To the Editor:

The recently published article titled “Proximal Radial and Distal Humeral Osteosarcoma” by Julius Liptak, et al. (JAAHA 2004;40:461-467) contains a number of numerical errors that are not supported by data presented in the Outcomes in the Table on page 463 of that article. In the published abstract, the results section on page 464, and the discussion on page 466, the median survival is listed as 824 days. According to the Table on page 463, 824 days was the longest survival of any dog, not the median survival; and the median survival of the dogs listed in the Table should actually be 238.5 days (or halfway between 182 and 295 days). This error should have been particularly visible to both authors and reviewers in the last sentence of the first full paragraph on page 464, which states, “The median survival time was 824 days (range 11 to 824 days).” Also, in the abstract, the results section on page 462, and the discussion on page 466, the claim for median metastasis-free interval is 356 days. On the Table on page 463, the metastasis-free interval is listed for six dogs, and the median metastasis-free interval should actually be 198 days (halfway between 153 and 243 days). Published conclusions reached from comparisons of the erroneous medians with the data from dogs with osteosarcoma at other appendicular sites (results, page 464) should be reevaluated using the corrected medians.

Median survival times from studies of this type are often quoted in support of patient-care decisions by casual readers without reference to or careful examination of the original published data. I would hope that authors of similar studies, and those who serve as scientific reviewers for the JOURNAL, would more carefully scrutinize the manuscript at each stage of publication to prevent final publication of such errors.

Cordially yours,

James K. Roush, DVM, MS, Diplomate ACVS
Professor and Section Head
Small Animal Surgery
Kansas State University

---

Response

Dear Dr. Roush,


The reported median survival time and median metastasis-free interval are correct, and no mistake has been made by either the authors or the reviewers. Kaplan-Meier survival analysis is the standard statistical test to calculate outcome in animals and humans with oncologic disease. Kaplan-Meier survival analysis includes animals that have died from tumor-related causes or are lost to follow-up, whereas animals that are alive or have died for reasons unrelated to the tumor are censored from analysis.

In our analysis, 10 dogs with osteosarcoma of the distal humerus or proximal radius were treated with curative-intent forequarter amputation and postoperative chemotherapy. Of these 10 dogs, four died because of metastatic disease, two dogs were lost to follow-up, three dogs died from unrelated causes, and one dog was alive. Hence, the oncologic outcome calculated using Kaplan-Meier survival analysis censored the latter four dogs. As a result, the 50% (or median) for dogs dead or presumed dead (i.e., lost to follow-up) because of tumor-related causes is 356 days for metastasis and 824 days for survival. This is demonstrated on the Kaplan-Meier survival curve on page 465.

The calculations provided in your letter are correct medians for the raw data but do not consider oncologic outcome and cause of death and, hence, are incorrect in the context of this paper and other papers reporting oncologic data.
Lastly, even for the casual reader, we clearly and unequivocally state in the abstract, results, discussion, and conclusion that metastasis-free interval and survival time for dogs with osteosarcoma of the distal humerus and proximal radius are not significantly different from osteosarcoma in other appendicular sites.

Yours sincerely,

Julius M. Liptak, BVSc, MVetClinStud, FACVSc
Assistant Professor in Small Animal Surgery
Ontario Veterinary College, University of Guelph
Effects of Clomipramine on Cats
Presented for Urine Marking

Twenty-five cats exhibiting at least four episodes of vertical urine marking per week were assessed. Following a medical workup, a 4-week clomipramine trial was instituted, using a mean dose of 0.54 mg/kg per os q 24 hours. No concurrent behavioral or environmental modifications were applied. There was a statistically significant ($P<0.0001$) decrease in urine spraying when the cats were on clomipramine, with 20 of 25 cats having a $\geq 75\%$ reduction in spraying within 4 weeks. Side effects were mild. Twenty cats were followed for an additional 5 months. Fifteen cats required medication to control the spraying, often at a reduced dose. J Am Anim Hosp Assoc 2005;41:3-11.

Introduction

Inappropriate elimination and urine spraying (vertical urine marking) are the most common feline behavior problems seen at behavior referral practices. In a study of feline behavior cases referred to the Ontario Veterinary College, 61% had a primary complaint of inappropriate elimination. Although sexually intact cats are most likely to spray, 12% of neutered males and 4% of spayed females may become problem sprayers. Spraying occurs when a cat backs up to a vertical surface and directs a stream of urine toward an object or surface. This marking behavior may be caused by territorial competition, anxiety-evoking situations, or arousing events, and it may be stimulated by novel sights, sounds, or odors, especially from other cats. Commonly sprayed sites include prominent objects such as plants and furniture, boundary and exit areas (such as doors, walls, or windows), and new objects in the home. Cats that spray use their litter for elimination of urine and feces, although some cats routinely use the spraying posture even in their litter boxes.

Although identifying and treating all initiating factors are essential if the urine spraying problem is to be successfully resolved, eliminating such factors may not be practical when they involve stray cats on the property or multiple cats within the home. In addition, eliminating factors such as residual urine odor may be difficult. In some cases, environmental adjustments that reduce access to the most common target areas or that decrease exposure to the inciting stimuli may be effective. Some cats are satisfied with marking a single area that is provided (allowed) by the owners. Feliway, a synthetic facial pheromone, may also be used to induce cheek gland marking (bunting) at the targeted sites in lieu of urine spraying. Feliway may reduce arousal, excitation, and anxiety, because cheek gland marking may have a calming effect. Feliway has been reported to reduce urine spraying in 74% to 97% of cats; but in a recent study, only 33.3% of treated households had a complete resolution of the spraying.
When other efforts to resolve the urine spraying are unsuccessful, pharmacological intervention may be useful. Combinations of environmental modification, pheromone therapy, and pharmacological intervention are often necessary to achieve satisfactory long-term control of urine spraying.\textsuperscript{2,4,5} For the drug trial reported here, only a single treatment modality was utilized in order to reduce the possibility of other variables affecting the outcome.

Since its introduction as a treatment for separation anxiety in dogs, the use of clomipramine hydrochloride has become increasingly common for a wide variety of behavioral problems, including urine spraying in cats.\textsuperscript{6-10} Clomipramine is licensed in Australia for this use.\textsuperscript{b} In countries such as Canada and Australia, a beef-flavored tablet is available in a 5-mg size that can be administered to cats at a dose of half a tablet per day.\textsuperscript{b}

Clomipramine is the most potent serotonin reuptake inhibitor of the tricyclic antidepressant class of drugs.\textsuperscript{6,8} Its active metabolite, desmethylclomipramine, also inhibits norepinephrine reuptake.\textsuperscript{6,8} Compared to amitriptyline, it appears to have fewer anticholinergic effects, although occasional urinary retention, constipation, or sedation may be seen.\textsuperscript{6,8} In a study of 26 cats given 5 mg once daily, a reduction in spraying was seen in 80% of the cats within 7 days, and complete cessation occurred in 33% of cats.\textsuperscript{11} However, no long-term or follow-up data was available. In two other studies, spraying improved in some cats and resolved in others.\textsuperscript{9,10} In a study where clomipramine was compared to cypreheptadine for the treatment of urine spraying, clomipramine was found to be more effective.\textsuperscript{12} Preliminary results comparing clomipramine and fluoxetine found the two drugs were equally effective at controlling urine marking during the first 8 weeks of treatment; but after 16 weeks, fluoxetine induced a significantly greater reduction in spraying.\textsuperscript{13}

It is recommended that clomipramine be used cautiously in animals with epilepsy, narrow angle glaucoma, or cardiac arrhythmias.\textsuperscript{b} However, therapeutic doses of clomipramine in dogs do not affect cardiac rate or rhythm and cause only benign cardiovascular changes, even with doses as high as 20 mg/kg for 7 days.\textsuperscript{14,15} Because of its potential anticholinergic effects, clomipramine should also be used cautiously in animals with a history of urine retention or reduced gastrointestinal motility.

The purpose of this study was to assess the efficacy and side effects of clomipramine administered for urine marking in cats over a short period of 30 days. Most cats were also monitored for an additional 5 months to assess long-term control and recurrence of spraying upon drug withdrawal.

Materials and Methods

Case Selection

Cats were recruited from veterinary hospitals across southern Ontario, Canada. Cats that were urine marking on vertical surfaces at least four times per week were recruited for the trial. Cats were housed indoors throughout the duration of the trial and were required to use a litter box for all other eliminations. Any previous drug therapy was withdrawn at least 30 days prior to the trial. No environmental changes or new forms of behavioral management were initiated during the trial, and no surgical procedures were allowed during the trial. A maximum of four cats was allowed for each household, provided the spraying cat could be positively identified and there was no history of intercat aggression. All cats with underlying medical conditions that might cause urinary abnormalities (e.g., hyperthyroidism, urinary tract disorders) or might preclude administration of clomipramine were discouraged from enrolling in the trial. However, five cats were admitted despite the presence of underlying medical problems, including four cats with chronic renal failure (one of which was also on corticosteroid therapy for anemia) and one cat with a grade I heart murmur and asymptomatic ventricular premature contractions (VPCs).

Cats that previously received medication for the treatment of urine marking were enrolled in the trial if the therapy had been unsuccessful or spraying had recurred after the drug was withdrawn. Fourteen cats in the trial had previously been treated with medication for urine marking. In all 14 cats, marking had recurred prior to the start of the trial. In 13 of the cats, the drugs were discontinued several months to several years earlier, well beyond any washout or withdrawal period for both behavioral and medicinal effects. In one cat that received medroxyprogesterone acetate approximately 2 months prior to the start of the trial, it is possible that some residual drug effects were still present, even though recurrence of the urine spraying occurred at least 1 month prior to the start of the trial.

Cats that met the enrollment criteria were examined by the referring veterinarian, and samples were collected and submitted to a central laboratory for a complete blood count, biochemical profile, serum thyroxine (T4) assay, and urinalysis. Each client completed a comprehensive behavioral history questionnaire, which was sent to the veterinary behaviorist (and trial coordinator) along with all laboratory results. Each owner was also required to complete 1 week of daily logs to determine the baseline (pretreatment) number of spraying events, against which future measurements would be compared. If there were four or more events of urine marking in the pretreatment, the owner was then supplied with enough drug and daily logs for the first month of the drug trial. A questionnaire to be completed at the end of the trial was also supplied. A dose of 2.5 mg clomipramine\textsuperscript{c} per os (PO) per day was given to most cats, although for cats >6 kg, the suggested dose was 3.75 to 5 mg PO per day. All cats were monitored closely for adverse effects.

Treatment Course

Owners completed a daily log in which they recorded all urine marking by location, as well as any adverse events or medication side effects. At the end of 1 month, a final questionnaire was completed, all forms were returned to the behaviorist, and the laboratory tests were repeated. If a cat’s clinical signs had sufficiently improved during the 1-month
trial, the clomipramine was continued for up to 5 additional months, and the cat was closely monitored. For cats in which the drug was effective, it was suggested that the drug dosage be maintained for an additional month (2 months in total) and then be reduced by 50% (by starting alternate-day therapy or reducing the daily dose by 50%) for another 2 months. If urine marking did not recur, the drug was further reduced by 50% for the next 2 months or was withdrawn. Follow-up data was collected on these cats 3 and 6 months after the start of the trial.

Data Analysis
The number of spraying events per week was recorded by owners for week 0 (pretreatment) and for the 4 weeks of therapy (weeks 1 through 4). The reduction of urine spraying was calculated as: Reduction = pretreatment spraying events at week 0 minus posttreatment spraying events at week n, where n = 1 through 4. The efficacy of treatment was calculated as: Efficacy = reduction ÷ pretreatment events × 100%.

As it could not be assumed that the data was normally distributed, applying analysis of variance (ANOVA) methods may not have been adequate; therefore, nonparametric methods were used. Since there was no control group, the only possible comparison was with pretrial (baseline) data, so that each animal acted as its own control. The number of spraying events at week “n” was compared to values from week 0, using the one-sample Wilcoxon signed rank test.

Results
Twenty-five cats (18 castrated males, seven spayed females) entered and completed the trial. Nineteen of the cats came from multicat households (two to four cats per household). Cats ranged in age from 2 to 15 years (mean 7.5 years) and in body weight from 3.2 to 8.2 kg (mean 5.26 kg). The actual dose of clomipramine given at the start of the trial ranged from 0.30 to 0.83 mg/kg (mean 0.54 mg/kg) PO q 24 hours. Owners were asked to indicate the sites of urine spraying within the house. Although a variety of locations were listed, including stereo speakers and various owner possessions, the most commonly sprayed sites were (in order) walls, windows, and doors.

Ten cats had abnormalities on pretreatment laboratory tests. Three cats were diagnosed with chronic renal failure, with blood urea nitrogen (BUN) values ranging from 8.8 to 18.3 mmol/L (reference range 4.0 to 10.7 mmol/L), creatinine concentrations ranging from 151 to 201 µmol/L (reference range 50 to 177 µmol/L), and urine specific gravities of 1.016 to 1.035. Five cats had elevations in alanine aminotransferase (ALT) ranging from 67 to 96 U/L (reference range 5 to 67 U/L), and one cat had proteinuria (3+). One of the cats with chronic renal failure was receiving 10 mg prednisone PO q 72 hours to control previously diagnosed immune-mediated anemia. One cat had a grade I systolic murmur and cardiac arrhythmia, which was diagnosed on electrocardiogram (ECG) as a normal sinus rhythm with occasional VPCs. Although it was recommended that these two cats not enter the trial, the clients and referring veterinarians requested that they participate, as the cats were to be euthanized if their urine spraying continued. Since their medical abnormalities were unlikely to be the cause of the vertical urine marking, the cats were entered into the trial.

Owners were advised to report any significant side effects to their veterinarian. No adverse effects were severe enough to necessitate removal of any cat from the trial. At the 30-day recheck, no new medical abnormalities were identified in any of the cats. The renal parameters remained stable in the three cats with chronic renal failure (creatinine 181 to 182 µmol/L; BUN 9 to 13.7 mmol/L). The ALT values were virtually unchanged in four cats with elevated ALT (62 to 90 U/L) and were mildly worse in one cat (71 to 109 U/L). The proteinuria of one cat decreased from 3+ to 2+, and the cat with the arrhythmia had a normal sinus rhythm with no VPCs on a subsequent ECG.

The mean numbers of baseline (pretreatment) spraying events for males, females, and all cats were 8.56±5.04, 9.71±6.92, and 8.88±5.50, respectively. The range for all cats was 4 to 22. In analyzing the owners’ logs, a statistically significant decrease in the number of sprays was noted for each of weeks 1 through 4 when compared to pretreatment values (P<0.0001; all cats). Twenty of the 25 cats had a ≥75% reduction in urine spraying (i.e., zero to one spraying event per week). Spraying resolved or improved by 90% in 17 (68%) of the 25 cats. Three cats had a 50% to 74% reduction in spraying, and two cats had a <50% improvement by week 4. The range and mean number of spraying events are listed in Table 1. For the 20 cats that had a ≥75% reduction, the spraying decreased to one or less event per week in seven cats by the end of week 1, in eight cats by the end of week 2, and in three more cats by the end of the third week. Two cats did not reach maximal improvement until the end of week 4 [see Figure].

There was no statistical difference between the results when age, weight, or breeds were analyzed; however, there were some differences noted between responses in males and females. The mean efficacy during weeks 1 to 4 was 77% for male cats (P<0.0001) and 80% for female cats (P<0.0156), with a mean overall efficacy of approximately 78% for all cats (P<0.0001). Responses were more or less constant for females during all 4 weeks of treatment, whereas the males showed a more gradual improvement [Table 1]. The larger P value of 0.0156 for females is likely a result of the small number (n=7) of female cats included in the trial. With seven subjects, the smallest possible P value for the Wilcoxon signed rank test is P=0.0156. This indicates that the number of spraying events was less than at baseline. There was no clinical evidence that the product was any less effective in females than in males.

Five cats sprayed ≥10 times during the pretreatment week (range 15 to 22). Two had complete resolution of spraying by week 4 (zero events per week); one had a reduction of 95.5% (one event per week); and the remaining two cats experienced <50% improvement (44.4% and 47.6% reduction). Of the remaining 20 cats with ≤10 pretreatment marking
events, all cats improved by ≥50%, 85% (17/20) improved by ≥75%, and 70% (14/20) improved by ≥90%.

Fourteen cats had previously received medication in an attempt to control the urine marking. Eight of these cats had been treated with amitriptyline at 5 to 10 mg per day, and a number of owners indicated they were unable to administer the medication. Six cats had been treated with an injection of medroxyprogesterone acetate at dosages ranging from 50 to 100 mg. Feliway spray was used in four households. Three cats were treated with buspirone at 5 mg \( q^{12} \) hours, and two cats were treated with diazepam at 1 mg \( q^{12} \) hours. One cat was treated with megestrol acetate at 5 mg per day initially, and then the dose was reduced to once or twice weekly. One cat had been treated with an amino acid/vitamin supplement containing tryptophan. A ≥50% improvement in urine marking was seen in 12 of these cats at the 4-week point of the study, with seven cats having no spraying [Table 2]. Of the two cats that did not improve by at least 50%, one had previously been given buspirone, medroxyprogesterone acetate, amitriptyline, and Feliway without success, and the other had not responded to diazepam therapy.

At the end of the 1-month trial, 17 owners elected to continue the clomipramine, and eight owners attempted to withdraw the medication. At the 3-month follow-up, 17 of the cats remained on medication to control the spraying. Three cats off medication had little or no recurrence of spraying, and one cat remained off medication because it was ineffective. Two cats were euthanized (one improved but was too difficult to medicate; the other did not improve sufficiently); one cat was given away when spraying recurred; and one cat was lost to follow-up (signs were controlled at last contact).

At the final 6-month follow-up, 15 cats still required medication, with the spraying either decreased or absent while on the clomipramine. Medication was discontinued in two additional cats with no recurrence of spraying. The three cats that had the medication successfully withdrawn at the 1-month follow-up continued to be normal or have only rare spraying events. For the 15 cats that remained on medication, the dose and frequency of clomipramine administration were variable. Doses ranged from 0.21 to 1.14 mg/kg PO, and frequency ranged from \( q^{24} \) hours to \( q^{72} \) hours. One cat was on an alternating schedule, with the drug given \( q^{24} \) hours for 2 days, then \( q^{48} \) hours [Table 3]. None of the treated cats received behavioral counseling or pheromone therapy, and no attempt was made to modify the household once the trial began.

### Table 1

Range and Mean Number of Spraying Events Per Week

<table>
<thead>
<tr>
<th>Sex of Cats</th>
<th>Wk of Trial</th>
<th>Range</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0 (pret)</td>
<td>4-22</td>
</tr>
<tr>
<td>All cats (n=25)</td>
<td>1</td>
<td>0-31</td>
<td>3.84</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0-16</td>
<td>1.84</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0-15</td>
<td>1.52</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0-11</td>
<td>1.32</td>
</tr>
<tr>
<td>Castrated males (n=18)</td>
<td>0</td>
<td>4-22</td>
<td>8.56</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0-31</td>
<td>4.83</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0-16</td>
<td>1.94</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0-15</td>
<td>1.11</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0-10</td>
<td>0.94</td>
</tr>
<tr>
<td>Spayed females (n=7)</td>
<td>0</td>
<td>4-21</td>
<td>9.71</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0-3</td>
<td>1.29</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0-5</td>
<td>1.57</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0-12</td>
<td>2.57</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0-11</td>
<td>2.29</td>
</tr>
</tbody>
</table>
Side effects, as reported by owners, occurred in 23 of 25 cats [Table 4]. Some cats had more than one clinical sign while on the medication, and some signs, such as increased sociability and decreased aggression to the other household cat, were considered desirable. Overall, side effects were mild, and only two cats (started at higher-than-recommended dosages) required a reduction in dosage for the signs to resolve. Signs in all other cats usually resolved within 1 week, despite continued administration of the clomipramine.

Discussion
Before drug therapy is started, every attempt should be made to identify and resolve the underlying causes of urine marking and to avoid the stimuli that incite the behavior. Pheromone therapy to reduce the cat’s motivation to mark territory with urine may also be tried, as well as making modifications to the environment. Increased attention must also be given to litter box location and hygiene before considering the use of drugs. In a recent study, environmental management alone (i.e., using enzymatic cleansers on previously soiled surfaces; increasing the number of litter boxes to the number of cats in the household plus one; cleaning the box daily; changing the box weekly) led to improvement in a number of cats that were vertically marking.17 In that study, owners were also advised to refrain from any form of punishment.17 Depending on a number of

---

**Table 2**

<table>
<thead>
<tr>
<th>Improvement by End of Wk 4</th>
<th>No. Cats</th>
<th>Previous Therapies Tried in These Cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>7</td>
<td>Methylprednisolone acetate, medroxyprogesterone acetate, buspirone, amitriptyline, Feliway</td>
</tr>
<tr>
<td>75%-99%</td>
<td>2</td>
<td>Tryptophan, amitriptyline, medroxyprogesterone acetate</td>
</tr>
<tr>
<td>50%-74%</td>
<td>3</td>
<td>Amitriptyline, megestrol acetate, diazepam, Feliway</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>2</td>
<td>Diazepam, buspirone, medroxyprogesterone acetate, amitriptyline, Feliway</td>
</tr>
</tbody>
</table>

* Improvement is defined as the percent reduction in spraying events per week compared to baseline (pretrial) data.

**Table 3**

<table>
<thead>
<tr>
<th>No. Cats</th>
<th>Clomipramine Dose (mg)</th>
<th>Dosage Range (mg/kg)</th>
<th>Frequency of Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>2.5</td>
<td>0.42-0.61</td>
<td>q 24 h</td>
</tr>
<tr>
<td>5</td>
<td>2.5</td>
<td>0.3-0.57</td>
<td>q 48 h</td>
</tr>
<tr>
<td>1</td>
<td>2.5</td>
<td>0.45</td>
<td>q 72 h</td>
</tr>
<tr>
<td>1</td>
<td>1.25</td>
<td>0.21</td>
<td>q 24 h</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>1.14</td>
<td>q 24 h</td>
</tr>
<tr>
<td>1</td>
<td>2.5</td>
<td>0.42</td>
<td>q 24 h × 2 d; then q 48 h; repeat</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>Signs remained under control after medication withdrawn</td>
</tr>
</tbody>
</table>

January/February 2005, Vol. 41 Clomipramine for Urine Marking 7
factors, improvement may not be achieved with these tech-
niques alone. Poor owner compliance or inability of the
owners to make significant changes to the household may
make it impractical to expect significant improvement.
Pharmacological therapy might be the most effective means
of controlling urine spraying in such homes.

To ensure consistent baseline and accurate data collec-
tion, and to minimize the possibility of owner and environ-
mental influences on outcome, the enrollment criteria for
this trial were strictly controlled. Although a double-blind-
ed placebo trial would have been preferable, it was consid-
ered impractical, because most of the owners were
desperate for some immediate improvement in the urine
marking. In addition, administration of clomipramine to all
cats in the study allowed more data on efficacy and side
effects to be collected over a shorter period of time.

The presence of concurrent laboratory abnormalities or
concomitant medical conditions in this study population is
consistent with prior reports. In one study of urine spray-
ing in cats, 20% of 34 cats had underlying medical condi-
tions, while another 17% had crystalluria. Although such
abnormalities may have had a causal relationship in some
individuals, a recent study indicated there were no statistical
differences in blood or urine test results of urine-marking
cats compared to cats with no history of marking. Conversely, a study of 100 clinically normal cats ≥8 years of age,
with no history of urine marking, found that 6% had
elevated serum T4 values, 9% were azotemic (urine specific
graphy <1.035 in five cats), one was diabetic, and one had a
urinary tract infection.

In the study reported here, the reduction in spraying in 23
of 25 cats and the ≥75% reduction in 20 cats indicated that
treatment with clomipramine alone may successfully
resolve many cases of urine spraying within 30 days. With
no concurrent behavioral modification, most of the cats in
the present study required medication (some at a reduced
dose) to control the urine marking. The use of a more com-
prehensive behavioral assessment and modification pro-
gram might provide even greater improvement and fewer
episodes of recurrence upon drug withdrawal. Concurrent
use of Feliway as well as environmental management might
also improve both short-term and long-term success rates.
The two cats that failed to improve to a level of ≥50% were
among the five cats with the highest number of pretrial
marking events (>10 marks per week; range 15 to 22). Three
other cats with very frequent pretrial marking all improved
(≥95%) with clomipramine therapy, however. While the
prognosis may be worse for cats with high numbers of
marking events (i.e., ≥15 per week), this study provided
some evidence that cats with frequent marking might also
improve significantly with clomipramine therapy.

Based upon studies in humans, it has been suggested that
antidepressants such as clomipramine may require 3 to 4
weeks to achieve a therapeutic effect in animals and that up
to 6 weeks may be required to achieve maximal therapeutic
effects. Steady-state plasma concentrations of

<table>
<thead>
<tr>
<th>Side Effects or Behavioral Changes</th>
<th>No. Cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lethargy, increased sleep, less active/interactive</td>
<td>17†</td>
</tr>
<tr>
<td>Anticholinergic effects: decreased frequency of urination (urinary retention, n=4) and defecation (constipation, n=3), dry mouth (n=3)</td>
<td>5‡</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>5‡</td>
</tr>
<tr>
<td>More restless/agitated, irritable, more vocal</td>
<td>3</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>1</td>
</tr>
<tr>
<td>Calmer, more friendly, more affectionate</td>
<td>6</td>
</tr>
<tr>
<td>Less demanding, less nervous, less needy</td>
<td>4</td>
</tr>
</tbody>
</table>

* As reported by the owner
† Cats may have had more than one side effect.
‡ Two cats accidentally received doses >0.5 mg/kg per os q 24 hours; signs resolved once dosage was lowered.
Clomipramine and its intermediate metabolite, desmethylclomipramine, are attained in dogs within 4 days. Clomipramine is a potent inhibitor of serotonin reuptake, and desmethylclomipramine inhibits noradrenaline reuptake, thus leading to enhanced neurotransmission of serotonin and noradrenaline. The initial increase in neurotransmitter concentrations in the area of the synapse leads to subsequent downregulation and inhibition of neurotransmitter release. Over time, further accumulation of neurotransmitters in the synapse causes desensitization of the autoreceptors and recovery of firing of the serotonergic neurons and a net elevation of neurotransmitter concentrations, which ultimately alters neuroreceptor function and structure. The full therapeutic effect may, therefore, take ≥4 weeks to be realized.

Interestingly, in the study reported here, improvement occurred in some cats within the first week of treatment, and 15 of 20 cats improved by the end of the second week. Similar results have been demonstrated in previous studies in which 80% of cats on clomipramine exhibited less spraying after 1 week, while cats on fluoxetine showed a significant reduction by the second week of treatment. Further evaluation is needed to determine whether the mechanism of action of antidepressants is different in cats than in humans and whether other factors (e.g., the initial anticholinergic side effects to which humans generally habituate in 3 to 7 days) play a role in the response. Five of the cats in the present study did not reach maximal improvement until the third or fourth week of the trial, which is consistent with the time that is expected in other species for stabilization of the neurotransmitter changes induced by antidepressant therapy.

One recent study suggested that long-term therapy of ≥6 months and a slower tapering process of clomipramine may improve efficacy and reduce the chances for recurrence. Chronic administration of serotonin reuptake inhibitors and tricyclic antidepressants in mice may lead to neurogenesis in the hippocampus, which appears to contribute to the long-term antianxiety effects of these drugs. Therefore, while some cats may improve within the first few weeks of therapy, extending the duration of therapy may be considered for those cats that do not immediately respond. It is also possible that an increased dosage may improve the efficacy, provided there are no adverse effects.

Most cats (male to female ratio of 2.6:1) in this study were castrated males from multicat households. This finding was consistent with other studies of vertical urine marking, in which male cats often outnumber females by at least 2 to 1 and by as much as 10 to 1. Cats from multicat households may have been over-represented because of increased competitive marking.

Of interest in this study is the number of cats that improved on clomipramine and had no previous response to a variety of other treatment modalities, including amitriptyline, medroxyprogesterone acetate injectable, megestrol acetate, buspirone, diazepam, Feliway, and tryptophan. In comparison to other drugs that have been utilized for urine marking in cats, clomipramine appeared to be an effective
alternative. Clomipramine can be used once daily in comparison to the twice-daily dosing of buspirone and diazepam.\textsuperscript{6,7,9,11,24,26} It appears to be easier to administer than amitriptyline, and it may have less toxicity than either diazepam or progestins.\textsuperscript{25-27} Clomipramine is more selective for its effects on serotonin transmission than any of these other compounds, which may explain its improved efficacy.\textsuperscript{6,7} This supposition is further supported by the success achieved in recent studies using fluoxetine (a selective serotonin reuptake inhibitor) for urine marking in cats.\textsuperscript{72}

Clomipramine caused urinary retention and constipation in some cats in the study reported here, especially when it was first initiated or when dosages $>0.5$ mg/kg per day were used. Cats should be monitored closely to insure normal elimination when clomipramine is first dispensed.\textsuperscript{28} Side effects were otherwise mild, with behavioral changes being the most common [Table 4]. Most of the behavioral changes reported were associated with the initial sedation or lethargy caused by the drug. While a few cats became more fearful, agitated, or less tolerant of petting, this may have been a response to the administration of the medication rather than to the medication itself. Some of the behavioral changes associated with clomipramine therapy were considered desirable by the owners [Table 4].

It is important to realize that it can be difficult to distinguish urine marking from inappropriate elimination. This difficulty can greatly affect therapy, as psychotropic drugs are not generally indicated in cases of inappropriate elimination. Little or no response can be expected in cases where pheromones and psychotropic drugs are used to treat horizontal elimination, since most of these cases do not have a marking or anxiety component.\textsuperscript{29} Clomipramine is recommended for only those cats with vertical urine marking.

**Conclusion**

Based on the results of this study, clomipramine was an effective and practical means of treating urine marking in cats. Eighty percent of treated cats improved $\geq75\%$ during the first 4 weeks of treatment. Side effects were minimal and generally resolved within the first week of therapy. Clomipramine is not licensed for use in cats in North America, so it must be used cautiously and with informed owner consent. Although five cats had no recurrence of urine marking when the drug was withdrawn, most cats required long-term therapy. Further investigation is needed to determine if identification and resolution of any underlying causes, increased attention to environmental management, and the concurrent use of products such as Feliway might improve treatment efficacy and allow for a greater number of cats to remain under control after the drug is ultimately withdrawn.

---

\textsuperscript{a} Feliway; Veterinary Products Laboratories, Phoenix, AZ 85013
\textsuperscript{b} Clomicalm package insert; Novartis Animal Health Australasia Pty Limited
\textsuperscript{c} Clomicalm 5 mg; Novartis Animal Health Canada Inc., Mississauga, Ontario, Canada LSN 1V9
\textsuperscript{d} Proc Univariate, SAS; SAS Institute Inc., Cary, NC 27511
\textsuperscript{e} Relaxum; Mark and Chappell Ltd., Luton, United Kingdom, LU31RJ
\textsuperscript{f} Garcia JL, Bruyette DS. Unpublished data, American College of Veterinary Internal Medicine Forum poster session, 1998
\textsuperscript{g} Hart BL. Personal communication, Annual American Veterinary Medical Association Conference presentation, Denver, CO 2003

**Acknowledgments**

The authors thank Dr. Wolfgang Seewalde for statistical analysis and support. The authors also thank the numerous veterinarians throughout southern Ontario who recruited and screened cases for this study.

**References**

The purpose of this 2-week, double-blinded, controlled clinical trial was to evaluate the efficacy of topical amino acid-complexed zinc gluconate formulated with boric acid (ZGB) or acetic acid (ZGA) versus a topical placebo in the treatment of yeast otitis externa in dogs. Included in the study were dogs with otitis externa and a cytopathological finding of yeast organisms in the affected ear. Ears were treated with the placebo, ZGA, or ZGB medications. Yeast counts as well as clinical appearance of the ears were monitored. Results revealed that ZGB significantly reduced the number of yeast organisms in cases of otitis externa.


Colleen L. Mendelsohn, DVM, Diplomate ACVD
Craig E. Griffin, DVM, Diplomate ACVD
Wayne S. Rosenkrantz, DVM, Diplomate ACVD
Larry D. Brown, DVM, MPVM, PhD, Diplomate ACVPM
Mona J. Boord, DVM, Diplomate ACVD

Introduction

A large variety and quantity of canine topical otic preparations are available and serve as a testament to the prevalence of ear disease in dogs. Otitis externa is one of the most common reasons for seeking veterinary care, accounting for up to 15% of all dogs presented. Primary causes of otitis externa include hypersensitivity disorders (e.g., atopy, food allergy), parasitic diseases, and metabolic disorders (e.g., primary keratinization defects, hypothyroidism, hyperadrenocorticism). Perpetuating factors such as proliferative changes, excessive cleaning, or the use of inappropriate cleaning products also contribute. Otitis externa may also occur secondary to infections. Malassezia pachydermatis is the most common isolate from diseased ears and often requires therapy. In some cases of atopic disease, controlling secondary infections (especially Malassezia spp.) helps alleviate the clinical signs. Most otic preparations are combinations of corticosteroids and antimicrobials. Frequent and repeated use of these products is often indicated; however, when such products are used repeatedly for management and prevention, problems of antibiotic resistance and glucocorticoid side effects (both cutaneous and systemic) may occur.

Products containing mild cleansers or disinfectants are valuable in the treatment of otitis externa, and they do not have as many potential risks as the long-term antibiotic or glucocorticoid therapies. Many otic products are available that are combinations of mild cleansers, drying agents, and disinfectants, with or without antimicrobial agents. In the authors' experience, some of these products can be used as maintenance therapy to prevent the recurrence of otitis externa. Common cleansing ingredients...
include boric acid, acetic acid, lactic acid, malic acid, fatty acids, enzymes, chelating agents, and minerals. Of these agents, acetic and boric acids have received attention for their abilities to kill yeast and bacterial organisms.

Acetic acid has been reported to be effective at concentrations from 0.5% to 5% in treating and preventing otic yeast infections. Acetic acid has been beneficial in people in the management of chronic suppurative otitis media. The effect was not solely related to pH, as other acidic products have not been as effective. Acetic acid may irritate already damaged otic epithelium, and its unpleasant odor creates problems with patient acceptance and client compliance.

Boric acid has also been shown to be effective against yeast infections. One study reported that boric acid was as efficacious as topical antibiotics in treating human otitis externa. In another study, 95% of vaginal yeast infections in people were eliminated with boric acid vaginal suppositories. The mechanism of action of boric acid is unknown. It has been proposed that boric acid may cleanse the lipids from the epithelium, which removes the metabolic substrates for Malassezia spp. or may inactivate a hygroscopic, neutrophilic chemo-attractant protein elaborated by Malassezia spp. In addition, an in vitro study of canine otitis isolates showed that a combination of 0.5% boric acid and 0.5% acetic acid was lethal to Staphylococcus intermedius.

Zinc has been studied for its effects on wound healing, and at the time this article was written, it was not incorporated into any commercial veterinary otic products. Zinc administered topically has had beneficial effects on wound healing, regardless of an individual’s systemic zinc levels. Like tris-ethylene diaminetetraacetic acid and silver-sulfadiazine, zinc also has chelating effects on cells. In humans, topical zinc oxide accelerated healing of diabetic leg ulcers. In pigs and mice, the topical application of zinc oxide enhanced reepithelialization of partial- and full-thickness wounds, and was as effective as streptokinase-streptodornase in removing necrotic tissue from pressure ulcers. When embedded in occlusive dressing, zinc decreased the inflammatory reaction typically seen during the formation of granulation tissue.

Zinc has also been demonstrated to have antimicrobial properties, specifically related to the topical application of zinc. Zinc gluconate lozenges have been shown to decrease the duration of cold symptoms, and the efficacy of zinc gluconate lozenges increases with the length of time the lozenge is present in the oral cavity. An in vitro study demonstrated that herpes simplex virus was inactivated after treatment with zinc gluconate. Zinc gluconate also specifically decreased the expression of certain inflammatory mediators by keratinocytes exposed to nickel, an allergen responsible for some cases of contact dermatitis.

The purpose of this double-blinded, placebo-controlled clinical trial was to evaluate the efficacy of topical amino acid-complexed zinc gluconate formulated with boric acid (ZGB) or acetic acid (ZGA) versus a placebo in the treatment of yeast otitis externa in dogs.

**Materials and Methods**

Dogs that were presented with clinical signs of otitis externa and a cytopathological finding of yeast in the affected ear(s) were eligible for the study. On examination of swabs of the ear, an average count of three yeast per oil-immersion field (OIF) was considered the minimum criterion for a diagnosis of yeast otitis [Figure 1]. Initially each slide was scanned on low power (100×) to select areas with keratinocytes or wax. Examination under oil immersion (1000×) was then performed, and yeast organisms were counted in 10 separate OIFs that contained keratinocytes. The numbers from these 10 counts were then averaged. Dogs were excluded from the study if they had received any topical or systemic antimicrobials or corticosteroids in the 2 weeks prior to presentation.

Each diseased ear was considered an individual case. An otoscopic examination was performed, a visible tympanum was verified, and the ear was randomly assigned to a ZGB, ZGA, or placebo control group. After cleaning the ear with a petrolatum-based squalene cleanser, 1 to 3 mL (depending on the size of the ear canal) of either ZGB, ZGA, or the placebo was applied to the ear twice daily for the entire study period. The ear was reevaluated and cleaned again on days 7 and 14 of the study by one of the available authors/investigators. The authors/investigators and the owners were blinded to the type of solution administered until the end of the study.

All study solutions contained deionized water, methylparaben (500 ppm), propylparaben (100 ppm), and propylene glycol at 1%. The placebo solution contained only these compounds. The zinc solutions also contained zinc gluconate, L-lysine, taurine, and either 1% acetic acid or 1% boric acid. The ZGB solution and the ZGA solution were compounded by Addison Biological Laboratory, Inc., but the ZGB solution has now become commercially available. The pH of all three test solutions was determined by a calibrated,
hand-held electronic pH meter. The pH of ZGA and ZGB solutions was 4.5, while the pH of the placebo solution was slightly higher at 4.93.

Yeast counts in the affected ears were evaluated (pre-cleaning) on days 0, 7, and 14. An average yeast count of ≤3 organisms per OIF was considered normal and given a score of 0. An average count of 3.1 to 8 organisms per OIF was assigned a score of 1; an average count of 8.1 to 14 organisms per OIF was given a score of 2; and yeast counts ≥15 yeast per OIF were assigned a score of 3. Bacteria present at levels >5 organisms per OIF were considered significant and were recorded. An aerobic bacterial culture and sensitivity were subsequently performed on these samples. The presence of bacteria in the original cytology and a positive culture did not preclude entrance of the case into the study.

For clinical scoring, the ear was divided into two regions. The external ear included the external aural orifice and the adjacent pinna. The ear canal included both the vertical and horizontal portions. The external ear was evaluated by visual inspection, while the ear canal was evaluated by otoscopic examination. Erythema, exudate, and stenosis of each region were evaluated by a single examiner and given scores of 0, 1, 2, or 3 representing none, mild, moderate, or severe changes, respectively. The scores for these three parameters were summed so that the highest possible clinical score was 9 for each region of the ear.

At each recheck visit, clients were questioned about their use of the test solutions and their perceptions as to response to treatment. In the event that the animal was worse (as determined by the owner) on day 7, the dog was removed from the study, and using the “intent to treat rule,” the values from day 7 were carried over to day 14.

Statistical Analysis

The three treatment groups included a control group, a ZGA treatment group, and a ZGB treatment group. Differences between groups were analyzed by analysis of variance (ANOVA) using a commercially available statistical software program. Three sets of scored data (i.e., yeast score, external ear clinical score, ear canal clinical score) were evaluated by Model I ANOVA for the control versus ZGA groups, the control versus ZGB groups, and the ZGA versus ZGB groups. A three-way (placebo control versus ZGA versus ZGB) analysis was also performed, comparing scores between all three groups. The statistical significance level (P=alpha or probability of committing a Type 1 error) applied to all comparisons was P≤0.05.

Results

Twenty-one dogs were included in the study. Fourteen had bilateral disease and seven had unilateral disease based on the inclusion criteria, resulting in a total of 35 ears. In 12 dogs (20 ears), atopic dermatitis was the primary condition (based on history, distribution of lesions, responsiveness to therapy, and absence of other hypersensitivity disorders), and 10 of these 12 dogs were under treatment with allergen-specific immunotherapy. The remaining two atopic dogs had mild seasonal signs and were not on any therapy. One dog (one ear) had both atopic dermatitis and food allergy; this dog was on allergen-specific immunotherapy and a restricted diet. One dog (two ears) had primary idiopathic seborrhea. Three dogs (five ears) had chronic recurrent otitis externa of undetermined cause, although atopic dermatitis was suspected in one. Four dogs (seven ears) were presented with no prior history of skin or ear disease.

Breed distribution was as follows: mixed-breed dogs (n=4), Labrador retriever (n=3), rottweiler (n=2), standard poodle (n=2), American cocker spaniel (n=2), dachshund (n=2), Dalmatian (n=2), and one each of beagle, golden retriever, Akita, and red bone coonhound. Ages ranged from 1.5 to 10 years, with a mean age of 4.3 years and a median of 4.0 years.

Control Group

Ten ears were treated with the placebo solution. These cases were assigned numbers 1 through 10 after the study was completed. The average yeast scores for the control dogs on days 0, 7, and 14 were 1.6, 1.1, and 1.1, respectively [Table 1]. The mean external ear clinical scores for days 0, 7, and 14 were 4.5, 3.5, and 2.7, respectively [Table 2]. The mean ear canal clinical scores for days 0, 7, and 14 were 5.0, 3.6, and 3.2, respectively [Table 2]. In case nos. 7 and 10, bacterial otitis and a worsening of the clinical signs were found on day 7, and systemic and topical antimicrobial treatments were initiated. These three cases were subsequently removed from the study.

Seven ears remained in the study for the full 14-day follow-up period. Yeast scores were increased in two cases on day 14, three scores remained the same, and five scores improved. In three cases (case nos. 3, 4, and 7), significant bacterial otitis was present on day 0. *Staphylococcus intermedius* was identified on day 0 in case nos. 4 and 7, but no organisms were initially isolated in case no. 3. In case no. 3, the bacterial component resolved by day 14. In case no. 7, the bacterial counts worsened and *Pseudomonas aeruginosa* was cultured on day 14. Case no. 10 was withdrawn from the study and had *Staphylococcus intermedius* isolated on day 14.

No discomfort occurred in association with medication application in any case. In two ears (case nos. 4, 9), owners felt their dog’s condition had slightly improved. For the remaining eight ears, owners reported either worsening or no change (even though clinically they had apparent improvement). An acute episode of lumbosacral pruritus occurred in case no. 8 on day 6.

Zinc Gluconate in Acetic Acid Treatment Group

Thirteen ears were treated with ZGA (assigned case numbers 11 through 23). The mean yeast scores on days 0, 7, and 14 were 2.4, 1.3, and 1.2, respectively [Table 3]. The mean external ear clinical scores for days 0, 7, and 14 were 4.2, 2.5, and 3.0, respectively [Table 4, Figures 2A, 2B]. The mean ear canal clinical scores for days 0, 7, and 14 were 5.2, 4.5, and 4.1, respectively [Table 4]. On day 7, case no. 23 had a significant increase in both yeast counts and clinical
scores, so it was removed from the study and started on sys-
temic and topical anti-yeast therapies. One yeast score was
increased at day 14, three scores remained the same, and
nine scores improved.

Case nos. 11, 14, and 21 had significant bacterial otitis at
the start of the study, and *Staphylococcus intermedius*
was cultured from all of the affected ears. Seven owners report-
ed improvement by day 14, and five owners reported no
change at day 14.

In seven cases, significant discomfort occurred in associ-
ation with application of the medication at various times
during the study. However, by day 14, four of the owners
reported that the initial discomfort associated with applica-
tion of the medication had resolved. All owners reported the
medication had an unpleasant odor similar to vinegar. In
three cases, generalized pruritus continued throughout the
study period.

### Zinc Gluconate in Boric Acid Treatment Group

Twelve ears were treated with ZGB (case nos. 24 through
35). The mean yeast scores on days 0, 7, and 14 were 2.0,
1.0, and 0.3, respectively [Table 5]. The mean external ear
clinical scores for days 0, 7, and 14 were 2.8, 1.3, and 1.8,
respectively [Table 6]. The mean ear canal clinical scores
for days 0, 7, and 14 were 3.6, 2.0, and 2.7, respectively
[Table 6]. No scores increased for any of the ears in this
group. No yeast counts increased, one count remained the
same, and 11 counts improved.

In seven cases, significant bacterial otitis occurred on day 0,
but the bacteria had subsided by days 7 or 14. Bacteria were isolated from only one culture (case no. 26)
and were identified as *Micrococcus* spp. In nine cases, the
owners reported significant improvement, while in three
cases the owners reported no change. No cases were with-
drawn from the study. In case no. 27, discomfort occurred

### Table 1

**Yeast Counts and Scores for 10 Dogs in the Control Group**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Day 0 Average Yeast Count (per OIF)*</th>
<th>Day 0 Assigned Score†</th>
<th>Day 7 Average Yeast Count (per OIF)</th>
<th>Day 7 Assigned Score</th>
<th>Day 14 Average Yeast Count (per OIF)</th>
<th>Day 14 Assigned Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;20</td>
<td>3</td>
<td>&gt;20</td>
<td>3</td>
<td>&gt;20</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>3.3</td>
<td>1</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>4.1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>8.5</td>
<td>2</td>
<td>2.1</td>
<td>0</td>
<td>1.4</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>6.0</td>
<td>1</td>
<td>14.1</td>
<td>3</td>
<td>&gt;20</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>5.0</td>
<td>1</td>
<td>&gt;20</td>
<td>3</td>
<td>&gt;20</td>
<td>3</td>
</tr>
<tr>
<td>7‡</td>
<td>8.5</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>&gt;20</td>
<td>3</td>
<td>4.0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>3.5</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3.0</td>
<td>1</td>
</tr>
<tr>
<td>10‡</td>
<td>5.0</td>
<td>1</td>
<td>2.0</td>
<td>1</td>
<td>2.0</td>
<td>1</td>
</tr>
</tbody>
</table>

Mean ± Standard Deviation 1.6 ± 0.84 1.1 ±1.37 1.1 ± 1.37
Mean ± Standard Error of Means 1.6 ± 0.27 1.1 ± 0.43 1.1 ± 0.43

* OIF=oil-immersion field; 10 OIFs per ear were counted and averaged
† See text for definition of Assigned Scores
‡ Bacterial otitis and worsening of clinical signs were detected on day 7; case was withdrawn from study for auxiliary treatments.

Day 7 scores were carried over to day 14 under ‘intent to treat’ rule.
after the medication was applied. In case no. 32, the owner reported continued generalized pruritus.

**Statistical Results**

At day 0, no statistical difference was found between groups for any of the scores evaluated. Within each treatment group, the yeast score and ear canal score gave the most obvious evidence of improvement. Within the ZGB group, a significant decrease in yeast score occurred over 2 weeks of treatment ($P \leq 0.00002$). Within the ZGA group, yeast scores also decreased significantly, but to a lesser degree ($P \leq 0.013$). The yeast scores in the control group did not change significantly.

When comparing results between groups, changes in yeast scores with ZGB were significantly better at day 14 than ZGA ($P \leq 0.034$) but not statistically significantly less than the placebo ($P \leq 0.085$) [Figure 3]. Day 14 yeast scores were not significantly different from each other for the control and ZGA groups.

The ZGB group had a reduced ear canal score on day 14, as compared to day 0 (baseline); however, the result was not statistically significant. Statistical comparisons (two- and three-way ANOVA) for all other within- or between-group yeast scores, external ear clinical scores, and ear canal clinical scores were not significant ($P > 0.05$).

**Discussion**

Both acetic and boric acid have been effective in treating yeast infections.2-9 In the study reported here, use of ZGA did not significantly eliminate or reduce yeast numbers when compared to placebo. Use of ZGB, however, did result in a significant decrease of yeast numbers. No significant differences in

---

**Figures 2A, 2B**—Affected ear canal before (A) and after (B) cleaning on day 0, demonstrating an intact tympanum, moderate erythema, and mild exudate from case no. 13 on day 7.

**Figure 3**—Ear yeast scores at three time points. SEM=standard error of means; PC=placebo control group; ZGA=zinc gluconate formulated with acetic acid treatment group; ZGB=zinc gluconate formulated with boric acid treatment group.
the degree of inflammation were noted between the treatment groups, and this result may have indicated continuing inflammation caused by the underlying primary disease, which was usually atopic dermatitis. This supposition was supported by the observation that the pinnae, which were not treated, remained more erythematous than the ear canal in the ZGB group.

Although acetic acid has been effective against many of the organisms that perpetuate canine otitis externa, the discomfort and inflammation induced by application of the acetic acid into the ear canal can result in worsening of the infection or inflammation.1-3 In this study, seven of the 13 owners in the ZGA group reported mild to severe discomfort with application of the eardrops, even after improvement of the infection. In the ZGB group, only one of the 12 ears had a mildly painful reaction to the topical medication.

The improvement noted in the control group on day 7 was an interesting finding and may have been related to the ear cleaning that was performed and/or the decreased pH of the placebo agent. Unlike the ZGB and ZGA treatment groups, bacterial growth appeared to worsen in some cases within the control group. It is possible that increased moisture in the absence of an antimicrobial agent contributed to this complication.1 The inability to demonstrate bacteria on cultures from the cases in which bacteria were visualized on cytopathology may have arisen from differences in the specific sites in the ear canal from which the samples were taken, from relatively low numbers of bacteria, from alterations in transport media, or from laboratory handling errors.

In clinical trials assessing the use of topical zinc to treat pressure wounds and diabetic foot ulcers, the duration of the clinical trials ranged from 6 to 12 weeks.11,12,14 It is possible that the 2-week duration of topical therapy used in the study reported here was not long enough to induce or recognize clinical improvement in the inflammatory component of otitis externa. In addition, the primary cause of otitis was not addressed during this study, as demonstrated by several instances of continued generalized or localized pruritus during the study period. Another possible explanation for lack of improvement in the clinical scores was the small sample size, which would not have

### Table 2

<table>
<thead>
<tr>
<th>Case No.</th>
<th>External Ear</th>
<th></th>
<th>Ear Canal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0 Day 7 Day 14</td>
<td>Day 0 Day 7 Day 14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>9 6 7</td>
<td>9 7 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 0 0</td>
<td>2 1 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>6 2 0</td>
<td>4 1 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3 2 0</td>
<td>5 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>7 6 1</td>
<td>6 4 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>3 6 5</td>
<td>4 7 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7†</td>
<td>6 9 9</td>
<td>7 8 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>4 3 0</td>
<td>7 3 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2 0 2</td>
<td>3 1 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10†</td>
<td>3 1 1</td>
<td>3 2 2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean ± Standard Deviation

<table>
<thead>
<tr>
<th>External Ear</th>
<th></th>
<th>Ear Canal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>Day 7</td>
<td>Day 14</td>
<td>Day 0</td>
</tr>
<tr>
<td>4.5 ± 2.37</td>
<td>3.5 ± 3.06</td>
<td>2.5 ± 3.31</td>
<td>5.0 ± 2.21</td>
</tr>
</tbody>
</table>

Mean ± Standard Error of Means

<table>
<thead>
<tr>
<th>External Ear</th>
<th></th>
<th>Ear Canal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>Day 7</td>
<td>Day 14</td>
<td>Day 0</td>
</tr>
<tr>
<td>4.5 ± 0.75</td>
<td>3.4 ± 0.97</td>
<td>2.5 ± 1.05</td>
<td>5.0 ± 0.70</td>
</tr>
</tbody>
</table>

* Score=sum of erythema, exudate, and stenosis scores; maximum=9
† Bacterial otitis and worsening of clinical signs were detected on day 7; case was withdrawn from study
compensated for subjective differences between investigators. The presence of otitis media and its potential impact on the clinical scores also could not be ruled out, although most of the dogs in this study had mild to moderate otic disease, and not all dogs had chronic otitis.22

Conclusion
Based on the results of this study, amino acid-complexed zinc gluconate with boric acid was efficacious against yeast otitis externa in dogs. It reduced ear canal inflammation, which is essential to promoting epithelial healing. Further studies are needed to examine the success of using boric acid alone by evaluating both organism numbers and the inflammatory response, and to determine whether concurrent use of low-potency topical corticosteroids alters the inflammation attributed to the primary disease, especially atopic dermatitis.

References

### Table 4

<table>
<thead>
<tr>
<th>Case No.</th>
<th>External Ear</th>
<th>Ear Canal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Day 7</td>
</tr>
<tr>
<td>11</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>13</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>14</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>15</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>16</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>17</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>19</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>21</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>22</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>23†</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

* Mean ± Standard Deviation

* Mean ± Standard Error of Means

<table>
<thead>
<tr>
<th></th>
<th>External Ear</th>
<th>Ear Canal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Day 7</td>
</tr>
<tr>
<td>Mean ± Standard Deviation</td>
<td>4.2 ± 3.14</td>
<td>2.5 ± 2.18</td>
</tr>
<tr>
<td>Mean ± Standard Error of Means</td>
<td>4.2 ± 0.87</td>
<td>2.5 ± 0.61</td>
</tr>
</tbody>
</table>

* Score=sum of erythema, exudate, and stenosis scores; maximum=9
† Worsening of clinical signs was detected on day 7; case was withdrawn from study
Table 5

Yeast Counts and Scores for 12 Dogs Treated With Zinc Gluconate in Boric Acid

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Day 0 Average Yeast Count (per OIF)</th>
<th>Day 0 Assigned Score†</th>
<th>Day 7 Average Yeast Count (per OIF)</th>
<th>Day 7 Assigned Score</th>
<th>Day 14 Average Yeast Count (per OIF)</th>
<th>Day 14 Assigned Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>12.0</td>
<td>2</td>
<td>8.1</td>
<td>2</td>
<td>4.1</td>
<td>1</td>
</tr>
<tr>
<td>25</td>
<td>16.5</td>
<td>3</td>
<td>1.4</td>
<td>0</td>
<td>&lt;1</td>
<td>0</td>
</tr>
<tr>
<td>26</td>
<td>12.0</td>
<td>2</td>
<td>12.0</td>
<td>2</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>27</td>
<td>3.4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>28</td>
<td>3.1</td>
<td>1</td>
<td>19.5</td>
<td>3</td>
<td>3.0</td>
<td>1</td>
</tr>
<tr>
<td>29</td>
<td>5.0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>&gt;20</td>
<td>3</td>
<td>10.0</td>
<td>2</td>
<td>5.0</td>
<td>1</td>
</tr>
<tr>
<td>31</td>
<td>5.0</td>
<td>1</td>
<td>5.0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>32</td>
<td>&gt;20</td>
<td>3</td>
<td>0.7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>33</td>
<td>5.5</td>
<td>1</td>
<td>1.9</td>
<td>0</td>
<td>1.5</td>
<td>0</td>
</tr>
<tr>
<td>34</td>
<td>14.7</td>
<td>3</td>
<td>10.2</td>
<td>2</td>
<td>7.9</td>
<td>1</td>
</tr>
<tr>
<td>35</td>
<td>15.0</td>
<td>3</td>
<td>&lt;1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Mean ± Standard Deviation 2.0 ± 0.95 1.0 ± 1.13 0.3 ± 0.49

Mean ± Standard Error of Means 2.0 ± 0.28 1.0 ± 0.33 0.3 ± 0.14

* OIF=oil-immersion field; 10 OIFs per ear were counted and averaged
† See text for definition of Assigned Scores

### Table 6
Sum of Clinical Scores* for 12 Dogs Treated With Zinc Gluconate in Boric Acid

<table>
<thead>
<tr>
<th>Case No.</th>
<th>External Ear</th>
<th></th>
<th></th>
<th>Ear Canal</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Day 7</td>
<td>Day 14</td>
<td>Day 0</td>
<td>Day 7</td>
<td>Day 14</td>
</tr>
<tr>
<td>24</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>25</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>26</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>27</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>28</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>29</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>31</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>32</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>33</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>34</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>35</td>
<td>5</td>
<td>4</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Mean ± Standard Deviation
- External Ear: 2.8 ± 2.37, 1.3 ± 1.15, 1.8 ± 1.90
- Ear Canal: 3.6 ± 1.62, 2 ± 1.13, 2.7 ± 2.06

Mean ± Standard Error of Means
- External Ear: 2.8 ± 0.68, 1.3 ± 0.33, 1.8 ± 0.55
- Ear Canal: 3.6 ± 0.47, 2 ± 0.33, 2.7 ± 0.59

* Score=sum of erythema, exudate, and stenosis scores; maximum=9

The medical records of 31 dogs treated for envenomation by the Eastern Diamondback Rattlesnake (Crotalus adamanteus) were reviewed. Twenty-four of 25 dogs that survived were hospitalized for an average of 4.3 days. The most common presenting signs were tachycardia, swelling/edema, depressed mentation, tachypnea, and bleeding puncture wounds. Thirteen (42%) of the 31 dogs were presented with or developed cardiac arrhythmias, predominantly ventricular premature contractions. Hematological disorders, including defibrination, elevated fibrin split products, hemolytic anemia, thrombocytopenia, and prolonged clotting times, were recorded in 81% of the dogs. Polyvalent crotalid antivenin was administered (mean of 4.0 vials per dog) to 88% of the surviving dogs and 50% of the nonsurviving dogs. J Am Anim Hosp Assoc 2005;41:22-33.

Jonathan R. Willey, BS
Michael Schaer, DVM,
Diplomate ACVIM,
Diplomate ACVECC

Introduction

Each year, approximately 20,000 people are treated in the United States for snakebites, with between 7000 and 8000 caused by venomous snakes.1 Although most practicing veterinarians have some familiarity with snakebites, there are no published data on the incidence of animal cases of envenomation. The southeastern United States is home to six native venomous snakes.2 The family Elapidae has short, fixed fangs and includes the Eastern Coral Snake (Micrurus fulvius). The family Crotalidae has larger, hinged fangs and includes the Eastern Diamondback Rattlesnake (Crotalus adamanteus), the Canebrake (Crotalus horridus atricaudatus, a subspecies of the Timber Rattlesnake), the Pygmy Rattlesnake (Sistrurus miliaris), the Copperhead (Agkistrodon contortrix), and the Cottonmouth or Water Moccasin (Agkistrodon piscivorus piscivorus).

Not all snakebites are true envenomations, because approximately 20% are “dry” bites with no venom inoculated.3 Various factors influencing the degree of envenomation include the species, age, and size of the snake; the time of year; the amount of venom regenerated during the period since the snake’s last strike; the number and depth of the strikes; and the nature of the strike (offensive, defensive, or agonal). The incidence of rattlesnake envenomations in animals is unknown. However, one study showed that the highest proportion of human cases of envenomation in the United States was caused by rattlesnakes, and another study attributed 74% of moderate to severe snake envenomations in Georgia to rattlesnakes.4,5 The Eastern Diamondback Rattlesnake causes more human fatalities annually than any other snake species.6,7 This is attributed to its high numbers in the southeast, an aggressive disposition, and a less reclusive nature than other species. Also, the Eastern Diamondback Rattlesnake is able to attain a much larger body size than other species, thereby allowing it to have the highest venom (dry weight) to body weight ratio of the native snake species.8
The nature of the two venoms, however, is different. Traditionally, in the dog, crotalid venom has been considered to be vasculotoxic and necrogenic, while elapid venom has been considered to be neurotoxic and hemolytic. While this is an oversimplification, it helps explain the difference in potencies. Eastern Diamondback Rattlesnake venom immobilizes a victim and begins digesting its tissues soon after envenomation occurs.\(^8,9\) Chemically, the content of Eastern Diamondback Rattlesnake venom is divided into enzymes and nonenzymes. The enzymes include hyaluronidase and collagenase, which aid in the spread of venom through interstitial spaces; proteases that cause tissue necrosis and coagulopathies; and phospholipases, which produce direct cytotoxic effects, including endothelial damage and inflammation.\(^10,11\) The nonenzymatic fraction of Eastern Diamondback Rattlesnake venom has direct effects on the cardiovascular and respiratory systems, causing ventricular arrhythmias, hypotension, and pooling of blood, especially in the splanchnic vascular beds. The nature of snake venom, including its toxicity, chemistry, and pathophysiological actions, has been reviewed elsewhere.\(^2,12\)

The main purposes of this study were to evaluate and characterize this clinical syndrome and to contribute to the published database on this condition in the dog.

Materials and Methods

The case records of 31 dogs examined at the University of Florida College of Veterinary Medicine Teaching Hospital (UF-VTH) that were treated for Eastern Diamondback Rattlesnake envenomation during the period 1982 through 2002 were reviewed. Computer-generated searches of medical records from 1982 through 2002 coded as “envenomation” or “snakebite” were evaluated for inclusion in the study. Criteria for inclusion were confirmed identification of the snake as an Eastern Diamondback Rattlesnake by the owner, and clinical lesions compatible with envenomation by this particular species. These lesions included sudden occurrence of puncture wounds (with or without overt bleeding), severe regional swelling and dependent edema, shock, and petechial/ecchymotic hemorrhages. Each dog included in the study was also from a region known to be indigenous for the Eastern Diamondback Rattlesnake. The data reviewed included the clinical features, treatments, and outcome of each case. An earlier study has also been published from the UF-VTH that described 20 cases of envenomation from 1978 through 1983.\(^13\) Although there was a slight overlap of the years covered by each study, there was no overlap of the individual cases reviewed.

Results

Distribution of Cases

The number of envenomations per month varied from one to six. One envenomation per month occurred in January, November, and December; August, September, and October had two per month; February, April, May, and June had three per month; March had four; and June had six. The majority of envenomations occurred during the spring and summer months. The time of the envenomation was noted in 20 of the 31 cases, with 11 occurring between 10 AM and 4 PM and seven occurring between 4 PM and 10 PM. Only two envenomations occurred between 10 PM and 10 AM.

Case Data

Of the 31 cases, 17 were male (eight were castrated) and 14 were female (eight were spayed). The dogs’ ages ranged from 7 months to 11.5 years, with a mean age of 3.8 years and median age of 3 years. The dogs’ weights ranged from 5.0 to 45 kg, with a mean of 25.3 kg. Twenty-two of the dogs weighed at least 20 kg. Eleven were mixed-breed dogs. Purebred dogs were represented by 13 different breeds, with no breed including more than three dogs.

The location of the snakebite was determined in all cases. A total of 44 strikes were identified. Nine of the 31 dogs were struck two to four times. Twenty-eight (63.6%) strikes were to the head, including the ears and tongue; six (13.6%) were to the neck; five (11.4%) were to the forelimbs and prescapular regions; three (6.8%) were to the thorax or abdomen; and two (4.5%) were to the hind limbs.\(^1,1,1\) Six of the 31 dogs did not survive, with three being euthanized and three dying spontaneously. Fifty of the six deaths occurred within 9 hours of presentation. One dog was euthanized following an aborted surgical procedure to remove necrotic tissue, more than a week after its initial presentation. Twenty-four of the 25 surviving dogs required hospitalization, with the length of stay ranging from 14 hours to 23 days (mean 4.3 days; median 2.5 days).\(^2\) The 23-day hospitalization of one dog was for treatment of renal failure, which was a very rare complication in this study population.

Elapsed time from envenomation to presentation at the referring veterinarian or the UF-VTH ranged from 15 minutes to >12 hours. Ten dogs were presented within 60 minutes (nine survived, one died); nine were presented between 60 minutes and 4 hours (seven survived, two died); and six were presented between 4 and 12 hours (all six survived). The interval from envenomation to presentation was unknown in the remaining six dogs (three survived, three died). Of the 25 with a known elapsed time until presentation, the mean was 3.5 hours.

Therapy

Three of the dogs that died received antivenin [Table 1], and three did not. Twenty-two of the 25 survivors received antivenin (from one to 10 vials; mean, four vials; median, four vials), and three did not. Each vial, when reconstituted, contained 10 mL of mixed crotalid antivenin.\(^6\) One of the 25 dogs receiving antivenin had signs of a hypersensitivity reaction, as characterized by facial pruritus and additional facial swelling.

Twenty-seven dogs received antibiotics; two that did not die during initial presentation, and two survived [Table 1]. Twenty-eight (90%) dogs received intravenous fluids. Flow
# Table 1
Clinical Information on Nonsurviving Dogs

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Time Elapsed Until Treatment</th>
<th>Bite Location (No. of Bites)</th>
<th>Initial Abnormal Clinical Findings</th>
<th>Antivenin Given (vials)</th>
<th>Corticosteroids Given†</th>
<th>Antibiotic Therapy</th>
<th>Total IV Fluid Therapy (Per Kg Body Weight; Time Period)‡</th>
<th>Blood Products Given§</th>
<th>Complications¶</th>
<th>Length of Hospitalization and Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>15 min</td>
<td>Muzzle (1)</td>
<td>Temperature 103.6˚F, tachycardia, progressive facial swelling, ventricular tachyarrhythmia</td>
<td>5</td>
<td>Prednisolone sodium succinate (500 mg IV)</td>
<td>Cephalothin</td>
<td>LRS (30 mL/kg over 9 h)</td>
<td>Fresh whole blood (amount unknown)</td>
<td>Thrombocytopenia, gross hemolysis, ventricular tachycardia, cardiac arrest</td>
<td>8 h, died spontaneously</td>
</tr>
<tr>
<td>11</td>
<td>&lt;2 h</td>
<td>Muzzle (1)</td>
<td>Severely swollen pharynx, distended abdomen, dyspnea, ecchymotic hemorrhages on mucous membranes and abdomen</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Ventricular fibrillation, cardiac arrest</td>
<td>Died shortly after presentation</td>
</tr>
<tr>
<td>22</td>
<td>Unknown</td>
<td>Hind limb/flank (3)</td>
<td>Unknown (seen at UF-VTH 13 d postenvenomation)</td>
<td>Amount unknown</td>
<td>Prednisolone sodium succinate (500 mg IV)</td>
<td>Cefazolin, metronidazole</td>
<td>LRS (45 mL/kg over 1 h)</td>
<td>None</td>
<td>Severe necrosis of limb, atrial standstill</td>
<td>8 d, euthanized after aborted surgery</td>
</tr>
<tr>
<td>26</td>
<td>4 h</td>
<td>Head (1)</td>
<td>Comatose, no brain-stem function</td>
<td>None</td>
<td>None</td>
<td>Yes, type unknown</td>
<td>None</td>
<td>None</td>
<td>Suspected arterial envenomation</td>
<td>Euthanized upon presentation</td>
</tr>
<tr>
<td>28</td>
<td>Unknown</td>
<td>Face (1)</td>
<td>Unconscious, temperature 103.4˚F, tachycardia, weak pulses</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>0.9% NaCl (40 mL/kg over 1 h)</td>
<td>None</td>
<td>Prolonged PT/PTT</td>
<td>2 h, euthanized</td>
</tr>
<tr>
<td>30</td>
<td>Unknown</td>
<td>Face (1)</td>
<td>Recumbent, tachycardia, tachypnea, gross hemolysis, ventricular tachyarrhythmia</td>
<td>3</td>
<td>None</td>
<td>Enrofloxacin, ampicillin</td>
<td>LRS (20 mL/kg over 8 h), Hetastarch (220 mL)</td>
<td>Fresh frozen plasma (750 mL), packed RBCs (250 mL)</td>
<td>Severe hematochezia, gross hemolysis, sustained ventricular tachycardia</td>
<td>8 h, died spontaneously</td>
</tr>
</tbody>
</table>

* UF-VTH=University of Florida Veterinary Teaching Hospital
† IV=intravenous
‡ IV=intravenous; LRS=lactated Ringer’s solution; NaCl=0.9% sodium chloride solution
§ RBCs=red blood cells
¶ PT=prothrombin time; PTT=partial thromboplastin time
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Time Elapsed Until Treatment</th>
<th>Bite Location (No. of Bites)</th>
<th>Initial Abnormal Clinical Findings</th>
<th>Antivenin Given (vials)</th>
<th>Corticosteroids Given</th>
<th>Antibiotic Therapy</th>
<th>Total IV Fluid Therapy (Per Kg Body Weight; Time Period)</th>
<th>Blood Products Given</th>
<th>Complications</th>
<th>Length of Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40 min</td>
<td>Forehead (1)</td>
<td>Temperature 104.8˚F, tachycardia, marked hemolysis, bleeding from puncture wounds</td>
<td>8</td>
<td>Prednisolone</td>
<td>Ampicillin</td>
<td>LRS (200 mL/kg over 3.5 d)</td>
<td>Fresh whole blood (500 mL on d 2)</td>
<td>Ventricular tachycardia, seizures, hemolytic anemia with hemoglobinuria</td>
<td>6 d</td>
</tr>
<tr>
<td>2</td>
<td>&lt;12 h</td>
<td>Elbow (1)</td>
<td>Tachycardia, temperature 103.6˚F, marked swelling of leg (shoulder to toes)</td>
<td>None</td>
<td>Dexamethasone</td>
<td>Amoxicillin</td>
<td>LRS (25 mL/kg over 24 h)</td>
<td>None</td>
<td>None</td>
<td>2.5 d</td>
</tr>
<tr>
<td>3</td>
<td>&lt;8 h</td>
<td>Muzzle (1)</td>
<td>Tachycardia, severely swollen face and ventral neck, large bruise on face</td>
<td>4</td>
<td>Prednisolone</td>
<td>Ampicillin then amoxicillin</td>
<td>LRS (53 mL/kg over 28 h)</td>
<td>None</td>
<td>Infrequent VPCs, prolonged ACT, mild anemia</td>
<td>2.5 d</td>
</tr>
<tr>
<td>4</td>
<td>&lt;2 h</td>
<td>Hind limb (1)</td>
<td>Tachycardia, severe leg bruising, bleeding puncture wounds</td>
<td>2</td>
<td>Dexamethasone</td>
<td>Gentamicin, ampicillin</td>
<td>NaCl/Dex (224 mL/kg over 3.5 d)</td>
<td>None</td>
<td>Infrequent VPCs, transient ventricular tachycardia, mild anemia, skin slough</td>
<td>5 d</td>
</tr>
<tr>
<td>5</td>
<td>&lt;8 h</td>
<td>Muzzle (1)</td>
<td>Tachycardia, tachypnea, temperature 102.9˚F, ecchymotic hemorrhages of mucous membranes, extreme swelling on nose and throat</td>
<td>4</td>
<td>Prednisolone</td>
<td>Gentamicin, ampicillin</td>
<td>NaCl/Dex (49 mL/kg over 24 h)</td>
<td>None</td>
<td>Thrombocytopenia, mild hemolysis, prolonged PT/PTT</td>
<td>1.5 d</td>
</tr>
</tbody>
</table>

Continued on next page
### Table 2 (cont’d)

Clinical Information on Surviving Dogs

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Time Elapsed Until Treatment</th>
<th>Bite Location (No. of Bites)</th>
<th>Initial Abnormal Clinical Findings</th>
<th>Antivenin (vials)</th>
<th>Corticosteroids Given†</th>
<th>Antibiotic Therapy</th>
<th>Total IV Fluid Therapy (Per Kg Body Weight; Time Period)‡</th>
<th>Blood Products Given</th>
<th>Complications§</th>
<th>Length of Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>&lt;2 h</td>
<td>Face (2), prescapular area (2)</td>
<td>Tachycardia, bleeding puncture wounds on face, marked edema</td>
<td>4</td>
<td>Prednisolone sodium succinate (300 mg IV), prednisolone (12.5 mg PO q 12 h)</td>
<td>Cephalexin, trimethoprim/sulfadiazine</td>
<td>LRS (370 mL/kg over 4.5 d)</td>
<td>None</td>
<td>Infrequent VPCs, prolonged ACT, increased FDP</td>
<td>5 d</td>
</tr>
<tr>
<td>8</td>
<td>Unknown</td>
<td>Face (1)</td>
<td>Tachycardia, weak pulses, temperature 102.6°F, anemia (packed cell volume=26%), ventricular tachyarrhythmia</td>
<td>3</td>
<td>Dexamethasone sodium phosphate (80 mg IV)</td>
<td>Ampicillin, enrofloxacin</td>
<td>LRS (183 mL/kg over 2.5 d)</td>
<td>Fresh whole blood (300 mL)</td>
<td>Ventricular tachycardia, mild anemia, thrombocytopenia, skin slough</td>
<td>7 d</td>
</tr>
<tr>
<td>9</td>
<td>&gt;12 h</td>
<td>Ventral neck (1)</td>
<td>Tachycardia, weak and lethargic, irregular pulses, petechial hemorrhages of mucous membranes, anemia (packed cell volume=29%), thrombocytopenia</td>
<td>None</td>
<td>Dexamethasone sodium phosphate (40 mg IV)</td>
<td>Gentamicin, cephalexin</td>
<td>LRS (282 mL/kg over 3.5 d)</td>
<td>Fresh whole blood (500 mL on d 4)</td>
<td>Infrequent VPCs, severe anemia, transfusion reaction, skin slough</td>
<td>8 d</td>
</tr>
<tr>
<td>10</td>
<td>&lt;1 h</td>
<td>Ventral neck (2)</td>
<td>Recumbent, tachycardia, respiration agonal, anemia (packed cell volume=8%)</td>
<td>5</td>
<td>Methylprednisolone sodium succinate (125 mg IV) and dexamethasone sodium phosphate (3 mg IM)</td>
<td>Ampicillin, chloramphenicol</td>
<td>LRS (222 mL/kg over 3 d)</td>
<td>Fresh whole blood (250 mL)</td>
<td>Ventricular tachycardia, severe anemia, skin slough</td>
<td>5 d</td>
</tr>
<tr>
<td>12</td>
<td>&lt;4 h</td>
<td>Face (1)</td>
<td>Tachycardia, anemia (packed cell volume=30%)</td>
<td>1</td>
<td>None</td>
<td>Cephalexin</td>
<td>NaCl/Dex (240 mL/kg over 2.5 d)</td>
<td>Fresh frozen plasma (750 mL)</td>
<td>Infrequent VPCs, mild anemia, thrombocytopenia, skin slough</td>
<td>9 d</td>
</tr>
</tbody>
</table>

Continued on next page
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Time Elapsed Until Treatment</th>
<th>Bite Location (No. of Bites)</th>
<th>Initial Abnormal Clinical Findings</th>
<th>Antivenin Given (vials)</th>
<th>Corticosteroids Given</th>
<th>Antibiotic Therapy</th>
<th>Total IV Fluid Therapy (Per Kg Body Weight; Time Period)</th>
<th>Blood Products Given</th>
<th>Complications</th>
<th>Length of Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>&lt;4 h</td>
<td>Nose (1), forelimb (1)</td>
<td>Tachycardia, weak, dyspnea, mucous membranes pale, ACT=175 sec</td>
<td>3</td>
<td>None</td>
<td>Enrofloxacin, ampicillin</td>
<td>LRS (1130 mL/kg over 23 d; also treated for ARF)</td>
<td>None</td>
<td>Enrofloxacin, LRS (1130 mL/kg over 23 d; also treated for ARF)</td>
<td>23 d</td>
</tr>
<tr>
<td>14</td>
<td>&lt;1 h</td>
<td>Muzzle (1)</td>
<td>Tachycardia, swollen upper and lower lips, bleeding puncture wounds</td>
<td>4</td>
<td>None</td>
<td>Enrofloxacin</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>23 d</td>
</tr>
<tr>
<td>15</td>
<td>Unknown (&gt;8 h)</td>
<td>Nose (1)</td>
<td>Tachycardia, anemia, marked hemolysis, bleeding puncture wounds, swollen muzzle, mucous membranes deep red</td>
<td>1</td>
<td>Dexamethasone</td>
<td>Enrofloxacin, ampicillin</td>
<td>LRS (56 mL/kg over 15 h)</td>
<td>None</td>
<td>Marked hemolysis, increased FDP</td>
<td>15 h</td>
</tr>
<tr>
<td>16</td>
<td>&gt;4 h</td>
<td>Forehead (1)</td>
<td>Disoriented, shocky, tachycardia, mucous membranes pale, severe facial edema, blood oozing from conjunctiva</td>
<td>8</td>
<td>Ampicillin</td>
<td>None</td>
<td>LRS (308 mL/kg over 2.5 d)</td>
<td>None</td>
<td>None</td>
<td>2.5 d</td>
</tr>
<tr>
<td>17</td>
<td>1 h</td>
<td>Muzzle (1)</td>
<td>Tachycardia, mild bleeding from puncture wounds</td>
<td>2</td>
<td>None</td>
<td>Cefazolin</td>
<td>LRS (35 mL/kg over 12 h)</td>
<td>None</td>
<td>None</td>
<td>14 h</td>
</tr>
<tr>
<td>18</td>
<td>Unknown</td>
<td>Forelimb (1), ventral thorax (1)</td>
<td>Mucous membranes congested, tachycardia</td>
<td>None</td>
<td>None</td>
<td>Gentamicin, cefazolin</td>
<td>LRS (67 mL/kg over 24 h)</td>
<td>None</td>
<td>None</td>
<td>1 d</td>
</tr>
</tbody>
</table>

Continued on next page
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Time Elapsed Until Treatment</th>
<th>Bite Location (No. of Bites)</th>
<th>Initial Abnormal Clinical Findings</th>
<th>Antivenin Given (vials)</th>
<th>Corticosteroids Given</th>
<th>Antibiotic Therapy</th>
<th>Total IV Fluid Therapy (Per Kg Body Weight; Time Period)</th>
<th>Blood Products Given</th>
<th>Complications</th>
<th>Length of Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>30 min</td>
<td>Dorsal neck (1), ventral neck (1)</td>
<td>Mucous membranes pale, tachycardia, hemoconcentration (packed cell volume=60%), gross hemolysis</td>
<td>4</td>
<td>Methylprednisolone sodium succinate (100 mg IV)</td>
<td>Cefazolin, ampicillin</td>
<td>NaCl and LRS (300 mL/kg over 5 d)</td>
<td>Fresh frozen plasma (125 mL), fresh whole blood (125 mL)</td>
<td>None</td>
<td>Mild azotemia, anemia, prolonged PT/PTT</td>
</tr>
<tr>
<td>20</td>
<td>&lt;3 h</td>
<td>Tongue (1)</td>
<td>Ataxia, shocky, sublingual hematoma, swelling of ventral neck, bleeding from mouth</td>
<td>5</td>
<td>None</td>
<td>None</td>
<td>LRS (52 mL/kg over 24 h)</td>
<td>None</td>
<td>None</td>
<td>25 h</td>
</tr>
<tr>
<td>21</td>
<td>1 h</td>
<td>Muzzle (1)</td>
<td>Tachycardia, extremely swollen muzzle</td>
<td>2</td>
<td>None</td>
<td>Ampicillin</td>
<td>LRS (82 mL/kg over 20 h)</td>
<td>None</td>
<td>None</td>
<td>1 d</td>
</tr>
<tr>
<td>23</td>
<td>30 min</td>
<td>Nose (2)</td>
<td>Tachycardia, severe swelling of face and neck, anemia, bleeding from oral cavity</td>
<td>6</td>
<td>None</td>
<td>Cefazolin</td>
<td>LRS (250 mL/kg over 3.5 d)</td>
<td>Fresh frozen plasma (100 mL), fresh whole blood (125 mL)</td>
<td>Chronic thrombocytopenia</td>
<td>3.5 d</td>
</tr>
<tr>
<td>24</td>
<td>1.5 h</td>
<td>Cheek (1), jaw (1)</td>
<td>Tachycardia, tachypnea, punctures oozing blood, swollen mouth and pharynx</td>
<td>6</td>
<td>None</td>
<td>Enrofloxacin, ampicillin</td>
<td>LRS (154 mL/kg over 45 h)</td>
<td>None</td>
<td>Thrombocytopenia, increased FDP, prolonged PT/PTT</td>
<td>52 h</td>
</tr>
</tbody>
</table>

Continued on next page
Table 2 (cont’d)
Clinical Information on Surviving Dogs

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Time Elapsed Until Treatment</th>
<th>Bite Location (No. of Bites)</th>
<th>Initial Abnormal Clinical Findings*</th>
<th>Antivenin Given (vials)</th>
<th>Corticosteroids Given†</th>
<th>Antibiotic Therapy</th>
<th>Total IV Fluid Therapy (Per Kg Body Weight; Time Period)‡</th>
<th>Blood Products Given</th>
<th>Complications§</th>
<th>Length of Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>&lt;6 h</td>
<td>Muzzle/orbital area (1)</td>
<td>Recumbent, temperature 103.9˚F, tachycardia, weak pulses, bleeding puncture wounds, bruising on ventral neck</td>
<td>10</td>
<td>None</td>
<td>Enrofloxacin, ampicillin</td>
<td>LRS (244 mL/kg over 4.5 d)</td>
<td>Fresh frozen plasma (500 mL)</td>
<td>VPCs, azotemia, increased FDP, prolonged PT/PTT, thrombocytopenia</td>
<td>5 d</td>
</tr>
<tr>
<td>27</td>
<td>&lt;1 h</td>
<td>Forehead (1)</td>
<td>Tachycardia, tachypnea, edema of chin/lips/face</td>
<td>2</td>
<td>None</td>
<td>Enrofloxacin, ampicillin</td>
<td>Normosol-R (167 mL/kg over 50 h)</td>
<td>None</td>
<td>Mild hematochezia</td>
<td>51 h</td>
</tr>
<tr>
<td>29</td>
<td>1 h</td>
<td>Pinna (1)</td>
<td>Unknown (seen at UF-VTH on second day)</td>
<td>1</td>
<td>None</td>
<td>Dexamethasone sodium phosphate IV and prednisolone PO (amounts unknown)</td>
<td>Enrofloxacin</td>
<td>LRS (55 mL/kg over 1 h)</td>
<td>None</td>
<td>Mild hemolysis, thrombocytopenia</td>
</tr>
<tr>
<td>31</td>
<td>&lt;2 h</td>
<td>Muzzle (1)</td>
<td>Tachycardia, tachypnea, mucous membranes dark pink, progressive facial swelling</td>
<td>3</td>
<td>None</td>
<td>None</td>
<td>LRS (58 mL/kg over 18 h)</td>
<td>None</td>
<td>Prolonged ACT</td>
<td>2 d</td>
</tr>
</tbody>
</table>

* ACT=activated clotting time; UF-VTH=University of Florida Veterinary Teaching Hospital
† IV=intravenous; PO=per os; IM=intramuscular
‡ IV=intravenous; LRS=lactated Ringer’s solution; NaCl=0.9% sodium chloride solution; NaCl/Dex=0.45% sodium chloride with 2.5% dextrose; ARF=acute renal failure
§ VPCs=ventricular premature contractions; ACT=activated clotting time; PT=prothrombin time; PTT=partial thromboplastin time; FDP=fibrin degradation products
\ Received subcutaneous epinephrine
† Owner was a licensed veterinarian.
rates of administration were adjusted according to the needs of the animal. Blood products were administered at the individual clinician’s discretion to 11 (35%) dogs based on the degree of anemia and total plasma protein deficiency. Thirteen (42%) dogs were administered corticosteroids by the referring veterinarian at the time of initial presentation. One dog received corticosteroids on the second day of hospitalization. Two of the six dogs that did not survive received corticosteroids. Eleven (44%) of the 25 survivors received corticosteroids initially or early in the course of therapy.

**Complications**

Thirteen (42%) of the 31 dogs had pathological cardiac arrhythmias (ventricular premature contractions, ventricular tachycardia, ventricular fibrillation) either at presentation or during hospitalization. Of these, three died. Arrhythmias resolved in five dogs after administration of antiarrhythmic drugs, and arrhythmias resolved spontaneously in five dogs. Two of the 13 dogs with cardiac arrhythmias did not receive antivenin. One of these dogs died, and the other survived after its arrhythmia resolved spontaneously.

Twenty-five (81%) of 31 dogs had hematological disorders, including defibrination, elevated fibrin split products, hemolytic anemia (with hemoglobinuria), thrombocytopenia, prolonged clotting times, or combinations of these abnormalities [Tables 1, 2].

**Discussion**

In the previous study of Eastern Diamondback Rattlesnake envenomations, 75% of cases occurred from April to October, with 55% of the cases occurring in July or August. In the study reported here, 68% of the envenomations occurred from April to October, but only eight (26%) were in July or August. The cause and significance of this difference are not known. One study in people reported that 95% of snakebites throughout the United States occurred from April to October, and most happened between the hours of 8 AM to noon or 4 PM to 10 PM, which correlated well with periods of human outdoor activity. In the authors’ study, 11 envenomations occurred between 10 AM and 4 PM, seven occurred between 4 PM and 10 PM, and only two occurred after 10 PM but before 10 AM. The milder fall and winter climate of the north central Florida region is less restrictive to both canine and human outdoor activity, and this may explain the more even monthly distribution of envenomations in this study.

The ages and sexes of the dogs in this study were similar to those in a prior study. The 19% mortality rate and the average number of days required for hospitalization were also similar. Overall, 71% of the dogs weighed at least 20 kg; however, three (50%) of the nonsurvivors weighed <15 kg. The high percentage of larger dogs envenomated could possibly be explained by breed popularity, the breeds generally favored for outdoor activities and sports, or the greater propensity for larger dogs to live entirely outdoors. The fact that smaller dogs had an increased representation in the nonsurvival group suggests that the prognosis is less optimistic for smaller dogs. All other things being equal, there is also a high likelihood of a greater venom-to-body weight ratio in smaller dogs.

Elapsed time from envenomation to presentation ranged from 15 minutes to >12 hours. Of the 25 cases with a known elapsed time until presentation, the mean was 3.5 hours. This was similar to the previous UF-VTH study, which documented a mean of 3.8 hours.

The high proportion of bites to the head and neck was consistent with other reports of rattlesnake envenomations and was probably associated with the manner in which the dog confronts the snake. An earlier study showed that 16 (80%) of 20 dogs were struck on the head region, with five (25%) of the 20 struck on the limbs. Interestingly, in spite of the profound swelling seen around the head and neck, airway obstruction was uncommon. Only one of the survivors received respiratory support via endotracheal intubation, while two of the nonsurviving dogs were intubated during efforts at cardiopulmonary resuscitation. In the experience of one of the authors (Schaer), most dogs are struck on the head or neck, while cats are struck more often on the thorax and abdomen. This phenomenon may be related to the confrontational posturing of cats and their faster evasive reactions, allowing them to spring away from the snakes and thereby exposing their lateral and ventral body surfaces to the striking snake.

As previously noted, 13 (42%) of the 31 dogs developed cardiac arrhythmias. Three of these dogs died, five resolved after administration of antiarrhythmic drugs, and five resolved spontaneously. Two of the 13 dogs did not receive antivenin; one died, and the other survived after its arrhythmia and illness resolved spontaneously. In the previous UF-VTH study, nine (47%) of 19 dogs evaluated had cardiac arrhythmias. It is interesting to note that in the previous study, three of the dogs that developed arrhythmias did not receive antivenin, and none of them survived.

Besides the three dogs that died from cardiac failure, three dogs in this study were euthanized. One was euthanized at presentation because of a total lack of brain-stem function, possibly caused by arterial envenomation and subsequent subdural bleeding. Another was euthanized owing to a combination of a guarded prognosis and financial constraints. The third dog was euthanized more than a week after presentation, from probable sepsis and multiple organ failure.

The rather high incidence of hematological disorders in the dogs of this study was consistent with the previous UF-VTH study, in which hematological disorders occurred in 12 (60%) of 20 dogs. Echinocytosis is a common finding (its presence occurred in 89% of rattlesnake-envenomated dogs in one study), but it is not pathognomonic because envenomation by the Eastern Coral Snake has also been reported to produce this same morphological red blood cell change.

The treatment goals for snake envenomation include (1) treatment or prevention of shock and associated arrhythmias, (2) neutralization of the venom with the hope of minimizing...
its local and systemic effects, (3) prevention of secondary bacterial infection, and (4) management of pain. Typical therapy entails the use of volume expansion with crystalloids and/or colloids, crotalid-specific antivenin, analgesia, and empirically chosen antibiotics. Cardiac antiarrhythmic drugs are used as indicated.

Twenty-eight (90%) dogs in the study reported here received intravenous fluids. Blood products (fresh whole blood, fresh frozen plasma) were given to 11 (35%) dogs. This was consistent with the previous UF-VTH study, in which 17 (85%) of 20 dogs received intravenous fluids while six (30%) of the 20 received blood products.13

Twenty-two of the 25 survivors received antivenin. Only one of the dogs receiving antivenin showed signs of hypersensitivity reaction, as characterized by facial pruritus and additional facial swelling. In the previous UF-VTH study, 12 (86%) of the 14 surviving dogs and three (50%) of the six dogs that did not survive received antivenin.13 None of the dogs in the previous study showed a reaction to the antivenin. Sixteen of the dogs that received antivenin received one to four vials, with the other nine dogs receiving five or more vials. This is similar to the previous UF-VTH study, in which 10 of 15 dogs received one to four vials, while five dogs with advanced clinical signs received five or more vials, based on the large amount of venom that can be injected by the Eastern Diamondback Rattlesnake.13

Analgesia may best be accomplished through the use of opioids like buprenorphine or fentanyl. However, the benefits of pharmacological pain management must be weighed against any depression of the animal’s mentation that might make clinical assessments more difficult. Only one (3%) dog in this study received analgesics, which were based on clinician preference. All of the dogs exhibited remarkable tolerance for their affliction, as based on their attitude, vocalization, and heart rates.

Thirteen (42%) dogs in the study reported here received corticosteroids at the initial presentation to the referring veterinarian, while 17 (54%) did not. The remaining animals
received corticosteroids on the second day of hospitalization at UF-VTH. In the previous study, four (31%) of 13 of the surviving dogs received corticosteroids, along with five (83%) of the six nonsurviving dogs. The use of corticosteroids remains controversial for snake envenomation. Some studies have shown corticosteroids to be effective in treating envenomation, while others have shown the opposite effect. Although the literature does not describe the effects of glucocorticoid drugs in dogs, the human literature finds no rationale for their use except to combat anaphylaxis. Corticosteroids might even be detrimental to local tissues in the early stages of envenomation. Some experts feel that glucocorticoids theoretically decrease the potency of the antivenin. Recommendations on the treatment of human cases of envenomation restrict the use of corticosteroids to treating hypersensitivity reactions from the antivenin. In the study reported here, 48% of the surviving dogs and 33% of the nonsurviving dogs received corticosteroids, thus making it difficult to determine the benefits (if any) derived from glucocorticoids. The senior author (Schaer) reserves the use of corticosteroid drugs for treating antivenin-induced hypersensitivity reactions.

Twenty-seven (87%) of the 31 dogs received antibiotics. Two of the four that did not receive antibiotics died during initial presentation (one spontaneously, one was euthanized), and two survived. In the previous UF-VTH study, 18 (90%) of the 20 dogs received antibiotics, and it was unclear if antibiotics had been administered to the remaining two dogs. Bacteriological studies have shown that the most commonly isolated natural microflora of the crotalid mouth includes *Pseudomonas aeruginosa*, *Proteus* spp., coagulase-negative *Staphylococcus* spp., *Clostridium* spp., and *Bacteroides fragilis*. Additionally, the oral cavity of the snake may harbor coliforms introduced while ingesting prey. Because the fangs can disrupt tissue integrity, bacterial invasion is possible both in the local tissues and systemically. However, studies have questioned the use of prophylactic antibiotics during the treatment of envenomation and have recommended their use only for severely contaminated wounds. Good topical wound management has been recommended instead. The decision to use antibiotics in the 27 dogs of this study was based on the preference of the primary clinician. It is entirely possible that antibiotics make no difference in the outcome of Eastern Diamondback Rattlesnake envenomation, because the necrogenic effects of the venom can cause considerable tissue damage.

One major difference between the routine medical management of human and canine envenomations is in the use of tetanus antitoxin in people. Because there have been no reported cases of tetanus associated with Eastern Diamondback Rattlesnake bites in the dog, none of the dogs in this study received tetanus antitoxin.

**Conclusion**

Envenomation by the Eastern Diamondback Rattlesnake was a potentially life-threatening situation in the dog. Because the degree of envenomation varied, treatment and prognosis were based on the presence of shock (tachycardia, tachypnea, pale mucous membranes, weakness), the occurrence and character of cardiac arrhythmias, and the presence and degree of hematological disorders (hemolytic anemia, defibrination, prolonged clotting times, thrombocytopenia). Hypovolemic shock was managed aggressively with intravenous fluid therapy. Although death may occur in spite of the timely use of crotalid-specific antivenin, a higher survival rate was seen in dogs administered antivenin than in those not receiving antivenin. Hospitalization was required for affected dogs in order to provide intravenous fluid therapy, cardiac monitoring, nursing care, and certain emergency procedures. Controversy surrounding the use of corticosteroids and antibiotics still exists, and their use should be determined on an individual case basis.

---

**References**


Percutaneous Drainage and Alcoholization of Hepatic Abscesses in Five Dogs and a Cat

Hepatic abscesses are rare and difficult to diagnose in dogs and cats. Ultrasonographic examination is essential to thoroughly examine hepatic abnormalities, and it may also help in the localization of hepatic abscesses. In this retrospective study, five dogs and one cat with focal hepatic lesions compatible with a hepatic abscess were treated with percutaneous ultrasound-assisted drainage and alcoholization using 95% ethanol. The procedure was performed rapidly under injectable anesthesia and provided excellent results in all animals. No complications or relapses were noted for 120 days following the procedure. The technique of percutaneous ultrasound-assisted drainage and alcoholization of hepatic abscesses in the dog and cat is also described. J Am Anim Hosp Assoc 2005;41:34-38.

Introduction
A variety of hepatic diseases occur in dogs and cats, although hepatic abscesses are rarely diagnosed. Because of the nonspecific clinical signs associated with hepatic abscesses, they are often misdiagnosed as infectious or inflammatory diseases of the liver. Ultrasonographic examination allows better identification of hepatic abscesses, which in turn has created the opportunity to attempt different therapies for this condition. In veterinary medicine, it has been reported that hepatic abscesses may be treated by percutaneous ultrasound-guided drainage, a technique that is both effective and minimally invasive. In humans, satisfactory results have been reported with drainage and alcoholization of hepatic abscesses, thus avoiding the need for hepatic resection, which is associated with high morbidity. Percutaneous drainage and alcoholization reduced hospitalization time, since the abscess was sterilized. The purposes of this retrospective study were to describe the technique for ultrasound-assisted percutaneous drainage and alcoholization of hepatic abscesses and to evaluate the success of the procedure in dogs and cats.

Materials and Methods
The clinical records of six animals (five dogs, one cat) treated with percutaneous drainage and alcoholization of hepatic abscesses between January 1999 and September 2001 were reviewed. In all animals, the diagnosis of hepatic abscess was confirmed by cytological evaluation of the drained material. Data evaluated from these cases included signalment, clinical signs, laboratory findings, ultrasonographic results, and results of follow-up examinations.

Ultrasonography/Alcoholization Procedure
All animals were fasted for 12 hours, after which abdominal ultrasonography was performed with the animal in dorsal recumbency. The liver
was thoroughly evaluated by sagittal and transverse scans. Hepatic lesions were classified as single or multiple, and the presence of septations was also determined for each lesion. The size of each lesion was determined in sagittal or transverse scans by measuring the longest dimension of the lesion. The outer hypoechoic parenchymal area (when found) was excluded from the measurement. The ultrasonographic appearance of the lesion was described and classified as reported by Schwarz, et al., into three types: anechoic (absence of internal echoes), hypoechoic or poorly echogenic (less echogenic than the surrounding liver), and mixed echogenicity (combination of echo patterns). The locations of the abscesses within the liver and the lobe affected were noted. Whether the abscess was deep within the parenchyma or in a peripheral subcapsular position was also recorded.

To perform drainage and alcoholization, all animals were anesthetized with diazepam (0.5 mg/kg intravenously [IV]) and ketamine (10 mg/kg IV) and were placed in dorsal recumbency. The abdominal area was clipped and prepared aseptically. A percutaneous ultrasound-assisted drainage of the abscess was performed using a biopsy needle (20 gauge × 10 cm) with the echo-tip attached to a 5- to 20-mL syringe and a 50-cm extension line. To avoid an excessive speed of aspiration of the abscess cavity, the amount of exudate to be removed was estimated, and a syringe with a volume twice that amount was chosen. The spinal needle was introduced into the abscess cavity under ultrasonographic guidance. When the tip of the needle was in the lesion, the stylet was removed, and the extension line with a sterile syringe of predetermined size was attached to the hub to permit drainage of the abscess contents. Before removing the spinal needle, alcoholization of the cavity was performed by infusing 95% ethanol. The amount of alcohol injected was equivalent to half the amount of the exudate removed. The alcohol-volume to syringe-volume ratio was never >1:2. The ethanol was left in the abscess cavity for 3 minutes and was then gently aspirated through the previously positioned spinal needle.

Follow-up Procedures

Each aspirated sample was submitted for aerobic bacterial culture and cytological evaluation. For bacterial culture, the sample was stored at 4˚ to 8˚C in a sterile container with transport media and was sent to the laboratory within 4 hours of collection. Five smears, one for each drained cavity from each case, were prepared for cytological evaluation. All the slides were stained with May-Grünwald-Giemsa stain and were assessed by a single individual (Bonfanti).

The detection of short-term complications associated with drainage and alcoholization of the abscess was based on results of physical examination, complete blood count (CBC), serum liver enzyme activities, and abdominal ultrasonography performed 24 and 48 hours after the procedure. Evaluation of the long-term results was assessed by abdominal ultrasonography repeated at 15, 30, 60, and 120 days after the procedure in all six animals.

Results

Clinical and Laboratory Findings

This retrospective study included five dogs of different breeds and one Siamese cat. The animals ranged in age from 2 to 15 years [see Table]. All animals had nonspecific signs including anorexia (6/6, 100%), cranial abdominal pain (4/6, 66.68%), pyrexia (4/6, 66.68%), vomiting (2/6, 33.34%), and abdominal ascites (1/6, 16.67%). Laboratory findings in all animals included leukocytosis with a left shift and increased concentrations of serum alanine transaminase (ALT) and aspartate transaminase (AST) [see Table].

Ultrasonographic Findings

On ultrasonography, all six animals had a single lesion, which appeared as either a hypoechoic or anechoic area with irregular, hyperechoic margins [Figures 1, 2]. In some cases, there was also reduced echogenicity of the surrounding liver [Figure 1]. Large lesions had less echogenicity, with anechoic to fine hyperechoic contents [see Table]. The anechoic lesions showed variable distal acoustic enhancement in some of the abscesses. No evidence of septation was identified in any of the lesions on ultrasonography. All lesions were located in the right hepatic lobe. Within the lobe, two lesions had a peripheral subcapsular location (case nos. 3, 4), while the others were deep within the parenchyma.

On days 1 and 2 following the alcoholization procedure, all animals were submitted to ultrasound examination, and in all cases, a hyperechoic area proportional in size to the original lesion and surrounded by hypoechoic hepatic tissue was identified. On days 15 and 30, the previously described areas were not as echogenic and the peripheral hypoechoic ring had disappeared. At days 60 and 120 posttherapy, no
Parenchymal abnormalities were evident on ultrasonography (e.g., cavitated structures or cicatricial areas) in those animals treated for small abscess lesions (<3 cm; case nos. 1, 4, 6). In animals with larger lesions (case nos. 2, 3, 5), the follow-up evaluations showed hyperechoic areas proportional in size to the drained lesions. No evidence of recurrence of the hepatic abscess or complications related to the procedure was detected in any of the animals at the follow-up examinations.

Cytological and Bacteriological Results
Cytological examination was suggestive of abscessation [Figure 3] and revealed necrotic debris in a background of highly degenerated neutrophils (case nos. 1-3, 5, 6) and a small number of rod-shaped bacteria compatible with Enterobacteriaceae (except in case no. 4). No neoplastic cells were found in any of the cytological samples. In case no. 4, the bacterial culture was negative. This dog had received antibiotics (i.e., enrofloxacin) for 72 hours prior to the aspirate, which may have affected the culture results. Culture results of all other animals were positive for Escherichia coli, suggesting a biliary origin from ascending cholangitis as previously described.6-10 All animals were treated with appropriate antibiotics based upon the microbial culture results for 30 days.

Complications and Follow-up
Based on the results of physical examination, CBC, serum biochemical profile, and abdominal ultrasonography performed 24 and 48 hours after the procedure, there was no evidence of any complications related to the technique. Anorexia, abdominal pain, and pyrexia resolved in all six animals within 48 to 72 hours after drainage and alcoholization, and all animals returned to a clinically normal state during the first week following the procedure. No animals were treated with analgesics, nonsteroidal antiinflammatory drugs, or opioids. Follow-up ultrasound evaluations at 15, 30, 60, and 120 days after drainage and alcoholization showed no evidence of complications and/or relapse of the abscess in any animal.

Discussion
In dogs and cats, ultrasonography facilitates the diagnostic approach to suspected hepatic abscesses. Sagittal and transverse scans permit a more accurate assessment of hepatic size, location, parenchymal echostructure, and vascular anatomy as well as structural features of the biliary tract.2 Since the advent of ultrasonography, the number of the hepatic abscesses identified has increased.3 The differential diagnoses for the hepatic lesions described in the study reported here included hepatic abscess, hematoma, metastatic neoplasia, and biliary cystadenoma.2 Biliary cystadenoma can appear as a cystic lesion or as a mass lesion, with increased or mixed echogenicity.2 Hematomas are typically located in the subcapsular area and usually have a thick and moderately hyperechoic wall, hypoechoic contents, and distal acoustic enhancement.2 Hepatic abscesses are often anechoic or hypoechoic, variable in size, and have irregular margins. The contents of hepatic abscesses may be mildly to moderately hyperechoic, and variable distal acoustic enhancement may be noted.2 The parenchyma surrounding hepatic abscesses may appear hypoechoic. Metastatic neoplastic lesions are usually multifocal and may also have a “target” appearance.2 However, a primary hepatic tumor may have an appearance similar to liver abscesses, especially if a necrotic center is present.2 Unlike abscesses, though, a tumor will generally have regular margins.2 The similar ultrasonographic findings for both liver neoplasia and hepatic abscesses require cytological and/or histopathological examination to reach a definitive diagnosis.
### Table

Clinical and Ultrasonographic Findings in Six Animals With Hepatic Abscesses

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Signalment*</th>
<th>Clinical Signs</th>
<th>Laboratory Abnormalities†</th>
<th>No. of Abscesses</th>
<th>Location of Abscess</th>
<th>Diameter of Abscess (cm)</th>
<th>Echogenicity of Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7-y-old, M, mixed-breed dog</td>
<td>Anorexia, abdominal pain</td>
<td>ALT 122 U/L&lt;br&gt;AST 106 U/L&lt;br&gt;WBC $16.8 \times 10^3$</td>
<td>1</td>
<td>Right lobe; deep within parenchyma</td>
<td>&lt;3</td>
<td>Hypoechoic</td>
</tr>
<tr>
<td>2</td>
<td>6-y-old, F schnauzer</td>
<td>Anorexia, abdominal pain, pyrexia</td>
<td>ALT 138 U/L&lt;br&gt;AST 113 U/L&lt;br&gt;WBC $18.2 \times 10^3$</td>
<td>1</td>
<td>Right lobe; deep within parenchyma</td>
<td>&gt;5</td>
<td>Anechoic</td>
</tr>
<tr>
<td>3</td>
<td>15-y-old, SF Yorkshire terrier</td>
<td>Anorexia, ascites, pyrexia</td>
<td>ALT 326 U/L&lt;br&gt;AST 187 U/L&lt;br&gt;WBC $28.4 \times 10^3$</td>
<td>1</td>
<td>Right lobe; peripheral subcapsular position</td>
<td>&gt;5</td>
<td>Anechoic</td>
</tr>
<tr>
<td>4</td>
<td>3-y-old, F cocker spaniel</td>
<td>Anorexia, vomiting, abdominal pain, pyrexia</td>
<td>ALT 213 U/L&lt;br&gt;AST 125 U/L&lt;br&gt;WBC $21.7 \times 10^3$</td>
<td>1</td>
<td>Medial right lobe; peripheral subcapsular position</td>
<td>&lt;3</td>
<td>Hypoechoic</td>
</tr>
<tr>
<td>5</td>
<td>11-y-old, M, mixed-breed dog</td>
<td>Anorexia, abdominal pain</td>
<td>ALT 154 U/L&lt;br&gt;AST 139 U/L&lt;br&gt;WBC $17.2 \times 10^3$</td>
<td>1</td>
<td>Right lobe; deep within parenchyma</td>
<td>&gt;5</td>
<td>Anechoic</td>
</tr>
<tr>
<td>6</td>
<td>2-y-old, CM Siamese</td>
<td>Anorexia, vomiting, pyrexia</td>
<td>ALT 182 U/L&lt;br&gt;AST 83 U/L&lt;br&gt;WBC $21.4 \times 10^3$</td>
<td>1</td>
<td>Right lobe; deep within parenchyma</td>
<td>&lt;3</td>
<td>Hypoechoic</td>
</tr>
</tbody>
</table>

* M=male; F=female; SF=spayed female; CM=castrated male
† ALT=alanine transaminase (dog reference range, 4 to 91 U/L; cat reference range, 13 to 75 U/L); AST=aspartate transaminase (dog reference range, <105 U/L; cat reference range, <51 U/L); WBC=white blood cells (dog reference range, 5.4 to $15.3 \times 10^3$; cat reference range, 3.8 to $19 \times 10^3$)
The lack of clinical signs and laboratory abnormalities specific for a hepatic abscess does not permit a definitive diagnosis without further investigation and testing. In the present study, anorexia was the most common clinical sign, followed by a hunched posture and pain on abdominal palpation. Laboratory findings showed both leukocytosis and elevations in liver enzyme activities, all of which may occur with other hepatic disorders. In this study, ultrasonographic evaluation and ultrasound-guided aspiration with cytological examination of material from the affected area proved to be very valuable in confirming the presence of a hepatic abscess.

Some authors have associated hepatic abscesses with concurrent diseases or certain predisposing factors, such as infectious diseases of the pancreas and/or biliary tract and immunosuppressive disorders (e.g., diabetes mellitus, hyperadrenocorticism). Based on laboratory tests and abdominal ultrasonography, there was no evidence of cholangitis, cholecystitis, pancreatitis, or immunosuppressive diseases in any of the animals in this report. In case no. 4, the peripheral subcapsular location of the abscess, an epigastric reactive inflammatory zone characterized by hypoechogenicity of the surrounding tissue and a thickened hypoechic gastric wall, suggested a transparietal infection possibly arising from a penetrating foreign body, even though it could not be identified upon standard radiography. In all of the cases presented here, the abscess occurred within the right liver lobe. According to reports in humans, the higher incidence of abscesses in the right lobe may reflect a biliary origin of the pathology. Only solitary hepatic abscesses were identified in this study, a finding that was consistent with previous reports in dogs.

The bacteria isolated from the hepatic lesions in this study were from the Enterobacteriaceae family, further suggesting a biliary origin from ascending cholangitis as previously described. Anaerobic bacterial cultures were not performed, and this may have limited the identification of etiological agents. In a prior study of dogs with hepatic abscesses, however, anaerobic cultures were all negative.

Possible complications of percutaneous drainage of hepatic abscesses include rupture of the abscess, leading to circumscribed or generalized peritonitis. These complications are most likely to occur with peripheral subcapsular abscesses, similar to peripheral complicated cysts. Abscesses may also rupture when a large amount of ethanol is used and/or if the alcohol is infused at a high rate of speed. Limiting the aspiration speed by keeping the estimated exudate-volume to syringe-volume ratio at 1:2 and injecting a precise amount of ethanol (equivalent to half the amount of the exudate removed) are believed to help prevent this complication. No complications occurred following these precautions in the animals of this report.

In dogs and cats, hepatic abscesses may be diagnosed and treated via laparotomy, laparoscopy, or percutaneous ultrasound-guided techniques. The drainage and 95% ethanol alcoholization technique used here was similar to the procedure reported in humans for the treatment of pyogenic liver abscesses. The advantages of this technique, when compared to drainage procedures alone, are the absence of complications and relapses, no requirement for maintaining indwelling catheters for continuous drainage, and no need for successive surgical intervention. The ultrasound-assisted drainage procedure reported by Schwarz et al. had a lower mortality rate and more favorable results compared to the temporary drainage technique described by Farrar et al. The technique presented here had no mortality, irrespective of the size of the lesion, and was followed by positive clinical results within a short period of time (e.g., absence of abdominal pain within 48 hours). The costs were also significantly lower than those incurred with classical surgical approaches.

Conclusion

The ultrasound-assisted percutaneous drainage and alcoholization technique for hepatic abscess in the dog and cat appeared to be an excellent alternative to surgical treatment. The procedure was rapid, was not accompanied by any complications or morbidity, resulted in complete resolution of the hepatic abscess, and cost less than other therapeutic procedures.

References

Trends in the Frequency of Calcium Oxalate Uroliths in the Upper Urinary Tract of Cats

Medical records from cats diagnosed with uroliths at nine United States veterinary teaching hospitals from 1980 to 1999, and records of cats with uroliths submitted for analyses to the Minnesota Urolith Center from 1981 to 2000, were evaluated. A 10-fold increase in frequency of upper tract uroliths occurred in cats during the 20-year interval at the nine veterinary teaching hospitals. Calcium oxalate emerged as the predominant mineral type in upper tract uroliths, having increased more than 50-fold during the study period. These results emphasize the need for increased awareness of the occurrence of upper urinary tract uroliths in cats. J Am Anim Hosp Assoc 2005;41:39-46.

Chalermpol Lekcharoensuk, DVM, PhD
Carl A. Osborne, DVM, PhD, Diplomate ACVIM
Jody P. Lulich, DVM, PhD, Diplomate ACVIM
Hasan Albasan, DVM, MS, PhD
Lisa K. Ulrich
Lori A. Koehler
Kathleen A. Carpenter
Laurie L. Swanson
Laura A. Pederson

Introduction

The Minnesota Urolith Center has analyzed uroliths from cats for more than two decades. Over this time, calcium oxalate (CaOx) has surpassed struvite as the most common mineral within uroliths. Whereas 78% of all the uroliths submitted in 1981 were primarily composed of struvite and 1% were composed of calcium oxalate, during the year 2000, 54% of all the uroliths were composed primarily of CaOx and 35% were composed of struvite.1,2 Recent information supports the impression that the frequency of CaOx uroliths affecting the upper urinary tract of cats has also been increasing.3,4 Clinical experience at the University of Minnesota Veterinary Teaching Hospital (UM-VTH) agrees with this impression. From 1980 to 1989, the hospital proportional morbidity rate (defined here as the frequency with which a disease is diagnosed in a veterinary teaching hospital) of upper tract uroliths at the UM-VTH was 19 cases per 10,000 cats. From 1990 to 1999, the hospital proportional morbidity rate for upper tract uroliths increased to 68 cases per 10,000 cats. With the objective of further evaluating this trend, an epidemiological study was designed to test two hypotheses. One hypothesis was that during the past two decades, there was an increase in the yearly hospital proportional morbidity rate of uroliths in the feline upper urinary tract. The other hypothesis was that during this time interval, the frequency of CaOx urolith occurrence in the upper urinary tract increased.

Materials and Methods

Study Populations

Because ureteral uroliths originate in the kidneys, relevant information about nephroliths and ureteroliths was combined and categorized as upper urinary tract uroliths. Because urethral calculi originate primarily from the urinary bladder, relevant information about cystoliths and urethral calculi was combined and categorized as lower urinary tract uroliths.

Information was retrieved from two databases. One database consisted of information retrieved from medical records of cats evaluated at Veterinary Teaching Hospitals (VTHs) in the United States between 1980 and 1999 and compiled by the Purdue Veterinary Medical Data Base (VMDB). Some colleges of veterinary medicine did not continuously contribute data to the VMDB from 1980 to 1999. Only those records from
nine VTHs (i.e., Michigan State University, University of Minnesota, Iowa State University, Purdue University, University of Georgia, University of Illinois, Colorado State University, Auburn University, and Texas A&M University) that submitted data continuously during this time period were reviewed.

Cats evaluated at each VTH were counted only once; data related to readmissions were excluded. Codes from the Purdue VMDB list were used to identify cats with nephroliths, ureteroliths, or both, and cats with cystoliths, urethral calculi, or both. Cats with uroliths retrieved from both the upper and lower urinary tract were grouped separately (i.e., into a third category). These cats were counted only once; data related to readmissions were excluded. Because of the retrospective nature of this study, it was not possible to determine the extent of the diagnostic evaluations performed on each cat. The Purdue VMDB did not distinguish between uroliths of different mineral composition; therefore, a diagnosis of nephrolith, ureterolith, and cystolith in this study encompassed all types of minerals. The yearly occurrence of upper tract uroliths identified at necropsy at nine VTHs from 1980 to 1999 and submitted to the Purdue VMDB was also evaluated.

The second database included records of cats with uroliths submitted for quantitative analyses to the Minnesota Urolith Center between 1981 and 2000. This database included urolith submissions from the nine VTHs described in the first data set. Uroliths were analyzed by means of optical crystallography, infrared spectroscopy, or X-ray diffraction. A urolith without a nidus or shell that contained ≥70% of one mineral was identified by that mineral. Uroliths retrieved from kidneys, ureters, or both were classified as upper tract uroliths. Lower tract uroliths included uroliths retrieved from the urinary bladder, urethra, or voided urine. Uroliths retrieved from both the upper and lower urinary tract were grouped separately (i.e., into a third category).

Statistical Analysis

The yearly hospital proportional morbidity rate of nephroliths or ureteroliths per 10,000 cats from the Purdue VMDB was calculated by dividing the number of cats diagnosed (with upper tract uroliths) during each year (x 10,000) by the total number of first-visit cats seen during each year. A linear regression (regress y on x; y = the yearly morbidity rate, x = years) method was used to test whether the yearly hospital proportional morbidity rate of nephroliths and/or ureteroliths at the nine VTHs increased from 1980 to 1999. In addition, data from necropsied cats with nephroliths and/or ureteroliths from the nine VTHs were also evaluated in the same manner.

Assumption of normality (tested by Wilks-Shapiro statistic), linearity (tested by plotting residuals versus fitted values), and constant variance (tested by analysis of residuals) for the yearly submission rates and the yearly morbidity rates were evaluated. A linear regression (regress y on x; y = the yearly submission rates, x = years) method was used to determine whether the yearly submission rate of all mineral types of upper tract uroliths (e.g., nephroliths or ureteroliths) from the Minnesota Urolith Center increased (slope of years >0) from 1981 to 2000. The test of parallelism of two regression lines was used to assess whether or not the Minnesota Urolith Center’s yearly submission rates of CaOx uroliths affecting the upper urinary tract from 1981 to 2000 were increasing at a faster rate than the CaOx uroliths affecting the lower urinary tract (i.e., slope of the yearly submission rates of upper tract CaOx uroliths was greater than the slope of the yearly submission rates of lower tract CaOx uroliths). Statistical analyses were performed using a commercial software program. Values of P<0.05 were considered significant.

Results

Data From the Purdue Veterinary Medical Data Base

From 1980 to 1999, 390,318 feline records were retrieved. After censoring records of multiple admissions for a single animal, records of 163,999 cats remained. Of nine VTHs that continuously submitted data to the VMDB from 1980 to 1999, the mean hospital proportional morbidity rate for nephroliths or ureteroliths (i.e., upper tract uroliths) was 22 cases per 10,000 cats. The mean morbidity rate for uroliths retrieved from both the upper and lower urinary tract was six cases per 10,000 cats. In contrast, the mean morbidity rate for cystoliths and/or urethral calculi (i.e., lower tract uroliths) was 70 cases per 10,000 cats. When nephroliths or ureteroliths were grouped by year [Table 1], a significant increase in morbidity (slope = 2.7; 95% confidence interval [CI] = 2.2 to 3.2) was observed [Figure 1]. In 1980, the hospital proportional morbidity rate of cats with upper tract uroliths was three cases per 10,000 cats. By 1999, the morbidity rate of cats with upper tract uroliths was 35 cases per 10,000 cats. From 1980 to 1999, 9402 necropsies were performed on cats at these nine VTHs. Upper tract uroliths were diagnosed in an average of six cases per 1000 necropsies. However, when upper tract uroliths identified at necropsy were grouped by year [Table 2], a significant increase over time was observed (slope = 0.62; 95% CI = 0.25 to 0.98) [Figure 2]. For example, in 1980, the necropsy rate of cats with upper tract uroliths was three cases per 1000 necropsies, whereas by 1998, the rate was 18 cases per 1000 necropsies.

Data From the Minnesota Urolith Center

Records from a total of 32,969 urolith assays were evaluated. Uroliths from the upper urinary tract were identified in 864 (2.6%) cases. Uroliths from only the lower urinary tract were identified in 31,851 (96.6%) cases. Uroliths from both the upper and lower urinary tract were identified in 254 (0.8%) of the cases.

Over the 20-year study period, upper tract uroliths represented approximately 2% to 4% (mean standard deviation [SD], 3.5±1.9) of each year’s total urolith submissions [Table 3]. Evaluation of the yearly submission rates of all mineral types of upper tract uroliths did not reveal a significant time-related increase (slope = -0.10; 95% CI = -0.24
to 0.04) [Figure 3]. Likewise, when this 20-year period was divided into two intervals (1981 to 1990 and 1991 to 2000), a significant increase in the percentage of all upper tract uroliths was not observed. From 1981 to 1990, the yearly totals of upper tract uroliths comprised approximately 4% (mean ± SD, 4.0±2.4) of each year’s total urolith submissions, and from 1991 to 2000, they represented approximately 3% (mean ± SD, 2.9±1.1) of each year’s total urolith submissions.

Of 864 upper tract uroliths, CaOx was the major component in 564 (65%) cases. Of 31,281 lower tract uroliths, CaOx was the major component in 15,459 (49%) cases. The yearly percentage of upper tract CaOx uroliths increased significantly (slope = 4.2; 95% CI = 3.2 to 5.1; R² = 0.81) [Figure 4] from 0% in 1981 to 30% in 1990, and to 75% in 2000 [Table 4]. The yearly percentage of lower tract CaOx uroliths increased (slope = 3.3; 95% CI = 2.7 to 4.0; R² = 0.84) [Figure 4] from 1.5% in 1981 to 53% in 2000 [Table 4]. The slope of the trend line depicting the yearly frequency of submissions of CaOx uroliths from the upper urinary tract was not significantly different from the slope of the trend line depicting the yearly frequency of submissions of CaOx uroliths from the lower urinary tract. In both the upper and lower urinary tracts, the number of CaOx uroliths increased approximately 3% to 4% per year.

Discussion

Until the 1990s, the prevailing opinion was that uroliths uncommonly affected the upper urinary tract of cats.8-12 Furthermore, the occurrence of CaOx nephroliths was considered to be rare. However, results of the study reported

<table>
<thead>
<tr>
<th>Year</th>
<th>Total No. Evaluated</th>
<th>No. of Cats With Upper Tract Uroliths</th>
<th>Morbidity Rate for Upper Tract Uroliths (Per 10,000 Cats)</th>
<th>No. of Cats With Lower Tract Uroliths</th>
<th>Morbidity Rate for Lower Tract Uroliths (Per 10,000 Cats)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>11,465</td>
<td>3</td>
<td>3</td>
<td>94</td>
<td>82</td>
</tr>
<tr>
<td>1981</td>
<td>8493</td>
<td>5</td>
<td>6</td>
<td>70</td>
<td>82</td>
</tr>
<tr>
<td>1982</td>
<td>7475</td>
<td>1</td>
<td>1</td>
<td>89</td>
<td>119</td>
</tr>
<tr>
<td>1983</td>
<td>8480</td>
<td>2</td>
<td>2</td>
<td>59</td>
<td>70</td>
</tr>
<tr>
<td>1984</td>
<td>8374</td>
<td>8</td>
<td>10</td>
<td>41</td>
<td>49</td>
</tr>
<tr>
<td>1985</td>
<td>8126</td>
<td>4</td>
<td>5</td>
<td>42</td>
<td>52</td>
</tr>
<tr>
<td>1986</td>
<td>8467</td>
<td>5</td>
<td>6</td>
<td>33</td>
<td>39</td>
</tr>
<tr>
<td>1987</td>
<td>8268</td>
<td>10</td>
<td>12</td>
<td>52</td>
<td>63</td>
</tr>
<tr>
<td>1988</td>
<td>8273</td>
<td>11</td>
<td>13</td>
<td>54</td>
<td>65</td>
</tr>
<tr>
<td>1989</td>
<td>8587</td>
<td>12</td>
<td>14</td>
<td>52</td>
<td>61</td>
</tr>
<tr>
<td>1990</td>
<td>8833</td>
<td>19</td>
<td>22</td>
<td>44</td>
<td>50</td>
</tr>
<tr>
<td>1991</td>
<td>8798</td>
<td>20</td>
<td>23</td>
<td>44</td>
<td>50</td>
</tr>
<tr>
<td>1992</td>
<td>8224</td>
<td>17</td>
<td>21</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>1993</td>
<td>7729</td>
<td>25</td>
<td>32</td>
<td>48</td>
<td>62</td>
</tr>
<tr>
<td>1994</td>
<td>7923</td>
<td>33</td>
<td>42</td>
<td>59</td>
<td>74</td>
</tr>
<tr>
<td>1995</td>
<td>7552</td>
<td>30</td>
<td>40</td>
<td>56</td>
<td>74</td>
</tr>
<tr>
<td>1996</td>
<td>7446</td>
<td>38</td>
<td>51</td>
<td>48</td>
<td>64</td>
</tr>
<tr>
<td>1997</td>
<td>7994</td>
<td>33</td>
<td>41</td>
<td>85</td>
<td>106</td>
</tr>
<tr>
<td>1998</td>
<td>6594</td>
<td>35</td>
<td>53</td>
<td>71</td>
<td>108</td>
</tr>
<tr>
<td>1999</td>
<td>6898</td>
<td>24</td>
<td>35</td>
<td>58</td>
<td>84</td>
</tr>
</tbody>
</table>
Figure 1—Trend line (solid line) and the hospital morbidity rates per 10,000 cats (black bars) of all mineral types of upper urinary tract uroliths diagnosed at nine veterinary teaching hospitals from 1980 to 1999.

Figure 2—Trend line (solid line) and the yearly rates of cats per 1000 cats necropsied (black bars) diagnosed with upper tract uroliths upon necropsy at nine veterinary teaching hospitals from 1980 to 1999.

Figure 3—Trend line (solid line) and frequency of all types of upper tract uroliths as a percentage of the total number of uroliths (black bars) submitted to the Minnesota Urolith Center from 1981 to 2000.
here indicated a 10-fold increase in the frequency of upper tract uroliths in cats evaluated at nine VTHs in the United States during the 20-year study period. Surprisingly, a corresponding increase in the percentage of upper tract uroliths submitted to the Minnesota Urolith Center was not observed during the same time interval. This difference was likely related, at least in part, to the fact that many upper tract uroliths (especially small nephroliths) diagnosed by radiography or ultrasonography were not removed surgically.13-15 In addition, the majority of uroliths received at the Minnesota Urolith Center were submitted by colleagues in private practice. It is probable that proportional morbidity rates of upper tract uroliths are higher at VTHs than in private practices, because cats with upper tract uroliths were more likely to be referred to specialists for diagnostic evaluations and/or surgery.

Results of this study indicated that CaOx is currently the predominant mineral type in upper tract uroliths submitted to the Minnesota Urolith Center. The frequency of CaOx uroliths increased more than 50-fold since 1981. Although the mineral types of upper tract uroliths were not specified in information compiled by the Purdue VMDB, the combined results derived from the Purdue VMDB and the Minnesota Urolith Center supported the hypothesis that the yearly percentage of upper tract CaOx uroliths of cats increased substantially during the 20-year study period. It should be noted that in the study reported here, the hospital proportional morbidity rate of upper tract uroliths represented the percentage of cats with nephroliths admitted to nine VTHs that submitted appropriate data to the Purdue VMDB continuously over a 20-year period. This morbidity rate may not have reflected the morbidity rate of upper tract

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Necropsies Performed in Cats</th>
<th>No. of Necropsies That Revealed Upper Tract Uroliths</th>
<th>Rate of Uroliths Per 1000 Cats Necropsied</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>634</td>
<td>2</td>
<td>3.2</td>
</tr>
<tr>
<td>1981</td>
<td>689</td>
<td>2</td>
<td>2.9</td>
</tr>
<tr>
<td>1982</td>
<td>590</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1983</td>
<td>575</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1984</td>
<td>599</td>
<td>2</td>
<td>3.3</td>
</tr>
<tr>
<td>1985</td>
<td>537</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
<td>1986</td>
<td>545</td>
<td>2</td>
<td>3.7</td>
</tr>
<tr>
<td>1987</td>
<td>530</td>
<td>3</td>
<td>5.7</td>
</tr>
<tr>
<td>1988</td>
<td>506</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>1989</td>
<td>505</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1990</td>
<td>456</td>
<td>2</td>
<td>4.4</td>
</tr>
<tr>
<td>1991</td>
<td>429</td>
<td>5</td>
<td>11.7</td>
</tr>
<tr>
<td>1992</td>
<td>359</td>
<td>2</td>
<td>5.6</td>
</tr>
<tr>
<td>1993</td>
<td>362</td>
<td>2</td>
<td>5.5</td>
</tr>
<tr>
<td>1994</td>
<td>380</td>
<td>6</td>
<td>15.8</td>
</tr>
<tr>
<td>1995</td>
<td>395</td>
<td>6</td>
<td>15.2</td>
</tr>
<tr>
<td>1996</td>
<td>377</td>
<td>6</td>
<td>15.9</td>
</tr>
<tr>
<td>1997</td>
<td>406</td>
<td>3</td>
<td>7.4</td>
</tr>
<tr>
<td>1998</td>
<td>328</td>
<td>6</td>
<td>18.3</td>
</tr>
<tr>
<td>1999</td>
<td>200</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Figure 4—Trend lines and frequency of upper and lower calcium oxalate (CaOx) uroliths submitted to the Minnesota Urolith Center from 1981 to 2000. Upper CaOx uroliths (black bars) are expressed as a percentage of total upper tract uroliths. Lower tract CaOx uroliths (gray bars) are expressed as a percentage of total lower tract uroliths. The solid line represents trend of upper tract CaOx uroliths. The interrupted line represents trend of lower tract CaOx uroliths.

Table 3

Frequency of Upper Tract Urolith Submissions of All Mineral Types to the Minnesota Urolith Center From 1981 to 2000

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Urolith Submissions</th>
<th>No. of Upper Tract Uroliths</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1981</td>
<td>69</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>1982</td>
<td>208</td>
<td>4</td>
<td>1.9</td>
</tr>
<tr>
<td>1983</td>
<td>140</td>
<td>5</td>
<td>3.6</td>
</tr>
<tr>
<td>1984</td>
<td>140</td>
<td>13</td>
<td>9.3</td>
</tr>
<tr>
<td>1985</td>
<td>78</td>
<td>4</td>
<td>5.1</td>
</tr>
<tr>
<td>1986</td>
<td>105</td>
<td>6</td>
<td>5.7</td>
</tr>
<tr>
<td>1987</td>
<td>138</td>
<td>3</td>
<td>2.2</td>
</tr>
<tr>
<td>1988</td>
<td>160</td>
<td>8</td>
<td>5.0</td>
</tr>
<tr>
<td>1989</td>
<td>329</td>
<td>13</td>
<td>4.0</td>
</tr>
<tr>
<td>1990</td>
<td>491</td>
<td>10</td>
<td>2.0</td>
</tr>
<tr>
<td>1991</td>
<td>526</td>
<td>31</td>
<td>5.9</td>
</tr>
<tr>
<td>1992</td>
<td>1325</td>
<td>30</td>
<td>2.3</td>
</tr>
<tr>
<td>1993</td>
<td>1429</td>
<td>42</td>
<td>2.9</td>
</tr>
<tr>
<td>1994</td>
<td>2164</td>
<td>50</td>
<td>2.3</td>
</tr>
<tr>
<td>1995</td>
<td>2557</td>
<td>60</td>
<td>2.3</td>
</tr>
<tr>
<td>1996</td>
<td>2995</td>
<td>90</td>
<td>3.0</td>
</tr>
<tr>
<td>1997</td>
<td>3959</td>
<td>119</td>
<td>3.0</td>
</tr>
<tr>
<td>1998</td>
<td>4755</td>
<td>111</td>
<td>2.3</td>
</tr>
<tr>
<td>1999</td>
<td>5091</td>
<td>125</td>
<td>2.5</td>
</tr>
<tr>
<td>2000</td>
<td>5740</td>
<td>139</td>
<td>2.4</td>
</tr>
</tbody>
</table>
uroliths diagnosed in private practice or the true incidence of upper tract uroliths in the general population of cats.

This study was not designed to identify factors associated with the increased occurrence of CaOx in upper tract uroliths. However, results of epidemiological studies indicate that some dietary factors (e.g., urine acidifying potential, magnesium restriction, moisture reduction) may increase the risk for CaOx uroliths in cats.\(^{16,17}\) Other factors such as age, sex, reproductive status, breed, and environment may also be involved.\(^{16,18}\) Nutritional and environmental factors have also been incriminated in the dramatic increase of CaOx upper tract uroliths observed in humans during the 20th century.\(^{19,20}\)

Upper urinary tract uroliths should be suspected in cats with clinical signs related to the kidneys (e.g., intrarenal azotemia, abdominal pain, renomegaly) and in cats with hematuria not associated with signs of lower urinary tract disease (e.g., dysuria, pollakiuria, urinating outside the litterbox). At the UM-VTH, nephroliths have been unexpectedly detected by survey radiography in 83 of 189 cats with naturally occurring chronic renal failure and intrarenal azotemia.\(^{6}\) Results of this study also emphasize the need to use caution when considering use of modified diets to dissolve nephroliths. Although protocols have been developed that are effective in dissolving feline sterile struvite uroliths, in the year 2002 only 9.4% of the upper tract uroliths submitted to the Minnesota Urolith Center were composed primarily of struvite.\(^{21}\)

### Conclusion

The frequency of detection of upper tract uroliths has significantly increased during the past 2 decades.

### Table 4

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of Upper Tract Urolith Submissions</th>
<th>No. of Upper Tract CaOx Urolith Submissions</th>
<th>%</th>
<th>No. of Lower Tract Urolith Submissions</th>
<th>No. of Lower Tract CaOx Urolith Submissions</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1981</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>67</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>1982</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>204</td>
<td>6</td>
<td>2.9</td>
</tr>
<tr>
<td>1983</td>
<td>5</td>
<td>1</td>
<td>20.0</td>
<td>135</td>
<td>6</td>
<td>4.4</td>
</tr>
<tr>
<td>1984</td>
<td>13</td>
<td>3</td>
<td>23.1</td>
<td>127</td>
<td>5</td>
<td>3.9</td>
</tr>
<tr>
<td>1985</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>74</td>
<td>4</td>
<td>5.4</td>
</tr>
<tr>
<td>1986</td>
<td>6</td>
<td>1</td>
<td>16.7</td>
<td>99</td>
<td>5</td>
<td>5.1</td>
</tr>
<tr>
<td>1987</td>
<td>3</td>
<td>1</td>
<td>33.3</td>
<td>135</td>
<td>40</td>
<td>29.6</td>
</tr>
<tr>
<td>1988</td>
<td>8</td>
<td>3</td>
<td>37.5</td>
<td>152</td>
<td>21</td>
<td>13.8</td>
</tr>
<tr>
<td>1989</td>
<td>13</td>
<td>7</td>
<td>53.8</td>
<td>315</td>
<td>118</td>
<td>37.5</td>
</tr>
<tr>
<td>1990</td>
<td>10</td>
<td>3</td>
<td>30.0</td>
<td>477</td>
<td>125</td>
<td>26.2</td>
</tr>
<tr>
<td>1991</td>
<td>31</td>
<td>19</td>
<td>61.3</td>
<td>492</td>
<td>269</td>
<td>54.7</td>
</tr>
<tr>
<td>1992</td>
<td>30</td>
<td>20</td>
<td>66.7</td>
<td>1288</td>
<td>372</td>
<td>28.9</td>
</tr>
<tr>
<td>1993</td>
<td>42</td>
<td>28</td>
<td>66.7</td>
<td>1380</td>
<td>567</td>
<td>41.1</td>
</tr>
<tr>
<td>1994</td>
<td>50</td>
<td>26</td>
<td>52.0</td>
<td>2091</td>
<td>1131</td>
<td>54.1</td>
</tr>
<tr>
<td>1995</td>
<td>60</td>
<td>51</td>
<td>85.0</td>
<td>2478</td>
<td>1324</td>
<td>53.4</td>
</tr>
<tr>
<td>1996</td>
<td>90</td>
<td>60</td>
<td>66.7</td>
<td>2884</td>
<td>1520</td>
<td>52.7</td>
</tr>
<tr>
<td>1997</td>
<td>119</td>
<td>71</td>
<td>59.7</td>
<td>3801</td>
<td>1992</td>
<td>52.4</td>
</tr>
<tr>
<td>1998</td>
<td>111</td>
<td>82</td>
<td>73.9</td>
<td>4617</td>
<td>2312</td>
<td>50.1</td>
</tr>
<tr>
<td>1999</td>
<td>125</td>
<td>84</td>
<td>67.2</td>
<td>4912</td>
<td>2690</td>
<td>54.8</td>
</tr>
<tr>
<td>2000</td>
<td>139</td>
<td>104</td>
<td>74.8</td>
<td>5553</td>
<td>2951</td>
<td>53.1</td>
</tr>
</tbody>
</table>
Diagnosticians should increase their index of suspicion of upper urinary tract uroliths in cats, especially those with chronic renal failure.

a Purdue Veterinary Medical Data Base. 1248 Lynn Hall, Purdue University, West Lafayette, IN 47906. Nephrolith is coded “722061500” and “710061500,” ureterolith is coded “723061500” and “723034324;” cystolith is coded “730061500,” “730061504,” and “730061505;” and urethral calculus is coded “740061500” and “740061505.”

b PROC GLM; SAS Institute, Cary, NC 27513-2414

Acknowledgment
The authors gratefully acknowledge the assistance of Yun Shen, Veterinary Medical Data Base, Purdue University, West Lafayette, Indiana.

References
Partial Foot Amputation in 11 Dogs

Eleven dogs with malignant tumors of the digits and feet were treated with partial foot amputation. Partial foot amputation involved amputation of one or both central weight-bearing digits. Lameness occurred in all dogs but resolved in eight dogs at a median of 37 days postoperatively. In the remaining three dogs, lameness improved but did not resolve. Tumor control was excellent, with no evidence of local recurrence in 10 dogs. One dog underwent limb amputation. Based on these results, partial foot amputation may be recommended in the management of malignant tumors of the canine foot in which more than one digit must be amputated to achieve adequate surgical margins. J Am Anim Hosp Assoc 2005;41:47-55.

Introduction

Tumors of the foot can originate from osseous or soft-tissue structures. Squamous cell carcinoma (SCC) and malignant melanoma are the most commonly described tumors of the canine digit, although soft-tissue sarcomas, osteosarcomas (OSA), mast cell tumors (MCT), and benign neoplasms have also been reported.1-3 Surgical options for the management of tumors of the foot include digit and limb amputation. Digit amputation provides adequate local tumor control for benign and malignant neoplasms confined to the nail bed, distal phalanges, and bones of the metacarpus or metatarsus.1-3 The 1- and 2-year survival rates in dogs with SCC of the digit not affecting the nail bed are significantly less than the survival rates in dogs with subungual SCC.2 Although the local recurrence rate and metastatic rate were not reported in this prior study, possible causes for the difference in survival rates included higher local recurrence from incomplete resection and/or a different or more aggressive biological behavior of SCC distant to the nail bed.2 Partial foot amputation and limb amputation are alternative surgical options for the management of malignant tumors of the proximal digit and those not confined to the skin, bone, or pads of a single digit.3-5

Limb amputation is a radical procedure, although most dogs adapt to ambulation on three legs within 1 month.6 However, the period of adaptation, especially initially, may be longer and more difficult in dogs without preexisting lameness. Most dogs with tumors of the digit or foot are presented because of the presence of a visible mass rather than for significant lameness.1 Partial foot amputation is a limb-sparing technique defined as the amputation of two adjacent digits. Partial foot amputation is not often recommended, as significant lameness has been reported following amputation of one or both weight-bearing digits.4,5 The purpose of this retrospective study was to examine the outcomes in 11 dogs following partial foot amputation for treatment of malignant tumors of the foot to determine whether partial foot amputation is a viable surgical option.
Materials and Methods

Medical records at Colorado State University Veterinary Teaching Hospital were reviewed for dogs that were treated with digit amputation from January 1992 to June 2002. Inclusion criteria included amputation of two adjacent digits exclusive of the first digit, the presence of a complete medical record, and follow-up telephone interviews with the owner and referring veterinarian that assessed tumor control, limb function, and the level of satisfaction with the outcome of surgery. Eleven dogs that underwent partial foot amputation for the treatment of neoplasia fulfilled the inclusion criteria.

Data retrieved from the records of each animal included signalment, site and type of the lesion of the digit or foot, presence or absence of lameness, surgical findings, adjunctive treatments, and postoperative outcome. Preoperative diagnostic tests and staging procedures, which were dependent on tumor type, were reviewed. The digits amputated and the level or point of amputation were recorded. The partial foot amputation was classified as "medial-foot" if the second and third digits were amputated, as "mid-foot" with amputation of the third and fourth digits, and as "lateral-foot" with amputation of the fourth and fifth digits. The levels of amputation were subdivided into metacarpophalangeal or metatarsophalangeal joint, metacarpal or metatarsal diaphysis, and carpometacarpal joint.

Four different outcomes were assessed, including survival, tumor control, limb function, and the degree of owner satisfaction with the procedure. Outcomes were assessed by telephone interviews with the owner and referring veterinarian. Survival parameters included whether the dog was still alive and, if not, the cause of death. Tumor control parameters included whether the tumor recurred at the surgical site, whether it metastasized, and if it had metastasized, the site and time of metastasis. Owners were asked to grade the degree of any lameness from 0 to 5, with 0 signifying no lameness and 5 representing nonweight-bearing lameness. The time to return of normal function in the affected limb and the degree of lameness during the postoperative recovery period were also determined. The characteristics of any lameness that persisted were also examined, especially in terms of whether it occurred at a walk, trot, and/or run, and whether the frequency of lameness was occasional, frequent, or constant. Owner satisfaction with the surgical procedure and outcome, both in terms of limb function and tumor control, was classified as dissatisfied, satisfied, or very satisfied.

Results

Signalment and Tumor Types

Eleven dogs with partial foot amputations satisfied the criteria for inclusion in this study. The median age of affected dogs was 8 years (range, 4 to 13 years). A variety of sizes of dogs was represented, and the median weight was 10 kg (range, 4.5 to 50 kg). Breeds of dogs in the study included four mixed-breed dogs, and one each of the cocker spaniel, golden retriever, Jack Russell terrier, Labrador retriever, Lhasa apso, miniature schnauzer, and rottweiler. Five dogs were neutered males, and six dogs were spayed females.

Partial foot amputation was performed for oncologic purposes in all dogs. The tumors treated included MCT (n=6, all grade II); OSA (n=2, one each of osseous and extraskeletal origin); and one each of a soft-tissue sarcoma (grade II), synovial cell sarcoma (grade I), and SCC [Table 1]. Partial foot amputation was performed for primary management of the mass in six dogs (case nos. 1, 2, 5, 6, 9, 10) [Figures 1, 2, 3], for incomplete prior excision of a tumor in four dogs (case nos. 3, 4, 8, 11), and following a complication of tumor resection in one dog (case no. 7) [Table 2]. In this last dog (case no. 7), surgical resection of a MCT between the third and fourth digits resulted in vascular interruption and avascular necrosis of the weight-bearing digits, requiring subsequent amputation. Tumors were located between the third and fourth digits of the foot of the right thoracic limb (n=4), left thoracic limb (n=2), right pelvic limb (n=2), and left pelvic limb (n=1). The fourth and fifth digits of the foot of the right pelvic limb (n=1) and the fourth metacarpus of the right thoracic limb (n=1) were also affected. Preoperative lameness was present in only two dogs, one with an extraskeletal OSA (case no. 1) and another with a synovial cell sarcoma (case no. 9).

Diagnostic Tests

Diagnostic tests and staging procedures included hematological tests (n=8), serum biochemical profiles (n=9), urinalyses
Table 1
Clinical Data on 11 Dogs With Partial Foot Amputations

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Signalment*</th>
<th>Tumor Location†</th>
<th>Amputated Digits‡‡</th>
<th>Amputation Level§</th>
<th>Postoperative Lameness</th>
<th>Lameness Severity and Conditions††</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9-y, 27.3-kg, SF golden retriever</td>
<td>LF 3-4</td>
<td>Mid LF</td>
<td>MC</td>
<td>Permanent, constant</td>
<td>2, W, T, R</td>
</tr>
<tr>
<td>2</td>
<td>13-y, 35.5-kg, SF Labrador retriever</td>
<td>LF 3-4</td>
<td>Mid LF</td>
<td>MCP joint</td>
<td>Temporary, 120 d</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>9-y, 9.1-kg, CM Jack Russell terrier</td>
<td>RF 3-4</td>
<td>Mid RF</td>
<td>MC</td>
<td>Temporary, 60 d</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>7-y, 10.0-kg, CM cocker spaniel</td>
<td>RH 3-4</td>
<td>Mid RH</td>
<td>MT</td>
<td>Temporary, 180 d</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>9-y, 28.6-kg, SF mixed-breed dog</td>
<td>RF 4</td>
<td>Lateral RF</td>
<td>MCC joint</td>
<td>Permanent, constant</td>
<td>2, W, T, R</td>
</tr>
<tr>
<td>6</td>
<td>8-y, 6.8-kg, SF miniature schnauzer</td>
<td>RH 4-5</td>
<td>Lateral RH</td>
<td>MT</td>
<td>Temporary, 14 d</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>8-y, 23.6-kg, SF mixed-breed dog</td>
<td>RF 3-4</td>
<td>Mid RF</td>
<td>MCP joint</td>
<td>Temporary, 60 d</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>4-y, 50.0-kg, CM rottweiler</td>
<td>LH 3-4</td>
<td>Mid LH</td>
<td>MT</td>
<td>Temporary, 7 d</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>7-y, 4.5-kg, SF mixed-breed dog</td>
<td>RF 3-4</td>
<td>Mid RF</td>
<td>MC</td>
<td>Temporary, 5 d</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>12-y, 6.8-kg, CM mixed-breed dog</td>
<td>RH 3-4</td>
<td>Mid RH</td>
<td>MTP joint</td>
<td>Permanent, occasional</td>
<td>1, R</td>
</tr>
<tr>
<td>11</td>
<td>7-y, 6.8-kg, CM Lhasa apso</td>
<td>RF 3-4</td>
<td>Mid RF</td>
<td>MCP joint</td>
<td>Temporary, 1 d</td>
<td>1</td>
</tr>
</tbody>
</table>

* SF=spayed female; CM=castrated male
† LF=left thoracic limb; RF=right thoracic limb; RH=right pelvic limb; LH=left pelvic limb; 3=third digit; 4=fourth digit; 5=fifth digit
‡‡ Mid=third and fourth digits; Lateral=fourth and fifth digits
§ MC=metacarpal; MCP=metacarpophalangeal; MT=metatarsal; MCC=carpometacarpal; MTP=metatarsophalangeal
†† 1=mild; 2=moderate; 3=severe; W=walk; T=trot; R=run
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diagnosis*</th>
<th>Adjunctive Therapy</th>
<th>Local Recurrence</th>
<th>Metastasis (d)</th>
<th>Metastasis Treatment</th>
<th>Alive</th>
<th>Survival Time (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OSA-ES</td>
<td>Transient cisplatin implant</td>
<td>No</td>
<td>None</td>
<td>-</td>
<td>Yes</td>
<td>455</td>
</tr>
<tr>
<td>2</td>
<td>MCT</td>
<td>Radiation therapy</td>
<td>No</td>
<td>None</td>
<td>-</td>
<td>No</td>
<td>464</td>
</tr>
<tr>
<td>3</td>
<td>Soft-tissue sarcoma</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>-</td>
<td>No</td>
<td>553</td>
</tr>
<tr>
<td>4</td>
<td>MCT</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>-</td>
<td>Yes</td>
<td>819</td>
</tr>
<tr>
<td>5</td>
<td>OSA</td>
<td>Chemotherapy</td>
<td>No</td>
<td>Lungs (634)</td>
<td>Metastasectomy</td>
<td>Yes</td>
<td>962</td>
</tr>
<tr>
<td>6</td>
<td>MCT</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>-</td>
<td>Yes</td>
<td>1198</td>
</tr>
<tr>
<td>7</td>
<td>MCT</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>-</td>
<td>No</td>
<td>1144</td>
</tr>
<tr>
<td>8</td>
<td>SCC</td>
<td>None</td>
<td>No</td>
<td>Lymph node (157)</td>
<td>Limb amputation</td>
<td>Yes</td>
<td>1312</td>
</tr>
<tr>
<td>9</td>
<td>Synovial cell sarcoma</td>
<td>Limb amputation</td>
<td>Not applicable</td>
<td>None</td>
<td>-</td>
<td>Yes</td>
<td>1766</td>
</tr>
<tr>
<td>10</td>
<td>MCT</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>-</td>
<td>No</td>
<td>2561</td>
</tr>
<tr>
<td>11</td>
<td>MCT</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>-</td>
<td>Yes</td>
<td>3028</td>
</tr>
</tbody>
</table>

* OSA=osteosarcoma; ES=extraskeletal; MCT=mast cell tumor; SCC=squamous cell carcinoma
(n=3), three-view thoracic radiographs (n=6), abdominal ultrasonography with guided aspirates of the liver and spleen (n=3), and bone marrow aspiration (n=6). Laboratory abnormalities were infrequent, nonspecific, and included elevated γ-glutamyl transferase (n=3) and mild hyperglycemia (n=2). There was no evidence of pulmonary metastasis on the thoracic radiographs of any dog. Abdominal ultrasonography and cytopathology of bone marrow aspirates and guided aspirates of the spleen and liver were performed for tumor staging in dogs with MCT. Systemic mastocytosis was not detected in any dog.

Surgical Technique
Partial foot amputation was performed in all dogs using a modified single-digit amputation technique. An elliptical incision was performed around the affected digits, extending from the distal aspect of the palmar or plantar surface of the base of the digits to the dorsal aspect of the metacarpus or metatarsus [Figure 4]. The incision included surgical margins of at least 2 cm around the tumor or the scar from previous incomplete tumor excision. In the fore foot, interosseous muscles were sectioned; tendons of the common and lateral digital extensors and superficial and deep digital flexors were transected; and branches of the dorsal and palmar common digital and metapodial artery and vein were either ligated or cauterized at the planned level of amputation.7 Similarly, in the hind foot, interosseous muscles were sectioned, and tendons of the long and lateral
digital extensors and superficial and deep digital flexors were transected. Branches of the dorsal and plantar metatarsal and common digital artery and vein were either ligated or cauterized at the planned level of amputation. A high-speed burr or bone cutters were used to perform amputations through the diaphysis of either the metacarpus or metatarsus (n=6). Disarticulation of either the metacarpophalangeal or metatarsophalangeal joint was completed by incising through the joint capsule and collateral and sesamoidean ligaments (n=5). The distal metacarpal or metatarsal condyles were not rongeured, and the palmar or plantar sesamoids were not routinely removed. The digits and tumor were removed en bloc with the digital pads, although metacarpal and metatarsal pads were preserved. Wound closure was usually performed in three layers, with the interosseous muscles and subcutaneous tissues apposed using absorbable suture material in an interrupted pattern, and the skin apposed with interrupted sutures of absorbable or nonabsorbable material [Figure 5].

A mid-foot amputation was performed in nine dogs [Figure 4], and a lateral-foot amputation was done in two dogs. Amputation was performed at the level of the metacarpophalangeal or metatarsophalangeal joint in four dogs, at the distal metacarpal or metatarsal diaphysis in six dogs, and at the carpometacarpal joint in one dog. Tumor margins were evaluated histopathologically in all cases, with the excision judged to be complete in eight dogs and incomplete in three dogs (case nos. 2, 9, 11).

**Adjunctive Therapies**

Postoperative management involved analgesics and bandages. Analgesia was provided in all cases with nonsteroidal anti-inflammatory drugs, opioids, or both. Carprofen (n=7) or piroxicam (n=4) was administered for 10 to 21 days following surgery. Opioid drugs administered included fentanyl in patch form (n=2) and morphine (n=5). Opioids were not used for more than 5 days postoperatively. A modified Robert-Jones bandage was applied to all operated limbs and was supplemented with a Mason metasplint in four dogs. The frequency of bandage changes and the duration of bandaging could not be determined from the medical records or from follow-up telephone calls.

Four dogs received additional therapy for their tumors [Table 2]. Radiation therapy was used in one dog (case no. 2) with an incompletely excised, grade II MCT of the mid-foot. External-beam radiation, consisting of 12 fractions of 3.2 Gy, was administered for a total dose of 38.4 Gy. The targetted radiation therapy protocol of 15 fractions was not reached in this dog, as acute radiation-induced moist desquamation and foot pad necrosis necessitated premature termination of radiation therapy. In one dog (case no. 9), thoracic limb amputation was performed 17 days after incomplete excision of a grade I synovial cell sarcoma. A local cisplatin implant was inserted at the surgical site in one dog (case no. 1), but it was removed 10 days postoperatively because of a surgical wound infection. One dog with a metacarpal OSA (case no. 5) was treated with an alternating protocol of intravenous doxorubicin (30 mg/m²) and carboplatin (300 mg/m²) administered every 3 weeks, for six total doses.

**Outcomes**

Surgical complications included lameness (n=11) and one superficial skin infection. In the dog with the surgical site infection (case no. 1), a biodegradable cisplatin implant was inserted into the wound cavity to reduce the risk of local tumor recurrence. The infection resolved following antimicrobial therapy and removal of the biodegradable sponge.

Lameness occurred in all dogs following surgery [Table 1]. Eight of the dogs returned to normal function, and lameness persisted in three dogs (case nos. 1, 5, 10). The median time to resolution of lameness was 37 days (range, 1 to 180 days). In one dog (case no. 2), the lameness that persisted for 120 days was partially attributed to digital pad necrosis secondary to adjunctive radiation therapy. The median severity of the immediate postoperative lameness
was 3 (range, 1 to 3). In the three dogs with persistent lameness, the lameness was graded as mild, with moderate to significant weight bearing, and was present either occasionally at a run (n=1) or constantly at a walk, trot, and run (n=2). These three dogs were diagnosed with OSA (n=2) or MCT (n=1). Both dogs with OSA weighed >25 kg, while the dog with MCT weighed 6.4 kg. Carpal hyperextension was diagnosed in one dog (case no. 5) following a lateral-foot amputation at the level of the carpometacarpal joint. Based on limb function and the degree of tumor control following partial-foot amputation, owners were either satisfied (n=4) or very satisfied (n=6).

Metastasis was diagnosed in two dogs. Metastasis of a digital SCC occurred to the popliteal lymph node of the same limb 157 days after a mid-foot amputation and was treated by pelvic limb amputation (case no. 8). This dog was disease-free and alive 1312 days after the initial partial foot amputation. In case no. 5, a single pulmonary metastasis was detected 574 days after a lateral-foot amputation for an osteosarcoma. Pulmonary metastasectomy was performed 60 days later, because the radiographic size of the pulmonary mass had increased by 40% (from 10-mm to 14-mm diameter), and no further pulmonary lesions were detected on thoracic radiographs and computed tomography scans.9 This dog was alive 962 days after partial foot amputation, with no evidence of local recurrence or distant metastasis.

There was no evidence of tumor in any dog at the termination of the study. The minimum follow-up time was 455 days, with a median of 1138 days (range, 455 to 2968 days). The median follow-up time for the six dogs with MCT was 1171 days (range, 464 to 3028 days). Individual follow-up times were 455 days for the dog with extraskeletal OSA; 553 days for the dog with soft-tissue sarcoma; 962 days for the dog with metacarpal OSA; 1312 days for the dog with digital SCC; and 1766 days for the dog with synovial cell carcinoma. Seven dogs were still alive (range, 455 to 3028 days), and four dogs had died from unrelated causes (range, 464 to 2561 days) by the end of the study.

Discussion

In the study reported here, partial foot amputation was performed in 11 dogs for local management of malignant tumors of the digits and foot. The locations of the tumors in these dogs precluded single-digit amputation, because the tumors involved the proximal digit or other areas of the foot, such as the interdigital webbing and pads of the digit, metacarpus, or metatarsus. Furthermore, adequate surgical margins could not be achieved with more conservative surgery because of the tumor size or the extent of surgical scar formation following incomplete tumor resection.10 Limb amputation was not initially performed in these dogs, as it was thought that partial foot amputation would provide comparable local control of the tumor while preserving limb function.

Local tumor control was excellent following partial foot amputation. Local recurrence was not reported in any dog, although two dogs had adjunctive therapy. The two dogs with histopathological evidence of incomplete tumor resection had either fractionated radiation therapy or a limb amputation to prevent local tumor recurrence. The use of adjunctive radiation therapy following incomplete excision of MCT is controversial, as there have been no significant differences reported in local recurrence rates following incomplete and complete MCT excision.11 One dog in the present study did not receive further treatment after incomplete excision of a MCT, but it was alive and disease-free 3028 days postoperatively.

Long-term systemic tumor control was good following partial foot amputation in the dogs of this report. Excluding the dog in which early limb amputation was performed, only two of 10 dogs had evidence of metastasis after a median follow-up time of 962 days (range, 455 to 3028 days).

Limb function following partial foot amputation was good to excellent. Partial foot amputation resulted in non-weight-bearing lameness in all dogs postoperatively. Pain control with analgesic drugs and bandaging were necessary during the immediate postoperative period. However, in most circumstances, analgesic drugs and bandages were discontinued within 21 days of the surgery. Eight (73%) dogs returned to normal limb function, while three (27%) dogs had varying degrees of persistent lameness. The degree of lameness in the latter three dogs was mild and did not seem to significantly impact the quality of life. The origin of lameness in these dogs was not determined, although possible causes included the dogs’ body weight and carpal instability arising from partial foot amputation at the level of the carpometacarpal joint (case no. 5).

Single-digit amputation of the third or fourth digit, amputation through a joint (phalangophalangeal, metacarpophalangeal, or metatarsophalangeal), and failure to remove metacarpophalangeal or metatarsophalangeal sesamoid bones have been reported as having a worse outcome.4,5,14 It should be realized, however, that minimal information has been published on single-digit amputation in dogs, and these results remain unsubstantiated.14,15 The findings of the study reported here contradict these earlier reports, as limb function was good to excellent even with removal of one or both weight-bearing digits, following amputation at different anatomical levels, and without removal of the sesamoid bones.

Amputations of the digits in ruminants and swine are analogous to partial foot amputation in dogs because of their different pedal anatomy.16-18 Prior reports of amputations of the digits in cattle have revealed poor results in heavier cattle and with amputation of the thoracic limb digits.18 In contrast, excellent results have been reported following amputation of the digits in sheep and pigs, both of which have a body weight closer to dogs.19,20 In the present study, the median body weight of affected dogs was only 10 kg, and permanent postoperative lameness was reported in the thoracic limb of two of four dogs with a body weight >25 kg. Postoperative lameness may be more likely in large dogs and following partial foot amputation in a thoracic limb, as higher weight-bearing loads are transmitted through the thoracic limb, and this load is proportionally greater in large dogs.21
In humans, ray resection is defined as the amputation of a digit and corresponding metatarsus. Ray resection of the hallux (first digit) and multiple ray resections are not recommended, as load redistribution results in transfer lesions, such as ulceration or trauma, in adjacent digits. In the study reported here, the weight-bearing portion of the foot was reconstructed with the second and fifth digits and included intact digital pads following mid-foot amputation. Reconstruction was not required after a lateral-foot amputation because of preservation of the third digit. The metacarpal or metatarsal pads were preserved in all cases. Ulceration or trauma of the digital, metacarpal, or metatarsal pads was not reported in any dog following partial foot amputation. Persistent lameness was uncommon in this study, possibly because foot reconstruction resulted in adequate load redistribution with acceptable absorption and transfer of weight-bearing forces. Further investigations using force-plate analysis are required to validate this supposition.

Partial ray resection, with preservation of the proximal metatarsus, is recommended in humans to prevent joint instability. One dog in this study (case no. 5) with a persistent weight-bearing lameness had a lateral amputation performed at the level of the carpometacarpal joint, resulting in carpal instability and mild carpal hyperextension. Amputation at the level of either the carpometacarpal or tarsometatarsal joint should be avoided because disruption of the collateral ligaments and palmar or plantar fibrocartilage may result in instability and lameness.

Owners of the dogs in this study were either satisfied or very satisfied with partial foot amputation for both local tumor control and limb function, regardless of the absence or presence of lameness. Pre- and postoperative orthopedic examination and kinetic and kinematic gait analysis would have been preferable to owner opinions for assessing subjective and objective degrees of lameness following partial foot amputation. These techniques were not performed because of the retrospective nature of the study. The subjective method utilized in this study for assessment of limb function following partial foot amputation was considered acceptable, as owner assessment and numerical grading scales are both regarded as reliable and reproducible in the evaluation of lameness and postoperative outcomes in animals.

Conclusion
Partial foot amputation was performed as a modification of the single-digit amputation technique in 11 dogs for local control of malignant foot tumors. Local tumor control following partial foot amputation was excellent, with no evidence of local recurrence after a median follow-up of 962 days. Limb function was good to excellent despite amputation of one or both weight-bearing digits. Further investigations are needed to determine whether the risk of permanent postoperative lameness is greater in dogs weighing >25 kg and following amputations at the level of the carpometacarpal or tarsometatarsal joints.

References


Comparison of Normograde and Retrograde Intramedullary Pinning of Feline Tibias

This study evaluated the effects of normograde and retrograde intramedullary pinning of mid-diaphyseal fractures of the feline tibia on the anatomical structures of the stifle joint. Using the paired pelvic limbs from five mature feline cadavers, a transverse, mid-diaphyseal osteotomy was performed, and each tibia was pinned in a normograde or retrograde fashion. The stifle joints were examined to determine the pin exit site and measure the distance from the exit site to pertinent anatomical structures of the stifle joint. Neither normograde nor retrograde intramedullary pinning resulted in damage to the cruciate ligaments, menisci, intermeniscal ligament, femoral condyles, or joint capsule. The patellar tendon was penetrated in all five tibias during retrograde pin insertion. J Am Anim Hosp Assoc 2005;41:56-60.

Introduction

Fractures of the tibia account for 15% to 20% of all fractures in small animals.1-4 In cats, tibial fractures most commonly occur in the diaphyseal region.5 Surgical stabilization of these fractures is often achieved by intramedullary pinning techniques, which are relatively easy to perform, require minimal equipment, and are less expensive than many other types of repair. Normograde pin insertion is an accepted and widely used method of fixation for tibial fractures in dogs and cats.2-4 Retrograde pin insertion is technically easier to perform and is commonly used to repair tibial fractures in clinical practice.

Studies performed in dogs indicate that retrograde insertion of intramedullary pins into the tibia involves a high risk of iatrogenic injury to structures of the stifle joint.1,6 Such injury is likely because the proximal bowing of the canine tibia aligns the diaphysis of the bone with the intracondylar eminence on the tibial plateau.6 As a result, intramedullary pins placed in a retrograde fashion often damage the cranial cruciate ligament, synovial membrane, or other stifle joint structures when the pin exits the proximal tibia.1,6

In fractures involving the proximal to mid-diaphyseal tibia, the risk of injury to the stifle joint can be minimized by intentionally directing the pin in a craniomedial direction during retrograde pin insertion, thus directing the pin away from the stifle joint.1 However, in mid-diaphyseal or distal diaphyseal fractures of the tibia, the pin follows the medullary cavity and exits the proximal tibia near the intercondylar eminence on the tibial plateau, resulting in penetration of the stifle joint and interference with the femoral condyle during joint motion.6 Subsequently, retrograde insertion of intramedullary pins for stabilization of mid-diaphyseal tibial fracture is not recommended in dogs.1,2,6

The effect of normograde and retrograde tibial pinning on anatomical structures within the stifle joint has not been extensively studied in cats.
Materials and Methods

Paired pelvic limbs from five, mature, domestic shorthair feline cadavers were collected, and the distal femurs, stifle joints, and tibias were radiographed. A limited surgical approach was made to expose the medial aspect of each tibia. A transverse osteotomy was performed at the mid-diaphysis using an oscillating bone saw. The location of the osteotomy was selected by determining the midpoint between the tibial plateau and distal aspect of the medial malleolus.

The left tibia from each pair was pinned using either a normograde or retrograde pinning technique (randomly assigned). The right tibia of each pair was pinned using the opposite technique. A double-trocar Steinmann pin, measuring 60% to 70% of the tibial diaphyseal diameter, was inserted using a Jacob’s hand chuck. For normograde pin insertion, the pin was started at a point midway between the tibial tuberosity and the medial tibial condyle on the medial ridge of the tibial plateau.\(^5\) The fracture was reduced and held in reduction with bone-holding forceps as the pin was driven into the distal tibial cortex. The stifle joint was held in 90˚ of flexion during pin insertion. The pin was left protruding from the skin proximally. For retrograde pin insertion, the Steinmann pin entered the medullary canal at the fracture site and was driven in a craniomedial direction into and through the proximal tibial cortex, surrounding soft tissue, and skin. The fracture was reduced and held in reduction with bone-holding forceps as the pin was directed in a retrograde fashion into the distal tibial cortex.\(^1\) The pin was left protruding from the skin proximally.

The stifle joints were exposed by careful dissection, and each pin was cut to a length of 3 to 4 mm above the tibial plateau.\(^5\) The joint was grossly inspected to determine each pin was cut to a length of 3 to 4 mm above the tibial plateau as evidenced by their distance to structures within the stifle joint. On the cadavers, calipers were used to measure the shortest distance (in mm) from the pin’s exit point to the insertion of the cranial cruciate ligament, the medial edge of the patellar tendon, the medial joint capsule, the medial and lateral menisci, and the cranial aspect of the tibial tuberosity.

The craniocaudal pin position was determined as described by Pard.\(^6\) The distance from the cranial aspect of the tibial tuberosity to the insertion of the medial collateral ligament on the tibia was measured. The distance from the pin’s exit site to the tibial tuberosity was also measured. The craniocaudal pin position was determined by the ratio:\(^6\)

\[
\text{Cranio-caudal pin position} = \frac{\text{Distance from pin tract to tibial tuberosity}}{\text{Distance from tibial tuberosity to \text{medial collateral ligament}}}
\]

The effect of the pinning technique (normograde or retrograde) on the distances from the pin’s exit site to anatomical structures of the stifle joint was analyzed using the paired t-test. The residuals from this model were examined using frequency histograms and normal probability plots. The data was reanalyzed using the Wilcoxon’s signed rank test if the normality assumption appeared to be substantially violated. The prevalence of penetration and direct damage to pertinent joint structures by the two pinning techniques were compared using McNemar’s test. The clinical importance of statistically significant differences was assessed using confidence intervals. A \(P\) value of \(\leq 0.05\) was considered significant for all tests.\(^a\)

Results

On visual assessments, neither normograde nor retrograde intramedullary pinning resulted in damage to the cranial cruciate ligament, medial or lateral menisci, intermeniscal ligament, femoral condyles, or medial joint capsule [Figures 1, 2]. However, during retrograde pinning, the patellar tendon was penetrated in all five cats. The pins penetrated the tendon 8.6±0.9 mm proximal to its insertion on the tibial tuberosity. Pins placed in normograde fashion exited 1.6±0.23 mm from the medial edge of the patellar tendon, but they did not penetrate or damage the tendon.

The distances from the pin’s exit site on the tibial plateau to structures of the stifle joint were measured after normograde and retrograde intramedullary pin insertions [see Table]. Pins placed in normograde fashion exited significantly closer to the cranial cruciate ligament than did pins inserted in retrograde fashion (\(P=0.01\)). Normograde pins were 2.9±0.34 mm from the cranial cruciate ligament. Retrograde pins were 4.2±0.10 mm from the cranial cruciate ligament. Pins placed in normograde fashion also exited significantly closer to the medial joint capsule than did pins inserted in retrograde fashion (\(P=0.02\)). Normograde pins were 1.9±0.11 mm from the joint capsule. Retrograde pins were 2.4±0.17 mm from the joint capsule. Pins placed in normograde fashion were not significantly closer to the medial (\(P=0.08\)) or lateral (\(P=0.15\)) menisci than those inserted in retrograde fashion.

Pins inserted in normograde fashion exited slightly more caudally on the tibial plateau as evidenced by their distance from the tibial tuberosity and measurements of cranio-caudal pin position. Pins placed in normograde fashion were 3.7±0.49 mm from the tibial tuberosity (cranio-caudal pin position, 0.29±0.05). Pins placed in retrograde fashion were 2.6±0.21 mm from the tibial tuberosity (cranio-caudal pin position, 0.08±0.05).
### Table

Mean Distances (mm) ± Standard Deviation Between the Exit Sites on the Tibial Plateau and Stifle Joint Structures for Normograde and Retrograde Intramedullary Pins Inserted in the Feline Tibia

<table>
<thead>
<tr>
<th></th>
<th>Cranial Cruciate Ligament</th>
<th>Patellar Tendon (medial edge)</th>
<th>Joint Capsule</th>
<th>Medial Meniscus</th>
<th>Lateral Meniscus</th>
<th>Tibial Tuberosity</th>
<th>Craniocaudal Pin Position *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normograde Pins (n=5)</td>
<td>2.9±0.34</td>
<td>1.6±0.23</td>
<td>1.9±0.11</td>
<td>2.9±0.35</td>
<td>5.4±0.32</td>
<td>3.7±0.49</td>
<td>0.29±0.05</td>
</tr>
<tr>
<td>Retrograde Pins (n=5)</td>
<td>4.2±0.10</td>
<td>0†</td>
<td>2.4±0.17</td>
<td>3.7±0.27</td>
<td>6.2±0.34</td>
<td>2.6±0.21</td>
<td>0.21±0.01</td>
</tr>
<tr>
<td>Comparison</td>
<td>0.01‡</td>
<td>0.003‡</td>
<td>0.02‡</td>
<td>0.08</td>
<td>0.15</td>
<td>0.09</td>
<td>0.12</td>
</tr>
</tbody>
</table>

* Craniocaudal pin position = Distance from pin tract to tibial tuberosity ÷ Distance from tibial tuberosity to medial collateral ligament
† All five pins inserted in retrograde fashion penetrated the patellar tendon.
‡ Significant difference between pins placed in normograde and retrograde fashion (P<0.05)
position, 0.21±0.01). These differences were not statistically significant (P=0.09 and 0.12, respectively).

**Discussion**

It is important to avoid damaging intraarticular and periarticular structures of the stifle joint when placing intramedullary pins for internal fixation of tibial fractures. Failure to do so can result in degenerative joint disease, fracture disease, and poor limb function. Retrograde placement of intramedullary pins in the tibia is technically easy and is commonly performed in clinical practice. However, studies in dogs found that retrograde pinning of mid-diaphyseal fractures resulted in a significantly greater risk of iatrogenic damage to stifle joint structures than normograde pinning.1,6 Because of the proximal bowing of the canine tibia, intramedullary pins placed in retrograde fashion often exit near (or actually damage) the cranial cruciate ligament, synovial membrane, or other stifle joint structures.1,6

The feline tibia is less angular and lacks the cranial bowing of the canine tibia. As a result, pins inserted into the feline tibia are positioned differently relative to the stifle joint than they are in dogs. The study reported here evaluated normograde and retrograde tibial pinning in cats in order to assess damage to joint structures and to determine pin positioning relative to the cruciate ligaments, medial and lateral menisci, medial joint capsule, and patellar tendon.

In cats, intramedullary pins placed in normograde fashion exited the tibia more caudally on the tibial plateau, placing them significantly closer to the cranial cruciate ligament and the medial joint capsule than pins inserted in retrograde fashion. This is opposite from the findings in the dog where normograde pins exited more cranially on the tibial plateau and were further from the cranial cruciate ligament and synovial cavity.6 However, pins inserted in normograde fashion in cats did not enter the joint or damage the cruciate ligaments, menisci, intermeniscal ligament, patellar tendon, or femoral condyles. In comparison, the frequency of patellar tendon penetration after normograde pinning in dogs was 0% to 10%.1,6

Intramedullary pins placed in retrograde fashion did not damage the cruciate ligaments, joint capsule, menisci, intermeniscal ligament, or femoral condyles in cats, which was in contrast to studies performed in dogs.1,6 In one canine study, retrograde pins interfered with the femoral condyle in 70% of 10 cases and penetrated the joint in 40%.6 In another study of dogs, the pin interfered with the femoral condyle in 96% of 25 cases when it was placed in retrograde fashion, and the pin interfered in 80% of 25 cases when it was placed in retrograde fashion and was directed craniomedially during insertion.1

However, in all the cats reported here, intramedullary pins placed in retrograde fashion (and directed craniomedially during insertion) penetrated the patellar tendon just proximal to its insertion on the tibial tuberosity. In one study of 25 dogs, 40% of pins placed in retrograde fashion penetrated the patellar tendon.1 In another canine study, pins placed in retrograde fashion penetrated the patellar tendon in 40% of 10 cases.

The straighter conformation of the feline tibia allowed insertion of pins in a retrograde fashion without damage to the cruciate ligaments, joint capsule, menisci, intermeniscal ligament, or femoral condyles, as occurs in dogs. The pins exited more cranially on the tibial plateau and thus avoided the stifle joint; however, damage to the patellar tendon occurred in all five cats, even when the pin was directed craniomedially during insertion.

**Conclusion**

The results of this study indicated that normograde pinning of the feline tibia does not result in damage to stifle joint structures.
structures and can probably be used safely for repair of mid-diaphyseal tibial fractures in cats. Retrograde pinning, while not causing damage to intraarticular structures of the stifle joint, did penetrate the patellar tendon and must be used with caution.

Acknowledgment
The authors acknowledge Dr. Carolyn Boyle for her assistance with the statistical analyses.

References
The Effects of Heated and Room-Temperature Abdominal Lavage Solutions on Core Body Temperature in Dogs Undergoing Celiotomy

To document the magnitude of temperature elevation obtained with heated lavage solutions during abdominal lavage, 18 dogs were lavaged with sterile isotonic saline intraoperatively (i.e., during a celiotomy). In nine dogs, room-temperature saline was used. In the remaining nine dogs, saline heated to 43±2°C (110±4°F) was used. Esophageal, rectal, and tympanic temperatures were recorded every 60 seconds for 15 minutes after initiation of the lavage. Temperature levels decreased in dogs lavaged with room-temperature saline. Temperature levels increased significantly in dogs lavaged with heated saline after 2 to 6 minutes of lavage, and temperatures continued to increase throughout the 15-minute lavage period. J Am Anim Hosp Assoc 2005;41:61-67.

Introduction

Hypothermia is common in dogs undergoing celiotomies.1 In a normal, awake dog, conductive heat loss is negligible because of the small surface area in contact with the ground and the insulated padding on the palmar and plantar aspects of the distal limbs.1 However, during anesthesia and celiotomy, the recumbent animal has greater surface area in contact with the table, and conductive heat loss increases. The low specific heat of stainless steel surgical tables compared to body tissues enhances conductive heat loss. Heat loss from radiation, convection, and evaporation is also increased during a celiotomy, because greater surface area is exposed when the abdominal cavity is opened. Anesthetic agents disrupt the normal vasoactive responses used to regulate body temperature and also contribute to heat loss during celiotomy.1 Factors affecting the development of hypothermia in surgical patients include duration of the procedure, choice of anesthetic agents, ambient temperature of the operating room, body condition score of the animal, size of the animal, and the nature of the surgical procedure.1-4

Numerous studies have documented an increase in anesthetic recovery time and increased morbidity and mortality in hypothermic patients (human and veterinary).1-9 Hypothermia of even a few degrees can increase recovery times in human surgical patients.1,6 For this reason, various methods are used to help maintain an animal’s body temperature during surgery, including circulating hot-water blankets, circulating heated air units, hot-water bottles, warmed intravenous fluids, and warmed inhaled anesthetic gases.10-13

Successful management of hypothermia in surgical patients requires an accurate means of recording and monitoring changes in core temperatures. Direct means of measuring core temperature, including the implantation of thermisters in a central vein, are limited by their invasiveness and the necessity of maintaining a sterile surgical field.13
Therefore, rectal thermography, esophageal thermography, and tympanic thermometers are often used to indirectly determine core body temperatures in animals undergoing abdominal surgery.1,4,7

During celiotomy, the abdominal cavity is typically lavaged with saline solution to dilute and remove contaminants. Warmed solution is recommended and is thought to help increase or maintain body temperature by convection of heat from the lavage solution to the animal.14,15 While the practice of using warm lavage solution is widely accepted, little is known regarding its effects on an animal’s core temperature. It is unclear if warmed lavage actually increases core temperature following abdominal exploratory surgery or simply slows heat loss; what the optimum temperature of the solution should be; and how long the solution must be present in the abdominal cavity to increase core temperature. The vasodilatation that occurs with warmed lavage may also predispose to additional heat loss during the procedure, as has been documented when warmed irrigants are used during arthroscopic procedures.16

The purpose of this study was to assess the benefits of warmed peritoneal lavage as a means of improving or maintaining core body temperature in anesthetized dogs during celiotomy. It was hypothesized that a significant difference in final core temperatures would be detected between dogs that received warmed lavage and dogs that received room-temperature lavage solutions.

Materials and Methods
This study was approved by the Mississippi State University’s Institutional Animal Care and Use Committee. Eighteen mixed-breed dogs (10 to 20 kg) scheduled for abdominal exploratory, as part of a veterinary student surgical teaching laboratory, were included in the study. Each dog was positioned in dorsal recumbency on a surgical table. A towel was placed between the table and the dog as insulation to minimize conductive losses to the table. Each dog was premedicated with intramuscular injections of butorphanol10 (0.2 mg/kg) and acepromazine10 (0.05 mg/kg). Anesthesia was induced with an intravenous injection of thiopental10 (6 to 10 mg/kg to effect) and maintained with isoflurane10 in oxygen administered via an endotracheal tube.

At the end of the surgical procedure and prior to performing abdominal lavage, a temperature probe10 was inserted into the esophagus of each dog to the level of the eighth intercostal space. A second probe was placed 6 cm into the rectum. The probes were connected to a physiograph unit10 to continuously record temperature measurements. The temperature probes were calibrated to within 0.1°C using a known temperature water bath prior to insertion into the esophagus and rectum. A tympanic thermometer was used to obtain tympanic temperatures.8 A thermistor was also placed in the abdominal cavity at the level of the left kidney and was connected to a physiograph unit to record the temperature of the abdominal lavage solution.8 The temperature of the operating room was also recorded throughout the lavage period.

Experimental Procedures
The dogs were randomly assigned to one of two groups. Dogs in Group 1 were lavaged with sterile isotonic saline at the ambient room temperature, which was maintained at 70±3°F (21±1°C). Dogs in Group 2 were lavaged with sterile saline heated to 110±4°F (43±2°C). The abdominal cavity of each dog was continuously filled to capacity with lavage solution. The lavage solution was allowed to sit for a period of 10 seconds, then continuous suction was applied. Continuous suction through a Poole suction tip1 was achieved by placing the suction device at the level of the right kidney. The suction tip was used to remove the lavage solution at the same rate as fluid was infused into the abdomen, ensuring that the abdominal cavity remained full and that the temperature of the saline remained constant. The temperature of the abdominal cavity lavage solution was continuously monitored via a thermistor probe that was located at the level of the left kidney.

Temperature recordings were obtained from the tympanic, rectal, esophageal, and abdominal probes every 60 seconds during the 15-minute lavage period. After the lavage period, the suction and temperature probes were removed, and the abdominal incisions were closed routinely.

Statistical Analysis
Sample size estimations were performed prior to the study10 using data from a previous report evaluating the effects of heated irrigation fluid used during arthroscopic surgery in humans.16 Comparable variations in body temperature were assumed for the study reported here. Data was initially analyzed using descriptive statistics (e.g., Student’s t-test, analysis of variance [ANOVA]) to evaluate the clinical importance of changes in body temperature associated with abdominal lavage. Temperature data from the esophagus, rectum, and tympanum was analyzed using a repeated measurements ANOVA with one between-subject factor (fluid temperature) and one within-subject factor (time). Means were further separated using the Least Significant Difference Test. Confidence intervals were calculated to characterize the clinical importance of these differences. Correlation between body temperature and lavage fluid temperature was assessed using Pearson’s product-moment correlation coefficient. Statistical computations were performed using the SAS System.8 The level of significance for all tests was set at $P<0.05$.

Results
Prior to initiation of the lavage, the mean temperature of the combined methods of temperature recording (tympanic, esophageal, and rectal) of the nine dogs in Group 1 (room-temperature lavage solution) was 94.8°F (34.8°C). The combined temperatures ranged from 89.4°F (31.9°C) to 98.4°F (36.9°C). The mean of the combined temperatures of the nine dogs in Group 2 (heated lavage solution) was 93.7°F (34.2°C). The combined temperatures ranged from 89.4°F (31.9°C) to 95.5°F (35.3°C). The difference in initial body temperature reflected the variable duration of the surgical
procedure prior to abdominal lavage. At completion of the lavage procedure, the dogs in Group 1 had a mean core temperature of 90.1°F (32.3°C), with a range of 82.7°F (28.2°C) to 94.0°F (34.4°C). The dogs in Group 2 had a mean post-lavage temperature of 97.4°F (36.4°C), with a range of 94.2°F (34.6°C) to 100.6°F (38.1°C). The ambient room temperature throughout the lavage procedure was maintained between 65°F (18.3°C) and 72°F (22°C).

In dogs lavaged with room-temperature saline (Group 1), body temperature was significantly lower by the end of the 15-minute lavage period as measured by the esophageal ($P<0.001$), rectal ($P<0.01$), and tympanic ($P<0.01$) probes. The core body temperature decreased significantly compared to prelavage levels (time 0) at 3 minutes after the initiation of the lavage as measured by the esophageal probe ($P=0.031$), at 4 minutes as measured by the rectal probe ($P=0.027$), and at 6 minutes as measured by the tympanic probe ($P=0.006$).

In dogs lavaged with heated saline (Group 2), body temperature was significantly higher at the end of the 15-minute lavage period as measured by esophageal ($P<0.001$), rectal ($P<0.001$), and tympanic ($P<0.001$) probes. The core body temperature increased significantly compared to prelavage levels at 2 minutes after the initiation of the lavage as measured by the esophageal probe ($P=0.009$), at 3 minutes as measured by the rectal probe ($P=0.022$), and at 6 minutes as measured by the tympanic probe ($P=0.019$).

Esophageal temperatures were significantly higher ($P=0.029$) in dogs lavaged with heated saline than in dogs lavaged with room-temperature saline beginning at the 6-minute mark of the procedure [Figure 1]. Rectal temperatures were significantly higher ($P=0.032$) in dogs lavaged with heated saline than in dogs lavaged with room-temperature saline beginning at the 5-minute mark of the procedure [Figure 2]. Tympanic temperatures were significantly higher ($P=0.004$) in dogs lavaged with heated saline than in dogs lavaged with room-temperature saline after 6 minutes of lavage [Figure 3]. A substantial difference in time was required for a statistically significant change in temperature to occur between Groups 1 and 2 (comparing heated versus room-temperature lavage), as compared to the time required for a significant change to occur in temperature from time 0 when Groups 1 and 2 were independently evaluated. This apparent lag time was caused by the slight difference in the mean core temperature recorded between Groups 1 and 2 at time 0, with the room-temperature lavage subjects having an overall higher initial core temperature than the heated lavage subjects. After 15 minutes of lavage, core temperatures were significantly higher in dogs lavaged with heated saline than in dogslavaged with room-temperature saline as measured by esophageal ($P<0.001$), rectal ($P<0.001$), and tympanic ($P<0.001$) thermometers.

No apparent change occurred in the temperature of the heated lavage solutions throughout the procedure. The room-temperature lavage solution maintained a constant temperature after attaining a steady-state temperature at around 3 minutes. The room-temperature lavage solution remained largely unchanged except for the 0- to 2-minute time period when the solution temperature increased from 69.7°F (20.9°C) to 85.4°F (29.7°C).

Lavage and core body temperature recordings were discontinued upon completion of the 15-minute lavage period. Grossly, no adverse effects were noted from the heated saline on the abdominal viscera prior to closure of the以外は、適切なテキストが提供されていません。
incisions. All the dogs in this study were euthanized prior to or at the end of surgery, so no specific comments could be made as to the effect of the heated lavage on the recovery of the animal. Several of the dogs were euthanized prior to complete closure of the abdomen, so no comments could be made on the postlavage effects of maintaining core temperature into the recovery period.

Pearson’s correlation coefficients were calculated between the temperature recording methods used in the study. The overall correlation for all dogs of tympanic to rectal and tympanic to esophageal temperatures were r=0.863 and 0.881, respectively. Esophageal and rectal temperature probes had a lower correlation coefficient (r=0.690). These findings were consistent with an individual study group correlation of r=0.849 (tympanic to rectal), r=0.903 (tympanic to esophageal), and r=0.766 (rectal to esophageal) for Group 2 (heated lavage). The correlation coefficients for Group 1 (room-temperature lavage) were r=0.851 (tympanic to rectal), r=0.770 (tympanic to esophageal), and r=0.534 (rectal to esophageal).

Discussion

Mild hypothermia is common in animals undergoing any surgical procedure, particularly celiotomy.1 The significant heat loss during abdominal surgery is attributed to the increased surface area present for heat exchange, the retardation of normal thermodynamic control of the body by anesthetic agents, and the direct exposure of the core body compartment to ambient room temperatures.1,4,5,7 Evidence suggests that hypothermia increases morbidity and mortality in animals and should be prevented whenever possible.3,5-7,9,12,13 When hypothermia occurs, effective treatment is needed to reduce complications.

Currently, many efforts that address perioperative hypothermia focus on preventing heat loss to the environment through the use of external heating systems. These
methods effectively reduce heat loss from the periphery of the body, but they do not improve the animal’s core temperature in many cases. Surface heating systems do not increase core temperatures unless the temperature of the heating system exceeds the patient’s core temperature. The heat must then pass through a thermal gradient to effectively increase core temperature. Additionally, complications occur when surface heating systems are used at higher temperatures. Surface burns are reported in animals with prolonged exposure to heating pads set at 42˚C.19 This consequence is greater during surgery, because animals are unable to shift their bodies to avoid prolonged exposure to the heating pads. The disruptive effects of anesthesia on peripheral circulation in animals may also increase the likelihood of thermal injury from surface heating systems.

Other methods of rewarming hypothermic surgical and nonsurgical patients have been evaluated.1,2,5,10,11 Extracorporeal warming and bypass technology are superior to external heaters, heated insufflation gases, and warmed lavage.1,2,17,18 However, their use is limited in animals by their expense, invasiveness, and the need for experienced personnel to operate the necessary equipment.17 As a result, more practical methods of rewarming animals have been sought. In humans, peritoneal lavage with warmed isotonic saline has been an excellent method of rewarming severely hypothermic patients compared to external warming methods and the use of heated inhalation agents. In a controlled comparison between peritoneal lavage and heated inhalation agents in severely hypothermic humans (i.e., core temperature of 25˚C), warmed peritoneal lavage required an average of 193 minutes to rewarm the people, compared to 332 minutes for heated inhalation.2 Gastric and thoracic lavage has also been shown to be more effective in increasing core temperature than exposure to an elevated ambient temperature, heated surface warmers, or heated insufflated gases in dogs.18 These findings suggest that the use of warmed peritoneal lavage may increase the animal’s body temperature and decrease postoperative recovery time and morbidity.5,7 Results of the study reported here confirmed that the use of warmed peritoneal lavage solutions increased body temperature in dogs undergoing celiotomy. Factors that may influence the efficacy of abdominal lavage include temperature of the solution, duration of the lavage, and the animal’s initial body temperature. In this study, at least 2 to 6 minutes of lavage with saline at 110±4˚F (43±2˚C) were required to significantly increase body temperature.

The optimum temperature of a peritoneal lavage solution for effectively increasing body temperature in dogs without causing injury to abdominal viscera is unknown. The room-temperature lavage used in Group 1 in this study actually decreased body temperature in dogs after only 3 to 6 minutes (depending on the method of temperature measurement). As expected, room-temperature lavage solutions were ineffective for warming, and they are not recommended for clinical use. This study demonstrated the importance of not allowing solutions intended for use as abdominal lavage to cool in the operating room prior to administration.

The heated saline solution used in this study was 110±4˚F (43±2˚C), and it effectively increased body temperature in dogs.

A limitation of the study was that the nonsurvival aspect of the laboratory exercise did not allow evaluation of core temperatures during closure of the abdominal incision or an evaluation of the effect on the overall recovery time. Further research in these areas is required. The study described here also did not investigate lavage solutions at higher temperatures. Intuitively, the use of warmer lavage solutions would decrease the time required for rewarming; however, the use of lavage solutions that are excessively warm could cause thermal injury to abdominal tissues.19

The duration of lavage required to effectively increase core temperature in a dog during celiotomy depends on the dog’s initial body temperature, the temperature of the lavage solution, and the magnitude of continued heat loss. The continued application of a warmed lavage solution increases the dog’s temperature as long as the solution is warmer than the animal’s core temperature. Throughout the lavage period, the abdomen remains open, and heat loss continues through radiation, convection, conduction, and evaporation. The application of a heated solution causes vasodilatation, which may increase heat loss from the viscera.1,16 The loss of heat from the abdomen caused by vasodilatation may impact the overall effectiveness of heated lavage to maintain normothermia during closure of the abdominal incision. This effect was not addressed in the study reported here. In this study, lavage with saline solution at 110±4˚F (43±2˚C) significantly increased core temperature after 2 to 6 minutes. Core temperature continued to increase throughout the 15-minute lavage period. Practically, the surgeon must weigh the advantages of continuing peritoneal lavage to further warm the animal against the risks of increased anesthetic and surgical time.

Difficulties in assessing the effects of lavage solution on core body temperature include the accurate measurement of core temperature without the invasive implantation of thermistors and measuring core temperature without compromising sterility of the surgical field. In this study, temperature measurements were obtained using esophageal, rectal, and tympanic temperature probes. Esophageal and rectal temperature measurements vary slightly from measurements taken via thermistors implanted in a central vein.20 This difference has been attributed to factors such as the metabolic processes within the stomach and colon, inconsistent placement of the temperature probes, the sensitivity of the equipment used, and the presence of fecal material within the rectum that may insulate the probe from the surrounding tissues.20,21 The rectal probe may also be affected by the temperature of the lavage solution as it is poured into the abdomen. The rectal temperature probes were consistently inserted 6 cm into the rectum to limit these variables. In the study reported here, the esophageal temperature probe was inserted to the level of the eighth intercostal space in order to place it directly over the heart and to reduce artifactual increases in temperature readings.
caused by metabolic activity in the stomach. Temperatures were recorded from three separate body locations to reduce the possibility that variation at an individual site would influence the results.

Differences were observed in the times at which the various temperature recording probes detected a change in body temperature. The rectal and esophageal probes consistently detected increases or decreases in temperature earlier than the tympanic thermometer. This faster detection may have arisen because the anatomical positions of the rectal and esophageal probes were closer to the body’s core. However, these probes were also in closer proximity to the lavage solution and may have been influenced by the temperature of the solution itself. Also, the tympanic thermometer was incapable of reading temperatures <92°F and would have failed to obtain some readings in the more hypothermic animals.

This study documented the efficacy of warmed peritoneal lavage solution in increasing body temperatures in dogs during celiotomy. The optimum temperature of the peritoneal lavage solution was not determined, although a solution warmer than the normal core temperature of the animal is required to allow sufficient transfer of heat. A peritoneal lavage solution heated to 110±4°F (43±2°C) effectively increased body temperatures in dogs undergoing celiotomy in the study reported here.

In this study, a lag time of 2 to 3 minutes was noted between initiation of room-temperature lavage and reaching a steady-state temperature of abdominal lavage solution. This period of temperature fluctuation likely occurred from a shift in heat from the animal to the lavage fluid, because the increase in temperature of the lavage fluid coincided directly with the reduction in body temperature as recorded by the temperature probes. This same effect can be anticipated with the use of warmed saline.

The length of time the abdomen should be lavaged to warm the animal depends on several factors, including the initial temperature of the animal, the temperature of the lavage solution, the weight of the animal, and body conformation. Larger animals and animals with higher fat stores in the abdomen require more heat energy to effectively increase their body temperatures, thus requiring potentially longer lavage periods to achieve an appreciable difference. The exact effects of body condition and size of the animal were beyond the scope of this study, so a standard range of body weight was used as a means to limit variability.

The volume of lavage used in clinical applications, and thus the length of duration of the lavage prior to closure of a celiotomy varies depending on animal size and level of contamination of the surgery. A more contaminated surgery usually requires a higher volume of lavage solution to be used in order to reduce the negative effects of the contamination. When lavage is indicated for dilution of contamination, the use of heated lavage solution is recommended in order to limit hypothermia and improve recovery time.

Variability exists between surgeons for closure times of abdominal incisions, and it is possible that a significant amount of heat could be lost during closure of the abdomen. Additional studies are needed to document an optimal time for closure of the incision in the line. In this study, a minimum of 2 to 6 minutes was required for effective heat exchange to begin between the lavage solution and the tissues. It can be assumed that once the heated solution is removed from the abdominal cavity, heat losses will continue until closure is completed and anesthesia is discontinued.

Conclusion

The use of heated abdominal lavage was an effective means of improving core temperatures in mildly hypothermic animals during celiotomy procedures. Significant increases in core temperatures were obtained after several minutes using a lavage solution heated to 110±4°F (43±2°C). Heated lavage was superior for maintaining or obtaining normo-thermia in animals compared to room-temperature lavage. Further research is required to determine an optimal lavage temperature and time. The vasodilatory effects of heated lavage may increase the rate of heat loss from the abdominal cavity following the lavage procedure; therefore, closure of the abdominal cavity should commence as soon as the lavage procedure is completed.

References

Heinz Body Hemolytic Anemia With Eccentrocytosis From Ingestion of Chinese Chive (Allium tuberosum) and Garlic (Allium sativum) in a Dog

A 4-year-old, intact male miniature schnauzer was presented with anorexia. The dog had ingested some Chinese steamed dumplings 2 days before, which contained Chinese chive (Allium tuberosum) and garlic (Allium sativum). Hematological examinations revealed severe Heinz body hemolytic anemia with eccentrocytosis and an increased concentration of methemoglobin, which was thought to result from oxidative damage to erythrocytes by constituents in these Allium plants. In this case, eccentrocytosis was a hallmark finding and could be detected easily, suggesting that this hematological abnormality is useful in diagnosing Allium plant-induced hemolysis. J Am Anim Hosp Assoc 2005;41:68-73.

Introduction

In dogs and cats, onion (Allium cepa) is known to be oxidatively toxic to erythrocytes, resulting in hemolytic anemia. Ingestion of garlic (Allium sativum) can also experimentally induce hemolysis in dogs as a result of oxidative damage to erythrocytes. Other members of the genus Allium are not known to cause hemolysis in dogs and cats, although wild onion (A. validum and A. canadense) and wild garlic (A. ursinum) are reported to cause hemolytic anemia in ruminants and horses.

Chinese chive (A. tuberosum) is a strong-flavored herb of commercial importance in East Asia, especially in Japan, Korea, and China. It has edible foliage leaves, but no bulbs. The external appearance of this plant resembles that of A. ampeloprasum, which includes several distinct crop types (i.e., leek, kurrat, great-headed garlic, pearl onion) from Europe and the United States. Chinese chive has not been reported to be toxic to domestic animals.

The following case report describes an adult dog that developed severe hemolytic anemia after ingesting Chinese food containing Chinese chive and garlic. To the authors’ knowledge, this is the first report of naturally occurring hemolytic anemia in a dog caused by Chinese chive and/or garlic.

Case Report

A 4-year-old, 7.2-kg, intact male miniature schnauzer was presented to a private animal hospital for anorexia unassociated with vomiting and diarrhea, starting the previous night. The owner reported the dog had ingested some Chinese steamed dumplings 2 days before and that the urine was dark in color for 1 day. The steamed dumpling was composed of minced pork and vegetables wrapped in a small pancake, and it contained Chinese chive and garlic. The amount of these Allium plants ingested by the dog was unknown. Initial physical examination revealed a mildly depressed dog with a rectal temperature of 102.4°F (39.1°C) and slightly...
pale, dark mucous membranes. Collected venous blood was
dark brown in color.

A complete blood count at admission (day 2 postingestion)
revealed a mild anemia (hematocrit [Hct] of 33%; reference
range, 36% to 54%), reddish plasma from hemolysis, and a
high mean corpuscular hemoglobin concentration (MCHC) of
36.5% (reference range, 30.5% to 36.1%) [Figure 1].
Moderate leukocytosis (17,500/µL; reference range, 5100 to
10,700/µL) with a neutrophilia (11,200/µL; reference range,
1400 to 8100/µL) and a left shift (bands 1663/µL; reference
range, 50 to 900/µL) were also noted [Figure 2]. Analysis of a
stained blood smear revealed many eccentrocytes with hemo-
globin that appeared dense and contracted to one side of the
cell, with a pale area on the other side and projections on the
cell surface that looked like Heinz bodies [Figure 3]. The per-
centage of eccentrocytes on day 2 was 37.5% of all erythro-
cytes [Figure 4]. Results of blood chemistry analyses at initial
presentation were within normal limits.

![Figure 1](image1.png)
**Figure 1**—Changes in hematocrit (Hct, A), mean corpuscu-
lar hemoglobin concentration (MCHC, B), and mean cell
volume (MCV, C) in a dog fed Chinese chive and garlic.
Days represent time after ingestion of *Allium* plants.

![Figure 2](image2.png)
**Figure 2**—Changes in leukocyte (A) and platelet (B)
counts in a dog fed Chinese chive and garlic. Days repre-
sent time after ingestion of *Allium* plants.

![Figure 3](image3.png)
**Figure 3**—Photomicrograph of a blood smear taken on
day 2 from a dog fed Chinese chive and garlic.
Eccentrocytes (closed arrows) and projections that look
like Heinz bodies (open arrows) are visible (Hemacolor
stain; bar=10 µm).
Based on these hematological findings, oxidative damage to erythrocytes was suspected from the ingestion of Chinese chive and garlic.

Initial therapy at the private animal hospital included subcutaneous lactated Ringer’s solution with B-complex vitamins to promote diuresis and prevent formation of hemoglobin casts and tubular nephrosis; famotidineb (0.7 mg/kg subcutaneously [SC]) to prevent gastric ulceration; and orbifloxacin (5 mg/kg SC) to prevent secondary infections. In addition, human recombinant erythropoietin (epoetin alpha, d 50 IU/kg SC) was administered to accelerate regeneration of erythroid cells. On day 3 postingestion, the Hct had decreased to 23%, and the MCHC had increased to 37.4% secondary to hemolysis [Figure 1].

On day 4 postingestion, the dog was presented to the Veterinary Teaching Hospital at Hokkaido University for evaluation of progressive anemia. Pale mucous membranes were observed on physical examination, and collected venous blood appeared dark brown. Hemolysis was not observed in the serum, and the MCHC had returned to normal (34.2%). The Hct reached a nadir (19%) on day 4 postingestion [Figure 1]. At the same time, the percentage of eccentricocytes remained high (21.6%), and erythrocytes containing Heinz bodies accounted for 44.3% of all the erythrocytes [Figure 4]. Methemoglobin concentration was measured using the method reported by Hegesh et al. and was found to be high (2.1%) [Figure 5] compared to the reference range (<1%). Methemoglobinemia was thought to be the cause of the dark color of the blood. Persistent leukocytosis (16,400/µL) and a decrease in the platelet count (114,000/µL; reference range, 160,000 to 600,000/µL) were also observed [Figure 2].

The dog’s anorexia and slight depression were treated with lactated Ringer’s solution SC, supplemented with vitamin B-complex and vitamin C, oral administration of a concentrated high-calorie liquid diet, and an oral vitamin and mineral supplement.

The antioxidative status of the dog was examined using erythrocytes collected on day 4 to rule out a high susceptibility to oxidative stress as a genetic trait. The concentration of reduced glutathione and the activities of superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, reduced nicotinamide adenine dinucleotide methemoglobin reductase, glucose-6-dehydrogenase, and 6-phosphogluconate dehydrogenase were measured according to the methods described by Beutler. The reduced glutathione concentration (8.5 µmol/gHb; reference range, 6.1 to 13.6 µmol/gHb) [Figure 5] and all the enzyme activities were within reference ranges or slightly higher than their reference ranges (probably because of the high percentage...
of young erythrocytes in circulation). In addition, results of an osmotic fragility test and analysis of hemoglobin composition using high-performance liquid chromatography were also normal.10,11 On day 5 postingestion, the Hct value had increased (21%), indicating a regenerative response. The regeneration of erythrocytes also resulted in a higher mean cell volume (MCV, 83.7 fL; reference range, 57 to 66 fL) and a greater percentage of circulating reticulocytes (4.5%) [Figure 6]. The oral administration of vitamin E (tocopherol acetate; 7 mg/kg q 12 hours) was also initiated to prevent further oxidative damage to erythrocytes.

On day 9, the dog’s appetite and activity level began to recover. The erythrocyte regenerative response was also dramatic, with an MCV of 93.3 fL [Figure 1] and a reticulocyte count of 10.1% [Figure 6]. The Hct had increased to 25%, and the reduced glutathione concentration in erythrocytes was also increased (9.4 µmol/gHb) [Figure 5]. The reduced glutathione elevation was probably attributable to the release of young erythrocytes. The number of eccentrocytes (1.6%), the number of erythrocytes with Heinz bodies (5.7%), and the methemoglobin concentration (0.6%) were markedly decreased. The platelet count continued to decline until day 9 (82,000/µL), while the leukocyte count (10,400/µL) returned to normal [Figure 2].

Fluid therapy and the concentrated high-calorie liquid diet were withdrawn on day 9, but the vitamin E (7 mg/kg q 24 hours) and a commercial supplement of vitamins and minerals were continued until day 22. At day 22 postingestion, the anemia was improved and all other hematological data were almost normal. Hemolytic anemia has not recurred, and the dog has remained hematologically normal for several years.

Figure 6—Changes in reticulocyte percentage in a dog fed Chinese chive and garlic. Days represent time after ingestion of Allium plants.

Discussion

Heinz bodies arise from the denaturation of hemoglobin through a sequence of oxidative steps.12,13 Methemoglobin forms when the iron moiety of heme protein is oxidized from the ferrous (II) to the ferric (III) state. Erythrocytes containing Heinz bodies are less deformable than normal erythrocytes.14 They tend to become sequestered in the reticuloendothelial system, where the Heinz bodies become pitted and the entire cell may be phagocytosed by macrophages.15 Eccentrocytes may form as a result of direct oxidative injury to erythrocyte membranes by adhesion of internal aspects of the cell membrane.16-19 Eccentrocytes are rigid and spheroid with intrinsic membrane alterations that make them susceptible to entrapment and removal by the mononuclear phagocytic system.16 Heinz bodies and collapsed membranes of eccentrocytes become pitted in the reticuloendothelial system, and residual spheroid regions have increased osmotic fragility that may result in intravascular hemolysis. In the case reported here, eccentrocytosis, Heinz body formation, methemoglobinemia, and evidence of hemolysis were all observed. These hematological abnormalities were speculated to result from oxidative damage to erythrocytes caused by constituents in Chinese chive and/or garlic.

Eccentrocytosis has been reported in dogs given high doses of acetaminophen and following the ingestion of dehydrated onions or hot-water extract of garlic.3,16,20,21 In garlic-induced oxidative injury, the appearance of eccentrocytes may be the most prominent hematological feature, suggesting that the formation of eccentrocytes is a primary cause of garlic-induced hemolysis.3 In the case reported here, eccentrocytosis seemed to be a hallmark of the disease. The eccentrocytes were easily detected using any staining method. In contrast, the demonstration of Heinz bodies often required supravital staining using new methylene blue, brilliant green, etc., although they are generally visible using Romanowsky-type stains. Based on these findings, the detection of eccentrocytes may be useful in the diagnosis of Allium plant-induced oxidative injury.

One of the major flavor components of onions, n-propyl disulfide, is generally believed to be responsible for onion-induced hemolytic anemia.22 Three alk(en)yl thiosulfates (i.e., sodium n-propyl thiosulfate, sodium trans-1-propenyl thiosulfate, and sodium cis-1-propenyl thiosulfate) extracted from boiled onions are also thought to be causative agents of onion-induced hemolytic anemia.23 In garlic-induced hemolysis, a novel alkenyl thiosulfate derivative, sodium 2-propenyl thiosulfate, has been isolated from boiled garlic and is considered to be one of the causative agents.24 In addition, other volatile organosulfur compounds that oxidize canine erythrocytes have been isolated from an aqueous ethanol garlic extract, and the composite effects of these compounds on erythrocytes may be responsible for garlic-induced hemolysis.25,26 Although no oxidants have been identified in Chinese chive, this plant is thought to contain oxidants similar to those in garlic, because Chinese chive and garlic possess similar flavor
precursors specific for *Allium* plants (i.e., S-alk(en)yl cysteine sulfoxides).27

Among Japanese and Korean purebred dogs (e.g., the Shiba and Jindo breeds), some individuals are particularly susceptible to onion-induced hemolytic anemia.28,29 The high susceptibility of these dogs occurs from inherited high concentrations of erythrocyte reduced glutathione, which accelerates the oxidative damage produced by the sodium n-propyl thiiosulfate and its derivatives found in onion and garlic.30,31 The dog reported here had a normal concentration of erythrocyte reduced glutathione, normal or slightly higher activities of antioxidative enzymes, and a normal composition of hemoglobin types, suggesting that the dog was genetically normal. It was therefore concluded that consumption of Chinese chive and garlic caused the hemolytic anemia experienced in this dog.

In the present case, human recombinant erythropoietin was used at a dosage of 50 IU/kg per day SC for 2 days in the early stages of the disease. This drug is generally administered for aplastic anemia associated with chronic renal failure, not for hemolytic anemia. However, the use of this drug in the initial stages of the anemia may have stimulated the production of erythrocytes earlier than the secretion of intrinsic erythropoietin, and this may have resulted in a more rapid resolution of the anemia. In addition, vitamin E was given at a dosage of 7 mg/kg q 12 to 24 hours from day 4, for about 3 weeks. The major physiological effect of vitamin E on erythrocytes is to act as a biological antioxidant protecting erythrocyte membranes from peroxidative damage.32,33 Vitamin E may be efficacious in the reduction of subsequent oxidative damage of erythrocyte membranes. Although no control dogs were utilized in this study, erythropoietin and vitamin E may have been beneficial in the dog’s recovery.

**Conclusion**

The ingestion of Chinese chive and garlic was followed by Heinz body hemolytic anemia with eccentricytosis in a genetically normal adult dog. Results of hematological examinations, especially the detection of eccentricytosis, supported the diagnosis of *Allium* plant-induced hemolysis in the affected animal. This was the first report of naturally occurring hemolytic anemia in a dog associated with the ingestion of Chinese chive and/or garlic. Foods containing Chinese chive and garlic, as well as onions, should be avoided when feeding dogs.

---

**References**


Intracranial Epidural Mucocele in a Cat

An 18-month-old, spayed female, domestic shorthaired cat was presented with clinical signs of depression and reluctance to walk, which progressed to nonambulatory tetraparesis. Increased opacification of both frontal sinuses and a cyst-like abnormality causing compression and displacement of the right frontal lobe were seen on computed tomography. Bilateral frontal sinus trephination and right transfrontal craniotomy revealed clear, viscous fluid in the right frontal sinus and rostral fossa, compatible with an intracranial mucocele. At a 6-month follow-up examination, no signs of recurrence were appreciated. J Am Anim Hosp Assoc 2005;41:74-77.

Introduction

Paranasal sinus mucoceles and sphenoid mucocoeles with intracranial extension are extremely rare in humans, and both disorders can be confused with other intracranial disease processes. Intracranial epidural mucocele has never been reported in cats. Paranasal sinuses are air-filled cavities that are often occupied by the nasal turbinates. Paranasal sinuses are located in the maxilla, frontal, and sphenoid bones. Paranasal sinuses are small at birth, enlarge with age, and are lined by a mucoperiosteum. The sinuses may be divided into several compartments that drain directly or indirectly into the nasal cavity. Mucoceles are thought to occur from occlusion of the natural orifice of the paranasal sinus, with subsequent intrasinus accumulation of excreted substances. If inflammation occurs, altered mucous secretion and obstruction of the sinus ostium may produce a mucocele. Sinus mucoceles are presumably rarer in dogs and cats because of their larger nasofrontal openings.

Case Report

An 18-month-old, spayed female, domestic shorthaired cat was referred because of a 7-day history of progressive lethargy, anorexia, and reluctance to walk. The owner also reported that vision was diminished 2 days prior to referral. Neurological examination revealed the cat had depressed mental status, ambulatory tetraparesis with severe proprioceptive deficits on both thoracic and pelvic limbs, and an absent menace reflex on the left side. Within several hours of admission, the cat’s neurological status deteriorated to a nonambulatory tetraparesis with blindness (i.e., lack of menace reflexes in both eyes).

The initial clinical signs were suggestive of a right forebrain lesion with subsequent, progressive, bilateral forebrain involvement. Differential diagnoses included feline infectious peritonitis; feline leukemia virus; feline immunodeficiency virus; bacterial, fungal, and protozoal (e.g., toxoplasmosis)
infections; neoplasia; metabolic encephalopathies; congenital defects (e.g., hydrocephalus); and vascular diseases (e.g., hemorrhage or ischemia). A complete blood count, serum biochemical profile, and urinalysis were within reference ranges. Serological test results for feline corona virus, feline leukemia virus, feline immunodeficiency virus, and toxoplasmosis were negative.

Pre- and postcontrast brain computed tomography (CT) scans, using a soft-tissue window in a transverse plane with 4-mm slices, were obtained. Postcontrast CT was conducted after intravenous (IV) injection of 2 mL/kg contrast medium. On precontrast CT, increased opacification within both frontal sinuses and the left paranasal sinus was observed. On postcontrast CT, a round, homogeneous, hypodense area with a peripheral, homogeneous line of contrast enhancement was also evident over the right frontal lobe [Figure 1]. This round lesion appeared to cause internal displacement of the right frontal lobe. Dorsal and sagittal plane CT confirmed the round shape of the lesion [Figures 2A, 2B]. The sagittal plane view showed extension of the lesion within the right frontal sinus [Figure 2B]. The CT abnormalities were suggestive of an abscess secondary to sinusitis, a congenital subarachnoid cyst, chronic subdural or extradural hematoma, or a parasitic cyst. Because of the risk of intracranial or foramen magnum herniation, cerebrospinal fluid was not collected. Because of the progressive worsening of the cat’s neurological status, an emergency surgical decompression was performed, with bilateral frontal sinus trephination and right transfrontal craniotomy. The cat was premedicated and induced with diazepam (0.3 mg/kg IV) and thiopental sodium (10 mg/kg IV). Anesthesia was maintained with isoflurane in oxygen. Thirty minutes before the craniotomy, mannitol (1 g/kg of an 18% solution, IV) was given over 15 minutes, followed with methylprednisolone sodium succinate (30 mg/kg IV). Methylprednisolone sodium succinate (15 mg/kg IV) was repeated after 3 and 6 hours. Before the
craniotomy, manual hyperventilation at 12 breaths per minute with 3.5 L per minute of oxygen flow and 1.5% of isoflurane was begun in order to lower the blood carbon dioxide level and prevent an increase in intracranial pressure. During surgery, isoflurane concentration was maintained between 2.5% and 3%. Near the end of surgery, spontaneous ventilation was achieved by reducing the oxygen flow to 1.5 L per minute and the respiratory frequency to four breaths per minute.

The cat was positioned in sternal recumbency with the head elevated and immobilized in a custom-made headstand that provided uninterrupted jugular venous drainage (to help reduce intracranial pressure). At the beginning of surgery, cefazolin (20 mg/kg) was given IV. A midline longitudinal skin incision was made over the frontal and nasal bones, starting from the caudal extent of the frontal sinus to the level of the medial canthus of the eyes. The underlying subcutaneous tissues, frontalis muscle, and periosteum were reflected laterally on each side of the incision. A standard bilateral frontal sinus trephination using a pneumatic air drill was performed, creating two holes approximately 0.5 cm in diameter. Colorless, watery, serous-mucoid fluid was collected from the right frontal sinus, and a yellowish mucoid material was aspirated from the left frontal sinus. No apparent communication was observed between the two frontal sinuses. Samples were taken for aerobic and anaerobic bacterial culture and antibiotic sensitivity testing, and both sinuses were flushed with a sterile saline solution. Unfortunately, the harvested fluid was not submitted for cytology. The septum between the two frontal sinuses was completely removed, and the nasosinus ostium was enlarged on both sides, breaking through the turbinates with a periosteal elevator. This latter procedure allowed adequate drainage into the nose, which was confirmed by observing the lavage fluid exiting from both nares during flushing of the sinuses.

The aperture on the right frontal bone was enlarged with Kerrison rongeurs and the air drill. For the craniotomy, an additional hole approximately 0.5 cm in diameter was made over the orbital portion of the right frontal bone. Abundant serous and colorless fluid that was under pressure rapidly flowed from the craniotomy opening, and it was collected for culture and sensitivity. The surgical site was flushed with sterile solution until the dura mater was visualized. The dura mater appeared intact but reddish in color. The discolored fluid was suspected to be secondary to an inflammatory process. The frontalis muscle and subcutaneous tissue were apposed with simple interrupted sutures using 3-0 polyglactin-910. The skin was closed using simple interrupted sutures using 3-0 silk. Postoperative cephalaxin (22 mg/kg per os [PO] q 8 hours) was administered for 10 days.

During the first 24 hours postoperatively, the cat had mild bilateral epistaxis. On the second day after surgery, the cat started eating and drinking, and over the following 10 days she made a full neurological recovery. Cultures yielded no bacterial growth. At a 6-month follow-up examination, no clinical signs of recurrence were appreciated.

Discussion
Cats and dogs possess both frontal sinuses and maxillary recesses. The maxillary recess is not a true sinus, because it does not lie between two plates of bone. The recess is bound laterally by the maxilla and medially by the ethmoid. The frontal sinus is the largest of the sinuses and occupies the brow ridge and supraorbital process of the frontal bone. Right and left frontal sinuses are separated by a median septum. In dogs, each frontal sinus is composed of three separate cavities (i.e., lateral, medial, and rostral), which communicate separately with the nasal fossa via the nasofrontal opening. This is not the case in the cat. It is not clear if this anatomical difference played a role in the occurrence of the mucocele in the case reported here.

The maxillary recess is found at the level of the carnassial tooth between the orbit and infraorbital canal. It communicates with the middle meatus by a spacious nasomaxillary opening, which is flanked by the nasal conchae. The maxillary recess houses the nasal gland on its lateral wall. Macroscopically the gland appears like thickened mucous membrane, and cytologically it is a serous salivary gland. The medial wall of the recess bears small compound alveolar glands.

Chronic sinusitis may occur in cats as the result of mucosal damage secondary to feline viral rhinotracheitis or calcivirus. Severe mucosal ulceration and turbinate resorption allow secondary bacterial infections to develop, primarily from *Streptococcus* spp., *Staphylococcus* spp., *Pasteurella* spp., or from the coliforms. Normal drainage of the frontal sinus fails from thickening of the mucosa and submucosa around the sinus ostium. Chronic infection occurs with or without mucocele formation. However, in this case no prior history of nasal discharge or upper respiratory infection was reported. The watery and colorless fluid from the right frontal sinus was macroscopically similar to the fluid drained from the brain cavity and differed from the mucoid, yellowish appearance of the fluid in the left frontal sinus. The watery, colorless-mucoid fluid collected from the right frontal sinus and in the cranial vault was considered to be mucus. The thick, yellowish mucoid material from the left sinus was also assumed to be mucus, probably at a different stage from that of the right side or of different origin. Cytological examination of both fluids would have been of great value to characterize the type and the origin of the fluids, but unfortunately it was not performed. Bacterial culture and sensitivity testing were negative on all collected fluids. By definition, a mucocele is a dilatation, cyst, or a cavity filled with mucous secretions. Based on CT and surgical findings as well as results of the limited fluid analysis, a presumptive diagnosis of intracranial epidural mucocele was made in this case.

Intracranial mucocele has been reported in people. In humans, intracranial mucoceles are usually, but not always, caused by a known defect in the skull that allows extension of a paranasal mucocele into the calvarium. Paranasal mucoceles in dogs have been reported as a consequence of trauma; however, there was no history of trauma in this
In humans, the frontal sinus is thought to be the most frequent site for mucoceles, followed by the ethmoid sinus and the sphenoid sinus. The primary site is not always identified because of the progressive osteolysis of bony walls adjacent to the mucous membranes. The dura mater is so resistant to pressure or inflammation that it is rarely penetrated. In human intracranial mucoceles, the color of the material in the sinuses ranges from gray-white to yellowish green or brown. The consistency of the fluid varies from a sticky, mucilaginous fluid to purulent-looking material, or a somewhat viscous, fibrous tissue. In humans, mucoceles usually have the same density as the brain on CT. Mucoceles also tend to fill the sinuses and compress the adjacent anatomical structures without infiltrating these structures. Hyperdense or hypodense mucoceles have also been reported on CT. In this report, the CT findings were consistent with a hypodense mucocele.

To the author's knowledge, this report contains the first description of a probable intracranial epidermal mucocele in the cat. Two different hypotheses were considered to explain the intracranial epidermal fluid accumulation in this case. The intracranial epidermal fluid accumulation may have occurred as a consequence of chronic sterile sinusitis, with secondary sinus ostium occlusion and subsequent infiltration into the cranial cavity through microscopic lesions within the orbital frontal bone. The different macroscopic appearances of the fluid within the two frontal sinuses could have represented different stages of the same pathological process or two separate entities. However, there was no historical evidence of chronic sinusitis and, unfortunately, no cytological analysis to support this theory. A second possible cause may have been obstruction of outflow from the salivary nasal gland contained in the maxillary recess. This type of obstruction might have explained the watery appearance of the fluid in the right frontal sinus and in the cranial cavity. This latter theory, however, doesn’t explain the macroscopic difference in appearance of the fluid in the left frontal sinus.

Case Description

A lesion compatible with an intracranial epidermal mucocele was diagnosed in a young domestic shorthaired cat with mental depression and progressive tetraparesis. Evidence of a cystic-type lesion was identified on CT over the right frontal lobe of the brain. Surgical drainage of the frontal sinuses and the mucocele was associated with a favorable outcome. The exact origin of the mucocele was not identified.

Acknowledgment

The author thanks Dr. Robert O’Brien for reviewing this manuscript.

References


a Toshiba TCT 300S; Toshiba Medical System, Amserdam, Netherlands
b Iopamiro 300; Bracco, Milan, Italy
c Diazepam 0.5%; Farmaceutici Gellini SpA, Aprilia (LT), Italy
d Pentothal Sodium; Farmaceutici Gellini SpA, Aprilia (LT), Italy
e Fluothane; Zeneca, Zeneca Ltd; Macclesfield, Cheshire, UK
f Mannitolo 18%; Pfizer Srl, Latina, Italy
g SoluMedrol; Pfizer Srl, Latina, Italy
h T otacef; Bristol-Myers Squibb, Sermoneta (LT), Italy
i Vicryl; Ethicon, Rome, Italy
j Silk; Ethicon, Rome, Italy
k Keflex; Eli Lilly Italia SpA Sesto Fiorentino (FI), Italy
Bilateral Stifle Osteochondritis Dissecans in a Cat

A 9-month-old, castrated male, domestic shorthaired cat was presented for progressive right hind-limb lameness. A diagnosis of osteochondritis dissecans of the lateral femoral condyle was made based on radiographs and physical examination, and was confirmed by right lateral stifle arthrotomy. The cartilage flap was removed, and the underlying bone was curetted. Seven months later, the cat was sound on the right leg but developed a left hind-limb lameness. A similar lesion was found in the left leg and was treated identically. Fourteen months after presentation, the cat was sound on both hind limbs. J Am Anim Hosp Assoc 2005;41:78-80.

Introduction

Osteochondritis dissecans (OCD) is a form of osteochondrosis in which a failure of endochondral ossification results in a zone of necrosis that extends into the subchondral bone.¹,² This necrotic, weakened cartilage is highly vulnerable to trauma, which may lead to flap formation.²,³ Once a cartilaginous flap has formed, the term OCD is applied.²,³ This condition may lead to synovitis, joint effusion, lameness, and degenerative joint disease.²,³

Osteochondritis dissecans is a common finding in pigs, horses, large-breed dogs, and poultry.² It may or may not result in clinical signs.² The etiology of OCD has not been determined, but it is considered to be multifactorial with both genetic and environmental factors playing a role.² In the dog, the caudal humeral head, the medial humeral condyle, the medial portion of the lateral condyle of the femur, and the medial or lateral trochlear ridges of the tarsus have been reported as common sites of OCD lesions.¹,³,⁴ To the author’s knowledge, osteochondritis lesions have not been previously reported in the stifle of cats. The purpose of this paper is to report on the diagnosis and treatment of bilateral osteochondritis dissecans in the stifle of a cat.

Case Report

A 9-month-old, castrated male, domestic shorthaired cat was presented with a 2-month history of progressive lameness of the right hind leg. At presentation, severe lameness was present, with pain on flexion and extension of the right stifle. The owner also reported increased drinking and urination in the weeks prior to presentation.

The complete blood cell count and serum biochemical profile were within normal reference ranges, and urine specific gravity was 1.045. Because of financial constraints, the observed polyuria/polydipsia problem was not pursued further. Radiographs taken of the right stifle [Figure 1]
revealed a subchondral defect and flattening of the lateral condyle of the femur with subchondral sclerosis. A moderate amount of soft-tissue swelling and faint mineral fragments were seen in the caudal aspect of the stifle joint. The radiographs were considered consistent with osteochondritis dissecans of the right femoral condyle. Other differential diagnoses included a nondisplaced fracture, traumatic injury, or a congenital lesion.

A standard right lateral stifle arthrotomy was performed. A cartilaginous flap was found on the lateral condyle [Figure 2]. This flap was removed, and the area was curetted until subchondral bone was reached. The joint was flushed thoroughly with physiological saline. The joint capsule, fascia, and subcutaneous tissues were closed separately with 4-0 polydioxanone in a simple continuous pattern. Skin was closed with 4-0 nylon using a cruciate pattern. The cat was sent home with a modified Robert Jones bandage and restricted activity for 2 weeks. The cat’s attitude immediately improved, and he seemed to be less painful. Once the bandage was removed, the cat rapidly regained full function of the leg and had no appreciable lameness.

At a 7-month follow-up, the cat was fully weight-bearing and was using the right hind leg well. However, the left hind leg was now lame. Radiographs taken of the left hind leg revealed a similar lesion to the OCD lesion originally seen in the right stifle. A standard left lateral stifle arthrotomy was performed, and a cartilaginous flap was visualized on the lateral femoral condyle. The stifle was surgically treated in a manner identical to the contralateral side.

Histopathologically, the specimen from the right stifle was composed of hyaline articular cartilage containing an irregular zone of mineralized cartilage in the deep articular cartilage, parallel to the articular surface [Figure 3]. Immediately subjacent to the zone of mineralized cartilage was a zone composed of chondrocyte clones. Subjacent to the chondrocytes, and forming the deep margin of the tissue, was a thin zone of necrotic cartilage. The histopathological appearance of this specimen was essentially identical to that of cartilage flaps removed from dogs with OCD.1,2 The
specimen from the left stifle was composed of a nodule of bone surrounded by fibrillated fibrocartilage or hyaline cartilage, depending on the location within the section. Although the appearance of this latter lesion was not classical for an OCD cartilage flap, it was still compatible with a diagnosis of OCD, given the clinical history, radiographic changes, and gross findings.

Discussion

Diagnosis of OCD is based on signalment, physical examination findings, and radiographic assessments. In the case reported here, the physical examination findings and radiographic lesions were consistent with OCD, but the signalment (i.e., feline patient) was very unusual. Only two prior reports exist of OCD in cats, both involving the humeral head. One of these cats was a domestic shorthaired cat, and one was a Burmese. Both were males. Surgical treatment in both cats consisted of removal of the cartilage flap with curettage of the area underlying the flap. Resolution of the lameness occurred after surgery in both cats.

Trauma, hereditary factors, rapid growth, nutritional factors, and ischemia have all been postulated to play a role in the etiology of OCD. Trauma is unlikely to be the sole cause of OCD, but it may play a secondary role in its development. Although the cat in this report had no known traumatic incident, trauma could not be ruled out as a contributor to the disease. Growth rate and hereditary factors are presumed to play a role in the development of OCD, particularly in those domestic species that are selected for desirable body characteristics, such as rapid growth. The cat reported here was adopted from a humane society, and its pedigree was unknown. The cat was not large, and it seemed unlikely that rapid growth was a significant contributing factor.

Early lesions of osteochondrosis in pigs and horses have been associated with abnormalities of blood vessels in the cartilaginous canals, which are thought to cause local ischemia and chondronecrosis. Because the lesion in this cat was not noticed until it had reached an advanced state, and because this type of lesion is so rare in cats, it is not known whether this mechanism played a role in the etiology of OCD in this case. Nutritional factors suspected to increase the risk of OCD are rapid growth from ad libitum feeding of high-energy foods, high calcium intake, and deficiencies in vitamins or trace elements. The early nutritional history of this cat was unknown. The current owner fed a commercially available cat food approved by the Association of American Feed Control Officials, so its nutritional needs were being met at the time of presentation. The cat also had an excellent body condition score (3/5).

Common treatments for animals with OCD include conservative and surgical therapies. Conservative management may be adequate for young animals with mild or absent clinical signs. Common surgical options include removal of the flap, any adjacent cartilage that is not adhered to the underlying tissues, and any free cartilage fragments. Removal of loose tissue is followed by curettage, forage (i.e., subchondral drilling, usually with a small Kirshner wire), or abrasion arthroplasty of the underlying subchondral bone to encourage reconstruction of the defect with fibrocartilage. Other surgical techniques such as microfracture, mosaicplasty, perichondral/periosteal grafting, and chondrocyte transplantation have been reported in humans and laboratory animals, but they are not commonly used in dogs and cats.

Osteochondritis dissecans of the stifle is common in dogs and most commonly affects the lateral femoral condyle. It may occur bilaterally in up to 72% of dogs. The prognosis for dogs with OCD of the stifle is reported to be guarded to fair because of progressive osteoarthritis even after surgical treatment of the lesion. However, the prognosis in dogs also depends on the method of treatment, size and location of the lesion, amount of degenerative changes present, age, breed, conformation, and temperament of the animal. Because of a dearth of clinical experience with OCD in cats, it is difficult to determine predictors of outcome. Similar to previously published reports in cats with OCD of the humeral head, the cat in this report had complete resolution of lameness after corrective surgery. The long-term outcome of this disease in cats is unknown, and osteoarthritis may lead to lameness later in life.

Conclusion

Osteochondritis dissecans was diagnosed initially in the right stifle of a young domestic shorthaired cat, and it was treated surgically. Seven months later, OCD was also diagnosed in the left stifle, and the lesion was treated in a similar fashion. The cat recovered uneventfully, with a full return of function in both legs. Based on this and previous case reports, OCD should be considered as a differential diagnosis in young cats with unilateral or bilateral lameness.

References


a PDS; Ethicon, Summerset, NJ 08876
b Ethibon; Ethicon, Summerset, NJ 08876