# Surgical Considerations in the Management of Pit Viper Snake Envenomation

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Envenomation by North American pit viper snakes (family *Viperidae*, subfamily *Crotalinae*, genera *Crotalus* [rattlesnakes], *Sistrurus* [pygmy rattlesnakes], and *Agkistrodon* [copperhead and cottonmouth snakes]) is a dynamic and potentially serious medical condition. Each year in the United States, approximately 9,000 patients are treated for pit viper snakebite and 5 die.<sup>1,2</sup>

Pit viper venoms are complex mixtures with up to 50 different active components, including enzymes, nonenzymatic polypeptides, glycoproteins, and nonprotein components. Metalloproteinases, phospholipases A2, and inflammatory mediator analogues produce tissue injury; activate complement; damage vascular endothelium; degrade fibrinogen; activate platelets; and cause systemic effects, including hemodynamically important fluid shifts, bleeding, and neurotoxicity.

The overall management of pit viper victims has been reviewed recently.<sup>3,4</sup> General care includes parenteral analgesia, antivenom administration, and serial assessments of limb swelling and laboratory tests. Despite the presence of soft tissue inflammation, prophylactic antibiotics are rarely required, and most patients achieve good outcomes with supportive care and antivenom alone. The case-fatality rate in rattlesnake envenomation is very low, approximately 1 per 700 patients about whom a poison center was consulted.<sup>5</sup> Death due to copperhead snake envenomation is extremely rare, with only 1 fatal case reported to US poison centers during a 5-year period.<sup>6</sup>

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Among patients with signs of envenomation, local tissue venom effects develop in at least 96% of pit viper victims, ranging from pain and swelling to tissue necrosis.<sup>7</sup> As a result, surgical evaluation and management is requested frequently, and in many institutions these patients are managed primarily by general, trauma, or orthopaedic surgeons. There is little consensus in the surgical literature about the indications for and extent of surgical intervention in the setting of pit viper snake envenomation. For example, a 2004 monograph from the American College of Surgeons Committee on Trauma notes this controversy, yet opines that "incision and suction of the fang marks may be beneficial if performed within 15 to 30 minutes from the time of the bite," a recommendation that is contradicted by evidence-based first-aid guidelines and the recommendations in a recent review article in this Journal.8-10

Because delays in the diagnosis and management of true muscle compartment syndrome are a major cause of preventable harm to patients and lost litigation, there is justifiable concern about timely diagnosis and treatment. Substantial variation in the management of suspected compartment syndrome after snake envenomation exists; published studies show a 5-fold variation in the proportion of patients who undergo fasciotomy, ranging from 3.4% to 13% of hospitalized patients. 11-14 Although there is little comparative literature, it is likely that compartment syndrome is more common among patients envenomated by rattlesnakes than among those envenomated by copperhead snakes. One recently published study of copperhead snake victims found no need for fasciotomy among 142 treated patients.<sup>10</sup> Limb amputations, major tissue loss, and ischemic contracture are extremely uncommon, affecting <1% of patients in published series. 10-16

Because of the variation in the extent and technique of surgical intervention and the lack of prospective comparative studies, 8,10,14,15,17-20 we sought to develop best practice guidelines for surgical interventions in the acute management of North American crotaline snake envenomation that are both evidence based and useful to the clinician.

# **METHODS**

Because of limitations in the available literature base, a formal meta-analysis could not be used for rule development. Therefore, we used a structured process to achieve evidence-informed consensus recommendations. Two authors (Dart, Lavonas) recruited panel members based on their published envenomation research and clinical experience. A panel of 4 members was chosen to provide sufficient diversity in subspecialty expertise, practice environment, and typical envenomating snake species. Background and qualifications of the panel members are summarized in Table 1.

The consensus process was managed by an independent professional facilitator. Before the in-person panel meeting, one conference call was used to define project scope and key clinical questions. Each clinical question was developed as a "foreground question" and, wherever possible, questions were structured in PICO (Patient, Intervention, Comparison, Outcome) format to improve the ability to address the question in an evidence-based fashion.<sup>21</sup> After the conference call, the facilitator completed one round of asynchronous panel deliberation, a modified Delphi technique, to work toward consensus before the panel meeting. This 1-day meeting was held in Denver, Colorado on September 7, 2012.

To provide the panel members with a complete literature base, a systematic literature search was completed to identify articles relevant to key clinical questions, using the search strategy outlined in Table 2. All citations identified from the search strategy were imported into an EndNote database (version X4). Duplicates were removed and an electronic filter was used to remove references containing the keywords mouse, rat, cellular, in vivo, or, in vitro. Two researchers (Khatri and Lavonas) reviewed the titles and abstracts of all articles to identify those that might contain original data about the issues identified in preliminary panel deliberations relevant to the study purpose. In the event of disagreement, the article was pulled and reviewed. A preliminary article list was circulated to the panel members before the conference call. After the call, panel members nominated additional articles for review. Each panel member received a summary and a full-text reproduction of each article for use during panel deliberations.

The panel defined consensus as at least 3 members voting to support a recommendation and no member expressing strong objection. One additional author (Lavonas) participated in the panel meeting but did not vote. Structured note taking and verbatim transcription were used to capture decisions and supporting reasoning accurately. Sponsor representatives were not present for the panel meeting and did not participate in the development of clinical questions, evidence evaluation, panel recommendations, or manuscript development.

**Table 1.** Background and Qualifications for Panel Members

Panel member	Background and qualifications
Dr Charles Bauer	Board certifications
	General Surgery
	Emergency Medicine
	Current positions
	Adjunct Professor of Surgery,
	Orthopedic Surgery, and
	Emergency Medicine
	Current institution
	University of Texas Health Science
	Center-San Antonio
Dr Richard Dart	Board certifications
	Emergency Medicine
	Medical Toxicology
	Current positions
	Director, Rocky Mountain Poison
	and Drug Center
	Professor of Emergency Medicine
	and Clinical Pharmacy
	Current institution
	Denver Health and Hospital
	Authority
	University of Colorado School
	of Medicine
Dr Edward Hall	Board certifications
	General Surgery
	Current positions
	General, Vascular and Non-Cardiac
	Thoracic Surgeon
	Current institution
	South Georgia Surgical Associates/
	Archbold Memorial Hospital
Dr Eric Toschlog	Board certifications
	General Surgery
	Surgical Critical Care
	Current positions
	Chief, Acute Care Surgery
	Current institution
	East Carolina University Brody
	School of Medicine/Vidant Healt
	System

Recommendations were developed using GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) methodology.<sup>22</sup> In keeping with GRADE guidelines, the quality of evidence was formally graded, then factors including importance of the outcomes that treatment prevents, magnitude, and certainty of the treatment effect, risks, and burdens of therapy, and costs were considered to generate a strong or weak recommendation.<sup>23</sup> Definitions used in GRADE evaluations are presented in Table 3. The use of GRADE methodology to formulate evidence-based treatment recommendations has been widely adopted, including by surgical specialty societies.<sup>25-29</sup>

Table 2. Search Strategy

Database	Search terms	Date of final search	Citations retrieved
PubMed (01/01/1997—04/30/2012)	Crotalid Venoms, Snake Venoms, Snake Bites, Viperidae, Agkistrodon, Crotalus (MeSH key word) or [CroFab or Crotaline immune Fab or FabAV].mp Limit: English language	7/27/2012	3,006
Ovid MEDLINE (1997—2012)	Crotalid Venoms, Snake Venoms, Snake Bites, Viperidae, Agkistrodon, Crotalus (MeSH key word) or [CroFab or Crotaline immune Fab or FabAV].mp Limit: English language	7/27/2012	2,769
EMBASE* (1997–2012)	Crotalid venoms, snake venoms, snake bites, Viperidae, Agkistrodon, Crotalus, Crotaline immune Fab, FabAV Limit: English language	7/27/2012	4,389

Medical Subject Headings (MeSH): Crotalid Venoms/po [Poisoning], Crotalid Venoms/to [Toxicity], Snake Venoms/po [Poisoning], Snake Venoms/to [Toxicity], Snake Bites/dt [Drug Therapy], Snake Bites/th [Therapy].

# **RESULTS**

The search identified 2,989 citations, 179 of which were retrieved for additional review. On full-text article review and reviewing references, 42 articles were selected by panel members for structured summaries. Only one randomized clinical trial involving the treatment of crotaline snakebite with antivenom has ever been published, and the report of this trial contained few data about surgical considerations.<sup>30</sup>

The panel identified 4 key questions highly relevant to surgeons who manage crotaline snakebite victims. These questions will be listed here. Unanimous consensus of the 4 panel members was achieved on all questions. The panel was determined to focus on issues specific to surgeons and to refer to a recently published treatment algorithm for overall management considerations.<sup>3</sup> These recommendations are specific to patients with North American *Crotalinae* envenomation; they do not apply to patients with coral snake envenomation (genera

Table 3. Definitions of Quality of Evidence

Quality of evidence	Definition
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is uncertain

(Reprinted from Guyatt et al,<sup>24</sup> with permission.)

Micrurus and Micruroides), nor to patients bitten by snakes that are not indigenous to the United States. These recommendations do not apply to out-of-hospital (eg, first aid, wilderness medicine, or low resource) settings. These recommendations are not meant to be applied to patients with mild envenomation for whom surgical intervention is historically neither requested nor performed. In this review, the term compartment syndrome is intended to include the equivalent of increased subcutaneous overpressure in the digits.

Question 1: In patients envenomated by crotaline snakes, does early excision of tissue near the bite site improve outcomes (ie, local and systemic venom effects), compared with standard care alone (including antivenom, if indicated)?

Recommendation: Excision of tissue to remove venom is not recommended because it has not been shown to improve outcomes, and can be harmful or disfiguring. (Strong recommendation based on moderate-quality evidence.)

Early removal of venom by surgical means is theoretically valuable, and this practice was once recommended and widely used. 31-36 Various authors describe surgical exploration of the wound with excision of all visibly envenomated tissue or, more simply, excision of an arbitrary margin of tissue surrounding the fang marks. These older articles, which were observational studies with no contemporaneous comparison group, provide very low-quality evidence for benefit. Patients in these studies typically did not receive antivenom and did receive interventions such as tourniquet administration and ice-water immersion, which have been shown to worsen tissue outcomes. 37,38 The outcomes of patients treated with early excision were dismal by modern standards; failed grafts

<sup>\*</sup>EMBASE: Crotalid venoms AND (intoxication OR toxicity), Snake venoms AND (intoxication OR toxicity), Snake bites AND (drug therapy OR therapy).

and flaps, osteomyelitis, and amputations, which are rarely described in modern series, were common. 32,33,35

Modern noninvasive therapy, including early antivenom administration, is generally safe and achieves better outcomes than are described in these historical articles. A recent meta-analysis found that acute hypersensitivity reactions occur in approximately 8% of patients treated with Crotalidae Polyvalent Immune Fab (ovine) (CroFab; BTG International).<sup>39</sup> These reactions are usually mild and rarely require discontinuation of antivenom treatment. Serum sickness develops in approximately 13% of patients, a rate less than half of that reported with older, equine-derived antivenom.<sup>39</sup> Antivenom administration reliably halts the progression of both local tissue and systemic effects of envenomation, although recurrence of both local tissue and hematologic venom effects can occur after initial successful treatment. 7,30,40-44 Studies conducted using equine antivenom, which is no longer available in the United States, show that, although pit viper venom initiates tissue injury cascades that cannot be fully halted by rescue therapy with antivenom, antivenom administration effectively limits the extent of necrosis in animal models. 45 A well-conducted rabbit study comparing equine antivenom alone, debridement and fasciotomy alone, or a combination found that antivenom was the most effective approach to reduce myonecrosis and preserve muscle mass and function. 46 These studies have not been repeated with ovine Fab antivenom. Although a prospective observational study collecting serial compartment pressure measurements before and after administration of ovine Fab antivenom plus mannitol was started, study results have not been published.47

It is important to note that no clinical trials have compared early excision to therapy with antivenom alone, and no trials have evaluated whether adding early excision to antivenom therapy improves outcomes. Although an observational study reported that, "wound excision after hospitalization was associated with a statistically significant decrease in overall complication rates in patients with grade II or greater envenomation," analysis of the data presented does not support that conclusion. There is strong concordance among clinical trials and observational studies showing that excellent results are usually achieved using antivenom therapy without incisions or excisions. 7,11,14,15,30,41-44,49-55

A related technique intended to remove venom from the site of injection, application of suction to the bite site, was once recommended as a first-aid technique to be applied by lay persons and other nonsurgeons, and sometimes applied in the hospital or emergency department setting. Incision over the bite site was sometimes recommended as an adjunct to suction. Neither incision nor suction is recommended as standard care by US and international organizations. <sup>9,56</sup> Good evidence shows that this practice is ineffective and poses risks to both the victim and rescuers. <sup>9,57-63</sup>

Debridement of necrotic tissue late in the clinical course is appropriate and should follow generally accepted surgical principles. No specific evidence could be found to define any situation in which wounds containing necrotic tissue from snake envenomation should be managed differently from wounds from other causes, such as localized pressure necrosis, burns, and acute or chronic vascular insufficiency. In their practice, the authors find that envenomated tissue that appears necrotic in the initial days after snake envenomation often survives, and that waiting for necrotic tissue to definitively declare itself can reduce the extent of debridement. This is concordant with an electron micrography study, which showed necrotic muscle fibers intertwined within muscle fascicles in which adjacent fibers are alive.<sup>64</sup> Similarly, no literature could be found that specifically addresses the management of snakebite puncture wounds to tendon sheaths; by default, management of these injuries should follow established surgical principles. Animal studies and rare human case reports demonstrate that viper venom metalloproteinases and phospholipases A2 cause cartilage destruction, suggesting that washout might be beneficial in cases involving venom injection into a joint. 65-67

Question 2: What is the most appropriate method of establishing or disproving the diagnosis of compartment syndrome in a victim with signs or symptoms suggestive of compartment syndrome?

Recommendation: Because snake envenomation often mimics compartment syndrome, the diagnosis of compartment syndrome should not be made based on "soft signs" (eg, firm compartments, pain out of proportion to apparent injury, pain with passive stretch) alone. Tissue pressure measurement is the preferred method to establish or disprove the diagnosis of compartment syndrome and should be performed whenever technically feasible to avoid misdiagnosis and unnecessary surgery. In anatomic locations where tissue pressure measurement cannot be performed (eg, digits), the diagnosis of compartment syndrome should be made only when clear evidence of neurologic dysfunction and/or vascular compromise are present. Clinical diligence, including serial re-examination, is often required. (Strong recommendation based on moderate-quality evidence.)

Crotaline envenomation often mimics compartment syndrome. Venom components, including histamine- and bradykinin-like factors, rapidly enter the lymphatic system. Careful animal studies have demonstrated that injection of venom into the subcutaneous space typically causes subcutaneous tissue hypertension with normal subfascial pressures.<sup>68</sup> Snake envenomation can produce pain, swelling, tenderness, induration, paresthesias, color changes (eg, bluish discoloration from bruising), and diminished pulses in the envenomated extremity, mimicking the initial signs of deep muscle compartment syndrome. However, true muscle compartment syndrome from snakebite is quite rare. A prospective observational study in patients with limb envenomations by rattlesnakes showed that most victims have greater blood flow in the envenomated limb than in the nonenvenomated limb.69 In one large case series of patients treated in a tertiary referral center with a large population of severely envenomated rattlesnake victims, only 8 of 236 (3.4%) patients were treated with a fasciotomy or digital dermotomy. 12,13 Although compartment syndrome remains a clinical diagnosis primarily, the trigger for fasciotomy and digital dermotomy must be based on something other than clinical appearance.

As with abdominal compartment syndrome, a combination of measured elevated pressures and consistent physical findings are optimal to establish the diagnosis of compartment syndrome. In contrast to the typical trauma situation, in which the index of suspicion for compartment syndrome should be high and fasciotomy performed at the first concerning signs, nearly all patients with firm, swollen limbs from snake envenomation do not have deep muscle compartment syndrome. The diagnosis of compartment syndrome requires confirmation, particularly if hard signs of neurovascular compromise are absent. Techniques for measuring compartment syndrome in the forearm and leg have been well described. 18,70-72 The threshold subfascial compartment pressure that should prompt intervention has been hotly debated; absolute tissue pressures in excess of 30 to 45 mmHg, tissue pressures within 30 mmHg of the diastolic blood pressure, and tissue pressures within 40 mmHg of the mean arterial pressure have all been proposed.<sup>72</sup>

Accurate and reliable measurement of tissue pressures in the digits and in subfascial portions of the hand and foot might not be possible; in these locations, physical examination and assessment of arterial blood flow by Doppler might be the only diagnostic tools available.

Question 3: In patients with crotaline snake envenomation to the extremities who do not have compartment syndrome, does prophylactic fasciotomy (ie, fasciotomy performed before the diagnosis of compartment syndrome is established), alone or in addition to standard therapy including antivenom, improve outcomes?

Recommendation: Prophylactic fasciotomy does not improve outcomes and should not be performed for the treatment of snakebite. (Strong recommendation based on moderate-quality evidence.)

In many centers, the practice of routinely performing fasciotomy in patients with snake envenomation and considerable limb swelling was once commonly advocated as a method of preventing compartment syndrome and avoiding the risk of allergic reaction to equine-derived, whole IgG antivenom. <sup>51</sup> Busy surgical centers that once advocated this approach have abandoned it, as the safety record of ovine Fab antivenom has become established, with attendant improvement in outcomes. <sup>11</sup>

In addition to problems with scarring and wound healing, fasciotomy can worsen muscle damage in snakebite victims. In a well-conducted porcine study, despite clear improvements in compartment pressure, envenomated limbs undergoing fasciotomy had considerably more myonecrosis than limbs not undergoing fasciotomy.<sup>73</sup> Because antivenom administration reduces limb swelling and improves elevated compartment pressures, antivenom administration is preferred over fasciotomy for patients who do not have elevated muscle compartment pressures and signs of syndrome. As with all cases in which compartment syndrome might be present or developing, clinical vigilance is essential to proper management.

Question 4: In patients with crotaline snake envenomation to the extremities for whom the diagnosis of compartment syndrome (or, in the digits, tissue overpressure syndrome) has been established, does fasciotomy, alone or in addition to standard therapy including antivenom, improve outcomes?

Recommendations: Fasciotomy is not recommended as first-line therapy in patients with snake venom—induced compartment syndrome because data from animals and humans does not establish that it improves outcomes. (Strong recommendation based on moderate-quality evidence.)

Administer antivenom to all patients with compartment syndrome because antivenom administration reduces tissue pressures and myonecrosis and can eliminate the need for fasciotomy. (Strong recommendation based on moderate-quality evidence.)

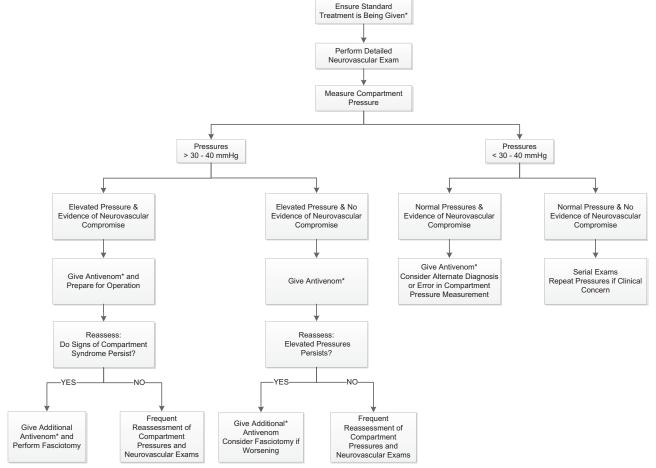
Fasciotomy is indicated for patients in whom the diagnosis of compartment syndrome is clearly established and who do not improve after appropriate doses of antivenom. (Strong recommendation based on moderate-quality evidence.)

In patients with very high tissue pressures or who have hard signs of compartment syndrome and delayed presentation, administer antivenom when preparing for fasciotomy. Although fasciotomy should not be delayed in patients at high risk of permanent injury, it is appropriate to reassess the patient before anesthesia/incision to determine whether compartment syndrome persists and fasciotomy is still required. (Weak recommendation based on low-quality evidence.)

Administration of adequate doses of antivenom reduces compartment pressure in animal experiments and human case reports and can eliminate the need for fasciotomy. <sup>11,42,63,74-77</sup> In contrast to fasciotomy, antivenom administration reduces myonecrosis in the envenomated limbs of experimental animals. <sup>73</sup> Therefore, antivenom administration is indicated in all cases of compartment syndrome,

and also for all cases involving substantial progressive limb swelling in which the clinician believes that compartment syndrome might develop. A typical dose is at least 4 to 6 vials of antivenom, repeated as necessary until the patient is stable; administration instructions are widely available.<sup>3,78</sup>

Although a recent evidence-based review concluded that, "the current evidence does not support the use of fasciotomy or dermotomy following *Crotalinae* envenomation with elevated intracompartmental pressures," it is clear that antivenom administration does not always prevent the need for fasciotomy, and delayed restoration of tissue perfusion causes harm. <sup>19,79</sup> In light of the large body of evidence supporting the use of fasciotomy in compartment syndrome caused by fractures, crush injuries, and electrical burns, it is logical that fasciotomy should be performed in cases where aggressive antivenom therapy fails to correct impaired tissue perfusion. Based on the experience of high-volume centers, these cases are uncommon, affecting <4% of both adults and children with snake envenomation. <sup>10,12,13,50,52</sup>



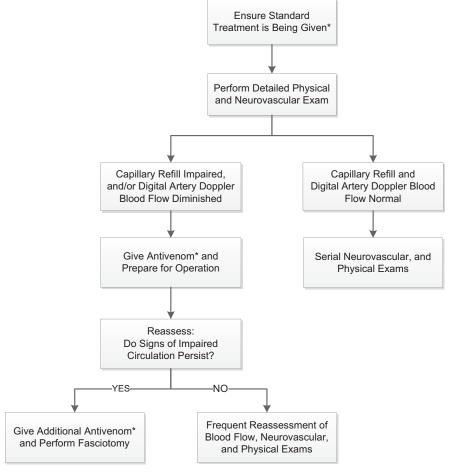
**Figure 1.** Evaluation and management of suspected extremity compartment syndrome (excluding digits). \*Standard treatment includes supportive care and antivenom as indicated. See http://www.biomedcentral.com/1471-227X/11/2.

A suggested treatment algorithm for patients with compartment syndrome is provided in Figure 1. Given the safety profile of modern Fab biologics, an adequate trial of antivenom (minimum of 4 to 6 vials, given intravenously over 1 hour) should be administered before fasciotomy is undertaken. The ideal dose of antivenom in this situation has not been studied. Although several of the authors recommend empiric administration of high antivenom doses (10 to 20 vials) to rapidly reduce compartment pressure in limb-threatening envenomations, no evidence supports this practice. Fasciotomy is sometimes required even in antivenom-treated patients.<sup>79</sup> A practical approach is to make preoperative arrangements during the antivenom infusion, particularly if tissue pressures are very high or if the patient's presentation was delayed. It is important to reassess the patient and repeat compartment pressure measurements before anesthesia to determine whether compartment syndrome still exists. The key, as with cases of traumainduced tissue injury, is clinical vigilance.

A modified treatment algorithm for patients with envenomation to body sites where accurate tissue pressure measurement is not possible, such as the digits and subfascial portions of the hand and foot, is provided in Figure 2. Digit dermotomy, if necessary, is performed under local anesthetic. A lateral incision is made through the skin of the finger and extended into a midlateral release by spreading to avoid damage to neurovascular structures.<sup>80</sup>

### DISCUSSION

The literature base for evaluating surgical interventions in crotaline snake envenomation consists primarily of wellconducted animal studies and human observational reports. Taken together, these data show a dramatic



**Figure 2.** Evaluation and management of suspected digit compartment syndrome. \*Standard treatment includes supportive care and antivenom as indicated. See http://www.biomedcentral.com/1471-227X/11/2.

improvement in outcomes achieved in moderate to severe snake envenomation cases since the widespread adoption of antivenom use. Accordingly, recent reviews show a strong consensus that mechanical removal of venom, whether by excision or incision/suction, should no longer be performed.

Compartment syndrome is a dreaded complication in acute care, trauma, and orthopaedic surgery. Delays in the diagnosis and treatment of compartment syndrome can lead to severe, permanent disability, and clinical vigilance is paramount.

Compartment syndrome caused by snake envenomation differs in 2 important ways from compartment syndrome caused by fractures, crush injury, or burns. First, unlike these other conditions, snake envenomation causes superficial edema and increased subcutaneous tissue pressure that often mimics compartment syndrome. Snake envenomated extremities are often swollen, tense, and tender, and patients report severe pain and pain with passive stretch. However, as noted previously, deep muscle compartment pressures can be normal in the face of elevated subcutaneous pressures, and envenomation typically produces increased, not decreased, limb perfusion. 68,69 To avoid unnecessary surgery, confirmation in the form of measured tissue hypertension, evidence of decreased distal perfusion, or impairment of nerve function should be present before the diagnosis of compartment syndrome is considered to be established in snakebite cases.

The second critical difference is that, unlike compartment syndrome from other causes, an effective medical therapy is available to prevent and treat compartment syndrome from snakebite. Antivenom reduces intracompartmental pressures and prevents myonecrosis in animal studies. 63,73,77,81 Antivenom administration is followed by decreased edema in most treated patients, and several case reports describe resolution of compartment syndrome after antivenom administration. 42,75,76 Because modern antivenom is safe and avoids the pain, scarring, and infection risk from fasciotomy, we advocate an aggressive antivenom-first strategy for patients with suspected compartment syndrome. Clinical vigilance is essential to this approach. Patients who fail to improve after antivenom administration and those who present for care only after compartment syndrome has been present for several hours require operative intervention to preserve the threatened limb. Clinical experience from busy centers suggests that these cases are, or should be, rare. 10-12,48,50,52

Although it is clear from these data that compartment syndrome is likely overdiagnosed and that timely antivenom administration can preclude the need for fasciotomy in most cases, the literature leaves more questions than answers. Perhaps the most important of these is whether fasciotomy, antivenom, or a combination of therapies improve functional outcomes in patients when compartment syndrome develops from pit viper envenomation. 82 Other important knowledge gaps include the dose of antivenom required to reduce compartment pressures, the role of subcutaneous vs deep compartment pressure measurements in man, the role (if any) of mannitol or hypertonic saline administration, and a cost—benefit analysis of antivenom- vs surgical-based treatment approaches.

# **CONCLUSIONS**

With the advent and widespread availability of safe antivenom, urgent surgical intervention in the form of incisions (fasciotomy) or excisions (debridement) is rarely required in the acute management of crotaline snake envenomation.

### **Author Contributions**

Study conception and design: Dart, Lavonas
Acquisition of data: Khatri, Lavonas
Analysis and interpretation of data: Toschlog, Bauer,
Hall, Dart, Khatri, Lavonas
Drafting of manuscript: Toschlog, Khatri, Lavonas
Critical revision: Toschlog, Bauer, Hall, Dart, Khatri,
Lavonas

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