Pulmonary resistance in dogs: a comparison of xenon with nitrous oxide

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Xenon (Xe) may cause an increase in airway resistance due to its high density and viscosity. The object of this study was to examine the effects of Xe on pulmonary resistance using dog models with normal and methacholine-treated airways. During anaesthesia 22 mongrel dogs' tracheas were intubated and the lungs were mechanically ventilated with 70% N_2/30% O_2 as a control gas. The gases 70% nitrous oxide (N_2O), 50% N_2O, 70% Xe and 50% Xe were administered in a random order for 25 min. Bronchoconstriction was produced by a continuous infusion of methacholine, 0.22 $mg \cdot kg^{-1} \cdot hr^{-1}$. Pulmonary resistance ($R_L$) was calculated by the isovolume method using flow at the airway opening, volume and transpulmonary pressure. In normal dogs, R_L breathing 70% Xe (mean ± SEM, 0.84 ± 0.12 cm $H_2O \cdot L^{-1} \cdot sec^{-1}$) was greater ($P < 0.05$) than with 70% N_2O, 50% N_2O or control gas (0.61 ± 0.08, 0.59 ± 0.06 and 0.62 ± 0.06 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$). Breathing 50% Xe the R_L (0.77 ± 0.10 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$) was not different from 50% N_2O or control. Methacholine infusion increased R_L 3.92 ± 1.98 (mean ± SD) times. The R_L breathing 50% Xe (2.55 ± 0.44 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$) was not greater than during 50% N_2O or control (2.08 ± 0.33 and 2.13 ± 0.33 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$) in methacholine-treated dogs. The data suggest that inhalation of high concentrations of Xe increases airway resistance, but only to a modest extent in dogs with normal or methacholine-treated airways.

A cause de sa densité et de sa viscosité élevées, le Xénon (Xe) peut augmenter la résistance des voies aériennes. Le but de ce travail consiste à étudier les effets du Xe sur la résistance pulmonaire de chiens aux voies aériennes normales ou traitées à la méthacholine. Pendant l'anesthésie, la trachée de 22 chiens batards est intubée et les chiens sont ventilés mécaniquement avec le gaz contrôle (70% N_2/30% O_2). Du protoxyde d'azote (N_2O) 70%, 50% N_2O, 70% Xe et 50% Xe sont administrés aléatoirement pour 25 min. La bronchoconstriction est produite par une perfusion continue de méthacholine, 0,22 $mg \cdot kg^{-1} \cdot hr^{-1}$. La résistance pulmonaire (R_L) est calculée selon la méthode de l'isovolume avec la mesure du débit à l'entrée des voies aériennes, du volume et de la pression transpulmonaire. Chez les chiens normaux, la R_L sous 70% Xe (moyenne ± SEM, 0,84 ± 0,12 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$) est plus élevée ($P < 0,05$) qu'avec 70% N_2O, 50% N_2O et qu'avec le gaz contrôle (0,61 ± 0,08, 0,59 ± 0,06 et 0,62 ± 0,06 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$). Sous 50% Xe, la R_L (0,77 ± 0,10 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$) ne diffère pas du 50% N_2O ou du contrôle. La perfusion de méthacholine augmente la R_L 3,92 ± 1,98 (moyenne ± SD) fois. Sous 50% Xe, la R_L (2,55 ± 0,44 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$) n'est pas plus élevée que sous 50% N_2O ou que sous le gaz contrôle (2,08 ± 0,33 et 2,13 ± 0,33 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$) chez les chiens traités à la méthacholine. Ces données suggèrent que l'inhalation de hautes concentrations de Xe augmente la résistance des voies aériennes, mais modérément seulement, chez les chiens aux des voies aériennes normales ou traitées à la méthacholine.

Key words
ANAESTHETICS, GASES: xenon; nitrous oxide;
LUNG: function; respiratory resistance.

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Since the anaesthetic effects of xenon gas (Xe) were reported by Cullen and Gross[1] in 1951, many studies have evaluated its anaesthetic properties. These indicate that Xe possesses advantages over nitrous oxide (N_2O). It probably does not undergo biotransformation; is non-toxic; and offers rapid induction and recovery from anaesthesia;[1-6] is free of cardiovascular side-effect.[7,8] Xenon also has an analgesic effect comparable with nitrous oxide in equipotent concentrations.[1,9] Were it not for high cost, Xe would be valuable alternative to N_2O; but costs may be minimized by using an anaesthesia system with minimal fresh gas flow.[10]

However, there is limited clinical experience of the effects of Xe on lung mechanics[8] and no studies about its effects on airway resistance. Airway resistance depends

not only on airway geometry but also on flow rate and gas density and viscosity.[11,12] Pressure-flow relationship is described as $P = K_1V + K_2V^2$, where k_1 is a constant that includes the influence of viscosity and K_2 is a constant that includes the influence of density. As Xe has higher density and viscosity (approximately 3 and 1.5 times those of N_2O, respectively), it may cause an increase in airway resistance during inhalation, especially in a patient with obstructive pulmonary disease.

The purpose of this study was to examine the effects of Xe on pulmonary resistance (RL) and gas exchange (PaO_2, $PaCO_2$), and to compare them with those of N_2O. We studied anaesthetized dogs with normal airways in Study 1 and with methacholine-treated airways in Study 2.

Methods

This study was approved by the Animal Care Committee of Osaka University Medical School. The animals used in the study were ten mongrel dogs of either sex weighing 8.5–11 kg in Study 1 and 12 weighing 9–11.3 kg in Study 2. Dogs were anaesthetized with an infusion of thiopentone (6 $mg \cdot kg^{-1}$) and alpha-chloralose (80 $mg \cdot kg^{-1}$) and anaesthesia was maintained with an infusion of alpha-choralose 10 $mg \cdot kg^{-1}$ every 15 min. After tracheal intubation, the animals were paralyzed with alcuronium, 0.2 $mg \cdot kg^{-1}$, which was maintained with 0.1 $mg \cdot kg^{-1}$ every 45 min. The endotracheal tube was a 7.5 mm cuffed tube (Deane Mallinckrodt, New York, USA), positioned just below the larynx. The tube has a side lumen at the tip for measurement of tracheal pressure. The lungs were mechanically ventilated by a piston-type ventilator (Sinano SN 480, Tokyo, Japan) to maintain end-tidal carbon dioxide (CO_2) in the normal range (35–45 mmHg) with 30% O_2/70% N_2 gas-mixture, tidal volume of 18–20 $ml \cdot kg^{-1}$ and at a flow rate below 0.5 $L \cdot sec^{-1}$ and a respiratory rate of 12 breaths $\cdot$ min^{-1}. To minimize the influences of respiratory rate and tidal volume on RL (11, 13) these settings were maintained constant throughout the measurements. End-tidal CO_2 concentration was monitored continuously using a capnograph (Capnomac, Datex, Helsinki, Finland).

A midline sternotomy was performed and the chest was widely opened to expose the lungs. As muscle paralysis and a midline sternotomy were performed, chest wall compliance was negated and it was not necessary to measure pleural pressure. The femoral artery was cannulated to permit arterial blood sampling and continuous monitoring for systemic arterial pressure. The femoral vein was cannulated for administration of fluid, anaesthetic and muscle relaxant. In Study 2, an additional femoral vein was cannulated for administration of bronchoconstriction-producing drugs. A #5 French, pulmonary artery catheter was inserted to monitor mean pulmonary artery pressure (Ppa) and central venous pressure (CVP). Losses of urine, saliva and stool fluid were replaced by lactated Ringer's solution (4–7 $ml \cdot kg^{-1} \cdot hr^{-1}$) and the CVP was maintained at about 6 mmHg. Metabolic acidosis was corrected with sodium bicarbonate (mean doses administered were 2.5 $mEq \cdot kg^{-1}$ in Study 1 and 5.1 $mEq \cdot kg^{-1}$ in Study 2). Rectal temperature was continuously monitored and maintained between 36–38°C with a thermostatically controlled heating blanket.

Flow at the airway opening was measured by a heated pneumotachograph (TV-142, Nihon Kohden, Tokyo, Japan) coupled to a differential pressure transducer (TP-602T, Nihon Kohden, Tokyo, Japan). The pneumotachograph was calibrated for each test gas using the experimental apparatus. When maximum air flow was <0.5 $L \cdot sec^{-1}$, the resistance of the pneumotachograph used in our study was 20 $mmH_2O \cdot L^{-1} \cdot sec^{-1}$. To measure the resistance of the pneumotachograph using the test gas mixtures, a large bag was partially filled with the test gas mixture and connected to a piston type ventilator used in the study. In the calibration system, the maximum flow rate was set <0.5 $L \cdot sec^{-1}$. As the flow rate at a given point in the ventilatory cycle was constant among different gas mixtures, the ratio of pressure differences of two gas mixtures across the pneumotachograph is equivalent to the viscosity ratio of these gas mixtures, because of the Poiseuille's law. Therefore, the viscosity ratios of the test gas mixtures of 70% N_2O/30% O_2, 50% N_2O/30% O_2/20% N_2, 70% Xe/30% O_2 and 50% Xe/30% O_2/20% N_2 to control gas mixture of 70% N_2/30% O_2 were determined (Table I). These ratios were used as correction coefficients to measure the gas flow ratio to the test gas mixtures. We also calculated the mixture gas viscosity by using the formula of Wilke,[14] and found that the calculated values were similar to measured values. Flow was electrically integrated to obtain tidal volume (VT) (EI-60IG, Nihon Kohden, Tokyo, Japan). As Xe and N_2O are anaesthetics, volume changes may occur because of changes to surfactant production or relaxation of cells located in Kapanci alveolar walls as well as tissue viscosity with alterations in fluid. Therefore, we monitored the tidal volume continuously during the experiments. Transpulmonary pressure (Ptp) was measured by a differential pressure transducer (TP-603T, Nihon Kohden, Tokyo, Japan), one side of which was connected to the tip lumen of the endotracheal tube whilst the other was left open to atmosphere. All recordings were displayed on a thermal array recorder (WS-641G, Nihon Kohden, Tokyo, Japan). Average total pulmonary resistance (RL) was calculated by using the isovolume

TABLE I Density, viscosity and viscosity ratios of gas mixtures

	Density ($kg \cdot m^{-3}$)	*Viscosity* ($\times 10^{-6} Pa \cdot sec^{-1}$)	*Viscosity ratio*
Control (70% N_2+30% O_2)	1.304	19.5	1.00
70% N_2O+30% O_2	1.812	16.7	0.87
50% N_2O+30% O_2+20% N_2	1.667	17.4	0.90
70% Xe+30% O_2	4.523	24.3	1.14
50% Xe+30% O_2+20% N_2	3.603	22.4	1.11

The densities were determined by calculating from the density and volume ratios of each gas. The viscosities were calculated from the formula of Wilke. Viscosity ratios of gas mixtures were measured using the experimental apparatus. These ratios were used as correction coefficients to measure gas flow of test gas mixtures using a pneumotachograph in the study.

method.[15] The RL was measured from the difference in Ptp and the difference in flow between the points of mid-tidal inspiratory and expiratory in the respiratory cycle. Peak inspiratory airway pressure (PIP) was obtained from the recordings. The control gas mixture of 70% N_2/30% O_2 and four test gas mixtures of 70% N_2O/30% O_2, 50% N_2O/30% O_2/20% N_2, 70% Xe/30% O_2 and 50% Xe/30% O_2/20% N_2 were administered via a semiclosed circuit of an anaesthetic machine.

Each gas concentration was monitored continuously at the airway opening; O_2 and N_2O with a gas analyzer (Capnomac, Datex, Helsinki, Finland) and Xe with a thermal conductivity gas analyzer (ZAF, Fuji Electric, Tokyo, Japan). Gas analyzers were calibrated with each standard gas before the measurement. Arterial blood gases were analyzed (ABL2, Finland) immediately after blood sampling.

The method used in this experiment was a repeated on/off stimulus bounded by two control periods. Study 1. Thirty minutes after the animal preparation was completed, measurements of each variable were made as the first control data with 70% N_2/30% O_2. Then, each dog received the four test gases. The gases were applied in random order and the lungs were ventilated for 25 min with each gas to obtain a steady state of end-tidal concentration. The lungs were ventilated with 70% N_2/30% O_2 for 20 min between the inhalation of the various test gases to eliminate their effects. Finally, the second control measurement was undertaken at the end of the experiment using 70% N_2/30% O_2.

Study 2. Fifteen minutes after induction of anaesthesia, the beta-adrenergic blocker, propranolol (1.6 $mg \cdot kg^{-1}$ *iv*) was administered followed by a continuous infusion (16 $\mu g \cdot kg^{-1} \cdot min^{-1}$).[16] After confirming a stable blood pressure and heart rate, infusion of methacholine was started at a rate of 0.22 $mg \cdot kg^{-1} \cdot hr^{-1}$ and adjusted to maintain RL at 200% greater than the pre-infusion value. The baseline measurement was made before administration of both drugs. Thirty minutes after administration of methacholine, the experiment was repeated following the same protocol as in Study 1, except that trials of 70% N_2O and 70% Xe were not performed.

Intergroup data were analyzed by one-way analysis of variance (ANOVA) with repeated measures and assessed by Scheffe's F-test. Data within each group were analyzed by two-way ANOVA with repeated measures and assessed by paired t test. A P value <0.05 was considered statistically significant.

Results

In three of 12 dogs used in Study 2, haemodynamic variables were unstable throughout the experiment and the second control values in RL did not return close to the first control values. Therefore, data obtained from these three dogs were excluded from the following analysis. We could not measure the RL with 70% Xe and 70% N_2O in Study 2 because of haemodynamic instability which was sometimes critical with the combined administration of methacholine and high dose of Xe or N_2O.

In Study 1, RL during 70% Xe was greater than during control, 70% N_2O and 50% N_2O ($P < 0.05$) (Table II). However, RL during 50% Xe was not different from control or from that with other gases. Peak inspiratory airway pressure during Xe inhalation did not change. The PaO_2 and $PaCO_2$ did not change with Xe gas mixtures.

In Study 2, infusion of methacholine caused bronchoconstriction and RL increased from 0.56 ± 0.07 (mean ± SE) to 2.13 ± 0.33 $cmH_2O \cdot L^{-1} \cdot sec^{-1}$ (Table III). Methacholine infusion reduced PaO_2 from 149 ± 8 to 94 ± 8 mmHg. The RL breathing 50% Xe gas mixture, was not different from those with control or 50% N_2O gas mixtures (Table IV). The PIP and VT did not change various gases both in Study 1 and 2. The PaO_2 and $PaCO_2$ did not change with Xe and N_2O gas mixtures. Circulatory data were not different among various gas mixtures both in Study 1 and 2.

TABLE II Cardiorespiratory data in Study 1

	C_1	70% N_2O	50% N_2O	70% Xe	50% Xe	C_2
RL ($cmH_2O \cdot L^{-1} \cdot sec^{-1}$)	0.62 ± 0.06	0.61 ± 0.08	0.59 ± 0.06	0.84 ± 0.12*	0.77 ± 0.10	0.64 ± 0.07
VT (ml)	218 ± 6	216 ± 6	216 ± 8	211 ± 7	209 ± 7	220 ± 5
PIP (cmH_2O)	6.6 ± 0.5	6.6 ± 0.6	6.7 ± 0.6	7.2 ± 0.4	7.3 ± 0.5	7.1 ± 0.6
pH	7.39 ± 0.01	7.39 ± 0.01	7.38 ± 0.01	7.37 ± 0.01	7.36 ± 0.01	7.41 ± 0.02
PaO_2 (mmHg)	155 ± 9	156 ± 7	143 ± 10	139 ± 10	140 ± 10	142 ± 9
$PaCO_2$ (mmHg)	35.2 ± 0.8	38.7 ± 2.2	40.5 ± 1.2	41.6 ± 1.7	41.2 ± 1.2	37.4 ± 1.0
HR (beats · min^{-1})	119 ± 4	126 ± 7	126 ± 6	115 ± 5	117 ± 5	125 ± 6
SBP (mmHg)	135 ± 6	137 ± 7	139 ± 7	129 ± 10	129 ± 9	140 ± 4
DBP (mmHg)	81 ± 3	88 ± 6	90 ± 5	83 ± 6	82 ± 5	87 ± 5
Ppa (mmHg)	15.8 ± 1.0	17.1 ± 0.8	17.1 ± 0.8	16.5 ± 0.7	17.2 ± 0.6	16.3 ± 0.7

Cardiorespiratory measurements during inhalation of control gas mixture of 70% N_2/30% O_2 and test gas mixtures of 70% N_2O/30% O_2, 50% N_2O/30% O_2/20% N_2, 70% Xe/30% O_2 and 50% Xe/30% O_2/20% N_2 with normal airway in Study 1 (mean ± SE, $n = 10$). C_1 = first control; C_2 = second control; RL = pulmonary resistance; VT = tidal volume; PIP = peak inspiratory airway pressure; PaO_2 = arterial oxygen tension; $PaCO_2$ = arterial carbon dioxide tension; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; Ppa = mean pulmonary arterial pressure.
*$P < 0.05$ compared with control, 70% N_2O and 50% N_2O.

TABLE III Response of cardiorespiratory measurements to methacholine infusion

	Baseline	*Postinfusion*
RL ($cmH_2O \cdot L^{-1} \cdot sec^{-1}$)	0.56 ± 0.07	2.13 ± 0.33‡
VT (ml)	229 ± 18	218 ± 17*
PIP (cmH_2O)	6.8 ± 0.5	13.2 ± 0.3‡
pH	7.41 ± 0.01	7.39 ± 0.02
PaO_2 (mmHg)	149 ± 8	94 ± 8†
$PaCO_2$ (mmHg)	37.9 ± 1.8	41.3 ± 2.0
HR (beats · min^{-1})	125 ± 5	93 ± 3†
SBP (mmHg)	142 ± 6	91 ± 5‡
DBP (mmHg)	89 ± 3	57 ± 2‡
Ppa (mmHg)	18.2 ± 1.5	21.1 ± 1.4

All values are mean ± SE, $n = 9$. Study 2.
RL = pulmonary resistance; VT = tidal volume; PIP = peak inspiratory airway pressure; PaO_2 = arterial oxygen tension; $PaCO_2$ = arterial carbon dioxide tension; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; Ppa = mean pulmonary arterial pressure.
*$P < 0.05$ compared with baseline.
†$P < 0.01$ compared with baseline.
‡$P < 0.001$ compared with baseline.

Discussion

This study has shown that 70% Xe increased pulmonary resistance in dogs with normal airways but 50% Xe did not cause increases either in normal airways or after bronchoconstriction. The PaO_2 and $PaCO_2$ were unaffected by inhalation of Xe both with normal airways and after bronchoconstriction. These results suggest that Xe may be safe anaesthetic gas as far as lung mechanics are concerned.

We used alpha-chloralose as a general anaesthetic in the study because it preserves myocardial function and maintains an intact bronchocontrictor-reflex in anaesthetized dogs.[17,18]

In this study we measured RL and took this to reflect airway resistance. Warner *et al.*[19] suggested that pulmonary resistance was composed of airway resistance and lung tissue resistance. As both of these components react to provocative challenges, the change in pulmonary resistance is the sum of these two components. Ludwig *et al.*[20] demonstrated that although pulmonary resistance was composed of these two separate entities, the percentage due to airway resistance was constant; therefore, a linear correlation exists between changes in RL and those in airway resistance. The relative contributions of airway and tissue resistance to RL vary with respiratory frequency and tidal volume in intact dog lungs.[13] To facilitate interpretation of our data, both of these variables were kept constant throughout the study.

We followed the methodology by Breen *et al.*[16] who used high tidal volumes of 18–20 ml · kg^{-1} at low flow rates. The disadvantages of high tidal volumes are that they would accentuate lung tissue resistance and diminish airway resistance as relative components, but its advantages include prolongation of expiratory time and a reduction of the gradient between the alveolae and atmosphere at end expiration.

Airway resistance has viscosity-dependent and density-dependent components. Airway resistance is viscosity-dependent in the presence of laminar flow and is density-dependent in turbulent flow. Jaffrin[12] has suggested, on theoretical grounds, that flow regimens ranging from nearly laminar to highly turbulent should be found in

TABLE IV Cardiorespiratory data in Study 2

	C_1	50% N_2O	50% Xe	C_2
RL ($cmH_2O \cdot L^{-1} \cdot sec^{-1}$)	2.13 ± 0.33	2.08 ± 0.33	2.55 ± 0.44	2.02 ± 0.30
VT (ml)	218 ± 17	216 ± 16	218 ± 17	218 ± 17
PIP (cmH_2O)	13.2 ± 0.3	13.2 ± 0.4	13.8 ± 0.4	13.4 ± 0.5
pH	7.39 ± 0.02	7.39 ± 0.01	7.41 ± 0.01	7.40 ± 0.02
PaO_2 (mmHg)	94 ± 8	97 ± 7	96 ± 9	89 ± 6
$PaCO_2$ (mmHg)	41.3 ± 2.0	44.1 ± 1.8	45.0 ± 2.0	40.5 ± 2.1
HR ($beats \cdot min^{-1}$)	93 ± 3	93 ± 3	90 ± 2	92 ± 2
SBP (mmHg)	91 ± 5	99 ± 10	87 ± 8	99 ± 7
DBP (mmHg)	57 ± 2	62 ± 4	55 ± 2	60 ± 4
Ppa (mmHg)	21.1 ± 1.4	22.0 ± 1.8	22.1 ± 1.9	21.5 ± 2.0

Cardiorespiratory measurements during inhalation of control gas mixture of 70% N_2/30% O_2 and test gas mixtures of 50% N_2O/30% O_2/20% N_2 and 50% Xe/30% O_2/20% N_2 with methacholine-treated airway in Study 2 (mean ± SE, $n = 9$). C_1 = first control; C_2 = second control; RL = pulmonary resistance; VT = tidal volume; PIP = peak inspiratory airway pressure; PaO_2 = arterial oxygen tension; $PaCO_2$ = arterial carbon dioxide tension; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; Ppa = mean pulmonary arterial pressure.

the lung. In peripheral airways, flow is laminar because the total air flow is divided among hundreds of thousands of tubes. In the more central airways, the resistance can change greatly with flow rate, at a flow rate of <1 $L \cdot sec^{-1}$, the effects of laminar flow pre-dominate but at high flow rate, the effects of turbulence dominate.[11]

The present data showed that with inhalation of 70% Xe RL increased by 1.3 times compared with control in normal airways. The gas mixture of 70% Xe has 1.14 times the viscosity of control gas and 3.47 times the density of controls, respectively (Table I). The results indicated that flow in the tracheobronchial tree is laminar or near laminar for Xe. As dog's normal airways are laminar flow-dominant, the density effect of Xe on the flow will be minimized. Therefore, inhalation of Xe gas may not cause large increases in airway resistance despite its higher density.

To evaluate the effect of Xe on pulmonary resistance in the bronchoconstricted state, we used methacholine-induced bronchoconstriction that has been used in some respiratory laboratory investigations.[16,21,22] Pretreatment with propranolol was used to increase methacholine reactivity.[16,23,24] Beta-adrenergic blockade with propranolol would also diminish the effect of sympathetic activity and indirectly increase the activity of methacholine rather than by a direct action. In the present study, continuous intraveous methacholine infusion increased RL by 3.92 ± 1.98 (mean ± SD) times and decreased PaO_2 systemic blood pressures. These results are consistent with the study reported by Breen and Becker.[16] They demonstrated that intravenous methacholine produced canine bronchoconstriction, gas trapping and hypoxia, and suggested these features of canine methacholine model may be important in studies of the optimal treatment of clinical status asthmaticus.

In this study, the effects of 50% Xe on RL are similar in normal and methacholine-treated dogs. There are two reasons which may explain this similarity. The first is derived from the physical properties of Xe. We had predicted that the Xe/O_2 mixture would increase the central airway component by a large amount (density-dependent) and increase peripheral resistance by only a small amount (viscosity-dependent). However, 50% Xe did not increase RL in methacholine-treated dogs as much as in normal dogs. This may have been because methacholine constricts peripheral rather than central airways[25] and resistance in peripheral airways is independent of gas density.[26] This indicated that the density effect of Xe is minimal in methacholine-induced bronchoconstricted airways. The second reason may be derived from the anaesthetic effect of Xe on the constricted airway. Some inhalational anaesthetics, such as halothane, have been shown to decrease RL considerably.[19] Xenon may directly attenuate the bronchoconstriction, resulting in a decrease of RL. This effect may have counterbalanced the density and viscosity effects of Xe.

Lachman *et al.*[8] compared the effects of 70% Xe/30% O_2 and 70% N_2O/30% O_2 on lung mechanics in ASA physical 1 or 2 patients, using a lung mechanics calculator. They demonstrated that expiratory lung resistance was higher in both Xe and N_2O groups than at baseline but there was no difference between the two groups. Oxygen saturation decreased below 92% in eight patients in the N_2O group but not in any patient in the Xe group. They concluded that there was only slight deterioration in lung mechanics during Xe anaesthesia, which suggests that Xe can be used safely in older patients and those with chronic lung diseases. Douglas *et al.*[27] reported that 50% N_2O decreased the specific airway conductance and interpreted the results as indicating bronchoconstrictive

effect of N_2O. In the present study, however, we did not find any effect of N_2O on R_L in both normal and methacholine-treated dogs.

Nemery *et al.*[28] demonstrated that the physical properties of the density of inhaled gas did not affect pulmonary gas exchanges in healthy humans because the changes were minimal and because they may compensate for each other. Moote *et al.*[29] reported that much greater increases in flow resistance induced by mechanical loads during anaesthesia do not detectably alter pulmonary gas exchange. Christopherson *et al.*[30] reported that the alveolar-arterial O_2 partial pressure difference decreased as carrier-gas density increased. We examined the effects of Xe and N_2O on pulmonary gas exchange (PaO_2 and $PaCO_2$) in normal and methacholine-treated dogs and did not find any differences.

In conclusion, the inhalation of high concentrations of Xe increases airway resistance, to a modest degree in dogs with normal or methacholine-treated airways.

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