DATE: April 2017

TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Evaluation & Management of Suspected U.S. Pit Viper Snakebites
Evidence Summary

Inclusion Criteria
- Patients <21 years of age with snakebites from suspected pit vipers (i.e., rattlesnakes, copperheads, or cottonmouths [also known as water moccasins])

Exclusion Criteria
- Patients ≥21 years of age
- Snakebites from coral snakes and other snakes that are not U.S. pit vipers (e.g., exotic breeds)

Background

The Crotalinae, commonly known as pit vipers, are the most common type of venomous snakes in Texas and include the copperhead, cottonmouth and rattlesnake. [1] Pit vipers are identified by their triangular head, elliptical pupils, and two curved fangs. Pit vipers make up 75-80% of bites resulting in envenomation. [2] According to the Texas Department of Health and Services, on average, 1 to 2 people in Texas die each year from venomous snakebites. Deaths typically occur in children, the elderly, and in those for whom treatment is not given, is postponed, or is administered in insufficient quantities.

Envenomation by pit vipers constitutes a medical emergency. The basis of treatment for all venomous snakebites include early transport to definitive care, the administration of antivenom when indicated, and monitoring for progression of disease and adverse reactions. Without timely intervention and administration of antivenom, pit viper envenomation can lead to significant morbidity and disability, or death in very rare cases.

Critically Analyze the Evidence

The **GRADE criteria** were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

PICO Question 1: In children younger than 21 years old presenting with snakebites from suspected pit vipers, what is the role of surgical intervention?

Recommendation(s): Strong recommendation with moderate quality evidence against surgical intervention with fasciotomy or dermotomy for suspected pit viper snakebites. If physical exam indicates suspected compartment syndrome, consultation with a medical toxicologist is recommended prior to any fasciotomy or digit dermotomy. [3-5]

Remarks: Consider noninvasive studies for blood flow.

A review of the literature yielded 1 randomized controlled trial and 2 observational studies regarding the use of surgical intervention for the treatment of snakebites. In a multi-center, double-blind, placebo randomized controlled trial, Gerardo (2016) compared the recovery of copperhead envenomated patients treated with antivenom to those receiving placebo. The study concluded that the intervention group that received antivenom had improved limb function at 14 days post envenomation. Darracq (2015), a retrospective observational study, compared the clinical characteristics and demographics of patients who underwent a fasciotomy to those where the procedure was discussed but not performed. Of 105 patients, 28 fasciotomies were performed. Only 2 of 28 patients had compartment pressure measurements and patients who underwent fasciotomies spent an additional 2 days in the hospital compared to those who did not receive the procedure. Shaw (2002) conducted a retrospective chart review of 24 children to investigate the roles of antivenin and

surgery in the treatment of rattlesnake envenomations. The study revealed that surgery was safely avoided in 19 patients with the aggressive use of polyvalent equine antivenin. For the three patients who received surgical intervention, two patients were managed with limited soft-tissue debridement and one patient, whom antivenin was withheld, was managed with a fasciotomy of the leg because of compartment syndrome. The studied concluded that children with severe envenomation from rattlesnakes should initially be treated with antivenin, rather than surgical intervention.

PICO Question 2: In children younger than 21 years old presenting with snakebites from suspected pit vipers, are prophylactic antibiotics necessary?

Recommendation(s): Strong recommendation with low quality evidence against the use of prophylactic antibiotics; antibiotics should only be administered if signs of infection develop, such as purulence. Isolated erythema does not warrant antibiotics (other signs of infection may be obscured by local tissue changes caused by venom). [6-9]

For the use of prophylactic antibiotics in the treatment of suspected snakebites, a review of literature produced 4 observational studies. Correra (2014) performed a retrospective chart review of 155 children with envenomated bites admitted to Texas Children's Hospital. 72 children received prophylactic antibiotics. Since the rate of wound infections with Crotalid bites is 3%, the study concluded that the utility of antibiotic administration is questionable. The impact of antibiotics on patient outcomes was undeterminable since the study was retrospective and follow-up was limited. In a prospective controlled trial, Kerrigan (1997) concluded that there were no statistically significant differences in patient outcomes between patients that received prophylactic antibiotics compared to patients that receive no antibiotics. LoVecchio (2002) conducted a prospective observational study to observe infection rates in patients treated with prophylactic antibiotics for rattlesnake bites. 81% of patients received antivenin but only 6% of patients received antibiotics at 7-10 day follow-up. The study determined that prophylactic antibiotics are not indicated for successful treatment of rattlesnake bites. Ruha (2014) observed the extent to which health care providers administer prophylactic antibiotics for snake envenomation. The study discovered that 11% if patients were treated with antibiotics, 53% in the emergency department, despite published evidence and recommendations against this practice.

PICO Question 3: In children younger than 21 years old presenting with snakebites from suspected pit vipers, what is the most efficient technique for reconstitution of CroFab?

Recommendation(s): Strong recommendation with low quality evidence to reconstitute CroFab with 25 mL of 0.9% sterile saline and gently rotated 180 degrees back and forth to dissolve the powder into solution. Once reconstituted the 4 to 6 vials should be further diluted with normal saline to a volume of 250 mL. [10,11]

Remarks: Although the manufacturer recommends reconstituting with 18 ml, 25 mL is associated with decreased dissolution times.

3 in vitro observational studies were discovered in the review of literature. Gerring (2013) performed an analytical study to compare reconstitution CroFab in 10 mL 0.9% NaCL to 18 mL. The study validated that more rapid reconstitution was achieved with the use of 18 ml of 0.9% NaCl and time to administration was significantly reduced. Quan (2010) compared CroFab reconstitution with 10 mL of sterile water for injection to 25 mL utilizing three mixing techniques: undisturbed; agitation with a mechanical agitator; and continuous hand rolling and inverting of vials. The study concluded that hand mixing after filling vials completely with 25 mL of sterile water resulted in shorter dissolution times than compared to the other methods.

PICO Question 4: In children younger than 21 years old presenting with snakebites from suspected pit vipers, which laboratory and diagnostic tests should be obtained and at what frequency?

Recommendation(s): Strong recommendation with low quality evidence to obtain a DIC panel for any suspected pit viper snakebites; further or serial labs at the discretion and consultation of medical toxicologist. [6,12-13]

Remarks: None

A review of literature yielded 3 observational studies. Ali (2015) conducted a retrospective chart review to determine the frequency and severity of abnormal laboratory measures of coagulation after suspected or known copperhead envenomation. The study results suggest to refrain from performing serial coagulation testing in both adult and pediatric patients in the absence of clinical evidence of bleeding for copperhead envenomation. Correra (2014) recommends obtaining the full profile of laboratory tests for all children who present with bites from unidentified snakes and reside in an area with a high probability of rattlesnake bites. The study also suggested that coagulation tests be reserved for patients with higher envenomation scores. Moriarity (2012) conducted a retrospective chart review for all snakebite patients. The study was unable to identify a group of patients that could be considered low risk or for whom coagulation marker testing could be omitted. The results of the study suggested that all patients presenting to the ED with snakebites should have routine coagulation tests.

PICO Question 5: In children younger than 21 years old presenting with snakebites from suspected pit vipers, what are the pediatric recommendations for administration of antivenom?

Recommendation(s): Strong recommendation with moderate quality evidence to administer the same adult dosage of antivenom to pediatric patients for suspected pit viper snakebites. [3,14-22]

Remarks: Pediatric snakebite patients should receive the same dose of antivenom as an adult. The antivenom counteracts snake venom and is dosed according to the amount of venom injected, not patient's body weight. Please consider and educate family on serum sickness and hypersensitivity as possible side effects of antivenom.

The review of literature revealed 1 meta-analysis, 2 randomized, controlled trials and 7 observational studies. The body of evidence regarding the pediatric recommendations for administration of antivenom concluded that CroFab antivenom is safe and effective in the pediatric population and pediatric dosing of CroFab is the same as adult dosing (4 to 22 vials, depending on severity of envenomation), regardless of size or age.

PICO Question 6: In children younger than 21 years old presenting with snakebites from suspected pit vipers, what medications should be used in pain management?

Recommendation(s): Strong recommendation with low quality evidence to use opioids, preferably fentanyl or hydromorphone, for pain management of suspected pit viper snakebites. [23]

Remarks: NSAIDs such as ibuprofen and aspirin are relatively contraindicated because of the theoretical risk of bleeding associated with NSAIDs in patients who may develop coagulopathy or thrombocytopenia secondary to envenomation. Avoid morphine sulfate when possible due to opiate-induced histamine release.

One observational study was discovered in the review of literature. Levine (2014), a retrospective cohort study, looked at the likelihood of bleeding complications for envenomation patients on antiplatelet or anticoagulant medications compared to those not on medication. Early bleeding occurred in three of 31 (9.7%) patients on antiplatelet or anticoagulant medications and four of 288 (1.4%) patients not on antiplatelet or anticoagulant medications (relative risk [RR] = 6.9; 95% confidence interval [CI] = 1.6 to 29.4; p = 0.022). The authors concluded that the risk of bleeding is increased in rattlesnake envenomation patients who use antiplatelet or anticoagulant medications. Therefore, providers should be vigilant of the risk assessment for patients on these medications.

PICO Question 7: In children younger than 21 years old presenting with snakebites from suspected pit vipers, what unit or floor should the patient be admitted to?

Recommendation(s): Strong recommendation with low quality evidence to admit patients with suspected pit viper snakebites to inpatient acute care for serial observation; admission consultation with medical toxicologist for admission to critical care status based on severity of envenomation. [24]

Remarks: Critical care admission should be reserved for patients with systemic toxicity and/or organ failure.

The review of literature yielded one observational study. Nara (2014) retrospectively examined resource utilization for treatment of envenomation under observation and inpatient status, and then compared patients in observation status receiving antivenom to all other patients in observation status. Results revealed that patients receiving antivenom had substantially higher costs due to pharmacy costs (mean cost: $17,665 for observation status, $20,503 for inpatient status). The mean costs for the patients in observation status with other diagnoses were $3,001 compared with $17,665 for observation-status patients who received antivenom. The observation-status designation for patients being treated for envenomation may be unwarranted since patients in observation status are likely exposed to a higher degree of cost-sharing, and hospitals receive lower reimbursements for care provided.

PICO Question 8: In children younger than 21 years old presenting with snakebites from suspected pit vipers, is the use of oral steroids beneficial in the reduction of limb edema?

Recommendation(s): Strong recommendation with low quality evidence to not routinely use steroids in the reduction of limb edema associated with snakebites [25,26]

Review included 2 randomized, controlled trial. Nuchprayoon (2008) randomized patients to either receive or not receive prednisolone after a green pit viper snakebite. Evaluation included degree of limb edema and limb circumference before and after intervention. No differences in outcomes were found. deSilva (2011) discovered that when compared with placebo, adrenaline significantly reduced severe reactions to antivenom by 43% (95% CI 25-67) at 1 hour and by 38% (95% CI 26-49) up to and including 48 hours after antivenom administration; hydrocortisone and promethazine did not. Also, adding hydrocortisone negated the benefit of adrenaline.

PICO Question 9: In children younger than 21 years old presenting with snakebites from suspected pit vipers, does the use of pressure immobilization or tourniquet, improve limb outcome?

Recommendation(s): Strong recommendation with very low quality evidence to avoid the use of tourniquets and pressure immobilization for the treatment of suspected snakebites. The affected extremity should be elevated to maintain at least 45 degree elevation. [27]

Review included 1 article, which discouraged the use of pressure immobilization or tourniquet.

Critical Points of Evidence

Evidence Supports

- Reconstitute CroFab with 25 mL of 0.9% sterile saline and gently rotated 180 degrees back and forth to dissolve the powder into solution. Once reconstituted, the 4 to 6 vials should be further diluted with normal saline to a volume of 250 mL. [10,11] – Strong recommendation, low quality evidence
- Obtain a DIC panel for any suspected pit viper snakebites; further or serial labs at the discretion and consultation of medical toxicologist.. [6,12,13] – Strong recommendation, low quality evidence
- Administer the same dosage of antivenom given to adults to pediatric patients for suspected pit viper snakebites. [3,14-22] – Strong recommendation, low quality evidence
- Administer opioids, preferably fentanyl or hydromorphone, for pain management of suspected pit viper snakebites. [23] – Strong recommendation, low quality evidence
- Admit patients with suspected pit viper snakebites to inpatient acute care for serial observation. [24] – Strong recommendation, low quality evidence
- Administer steroids to treat anaphylaxis to antivenom. [25] – Strong recommendation, low quality evidence

Evidence Against

- Surgical intervention by fasciotomy or dermotomy for suspected pit viper snakebites. [3-5] – Strong recommendation, moderate quality evidence
- The use of prophylactic antibiotics for the treatment of suspected pit viper snakebites. [6-9] – Strong recommendation, low quality evidence
- The use of oral steroids to reduce limb edema associated with snakebites. [26] – Strong recommendation, low quality evidence
- The use of pressure immobilization or tourniquet. [27] – Strong recommendation, very low quality evidence

DATE: April 2017

TCH Evidence Based Outcomes Center
Clinical Algorithm for Emergency Department Evaluation & Management of Pit Viper Snakebite

Patient arrival to ED with suspected pit viper snakebite

Inclusion criteria:
- Patients less than 21 years of age with snake bites from suspected US pit vipers (i.e. rattlesnakes, copperheads or cottonmouths [also known as water moccasins])

Exclusion criteria:
- Patients 21 years of age and older
- Patients with snake bites from coral snakes and other snakes than US pit vipers (i.e. exotic breeds)

Assess Patient
- Mark leading edge of swelling and tenderness every 15-30 minutes
- Immobilize and elevate extremity
- Treat pain (IV opioids preferred)
- Obtain initial lab studies (protime, Hgb, platelets, fibrinogen)
- Update tetanus

Check for Signs of Envenomation
- Swelling, tenderness, redness, ecchymosis, or bites at the bite site, or
- Elevated protime, decreased fibrinogen or platelets, or
- Systemic signs, such as hypotension, bleeding beyond the puncture site, refractory vomiting, diarrhea, angioedema, neurotoxicity

None →

Apparent Dry Bite/No Bite
- Do not administer antivenom
- Observe patient ≥ 8 hours
- Repeat labs prior to discharge
- ***If patient develops signs of envenomation, return to "Check for Signs of Envenomation" box***

Present ↓

Check for Indications for Antivenom
- Swelling that is more than minimal and that is progressing, or
- Elevated protime, decreased fibrinogen or platelets, or
- Any systemic signs

None →

Apparent Minor Envenomation
- Do not administer 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 " Check for Indications for Antivenom" box***

Present ↓

Administer Anitvenom
- Establish IV access and give IV fluids
- Pediatric antivenom dose = adult dose
- Mix 4-6 vials of crotaline Fab antivenom (CroFab) in 250 ml NS and infuse IV over 1 hour
  - For patients in shock or with serious active bleeding
    - Increase initial dose of antivenom to 8-12 vials
    - Call medical toxicologist
- Initiate first dose of antivenom in ED or ICU
  - For suspected adverse reaction: hold infusion, treat accordingly, and call medical toxicologist
- Re-examine patient for treatment response within 1 hour of completion of antivenom infusion

Has Initial Control of Envenomation been Achieved?
- Swelling and tenderness not progressing
- Protime, fibrinogen, and platelets normal or clearly improving
- Clinically stable (not hypotensive, etc.)
- Neurotoxicity resolved or clearly improving

No →

Repeat antivenom until initial control is achieved
If initial control is not achieved after 2 doses of antivenom, call Medical Toxicologist

Yes ↓

Monitor Patient
- Perform serial examinations
- Maintenance antivenom therapy may be indicated (read Maintenance Antivenom Therapy box)
- Observe patient 16-24 hours after initial control for progression of any venom effect
- Follow-up labs 6-12 hours after initial control and prior to discharge
- If patient develops new or worsening signs of envenomation, administer additional antivenom per Administer Antivenom box

Maintenance Antivenom Therapy
- Maintenance therapy is additional antivenom given after initial control to prevent recurrence of limb swelling
  - Maintenance therapy is 2 vials of antivenom q 6 hours x 3 (given 6, 12, and 18 hours)
- Maintenance therapy may not be indicated in certain situations, such as
  - Minor envenomations
  - Facilities where close observation by a medical toxicologist is available
- Follow advice of medical toxicologist

Does patient meet discharge criteria
- No progression of any venom effect during the specified observation period
- No unfavorable laboratory trends in protime, fibrinogen or platelets

Post-Discharge Planning
- 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

Treatments to Avoid in US Pit Viper Snakebite
- Cutting and/or suctioning of the wound
- Ice
- Tourniquets or constriction bands
- Pressure immobilization
- Prophylactic antibiotics
- Prophylactic fasciotomy
- Routine use of blood products
- Steroids

References

1. Texas Department of State Health Services (2017). Snakebite statistics. Retrieved from http://tpwd.texas.gov/education/resources/texas-junior-naturalists/snakes-alive/snake-bite-statistics
2. Lavonas, E. J., Ruha, A. M., Banner, W., Bebarta, V., Bernstein, J. N., Bush, S. P., . . . & Curry, S. C. (2011). Unified treatment algorithm for the management of crotaline snakebite in the United States: Results of an evidence-informed consensus workshop. *BMC Emergency Medicine*, *11*(1), 2.
3. Gerardo, C. J., & Lavonas, E. J. (2016). The efficacy of early fab antivenom versus placebo plus optional rescue therapy on recovery from copperhead snake envenomation. *Toxicon*, (117), 102.
4. Darracq, M. A., Cantrell, F. L., Klauk, B., & Thornton, S. L. (2015). A chance to cut is not always a chance to cure-fasciotomy in the treatment of rattlesnake envenomation: A retrospective poison center study. *Toxicon*, *101*, 23-26.
5. Shaw, B. A., & Hosalkar, H. S. (2002). Rattlesnake bites in children: Antivenin treatment and surgical indications. *Journal of Bone and Joint Surgery*, *84*(9), 1624-1629.
6. Correa, J. A., Fallon, S. C., Cruz, A. T., Grawe, G. H., Vu, P. V., Rubalcava, D. M., ... & Brandt, M. L. (2014). Management of pediatric snake bites: Are we doing too much? *Journal of Pediatric Surgery*, *49*(6), 1009-1015.
7. Kerrigan, K. R., Mertz, B. L., Nelson, S. J., & Dye, J. D. (1997). Antibiotic prophylaxis for pit viper envenomation: Prospective, controlled trial. *World Journal of Surgery*, *21*(4), 369-373.
8. LoVecchio, F., Klemens, J., Welch, S., & Rodriguez, R. (2002). Antibiotics after rattlesnake envenomation. *Journal of Emergency Medicine*, *23*(4), 327-328.
9. Ruha, A. M., Kang, A. M., Onisko, N. S., Greene, S., Vohra, R., Seifert, S. A., . . . & Padilla-Jones, A. (2014). Antibiotic use in the management of snake envenomation. *Journal of Medical Toxicology, 11*, 36-37.
10. Gerring, D., King, T. R., & Branton, R. (2013). Validating a faster method for reconstitution of Crotalidae Polyvalent Immune Fab (ovine). *Toxicon*, *69*, 42-49.
11. Quan, A. N., Quan, D., & Curry, S. C. (2010). Improving Crotalidae polyvalent immune Fab reconstitution times. *American Journal of Emergency Medicine*, *28*(5), 593-595.
12. Ali, A. J., Horwitz, D. A., & Mullins, M. E. (2015). Lack of coagulopathy after copperhead snakebites. *Annals of emergency medicine*, *65*(4), 404-409.
13. Moriarity, R. S., Dryer, S., Repogle, W., & Summers, R. L. (2012). The role for coagulation markers in mild snakebite envenomations. *Western Journal of Emergency Medicine*, *13*(1).
14. Schaeffer, T. H., Khatri, V., Reifler, L. M., & Lavonas, E. J. (2012). Incidence of immediate hypersensitivity reaction and serum sickness following administration of crotalidae polyvalent immune Fab antivenom: A meta-analysis. *Academic Emergency Medicine*, *19*(2), 121-131.
15. Bush, S. P., Ruha, A. M., Seifert, S. A., Morgan, D. L., Lewis, B. J., Arnold, T. C., ... & Figge, G. R. (2015). 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.
16. Gale, S. C., Peters, J. A., Allen, L., Creath, R., & Dombrovskiy, V. Y. (2016). FabAV antivenin use after copperhead snakebite: Clinically indicated or knee-jerk reaction? *Journal of Venomous Animals and Toxins including Tropical Diseases*, *22*(1), 2.
17. Gerardo, C. J., Scott Evans, C., Kuchibhatla, M., Mando-Vandrick, J., Yen, D. M., Weiying, G., . . . & Lavonas, E. J. (2015). Time to antivenom administration is not associated with total antivenom dose administered in a copperhead-predominant snakebite population. *Academic Emergency Medicine*, *22*(3), 308-314.
18. Lavonas, E. J., Kokko, J., Schaeffer, T. H., Mlynarchek, S. L., Bogdan, G. M., & Dart, R. C. (2011). Short-term outcomes after Fab antivenom therapy for severe crotaline snakebite. *Annals of Emergency Medicine*, *57*(2), 128-137.
19. Offerman, S. R., Bush, S. P., Moynihan, J. A., & Clark, R. F. (2002). Crotaline Fab antivenom for the treatment of children with rattlesnake envenomation. *Pediatrics*, *110*(5), 968-971.
20. Pizon, A. F., Riley, B. D., LoVecchio, F., & Gill, R. (2007). Safety and efficacy of Crotalidae polyvalent immune Fab in pediatric crotaline envenomations. *Academic Emergency Medicine*, *14*(4), 373-376.
21. Walker, J. P., & Morrison, R. L. (2011). Current management of copperhead snakebite. *Journal of the American College of Surgeons*, *212*(4), 470-474.
22. Watson, L. I., Spivey, C., Menon, C. R., Kotwall, C. A., Clancy, T. V., & Hope, W. W. (2010). An evaluation of snake bites and antivenin use at a regional medical center. *The American Surgeon*, *76*(7), 755-758.
23. Levine, M., Ruha, A. M., Padilla-Jones, A., Gerkin, R., & Thomas, S. H. (2014). Bleeding following rattlesnake envenomation in patients with preenvenomation use of antiplatelet or anticoagulant medications. *Academic Emergency Medicine*, *21*(3), 301-307.
24. Narra, A., Lie, E., Hall, M., Macy, M., Alpern, E., Shah, S. S., . . . & Fieldston, E. (2014). Resource utilization of pediatric patients exposed to venom. *Hospital pediatrics*, *4*(5), 276-282.
25. de Silva, H. A., Pathmeswaran, A., Ranasinha, C. D., Jayamanne, S., Samarakoon, S. B., Hittharage, A., . . . & Armitage, J. M. (2011). Low-dose adrenaline, promethazine, and hydrocortisone in the prevention of acute adverse reactions to antivenom following snakebite: A randomised, double-blind, placebo-controlled trial. *PLoS medicine*, *8*(5), e1000435.
26. Nuchprayoon, I., Pongpan, C., & Sripaiboonkij, N. (2008). The role of prednisolone in reducing limb oedema in children bitten by green pit vipers: A randomized, controlled trial. *Annals of Tropical and Parasitology, 102*(7), 643-649.
27. Norris, R. L., Ngo, J., Nolan, K., & Hooker, G. (2005). Physicians and lay people are unable to apply pressure immobilization properly in a simulated snakebite scenario. *Wilderness & Environmental Medicine*, *16*(1), 16-21.

Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

Snakebites Content Expert Team
Spencer Greene, MD, Medical Toxicology
Jeanine Graf, MD, Critical Care
Nichole Gubbins, MD, Emergency Medicine & Global Health Fellow
Ashley Joshi-Patel, DO, Pediatric Hospital Medicine
Sara Liechti, PharmD, Pharmacy
Monica Lopez, MD, Surgery

EBOC Team
Sheesha Porter, MSN, RN, CNOR, Research Specialist
Charles Macias, MD, MPH, Medical Director

Additional EBOC Support
Tom Burke, Research Assistant
Sherin Titus, Research Assistant
Karen Gibbs, MSN/MPH, RN, Research Specialist
Andrea Jackson, MBA, RN, Research Specialist
Betsy Lewis, MSN, RN, Research Specialist
Jennifer Loveless, MPH, Research Specialist
Ellis Arjmand, MD, MMM, PhD, Associate Director
Christina Davidson, MD, Associate Director
Anne Dykes, MSN, RN, Assistant Director
Kathy Carberry, MPH, RN, Director

No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing Internal and External Guidelines
   - Unified treatment algorithm for the management of crotaline snakebite in the United States: Results of an evidence informed consensus workshop
   - Venomous Snakebites in the United States: Management Review and Update
   - Wilderness Medical Society Practice Guidelines for the Treatment of Pitviper Envenomations in the United States and Canada
   - Surgical Considerations in the Management of Pit Viper Snake Envenomation
3. Literature Review of Relevant Evidence
   - Searched: PubMed, American Academy of Pediatrics, Cochrane Library, AHRQ, and UptoDate.
4. Critically Analyze the Evidence
   - 1 meta-analysis, 2 randomized controlled trials, and 20 nonrandomized studies
5. Summarize the Evidence
   - Materials used in the development of the guideline, evidence summary, and order sets are maintained in an Evaluation and Management of Suspected Pit Viper Snakebites evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.

"Evidence Supports" provides clear evidence that the benefits of the intervention exceed harm.

"Evidence Against" provides clear evidence that the intervention is likely to be ineffective or that it is harmful.

"Evidence Lacking/Inconclusive" indicates there is currently insufficient data or inadequate data to support or refute a specific intervention.

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
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Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the evaluation and management of suspected pit viper snakebites in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care, and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient family, to make the ultimate judgment regarding care.

Version History

Date	Action	Comments
Apr 2017	Originally completed	