In the past, it was estimated that mortality from venomous snakebite approached 25 percent. Because of the availability of antivenom and advances in emergency and critical care, mortality rates today are below 0.5 percent. Approximately 5 to 10 deaths occur per year.

Except for bites by imported species, North American venomous snakebite involves the pit vipers (Crotalidae family) or coral snakes (Elapidae family). The crotalids are represented by the rattlesnakes (Crotalus species), pygmy rattlesnakes and massasauga (Sistrurus species), and the copperheads and water moccasins (Agkistrodon species).

**Crotalid Bites:**
**Pathophysiology**
Crotalid venom is a complex enzyme mixture that causes local tissue injury, systemic vascular damage, hemolysis, fibrinolysis, and neuromuscular dysfunction, resulting in a combination of local and systemic effects. Crotalid venom quickly alters blood vessel permeability, leading to loss of plasma and blood into the surrounding tissue and causing hypovolemia. It also consumes fibrinogen and platelets, causing a coagulopathy. In some species, specific venom fractions block neuromuscular transmission, leading to ptosis, respiratory failure, and other neurologic effects.
Clinical Features

*Up to 25 percent of crotalid snake bites are termed dry:* venom effects do not develop. The manifestations of crotalid venom poisoning involve a complex interaction of the venom and the victim. The species and size of the snake, the age and size of the victim, the time elapsed since the bite, and characteristics of the bite (location, depth, and number, the amount of venom injected) all affect the clinical appearance. The severity of poisoning following a crotalid bite is therefore variable. Crotalid bites are generally classified as *minimal, moderate,* or *severe,* depending on the degree of local and systemic injury. An initially minimal bite may evolve into a moderate or severe bite and require large amounts of antivenin.

Grading of Envenomation by Crotalid Snakes

- **No envenomation:** No swelling or erythema (dry bite).
- **Minimal envenomation:** Swelling, erythema, or ecchymosis limited to immediate area of the bite site. Systemic signs and symptoms not present or minimal. Coagulation parameters all normal. No other significant laboratory abnormalities.
- **Moderate envenomation:** Swelling, erythema, or ecchymosis present, may involve most of an extremity, and may be spreading slowly. Systemic signs and symptoms present, but not life threatening. These may include nausea, vomiting, oral paresthesia or unusual tastes, mild hypotension (systolic blood pressure >80 mmHg), mild tachycardia, and tachypnea. Coagulation parameters may be abnormal, but no clinically significant bleeding is present. Severe abnormalities of other laboratory tests are not present.
- **Severe envenomation:** Swelling or ecchymosis involve the entire extremity and are spreading rapidly. Systemic signs and symptoms are markedly abnormal, including severe alteration of mental status, nausea and vomiting, hypotension (systolic blood pressure <80 mmHg), severe tachycardia, tachypnea, or other respiratory compromise. Coagulation parameters abnormal with serious bleeding present or threat of spontaneous bleeding, including prothrombin time unmeasurable, partial thromboplastin time unmeasurable, platelets <20,000/ml, or fibrinogen undetectable.

Treatment

1. Advanced Life Support Stabilization
2. Do not use ice
3. Tourniquets are contraindicated. (Previously placed tourniquets and constriction bands should not be removed until intravenous access is established.)
4. Immobilize bitten area and if on a limb keep dependent and splint in a functional position.
5. Remove constrictive jewelry or clothing.
6. Grade bite (measure limb circumference, monitor neurovital signs central and distal to wound, coagulation abnormalities) and note time.
7. Labs: CBC, electrolytes, BUN, Cr, urinalysis, PT, PTT, fibrinogen, fibrin split products, and D-dimer.
8. Tetanus Prophylaxis.
9. Clean & Dress Wound
10. Provide Pain Management
11. Notify Poison Center
12. Administer antivenom as indicated. (see flow diagram)
13. Treatment with blood products not recommended until after adequate antivenom administration as blood components provide additional substrate for development of
14. No indication for routine antibiotic use.
15. No NSAIDs or ASA.
16. Avoid opiates when neurologic status potentially compromised by toxin (coral and Mojave rattlesnake)
17. Compartment syndrome associated with snakebites is more likely due to direct myonecrosis from venom effects rather than edema and vascular compromise, therefore the treatment for potential compartment syndrome is more antivenom and reassessment. Fasciotomy is not routinely recommended unless treatment with antivenom fails. It does not obviate the need for additional antivenom, may lengthen the course of treatment, and has risks of its own.

- **CroFab antivenom**

Crotalidae Polyvalent Immune Fab (Ovine) (CroFab) is now the mainstay of therapy for poisonous snakebites. *CroFab is derived from sheep serum.* It has replaced the previous antivenin (Crotalidae) Polyvalent that was derived from horse serum. CroFab does not contain the Fc antibody fragments; therefore acute allergic reactions are rare. An intradermal skin test is not needed and not recommended.

- **Safety:**
  - **Allergic Reaction:** No patient has experienced an anaphylactic or anaphylactoid response from CroFab. Therefore, skin testing prior to use is not recommended. Some patients (14%) had mild to moderate side effects (rash, urticaria, pruritis, or wheezing). These patients were treated with discontinuation of the antivenom, antihistamines, and beta-agonists. If the reaction was mild and the envenomation rapidly progressing, CroFab was restarted.
  - **Coagulopathy Recurrence:** Half of the patients who received CroFab developed a Coagulopathy 1-2 weeks after successful initial treatment (similar to the Wyeth antivenin). The etiology and clinical significance of this finding is not clear, but some of these patients may require repeat dosing. Patients who develop coagulation abnormalities should have follow up studies repeated for up to two weeks.
  - **Local Recurrence:** If the maintenance doses are omitted, then a recurrence of local signs and symptoms may occur. Local recurrence is treated by giving 2 additional vials of CroFab.

- **Indications:**
  - CroFab is prepared from the blood of sheep immunized with the venoms of 3 different rattlesnakes and the cottonmouth (or water moccasin). It is effective at neutralizing the venom of the 10 clinically important North American crotalid snakes. CroFab is indicated when significant clinical effects from a crotalid envenomation can be reversed or prevented. It should be administered to snakebite victims who have a progression of:
    - Local pain, swelling, or ecchymosis
    - Coagulopathy
Systemic effects such as hypotension, vomiting, fasciculation, or confusion.

Tissue reaction to snake venom is a dynamic process. Therefore, CroFab should be administered as soon as it can be determined that a patient has suffered even a minimal or moderate envenomation and the patient has progression of symptoms.

Contraindications: CroFab should not be given to patients who have “dry bite” (no venom) or have a history of allergy to:

- CroFab
- Sheep serum (not just reaction to wool)
- Papaya or papain

Dosing:
CroFab is provided in packages containing 2 vials. CroFab must be reconstituted before use, but this process should take only 10-40 minutes which is less time than the Wyeth reconstitution process. Each vial is reconstituted with 10 ml of sterile water and mixed by gentle swirlring.

1. Administer the initial dose of 4-6 vials intravenously over 60 minutes. The entire dose (after reconstitution) is injected into 250 ml normal saline. Over the first 10 minutes, infuse slowly at 25-50 ml/hour (about 5 ml). If no allergic reaction is observed, then infuse the remainder over the next 50 minutes (250 ml/hr).

2. Immediately after the initial dose, determine if initial control has been obtained. Initial control is defined as the cessation of the progression of the signs and symptoms (swelling, ecchymosis, pain, hypotension, and coagulopathy) of the snakebite. If the progression of signs and symptoms has not been stopped, continue to administer additional doses of 4-6 vials each until initial control is obtained. Up to 18 vials have been given without any observed adverse effects.

3. After initial control is achieved (usually after the first 4-6 vials), administer the maintenance dose of 2 vials every 6 hours for 3 doses (6 additional vials).

4. May consider not giving additional maintenance doses if envenomation is deemed to be minimal with no further progression. Watch for recurrence and progression; observe patient for up to 24 hours.

5. Copperhead venom is not used in the preparation of CroFab, but CroFab has been used effectively in victims of copperhead bites.

Cost:
About $1000/vial.

Elapid Bites:
North American coral snakes include the eastern coral snake (*Micrurus fulvius fulvius*), the Texas coral snake (*Micrurus fulvius tenere*), and the Arizona (Sonoran) coral snake (*Micruroides euryxanthus*). Coral snakes account for 20 to 25 bites a year. All coral snakes are brightly colored with black, red, and yellow rings. The red and yellow rings touch in coral snakes, but they are separated by black rings in nonpoisonous snakes, creating the well known rhyme: A red on yellow, kill a fellow; red on black, venom lack. **This rule is not true outside of the United States.**
Coral snake venom is primarily composed of neurotoxic components that do not cause marked local injury. Elapid bites produce primarily neurologic effects: tremors, salivation, dysarthria, diplopia, bulbar paralysis with ptosis, fixed and contracted pupils, dysphagia, dyspnea, and seizures. The immediate cause of death is paralysis of respiratory muscles. Signs and symptoms may be delayed up to 12 h. The potential coral snake victim should be admitted to the hospital for observation. Coral snake venom effects may develop hours after a bite and are not easily reversed. It is suggested that 3-5 vials of the Antivenin (*Micrurus fulvius*) be administered to patients who have definitely been bitten because it may not be possible to prevent further effects or reverse effects that have already developed.

**REFERENCES**

Patient with indication for FabAV treatment

Establish initial control of envenomation
Administer 4-6 vials of FabAV

Administer over 1 hour

Initial control achieved?
(No progression within 30 minutes of initial dose)

Yes

Infuse additional 2-vial doses at 6, 12, and 18 hr

No

Administer additional 4-6 vials of FabAV

Initial control achieved?

Yes

Infuse additional 2-vial doses at 6, 12, and 18 hr

No

Administer additional 4-6 vials of FabAV

Initial control achieved?

Yes

Infuse additional 2-vial doses at 6, 12, and 18 hr

No

Reconsider diagnosis

Venomous Snake Bite Algorithm

- Each vial is reconstituted and the entire dose diluted to a volume of 250ml in a crystalloid fluid and administered over the course of one hour.
- For copperhead or minimal envenomation may consider not giving scheduled maintenance doses, but observe for up to 24 hours.
- THIS DOCUMENT SERVES AS A GUIDELINE FOR PATIENT CARE BUT SHOULD NOT SUPERSEDE PHYSICIAN JUDGEMENT.