Effects of alfaxalone administered intravenously to healthy yearling loggerhead sea turtles (Caretta caretta) at three different doses

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OBJECTIVE
To compare physiologic and anesthetic effects of alfaxalone administered IV to yearling loggerhead sea turtles (Caretta caretta) at 3 different doses.

DESIGN
Randomized crossover study.

ANIMALS
9 healthy yearling loggerhead sea turtles.

PROCEDURES
Animals received each of 3 doses of alfaxalone (3 mg/kg [1.4 mg/lb], 5 mg/kg [2.3 mg/lb], or 10 mg/kg [4.5 mg/lb]) administered IV in randomly assigned order, with a minimum 7-day washout period between doses. Endotracheal intubation was attempted following anesthetic induction, and heart rate, sedation depth, cloacal temperature, and respirations were monitored. Times to first effect, induction, first voluntary muscle movement, first respiration, and recovery were recorded. Venous blood gas analysis was performed at 0 and 30 minutes. Assisted ventilation was performed if apnea persisted 30 minutes following induction.

RESULTS
Median anesthetic induction time for all 3 doses was 2 minutes. Endotracheal intubation was accomplished in all turtles following induction. Heart rate significantly increased after the 3- and 5-mg/kg doses were administered. Median intervals from alfaxalone administration to first spontaneous respiration were 16, 22, and 54 minutes for the 3-, 5-, and 10-mg/kg doses, respectively, and median intervals to recovery were 28, 46, and 90 minutes, respectively. Assisted ventilation was required for 1 turtle after receiving the 5-mg/kg dose and for 5 turtles after receiving the 10-mg/kg dose. The 10-mg/kg dose resulted in respiratory acidosis and marked hypoxemia at 30 minutes.

CONCLUSIONS AND CLINICAL RELEVANCE
IV alfaxalone administration to loggerhead sea turtles resulted in a rapid anesthetic induction and dose-dependent duration of sedation. Assisted ventilation is recommended if the 10 mg/kg dose is administered. (J Am Vet Med Assoc 2017;250:909–917)

Alfaxalone (3-α-hydroxy-5-α-pregnane-11, 20-dione) is a neurosteroid anesthetic agent recently reintroduced into veterinary medicine in the United States.1 The previously marketed formulation contained alphadolone solubilized in a 20% polyoxyethylated castor oil–based surfactant. This formulation was removed from the market after it was associated with histamine release and severe edema in cats and death in dogs.1 The currently marketed formulation contains a different solubilizing compound (cyclodextrin) that does not promote histamine release.

A GABA_A receptor agonist, alfaxalone inhibits action potential propagation and consciousness pathways.1 This drug produces smooth anesthetic inductions when administered to dogs, with dose-dependent cardiovascular depression in both dogs and cats.2,3 Alfaxalone is effective by both IV and IM routes of administration, but the currently marketed formulation is approved only for IV use in dogs and cats in the United States. It also supports less microbial growth than propofol.4

Alfaxalone has been evaluated in reptiles as an anesthetic agent and used clinically as an anesthetic induction agent.5,6 Dose-dependent sedation was observed in green iguanas (Iguana iguana) and Horsfield tortoises (Agrionemys horsfieldii) following IM administration.7,8 In red-care sliders (Trachemys scripta elegans), IM alfaxalone administration resulted in rapid anesthetic induction, increased loss of muscle tone at increased doses, and longer interval from administration.
tion to anesthetic recovery when given at lower temperatures. In juvenile estuarine crocodiles (Crocodylus porosus) and Australian freshwater crocodiles (Crocodylus johnstoni), IV alfaxalone administration at 4 temperatures resulted in variable duration of sedation, hypersensitivity to stimulation during anesthetic recovery, and apnea 1 to 2 hours following recovery. It was hypothesized that alfaxalone administration would provide smooth induction and recovery from anesthesia and that anesthetic effects (total sedation score, heart and respiratory rate, and recovery time) would be dose dependent in these turtles.

**Materials and Methods**

**Animals**

Nine yearling loggerhead sea turtles from a research colony were used for the study. They were transferred to the North Carolina Wildlife Resources Commission from the research colony and housed at the North Carolina Aquarium at Pine Knoll Shores, North Carolina, where they were allowed to acclimate to the study environment for 1 week before the study began. Three weeks prior to the first anesthesia session, a full physical examination was performed on each animal and blood samples were collected for CBC and plasma biochemical analysis. Although several turtles had a plasma albumin concentration that was slightly less than the lower reference limit reported for this species, plasma total protein concentrations were within reference limits. None of the turtles had any signs of abnormalities, such as positive or asymmetrical buoyancy, locomotive defects, or lower than typical appetite, and all were deemed healthy.

At the beginning of the anesthesia sessions, body weight ranged from 0.783 to 0.957 kg (1.723 to 2.105 lb), with a median value of 0.827 kg (1.819 lb), and these initial measurements were used for all dose calculations. Median straight carapace length (notch to notch) was 17.6 cm (range, 16.3 to 18.6 cm), and median straight carapace length (notch to tip) was 179 cm (range, 16.6 to 18.6 cm). Median straight carapace width was 14.6 cm (range, 13.1 to 15.0 cm). The study protocol was approved by the North Carolina State University Institutional Animal Care and Use Committee.

**Husbandry**

Each loggerhead sea turtle was individually maintained in an oval tank. Tank water was emptied and refilled once every 24 hours. The pH of the natural seawater source ranged from 8.0 to 8.3, salinity ranged from 28 to 32 g/L, and ammonia concentration was 0 mg/L. Water temperature ranged from 23.8°C to 24.7°C, with a median value of 24.4°C. Ambient air temperature ranged from 19.5°C to 22.4°C, with a median value of 20.6°C.

Six days per week, turtles were fed at approximately 1% of their body weight an omnivore diet supplemented with vitamin D3 and calcium powder, clam (Mercenaria mercenaria), shrimp (Penaeus sp), and lake smelt (Osmerus mordax). Each turtle was assessed daily throughout the study period by aquarist staff for activity level and appetite during scheduled feedings.

**Selection of alfaxalone doses**

To select appropriate doses of alfaxalone for use in the study, a preliminary evaluation was conducted with three 2-year-old loggerhead sea turtles housed as education animals at the North Carolina Aquarium at Pine Knoll Shores. Intravenous administration of alfaxalone injectable solution at a dose of 3 mg/kg (1.4 mg/lb), 5 mg/kg (2.3 mg/lb), or 10 mg/kg (4.5 mg/lb) resulted in no detected adverse effects (eg, prolonged apnea > 2 hours), severe bradycardia (< 4 beats/min, comparable to some cold-stun cases), or failure to recover fully from anesthesia. On the basis of these findings, these 3 doses were selected.

**Study design**

A crossover study design was used. Three anesthesia sessions were planned, each separated by a minimum washout period of 7 days. Turtles were randomly assigned (by rolling of 2 dice) to receive the 3- (n = 3), 5- (3), or 10- (3) mg/kg dose of alfaxalone first during the first session. 1 of the remaining 2 doses during the second session, and the remaining dose during the third session, resulting in all turtles receiving all doses by the end of the study. This scheme allowed assessment of all 3 doses during each session, but in different turtles each time.

During each of the 3 sessions, turtles assigned to receive the 3-mg/kg dose on that day were treated first, those assigned to receive the 5-mg/kg dose on that day were treated second, and those assigned to receive the 10-mg/kg dose on that day were treated last. The ascending dose series was adopted as a safety feature for this protected species, so that planned higher doses could be omitted if adverse effects occurred at an earlier lower dose.

**Alfaxalone administration**

For each anesthesia session, each turtle was removed from its tank and placed in a 38-L plastic tub containing dry towels, and remained in this tub for the duration of the anesthesia session. Approximately
10 minutes was provided for the turtle to acclimate to this enclosure, after which baseline measurements were obtained of heart rate (measured via Doppler ultrasonic flow detector), cloacal temperature, ambient temperature, and sedation score. Respirations were monitored and recorded for the next 10 minutes. Following respiration monitoring, each turtle was manually restrained and the neck was scrubbed with dilute povidone iodine solution for venipuncture of the left dorsal cervical sinus. The assigned alfaxalone dose was administered slowly over 15 seconds into the left dorsal cervical sinus by use of a 22-gauge, 2.5-cm needle and 1.0-ML syringe.

**Monitoring**

During each anesthesia session, heart rate was assessed at 2 minutes and then every 5 minutes after alfaxalone administration. Cloacal temperature was measured with a thermocouple thermometer at times of blood sample collection for blood gas analysis (0, before administration, 30, and if applicable, 60 minutes). The time at which each respiration occurred was recorded, and the number of breaths for each 5-minute interval was calculated. Monitoring continued until turtles had fully recovered from anesthesia. Timings of first noticed effect, achievement of anesthetic induction, first voluntary muscle movement, and anesthetic recovery were recorded. First effect was defined as the first noticed decrease in muscle tone (sedation score of 1 or 2). Anesthetic induction was defined as loss of muscle tone (sedation score of 2) and mild-to-no jaw resistance (sedation score of 2 or 3). Anesthetic recovery was defined as return of voluntary coordinated movement and to baseline sedation scores. Turtles remained in plastic tubs for a total of 60 minutes after anesthetic recovery, after which heart rate was measured and turtles were returned to their tanks.

**Intubation and ventilation protocol**

To determine whether the alfaxalone dose administered provided sufficient anesthesia to allow endotracheal intubation, each turtle was intubated with a 2-mm uncuffed endotracheal tube at the point immediately following anesthetic induction (determined on the basis of sedation scores) in each anesthesia session. The endotracheal tube was then promptly removed to permit monitoring of unassisted spontaneous ventilation. Free-ranging loggerhead sea turtles typically dive for durations up to 308 minutes. In comparison, loggerhead sea turtles raised and evaluated in a laboratory setting reportedly had voluntary submergences that ranged from 5 to 40 minutes, with periods of 2 to 10 breaths between dive periods. Typically dive for durations up to 308 minutes.

**Sedation scoring**

Sedation scoring began after physiologic variables had been recorded at 2 minutes and at each 5-minute interval following alfaxalone administration and was performed by the same investigator during all anesthesia sessions for consistency. By this system, scores were assigned for palpebral reflex, jaw tone, muscle tone, and response to painful stimuli. For palpebral reflex scoring, 0 represented an intact reflex, 1 represented a slowed reflex, and 2 represented an absent reflex. For jaw tone scoring, the ability of a turtle to open its mouth was tested with the investigator applying 2 fingers to open the lower jaw. A score of 0 indicated notable resistance, with the mouth unable to be opened with 2 fingers; 1 indicated moderate resistance, with force required to open the mouth with 2 fingers; 2 indicated mild resistance, with the mouth able to be opened with 2 fingers with light force; and 3 indicated no resistance, with the mouth easily opened with 2 fingers. For muscle tone scoring, 0 represented head and neck actively held up, with active movement of all 4 flippers; 1 represented head and neck limp, with intermittent flipper movement when stimulated; and 2 represented head and neck limp, with no flipper movement.

For testing of response to painful stimuli, a pair of small curved hemostats was applied to the trailing edge of a foreflipper on each turtle by the same investigator (BEF) for up to approximately 2 seconds. The investigator avoided closing the hemostats to a ratchet to minimize potentially harmful injuries. A score of 0 indicated reaction to pain, movement of the head, or withdrawal of the flipper; 1 indicated slow withdrawal of the flipper and slow reaction of the head; 2 indicated no head movement, with slow reaction of the flipper; and 3 indicated no response to stimulation. Sedation scores were recorded until the time a turtle had fully recovered from anesthesia. The maximum possible total sedation score was 10.

**Blood gas measurement**

A baseline (0 minutes) venous blood gas sample was obtained immediately prior to alfaxalone administration. A second blood sample, this time from the right dorsal cervical sinus, was collected at 30 minutes from all turtles and at 60 minutes only from those that had not yet recovered from anesthesia. These samples were obtained following measurement of physiologic variables and assignment of sedation scores at these assessment points. In preparation for collection, the dorsal cervical region was gently scrubbed with dilute povidone iodine solution. Venipuncture was performed by use of a 22-gauge, 2.5-cm needle connected to a syringe containing sodium heparin (total volume of blood collected, 0.2 mL).
Venous blood gas analysis was performed with a point-of-care analyzer. The total volume of blood used for this analysis (0.6 mL) represented 0.35 mL/kg for the smallest turtle in this study. Blood pH, PaCO₂, PaO₂, and lactate concentration were measured at 37°C. Blood HCO₃⁻ concentration was calculated by use of the Henderson-Hasselbalch equation. Temperature-corrected values were calculated by use of equations more applicable to sea turtles than the human-based algorithms used by the analyzer. The analyzer can also be used to calculate percentage of oxygen saturation and base excess, but these values were excluded from analysis because the calculations rely on assumptions of hemoglobin and plasma protein concentrations for humans and species-specific blood-oxygen affinity that do not apply to sea turtles.

### Statistical analysis

Morphological and physiologic data, sedation scores, and blood gas data were analyzed by use of statistical software. The Shapiro-Wilk test was used to test the data for a normal distribution. Because data were not normally distributed, nonparametric analysis was performed. The Friedman test was used to compare ambient temperature, intervals to anesthetic effects and first respiration, cloacal temperature, baseline and peak total sedation scores, baseline heart rate, and heart rate at peak sedation score among the 3 alfaxalone doses. Blood gas values were compared between 0 and 30 minutes for the 3-mg/kg dose and the 5-mg/kg dose (all but 1 turtle were fully recovered by 60 minutes, and a 60-minute sample was not collected) by use of the Wilcoxon signed rank test. Pairwise comparison was also performed between baseline and peak total sedation scores for each alfaxalone dose by use of the same test. Baseline heart rate and heart rate at peak sedation score were compared within doses by use of the same test. The Friedman test was used to compare blood gas values over time for the 10-mg/kg dose. Values of $P < 0.05$ were considered significant.

### Results

All loggerhead sea turtles recovered fully from the anesthesia sessions and were returned to water after 1 hour of recovery, with no observed recurrence of sedative effects. No significant difference in ambient and water temperatures was identified among turtles when they received the 3-, 5-, or 10-mg/kg dose.

Intervals from alfaxalone administration to first effect, anesthetic induction, first voluntary muscle movement, and anesthetic recovery; interval from first muscle movement to recovery; and interval from alfaxalone administration to first spontaneous breath for each alfaxalone dose were summarized (Table 1). For all doses (3, 5, and 10 mg/kg), median interval from alfaxalone administration to anesthetic induction was 2 minutes. Endotracheal intubation was successfully achieved in all turtles at all doses between 6 and 7 minutes after alfaxalone administration, except for 1 turtle with a prolonged anesthetic induction and incomplete anesthesia after receiving the 5-mg/kg dose, for which intubation was not attempted.

During the acclimation period before alfaxalone administration (baseline), respirations ranged from 0 to 26 breaths/10 min. There was no significant difference in baseline respirations among doses. Interval from alfaxalone administration to first spontaneous respiration was significantly longer for the 10-mg/kg dose than for the 3-mg/kg dose (Table 1). No intubation or assisted ventilation was required for turtles after receiving the 3-mg/kg dose of alfaxalone. One turtle after receiving the 5-mg/kg dose and 5 turtles after receiving the 10-mg/kg dose required intubation and IPPV after 30 minutes of apnea. The turtle that became apneic after the 5-mg/kg dose received IPPV for 16 minutes. Assisted ventilation was provided for a median of 23 minutes (range, 6 to 43 minutes) to the turtles that became apneic after the 10-mg/kg dose. During the first and second 5-minute intervals after the first spontaneous respiration, no significant differences in respiratory rates were identified among the 3 doses, nor were any differences detected from baseline respiratory rates. The median number of respirations for all doses during the first and second 5-minute intervals were 3 (range, 1 to 15) and 2 (range, 0 to 8), respectively.

Median baseline heart rate before administration of each of the 3 doses was 32 beats/min (Figure 1). No significant difference in baseline heart rates was identified among the doses. At the time of peak sedation following administration of the 3- and 5-mg/kg doses

### Table 1—Median (range) intervals (min) for various events following IV administration of alfaxalone at 3, 5, or 10 mg/kg (1.4, 2.3, or 4.5 mg/lb) to 9 loggerhead sea turtles (Caretta caretta) in a crossover study design.

<table>
<thead>
<tr>
<th>Interval</th>
<th>3 mg/kg</th>
<th>5 mg/kg</th>
<th>10 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>From alfaxalone administration to first effect</td>
<td>0.5 (0–2)</td>
<td>0* (0–1.5)</td>
<td>0* (0–0.5)</td>
</tr>
<tr>
<td>From alfaxalone administration to anesthetic induction</td>
<td>2* (1–2)</td>
<td>2* (0–25)</td>
<td>2* (1–2)</td>
</tr>
<tr>
<td>From alfaxalone administration to first muscle movement</td>
<td>13* (12–17)</td>
<td>17* (9–31)</td>
<td>51* (26–62)</td>
</tr>
<tr>
<td>From alfaxalone administration to anesthetic recovery</td>
<td>28* (20–46)</td>
<td>46* (40–75)</td>
<td>90* (82–130)</td>
</tr>
<tr>
<td>From first muscle movement after alfaxalone administration to anesthetic recovery</td>
<td>14* (8–29)</td>
<td>28* (9–59)</td>
<td>61* (18–89)</td>
</tr>
<tr>
<td>From alfaxalone administration to first spontaneous respiration</td>
<td>16 (11–21)</td>
<td>22 (17–55)</td>
<td>54 (33–82)</td>
</tr>
</tbody>
</table>

*For a given interval, values with the same superscript letter differ significantly ($P < 0.05$).

Loggerhead sea turtles received each alfaxalone dose in a different anesthesia session, with a minimum 7-day washout period between sessions.
A significant increase in heart rate from baseline was identified. Beginning 15 minutes after alfaxalone administration at 10 mg/kg, median heart rate started to decrease and continued to do so until the 30-minute assessment point. The lowest median heart rates occurred at the 25- and 30-minute assessment points and were significantly lower than at baseline. At the 35-minute assessment point, median heart rate for the 10-mg/kg dose began to increase, corresponding with the point of either first spontaneous respiration or initiation of IPPV.

Median peak total sedation score was achieved at 2, 5, and 10 minutes after alfaxalone administration at 5, 5, and 10 mg/kg, respectively (Figure 2). These
peak tone were significantly higher than at baseline for all 3 doses. Sedation scores were no longer significantly higher than at baseline by 25, 45, and 90 minutes after alfaxalone administration at 3, 5, and 10 mg/kg, respectively. At the peak total sedation score, heart rate of turtles after receiving the 10-mg/kg dose was significantly lower than when they received the 3- or 5-mg/kg dose.

Loss of palpebral reflex was observed in 7 of the 9 turtles after receiving the 10-mg/kg dose of alfaxalone, 3 turtles after receiving the 5-mg/kg dose, and none of the turtles after receiving the 3-mg/kg dose. Only 3 turtles had a slow palpebral reflex after receiving the 3-mg/kg dose. All turtles had loss of muscle tone after receiving any of the 3 doses, and all had loss of jaw tone after receiving the 5- or 10-mg/kg doses. Only 5 turtles had loss of jaw tone after receiving the 3-mg/kg dose, and the other 4 retained slight jaw tone. All turtles lacked a response to painful stimulation after receiving the 5- or 10-mg/kg doses, whereas only 4 turtles had no such response after receiving the 3-mg/kg dose. Complete loss of response to painful stimulation after alfaxalone administration was observed up to the 15-minute assessment point for the 5-mg/kg dose and up to the 25-minute assessment point for the 10-mg/kg dose. An increase in jaw resistance was identified prior to the first voluntary muscle movement for all doses.

Cloacal temperatures decreased significantly from baseline to the 30-minute assessment point for all doses and from baseline to the 60-minute assessment point for the 10-mg/kg dose (Table 2; cloacal temperature was not assessed at the 60-minute point for the 3- and 5-mg/kg dose). No significant differences in cloacal temperature were identified among the doses at the baseline or 30-minute assessment points.

Venous blood gas analysis was performed at 0 and 30 minutes for all 3 doses and at 60 minutes for the 10-mg/kg dose (Table 3). No significant differences were identified among doses in any analyte value at 0 minutes. For the 3 mg/kg dose, no significant differences were identified for any analyte between 0 and 30 minutes. For the 5 mg/kg dose, only significant differences were identified at 30 minutes for all 3 doses and at 60 minutes for the 10-mg/kg dose (Table 3). For the 3 mg/kg dose, no significant differences were identified among doses in any analyte value at 30 minutes.
fied between 0 and 30 minutes was an increase in PaCO₂ at 37°C, but not in temperature-corrected PaCO₂. For the 10-mg/kg dose, significant decreases from 0-minute values in pH and PaO₂ and an increase in PaCO₂ were identified at the 30-minute assessment point, with pH, PaO₂ and temperature-corrected PaCO₂ no longer significantly different from 0-minute values at the 60-minute assessment point. For the 3- and 5-mg/kg doses, PaO₂ was significantly lower than for the 10-mg/kg dose at the 30-minute assessment point.

**Discussion**

Intravenous administration of alfaxalone to yearling loggerhead sea turtles at a dose of 3, 5, or 10 mg/kg was performed without any immediate adverse effects in the study reported here. A smooth and rapid induction of anesthesia was achieved at all 3 doses. The median interval from administration to anesthetic induction (2 minutes for all 3 doses) was comparable to reported induction times for IV alfaxalone administration in green iguanas, red-eared sliders, and 2 species of crocodiles. One hour after recovery from anesthesia, all turtles in the present study were returned to water with no observed recurrence of sedative effects, in contrast to reported findings for IV alfaxalone administration to crocodiles and the experience of the authors and others regarding clinical use of propofol in loggerhead sea turtles. However, the 10-mg/kg dose of alfaxalone resulted in significantly greater intervals from administration to anesthetic recovery and to first respiration, compared with the other 2 doses as well as marked venous blood gas alterations.

Intravenous alfaxalone administration at 3 and 5 mg/kg resulted in a significant increase in heart rate at time of peak sedation in the study reported here. This finding was contrary to the study hypothesis as well as to the cardiovascular effects of alfaxalone reported for other reptile species. A significant decrease in heart rate following IM alfaxalone administration was identified in green iguanas and Horsfield tortoises. A nonsignificant trend of increase in heart rate was identified in red-eared sliders. Although IV administration of the 10-mg/kg dose of alfaxalone did not result in a significant change in heart rate between baseline and time of peak sedation in the loggerhead sea turtles of the present study, heart rate decreased after peak sedation.

In domestic mammals, alfaxalone also has varied effects on the cardiovascular system. For example, heart rate increased following alfaxalone administration in dogs but was associated with a dose-dependent decrease in cats. The mechanism underlying an increase in heart rate is unknown but may reflect a response to peripheral hypotension associated with alfaxalone administration. Invasive techniques would be required to measure blood pressure in loggerhead sea turtles, but such information may be valuable in furthering the understanding of the cardiovascular effects of alfaxalone in this species.

Alfaxalone administration in reptiles and domestic mammals causes a decrease in respiratory rate and periods of apnea. Horsfield tortoises given alfaxalone 1M at 10 and 20 mg/kg (4.5 and 9.1 mg/lb) reportedly have a decrease in respiratory rate. Variable periods of apnea occurred in green iguanas, estuarine crocodiles, dogs, and cats following alfaxalone administration. In the study reported here, different durations of apnea resulted from each of the 3 alfaxalone doses administered to loggerhead sea turtles. The 10-mg/kg dose resulted in the longest period of apnea (median, 54 minutes), and more turtles required IPPV at this dose than at lower doses. In addition, the 10-mg/kg dose resulted in marked hypoventilation and hypoxemia 30 minutes after administration.

Sea turtles perform voluntary dives of various durations, depending on species and size class. Adult free-ranging loggerhead sea turtles can perform voluntary dives for as long as 308 minutes. In contrast, juvenile and hatchling green sea turtles have mean dive durations of 7.7 minutes (maximum, 17 minutes) and 82 seconds (maximum, 6 minutes). Dive durations for yearling loggerhead sea turtles such as those in the present study have not been reported, but given the marked hypoxemia achieved at 30 minutes with the 10 mg/kg dose of alfaxalone in the present study (median temperature-corrected PaO₂, 7 mm Hg), this duration of apnea likely exceeded a typical dive period for this age class. Therefore, IV administration of alfaxalone at 10 mg/kg to this species should be complemented with endotracheal intubation and IPPV, which if initiated early after anesthetic induction may prevent the marked hypoxemia and respiratory acidosis observed with this dose.

In domestic mammals, IV administration of high doses of alfaxalone causes blood gas alterations similar to those achieved in turtles in the present study at the 10-mg/kg dose, including an increase in PaCO₂ and decreases in pH and PaO₂. In dogs and cats, such arterial blood gas changes are suspected to be due to respiratory depression and apnea achieved with high doses of alfaxalone. Voluntary submergences of loggerhead sea turtles are mostly aerobic and are typically associated with minimal changes in venous blood gas analytes. Longer dive durations are associated with respiratory acidosis and anaerobic metabolism. The prolonged period of apnea achieved in the present study at the 10-mg/kg dose of alfaxalone likely resulted in the marked hypoxemia. At 30 minutes after alfaxalone administration at 10 mg/kg, the 5 apneic turtles were provided with IPPV, and the marked hypoxemia resolved by 60 minutes after administration, likely owing to manual ventilation or return of spontaneous respiration.

Cloacal temperature decreased with time by a median of 1.3° to 1.5°C (2.3° to 2.7°F) at all doses in the present study, as body temperature equilibrated from water temperature toward air temperature. These changes may have had a minor effect on anesthetic depth and duration. Environmental temperature and associated decrease in body temperature
reportedly has an effect on alfaxalone sedation in sliders. Intramuscular administration of alfaxalone at 20 mg/kg and a low environmental temperature (20°C) resulted in a longer duration of anesthesia with greater loss of muscle tone and palpebral reflex than did IM administration of a 10-mg/kg dose at a higher temperature (35°C). A similar study involving red-eared sliders revealed that IM alfaxalone administration at 20 mg/kg and 20°C resulted in a significantly longer recovery period than administration at 10 mg/kg at 35°C, but with no significant effects of dose or temperature on response to painful stimuli. The lack of environmental temperature control in the present study led to the observed decrease in clonic temperature, but the resulting temperature differences were minor compared with those reported for red-eared sliders. Ambient temperature and clonic temperature of loggerhead sea turtles should be monitored during alfaxalone anesthesia if water and air temperature differ appreciably, given that a continued decrease in body temperature may result in a prolonged anesthetic recovery. A supplemental heat source should be provided when necessary to minimize such a change.

Total sedation scores significantly increased after alfaxalone administration in the present study, and the duration of sedation corresponded with the alfaxalone dose. The sedation period for the 3-mg/kg dose was shortest and characterized by loss of muscle tone, intact or slowed palpebral reflex, decreased or absent jaw tone, and slow or absent response to painful stimuli. This dose still allowed for endotracheal intubation and maintenance with inhaled anesthesia. Alfaxalone administered IV at 10 mg/kg resulted in a significant decrease in heart rate, prolonged period of apnea, and venous blood gas alterations over a 30-minute period. These doses may be sufficient for IV induction of anesthesia for diagnostic procedures, brief surgical procedures, or endotracheal intubation and maintenance with inhalation anesthesia. Alfaxalone administered IV at 10 mg/kg resulted in a significant decrease in heart rate, prolonged period of apnea, and venous blood gas alterations including respiratory acidosis and hypoxemia. This higher dose should be used clinically only if the turtle can be intubated and provided with IPPV.

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Footnotes
a. Alfaxan-CD RTU (10 mg/mL), Jurox Pty Ltd, Rutherford, Australia.
c. Pocket Dop 3 Doppler flow probe, CareFusion, Middleton, Wis.
d. Barnant Thermocouple Thermometer, Barnant Co, Barrington, Ill.
e. VetScan i-STAT 1 analyzer with CG4+ cartridges, Abaxis, Union City, Calif.
f. JMP Pro, version 11. SAS Institute Inc, Cary, NC.
g. Boylan S, South Carolina Aquarium, Charleston, SC: Personal communication, 2015.

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4. Strachan FA, Mansel JC, Clutton RE. A comparison of micro-