

## Clinical Practice Statement

### ***How Should Native Crotalid Envenomation Be Managed in the Emergency Department?***

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#### Disclosures:

- Dr. Greene has disclosed a conflict of interest-served as a speaker for BTG/Boston Scientific.
- Drs. Cheng, Giwa and Mills have disclosed no commercial relationships or conflicts of interest.

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#### Recommendations:

- 1. Address airway, breathing, circulation, then assess for local, hematologic, and/or systemic toxicity indicative of envenomation.**
- 2. Assess and determine the antivenom dosage needed.**
- 3. Prophylactic antibiotics and surgical intervention are unnecessary and should be avoided.**

#### Executive Summary

##### **1. How should patients with potential snake envenomation be assessed?**

After life-threatening airway, breathing, or circulatory conditions are identified and corrected, snakebite victims should be assessed for local, hematologic, and systemic toxicity. Clinicians should examine the affected extremity for swelling, tenderness, and hemorrhagic blebs every 15 – 30 minutes for a minimum of eight hours and until progression has halted [1].

All patients with possible snakebite envenomation should have the following laboratory tests performed:

- Complete blood count (CBC), Basic metabolic profile (BMP)
- Prothrombin time (PT), Fibrinogen, Creatine kinase (CK)

Serial dynamometry and negative inspiratory force (NIF) assessments should be measured on patients with bites from potentially neurotoxic rattlesnakes. Capnography should also be used to identify patients with mild respiratory insufficiency.

##### **2. What are the initial steps in snakebite management?**

Life-threatening conditions must be immediately stabilized. Ensure airway patency and adequate oxygenation and ventilation. Euvolemia must be maintained, but aggressive fluid resuscitation should be avoided.

Analgesia is an essential component to snakebite management. Intravenous opioids are preferred initially. NSAIDs are discouraged because of the potential inhibition of platelet function. The use of topical ice packs is discouraged because prolonged cryotherapy is harmful to tissue [2].

The crotalid-envenomated limb should be elevated once the patient has arrived at the hospital. This prevents the venom from accumulating in the extremity and reduces the hydrostatic pressures that can exacerbate tissue swelling.

### **3. What are the indications for antivenom?**

Administer antivenom for any of the following:

- significant or progressive local tissue damage e.g. tenderness, swelling, hemorrhagic bleb
- hematologic toxicity, e.g. PT > 15 s, fibrinogen < 150 mg/dL, platelets < 150K/ $\mu$ L
- systemic toxicity, e.g. hypotension, airway swelling, neurological toxicity

If the swelling and tenderness are more than minimal and have extended beyond a major joint (e.g. wrist, ankle), antivenom is warranted [1]. If there is significant local tissue injury, e.g. necrosis, antivenom is also indicated, even if the swelling has not progressed across a joint. Antivenom is most effective when given early [3].

### **4. How should antivenom be dosed?**

There are currently two antivenoms used in the treatment of native crotalid envenomations. Crotalidae Polyvalent Immune Fab Ovine (CroFab®) is FDA-approved for the treatment of all North American crotalid envenomations [4]. Initial dosing of CroFab® is 4 – 12 vials. If control is achieved within one – two hours, maintenance dosing consisting of two vials of every six hours for three doses is recommended starting six hours after the initial dose. If control is not initially achieved, another 4 – 6 vials should be administered. If initial control is not achieved after two doses, a medical toxicologist or other snakebite expert should be consulted. CroFab® should be used with caution in patients with allergy to latex, papaya, pineapple, papain, bromelain, and sheep.

Crotalidae Immune F(ab')<sub>2</sub> Equine (Anavip®) is FDA-approved for the treatment of North American rattlesnake bites but not envenomations from copperheads or cottonmouths [5]. The recommended starting dose of Anavip® is 10 vials. An additional 10 vials should be given if initial control is not attained within one – two hours. Maintenance dosing is not recommended for Anavip®, and it should be used with caution in patients with allergy to horses, pepsin, and cresol.

As of August 2020, only CroFab® is FDA-approved for all North American crotalids, so it can be used for any copperhead, cottonmouth, or rattlesnake envenomation, including when the species cannot be determined. Both CroFab® and Anavip® are FDA-approved for rattlesnake envenomations, and the choice of one over the other should be based on patient allergies, prior adverse reaction to either product, availability, and familiarity with each product.

### **5. Should copperhead envenomations be managed differently from other crotalid envenomation?**

Copperhead envenomations should be treated like other native crotalid envenomation. Although the average copperhead envenomation tends to be less severe than a typical rattlesnake envenomation, any native crotalid envenomation can result in significant local and systemic toxicity, and many snakes go unidentified or misidentified.

A randomized clinical trial demonstrated that copperhead envenomations recover more quickly when treated with CroFab® compared to placebo [6]. CroFab® also reduced total opioid requirements [7].

### **6. To what unit should snakebite patients be admitted?**

Many crotalid envenomations can be safely managed on a general medical floor. Admission to the ICU is recommended for patients with significant systemic toxicity. Early medical toxicology consultation is recommended.

Hospital length of stay is decreased by an average 21 hours when a toxicologist is involved in patient care, with no difference in readmission rates [8]. Poison control should be contacted for complex cases when medical toxicology is unavailable.

**7. What is the role of antibiotics following crotalid envenomation?**

Infection is uncommon following crotalid envenomation [9]. Prophylactic antibiotics have not proven to be beneficial, and indiscriminate use of antibiotics can cause side effects and contribute to antimicrobial resistance [9,10].

**8. What are the indications for surgical consultation for snakebite in the ED?**

Acute surgical intervention is rarely necessary following crotalid envenomation. Excising tissue around the bite site confers no benefit and will exacerbate local tissue damage [11]. Compartment syndrome is an exceptionally uncommon complication from crotalid envenomation, and prophylactic fasciotomies are not recommended. Even in a confirmed compartment syndrome, the initial treatment should be additional doses of antivenom, not fasciotomy. Fasciotomy should only be considered in those patients with persistently elevated compartment pressures despite adequate antivenom therapy [11,12].