EVIDENCE WORKSHEET

Guideline 9.4.8: Envenomation - Pressure Immobilisation Technique
Guideline 9.4.1: Envenomation – Australian Snake bite

ARC Subcommittee: BLS	**Worksheet author**: Suzanne DAVIES **Guideline author:** Peter LEMAN

Clinical questions:

1. In patients in Australia who have sustained snakebite (P) does the application of a pressure immobilisation technique (I) compared with other interventions, or no immobilisation (C) improve any outcomes (O)?
2. In patients in Australia who have sustained a snakebite and have pressure immobilisation bandaging applied (P), is any one technique of immobilisation (I) better than any other (C) in improving any outcomes (O)?

Search Strategies:

A. The Cochrane Library (CDSR, CENTRAL, DARE)

Bites and Stings / exp OR Bandages / exp OR Pressure / exp OR Immobilization / exp
Search results: 56

B. MEDLINE (1950 – current)

[Snake Bites/th OR exp snake venoms/ OR "Bites and Stings"/th] AND [Bandages/mt,ut OR Constriction/mt,ph,th OR Pressure/mt,ut OR Immobilization/mt,ph,ut OR (pressure adj (immobili?ation or bandag$)).ti,ab. OR ((compressi$ or constrict$) adj bandag$).ti,ab. OR First Aid/] *Search Results: 222*

C. EMBASE

['Bites and Stings' / exp OR 'bites and stings'] AND ['Bandages and Dressings' / exp OR 'bandages and dressings' OR immobilization / exp OR ' immobilization'] *Search Results: 226*

Databases / sources searched:

In addition to the electronic databases detailed above, backward and forward searching was undertaken in Scopus, hand-searching of reference lists of relevant articles, text-word based grey literature searches in Google Scholar and searches of relevant academic institutions' published texts.
A good topic-specific database of studies and general information can be found at:
The Australian Venom Research Unit http://www.avru.org

Inclusion / exclusion criteria:

Included were prospective animal or human studies comparing any techniques or interventions to minimise snake envenomation, efficacy studies examining the application of pressure immobilisation bandaging in the treatment of snake envenomation and systematic reviews of intervention studies. Excluded were case studies, non-systematic reviews, letters, editorials and opinion pieces. Studies not available in English and studies not available in full (abstract-only) were also excluded.

Search results:

The combined searches outlined above yielded 64 studies, these papers were retrieved and assessed for inclusion as evidence.

Number of papers / studies meeting criteria for further review: 12

Six LOE III-2 trials and one LOE IV case series provided clinical evidence for the guideline. A further 5 animal studies not meeting the NHMRC criteria for classification as evidence for an intervention were also used to support the guideline construction.

Level of Evidence	Definitions	Study
I	Evidence obtained from a systematic review of all relevant randomised controlled trials	
II	Evidence obtained from at least one properly designed randomised controlled trial	
III-1	Evidence obtained from well designed properly pseudo-randomised controlled trials (alternate allocation or other method)	
III-2	Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case control studies, or interrupted time series with a control group	**Ankler *et al* 1982** **Canale *et al* 2009** **Howarth *et al* 1994** **Norris *et al* 2005** **Simpson *et al* 2008** **Pe *et al* 1994**
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group	
IV	Evidence obtained from case series, either post-test or pre-test and post-test	**Pe *et al* 2000**
Other	Animal, manikin etc	**Bush *et al* 2004 (Animal study)** **German *et al* 2005 (Animal study)** **Meggs *et al* 2010 (Animal study)** **Sutherland & Coulter 1981 (Animal study)** **Sutherland *et al* 1979**

Methodological quality, levels of evidence & outcomes of studies examining Pressure Immobilisation Technique (PIT) for Australian snakebite:

Good	**Fair**	**Poor**
The methodological quality of the study is high with the likelihood of any significant bias being minimal	The methodological quality of the study is reasonable with the potential for significant bias being likely.	The methodological quality of the study is weak possessing considerable and significant biases

1.Studies *supportive* of PIT for the treatment of Australian snakebite:

Good							
Fair				**Ankler 1982 E** **Howarth 1994 E**			**Bush 2004 B** **Meggs 2010 B** **German 2005 B**
Poor				**Pe 1994 E**		**Pe 2000 E**	**Sutherland 1981 E** **Sutherland 1979 E**
	I	**II**	**III-1**	**III-2**	**III-3**	**IV**	**Other**
	NH&MRC levels of evidence						

2.Studies with *neutral* findings for PIT for the treatment of Australian snakebite:

Good							
Fair							
Poor							
	I	**II**	**III-1**	**III-2**	**III-3**	**IV**	**Other**
	NH&MRC levels of evidence						

3.Studies with *negative* findings for PIT for the treatment of Australian snakebite:

Good							
Fair							
Poor							
	I	**II**	**III-1**	**III-2**	**III-3**	**IV**	**Other**
	NH&MRC levels of evidence						

Endpoints:

A = Return of spontaneous circulation **C** = Survival to hospital discharge
B = Survival of event **D** = Intact neurological survival
E = retardation of the systemic dissemination of venom / mock venom
F = other endpoint

Class of recommendation:

Class A: Pressure immobilisation bandaging and limb splinting is recommended for the treatment of any suspected snake envenomation in Australia, using a firm or elasticised bandage over the entire limb, applied in a distal to proximal direction, and ensuring the applied pressure is similar to that used with a sprained ankle. The patient should avoid unnecessary movement. The bandage should remain in place until anti-venom is administered. Regular repeated training in PIT is highly recommended.

Reviewer's final comments and assessment of benefit / risk:

No high level evidence exists supporting the use of pressure immobilisation techniques (PIT) for increasing survival rates after Australian snake bite. However, a number of lower level studies consistently report improved surrogate outcomes (decreased systemic dissemination) of mock venom in humans, or snake venom in animal studies. Of concern is the dearth of studies examining PIT for the treatment of Australian elapid envenomation. No studies reported any adverse effects associated with the application of PIT.

Of the 12 studies that were identified examining the effect of PIT for the first-aid treatment of Australian snakebite, 5 were animal studies, 3 examined the ability of people to administer the treatment, one was an observational study of presentations of viper envenomation in Myanmar (of limited value in the Australian context, as there are no Australian vipers) and the remaining 3 were the only clinical trials in humans (all were non-randomised, small and used different 'mock' venoms).

Animal Studies:
The porcine studies of both Bush (2004) and Meggs (2010) compared the efficacy of PIT in the treatment of *Crotalus atrox*, an American species of viper. Both found that PIT significantly increased the survival time compared to no treatment, however again the concern of confidently extrapolating viper studies to the Australian setting must be considered. Recent pharmacological analyses (Graham et al 2008) differentiate the neurotoxic actions of the Elapidae family from the haemorrhagic actions of the Viperidae family. The 1981 Sutherland & Coulter study examined the efficacy of PIT for reducing plasma levels of venom compared with no treatment for rattlesnake envenomation (another American viper) in four monkeys, reporting that PIT was associated with lower venom plasma levels (actual levels were not reported).
Only two animal studies examined the efficacy of PIT in elapid envenomation. German (2005) studied PIT for the treatment of *Micrurus fulvius fulvius* (an American elapid) envenomation, finding that PIT resulted in increased 24 hour survival rates in the treatment group (4/5) compared to the control group (0/5). The 1979 Sutherland study compared plasma Australian tiger snake venom levels of three monkeys treated with PIT, compared with no treatment in another three envenomated monkeys. The study was of poor quality, as results were given only as graphs (no figures) and 14 animals were unaccounted for at the end of study.
Human studies using 'mock' venom
Ankler (1982) reported that application of pressure immobilisation using a pad, inelastic bandages & splinting was more effective at preventing mock venom entering the systemic

circulation in human subjects than an airsplint, elastic bandaging & splint or no treatment. A possible confounder is that the inelastic bandaging was applied at a pressure of 70mmHg, whereas the elastic bandaging and airsplint were applied at a pressure of 55mmHg.
Howarth's 1994 non-randomised, non-blinded study compared PIT (applied at irregularly different pressures for each subject) with no treatment in 15 human subjects (using their opposite limbs as controls). The authors' reported that, in this sample, PIT applied between 40-70mmHg (upper limb) and 55-70mmHg (lower limb) prevented the migration of mock venom to inguinal or axillary nodes at 30 minutes when subjects remained supine and immobile. All subjects showed node involvement after 10 minutes of walking. This one small study remains the basis for pressure recommendations for PIT.
Pe's 1994 study reported that PIT (6ommHg with pad and splinting) was associated with a slower rate of transit of mock venom (50-87 minutes) than no treatment (40-57 minutes).

Human studies examining PIT training:
Canale (2009) in a well-designed and powered study reported that both health professionals and lay-persons were able to achieve PIT pressures of close to 55-70mmHg only after intensive training and using elasticized bandages (not crepe bandages).
Norris (2005) also found in a series of 200 applications, that effective PIT was rarely administered by either healthcare professionals (13/100) or lay-persons (5/100), even after they read comprehensive instructions. Simpson (2008) reported equally poor retention of PIT skills after either intensive training or written instruction.
These three studies identify the need for effective and regularly repeated training in PIT, even for healthcare professionals.

The one remaining prospective observational study was undertaken in Myanmar and examined the effectiveness of PIT in preventing systemic envenomation from viper envenomations. The study concluded that PIT was ineffective as 16/19 cases showed signs of systemic involvement. Study results were particular to the local context, examining the barriers to implementation of PIT as a first aid measure in the developing world.

Citation List:

Anker RL, Straffon WG, Loiselle DS and Anker KM, Retarding the uptake of "mock venom" in humans: comparison of three first-aid treatments. Medical Journal of Australia 1982: 1(5);212-4
We compared, for the first time in human subjects, first-aid measures to treat bites from Australian snakes using a "mock venom" (congruent to 0.2 mL of Na 131I at 7.4 kBq or 11.1 kBq (0.2 muCi/kg or 0.3 muCi/kg)) as a subcutaneous injection in the lateral aspect of the leg. After application of either a full-length lower-limb air-splint (inflated to 7.3 +/- 0.7 kPa (55 +/- 5 mmHg) pressure) or the currently recommended treatment (elastic bandages at 7.3 +/- 0.7 kPa (55 +/- 5 mmHg) pressure and supporting splint) the rate of appearance of the Na 131I in the peripheral blood was approximately the same as the ratio for the untreated controls. However, application of a large firm pad over the injection site and its immediate surrounds, retained by a non-elastic bandage (at least 9.3 kPa (70 mmHg) pressure over the injection site), completely prevented "mock venom" uptake until the pad was removed.
LOE III-2, small (n=3 in each group), non-randomised controlled trial comparing PIB with elastic bandaging & splint (55mmHg), PIB with an airsplint (55mmHg), 'Monash Method'

of PIB (non-elastic bandage, pad and splint) and no treatment for preventing venom uptake after simulated envenomation. The outcome was time to appearance of venom in the systemic circulation. After pressure bandaging with an inelastic material ('Monash Method') study authors were unable to detect radioactively-labelled mock venom in systemic blood. Other methods showed no advantage over no intervention (control). Small study size and use of an 'unvalidated' model of envenomation reduce the weight of this evidence.

Bush SP, Green SM, Laack TA, Hayes WK, Cardwell MD and Tanen DA, Pressure immobilization delays mortality and increases intra-compartmental pressure after artificial intramuscular rattlesnake envenomation in a porcine model. Annals of Emergency Medicine 2004: 44(6);599-604

Determination of the effect of pressure immobilization on mortality and intra-compartmental pressure after artificial intramuscular *Crotalus atrox* envenomation in a porcine model. METHODS: We prospectively studied 20 pigs using a randomized, controlled design. After anaesthesia, *C atrox* venom (20 mg/kg) was injected with a 22-gauge needle 10 mm deep into the tibialis anterior muscle of the hind leg. Pigs were randomized to receive either pressure immobilization (applied 1 minute after envenomation and maintained throughout the duration of the experiment) or no pressure immobilization. We measured time to death, intra-compartmental pressure before venom injection and at 2 hours after injection, and leg circumference at a standardized location before injection and immediately post-mortem. Duration of survival was compared using Kaplan-Meier survival analysis. RESULTS: The dose of venom resulted in 100% mortality. The median survival was longer in the pressure immobilization group (191 minutes, range 140 to 240 minutes) than in the control group (median 155 minutes, range 119 to 187 minutes). The difference between the groups was 36 minutes (95% confidence interval [CI] 2 to 64 minutes; P =.0122). The mean intra-compartmental pressures were 67+/-13 mm Hg+/-SD with pressure immobilization and 24+/-5 mm Hg without pressure immobilization. The difference between groups was 43 mm Hg (95% CI 32 to 53 mm Hg). The mean circumferences were 14.3 cm in the pressure immobilization group and 19.1 cm in the control group. The difference between groups was -4.8 cm (95% CI -5.7 to -3.9 cm). CONCLUSION: Compared with control animals without treatment, the pressure immobilization group had longer survival, less swelling, and higher intra-compartmental pressures after artificial, intramuscular *C atrox* envenomation in our porcine model.

Randomised, non-blinded, controlled trial of pressure immobilisation bandaging versus no treatment in a porcine model of snake envenomation. Pressure bandaging increased survival time by a mean of 36 minutes, with a wide confidence interval for the difference of 2 – 64 minutes. C. atrox is an American viper – care must be taken generalising the study results to the Australian Elipidae context. Venom was injected intra-muscularly (as opposed to sub-cutaneously, as is generally considered the case with Australian snake envenomation)

Canale E, Isbister GK and Currie BJ, Investigating pressure bandaging for snakebite in a simulated setting: bandage type, training and the effect of transport. Emergency Medicine Australasia 2009: 21(3);184-90

This study aimed to investigate if pressure bandages (PB) generated and maintained presumptive optimal pressures in a simulated setting. METHODS: A total of 96 subjects

were recruited, 78 health professionals and 18 from the general public. Participants were asked to apply PB with crepe and with an elasticized bandage without instruction. A paediatric blood pressure cuff attached to a pressure transducer was used to measure the pressure generated. PB application with elasticized bandages was repeated by 36 participants (18 general public and 18 health professionals) with feedback on pressures attained, and reassessment on the sixth subsequent attempt. Pressure was also measured under correctly applied bandages during an ambulance ride. RESULTS: The median pressure generated under crepe bandages was 28 mmHg (interquartile range [IQR]: 17-42 mmHg) compared with 47 mmHg (IQR 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 the 36 participants was 65 mmHg (IQR 56-71 mmHg), closer to the optimal range than initial attempts. On initial bandaging, 5/36 (14%) participants achieved optimal pressure range with elasticized bandages, compared with 18/36 (50%) after training (P = 0.002). Crepe bandages initially correctly applied did not maintain desired pressure during ambulance transport on urban roads over 30 min. Elasticized bandages maintained pressure. CONCLUSIONS: PB was poorly done by the general public and health professionals. Crepe bandages rarely generated optimal pressures compared with elasticized bandages, but training did improve participants' ability to apply elasticized bandages. PB recommendations should be modified to specify appropriate bandage types.
LOE III-2 cohort study comparing the efficacy of elastic bandages to crepe bandages for achieving and maintaining the recommended optimal pressure for treatment of snake envenomation (stated as 55-70mmHg). Study participants bandaged the lower limb of either a human volunteer or a manikin arm. Pressure measurements were taken before and after study participants were trained; study participants were a mix of various health professionals and lay persons. Close to optimal pressures (mean 65mmHg) were obtained using an elastic bandage after training and feedback. Health professionals and lay persons were equally inept. Crepe bandages (with or without splinting) were not able to generate or maintain optimal pressures during a 30minute ambulance transport.

German BT, Hack JB, Brewer K and Meggs WJ, Pressure-immobilization bandages delay toxicity in a porcine model of eastern coral snake (*Micrurus fulvius fulvius*) envenomation. Annals of Emergency Medicine 2005: 45(6);603-8
STUDY OBJECTIVES: Pressure-immobilization bandages are used in countries where neurotoxic snake envenomations are common. They impede lymphatic egress from the bite site and delay systemic venom toxicity. The effectiveness of these devices has not been evaluated in coral snake envenomations. We investigated the efficacy of pressure-immobilization bandages in delaying the onset of systemic toxicity in a porcine model of coral snake envenomation. METHODS: A randomized controlled trial of pressure-immobilization bandages was conducted in a university animal care centre. Subjects were 12 anaesthetized spontaneously breathing pigs, ranging from 9.1 to 11.4 kg. After injection with 10 mg of *Micrurus fulvius fulvius* venom in the subcutaneous tissue of the distal foreleg, subjects were randomized to receive no treatment or application of a pressure-immobilization bandage at 1 minute after injection. Treated animals had elastic bandages applied to the extremity and splinting for immobilization. Vital signs and quality of respirations were recorded. Outcome was the onset of respiratory failure or survival to 8 hours. Necropsies and histological analysis of the envenomation site was performed. RESULTS: One animal from each group was removed because of the discovery of pre-

existing respiratory pathology. Four of 5 pigs in the treatment group survived to 8 hours, but none in the control group survived. Mean time to onset of respiratory compromise was 170.4 +/- 33.3 minutes in the control group. None of the pigs had histological changes at the envenomation site consistent with ischemia or pressure-related injury. CONCLUSION: Pressure-immobilization bandages delayed the onset of systemic toxicity in our porcine model of *M fulvius* envenomation.
Small (n=10) randomised controlled trial of pressure immobilisation versus no treatment in a porcine model of human envenomation. Animals were injected with the venom of the eastern coral snake, an American elapid. Pressure immobilisation was achieved with elastic bandages and full limb splinting. Outcomes were mean time to onset of respiratory failure and survival to 8 hours. Four of the five animals in the intervention group survived to eight hours, none survived in the control group (P= 0.0036). The one animal that died in the intervention group developed respiratory difficulty at 300 minutes; the mean onset to respiratory failure in the control group was 170.4 +/- 33 minutes. A histological examination of tissue that was subjected to pressure bandaging showed no evidence of ischaemic injury in any animal.

Howarth DM, Southee AE and Whyte IM, Lymphatic flow rates and first-aid in simulated peripheral snake or spider envenomation. Medical Journal of Australia 1994: 161(11-12);695-700
OBJECTIVES: To demonstrate and define normal lymphatic transit times by lymphoscintigraphy and to evaluate the efficacy of the currently recommended first-aid measures for the management of snake or spider envenomation. SETTING: The nuclear medicine department of a major teaching hospital. PARTICIPANTS AND DESIGN: Twenty-four subjects received either intradermal or subcutaneous injections of 99mtechnetium antimony sulphur colloid (0.1 mL) in both hands/forearms and feet/legs. This simulated a snake or spider bite. Fifteen of the subjects had first-aid in the form of firm bandages and splints applied to an upper and a lower limb immediately after injection. MAIN OUTCOME MEASURES: The progress of the radiotracer was followed with a large field of view gamma camera. If no egress of radiotracer was seen in the bandaged limbs, the subject walked until radioactivity was detected. RESULTS: The mean (+/- SEM) periphery-to-systemic circulation transit time after subcutaneous injection was 58 (+/- 7) minutes. The first-aid was found to be very effective when applied with bandage pressures ranging from 40 to 70 mmHg (5.3-9.3 kPa) in the upper limb and 55 to 70 mmHg (7.3-9.3 kPa) in the lower limb. Lower and higher bandage pressures were ineffective. However, despite first-aid measures, egress of radiotracer, even in the upper limbs, was seen in all subjects who walked for 10 minutes or more. CONCLUSIONS: Firm pressure bandaging is an effective means of restricting the lymphatic flow of toxins after envenomation, provided the bandage is applied within the defined pressure range. Strict limb immobilisation is necessary to minimise lymphatic flow, and walking after upper or lower limb envenomation will inevitably result in systemic envenomation despite first-aid measures.
LOE III-2 cohort study (n=24) examining the efficacy of pressure immobilisation (achieved with crepe bandages and splinting) in retarding the movement of 'mock' radio-labelled venom. Mock venom was injected either subcutaneously or intradermally into the wrists and/or ankles of healthy human subjects. One side (one arm, one leg) was bandaged, with the other limbs acting as controls. Movement of the mock venom to the axillary and inguinal nodes was timed, both with subjects resting in a supine position, and after walking. Supine, resting subjects with bandages applied at pressures between 55-70mmHg

(lower limb) or 40-70mmHg (upper limb) showed no evidence of radiotracer in inguinal or axillary nodes at 30 minutes, however pressures under (4 subjects) or over (7 subjects) this range showed shorter times to lymph node involvement. When subjects walked, all showed radiotracer movement at 10 minutes. This study used a non-systematic combination of pressures and times, leading to difficulty in extracting any meaningful data.

Meggs WJ, Courtney C, O'Rourke D and Brewer KL, Pilot studies of pressure-immobilization bandages for rattlesnake envenomations. Clinical Toxicology: The Official Journal of the American Academy of Clinical Toxicology & European Association of Poisons Centres & Clinical Toxicologists 2010: 48(1);61-3

STUDY OBJECTIVE: Pressure-immobilization bandages sequester venom in extremities and are recommended for snakebites without local toxicity. Pilot studies were performed to determine the time of onset of toxicity and efficacy of pressure-immobilizations bandages in a porcine model of rattlesnake envenomation. METHODS: After IACUC approval, anesthetized pigs were injected subcutaneously in a distal hind leg with 200 mg of Crotalus atrox venom. After 1 min, pigs received either a pressure-immobilization bandage (N = 3) or no treatment (N = 3). At 24 h, surviving pigs received antivenin and then the pressure-immobilization bandages were removed. Surviving subjects were followed for 1 week. Chi-square analysis and paired t-test were used. RESULTS: Pigs with pressure-immobilization bandages survived for 24 h, whereas untreated pigs died at 13.68 +/- 3.42 h ($p = 0.014$). Surviving pigs walked on the extremity at 7 days. Potassium rose from 4.033 +/- 0.252 at baseline to 17.767 +/- 5.218 mEq/L ($p < 0.0001$) at time of death in untreated pigs but was normal at 24 h in treated subjects. Widespread tissue necrosis was seen in the untreated group but only local necrosis in the treatment group. CONCLUSIONS: Pressure-immobilization bandages prevented death from severe *C. atrox* envenomations with a 24 h delay to treatment. Surviving pigs had recovery of limb use at 1 week.

Small (n=6) controlled trial comparing pressure immobilisation bandaging to no treatment in a porcine model of human rattlesnake envenomation. The primary outcome was survival at 24 hours. All animals in the treatment group survived to 24hours, all animals in the control group were dead at 24hours (mean time to death 13.68 +/-3.42hours) P = 0.014.

Norris RL, Ngo J, Nolan K and Hooker G, Physicians and lay people are unable to apply pressure immobilization properly in a simulated snakebite scenario. Wilderness & Environmental Medicine 2005: 16(1);16-21

OBJECTIVE: To determine whether volunteers (with or without prior medical training) can correctly apply pressure immobilization (PI) in a simulated snakebite scenario after receiving standard instructions describing the technique. METHODS: Twenty emergency medicine physicians (residents and attendings) and 20 lay volunteers without prior formal medical training were given standard printed instructions describing the application of PI for field management of snakebite. They were then supplied with appropriate materials and asked to apply the technique five separate times (twice to another individual [one upper and one lower extremity] and three times to themselves [non-dominant upper extremity, dominant upper extremity, and one lower extremity]). Successful application was defined a priori by four criteria previously published in the literature: wrap begins at the bite site, entire extremity is wrapped, splint or sling is applied, and pressures under the dressing are between 40 and 70 mm Hg in upper-extremity application and between 55 and 70 mm Hg in lower-extremity use. Pressures were determined using a specially designed skin interface pressure-measuring device placed at the simulated bite site.

RESULTS: The technique was correctly applied as judged by the preset criteria in only 13 out of 100 applications by emergency medicine physicians and in only 5 out of 100 applications by lay people. There was no significant difference in success rates between physicians and lay volunteers. Likewise, there was no significant difference in success based on which extremity was being wrapped. More detailed analysis revealed that the major contributor to failure was inability to achieve recommended target pressures. CONCLUSIONS: Volunteers in a simulated snakebite scenario have difficulty applying PI correctly, as defined in the literature. The major source of failure is an inability to achieve recommended pressure levels under the dressing. New methods of instructing people in the proper use of PI or new technologies to guide or automate application are needed if this technique is to be used consistently in an effective manner for field management of bites by venomous snakes not known to cause significant local wound necrosis.
LOE III-2 comparative study (n=40) examining the ability of healthcare professionals to apply adequate PIB compared with lay-persons, after reading the same printed training material. Adequacy was assessed as correct pressure, entire limb wrapped, splint/sling applied and distal to proximal wrapping technique. Both groups were equally poor at PIB; 13/100 attempts by healthcare professionals were deemed adequate, 5/100 attempts by lay-persons were adequate. The major problem was with attaining the recommended pressure.

Pe T, Mya S, Myint AA, Aung NN, Kyu KA and Oo T, Field trial of efficacy of local compression immobilization first-aid technique in Russell's viper (Daboia russelii siamensis) bite patients. Southeast Asian Journal of Tropical Medicine & Public Health 2000: 31(2);346-8

A field trial of efficacy of local compression immobilization first-aid technique in 42 Russell's viper bite cases was studied and only 19 were envenomed. Proper immobilization was carried out in 3/13 immobilized cases. The average time of application of the pad was 1.12 hours (range 5 minutes to 7 hours) and the total duration of the pad application was 3 hours 40 minutes (range 30 minutes to 9 hours). Venom levels measured at the hospital before and at 15 and 30 minutes after release of the pad (n=10) showed a rise of 5 to 30 ng/ml of venom following release. Movement of venom antigen was found to be retarded in all cases (n=9) whose venom levels were measured at 15 and 30 minutes with the pad in place. Sixteen out of 19 cases had systemic envenoming; indicating that pad or immobilization alone is not effective in delaying spread of venom. The incidence of local necrosis 3/42 (8%) following use of the pad was comparable to that of the systemic cases without the pad. No ill effects were observed following its application for as long as 9 hours. Local blackening seen in 4/36 (10%) cases was likely to be result of a local venom effect.
Level IV observational study of the efficacy of pressure immobilisation bandaging (PIB) for the first-aid treatment of Russell's viper envenomation. 19 patients presented to a local hospital after envenomation, with PIB in place. Serum venom antigen levels were taken for these pts with the PIB in place. In 9/19 a further serum level was taken 15 minutes later, with the pad still in place; only one patient had an increase in antigen levels. 10/19 patients had the PIB removed and a further serum level taken 15 minutes later, all 10 had a marked increase in antigen levels. 16/19 patients had systemic envenomation – authors propose this was due to inadequate immobilisation and a delay to application of PIB ($\bar{x}$ = 1.12hrs).

Simpson ID, Tanwar PD, Andrade C, Kochar DK and Norris RL, 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. Transactions of the Royal Society of Tropical Medicine & Hygiene 2008: 102(5);451-9
Pressure immobilisation (PIM) has been recommended for field management of bites by some venomous snakes. A narrow range of pressures under the encompassing wrap is necessary for PIM to limit venom spread. This study sought to evaluate the effect of focused training on volunteers' ability to apply PIM and to retain such skill over time. Forty volunteers were randomly divided into two groups: Group 1 (N=20; controls) received standard written instructions in PIM application; and Group 2 (N=20) received focused instruction during a 4-h training session (including hands-on practice and real-time feedback regarding pressures achieved). After voicing confidence with the technique, volunteers were tested at 1h, 1 day, 3 days and 3 months post training. One-hour post training, no volunteers in the control group were successful in applying PIM with the correct pressure. Twelve volunteers (60%) in Group 2 achieved target pressures 1h after training. However, there was rapid loss of ability to apply PIM correctly by Group 2, falling to just 25% success at 3 days, with little further deterioration at 3 months. Neither written instructions nor intense training with feedback adequately prepares individuals to apply PIM with correct pressures under the wrap.
LOE III-2 comparative study (n=40) comparing the retention of pressure immobilisation skills between two groups in rural India. One group received written instructions, the other intensive, focussed instruction. The intensively trained group displayed significantly better skills at 1 hour post training, however this rapidly fell, with retention being equally poor for both groups by 3 days after training. This study questions the role of PIB in developing countries, where training and equipment are significant economic barriers, and the domination of Viperidae species limits the usefulness of the PIB technique.

Sutherland SK and Coulter AR, Early management of bites by the eastern diamondback rattlesnake (Crotalus adamanteus): studies in monkeys (Macaca fascicularis). American Journal of Tropical Medicine & Hygiene 1981: 30(2);497-500
Monkeys were injected subcutaneously with 6 mg of *Crotalus adamanteus* venom and a solid phase radioimmunoassay was used to measure levels of venom in plasma and urine. When no attempt was made to retard venom movement from the site of injection, plasma levels as high as 1,300 ng/ml occurred within 15 min of injection and progressive swelling developed in the injected limb. When first aid was employed (firm pressure to the injection site and immobilization of limb with a splint), plasma levels remained very low until cessation of first aid. No swelling of the injected limb occurred while the first aid measures were in position and animals which received first aid and antivenom fared much better than did those which received antivenom alone. The best result was obtained when antivenom was infused prior to removal of the pressure bandages and splint. This first aid procedure is effective in delaying venom movement, and its simplicity and safety suggest it should be considered for use in cases of human envenoming by *C. adamanteus.*
Small (n=4) comparative study of the efficacy of PIB and timing of antivenom administration in a monkey model of rattlesnake envenomation. Outcomes were plasma and urine levels of venom. The two monkeys that were treated with PIB had lower plasma levels and survived, the two monkeys with no PIB (but did receive antivenom) both had high plasma levels of venom and died.

Sutherland SK, Coulter AR and Harris RD, Rationalisation of first-aid measures for elapid snakebite. Lancet 1979: 1(8109);183-5

The plasma of monkeys envenomated with tiger snake (*Notechis scutatus*) venom was monitored by radioimmunoassay for both crude venom and a neurotoxin. When the injected limb was immobilised and a pressure of 55 mm Hg applied to the injection site, only very low levels of circulating venom or neurotoxin were detectable. In practical terms, venom movement can be effectively delayed for long periods by the application of a firm crepe bandage to the length of the bitten limb combined with immobilisation by a splint. Pressure alone or immobilisation alone did not delay venom movement.

Small (n=6) comparative study of the effect of PIB (crepe bandage and splint) with no treatment in a monkey model of human envenomation by tiger snake. After injection of venom into 25 monkeys, only 11 were reported on (no follow up for other 14). Of the 11 described, 3 had PIB, 3 had no treatment with the remaining 5 monkeys receiving a variety of other treatments. The three monkeys treated with PIB for 60 minutes had lower levels of circulating venom at 120 minutes than did the three monkeys not treated. Results were presented as graphs, no figures given.

Pe T, Muang Muang T, Myint Myint T, Aye Aye M, Kyaw M and Thein T, The efficacy of compression immobilization technique in retarding spread of radio-labeled Russell's viper venom in rhesus monkeys and 'mock venom' NaI131 in human volunteers. Southeast Asian Journal of Tropical Medicine & Public Health 1994: 25(2);349-53

The efficacy of the modified compression immobilization technique in retarding spread of radio-labelled Russell's viper venom in 3 rhesus monkeys (*Macaca mulata*) and "mock venom" NaI131 in 14 human volunteers was studied. 0.1 microgram of Russell's viper venom having 10 microCi radio-activity in 0.2 ml normal saline containing 0.5% bovine serum albumin was injected subcutaneously at the lateral aspect of the right hind limb of a rhesus monkey. A hand-tight bandaging of a rubber pad measuring 55 x 28 x 16 mm over the injection site and splinting effectively retard spread of radio-labelled venom for the entire length of time applied, although complete immobilization was not achieved. In human volunteers, application of a pad measuring 60 x 50 x 17 mm over the subcutaneous injection site of 20 microCi or 12 microCi/0.2 ml NaI131 with a hand-tight bandaging (60 +/- 10 mmHg) and immobilization of limb was found to be effective in retarding the movement of radioactive NaI131. These results suggested that the compression pads tried in this study effectively retard the spread of radio-labelled Russell's viper venom (MW ranging from 20,000-90,000) and radioactive NaI131 (MW 150) from the site of injection. Thus, it is highly likely that the present compression pad will be useful as a first-aid measure in Russell's viper bite victims.

Small (n=3) observational study of the efficacy of a modified 'rubber block' pressure bandaging technique in retarding the systemic dissemination of radio-labelled venom in a monkey model of human envenomation. Authors' report that the range of times for appearance of 80% maximum radioactivity was 53.6 – 70minutes and this was 'effective'. There is a problem with the generalisibility of these results to the Australian context where snake envenomation is from the Elipidae family (not Viperidae)

The second part of the study was a LOE III-2 controlled trial comparing the same modified PIB technique for retarding the movement of radio-labelled mock venom with no treatment in 22 human volunteers. Results were again reported as time to reach 80% maximum systemic radioactivity. The control subjects ranged from 40-54 minutes to detection, the PIB treated group reported a range of 50-87 minutes. Authors' report this as an indication that

the treatment is 'effective'.