American Red Cross

Scientific Advisory Council

ARC SAC SCIENTIFIC REVIEW
(Pressure Immobilization Bandaging for North American Snakebites)

Questions to be addressed:

- For adults and children with possible venomous snakebites sustained in North America (P), does the use of a pressure immobilization bandage (PIB) on the affected extremity (I) compared to no PIB or immobilization alone (C) change degree of envenomation, healing, complications, mortality(O)?
- For adults and children with possible venomous snakebites sustained in North America (P), are lay providers able to learn and retain the skill of pressure immobilization bandaging (I) in order to provide treatment within the recommended pressure ranges (C).

Introduction/Overview:

There are approximately 45,000 snake bites occurring per year in the United States (US), with about 7000-9000 bites resulting from venomous snakes per year. Death from a venomous snakebite in the US is very rare, with only 5-10 deaths per year.[1,2] Worldwide there are an estimated 100,000 deaths annually due to venomous snake bites.[3,4] Globally, first aid treatment has the potential to save many lives.

Venomous snakes come primarily from two families, *Elapidae* and *Viperidae*. Snake venoms are complex toxins that vary in composition and toxicity between and within species. In general, *Elapidae* have more neurotoxic effects and includes snakes such as coral snakes, cobras, and mambas. *Viperidae* generally have cyto- and hemotoxic venoms and include snakes such as the rattlesnakes, copperhead and other species of vipers. In the US and Canada, all snakes of the *Viperidae* family are in the subfamily of *Crotalinae*, or pit vipers. Bites from pit vipers constitute the majority of envenomations in the US, with a much smaller percentage coming from coral snakes, the only species of *Elapidae* indigenous to the US. [1,5]As there are very few deaths from venomous snakes each year in the US and Canada, the primary concern is morbidity from damage to local tissues.

While data from the 2010 International Liaison Committee on Resuscitation (ILCOR) Consensus on Science with Treatment Recommendations review demonstrated that PIB appeared to be beneficial in delaying mortality, when analysis of the available global literature was performed, it was noted that this data was not broken down by region or type of snake, and less data was available to suggest that this treatment would be beneficial to patients with venomous snake bites in the US and Canada. The current American Red Cross First Aid Manual provides information about treatment of US snake bites that includes advice to call 9-1-1 or a local emergency response number if the bite is from a venomous snake, wash the wound and apply an elastic (pressure immobilization) bandage to the bitten extremity.

Current General Recommendations for Venomous Snake Bites, Published in Red Cross First Aid Manual:

Venomous Snake Bites

Snakebites kill few people in the United States. Of the estimated 7000 people bitten annually, fewer than 5 die (Fig. 6-12, A–D). Most snakebites occur near the home, not in the wild. Rattlesnakes account for most snakebites, and most of the deaths from snakebites in the United States. Most deaths occur because the bitten person has an allergic reaction, is in poor health or because too much time passes before he or she receives medical care.

What to Look For

Signals of a possibly venomous snakebite include:

- A bite mark.
- Pain.
- Swelling.

When to Call 9-1-1

If the bite is from a venomous snake such as a rattlesnake, copperhead, cottonmouth or coral snake call 9-1-1 or the local emergency number immediately.

What to Do Until Help Arrives

To care for a venomous snake bite:

- Wash the wound.
- Apply an elastic (pressure immobilization) bandage to slow the spread of venom through the lymphatic system by following these steps:
  - Check for feeling, warmth and color of the limb and note changes in skin color and temperature.
  - Place the end of the bandage against the skin and use overlapping turns.
  - The wrap should cover a long body section, such as an arm or a calf, beginning at the point farthest from the heart. For a joint, such as the knee or ankle, use figure-eight turns to support the joint.
  - Check above and below the injury for feeling, warmth and color, especially fingers and toes, after you have applied an elastic roller bandage. By checking before and after bandaging, you may be able to tell if any tingling or numbness is from the elastic bandage or the injury.
  - Check the snugness of the bandaging—a finger should easily, but not loosely, pass under the bandage.
  - Keep the injured area still and lower than the heart. The person should walk only if absolutely necessary.
- Do not apply ice.
- Do not cut the wound.
- Do not apply suction.
- Do not apply a tourniquet.
- Do not use electric shock, such as from a car battery.

Since the 2010 ILCOR Summary of CoSTRs there have been two additional studies published with animal models that investigate the use of PIB for snake envenomation in North America. In

the context of the low mortality from US and Canadian viper bites and concern for morbidity from local tissue injury, this review reexamines both the old scientific literature and any new scientific literature in regards to the first aid use of pressure immobilization bandaging for US and Canadian snake bites and any literature addressing the ability of lay providers to perform PIB correctly. This review did not encompass snake bites sustained in the regions of Central America or the Caribbean as the epidemiology is thought to be significantly different from the incidence and mortality in US and Canada. [28] Two reviewers independently reviewed titles or abstracts to determine eligibility for inclusion and after a consensus was met, the included studies were reviewed for quality of evidence and interventions, comparison (if any), outcomes and snake species evaluated.

American Red Cross Scientific Advisory Council (Pressure Immobilization Bandaging for North American Snakebites) Scientific Review

Action Recommended
☒ **Re-affirm** ☐ **Revise** ☐ **Retire**

2020 Review Process and Literature Search of Evidence Since Last Approval Performed

Pubmed was searched with the following terms:

Search ((((("Snake Venoms/poisoning"[Mesh]) OR ("Snake Bites/mortality"[Mesh] OR "Snake Bites/therapy"[Mesh]))) AND (((((("Clinical Competence"[Mesh]) OR "First Aid"[Majr]) OR "First Aid/methods"[Majr]) OR "Emergency Treatment/methods"[Mesh]) OR "Emergency Treatment/standards"[Mesh])) AND ((((((("Bandages"[Mesh] OR "Compression Bandages"[Mesh]) OR "Constriction"[Mesh]) OR "Immobilization"[Mesh]) OR "Immobilization/methods"[Mesh]) OR "Pressure"[Mesh]) OR "Pressure"[Majr])

To additional articles were found that were determined not to fit inclusion criteria and we therefore excluded. Additional hand search of the references did not reveal any new studies that were not included in the prior Scientific Review.

First Aid and Pre-Hospital Management of Venomous Snakebites.
Parker-Cote J, Meggs WJ.
Trop Med Infect Dis. 2018 Apr 24;3(2). pii: E45. doi: 10.3390/tropicalmed3020045. Review.

Knowledge of first aid methods and attitude about snake bite among medical students: a cross sectional observational study.
Subedi N, Paudel IS, Khadka A, Shrestha U, Mallik VB, Ankur KC.
J Occup Med Toxicol. 2018 Aug 15;13:26. doi: 10.1186/s12995-018-0210-0. eCollection 2018.

2017 Search Strategy and Literature Search Performed

Answer all questions and complete PRISMA flow sheet below
Key Words Used
Treatment:
Search snake bite and AND (pressure immobilization bandage OR pressure OR compression OR immobilization OR banding)

Education:
Search ((((("Snake Venoms/poisoning"[Mesh]) OR ("Snake Bites/mortality"[Mesh] OR "Snake Bites/therapy"[Mesh]))) AND (((((("Clinical Competence"[Mesh]) OR "First Aid"[Majr]) OR "First Aid/methods"[Majr]) OR "Emergency Treatment/methods"[Mesh]) OR "Emergency Treatment/standards"[Mesh])) AND ((((((("Bandages"[Mesh] OR "Compression Bandages"[Mesh]) OR "Constriction"[Mesh]) OR "Immobilization"[Mesh]) OR "Immobilization/methods"[Mesh]) OR "Pressure"[Mesh]) OR "Pressure"[Majr])

Inclusion Criteria (time period, type of articles and journals, language, methodology)

American Red Cross Scientific Advisory Council (Pressure Immobilization Bandaging for North American Snakebites) Scientific Review

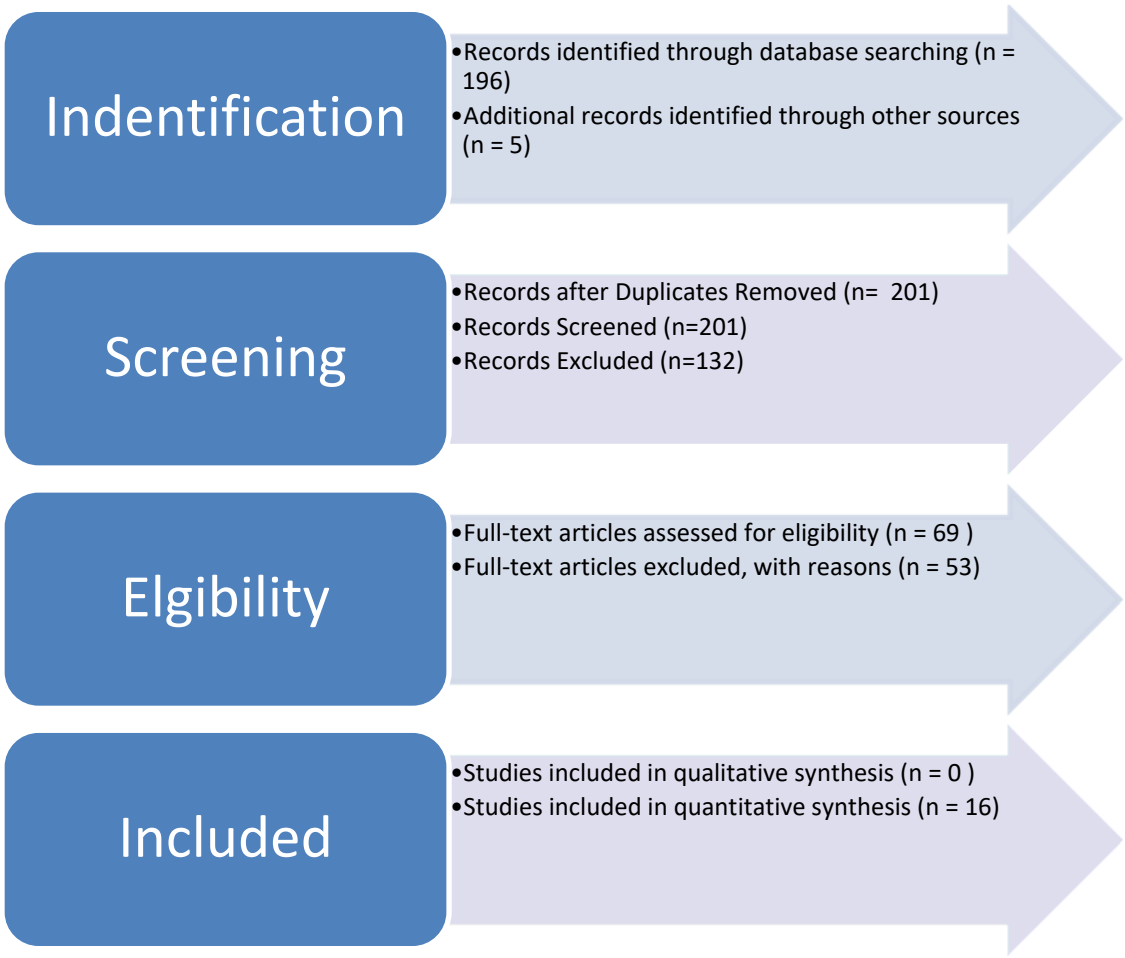
All publication dates; human and animal, all study types, systematic reviews

Exclusion Criteria (only human studies, foreign language, etc…)
English only

Databases Searched and Additional Methods Used (references of articles, texts, contact with authors, etc...)

We searched the following database: PubMed.
Additional hand searching was conducted based on review of the articles discovered in the initial search.

Treatment



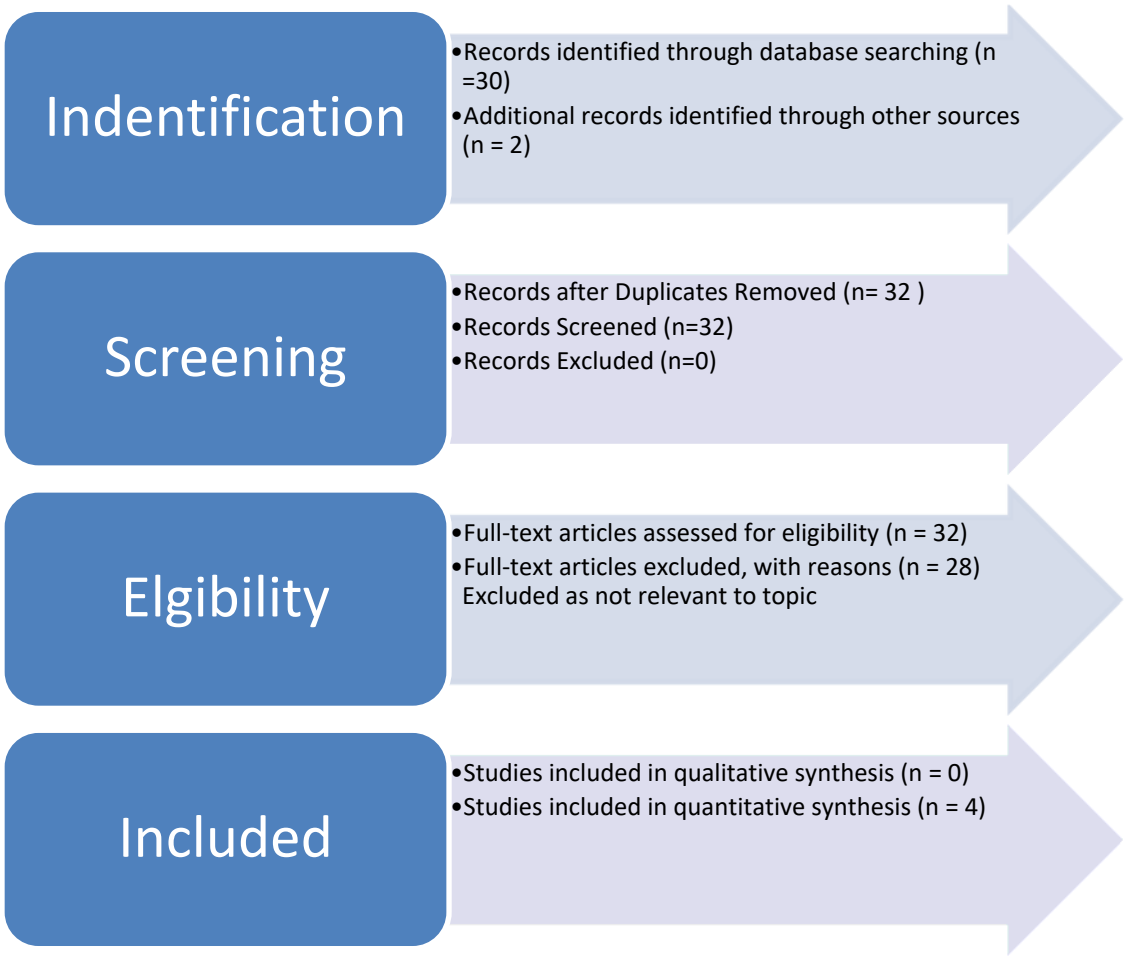
Studies included for final review for data analysis:

Title	Author(s)	Journal	Vol	Issue	Page(s)	Year
Rationalisation of first-aid measures for elapid snakebite	Sutherland SK, Coulter AR, Harris RD	Lancet	1	8109	183-5	1979
Early management of bites by the eastern diamondback rattlesnake (*Crotalus adamanteus*): studies in monkeys (*Macaca fascicularis*)	Sutherland SK, Coulter AR	Am J Trop Med Hyg	30	2	497-500	1981
A study of the major Australian snake venoms in the monkey (*Macaca fascicularis*). II. Myolytic and haematological effects of venoms.	Sutherland SK, Campbell DG, Stubbs AE	Pathology	13	4	705-715	1981

A study of the major australian snake venoms in the monkey (*Macaca fascicularis*). I. The movement of injected venom, methods which retard this movement, and the response to antivenoms.	Sutherland SK, Coulter AR, Harris RD, Lovering KE, Roberts ID	Pathology	13	1	13-27	1981
First aid for cobra (*Naja naja*) bites	Sutherland S K, Harris RD, Coulter AR, Lovering KE	Indian J Med Res	73		266-8	1981
Retarding the uptake of "mock venom" in humans: comparison of three first-aid treatments	Anker RL, Straffon WG, Loiselle DS, Anker KM	Med J Aust	1	5	212-4	1982
Snakebite. Comparison of three methods designed to delay uptake of 'mock venom'	Anker RL, Straffon WG, Loiselle DS, Anker KM	Aust Fam Physician	12	5	365-8	1983
Effects of constriction bands on rattlesnake venom absorption: A pharmacokinetic study.	Burgess JL, Dart RC, Egen NB, Mayersohn M	Ann Emerg Med	21	9	1086-93	1992
The efficacy of compression immobilization technique in retarding spread of readio-labeled russell's viper venom in rhesus monkeys and "mock venom" NaI in human vomunteers	Pe T, Thwin MM, Than MM, Myint AA, Myint K, Than T	Southeast Asian J Trop Med Public Health	25	2	349-353	1994
Lymphatic flow rates and first-aid in simulated peripheral snake or spider envenomation	Howarth DM, Southee AE Whyte IM	Med J Aust	161	12-Nov	695-700	1994
Local compression pads as a first-aid measure for victims of bites by Russell's viper (*Daboia russelii siamensis*) in Myanmar	Pe T, Myint AA, Han KE, Ha T, Swe TN	Trans R Soc Trop Med Hyg	89	3	293-5	1995

Field trial of efficacy of local compression immobilization first-aid technique in Russell's viper (*Daboia russelii siamensis*) bite patients	Pe T, Mya S, Myint AA, Aung NN , Kyu KA, Oo T	Southeast Asian J Trop Med Public Health	31	2	346-8	2000
Pressure immobilization delays mortality and increases intracompartmental pressure after artificial intramuscular rattlesnake envenomation in a porcine model	Bush SP, Green SM, Laack TA, Hayes WK, Cardwell MD, Tanen DA	Ann Emerg Med	44	6	599-604	2004
Pressure-immobilization bandages delay toxicity in a porcine model of eastern coral snake (*Micrurus fulvius fulvius*) envenomation	German BT, Hack JB, Brewer K, Meggs WJ	Ann Emerg Med	45	6	603-8	2005
Pilot studies of pressure-immobilization bandages for rattlesnake envenomations	Meggs WJ, Courtney C, O'Rourke D, Brewer KL	Clin Toxicol	48	1	61-3	2010
Long-term efficacy of pressure immobilization bandages in a porcine model of coral snake envenomation	Smyrnioudis ME, O'Rourke DP, Rosenbaum MD, Brewer KL, Meggs WJ	Am J Emerg Med	32	9	1024-6	2014

PIB Education



Title	Author(s)	Journal	Vol	Issue	Page(s)	Year
Physicians and lay people are unable to apply pressure immobilization properly in a simulated snakebite scenario	Norris RL, Ngo J, Nolan K, Hooker G	Wilderness Environ Med	16	1	16-21	2005
The Ebbinghaus retention curve: training does not increase the ability to apply pressure immobilisation in simulated snake bite--implications for snake bite first aid in the developing world	Simpson ID, Tanwar PD, Andrade C, Kochar DK, Norris RL	Trans R Soc Trop Med Hyg	102	5	451-459	2008

Effectiveness of pressure-immobilization first aid for snakebite requires further study	Currie BJ, Canale E, Isbister GK	Emerg Med Australas	20	3	267-270	2008
Investigating pressure bandaging for snakebite in a simulated setting: bandage type, training and the effect of transport	Canal E, Isbister GK, Currie BJ	Emerg Med Australas	21	3	184-190	2009

2020 Updated Scientific Foundation:

Only two studies were found with the updated literature search. The first, Meggs et al, is a review article of prior literature and did not present any new information that would change these recommendations. The second article, Subedi et al, is a cross sectional survey of students regarding their knowledge of snake bite first aid and did not provide any evidence pertaining to the clinical question. With the lack of any new data, there is no new science with which to update the original Scientific Review.

2017 Scientific Foundation:

Background

Venomous snakes in North America belong to two families: *Elapidae* and *Viperidae*. All snakes of the family *Viperidae* in the US and Canada belong to the subfamily *Crotalinae*, which are also known as pit vipers.[1] Both *Elapidae* and *Viperidae* species of snakes are found throughout the world and both families result in significant morbidity and mortality worldwide. Throughout the world it is estimated that up to 100,000 fatalities occur each year with many more bites occurring each year and resulting in significant morbidity.[3,4] In the US the majority of bites and envemomations occur secondary to *Crotalinae* species. However, only approximately 5-10 deaths occur each year in the US. [1,2] There are only two types of snakes regarded as having significant neurotoxic features in the US: Coral snake species of the genus *Micrus* and the Mohave rattlesnake (*Crotalus scutulatus*). Envenomation from these snakes could result in mortality secondary to respiratory paralysis and would be more similar to neurotoxic envenomation from other venomous snakes worldwide.

Recommendations for use of pressure immobilization bandages vary worldwide, in part due to wide variability in envenomation profiles among various species of snakes. *Elapidae* envenomation in Australia results in primarily neurotoxic symptoms, with few localized symptoms of tissue toxicity. Pressure immobilization bandaging was first used in Australia in the 1970's and has become a standard for the treatment of neurotoxic *Elapidae in Australia* (Australian Resuscitation Council Guideline 9.4.8 Aug 2011). PIB is not recommended for snakebite on the Indian Subcontinent (Indian National Snakebite Protocols 2007). In Southeast Asia it is recommended for bites by neurotoxic elapid snakes, but not for viper bites because of the possible danger of increasing the local effects of the necrotic venom. (WHO Guidelines for the Clinical Management of Snake Bite in the South-East Asia Region. Southeast Asian Journal of Tropical Medicine & Public Health, Vol 30, Supplement 1, 1999.) It is not recommended by the Wilderness Medical Society for North American crotaline envenomation (Practice Guidelines for the Treatment of Pit Viper Envenomations in the United States and Canada. WEMJ, 26, 472–487 (2015). The 2016 International First Aid and Resuscitation guidelines by the International Federation of Red Cross and Red Crescent Societies do not recommend the use of PIB due to concerns of the ability of the lay provider to properly apply the dressing and thus potentially worsening the outcome. (International first aid and resuscitation guidelines 2016, International Federation of Red Cross and Red Crescent Societies, 2016)

In 2010, pressure immobilization bandaging was reviewed by ILCOR and the treatment recommendation stated that "properly performed pressure immobilization of extremities should be considered in first aid following snake envenomation." Published American Red Cross/AHA guidelines in 2010 stated: "Initially it was theorized that slowing lymphatic flow by external pressure would only benefit victims bitten by snakes producing neurotoxic venom, but the effectiveness of pressure immobilization has also been demonstrated for bites by non-neurotoxic American snakes in an animal model." These guidelines also acknowledged: "The challenge is to find a way to teach the application of the correct snugness of the bandage because inadequate pressure is ineffective and too much pressure may cause local tissue damage. It has also been demonstrated that, once learned, retention of the skill of proper pressure and immobilization application is poor." The application of PIB to US snakes, that are regarded as having low neurotoxicity, generated controversy among multiple organizations in the Medical Toxicology specialty. [6] Among these organizations it was thought that the risk of compartment syndrome and worsening local tissue necrosis by sequestering the venom at the site would generate greater morbidity than the extremely small risk of mortality that is typical of US and Canadian snakes.

The Extent of the Problem

There are approximately 45,000 snake bites occurring per year in the US. In the US, bites from venomous snakes only occur about 7000-9000 times per year, and death from a venomous snakebite in the US is very rare, with only 5-10 deaths per year.[1,2] In the US, bites from the neurotoxic coral snake only occur approximately 70 times per year, accounting for <1% of all venomous snake bites.[20] Death from coral snakes occurs even more rarely, with far less than 1 death occurring per year.[27] The vast majority of envenomations in the US and Canada occur from vipers that are much more likely to cause local morbidity than mortality.

Traditional First Aid

While a variety or therapies have been used to treat venomous snake bites in the US, the majority of these treatments have been shown to be either non efficacious or harmful for victims of snake envenomation. Both scientific literature and expert opinion for first aid therapy for venomous snake bites in US and Canada support the use of immobilization of the bitten extremity and transport to a health care facility for definitive treatment.

RESULTS

Treatment

In **1979, Sutherland et al**[7] (LOE 4) conducted an observational **animal** trial that evaluated the use of PIB in adult monkeys (*Macaca fascicularis*). In this study, the monkey's upper and left lower extremities were restrained. Monkeys were injected with 300 mcg of tiger snake (*Notechis scutatus*), an **elapid**, venom with a 25 gauge needle at a depth of 2.5 mm over the lower third of the lateral gastrocnemius of the right leg. A variety of first aid measures were studied including PIB with a crepe bandage (i), a pressure chamber, arterial tourniquet and no treatment (c). In this study data is reported from 11 of 25 monkeys, 3 are from a control group that received no first aid treatment. In the treatment group, PIB using crepe bandages was applied to either the entire envenomed extremity or below the knee only to approximate 55mmHg and the extremity was

then splinted. PIB was performed without manometry. PIB was kept in place for 60 minutes following envenoming. A crude tiger snake venom assay and an assay for notexin, the major neurotoxin, were used to evaluate the effectiveness of various first aid techniques. Data are poorly reported and graphs of the data as it was presented in the article are copied below. This animal study presented very low quality data with additional downgrades for bias, inconsistency, indirectness and imprecision. The data appear to show that PIB delays systemic absorption of tiger snake venom. The authors concluded that the application of PIB was an excellent method of retarding the absorption of elapid venom.

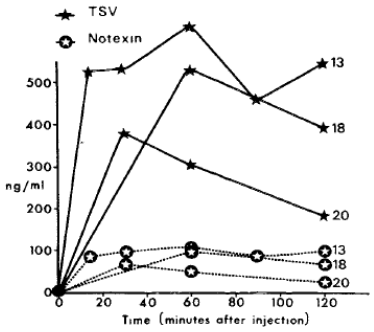


Fig. 2—Venom and neurotoxin levels in conscious monkeys (nos. 13, 18, and 20); no first-aid measures applied to envenomated limb.

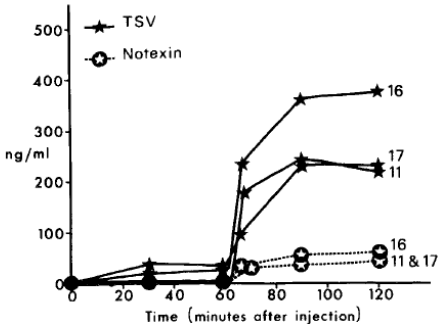


Fig. 7—Venom and neurotoxin levels in monkeys which had crepe bandage firmly applied for 60 min to the whole limb (monkeys no. 11 and 16) or below the knee only (monkey no. 17).

In **1981, Sutherland et al**[8] (LOE 4) published a small observational **animal** study in which the studied the effects of PIB on Indian cobra (*Naja naja*), an **elapid**, envenoming in two monkeys (*Macaca fasicularis*). Anaesthetized monkeys were restrained and injected with 300mg of venom into the right lower leg. One monkey was treated with PIB using a crepe bandage (i) with splinting. PIB was performed without manometry. The other monkey remained untreated (c). It does not appear that this study was blinded. The control monkey developed neurotoxic effects at 65 minutes and required antivenin at that point. The treated monkey had the PIB removed at 60 minutes and did not develop neurotoxic symptoms until approximately 40 min after removal of the PIB. No local necrosis was noted at the site of injection. Plasma venom levels were also collected during the study. No specific data is given but is plotted as shown in the figure below. No local necrosis was seen at the site of venom injection (time unknown). This animal study provided very low quality evidence with additional downgrades for bias, indirectness and imprecision. The authors of this study recommended PIB for necrotizing venom as they propose that necrosis would be limited to the bite site and not extend up the limb.

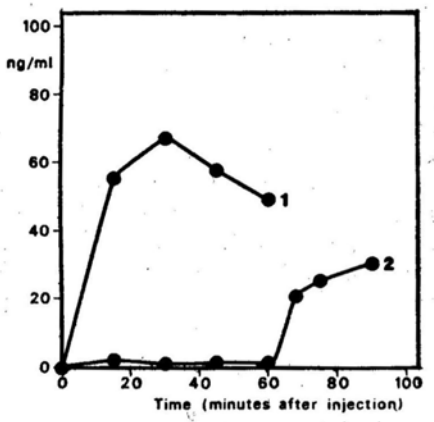


Fig. Plasma venom levels in monkeys injected with 300 μg of *Naja naja* venom. Monkey 1 had no first aid and monkey 2 had the described first aid for 60 min. Antivenom was infused at 65 and 100 min respectively, after which times venom can no longer be quantified by radioimmunoassay.

In **1981**, **Sutherland et al**[9] (LOE 4) published an observational **animal** study evaluating the effects of PIB on Eastern diamondback rattlesnake (*Crotalus adamanteus*), a **viper**, venom in monkeys. Monkeys (*Macaca fascicularis*) were restrained and unanesthetized. Four monkeys were injected into the right lower leg with four 1.5 mg injections (6mg total) of *Crotalus adamanteus* venom in close vicinity. Within 5 minutes of injection, two monkeys received PIB with a crepe bandage (i) and immobilization with a splint. PIB was performed without manometry. Two control monkeys received no first aid(c). In the treatment group PIB remained in place for 60 min in 1 monkey and 135 min in the other. Plasma levels of *C. adamanteus* venom were collected and are displayed in figure 1 (no data is given). All animals received antivenin, however, both animals in the control group still died (75 min and 250 min) whereas both animals in the treatment groups survived. Monkey 4, who had PIB applied for 120 min and antivenin was given before removal of the PIB had the lowest levels of detectable venom. Venom was not detectable in any animal after antivenin was given. Monkey 4 was described as having the most rapid recovery. In the treatment groups rapid swelling of the injected limb occurred within a few minutes of release of the PIB and within 30 minutes of removing the PIB the local color changes around the injection sites were more severe in the treatment group than in the control group (figure 2, data poorly described). This animal study provided very low quality evidence with additional downgrades for bias, indirectness and imprecision. The authors of this study concluded that this method of PIB appears promising for reducing systemic symptoms and suggested that this method would not cause harm in a non-envenomed snakebite (dry bite).

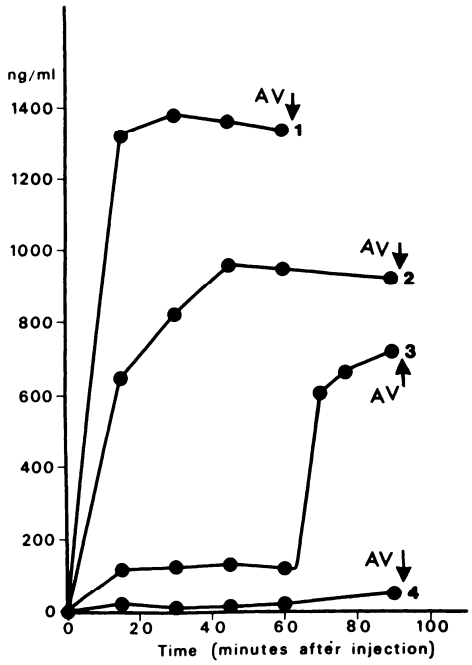


FIGURE 1. Plasma levels of *C. adamanteus* venom in monkeys injected subcutaneously with 6 mg of venom. Monkeys 1 and 2 received no first aid; monkeys 3 and 4 had the described first aid procedure (firm pressure to the injection site and immobilization of limb with a splint) for 60 and 120 min, respectively. Venom was no longer detectable by the radioimmunoassay after infusion of the antivenom (AV). Monkeys 1 and 2 died 75 and 250 min, respectively, after injection; monkeys 3 and 4 fully recovered.

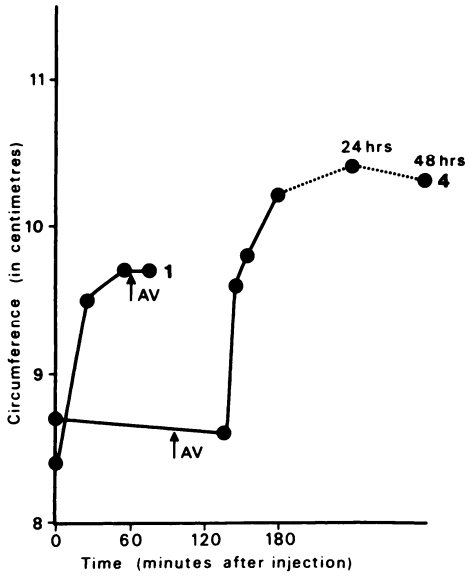


FIGURE 2. Changes in the circumference of limbs of monkeys injected with 6 mg of *C. adamanteus* venom. Monkey 1, which received no first aid, died 75 min after injection despite the infusion of antivenom (AV) at 60 min. Monkey 4 had the described first aid (firm pressure to the injection site and immobilization of limb with a splint) for 135 min but received antivenom at 90 min. At no stage did this animal exhibit systemic signs and local changes resolved very satisfactorily. (Measurements were not made on monkeys 2 and 3.)

In **1981, Sutherland et al**[10] (LOE 4) published an observational **animal** study evaluating the use of PIB (i) as a first aid measure in *Macaca facicularis* monkeys. In this study monkeys were restrained with the use of a frame; monkeys were not anesthetized. Venom was injected to a depth of 3.5 mm at the top of the lower third of the monkey's right legs. Multiple different snake venoms were used in this study, however all were from the ***Elapidae*** family of snakes. PIB was applied with a firm crepe bandage (i) over the envenomed limb and then immobilized with a splint. No manometry was used in for PIB. Control animals had no first aid applied(c). Data is variable and poorly presented; much of the raw data is not available. In tiger snake (*Notechis scutalus*) venom studies, 3 monkeys with no first aid died at an average time of 208 minutes, whereas 3 monkeys that had PIB applied for 60 min lived for 288 minutes. A monkey injected with copperhead snake (*Austrelaps superba*) venom and not treated with PIB showed muscle weakness at 97 minutes, whereas the monkey treated with PIB for 60 minutes did not develop weakness until 140 minutes. A monkey injected with beaked sea snake (*Enhydrina schistose*) venom not treated with PIB became "very symptomatic" at 50 minutes, the monkey treated with PIB for 60 minutes became "very symptomatic" at 150 minutes. Two monkeys received small-scaled snake (*Oxyuranus microlepidotus)* venom; without PIB the monkey had weakness by 90 minutes, while for the monkey who received PIB for 60 minutes, symptoms did not develop until 150 minutes. This study provided very low quality evidence with additional downgrades for bias, inconsistency, indirectness and imprecision. The authors concluded that PIB significantly delayed venom movement and suggested that this technique should be used as first aid for Australian snake bites.

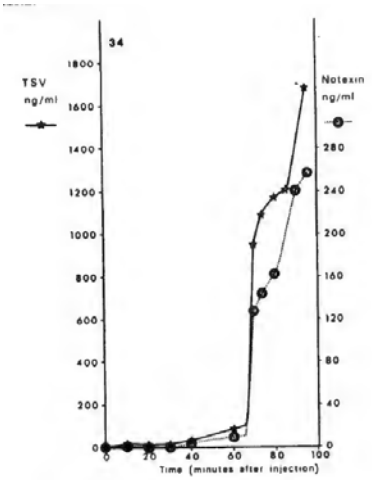


FIG. 1 Monkey No. 34 injected with 3000 μg of Tiger snake venom. Crepe bandages and splint applied to injected limb for 60 min. Plasma levels of both Tiger snake venom (TSV) and the specific neurotoxin (notexin) are shown

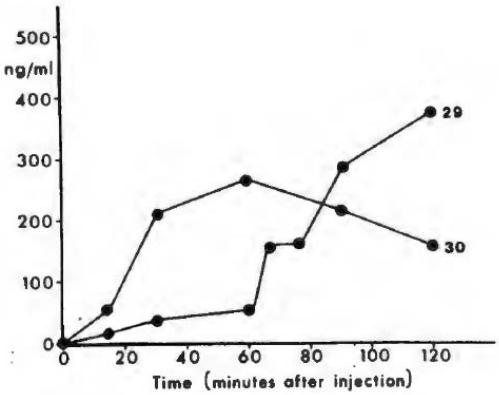


FIG. 2

FIGS 2–13 Plasma venom levels in monkeys injected with venom at time 0

FIG. 2 Monkeys Nos 29 and 30, both injected with 300 μg of Brown snake venom. Crepe bandages and splint to No. 29 for 60 min

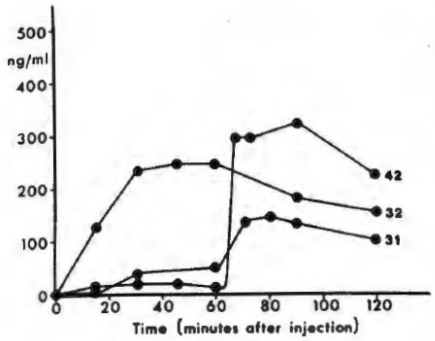


FIG. 3

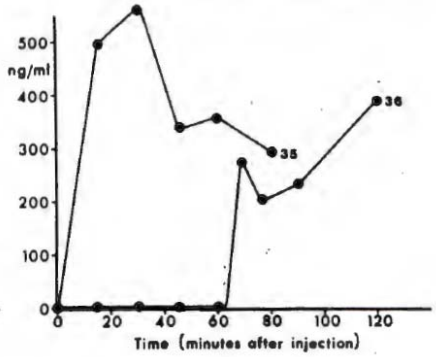


FIG. 4

FIG. 3 Monkeys Nos 31, 32 and 42, all injected with 300 μg of Taipan venom. Crepe bandages and splints applied to injected limbs of Nos 31 and 42

FIG. 4 Monkeys Nos 35 and 36, both injected with 300 μg of Death Adder venom. Crepe bandages and splints applied to injected limb of No. 36 for 60 min

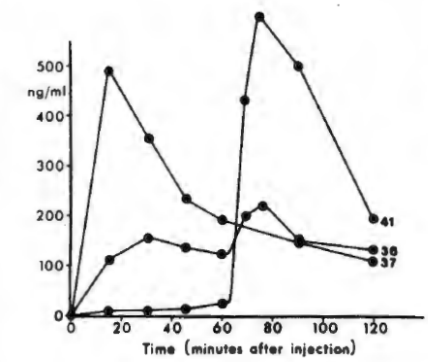


FIG. 5

FIG. 5 Monkeys Nos 37, 38 and 41, all injected with 1200 μg of King Brown snake venom. Crepe bandages and splints applied to injected limbs of Nos 38 and 41 for 60 min

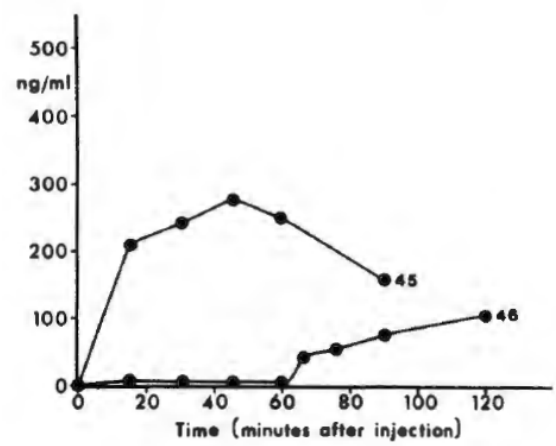


FIG. 8

FIG. 8 Monkeys Nos 45 and 46, both injected with 300 μg of Copperhead venom. Crepe bandages and splint applied to No. 46 for 60 min

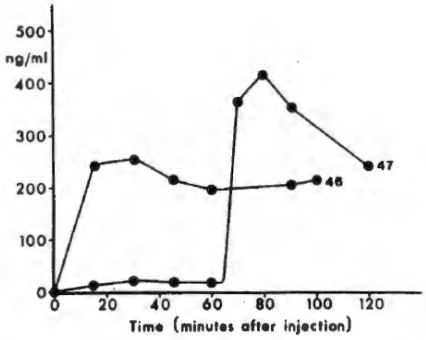


FIG. 9 Monkeys Nos 47 and 48, both injected with 1200 μg of Red-Bellied Black snake venom. Crepe bandages and splint applied to No. 47 for 60 min

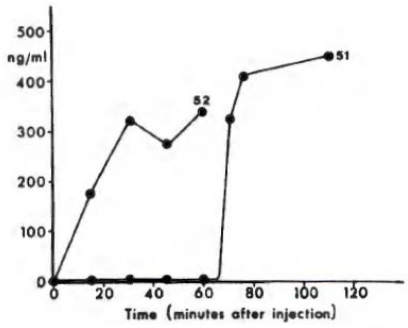


FIG. 12 Monkeys Nos 51 and 52, both injected with 300 μg Beaked Sea snake venom. Crepe bandages and splint applied to No. 51 for 60 min

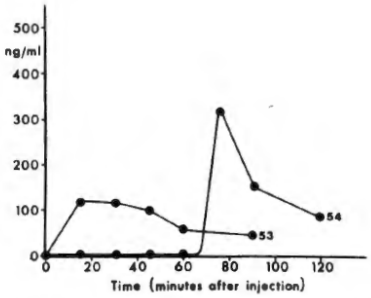


FIG. 13 Monkeys Nos 53 and 54, both injected with 300 μg of Small-Scaled or Fierce snake venom. Crepe bandages and splint applied to No. 54 for 60 min

In **1981, Sutherland et al**[11] (LOE 4) published hematologic results from an observational **animal** study of what appears to be the same population of monkey of the earlier 1981 study. To review, this was an observational study evaluating the use of PIB as a first aid measure in *Macaca facicularis* monkeys. In this study monkeys were restrained with the use of a frame, monkey were not anesthetized. Venom was injected to a depth of 3.5 mm at the top of the lower

third of the monkey's right legs. Multiple different snake venoms were used in this study, however, all were from the ***Elapidae*** family of snakes. A firm crepe bandage (i) was applied over the envenomed limb and then immobilized with a splint. No manometry was used in crepe application. The control group receive no first aid (c). Data is variable and poorly presented; much of the raw data is not available. Descriptive statements made by the authors include that the rise in CK when PIB was applied was usually less marked than when no first aid was used and PIB was found to invariably delay the development of coagulopathy. However, no statistical comparison was made. The authors did include specific data on CK elevation for one snake species which is recorded in the table below. In 3 monkeys injected with taipan (*Oxyuranus scuttellatus*) venom the control group (unknown n value) had a PTT of 61 seconds at 120 minutes. When PIB was used for 60 minutes the PTT was only 37 seconds at 120 minutes (unknown n value; distribution was not recorded). This animal study provided very low quality evidence with additional downgrades for bias, inconsistency, indirectness and imprecision.

TABLE 2 Elevation of Plasma Creatine Kinase (IU/l) in two monkeys injected with 300 μg of Beaked Sea snake venom

Time after injection (min)	0	15	30	45	75	120	180
No first aid	346	1074	1793	1892		3376	>4000
First aid for 60 min	152	277	297	511	711	1367	1249

In **1982, Anker et al**[12] (LOE 4) designed a controlled trial to test three different methods of first aid pressure application on **mock venom** in 12 adult human subjects. It is unclear if the researchers randomized the subjects or if it was blinded (although due to the nature of the study this is unlikely). Radioactive sodium iodide ($Na^{131}I$) was administered "immediately beneath the skin," 10 cm distal to the head of the fibula on the lateral aspect of the leg. Patients were either treated with PIB (i) (n=3), a full length lower extremity pneumatic splint (n=3), a pressure immobilization pad (n=3) or control receiving no first aid treatment (c) (n=3). For the PIB method (i), an elastic or crepe roller bandage was applied at the site of the injection and wrapped proximally. It is not clear which patients received what type of bandage. A pediatric sphygmomanometer was placed between the dressing and bandage and the bandage was applied to this region until 55 mmHg pressure registered on the attached mercury manometer. A padded straight wooden splint was applied to the medial side of the lower limb. In three subjects a lower-limb pneumatic splint made of rubberized cloth was inflated and pressure maintained at 55 mmHg. In three subjects a 8 cm x 8 cm x 3 cm firm cloth pad was placed over the injection site and was held in place by two broad bandage firmly bound around the leg. Pressure was evaluated by placement of a pediatric sphygmomanometer cuff, interposed between dressing and pad and connected to a mercury manometer. The limb was elevated. The pressure attained in each for the three subjects was 70, 90, and 120 mmHg, respectively. Endpoint in the study was time to 80% maximum blood counts in minutes. Despite the first-aid treatments administered by PIB and pneumatic splint the radioactivity level in the blood of subjects rose nearly as rapidly as it did in the untreated subject: control: median (IQR) 27 minutes (7), pneumatic splint: median (IQR) 22 minutes (15), PIB: median (IQR) 21 minutes (33). Mean difference between PIB (i) and control (c) was 0 minutes (95% CI -28.01 – 28.01). In contrast, blood radioactivity for subjects treated with the pressure pad remained at background level until the first-aid treatment was discontinued (approximately 60 minutes); only then did the characteristic rise appear:

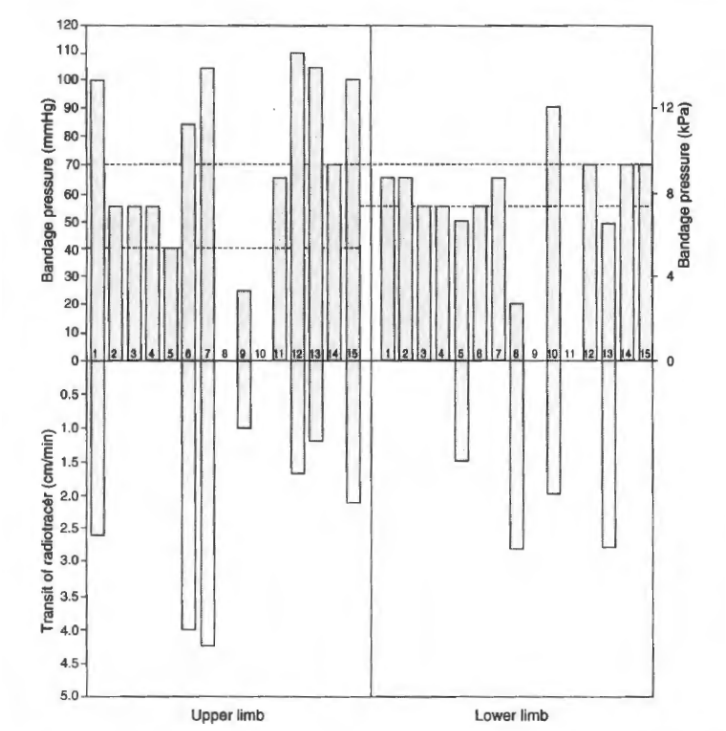
median (IQR) 76 minutes (7). There were no comments made regarding pain or adverse effects. This study provided low quality evidence downgraded for bias, indirectness and imprecision. The authors concluded that the pressure pad (Monash method) is superior to either pneumatic splint or PIB for delaying uptake of mock venom.

In **1983, Anker et al**[13] (LOE 4) published a controlled trial investigating the use of three different first aid techniques on the uptake **of mock venom** in human subjects. Twelve adult subjects were injected with radioactive (^{125}I) insulin in a manner similar to the 1982 Anker study. It is unclear if the researchers randomized the subjects or if it was blinded (although due to the nature of the study this is unlikely). Radioactive insulin was administered "immediately beneath the skin," 10 cm distal to the head of the fibula on the lateral aspect of the leg. Patients were either treated with PIB (i) (n=3), a full length lower extremity pneumatic splint (n=3), a pressure immobilization pad (n=3) or control receiving no first aid (c) (n=3). For the PIB method (i), an elastic roller bandage was applied at the site of the injection and wrapped proximally. Similar to the prior study, it appears that a pediatric sphygmomanometer was placed between the dressing and bandage and the bandage was applied to this region until 55 mmHg pressure registered on the attached mercury manometer. A padded straight wooden splint was applied to the medial side of the lower limb. In three subjects a lower-limb pneumatic splint made of rubberized cloth was inflated and pressure maintained at 50, 55 and 60 mmHg for each subject, respectively. In three subjects a 8 cm x 8 cm x 3 cm firm cloth pad was placed over the injection site and was held in place by two broad bandage firmly bound around the leg. Pressure was evaluated by placement of a pediatric sphygmomanometer cuff, interposed between dressing and pad and connected to a mercury manometer. The limb was elevated. The pressure attained in each for the three subjects was 80, 90, and 100 mmHg, respectively. Outcomes included the percent of maximum radioactivity in blood by 60 min and the percent of maximum radioactivity in blood at release of treatment. Percent of maximum radioactivity in blood by 60 min for control, pneumatic splint, PIB and pressure pad were [median(IQR)] 37% (28), 34% (4), 41% (9), and 4.5% (6.5), respectively. Mean difference between PIB (i) and control (c) was -5.6% (95% CI -32.6 – 21.4). The percent of maximum radioactivity in the blood at release of treatment was as follows [median(IQR)]: pneumatic splint 67% (5), PIB 61% (26), pressure pad 11% (14). No comments on pain or adverse effects. This study provided very low quality evidence and was downgraded for bias, inconsistency, indirectness and imprecision. The authors concluded that pressure pad is superior to either pneumatic splint or PIB for delaying uptake of mock venom.

In **1992, Burgess et al**[14] (LOE 4) published an observational **animal** study to evaluate the use of a constriction band in pigs. Five pigs were used in this crossover trail. A 6-day interval was observed between trials and each animal severe as its own control. Half the animals started in the treatment group and half started in the control group. Testing for venom concentrations at 6 days revealed negligible levels. ^{125}I labeled Western Diamondback rattlesnake (*Crotalus atrox*), a **viper**, venom was injected in anesthetized pigs with a 22 gauge needle 7mm deep at the center of the footpad 2 cm distal to the metatarsophalangeal joint. A pediatric sphygmomanometer was applied proximal to the metatarsophalangeal joint and inflated to 45 mmHg to serve as a pressure band. The cuff was kept inflated for 4 hours and then removed. The pig was kept immobile for 5 hours after injection with sedation and then was placed back into its cage and allowed to ambulate *ad libitum*. Serial circumferential limb measurements and serial blood draws were performed. A cross over was done 6 days after the initial injection. Total venom absorption for

the initial four hour period, measured by area under the curve of mean plasma venom concentration (counts/min/mL), was 33% less for the constriction band than the control group ($p<0.05$). Maximum plasma venom concentration was also decreased during this four hour period by 25% ($p<0.05$). Total venom absorption during the 96 hour monitoring period did not differ between groups. There was no statistically significant difference in leg circumference between the groups over the 96 hours of measurements. All animals walked without difficulty by 96 hours. This animal study provided very low quality evidence with additional downgrades for bias, indirectness and imprecision. The authors concluded that the application of a constriction band reduced the rate of systemic absorption and the peak venom concentration during a four hour monitoring period in pigs.

In **1994, Howarth et al**[15] (LOE 4) published a controlled trial evaluating PIB (i) on lymphatic flow rates in a **human model** of simulated envenomation. It is unclear if any form of randomization occurred; it does not appear to have been blinded. 15 healthy subjects were injected subcutaneously at approximately 3 mm depth with radioactive technetium antimony sulfur colloid in the lateral dorsal aspect of both wrists and the lateral aspect of both legs just above the ankle. However, 2 of these subjects had only upper extremities bandaged and 2 subjects had only lower extremities bandaged. Within 30 seconds of the injection 15 subjects had one lower and one upper extremity bandaged with a crepe bandage (i) with an approximate pressure of 50-70 mm Hg. Pressure was measured with a sphygomomanometer cuff bladder under the bandage. The bandaged limbs were then immobilized. The opposite unbandaged extremity served as a control (c). Radioactivity transit times were determined by a gamma camera. For control extremities (c), mean transit time from the foot to inguinal lymph node was 47 minutes (+/-27 min) and from the wrist to the axillary lymph node was 22 minutes (+/- 5 min). Mean transit rate from the ankle to the inguinal lymph node was 3.4 (+/0.7) cm/min and from the wrist to the axillary lymph node 1.9 (+/-0.4) cm/min. PIB completely prevented transit to the inguinal lymph node in 9/13 subjects and completely prevented transit to the axillary lymph nodes in 6/13 subjects. Exercise (walking) greatly increased transit times of the tracer. In this study there was the suggestion that bandages applied below the lower limit (40 mmHg for the UE and 55 mmHG for the LE) did not prevent lymphatic flow. Pressures above 70 mmHg also seemed to fail to prevent lymphatic flow. Some subjects reported numbness and paresthesias in the fingers and toes, in addition, cyanosis was observed by the researchers some subjects. This study provided very low quality evidence downgraded for bias, inconsistency, indirectness and imprecision. The authors concluded that proper PIB is effective for limiting lymphatic flow but only works at rest.



Pressure bandage thresholds in upper and lower limbs. Dashed lines represent the effective bandage pressure range to prevent lymphatic transit.

In **1994, Pe et al**[16] (LOE 3b) published an observational study evaluating the use of pressure pads (Monash method) in retarding flow of radioactive **mock venom** in humans and radioactive Russell's **viper** (*Daboia russelli siamensis*) venom in monkeys. In the animal studies, three monkeys (*Macaca mulata*) were restrained and injected subcutaneously (5mm deep) 4 cm proximal to the lateral malleolus of the right hind limb with radioactive ^{125}I Russell's viper venom. A rubberized pad 55 x 28 x 16 mm was applied over the injection site and secured with hand-tight cotton bandage and the limb was immobilized with a bamboo splint. No manometry was used to measure pressures. This study was not blinded. The duration of treatment time for the monkeys was 52, 51 and 44 minutes, respectively. Time to 80% maximum blood counts of radioactivity as measured by as Autogamma spectrophotometer was 70 min, 53.6 minutes and 65.6 minutes, respectively. The authors concluded that the "slow leak" of radioactivity into the blood in 2 monkeys was the result of leg muscular contraction, but that overall the technique was effective in preventing the spread of venom.

In the human studies, 22 healthy male volunteers (14 treatment; 8 control) were injected with Na ^{131}I subcutaneously 10 cm proximal to the lateral malleolus (5mm deep) or 10 cm distal to the head of the fibula (15 mm deep). A firm rubber pad measuring 60 x 50 x 17 mm was secured with a cotton bandage (25 mm x 2.5 m) applied immediately over the site of the injection. The limb was immobilized with a bamboo splints. There does not appear to be any randomization or blinding for this part of the study The time to 80% of the maximum blood counts of radioactivity in the control groups averaged 40 minutes for those injected 10 cm proximal to the lateral malleolus and averaged 43.8 minutes for those injected 10 cm distal to the head of the fibula. Time to reaching 80% of the maximum blood counts of radioactivity in the 14 pad treated

patients was at or after discontinuation of treatment. This averaged 66.9 minutes in those injected 10 cm proximal to the lateral malleolus and 62.5 minutes in those patients injected 10 cm distal to the head of the fibula. Mean difference in pressure pad versus control was 26.9 minutes (95% CI 12.0 – 41.8) and 18.7 minutes (95% CI 6.25 – 31.15) for injections 10 cm proximal to the lateral malleolus and for those injected 10 cm distal to the head of the fibula, respectively. In this study no manometry was used, however, to test the amount of pressure applied by the band, ten volunteers were separately asked to apply a rubber pad and bandage the leg over the top of an adult sphygmomanometer. Pressure resulted from each wrap of the hand-tight bandage was found to be approximately 60 +/- 10 mm Hg. The authors reported side effects of the human subjects included paresthesias starting at 30 minutes. Overall this study provided very low quality evidence downgraded for bias, inconsistency, indirectness and imprecision. The authors concluded that the pressure pad technique was effecting in preventing the spread of mock venom and concluded that the leakage of radioactivity present in 2 of the 14 in the treatment groups resulted from insufficient pressure being applied on the pad.

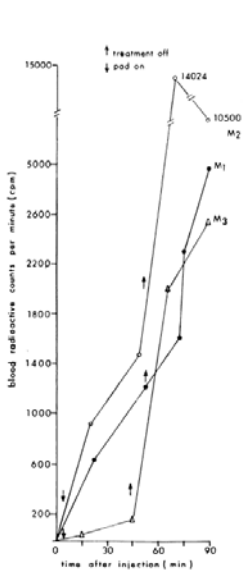


Fig 2—Trend of appearance of radioactivity in the blood of monkeys injected with a dose of I^{131} RVV, 10 μCi containing 0.1 μg venom and 0.5% BSA, subcutaneously.

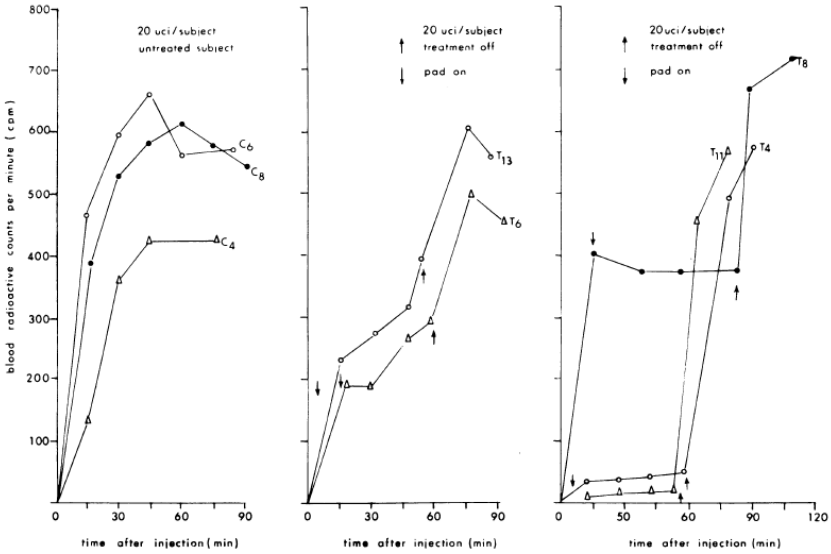


Fig 3—Trend of appearance of radioactivity in the blood of untreated controls and pad-treated human volunteers injected with a dose of "mock venom" NaI^{131}, subcutaneously.

In **1995, Pe et al**[17] (LOE 3b) published and observational trial that studied the effect of a pressure pad with immobilization in 40 patients with suspected Russell's **viper** bite (*Daboia russelii siamensis*) who were being kept under observation in the hospital for mild signs of envenomation (still had clottable blood). Each patient was kept supine in bed and a rubber pad (65 x 65 x 25 mm) was applied over the site of the bite and secured with a cotton bandage (65 mm x 1.6 m) with hand tightness. If the bites occurred on the fingers or toes a smaller rubber pad, appropriate for the size of the appendage was used. The affected limb was immobilized. There were no controls present and there appears to be no blinding. Blood samples were collected during the treatment, which in most cases occurred for 1 hour, but one was extended to two hours to study extended efficacy and side effects. Serum venom antigen levels were measured and were detected in 23 of 40 patients (17 patients, therefore, were presumed to have a bite with no envenomation). One patient was excluded due to insufficient data. 15 of 22 subjects had an increases in antigen levels once the pad was removed (range 10-40 ng/mL). In 7 patients

venom antigen disappeared during the course of pad treatment and were presumed to have minimal envenomation and were excluded from further analysis. 13/15 patients had arrest of the venom movement during pad treatment. 2/15 had continued increases in venom antigen detected in the blood while the pad was placed. Side effects were tolerated by all but 2 patients, which removed the pad early due to increased pain. A small hematoma (approximately 2x2 mm) occurred in 3/15 cases bit on a digit. The extent of bruising increased in 1/22 patients and it was noted that local necrosis occurred in 1/22 patients. Data is poorly presented and is depicted in the figure below. This study provided very low quality data downgraded for bias, indirectness and imprecision. The authors conclude that pressure pad immobilization is efficacious in arresting the progression of venom spread in victims of Russell's viper envenomation.

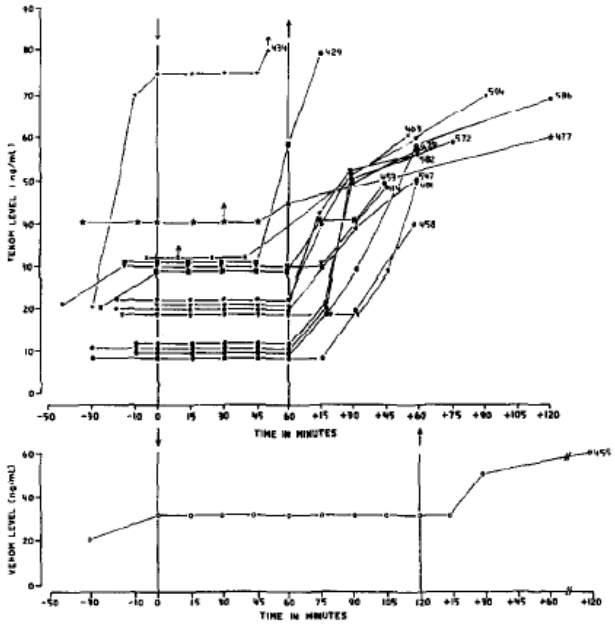


Fig.2. Venom levels in the 15 pad-treated Russell's viper bite cases treated with compression pads; ↓ pad placed on; ↑ pad removed.

In **2000, Pe et al**[18] (LOE 3b) conducted an observational field trial of the efficacy of pressure pad immobilization on victims of Russell's **viper** (*Daboia russelii siamensis*) bites. In this study 800 pads with instructions were distributed to 40 villages in the Taungdwingyi township of Myanmar. Victims were instructed to apply the pad as soon as possible after the bite, immobilize the limb with a splint and go to the nearest health facility. The study took place from 1995-1996. Blood samples were collected for antigen testing. Data is very poorly recorded. 42 patients attempted to apply the pressure pad, this took an average of 1 hour and 12 minutes to obtain and apply, and these patients had to travel an average of 16 km to obtain the pressure pad. Twenty-six patients were available for analysis and only 19 patients appeared to be envenomed by evidence of antigen testing. In 10 patients whose antigen levels were measured before pad release and after pad release showed an antigen rise of 5 ng/mL to 30 ng/mL. Of 9 patients with antigen levels measured only with the pad in place venom antigen levels remained stable. However, of those with pad immobilization and antigen test, 16/19 had systemic symptoms, suggesting that the pad in the manner applied, was not effective in preventing systemic symptoms. The incidence of local necrosis was reported at 8%, however, this was consistent with

historic levels of local necrosis in the area (10%). Only 3 patients properly immobilized the bitten limb, even in spite of pad application. Authors report that localized pain was twice as common in pad treated cases, but no cases demanded removal of the pad. This study provided very low quality evidence downgraded for bias, indirectness and imprecision. Authors conclude that this report adds further data that a pressure pad retards the spread of venom from the bite site, note that the majority of snake bite victims fail to properly immobilized the effected limb, and that better education and access is needed for PIB.

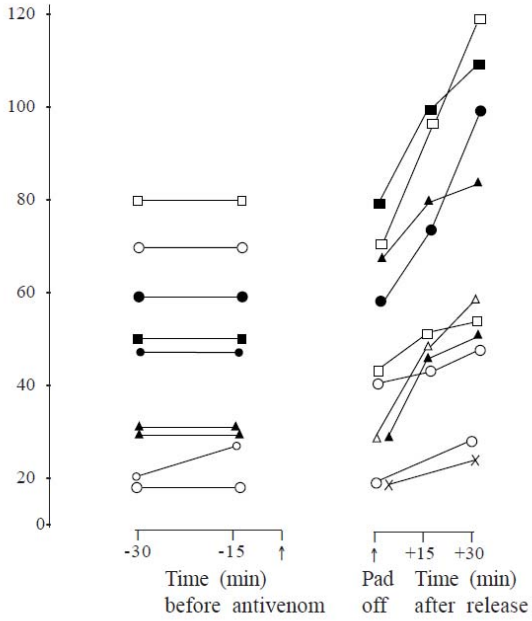


Fig 2–Venom levels of cases with the pad in place, before and after release of the pad.

In **2004, Bush et al**[19] (LOE 4) performed a randomized controlled un-blinded **animal** trial studying the efficacy of PIB (i) on a porcine model of viper envenoming. Western Diamondback rattlesnake (*Crotalus atrox*), a **viper**, venom was injected intramuscularly in 20 anesthetized pigs and PIB (i) was applied within 1 minute in the treatment group and no PIB (c) in the control group. PIB was performed without manometry with an elastic bandage and splinted. The 20mg/kg dose of venom resulted in 100% mortality. One pig in the control group died immediately after injection leaving 19 pigs available for analysis (10 treatment; 9 control). The median survival was 191 minutes (range 140 to 240 minutes) in the PIB (i) group and 155 minutes (range 119 to 187 minutes) in the control group (c). The effect size was 36 minutes (95% CI: 2 - 64 minutes; P=.0122). The mean intracompartmental pressure in the pressure immobilization group was 67±13 mm Hg (mean±SD) with PIB (i) and 24±5 mm Hg without pressure immobilization (c) (effect size: 43 mm Hg, 95% CI 32 to 53 mm Hg). There was no non-envenomed PIB control group in which to compare compartmental pressures. The mean leg circumference was 14.3±0.8 cm with pressure immobilization and 19.1±1.0 without pressure immobilization (effect size: –4.8cm, 95%CI: –5.7 to –3.9 cm). This animal study provided very low quality evidence with additional downgrades for bias, indirectness and imprecision. The

authors of the study concluded that PIB had a statistically and clinically significant survival time but expressed great concern about the increase in intracompartmental pressures in the PIB group and, therefore, did not recommend PIB for routine use in viper envenomation.

In **2005, German et al**[20] (LOE 4) published a randomized controlled **animal** study evaluating the use of PIB for Eastern coral snake, an **elapid**, envenomation. Twelve anesthetized swine received 10 mg of coral snake (*Micrurus fulvius fulvius*) venom subcutaneously (3mm using a 27 gauge needle) in the left distal foreleg. The dose was approximately 1 mg/kg and reliably produced fatal respiratory failure within 200 minutes. Pigs were then randomized to either no treatment (c) (n=6) or PIB (i) (n=6) 1 minute after injection. Investigators were not blinded. PIB was performed without manometry with an elastic bandage starting at the site of the bite, wrapped proximally and splinted. Two pigs, 1 from each group, developed fulminant sanguinous bronchorrhea and were excluded from the analysis. The endpoint was onset of respiratory distress or survival to 8 hours (both followed by euthanasia). 4/5 subjects in the PIB group and 0/5 in the control group survived to 8 hours, (P=.0036). Mean time to death in the PIB group (i) was 450 minutes (95% CI 366.71 - 533.29 minutes; median 480 minutes; IQR 37.5) and 182 minutes (95% CI 148.35 - 236.45 minutes; median 182 minutes; IQR 70) in the control group (c). For the difference of the mean time to death, the 95% CI was 179.34 to 335.86 minutes. The one animal in the treatment group who did not survive the 8-hour observation period of investigation developed respiratory difficulty at 310 minutes. All animals were subject to necropsy by a veterinary pathologist. Histologic examination revealed no evidence of pressure or ischemic-induced injury at any of the envenomation sites. Minor localized hemorrhage was observed in all envenomation sites, possibly because of venom effects. This animal study provided very low quality evidence with additional downgrades for bias, indirectness and imprecision. Based on the results of these studies the authors proposed that PIB be considered in the management of coral snake envenomation until definitive care is available.

In **2010, Meggs et al**[21] (LOE 4) conducted an observational **animal** trial to study the effects of PIB in a porcine model of Western Diamondback rattlesnake (*Crotalus atrox*), a **viper**, envenomation. This study was unblinded. Six anesthetized pigs were injected with 200 mg of *C. atrox* venom subcutaneously in a distal hind leg. One minute after injection, pigs received either no treatment (c) (n = 3) or PIB (i) (n = 3) using an elastic wrap, beginning at the site of the bite and wrapping proximally, and splint by a single researcher. It is unclear if randomization occurred. PIB was performed without manometry. All subjects surviving to 24 h received 10 vials of antivenin and bandages were then removed immediately after the administration of antivenin. The surviving subjects were followed for 1 week for evaluation of recovery from local toxicity. Control group (c) pigs died at 13.68 ± 3.42 h, whereas all PIB (i) treated pigs survived to 24 h ($p = 0.014$). Potassium was 17.767 ± 5.218 mEq/L in the control group (c) and normal at 24 h in treated (i) animals. One pig in the treatment group died 25 min after PIB was removed. Serum potassium level before removal was 3.6 mEq/L and 10.7 mEq/L at the time of death. For pigs who survived the 7-day trial other laboratory tests were normal. In the control group, postmortem examination revealed widespread hemorrhagic necrosis of subcutaneous tissue and inguinal lymph nodes but gross examination of muscle did not reveal obvious necrosis. In the PIB treated pigs, gross necrosis was highly localized and pigs who survived the 7-day study period regained use of the extremity. This study provided very low quality evidence with additional downgrades for bias, indirectness and imprecision. The authors concluded that PIB

bandages prevented fatality at 24 h and did not recommend the routine use of PIB, but suggested that consideration of the use of PIB in severe envenoming with a long time period to definitive treatment is reasonable.

In **2014 Smyrnioudis et al**[22] (LOE 4) published an observational study on the effects of PIB on Eastern coral snake (*Micrurus fulvius fulvius*), an **elapid**, envenomation using an **animal** model. The study was not blinded. Ten anesthetized pigs were injected subcutaneously with a 27-gauge needle at a depth of 3mm in the left distal foreleg with 10 mg of lyophilized *M. fulvius fulvius* venom. Pigs were then randomized to either no treatment (c) or a PIB (i) using an elastic wrap, beginning at the site of the bite and wrapping proximally and having a circumferential fiberglass cast applied approximately 1 minute after envenomation. PIB was performed without manometry. The pigs were monitored every 15 minutes for approximately 5 hours for signs of distress and then anesthesia was discontinued and pigs were allowed to ambulate *ad libitum*. For signs of distress pigs were euthanized and time to death was recorded. Surviving pigs were monitored daily until the end point of 21 days. Bandages and splints were evaluated for correct placement and excessive compression daily throughout course of study and adjusted if needed. Pigs receiving PIB (i) were more likely to survive to the 24-hour period than pigs in the control group (c) (3/5 (60%) vs 0/5 (0%); P = .08). Two pigs in the PIB group survived to 21 days. Of those that died in the PIB group, the median time to death was 1172 minutes versus 307 minutes in the control group (P = .10). The pigs in the PIB group that survived to the end point showed necrosis of the injected distal lower extremity and had nearly autoamputated limbs at time of death, however necropsy reveals no other findings except for those on the envenomated extremity. This study provided very low quality evidence, with additional downgrades for bias, indirectness and imprecision. The authors conclude that long term survival is possible with PIB treatment for Eastern coral snake bites, but there is insufficient data at this time to recommend the long term use of PIB for Eastern coral snake bites.

PIB Education

In **2005, Norris et al**[23] (LOE 3b) published an observational study evaluating the ability of medical personnel and lay volunteers to properly apply PIB following standard printed instructions. Subjects were given written instructions with illustrations on how to apply PIB as published by Sutherland. Subjects were not informed of the purpose of the study. Subjects were asked to apply the PIB five separate times. The simulated bite was on their non-dominant arm, dominant arm, their dominant leg, an investigators arm and investigators leg. A pressure measuring device was placed at the site of a simulated snake bite. In this study all subjects immobilized with a splint or sling. A single observer graded the application of each application on 4 different variables defined *a priori*. The 40 subjects performed 200 PIB applications. PIB was done completely correctly only 18 times (13/100 medical personnel, 5/100 lay volunteers). The main variable resulting in failure was inability to apply the bandages within the appropriate pressure range (correct applications: 17/100 medical personnel, 14/100 lay volunteers). This study provided low quality evidence downgraded for bias and imprecision. The authors concluded that subjects have difficulty applying PIB in a simulated setting and suggested that either a new method of teaching or automated methods of PIB be adopted to improve application.

In **2008, Simpson et al**[24] (LOE 2a) conducted a randomized trial evaluating the effect of training on the ability to correctly apply PIB and retain the skill over time. In this study 40 volunteers were selected from individuals who were visiting a health care facility. Group 1 (c) received only written instructions whereas group 2 (i) received more focused training involving 4 hours of training on the proper application technique, this included hands on training. Group 1 participants were randomized to PIB application using crepe bandages or turban cloth and to application to either the upper or lower extremity. Group 2 subjects (i) were further divided into two subgroups' that used either crepe bandages to apply PIB or turban cloth to apply PIB. A research assistant was used as the standardized simulation patient and PIB was applied over a pressure transducer to monitor applied pressures. Participants were blinded to the pressure readings only one researcher collected the pressure recording which otherwise remained blinded until the end of the study. Successful application was defined as application within a pressure range of 55-70 mmHg. The control group only performed one application of PIB. In group 2, following successful training (defined as successful application of PIB three times in succession after the 4 hour training session) retention training was conducted at 1 hour, 1 day, 3 days and 3 months. In comparing initial (1 hour) applications, 12/20 in the experimental group (i) and 0/20 in the control groups (c) ($p<0.001$) applied PIB successfully. Ability to successfully apply PIB in the experimental group diminished over time with a 7/20 successful applications at 1 day, 5/20 at 3 days, and an average of 4/20 at 3 months. A statistically significant difference in pressures generated using the turban vs crepe bandage was only seen at 1 day and 3 months in the lower extremity, but this is of unclear meaning. This article provides low quality data downgraded for bias and imprecision. From this data the researchers concluded that written instructions were insufficient for training of PIB, and that even with hands on training successful application of PIB declined from 60% at 1 hour to approximately 25% by 3 days (95% CI 6-44%) and therefore PIB is not a practical first aid recommendation for venomous snake bite.

In **2008, Currie et al**[25] (LOE 3a) published data from an observational trial on PIB in Australia. This study evaluated 348 subjects from the Australian Snakebite Project regarding the use of PIB (i). In this study PIB was evaluated qualitatively as of adequate quality (still firm and whole limb bandaged) or poor quality (loose and/or not covering the limb as required). It is unclear who did this assessment. Two hundred and seventy-one patients had evaluable data. Of these 214 (79%) attempted PIB. The bandage was assessed as adequate quality in 70% (149/191; 23 not assessed) of these patients. Formal immobilization was determined to be inadequate in 70 of the 127 patients in whom this data was available. This study offered very low quality data, downgraded for bias, indirectness and imprecision. The authors concluded that while they would still promote the use of PIB, further research is needed to determine the utility and optimal application of this treatment.

In **2009, Canale et al**[26] (LOE 2a) performed an observational study investigating the ability to perform PIB and whether training improved correct application. In the initial study 96 participants (78 health care workers and 18 lay persons) were randomized to perform PIB with both a crepe bandage and an elastic bandage. In the initial phase, participants performed PIB two times each with randomization of the first attempt method. Two subjects served as simulated patients for all the trails. A blood pressure cuff placed positioned under the PIB and attached to a pressure transducer was used to measure the pressure generated. In the second phase of the study PIB application with elasticized bandages was repeated by 36 participants (18 general

public and 18 health professionals) with feedback (i) on pressures attained during these attempts. On the subsequent sixth attempt, data regarding the adequacy of PIB was collected. In a final phase of the study, pressure was also measured under correctly applied bandages during an ambulance ride. The median pressure generated under crepe bandages was 28 mmHg (IQR 17-42 mmHg) compared with 47 mmHg (26 - 83 mmHg) with elasticized bandages, with most subgroups applying the elasticized bandage closer to the estimated optimal pressure (55–70 mmHg). Following training, the median pressure for closer to the optimal range than initial attempts [65 mmHg (IQR 56-71 mmHg versus 47 mmHg (IQR 27-75 mmHg)]. On initial bandaging, 14% (5/36) achieved optimal pressure range with elasticized bandages, compared to 50% (18/36) after training (p=0.002). Crepe bandages that initially were correctly applied did not maintain desired pressure during ambulance transport on urban roads over 30 min whereas elasticized bandages maintained pressure (raw data not given). This study provided low quality evidence downgraded for bias and imprecision. In this study crepe bandages rarely generated optimal pressures compared with elasticized bandages, but training did improve participants' ability to apply elasticized bandages. Overall, PIB was poorly done by the general public and health professionals. However, authors recommended that PIB should continue to be promoted as the standard in Australia, but PIB recommendations should be modified to specify the use of elastic bandages.

Summary of Evidence and Rationale

While the data is limited, pressure techniques, including PIB, combined with immobilization appear to prevent systemic absorption of venom and improves mortality following both *Elapidae* and *Viperidae* envenomation.

However, there are potential risks when using PIB.

- **There is some evidence that localized necrosis may occur at the site of envenomation with necrotizing venoms.[9,17,21]**
- **There is some evidence that PIB increases intra-compartmental pressures, potentially increasing the risk of compartment syndrome.[19]**
- **Some subjects experience increased pain, numbness and paresthesias when using PIB. Cyanosis was reported with PIB in some non-envenomated subjects. [15-18]**

PIB appears to be a technique that must be applied in a fairly specific manner in order to be effective.

- **Evidence from a study using a radioactive tracer suggested that an improper pressure when using PIB does not prevent lymphatic flow.[15]**
- **Evidence suggests that PIB does not work well without proper immobilization.[15,16,18]**
- **Studies demonstrate that PIB is often inadequately performed by both medical and lay providers and that retention of training is poor.[23-26]**

In the United States and Canada, where most of the dangerous snakes have necrotizing venoms and the overall mortality rate is low, the risk of necrosis, increased intra-compartmental pressures and training needed to achieve and maintain competency with this unproven treatment outweigh the benefit of PIB in possibly preventing mortality. PIB may have a greater benefit to risk ratio when used for non-necrotizing venoms (i.e. coral

snakes) and possibly envenomations with a higher risk of mortality (e.g. prolonged transport time in a rattlesnake bite).

PIB has been researched as a first aid treatment for envenomations since the 1970's. The majority of studies on treatment are of poor quality, with numerous limitations (LOE 3b or below). In general, studies evaluating the use of various types of PIB on mock venoms in humans demonstrate restricted mock venom flow compared to control.[12,13,15,16] They also demonstrate that movement of the immobilized extremity reverses the effect of pressure suggesting immobilization is an essential component of the treatment.[15] Horvath's study demonstrated the complexity of PIB, in that pressures that were lower or higher than the recommended pressure limits failed to prevent lymphatic flow, suggesting that PIB that is applied inappropriately is not helpful in preventing the systemic absorption of venom.[15] These studies also provided some evidence of potential complications in non-envenomated patients as numbness, paresthesias and cyanosis were experienced by some patients.[15,16] Education studies consistently demonstrate that both lay and medical often do not appropriately apply PIB.[23-26] These data also suggest that hands on teaching is of greater benefit for education of proper technique than only using written instructions.[24,26]

United States Coral Snake Bites

The original studies regarding PIB were performed in Australia using Australian snake venoms. These snakes come from the *Elapidae* family and are primarily neurotoxic venoms. In the US the coral snake is the only indigenous snake from the *Elapidae* family. Sutherland's early animal studies on *Elapidae* venom had small numbers and limitations but suggest that PIB retarded venom flow.[7,8] Sutherland also published a series of articles in the early 1980's that investigated the use of PIB in an animal model of various *Elapidae* venoms.[10,11] Again, in this series of studies methods and results are poorly recorded, but those monkeys in which PIB was applied appeared to have lower systemic venom concentrations, fewer symptoms, delayed creatine kinase concentrations and delayed coagulopathy compared to untreated animals. Later animal studies evaluating coral snake venom demonstrated improved survival with the use of PIB.[20,22] Short term treatment in the coral snake venom studies showed no evidence of necrosis.[20] There is consistent evidence of improved mortality and little evidence of morbidity with proper application of PIB for a coral snake envenomation. PIB is unlikely to offer benefit in the vast majority of cases of coral snake envenomation when transport to definitive care is readily available. Although education studies demonstrate poor application, if mortality is of concern due to markedly delayed transport to definitive care, the benefit of PIB in coral snake envenomation likely outweighs the risk of PIB.

Pit Viper Bites in the United States and Canada

The use of PIB for *Crotalinae* bites in the US and Canada is even more uncertain. Sutherland performed an animal study using Eastern Diamondback rattlesnake venom (from the family *Viperidae*) which appears to show that PIB retards venom flow and improves survival with viper venom.[9] Later animal studies using rattle snake venom demonstrate improved survival in pigs treated with PIB.[19,21] One of these studies demonstrated localized necrosis (versus more widespread necrosis)[21] and one study demonstrated increased intra-compartmental pressures with

the use of PIB (however there was no non-envenomed control group to determine the effect of PIB on a compartment without envenomation).[19] While animal and human studies demonstrate improved mortality, there is debate over the morbidity that could be caused by increasing compartments pressures up to the range that have been associated with compartment syndrome and demonstrating localized necrosis at the site.[19] In contrast, some authors have speculated that localized necrosis is advantageous over more widespread necrosis following envenomation with a necrotizing venom.[8,9] Again, education studies demonstrate that both lay and medical providers are poorly able to apply PIB. In the US and Canada, where overall mortality is low, the risk of necrosis and possible compartment syndrome in almost all circumstances would outweigh the benefit of decreased risk of mortality with PIB.

Recommendations and Strength (using table below):

2020Textual Summary of Recommendation for Revision, Reaffirmation or Retire

With no new literature available, the recommendations regarding the care of snake bites in North America will remain the same as the original systematic review. However, as was discussed with the ARC SAC FA Sub-council, placement of a PIB dressing for a suspected coral snake bite can be considered by a trained provider in a rural or isolated setting when prolonged extrication is anticipated. Given the risk of neurotoxicity resulting from coral snake envenomation, this current recommendation only applies to this type of snake bite.

Standards:

None

Guidelines:

- Immobilize the bitten extremity or keep it still (LOE 4).
- Do not ambulate on the immobilized extremity unless no other option is available (LOE 4).
- PIB is not recommended following bites from a pit viper in the United States and Canada (LOE 4)

Options:

- PIB, with the use of an elastic bandage, can be considered by those trained in proper application following the bite of a suspected coral snake in the United States if the transport time to the hospital may be prolonged (LOE 4).
- It is reasonable to keep the injured area at or lower than the level of the heart (LOE 6).
- It is reasonable to wash the wound if this does not delay hospital transport (LOE 6).

Knowledge Gaps and Future Research:

Please describe any knowledge gaps in your scientific review and how they altered or limited your review and conclusions. Also please provide a description of necessary future research in this area.

1. What is the role of PIB in the United States and Canada in victims of snake bite with a prolonged transport time?
2. Can first aid providers identify venomous snakes?
3. Is there harm from PIB used for non-venomous snakebites?
4. What is the effect of immobilization alone versus immobilization and pressure wrap?
5. What methods of education would better prepare rescuers for treatment with PIB?

Implications for ARC Programs:

Previously PIB was listed as a treatment for all snake envenomations in the United States and Canada. With these recommendations, PIB is considered an option only for United States coral snake envenomations if transport time to definitive care is expected to be prolonged. While the Subcouncil felt that the science supported the use of PIB in preventing death in coral snake envenomation, the low incidence of coral snake envenomation and extremely low incidence of death (less than one per year) makes teaching PIB in courses impractical for the extremely few patients that this treatment would benefit. Therefore, teaching PIB in courses is NOT recommended by the First Aid Science Advisory Subcouncil. Immobilization and transport will be the mainstay of treatment.

Attach Any Lists, Tables of List of Recommendations Created As Part of This Review Summary of Key Articles/Literature Found and Level of Evidence/Bibliography:

American Red Cross

Scientific Advisory Council

ARC SAC SCIENTIFIC REVIEW
(Pressure Immobilization Bandaging for North American Snakebites)

Author(s)	Full Citation	Summary of Article (provide a brief summary of what the article adds to this review including which question(s) it supports, refutes or is neutral)	Methodology	Bias Assessment	Indirectness/ Imprecision/ Inconsistency	Key results and magnitude of results	Support, Neutral or Oppose Question	Level of Evidence (Using table below)	Quality of study (excellent, good, fair or poor) and why

Treatment

Sutherland SK, Coulter AR, Harris RD	Rationalisation of first-aid measures for elapid snakebite. Lancet. 1979;1(8109):183-5.	Original monkey study using elapid venom. Control animals were used, but full reporting on those animals was not part of this paper.	Observational	Serious	Serious	Data poorly presented. Results showed longer survival for monkeys treated with PIB	Neutral	4	Poor
Sutherland SK, Coulter AR	Early management of bites by the eastern diamondback rattlesnake (Crotalus adamanteus): studies in monkeys (Macaca fascicularis) Am J Trop Med Hyg. 1981;30(2):497-500.	Increased survival with PIB in NA pit viper envenomation in animal model.	Observational	Serious	Serious	Data poorly presented. Results showed longer survival for monkeys treated with PIB	Support	4	Poor

Sutherland SK, Harris RD, Coulter AR, Lovering KE	First aid for cobra (Naja naja) bites. Indian J Med Res. 1982;73:266-8.	2 monkeys injected with elapid venom and PIB used in one	Observational	Serious	Serious	Data poorly presented. PIB delayed absorption of venom in PIB treated animal.	Neutral	4	Poor
Sutherland SK, Coulter AR, Harris RD, Lovering KE, Roberts ID.	A study of the major australian snake venoms in the monkey (Macaca fascicularis). I. The movement of injected venom, methods which retard this movement, and the response to antivenoms. Pathology. 1982;13(1):13-27.	Observational study with multiple elapid venoms and procedures being performed.	Observational	Very Serious	Serious	Data poorly presented. Authors conclusions supportive of PIB in elapid bites	Neutral	4	Poor
Sutherland SK, Campbell DG, Stubbs AE.	A study of the major Australian snake venoms in the monkey (Macaca fascicularis).	Observational study of effects of various elapid venoms	Observational	Very Serious	Serious	Data poorly presented. First aid measures (PIB) used but impossible to	Neutral	4	Poor

	II. Myolytic and haematological effects of venoms. Pathology. 1981;13(4):705-715.					follow the method or the results			
Anker RL, Straffon WG, Loiselle DS, Anker KM	Retarding the uptake of "mock venom" in humans: comparison of three first-aid treatments Med J Aust. 1982;1(5):212-4.	Tested 3 methods of PIB (PIB, air splint, local pad) w radioactive mock venom	RCT	Serious	Serious	Time to 80% maximum blood counts: control: median (IQR) 27 minutes (7), pneumatic splint: median (IQR) 22 minutes (15), PIB: median (IQR) 21 minutes (33). Mean difference between PIB and control 0 minutes (95% CI -28.01 – 28.01). Pressure pad remained at	Neutral	4	Poor

						background level until the first-aid treatment was discontinued (approximately 60 minutes); only then did rise appear: median (IQR) 76 minutes (7). Pressure pad was superior but low quality evidence limits conclusions			
Anker RL, Straffon WG, Loiselle DS, Anker KM	Snakebite. Comparison of three methods designed to delay uptake of 'mock venom Aust Fam Physician. 1983;2(5):365-8.	Tested 3 methods of PIB (PIB, air splint, local pad w radioactive mock venom	RCT	Serious	Serious	Percent of maximum radioactivity in blood by 60 min for control, pneumatic splint, PIB and pressure pad were [median(IQR)] 37% (28),	Neutral	4	Poor

						34% (4), 41% (9),and 4.5% (6.5), respectively. Mead difference between PIB and control was -5.6% (95% CI -32.6 – 21.4). The percent of maximum radioactivity in the blood at release of treatment was: median(IQR) pneumatic splint 67% (5), PIB 61% (26), pressure pad 11% (14). Pressure pad was superior but low quality evidence limits conclusions			

Burgess JL, Dart RC, Egen NB, Mayers ohn M	Effects of constriction bands on rattlesnake venom absorption: A pharmacokinetic study. Ann Emerg Med. 1992;21(9):1086-93.	Pig study of Western Diamondback rattlesnake venom absorption with PIB Tx.	Observational	Serious	Serious	Total venom absorption for the initial four hour period, measured by AUC of mean plasma venom concentration (counts/min/mL), was 33% less for the constriction band than the control group ($p<0.05$). Maximum plasma venom concentration decreased during this four hour period by 25% ($p<0.05$). There was no statistically significant difference in leg	Support	4	Fair

						circumference between the groups over the 96 hours of measurements. Venom absorption was less with PIB. No increase in local swelling.			
Howarth DM, Southee AE, Whyte IM	Lymphatic flow rates and first-aid in simulated peripheral snake or spider envenomation Med J Aust. 1994;161:695-700.	Human model of lymphatic flow rates with PIB treatment. 24 human subjects	RCT	Very Serious	Serious	PIB completely prevented transit to the inguinal lymph node in 9/13 subjects and completely prevented transit to the axillary lymph nodes in 6/13 subjects. Exercise (walking) greatly increased transit times	Neutral	4	Fair

						of the tracer. PIB reduced venom movement.			
Pe T, Thwin MM, Than MM, Myint AA, Myint K, Than T	The efficacy of compression immobilization technique in retarding spread of readio-labeled russell's viper venom in rhesus monkeys and "mock venom" NaI in human vomunteers Southeast Asian J Trop Med Public Health. 1994;25(2):349-353.	Monash (local pad) method of pressure in both monkeys and humans using viper venom.	Observational	Serious	Serious	Mean difference in pressure pad versus control was 26.9 minutes (95% CI 12.0 – 41.8) and 18.7 minutes (95% CI 6.25 – 31.15) for injections 10 cm proximal to the lateral malleolus and for those injected 10 cm distal to the head of the fibula, respectively. Pad was effective in reducing spread of venom. Local effects unclear.	Neutral	3b	Poor

Pe T, Myint AA, Han Khin E, Ha T, Swe TN	Local compression pads as a first-aid measure for victims of bites by Russell's viper (Daboia russelii siamensis) in Myanmar Trans R Soc Trop Med Hyg. 1995;89(3):293-5.	Venom level checked before and after PI removal.	Observational	Serious	Serious	13/15 patients had arrest of the venom movement during pad treatment. Side effects were tolerated by all but 2 patients, which removed the pad early due to increased pain. Venom levels remained low while PI was in place, but upon PI discontinuation venom levels increased significantly	Neutral	3b	Poor
Pe T, Mya S, Myint AA, Aung NN,	Field trial of efficacy of local compression immobilization first-aid	Field trial of PIB as a first-aid intervention in 19 Russell's	Observational	Serious	Serious	In patients whose antigen levels were measured before pad	Neutral	3b	Poor

Kyu KA, Oo T	technique in Russell's viper (Daboia russelii siamensis) bite patients Southeast Asian J Trop Med Public Health. 2000;31(2):346-8.	vipers bites with envenomation.				release and after pad release showed an antigen rise of 5 ng/mL to 30 ng/mL. Of 9 patients with antigen levels measured only with the pad in place venom antigen levels remained stable. Minimal local effects seen. Limited control analysis..			
Bush SP, Green SM, Laack TA, Hayes WK, Cardwell MD,	Pressure immobilization delays mortality and increases intracompartmental pressure after artificial intramuscular rattlesnake	Pig model for rattlesnake envenomation and PIB. PIb increased survival but also	RCT	Serious	Serious	The median survival was 191 minutes (range 140 to 240 minutes) in the PIB group and 155 minutes (range 119 to 187 minutes)	Neutral	4	Fair

Tanen DA	envenomation in a porcine model Ann Emerg Med. 2004;44(6):599-604.	compartment pressure.				in the control group. The effect size was 36 minutes (95% CI: 2 - 64 minutes; P=.0122). The mean intracompartmental pressure in the pressure immobilization group was 67±13 mm Hg (mean±SD) with PIB and 24±5 mm Hg without pressure immobilization (effect size: 43 mm Hg, 95% CI 32 to 53 mm Hg). Pigs who received PI survived longer than those that did			

						not and had less swelling. Intracompartmental pressure was higher in the PI group			
German BT, Hack JB, Brewer K, Meggs WJ	Pressure-immobilization bandages delay toxicity in a porcine model of eastern coral snake (Micrurus fulvius fulvius) envenomation Ann Emerg Med. 2005;45(6):603-8	Pig model of a coral snake envenomation w PIB.	RCT	Serious	Serious	4/5 subjects in the PIB group 0/5 in the control group survived to 8 hours, (P=.0036). Mean time to death in the PIB group was 450 minutes (95% CI 366.71 - 533.29 minutes; median 480 minutes; IQR 37.5) and 182 minutes (95% CI 148.35 - 236.45 minutes; median 182	Support	4	Fair

						minutes; IQR 70) in the control group. For the difference of the mean time to death, the 95% CI was 179.34 to 335.86 minutes.Increased survival w PIB use. No local effects observed.			
Meggs WJ, Courtney C, O'Rourke D, Brewer KL	Pilot studies of pressure-immobilization bandages for rattlesnake envenomations Clin Toxicol. 2010;48(1):61-3	Pig model for rattlesnake envenomation and PIB	Observational	Serious	Serious	Control group pigs died at 13.68 ± 3.42 h, PIB treated pigs survived to 24 h (p = 0.014). Potassium was 17.767 ± 5.218 mEq/L in the control group and normal at 24 h in treated animals.	Neutral	4	Poor

						Increased survival w PIB w local tissue damage observed			
Smyrniodis M E, O'Rourke DP, . Rosenbaum MD, Brewer KL, Meggs WJ	Long-term efficacy of pressure immobilization bandages in a porcine model of coral snake envenomation Am J Emerg Med. 2014;32(9): 1024-6.	Pig model of coral snake envenomation w PIB treatment	RCT	Serious	Serious	Pigs receiving PIB were more likely to survive to the 24-hour period than pigs in the control group (3/5 (60%) vs 0/5 (0%); P = .08). Two pigs in the PIB group survived to 21 days. Of those that died in the PIB group, the median time to death was 1172 minutes versus 307 minutes in the control	Neutral	4	Fair

						group (P = .10). Increased survival w PIB w local tissue damage observed			

Education

Norris RL, Ngo J, Nolan K, Hooker G	Physicians and lay people are unable to apply pressure immobilization properly in a simulated snakebite scenario. Wilderness Environ Med. 2005:16(1):16-21.	Observational study evaluating the ability of medical personnel and lay volunteers to properly apply pressure immobilization following standard printed instructions	Observation	Serious	Not serious	PIB applied correctly only 18 out of 200. Main error was incorrect pressure.	Oppose	3b	Good
Simpson ID, Tanwar PD, Andrade C,	The Ebbinghaus retention curve: training does not increase the	Studied the effect of training on PIB skill and	RCT	Serious	Not Serious	12/20 in the experimental group and 0/20 in the control groups	Oppose	2a	Fair

Kochar DK, Norris RL	ability to apply pressure immobilisation in simulated snake bite--implications for snake bite first aid in the developing world. Trans R Soc Trop Med Hyg. 2008;102(5):451-459.	retention of skill				($p<0.001$) applied PIB successfully. Successful application of PIB declined from 60% at 1 hour to approximately 25% by 3 days (95% CI 6-44%). With both written instructions and hands on training successful application of PIB declined. PIB is not a practical first aid recommendation from venomous snake bite.			
Currie BJ, Canale E,	Effectiveness of pressure-immobilization first aid for	This study evaluated 348 subjects in	Observational	Serious	Serious	The bandage was assessed as adequate quality in	Oppose	3a	Poor

Isbister GK	snakebite requires further study. Emerg Med Australas. 2008;20(3):267-270.	this study regarding the use of PIB in elapid bites				70% (149/191) Formal immobilization was determined to be inadequate in 70 of the 127 patients. Inconsistent to poor performance of PIB.			
Canale E, Isbister GK, Currie BL	Investigating pressure bandaging for snakebite in a simulated setting: bandage type, training and the effect of transport. Emerg Med Austral. 2009;21(3):184-90	PIB dressings tested before and after training and during ambulance transport.	Observational	Serious	Not Serious	Median pressure generated under crepe bandages was 28 mmHg (IQR 17- 42 mmHg) compared with 47 mmHg (26 - 83 mmHg) with elasticized bandages, Following training, the median	Oppose	2a	Fair

						pressure was closer to the optimal range than initial attempts [65 mmHg (IQR 56-71 mmHg versus 47 mmHg (IQR 27-75 mmHg)). On initial bandaging, 14% (5/36) achieved optimal pressure range with elasticized bandages, compared to 50% (18/36) after training (p=0.002). PIB was poorly done before and after instruction.			

American Red Cross

Scientific Advisory Council

ARC SAC SCIENTIFIC REVIEW
(Pressure Immobilization Bandaging for North American Snakebites)

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Level of Evidence	Definitions (See manuscript for full details)
Level 1a	**Experimental and Population based studies -** population based, randomized prospective studies or meta-analyses of multiple higher evidence studies with substantial effects
Level 1b	**Smaller Experimental and Epidemiological studies -** Large non-population based epidemiological studies or randomized prospective studies with smaller or less significant effects
Level 2a	**Prospective Observational Analytical** - Controlled, non-randomized, cohort studies
Level 2b	**Retrospective/Historical Observational Analytical** - non-randomized, cohort or case-control studies
Level 3a	**Large Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 3b	**Small Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 4	**Animal studies or mechanical model studies**
Level 5	**Peer-reviewed Articles** - state of the art articles, review articles, organizational statements or guidelines, editorials, or consensus statements
Level 6	**Non-peer reviewed published opinions -** such as textbook statements, official organizational publications, guidelines and policy statements which are not peer reviewed and consensus statements
Level 7	**Rational conjecture** (common sense); common practices accepted before evidence-based guidelines
Level 1-6E	**Extrapolations** from existing data collected for other purposes, theoretical analyses which is on-point with question being asked. Modifier E applied because extrapolated but ranked based on type of study.