Determination of minimum alveolar concentration and cardiovascular effects of desflurane in positive-pressure ventilated sheep

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OBJECTIVE
To determine the minimum alveolar concentration of desflurane (MAC_{DES}) and effects on cardiovascular variables in positive-pressure ventilated sheep.

ANIMALS
13 adult female sheep.

PROCEDURES
Anesthesia was induced with desflurane. After a 30-minute equilibration at an end-tidal concentration of desflurane (ET_{DES}) of 10.5%, an electrical stimulus (5 Hz/ms and 50 mA) was applied for 1 minute or until gross purposeful movement occurred. The ET_{DES} was then changed by 0.5% (modified up-down method), depending on whether a positive motor response had been elicited, and stimulation was repeated. The MAC_{DES} was the ET_{DES} midway between a positive and negative response. After MAC_{DES} was determined, ET_{DES} was increased to 1.3 and 1.6 MAC_{DES}. Animals were allowed to equilibrate for 15 minutes, and cardiovascular, blood gas, acid-base, and hematologic variables were measured. Times to induction of anesthesia, extubation, attainment of sternal position, and standing and duration of anesthesia were recorded.

RESULTS
Mean ± SD MAC_{DES} was 9.81 ± 0.79%. Times to intubation, extubation, and standing were 4.81 ± 2.21 minutes, 14.09 ± 4.05 minutes, and 32.4 ± 12.5 minutes, respectively. Duration of anesthesia was 226 ± 22 minutes. Heart rate increased significantly at induction of anesthesia but otherwise remained at preanesthetic rates. Arterial blood pressures progressively decreased with increasing ET_{DES}; pressures increased slightly only in response to noxious stimulation.

CONCLUSIONS AND CLINICAL RELEVANCE
The MAC_{DES} determined here compared favorably with that determined for other sheep populations and indicated similar anesthetic potency as in other species. Desflurane caused dose-dependent arterial hypotension, which indicated the need for careful blood pressure monitoring. (*Am J Vet Res* 2018;79:727–732)

Desflurane is 1 of 3 contemporary ether-derived volatile anesthetics that was developed in the 1960s. However, it was not used in clinical practice throughout North America and Europe until the 1990s. In contrast to the other volatile anesthetics, desflurane is characterized by a boiling point close to room temperature; thus, it requires a specially designed and electrically heated vaporizer for safe use in both clinical practice and research settings.[1–3] This requisite and the higher cost per milliliter of agent (compared with the cost for isoflurane) have curtailed the widespread use of desflurane in veterinary practice and for larger research animals (eg, sheep and pigs). However, patent protection for desflurane has expired, and drug costs are likely to decrease soon; thus, use of desflurane will probably increase.

The overall pharmacodynamic profile of desflurane is similar to those of isoflurane and sevoflurane, the other 2 ether-derived anesthetics used in clinical practice.[1–3] However, desflurane is characterized by relatively unique properties that may offer advantages for its use in certain clinical and research situations. It has the lowest rate of biodegradation (< 0.02% vs 0.2% for isoflurane and 2% to 3% for sevoflurane) among all volatile anesthetics, which explains the reason that the increase in serum inorganic fluoride concentration is much smaller with desflurane than with isoflurane and sevoflurane.[3] In contrast, desflurane may result in

ABBREVIATIONS

DAP	Diastolic arterial blood pressure
ET_{DES}	End-tidal concentration of desflurane
IQR	Interquartile (25th to 75th percentile) range
MAC	Minimum alveolar concentration
MAC_{DES}	Minimum alveolar concentration of desflurane
MAP	Mean arterial blood pressure
P_{ETCO_2}	End-tidal partial pressure of carbon dioxide
Sa_{O_2}	Arterial oxygen saturation
SAP	Systolic arterial blood pressure

higher amounts of CO, compared with the amounts of CO when isoflurane or sevoflurane are used, when the anesthetic agent is in contact with dry CO_2 absorbents, with higher amounts of CO formed in calcium hydroxide–barium hydroxide compounds than in soda lime, which favors use of desflurane under low-flow anesthesia conditions that result in much less desiccation of CO_2 absorbents.[4] The extremely low solubility of desflurane in blood (blood gas partition coefficient, 0.424 at 37°C) and tissues allows for rapid induction and emergence from anesthesia as well as precise control over anesthetic depth and other clinical drug effects.[2,3] Thus, desflurane may offer important advantages over the use of isoflurane and sevoflurane for induction and maintenance of anesthesia, particularly when clinical or research circumstances restrict the use of injectable anesthetics or anesthetic adjuvants.

The MAC of a volatile anesthetic is the concentration that prevents gross purposeful movement in response to a defined supramaximal noxious stimulus in 50% of subjects, and it determines the potency of an inhalation anesthetic.[3,5] The MAC_{DES} has been determined in humans and various other species, including cats, dogs, horses, mice, pigs, rats, and rabbits[3] as well as sheep.[6,a] In most of the studies that involved domestic animals, noxious stimulation involved a mechanical stimulus (eg, forceps clamping).

The purposes of the study reported here were to determine the MAC_{DES} in sheep by applying a train of electrical impulses instead of mechanical stimulation as the supramaximal nociceptive stimulus and to describe the effects of various doses of desflurane (ie, MAC multiples) on hemodynamic variables. We hypothesized that desflurane would have similar anesthetic potency and cardiovascular effects of similar magnitude in sheep as has been reported for other animal species.

Materials and Methods

Animals

Thirteen healthy adult nonpregnant female Sardinian sheep were included in the study. The sheep were 5 to 7 years old and had a mean ± SD body weight of 35.3 ± 2.7 kg. All sheep were deemed to be healthy on the basis of results of physical examination, hematologic assessment, and serum biochemical assay. The study was performed in Sassari, Italy, which is located at 225 m above sea level. Atmospheric pressure during the period of MAC_{DES} determinations was between 101 and 102 kPa. The study protocol was approved by the Institutional Animal Care and Use Committee at the University of Sassari (protocol No. 132/11) in accordance with Italian legislation.

Study protocol

Food was withheld for 12 hours prior to anesthesia, but animals had unlimited access to water. On the day of the procedure, body weight, heart rate, respiratory rate, and rectal temperature were recorded for each animal while at rest. Sheep then were positioned in right lateral recumbency on a preparation table. The subcutaneous tissues over a rostral auricular artery were infiltrated with lidocaine 2% solution, and a 20-gauge, 3.1-cm catheter[b] was aseptically inserted in the artery; that catheter was used to obtain invasive arterial blood pressure measurements and for collection of blood samples. Wool was clipped over the lateral surface of a saphenous vein, and the region was aseptically prepared. An 18-gauge, 4.5-cm catheter[b] was inserted into the vein and used for administration of lactated Ringer solution (5 mL/kg/h) to maintain normovolemia during anesthesia.

Sheep then were moved onto a surgery table and gently physically restrained. Sheep were not given premedicants but were preoxygenated (3 L/min) for at least 3 minutes by use of a tight-fitting face mask connected to a standard rebreathing system. The rebreathing system was connected to an anesthesia workstation[c] that included soda lime[d] and a desflurane vaporizer[e] and was equipped with an electrically driven and electronically controlled turbo ventilator.[f] Baseline measurements (including invasively measured blood pressures, heart rate, and arterial oxygenation) and an ECG were continuously recorded.

Anesthesia was induced with desflurane[g] (vaporizer dial setting, 14%) administered in O_2 (flow rate, 3 L/min) by use of a face mask, which allowed a rapid arrival at an ET_{DES} that resulted in an adequate depth of anesthesia as determined by lack of a palpebral reflex, decreased jaw tone, and cessation of swallowing. Once an adequate depth of anesthesia was achieved, a cuffed 9.0-mm (internal diameter) Murphy endotracheal tube was placed and the animal connected to the rebreathing circuit. Sheep received volume-limited positive-pressure ventilation and were maintained at a P_{ETCO_2} of 35 to 45 mm Hg throughout the remainder of the study.

The ECG; heart rate; invasively measured SAP, DAP, and MAP; Sa_{O_2}; and esophageal body temperature were continuously monitored by use of a multiparameter vital monitor.[h] Respiratory rate, tidal volume, and O_2 flow rate were monitored via the anesthesia workstation screen.[i] The O_2 flow rate was maintained at 3 L/min throughout the experiment to ensure the fraction of inspired O_2 remined > 0.96. The fraction of inspired O_2, ET_{DES}, and P_{ETCO_2} were continuously monitored via the workstation integrated gas module[j] as a side-stream analyzer (250 mL/min) through a nylon catheter positioned in the distal end of the endotracheal tube. The gas module was calibrated before each experiment with gas standards[k] (5% desflurane, 5.5% CO_2, 43% N_2O, and 46.5% O_2).

Supramaximal noxious stimulation

Preliminary experiments conducted by one of the investigators (NC) revealed that repeated brief stimulations of the lateral palmar nerves with 60-second trains of constant-current electrical impulses caused motor responses without noticeable tissue damage and thus proved superior to repeatedly clamping a body part such as the tail, as has been commonly applied

in other MAC studies.[7] Therefore, disposable low-resistance silver–silver chloride electrodes[l] with an interelectrode distance of 1 cm were applied on the lateral surface of the metacarpus midway between the carpal and metacarpophalangeal joints and secured in place with self-adhesive bandages. Stimuli were delivered by a 220-V constant-current stimulator[m] triggered by a 9-V battery-powered digital timer.[n] Supramaximal noxious stimulation consisted of trains of square-wave impulses (1 millisecond in duration, 5 Hz, and constant current of 50 mA) delivered for 60 seconds or until a gross purposeful motor response was detected. A response was considered positive when major motor responses were observed in nonstimulated body areas (eg, flexion or extension of the contralateral hind limb or gross movement of the neck). Muscle tremors, occasional swallowing, nystagmus, and changes in cardiorespiratory variables were not considered a positive response. Because the maximum voltage delivered by the stimulator was 200 V, the electrical resistance between electrodes was measured with an ohmmeter[o] before each stimulation to ensure resistance remained at < 3 kΩ to discharge a current of 50 mA. If resistance increased to > 3 kΩ, the electrodes were replaced. A 1-second train of electrical stimulation was applied once after placement of electrodes to verify appropriate function of the equipment.

Determination of MAC_{DES}

A modified protocol of the up-down method was used.[8] Anesthetized sheep were allowed a 30-minute equilibration period at an ET_{DES} of 10.5%; the previously described supramaximal noxious stimulation procedures were then applied. When gross purposeful movement (positive response) was elicited prior to the end of the 60-second stimulation cycle, noxious stimulation was immediately discontinued. When the noxious stimulation elicited a positive response, the ET_{DES} was increased by 0.5%; a 15-minute equilibration period was then allowed before the noxious stimulus was applied again. When noxious stimulation did not elicit gross purposeful movement (negative response), the ET_{DES} was decreased by 0.5%; a 15-minute equilibration period was allowed before the noxious stimulation was repeated. The MAC_{DES} for each sheep was calculated as the mean of 2 successive ET_{DES} values (1 that did not prevent gross purposeful movement and 1 that prevented gross purposeful movement) in response to the supramaximal electrical stimulation. Each determination of MAC_{DES} was performed in duplicate. The population MAC_{DES} was calculated as the arithmetic mean ± SD of the MACs of all 13 sheep.

Determination of dose-dependent effects of desflurane on body temperature and cardiovascular variables

After MAC_{DES} was determined for each sheep, ET_{DES} was adjusted to 1.3 MAC_{DES} for each animal. This ET_{DES} was then maintained for 15 minutes before variables were recorded. The ET_{DES} then was adjusted to 1.6 MAC_{DES} for each animal. This ET_{DES} was then maintained for 15 minutes before variables were again recorded. The sheep then were allowed to recover from anesthesia, and the interval until extubation, sternal recumbency, and standing were recorded.

Data collection

Body temperature, respiratory rate, P_{ETCO_2}, heart rate, SAP, DAP, and MAP were recorded in each awake sheep before administration of desflurane (awake), immediately after intubation (ET_{DES}, 10.5%), after intubation), at the end of the 30-minute equilibration period (equilibration), during the first MAC_{DES} determination (first MAC), during the second MAC_{DES} determination (second MAC), at the end of the 15-minute equilibration period when sheep received an ET_{DES} of 1.3 times MAC_{DES} (1.3 MAC), at the end of the 15-minute equilibration period when sheep received an ET_{DES} of 1.6 times MAC_{DES} (1.6 MAC), and immediately before discontinuation of desflurane administration (ET_{DES} corresponded to 1.45 ± 0.43 MAC_{DES}; end of procedures). The ET_{DES} was also recorded at all those time points, except for awake.

At various time points, an arterial blood sample (1 mL) was collected from each sheep into a heparin-coated syringe and immediately analyzed by use of a blood gas analyzer.[p] Samples were collected at the awake, equilibration, and end of procedures time points.

Arterial blood gas variables (Pa_{O_2}, Pa_{CO_2}, and Sa_{O_2}), arterial acid-base variables (pH, HCO_3^- concentration, base excess, and lactate concentration), electrolytes (concentrations of Na^+, K^+, Ca^{2+}, and Cl^-), anion gap, Hct, hemoglobin content, glucose concentration, and creatinine concentration were recorded at the awake, equilibration, and end of procedures time points. Intervals from mask induction with desflurane to intubation and from cessation of positive-pressure ventilation after discontinuation of desflurane administration to spontaneous ventilation were recorded. Times to sternal recumbency and to standing without ataxia as well as total anesthesia time were also recorded.

Statistical analysis

An ad hoc electronic data set[q] was used for all variables. Continuous data were summarized as mean ± SD or median and IQR on the basis of their parametric distribution. To reduce variability, cardiovascular variables were logarithmically transformed. Student *t* or Wilcoxon rank tests were performed for normally and nonnormally distributed quantitative variables, respectively. A repeated-measures ANOVA was used to assess significant differences among time points for normally distributed quantitative variables. Values of $P < 0.05$ (2-tailed test) were considered significant.

Results

Animals

Mean ± SD time to induce anesthesia with desflurane administered via face mask was 4.81 ± 2.21

Table 1—Mean ± SD values for body temperature and heart rate in 13 adult nonpregnant female sheep anesthetized with desflurane at various MAC multiples.

Variable	Awake	After intubation	Equilibration	First MAC	Second MAC	1.3 MAC	1.6 MAC	End of procedures
ET_{DES}	0	1.06 ± 0.15	1.06 ± 0.10	1	1	1.3	1.6	1.45 ± 0.43
Body temperature (°C)	39.1 ± 0.6	38.9 ± 0.5*	38.4 ± 0.7*	38.0 ± 0.8*	37.4 ± 0.8*	37.2 ± 0.7*	36.9 ± 1.0*	36.9 ± 1.0*
Heart rate (beats/min)	79 ± 16	103 ± 28*	85 ± 18	87 ± 15	88 ± 13	81 ± 10	77 ± 6	75 ± 8

Value for ET_{DES} is the MAC_{DES} multiple. Time points were before induction of anesthesia with desflurane (0 MAC_{DES}; Awake), immediately after intubation (ET_{DES} of 1.06 MAC_{DES}; After intubation), after a 30-minute equilibration period at an ET_{DES} of 10.5% (corresponding to 1.06 MAC_{DES}; Equilibration), during the first MAC_{DES} determination (1 MAC_{DES}; First MAC), during the second MAC_{DES} determination (1 MAC_{DES}; Second MAC), after a 15-minute equilibration period at 1.3 MAC_{DES} (1.3 MAC), after a 15-minute equilibration period at 1.6 MAC_{DES} (1.6 MAC), and immediately after discontinuation of desflurane administration (mean, 1.45 MAC_{DES}; End of procedures).

*Value differs significantly ($P < 0.05$) from the value for Awake.

minutes. Ten of 13 sheep were apneic immediately after intubation (ET_{DES} was 10.5%, which corresponded to 1.06 ± 0.15 MAC_{DES}). Mean total anesthesia time was 226 ± 22 minutes. Mean time to extubation was 14.09 ± 4.05 minutes after discontinuation of desflurane administration and cessation of positive-pressure ventilation. Median time to sternal recumbency was 17.1 minutes (IQR, 15.9 to 18.8 minutes), and mean ± SD time to standing without ataxia was 32.4 ± 12.5 minutes.

MAC_{DES}

Mean ± SD MAC_{DES} for the 13 adult nonpregnant female Sardinian sheep was 9.81 ± 0.79%. There was no significant difference in MAC_{DES} between the first MAC (mean ± SD, 9.89 ± 0.87%) and second MAC (mean ± SD, 9.73 ± 0.83%) determination.

Dose-dependent effects of desflurane on body temperature and cardiovascular variables

Body temperature decreased steadily during the experimental procedures, and all temperature values recorded during anesthesia were significantly (all $P < 0.01$) lower than values measured in the awake sheep **(Table 1)**. Because positive-pressure ventilation was used, respiratory rate and P_{ETCO_2} did not change with increasing ET_{DES}. Heart rate increased significantly at induction of anesthesia and intubation, but it then returned to values not significantly different from the heart rate in awake sheep. Arterial blood pressures (SAP, MAP, and DAP) began to significantly decrease from the values in awake animals by 25% to 30% as soon as desflurane was administered. Arterial blood pressures increased for a short period during and after noxious stimulation as part of the MAC determination procedure before they decreased again to prestimulation values. When ET_{DES} was increased to 1.3 and 1.6 MAC_{DES} without further noxious stimulations, arterial blood pressures decreased significantly with increasing ET_{DES} **(Figure 1)**.

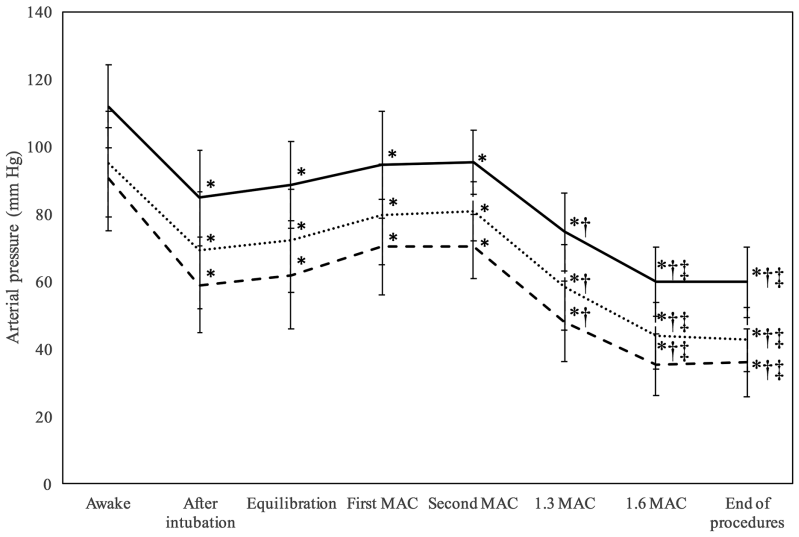

Figure 1—Mean ± SD values of SAP (solid line), MAP (dotted line), and DAP (dashed line) for 13 adult nonpregnant female sheep anesthetized at various MAC multiples. Time points were before induction of anesthesia with desflurane (0 MAC_{DES}; Awake), immediately after intubation (ET_{DES} of 1.06 MAC_{DES}; After intubation), after a 30-minute equilibration period at an ET_{DES} of 10.5% (corresponding to 1.06 MAC_{DES}; Equilibration), during the first MAC_{DES} determination (1 MAC_{DES}; First MAC), during the second MAC_{DES} determination (1 MAC_{DES}; Second MAC), after a 15-minute equilibration period at 1.3 MAC_{DES} (1.3 MAC), after a 15-minute equilibration period at 1.6 MAC_{DES} (1.6 MAC), and immediately after discontinuation of desflurane administration (mean, 1.45 MAC_{DES}; End of procedures). *Value differs significantly ($P < 0.05$) from the value for Awake. †Value differs significantly ($P < 0.05$) from the values for After intubation, Equilibration, First MAC, and Second MAC. ‡Value differs significantly ($P < 0.05$) from the value for 1.3 MAC.

Ten of 13 sheep remained apneic for 5.25 ± 1.43 minutes after desflurane administration and positive-pressure ventilation was discontinued. At that time point, mean ± SD ET_{DES} was 15.40 ± 1.53% (1.56 ± 0.10 MAC_{DES}), median Sa_{O_2} was 100% (IQR, 100% to 100%), and mean ± SD Pa_{CO_2} was 47.3 ± 5.7 mm Hg. The mean ET_{DES} and Pa_{CO_2} in the 3 sheep that immediately resumed spontaneous breathing after discontinuation of desflurane administration and positive-pressure ventilation were 14.80% and 50.5 ± 5.5 mm Hg, respectively; these values did not differ significantly (ET_{DES}, $P = 0.60$; Pa_{CO_2}, $P = 0.49$) from values measured in the other 10 sheep.

Table 2—Values for arterial blood gas variables, electrolyte concentrations, and hematologic variables for 13 adult nonpregnant female sheep anesthetized with desflurane at various MAC multiples.

Variable	Awake	Equilibration	End of procedures
pH	7.50 ± 0.04	7.43 ± 0.06*	7.41 ± 0.06*
Pa_{CO_2} (mm Hg)	33.8 ± 2.3	44.7 ± 4.6*	47.9 ± 5.5*
Pa_{O_2} (mm Hg)	74.1 ± 11.7	424.4 ± 156.6*	409.9 ± 105.5*
HCO_3^- (mmol/L)	28.0 ± 3.7	29.9 ± 2.8*	30.2 ± 3.4
Base excess (mmol/L)	0.74 ± 0.55	1.22 ± 1.15	1.14 ± 1.22
Sa_{O_2} (%)	96.3 (95.2–97.1)	100 (99.9–100)*	100 (100–100)*
Na^+ (mmol/L)	145 ± 2	144 ± 2	145 ± 2
K^+ (mmol/L)	4.0 ± 0.5	4.1 ± 0.7	3.9 ± 0.6
Ca^{2+} (mmol/L)	1.15 ± 0.09	1.08 ± 0.12	1.08 ± 0.15
Cl^- (mmol/L)	104 (102–105)	105 (103–107)	105 (101–108)
Anion gap (mmol/L)	19 ± 2	15 ± 2*	14 ± 2*
Hct (%)	23 ± 3	18 ± 2*	16 ± 3*
Hemoglobin (g/dL)	7.7 ± 0.8	5.9 ± 0.8*	5.4 ± 1.0*
Lactate (mmol/L)	2.34 (1.84–2.73)	1.20 (1.02–1.76)*	0.96 (0.82–1.37)*
Glucose (mg/dL)	103 ± 34	94 ± 30	84 ± 16
Creatinine (mg/dL)	1.14 ± 0.20	1.04 ± 0.27	0.96 ± 0.21

Values reported are mean ± SD or median (IQR).
See Table 1 for remainder of key.

Changes in values for arterial blood gas measurements (Pa_{O_2}, Pa_{CO_2}, and Sa_{O_2}), acid-base variables (pH, HCO_3^- concentration, base excess, and lactate concentration), electrolytes (concentrations of Na^+, K^+, Ca^{2+}, and Cl^-), and other hematologic variables at 3 time points during the study (awake, equilibration, and end of procedures) were summarized **(Table 2)**. Some values differed significantly from values for awake animals.

Discussion

Mean ± SD MAC_{DES} for the sheep of the present study was 9.81 ± 0.79%. This value is in accordance with the median MAC of 9.5% (range, 8.4% to 11.1%) reported for administration of desflurane to nonpregnant ewes (1 to 8 years of age) in one study[a] and the only slightly higher MAC of 8.6 ± 0.2% determined for 8 adult nulliparous sheep of another study.[6] Investigators in both of those studies[6,a] applied mechanical stimulation (forceps clamping) instead of electrical stimulation, as was used in the study reported here, for supramaximal noxious stimulation. Because the MAC_{DES} results for the present study were similar to those previously reported, they confirmed the findings for dogs[7,9] and rabbits[7] that electrical stimulation with current intensities of 30 mA and 50 mA (independent of the location of electrical stimulation) and mechanical stimulation in the form of tail or paw clamping result in supramaximal noxious stimulation and lead to determination of comparable MAC values. In contrast for humans, in which skin incision and electrical stimulation are of similar nociceptive strength and yield similar MAC values,[5] a study[7] involving rabbits and dogs revealed that a skin incision results in a much lower MAC, compared with the MAC for mechanical clamping or electrical stimulation.

The MAC_{DES} data for sheep of the present study and other studies indicate an anesthetic potency of desflurane of similar magnitude to that reported for dogs,[10–12] cats,[13] rabbits,[10] pigs,[14] horses,[15,16] and 18- to 30-year-old humans.[1] Differences between the MAC_{DES} for sheep of the present study and values reported for other species are likely attributable to variability that is common among species and reflect primarily biological variation.[3] However, differences in experimental methods and breed, age, body temperature, and circadian rhythm among subjects and among species may also account for some of the variability in results.[5,7]

All sheep received positive-pressure ventilation throughout the experimental period to prevent arterial CO_2 retention. Therefore, it was not surprising that at the end of the experiment, when the administration of desflurane was discontinued and positive-pressure ventilation ceased, analysis of arterial blood gas samples revealed only mild hypercapnia. However, 10 of 13 sheep were apneic for several minutes. The ET_{DES} at that time was 1.45 ± 0.43 MAC_{DES}. Only as desflurane was washed out with fresh O_2 (flow rate, 3 L/min) did animals resume spontaneous breathing. Progressive respiratory depression attributable to desflurane has also been observed in other species.[3] In swine, which have a MAC_{DES} of 10% (almost identical to that of sheep), the apneic index for desflurane (ie, ratio of the ET_{DES} at apnea and MAC_{DES}) is reportedly 1.6.[3] Also, rabbits rapidly became apneic during mask induction with desflurane once the vaporizer setting reached values ≥ 6%.[17] In contrast, dogs have an apneic index of 2.4,[3] which indicates less respiratory depressant effects in that species. However, desflurane has a strong respiratory depressant effect in horses.[16]

Results of studies of sheep,[6] horses,[16] and pigs[18,19] and the sheep of the study reported here indicated no significant dose-dependent change in heart rate when the desflurane concentration increased from 1.0 to 1.6 MAC_{DES}. The only significant increase in heart rate was detected during the induction of anesthesia. This might have been related to stage 1 of inhalation anesthesia, which commonly is associated with CNS excitement and tachycardia,[20] and possibly to stimulation associated with orotracheal intubation of the sheep. In

contrast to heart rate, arterial blood pressures rapidly decreased (by 25% to 30%) from baseline values in awake animals as ET_{DES} began increasing to concentrations of approximately 1 MAC_{DES} and then remained relatively stable during the equilibration period. As expected, mild recovery of blood pressures was detected during the period of MAC determinations, most likely as a result of repetitive noxious stimulation and related activation of the sympathetic nervous system.[3] Thereafter, arterial blood pressures decreased further in a concentration-dependent manner as ET_{DES} increased to 1.3 and 1.6 MAC, reaching a dangerously low mean MAP of 44 mm Hg. A similar concentration-dependent decrease in arterial blood pressures as a result of pronounced peripheral vasodilation has been recognized in previous studies of sheep,[6] horses,[16] pigs,[18,19] and humans.[21] It is important to mention the reduction (approx 30%) in the hemoglobin concentration by the end of the experimental procedures, which was potentially related to both constant administration of IV fluids and sequestration of erythrocytes in the spleen and other organs (eg, liver, skin, and skeletal muscles), as has been reported for dogs[22] and cats.[23] Because lactate and creatinine concentrations did not increase toward the end of the experimental procedures, it is unlikely that systemic tissue or organ perfusion and, hence, aerobic function were severely compromised by the relatively brief period of pronounced arterial hypotension toward the end of the experimental procedures.

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Footnotes

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k. Air Liquide Healthcare America, Plumsteadville, Pa.
l. Norotrode 20 bipolar SEMG electrodes, Myotronics-Noromed Inc, Kent, Wash.
m. DS7A, Digitimer Ltd, Letchworth Garden City, England.
n. DG2A train/delay generator, Digitimer Ltd, Letchworth Garden City, England.
o. Personal 20, Mega Elettronica, Milan, Italy.
p. ABL 80 CO-OX flex, Radiometer, Copenhagen, Denmark.
q. Excel, version 2016, Microsoft Corp, Redmond, Wash.

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