

# Effect of variable-dose propofol alone and in combination with two fixed doses of ketamine for total intravenous anesthesia in cats

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**Objective**—To determine the minimum infusion rate (MIR<sub>50</sub>) for propofol alone and in combination with ketamine required to attenuate reflexes commonly used in the assessment of anesthetic depth in cats.

**Animals**—6 cats.

**Procedure**—Propofol infusion started at 0.05 to 0.1 mg/kg/min for propofol alone or 0.025 mg/kg/min for propofol and ketamine (low-dose [LD] constant rate infusion [CRI] of 23 µg/kg/min or high-dose [HD] CRI of 46 µg/kg/min), and after 15 minutes, responses of different reflexes were tested. Following a response, the propofol dose was increased by 0.05 mg/kg/min for propofol alone or 0.025 mg/kg/min for propofol and ketamine, and after 15 minutes, reflexes were retested.

**Results**—The MIR<sub>50</sub> for propofol alone required to attenuate blinking in response to touching the medial canthus or eyelashes; swallowing in response to placement of a finger or laryngoscope in the pharynx; and to toe pinch, tetanus, and tail-clamp stimuli were determined. Addition of LD ketamine to propofol significantly decreased MIR<sub>50</sub>, compared with propofol alone, for medial canthus, eyelash, finger, toe pinch, and tetanus stimuli but did not change those for laryngoscope or tail-clamp stimuli. Addition of HD ketamine to propofol significantly decreased MIR<sub>50</sub>, compared with propofol alone, for medial canthus, eyelash, toe pinch, tetanus, and tail-clamp stimuli but did not change finger or laryngoscope responses.

**Conclusions and Clinical Relevance**—Propofol alone or combined with ketamine may be used for total IV anesthesia in healthy cats at the infusion rates determined in this study for attenuation of specific reflex activity. (*Am J Vet Res* 2003;64:907–912)

In dogs and cats, anesthesia is usually maintained by administration of the potent inhalant anesthetics halothane, isoflurane, or sevoflurane. These agents provide progressive controlled depression of the CNS; however, they also induce cardiovascular and respiratory depression in a dose-dependent manner.<sup>1,2</sup> Inhalant techniques also require expensive equipment, contribute to atmospheric pollution, and are unsuitable for animals with conditions such as

malignant hyperpyrexia and in clinical situations such as bronchoscopy in smaller animals. Total intravenous anesthesia (TIVA) has become a popular technique in humans because of the advantages it offers, compared with inhalant techniques, and the development of drugs such as propofol. Although propofol allows for easy control of anesthetic depth and rapid recovery, it reportedly does not attenuate autonomic responses to noxious stimuli, and administration in animals is often associated with respiratory depression and hypotension. Ketamine, conversely, induces profound analgesia and stimulation of the sympathetic nervous system with increased heart rate and blood pressure, but recovery is associated with emergence delirium. Studies<sup>3,4</sup> in humans indicate that the cardiovascular depressant effects of propofol can be offset by the sympathomimetic effects of ketamine, resulting in cardiovascular stability and minimal emergence phenomena.

The purpose of the study reported here was to determine the minimum infusion rate (MIR) in 50% of a population (MIR<sub>50</sub>) for propofol alone and propofol in combination with ketamine required to attenuate reflexes commonly used in the assessment of anesthetic depth in cats. Effects of propofol alone or in combination with ketamine on hemodynamic responses to various noxious stimuli were also studied.

## Materials and Methods

**Animal care and instrumentation**—Six conditioned spayed female domestic cats were assigned to this study after approval by the Animal Care and Use Committee of the University of California, Davis. Cats were housed in a large room in compliance with established standards and fed a commercial dry cat food ad libitum. Cats weighed (mean ± SEM) 4.8 ± 0.1 kg and were 3.62 ± 0.05 years old.

Each cat received all 3 treatments with at least 2 weeks between treatments. The 3 treatments were propofol<sup>a</sup> administered alone by constant rate infusion (CRI) and propofol CRI combined with ketamine<sup>b</sup> as a low-dose (LD; loading dose, 2 mg/kg; CRI, 23 µg/kg/min) or high-dose (HD; loading dose, 4 mg/kg; CRI, 46 µg/kg/min) CRI. All CRIs were delivered by use of syringe pumps.<sup>c</sup> The LD and HD ketamine regimens were designed by use of previously published pharmacokinetic values of ketamine in cats<sup>5</sup> to provide targeted plasma ketamine concentrations of 0.6 and 1.2 µg/mL, respectively.

Before each experiment, food was withheld for 12 hours, and a catheter was placed percutaneously in a cephalic vein for drug and fluid administration. Anesthesia was induced by IV administration of propofol at 5 mg/kg/min until the cat assumed lateral recumbency and had a sluggish withdrawal response to a toe pinch applied manually. Propofol infusion was decreased to a maintenance rate of 0.1 to 0.25 mg/kg/min, and an arterial catheter was placed into the

Received June 17, 2002.

Accepted November 22, 2002.

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Supported by grants from the Miller Foundation and Center for Companion Animal Health, University of California, Davis.

Presented in part at the Annual General Meeting of the American College of Veterinary Anesthesiologists, New Orleans, October 1996.

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abdominal aorta via the femoral artery. This catheter was used for continuous measurement of arterial blood pressure and repeated collection of arterial blood samples for measurement of plasma pH, gas pressures, PCV, and plasma ketamine and plasma protein concentrations. Systolic, diastolic, and mean arterial pressures were measured by use of a pressure transducer that was calibrated before each treatment against a mercury manometer, with zero set at the level of the thoracic inlet in laterally recumbent cats. Limb leads were attached to record an ECG, and all measurements were recorded by use of a physiograph. The PaO<sub>2</sub>, PaCO<sub>2</sub>, and pH were measured by use of a blood gas analyzer.<sup>4</sup> Blood gas and pH values were corrected on the basis of rectal temperature.<sup>6</sup> Arterial bicarbonate concentration and base deficit were calculated by use of standard formulas.<sup>7,8</sup> Plasma ketamine concentrations were determined by use of gas chromatography-mass spectrometry with selective ion monitoring. The limit of quantification was approximately 100 ng/mL. Rectal temperature was measured and maintained at 37 to 39°C by use of external warming blankets.<sup>c</sup> At completion of the study, the catheter in the femoral artery was removed, and incisions in the femoral artery, subcutaneous tissue, and skin were sutured. Combined propofol and ketamine administration was discontinued, and cats were watched closely until they recovered from anesthesia.

**Experimental protocol**—After instrumentation, the propofol infusion was decreased to the lowest possible dose that would allow the reflexes to be tested (propofol alone, 0.05 to 0.1 mg/kg/min; propofol and ketamine, 0.025 mg/kg/min). When the cat was also scheduled to receive ketamine, the loading dose was administered IV for a period of 5 minutes, and the LD or HD CRI was delivered until completion of the study. After a period of 15 minutes to enable stabilization, responses of reflexes (blinking in response to touching the medial canthus or eyelashes; swallowing in response to placement of a finger or a laryngoscope in the pharynx; or purposeful response to placement of a 10-inch hemostat caught to the second ratchet on a phalanx for 10 seconds, tetanic stimulus to the ulnar nerve for 10 seconds by use of a peripheral nerve stimulator,<sup>f</sup> or placement of a 10-inch hemostat caught to the first ratchet at the base of the tail for 1 minute) were tested. Following a response to any reflex, the propofol dose was increased by 0.05 mg/kg/min for propofol alone or 0.025 mg/kg/min for propofol and ketamine, the cat was allowed to stabilize for 15 minutes at the new plane of anesthesia, and reflexes were retested, until there were no responses to 2 consecutive increases in infusion rates.

At each infusion rate, heart rate and arterial blood pressure were measured, and blood was collected for measurement of gas pressures and pH before testing reflexes. Heart rate and arterial blood pressure were measured continuously during testing of responses to toe pinch, tetanus, and tail-clamp stimuli.

**Statistical analyses**—Unless stated otherwise, all results were expressed as mean ± SEM, and differences were considered significant at *P* < 0.05. The MIR<sub>50s</sub> for medial canthus, eyelash, finger, laryngoscope, toe pinch, tetanus, and tail-clamp stimuli were reported as the median value and SE of

the median and calculated as the SEM × (π/2)<sup>0.5</sup>, which is a functional relationship between the 2 values for normally distributed data. The effect on MIR<sub>50</sub> with addition of ketamine (LD or HD) to propofol for various reflexes was tested by use of pairwise Wilcoxon signed rank tests. Effects of toe pinch, tetanus, and tail-clamp stimuli on heart rate and arterial blood pressure were analyzed by use of several repeated-measures ANOVA with 1 or 2 within-factor (dosages of propofol alone and with ketamine) analyses. When these effects were significant, an orthogonal decomposition was used to determine whether there was a significant linear component.

## Results

Propofol MIR<sub>50s</sub> were determined for medial canthus, eyelash, finger, laryngoscope, toe pinch, tetanus, and tail-clamp stimuli (Table 1). Addition of LD ketamine to propofol significantly decreased MIR<sub>50s</sub> for medial canthus, eyelash, finger, toe pinch, and tetanus stimuli but did not change those for laryngoscope or tail-clamp stimuli. Addition of HD ketamine to propofol significantly decreased MIR<sub>50s</sub> for medial canthus, eyelash, toe pinch, tetanus, and tail-clamp stimuli but did not change those for finger or laryngoscope stimuli. There were no significant differences between the ketamine doses for MIR<sub>50s</sub> in response to any of the reflexes.

Plasma ketamine concentrations reached a steady state quickly and often remained there until all reflexes being evaluated had disappeared. At these times, plasma ketamine concentrations increased slightly in certain cats. Measured plasma ketamine concentrations of

Table 1—Minimum infusion rate required to abolish reflexes in at least 3 of 6 cats that received propofol (mg/kg/min), propofol with low-dose (LD) ketamine (23 μg/kg/min), and propofol with high-dose (HD) ketamine (46 μg/kg/min)

Reflex	Propofol	Propofol and LD ketamine	Propofol and HD ketamine
Blinking in response to touching medial canthus	0.28 ± 0.02 <sup>a</sup>	0.16 ± 0.02 <sup>b</sup>	0.15 ± 0.01 <sup>b</sup>
Blinking in response to touching eyelash	0.25 ± 0.03 <sup>a</sup>	0.13 ± 0.03 <sup>b</sup>	0.15 ± 0.01 <sup>b</sup>
Swallowing in response to placement of finger in pharynx	0.18 ± 0.04 <sup>a</sup>	0.05 ± 0.02 <sup>b</sup>	0.09 ± 0.01 <sup>ab</sup>
Swallowing in response to placement of laryngoscope in pharynx	0.19 ± 0.04	0.10 ± 0.01	0.10 ± 0.01
Purposeful movement in response to toe pinch	0.21 ± 0.02 <sup>a</sup>	0.14 ± 0.01 <sup>b</sup>	0.14 ± 0.01 <sup>b</sup>
Purposeful movement in response to tetanic stimulation	0.10 ± 0.02 <sup>a</sup>	0.01 ± 0.03 <sup>b</sup>	0.01 ± 0.02 <sup>b</sup>
Purposeful movement in response to tail clamp	0.15 ± 0.03 <sup>a</sup>	0.11 ± 0.01 <sup>ab</sup>	0.11 ± 0.01 <sup>b</sup>

Values represent mean ± SEM (mg/kg/min) results obtained from 6 cats.  
<sup>a,b</sup>Within a row, values with different superscript letters are significantly (*P* < 0.05) different.

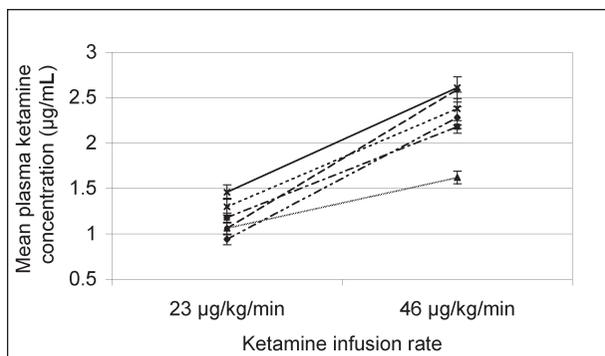


Figure 1—Mean ± SEM plasma ketamine concentrations in 6 cats that received low-dose (LD; 23 μg/kg/min) and high-dose (HD; 46 μg/kg/min) ketamine infusions IV.

LD and HD ketamine infusions (LD,  $1.17 \pm 0.04 \mu\text{g/mL}$ ; HD,  $2.27 \pm 0.09 \mu\text{g/mL}$ ) were higher than targeted concentrations (0.6 and 1.2  $\mu\text{g/mL}$ , respectively). For individual cats, mean  $\pm$  SEM plasma ketamine concentrations differed between LD and HD ketamine (Fig 1).

As drug concentrations increased (Fig 2 and 3), cardiovascular and respiratory functions were well maintained, even at concentrations in which somatic responses to various stimuli had disappeared (Table 2).

For tetanus and tail-clamp stimuli, but not toe pinch, significant treatment effects on hemodynamic responses were seen. Interactions between propofol and ketamine or overall effects of ketamine on hemodynamic responses could not be detected. During tetanus and tail-clamp stimuli, systolic blood pressure, mean blood pressure, and heart rate responses with propofol alone decreased significantly with increasing doses of all propofol treatments that included ketamine (Fig 4 and 5).

Table 2—Mean  $\pm$  SEM values for cardiovascular and respiratory effects for administration of propofol, propofol with LD ketamine, or propofol with HD ketamine to an endpoint at which reflexes were abolished in 6 cats

Variable	Propofol	Propofol and LD ketamine	Propofol and HD ketamine
Heart rate (beats/min)	161 $\pm$ 13	165 $\pm$ 15	165 $\pm$ 7
Systolic blood pressure (mm Hg)	144 $\pm$ 15	137 $\pm$ 7	142 $\pm$ 14
Diastolic blood pressure (mm Hg)	101 $\pm$ 11	91 $\pm$ 4	98 $\pm$ 10
Mean blood pressure (mm Hg)	115 $\pm$ 13	106 $\pm$ 5	113 $\pm$ 13
PaO <sub>2</sub> (mm Hg)	97.0 $\pm$ 2.8	102.6 $\pm$ 4.8	101.1 $\pm$ 3.7
PacO <sub>2</sub> (mm Hg)	39.2 $\pm$ 2.1	39.0 $\pm$ 1.5	39.7 $\pm$ 1.5
pH	7.331 $\pm$ 0.014	7.321 $\pm$ 0.014	7.316 $\pm$ 0.011
Bicarbonate concentration (mmol/L)	19.8 $\pm$ 0.5	19.4 $\pm$ 0.5	19.6 $\pm$ 0.5
Base deficit (mmol/L)	4.6 $\pm$ 0.2	5.4 $\pm$ 0.6	5.3 $\pm$ 0.5

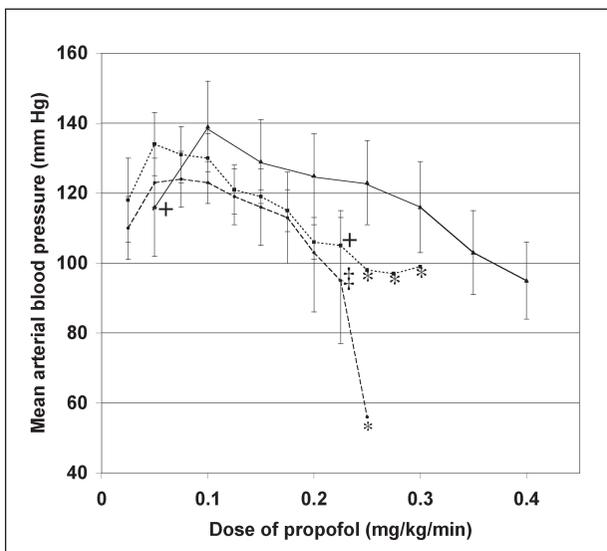


Figure 2—Mean  $\pm$  SEM arterial blood pressure in response to increasing doses of propofol (triangles), propofol and LD ketamine (23  $\mu\text{g/kg/min}$ ; squares), and propofol and HD ketamine (46  $\mu\text{g/kg/min}$ ; circles) in cats. + = Data from 4 cats.  $\pm$  = Data from 3 cats. \* = Data from 1 cat.

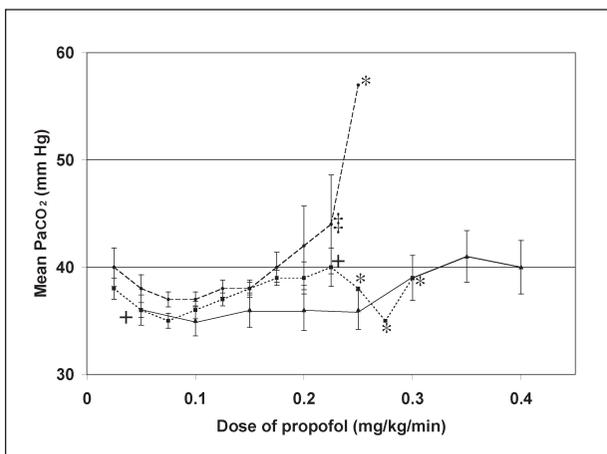


Figure 3—Mean  $\pm$  SEM PaCO<sub>2</sub> in response to increasing doses of propofol in cats. See Figure 2 for key.

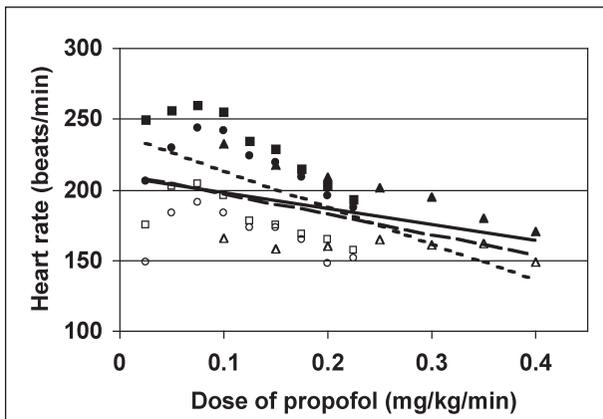


Figure 4—Heart rate response following a tetanic stimulus to the ulnar nerve with increasing doses of propofol (before stimulation [open triangles], after stimulation [closed triangles], linear regression [line]), propofol and LD ketamine (23  $\mu\text{g/kg/min}$ ; before stimulation [open squares], after stimulation [closed squares], linear regression [dotted line]), and propofol and HD ketamine (46  $\mu\text{g/kg/min}$ ; before stimulation [open circles], after stimulation [closed circles], linear regression [dashed line]) in cats.

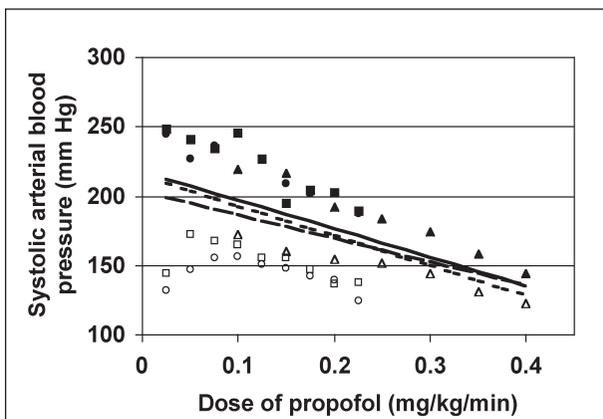


Figure 5—Systolic arterial blood pressure response to application of a tail clamp with increasing doses of propofol (before stimulation [open triangles], after stimulation [closed triangles], linear regression [line]), propofol and LD ketamine (23  $\mu\text{g/kg/min}$ ; before stimulation [open squares], after stimulation [closed squares], linear regression [dotted line]), and propofol and HD ketamine (46  $\mu\text{g/kg/min}$ ; before stimulation [open circles], after stimulation [closed circles], linear regression [dashed line]) in cats.

## Discussion

With injectable anesthetics, pharmacologic effects are difficult to measure, because they are most closely related to the concentration of free drug in the biophase, which are cells within the brain where anesthetics are believed to exert their effects. Therefore, to measure pharmacodynamic responses, one must rely on achieving a quasi-steady state by maintaining a stable blood concentration of the relevant drug on the basis of the premise that there will be equilibrium between blood and biophase concentrations after a period and that responses of the brain will be determined by those concentrations. For this reason, propofol and ketamine in this study were administered by CRI. To decrease the time required to obtain initial steady-state concentrations, loading doses of propofol and ketamine were administered. Infusion rates for ketamine reached a steady state quickly and did not change until all reflexes being evaluated had disappeared. At this level in certain cats, plasma ketamine concentrations increased slightly, possibly because of the effects of propofol on liver blood flow. Propofol reportedly reduces the clearance of other drugs, such as alfentanil, by reducing liver blood flow,<sup>9</sup> and drugs that reduce liver blood flow reportedly reduce ketamine clearance.<sup>10</sup> Propofol infusions were held constant for at least 15 minutes before reflex responses were tested. However, in our study, propofol blood concentrations were not measured, and we were unable to determine whether steady-state concentrations were obtained with each increase in the propofol infusion dose.

The concept of a MIR (effective dose in 50% of a population [ED<sub>50</sub>]) of an IV administered anesthetic and its associated blood concentration effective in 50% of a population under conditions of stable anesthesia, which are required to suppress somatic motor movement in response to a surgical incision, is established for TIVA.<sup>11,12</sup> Recently, measurement of plasma drug concentrations (CP) and use of a concentration that induces 50% of the maximum possible drug effect (CP<sub>50</sub>) have been advocated. Advantages of CP<sub>50</sub> over MIR<sub>50</sub> are that CP<sub>50</sub> is independent of duration of infusion and pharmacokinetic variability.<sup>13</sup> Because we did not measure plasma propofol concentrations, we have reported our results as an MIR<sub>50</sub> (response), which is the MIR at which 50% of the cats did not respond to the particular stimulus.

In our study, propofol infusion rates of  $0.10 \pm 0.02$  to  $0.28 \pm 0.02$  mg/kg/min were required to achieve MIR<sub>50</sub>. These values are lower than that of 0.51 mg/kg/min, which has been reported in cats during surgery.<sup>14</sup> In the latter study, which was performed in a clinical setting, propofol was not administered as a CRI but was instead given as bolus doses when needed, and the maintenance rate was calculated. Our MIR<sub>50</sub> values for propofol were lower, because maintenance of anesthesia by bolus administration rather than CRI requires more drug.<sup>15</sup> During surgery in dogs, the MIR for propofol was 0.3 to 0.35 mg/kg/min, and surgical anesthesia was induced in all dogs at 0.4 mg/kg/min.<sup>16</sup> These values are also higher than our values, but these values are closer to ED<sub>95</sub> values, whereas our values were ED<sub>50</sub> values.

In our study, the lowest MIR<sub>50</sub> for propofol alone was that required to prevent movement in response to a tetanic stimulus to the ulnar nerve for 10 seconds ( $0.10 \pm 0.02$  mg/kg/min), whereas the highest MIR<sub>50</sub> for propofol alone was that required to prevent blinking in response to touching the medial canthus of the eye ( $0.28 \pm 0.02$  mg/kg/min). In humans, tetanus is suppressed at doses that are lower than those required for surgical incision.<sup>4,17,18</sup> We included medial canthus and eyelash reflex responses for 2 reasons. First, these reflexes are commonly used to judge depth of anesthesia. Second, on the basis of our clinical experience, it appeared that the eyelash reflex persisted to deeper levels of anesthesia with propofol than with inhalants or thiopental. In our study, medial canthus and eyelash reflexes were the last reflexes to be lost and persisted to deeper levels of anesthesia, compared with reflexes for noxious stimuli, such as toe pinch, tail clamp, and pharyngeal placement of a laryngoscope. This is an important clinical feature, because the eyelash reflex in cats anesthetized with inhalants usually indicates a light plane of anesthesia. Persistence of this reflex has also been reported in humans where suppression of the eyelash reflex appeared to develop later than loss of consciousness during the induction of propofol anesthesia.<sup>19</sup> We are aware that the corneal reflex persists to deep levels of anesthesia, and we were careful not to elicit a corneal reflex when testing medial canthus and eyelash reflexes. Similarity in MIR<sub>50</sub> for medial canthus and eyelash reflex responses in the study reported here supports that we were testing the eyelash reflex. Furthermore, the most intense noxious stimulus used for a somatic response in our study appeared to be the toe pinch.

We are not aware of any similar studies that have been conducted in animals, although infusion doses of propofol required to suppress consciousness and the response to various graded, non-noxious and noxious stimuli have been reported in humans.<sup>20,21</sup> In 1 study,<sup>20</sup> ED<sub>50</sub> infusion rates for the abolition of a number of responses in young patients ranged from 0.085 to 0.105 mg/kg/min.

In humans, addition of ketamine to propofol has been advocated to attenuate respiratory depression,<sup>22,23</sup> provide analgesia and lower analgesic requirements after surgery,<sup>23,24</sup> and promote hemodynamic stability.<sup>22,24</sup> In our study, 2 ketamine infusion doses were selected to determine whether purported beneficial effects were dose-related factors. Pharmacokinetic values for ketamine that were determined in cats<sup>3</sup> were used to calculate target CPs of 0.6 and 1.2 µg/mL, which were selected from reported requirements in humans.<sup>13</sup> In humans, plasma ketamine concentrations of 0.1 to 1 mg/mL were required for analgesia, and 1 to 2 µg/mL was required for minor surgery when combined with nitrous oxide.<sup>13</sup> Without nitrous oxide, plasma ketamine concentrations of  $9.3 \pm 0.8$  µg/mL were required for surgery in patients recovering at concentrations of  $2.7 \pm 0.9$  µg/mL.<sup>25</sup> Analgesia without nitrous oxide has been reported in humans at plasma ketamine concentrations  $> 0.16$  µg/mL.<sup>26</sup> However, in our study, measured plasma ketamine concentrations of LD and HD ketamine infusions (LD,  $1.17 \pm 0.04$

$\mu\text{g/mL}$ ; HD,  $2.27 \pm 0.09 \mu\text{g/mL}$ ) were higher than targeted concentrations (0.6 and  $1.2 \mu\text{g/mL}$ , respectively). The reason for this is unknown, but it could be attributable to inaccuracies in the pharmacokinetic values used to compute dose calculations or changes in the pharmacokinetics of ketamine induced by simultaneous administration of propofol. The pharmacokinetic model we used was determined by a small sample size, and use of population pharmacokinetic models has been reported to improve predictions of measured concentrations. Population pharmacokinetic models allow the variability between individuals, as well as within individuals, to be quantified and covariates (eg, age and weight) to be added.<sup>27</sup> Such models are not available for use in animals. Propofol reportedly changes the pharmacokinetics of alfentanil.<sup>9</sup> In that study, a reduction in the volume of distribution, possibly caused by reduced tissue binding, and a reduction in clearance, caused by changes in liver blood flow, were postulated as causes for the higher-than-expected plasma alfentanil concentrations. Other drugs that reduce liver blood flow, such as halothane, reportedly reduce ketamine clearance.<sup>10</sup>

In our study, addition of LD ketamine to propofol significantly decreased the  $\text{MIR}_{50}$  for medial canthus, eyelash, finger, toe pinch, and tetanus stimuli but did not change the dose for laryngoscope or tail-clamp stimuli. Increasing the dose (HD ketamine) did not result in a further significant decrease in  $\text{MIR}_{50}$  for any of the responses. Similar studies have not been conducted in domestic animals or humans, although the literature supports the conclusion that addition of ketamine to propofol will decrease the dose of propofol for a number of endpoints.<sup>4,22,28</sup> The dose of propofol alone for maintenance of anesthesia in horses during surgery was  $0.33 \text{ mg/kg/min}$ , whereas when used in combination with ketamine infused at  $40 \mu\text{g/kg/min}$ , the dose of propofol required for anesthesia decreased to  $0.12 \text{ mg/kg/min}$ .<sup>22</sup>

Although cardiopulmonary effects were not a specific objective of the study reported here, arterial blood pressure and blood gases were determined. Cardiovascular and respiratory function was well maintained, even at doses in which all somatic reflex responses were lost. At this level, there were little differences among propofol, propofol and LD ketamine, or propofol and HD ketamine for any of the variables. This was an unexpected finding for 2 reasons. First, propofol alone has depressant effects on the cardiovascular<sup>29,30</sup> and respiratory systems.<sup>31,32</sup> Second, when ketamine is administered with propofol, those effects are offset by the stimulatory effects of ketamine.<sup>4,23</sup>

In our study, depending on the type of stimulus applied, a linear relationship was found between the propofol dose and hemodynamic response, such that as propofol dose increased, the magnitude of the hemodynamic response to stimulus decreased. Ketamine did not appear to alter this response, suggesting that this response was caused by propofol. The hemodynamic components of this response were systolic blood pressure and heart rate, and the types of stimuli most affected were tail clamp and tetanus. We are not aware of published data on hemodynamic responses during

anesthesia with propofol and ketamine, although several studies<sup>20,33,34</sup> investigated hemodynamic responses during anesthesia with propofol and fentanyl.

<sup>a</sup>Diprivan, Stuart Pharmaceuticals, Wilmington, Del.

<sup>b</sup>Ketaset, Aveco Co Inc, Fort Dodge, Iowa.

<sup>c</sup>Medfusion 2010i syringe pump, Medexinc, Duluth, Ga.

<sup>d</sup>ABL505, blood gas and electrolyte system, Radiometer Medical A/S, West Lake, Ohio.

<sup>e</sup>Model K-20, American Pharmaseal Co, Valencia, Calif.

<sup>f</sup>Ministim, model MS-1, Life-tech Inc, Houston, Tex.

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