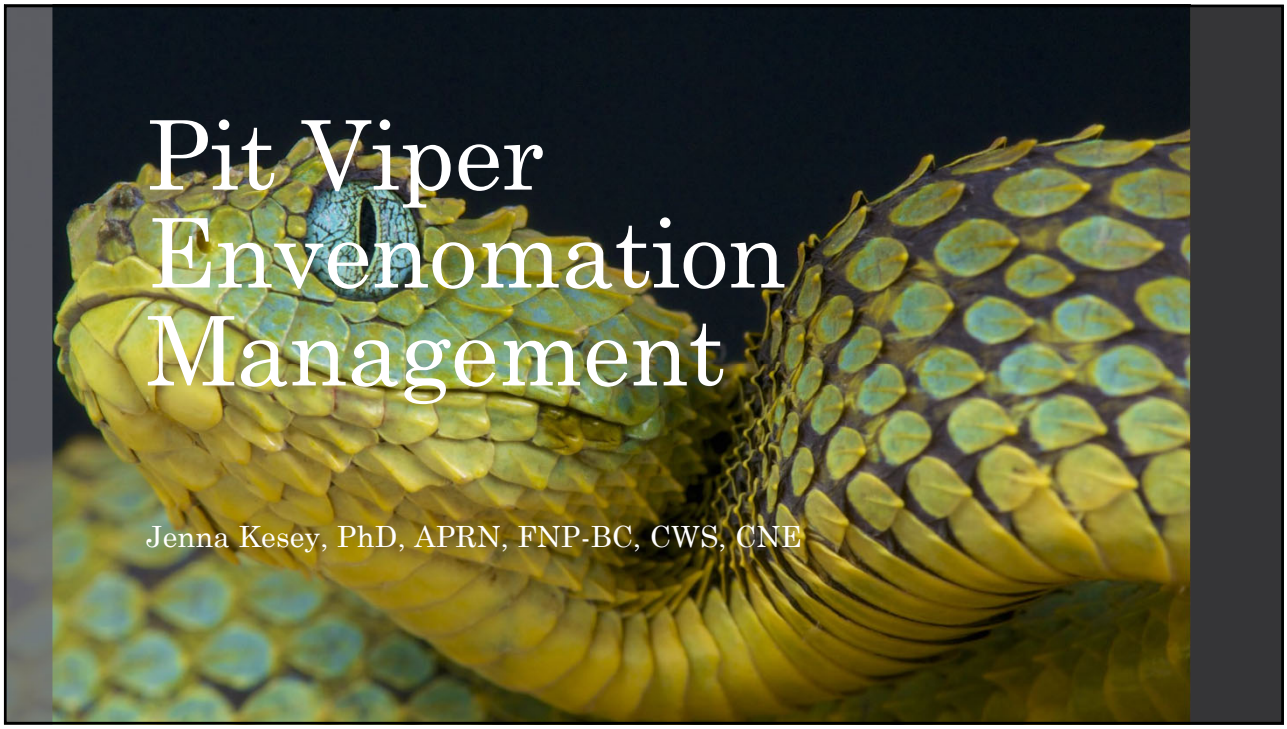


Pit Viper Envenomation Management

Jenna Kesey, PhD, APRN, FNP-BC, CWS, CNE

Objectives

1. Describe the epidemiology and impact of Pit Viper envenomation in the Southwestern United States.
2. Apply principles of assessment, treatment, and risk reduction in the management of Pit Viper envenomation.
3. Synthesize evidence for the management of Pit Viper Envenomation in the prehospital, acute, and critical care settings.

Huang et al., 2022

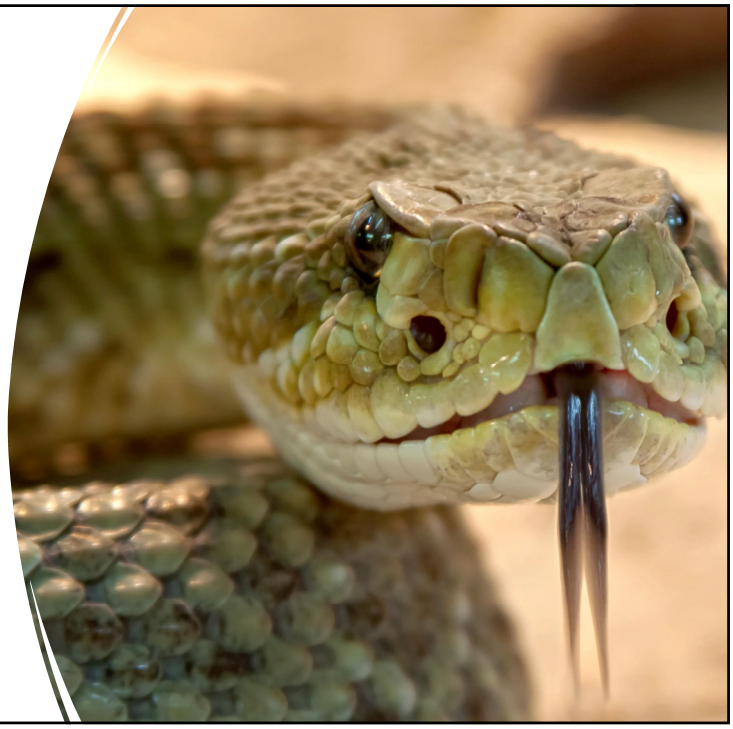
Epidemiology

- 5.4 Million snakebites per year worldwide (2.7 million venomous)
- Snakes exist on 6/7 continents (excluding Antarctica)
- 15% of the 3,700 species of snakes are venomous
- *Viperidae* and *Elapidae* are the venomous snake families
  - Of the *Viperidae* – 3 genera have hemotoxic venom
    - *Crotalinae* (subfamily) are the only ones existing in North America
      - Bothrops (genus) have hemotoxic venom
      - Crotalus (genus) have both hemotoxic and neurotoxic venom
- 98% of US snake envenomations are Viperidae

Huang et al., 2022; Gerardo et al., 2019; WHO, 2021

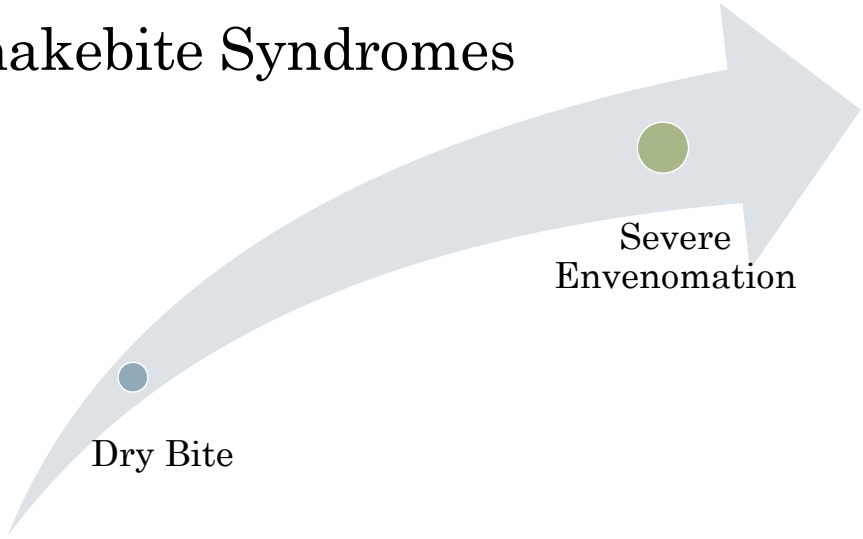
Introduction

- Most providers may only encounter a snake envenomation a few times in their careers
- Accurate assessment is key for positive patient outcomes and fiscal responsibility



Gerardo et al., 2019

Snakebite Syndromes



Severity and Outcomes with Snakebite

- Size of victim
- Comorbidity
- Part bitten
- Exercise
- Sensitivity
- Bite characteristics
- Snake species
- Secondary infection
- Treatment

Ahmed et al., 2008

Venom Effects

- Tissue Injury – connective tissue destruction and local spread with an inflammatory response, lymphatic absorption
- Hematologic Effects– both procoagulant and anticoagulant toxins, mixed platelet effects including aggregation and sequestration
- Neurologic Effects - local neuromuscular effects → cranial neuropathy
- Systemic Effects - cardiovascular toxicity, vasodilation, SIRS

Ahmed et al., 2008; Gerardo et al., 2019; Lavonas et al., 2011

Etiology

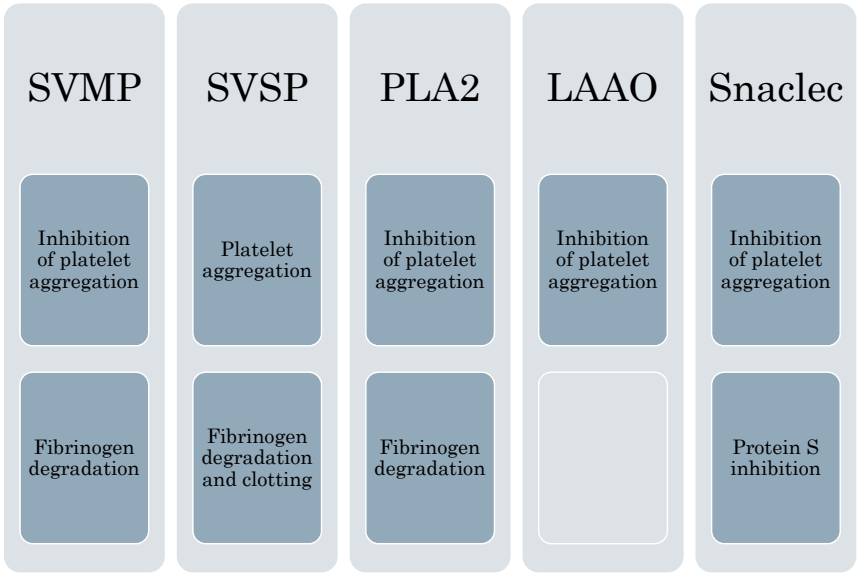
Hemotoxic effects (consumptive coagulopathy)

- Snake-venom serine proteases (SVSPs)
- Hemotoxic enzymes snake-venom metalloproteinases (SVMPs)
  - Endothelial damage (proteolytic destruction of the basement membrane)
  - Vascular permeability
  - Disordered coagulation

Neurotoxic effects

- Local numbness, ptosis, respiratory paralysis, cerebral anoxia, encephalopathy

Huang et al., 2022



Huang et al., 2022

Severe Envenomation Predictors

Demographic Predictors:

- Greater than 6 hours before treatment
- Age < 12 years
- Large snake (based on observer report)
- Rattlesnakes

Physiologic Predictors:

- Ptosis
- Bleeding distant to the bite site
- Bite to the digit or upper extremity

Gerardo et al., 2019;

Severe Hematologic Venom Effects – Laboratory Assessment

Severity Predictors

- Fibrinogenemia
- Thrombocytopenia (<150,000/mm3)
- Elevated Prothrombin time

Protective Findings

- Initial fibrinogen at or above normal
- Absence of thrombocytopenia

Gerardo et al., 2019;

Snakebite Severity Scale

Local Effects

- Ecchymosis
- Edema
- bullae

Hematologic Effects

- Bleeding
- Lab abnormalities

Systemic Effects

- Resp
- CV
- GI
- CNS

Gerardo et al., 2019

Unified treatment algorithm for the management of crotaline snakebite in the United States: results of an evidence-informed consensus workshop

Lavonas *et al.*

BioMed Central

Lavonas et al. *BMC Emergency Medicine* 2011, **11**:2
http://www.biomedcentral.com/1471-227X/11/2 (3 February 2011)

Lavonas et al., 2011

"Administration of antivenom, in adequate doses, effectively halts the spread of local tissue effects, reduces hematologic venom effects, and reduces systemic effects"

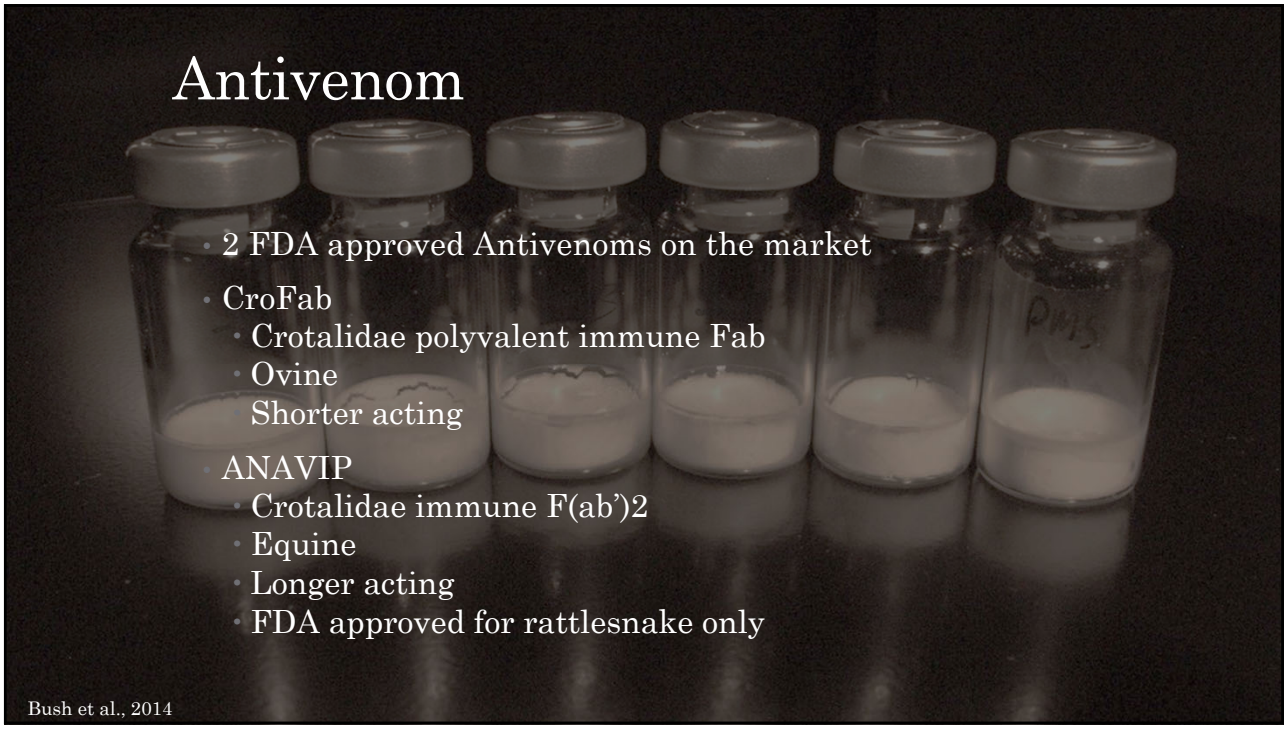
Lavonas et al., 2011, p. 6

However …

it may not be necessary for <u>every</u> snake bite

Bowden et al., 2022

Antivenom



- 2 FDA approved Antivenoms on the market
- CroFab
  - Crotalidae polyvalent immune Fab
  - Ovine
  - Shorter acting
- ANAVIP
  - Crotalidae immune F(ab')2
  - Equine
  - Longer acting
  - FDA approved for rattlesnake only

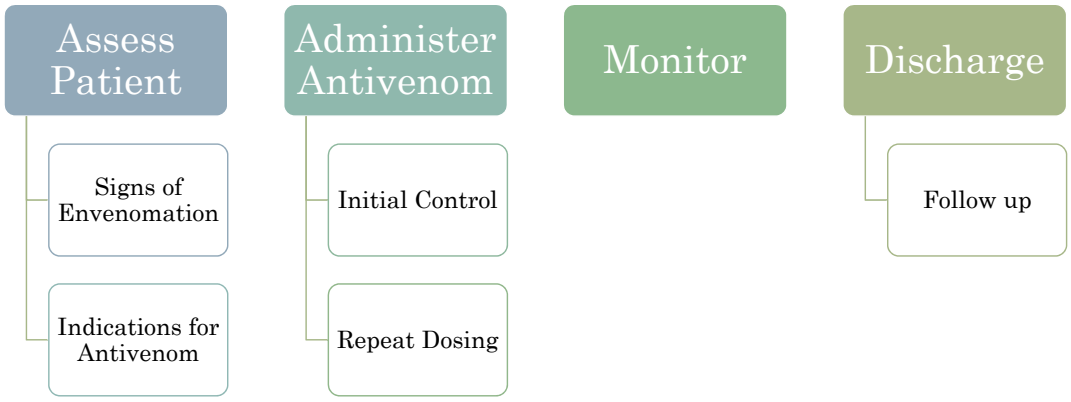
Bush et al., 2014

Antivenom

- Misidentification of snake species can cause irreversible damage and fatality
- Antivenom binds to the active venom to mitigate effects
- Current treatment calls for AV for both severe and non-severe bites however dosing adjustments are prudent
- Interspecies variation and intraspecies variation limit effectiveness

BTG International, 2018; Casewell et al., 2020; Huang et al., 2022; Gerardo et al., 2019; Waiddyanatha et al., 2019

Unified Treatment Algorithm



Lavonas et al., 2011

Treatment Algorithm Caveats

- Allergy (weigh benefits and risks carefully – but still probably give antivenom and be ready for mitigation of AE)
- Poison Control
  - Life threatening, hard to control, recurrence phenomena, allergic reactions, uncommon situations
- Maintenance Therapy
  - May not always be indicated in certain situations
- Discharge planning
  - Patient education, follow-up, bleeding precautions, lab assessment

BTG International, 2018; Lavonas et al., 2011

Dry Bite vs Mild Envenomation

- Any systemic effects or hematologic effects must be treated with antivenom
- Observation only may be indicated if no signs or only mild local effects exist
- Observation time (8-24 hours) depends on
  - Local signs
  - Age and health
  - Limb
  - Snake
  - Social support

Maintenance Therapy

- Crotalidae Polyvalent Immune Fab: 2 vials every 6 hours X 3 doses
- Unknown benefit: Some studies show it decreases the risk of local recurrence phenomena however most studies show equal administration of antivenom when compared to using a rescue approach if symptoms worsen
- Likely beneficial for any severe envenomation but may be clinically appropriate to only monitor without maintenance therapy for mild envenomations

BTG International, 2018; Lavonas et al., 2011

Treatments to AVOID

- Cutting or suctioning of the wound
- Ice or cryotherapy
- NSAIDS
- Prophylactic antibiotics
- Prophylactic fasciotomy or digital dermotomy
- Blood product transfusion
- Steriods (unless for allergic reaction)
- Tourniquets

Lavonas et al., 2011

Max dose???

Very few patients have an improvement in outcomes after 18 vials of antivenom

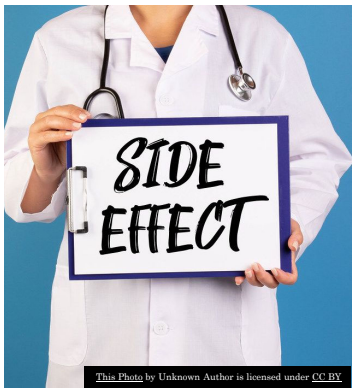
After the 20th vial of antivenom, if a patient has not achieved initial control, they are unlikely to respond any further

Expert consultation (Poison Control)

BTG International, 2018; Lavonas et al., 2011

Side Effects of Antivenom

- Side effects very common (up to 76%!)
- Serum sickness (fever, myalgias, arthralgias, rash, etc.)
  - antihistamines and corticosteroids
- 5-6% rate of an allergy (pruritis, urticaria, wheezing or anaphylaxis)
- Infusion reaction (fever, back pain, wheezing, nausea)
- Hypotension from histamine release in combination with relative hypovolemia due to the vasodilation



BTG International, 2018; Lavonas et al., 2011

Hospitalization

- Monitor for 18-24 hours after initial control with assessment and lab draws
- This can be decreased with Copperhead bites since they are rarely clinically significant

Lavonas et al., 2011

Recurrence Phenomena

2 phases

6-36 hours after initial control
- Typically local tissue effects
- Responds well to retreatment with antivenom

2-7 days after initial control
- Hematologic venom effects (defibrination and thrombocytopenia)
- Attenuated treatment response
- Clinically occult, rare to have medically significant bleeding

Lavonas et al., 2011

Complications

- Clinically significant bleeding
- Venom-induced angioedema or anaphylaxis
- Compartment syndrome
- Soft tissue infection
- Long-term limb dysfunction
- Intracranial hemorrhage
- Cerebral infarction or ischemic stroke
- Ocular

Huang et al., 2022; Waiddyanatha et al., 2019

Complications

- Kidney Disease
- Psychological effects

Waiddyanatha et al., 2019

Pearls & Pitfalls

- Disproportionally poor outcomes in the socioeconomically disadvantaged
- Long-term sequelae are poorly understood and reported because of a lack of follow up
- Petshop snakebites vs indigenous species

Huang et al., 2022; Waiddyanatha et al., 2019

Discharge and Follow-up

- ADLs
- Repeat labs
- Instructions
  - Elevation
  - ROM
  - Bleeding precautions
  - Serum sickness
  - Recurrence phenomena

Lavonas et al., 2011

Future Research

- Quality of life after snake envenoming – likely that many patients suffer from local and systemic symptoms months to years after bite with severe envenomation
- Severe local effects (short-term) or mild local effects (long-term) may be important to our patients

Huang et al., 2022

References

- Ahmed, S.M., Ahmed, M., Nadeem, A., Mahajan, J., Choudahary, A., & Pal, J. (2008). Emergency treatment of a snake bite: Pearls from literature. Journal of Emergency Trauma & Shock, 1(2): 97-105. https://www.doi.org/10.4103/0974-2700.43190
- BTG International. (2018). CROFAB ® Crotalidae Polyvalent FAB (Ovine) [package insert]. West Conshohocken, PA. Retrieved from https://crofab.com/getmedia/e01143d2-0638-4d8e-bc29-d6f63d515751/CroFab-Prescribing-Information.pdf
- Bowden, M.B., Christie, D.B., Hand, K.H., & Montgomery, A. (2022). Crotalidae Polyvalent Immune Fab and cost-effective management of hospital admissions for snakebites. *The American Surgeon, 88*(3): 368-371. https://www.doi.org/10.1177/00031348211054566
- Bush, S.P., Ruham A.M., Seifert, S.A., Morgan, D.L., Lewis, B.J., Arnold, T.C., Clark, R.F., Meggs, W.J., Toschlog, E.A., Borron, S.W., Figge, G.R., Sollee, D.R., Shirazi, F.M., Wolk, R., Chazal, I., Quan, D., Garcia-Ubbelohde, W., Alagon, A., Gerkin, R.D., & Boyer, L.. (2014). Comparison of F(ab')2 versus Fab antivenom for pit viper envenomation: A prospective, blinded, multicenter, randomized clinical trial. *Clinical Toxicology, 53*(1): 37-45. https://www.doi.org/10.3109/15563650.2014.974263
- Casewell, N.R., Jackson, T.N.W., Laustsen, A.H., & Sunagar, K. (2020). Causes and consequences of snake venom variation. *Trends in Pharmacological Sciences, 41*(8): 570-581. https://www.doi.org/10.1016/j/tips.2020.05.006
- Gerardo, C.J.., Vissoci, J.R.N., Evans, C.S., Simel, D.L., & Lavonas, E. J. (2019). Does this patient have a severe snake envenomation? The rationale clinical examination systematic review. *JAMA Surg, 154*(4): 346-354. https://www.doi.org/10.1001/jamasurg.2018.5069
- Huang, Y., Chen, Y., Liu, C., Cheng, H., Tu, A., & Chang, K. (2022). Cerebral complications of snakebite envenoming: Case studies. *Toxins, 14*(432). https://www.doi.org/10.3390/toxins14070436
- Waiddyanatha, S., Silva, A., Siribaddana, S., & Isbister, G.K. (2019). Long-term effects of snake envenoming. Toxins, 11(193). https://www.doi.org/10.3390/toxins11040193
- World Health Organization. (2021). *Snakebite envenoming*. https://www.who.int/news-room/fact-sheets/detail/snakebite-envenoming


Questions?