Anaphylaxis is defined by the World Allergy Organization as a serious allergic reaction that is rapid in onset and may cause death.\(^1\) Rapid release of preformed mediators and subsequent activation of the inflammatory cascade results in the target organ system effects responsible for the clinical manifestations of anaphylaxis.\(^2,3\)

Many common clinical findings of anaphylaxis in veterinary patients can be explained by alterations in blood flow and acute hepatic insult. Systemically, the surge of vasoactive and inflammatory mediators, most notably histamine, causes concurrent hepatic arterial vasodilation and hepatic venous outflow obstruction within seconds. The cascade of effects resulting from the ensuing hepatic congestion includes hepatocellular necrosis, substantially decreased venous return, visceral blood pooling, acute portal hypertension, and splanchnic hypoperfusion all leading to cardiovascular collapse and multiple organ dysfunction.\(^2,4,5\)

In dogs, the severity of systemic manifestations of anaphylaxis has been linked to the degree of hepatobiliary congestion induced.\(^6\)

Clinical signs associated with anaphylaxis are categorized according to involvement of 4 predominant body systems: cutaneous, cardiovascular, gastrointestinal, and respiratory.\(^2,7\) Anaphylaxis may progress quickly resulting in death in \(<1\) hour. Clinical signs in veterinary patients may vary widely from patient to patient and species to species, potentially impeding rapid diagnosis and appropriate treatment.

Mortality rates in humans with anaphylaxis are \(\leq\) 1% to 2%.\(^8,9,10\) However, cardiopulmonary arrest
Rates in humans with anaphylaxis are higher (up to 5.5%); the comparably lower mortality rates in these patients are the result of successful resuscitation.\textsuperscript{11-13} Scrutiny of low mortality rates reported for humans with anaphylaxis reveals lack of inclusion of cardiac arrests that occur outside the hospital, unrecognized anaphylaxis, and poor reporting practices.\textsuperscript{14,15} Old age, preexisting cardiovascular or chronic pulmonary disease, obesity, and some medications (eg, angiotensin-converting-enzyme inhibitors and β-adrenoceptor antagonists) have been identified as risk factors for severe and fatal anaphylactic events in humans.\textsuperscript{8,15}

Available information on mortality rate or prognosis for small animals with anaphylaxis is minimal. One case series\textsuperscript{16} of anaphylaxis in cats reported a 13% mortality rate. Results of 2 recent small population studies\textsuperscript{7,17} in dogs with anaphylaxis indicated 100% survival rates. However, such rates are unlikely to reflect actual mortality rates in dogs with anaphylaxis because reports of fatal anaphylaxis in dogs do exist.\textsuperscript{18-20} The objectives of the study presented here were to determine mortality rates in dogs with severe manifestations of anaphylaxis and identify potential prognostic factors.

Materials and Methods

Case selection criteria

Medical records were searched for dogs admitted to 2 regional private specialty practices and a university teaching hospital between January 2016 and April 2018 with a diagnosis of suspected anaphylaxis. Diagnostic codes and medical record notes were electronically searched for the following terms: anaphylaxis, anaphylactic shock, and allergic reaction. Medical records were reviewed for information in agreement with a diagnosis of anaphylaxis. For the present study, a diagnosis of anaphylaxis was made from a combination of peracute onset of clinical signs, evidence of involvement of at least 2 organ systems (eg, skin, gastrointestinal, cardiovascular, or respiratory), and diagnostic findings (eg, high serum ALT activity or gallbladder edema) consistent with the disease.

Organ system involvement was defined from the presence of ≥ 1 clinical sign associated with compromise of that organ system on initial examination or in the patient’s immediate history.\textsuperscript{7} Signs consistent with cutaneous involvement included urticaria, angioedema, skin flushing, and pruritus. Gastrointestinal signs included signs of abdominal pain, vomiting, and diarrhea (with or without hematochezia). Acute collapse, bradycardia (heart rate ≤ 60 beats/min), tachycardia (heart rate > 150 beats/min), mucous membrane pallor, hypotension (systolic blood pressure < 90 mm Hg), and cardiac arrest were considered indicators of cardiovascular involvement. Respiratory signs included dyspnea, tachypnea (respiratory rate > 35 breaths/min), bradypnea (respiratory rate < 10 breaths/min), cyanosis, and respiratory arrest.

Disease severity was graded retrospectively according to allergy and anaphylaxis severity criteria adapted for dogs.\textsuperscript{7} The clinical signs associated with the most severely affected organ systems formed the basis of the severity grade assigned. Anaphylaxis was graded in patients as follows: grade 0 (absent) = only cutaneous signs; grade 1 (mild, minor systemic effects) = cutaneous signs along with a single episode of vomiting or diarrhea or a single episode of both; grade 2 (moderate, modest but non–life-threatening systemic effects) = a combination (ie, ≥ 2 body systems) of cutaneous signs, persistent gastrointestinal signs, evidence of compensated cardiovascular function (eg, transient mucous membrane pallor or tachycardia without concurrent hypotension), or respiratory compromise (ie, tachypnea or dyspnea); and grade 3 (severe) = life-threatening systemic effects such as decompensated cardiovascular compromise (eg, acute collapse, bradycardia, cardiac arrest, or any of the previously mentioned cardiovascular signs with concurrent hypotension) or respiratory failure (bradypnea, cyanosis, or respiratory arrest) with or without any of the previously mentioned lower-grade organ system signs (Appendix).

Eligibility for inclusion in the present study required complete medical records, hospital admission within 12 hours of onset of clinical signs, serum biochemical analysis and Hct results at the time of hospital admission, and an anaphylaxis severity grade of severe (grade 3). Exclusion criteria included incomplete medical records, missing serum biochemical analysis results, hospital admission > 12 hours after onset of clinical signs, missing outcome data, and a severity grade of less than severe (grades 0 through 2). Dogs were excluded if any preexisting health conditions were identified that could otherwise explain the clinical signs.

Medical records review

Data collected from the medical records included signalment, physical examination findings, time to hospital admission from onset of clinical signs, initial serum biochemical analysis values, Hct, vital parameters, and clinical outcome. For blood glucose concentration, values < 80 mg/dL were considered hypoglycemic. Doppler ultrasonographic measurements of systolic blood pressure were recorded at the time of hospital admission. Values of < 90 mm Hg were considered hypotensive; values of 90 to 150 mm Hg were considered normotensive, and values of > 150 mm Hg were considered hypertensive. Patients in which a blood pressure reading could not be obtained were considered to have a systolic blood pressure of < 60 mm Hg. Additional information collected, if available, included CBC data, PT, PTT, and findings on ultrasonography of gallbladder wall edema, peritoneal effusion, and other effusion characteristics. Initial treatment, defined as those modalities initiated within the first 6 hours of hospital admission, was recorded for analysis, specifically including the use of epinephrine, diphenhydramine, corticosteroids, antimicrobials, fresh-frozen plasma, and supplemental dextrose.
Sometimes values of serum biochemical analysis (ie, ALT activity) and coagulation testing (ie, PT and PTT) were above the measurable limits of an analyzer; these values did not undergo further quantification. Instead, stratification of ALT activity and PT and PTT values was used, which also compensated for the use of multiple biochemical and coagulation analyzers across institutions. Values of serum ALT activity and PT and PTT that were above the reference range limit for dogs were converted to percentage values. Values of PT and PTT above the reference range limits for dogs were stratified according to the degree of the increase as < 25%, 25% to 50%, and > 50% signifying mild, moderate, and severe increases, respectively. Values of ALT activity above the reference range limit for dogs were stratified according to the degree of the increase as < 300%, 300% to 1,000%, and > 1,000% signifying mild, moderate, and severe increases, respectively.21

Outcome data were defined as nonsurvival or survival to discharge. The nonsurvivor group consisted of patients that died naturally or were euthanized. For patients that were euthanized, the reason for euthanasia was determined from the medical records and communication log entries. Patients euthanized for reasons other than disease state or progression were not included in the outcome analysis.

Statistical analysis

The distributions of the continuous data were evaluated by use of the Shapiro-Wilk test, skewness, kurtosis, and Q-Q plots. Nonnormally distributed data were log transformed for parametric testing. An independent-samples t test was used to determine whether individual CBC and biochemical variables (continuous variables) were significantly different by outcome. The Levene test was used to assess homogeneity of variance. Several continuous variables (ALT activity, PT, and PTT) were further characterized into categorical data and analyzed by use of \( \chi^2 \) tests to determine whether there was an association between the category and survival. Values of PT, PTT, and ALT activity were each categorized into 3 categories. Combinations of PT and PTT values above the reference range limits were additionally categorized into 3 categories (both increased < 50%, 1 of either value increased > 50%, and both increased > 50%) to determine differences by outcome. Fisher exact or \( \chi^2 \) tests were used to determine whether binary independent variables (individual treatment modalities) were different by outcome. Odds ratios and 95% CI were calculated for values determined to be significant. Data were analyzed with a commercial statistics program.6 A value of \( P < 0.05 \) was used to determine significance.

Results

The initial search returned 346 cases. Of those, 114 cases fulfilled the clinical criteria for diagnosis of anaphylaxis with a grade of severe. Thirty-six cases were excluded because of incomplete diagnostic data, 6 cases were excluded for the presence of concurrent disease that may display similar clinical signs, 4 cases were excluded because of hospital admission > 12 hours after onset of clinical signs, and 1 case was excluded because of missing outcome data.

Inclusion criteria were met in 67 dogs. Twenty-nine males (7 sexually intact and 22 neutered) and 38 females (7 sexually intact and 31 neutered) were included in the present study. The mean patient age was 41 months (range, 5 to 120 months). The mean patient weight was 18.4 kg (40.5 lb) with a range of 2.9 to 39.4 kg (6.4 to 86.7 lb). Dogs included mixed-breed dog (n = 30), Labrador Retriever (6), Catahoula Leopard Dog (4), pit bull-type dog (4), Boxer (3), Yorkshire Terrier (2), Jack Russell Terrier (2), and 1 each of American Eskimo Dog, Beagle, Bichon Frise, Standard Dachshund, Doberman Pinscher, English Bulldog, French Bulldog, German Shepherd Dog, German Shorthair Pointer, Golden Retriever, Husky, Maltese, Miniature Dachshund, Miniature Pinscher, Miniature Poodle, and Shih Tzu. No significant differences were found between the survivor and nonsurvivor groups in terms of signalment, age, or sex.

Initial examination findings indicated the median number of body systems affected as 3 (range, 2 to 4) in the survivor group and as 2.5 (range, 2 to 4) in the nonsurvivor group, as defined by the severity grading scheme. All patients displayed ≥ 1 clinical sign of cardiovascular compromise (ie, acute collapse, tachycardia, bradycardia, arrhythmia, hypotension, and pallor). Sixty-three of 67 (94%) patients had ≥ 1 gastrointestinal sign (ie, signs of abdominal pain, vomiting, ptalism, diarrhea, and hematochezia). Forty-five of 67 (67.2%) patients had ≥ 1 respiratory sign (ie, tachypnea, bradypnea, dyspnea, wheezing, coughing, and cyanosis). Eighteen of 67 (26.9%) patients had ≥ 1 cutaneous sign (ie, erythema, angioedema, urticaria, and pruritus).

Vital signs and systolic blood pressure measurements at hospital admission were available for all but 1 patient. Body temperature at the time of hospital admission was significantly (\( P = 0.019 \)) lower in the nonsurvivor group (median, 36.5°C [97.5°F]; range, 35.5°C to 39.2°C [95.9°F to 102.5°F]), compared with the survivor group (median, 37.7°C [99.9°F]; range, 34.2°C to 39.7°C [93.5°F to 103.4°F]). No other vital parameters were significantly different between groups. Of 66 dogs, 44 (66.7%) were hypotensive, 18 (27.3%) were normotensive, and 4 (6.0%) were hypertensive. Of the 57 dogs classified as survivors, 37 were hypotensive, 16 were normotensive, 3 were hypertensive, and 1 was undocumented. Of the 10 dogs classified as nonsurvivors, 7 were hypotensive, 2 were normotensive, and 1 was hypertensive. Of the 44 hypotensive patients, 30 (23 survivors and 7 nonsurvivors) had a systolic blood pressure of ≤ 60 mm Hg at the time of hospital admission. Initial systolic blood pressure categorization was not significantly (\( P = 0.244 \)) associated with death. Time from onset of clinical
signs to hospital admission did not differ significantly between survivor and nonsurvivor groups.

Of 67 dogs, 63 had full CBC data available from the time of hospital admission. No significant differences were found in Hct, platelet count, or WBC count between dogs in the survivor and nonsurvivor groups. Serum biochemical analysis results were available for 67 patients at the time of hospital admission, with the exception of serum cholesterol (available for 53 dogs) and chloride (available for 65 dogs) concentrations. At the time of hospital admission, serum ALT activity was high in 64 of 67 (94%) dogs. Of the 57 dogs classified as survivors, 55 had high serum ALT activity. Of the 10 dogs classified as nonsurvivors, 8 had high serum ALT activity. No significant \((P = 0.794)\) difference was found in the serum ALT activity between dogs in the survivor versus nonsurvivor groups. Patients in the nonsurvivor group had significantly \((P = 0.008)\) higher serum phosphorus concentration (mean, 10.1 ± 3.8 mg/dL; range, 6.3 to 16.2 mg/dL), compared with patients in the survivor group (mean, 5.9 ± 2.1 mg/dL; range, 2.8 to 11.2 mg/dL; Figure 1). Patients with serum phosphorus concentrations > 12.0 mg/dL were 79.6 times (95% CI, 3.83 to 1,651.57; \(P = 0.005\)) as likely to die as patients with lower values in serum phosphorus concentrations. Initial blood glucose concentrations were not significantly different between groups; however, the presence of hypoglycemia (< 80 mg/dL) at any point within 6 hours of hospital admission was significantly \((P = 0.005)\) associated with death. Patients that developed hypoglycemia were 5.7 times (95% CI, 1.39 to 23.35; \(P = 0.016\)) as likely to die as patients that did not. No other serum biochemical variables were significantly different between dogs in the survivor and nonsurvivor groups.

Coagulation testing was performed on 39 patients (31 survivors and 8 nonsurvivors) at the time of hospital admission. Of the 39 dogs, 34 (87.2%; 26 survivors and all 8 nonsurvivors) had PT values above the reference range limit. A significantly \((P = 0.013)\) larger proportion of nonsurvivors (7/8 [87.5%]) had PT values > 50% above the reference range limit, compared with the proportion of survivors (10/31 [32.2%]). Patients with PT values > 50% above the reference range limit were 11.0 times (95% CI, 2.41 to 49.89; \(P = 0.002\)) as likely to die as patients with PT values within the reference range interval or patients with PT values of lesser increases above the reference range limit. Of the 39 dogs, 34 (87.2%; 26 survivors and all 8 nonsurvivors) also had PTT values above the reference range limit. Although a PTT value > 50% above the reference range limit was found in 24 of the 39 (61.5%) patients (17/31 survivors and 7/8 nonsurvivors), no significant \((P = 0.160)\) difference was found between survivors and nonsurvivors in the degree of increase in PTT values at the time of hospital admission. All but 2 of the 39 patients tested had concurrent increases of PT and PTT values.

Combinations of PT and PTT values were evaluated by outcome and were found to have significant differences \((\chi^2 = 8.0; P = 0.018)\). Fifteen patients (group 1; 14 survivors and 1 nonsurvivor) had both PT and PTT values that were < 50% increased above the reference range limit. Seven patients (group 2; 7 survivors and 0 nonsurvivors) had a single PT or PTT value that was increased > 50% above the reference range limit. Seventeen patients (group 3; 10 survivors and 7 nonsurvivors) had both PT and PTT values that were increased > 50% above the reference range limit. A significant \((P = 0.041)\) difference was found in outcome between patients in group 1 and those in group 3. No significant differences in outcomes were found between patients in group 1 and group 2 \((P = 1.0)\) or between patients in group 2 and group 3 \((P = 0.065)\).

Abdominal ultrasonography was performed in 58 patients at the time of hospital admission; 49 (84.5%) had gallbladder edema, and 38 (65.5%) had abdominal effusion. Abdominal fluid samples were obtained from 19 patients that had abdominal effusion. Fluid analysis results were consistent with a hemorrhagic effusion in 16 of 19 (84.2%) patients and a protein-rich (modified) transudate with hemorrhagic characteristics in the remaining 3 of 19 (15.8%) patients. No significant differences were found between outcome groups (ie, survivors vs nonsurvivors) in regard to the presence or absence of abdominal effusion or gallbladder edema.

Initial treatment data on all patients was assessed and summarized. Patients receiving epinephrine were...
listed separately as those receiving bolus treatment (0.1 to 0.2 mg/kg [0.05 to 0.09 mg/lb], IM or IV) and those receiving a constant rate infusion (0.05 to 0.1 µg/kg/min [0.023 to 0.045 µg/lb/min], IV). All patients receiving a constant rate infusion of epinephrine received a bolus treatment prior to receiving the infusion. Administration of supplemental dextrose because of hypoglycemia was significantly associated with death (P = 0.005). Odds of death for patients requiring supplemental dextrose, compared with those that did not, were identical to those of patients developing hypoglycemia. All patients that were given supplemental dextrose had blood glucose values of ≤68 mg/dL at the time of dextrose administration. Notably, blood glucose concentrations for all survivor group patients receiving supplemental dextrose normalized after treatment, whereas all nonsurvivor group patients remained refractory despite treatment. Treatment with epinephrine, diphenhydramine, corticosteroids, antimicrobials, or fresh-frozen plasma was not significantly different between groups.

The overall mortality rate was 14.9% (10/67) for dogs with anaphylaxis graded as severe. Four patients died and 6 were euthanized because of poor prognosis or disease progression. No exclusions from the present study because of euthanasia for other reasons were necessary.

Discussion

The overall mortality rate for dogs with severe anaphylaxis was 14.9% in the present study. This finding contrasts with a reported 100% survival rate in 2 recent small population studies6,17 that included a group of dogs with anaphylaxis. Case selection in 1 study17 required those patients in the anaphylaxis group to have completely resolved clinical signs within 72 hours of admission as a criterion of inclusion, which may select for a population that is more likely to survive. Additionally, these studies may have included patients of a lesser grade of anaphylaxis than severe, which would skew the resultant mortality rates in favor of survival. Our results more closely resemble the reported 13% mortality rate in a case series of cats with anaphylaxis.16 To the authors’ knowledge, the present study is the first to specifically report on the mortality rate associated with anaphylaxis in dogs.

Body temperature was significantly (P = 0.019) lower in patients that died, compared with those that survived. Hypothermia (<37.5°C [<99.5°F]) has been previously described as a common finding associated with anaphylactic shock in dogs.22 Histamine has largely been implicated for this change owing to heat loss due, directly, to histamine activity causing peripheral vasodilation and, indirectly, to negative effects on cardiac output and perfusion as a result of the ensuing shock state.5,22 Additionally, histamine has been found to influence development of hypothermia centrally at the level of the hypothalamus in mice with anaphylaxis.23 Whether this effect translates to dogs has yet to be determined.

An unexpected finding was that hyperphosphatemia was significantly (P = 0.008) associated with death in the present study. The highest serum phosphorus concentration of patients that survived was 11.2 mmol/L, whereas 40% of patients that died had values >12.0 mmol/L. A link between death and hyperphosphatemia in patients with acute liver injury is established in humans.24-27 Proposed mechanisms of hyperphosphatemia pertaining to acute liver injury include release from the intracellular compartment resulting from hepatocellular necrosis and impaired hepatic uptake and utilization of phosphates.25,26,28 High serum ALT activity indicative of hepatocellular damage was found in 94.0% of patients in the present study and has consistently been a prominent finding in dogs with anaphylaxis, suggesting that such mechanisms could be possible in these patients.2,17,22 Another potentially relevant mechanism is rhabdomyolysis resulting in release of cellular phosphates.29 Rhabdomyolysis has been reported to occur in humans with anaphylaxis.29,30 In the present study, 13 of 16 patients in which serum creatine kinase activity was measured had high creatine kinase activity indicating some degree of muscle damage. Unfortunately, no determination could be made regarding the prognostic usefulness or implications of serum creatine kinase activity on clinical progress in the present study because the value was not measured in any of the patients in the nonsurvivor group. Further investigation will be required to determine a definitive mechanism for development of hyperphosphatemia in dogs with anaphylaxis. No other hematologic or serum biochemical variables were associated with death in the present study and the alterations in this patient population were consistent with findings in previous studies of dogs with anaphylaxis.6,17,22

Most patients tested (37/39 [94.9%]) had varying degrees of increases of PT, PTT, or both. Most of these patients (34/39, [87.2%]) had high PT and PTT values concurrently, however, the degree of increase in PT was the only individual coagulation parameter significantly (P = 0.013) associated with death in the present study. No patients in the present study had a high PT value alone (ie, without an increase in PTT). Additionally, concurrent increases of PT and PTT values >50% above the reference range limits were associated with death, compared with increases <50%. Coagulopathy, determined on the basis of increases in PT and PTT values concurrently, however, the degree of increase in PT was the only individual coagulation parameter significantly (P = 0.013) associated with death in the present study. No patients in the present study had a high PT value alone (ie, without an increase in PTT). Additionally, concurrent increases of PT and PTT values >50% above the reference range limits were associated with death, compared with increases <50%. Coagulopathy, determined on the basis of increases in PT and PTT values concurrently, however, the degree of increase in PT was the only individual coagulation parameter significantly (P = 0.013) associated with death in the present study. No patients in the present study had a high PT value alone (ie, without an increase in PTT). Additionally, concurrent increases of PT and PTT values >50% above the reference range limits were associated with death, compared with increases <50%. Coagulopathy, determined on the basis of increases in PT and PTT values concurrently, however, the degree of increase in PT was the only individual coagulation parameter significantly (P = 0.013) associated with death in the present study. No patients in the present study had a high PT value alone (ie, without an increase in PTT). Additionally, concurrent increases of PT and PTT values >50% above the reference range limits were associated with death, compared with increases <50%.
of factors V and fibrinogen, which may better explain the involvement of increased PT values in some of these patients.¹² Coagulation derangement caused by altered factor activation or hepatic synthetic failure as a result of the acute liver insult could also be possible in patients with anaphylaxis.¹⁰ Despite these hemostatic alterations, spontaneous resolution is documented in some instances in both human and veterinary literature.¹³,¹⁶,¹⁷

Dextrose administration and hypoglycemia (<80 mg/dL) within 6 hours of hospital admission were also significantly (both P = 0.005) associated with death, particularly if the hypoglycemia was refractory to treatment. Hypoglycemia can be a sequela of increased cellular utilization or a decrease in hepatic production or mobilization of glucose, either of which could be feasible in an anaphylactic patient. Alternatively, hypoglycemia could be the result of sepsis induced by bacterial translocation brought on by compromised gastrointestinal mucosal defenses. Gastrointestinal mucosal barrier breakdown can occur secondary to hypoperfusion from cardiovascular collapse or because of tissue hypoxia related to congestion and edema resulting from acute portal hypertension.²,⁴¹ Hypoglycemia has been described to exacerbate the severity of anaphylactic shock in laboratory animals, but whether this effect occurs in dogs is currently undetermined.⁴² The mechanisms behind the spontaneous development of hypoglycemia in patients with anaphylaxis have yet to be definitively resolved and require further study.

Gallbladder wall edema was evident in 84.5% of patients in the present study for which abdominal ultrasonography was performed. Our study demonstrated a slightly lower prevalence of gallbladder wall edema than that reported by Quantz et al.²² The development of gallbladder wall edema in anaphylaxis has been postulated to be caused by congestion associated with impaired hepatic venous drainage or caused by an inflammatory response.²,¹⁷ The exact mechanism has not yet been elucidated.

In the present study, peritoneal effusion was noted in 65.5% of the patients evaluated ultrasonographically. This agreed with the incidence noted in a recent study inclusive of a group of dogs with anaphylaxis. This finding suggested that the presence of effusion is a relatively common clinical feature of severe anaphylaxis in dogs. Specifically, a hemorrhagic effusion has been described in a recent case report involving Hymenoptera envenomation.⁵ In the present study, most of the abdominal fluid samples analyzed were characterized as hemorrhagic effusions on the basis of PCV and cytologic findings. The remaining samples were classified as protein-rich transudates with a hemorrhagic component (PCV > 2%). It is possible that the presence of hemorrhagic effusions in anaphylaxis could be linked to the induced coagulopathies previously mentioned. On the other hand, the presence of effusion could be the result of increased vascular permeability as the result of massive cytokine release, exudation associated with acute hepatic congestion and portal hypertension, or a combination of both.²,³,¹³,¹⁴ No definitive mechanism is currently understood for the presence of these effusions, and future studies will be required to elucidate the cause.

There are several important limitations to the present study. First, the criteria for diagnosis of anaphylaxis are broad and heavily dependent on patient history. With the use of specific clinical criteria and meticulous review of records, this error is thought to have been mitigated substantially. However, because there are no readily available tests to confirm the diagnosis in veterinary patients, it is possible that the diagnosis was incorrect in some dogs. Additionally, it is equally possible that some affected dogs may have been missed as the result of poor coding, misdiagnosis, or death before diagnosis. Occasional missing data points and case exclusions may have resulted in diminished sample sizes for some study variables. This could cause some of those variables to be skewed toward or away from statistical significance, which may not be representative of the population of dogs with anaphylaxis. Any such exclusions were deemed necessary to ensure the most homogenous population possible. Because the present study involved several clinicians over multiple institutions, the treatment approaches and diagnostic testing used could have influenced the results. Lastly, the retrospective nature of the present study cannot account for extraneous factors (such as personal or financial limitations) on the course of treatment provided to individual patients. Although our selection criteria attempted to eliminate these factors with regard to nonsurvival, it is improbable to have completely done so.

In conclusion, findings in the present study indicated that the survival rate of dogs with severe anaphylaxis is high (85.1%) regardless of the initial clinical appearance. Coagulopathy and effusions appear to be relatively common findings in dogs with severe anaphylaxis, which should prompt additional points of evaluation for these patients. Hypothermia (<37.5°C [99.5°F]), high serum phosphorus concentration (≥12.0 mmol/L), high PT values (particularly >50% above the reference range limit), concurrent increase of both PT and PTT values (>50% above the reference range limits), hypoglycemia (<80 mg/dL) within 6 hours of hospital admission, and the need for supplemental dextrose administration appeared to carry a worse prognosis in this patient population. Prospective studies are necessary to further evaluate these findings.

Acknowledgments

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Footnotes

a. Olympus Model AU640, Beckman Coulter Inc, Brea, Calif.
b. Catalyst Dx, Idexx Laboratories Inc, Westbrook, Me.
c. Start 4 Coagulation Analyzer, Diagnostica Stago, Parsippany, NJ.
d. Coag Dx, Idexx Laboratories Inc, Westbrook, Me.
e. SPSS, version 24.0, IBM Statistics, Armonk, NY.
References


Continued on next page.
### Appendix

A simplified grading scale of anaphylaxis severity adapted for dogs. Severity grades for anaphylaxis in dogs are assigned on the basis of the clinical signs of the most severely affected organ system.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Severity</th>
<th>Definition</th>
<th>Body systems</th>
<th>Organ system severity criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Absent</td>
<td>Allergic reaction lacking systemic effects</td>
<td>Cutaneous only</td>
<td>Cutaneous &lt;br&gt; Urticaria &lt;br&gt; Angioedema</td>
</tr>
<tr>
<td>1</td>
<td>Mild</td>
<td>Multisystemic reaction with mild systemic effects that are not life-threatening</td>
<td>Cutaneous and gastrointestinal</td>
<td>Cutaneous &lt;br&gt; Any grade 0 criteria &lt;br&gt; Flushing &lt;br&gt; Pruritus &lt;br&gt; Gastrointestinal &lt;br&gt; Vomiting (single episode) &lt;br&gt; Diarrhea (single episode)</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
<td>Multisystemic reaction with increasing severity of systemic effects but that are not life-threatening</td>
<td>Any combination of cutaneous, gastrointestinal, cardiovascular, and respiratory</td>
<td>Cutaneous &lt;br&gt; Any grade 0 and 1 criteria &lt;br&gt; Gastrointestinal &lt;br&gt; Vomiting (persistent or ongoing) &lt;br&gt; Diarrhea (persistent or ongoing) &lt;br&gt; Abdominal pain &lt;br&gt; Cardiovascular compromise &lt;br&gt; Tachycardia without hypotension &lt;br&gt; Mucous membrane pallor (transient) &lt;br&gt; Respiratory compromise &lt;br&gt; Dyspnea &lt;br&gt; Tachypnea</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
<td>Multisystemic reaction with life-threatening systemic effects</td>
<td>Cardiovascular, respiratory, or both with or without any additional grade 0, 1, and 2 signs</td>
<td>Cardiovascular collapse &lt;br&gt; Acute collapse &lt;br&gt; Bradycardia &lt;br&gt; Cardiac arrest &lt;br&gt; Any grade 2 criteria with hypotension &lt;br&gt; Respiratory failure &lt;br&gt; Cyanosis &lt;br&gt; Bradypnea &lt;br&gt; Respiratory arrest</td>
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</tbody>
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