas analyzer[o] and corrected on the basis of body temperature. Lactate concentration,[p] PCV (via a microcentrifugation technique), and **total protein (TP)** concentration (by use of a refractometer) were measured in arterial blood samples. Arterial and mixed-venous blood samples were stored for subsequent determination of hemoglobin concentration by use of a hemoximeter.[q] Cardiac output was determined in triplicate by use of a thermodilution technique, which used a cardiac output computer.[r] Three milliliters of iced 5% dextrose was injected through the proximal port of the thermodilution catheter for each determination. Mean of the 3 measurements was then calculated. Core body temperature was maintained between 38° and 39°C throughout the study by the use of warm-water circulating blankets and forced-air blankets as needed.

Cardiac index (CI), **stroke index (SI)**, **rate-pressure product (RPP)**, **systemic vascular resistance index (SVRI)**, **pulmonary vascular resistance index (PVRI)**, **left ventricular stroke work index (LVSWI)**, **right ventricular stroke work index (RVSWI)**, **arterial oxygen content** (Ca_{O_2}), **mixed-venous oxygen content** ($C\bar{v}_{O_2}$), **oxygen delivery** (D_{O_2}), **oxygen consumption** ($\dot{V}_{O_2}$), oxygen extraction ratio (ie, O_2 extraction), **alveolar-to-arterial oxygen difference** ($P_{AO_2} - Pa_{O_2}$), and **venous admixture** (Q_S/Q_T) were calculated by use of standard equations. Barometric pressure at the time of the study that was used to calculate alveolar P_{O_2} was obtained from the Climate Station at the University of California–Davis.

Protocol—Ninety minutes after induction of anesthesia, the end-tidal isoflurane concentration was set at 1.25 times the individual MAC, and that concentration was maintained for the remainder of the study. After a period of 25 minutes (to allow for stabilization), end-tidal gas samples were manually collected for measurement of isoflurane concentration. Heart rate, SAP, DAP, MAP, CVP, PAP, and PAOP were recorded. Arterial and mixed-venous blood samples were anaerobically collected and immediately placed on ice until analyzed; these samples were analyzed within 20 minutes after collection. Cardiac output was measured. A tail clamp was then applied for 5 minutes, and measurements were repeated with the noxious stimulation ongoing.

Nitrous oxide was randomly administered at 0, 30, 50, and 70% in accordance with a Latin-square design. Each concentration was administered for 25 minutes to allow for stabilization. At the end of that time, end-tidal gas samples were manually collected for end-tidal isoflurane and nitrous oxide measurements. The same measurements that had been obtained during the initial collection of data (ie, isoflurane alone) were again obtained before and during application of the tail clamp. The next concentration of nitrous oxide was then administered and collection of data repeated.

At the end of the study, the thermodilution catheter and introducer were removed, and a compressive bandage was applied for 15 minutes to the tissues overlying the jugular vein. The catheter in the femoral artery catheter was removed, the femoral artery was sutured, and the skin was closed in a routine manner. Cefazolin[s] (22 mg/kg, IV) was administered to each cat, and the cats were allowed to recover from anesthesia.

Statistical analysis—Data were analyzed by use of a repeated-measures Latin-square followed by a Tukey test for 2 × 2 comparisons.[12] Data were reported as mean ± SEM. Significance was designated at $P < 0.05$.

Results

Anesthetic concentrations—Mean ± SEM MAC of isoflurane used in the study reported here was 1.93 ± 0.06% (range, 1.50 to 2.21%). Ratio for the measured-to-target isoflurane concentration was 1.008 ± 0.002 for all cats at all measurement times. Mean measured nitrous oxide concentrations were 0.55 ± 0.17, 29.45 ± 0.22, 49.26 ± 0.16, and 69.73 ± 0.19% for the administration of 0, 30, 50, and 70%, respectively.

Effects of nitrous oxide before noxious stimulation—Heart rate, CI, SI, LVSWI, RVSWI, **mixed-venous** P_{CO_2} ($P\bar{v}_{CO_2}$), arterial and mixed-venous bicarbonate concentrations, TP concentration, Ca_{O_2}, $C\bar{v}_{O_2}$, D_{O_2}, $\dot{V}_{O_2}$, O_2 extraction, and Q_S/Q_T did not change significantly during administration of various concentrations of nitrous oxide (**Fig 1**; **Tables 1–4**). Values for MAP, CVP, PAP, RPP, PVRI, Pa_{CO_2}, and PCV were significantly higher when nitrous oxide was administered at 70%, compared with values obtained when nitrous oxide was administered at 0% (**Fig 2**). Values for SVRI were significantly higher when nitrous oxide was administered at 50 and 70%, compared with SVRI values when nitrous oxide was administered at 0% (**Fig 3**). The PAOP was significantly lower for the administration of nitrous oxide at 30%, compared to PAOP for administration of nitrous oxide at 70%. Mixed-venous pH and **mixed-venous** P_{O_2} ($P\bar{v}_{O_2}$) were significantly lower when nitrous oxide was administered at 70%, compared with values when nitrous oxide was admin-

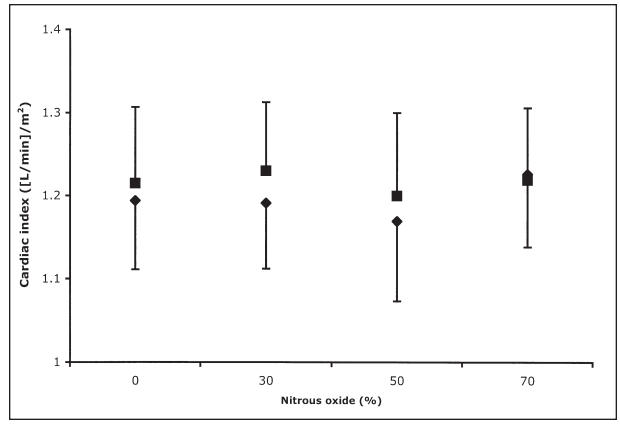

Figure 1—Mean ± SEM values for cardiac index in 12 cats anesthetized by use of 1.25 times the minimum alveolar concentration (MAC) of isoflurane and administration of various concentrations of nitrous oxide before (solid diamond) and during (solid square) noxious stimulation. Notice that cardiac index did not change during administration of nitrous oxide.

Table 1—Effects of administration of various concentrations of nitrous oxide (N_2O) before and during noxious stimulation on mean ± SEM values for selected hemodynamic variables in 12 cats anesthetized by use of isoflurane at 1.25 times the minimum alveolar concentration (MAC)

	HR (bpm)		CVP (mm Hg)		PAP (mm Hg)		PAOP (mm Hg)	
N_2O (%)	Before	During	Before	During	Before	During	Before	During
0	174 ± 6.3	175 ± 5.9	11.67 ± 1.07	12.42 ± 0.72	20.08 ± 0.78	21.33 ± 0.73	15.17 ± 0.63	15.67 ± 0.62
30	176 ± 4.7	178 ± 4.2	12.42 ± 0.80	13.25 ± 0.87	20.75 ± 0.75	21.33 ± 0.81	14.17 ± 0.71	15.08 ± 0.62
50	180 ± 4.7	179 ± 4.2	12.92 ± 0.68	14.67 ± 1.18*	21.58 ± 1.01	22.50 ± 0.77	16.00 ± 0.84	15.75 ± 0.80
70	182 ± 6.1	183 ± 6.0*	14.42 ± 1.03*	14.42 ± 1.01*	23.83 ± 0.71*	24.08 ± 0.85*	16.33 ± 0.60	17.17 ± 0.74

*Within a column, value differs significantly ($P < 0.05$) from value for 0%.
HR = Heart rate. bpm = Beats per minute. CVP = Central venous pressure. PAP = Mean pulmonary arterial pressure. PAOP = Pulmonary artery occlusion pressure.

Table 2—Effects of administration of various concentrations of N_2O before and during noxious stimulation on mean ± SEM values for selected hematologic variables in 12 cats anesthetized by use of 1.25 MAC isoflurane

	SI ([mL/beat]/m²)		RPP (beat X mm Hg)		PVRI ([{dynes X s}/cm⁵]/m²)	
N_2O (%)	Before	During	Before	During	Before	During
0	6.90 ± 0.45	6.94 ± 0.48	17,722 ± 1,593	18,461 ± 1,437	327.6 ± 46.8	388.1 ± 45.3
30	6.79 ± 0.44	6.90 ± 0.44	18,048 ± 1,099	19,158 ± 1,298	459.8 ± 59.2*	424.6 ± 59.1
50	6.47 ± 0.47	6.68 ± 0.51	19,234 ± 1,359	20,505 ± 2,163	387.0 ± 57.3	488.7 ± 65.5
70	6.77 ± 0.46	6.69 ± 0.42	21,667 ± 1,947*	22,614 ± 2,034*	507.0 ± 48.2*	491.0 ± 75.6

SI = Stroke index. RPP = Rate-pressure product. PVRI = Pulmonary vascular resistance index.
See Table 1 for remainder of key.

Table 3—Effects of administration of various concentrations of N_2O before and during noxious stimulation on mean ± SEM values for selected hematologic variables in 12 cats anesthetized by use of 1.25 MAC isoflurane

	Arterial pH		$Paco_2$ (mm Hg)		$PAo_2 - Pao_2$ (mm Hg)		Mixed-venous pH	
N_2O (%)	Before	During	Before	During	Before	During	Before	During
0	7.33 ± 0.02	7.33 ± 0.02	34.27 ± 1.74	33.18 ± 1.52	210.42 ± 16.84	196.64 ± 16.41	7.27 ± 0.02	7.28 ± 0.02
30	7.31 ± 0.01	7.31 ± 0.02	36.98 ± 1.80	36.78 ± 1.98	127.39 ± 15.09*	129.43 ± 14.09*	7.27 ± 0.01	7.27 ± 0.01
50	7.30 ± 0.01*	7.29 ± 0.03	38.59 ± 1.92	40.03 ± 4.32	84.97 ± 12.52*	84.39 ± 10.21*	7.26 ± 0.01	7.25 ± 0.02
70	7.25 ± 0.02*	7.25 ± 0.02	43.64 ± 3.79*	41.58 ± 3.34	24.02 ± 4.42*	30.94 ± 5.19*	7.22 ± 0.02*	7.22 ± 0.02*

$PAo_2 - Pao_2$ = Alveolar-to-arterial oxygen difference.
See Table 1 for remainder of key.

Table 4—Effects of administration of various concentrations of N_2O before and during noxious stimulation on mean ± SEM values for selected hematologic variables in 12 cats anesthetized by use of 1.25 MAC isoflurane

	$P\bar{v}o_2$ (mm Hg)		$P\bar{v}co_2$ (mm Hg)		PCV (%)		Lactate(mmol/L)	
N_2O (%)	Before	During	Before	During	Before	During	Before	During
0	66.35 ± 3.20	62.26 ± 2.23	42.37 ± 1.79	40.63 ± 1.70	30.67 ± 0.87	30.00 ± 0.76	2.33 ± 0.36	2.26 ± 0.32
30	59.07 ± 1.58	58.38 ± 1.74	43.30 ± 1.86	42.59 ± 2.10	31.88 ± 0.80	30.92 ± 0.83	2.17 ± 0.30	2.08 ± 0.29
50	58.57 ± 2.47	57.54 ± 2.53	44.80 ± 2.02	45.89 ± 3.51	31.71 ± 0.87	31.54 ± 1.44	2.07 ± 0.23	2.07 ± 0.22
70	57.14 ± 1.31*	56.54 ± 1.37*	47.71 ± 2.77	46.98 ± 2.69*	35.92 ± 1.05*	34.00 ± 0.96*	2.51 ± 0.31	2.71 ± 0.31

$P\bar{v}o_2$ = Mixed-venous Po_2. $P\bar{v}co_2$ = Mixed-venous Pco_2.
See Table 1 for remainder of key.

istered at 0%, whereas arterial pH was significantly lower when nitrous oxide was administered at 50 and 70%, compared with pH when nitrous oxide was administered at 0%. As expected, Pao_2 varied in relation with the decrease in **fraction of inspired oxygen** (Fio_2). However, the ratio of Pao_2 to Fio_2 did not change significantly. The $PAo_2 - Pao_2$ value decreased in a dose-dependent manner with the administration of nitrous oxide. Arterial lactate concentration was slightly higher during the administration of nitrous oxide at 70%, compared with the concentration when nitrous oxide was administered at 0%. A significant difference was found when comparing values for nitrous oxide administered at 30 and 70%. Moreover, lactate concentration was significantly affected by time (ie, duration of anesthesia).

Effects of noxious stimulation—Values observed during noxious stimulation were not significantly different from values observed before stimulation for any variable in the study. However, the effects of nitrous oxide on some variables differed before and during noxious stimulation. During stimulation, HR and $P\bar{v}co_2$ were significantly higher during administration of nitrous oxide at 70%, compared with values during administration of nitrous oxide at 0% (Tables 1–4). Values for CVP increased significantly during administration of nitrous oxide at 50 and 70%, and

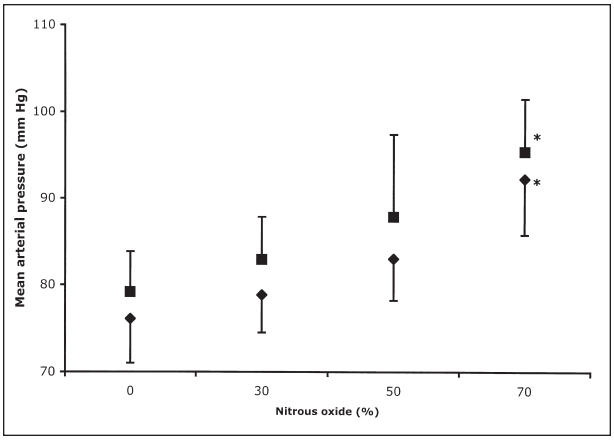

Figure 2—Mean ± SEM arterial pressure in 12 cats anesthetized by use of 1.25 MAC isoflurane and administration of various concentrations of nitrous oxide before (solid diamond) and during (solid square) noxious stimulation. Notice that mean arterial pressure increased significantly ($P < 0.05$) during administration of nitrous oxide at 70%. *Value differs significantly ($P < 0.05$) from value for administration of nitrous oxide at 0%.

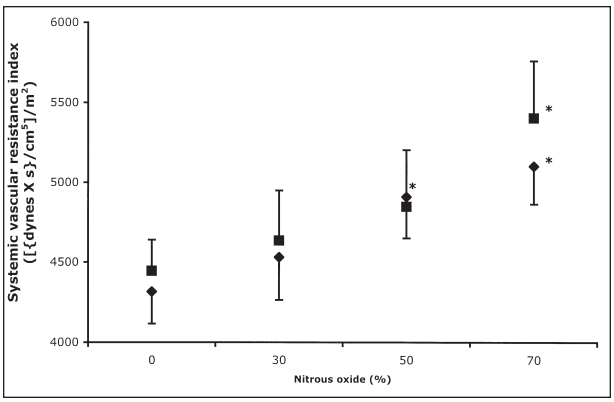

Figure 3— Mean ± SEM values for systemic vascular resistance index in 12 cats anesthetized by use of 1.25 MAC isoflurane and administration of various concentrations of nitrous oxide before (solid diamond) and during (solid square) noxious stimulation. Notice that systemic vascular resistance index increased significantly ($P < 0.05$) during administration of nitrous oxide at 70% before and during noxious stimulation and at 50% before noxious stimulation. *See* Figure 2 for key.

SVRI increased significantly only during administration of nitrous oxide at 70% (Fig 3). Values for $P\bar{v}O_2$ decreased significantly during administration of nitrous oxide at 50 and 70%. We did not detect a significant change in PAOP or PVRI. A significant difference in lactate concentration was observed when nitrous oxide was administered at 30 or 50%, compared with the lactate concentration when nitrous oxide was administered at 70%.

Discussion

Hemodynamic effects of nitrous oxide administered at 0, 30, 50, and 70% in isoflurane-anesthetized cats were determined in the study reported here. Each concentration of nitrous oxide was administered for 25 minutes to allow stabilization before measurements were obtained. This amount of time should be sufficient to enable equilibration with the brain, given the low blood and tissue solubility of nitrous oxide.[13] Measured isoflurane and nitrous oxide concentrations were extremely close to target concentrations. Individual MAC isoflurane values that had been determined in another study[a] were used to increase accuracy. A value of 1.25 times times the individual MAC of isoflurane was selected to provide a light surgical plane of anesthesia.[14]

Nitrous oxide concentrations were added to 1.25 MAC isoflurane without accounting for individual changes of isoflurane MAC related to the addition of nitrous oxide. Therefore, any decreases in isoflurane requirements induced by adding nitrous oxide were ignored in this study. This was decided on the basis of results of another study[a] conducted on the same cats; in that study, nitrous oxide did not consistently decrease the isoflurane MAC in some of the cats. Moreover, when the aforementioned study was repeated in the same cats, the reduction (or lack of reduction) in isoflurane MAC in any given animal was inconsistent. However, in the study reported here, this may have resulted in a deeper plane of anesthesia than expected in some cats, as suggested by subjective signs of anesthetic depth, such as jaw tone. If this were the case, beneficial cardiovascular effects of nitrous oxide may have been obscured by the depressant cardiovascular effects attributable to a deeper degree of anesthesia.

Spontaneous ventilation was used in the study to enable observation of the effects of nitrous oxide on blood gas tensions and pH and to avoid the cardiovascular depression induced by use of intermittent positive-pressure ventilation. In this study, an effect of increased $PaCO_2$ or decreased PaO_2 on cardiovascular variables was unlikely, because even during administration of nitrous oxide at 70%, $PaCO_2$ was only moderately increased (from 33.72 ± 1.13 mm Hg at 0% to 42.61 ± 2.47 mm Hg at 70%), and PaO_2 remained within the physiologic range (mean, 117.73 ± 4.69 mm Hg at 70%). Moreover, cardiovascular changes observed were not consistent with the circulatory response to decreased oxygen concentration (ie, increase in CI and HR and decrease in SVRI).[15]

Nitrous oxide reportedly has dual hemodynamic effects: direct myocardial depression and vasodilatory activity, resulting in decreased cardiac output, vascular resistance, and arterial pressure and an indirect cardiovascular stimulation neurally mediated by sympathetic activation.[9-11,16-24] The direct depressant effect is believed to be attributable to decreased calcium availability, whereas sympathetic stimulation may be attributable to a direct effect on nerve endings or suprapontine centers.[16,18,20,21,24] Therefore, nitrous oxide induced different effects depending on the species studied, other drugs administered, and the predominance of direct or indirect actions.

Baseline values in the study reported here are similar to other values reported for isoflurane-anesthetized cats.[1,3] The addition of nitrous oxide to 1.25 MAC isoflurane induced hemodynamic changes characterized by an increase in arterial pressures, CVP, PAP, SVRI, and PVRI. Changes were mainly observed during administration of nitrous oxide at 70% (and sometimes 50%), whereas administration at 30% did not result in

substantial cardiovascular effects. This probably reflects the low potency of nitrous oxide in cats.[5]

Heart rate increased during administration of nitrous oxide, although the values differed significantly only during noxious stimulation. Heart rate can increase, decrease, or remain constant when nitrous oxide is administered. In isoflurane-anesthetized humans, HR increases significantly during the administration of nitrous oxide at 75% but only when high isoflurane concentrations are used.[8] In halothane-anesthetized dogs, nitrous oxide administered at 75% induces a moderate increase in HR at 2 MAC.[6] Because nitrous oxide administered at 75% accounts for approximately 0.75 MAC, the halothane concentration in this combination is approximately 1.25 MAC. In halothane-anesthetized cats, HR increases moderately in response to nitrous oxide administered at 70%.[21] This increase is attributable to sympathetic activation.

In the study reported here, increases in arterial pressures and PAP were related to a vasoconstrictive effect of nitrous oxide as illustrated by the effects on SVRI and PVRI, respectively. Venoconstriction was also probably induced, because CVP increased without a concomitant decrease in cardiac output or increase in circulating volume. Similar changes have been observed in some studies[7,10,21,25]; investigators attributed these changes to sympathetic stimulation. Nitrous oxide can directly affect nerve endings to cause an increase in norepinephrine release from the pulmonary artery in dogs.[18] However, in other studies,[8,9] SVRI and arterial pressures decreased.

In the study reported here, CI and SI did not change in response to the administration of nitrous oxide. This contrasts the results of several studies[6,7,11,26-28] in which cardiac output increased in response to nitrous oxide. However, when administered concurrently with an inhalant anesthetic in those studies, the concentration of the inhalant anesthetic agent was reduced following the introduction of nitrous oxide to account for the anesthetic-sparing effect of nitrous oxide. Therefore, the increase in cardiac output observed could have been related to the decreased concentration of a more potent cardiovascular depressant rather than to an actual stimulating effect of nitrous oxide. The lack of effect observed in the study reported here may also have reflected a balance between the indirect stimulant effect and the direct depressant effect.

Rate-pressure product has been used as an index of myocardial oxygen consumption. Values for RPP increased as a result of the increase in arterial pressures and the increase in HR. Therefore, this effect was probably related to sympathetic stimulation.

The Pa_{O_2}-to-F_{IO_2} ratio did not change, illustrating that the decrease in Pa_{O_2} was mainly related to the changes in F_{IO_2} in reponse to the administration of nitrous oxide. The value for $P_{AO_2} - Pa_{O_2}$ decreased with increasing concentrations of nitrous oxide. This was expected; ventilation-perfusion scatter results in a larger change in Pa_{O_2} when P_{AO_2} is higher, because most of the oxygen is then lost from physical solution.[29]

Values for Pa_{CO_2} and $P\bar{v}_{CO_2}$ increased during the administration of nitrous oxide. This has been reported in several studies[8,9,11,27] and has been attributed to an increase in dead-space ventilation or CO_2 production, because minute volume tends to increase in response to administration of nitrous oxide.

Arterial lactate concentration increased during administration of nitrous oxide. Again, this was consistent with sympathetic stimulation. However, the fact we detected a significant effect of time may indicate that the increase was more related to time-related accumulation of this metabolite. The PCV increased in response to administration of nitrous oxide, probably as a result of vasoconstriction that induced fluid shifts from the vascular space to the interstitial space.[30]

To mimic clinical conditions, a noxious stimulus was applied, and cardiovascular measurements were repeated. We used the tail-clamp technique, because it is one of the most commonly used tests in MAC studies of animals and is considered to be a supramaximal noxious stimulus. Lack of significant hemodynamic changes during noxious stimulation observed here may have been related to several factors. The intensity of pain may have been insufficient, although this is unlikely if the assumption that the application of a tail clamp provides a supramaximal stimulus were true. Anesthesia may have been deeper than expected, resulting in sufficient depression of the CNS to inhibit a reaction to noxious stimulation. Although 1.25 MAC of an inhalant anesthetic can reportedly result in a light plane of surgical anesthesia, subjective assessment seemed to indicate that the cats achieved a deeper plane of anesthesia.

Administration of nitrous oxide at 70% in isoflurane-anesthetized cats resulted in less hypotension than when isoflurane was administered alone, whereas lower concentrations of nitrous oxide may be ineffective in improving blood pressure. The increase in blood pressure was related to a vasoconstrictive effect, whereas CI remained unchanged. Vascular effects were consistent with sympathetic activation, and the cardiac effects may have represented a balance between sympathetic activation and direct myocardial depression. However, the results may not be true for all cats at all times, because if nitrous oxide induces a reduction in MAC, and this is taken into account when administering a more potent inhalant anesthetic, there may be beneficial effects on CI. In addition, the study reported here may not reflect clinical conditions, because inhalation anesthetics are not commonly used without adjunctive medications that may modify their hemodynamic effects. Moreover, various disease processes could also change the cardiovascular response to the agents studied. Additional studies are warranted to determine whether the effects of nitrous oxide are beneficial to overall cardiovascular function in other situations (eg, evaluation of outcome in clinical patients).

[a]Imai A, Ilkiw JE, Pypendop BH, et al. Nitrous oxide does not consistently reduce isoflurane requirement in cats (abstr). *Vet Anaesth Analg* 2002;29:98.

[b]Insyte catheter, Becton-Dickinson, Sandy, Utah.

[c]Introducer kit, Arrow International, Reading, Pa.

[d]Thermodilution balloon catheter, Arrow International, Reading, Pa.

[e]Central venous catheterization kit, Arrow International, Reading, Pa.

[f]Physiograph, Gould Instrument Systems, Valley View, Ohio.
[g]Ponehma version 3.0, Gould Instrument Systems, Valley View, Ohio.
[h]Rascal II, Ohmeda, Salt Lake City, Utah.
[i]0.5% isoflurane primary standard, Matheson Gas Products, Newark, Calif.
[j]1.5% isoflurane primary standard, Matheson Gas Products, Newark, Calif.
[k]2.5% isoflurane primary standard, Matheson Gas Products, Newark, Calif.
[l]25% nitrous oxide primary standard, Matheson Gas Products, Newark, Calif.
[m]50% nitrous oxide primary standard, Matheson Gas Products, Newark, Calif.
[n]75% nitrous oxide primary standard, Matheson Gas Products, Newark, Calif.
[o]ABL 505, Radiometer, Copenhagen, Denmark.
[p]1500 Sport Lactate analyzer, Yellow Springs Instruments, Yellow Springs, Ohio.
[q]OSM3, Radiometer, Copenhagen, Denmark.
[r]COM-1, American Edwards Laboratories, Irvine, Calif.
[s]Cefazolin, Apothecon, Princeton, NJ.

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