Effect of gantacurium on evoked laryngospasm and duration of apnea in anesthetized healthy cats

Manuel Martin-Flores DVM
Jonathan Cheetham VetMB, PhD
Luis Campoy IV
Daniel M. Sakai DVM
Paul M. Heerdt MD, PhD
Robin D. Gleed BVSc

OBJECTIVE
To evaluate whether the ultrashort-acting neuromuscular blocking agent gantacurium can be used to blunt evoked laryngospasm in anesthetized cats and to determine the duration of apnea without hemoglobin desaturation.

ANIMALS
8 healthy adult domestic shorthair cats.

PROCEDURES
Each cat was anesthetized with dexmedetomidine and propofol, instrumented with a laryngeal mask, and allowed to breathe spontaneously (fraction of inspired oxygen, 1.0). The larynx was stimulated by spraying sterile water (0.3 mL) at the rima glottidis; a fiberscope placed in the laryngeal mask airway was used to detect evoked laryngospasm. Laryngeal stimulation was performed at baseline; after IV administration of gantacurium at doses of 0.1, 0.3, and 0.5 mg/kg; and after the effects of the last dose of gantacurium had terminated. Duration of apnea and hemoglobin oxygen saturation (measured by means of pulse oximetry) after each laryngeal stimulation were recorded. Neuromuscular block was monitored throughout the experiment by means of acceleromyography on a pelvic limb.

RESULTS
Laryngospasm was elicited in all cats at baseline, after administration of 0.1 mg of gantacurium/kg, and after the effects of the last dose of gantacurium had terminated. The 0.3 and 0.5 mg/kg doses of gantacurium abolished laryngospasm in 3 and 8 cats, respectively, and induced complete neuromuscular block measured at the pelvic limb; the mean ± SE duration of apnea was 2 ± 1 minutes and 3 ± 1.5 minutes, respectively. Hemoglobin oxygen saturation did not decrease significantly after administration of any dose of gantacurium.

CONCLUSIONS AND CLINICAL RELEVANCE

Tracheal intubation is not a benign procedure, especially in cats, a species in which prominent protective laryngeal reflexes are present. Stimulation of the larynx of cats often results in laryngospasm, and lesions as a consequence of tracheal intubation, such as tears adjacent to the larynx or tracheal lacerations associated with the use of stylets, have been reported. Moreover, tracheal intubation in this species has been associated with increased odds of anesthetic-related death.

An NMBA can be administered during induction of anesthesia and prior to intubation to prevent laryngospasm and facilitate insertion of the tracheal tube. It has been well established in humans that use of NMBA results in better intubation conditions and less laryngeal trauma. A major drawback of the use of conventional NMBAs in veterinary patients is the development of prolonged apnea. Modern, ultrashort-acting NMBAs might solve this problem if they obtund laryngeal reflexes sufficiently to allow tracheal intubation while inducing very transient apnea. Gantacurium, a novel olefinic isoquinolinium fumarate, is an ultrashort-acting, nondepolarizing NMBA that might fulfill these criteria. The brief duration of neuromuscular blockade induced by gantacurium is primarily the result of rapid inactivation of the drug through adduction of cysteine. This irreversible chemical reaction markedly decreases the affinity of gantacurium for nicotinic receptors at the motor end plate, rendering the drug devoid of neuromuscular blocking effects. Secondary elimination of gantacurium occurs via pH-sensitive hydrolysis. In human trials, the duration of neuromuscular blockade, defined as recovery to a train-of-four ratio ≥ 0.9, was found to be 10 to 15 minutes over a dose range of 1 to 4 times the ED95.

In cats, gantacurium is approximately half as potent as it is in humans (ED95, 0.11 mg/kg) but has an even shorter duration of effect (mean ± SE duration,

ABBREVIATIONS
ED95 Effective dose required to produce 95% depression of an evoked muscle response
MAP Mean arterial blood pressure
NMBA Neuromuscular blocking agent
PETCO2 End-tidal partial pressure of CO2
SpO2 Oxygen saturation as measured by pulse oximetry
T1 First twitch of the train-of-four
induced 15 minutes later with propofolc (2 mg/kg, IV), and neuromuscular monitoring. General anesthesia was approved by the Cornell University Institutional Animal Care and Use Committee. Experiments (5 tests completed for each cat during 1 anesthetic episode) were approved by the Cornell University Institutional Animal Care and Use Committee, and the concomitant duration of apnea and extent of hemoglobin desaturation were measured.

**Materials and Methods**

Eight healthy adult (1- to 4-year-old) domestic shorthair cats (5 males and 3 females), weighing between 2.3 and 5.6 kg, were evaluated. Food but not water was withheld overnight prior to anesthesia. The temperature was maintained between 2.3 and 5.6 kg, were evaluated. Food but not water was withheld overnight prior to anesthesia. The experiments (5 tests completed for each cat during 1 anesthetic episode) were approved by the Cornell University Institutional Animal Care and Use Committee.

**GENERAL ANESTHESIA AND NEUROMUSCULAR MONITORING**

Each cat received dexmedetomidine (10 µg/kg, IM) and butorphanol (0.1 mg/kg, IM). Anesthesia was induced 15 minutes later with propofol (2 mg/kg, IV), and a laryngeal mask (size No. 1.5 or 2) was placed orally. Anesthesia was maintained with IV administration of propofol (0.2 mg/kg/min) and dexmedetomidine (2 µg/kg/h). The laryngeal mask airway was connected via a 3-way swivel adaptor to a nonrebreathing system that provided 100% oxygen (1.5 to 2.0 L/min). Each cat was positioned in sternal recumbency and breathed spontaneously throughout the experiment. Oxygen saturation, ECG, and rectal temperature were monitored continuously, and arterial blood pressure was measured oscillometrically at 2-minute intervals. A sidestream capnograph was used to obtain and analyze gas samples from the lumen of the laryngeal mask airway. Rectal temperature was maintained between 38° and 39°C with a heated surgical table and forced warm air blanket, when necessary.

Neuromuscular function was measured by means of acceleromyography. With each cat in sternal recumbency, both pelvic limbs were positioned toward the right side of the body (ie, the pelvic limbs were arranged in a left-lateral position, but the rest of the cat’s body remained in sternal recumbency). The right pelvic limb was supported so that it would remain parallel to the surgical table and the tarsus could undergo free and unopposed flexion. Two 25-gauge needles were passed subcutaneously over the common fibular (peroneal) nerve and attached to the stimulating cables of the acceleromyography device. The acceleration sensitive crystal of the acceleromyography device was taped to the dorsal aspect of the metatarsus. The common fibular nerve was stimulated with a train-of-four pattern (frequency, 2 Hz; pulse duration, 0.2 milliseconds) and supramaximal current. The acceleromyography monitor was calibrated, and the amplitude of T1 was set automatically to 100%. The amplitude of the T1 and the fourth twitch of the train-of-four and the train-of-four ratio (ie, amplitude of the fourth twitch divided by amplitude of T1) were measured every 15 seconds thereafter.

**EVALUATION OF LARYNGOSPASM**

To assess the laryngeal response to physical stimulation, a 3-mm fiberscope fitted with a high-definition camera was inserted through the free port of the 3-way adapter into the lumen of the laryngeal mask airway and placed rostral to the larynx. The larynx (arytenoid cartilages and dorsal aspect of the epiglottis) were observed on a monitor in real time. A 20-gauge 90-mm closed-tip epidural catheter was placed alongside the fiberscope and advanced until the tip was positioned between the arytenoid cartilages. Protective laryngeal reflexes were evoked by injecting 0.3 mL of sterile water through the catheter so that the mucous membrane of the rima glottidis was irrigated by the spray. The injection was performed as quickly as possible by the same investigator (MMF) on each occasion. A similar procedure has been used in children, and results indicated that the stimulus was repeatable at 10-minute intervals. Laryngospasm was deemed to be present when the arytenoid cartilages closed immediately in response to the water spray and deemed to be absent when no such movement occurred.

**SEQUENCE OF OBSERVATIONS**

After at least 20 minutes of anesthesia, a baseline laryngeal response for each cat was evaluated by spraying the rima glottidis in the absence of the NMBA. Fifteen minutes after the baseline response was evoked, gantacurium (0.1 mg/kg, IV) was administered. When the lowest T1 amplitude was observed (no reduction in 3 consecutive measurements), neuromuscular blockade was considered to be maximal; at this time, sterile water was again sprayed at the larynx and the presence or absence of laryngospasm was observed. Recovery of neuromuscular function after gantacurium administration occurred spontaneously. Once the train-of-four ratio reached at least 1.0, a 30-minute washout interval was allowed before the next dose of the NMBA was evaluated. Then the procedures were repeated for a 0.3 mg/kg dose of gantacurium and subsequently for a 0.5 mg/kg dose of gantacurium. In all instances, laryngeal stimulation occurred (and laryngeal response recorded) when the effects of gantacurium were maximal, and a 30-minute interval was allowed between complete recovery of neuromuscular function and evaluation of the next higher dose. The 0.1, 0.3, and 0.5 mg/kg doses of gantacurium approximated 1, 3, and 5 times the ED95.
in cats, respectively.7 Fifteen minutes after complete recovery from the last dose of gantacurium, the laryngeal response to water spraying was evaluated again; the latter test established whether laryngeal response at the end of the procedure (in the absence of the effects of gantacurium) was similar to the initial baseline laryngeal response.

DATA COLLECTION

After each of the 5 laryngeal stimulation tests, presence or absence of laryngospasm was determined. Duration of apnea was defined as the interval after laryngeal stimulation when no capnographic evidence of ventilation could be detected; apnea was considered to end as soon as CO2 was registered by the capnograph. If apnea occurred for ≥ 5 minutes or SpO2 was ≤ 90%, positive pressure ventilation was implemented.

Oxygen saturation as measured by pulse oximetry and PETCO2 were recorded before each application of water spray. Following laryngeal stimulation, the lowest SpO2 and the highest PETCO2 detected after restoration of spontaneous ventilation (during a 10-minute period) were recorded. Prestimulation and poststimulation data for these 2 variables were collected for each of the 5 tests. Because it is known that gantacurium can induce arterial hypotension as a result of histamine release,9 the prestimulation MAP and the lowest MAP during the 10-minute interval after laryngeal stimulation were recorded. Thus, prestimulation and poststimulation data for this variable were collected for each of the 3 drug tests.

Time of onset of neuromuscular blockade was defined as the time elapsed between gantacurium administration and maximal depression of the T1 amplitude. Percentage depression of T1 amplitude after each dose of gantacurium was calculated as follows: (1 - [minimal T1 amplitude/baseline T1 amplitude]) × 100%, where baseline T1 amplitude was the mean of the 3 T1 measurements obtained immediately prior to administration of each dose of gantacurium. The recovery index was defined as the interval between recovery of T1 amplitude to 25% and 75% of baseline T1 amplitude. Duration of neuromuscular blockade was defined as the interval between administration of a dose of gantacurium and return to train-of-four ratio to ≥ 1.0.

STATISTICAL ANALYSIS

Distribution of data was tested for normality by means of the Shapiro-Wilk test. Results were summarized as mean ± SE for parametric data and median (range) for nonparametric data. Values of P ≤ 0.05 were considered significant. Statistical tests were performed with the aid of computer software.9

Results

All cats recovered from anesthesia without complications. Mean ± SE duration of anesthesia was 133 ± 5 minutes (range, 120 to 150 minutes). Laryngospasm was evoked in all cats at baseline and after administration of gantacurium at a dose of 0.1 mg/kg. Laryngospasm was observed in 5 of the 8 cats after administration of gantacurium at a dose of 0.3 mg/kg, a finding that was not significantly different (P = 0.24) from baseline. No cat had laryngospasm after administration of gantacurium at a dose of 0.5 mg/kg, a finding that was significantly different from baseline. At the end of the experiment (15 minutes after recovery from the last dose of gantacurium) and in the absence of neuromuscular blockade, laryngospasm was evoked again in all cats.

In the absence of gantacurium, laryngeal stimulation caused apnea for a period of approximately 15 seconds; gantacurium at a dose of 0.1 mg/kg did not significantly prolong this period of apnea (Figure 1). However, duration of apnea was significantly longer after administration of gantacurium at a dose of 0.3 or 0.5 mg/kg. Duration of apnea was never ≥ 5 minutes and SpO2 was never ≤ 90%, so positive pressure ventilation was not used for any cat at any time.

Compared with prestimulation findings, no significant changes in SpO2 were observed after laryngospasm or during apnea at any testing time (all P ≥ 0.2). The SpO2 remained ≥ 96% in all cats at all times except for 2 individuals with an SpO2 of 93% after administration of gantacurium at a dose of 0.3 mg/kg and 2 others with an SpO2 of 94% and 91% after administration of gantacurium at a dose of 0.5 mg/kg. In those cats, SpO2 increased on return of spontaneous ventilation. Laryngospasm and apnea were followed by significant increases in PETCO2 at the time of restoration of spontaneous ventilation. All peak PETCO2 measurements were registered within 2 minutes after return of spontaneous ventilation (Figure 2). The MAP measured prior to laryngeal stimulation (and thus prior to gantacurium administration) did not differ among tests. Administration of gantacurium at all doses resulted in significant decreases in MAP (Figure 3).

Increasing the dose of gantacurium from 0.1 to 0.3 mg/kg and from 0.3 to 0.5 mg/kg resulted in fast-
registered by the capnograph. Values with different letters are significantly different. \( P < 0.05 \) for the difference between that data pair.

et onset times and longer duration of action, but did not prolong the recovery index (Table 1). Maximal depression of T1 amplitude was < 75% in 4 cats given gantacurium at a dose of 0.1 mg/kg; therefore, the recovery times to 25% of the T1 amplitude were not available for those individuals. Recovery index for that dose was derived from data for 4 cats.

**Discussion**

In the present study, administration of gantacurium at a dose of 0.5 mg/kg to healthy cats anesthetized with dexmedetomidine, butorphanol, and propofol abolished laryngospasm in response to a mechanical stimulus in all the animals studied, while causing apnea for a period of < 5 minutes and inducing no hemoglobin desaturation (defined as \( \text{SpO}_2 \leq 90\% \)). Results of this study also indicated that doses of gantacurium required to abolish laryngospasm are larger than those required to provide complete neuromuscular blockade measured at a pelvic limb in cats. In the study cats, duration of apnea after each dose of gantacurium was brief. A dose of 0.1 mg/kg resulted in an average of 2 to 3 minutes' duration in the cats of the present study. The short duration of apnea observed was probably the result of the termination of the neuromuscular blocking effects of this agent through l-cysteine adduction. The inactivation of gantacurium by l-cysteine is so rapid that a substantial proportion of the drug might even be inactivated before any effects can be induced. A similar observation has been made in regard to mivacurium chloride, for which it has been postulated that in humans, as much as 40% of the agent can be hydrolyzed during its passage from the site of injection, prior to it reaching nicotinic receptors on muscle. The duration of action and recovery index of gantacurium is much shorter than that of other commonly used NMBAs such as rocuronium bromide. Under inhalation anesthesia, the duration of neuromuscular blockade achieved by rocuronium in cats is approximately 20 minutes, with a recovery index of approximately 5 minutes (maximum of almost 11 minutes). In contrast, the duration of neuromuscular blockade achieved by gantacurium to a train-of-four ratio of 1.0 in the present study was only approximately 7 minutes after the highest dose, with recovery indices of approximately 1 and 1.5 times.
minutes after administration of doses of 0.3 and 0.5 mg/kg, respectively. Once spontaneous recovery from gantacurium begins, it appears to proceed rapidly and reliably.

It is interesting that duration of apnea was shorter than the duration of neuromuscular blocking measured at the pelvic limb in the cats of the present study. We have previously shown that restoration of ventilation occurs early during recovery from neuromuscular blockade in dogs,\textsuperscript{13} and the same was observed in these cats. This observation has an important clinical implication: recovery of spontaneous ventilation (ie, recovery of diaphragmatic function) does not indicate that neuromuscular function has been restored in all nerve-muscle groups.

The capacity to prevent laryngospasm while inducing only a brief period of apnea in cats is of potential clinical importance; it suggests that it might be feasible to improve intubation conditions by preventing laryngospasm, thereby reducing the risks associated with prolonged apnea. Because a cannot-intubate, cannot-ventilate scenario has a potentially fatal outcome when NMBAs are used during induction of anesthesia, the benefits of a quick return of spontaneous ventilation are self-evident and contrast with observations for more traditional NMBAs such as rocuronium. When cats were treated with rocuronium, the quality of intubation was improved (compared with findings for cats that did not receive rocuronium), but mechanical ventilation was needed for up to 28 minutes.\textsuperscript{14} The short duration of apnea observed in cats in the present study should not be interpreted as justification to use NMBAs without the skills and means for placing an orotracheal tube and providing positive-pressure ventilation.

Succinylcholine chloride has also been used in cats to prevent laryngospasm.\textsuperscript{15} In that study,\textsuperscript{15} positive-pressure ventilation was provided for 15 minutes. When succinylcholine (0.6 mg/kg) was used to facilitate intubation in people, spontaneous breathing had returned by the fourth minute after administration.\textsuperscript{16} However, administration of succinylcholine might be associated with several adverse effects, including intracranial and intraocular hypertension, bradycardia, hyperkalemia, and malignant hyperthermia. Nondepolarizing agents such as gantacurium are not asso-

![Figure 3](image-url) - Mean ± SE MAP immediately before (white bars) and after (gray bars) IV administration of 0.1, 0.3, or 0.5 mg of gantacurium/kg (in order of increasing dose) and laryngeal stimulation in the cats described in Figure 1. The lowest MAP recorded during a 10-minute interval after laryngeal stimulation (and thus gantacurium administration) was used for analysis. The value above each bracketed data pair represents the P value for the difference between that data pair.

Table 1 - Mean ± SE onset time, maximal depression of T1 amplitude, recovery index, and duration of neuromuscular blockade after IV administration of 0.1, 0.3, or 0.5 mg of gantacurium/kg (in order of increasing dose) in 8 anesthetized healthy cats.

<table>
<thead>
<tr>
<th>Dose of gantacurium (mg/kg)</th>
<th>Onset time (s)</th>
<th>Maximal T1 depression (%)</th>
<th>Recovery index (s)</th>
<th>Duration (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>96 ± 9\textsuperscript{a}</td>
<td>75 ± 7</td>
<td>64 ± 15\textsuperscript{b}</td>
<td>238 ± 21\textsuperscript{c}</td>
</tr>
<tr>
<td>0.3</td>
<td>62 ± 7\textsuperscript{a}</td>
<td>100</td>
<td>67 ± 23\textsuperscript{a}</td>
<td>360 ± 33\textsuperscript{c}</td>
</tr>
<tr>
<td>0.5</td>
<td>55 ± 7\textsuperscript{a}</td>
<td>100</td>
<td>94 ± 29\textsuperscript{a}</td>
<td>440 ± 40\textsuperscript{c}</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Data for only 4 cats were available.

\textsuperscript{b}Within a column, values with different superscript letters are significantly (P < 0.05) different.

Neuromuscular function was measured by means of acceleromyography. Two 25-gauge needles were passed subcutaneously over the common fibular (peroneal) nerve and attached to the stimulating cables of the acceleromyography device. The acceleration sensitive crystal of the acceleromyography device was taped to the dorsal aspect of the right metatarsus. The common fibular nerve was stimulated with a train-of-four pattern (frequency, 2 Hz; pulse duration, 0.2 milliseconds) and supramaximal current. The acceleromyography monitor was calibrated, and the amplitude of T1 was set automatically to 100%. The amplitude of the T1 and the fourth twitch of the train of four and the train-of-four ratio (ie, amplitude of the fourth twitch divided by amplitude of T1) were measured every 15 seconds thereafter. When the lowest T1 amplitude following each administration of gantacurium was observed (no reduction in 3 consecutive measurements), neuromuscular blockade was considered to be maximal. Recovery of neuromuscular function after gantacurium administration occurred spontaneously. Once the train-of-four ratio reached at least 1.0, a 30-minute washout interval was allowed before the next dose of the NMBAs was evaluated. Time of onset of neuromuscular blockade was defined as the time elapsed between gantacurium administration and maximal depression of the T1 amplitude. Percentage depression of T1 amplitude after each dose of gantacurium was calculated as follows: (1 – [minimal T1 amplitude/baseline T1 amplitude]) X 100, where baseline T1 amplitude was the mean of the 3 T1 measurements obtained immediately prior to administration of each dose of gantacurium. The recovery index was defined as the interval between recovery of T1 amplitude to 25% and 75% of baseline T1 amplitude. Duration of neuromuscular blockade was defined as the interval between administration of a dose of gantacurium and return to train-of-four ratio ≥ 1.0.
associated with such adverse effects. Another alternative for blunting or preventing laryngospasm is to desensitize the laryngeal mucosa with a local anesthetic prior to intubation. It has been shown in cats that 2% lidocaine (2 mg/kg) placed on the laryngeal mucosa results in a lower number of attempts to intubate the trachea, compared with findings in a control group that received no treatment prior to intubation.17 Efficacy of this technique depends, at least in part, on sufficient time for the local anesthetic agent to desensitize the laryngeal mucosa. Intervals required for complete desensitization of the larynx following application of lidocaine in cats are between 1.5 and 2 minutes, even when concentrations of lidocaine > 2% are used.17,18

This latent period for laryngeal desensitization is longer than was the onset time for neuromuscular blockade following administration of gantacurium at a dose of 0.5 mg/kg in cats of the present study (55 seconds). Topical application of lidocaine to the laryngeal mucosa prior to intubation is widely practiced in veterinary medicine; however, a study19 of 1,000 children revealed that topical laryngeal anesthesia did not reduce the incidence of laryngospasm or coughing during airway instrumentation.

Similar to other muscles responsible for ventilation, the laryngeal musculature is more resistant to the effects of NMABs than are limb muscles.15,20–22 At a gantacurium dose approximately 3 times the ED₅₀ measured at the pelvic limb, laryngospasm was prevented in only 3 of 8 cats in the present study; therefore, the dose required to reliably block laryngospasm must be greater. Even though we expected that doses required for preventing laryngospasm would be larger than the doses required for inducing complete neuromuscular blockade at the pelvic limb, we did not foresee that the difference would be of this magnitude. However, one should note that the design of the present study did not allow accurate measurement of the ED₅₀ at the larynx, but it is likely to be > 0.3 and ≤ 0.5 mg/kg. Also, although a dose of 0.1 mg of gantacurium/kg resulted in approximately 95% depression of T₁ amplitude in cats in a previous study,9 that dose only resulted in approximately 75% depression of T₁ amplitude in the cats of the present study. Differences in anesthetic techniques and neuromuscular monitoring between the 2 studies might account this discrepancy; the potency of gantacurium in cats was established previously when the animals were under α-chloralose and pentobarbital anesthesia.9 In addition, force, instead of acceleration, was measured to quantify neuromuscular function in that previous study.9

The design of the present study did not allow intermediate responses to laryngeal stimulation to be recorded; we used a yes or no score for the presence of evoked laryngospasm. It is possible that doses of gantacurium < 0.5 mg/kg might be useful to improve intubation in cats: improved intubation conditions have been achieved in humans with doses of NMABs that only resulted in partial neuromuscular blockade.23,24 Reductions in muscular tone at the larynx, even if submaximal, could improve the quality of intubation and reduce the risks of trauma.

On the basis of the a priori criteria, no cat in the present study required mechanical ventilation during the time of gantacurium-induced apnea, although mechanical ventilation was almost initiated for 1 cat: SpO₂ of 91% was measured and spontaneous ventilation was restored approximately 10 seconds before the 5-minute time point. It is important to note that all cats were receiving oxygen at approximately 100% via the laryngeal mask airway prior to NMBA administration. Lower SpO₂ can be anticipated in patients that do not receive supplemental oxygen at this concentration prior to induction of apnea; it has been shown in dogs that the mean time to desaturation (SpO₂ ≤ 90%) during anesthetic induction with propofol in the absence of oxygen supplementation was only 70 seconds.25 Because of the implicit risk of apnea and hemoglobin desaturation during induction of anesthesia, the inspired fraction of oxygen should be augmented prior to administration of the anesthetic agents. In the cats of the present study, the most substantial change associated with apnea was an increase in PETCO₂. Even breath-holding for a few seconds after laryngospasm in the absence of neuromuscular blockade resulted in significant increases of PETCO₂. Apnea after doses of 0.3 and 0.5 mg of gantacurium/kg resulted in peak PETCO₂ that ranged between 92 and 97 mm Hg in all but 1 cat. Peak values were observed during the first 2 minutes after restoration of spontaneous ventilation. Values of that magnitude are expected to result in substantial reductions in blood pH; however, hypercapnia was of very short duration and quickly decreased as spontaneous ventilation returned. Blood pH was not measured in the present study. It can also be anticipated that such levels of hypercapnia will exacerbate hypoxemia by displacing oxygen from the alveolar gas if oxygen supplementation is not provided.

In the cats of the present study, gantacurium administration resulted in reductions in MAP. The mean decrease in MAP was 10% for doses of 0.1 mg/kg and 35% for doses of 0.5 mg/kg. In all cats, MAP returned to values similar to those observed before NMBA administration within 5 to 10 minutes and without any additional treatment. Gantacurium increases the circulating concentration of histamine, which is probably responsible for the transient decreases in MAP.26 Decreases in MAP in the cats of the present study could have been blunted by the presence of dexmedetomidine, which has vasoconstrictive effects. It is possible that more severe reductions in MAP would be observed in cats that did not receive dexmedetomidine.

In the present study, cats were anesthetized with an infusion of propofol instead of inhalation anesthetic agents, which potentiate NMABs.27 We wanted to avoid such an effect so that the data obtained would be more relevant to the conditions during induction of anesthesia with IV administered agents such as propofol. The drawback of this approach was that constant infusion of propofol might result in accumulation of...
the agent; with regard to propofol, the total recovery time is longer with increasing duration of infusion. It is possible that increments in plasma concentrations of propofol could result in increasing depths of anesthesia over time. Although this was a possibility in the present study, the laryngeal response to water spraying at the end of the experiment was evaluated and did not differ from that observed at baseline (ie, prior to any drug treatment). Hence, even if depth of anesthesia increased with time, that change appears to be insufficient to affect laryngospasm in response to mechanical stimulation.

We did not randomize the order of the gantacurium doses given to the cats of the present study; the dose administered was increased incrementally. Because the plasma half-life of gantacurium is short, a similar approach was used when the potency of gantacurium was assessed in dogs, monkeys, and cats. Although we cannot exclude the possibility that the data obtained in the present study were biased by the nonrandom order of administration of gantacurium doses, the fact that duration of action of neuromuscular block and duration of apnea achieved with doses of 0.3 and 0.5 mg of gantacurium/kg were indistinguishable suggests that no substantial accumulation of the drug in the circulation occurred.

The results of the present study in cats indicated that it was possible to blunt laryngospasm in response to a mechanical stimulus by administration of an NMBA without the need for mechanical ventilation. Because the data set was small and because gantacurium is not yet commercially available, it would be premature to recommend broad clinical application of gantacurium as an aid to tracheal intubation in cats. However, these data have suggested that this or another of the other new ultrashort-acting NMBA s might merit further investigation to establish whether they facilitate tracheal intubation in cats.

Acknowledgments
Supported by the Feline Health Center, College of Veterinary Medicine, Cornell University.

Footnotes
b. Torbugesic, Fort Dodge Animal Health, Fort Dodge, Iowa.
c. Propofol, Abbott Laboratories, Abbott Park, Ill.
d. AES laryngeal mask, AES Inc. Black Diamond, Wash.
e. TOF-Watch SX, Organon Ltd, Dublin, Ireland.
f. Specialty Fiberscope, Karl Storz Endoskope, Tuttingen, Germany.
g. Gantacurium, Cedarburg Laboratories, Grafton, Wis.
h. Minitab, version 16.2.4, Minitab Inc, State College, Pa.
i. Ezzine S, Donati E, Varin F. Arterial-venous gradient under mi-
vacurium steady-state concentrations in anesthetized patients (abstr). Anesthesiology 2001;95:A68.

References
1. Rex MA. Laryngospasm and respiratory changes in the cat pro-
duced by mechanical stimulation of the pharynx and respira-
2. Dyson DH, Grant Maxie M, Schnurr D. Morbidity and mortality associated with anesthetic management in small animal veteri-
4. Wong WT, Brock KA. Tracheal laceration from endotracheal in-
5. Mitchell SL, McCarthy R, Rudloff E, et al. Tracheal rupture asso-
6. Brodbelt DC, Pfeiffer DU, Young LE, et al. Risk factors for an-
8. Lundstrom LH, Moller AM, Rosenstock C, et al. Avoidance of neuromuscular blocking agents may increase the risk of dif-
cology of GW280430A (AV430A) in the rhesus monkey and in the cat: a comparison with mivacurium. Anesthesiology 2004;100:835–845.
11. Erb TO, von Ungern-Sternberg BS, Kellor F. Pentanyl does not reduce the incidence of laryngospasm in children aneste-
thized with sevoflurane. Anesthesiology 2010;113:41–47.
12. Auer U, Mosing M. A clinical study of the effects of rocuroni-
13. Martín-Flores M, Sakai DM, Campoy L, et al. Recovery from neu-
14. Moreno-Sala A, Ortiz-Martínez R, Valdivia AG, et al. Use of neu-
15. Rex MA. The effects of other drugs on the stimulation of la-
16. El-Orbany MJ, Joseph NJ, Salem MR. Tracheal intubating con-
22. Hemmerling TM, Schmidt J, Hanusa C, et al. Simultaneous de-
23. Siddik-Sayyid SM, Taha SK, Kanazi GE, et al. Excellent intubating conditions with remifentanil-propofol and either low-dose ro-
24. Kopman AF, Kiewicka MM, Neuman GG. Reexamined: the


