GUIDELINE

Title:	Snakebite Management				
Department/Service Line:	Pharmacy				
Approver(s):	Vice President of Pharmacy Services; BSWH Pharmacy & Therapeutics Council				
Location/Region/Division:	BSWH				
Document Number:	BSWH.RX.032.G				
Effective Date:	07/05/2021	**Last Review/ Revision Date:**	06/02/2021	**Origination Date:**	06/02/2021

SCOPE

This document applies to Baylor Scott & White Health including Controlled Affiliates ("BSWH") hospitals.

DEFINITIONS

When used in this document with initial capital letter(s), the following word(s)/phrase(s) have the meaning(s) set forth below unless a different meaning is required by context. Additional defined terms may be found in the BSWH P&P Definitions document.

PRN: as needed

GUIDELINE

To establish a guideline for the care of patients with venomous snake bite.

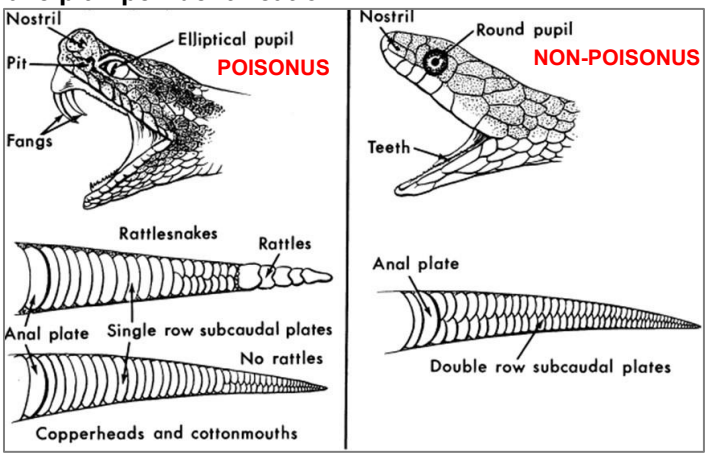
Background/Assessment

North American venomous snakebites involve the pit vipers (Crotalidae family) or coral snakes (Elapidae family) with the exception of imported snake species. The crotalids are represented by the rattlesnakes (Crotalus species), pygmy rattlesnakes, massasauga (Sistrurus species), and copperheads, water moccasins/cottonmouth (Agkistrodon species).

Identification

1. **Rattlesnakes, Copperheads, and Water Moccasins (Crotalidae family):** Typically difficult to identify. If question is raised to whether the snake is poisonous, anatomical features of the head and tail can be utilized to identify poisonous verses non-poisonous species. (Figure 1)
2. **Coral snakes (Elapidae family):** Often easily identified due to their bright colors (black, red, and yellow rings). Coral snakes in the United States are poisonous if the color red touches yellow. Red on black are not native poisonous snakes to the U.S. This general principle reliably applies only to coral snakes native to North America.
3. **Exotic snakes**: Identification of the snake is of key importance in providing appropriate care as envenomation by some of these snakes requires a specific antivenin. If possible, a herpetologist sees the snake or a high-quality photograph of the snake in order to identify the snake as precisely as possible.

Figure 1. US poisonous snake/pit viper identification



Crotalid Bites

- Crotaline venom is a mixture of proteolytic enzymes, hemotoxins, and neurotoxins that can cause direct tissue damage, increase blood vessel permeability, activate coagulopathy and alter nerve cell transmission. The content and potency of the venom can vary widely depending on the snake's age, size, diet, climate, season and possible crossbreeding with different snakes. Approximately 20-25% of crotalid bites are dry bites (no envenomation).
- Signs/Symptoms
  - *General*: anxiety, fear, nonspecific weakness, malaise, metallic taste in mouth, rhabdomyolysis and rarely anaphylaxis
  - *Local*: swelling, blistering, edema, pain at site, ecchymosis, tissue necrosis
  - *Neurologic*: altered level of consciousness, weakness, paresthesia, fasciculation
  - *Cardiovascular*: tachycardia, hypotension
  - *Hematologic*: coagulopathy, thrombocytopenia, spontaneous bleeding (epistaxis, gingival, etc.)
- Snakebite Severity Assessment
  - Establishing the clinical severity of the envenomation is essential to guide management. Dart and colleagues developed and validated the Snakebite Severity Score which is an objective symptom severity scoring tool for crotalid bites. The Snakebite Severity Score has been shown to reduce antivenom utilization without an increase in other health care costs (length of stay, readmission, etc.). BSWH has developed a modified Snakebite Severity Score ("mSSS") ranging from 0-8 to guide management of crotalid bites. Refer to attachment 1 for detailed BSWH mSSS assessment.

Coral Snake Bites

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 & symptoms may be delayed for up to 12 hours.

PROCEDURE

General Management

Wound Care

- Clean wound and loosely cover with a dry dressing
- Label demarcation of swelling every 30 minutes to monitor progression until stable (normalization of vital signs and the cessation of progression of swelling of the extremity)
- Remove all jewelry (watches, earrings, piercings, etc.) and restrictive clothing
- Maintain bite area level with heart until definitive care, then may elevate to reduce swelling
- **DO NOT**
  - Apply ice or heat

- Incise the wound
- Apply suction to wound
- Apply a tourniquet to bitten extremity
  - If tourniquet or constriction band previously placed do not remove until definitive care, intravenous access is established, and antivenom initiated (if indicated)

General Care

- Consider contacting local poison control center (1-800-222-1222)
- Assess mSSS for crotalid envenomation (refer to attachment 1 for detailed mSSS assessment)
- Ensure tetanus vaccination up to date
- Pain control as needed
- **AVOID**
  - Prophylactic antibiotics
  - Corticosteroids (unless for allergic reaction or serum sickness)
  - Transfusion of blood products (Fresh frozen plasma/Cryoprecipitate/Platelets) in the management of coagulopathy. The only treatment for coagulopathy is the administration of antivenom.

Crotalid Management

Indication for Crotalid Antivenom Therapy (Refer to attachments 1 and 2 for additional guidance)

- mSSS 3-8 (moderate to severe)
  - Antivenom may not be required in mild to moderate confirmed copperhead envenomation as data suggests patients perform well *regardless* of antivenom administration

	Anavip® **crotalidae immune F(ab')2 [equine]**	**CroFab®** **crotalidae polyvalent immune FAB [ovine]**
FDA Approved Indications	Rattlesnake, copperhead, or cottonmouth	
Dosing¥	Initial dose: 10 vials Initial Control* NOT Achieved: repeat 10 vials q1hr PRN until initial control achieved Symptom-triggered**: 4 vials PRN mSSS of 3-8	Initial dose: 4 vials (range 4-6) Initial Control* NOT Achieved: repeat 4 vials q1hr PRN until initial control achieved Symptom-triggered**: 2 vials PRN mSSS 3-8
Administration	• For the first 10 minutes infuse at a 25-50 mL/hour rate, carefully monitoring for any allergic reactions, including any anaphylactic reactions. Discontinue the infusion if any allergic reaction occurs and institute appropriate emergency treatment. If an infusion reaction occurs, slow infusion rate and immediately notify physician. • If no reactions occur, the infusion rate may be incrementally increased to the full 250 mL/hour rate until completion.	• Begin initial infusion at 50 mL/hr for 10 minutes to monitor for signs of acute reaction • If no reaction noted, increase rate to 250 mL/hr until infusion complete (total dose should infuse over 1 hr) • If an infusion reaction occurs, slow infusion rate and immediately notify physician
Precautions	• Known allergies to horse protein are at risk for an anaphylactic reaction. • Product may contain cresol; local reactions and generalized myalgias may occur. • Product derived from equine (horse) plasma; may potentially contain infectious agents. • Delayed allergic reactions or serum sickness may occur, usually within 2 weeks (rash, fever, myalgia, arthralgia, pruritus, urticarial rash).	• Use is contraindicated in patients with a known hypersensitivity to papaya or papain • Acute hypersensitivity reaction possible in patients previously treated with CroFab®

¥Pediatric dose = adult dose

*Initial control: No increase in mSSS or cessation of the progression of the signs and symptoms (swelling, ecchymosis, pain, hypotension, and coagulopathy) within 1 hour of completion of antivenom administration
**CroFab® symptom-triggered vs maintenance dosing. Literature suggests a symptom-triggered (PRN) antivenom dosing strategy results in less antivenom use and shorter hospital length of stay. If CroFab® utilized and scheduled maintenance indicated, CroFab® 2 vials every 6 hours x 18 hours may be utilized. Scheduled maintenance dosing is NOT recommended for Anavip®.

Monitoring/Follow-up

- **Modified Snakebite Severity Score (mSSS)**
  - Assess at baseline, every 1 hour x 6 followed by every 6 hours
  - *Exception*: mild envenomation can be assessed every 6 hours
  - Refer to appendix for assessment and flow sheet
- **Vital signs**
  - Check and document vital signs every 1 hour x 6 followed by every 6 hours
  - Once stable, monitor vital signs in accordance with unit of admission
- **Laboratory**
  - Consider CMP, CBC or platelets, PT, INR, aPTT, and fibrinogen every 6 hours and prior to discharge
  - Consider UA, CPK, and myoglobin if urine dark (concern for rhabdomyolysis)
  - Consider thromboelastography (TEG) as it may be used as an adjunct to standard coagulation studies in patients with coagulopathies
- **Observation Period**
  - Dry Bite: Observe patient for <u>at least</u> 4 hours from time of bite
  - Antivenom <u>NOT</u> given: Observe 12 to 24 hours from time of bite (mSSS 0-2)
  - Antivenom GIVEN: Observe at least 24 hours post-antivenom (mSSS 3-8)

Post-Discharge Planning

- Instruct patient to return for worsening swelling not relieved by elevation, abnormal bleeding (gums, easy bruising, melena, etc.), or symptoms of delayed allergic reactions or serum sickness (fever, rash, muscle/joint pain, etc.)
- Bleeding precautions for 2 weeks in patients with <u>rattlesnake</u> envenomation **OR** abnormal INR, PT, fibrinogen, or platelet count at any time
- Pain control as needed
- Follow-up visits:
  - Antivenom <u>NOT</u> given: PRN only
  - Antivenom recipient:
    - Copperhead/water moccasin victim: PRN only
    - Rattlesnake victim: repeat labs at 5-7 days, then PRN
      - Patient may be discharged from clinic/office if coags are normal (INR < 1.5, Fibrinogen > 200 mg/dL, Platelets > 100 k/uL (or 10^9/L), Fibrin Split Products < 5 ug/mL)
      - Patient may need to return to clinic/office at day 5-7 post discharge if any of the following coagulation abnormalities are present:
        - INR > 1.5 and < 3
        - Fibrinogen 100 – 200 mg/dL
        - Platelet Count 50k – 100 k/uL (or 10^9/L)
        - Fibrin Split Products >5 and < 20 ug/mL
      - Patient may need to be re-admitted for antivenom if any of the following coagulation abnormalities are present:
        - INR > 3
        - Fibrinogen < 100 mg/dL
        - Platelet count < 50 k/uL (or 10^9/L)
        - Fibrin Split Products > 20 ug/mL

<u>Coral Snake Management</u>

- Notify local poison control center (1-800-222-1222) for management and antivenom recommendations
- Patients with suspected Coral Snake bite should be admitted to ICU for neurologic and respiratory monitoring for 24 hours

- Signs & Symptoms may be delayed for up to 12 hours
- Patients may require intubation for respiratory failure

Exotic Snake Management

- Notify local poison control center (1-800-222-1222) for management and antivenom recommendations.

ATTACHMENTS

Modified Snakebite Severity Score Assessment (BSWH.RX.032.A1)
Snakebite Management Algorithm (BSWH.RX.032.A2)

RELATED DOCUMENTS

None.

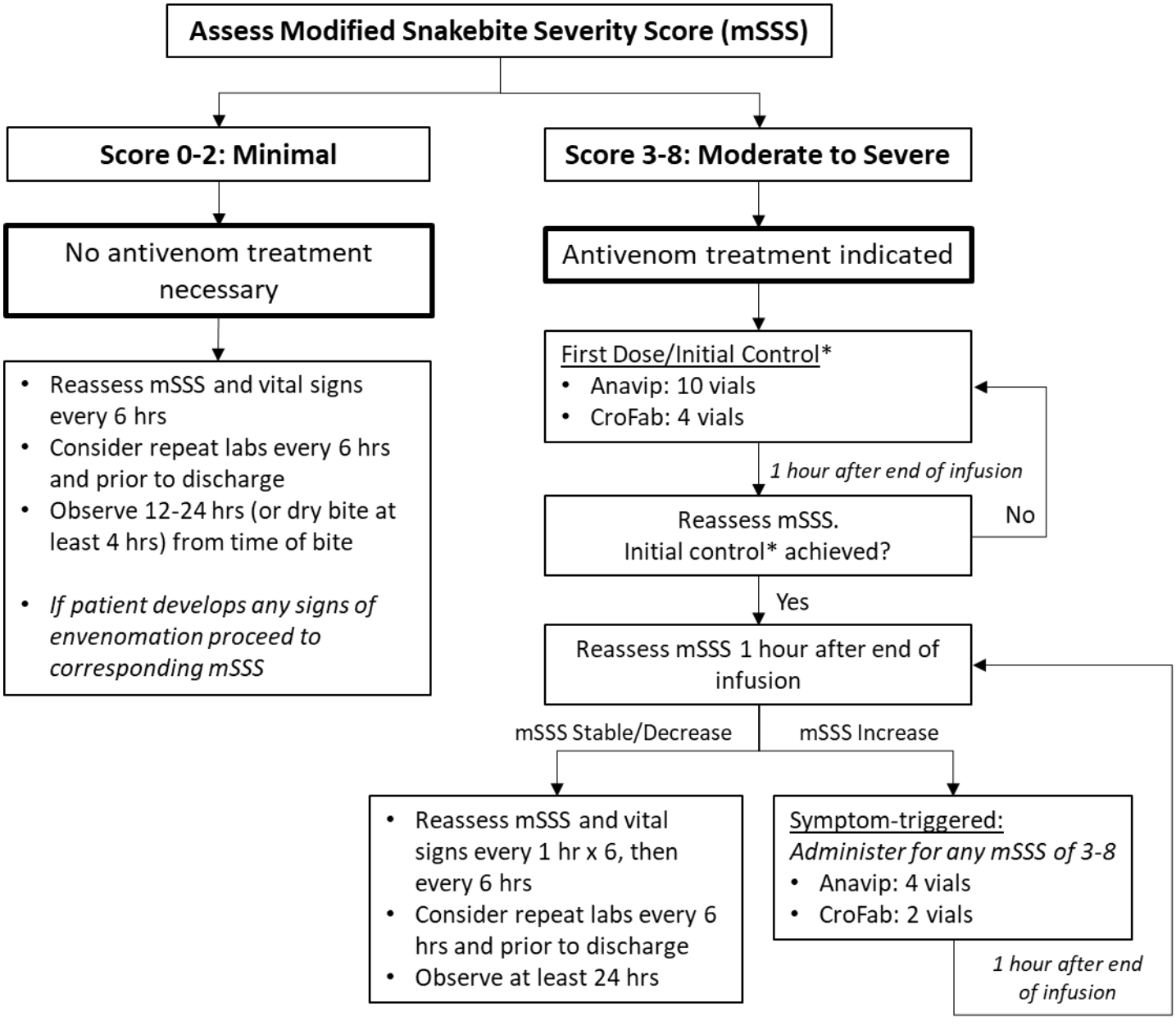
REFERENCES

1. Dart RC, Hurlbut KM, Garcia R, Boren J. Validation of a severity score for the assessment of crotalid snakebite. *Ann Emerg Med.* 1996;27(3):321-6.
2. Fowler AL, Hughes DW, Muir MT, et al. Resource utilization after snakebite severity score implementation into treatment algorithm or crotaline bite. *J Emerg Med*. 2017 Dec;53(6):854-861.
3. Anavip (Crotalidae Immune F[ab']2 [Equine]) [prescribing information]. Franklin, TN: Rare Disease Therapeutics Inc; April 2021.
4. Weant KA, Johnson PN, Bowers RC, Armitstead JA. Evidence-based, multidisciplinary approach to the development of a crotalidae polyvalent antivenin (CroFab) protocol at a university hospital. *Ann Pharmacother.* 2010;44(3):447-55.
5. Lavonas EJ, Ruha AM, Banner W, et al. Unified treatment algorithm for the management of crotaline snakebite in the United States: results of an evidence-informed consensus workshop. *BMC Emerg Med.* 2011;11:2.
6. Bush SP, Ruha AM, Seifer SA, et al. Comparison of F(ab')2 versus Fab antivenom for pit viper envenomation: a prospective, blinded, multicenter, randomized clinical trial. *Clin Toxicol (Phila).* 2015;53(1):37-45.
7. Spyres MB, Skolnik AB, Moore EC, Gerkin RD, Padilla-Jones A, Ruha AM. Comparison of antivenom dosing strategies for rattlesnake envenomation. *Crit Care Med.* 2018;46(6):e540-e544.
8. Walker JP, Morrison RL. Current Management of Copperhead Snakebite. *J AM Coll Surg.* 2011;212:470-475
9. Gale SC, Peters JA, Allen L, Creath R, Dombrovskiy VY. FabAV antivenin use after copperhead snakebite: clinically indicated or knee-jerk reaction? *Journal of Venomous Animals and Toxins including Tropical Diseases.* 2016;22:2.

Attachment Name:	Modified Snakebite Severity Score Assessment		
Attachment Number:	BSWH.RX.032.A1	Last Review/Revision Date:	06/02/2021

Modified Snakebite Severity Score (mSSS)	Date											
	Time											
Criterion	**Points**											
Local Wound												
No symptoms/signs	0	0	0	0	0	0	0	0	0	0	0	
Pain, swelling, or ecchymosis within 5-7.5 cm of bite site	1	1	1	1	1	1	1	1	1	1	1	
Pain, swelling or ecchymosis involving less than half the extremity [7.5-50 cm from bite site]	2	2	2	2	2	2	2	2	2	2	2	
Pain, swelling or ecchymosis involving half to all of extremity [50-100 cm from bite site]	3	3	3	3	3	3	3	3	3	3	3	
Pain, swelling or ecchymosis extending beyond affected extremity [more than 100 cm from bite site]	4	4	4	4	4	4	4	4	4	4	4	
Hematologic Symptoms												
No symptoms/signs	0	0	0	0	0	0	0	0	0	0	0	
Coagulation parameters slightly abnormal: INR < 1.5; platelets 100-150 k/uL (or 10^9/L); or fibrinogen 10 – 15 mg/dL	1	1	1	1	1	1	1	1	1	1	1	
Coagulation parameters abnormal: INR $\geq$ 1.5 and < 3; platelets 50-100 k/uL (or 10^9/L); or fibrinogen 5 – 10 mg/dL	2	2	2	2	2	2	2	2	2	2	2	
Coagulation parameters abnormal: INR $\geq$ 3; platelets 20-50 k/uL (or 10^9/L); or fibrinogen < 5 mg/dL	3	3	3	3	3	3	3	3	3	3	3	
Coagulation parameters markedly abnormal, with serious bleeding or the threat of spontaneous bleeding; unmeasurable PT, INR, or PTT; platelets <20 k/uL (or 10^9/L); or undetectable fibrinogen; severe abnormalities of other laboratory values also fall into this category	4	4	4	4	4	4	4	4	4	4	4	
Total Score												

	Severity of Envenomation		
Modified Snakebite Severity Score	0 – 2	3 – 5	6 – 8
Severity of Envenomation	Minimal	Moderate	Severe



***Initial control:** No increase in mSSS or cessation of the progression of the signs and symptoms (swelling, ecchymosis, pain, hypotension, and coagulopathy) within 1 hour of completion of antivenom administration