Snake Bite Treatment

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Speaker Disclosure

I have no financial relationships or affiliations to disclose.

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Objectives

- Identify the different types of venomous snakes native to our area
- Analyze a patient for indications to treat with antivenom for Pit Viper snake bites
- Initiate an appropriate evidence based medicine treatment regimen that includes appropriate
    - Initial and Maintenance Dosing
    - Safety and Efficacy Monitoring
    - Discharge Counseling
    - Follow-up Visits

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Epidemiology

- Worldwide
  - 2.5 million envenomations per year
  - 81,000-138,000 deaths per year
- United States
  - 7,000–8,000 venomous snakes bites per year
  - Average of 5 deaths per year
- In Alabama, on average 1 person dies every 10 years

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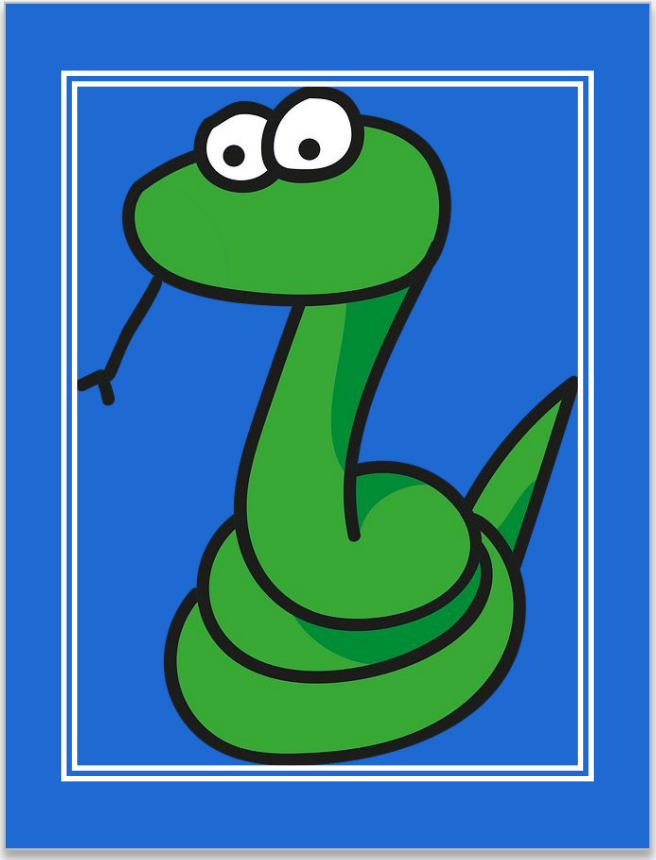
Snake Facts

- Optimal Temperature Range
- Striking Range and Top Speed
- Baby Snakes
- Amount of Venom Released



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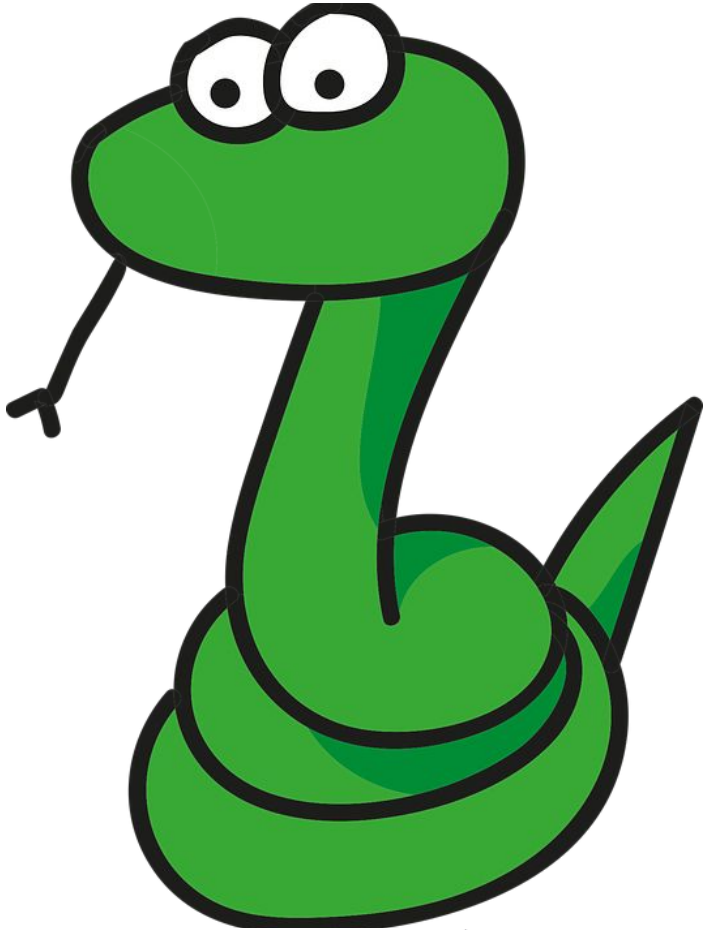
Snakes in Alabama

- 43 different species of snakes
- Only 6 snake species are venomous
    - Pit Vipers and Coral Snake



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Pit Viper

- Five of the six venomous snakes in Alabama are in the pit viper (crotalinae) group
  - Eastern Diamondback Rattlesnake, Timber Rattlesnake, Pigmy Rattlesnake, Copperhead, and Cottonmouth
- Pit vipers get their name from the presence of pits on both sides of the face between the eye and nostril
- Pit vipers have vertical or “cat-like” pupils, thin necks, triangular heads, and heavy bodies
- Pit vipers are also characterized by having retractable, hollow fangs near the front of the mouth

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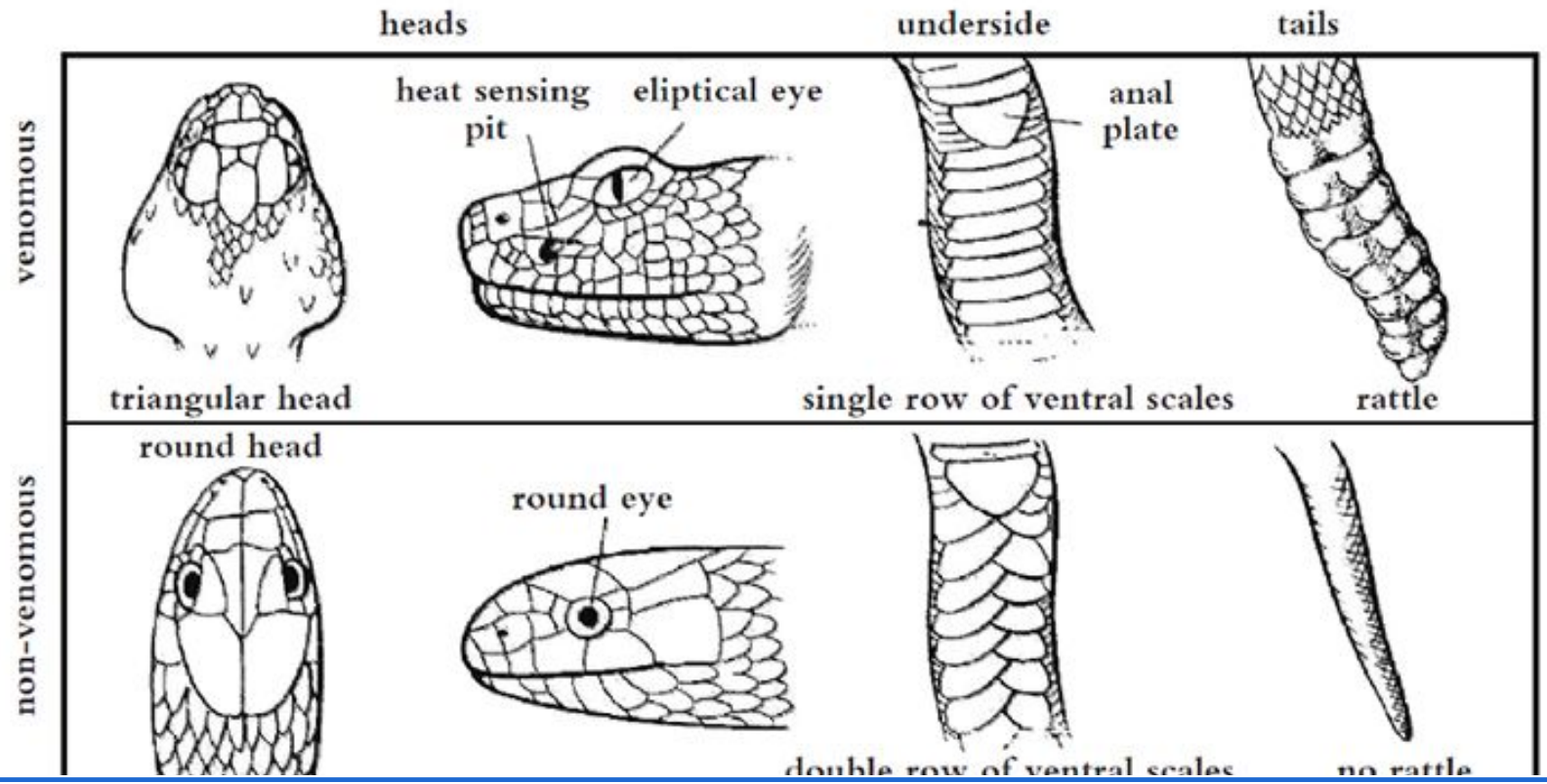

https://www.aces.edu/blog/topics/forestry-wildlife/identification-and-control-of-snakes-in-alabama/.

Eastern Diamondback Rattlesnake

Timber Rattlesnake

Pygmy Rattlesnake

Copperhead

Cottonmouth

https://www.aces.edu/blog/topics/forestry-wildlife/identification-and-control-of-snakes-in-alabama/.

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Coral Snake

- Located mostly in coastal areas
- Close relative of the cobra
- Small head, round pupils, and a slender body
- “Red on yellow, kill a fellow. Red on black, friend of Jack. Black on snout, look out!”

Coral Snake

https://www.aces.edu/blog/topics/forestry-wildlife/identification-and-control-of-snakes-in-alabama/.

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Envenomation

Dry Bites

- A very small amount of venom or no venom is injected which may cause slight bleeding, pain, and swelling at the bite injury
- 20-25% of bites are dry
- If no symptoms are present within 8 to 12 hours, the snake might not have injected any venom

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Level of Severity

Category	Tissue effect	Systemic signs and symptoms	Coagulopathy and bleeding
Minimal	Swelling, pain, and ecchymosis adjacent to the bite site	None	Normal coagulation parameters¶; no bleeding
Moderate	Swelling, pain, and ecchymosis less than full extremity or less than 50 cm if bite on head, neck, or trunk	Present but not life-threatening (eg, nausea, vomiting, diarrhea, oral paresthesia, unusual tastes, tachycardia, tachypnea, mild hypotension [eg, systolic BP >90 mmHg in an adult or >5th percentile for age in children])	Abnormal coagulation parameters¶; no bleeding or minor hematuria, gum bleeding, and/or epistaxis
Severe	Swelling, pain, ecchymosis involving more than the entire extremity; greater than 50 cm if bite on head, neck, or trunk; threatens the airway; OR signs of compartment syndrome	Present and life-threatening (eg, respiratory insufficiency, marked tachycardia for age with severe hypotension, obtundation, seizures)	Markedly abnormal coagulation parameters¶ with serious bleeding

https://www.uofmhealth.org/health-library/th142

Snake Bite Severity Score

	Criterion Points
Pulmonary symptoms	
• No symptoms/signs	0
• Dyspnea, minimal chest tightness, mild or vague discomfort, or respirations of 20-25 breaths/minute	1
• Moderate respiratory distress [tachypnea, 26-40 breaths/minute; accessory muscle use]	2
• Cyanosis, air hunger, extreme tachypnea, or respiratory insufficiency/failure	3
Cardiovascular system	
• No symptoms/signs	0
• Tachycardia [100-125 BPM], palpitations, generalized weakness, benign dysrhythmia, or hypotension	1
• Tachycardia [126-175 BPM]	2
• Extreme tachycardia [>175 BPM], hypotension, malignant dysrhythmia, or cardiac arrest	3
Local wound	
• No symptoms/signs	0
• Pain, swelling, or ecchymosis within 5-7.5 cm of bite	1
• Pain, swelling or ecchymosis involving less than half the extremity [7.5-50 cm from bite]	2
• Pain, swelling or ecchymosis involving half to all of extremity [50-100 cm from bite]	3
• Pain, swelling or ecchymosis extending beyond affected extremity [more than 100cm from bite]	4
Gastrointestinal system	
• No symptoms/signs	0
• Pain, tenesmus, or nausea	1
• Vomiting or diarrhea	2
• Repeated vomiting, diarrhea, hematemesis, or hematochezia	3
Hematologic symptoms	
• No symptoms/signs	0
• Coagulation parameters slightly abnormal: PT 13-20 secs; PTT 36.5-50 secs; PLTs 100-150K/mL; or fibrinogen 100-150 mcg/mL	1
• Coagulation parameters abnormal: PT 20-50 secs; PTT 50-75 secs; PLTs 50-100K/mL; or Fibrinogen 50-100 mcg/mL	2
• Coagulation parameters abnormal: PT 50-100 secs; PTT 75-100 secs: PLTs 20-50K/mL; or Fibrinogen <50 mcg/mL	3
• Coagulation parameters markedly abnormal, with serious bleeding or the threat of spontaneous bleeding; unmeasurable PT or PTT: PLTs <20K/mL; or undetectable fibrinogen; severe abnormalities of other laboratory values also fall into this category	4
Central nervous system	
• No symptoms/signs	0
• Minimal apprehension, headache, weakness, dizziness, chills, or paresthesia	1
• Moderate apprehension, headache, weakness, dizziness, chills, paresthesia, confusion, or fasciculation in area of bite site	2
• Severe confusion, lethargy, seizures, coma, psychosis, or generalized fasciculation	3

https://www.universityhealthsystem.com/-/media/Files/Clinical-Pathways/Snakebite-Severity-Score-Flowsheet-Algorithm.ashx

First-Aid

DO's

- Call 911
- Take a photograph of the snake
- Remove rings and watches
- Wash the bite with soap and water
- Cover the bite with a clean, dry dressing.
- Mark the leading edge of tenderness/swelling on the skin and write the time alongside it

DON'Ts

- Do not pick the snake up
- Do not wait for symptoms to appear
- Do not apply a tourniquet
- Do not slash the wound with a knife
- Do not try to suck out the venom.
- Do not apply ice or immerse the wound in water
- Do not drink alcohol as a painkiller
- Do not take pain relievers (such as aspirin, ibuprofen, naproxen)

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Initial Treatment

- Gather subjective information
- Mark leading edge of swelling and tenderness every 15-30 minutes
- Immobilize and elevate extremity
- Treat pain (IV opioids preferred)
- Update tetanus
- Call Poison Control (1-800-222-1222)

- Obtain initial lab studies
  - Complete blood count (CBC)
  - Complete metabolic panel (CMP)
  - Serum creatine kinase (CK)
  - Prothrombin time (PT)
  - International normalized ratio (INR)
  - Fibrinogen
  - D-dimer
  - Electrocardiogram (ECG)

Check for Signs of Envenomation

- Check for Signs of Envenomation
  - Swelling, tenderness, redness, ecchymosis, or blebs at the bite site
  - Prolonged prothrombin time, decreased fibrinogen level or decreased platelets
  - Systemic signs, such as hypotension, bleeding beyond the puncture site, refractory vomiting, diarrhea, angioedema, neurotoxicity
- If none of the above signs: Dry Bite/ No Bite
  - Do not administer antivenom
  - Observe patient ≥ 8 hours
  - Repeat labs prior to discharge

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Indication for Antivenom

- Swelling that is more than minimal and that is progressing
- Abnormal laboratory coagulation parameters
- Any systemic signs
- If none of the above is present
  - Do not administer antivenom
  - Observe patient 12-24 hours
  - Repeat labs at 4-6 hours and prior to discharge

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Antivenom Agents

2 FDA Approved Options

- Anavip (crotalidae immune $F(ab)_2$) (Fab2AV)
  - FDA approved May 2015: Rattlesnake envenomation
  - FDA approved April 2021: All North American Pit Viper envenomation
- CroFab (crotalidae polyvalent immune fab) (FabAV)
  - FDA approved October 2000: Mild-moderate pit viper envenomation
  - FDA approved 2009: Severe pit viper envenomation

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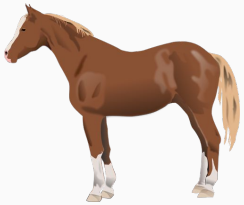
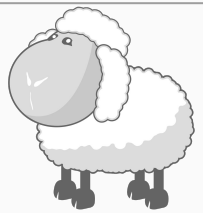
Antivenom Development

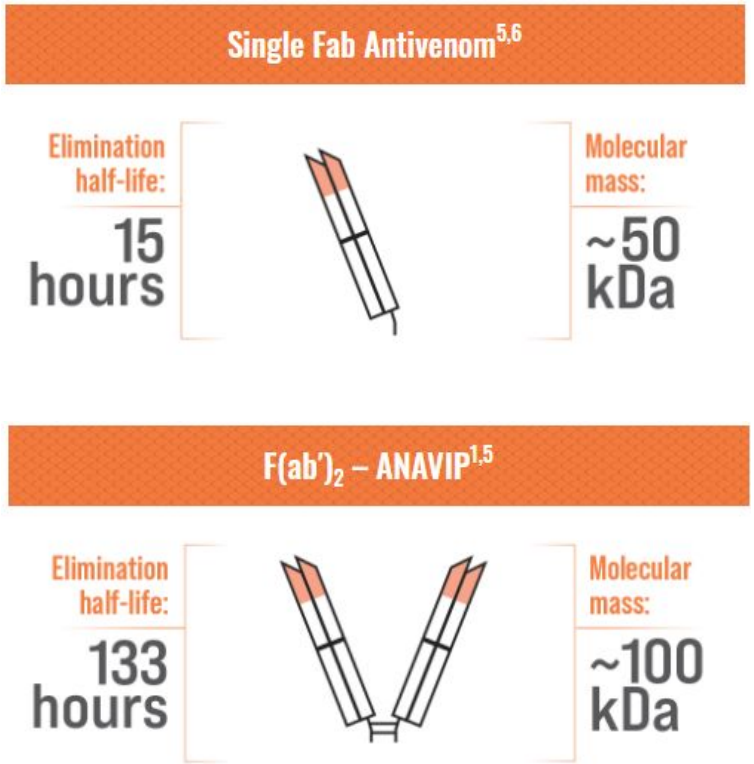
	Anavip	**CroFab**
Animal Source	Horse 	Australian Sheep 
Venom Used	Fer-de-lance Central American Rattlesnake Western Diamondback Eastern Diamondback MoJave Rattlesnake Copperhead Cottonmouth	Western Diamondback Eastern Diamondback Mojave Rattlesnake Cottonmouth

Antivenom Comparison

Spectrum of Activity: Anavip and CroFab

- Eastern Diamondback Rattlesnake
- Timber Rattlesnake
- Pigmy Rattlesnake
- Copperhead
- Cottonmouth

98% of venomous snakebites in the United States are from the North American Pit Viper



https://anavip-us.com/

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Preparation and Administration

	Anavip	Crofab
Storage	Up to 25 ºC (77 ºF) for up to 3 years	2° to 8°C (36° to 46°F) for 60 months
Reconstitution	10 mL normal saline per vial Swirl for 8-26 seconds until fully mixed Use within 6 hours	18 mL normal saline per vial (slowly) Invert for 3-6 minutes until fully mixed Use within 4 hours
Fluid	250 mL 0.9% NaCl	250 mL 0.9% NaCl
Infusion time	60 minutes	60 minutes

Comparison of F(ab')$_2$ versus Fab antivenom for pit viper envenomation: A prospective, blinded, multicenter, randomized controlled trial

- 123 patients
- Three comparison groups
  - Anavip® + maintenance dosing: 10 vials x1, then 4 vials q6h x 3 doses
  - Anavip® + placebo maintenance: 10 vials x1, then 250 ml NS q6h x 3 doses
  - CroFab® + maintenance: 5 vials q2h until initial control, then 2 vials q6h x 3 doses
- Primary efficacy endpoint
  - Coagulopathy after the last maintenance dose
  - Defined as platelets <150,000/mm^3 or fibrinogen <150 mg/dL, or the use of antivenom between the end of maintenance and study day 5
- 102 patients were bitten by either a rattlesnake or unidentified snake
- Primary endpoint results:
  - Anavip/Anavip vs CroFab/CroFab: 4 (10.3) vs 11 (29.7); p <0.05; ARR 0.195 (0.014 - 0.367); NNT ~5
  - Anavip/placebo vs CroFab/CroFab: 2 (5.3) vs 11 (29.7); p< 0.05; ARR 0.245 (0.073 - 0.410); NNT ~4
- Conclusion
  - For envenomation by North American Pit Viper snakes, this study found that management with longer-half-life Anavip antivenom reduces the risk of post-treatment recurrence and late-onset coagulopathies following treatment when compared with management with CroFab.

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Antivenom Dosing

Phase 1: Initial Control

Determine if Initial Control of Envenomation has been Achieved

- Swelling and tenderness not progressing
- Prothrombin, fibrinogen, and platelets normal or clearly improving
- Clinically stable
- Neurotoxicity resolved or clearly improving

Phase 2: Maintenance Phase

- Maintenance therapy is additional antivenom given after initial control to prevent recurrence of limb swelling
- Maintenance therapy may not be indicated in certain situations, such as
  - Minor envenomations
  - Facilities where close observation by a physician expert is available.
  - Not routinely used with Anavip
- Follow local protocol or contact a poison center or physician-expert for advice

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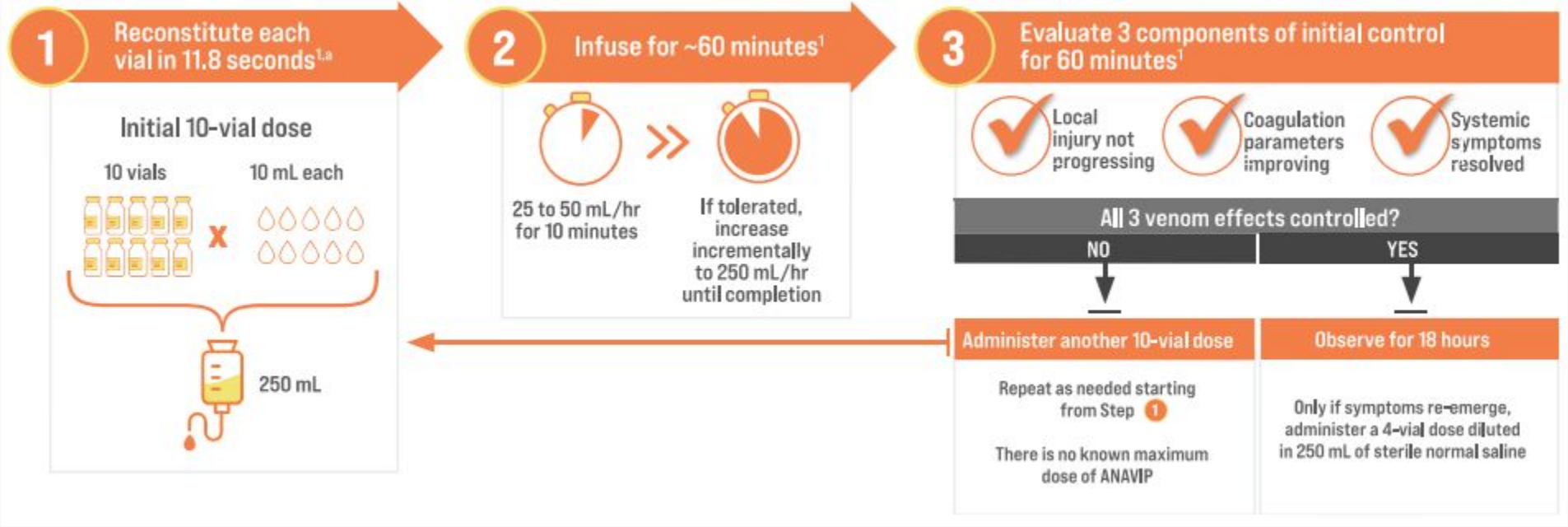
Anavip (crotalidae immune F(ab)$_2$) (Fab2AV) Dosing



https://anavip-us.com/

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Anavip (crotalidae immune $F(ab)_2$) (Fab2AV)

- Contraindications: none
- Efficacy
  - Monitor for ≥18 hours following initial control of signs and symptoms
  - Size of bite area (every 15 to 30 minutes)
  - Vital signs
  - CBC, platelet count, fibrinogen levels, and coagulation times (evaluated every 6 hours until patient is stable)
- Safety
  - Pruritus
  - Nausea/vomiting
  - Rash
  - Arthralgia
  - Peripheral edema
  - Erythema
  - Headache
  - Myalgia
  - Pain in extremity

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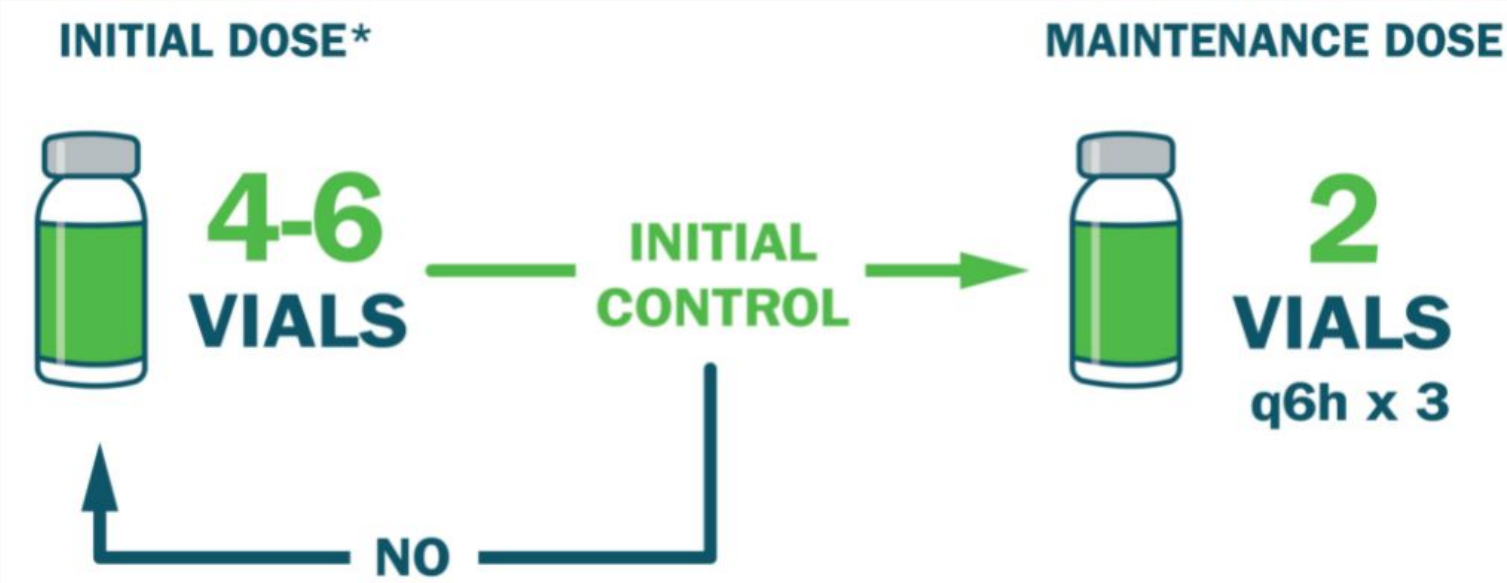
Crofab (crotalidae polyvalent immune fab) (FabAV) Dosing



Administer an initial dose of 4-6 vials* and monitor for signs of progression.

- Administer an additional 4-6 vials if initial control is not achieved ~1 hour after initial dose
- Once initial control is achieved, administer an additional 2 vials every 6 hours for up to 18 hours (total of 3 doses)
- Scheduled maintenance dosing reduced the incidence of coagulation abnormalities due to residual venom[1]

*Initial dose may vary from 4-12 vials based on clinical judgment and severity of envenomation. Dosing is the same in adult and pediatric patients.[1]

Crofab (crotalidae polyvalent immune fab) (FabAV)

- Contraindications:
  - History of hypersensitivity to any of its components, or to papaya or papain unless the benefits outweigh the risks of anaphylaxis
- Monitoring Parameters
  - Size of bite area (every 15 to 30 minutes)
  - Vital signs
  - CBC, platelet count, fibrinogen levels, and coagulation times (evaluated every 6 hours until patient is stable)
- Safety
  - Urticaria/rash/pruritus
  - Hypotension
  - Nausea
  - Cough
  - Dyspnea
  - Wheezing
  - Hypersensitivity reaction (5%–19%)
  - Serum sickness (5%)
  - Disease-related concerns: recurrent coagulopathy

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When to Call a Physician-Expert

Direct consultation with a physician-expert is recommended in certain high-risk clinical situations:

- Life-threatening envenomation
  - Shock
  - Serious active bleeding
  - Facial or airway swelling
- Hard to control envenomation
  - Requires more than 2 doses of antivenom for initial control
- Recurrence or delayed-onset of venom effects
- Allergic reactions to antivenom
- If transfusion is considered
- Uncommon clinical situations
  - Bites to the head and neck
  - Rhabdomyolysis
  - Suspected compartment syndrome
  - Venom-induced hives and angioedema
- Complicated wound issues

Physician-expert can be reached through a poison center (1-800-222-1222) or a CroFab expert at (1-877-377-3784)

Discharge Counseling

- Instruct patient to return for:
  - Worsening swelling that is not relieved by elevation
  - Abnormal bleeding
- Instruct patient to seek care if symptoms of serum sickness develop
- Bleeding precautions for 2 weeks in patients with:
  - Rattlesnake envenomation
  - Abnormal prothrombin time, fibrinogen, or platelet count at any time

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Follow-Up Visits

- Follow-up visit for Anavip
  - Monitor patients with follow-up visits for signs and symptoms of delayed allergic reactions or serum sickness
- Follow-up visits for CroFab
  - Copperhead victims: PRN only
  - Other snakes: follow up with labs twice (2-3 days and 5-7 days), then as needed

Patient Cases

Patient Case: AH

AH is a 19 yo male presenting to the ED via ambulance for a snake bite. He was bitten approximately 1 hour ago by an unknown snake with rattles. The patient applied a tourniquet.

BP 126/72, HR 80, RR 18, Temp 98.2º, 100kg, 182cm

Allergy: None PMH: None

Labs: WNL

What are the appropriate next steps?

A. Give the initial dose of antivenom
B. Discharge patient home
C. Watch and observe the foot for swelling for 8 hours and repeat labs in 6 hours
D. Open wound to drain venom

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Patient Case: RC

RC is a 35 yo male presenting to the ED via his personal car with a snake bite. He was bitten approximately 30 minutes ago. He did not provide any first aid.

BP 100/65, HR 100, RR 18, 98.9°, 120 kg, 182 cm

Allergy: PCN PMH: HTN, T2DM

Labs: Plt 120, PT 15.3

What is the most appropriate management for this bite?

A. Wait and watch since the swelling has not progressed to the entire extremity
B. Administer the initial dose of antivenom

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Questions?

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