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A comprehensive approach to managing a neglected, neglected tropical disease; The Myanmar Snakebite Project (MSP)

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ABSTRACT

Snakebite is predominantly an occupational disease affecting poor rural farmers in tropical regions and was recently added to the World Health Organisation list of Neglected Tropical Diseases (NTD). We document an overview of methodologies developed and deployed in the Myanmar Snakebite Project, a foreign aid project largely funded by the Australian Government, with the core aim to "improve outcomes for snakebite patients". A multidisciplinary team of experts was assembled that worked in a collaborative manner with colleagues in Myanmar, first to identify problems related to managing snakebite and then develop interventions aimed to improve selected problem areas. A broad approach was adopted, covering antivenom production, antivenom distribution and health system management of snakebite. Problems identified in antivenom production included poor snake husbandry resulting in poor survival of captive specimens, lack of geographical diversity; poor horse husbandry, resulting in high mortality, inadequate stock acquisition protocols and data collection, and inappropriate immunisation and bleeding techniques; and inadequate production capacity for freeze dried antivenoms and quality control systems. These problems were addressed in various ways, resulting in some substantial improvements. Antivenom distribution is being reorganised to achieve better availability and utilisation of stock. Health system management of snakebite was assessed across all levels within the area selected for the study, in Mandalay region. A comprehensive community survey indicated that hospital statistics substantially underestimated the snakebite burden, and that access to care by local villagers was delayed by transport and cost issues compounded by lack of antivenom at the most peripheral level of the health service. A health system survey confirmed under-resourcing at the local village level. Prospective case data collection initiated at tertiary hospitals indicated the extent of the snakebite burden on health resources. Interventions initiated or planned include training of health staff, development of a core of senior trainers who can "train the trainers" nationwide in a sustainable way, development and deployment of management guidelines and algorithms for snakebite and a distribution of solar powered fridges to remote health facilities to allow storage of antivenom and prompt treatment of snakebite cases before transfer to major hospitals, thereby reducing the "bite to needle" time.

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1. Introduction

Snakebite is arguably the most important venom induced disease (VID) (WHO, 2007) globally. Estimates of its annual incidence and mortality, range up to >5 million cases and >100,000 deaths annually (Chippaux, 1998; Kasturiaratne et al., 2008; Swaroop and Grab, 1954). A detailed community study in India provided a strong data set indicating at least 45,000 deaths annually due to snakebite, significantly in excess of the "high" estimates in a global study estimating snakebite rates and mortality, where "South Asia" (included India, Pakistan, Bangladesh) had a stated mortality range of 14 k to 33 k deaths/year (Mohapatra et al., 2011). The World Health Organisation (WHO) currently lists the annual global mortality from snakebite as 81,000 to 138,000 (WHO, 2017). Snakebite also extracts a financial burden, causing victims, their families and health services significant economic loss (Habib et al., 2015; Kasturiaratne et al., 2017). The plight of snakebite patients in the developing world, where this is predominantly an occupational disease of poor rural farmers, has been highlighted by groups such as the Global Snakebite Initiative (Gutierrez et al., 2010, 2013; Warrell, 2010), culminating in listing of snakebite as a global health issue at the World Health Assembly in Geneva in May 2016, followed by its inclusion in the WHO list of Neglected Tropical Diseases (NTDs) in 2017. These efforts highlight the urgent need to develop strategies to improve outcomes for snakebite patients, especially in the rural tropics where incidence is highest.

Most published approaches to tackling the global snakebite problem focus on restricted aspects, mainly the inadequate availability of safe, effective and affordable antivenoms (Gutierrez et al., 2014; Warrell et al., 2013; Williams et al., 2010, 2011). Ensuring availability of appropriate antivenom (AV) is a priority, but availability of AV alone is not the complete solution for improving patient outcomes in snakebite (Gutierrez, 2014; Harrison et al., 2011, Harrison and Gutiérrez, 2016).

We herein report the development and deployment of a comprehensive strategy to deliver a sustainable solution for snakebite in impoverished rural areas of a developing nation with a known high snakebite burden.

2. Methods

The Myanmar Snakebite Project is a joint Australia-Myanmar project funded through the Australian Government Department of Foreign Affairs and Trade (DFAT), with support from the Government of Myanmar (Ministry of Industry and Ministry of Health and Sports) and in-kind support from the University of Adelaide, SA Health (Women's & Children's Hospital, Royal Adelaide Hospital), Seqirus Ltd, Venom Supplies Ltd., University of Sydney, CSIRO Australian Animal Health Laboratory and a number of volunteer experts. Its stated aim is "to improve outcomes for snakebite patients".

The Project was established under the auspices of the University of Adelaide, Faculty of Health Sciences, with executive control (Executive Team; ET) by 3 university staff (full time or clinical associates) providing skills and experience in clinical toxinology, renal medicine and public health, all of whom had prior contact with the health sector in Myanmar. Through this contact these individuals were approached in 2014 by colleagues in Myanmar, requesting assistance with their snakebite problem. The Project proposal was developed by the ET and colleagues in the Myanmar Ministry of Health and Ministry of Industry, in consultation with colleagues in Australia.

This process, through both discussions and visits to Myanmar to identify issues, prior to funding being granted, ascertained that there were 3 principal areas requiring intervention, in the interests of a broad approach to the problem, rather than concentration on a single aspect such as antivenom. The 3 principal areas were:

- Antivenom production
- Antivenom distribution
- Health system strengthening for more effective management of snakebite

The ET assembled a team encompassing a broad range of relevant skills and experience (Fig. 1). Team members were drawn from those with relevant expertise, both in Myanmar, and from elsewhere, most notably Australia, as the nation funding the Project. In this paper, where the "Project" undertakes an activity, this implies relevant members of the Project team undertook the activity, including both non-Myanmar members of the team and Myanmar members of the team and, where appropriate, other Myanmar personnel, in a collaborative and cooperative manner. A key Project requirement was that activities jointly involved those from within and outside Myanmar, as equal partners. Without that equal partnership involving many colleagues in Myanmar, the Project could not have achieved the results it has and this is therefore a core component of methodology (i.e. development and implementation of interventions to address AV production, distribution and health system strengthening).

2.1. Selection of project sites for activity and intervention

Myanmar is sufficiently large (676,578 km^2) and well populated (>52 million) to make it impossible to conduct activities across the entire country with the resources available to the Project, therefore it was necessary to select a suitable site and sub-sites as interventional foci. To achieve this the Project team consulted senior Ministry of Health and Sport officials, examined Ministry statistics on recorded rates of snakebites in each region and shortlisted several potential sites that met the criteria of significant snakebite case load, accessibility, and local resources and enthusiasm for the aims of the Project. Senior team members then undertook visits to selected sites, and, using these criteria, selected a major focus site and two sub-sites.

2.2. Antivenom production

The Project supported initial fact-finding visits to the Myanmar government antivenom production facility, with strong support from the Government of Myanmar through the Minister/Deputy Minister of Industry and key staff at the facility. This identified several problem areas:

2.2.1. Venom production

Globally accepted methodology for antivenom production involves venom collection followed by inoculation into the production animals. This requires collection, housing and regular venom extraction from snakes. In Myanmar, at present, there are 2 monospecific antivenoms, raised against Russell's viper (*Daboia siamensis*) and monocled cobra (*Naja kaouthia*). Within a given species there may be considerable venom variability across its geographic range, a problem well documented for the Western Russell's viper *Daboia russelii* (Prasad et al., 1999).

Snakes must be healthy and preferably be long lived in captivity. The Project therefore determined, through visits by experts in clinical toxinology and herpetology, the health of captive snakes used, their care in captivity, seeking potential problems and possible solutions.

2.2.2. Antibody production

As is usually the case in antivenom production, horses are the principal production animals in Myanmar. The WHO global standard for antivenom production includes measures of horse health and longevity in production, in addition to immunisation and plasma product processing requirements. The Project determined, through its advisory visits by experts in clinical toxinology, veterinary medicine, antivenom production, the health of the horses and the facilities available for their care, immunisation and plasma collection. During this process it became apparent that documentation of the health of individual horses was inadequate. A database was therefore developed and deployed to improve data collection. Equipment was provided, with associated staff

training, to allow key variables to be collected relating to the horses' health (haematocrit (PCV) and Equine Infectious Anemia (EIA) exposure status). In addition, staff were trained to conduct autopsies on horses dying during production, to ascertain causes of death.

2.2.3. Antivenom processing and production

The Project assessed the existing antivenom production methodologies against WHO global standards, using advisory visits by experts in clinical toxinology and antivenom production.

2.3. Antivenom distribution

The Project investigated problems relating to antivenom distribution (quantity, availability to users in the health system, factors restricting availability) through exploratory visits by experts in clinical toxinology, public health, antivenom production and through subsequent meetings and discussions with local stakeholders in the Ministry of Industry and Ministry of Health and Sports. This approach was supplemented by data collected through other Project activities, including community surveys, health system analyses and prospective case data collection.

2.4. Health system management of snakebite

The Project identified some key questions that demanded answers, through some initial visits before funding was secured, followed by further enquiries:

What is the true extent of snakebite in the community?

The Project undertook a comprehensive, random sample community survey designed to capture data on rates of snakebite, outcomes, first aid knowledge and practices, care-seeking behaviour, sources of local care, availability of health system resources, utilisation of those resources and impediments to their implementation.

Within the chosen project areas 150 villages were randomly selected with probability proportional to size. This resulted in a spread of villages that optimized varying levels of health system access and in which access to and use of various resources might be improved [Rural Health Centers (RHCs), Station Hospitals (SHs), Township Hospitals (THs)]. Within villages selection of study households was rigorously randomised. A team of Myanmar enumerators was recruited through the Myanmar Ministry of Health and Sport. They were trained to conduct the survey and were deployed under the supervision of Project team leaders in public health and epidemiology.

Which data about snakebite are currently available in the health system?

Initially, the Project team was given access to data on snakebite rates and outcomes in the Myanmar government's health management information system. However, these datasets lack data at population level, because patients may not seek help through the formal health system, or may leave the system for social or economic reasons so that their data are lost to the system.

Which data should be available to the health system to guide snakebite management?

The Project team, using global standards, expert experience and discussions with Myanmar colleagues, developed a set of core pieces of information that would assist decision making processes in snakebite management within the health system.

What is the capacity of the health system to manage snakebite and what skills are currently available among health system staff for snakebite management?

The capacity of the health system to manage snakebite was assessed through discussions with local experts and through a survey at each level of the system within the Project study sites using a specifically developed questionnaire.

What training is required for health system staff to improve snakebite management?

The Project team, in collaboration with other Myanmar colleagues, through a consultative process, guided by local conditions and knowledge of clinical toxinology training developed by some team members over a 20 year period, developed a curriculum for training that allowed training of health staff to start in Project sites. Experiences and feedback from this initial training allowed refinement of the in-service training curriculum and training.

What resources are required by the health system to improve snakebite management?

Through the processes outlined above, we initially determined which resources were needed. Snakebite management algorithms and guidelines were then produced (Figs. 2–6), through a review process involving local users, to ensure their practicability, applicability and, most importantly, local acceptance.

3. Results

3.1. Selection of project sites for activity and intervention

Several key geographic sites were considered including in Yangon and Magwe Divisions, but Mandalay Division proved to be the best, centered on Mandalay General Hospital (MGH; a 2,500 bed teaching hospital), which is a regional centre that admits at least 600 snakebite patients annually, many with severe envenoming, including acute kidney injury. Within the Mandalay health division, Madaya township (MTH) and Kyaukse township (KTH) were chosen as sub-sites. In each, a central township hospital serves a region with numerous smaller towns and villages with Station Hospitals (SHs) or Rural Health Centers (RHCs).

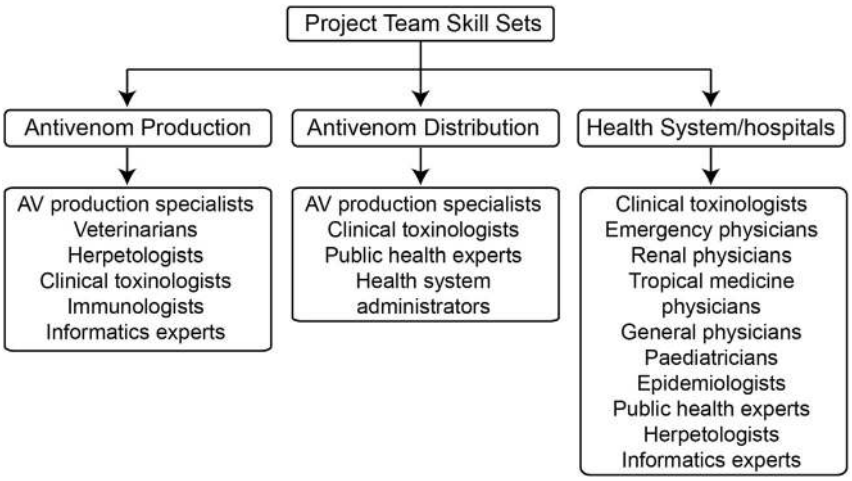
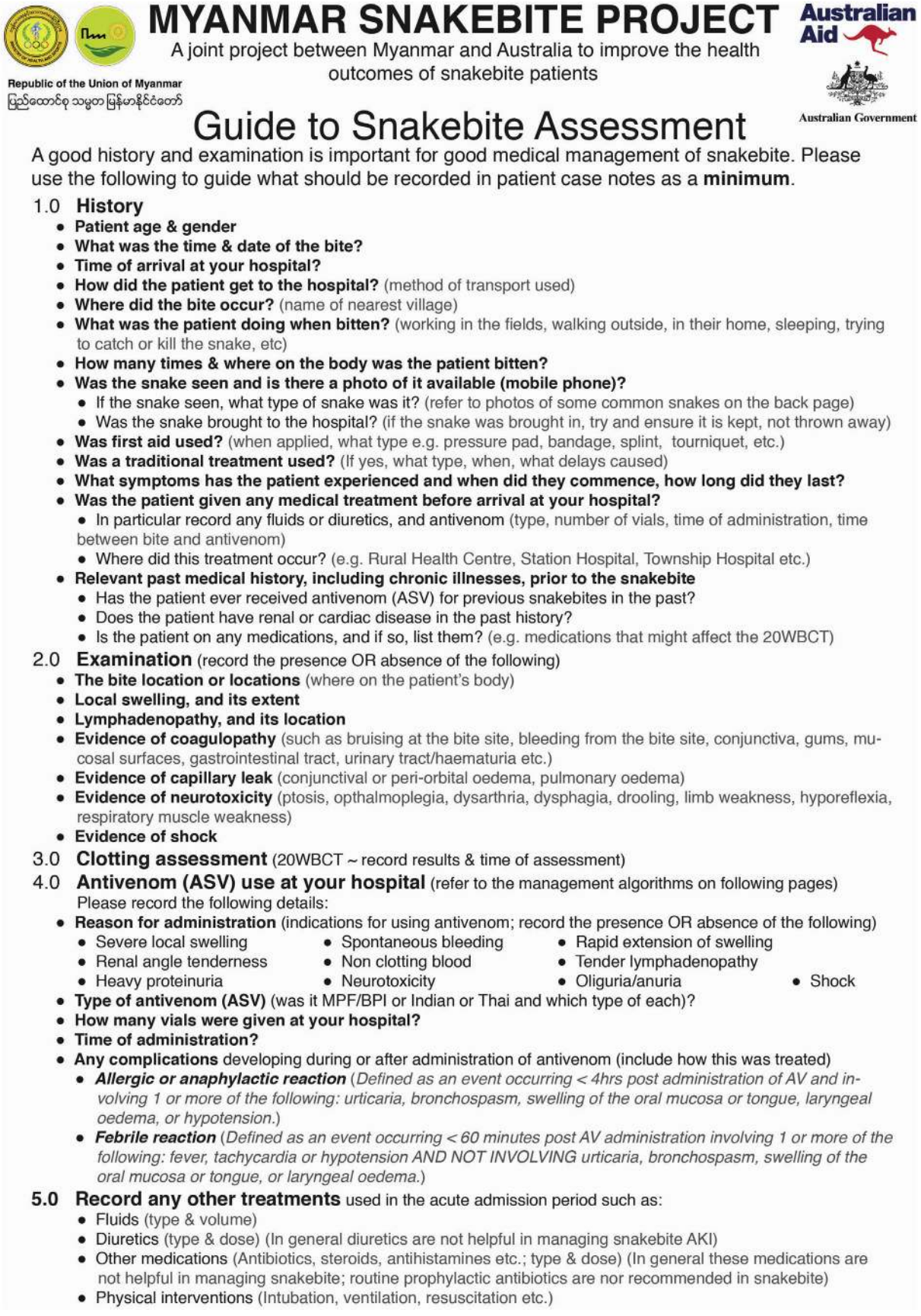


Fig. 1. Diagrammatic representation of Project staff skill sets involved in each of the 3 project sections.



MYANMAR SNAKEBITE PROJECT

A joint project between Myanmar and Australia to improve the health outcomes of snakebite patients

Republic of the Union of Myanmar
ပြည်ထောင်စု သမ္မတ မြန်မာနိုင်ငံတော်

Australian Aid

Australian Government

Guide to Snakebite Assessment

A good history and examination is important for good medical management of snakebite. Please use the following to guide what should be recorded in patient case notes as a **minimum**.

1.0 History

- **Patient age & gender**
- **What was the time & date of the bite?**
- **Time of arrival at your hospital?**
- **How did the patient get to the hospital?** (method of transport used)
- **Where did the bite occur?** (name of nearest village)
- **What was the patient doing when bitten?** (working in the fields, walking outside, in their home, sleeping, trying to catch or kill the snake, etc)
- **How many times & where on the body was the patient bitten?**
- **Was the snake seen and is there a photo of it available (mobile phone)?**
  - If the snake seen, what type of snake was it? (refer to photos of some common snakes on the back page)
  - Was the snake brought to the hospital? (if the snake was brought in, try and ensure it is kept, not thrown away)
- **Was first aid used?** (when applied, what type e.g. pressure pad, bandage, splint, tourniquet, etc.)
- **Was a traditional treatment used?** (If yes, what type, when, what delays caused)
- **What symptoms has the patient experienced and when did they commence, how long did they last?**
- **Was the patient given any medical treatment before arrival at your hospital?**
  - In particular record any fluids or diuretics, and antivenom (type, number of vials, time of administration, time between bite and antivenom)
  - Where did this treatment occur? (e.g. Rural Health Centre, Station Hospital, Township Hospital etc.)
- **Relevant past medical history, including chronic illnesses, prior to the snakebite**
  - Has the patient ever received antivenom (ASV) for previous snakebites in the past?
  - Does the patient have renal or cardiac disease in the past history?
  - Is the patient on any medications, and if so, list them? (e.g. medications that might affect the 20WBCT)

2.0 Examination (record the presence OR absence of the following)

- **The bite location or locations** (where on the patient's body)
- **Local swelling, and its extent**
- **Lymphadenopathy, and its location**
- **Evidence of coagulopathy** (such as bruising at the bite site, bleeding from the bite site, conjunctiva, gums, mucosal surfaces, gastrointestinal tract, urinary tract/haematuria etc.)
- **Evidence of capillary leak** (conjunctival or peri-orbital oedema, pulmonary oedema)
- **Evidence of neurotoxicity** (ptosis, opthalmoplegia, dysarthria, dysphagia, drooling, limb weakness, hyporeflexia, respiratory muscle weakness)
- **Evidence of shock**

3.0 Clotting assessment (20WBCT ~ record results & time of assessment)

4.0 Antivenom (ASV) use at your hospital (refer to the management algorithms on following pages)

Please record the following details:

- **Reason for administration** (indications for using antivenom; record the presence OR absence of the following)
  - Severe local swelling
  - Spontaneous bleeding
  - Rapid extension of swelling
  - Renal angle tenderness
  - Non clotting blood
  - Tender lymphadenopathy
  - Heavy proteinuria
  - Neurotoxicity
  - Oliguria/anuria
  - Shock
- **Type of antivenom (ASV)** (was it MPF/BPI or Indian or Thai and which type of each)?
- **How many vials were given at your hospital?**
- **Time of administration?**
- **Any complications** developing during or after administration of antivenom (include how this was treated)
  - ***Allergic or anaphylactic reaction*** *(Defined as an event occurring < 4hrs post administration of AV and involving 1 or more of the following: urticaria, bronchospasm, swelling of the oral mucosa or tongue, laryngeal oedema, or hypotension.)*
  - ***Febrile reaction*** *(Defined as an event occurring < 60 minutes post AV administration involving 1 or more of the following: fever, tachycardia or hypotension AND NOT INVOLVING urticaria, bronchospasm, swelling of the oral mucosa or tongue, or laryngeal oedema.)*

5.0 Record any other treatments used in the acute admission period such as:

- Fluids (type & volume)
- Diuretics (type & dose) (In general diuretics are not helpful in managing snakebite AKI)
- Other medications (Antibiotics, steroids, antihistamines etc.; type & dose) (In general these medications are not helpful in managing snakebite; routine prophylactic antibiotics are nor recommended in snakebite)
- Physical interventions (Intubation, ventilation, resuscitation etc.)

Fig. 2. Page 1 of snakebite management guide for Myanmar; overview of important assessment points. [Original graphic copyright © Julian White, used with permission].

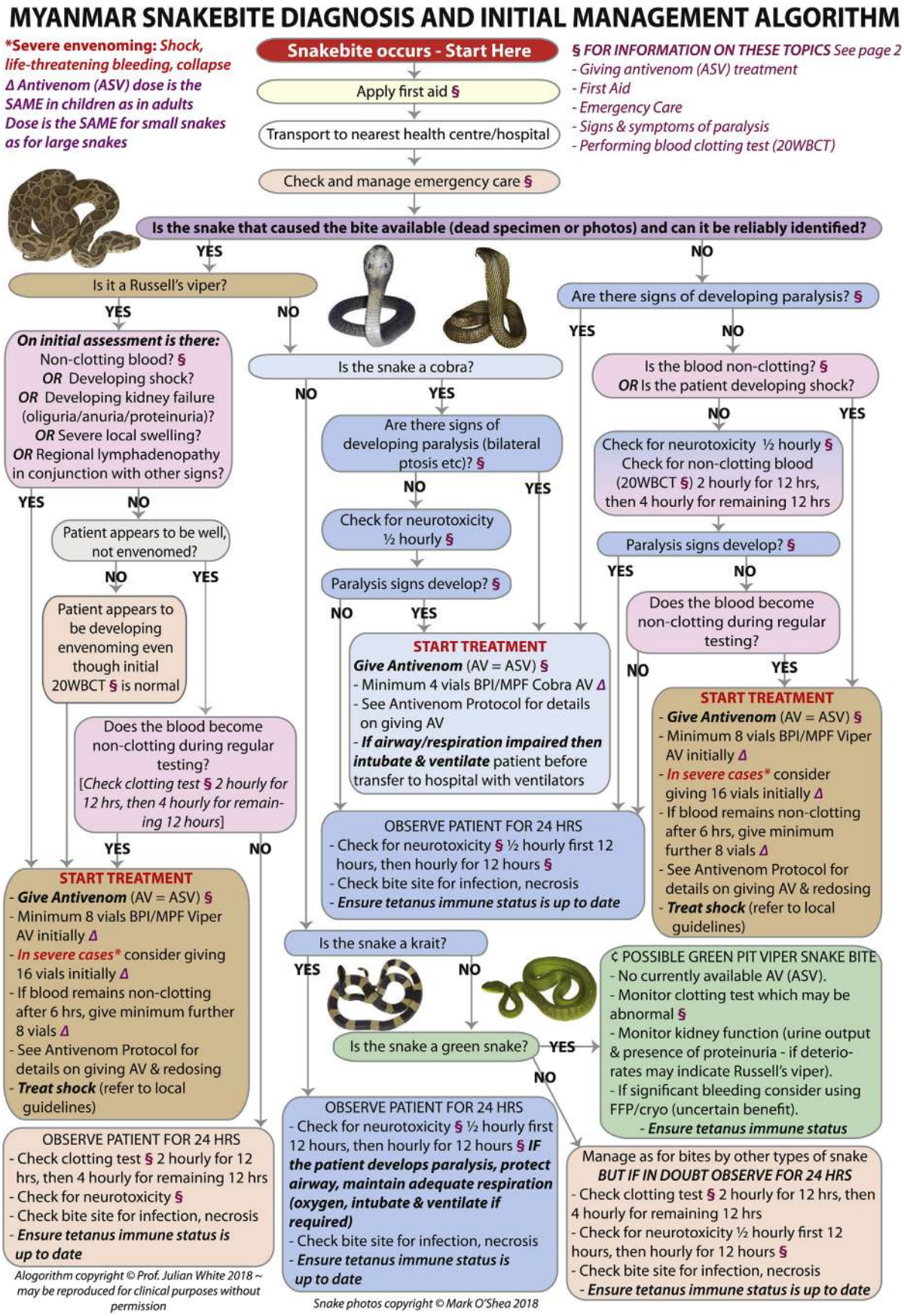


Fig. 3. Page 2 of snakebite management guide for Myanmar; management algorithm. [Original graphic copyright © Julian White, used with permission].

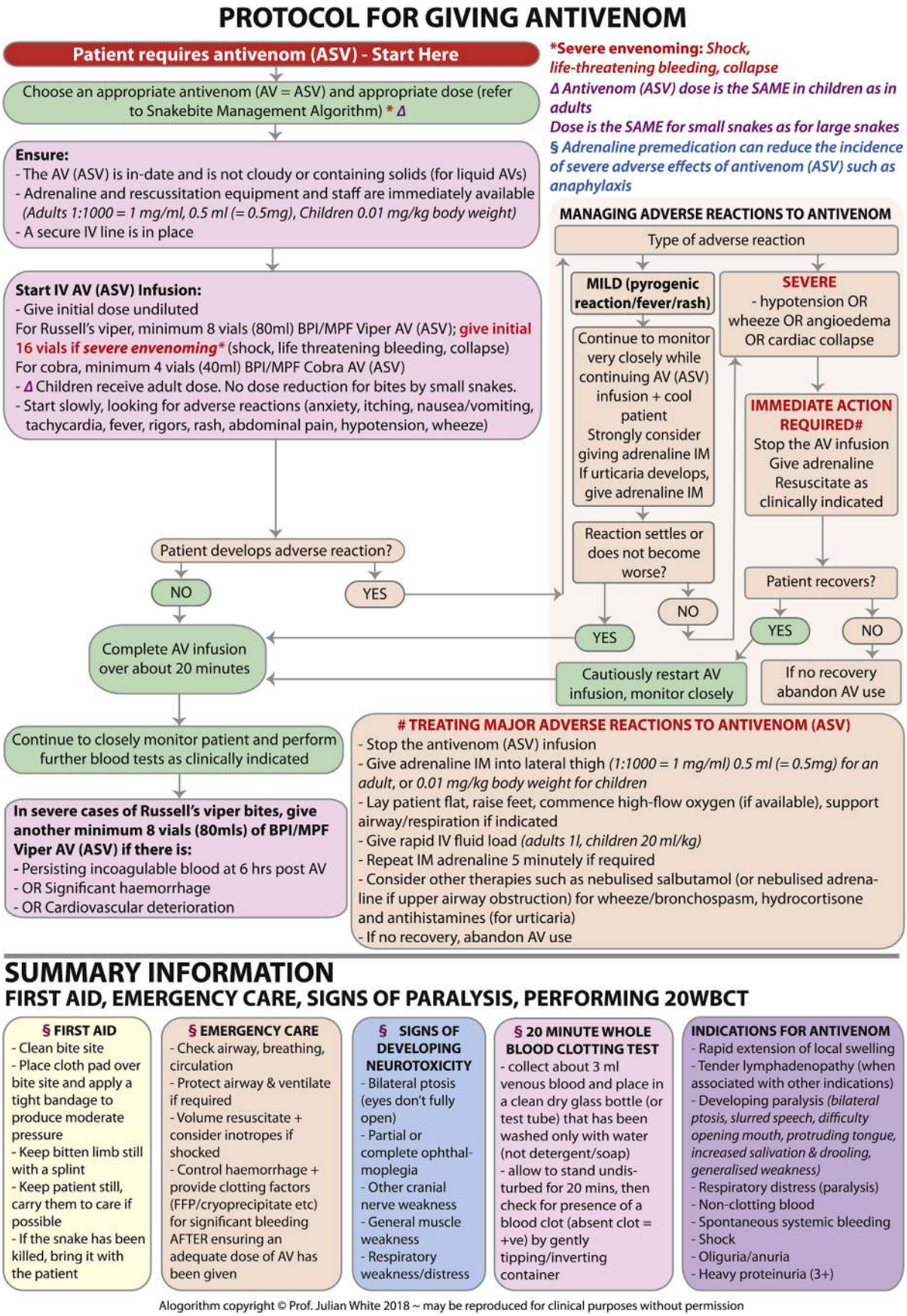


Fig. 4. Page 3 of snakebite management guide for Myanmar; algorithm guiding administration of antivenom. [Original graphic copyright © Julian White, used with permission].

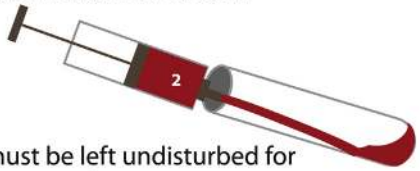
Fig. 5. Page 4 of snakebite management guide for Myanmar; list of clinical issues to consider. [Original graphic copyright © Julian White, used with permission].

Myanmar Snakebite Project

Instructions for Performing the 20 Minute Whole Blood Clotting Test (20WBCT)

The only bedside clotting test that has been scientifically validated to detect coagulopathy in snakebite patients is the 20WBCT. Therefore, we recommend only the 20WBCT.

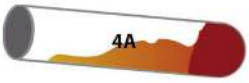
1. The tube used to test the 20WBCT **must be made of *glass*** (NOT plastic) and **must be clean and dry**. Ideally, it should also be new and made from soda-lime glass. Exposure to washing detergent or soap will stop the blood from clotting, a so-called false-positive test result. We recommend that you use only disposable soda-lime glass tubes. If disposable glass tubes are not available, you can use clean glass antibiotic vials after they have been boiled with salt only, never with detergent, soap or other chemicals, and dried afterwards with hot air.



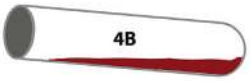
2. **Place about 2mls of venous blood** in the ***glass*** tube.

3. **Let it stand for 20 minutes.** The ***glass*** tube with blood must be left undisturbed for 20 minutes. The tube must not be flicked or agitated whilst waiting for 20 minutes.

4. **At 20 minutes gently invert/tip** the ***glass*** tube checking for the presence of a blood clot. Sometimes, after 20 minutes, a thin layer of serum appears on top of the clot, and this serum may run slightly down the side of the tube when gently inverted. If the tube is left for 30 minutes or longer after the blood has been placed in it, the clot may start to break down, leading to a false-positive result. Therefore, try to read the test at exactly 20 minutes.



4A. **Clot present = negative test** (no coagulopathy present). On gently inverting the tube, ***if there is any clot in the bottom of the tube, the blood has clotted = a negative test***. If a clot has formed after 20 minutes (a negative test), the clot will stop any whole blood from running freely down the side of the tube when gently inverted, but serum on top of the clot may run down the tube. The serum may be yellow or red in colour, but does not have the denser consistency of whole blood. In this case, you can ignore the serum on top of the clot.



4B. **Clot absent = positive test** (coagulopathy present). On gently inverting the tube, if the blood runs down the side of the tube, and ***there is no clot***, it is unclotted (non-clot).

5. If there is any uncertainty about the result of the 20WBCT, a separate 20WBCT ought to be done in parallel using blood from a healthy individual to prove that normal blood will clot after 20 minutes. This is your negative control.

6. If blood from a healthy individual clots after 20 minutes, the finding that blood from a snakebite patient does not clot is a very significant positive test result.

7. If blood from a healthy individual clots after 20 minutes, the finding that blood from a snakebite patient also clots after 20 minutes implies that the patient does not have coagulopathy at that time.

8. If blood from a healthy individual does not clot after 20 minutes, it will be difficult to interpret the result of the 20WBCT from the patient. The most common problem here is contamination of the tube with washing using detergent or soap.

9. Note that the 20WBCT must be repeated at regular intervals after the initial test to detect late-onset coagulopathy.

Fig. 6. How to perform the 20 Minute Whole Blood Clotting Test (20WBCT) provided together with the management guide for Myanmar (Figs. 1–4). [Original graphic copyright © Julian White, used with permission].

Within MGH the Project established strong working relationships with key medical consultant staff who became actively involved in developing both teaching and educational material and programs and advising on development and deployment of case data collection. To achieve this, the active support of the Ministry of Health and Sport and direct involvement as a senior Project team member of the national Director of the Ministry Snakebite Program were vital, emphasising the collaborative approach of this Project.

3.2. Antivenom production

Ministry of Industry; Burma Pharmaceutical Industries factory site (BPI), Insein, Yangon and Hmawbe site, near Yangon.

3.2.1. Venom production

Early scoping visits identified major problems in snake husbandry, specifically a poor snake house, multiple snakes per cage, poor snake health and markedly reduced life span and poor geographic spread of utilised snakes. The Project team, specifically experts in herpetology and clinical toxinology, worked with the local Myanmar staff managing snakes to advise on new methods of snake care, including providing on-site training for key staff at a model snake venom extraction facility in Australia. Snakes were moved to a new purpose-built facility, housed in individual clear plastic containers and managed appropriately, resulting in improvement in snake health. Longevity for Russell's viper remains a problem because of difficulty persuading most snakes to feed appropriately, and solutions to this problem continue to be explored. The issue of geographic variability of snakes to ensure adequate venom variability within pooled venom was identified, and a program to more widely source snakes from within Myanmar has been proposed.

3.2.2. Antibody production

Horse husbandry and high horse mortality were identified as key problems impeding antivenom production. The high horse mortality resulted in an inability to supply local demand, thereby requiring importation of foreign antivenoms that were less well targeted against Myanmar snake venoms. The causes of poor horse health and high mortality were not immediately apparent as horse health data was poorly recorded and many variables were in operation. As this was a critical problem the Project initiated multiple changes simultaneously to ensure rapid improvement. For this part of the Project, team experts in veterinary medicine and antivenom production were critical.

The Project sourced simple technology to allow routine PCV measurement to assess horse health at all stages of the induction, immunisation and bleeding process. This was combined with better assessment of EIA status and vet-supervised visual assessment of horse health. Moving horses to a healthier environment allowing free paddock use rather than limitation to stalls, plus dietary improvements were also initiated. Veterinary assessments revealed that poor horse paddock and facility design were resulting in avoidable injuries to horses with health and mortality consequences, therefore changes to facilities to mitigate against such hazards were initiated. Horse facility staff were provided training on clinical and post-mortem examination techniques, both in Australia and on-site. Reuse of needles used in immunisation was noted and introduction of single-use needles recommended. Replacement of multiple-use bleeding systems with single use isolated systems to maintain sterility was recommended and suitable systems sourced and introduced. Physical separation (quarantine) of incoming stock horses from existing horses, prior to clearance for infectious disease was recommended and initiated and similar separation of horses positive for EIA from the rest of the herd was recommended and initiated.

The horse database was developed specifically for this facility and a staff person employed to ensure accurate data entry, with a view to implementing this database as an ongoing live management system to replace the pre-existing and limited manual card system. The horse database will be handed over to BPI as the Project winds down and BPI have indicated they intend using it as an ongoing management tool.

Another staff member was provided training in Australia to develop ELISA-based detection systems to determine antibody response levels in immunised horses, thereby reducing reliance on destructive small animal (mouse) testing. This ELISA assay is now in routine use at BPI.

The combined effect of these multiple interventions was, over the first 3 years of the project, a dramatic fall in horse mortality (Fig. 7), with improved horse health, longevity, a reduced requirement for annual replacement of horses and a consequent significant rise in production capacity and fall in cost per vial. At time of writing the facility is on track to regain sustainable sufficient antivenom production to meet all Myanmar needs.

3.2.3. Antivenom processing and production

In the first 2 years of the project the principal focus was increasing antibody output. Subsequent efforts have targeted a move towards production of a higher proportion of freeze dried antivenom, and improved quality control of final product. The former is of importance because it became apparent early in the Project that electricity supply throughout Myanmar, especially in rural areas, is unreliable, thus causing cold chain maintenance issues for liquid antivenoms. Freeze dried antivenoms do not have such rigorous cold chain requirements and generally have a longer shelf life which is advantageous if deployed to isolated rural environments where usage may be low, but availability should be maintained given the potentially long delays in seeking antivenom at a larger (but distant) health facility.

The Myanmar producer already had identified this issue and sought Project funding support to assist in the purchase of a suitable freeze drier. The Project contributed a substantial sum to enable purchase of the freeze drier which came online in 2017. As an interim measure the Project funded purchase of a limited number of solar powered fridges for deployment to selected isolated RHCs and SHs to allow storage of current liquid antivenoms, thereby allowing reduced “bite to needle” time in administering antivenom.

The issue of ongoing antivenom quality control will now be addressed, involving input from Australian and other antivenom production experts and training of Myanmar staff in required techniques. The importance of good quality control of antivenom product cannot be over-emphasised. An ongoing challenge is persuading local producers to mount the required clinical trials for newly developed antivenom

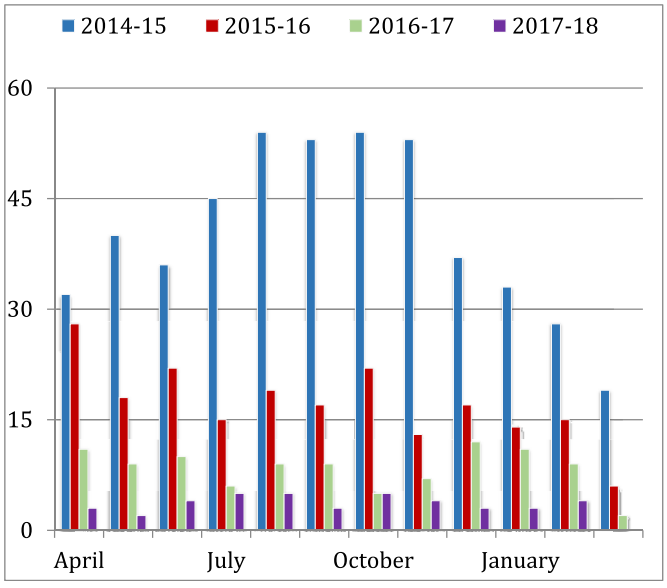


Fig. 7. Monthly horse mortality over 3½ years showing dramatic decline as the Project progressed and interventions were implemented. The Project work commenced towards the end of 2014. Data provided up to February 2018.

products, notably the freeze dried antivenom newly produced from upgraded production facilities, utilizing new equipment and processes.

3.3. Antivenom distribution

The Project, having better established rates of bites and antivenom requirements through activities in other parts of the Project, has now established a coordinating committee, bringing together relevant senior personnel from the Ministry of Industry and Ministry of Health and Sport, to determine a policy on antivenom distribution nationally and develop and deploy a process to achieve this.

3.4. Health system management of snakebite

3.4.1. Community survey

The community health survey involved 144 villages, 4276 households and 19,877 people. Detailed analysis of this data is ongoing, but initial analysis indicates that snakebite is more common and deaths more frequent than currently recorded through the health system. This will have clear implications for health system resource allocation in future and may provide key data to design strategies to improve patient and system outcomes.

3.4.2. Community empowerment

Education and training directed towards disease prevention, first aid skills and information promoting early transfer of patients to suitable health care facilities where appropriate is amongst the most important aspects of addressing public health problems. Therefore the Project focused on community empowerment through education and skills development. This was achieved through various interventions. As part of the process of gathering data, the Project staff and all primary care outreach workers in the government sector were trained to deliver public education on prevention of snakebite. The data collecting staff provided education to more than 4,000 respondents for the community survey. The primary care outreach workers were also trained to conduct community meetings and provide health education and basic first aid skills. These meetings were conducted in more than 200 villages in the Project sites, providing education to another 6,000 people. Furthermore, the project, in collaboration with government health care staff, identified community health activists in 150 villages and working with the Myanmar Red Cross Society, provided extensive training to these community 'champions' who will act as a community resource and can pass on knowledge and skills to the rest of the local community.

3.4.3. Primary care staff training

Consultations with the healthcare staff across primary and secondary care facilities indicates that if "bite to needle" time is to be reduced, staff training in newly provided RHC resources (particularly antivenom use) is essential. The Project has commenced training of RHC staff within the study areas.

3.4.4. Case data collection

Through a collaborative process a case data collection system using a tailor-designed and built database and derived data collection forms has been developed and data collection commenced, first at MGH and now at a number of other hospitals. Site specific data on snakebite incidence, antivenom utilisation and clinical outcomes is now provided to Myanmar based clinicians and health administrators via quarterly reports generated by the Project.

3.4.5. Provision of education to health workers

The Project has worked with Myanmar colleagues to develop health worker training in snakebite management, based on pre-existing resources developed in Myanmar and supplemented by skills and knowledge provided through Project senior team members. Initial training has been provided to health staff at multiple levels within the Project activity zones. The long term requirement is to develop a core of senior trained personnel ("master trainers") within the Ministry of Health and Sport who will "train the trainers", allowing deployment of training in snakebite management to be deployed in a sustainable manner nationwide. Project senior team members are working with senior Ministry staff to develop a process to achieve this goal and once staff are identified and appointed by the Ministry, high level training of these "trainers" will commence using materials and information already developed (Figs. 2–6). In coordination with this, new curricula for snakebite are being developed at the undergraduate level (medicine, nursing, allied health), for implementation country-wide.

Management plans and algorithms to guide treatment of snakebite patients have been officially developed by the Project team and the government regional health services in Mandalay (Figs. 2–6). These clinical support documents have been provided directly to clinicians in all Project sites. The acceptance and utilisation of these tools has been so high amongst local Myanmar health workers that they are now being adopted in other regions within the country independent of Project activity. The Ministry of Health and Sports have indicated they will deploy this written material countrywide.

4. Discussion

Snakebite is still an important disease in many parts of the rural tropics and affects particularly the rural poor, hence it is a predominantly occupational disease affecting farmers. The numbers of people affected dwarfs those affected by many officially recognised Neglected Tropical Diseases, yet snakebite does not yet enjoy the international resources brought to bear on those NTDs. It is hoped that official WHO recognition of snakebite as an NTD will now allow focus of international resources to tackle this problem. This issue has been, in recent times, highlighted in the literature, as earlier mentioned (Gutiérrez, 2014; Gutierrez et al., 2010, 2013, 2014, Habib et al., 2015; Harrison et al., 2011, Harrison and Gutiérrez, 2016; Kasturiaratne et al., 2017; Warrell, 2010; Warrell et al., 2013; Williams, 2015; Williams et al., 2011). The Myanmar Snakebite Project provides a practical model for addressing snakebite as a health issue in these environments, with a holistic approach covering many aspects.

Addressing public health problems requires a people-centered primary health care (PHC) approach, which incorporates comprehensive and integrated health care with the community at the centre of development (WHO, 2008). Integrated care is about making available to people a continuum of health education, preventive actions, and effective treatment and rehabilitation. The project adopted the PHC approach and continuum of care through education, first aid training, training of primary care workers, training of hospital based staff and strengthening of services and resources at all facilities from rural health centers to hospitals. It has been noted that the key to successful international assistance, in terms of strengthening health systems and effective management of public health problems, by collaborative projects, is to strengthen rather than undermine the local control, facilitate strengthening of governmental health service structures, and working through sustained equitable professional relationships between locals and expatriates (Feiffer, 2003). With this in mind, the Project international experts worked hand in hand with the local partners to facilitate development within the government sector rather than opening up the Project's own "shop-front". The collaborative, cooperative nature of the intervention, emphasised foreign experts working with and alongside Myanmar colleagues to consider and develop and deploy solutions. Technology and skills transfer, with a focus on strengthening the existing resources, is a key to achieve long term local sustainability rather than reliance on outside support.

The community survey provided clear evidence that the actual community impact of snakebite was more substantial than official government hospital-based data might indicate, in line with studies elsewhere (Ediriweera et al., 2016; Iliyasu et al., 2015; Lam et al., 2016;

Vongphoumy et al., 2015). We consider that such a community-based epidemiologic study, managed by experts in public health, provides essential information required for understanding the health impact of snakebite and the development of appropriate system-level responses to improve outcomes.

The case data collection, once fully analysed, will provide valuable information that can be correlated with the community survey to indicate specific problem areas requiring intervention. However, even crude data from this process provides useful information for other areas of health system planning. An example is antivenom use in total vials; the current case data indicates that in the MGH it is BPI Viper Antivenom that is used predominantly (8,848 vials), with only a small amount of BPI Cobra Antivenom used (30 vials), information which can be used to ensure appropriate antivenom stocking by the Ministry of Health and Sport and efficient production targets for each antivenom, to meet actual need, by the Ministry of Industry, potentially avoiding wasteful overproduction of Cobra Antivenom. Similar data, once available for other parts of Myanmar, can indicate whether this pattern is universal, or whether the patterns of antivenom use are region-specific, again allowing better targeting of antivenom production, inter-Ministry purchasing, and deployment to areas of need.

The dramatic improvements in horse health and longevity have allowed rapid progress towards national antivenom self-sufficiency for Myanmar, a result which arguably justifies the simultaneous deployment of interventions in multiple areas, even though that compromised ability to isolate specific factors contributing to poor horse outcomes. It is likely that horse health is impacted in a complex multifactorial manner by diverse variables including a multitude of potential infections, immediate environment, nutrition, pre-existing health, genetics, levels of care provided, staff skills and training, production requirements, the latter potentially conflicting with best practice horse health care. By continuing to closely monitor aspects of horse health and husbandry, alongside antivenom production parameters such as immunisation and bleeding schedules, emerging issues can quickly be detected and remedial action taken. Implementing a database driven field management system for this aspect of antivenom production poses challenges, including resistance amongst older or long-time staff used to old methodologies and uncomfortable with newer technology and methods. Adequate education, training and encouragement may be applied to overcome this unfamiliarity. Demonstrated success of interventions and new methodologies of care may assist in enthusing existing staff about support for a process of continuous improvement.

While it may be too soon to determine the effectiveness of Project interventions in the area of pre-hospital and in-hospital care of snakebite patients, studies elsewhere have indicated the importance of appropriate training at all levels within the health system and, similarly, the value of a coordinated national approach and use of guiding protocols (Monzavi et al., 2015). The Ministry of Health and Sports, Myanmar, have indicated a desire to fully implement Project recommendations, including a nation-wide adoption of the snakebite diagnostic and treatment algorithms and information developed by the Project and continuation of snakebite case data collection across many hospitals, to monitor patient outcomes and resource utilisation.

Limitations of this study include the necessity to limit epidemiologic studies, community education and case data collection to circumscribed areas because of the logistics involved. A wider community survey of snakebite, across a diverse array of regions and habitats may have delivered a more comprehensive view of the impact of snakebite. However, by selecting areas with known or expected significant snakebite incidence, representative of the broad areas of risk involving much of the Myanmar rural farming population, we consider our data is representative and scalable to estimate approximate national risk profiles. It will not cover lesser populated regions with different habitat and snake fauna, such as hilly forested areas and coastal areas where traditional fishing may risk exposure to sea snake bites. Our success with establishing collection, preservation and expert identification of snakes involved in snakebite was less successful than we had hoped for, in part because it proved more difficult than anticipated to gain permission for and successfully establish systems to enable snake collection. We recommend that establishing viable snake collection systems be prioritized early in future projects similar to ours. Similarly, early prioritization of field snake collection by herpetologists would have provided our project with valuable data. Unfortunately, logistic issues prevented us from undertaking such field work until late in the Project, limiting effectiveness. Conversely, the delayed field collection allowed us to better prioritise which snakes were of particular interest. Establishing effective working relationships between locals and external project staff is critical, but can take considerable time and effort, particularly in relation to senior bureaucrats within key areas of government. We were fortunate to already have some key contacts at the commencement of our project. In developing and undertaking foreign aid projects such as ours there is a risk that scarce government resources may be stretched too thinly by trying to meet project requests, with potentially adverse outcomes. We managed this problem by ensuring we funded sufficient local resources as part of the project, to avoid such negative impacts on existing resources, a particular issue when interfacing with a very busy health system.

Conflict of interest statement

The Myanmar Snakebite Project, documented in this paper, is a foreign aid project with a central aim to “improve outcomes for snakebite patients in Myanmar” and has been principally funded by the Australian Government Department of Foreign Affairs and Trade. The Project relies on “in kind” contributions, principally donation of time by individuals, mostly employed by other institutions. These involved institutions are Myanmar government Ministry of Industry and Ministry of Health and Sports; University of Adelaide; Women's & Children's Hospital, Adelaide; Royal Adelaide Hospital; CSIRO Animal Health Laboratories; Seqirus Ltd; Venom Supplies; University of Sydney.

David Bacon is employed by the Project, through the University of Adelaide, as a manager, based in Myanmar. His income is therefore derived directly from Project funds.

Conflicts of interest

The authors declare no conflicts of interest in relation to this work.

Ethical statement

This paper has no ethical issues. There are no financial conflicts for authors. No patient information is provided which might allow identification of a patient. No clinical trial studies are herein reported. No animal research studies are involved. Ethics approval for all Myanmar Snakebite Project work has been granted by both the University of Adelaide and the Department of Medical Research, Myanmar.

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Transparency document

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