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SNAKEBITE / CROTALID ENVENOMATION

Evidence Based Medicine Guideline

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SUMMARY
Snakebite / crotalid envenomations are characterized by an erratic and unpredictable clinical course. They should be considered medical emergencies requiring close monitoring. Manifestations of crotalid envenomations may include local tissue injury, coagulopathy, and severe systemic effects. Treatment for venomous snakebites includes aggressive supportive care and prompt administration of antivenom to selected patients. Although prospective data on crotalid antivenoms are limited, use of antivenom in progressive crotalid envenomations should be considered as standard of care.

RECOMMENDATIONS

- **Level 1**
  - **None**
- **Level 2**
  - **Antivenom therapy should be administered for the following indications:**
    - **Swelling that is more than minimal and progressing, particularly proximal progression past a major joint**
    - **Elevated prothrombin time; downward trending fibrinogen or platelet count**
    - **Systemic signs: severe hypotension, altered sensorium, tachycardia, tachypnea, and/or respiratory distress**
  - **Antivenom dosing regimen should be based on agent used:**
    - **Crotalidae**
      - **Anavip® initial dose is ten vials IV infused over 60 minutes.**
      - **Crofab® initial dose is four to six vials IV over 60 minutes, or ten vials depending on the severity of the envenomation.**
      - **Initial bolus dosing should be repeated every hour until control of progression and symptoms is achieved.**
    - **Elapidae (Coral snakebites)**
      - **Antivenin Micrurus Fulvius initial dose is three to five vials IV administered over 30 minutes.**
- **Level 3**
  - **Patients receiving antivenom therapy should be provided with education and counseling regarding serum sickness prior to discharge and signs and symptoms of delayed coagulopathies for up to two weeks. Anavip® is the preferred agent at Orlando Health due to the potential benefit in reducing delayed coagulopathies.**
  - **Patients started on Crofab® at an outside facility may continue with Crofab® upon transfer.**
  - **Patients with allergic reactions to either product may change to the alternate product, restarting therapy with initial dosing.**
  - **Continuous infusion of Crofab® should be considered in patients with recurrent, late-onset coagulopathies that do not respond to traditional or alternative agents.**

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

DISCLAIMER: These guidelines were prepared by the Department of Surgical Education, Orlando Regional Medical Center. They are intended as a general statement regarding appropriate patient care practices based on the medical literature and clinical expertise at the time of development. They should not be considered protocol or policy nor are intended to replace clinical judgment or dictate care of individual patients.

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INTRODUCTION

About 9,000 patients per year are bitten by venomous snakes in the United States, five of which die from their injuries (1). Over 99% of the venomous snake bites in the US are caused by snakes of the subfamily Crotalidae, also known as pit vipers. These snakes include rattlesnakes, cottonmouths/water moccasins, and copperheads (2). Snakebite envenomation is characterized by an erratic and unpredictable clinical course, making assessment and determination of the severity of envenomation difficult. They should be considered medical emergencies that require observation in a hospital setting. Manifestations of crotalid envenomation may include local tissue injury, such as marked tissue swelling, pain with potential soft tissue necrosis and severe coagulopathies characterized by hypofibrinogenemia, prolonged prothrombin time (PT), variable changes to activated partial thromboplastin time (aPTT), and decreased platelet count (3). These coagulopathies have been reported to cause episodes of gingival bleeding, epistaxis, gastrointestinal hemorrhage, and potential intracranial bleeding. Severe systemic effects including hypotension, cardiovascular toxicity and neurotoxicity may also occur. Treatment for venomous snakebites includes prompt administration of antivenom in the case of progressive symptoms from envenomation (1).

Initial Triage and Management

When a patient arrives to the emergency department after a venomous snake bite, a detailed history should be collected to determine the nature of the envenomation and identify the snake, if possible. Therapy should begin by administering tetanus vaccine and/or booster; data suggests that seldom are snake bites associated with Clostridium tetani, however, this has become standard practice throughout multiple World Health Organization and local guidelines (1,2,4). The Poison Control center should be notified immediately. Venom metalloproteases cleave cell-cell junctions that weaken vascular walls and increase capillary permeability. There is an increase in vasodilation and third-spacing of fluid and blood. Intravenous fluid should be administered to these patients. Blood should be drawn from an unaffected extremity and a CBC, aPTT, PT/INR, and fibrinogen (2). Routine D-Dimer and fibrin split product measurements are not needed as these tests do not affect patient management The presence of fibrinogen split-products in the first 12 hours after envenomization is 87% sensitive and 69% specific for the presence of coagulopathy (1). Other test considerations include liver function tests, blood type and crossmatch, venous blood gas, and thromboelastography.

Serial examinations should be performed to identify fang marks, measure the circumference of the affected sites, and the circumference about 4 inches and 8 inches proximal to the bite site, marking the measurement sites with a surgical skin pen. The measurements should be repeated every 15 minutes for one hour, followed by every 30 minutes for one hour, followed by every hour for four hours, and every 6 hours while hospitalized. Serial measurements should be documented for at least 24 hours in patients who receive antivenom from time of last dose administration. If a retained fang is suspected, a bedside ultrasound or x-ray should be considered for rule out.

Applying a tourniquet or constrictive band to the affected extremity above the snake bite has been advocated in the past, but there is no evidence to support this therapy. In fact, applying a tourniquet may precipitate additional local tissue destruction and necrosis. Tourniquets are therefore not recommended. Ice application and wound incisions have also been debunked as beneficial therapies after venomous snake bites (2). Though mostly supported by anecdotal evidence, immobilization of the affected extremity has been theoretically proposed to prevent the spread of venom. Immobilization, elevation, and use of a wide block of compression on an affected extremity (applying up to 20 mmHg of pressure) to assist in compressing superficial veins and lymphatics, have been advocated to be safe initial measures after snake bites with little deleterious effects to the patient. However, the benefit of these therapies is without quality evidence (1,2).

For patients that are asymptomatic after snake bite, they may be safely observed without administration of antivenom. If there is swelling of an extremity, the borders should be marked and re-marked every 30 minutes to monitor for progression of edema (2). Previously, prophylactic fasciotomies were debated as standard of care, however, this has fallen out of favor. Venom may cause edema and local tissue destruction, but compartment pressures are rarely elevated. Increasing edema of an extremity after envenomization often resolves with administration of antivenom therapy without need for fasciotomy. Previous reports in the literature suggest measuring creatinine kinase levels to detect potential rhabdomyolysis following venomous bite. There is poor clinical

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evidence that snake bites cause rhabdomyolysis however. Clinical judgement should support laboratory studies, but creatinine kinase is no longer recommended as an initial laboratory marker (1).

Pain control should include narcotics. From a theoretical perspective, NSAIDs have been historically avoided for pain control after snakebite due to concern for possible increased bleeding risk. However, in a retrospective chart review of patients at St. Louis Children's Hospital between 1998 to 2016 and from Barnes Jewish Hospital from 2001 to 2016, 147 copperhead snake bite victims were identified (5). Of those, 52% received NSAIDs in the form of IV ketorolac, IV ibuprofen or oral naproxen. The authors concluded that there was no significant association between treatment with NSAIDs and bleeding in patient who sustained copperhead bites (Class III). It should be mentioned that, of all the crotalid snakes, copperheads have the mildest and least-coagulopathic venom. Further investigation should be undertaken to fully elucidate whether NSAID use is safe in all crotalid snake bites. In addition, a consensus workshop for the management of crotaline snakebites recommends avoiding the use of NSAIDs because of the theoretical harm associated with platelet dysfunction caused by NSAIDs in a potentially thrombocytopenic patient (24).

Some case reports have detailed nerve blocks as effective analgesia after extremity snake bites; this information has only been taken from anecdotal case reports and will require further investigation to detail efficacy in a larger patient population (6).

Antivenom Therapy

Antivenom therapy is derived from IgG fragments from horses, mules, donkeys, or sheep. Due to its immunologic nature, there is potential for severe anaphylactoid reactions and guidelines recommend only administering antivenom in cases of progressive venom injury, defined as worsening local injury (e.g., swelling, ecchymosis), development of a clinically important coagulation abnormality (elevated protime, downward trending fibrinogen or platelets), or systemic effects (e.g., severe hypotension, altered mental status, tachycardia, tachypnea, or respiratory distress). Therapy may be held in cases of only localized pain and swelling (1,7). In fact, 20-25% of venomous snake bites are "dry" and provide no venom to the victim; antivenom in these cases will provide no benefit. Patients who do not receive antivenom therapy and do not present with local or systemic signs of toxicity should be monitored for a minimum of eight hours and undergo serial measurements drawn six hours after initial labs to confirm no signs of envenomation. Patients who show minimal symptoms of envenomation should be monitored for a minimum of 24 hours and labs should be drawn every six hours.

The severity of envenomation by North American pit vipers can be assessed by using the guidelines provided below.

Guidelines for Assessing the Severity of North American Pit-Viper Envenomations (8)			
Signs and Symptoms	**Severity of Envenomation***		
	Minimal	**Moderate**	**Severe**
Local	Swelling, erythema, or ecchymosis confined to the site of the bite	Progression of swelling, erythema, or ecchymosis beyond the site of the bite	Rapid swelling, erythema, or ecchymosis involving the entire body part
Systemic	No systemic signs or symptoms	Non-life-threatening signs and symptoms (nausea, vomiting, perioral paresthesias, and mild hypotension)	Markedly severe signs and symptoms (hypotension [systolic blood pressure <80 mm Hg], altered sensorium, tachycardia, tachypnea, and respiratory distress)
Coagulation	No coagulation abnormalities or other important laboratory abnormalities	Mildly abnormal coagulation profile without clinically significant bleeding; mild abnormalities on other laboratory tests	Markedly abnormal coagulation profile with evidence of bleeding or threat of spontaneous hemorrhage (unmeasurable INR, APTT, and fibrinogen; severe thrombocytopenia with platelet count <20,000 per mm_3); results of other laboratory tests may be severely abnormal
* The ultimate grade of severity of any envenomation is determined based on the most severe sign, symptom, or laboratory abnormality.			

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Antivenom Crotalidae Polyvalent (ACP) - no longer available

Antivenom treatment was first introduced by Albert Calmette in the 1890s as an immunoglobulin fragment derived from horse (equine) or sheep (ovine) (4). One of the first commercially available antivenoms was Antivenom (Crotalidae) Polyvalent (ACP), which was introduced in the early 1950's by Wyeth Laboratories. Although the equine-derived antivenom was used clinically for many years and resulted in a marked decrease in mortality rate, there are no prospective data available regarding its efficacy (3,7). In addition, the use of ACP is limited by the frequency of adverse effects, including acute reactions, ranging from minor rashes to anaphylaxis, in 23-56% of patients and serum sickness, a delayed type III hypersensitivity reaction causing fever, chills, malaise, and arthralgia, in 50 to 75% of patients (2,9). Due to the high incidence of hypersensitivity reactions, the manufacture of ACP was discontinued in April 2007.

Crotalidae Polyvalent Immune Fab (FabAV or Crofab®)

Approved by the FDA in October 2000, Crotalidae Polyvalent Immune Fab (FabAV) or Crofab® was the first crotalid snake antivenom approved in almost 50 years. Crofab® is the Fab fragment of antibodies derived from ovine sources immunized with venom from Crotalus atrox (Western Diamondback rattlesnake), Crotalus adamanteus (Eastern Diamondback rattlesnake), Crotalus scutulatus (Mojave rattlesnake), and Agkistrodon piscivorus (Cottonmouth or Water Moccasin), in which the immunogenic Fc portions of the antibody and the non-neutralizing components of the serum are eliminated during purification. As such, Crofab® may be associated with a lower risk of allergic and serum sickness type reactions. Crofab® is associated with an improved reconstitution profile and animal studies indicate that Crofab® is up to 5 times more potent than ACP (9). Anaphylactoid reactions have been reported in up to 6% of patients but have been reported as mild in nature (1). Therapy is most effective if started within 4 hours after insult. The premarketing trial of Crofab® advocated four to six vials of antivenom as an initial dose for progressive venom injury and this has become the standard initial treatment. Antivenom infusion has been associated with histamine release and this, along with the vasodilatory effects of venom, has required antivenom to be administered with IV fluid. In the cases of moderate envenomation (progressing tissue, hematologic, and systemic effects), four to six vials of Crofab® should be diluted in 250 mL of normal saline and administered over 1 hour. In severe envenomation (shock or active bleeding), ten vials should be administered. Previous reports suggest infusing the initial dose slowly over 10 minutes at a rate of 25-50 mL/hr to observe for allergic reaction, however, this slow infusion is controversial and expert consensus data suggests no standard infusion rate for initial administration (1,10). All patients receiving initial antivenom therapy should be observed in the ICU. Epinephrine, H1 and H2 blockers and instruments for intubation should be bedside in the case of an anaphylactic reaction. There is no evidence that pre-treatment with antihistamines is beneficial to prevent potential anaphylactic reactions. If a patient tolerates initial antivenom infusion, it is safe to observe the patient in the ward versus the intensive care unit (1).

Laboratory data should be repeated within one hour of initial infusion of antivenom to assess response. There is no evidence for following fibrin split-products after treatment; instead, fibrinogen is a more specific marker of response (1). There is some evidence to suggest thromboelastometry may help drive treatment. Although initial treatment should be antivenom, blood products may aid in resuscitation in the case of continued coagulopathy despite antivenom infusion (11). If labs do not reveal a response to antivenom therapy, initial bolus dosing should be repeated every hour with an additional four to six vials of Crofab® for moderate envenomation and ten vials for severe envenomations until response is achieved. Response is defined as cessation of swelling progression, reversal of coagulopathy, and normalization of systemic signs of envenomation. Reportedly, few patients fail to respond after 18 vials of therapy (1,4,10). Once control is achieved, two vials every 6 hours should be administered for up to 18 hours.

Crotalidae immune F[ab']2 (Anavip®)

In May 2015, Crotalidae immune F[ab']2 or Anavip® was FDA approved for envenomations from the North American rattlesnake, with the indication expanding in April 2021 to cover all rattlesnake, copperhead, and cottonmouth/water moccasin envenomations. Anavip® is a F(ab')2 fragment with two venom binding sites, compared to Crofab® which is a single Fab fragment with one venom binding site. It is derived from equine sources immunized with venom from Bothrops asper (Central American lancehead pit viper) and Crotalus durissus (South American rattlesnake) (20). Compared to Crofab®, Anavip® has a longer elimination half-life and was found to result in significantly lower rates of recurrent or late thrombocytopenia. In addition, Anavip® eliminates the need for additional doses commonly required with shorter-acting antivenom, Crofab®.

Anavip® is the recommended antivenom due to potential benefits in reducing delayed coagulopathies and cost savings. Ten vials should be infused over 60 minutes. The rate should be 25-50 mL/hr for the first 10 minutes and

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increased to 250 mL/hr if no adverse reaction is observed. In cases of incomplete response, the bolus may be repeated every hour until control is achieved. Maintenance dosing is not routinely required (20).

Antivenoms work by binding and neutralizing venom toxins, facilitating redistribution away from target tissues and elimination from the body (10). For this reason, pediatric doses of antivenom are similar to adult dosages (1).

Recurrence

An unexpected observation identified during clinical trials was the recurrence of local symptoms or coagulation abnormalities after completion of treatment. Recurrence is defined as the occurrence of any venom effect following resolution of that abnormality. Recurrent coagulopathy was especially noted among patients with coagulopathy at presentation. Multiple explanations have been proposed for the pathophysiology of symptom recurrence, including prolonged venom absorption from the bite site and dissociation of the venom-FabAV complex (9). Recurrence has been documented to have occurred in up to 50% of patients receiving Crofab®. To monitor for recurrence, physicians should observe patients with serial labs, although, local tissue recurrence with pain and swelling may become evident six to 36 hours after treatment. Treatment for recurrence includes a dose of antivenom (Crofab® – four to six vials or Anavip® - four vials), although response may be attenuated. Continuous infusion can be considered in patients who do not respond to treatment.

Allergic Reactions to Antivenom

There is no absolute contraindication to antivenom treatment. Patients with previous reactions to equine or ovine serum and patients with severe atopic disease may be most susceptible to anaphylactic response after administration (4). Because papain is used to cleave the whole antibody into Fab, Crofab® should be administered cautiously to patients with a history of hypersensitivity to papaya. Appropriate management for anaphylactic reactions should be readily available. Patients with allergies to papain, chymopapain, other papaya extracts, or the pineapple enzyme bromelain may also be at risk of an allergic reaction. Because some dust mite and latex allergens share a similar structure with papain, patients with these allergies may also demonstrate hypersensitivity to Crofab® (10). Premedication has been described with Benadryl and cimetidine. There is poor data to support applying antivenom in a skin test to assess allergenicity as there is a 10-36% false negative rate and this can precipitate anaphylaxis. Awaiting the results of a skin test may also delay treatment (2).

In cases of a mild-moderate allergic reaction (rash, flushing, gastrointestinal symptoms), stop infusing the antivenom and re-start at a slower rate. In cases of severe, anaphylactic reactions, promptly administer epinephrine 0.5 mg for adults or 0.01 mg/kg body weight for children. After initial dosing with epinephrine, antihistamines and corticosteroids should be administered (4).

Follow-Up

After sustaining a snake bite from a venomous snake, consensus guidelines suggest a period of 18-24 hours of observation to be sufficient. During this observation period, laboratory studies should be repeated serially every six hours while hospitalized. Some physicians argue that antivenom therapy should be maintained even after resolution of symptoms and normalization of laboratory blood work to prevent recurrence; this is controversial and there is currently no consensus data to support or refute this. After the first 24 hours of observation, patients are often able to be discharged from the hospital with close follow-up as an outpatient (1). There is a 3% risk of wound infection after snake bite and prophylactic antibiotics at discharge are not recommended (2). Patients should be advised to return to the hospital if they have recurrence of pain or swelling or signs of bleeding such as gingival bleeding or epistaxis.

Serum sickness, a type III hypersensitivity reaction, may manifest with fever, rash and arthralgias in 5-10% of patients treated with antivenom. This can occur within one to four weeks after treatment with antivenom. Serum sickness often responds to a five-day course of antihistamines and systemic corticosteroids (1,4).

Coral Snake Envenomation

Coral snakes belong to the Elapidae family and are the only other native venomous snakes in the United States. Due to the reclusive nature and short, fixed fangs of the coral snake, the incidence of coral snakebites is rare in the United States, accounting for only 20 to 25 bites per year (3). Coral snake envenomation produces little or no local effects, but may result in changes in mental status, such as euphoria and drowsiness, and are characterized by their neurotoxic effects. Neurologic manifestations are usually cranial nerve palsies, including ptosis and dysphagia, and left untreated, may progress to respiratory paralysis (8). The onset of neurotoxic effects may be delayed up to 12 hours and once present, may progress rapidly and are difficult to reverse. The definitive treatment for coral snake

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envenomation is the immediate administration of antivenom. The only approved, coral snake antivenom available in the United States is Antivenin Micrurus Fulvius, which is derived from the Eastern Coral Snake. Initial dosing is three to five vials administered at 250 – 500 mL over 30 minutes. The first one to two mL should be administered over three to five minutes with careful observation for any allergic reaction. Normal saline at 250 – 500 mL per hour should be started at the same time as antivenom administration (21). Supportive treatment alone can be effective, as death is due to the failure to initiate ventilatory support when symptoms develop. Mechanical ventilation may be required. Even with treatment, neurotoxic effects can last three to six days (3). Alternatively, Coralmyn, produced by the Mexican company Bioclon has been shown to be effective in neutralizing coral snake venom (14). However, the rarity of bites and expense of required testing for FDA approval make manufacture in the United States financially unlikely.

LITERATURE REVIEW

In a prospective, open-label, multicenter trial, Dart et al. evaluated the efficacy and safety of Crofab® in 11 patients age 10 years or older with progression of envenomation syndrome (defined by worsening of local injury, coagulation abnormalities, or systemic symptoms) after mild or moderate crotalid envenomation in the six hours preceding presentation (15). All patients received an initial intravenous dose of four vials. If clinical symptoms continued to worsen, an additional 4 vials were permitted. All patients demonstrated clinical improvement following antivenom administration. At the four-hour assessment, all patients had improved clinically with snakebite severity scores (SSS), a validated measure of limb swelling, coagulation tests, and gastrointestinal, neurologic, and cardiac signs, having remained the same or decreased, indicating a halt to envenomation progression. Five patients received four vials and six patients required eight vials of study antivenom. The mean severity score was 3.9±2.2 before antivenom administration and 2.6±1.0 12 hours after administration. Two patients required additional antivenom for recurrent swelling approximately 15 hours after initial improvement from antivenom administration and one patient was found to have recurrent coagulopathy at the one-week follow-up visit, which resolved over several days. No patients experienced anaphylaxis or serum sickness from antivenom administration at follow-up visits seven and 14 days after discharge (Class II).

To suppress recurrence, Dart et al. conducted a prospective, randomized, open-label trial comparing two dosing schedules of Crofab® in 31 patients, aged 10 years or older, with minimal or moderate crotaline envenomations within the six hours preceding antivenom administration showing evidence of progression (9). Patients were initially treated with six vials of Crofab® and, if necessary, a second dose of six vials was allowed. After initial control was achieved, the scheduled group received an additional two doses every six hours for 18 hours while the PRN group received no planned additional doses. All patients, both in the scheduled and PRN groups, had a decrease in mean total SSS with mean severity score decreasing from 4.35 to 2.39 ($p<0.001$) after antivenom administration in the 12-hour evaluation period; however, half of the patients in the PRN group required unplanned doses of Crofab® for recurrence of local wound progression during the first 12 hours. The total amount of antivenom administered was not statistically different between groups, indicating a continued need for antivenom for adequate treatment. Nineteen percent of patients developed an acute reaction during infusion and 23% developed serum sickness. It should be noted, however, that five of the six patients who developed serum sickness were treated with a batch of Crofab® that was incompletely purified due to a flawed manufacturing process (Class II).

Although bites by the copperhead snake (Agkistrodon contortrix) were an exclusion criterion in safety and efficacy trials of Crofab®, this agent is being used for copperhead envenomation (16,17). In a retrospective chart review of 32 copperhead snake envenomations, primarily moderate in nature, rapid initial response was achieved in 28 cases (17). There were four treatment failures, defined as progression of envenomation or failure to achieve initial control within 12 hours. Recurrent local effects developed in six patients and repeated, planned doses of antivenom did not reduce the incidence of recurrent swelling (Class II).

Case reports demonstrate that delayed administration of antivenom may be beneficial for patients with coagulopathies and local symptoms greater than six hours after envenomation (18,19). A case series by Lavonas et al. reported 28 patients with severe envenomation, all with clinical improvement after receiving Crofab® (Class III) (12).

Optimal dosing beyond an 18-hour period has not been established to-date and there are no prospective data evaluating the efficacy of Crofab® in patients presenting with severe envenomation. Additionally, no prospective studies have been conducted comparing Crofab® to other treatments for snakebite envenomations, such as ACP or observation alone.

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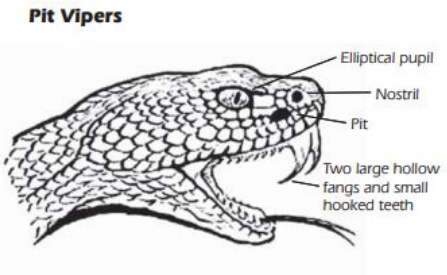
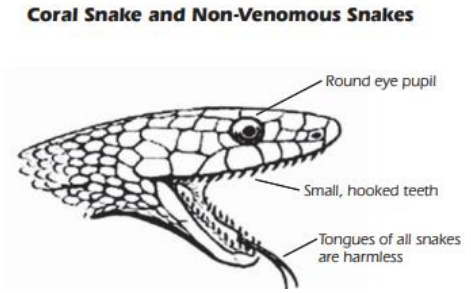
In patients who do not respond to initial therapy, a continuous infusion of Crofab® can be considered. A case series by Bush et al. reported five patients that received continuous infusions of Crofab® due to profound late hematological abnormalities or bleeding complications. Patients received 2-4 vials per day, titrated to effect and continued for 6 to 14 days post-envenomation. All patients responded to management with cessation of progression or improvement in hematological abnormalities (25).

To compare the efficacy of Crofab® to Anavip®, Bush et al. conducted a prospective, double-blind, randomized clinical trial comparing late coagulopathy in snakebitten patients. Patients were randomized to one of three groups: 1) Anavip® ten vials followed by maintenance dosing of four vials every six hours for three doses (n=39) 2) Anavip® ten vials followed by maintenance dosing of placebo every six hours for three doses (n=38) 3) Crofab® five vials every two hours followed by maintenance of two vials every six hours for three doses (n=37). Four vials of Anavip® or two vials of Crofab® could be repeated as needed for ongoing envenomation signs. The primary outcome was coagulopathy which was defined as platelet count <150,000, fibrinogen <150 mg/dL, or use of antivenom to treat coagulation abnormality between the end of maintenance dosing and day five. Coagulopathy was significantly lower in the Anavip® groups than in the Crofab® group (10.3% vs 5.3% vs 29.7% for groups 1, 2, and 3 respectively). Mean antivenom dose in terms of vials was higher among the Anavip® group (22). A post-hoc analysis was conducted in patients with copperhead snakebites and found no significant difference in the number of repeat doses required for initial control, number of patients requiring unscheduled doses during maintenance, and the time from antivenom administration to initial control (23).

Sánchez et al. compared neutralization between the Wyeth coral snake and Coralmyn antivenoms with the North American coral snake venoms. The venom lethal doses (LD50) and antivenom effective doses (ED50) were determined in 18–20 g, female mice. Coralmyn antivenom was able to effectively neutralize three LD50 doses of all venom from both Micrurus tener tener and Micrurus fulvius fulvius (14).

General Snake Information





Pit Vipers (Crotalidae)	Elapidae
• Eastern Diamondback Rattlesnake (Crotalus adamanteus) • Pigmy Rattlesnake (Sistrurus miliarius) • Cottonmouth/Water Moccasin (Agkistrodon piscivorus) • Copperhead (Agkistrodon contortrix) • Canebrake Rattlesnake (Crotalus horridus)	• Coral Snake (Micrurus Fulvius)

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