Inclusion Criteria:
Snakebite by Pit Viper
Snake Species: rattlesnakes, copperheads, water moccasins (cottonmouths)

Patient assessment
- Mark leading edge of swelling and tenderness every 30 – 60 minutes
- Immobilize and elevate extremity
- Treat pain (IV opioids preferred)
- Obtain initial lab studies (CBC, protime, fibrinogen)
- Update Tetanus
- Providers contact Arkansas Poison and Drug Information Center (1-800-376-4766)

Treatments to AVOID in Pit Viper Snakebite
- Ice
- NSAIDs
- Tourniquets
- Cutting
- Steroids (except for allergic phenomena)
- Prophylactic antibiotics
- Prophylactic fasciotomy
- Routine use of blood products

Notify ACH ED of incoming patient
- Place in expected ER status and document all clinical information
- Contact pharmacology/toxicology for any questions or concerns

Normal Coagulation Markers
- International Normalization Ratio (INR) <1.1
- Prothrombin Time (PT) 11-15
- Partial Thromboplastin Times (PTT) 25-35

CroFab® Information

ACH only has CroFab® on formulary but patients may be transferred having received Anavip®

Anavip® Crotalidae immune F(ab’); [equine]
These antivenoms are dosed differently initially; initial dose of Anavip® is 10 vials for all patients of all ages.
**Check for Indications for CroFab® Antivenom**
- Swelling that is more than minimal and that is progressing, or
- Elevated protiene, decreased fibrinogen or platelets, or
- Any systemic signs (i.e. vomiting, diarrhea, hypotension, syncope, muscle fasciculations/weakness)

**How Much**
- Initial dose 4 – 6 vials.
  - Dose is NOT weight based, but is based on the severity of the bite
  - If patient is in shock or with serious active bleeding, increase initial dose to 8 – 12 vials

**How to mix**
- Dissolve vials with normal saline per package insert
- Mix 4-6 Vials CroFab in NS 250 ml

**How to administer**
- Administer 25 ml/hour for 10 minutes. If no signs of anaphylaxis increase to 250 ml/hour
- If patient develops anaphylaxis or hypersensitivity reaction, STOP the infusion, treat with epinephrine, diphenhydramine, and steroids as indicated
- Contact Pharmacology/Toxicology for concerns

**What to monitor**
- Monitor progression of swelling or worsening lab abnormalities.
- Observe for 1 hour after each antivenom administration,
  - If progressive swelling or systemic signs/symptoms still occur, consider redosing with CroFAB. Contact Pharm/Tox for recommendations
- Monitor for signs and symptoms of anaphylaxis
Pit Viper Snakebite Management: ED

**Inclusion Criteria:**
Snakebite by Pit Viper
Snake Species: Rattlesnakes, copperheads, water moccasins (cottonmouths)

**Assess Patient**
- Mark leading edge of swelling and tenderness every 30-60 minutes
- Immobilize and elevate extremity
- Treat pain (IV opioids preferred)
- Obtain initial lab studies (CBC, protime, fibrinogen)
- Update Tetanus
- Contact poison center (1-800-222-1222)

**Check for Signs of Envenomation**
- Swelling, tenderness, redness, ecchymosis, or blebs at the bite site, or
- Elevated protein; decreased fibrinogen or platelets, or
- Systemic signs, such as hypotension, bleeding beyond the puncture site, refractory vomiting, diaphoresis, neurotoxicity

**Check for Indications for CroFab® Antivenom**
- Swelling that is more than minimal and that is progressing, or
- Elevated protein; decreased fibrinogen or platelets, or
- Any systemic signs

**Administer CroFab® Antivenom**
- Establish IV access and give IV fluids
- Pediatric CroFab® antivenom dose = adult dose
- Mix 4-6 vials of crotaline Fab antivenom (CroFab®) in 250mL NS and infuse IV over 1 hour
- For patients in shock or with serious active bleeding
  - Increase initial dose of CroFab® antivenom to 8-12 vials
- Call Clinical Pharmacology/Toxicology or APDRC
- Initiate first dose of antivenom in ED or ICU
  - For suspected adverse reaction (see Background pg. 1): hold infusion, treat accordingly, and call Medical Toxicologist
- Re-examine patient for treatment response within 1 hour of completion of antivenom infusion

**Determine if initial control of envenomation has been achieved:**
- Swelling and tenderness not progressing
- Protein, fibrinogen, and platelets normal or clearly improving
- Clinically stable (not hypotensive, etc)
- Neurotoxicity resolved or clearly improving

**Monitor Patient**
- Perform serial examinations
- Maintenance CroFab® antivenom therapy may be indicated
- See Maintenance CroFab/Antivenom Therapy
- Observe patient 1-2 hours after initial control for progression of any venom effect
  - Shorten observation times and less laboratory monitoring may be acceptable for known copperhead bites. Consult Clinical Pharmacology/Toxicology for recommendations.
- Follow-up labs 6-12 hours after initial control and prior to discharge
- If patient develops new or worsening signs of envenomation, administer additional CroFab® antivenom

**Determine if Patient Meets Discharge Criteria**
- No progression of any venom effect during the specified observation period
- No unfavorable laboratory trends in protein, fibrinogen, or platelets

**Treatments to AVOID in Pit Viper Snakebite**
- Cutting and/or suctioning of the wound
- Ice
- NSAIDs
- Prophylactic antibiotics
- Prophylactic fasciotomy
- Routine use of blood products
- Shock therapy (electricity)
- Steroids (except for allergic phenomena)
- Tourniquets

**Apparent Dry Bite / No Bite**
- Do not administer CroFab® antivenom
- Observe patient 2 hours
- Repeat labs prior to discharge
- If patient develops signs of envenomation, return to previous box

**Apparent Minor Envenomation**
- Do not administer CroFab® antivenom
- Observe patient 12-24 hours
- Repeat labs at 4-6 hours and prior to discharge
- If patient develops progression of any signs of envenomation, return to previous box

**Repeat antivenom until initial control is achieved**
- If initial control is not achieved after 2 doses of CroFab® antivenom, call Clinical Pharmacology/Toxicology
- Patient receives 10 vials of Anavip® at outside hospital

**Notes:**
All treatment recommendations in this algorithm refer to CroFab®. This worksheet represents general advice from a panel of US snakebite experts convened in May, 2010®. No algorithm can anticipate all clinical situations. Other valid approaches exist, and deviations from this worksheet based or individual patient needs, local resources, local treatment guidelines, and patient preferences are expected. This document is not intended to represent a standard of care. For more information, please see biomedcentral.com
Maintenance therapy is additional CroFab® antivenom given after initial control to prevent recurrence of limb swelling.

- Maintenance therapy is 2 vials of CroFab® antivenom Q6H x 3 (given 6, 12, and 18 hours after initial control).

Maintenance therapy may not be indicated in certain situations, such as:

- Minor envenomations
- Some copperhead bites
- Facilities where close observation by a medical toxicologist is available

Contact Arkansas Poison and Drug Information (1-800-222-1222) or contact Clinical Pharmacology/Toxicology Service at ACH if patient is at ACH or ACNW.
When to Consult Clinical Pharmacology/Toxicology or Medical Toxicologist either at ACH or APDIC

Direct consultation with a medical toxicologist is recommended in certain high-risk clinical situations.

- Life-threatening envenomations
  - Shock
  - Serious active bleeding
  - Facial or airway swelling

- Hard to control envenomation
  - Envenomation that requires more than 2 doses of antivenom for initial control

- Recurrence or delayed-onset of venom effects
  - Worsening swelling or abnormal labs (protime, fibrinogen, platelets, or hemoglobin) on follow-up visits

- Allergic reactions to antivenom

- If transfusion of blood products is considered

- Uncommon clinical situations
  - Bites to the head and neck
  - Rhabdomyolysis
  - Suspected compartment syndrome
  - Venom-induced hives and angioedema

- Complicated wound issues

*Call APDIC (1-800-222-1222) and request to speak with Medical Toxicologist on-call or consult with Clinical Pharmacology/Toxicology Service at ACH if patient is at ACH or ACNW.*
• Instruct patient to return for:
  • Worsening swelling that is not relieved by elevation
  • Abnormal bleeding (gums, easy bruising, melena, etc)

• Instruct patient where to seek care if symptoms of serum sickness (fever, rash, muscle/joint pains) develop

• Bleeding precautions (no contact sports, elective surgery or dental work, etc) for 2 weeks in patients with:
  • Rattlesnake envenomation
  • Abnormal protime, fibrinogen, or platelet count at any time

• Follow-up visits:
  • Antivenom not given:
    • PRN only
  • Antivenom given:
    • Copperhead victims: PRN only
    • Other snakes including unknown species with extensive local reaction, abnormal coagulation studies, and/or any hand envenomation: Follow-up with physical exam, labs (CBC, protime, fibrinogen) twice (2-3 days and 5-7 days), then PRN
BACKGROUND

- Pit Viper snake envenomation is a dynamic clinical process.
- Pit Viper snakes include copperheads, rattlesnakes, and water moccasins (cottonmouths).
- Clinical toxicity is manifested by local toxicity, systemic toxicity, and a multicomponent coagulopathy. The development and progression of these toxicities depends on the type of snake, the number of bites, and/or the potency of the venom.
- Serial examinations and laboratory studies are necessary to detect ongoing, recurrent, or delayed-onset venom effects.
- A photo of the snake may be helpful in its identification and in anticipating the potential severity of toxicity, observation times, and need for serial laboratory monitoring. Do NOT bring snake into the healthcare facility.
- Copperhead snakebites many times don’t result in as severe envenomation as those from rattlesnakes and water moccasins (cottonmouths). Shorter observation times and less frequent laboratory monitoring may be acceptable for known envenomations from these snakes.
- Anaphylactic and anaphylactoid reactions to the snake venom itself are uncommon manifestations of snakebites but can occur and range in severity from urticarial rash to multisystem organ failure and angioedema causing airway loss.
- This clinical pathway is NOT for coral snake envenomations.

ANTIVENOM

Types:
- There are 2 antivenoms approved for pit viper envenomation in the United States
  - CroFab® Crotalidae polyvalent immune Fab [ovine] – on ACH Formulary
  - Anavip® Crotalidae immune Fab(αb')2 [equine]
- ACH only has CroFab® on formulary but patients may be transferred having received Anavip®
- These antivenoms are dosed differently initially: initial dose of Anavip® is 10 vials for all patients of all ages.

Infusion of Antivenom:
- Initial dose: start antivenom infusion at a slow initial rate (e.g., 25mL/hr for 10 minutes) followed by an increased infusion rate (balance of dose administered over 50 minutes) if no acute hypersensitivity reaction is observed.
- First dose of antivenom should be administered in a clinical setting such as an emergency department or intensive care unit where the medications, equipment, and skilled personnel required to manage an airway emergency are immediately available.
- If there is no acute reaction to initial dosing, subsequent doses of antivenom can be administered in a less monitored setting.

Adverse effects of antivenom:
- CroFab® antivenom is contraindicated in patients allergic to papain or papaya.
- Symptoms of anaphylactoid reactions, such as pruritus, urticaria, or wheezing occur in approximately 6% of patients.
- Carefully monitor patients for signs and symptoms of an acute allergic reaction (e.g., urticaria, pruritus, erythema, angioedema, bronchospasm with wheezing or cough, stridor, laryngeal edema, hypotension, tachycardia).
- Most cases are mild and do not preclude continued administration of antivenom.
- Infusion reactions such as fever, back pain, wheezing, and nausea may be related to the rate of infusion and can be controlled by decreasing the rate of infusion.
- If patient develops allergic or other reaction (hives, pruritus), stop infusion and administer antihistamines and restart the infusion at a lower rate.
- Severe acute hypersensitivity reactions or true immune-mediated anaphylaxis demonstrated by airway compromise or hypotension are rare but can occur. Discontinue antivenom and institute appropriate emergency treatment (epinephrine, IV antihistamines, albuterol, steroids). See Anaphylaxis Clinical Pathway
- There are a few published reports of developing anaphylactic reactions to CroFab who were found to be sensitized to alpha-Gal or galactose-α-1,3-galactose and suggest that IgE to α-gal may have been relevant to that reaction. Alpha-Gal sensitization is caused by tick bites and alpha-gal syndrome/allergy may occur after people eat red meat. In the United States, IgE to alpha-Gal has a regional distribution that is most pronounced in southeastern states where mammalian meat allergy is common.
- The decision to resume or discontinue antivenom therapy involves a complex balancing of risk and benefit and should be in consultation with Clinical Pharmacology/Toxicology attending and other specialists as needed.
Metrics

1. Length of stay
2. Total vials of antivenom – CroFab + Anavip from OSH
3. Fibrinogen ordered: Yes or No
4. Development of coagulopathy: PT > 15 or Fibrinogen < 170 mg/dL
5. Order set utilization
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References


