Clinical findings associated with prairie rattlesnake bites in dogs: 100 cases (1989–1998)

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Objective—To identify clinically relevant variables and treatments for dogs bitten by prairie rattlesnakes (Crotalus viridis viridis).

Design—Retrospective study.

Animals—100 client-owned dogs.

Procedure—Records of dogs evaluated for rattlesnake envenomation from 1989 to 1998 were reviewed. Analysis was performed to test for significant associations among clinical variables or treatments and cell counts, costs, and duration of hospitalization.

Results—Most prairie rattlesnake bites occurred between May and September. Dogs were 3 months to 12 years old (median, 3.7 years); most were bitten on the head in the late afternoon. There was no sex predilection. Median time to evaluation was 1 hour (range, 15 minutes to 13 hours). Swelling in the area of the bite was the primary physical abnormality. Principal initial laboratory findings were echinocytosis, thrombocytopenia, leukocytosis, and prolonged activated clotting time. Ninety-four dogs were hospitalized; 48 were discharged the following day. Antimicrobials and crystalloid fluids, glucocorticoids, and antivenin administered IV were the most commonly used treatments. One dog died, and small dogs were hospitalized longer than large dogs. Antivenin administration was not significantly associated with duration of hospitalization but was associated with higher platelet counts after treatment and higher total hospital costs.

Conclusions and Clinical Relevance—Prairie rattlesnake envenomation in dogs is associated with high morbidity rate but low mortality rate. The efficacy of administration of antivenin for dogs with bites from this snake species is questionable. (J Am Vet Med Assoc 2002;220:1675–1680)

Pit vipers occur throughout North America and in many parts of the world and include rattlesnakes (Crotalus spp); copperheads, cottonmouths, and water moccasins (Agkistrodon spp); and pygmy rattlesnakes and massasaugas (Sistrurus spp).1 Rattlesnakes comprise 20 species that vary in habitat, size, and, most importantly, relative toxicity of venom.1,3 As humans and their dogs encroach on the snakes’ habitats, dangerous encounters are bound to occur. Because rattlesnakes usually warn before they strike, most bites can be avoided. Human snakebite victims are disproportionately represented by young males < 30 years old, and the bites are often associated with use of intoxicants and other illicit substances.3

There are many review articles regarding the management of snakebite and rattlesnake envenomation in humans and other animals.3,4 However, there is little in the veterinary literature about the actual morbidity rate and mortality rate associated with rattlesnake envenomation in dogs. A single retrospective report5 of snakebite in dogs (n = 109) bitten by the Palestine viper Vipera xanthina palestina indicated that most bites occurred in the summer months, median age of dogs was 3 years, and 66.7% of the dogs had bites to the head. Important clinical findings included localized swelling at the site of the bite (98%), neutrophilia (67.6%), thrombocytopenia (51.9%), and an overall mortality rate of 3.7%; treatments were not reported.

The lack of similar clinical information in North America makes it difficult to recommend ideal treatments for rattlesnake envenomation in this country. Data provided by a manufacturer of antivenom indicated that 16 practicing veterinarians had uniformly successful results with antivenom in dogs with mild clinical signs at the time of treatment.6 Of 103 dogs with acute clinical signs, 72% survived after a single 10-ml dose; there was a higher percentage (83%) of recovery when 20 to 70 ml was given. Overall, 82% of antivenin-treated dogs survived; most that did not receive antivenin died. With no mention of snake species involved, clinical problems, or other treatments, it is difficult to draw practical treatment recommendations from this information. There are many genera and species of snakes in North America, with a wide array of species-specific venom potency and clinical envenomation patterns7; therefore, optimal treatments might differ. For example, the ideal treatment for a bite by Arizona’s deadly Mojave rattlesnake (C scutulatus) or the Eastern diamondback rattlesnake (C adamanteus) may need to be much more aggressive than for that of the Southern copperhead (A contortrix contortrix), which is reported to have much less toxic venom.3

The Western diamondback rattlesnake (C viridis) is the most widely distributed rattlesnake in the western United States and Canada.8 It is also the most variable rattlesnake in North America, with 9 recognized subspecies. Of all the subspecies, the prairie rattlesnake (C viridis viridis) has the largest range, extending north to Alberta, Canada, and south to Coahuila province in Mexico (Fig 1). The prairie rattlesnake is the only wild venomous snake in northeastern Colorado and is therefore the only species respon-

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sible for snakebite in animals living within approximately a 200-mile radius of the Colorado State University Veterinary Teaching Hospital.

The purpose of the study reported here was to describe demographic variables, clinical and laboratory abnormalities, and morbidity and mortality rates and to assess clinical efficacy of different treatment modalities.

**Criteria for Selection of Cases**

A retrospective, computer-generated search of all medical records of snakebite in dogs treated at the Colorado State University Veterinary Teaching Hospital during a 10-year period (1988 to 1998) was conducted. Cases were included if contact with a rattlesnake was witnessed or the dog had compatible clinical signs of severe swelling around paired puncture wounds. Cases were excluded if there was any doubt in the medical record of the diagnosis of rattlesnake envenomation.

**Procedures**

Records were screened and pertinent clinical data abstracted to flow sheets and collated. The following data were sought: patient signalment, geographic location of the snakebite incident, date and time of envenomation, time to reach the hospital, anatomic location of the bite, clinical laboratory abnormalities, treatments, costs of all treatments, duration of hospitalization, complications, and clinical outcome. Clinical data were entered into a spreadsheet and assessed with a statistical package. Multiple linear regression was performed to model each response (logarithm of cell counts, cost, or days in hospital) as a function of variables determined at initial evaluation (age, weight, sex, PCV, and anatomic location of the bite) and treatments received (antimicrobials, glucocorticoids, antihistamines, analgesics, and antivenin). For all comparisons, significance was set at a value of $P \leq 0.05$.

**Results**

Patient signalment and date and time of snakebite and hospital evaluation—During the 10-year period from 1989 to 1998, 100 cases of rattlesnake bite in dogs were identified. Dogs ranged from 3 months to 12 years of age, with a median age of 3.7 years (Fig 2). Female (52%) and male (48%) dogs were nearly equally represented. Dogs weighed a mean of 26.2 kg (57.6 lb), with a range of 3.8 to 58.2 kg (8.4 to 128 lb). Date of the bite was determined from the medical record for 72 of 100 dogs (Fig 3). The time to receipt of medical attention ranged from 15 minutes to 13 hours, with a median time of 1 hour. Dogs were bitten between April 19th and October 14th, with most bites occurring between May and September (Fig 4).
Clinical findings—Anatomic location of the bite was noted in the record for 96 patients. Of the 96 bites, 78 (81.2%) occurred to the head, 12 (12.5%) to a forelimb, and 9 (9.4%) to a hind limb. When evaluated using multiple logistical regressions, the location of the bite was not associated with any other clinical variable. Swelling in the region of the bite was observed in all dogs, although severity of the swelling often could not be determined from the medical record. Many dogs evaluated within 1 hour of a witnessed bite had only mild swelling at initial evaluation, but swelling continued for several hours after admission. Estimation of signs of pain associated with the bites was not available from the medical records.

Results of initial CBC included echinocytosis (48/52 [92%]; Fig 5), thrombocytopenia (44/50 [88%]) with a median platelet count of 135,000 platelets/µl (range, 6,000 to 363,000 platelets/µl), leukocytosis (37/70 [53%]) with a median nucleated cell count of 11,700 cells/µl (range, 5,500 to 28,600 cells/µl), and a median serum total solids of 6.4 g/dl (range, 3.0 to 8.6 g/dl). The activated clotting time (ACT) was > 120 seconds in 8 of 86 (9%) patients tested, with a median ACT of 95 seconds (range, 60 to 480 seconds). The median activated clotting time increased in 20 of 78 (26%) dogs tested the next day; however, the change was not significant, with median ACT on day 2 of 104 seconds (range, 60 to 480 seconds). Mild hemocoagulation was observed, with median PCV of 53.5% (range, 26 to 68%).

Median platelet count at admission (n = 63) was 135,000 platelets/µl. The reference range for platelets in our laboratory is 200,000 to 500,000 platelets/µl. For dogs still hospitalized on days 2 and 3 after the snakebite for which recheck platelet counts were available (n = 44 on days 2 and 3), median counts decreased to 130,000 platelets/µl (range, 11,000 to 302,000 platelets/µl) and 69,000 platelets/µl (range, 13,000 to 239,000), respectively. Dogs that received antivenin (n = 22) had a higher median day-2 platelet count of 199,000 platelets/µl (range, 85,000 to 362,000 platelets/µl), compared with median count of 97,500 platelets/µl (range, 11,000 to 251,000 platelets/µl) in dogs that did not receive antivenin (78; P = 0.004).

Supportive care—Of the 100 dogs, 94 were hospitalized for observation and treatment, and 6 were treated as outpatients. Eighty-four of 100 dogs received IV administration of crystalloid fluids (either 0.9% NaCl solution, lactated Ringer’s solution, or another balanced electrolyte). Most hospitalized dogs received 25% of their blood volume (22 ml/kg [10 ml/lb]) as an initial crystalloid bolus, followed by maintenance volumes until discharge. Other treatments included 1 unit of fresh whole blood (3 dogs), 1 unit of fresh frozen plasma (1), and SC administration of heparin (10; dose range, 45 to 180 U/kg [20.5 to 81.8 U/lb], SC, q 8 h to q 6 h). Narcotic analgesics, including morphine (0.11 to 0.5 mg/kg [0.5 to 0.23 mg/lb], IM and SC), oxymorphone (0.04 to 0.2 mg/kg [0.02 to 0.09 mg/lb], SC), and fentanyl (2 to 4 µg/kg/h [0.9 to 1.8 µg/lb/h]), were administered to 15 dogs. One dog received ketoprofen (1.5 mg/kg [0.68 mg/lb], IV). Supportive care was not significantly associated with any other clinical variables.

Antivenin—Antivenin was administered to 23 of the 100 dogs. Unfortunately, we were unable to determine which brand of equine-derived antivenin was used in each case. Two dogs referred by the same owner were administered 5 ml of reconstituted antivenin each. One dog received 2 vials (2 doses of 10 ml of reconstituted antivenin, 6 hours apart). The remaining dogs that received antivenin were given one 10-ml vial. Data were reviewed to determine the relationship between the administration of antivenin and differences in clinical variables. Antivenin was not significantly associated with duration of hospitalization (P = 0.67) but was associated with higher platelet count after treatment (P = 0.004) and higher total hospital costs (P < 0.001). No adverse reactions to the antivenin were reported. No other significant associations between use of antivenin and other variables were detected.

Glucocorticoids and antihistamines—Glucocorticoids were administered to 87 of 100 dogs. Most dogs were administered 1 dose of dexamethasone sodium phosphate IV. The dose ranged from 0.2 to 4.2 mg/kg (0.09 to 2 mg/lb), with a median dose of 2 mg/kg. Glucocorticoids alone were administered to 32 dogs, and 4 dogs were treated with antihistamines alone. Antihistamines included diphenhydramine (median dose, 2.1 mg/kg [0.95 mg/lb], IV) and pyrilamine (median dose, 1.3 mg/kg [0.59 mg/lb], IV). A glucocorticoid and an antihistamine were administered to 55 dogs. The only significant effect observed regarding glucocorticoid, antihistamine, or combined treatment was a significantly higher leukocyte count following glucocorticoid treatment (median, 20,350 cells/µl), compared with the leukocyte count of those that did not receive glucocorticoids (median, 16,300 cells/µl).

Antimicrobials—Antimicrobials were administered parenterally to 87 of 100 dogs in standard dosages. Ampicillin alone (54/87 dogs) or in combination with enrofloxacin (5/87), amoxicillin alone (9/87) or in combination with enrofloxacin (5/87), cefazolin
(3/87), or cefoxitin (2/87) were most commonly prescribed. One dog received gentamicin, another received trimethoprim sulfamethoxazole, and a third was treated with procaine penicillin G. No wound-related complications (infections, abscessation, necrosis) were identified in the medical records. There was no significant association between antimicrobial treatment and any outcome variables.

**Outcome**—Hospital stay ranged from < 1 day to 5 days, with a median of 1 overnight stay in the hospital. Significant differences in duration of hospitalization were not detected among any of the treatment groups. Body weight, however, was inversely correlated with duration of hospitalization (P < 0.05). There was no association between days hospitalized and any of the other clinical variables.

Only 1 dog, a 2-year-old 5.5-kg (12-lb) sexually intact female miniature Dachshund, died. This dog was referred to our hospital 24 hours after a witnessed rattlesnake bite to the nose. At admission, the dog had signs of obtundation and swelling of the head and neck. The dog had signs of dyspnea and circulatory shock. Oxygen was given by face mask, and 400 ml of balanced electrolyte was administered IV. One vial of antivenin and dexamethasone sodium phosphate (2 mg/kg, IV) were also administered. Forty-five minutes after referral, the dog suffered cardiopulmonary arrest and died. Necropsy revealed severe subcutaneous hemorrhage and edema surrounding the head and neck. Multifocal echymotic hemorrhages were detected on the heart, stomach, intestines, and urinary bladder. It was not found in the record or in the necropsy report whether the larynx or airway was swollen.

**Discussion**

The prairie rattlesnake bites were associated with swelling of the affected area, echinocytosis, and thrombocytopenia in most dogs. Snakebites generally were located on the face (81%); almost equal numbers of bites affected the forelimbs (12.4%) and the hind limbs (9.4%). Despite serious clinical signs on admission, results of this study indicate that most dogs referred to a veterinary hospital survive the bite with basic supportive care.

Most dogs were bitten in the late afternoon, with a large number of bites also occurring around noon. It would seem logical that most witnessed bites occur when dogs are roaming through snake habitat on walks with owners during their lunch hour and after work in the early evening.

All bites in this series occurred between April 19 and October 14. This is best explained from observations that prairie rattlesnakes in Colorado begin hibernation or denning in mid October and emerge in the spring between March 20 and April 20.1 Lower number of bites in April and October may reflect more torpid behavior observed during the spring and fall laying-out period when the snakes sun near the entrance to their den.

The hematologic changes associated with the *C. viridis viridis* envenomation included echinocytosis, thrombocytopenia, and leukocytosis. Echinocytosis is the most common change and was evident even before substantial swelling took place. Possible mechanisms for the echinocytosis include depletion of ATP from cell membrane cation pumps by ATPase enzymes and alteration of erythrocytic membrane composition by phospholipases, both of which are present in rattlesnake venom.10 In a study11 to define the mechanisms of echinocyte formation, the addition of ethylenediaminetraacetic acid prevented formation of echinocytes in vitro, suggesting that a change in calcium or a metalloprotein participated in the formation of echinocytes. Although echinocytosis can be found in association with many diseases, > 90% of the dogs reported here had echinocytosis on admission, so it would seem that echinocytes are a reasonably good marker for prairie rattlesnake envenomation in dogs.

Thrombocytopenia was detected in 88% of the dogs in which platelet counts were performed. Both the enzymatic and nonenzymatic components of rattlesnake venom can cause platelet aggregation and induce thrombocytopenia by a variety of mechanisms.12 Some mechanisms culminate in formation of thromboxane A2 either by direct release of arachidonic acid or indirectly by activating endogenous phospholipase A2. Other venom components can induce a conformational change in platelet glycoproteins that allows fibrinogen binding and platelet aggregation, whereas still others activate prothrombin or generate thrombin-like proteases that will induce platelet aggregation.13 In an experimental snakebite model, rabbits injected with the venom of the Western diamondback rattlesnake (*C. atrox*) had substantial consumption of platelets. When tissue samples from the site of envenomation were compared with the unaffected contralateral limb, a large proportion of labeled platelets were found to be sequestered at the site of actual tissue injury.13

Among the variables we studied, thrombocytopenia was the only clinical variable associated with antivenin treatment. However, whether thrombocytopenia or its magnitude is an indication for antivenin treatment is controversial. For example, bites of the timber rattlesnake (*C. horridus*) are associated with severe thrombocytopenia in humans. In 1 case report,14 a man bitten by *C. horridus* received more than 50 vials of antivenin with no improvement in platelet count. Following that report, there was some discussion in letters to the editor regarding the futility of treating a laboratory abnormality instead of the patient (who continued to improve clinically, despite platelet count below reference range).15 Most of the dogs in our study were discharged from the hospital with platelet counts below reference range, whether they received antivenin or not, and all discharged dogs survived.

Several factors may explain the apparent lack of clinical response to antivenin observed in our study. Crotalid polyvalent antiserum is a refined, concentrated preparation of equine serum globulins obtained from horses immunized with venom from the Eastern diamondback rattlesnake (*C. adamanteus*), Western diamondback rattlesnake (*C. atrox*), Central and South American rattlesnake (*C. terrificus*), and the fer-de-lance (*Bothrops atrox*). Because none of the subspecies...
of the Western diamondback rattlesnake are represented by use of ELISA. 18 Quantitation of venom has been evaluated by use of prospective controlled studies because of inter- and intraspecies variation, these findings cannot and should not be extrapolated to all species differences, age of the snake and time since the last meal are variables unknown to the clinician. Twenty to 25% of North American pit viper bites are termed dry bites, with no clinical evidence of envenomation.22 Conservative treatment (ie, IV administration of fluids, use of analgesics, and local wound care) has been advocated for humans bitten by copperheads and other pit vipers with low-toxicity venom.23,24 Others have proposed severity-of-envenomation scoring to identify patients who would benefit from more aggressive treatments, including antivenin.3,25 Without a validated scoring system for dogs, canine snakebite victims must be evaluated and treated individually. Clinical findings should provide the clinician enough information to institute appropriate supportive care.

Not all pet owners can afford the cost of antivenin (several hundred dollars per unit). Recently, practitioners have also faced shortages of equine-source polyvalent antivenin. A new polyvalent antivenin made from purified ovine fragmented antibody is now available and costs more than 4 times as much as standard polyvalent antivenin. This Fab product has not yet been evaluated by use of prospective controlled studies in dogs.

Data regarding infection of snakebite wounds are scarce, and opinions have been divided about the need for prophylactic antimicrobial treatment.20 In a report from Brazil, 40 humans bitten by the pit vipers Bothrops jararaca who developed bite wound-related abscesses were evaluated, and cultures revealed both aerobic (mainly enterobacteria) and anaerobic (mainly Bacteroides spp) infections. According to the authors, during the year the study was conducted, 21,463 cases of snakebite were reported to the Brazilian Ministry of Health. In a prospective study21 of 54 human snakebite patients in California, only 1 patient developed a wound-related infection. Only 12 of these patients received antimicrobials, and the authors concluded that routine prophylactic use of antimicrobials in such patients may not be warranted. Presently, prophylactic use of antimicrobials is not routinely recommended for human snakebite victims.3 Although wound infection was not reported in any dog in our study, the small number of dogs that did not receive antimicrobials and the lack of follow-up make it difficult to determine treatment recommendations. Serious complications that developed after discharge may have been overlooked.

Our results suggest that antivenin may not be necessary for most dogs bitten by the prairie rattlesnake. However, with no signs of hypotension or cardiovascular collapse in most of the dogs, it was impossible to draw conclusions about the optimal treatment for severely affected dogs. It should also be noted that because of inter- and intraspecies variation, these findings cannot and should not be extrapolated to all Crotalidae envenomations or envenomation by C. viridis viridis in other species.

Many variables have been reported to affect the amount of venom injected at the time of the bite.4 In addition to species differences, age of the snake and time since the last meal are variables unknown to the clinician. Twenty to 25% of North American pit viper bites are termed dry bites, with no clinical evidence of envenomation.22 Conservative treatment (ie, IV administration of fluids, use of analgesics, and local wound care) has been advocated for humans bitten by copperheads and other pit vipers with low-toxicity venom.23,24 Without a validated scoring system for dogs, canine snakebite victims must be evaluated and treated individually. Clinical findings should provide the clinician enough information to institute appropriate supportive care.

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References


