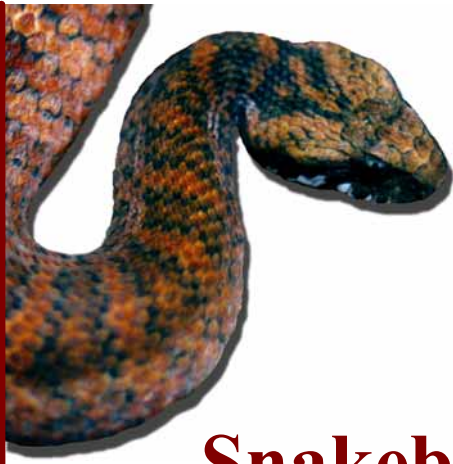


2004 Course Handbook



Clinical Management of Snakebite in Papua New Guinea

Editors: David Williams, Dr Simon Jensen & Dr Kenneth D Winkel



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Table of contents

Acknowledgements

Introduction

1	Snakebite in Papua New Guinea: Facts & Fiction	1.1
2	The snakes of Papua New Guinea	2.1
3	The composition and actions of Papua New Guinean snake venoms	3.1
4	Symptoms and signs of snakebite in Papua New Guinea	4.1
5	First aid for snakebite in PNG	5.1
6	Patient Assessment and Diagnosis	6.1
7	Treatment Overview	7.1
8	Clinical assessment and treatment of neurotoxicity	8.1
9	The assessment and treatment of coagulopathy	9.1
10	Treating other effects of envenomation	10.1
11	The role and use of antivenom in Papua New Guinea	11.1
12	The use of anticholinesterase therapy	12.1
13	Managing the respiratory effects of snake envenomation	13.1
14	Management plans for snakebite patients	14.1

Appendix: CSL snake venom detection kits

Glossary of medical terms

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David Williams

Course Co-ordinator 2004

Introduction

David Williams

Many of us know the feelings of urgency and helplessness that come when a sudden knock at the door in the early hours of morning brings the news of yet another seriously ill snakebite patient arriving at our aid posts, health centres and hospitals. Often these patients will already be in the terminal stages of severe neurotoxic paralysis, and without transport, medicines or modern hospital equipment, we are left with little to do but stand by and watch as they slowly slip away to become yet another victim of the deadly reptiles that live in our midst.

Snakebite is a medical emergency, and we live in a country where venomous snakes, although few in variety, are many in number. As you will hear during this course, the incidence and mortality rates after snakebite in Papua New Guinea are among the highest reported in any part of the world. This is in stark contrast to the experience of our neighbour Australia. Despite having many of the same species, and much higher populations living in areas with abundant snake populations, snakebite in Australia is a very minor problem at community level. With just one quarter of Australia's population, and perhaps 200 more deaths from snakebite each year, PNG's snakebite mortality rate may be as much as 800 times greater than Australia. The gap between PNG's snakebite problem and snakebite in Australia does not end there.

With a much larger revenue-contributing population, stronger resource base and solid economic foundation, Australia has some of the best medical facilities in the world. Even in many of our smaller towns and villages, there are qualified doctors working in hospitals that are well equipped. In our most remote areas we are able to extend viable emergency medical services with a long-established privately-funded aeromedical retrieval service, the Royal Flying Doctor Service. A person bitten by a venomous snake in Australia's arid heart can be retrieved using a well-equipped medical airplane, and may find themselves recovering in a large, modern city hospital in just a matter of hours. Snakebite is, nevertheless, still considered to be a very serious medical condition, and even in the most modern Australian intensive care units, snakebite patients may still have a guarded prognosis.

Here in PNG, where the economic base of the country remains in its formative years, the challenges of basic service delivery, education, transport, health, housing and policing remain great. With limited resources, and a plethora of important health issues to overcome, PNG faces a much more difficult road to prosperity. Common diseases like measles kill hundreds every year, malaria and other tropical illnesses are endemic, and the spectre of HIV/AIDS currently looms like a guillotine above the head of a condemned man. Rural hospitals and clinics do not usually have qualified doctors on hand, and resources, equipment and essential drugs are often in short supply. Medical evacuations, if and when they are carried out, come at a high cost, one beyond the economic means of most grassroots Papua New Guineans. Relative antivenom costs in PNG are much higher than in Australia, and high prices mean that even with increases in funding allocations, there simply is not enough money available to purchase sufficient antivenom for all cases. Without the benefits of modern medical facilities, a Papua New Guinean snakebite victim faces a struggle to survive that is frequently lost.

With so many challenges to overcome, one could be forgiven for thinking that survival after snakebite is a slim possibility, and while the chances of death are certainly higher in PNG than in Australia, the reality is that many people do survive snakebite.

A good part of that survival is due to the dedication and experience of health personnel who work hard against numerous obstacles to provide their patients with the best care they can provide. Well-trained and well-informed health workers are vital to the delivery of health services, and, for that reason, we have developed this training course to equip rural and urban health workers with the skills and knowledge needed to improve their snakebite assessment and management skills even further.

We aim to show you how to work with the resources that are at your disposal in the most effective and efficient manner. We will teach you the most appropriate, practical snakebite treatment techniques for your service delivery environments, and we are going to build up your knowledge base and ability to make the most of the resources that you already have. By addressing issues concerning the timeliness and use of safe, efficacious first aid treatments, the assessment, diagnosis and treatment of patients, and the care and support of patients with respiratory distress, we will try to help you learn to make the most of your resources in order to improve the prognosis for snakebite patients.

At the completion of this course we hope that you will return to your communities with the skills and knowledge to approach the treatment of snakebite with new confidence. We also hope to stimulate, in all of you, an interest in teaching what you have learned to your colleagues and staff, and in proactively helping your communities to learn proper snakebite first aid techniques as a way of improving their chances of survival even further.

Finally, we would like to see some of you take an active interest in snakebite research, and to perhaps, one day, be able to replace us as the instructors of this course.

Snakebite in Papua New Guinea

Facts & Fiction

David Williams

Introduction

Snakes are widely feared in Papua New Guinea, and with very good reason. In many parts of PNG snakebite is an almost daily occurrence and venomous snakebite is a serious public health problem, with localized incidence rates that are among the highest of any tropical region in the world. Medical and epidemiological studies of snakebite in different parts of the country have given us detailed snapshots of some of the outcomes of snakebite, and although there are still many gaps in our knowledge, there is a significant amount of factual data available.

Ask anyone about snakebite and they will undoubtedly have a story to tell about someone they know who was bitten by a snake, or who died of snakebite. It would in fact be very easy to believe that venomous snakes lie in wait for unsuspecting people at every turn, and that right across PNG snakebite is claiming dozens of lives every day. If you ask Papua New Guineans about which snakes are responsible for snakebite one species above all others will feature at the forefront of every conversation; the fearsome ‘Papuan (Pap) black’.

Of course the challenge for clinicians, health workers and scientists when it comes to snakebite is to separate the finely woven threads of fact and fiction:

- *Just how many people really are bitten by snakes, and in what parts of the country do these bites occur?*
- *Are there as many deaths as either the scientific data, or the local people would have us believe?*
- *Which species are dangerous and bite the most people and which are not?*
- *What types of antivenom will best suit the needs of certain areas of the country?*

We have to be able to answer these and many other questions in order to provide the victims of snakebite with the most appropriate medical care. Having factual data enables resources (including antivenoms) to be distributed to the right places, and most importantly of all, reliable data provides health managers with the information they need to be able to make the right funding decisions to address community needs.

At the present time however the extent of our knowledge lacks national clarity; there are many provinces throughout the country for which we simply have no reliable data. Without even basic information it is extremely difficult to give clinicians and health workers exact information about snakebite in their communities, and it is completely impossible to provide sound advice to health administrators. As you will learn in this chapter, research into the epidemiology and clinical consequences of snakebite is taking place, and we have learned quite a lot about snakebite over the last fifty years. We hope to stimulate your enthusiasm to assist in ongoing research and to develop our knowledge even further.

Local beliefs & perceptions of snakes and snakebite

Snakes occupy an important role in local culture and tradition, and it is these beliefs and perceptions that affect the ways in which Papua New Guineans deal with the issue of snakebite and snakes in general. In many communities across PNG snakes are considered to be the mortal shells of bush spirits, demons, or deceased ancestors, enemies and sorcerers. There are numerous legends that tell of fearsome demons which take the natural form of snakes. The Marind-anim people from south-western PNG and eastern Papua believe, for example, that a demonic old woman known as the *pathogu* steals young children while in the body of a snake. To the Orokolo people living to the west of Kerema in Gulf province, snakes are the homes of mythical bush spirits – dark and dangerous creatures that can cause untold trouble.

Many Mekeo people believe that the dreaded ‘Papuan black’ attacks people at the behest of a sorcerer who may have first stolen something personal from the victim and have placed it into a heated pot containing the body of a snake. A similar belief is held by the Kiwai people from the Fly River delta; the *ove-devenar* sorcerer will collect the faeces of his victim and put it into the mouth of a snake model made from wood or clay which he then places in an area that the victim is likely to visit. The model becomes a living snake which hunts and kills the *ove-devenar*'s target. The Elema people of Gulf province believe in an evil spirit called *ove-hahu* who is the cause of accidents, serious sudden illnesses and snakebite. Similar traditional beliefs about snakes are held by the Arapesh people from the Sepik region, and by many other clans throughout PNG.

In Central province, the coastal Motu-Koitabu and mountain Koiari peoples often believed that snakebite, as well as being a tool of the *vada* (sorcerer), was sometimes a punishment meted out by good spirits such as the *birava* for social and traditional crimes like adultery. The Keakalo people of Marshall Lagoon also believed that snakebite was a common punishment for social transgressions such as adultery, theft, spousal abuse or taboo-breaking. As well as this, their *mega mega auri* (snake senders) could not only use magic to send out a snake to bite someone, but could also be sought out and paid to administer a cure. Dr Charles Campbell, a physician who conducted the first medical studies of snakebite in PNG learned that this cure usually involved obtaining a variety of tree bark called *paia* and a rainforest vine *wamela* which were chewed by the *mega mega auri* and then blown onto the face and body of the victim, who would also be massaged with coconut flesh or milk and *kiki* leaves. Chewing the *paia iwoa* (ginger leaves) and *wamela* was also considered to be a way of deterring snakes from biting.

Just as snakes are associated with evil deeds, dark spirits and sudden death, they are also widely held to play an important role in fertility and the guardianship of important traditional sites. The Kamea people (known as the Kukukuku by outsiders) live in the remote highlands of Gulf and Morobe provinces. These small, strongly built people, with an infamous warrior tradition and a fearsome reputation, have many animistic beliefs and some of them believe strongly that an enormous snake keeps the world functioning and protects us all. This creature is guarded by benevolent sorcerers who engage in a constant struggle to protect the snake from evil sorcerers who would kill it, a calamity that would spell the end of the world.

Kiwai people in Western province believe that the mythical *maigidubu* snake spirit is crucial to the success of yam crops, and that if the *maigidubu* leaves its tracks through the crop around the time of the yam festival, then success will be assured. Also, their guardian spirits the *etengena*, would often take the form of snakes and stand guard over their gardens, biting intruders to send them away.

Trobriand Islanders believe that some snakes are sacred and either house the spirits of great chiefs, or are their reincarnations. All the same, finding such a snake in a village was not considered a good sign, and unless the creature could be tempted to leave with prayers or other offerings, sudden illness was likely to befall the entire community. Despite this dreadful possibility, it was taboo to kill the snake, as this would only make the consequences worse.

The Bariai of West New Britain tell the tale of Moro, a snake-man who started the tradition of pig exchanges and other ceremonies in honour of firstborn children, and to give praise to the dead. Legend has it that Moro's father Kamaia had been killed in a disagreement with his brothers-in-law, and his liver cut out and cooked. Later during his funeral Moro was tricked into eating some of the liver by his cousin-in-law Kaukave whereupon his two legs immediately became fused together and the entire lower half of his body was transformed into that of a snake. Moro's transformation is ascribed to the vengeful punishment of his father's ghost for the having consumed the liver, albeit unknowingly. Pursued by the ghost of his father, Moro and his mother escape after Moro uses magic to carve out the Amara River, and then tricks the ghost into trying to cross, only to be eaten by a large crocodile!

Distinctions between different types of venomous snakes are made by many of the people living in southern PNG although different names may sometimes be used by different clans of the same language groups for exactly the same snake, and other groups use just one name to describe different venomous snakes:

Papuan taipan (*Oxyuranus scutellatus canni*)

Moveave (Gulf)	<i>Lavai</i> – 'black snake with a red stripe that lives in long grasses'
Mekeo (Central)	<i>Auguma</i> – 'black snake that bites again'
Motu-Koitabu (Central)	<i>Kabagi</i> – 'red snake' by the people of Barune <i>Larana Karo</i> – 'long blacksnake' by the Barune people <i>Duba</i> – dark coloured snake by the Kila Kila people
Keakalo (Central)	<i>Relena Gamara</i> – 'big brown snake'

Papuan blacksnake (*Pseudechis papuanus*)

Moveave (Gulf)	<i>Mito</i> – 'black snake that lives in Sago swamps'
Mekeo (Central)	<i>Auguma</i> – 'black snake that bites again'
Motu-Koitabu (Central)	<i>Larana Karo</i> – 'long blacksnake' by the Barune people <i>Duba</i> – dark coloured snake by the Kila Kila people
Keakalo (Central)	<i>Gelema rupa</i> – 'black snake'

Death adder (*Acanthophis* spp.)

Mekeo (Central)	<i>Afi</i> – 'sharp-eyed snake'
Motu-Koitabu (Central)	<i>Asenamo Api</i> or just <i>Api</i> – 'short sharp-tailed snake'
Keakalo (Central)	<i>Vanaame</i> – 'short snakes that jumps'

Neither the Mekeo nor Kila Kila Motu people make a significant distinction between taipans and blacksnakes and use just one name each to describe the two different species. Even the people of the Moveave region in the east of Gulf province, while using different names to describe taipans and blacksnakes, identify both as 'blacksnakes'. The majority of people are also able to distinguish venomous snakes from non-venomous pythons and other snakes. The Motu people know pythons as *Navara*, while their Koitabu cousins use *Lavara*, and the Keakalo call large pythons *Kapari* and may consider some of them sacred spirit animals.

When is a *black* snake not a blacksnake?

The use of colour to describe and identify snakes is common all over the world. In Australia snakes with stripes are called ‘tiger snakes’ (although the reality is that not all of them have stripes), and even in Papua the small-eyed snake (*Micropechis ikaheka*) is called a ‘tiger snake’ because of the striped appearance of some specimens. Brown-coloured snakes in Australia were given the obvious name ‘brown snake’ while black-coloured snakes are called ‘blacksnakes’; even though at least one member of the ‘blacksnake’ taxonomic group is called a ‘king brown snake’ (*Pseudechis australis*) because it is actually a brown-coloured ‘blacksnake’!

In Papua New Guinea people tend to do exactly the same thing. All black-coloured snakes are called ‘blacksnakes’ based entirely on the colour of their bodies. Whether or not they happen to really be venomous Papuan blacksnakes (*Pseudechis papuanus*) is an entirely different issue. There are in fact many different types of black-coloured snakes in Papua New Guinea, some of them non-venomous, some moderately venomous and three that are highly venomous and very dangerous; they include:

Black whipsnakes (<i>Demansia vestigiata</i>)	Moderately venomous
Boelen’s pythons (<i>Morelia boeleni</i>)	Non-venomous
Brown-headed snakes (<i>Furina tristis</i>)	Moderately venomous
Common tree snakes (<i>Dendrelaphis punctulatus</i>)	Non-venomous
D’Albert’s pythons (<i>Leiopython albertisi</i>)	Non-venomous
Death adders (<i>Acanthophis</i> spp.)	Highly venomous & dangerous
Forest snakes (<i>Toxicocalamus</i> spp.)	Moderately venomous
Javan file snakes (<i>Acrochordus granulatus</i>)	Non-venomous
Mangrove snakes (<i>Myron richardsoni</i>)	Moderately venomous
Muller’s crowned snakes (<i>Aspidomorphus Muelleri</i>)	Moderately venomous
New Guinea ground boas (<i>Candoia aspera</i>)	Non-venomous
Papuan blacksnakes (<i>Pseudechis papuanus</i>)	Highly venomous & dangerous
Papuan taipans (<i>Oxyuranus scutellatus canni</i>)	Highly venomous & dangerous
Slatey-grey snakes (<i>Stegonotus cucullatus</i>)	Non-venomous
Solomon’s coral snakes (<i>Salomonelaps par</i>)	Moderately venomous
Water pythons (<i>Liasis mackloti</i>)	Non-venomous

With so many different ‘Papuan (Pap) blacks’ distributed throughout the country it should be very obvious why this almost supernatural snake ends up being blamed for virtually every snakebite that occurs in PNG!

It should also be very clear why some bites by ‘Papuan blacks’ cause absolutely no clinical illnesses at all, while other may produce minor signs, and still others are lethal.

There is **ONE** snake in this list that really is a Papuan blacksnake (*Pseudechis papuanus*) both in colour and scientific identity. It is a highly venomous species, but the reality is that, of the venomous snakes in this list of sixteen different types of snakes, only three are highly venomous, and of these, the one which causes the majority of snakebites is not a ‘Papuan black’ at all, but the actually the much more dangerous and much more venomous Papuan taipan (*Oxyuranus scutellatus canni*). In Central province taipans cause more than 80% of all snakebites, while Papuan blacksnakes (*Pseudechis papuanus*) cause less than 5% of the serious snakebites admitted to PMGH.

Can you pick the REAL Papuan blacksneke?



A



B



C



D



E



F



G



H

Turn to the last page of this Chapter to see if your attempt at identification was correct or not.

Common misconceptions about snakebite

There are several common misunderstandings and misconceptions about snakes and snakebite in Papua New Guinea:

Belief: **The majority of snakebites are caused by the Papuan blacksnake.**

Reality: From a medical perspective, this is a particularly dangerous misconception that can seriously harm a snakebite patient.

The clinical reality is that there is little evidence to show that the **real** Papuan blacksnake (*Pseudechis papuanus*) causes large numbers of snakebites, particularly in Central province where investigations using venom identification assays have shown that only 4.3% of the serious snakebites admitted to Port Moresby General Hospital were caused by this species.

In Milne Bay, Gulf and Western provinces, it is still possible that a larger proportion of snakebites are caused by the Papuan blacksnake, but at the present there is very little reliable evidence available. Papuan blacksnakes do not occur in any other parts of Papua New Guinea.

In Central province the evidence suggests very strongly that the majority (more than 80%) of serious snakebites admitted to PMGH are caused by Papuan taipans (*Oxyuranus scutellatus canni*). In the past people have died as a result of the mis-identification of taipans as ‘blacksnakes’.

Belief: **The death adder uses a poison spine on its tail to harm people.**

Reality: This is completely untrue. The soft spine-like projection on the end of a death adders (*Acanthophis* spp.) tail contains nothing toxic, and has no role in the injection of venom.

The ‘spine’ is nothing more than a lure that is wriggled by the snake in order to attract food – just like dangling a worm on a fishing hook. When a small lizard or frog tries to eat the lure, the snake bites the animal killing it with venom injected through fangs in the roof of the mouth.

Belief: **The forked tongue of a snake is a poisonous sting.**

Reality: The tongue of a snake is completely harmless. It is a specialised scent organ that is used to collect odours from the air and deposit them in a special organ on the roof of the mouth (Jacobson’s organ) that contains the same types of olfactory cells that occur in the human nose, and which allow us to smell – the tongue does nothing more than help the snake detect smells and odours.

Belief: **All snakes are venomous.**

Reality: This belief could not be further from the truth; of the 112 species of snakes that occur in Papua New Guinea and Papua, only a third are venomous, and of 37 species, there are currently only 6 land snake species known to have the ability to cause human fatality. The two species of sea krait (*Laticauda* spp.) can also cause death, as can several species of true sea snakes; but sea snake related deaths are very rare in PNG.

Epidemiology of snakebite in PNG

Although the first published medical report of snakebite in Papua New Guinea did not appear in the literature until 1961, the risk to public health presented by venomous snakes was well known, and snakes generally were (and remain) widely feared.

While the Papua New Guinean perception of snakebite may have revolved around the traditional beliefs of the various cultural and social groups throughout the country, the perceptions of colonial medical officers was tempered by 'western' attitudes which had by the start of the 20th Century largely turned away from belief in supernatural forces towards acceptance of 'scientific' conclusions that were based on rational hypotheses, demonstrable facts and clinical reality. Significant advances in human understanding of basic physiology and biology provided a vastly different perspective of the causes of the clinical effects seen after snakebite. Rather than being considered as the result of sorcery, colonial doctors had a strong belief that snakebite was the consequence of the physiological changes produced by organic toxins.

Over the last 5 decades there has been considerable interest in the problems associated with snakebite in PNG, and a number of epidemiological and clinical studies, aimed at learning more about the consequences of snakebite and the outcomes of various treatment strategies, have been carried out. As a result there exists a considerable body of information to help us in understanding why snakebite occurs, what the consequences may be, and what we should be doing to improve the prognosis for snakebite patients.

Incidence and Mortality Rates

Early publications about snakebite in Papua New Guinea give no data on the overall incidence of morbidity or mortality, and concentrate predominantly on the reporting of case series that describe clinical syndromes of envenoming and their treatment. Campbell & Young (1961) reported 15 cases of serious envenoming from Central province between November 1959 and August 1960. The single death in this series was due to pulmonary oedema. Campbell (1964) reported an additional 41 cases in addition to further discussion of 11 cases from the earlier study. All of these cases occurred between mid-February 1960 and September 1962, with 38 cases originating within 80 kilometres of Port Moresby. As with the earlier paper, no data is presented to explain whether these represent all of the cases treated, or whether they only represent cases treated by the author.

Campbell also published three papers describing clinical syndromes of envenoming by presumed death adders *Acanthophis antarcticus*¹ (1966), Papuan taipans *Oxyuranus scutellatus canni* (1967a), and Papuan blacksnakes *Pseudechis papuanus* (1967c), but again gives no indications as to whether the cases reported represent all cases during particular periods, or are simply representative case histories. None of the cases were fatal. In a report on antivenom use Campbell (1967b) records a case fatality rate of 7.1% from 28 cases treated over a 21 month period from March 1964 to November 1965. In discussing the management of 73 cases between 1959 and 1965, Campbell (1969a) records 5 fatalities (CFR of 6.8%). Campbell (1969b) recorded mean admissions for snakebite in Papuan hospitals as 155.5 cases per annum for the period 1961-1967, and says that there were 6.3 admissions for snakebite per 1,000 patients (0.63%).

¹ *Acanthophis antarcticus* is not currently believed to occur in Papua New Guinea, and ongoing taxonomic investigations suggest that the genus is represented by several distinct species including *Acanthophis rugosus* and *Acanthophis laevis*.

Hudson & Pomat (1988) provide data on the incidence of snakebite in Madang province during the 10-year period from 1977 to 1986, but do not calculate actual incidence rates despite giving general population data. Using the data, the mean annual incidence can be calculated as 8.3 cases per 100,000 population. Clinical data for all of the cases is not available, and consequently any estimate of envenomation incidence would most likely underestimate the true figure. Only 2 deaths were recorded, giving a mortality rate estimate of 0.09 cases per 100,000 population and a case fatality rate of 1.14%. Brian & Vince (1988) examined snakebite in children admitted to Port Moresby General Hospital and reported a case fatality rate of 7.7% among 54 2-16 year olds over 38 months.

Currie *et al* (1991) produced incidence rates for envenoming snakebite and snakebite mortality in Papua New Guinea based on antivenom usage data from hospital admissions in Port Moresby (1987-1989) and Madang (1978-1988), and from CSL antivenom usage reporting forms (1983-1988). The authors acknowledged that these sources represented incomplete data on antivenom usage in Papua New Guinea. The annual incidence rates (January 1987-June 1989) of envenomation in rural central Papua and urban Central Papua were 81.8 and 21.8 cases per 100,000 population respectively. Corresponding annual mortality rates were given as 4.3 and 2.1 cases per 100,000 population. For the Madang region (1978-1988) they reported the annual envenomation incidence to be 3.0 cases per 100,000 population, with an annual mortality rate of <1.0 case per 100,000 population. Examined critically, these rates must underestimate the true rates, since antivenom supplies rarely meet demand, and many patients with envenomation never receive antivenom. Currie *et al* (1991) argue that the intention was to reduce diagnostic error by only considering cases in which antivenom was administered. A more appropriate design would have been a prospective study using enzyme immunosorbent assay technology to positively confirm the presence of venom antigen in the serum of patients in which snakebite was a suspected diagnosis.

Laloo *et al* (1995b) examined the epidemiology of snakebite in the Central province of Papua New Guinea as part of an extensive study supported by Oxford University and the Wellcome Trust. Retrospective analysis of admissions for snakebite at five rural health centres and at Port Moresby General Hospital (1987-1991) was combined with prospective Port Moresby General Hospital data for the period 1990-1992. Annual incidence and mortality rates for each of five sub-provinces were calculated as well as overall provincial rates. The annual incidence of snakebite ranged from 20.6 to 526.2 cases per 100,000 population at sub-province level. Provincial annual incidence was calculated as 215.5 cases per 100,000 population. The rate of actual envenoming was given as 62.6 cases per 100,000 population per annum, but no criteria used to identify these patients are provided. They reported that case fatality rates ranged from 2.9% to 30% at five rural health centres in Central province. For Central province annual mortality is reported as 7.9 cases per 100,000 population, and the combined Central province/National Capital District annual mortality is given as 3.7 cases per 100,000 population. From 1987 to mid-1992 the case fatality rate at Port Moresby General Hospital was 4.4% overall, however the rate in children under 10 years (10.0%) was significantly higher than the rate for adults (3.3%).

Williams *et al* (2003) studied snakebite admissions to health centres in the Mekeo region of Central province between 1997 and 2001 and reported that the average annual incidence of snakebite was 561.9 cases per 100,000 population. This figure compares very favourably to the rate of 526.2 cases per 100,000 population provided by Laloo *et al* (1995b). Localised community incidence rates reported by Williams *et al* (2003) were however significantly higher with three large communities having average annual incidence rates of between 1,041 and 1,448 cases per 100,000 population.

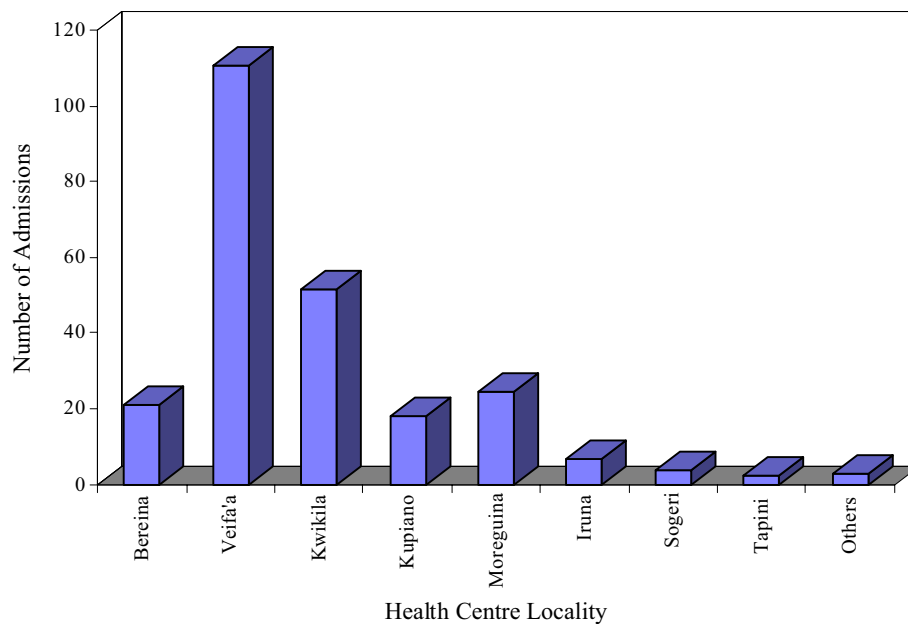


FIGURE 1: Average annual admissions for snakebite at major health centres in Central province 1987-1991 (SOURCE: Lalloo *et al*, 1995)

Not all snakebites resulted in envenomation. The average annual incidence rate for envenomation was 326.9 cases per 100,000 population; effectively 58.2% of snakebites resulted in the development of clinical envenoming. Annual mortality rates ranged from 7.5 to 19.3 cases per 100,000 population with an average mortality rate of 13.8 cases per 100,000 population. This is significantly higher than has been demonstrated in the past.

Williams *et al* (2002) determined case fatality rates for 283 patients admitted to the Intensive Care Unit at Port Moresby General Hospital for the treatment of snakebite between January 1998 and December 2001. The overall case fatality rate was 9.54% but annual case fatality rates ranged from 4.4% to as high as 20.6%. Case fatality rates among males (7.7%) were significantly different ($X^2=24.6$, $P<0.001$) to females (13.5%). There was also a significant difference ($X^2=37.4$, $P<0.001$) between case fatality rates of children² (15.7% overall; 14.3% for males; 17.9% for females) and older patients (7.5% overall; 5.9% for males; 11.5% for females). McGain *et al* (2004), examining snakebite mortality at Port Moresby General Hospital in the period from January 1992 to December 2001, reported a total of 87 deaths among 722 admissions for envenoming, giving a case fatality rate of 12.0%. The snakebite case fatality rate for ventilated children in the Intensive Care Unit was 16.2% compared to 10.2% for ventilated adults. At the present time no data on the incidence of morbidity or mortality following snakebite in other regions of Papua New Guinea is available.

Age Distributions and Sex Ratios

Campbell & Young (1961) and Campbell (1964, 1966, 1967a, 1967b) give an elementary profile of the epidemiology of snakebite during the 1960's. The mean age of 57 male victims was 26.8 years (SD=10.6 yrs) and 20 years (SD=9.8 yrs) for 10 female patients. Twelve patients (17.9%) were under 15 years of age. Patients ranged from 3 years to 45 years of age.

² Paediatric cases 10 years of age or under.

Hudson & Pomat (1988) examined 129 cases (83 males; 46 females) from Madang province for which medical records were available. There were 111 adults and 18 children under 12 years of age; however no further data on age distribution is given.

Currie *et al* (1991) report that the mean age of 347 patients (215 males; 132 females) in their study was 24.5 years (SD=13.8 yrs), but give no sex-related data. The youngest patient was 2 years old and the oldest was 67 years of age. Ninety patients (25.9%) were under 15 years of age, and 69% of these were males. The overall male:female sex ratio was 1.6:1. Lalloo *et al* (1995) state that the mean age of patients in their study was 25.0 years; but, like Currie *et al* (1991), give no sex-related data. Of the admitted patients, 8.5% were children 10 years old or younger, and children comprised 16% of envenomed and 6.9% of non-envenomed patients. Lalloo *et al* (1995b) report an overall male:female sex ratio of 1.39:1 based on 1,421 admissions to Central province health centres and Port Moresby General Hospital between 1987 and 1991. At Veifa'a in the north-west of the province the male:female sex ratio was 0.87:1. The lack of sex-specific age data in both of these large recent studies is unfortunate. In Lalloo *et al* (1995b) the mean age of all admitted patients (25.0 years) differs from the mean (21.1 yrs, SD=17.7) and median (15.5 yrs) ages of 20 patients who died from snakebite in their study. Median ages of male (14 yrs, n=11) and female (16 yrs, n=9) fatalities are at variance with the mean age given for all admissions. However, it is not possible to compare this data further as no sex-specific calculations are provided.

Williams *et al* (2003) do give age-specific data for snakebite in Mekeo, with a mean age for males of 23.1 years and 22.7 years for females and a median age of 20 years for both sexes. There were a disproportionate number of 16-30 year old males and females bitten by snakes in Mekeo; 49.7% of all male snakebite victims and 53.6% of all female snakebite victims in Mekeo fell into this age range despite that fact that only 27.5% of males and 27.1% of females in Mekeo were aged between 16 and 30 years. Although 43.5% of the male population, and 41.1% of the female population were aged between 0-15 years old, snakebite victims of these ages were under-represented; 28.6% of males and 23.4% of females were 0-15 years old.

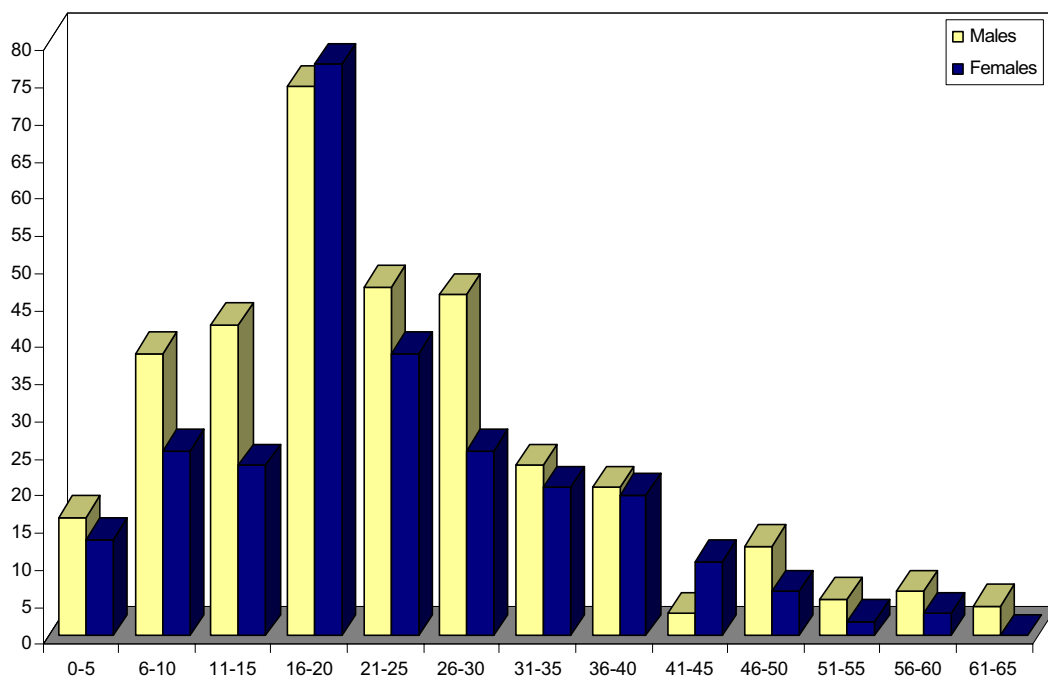


FIGURE 2: Age distribution of 336 male and 261 female patients admitted to health centres in Mekeo between 1997 and 2001 for whom actual age was recorded (SOURCE: Williams *et al*, 2003)

Williams *et al* (2002) give age and sex-specific data for their series of 283 seriously envenomed patients at Port Moresby General Hospital. Mean age for males was 21.5 years (n=170, SD=14.9 yrs, median=16 yrs) and 21.1 years (n=77, SD=16.5yrs, median=14 yrs) for females. Children 15-years old or under comprised 39.9% of cases. The overall male:female sex ratio was 2.2:1. However, in the 15-29 year age group the ratio of males to females was 4.1:1. Males under the age of 30 years comprised 46% of cases. McGain *et al* (2004) examining fatal snakebite at Port Moresby General Hospital report that 47% (n=41) were under 15 years of age, and that males were involved in 53% (n=46) of all cases.

Circumstances of Injury

In the first report on snakebite in Papua New Guinea, Campbell & Young (1961) state that all 15 patients were bitten on either the foot or the leg during daytime hours while the victims were either walking in or near long grass. Campbell (1964) reported that all but 2/52 patients were bitten in daylight hours; 96% of cases were from Central province and 73.1% came from within 80 kilometres of Port Moresby. All but one bite occurred on the lower limbs with 17.3% on the toes, 32.7% on the foot, 15.4% on the ankle and 32.7% on the legs themselves. Bites occurred when the victims were walking on paths near long grass, or through long grass, and 23% actually trod on the snake itself.

In his series of 15 cases of *Acanthophis* spp. bites over a six-year period, Campbell (1966) reported that all but one bite occurred on the lower limbs, typically on either the dorsum of the foot or the toes. Eight bites happened when the person stood on the snake. In one case a man laid down on a snake concealed beneath leaf litter and was bitten on the leg, and another was bitten on the finger by a snake he accidentally picked up in a pile of cut grass. The other 13 bites were on either the feet or ankles. Three cases involved patients bitten between 6.30pm and 7.30pm, while a fourth patient was bitten at 3.00am in the morning. The other cases occurred between 8.30am and 5.30pm. In the only other study of proven *Acanthophis* spp. envenomation in Papua New Guinea, Lalloo *et al* (1996) found that 22 of the 32 EIA-confirmed cases occurred in daylight, and that only two bites did not occur on the lower limbs.

Reporting bites by *Oxyuranus scutellatus canni*, Campbell (1967a) shows that all bites occurred on a lower limb (one of these was bitten on the “middle third” of the leg, and another on the “lower third”), and occurred between 10.00am and 4.00pm. Lalloo *et al* (1995a) observed that 85% of proven *Oxyuranus scutellatus canni* bites occurred during daylight among people working in gardens or walking along bush tracks, and that 96.4% of all the bites were to the lower limbs. All nine cases of presumed *Oxyuranus scutellatus canni* envenomation reported by Williams & Bal (2003) took place during daylight and involved bites to the legs, ankles or feet. One patient was bitten at home, two were bitten in the garden and the other six cases occurred when patients were walking along bush tracks or dirt roads.

Among Campbell's (1967c) 13 cases of presumed *Pseudechis papuanus* bites, most (n=10) were bitten on either the foot or ankle, while 2 were bitten on the hand or arm and 1 was bitten on the shoulder. Positive identification of the biting snake was only made in one case (specimen brought to PMGH), and all of the other cases were more likely to have been caused by Papuan taipans (*Oxyuranus scutellatus canni*). Only two positive identifications of *P. papuanus* snakebite were made during Campbell's 7 years at PMGH, and his contention that it was the most common cause of snakebite in southern PNG is almost certainly erroneous. All of the bites occurred in daylight. All nine cases of snakebite involving *Pseudechis papuanus* discussed in Lalloo *et al* (1994) involved bites to the lower limb that occurred during daylight.

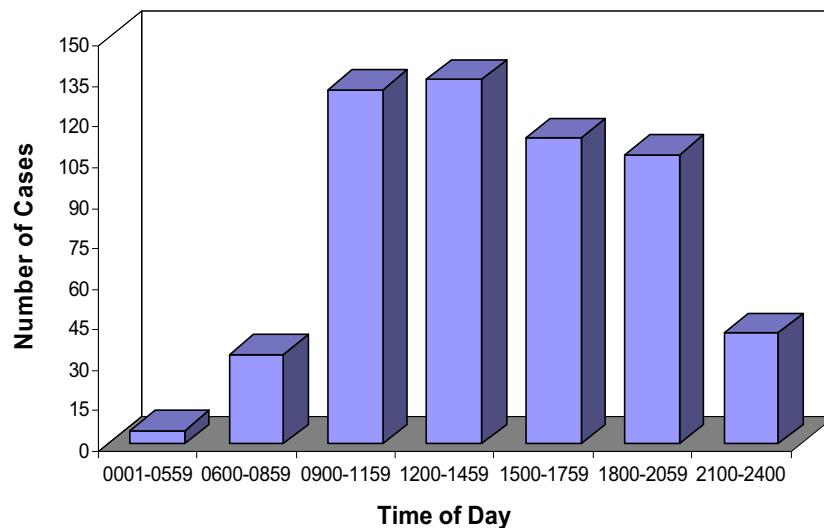


FIGURE 3: Time of day for snakebites in the Mekeo region of Central province between January 1997 and December 2001; increased frequency (43.9%) during the afternoon (1200-1759 hours) was statistically significant ($p < 0.005$) making this the major danger time for snakebite.

(SOURCE: Williams *et al*, 2003).

On the northern side of PNG, Hudson & Pomat (1988) reported that 81% of patients in their series of 129 patients were bitten on a lower limb; and that 87.6% of these were bites on the feet. Ten of the 129 patients (7.75%) were bitten on the hands. Sixty-two% of the bites occurred during the day and 33% in the night, while no time was recorded for 5% of the series. In Blasco & Hornabrook's (1972) report of a case of fatal *Micropechis ikaheka* envenomation, the patient was bitten at approximately 6.00pm while alone in the bush, and in Warrell *et al*'s (1996) case series of 11 bites by this species, which were confirmed by venom-antigen specific EIA, 3 of 7 cases for which a time of injury was recorded occurred after 8.00pm at night. One of the two patients who died was killed after being bitten while playing with the decapitated head of a snake he "killed" in the bush. Six of the patients in this series stood on the snake, and two were handling snakes they had found.

Currie *et al* (1991) found that 281 (81%) of 347 snakebite victims were bitten between 6.00 am and 6.00 pm, and that 53 bites (15.3%) occurred at night. Of 334 patients for whom data was available, 316 (94.7%) were bitten on the lower limbs; 204 of these (64.5%) were bites on the foot or the toes. No data was provided regarding what the victims were doing when bitten. Lalloo *et al* (1995b) report details for 335 cases of snakebite. The majority (89.4%) of 205 envenomed patients were bitten during daylight compared to 54% of the 130 non-envenomed patients. As with other studies, 86% of all bites occurred on the lower limbs. The three most common circumstances under which bites occurred were while victims were walking (34.5%), in the garden (19%) or in the bush (14.8%). In 86 cases of fatal snakebite discussed in detail by McGain *et al* (2004), 89% of the bites occurred on the lower limbs, and 60% of the bites for which time of injury was recorded occurred between 12.00pm and 6.00pm.

Identification of Biting Species

Throughout Papua New Guinea there are only four species of venomous snake that contribute to the majority of serious envenomations, along with perhaps two other species that can cause human fatality. The best information available to date shows that on the basis of

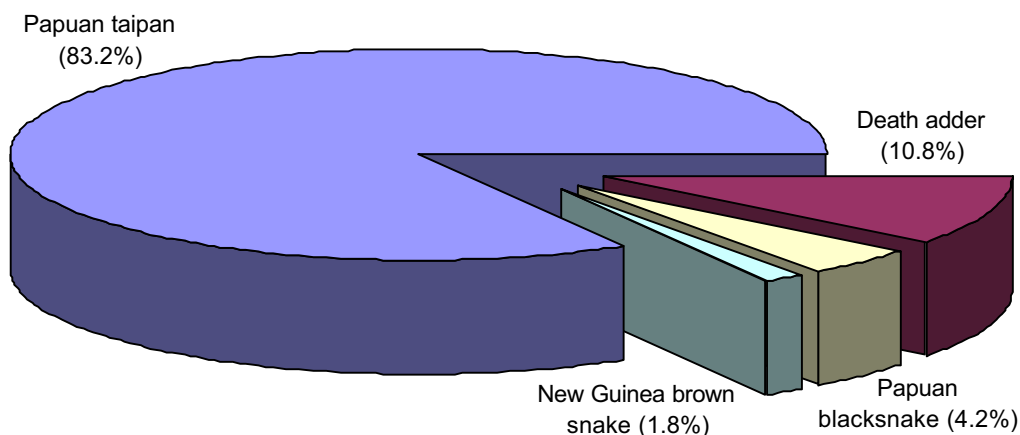
identifications made with the aid of species-specific venom enzyme immunosorbent assay (EIA) by Laloo *et al* (1995b), the snake responsible for the majority of serious snakebites admitted to PMGH is the Papuan taipan (*Oxyuranus scutellatus canni*) and not the Papuan blacksnake (*Pseudechis papuanus*). Papuan taipans caused an incredible 83.2% of envenomations compared to just 4.2% that were attributable to Papuan blacksnakes.

Reliable identification of the biting species is a major shortcoming in most studies of Papua New Guinean snakebite. In the 1950's herpetologist Ken Slater believed that the Papuan black snake *Pseudechis papuanus* was the commonest venomous snake in southern PNG, and even today, the perception of Papua New Guineans is that this snake is responsible for almost all snakebites. Slater (1956) wrote that it was most abundant along the coastline to the east of Port Moresby, and Campbell (1967c) claimed that it was responsible for more hospital admissions than any other species. In spite of this statement only two cases seen by Campbell between 1959 and 1967 could be conclusively attributed to this species on the basis of positive identification of the biting snake at the hospital. Campbell's (1967c) description of a syndrome of envenoming attributable to Papuan black snake *Pseudechis papuanus* bites must therefore be treated with scepticism.

The much more dangerous Papuan taipan *Oxyuranus scutellatus canni* often has a distinctive reddish-orange vertebral stripe as a distinctive feature, and Campbell appears to have relied upon this colouration as a means of presuming that large dark coloured snakes *apparently* lacking it were *Pseudechis papuanus*.

Although the Papuan taipan is the only large snake in PNG that may have a red or orange vertebral marking, this is a feature that many snakebite patients simply do not notice in the heat of the moment. There are no reliable means of visually distinguishing *all* specimens of *Pseudechis papuanus* and *Oxyuranus scutellatus canni*. One patient in Campbell's (1967c) series of 13 victims presented with a dead 1.5 metre snake for identification. Identification in the other 12 cases appears based on non-reporting of a vertebral stripe and these cannot be accepted as confirmed bites by *Pseudechis papuanus*. The only reliable recent description of envenomation by *Pseudechis papuanus* was given by Laloo *et al* (1994) who detailed the clinical syndromes of 9 patients bitten between January 1990 and June 1992 identified by specific venom-antigen enzyme immunosorbent assay.

FIGURE 4: Species responsible for serious snakebites admitted to Port Moresby General Hospital between January 1990 and June 1992 (SOURCE: Laloo *et al.* 1994, 1995)



Campbell (1964) states that 5 patients in a series of 52 arrived at hospital with a dead snake - 3 with death adders *Acanthophis* spp, 1 with a Papuan black snake *Pseudechis papuanus* and 1 with a Papuan taipan *Oxyuranus scutellatus canni*. Campbell (1966), describing the clinical syndrome of death adder *Acanthophis* spp envenoming reports 15 cases. The biting snake was killed in 11 of these cases and 8 of the victims brought the snake to the hospital where it was identified. Death adder envenoming is presumed in 5 cases on the basis of statements by either the patient or a third party, and in the last 2 cases Campbell presumes identification on the basis of haematological tests. Death adders have a distinctive body plan and appearance that makes visual identification easier than for other species. Laloo *et al* (1995b) used species-specific venom EIA and found that 10.8% of serious snakebites admitted to PMGH were caused by death adders. Enzyme immunosorbent assay confirmed 32 cases of envenomation by *Acanthophis* spp. that involved a syndrome of progressive neurotoxicity without coagulopathy (Laloo *et al*, 1996), and the 15 cases reported by Campbell (1966) conform to this profile, lending support to Campbell's diagnosis. Hudson & Pomat (1988) give an excellent case report of a death adder bite treated at Madang Hospital where the dead snake was identified at the hospital.

Campbell (1967a) reports six cases that he believed were attributable to envenoming by Papuan taipans *Oxyuranus scutellatus canni* based on positive identification of two dead snakes brought in with the victims, and a description of an orange or red coloured vertebral stripe in the remaining four cases. Laloo *et al* (1995a) examine the syndrome of envenoming by *Oxyuranus scutellatus canni* in detail on the basis of 166 cases in which this species was implicated by specific venom-antigen EIA. Although they report the specificity for specific taipan venom-antigen as 87%, only cases in which this was the sole antigen detected were regarded as cases of definite *Oxyuranus scutellatus canni* snakebite. Williams & Bal (2003) reported nine cases of presumed envenoming by *Oxyuranus scutellatus canni* on the basis of clinical presentation and/or description of the biting species. In the future it is hoped that the widespread use of venom detection kits to diagnose snakebite will make it possible to assemble nationwide data on the species responsible for envenomation.

Hudson & Pomat (1988) reported on 64 cases of envenomation reported in Madang Province between 1977 and 1986; 15 presented with symptoms suggestive of bites by the small-eyed snake (*Micropechis ikaheka*). Warrell *et al* (1996) reported that in a more recent series, 4/46 (8.7%) cases of snakebite treated at Madang Hospital, and 5/13 (38.5%) treated at Gaubin Hospital on nearby Karkar Island were identified by EIA as attributable to *M. ikaheka*. No cases of *M. ikaheka* were identified in any of the patients studied using EIA by Laloo *et al* (1994). Brown snake *Pseudonaja textilis* spp. envenomation has been reported among 1.8% of EIA-tested snakebite patients admitted to Port Moresby General Hospital between January 1990 and June 1992 (Laloo *et al*, 1994).

Climate and Seasonality

There have been few attempts to determine whether bites by certain species are more likely to occur under specific climatic conditions (temperature, rainfall, etc.) or during particular seasons throughout the year.

Campbell (1966) reported that for *Acanthophis* spp., 12 of the 15 cases occurred between August and December. Campbell (1967a) reports *Oxyuranus scutellatus canni* bites in June (2), August (1), December (1), January (1) and March (1). Currie *et al* (1991) reported that 56.8% of snakebites occurred between the 'wet season' months of from November to April.

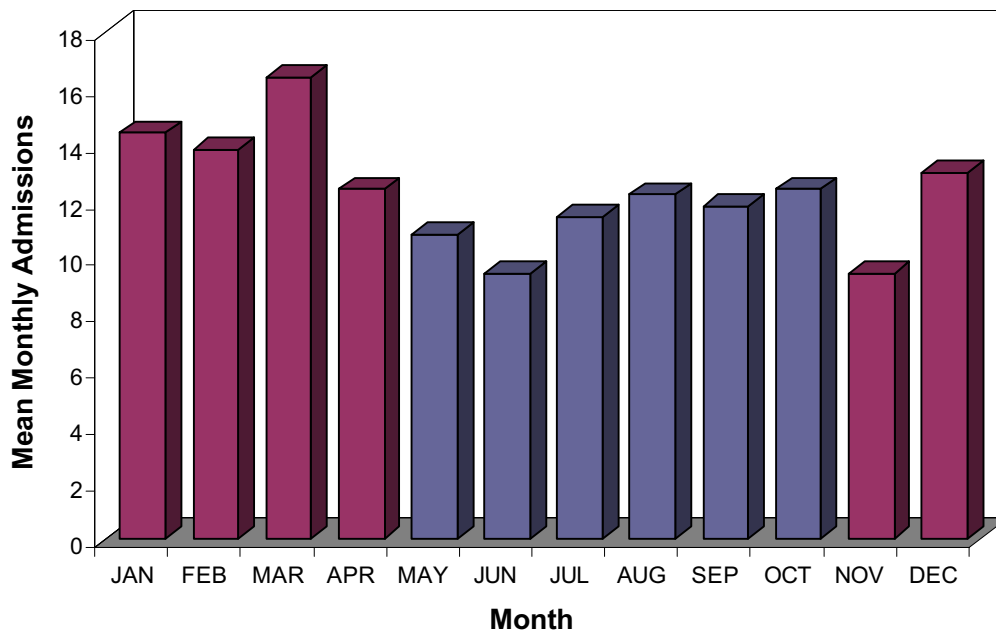


FIGURE 5: Seasonal frequency of admissions for snakebite in the Mekeo region of Central province between January 1997 and December 2001; increased frequency during the dry season months of November to April is statistically significant ($p=0.04$). (SOURCE: Williams *et al*, 2003).

Laloo *et al* (1995b) state that 57.9% of 221 envenomed patients and 51.6% of 128 non-envenomed patients were bitten between November-April. Data on monthly admissions for snakebite were compared to monthly rainfall; however rainfall itself was not shown to be a significant contributing factor.

Williams *et al* (2002), reporting cases admitted to the PMGH ICU from January 1997 to December 2001 from across PNG, found that 54% occurred between November-April, and Williams *et al* (2003) found that 53.9% of snakebites in Mekeo occurred during the same months during this same period. McGain *et al* (2004) reported that 60% of fatal cases in the 10 years from January 1992 to December 2001 occurred between November and April.

Clinical Epidemiology and Envenomation Syndromes

Local Indications of Envenomation

The clinical syndromes of envenomation after snakebite in Papua New Guinea have been reported by several authors. Most reports relate to small case series of patients and, in most, the identification of the biting species is equivocal. Some of the consistently reported symptoms of snakebite over the last 40 years are shown in Table 1.

Lymph node pain is a consistent feature after snakebite in Papua New Guinea, and tender enlargement of regional lymph nodes is reported in all published accounts. Venom injected subcutaneously typically enters the lymphatic system and drains via lymph nodes into the circulation, and tenderness or swelling of lymph nodes may be an indication of venom absorption. Trevett *et al* (1994a) stated that lymphadenitis was a particularly sensitive positive indication of envenomation and occurred in 93% of envenomed patients.

TABLE 1: Symptoms reported in various studies of snakebite in Papua New Guinea between 1964 and 2004.

Author	Local Pain	Lymph Nodes	Oedema	Headache	Vomiting or Nausea	Abdominal Pain	Spit/Vomit Blood	Visual Disturbances
Campbell & Young, 1964	+	+	+	+	+	+	+	+
Campbell, 1964	+	+	+	+	+	+	+	+
Campbell, 1966	+	+	+	+	+	-	-	+
Campbell, 1967a	-	+	-	+	+	+	-	-
Campbell, 1967c	+	+	+	+	+	+	+	+
Campbell, 1969a	-	+	-	+	+	+	+	-
Hudson & Pomat, 1988	+	+	+	+	+	+	-	+
Laloo <i>et al</i> , 1994	+	+	+	+	+	+	+	+
Laloo <i>et al</i> , 1995a	-	+	-	+	+	+	+	+
Laloo <i>et al</i> , 1996	-	+	-	+	+	+	-	+
Warrell <i>et al</i> , 1996	+	+	+	+	+	+	-	+
Williams & Bal, 2002	-	+	-	+	+	+	+	+
Williams <i>et al</i> 2003	+	+	+	+	+	+	+	+
McGain <i>et al</i> 2004	-	+	-	+	+	+	+	+

The extent and severity of local symptoms such as pain or oedema is significantly lower than in reports of elapid snakebite from Australia. Campbell & Young (1961) reported severe local pain and oedema in a single patient; however this was most likely caused by prolonged tourniquet use. Three other patients experienced minor oedema, and local pain was either absent completely or mild. Campbell (1964) found severe pain in 3 patients and severe oedema occurred in two individuals as a result of lengthy tourniquet application.

A third of the patients bitten by death adders *Acanthophis* spp. in Campbell (1966) had local pain, and 27% had slight oedema. Neither symptom was present in any of the 6 patients with *Oxyuranus scutellatus canni* envenomation reported by Campbell (1967a); however severe pain, oedema and extensive ecchymoses were seen in a patient bitten on the shoulder (Campbell, 1967c) and this may have been due to a Papuan blacksnake (*P. papuanus*) bite.

Pain was a feature in 36% of cases reported by Hudson & Pomat (1988) and 14% of patients had local oedema and localised muscle pain, most probably associated with rhabdomyolysis after *Micropechis ikaheka* envenomation. One patient in a series of eleven bitten by *Micropechis ikaheka* reported local pain and two patients had oedema (Warrell *et al*, 1996). Laloo *et al* (1994) observed slight oedema in one patient bitten by a Papuan black snake *Pseudechis papuanus*. In a series of 166 bites by *Oxyuranus scutellatus canni* (Laloo *et al*, 1995a) there were no reports of local pain or swelling. Clinical experience in Australia is that the bites by members of the blacksnake genus *Pseudechis* are painful locally and often associated with local oedema that may be mild to pronounced in severity. Williams *et al* (2004) reported severe local pain after a bite by an Australian Collett's blacksnake (*Pseudechis colletti*) and Isbister & Currie (2003) presents a case of mulga snake (*Pseudechis australis*) envenomation in a child with persistent bite site pain and swelling. Although uncommonly reported in PNG (perhaps because bites are uncommon) it should be anticipated that Papuan blacksnake (*Pseudechis papuanus*) and Papuan mulga snake (*Pseudechis cf.*

australis) bites may also produce significant local pain and oedema. Local pain and swelling caused by snakebite should not be confused with the pain and swelling that can be associated with ischemic injury due to prolonged tourniquet use.

Non-specific Indications of Envenomation

A number of non-specific features have been reported consistently in patients with snakebite envenomation. Campbell & Young (1961), and Campbell (1964; 1966; 1967a; 1967c; 1969a) reported that headache often followed envenomation, and headache has been universally reported in virtually all published accounts of snakebite in PNG. Headaches are reported to have last from a few hours to several days. Hudson & Pomat (1988), Laloo *et al* (1996) and Warrell *et al* (1996) report headache as common following bites by death adders (*Acanthophis* spp.) and small-eyed snakes (*Micropechis ikaheka*). Herpetologist Ken Slater had persistent severe headache for two days after a bite from *Micropechis ikaheka*. Laloo *et al* (1994) noted headache in 2 of 9 patients with confirmed Papuan blacksnake (*Pseudechis papuanus*) bite, and Laloo *et al* (1995a) reported headache in 54.5% of positively identified Papuan taipan (*Oxyuranus scutellatus canni*) victims. In an analysis of referral letters written by rural health workers during the early 1990's, Trevett *et al* (1995) found that headache was reported in 37% of patients at the health centre, and in 58% of the same patients on admission to PMGH. Headache was reported in 51.9% of 564 patients bitten by snakes in Mekeo (Williams *et al* 2003). Headache was a documented non-specific symptom in 38 (63.3%) of 60 fatal snakebites treated at PMGH between 1992 and 2001 (McGain *et al*, 2004).

Vomiting and abdominal pain or tenderness typically occurs in unison. Campbell & Young (1961) observed concurrent vomiting and abdominal pain in 3 patients, while another 3 patients had vomiting without abdominal pain. One patient with severe abdominal pain and vomiting in conjunction with abdominal tenderness was mistakenly diagnosed with acute appendicitis. Vomiting was reported in 42% and abdominal pain in 34.6% of patients described in Campbell (1964). Vomiting was a typical non-specific indication in patients of death adder (*Acanthophis* spp.) bites reported by Campbell (1966), and was also recorded in three patients with presumed Papuan taipan (*Oxyuranus scutellatus canni*) bite (Campbell, 1967a). In the series of 13 bites dubiously ascribed to Papuan blacksnake (*Pseudechis papuanus*) envenomation, but most probably really having been caused by Papuan taipans (*Oxyuranus scutellatus canni*), 8 patients had early vomiting and 4 had severe abdominal pain (Campbell, 1967c). Vomiting after bites from the small-eyed snake (*Micropechis ikaheka*) has been reported by Blasco & Hornabrook (1972) and Warrell *et al* (1996). Abdominal pain was reported in 2 of the 6 patients reported in Warrell *et al* (1996). Hudson & Pomat (1988) reported abdominal pain in 56% and vomiting in 25% of 64 envenomed patients treated for either death adder (*Acanthophis* spp.) or small-eyed snake (*Micropechis ikaheka*) bites in Madang during the 1980's.

Of 9 patients with confirmed Papuan blacksnake (*Pseudechis papuanus*) envenomation, 2 vomited and 5 had abdominal pain (Laloo *et al*, 1994). In a large series of Papuan taipan (*Oxyuranus scutellatus canni*) bite victims, 64.4% vomited and 59.8% had abdominal pain. In the analysis of referral letters conducted by Trevett *et al* (1994a), 38% had abdominal pain and 30% had vomited at the health centre; on admission to PMGH 58% had abdominal pain and 62% had reported vomiting. Williams & Bal (2003) reported vomiting in 4 of 9 patients with likely Papuan taipan (*Oxyuranus scutellatus canni*) envenomation and 3 of these 4 patients had concurrent abdominal pain. Williams *et al* (2003) reports abdominal pain in 48.9% of 564 patients bitten by snakes in Mekeo; however, nausea or vomiting was only reported for 6.2%. Abdominal pain was documented in 48 (80%), and vomiting in 40 (66%) of the 60 fatal snakebites discussed by McGain *et al* (2004).

Specific Indications of Envenomation: Coagulation defects

Evidence of coagulopathy is an absolute indication for antivenom if observed in conjunction with a history of snakebite in PNG.

Campbell & Young (1961) reported that 6 of the 15 patients had 'bleeding tendencies' and that 3 patients vomited blood-stained material. Campbell (1964) notes that 11/52 (21.2%) patients were recorded as either spitting blood or having haematemesis, while 3 patients also passed 'blood-stained' urine. Campbell (1967a) notes bleeding problems in 2 of 6 patients; one of these had persistent bleeding from a superficial facial wound, while another had haemoglobinuria and incoagulable blood. Haematemesis was seen in 3 patients and another 2 had haemoptysis among the group of 13 that Campbell (1967c) thought to have been bitten by Papuan blacksnakes (*Pseudechis papuanus*). Three of 4 patients in this series had haemoglobinuria and fibrinogenolysis, and other signs of coagulopathy (spitting blood; gingival bleeding; bleeding bite wounds) were reported in 8 of the 13 patients. As has been stated before, Campbell's presumptive identifications were based on whether or not the patient reported seeing a red marking on the back of the snake, and while the presence of reddish-orange marking is a strong indication that the culprit was a Papuan taipan (*Oxyuranus scutellatus canni*), it is important to again emphasize that not seeing this type of marking does not mean the snake was not a Papuan taipan.

Spontaneous bleeding has been reported in two cases of envenomation by the small-eyed snake (*Micropechis ikaheka*) that was reported in Warrell *et al* (1996). Hudson & Pomat (1988) did not report bleeding disorders in any of the 64 cases of snakebite from Madang province during the 1980's. In a study of 32 patients shown to have been bitten by death adders (*Acanthophis* spp.) by EIA, there was no clinical evidence of coagulopathy although elevation in leucocyte counts and slight thrombocytopenia was found on laboratory investigation (Lalloo *et al*, 1996). Prothrombin time was significantly prolonged in 13 patients. Broad clinical experience in Australia and PNG indicates that bites by these snakes do not involve bleeding disorders.

Blood-stained saliva and bleeding from the mouth or nose was reported in 1 patient with confirmed Papuan blacksnake (*Pseudechis papuanus*) envenomation, while 2 others had either epistaxis or gingival bleeding (Lalloo *et al*, 1994). Laboratory studies on blood from 2 of these patients showed a mild thrombocytopenia (platelet counts: $91-93 \times 10^9/L$), and that three patients had lower than normal levels of several important clotting factors including protein C, fibrinogen, Factors V, VIII, XIII_a, anti-thrombin III, plasminogen and α_2 -antiplasmin. Prothrombin time (PT) and activated partial thromboplastin times (APTT) were prolonged briefly and FDP was elevated.

Coagulopathy can be a very prominent feature of bites by Papuan taipans (*Oxyuranus scutellatus canni*), and in addition to Campbell's early reports of bleeding after bites by large dark coloured snakes, there is a substantial body of evidence from recent studies. Lalloo *et al* (1995a) report that 77% of patients with EIA proven bites by Papuan taipans had incoagulable blood on the basis of 20WBCT > 20 minutes. Systemic bleeding occurred in 43.7% of patients, and bite site bleeding occurred in 16.3%. Most reported bleeding from either the gingival sulci (37%) or by haematemesis (12.6%). Three patients had epistaxis; 11% bled from superficial cuts and scratches; 8.8% bled from venepuncture sites. On laboratory investigation 52.8% had moderate to severe leucocytosis and 27.5% developed mild thrombocytopenia.

Brian & Vince (1987) reported that 40 of 54 children bitten by snakes developed evidence of coagulopathy and that 33 had clotting times greater than 15 minutes. Bleeding problems were

mentioned in 40% of referral letters written by rural health workers, and 60% of the referred patients were found to have incoagulable blood upon admission to PMGH (Trevett *et al*, 1994a). According to Trevett *et al* (1994a), a 20WBCT > 20 minutes had a positive predictive value (PPV) of 93.5% for a diagnosis of Papuan taipan (*Oxyuranus scutellatus canni*) envenomation. Williams *et al* (2003) reviewed 553 cases of snakebite from the Mekeo region in which the 20WBCT was used, and found that this simple diagnostic test had a positive predictive value of 98.4% and a specificity of 99.6% for the subsequent development of neurotoxicity. The PPV for subsequent coagulopathy was 67.7% with specificity of 95.7%; however, because the other signs and symptoms of incoagulable blood were often not reported in the clinical notes, it is probable that the actual PPV for disseminated intravascular coagulopathy is actually higher. In 60 fatal cases of snakebite reported by McGain *et al* (2004), 75% had a 20WBCT > 20 minutes and 35 patients (53.3%) had demonstrable spontaneous bleeding.

Specific Indications of Envenomation: Myotoxicity

There are few early reports of myotoxicity following snakebite in PNG, although some cases with 'haemoglobinuria' may actually have been patients with myoglobinuria instead. Blasco & Hornabrook (1972) mention that Ken Slater had 'weakness' after a bite from the small-eyed snake (*Micropechis ikaheka*), and this is often a sign of rhabdomyolysis. Hudson & Pomat (1988) report renal failure in 6 patients from Madang province who presented with dark-coloured urine. Hudson (1988b) reported two cases of presumed small-eyed snake (*Micropechis ikaheka*) envenomation. A 13 year-old girl bitten on the finger developed generalized muscle pain and tenderness and had urine that was dark reddish-brown, but was erythrocyte-free; and a 50 year-old man bitten on the finger while reaching into a bandicoot burrow by a 'black-headed snake with a white belly' also developed muscle pain and passed dark urine. This second patient's muscle pain was mild initially but became more severe over the next 2 days; at Modilon hospital in Madang his urine was grossly discoloured, but once again was erythrocyte-free. He received one ampoule of death adder antivenom and three ampoules of polyvalent antivenom. Both patients were said to be anicteric and without coagulopathy, and had neurotoxicity; the 13 year old girl subsequently died. Other cases of presumed *Micropechis ikaheka* envenoming treated in Madang also showed signs and symptoms of generalized rhabdomyolysis and myoglobinuria. Warrell *et al* (1996) describes classical signs of myolysis (generalised muscle pain and tenderness; trismus; dark urine) in three patients with EIA proven small-eyed snake envenomation.

The creatine kinase (CK) levels of 8 out of 12 patients bitten by death adders (*Acanthophis* spp.) was elevated (164-4,220 IU/L). Similar studies in victims of Papuan taipan (*Oxyuranus scutellatus canni*) bites found that creatine kinase levels were raised in 74.7% (43-8,110 IU/L) and levels of the liver enzyme aspartate transaminase (AST) were >50 IU/L in 52.6% of patients. Serum myoglobin exceeded 80 ng/ml in 52.2% of patients at the time of their admission. The serum creatine kinase levels of 2 of the 9 patients with proven Papuan blacksnake (*Pseudechis papuanus*) envenomation were slightly elevated; however there were no indications of rhabdomyolysis in any patient (Lalloo *et al*, 1994). In Australia, gross rhabdomyolysis and myoglobinuria after bites by members of the *Pseudechis* genus are relatively common, and creatine kinase levels may exceed 200,000 IU/L. Acute renal failure is a potential complication of myotoxicity, and McGain *et al* (2004) reported muscle pain in 41.7% of 60 fatal snakebites treated at PMGH. Renal complications were contributing factors in the deaths of 16 (26.7%) patients. Testing for creatine kinase, lactate dehydrogenase and other isoenzymes that quantitatively measure rhabdomyolysis products is not routine in PNG at present so it is possible that this important syndrome is seriously under-reported.

Specific Indications of Envenomation: Neurotoxicity

The neurotoxic effects of Papua New Guinean snake venoms are well defined in the available literature, and the balance of evidence demonstrates that snake venom neurotoxins are the major contributors in the deaths of patients due to the development of progressive flaccid paralysis that inhibits and compromises respiration.

The earliest signs of neurotoxicity often manifest themselves in the craniofacial nerves producing a sequential syndrome that often starts with diplopia and ptosis before progressing to ophthalmoplegia, dysarthria, dysphagia and bulbar palsy and eventually involving the intercostal, diaphragm and peripheral musculature. Ataxia and progressive muscle weakness results in a loss of locomotor function; patients eventually lose the ability to walk, stand, sit or even raise their limbs, or control head movements ('broken neck syndrome'). Deep tendon reflexes may be lost and failing respiration often leads to 'abdominal' breathing.

Campbell & Young (1961) graded the neurotoxic effects in 15 snakebite victims according to severity. Ptosis was moderate in 10 cases and severe in 4, while ophthalmoplegia was moderate in 4 patients and severe in 8 others. 10 patients were reported to have had 'visual disturbances'; most probably diplopia. 6 patients had moderate to severe facial palsies and there was moderate to severe paralysis of the tongue and palate in 9 patients. Paralysis of intercostal muscles was severe in 7 patients with 3 patients experiencing moderate diaphragmatic paralysis. Paralysis of the diaphragm was severe in only 1 patient. 7 patients had moderate, and 2 patients had severe, peripheral flaccid paralysis.

Campbell (1964) reports 'visual disturbances' in 26.9% of patients, noting both diplopia and blurred vision. Ptosis was regarded as the earliest sign of neurotoxicity and Campbell comments that many patients would go to sleep only to awake the next morning with severe facial palsy. Ptosis was often associated with either partial or complete ophthalmoplegia, and was observed in 75% of patients in this series. Campbell (1966) says that bites by death adders (*Acanthophis* spp.) produced either blurring of vision or an inability to see clearly, and that ocular and facial paralysis generally followed; however these signs were present in only 3 of the 15 patients. Campbell (1967a) states that 'muscular paralysis' was present in only 3 of 6 presumed Papuan taipan (*Oxyuranus scutellatus canni*) victims yet says that paralysis was present after 9 of 13 supposed Papuan blacksnake (*Pseudechis papuanus*) bites. Campbell's assertion that during the 1960's the Papuan blacksnake was the most common venomous snake in southern PNG and cause of the most snakebites is a fallacy that persists even today, and has resulted in many patients being treated incorrectly with inappropriate antivenoms.

Blasco & Hornabrook (1972) describe a fatal case of small-eyed snake (*Micropechis ikaheka*) envenoming marked by peripheral limb weakness, shortness of breath and profound respiratory failure with cyanosis. Warrell *et al* (1996) reviewed 6 cases of envenomation by this species (identity confirmed by EIA) and reported ptosis in 4 patients, bulbar paralysis in 3, and peripheral limb weakness in 3 cases. Ptosis was present between 6 and 12 hours post-bite. Two patients died of respiratory paralysis at 19 and 38 hours respectively. A patient from Papua developed dysarthria, facial paralysis and ataxic gait resulting in an inability to stand unassisted. Paralysis of the cranial muscles and intercostals was pronounced.

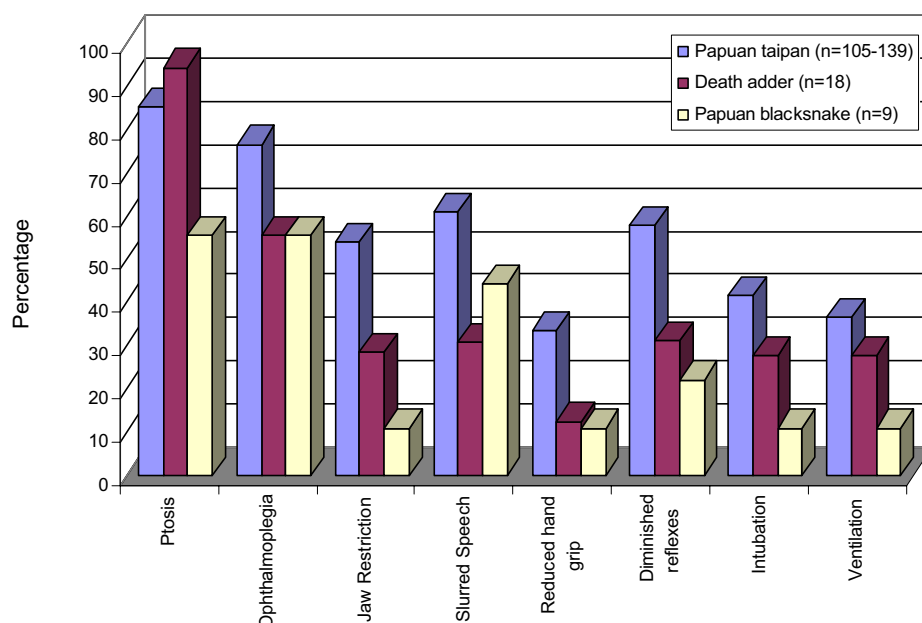
In a study of 32 cases of proven death adder (*Acanthophis* spp.) bites, Lalloo *et al* (1996) found that 18 developed symptoms and signs of envenomation. Ptosis was a symptom in 15/18 (88.2%) and a sign in 17/18 (94.4%). Other symptoms included dysphagia (29.4%), dysarthria (37.5%), diplopia (18.8%), and respiratory difficulty (20%). On examination there were signs that these patients had ophthalmoplegia (55.6%), slurring of speech (30.3%), jaw restriction (28.6%), diminished hand grip (31.3%) and reduced reflexes (12.5%). A total of 5 patients (27.8%) had to be intubated and ventilated, with the median ventilation time being 13

hours. The range of ventilation times was between 2 and 23.5 hours, considerably less than for victims of Papuan taipans (*Oxyuranus scutellatus canni*). Lalloo *et al* (1995a) reported that the median ventilation time after bites by Papuan taipans was 88 hours with a range of from 3 to 176 hours.

Hudson & Pomat (1988) reported ptosis as a symptom in 55% and as a sign in 53% of snakebite envenomations in Madang province. Dysphagia and dysarthria were symptoms in 31%, and 20% reported diplopia. Respiratory distress was a symptom in 9% of bites. Other signs included bulbar paralysis (17%) and external ophthalmoplegia (13%). Only 5% of patients subsequently developed respiratory failure. The only highly venomous species in the province are death adders (*Acanthophis* spp.) and small-eyed snakes (*Micropechis ikaheka*). Hudson (1988a) reports complete bilateral ptosis, ophthalmoplegia and paralysis of tongue, jaws and pharynx in a man bitten by a death adder. Peripheral limb weakness was present as well as paralysis of the intercostal muscles. Hudson (1988b) reports bilateral ptosis, ophthalmoplegia, diplopia, bulbar and peripheral paresis in two patients presumed to have been bitten by small-eyed snakes (*Micropechis ikaheka*) in Madang province. Respiratory distress was evident in both patients, and one of them, a 13 year old girl, eventually died from cardiorespiratory failure 42 hours post bite. Resolution of ptosis, bulbar paresis and limb weakness took more than 14 days in the other patient despite the use of a large quantity of antivenom.

The study of Papuan taipan (*Oxyuranus scutellatus canni*) envenomation by Lalloo *et al* (1995a) remains the most comprehensive investigation of neurotoxicity by this large and very dangerous snake. Of 166 patients with confirmed bites by taipans, 139 (83.7%) developed signs and symptoms of envenomation. Ptosis was present in 84/131 (64.1%) patients and was the most frequently reported symptom followed by dysarthria in 39/121 (32.2%) and dysphagia in 39/124 (31.5%). Diplopia was reported in 26/120 (21.7%) and 17/121 (14%) had dyspnoea; 41.7% of patients required intubation as paralysis deepened, and ventilation was required by 36.7% of envenomed patients. Progression to the point where intubation was required ranged from 3 to 55 hours with a median time point of 13.5 hours.

FIGURE 6: Comparison of clinical signs of neurotoxicity after the EIA-proven bites of three different species of highly venomous Papua New Guinean snakes. (SOURCES: Lalloo *et al*, 1994; Lalloo *et al*, 1995a; Lalloo *et al*, 1996)



Williams & Bal (2003) reported ptosis and dysphagia in all 9 patients with presumed Papuan taipan (*Oxyuranus scutellatus canni*) envenoming, 5 had diplopia, 6 had dysarthria, 5 had general bulbar paralysis, 4 had dyspnoea and 2 had peripheral limb weakness. Eight of the 9 patients died from respiratory failure. McGain *et al* (2004) reported neurotoxicity (one or more of ptosis, dysphagia or dyspnoea) in all 60 patients in their series who died from snakebite in the PMGH ICU between January 1992 and December 2001.

Brian & Vince (1987) reported ptosis (88%), drowsiness (56%), ophthalmoplegia (48%), respiratory weakness (42%), difficulty swallowing (40%), slurred speech (38%), limb weakness (27%) and jaw weakness (23%) in a series of 49 paediatric cases of snakebite admitted to PMGH between August 1981 and October 1984. Sixteen of these patients required subsequent intubation, although all 49 had received antivenom. In Trevett *et al*'s (1994a) examination of referral letters submitted with patients brought to PMGH from outlying health centres in Central and Gulf provinces, ptosis (either with or without concurrent ophthalmoplegia) was identified at the health centre in only 33% of cases, despite the fact that 82% of the patients had signs of ptosis/ophthalmoplegia on arrival at the hospital. Other signs and symptoms of neurotoxicity were not provided in the referral letters.

Williams *et al* (2003) reported symptoms and signs of neurotoxicity in 423 patients admitted to health centres in the Mekeo region between January 1997 and December 2001. Ptosis was reported in 68.6% of these cases. Other conditions were less frequently reported: ophthalmoplegia (2.8%), diplopia (21.7%), dysarthria (22.7%), dysphagia (41.4%), and dyspnoea (17.7%).

Other clinical effects of envenomation

Many of the victims of snakebite present at rural health centres with symptoms and signs that do not neatly fit into the three major clinical categories of coagulopathy, myotoxicity and neurotoxicity.

Campbell & Young (1961) note that transient tachycardia was an occasional feature of envenomation. Blasco & Hornabrook (1972) reports tachycardia during the terminal stages of small-eyed snake (*Micropechis ikaheka*) envenomation. Both tachycardia and bradycardia were observed in patients with proven envenoming by this species reported by Warrell *et al* (1996). One victim of death adder (*Acanthophis* spp.) envenoming from Western province presented to the rural health centre with a heart rate of 100 bpm, and subsequently developed both renal failure and a second-degree atrioventricular block (ventricular rate of 36 bpm). Laloo *et al* (1997) reported a single case of a death adder victim with septal T-wave inversion, as well as in a single case of New Guinean brown snake (*Pseudonaja cf. textilis*) envenomation. Laloo *et al* (1995a) found that 24.1% of Papuan taipan (*Oxyuranus scutellatus canni*) victims presented to hospital with bradycardia but were rarely hypotensive, and 52.2% of those tested had electrocardiograms that demonstrated abnormalities, particularly septal T-wave inversion (31.9%).

Tachycardia was an early feature in 5 fatal cases of presumed Papuan taipan (*Oxyuranus scutellatus canni*) envenomation reported by Williams & Bal (2003). Williams *et al* (2003) reported tachycardia in 20% of 564 snakebite patients from Mekeo for whom hourly blood pressure readings were available, while 19.8% had bradycardia, 24.1% were hypertensive and 25.5% were hypotensive. Campbell (1967a) notes that sudden collapse after snakebite is common following bites by Australian species. Laloo *et al* (1995a) reported sudden early collapse with transient loss of consciousness as a feature in 23% of Papuan taipan (*Oxyuranus scutellatus canni*) bites. McGain *et al* (2004) reported early collapse in 13.3% of the 60 fatal cases reported in the ICU at PMGH.

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Answers to ‘Can you pick the REAL Papuan blacksnake?’

- | | |
|---|-----------------------------|
| (A): D’Albert’s python (<i>Leiopython albertisi</i>) | Non-venomous |
| (B): Papuan taipan (<i>Oxyuranus scutellatus canni</i>) | Highly venomous & dangerous |
| (C): Brown-headed snake (<i>Furina tristis</i>) | Moderately venomous |
| (D): Papuan blacksnake (<i>Pseudechis papuanus</i>) | Highly venomous & dangerous |
| (E): Solomon’s coral snake (<i>Salomonelaps par</i>) | Moderately venomous |
| (F): Papuan taipan (<i>Oxyuranus scutellatus canni</i>) | Highly venomous & dangerous |
| (G): Papuan blacksnake (<i>Pseudechis papuanus</i>) | Highly venomous & dangerous |
| (H): Slatey-grey snake (<i>Stegonotus cucullatus</i>) | Non-venomous |

Snakes of Papua New Guinea

David Williams

Introduction

Papua New Guinea is home to a wide diversity of snake species which have adapted to live in almost all habitats; from coastal mangroves through to highland forests. Virtually all of them are openly feared, and many snakes are killed through fear, despite that fact that of more than 112 different varieties, fewer than half a dozen have killed humans, and the majority of human deaths have been due to just one snake in particular.

The snakes of PNG fall into six taxonomic Families:

NON-VENOMOUS Blind snakes or worm snakes (Family *Typhlopidae*) **11 species**

- ? Small burrowing snakes with rudimentary eyes (hence the name ‘*blind snake*’).
- ? Characteristic small smooth scales with a down turned spine on the tip of the tail that is used as an anchor (and contains **NO** poisonous sting).
- ? Shovel-shaped head for use when burrowing.
- ? Typically nocturnal, but may come to the surface during rain.

NON-VENOMOUS File snakes (Family *Acrochordidae*) **2 species**

- ? Aquatic snakes in both brackish water and estuaries.
- ? Named for their very rough, loose fitting skin; also called ‘*wart snakes*’ or ‘*elephant trunk snakes*’.
- ? Very agile in the water but have difficulty moving on land.

NON-VENOMOUS Pythons and boas (Family *Boidae*) **11 species**

- ? The three small (< 1 metre) boa species are viviparous – they produce live young.
- ? Two harmless species resemble highly venomous death adders in body size, shape and habits, and are often needlessly killed.
- ? Pythons range in size from 1 to 6 metres in length and reproduce by laying eggs.
- ? Nearly all Papuan pythons are nocturnal, and have heat-sensing pits which they use for tracking prey in total darkness.
- ? Large pythons are extremely strong and can easily suffocate an adult human being, although it is very unlikely that they could swallow one. There are anecdotal claims of children having been eaten by large pythons.
- ? PNG’s only legally protected snake is Boelen’s python (*Morelia boeleni*); a large black and white snake that occurs in cool Highland forests.

NON-VENOMOUS or MILDLY VENOMOUS Colubrid snakes (Family Colubridae) 35 species

- ? Representatives of the world's largest group of snakes; there are more than 2,000 species worldwide.
- ? There are five subfamilies in PNG and the members of two of these are mildly venomous, but most are unlikely to be a danger to man.
- ? One species, the brown tree snake (*Boiga irregularis*) has caused moderate envenomation in children on the island of Guam, and therefore may be potentially dangerous.
- ? The 35 species include a number of tree-climbing species; several aquatic species that occur in both freshwater as well as in brackish water, muddy estuaries and swamps; and a number of small ground-dwelling snakes.
- ? Most of these species grow to no more than 1-1.5 metres in length; the majority reproduce by laying eggs, although the aquatic species bear live young.

VENOMOUS Front-fanged snakes (Family Elapidae)**30 species**

- ? The Family which includes the species that are known to kill humans; snakes in 6 of the 14 genera can cause fatalities.
- ? There are 13 genera of land-dwelling snakes and a single genus containing two species of marine-dwelling snakes which can return to land.
- ? Most of the snakes in this Family should be considered potentially dangerous (with the possible exception of the very small ground-dwelling forest snakes); however very little is known about the venoms of most species.
- ? All species, with the exception of death adders (*Acanthophis* spp.), are oviparous (reproducing by laying eggs).
- ? All species produce venom in specialized salivary glands; venom is injected through the grooves in fangs situated at the front of the maxillary bone in the upper jaw.
- ? Species may be either diurnal (active by day) or nocturnal (active by night), and some species are active during both the day and the night.

VENOMOUS True sea snakes (Family Hydrophiinae)**23 species**

- ? True sea snakes are not able to survive for long periods on land, and all have broad, paddle-shaped tails that have evolved specifically for life in the ocean.
- ? Some estuarine species have been found long distances from the open ocean in coastal rivers, and sea snake bites have occurred in rivers in Papua New Guinea.
- ? Sea snakes have a number of highly specialized adaptations to life in the sea, including valves on the nostrils that prevent water entering the lungs; the ability to absorb oxygen from sea water through the skin; salt excreting glands that protect them from dehydration; and an enlarged lung that can store air for deep diving.
- ? Some species in the open sea can dive to depths of more than 100 metres.
- ? Many are highly venomous and some are extremely dangerous to man, especially the very large fish or crustacean eating species.
- ? All reproduce by bearing live young.

General biology and ecology of snakes

All snakes share a number of common biological characteristics that make them unique among all other members of the animal kingdom. No other animal is as uniquely handicapped. Despite their lack of limbs; technical deafness; and imprecise long-range vision, snakes have managed to successfully colonize virtually every corner of the planet with the exception of the two poles. Snakes reside in the depths of the oceans; the thickest of rainforests, driest of deserts, and even in sub-arctic tundras where temperatures plummet to many degrees below freezing. Even though most of us are fearful of snakes, few will not admit to admiring their incredibly successful occupation of our planet.

Snakes occupy important ecological roles, and in many parts of the world (particularly Australia and New Guinea) without carnivorous mammals, they are among the highest order predators and fulfil a very important role in the delicate balance of complex ecosystems. The removal of snakes from the environment might be a blessing for human safety, however in ecological terms their loss can be catastrophic; many species play crucial roles in the control of agricultural pests such as rats and mice, and there are examples from around the world of huge increases in rodent-related crop losses in the absence of natural predators like snakes.

Biogeographical Radiation

The earliest fossil snakes appeared approximately 50-60 million years ago and were boid (python-like) snakes of moderate size. In the Australasian region the first front-fanged elapid snakes appear between 23-34 million years ago. Venomous snakes appear to have evolved from a common ancestor and to have radiated across the Australian landmass. During this time the island of New Guinea was connected to Australia by now-submerged land bridges in the Arafura Sea and Torres Strait, and this allowed considerable sharing of biodiversity. While some snake species such as the green tree python (*Morelia viridis*) and the amethystine python (*Morelia amethystina*) appear to have migrated south from New Guinea into north Queensland, the venomous species have done the opposite; migrating northwards in separate radiations into New Guinea where they became isolated and diversified into new species.

Our most highly venomous snakes are believed to have reached New Guinea around 6-8 million years ago. At this time two species complexes crossed to New Guinea from northern Australia; the smooth-scaled death adders (*Acanthophis laevis*) (6.4-7.5 Mybp) and the mulga snakes (*Pseudechis cf. australis*) (6.2-7.4 Mybp). The *A. laevis* group diversified right throughout New Guinea and as far west as the Indonesian island of Seram, while *P. cf. australis* seems content to have remained living in the open forests and savannah's of the Oriomo plateau and Wasur lowlands on the west of the Fly river.

The Papuan black snake (*Pseudechis papuanus*), whose closest relative can be found in central-western Queensland, probably arrived here across the trans-Torresian land bridge around 2.9-3.6 million years ago. The rough-scaled death adders (*Acanthophis rugosus*) are only recent colonialists having arrived from Australia sometime in the last 0.6-1.0 million years. Remarkably genetic studies suggest that the most highly venomous of all New Guinea's snakes, the Papuan taipan (*Oxyuranus scutellatus canni*) only made its way north during the very late Pleistocene before the loss of the most recent land bridge approximately 8,000 to 10,000 years ago. This snake is such a recent arrival that in genetic terms its status as a different subspecies to the Australian taipan (*Oxyuranus scutellatus scutellatus*) is tenuous.

Physiology

All snakes share a common physiological structure:

- ? An elongated backbone that can comprise more than 400 individual vertebrae and rib pairs which can articulate horizontally, vertically and diagonally to give extreme flexibility and fluidity of motion.
- ? Dry waterproof skin composed of keratinous material similar to that of human fingernails; the texture of the skin varies – in some species it is smooth, while in others it can be slightly to extremely rough to the touch.
- ? Flexible skulls with loosely joined bones that can separate from each other to enable the snake to swallow prey items many times larger in diameter; the lower jaw bones are joined in the middle by elastic ligaments to enable wide separation.
- ? Ectothermic metabolism which relies on external heating rather than self-generation of body heat (i.e. as in mammals and birds). The key advantage of this is that snakes have a metabolic rate that is only 10-15% of that of a ‘warm-blooded’ animal, and can therefore survive much longer without eating.
- ? Completely absent external ear openings; despite this they are not deaf – snakes ‘hear’ by detecting sound vibrations through their bodies and these vibrations are picked up by internal ear structures.
- ? A bifurcated (‘forked’) tongue which is the primary scent organ; the tongue is flicked out to collect scent particles in the air which are then transferred to a special groove in the roof of the mouth (Jacobson’s Organ) that contains chemoreceptors similar to those present in the noses of other animals.
- ? Binocular vision of variable acuity and absent eyelids. Snakes track movement rather than identifying shapes, and some can detect movement at considerable distances.
- ? With the exception of crocodiles all reptiles have a three-chambered heart. In snakes the position of the heart largely depends on the behaviour of the species; tree climbing pythons and colubrids have hearts positioned closer to the head, while diving sea snakes have a heart that is more centrally located.
- ? A single functional lung that is elongated and may extend up to two-thirds of the body length. The second lung is much smaller and is little more than an air sac.

Reproduction

Different species of snakes employ different reproductive strategies, however reproduction is sexual in nature despite the fact that female snakes of some species can ‘retain’ sperm in their bodies and produce successive clutches/broods of young without a second mating.

In Papua New Guinea nearly all species mate in late winter and spring (between June and October) although some may mate all year round in favourable conditions. The males of some species such as Papuan taipans (*Oxyuranus scutellatus canni*) engage in ritual fighting prior to mating. This typically involves two or more combatants entwining around each other like corkscrews and attempting to push each others head to the ground. Biting rarely occurs until one snake attempts to flee, and then he may be bitten by the pursuing victor. Most snakes are immune to their own venom, so such bites do not result in death.

A successful mate may mate with a female for many hours over many days. After mating is complete it is very rare for the two snakes to remain together, as snakes are typically solitary creatures.

In egg-laying (oviparous) species (such as all pythons and most venomous land species) the fertilized embryos develop in the female over a period of 6-10 weeks. At the end of this time the female will find a secluded location such as a deserted animal burrow, or the space under a large rock or log to use as a laying chamber. Pythons typically coil around their eggs to protect them from predators and to ensure an even incubation temperature. Female pythons do not feed while incubating eggs, however many use muscle contractions to generate slight increases in body heat to warm the eggs, and this added reproductive cost means that they may lose a considerable amount of body weight during this time.

Most other egg-laying snakes deposit their eggs and then leave them to incubate at ambient temperature. Many ground-dwelling snakes lay their eggs in rotting vegetation in order to take advantage of higher temperatures due to decomposition. These snakes are then able to resume feeding immediately, and many may subsequently produce additional clutches of eggs in the same year.

The death adders (*Acanthophis* spp.) are unique among PNG's venomous snakes in that they, like the marine sea snakes of the Family *Hydrophiinae*, produce live young (viviparous). The embryos develop inside the body of the female over a lengthy period (from 4 to 6 months in some species) before being born alive inside a thin membrane from which the young snakes rapidly break free and disperse. Once the baby snakes hatch, or are born, their parents have no interest in them, and adult snakes do not protect or guard their young – in fact many species will eat their own babies if the small snakes do not move away quickly.

Life Expectancy

There is very little information available about how long a snake can live in the wild. Snakes which are born and raised in captivity may live for more than 15-20 years; however this is not an accurate estimate of wild life expectancy because captive snakes do not have the same risks of predation or death through disease.

What is known is that most juvenile snakes do not reach reproductive maturity until they are between 2 and 3 years of age. Reproduction is the driving force in all organisms and for a species to be successful it must reproduce at least once and have at least two juveniles survive long enough to reproduce themselves. The higher the risk to juveniles, the more young a snake is likely to produce in a single clutch or brood.

Captive pythons have been known to live for more than 25 years, and some captive venomous snakes have also lived for between 15-20 years, although most live only for 8-10 years. With this in mind it is likely that the average life expectancy of most wild snakes would be from 5 to 8 years depending on the species.

Aggressive Behaviour

It is very important to realise that snakes are not aggressive animals, although most will attempt to defend themselves if threatened or approached.

All snakes are secretive. Their absence of limbs despite enabling them to adapt to many different environments does leave them with vulnerabilities, and most snakes spend the majority of their time being as elusive and secretive as possible in order to avoid potential predators. If a snake is given an opportunity to escape from a predator it will always take this option rather than attacking. At the same time however, different species may be more easily threatened than others; a death adder (*Acanthophis* spp.) has to be touched before it will bite, but a Papuan taipan (*Oxyuranus scutellatus canni*) may only need to be approached closely

(within 5-6 metres) before feeling sufficiently threatened to bite what it perceives to be a potential threat. Understanding this sort of behaviour by different species can be important when teaching people how to avoid snakebite, and it is often useful to use the analogy of the frightened dog that barks loudly when you are distant, but which may bite if you walk to close to it. Many snakes are exactly the same – at a distance they may hiss and puff themselves with air to make themselves look more dangerous, but if you come too close, they become afraid and defend themselves in the only way possible – by biting.

There is no truth in the common misconception that venomous snakes will attack people during the ‘breeding season’; the only reality is that male snakes are more likely to be encountered when they are actively looking for females.

If a person sees a snake and either stands completely still or slowly backs away there is a 99.9% chance that the snake will use the opportunity to escape as quickly as possible. The only exception to this rule of thumb are the death adders (*Acanthophis* spp.) which are ambush hunters and rely on sitting perfectly still to all their prey to come towards them. A death adder will sit completely still even if a person walks right up to it, and if the person is unfortunate enough to touch the snake or stand on it, then the death adder will bite.

Feeding

Most snakes have particular dietary preferences, although some are more specific about what they eat than others. The small ‘blind snakes’ feed solely in ant and termite eggs, and consequently spend much of their lives underground in ant and termite nests satisfying this peculiar appetite. Some species of sea snakes feed solely on fish eggs, while others live upon crabs and other crustaceans, and still others prefer eels or fish.

Many colubrid snakes live on small fast moving lizards, and have slender streamlined bodies and great agility to enable them to catch such prey. Some semi-aquatic colubrids live only on frogs and toads, and in particular the Keelbacks (*Tropidonophis* spp.) are such successful amphibian-eaters that they are able to consume poisonous cane toads (*Bufo marinus*) without succumbing to the potent cardiotoxins the toad has in its parotid gland secretions.

Small aboreal pythons such as the green tree python (*Morelia viridis*) have extremely long front teeth that they use to snatch birds and small bats out of the air as they fly close by. Ground dwelling giants such as the Papuan python (*Apodora papuana*) are opportunistic feeders and will eat almost anything they can overpower including lizards, other snakes, ground birds and mammals like bandicoots and wallabies. Large Papuan pythons have been known to eat wallabies up to 23kg in weight – the size of a small child!

Small venomous snakes like death adders (*Acanthophis* spp.), brown-headed snakes (*Furina tristis*), and whipsnakes (*Demansia* spp.) feed primarily on small lizards and occasionally small rodents. The New Guinea forest snakes (*Toxicocalamus* spp.) have been reported feeding on earthworms and other small invertebrates that live among the leaf litter on the forest floor. Larger venomous snakes tend to be opportunistic, and this is certainly the case with species like the New Guinea small-eyed snake (*Micropechis ikaheka*) which feeds on lizards, frogs, small rodents and even other snakes. Papuan blacksnakes (*Pseudechis papuanus*) are believed to be largely frog-eaters (although they may also eat lizards and rodents) and this is one of the reasons their numbers appear to have declined rapidly with the spread of the introduced cane toad (*Bufo marinus*) which is extremely poisonous if eaten. Papuan taipans (*Oxyuranus scutellatus canni*), on the other hand, are highly specialized mammal feeders, and this is the major reason for their extreme toxicity towards humans; the venom of these snakes has specifically evolved to target mammalian nervous systems.

Differences between non-venomous and venomous snakes

The accepted means of distinguishing one species of snake from another has for many years been based upon counting the numbers and arrangements of scales on their bodies (FIGURES 1 & 2). This works very well for zoologists and museum technicians, but unfortunately is fraught with obvious dangers for everyone else. As a consequence it is very difficult for untrained people to identify one snake from another, and this has special significance when dealing with cases of snakebite.

In southern PNG the vast majority of snakebite victims who see a snake identify the offending animal as a 'Pap black'; literally taken to mean a Papuan blacksnake (*Pseudechis papuanus*). Accepting such an identification at close quarters can, however, have disastrous consequences, given that:

- there are several species of snakes (assuming a snake is actually involved at all) that may have been responsible for the snakebite; and while,
- some of them are completely non-venomous species, at least two species of black-coloured snake are extremely venomous; and
- administration of the either the incorrect antivenom, or an antivenom when one is not required can result in serious medical complications or the death of the patient.

Studies of snakebite in Papua New Guinea have demonstrated that the reality is that less than 5% of serious snakebites admitted to PMGH are caused by Papuan blacksnakes (*Pseudechis papuanus*), and that an overwhelming majority (83.2%) of 'Pap black' bites are actually caused by the much more dangerous Papuan taipan (*Oxyuranus scutellatus canni*).

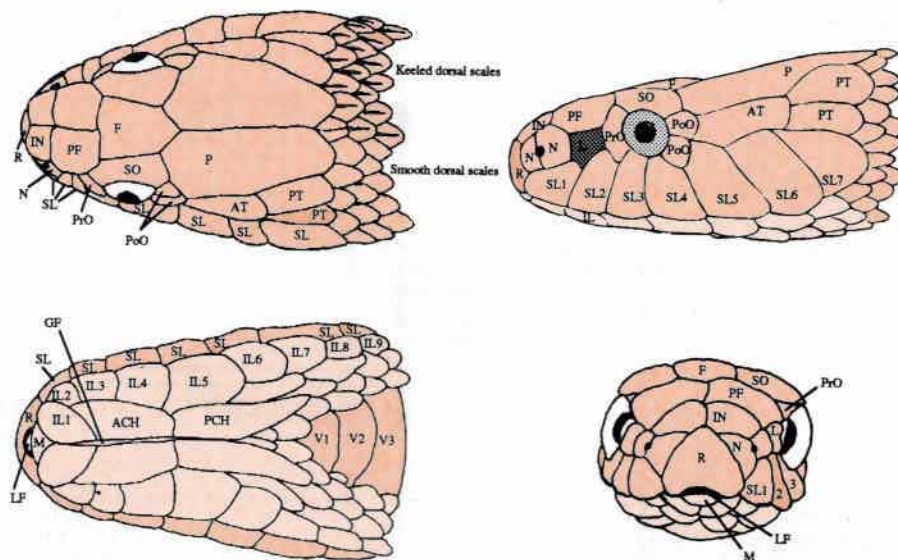


FIGURE 1: IDENTIFICATION FEATURES OF SNAKES: HEAD SCALATION

Typical arrangement of head scales that are used in the identification of different species of snakes. **KEY:** (ACH) anterior chin shield; (AT) anterior temporals; (F) frontal; (GF) gular fold; (IL) infralabials; (IN) internasal; (LF) lingual fossa; (M) mental; (N) nasal; (P) parietal; (PCH) posterior chin shield; (PF) prefrontal; (PoO) postoculars; (PrO) preoculars; (PT) posterior temporals; (R) rostral; (SL) supralabials; (SO) supraocular; (V) ventrals.

SOURCE: *A Guide to the Snakes of Papua New Guinea* by MT O'Shea (Independent Publishing) (1996)

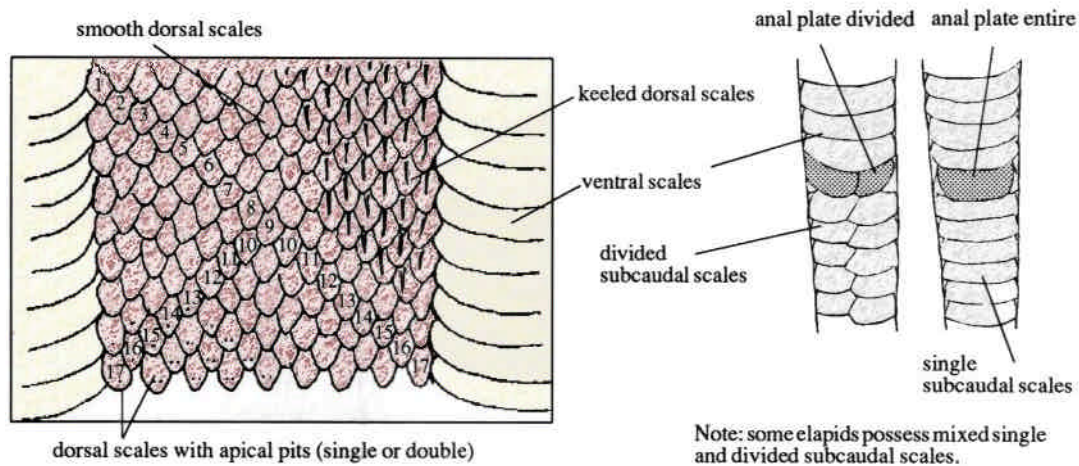


FIGURE 2: IDENTIFICATION FEATURES OF SNAKES: BODY SCALATION

A key means of differentiating species rapidly is to count the numbers of scale rows across the dorsal (back) surface at the middle of the body. Scales are counted diagonally. Additional counts of the total numbers of ventral (belly) scales and subcaudal (beneath tail) scales provide further information for identification purposes, as does the structure of the larger anal scale covering the cloaca (it may be either singular or split into two halves). **WARNING: Inexperienced people should never attempt to count the scales of a live snake.**

SOURCE: *A Guide to the Snakes of Papua New Guinea* by M T O'Shea (Independent Publishing) (1996)

On the other side of the island, many people who are bitten by a 'short, sharp-tailed snake' or a 'death adder' present to health centres in an extremely anxious state, with tachycardia, shortness of breath and anxiety (to the point of causing nausea or vomiting). Despite the seemingly clear-cut identification the reality is that the real culprit is not a highly venomous death adder (*Acanthophis* spp.), but a completely non-venomous ground boa (*Candoia aspera*) with a bad temper!

So how then can a casual observer tell the difference between a non-venomous and venomous snake, or for that matter between two different varieties of any snake?

There is no simple answer.

There are however some approximate rules of thumb that may help to distinguish some species:

- (1) A description of either a black or brown-coloured snake 'with a red stripe on the back' refers invariably to the highly venomous Papuan taipan (*Oxyuranus scutellatus canni*).
- (2) All snakes can climb, and even small snakes like death adders (*Acanthophis* spp.) can climb very well. **HOWEVER**, as a general rule, the majority of snakes encountered more than 2 metres above the ground are non-venomous.
- (3) A description of a 'white snake with pink stripes' typically refers to the highly venomous New Guinea small-eyed snake (*Micropechis ikaheka*); 'white snake' is the common name for this snake in the Madang and Karkar Island districts.
- (4) Aquatic snakes with laterally flattened 'paddle-shaped' tails are venomous sea snakes.
- (5) If a suspected snakebite is involved and you are in doubt – follow the management plan, perform appropriate diagnostic tests and observe the patient closely over a period of at least 24 hours.

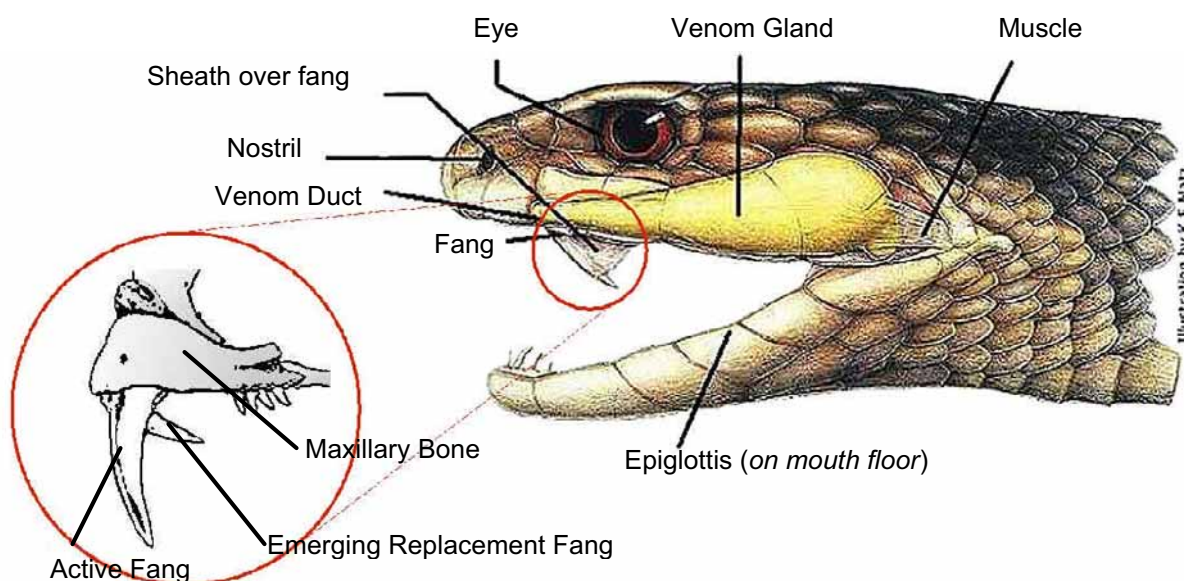
Venom delivery system

All venomous snakes produce their toxins in modified salivary glands comprised of densely packed epithelial cells which secrete the proteins, carbohydrates and other compounds that constitute “venom”. Each snake has two separate glands located on either side of the head just below, and to the rear of, the eyes. The glands are encased in powerful muscles which are used to compress the venom glands and expel venom along narrow ducts which connect to the tops of thickly grooved fangs at the front of the upper jaws.

Papua New Guinea’s front-fanged land snakes and sea snakes differ from some other venomous snakes in the degree of evolutionary development present in the highly modified teeth that are used to inject venom into their prey. The fangs of more primitive venomous colubrid snakes such as the brown tree snake (*Boiga irregularis*) are located at the rear of maxillary bones (hence: ‘rear-fanged’) in the upper jaw, are relatively short, and are only slightly grooved. This system is relatively inefficient and these snakes need to be able to grasp prey firmly and ‘chew’ in venom in order to inject venom. In the most highly evolved venomous snakes, such as the African vipers (i.e.: *Bitis* spp., *Echis* spp.) and North American rattlesnakes (*Crotalus* spp.), the fangs are extremely large (up to 4.5 centimetres!), are completely hollow and fused (like hypodermic needles) and are located at the front of a highly mobile maxilla; both the fangs and the maxillary bones rotate forward to project the fangs outward and down when these snakes bite. The elapid and hydrophiid snakes that occur in PNG and Australia are intermediate between these two groups in terms of evolutionary fang development (FIGURE 3).

FIGURE 3: VENOM DELIVERY SYSTEM OF ELAPID SNAKES

Elapid snakes are proteroglyphous, meaning that the fangs are grooved rather than completely hollow, and are located at the front of the maxillary bone. The fangs of venomous snakes are replaced periodically throughout their lives, and replacement fangs are always under development. The fangs of most elapid snakes in Papua New Guinea are extremely short; between 1 and 4 millimetres. The notable exceptions are the Papuan taipan (*Oxyuranus scutellatus canni*) which can have fangs more than 1 centimetre long; and the death adders (*Acanthophis* spp.) – large specimens can have fangs up to 6-7 millimetres long.



Venomous Papua New Guinean snakes

There are 37 species of semi-aquatic and land-dwelling venomous snakes in Papua New Guinea that are currently known to science. The majority of these are not considered to be dangerous to humans, but this is based more on a lack of information than on specific scientific evidence.

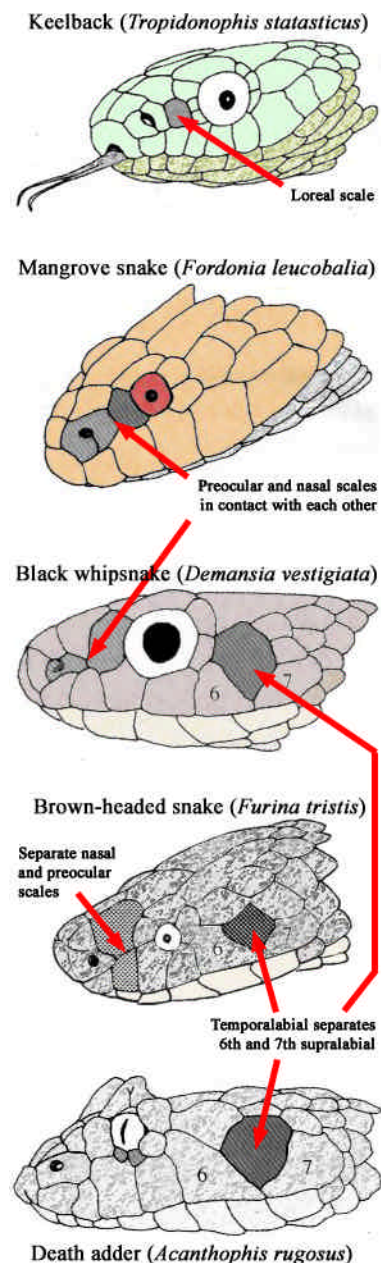


FIGURE 4: HEAD SCALES

Non-venomous snakes typically have a loreal scale between the nasal and preocular scales; a feature absent in venomous species. Elapid snakes have a large temporalabial scale that wedges between supralabial scales on the upper lip.

The bites of rear-fanged semi-aquatic species such as the white-bellied mangrove snake (*Fordonia leucobalia*) are not known to be dangerous, and while there have been cases of envenomation (mainly among children) by the aboreal brown tree snake (*Boiga irregularis*) on the island of Guam, these were unusual cases, and the majority of bites by this species produce no effects.

Nothing is currently known about the venoms of most of the 30 species of elapid snakes present in Papua New Guinea. Among nine species of New Guinean forest snakes (*Toxicocalamus* spp.) there are several species that grow large enough to be considered potentially dangerous. The widely distributed Loria forest snake (*Toxicocalamus loriae*) and Preuss's forest snake (*Toxicocalamus preussi*) both reach maximum lengths of between 70-80 centimetres and should be considered to be of potential medical importance.

Other small elapid snakes that could be dangerous include the black-striped snake (*Rhinoplocephalus nigrostriatus*) from the Oriomo plateau in Western province; the brown-headed snake (*Furina tristis*) that occurs right across southern PNG; and the Solomon's coral snake (*Salomonelaps par*) from Buka, Bougainville, Fauro and Shortland Islands.

The Papuan whipsnake (*Demansia vestigiata*) attains a maximum length of approximately 1.5 metres and is often mistakenly called a 'Pap black'. This slender, very fast snake has a characteristic long whip-like tail and large eyes that are sometimes surrounded by a yellowish ring of colour on the ocular scales. Bites by whipsnakes can cause severe local pain and swelling but there are no current reports of systemic illness other than allergic reactions in people who have histories of repeated snakebites.

The bites of seven species are known to be potentially fatal:

- ? Papuan taipan (*Oxyuranus scutellatus canni*)
- ? New Guinea death adders (*Acanthophis rugosus* and *Acanthophis laevis*)
- ? New Guinea small-eyed snake (*Micropechis ikaheka*)
- ? Papuan blacksnake (*Pseudechis papuanus*)
- ? Papuan mulga snake (*Pseudechis cf. australis*)
- ? New Guinea brown snake (*Pseudonaja cf. textilis*)

Photographs of some non-venomous PNG snakes



Blind snake (*Ramphotyphlops*) spp.



Arafuran file snake (*Acrochordus arafurae*)



Common keelback (*Tropidonophis mairii*)



Coconut treesnake (*Dendrelaphis calligastra*)



Slatey-grey snake (*Stegnotus cucullatus*)



Papuan carpet python (*Morelia variegata*)



Green tree python (*Morelia viridis*)



Boelen's python (*Morelia boeleni*)



Papuan olive python (*Apodora papuana*)



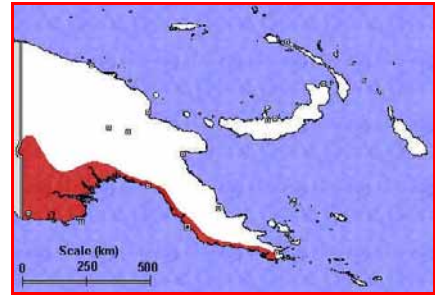
D'Albert's python (*Leiopython albertisi*)

Papuan taipan (*Oxyuranus scutellatus canni*)

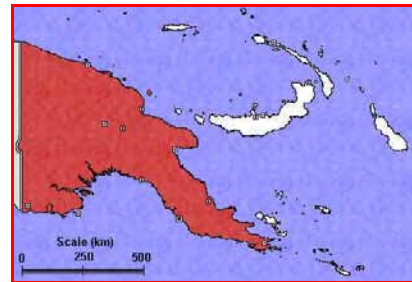
- DESCRIPTION:** A large snake that is typically dark-brown to black above with a broad orange-red dorso-vertebral stripe extending along most of the back. The ventral surface can be white to orange in colour. The tip of the nose and the sides of the lips are usually creamish.
- SCALATION:** Dorsal scales in 21-23 rows at mid-body; 220-250 ventrals; anal single; 45-80 paired subcaudals.
- BODY SIZE:** Average length is from 1.8-2.4 metres; maximum length is 3.36 metres.
- DISTRIBUTION:** Milne Bay, Central, NCD, Gulf and Western Provinces and as far west as the Wildoman River in West Papua.
- HABITAT:** Inhabits grasslands and savannah woodland to an altitude of around 400 metres. Adapts well to areas of human habitation and is a frequent inhabitant of village gardens and residential areas. Specimens have been collected in Port Moresby on Ela Beach Road.
- DIET:** Feeds on warm-blooded prey; primarily rodents and small mammals to the size of bandicoots, but also known to eat ground-dwelling birds. Does not appear to have been affected by the introduction of the cane toad (*Bufo marinus*), which is hypothesized as a cause of declines in frog-eating species. If other species continue to decline, the proportion of snakebites involving this species will only continue to rise.
- REPRODUCTION:** Oviparous producing 1-2 clutches of 16-22 eggs each year.
- ACTIVITY:** Active by day but may be nocturnal just after dark in very hot weather.
- BEHAVIOUR:** Unless approached closely this is a very shy, extremely nervous snake that endeavours to avoid human contact. Veteran snakeman Ken Slater (who described this species in 1956) said of the Papuan taipan that he knew of "*no other snake more formidable or adept in defence when at close quarters nor more capable of clearing the Papuan grasslands of man if it did adopt truly aggressive behaviour*".
- If provoked or frightened this very large snake is indeed capable of unparalleled ferocity and may inflict multiple bites in rapid succession using a 'snap and release' strategy in which larger amounts of venom are injected with each subsequent bite. Taipans also tend to strike much higher than other venomous species; bites to the calves or even above the knee are not uncommon. This is the only snake in Papua New Guinea that will pursue an attack against a perceived threat.
- MEDICAL IMPORTANCE:** The most venomous snake in Papua New Guinea, with the highest venom yield and the longest fangs (*see* CHAPTER 3).
- There is considerable evidence that this species is responsible for the majority of serious snakebites admitted to health centres in Central Province and to PMGH. In a study by Laloo et al (1995), it was shown, using a specific diagnostic test (EIA), that 82.3% of serious snakebites in Central Province were caused by this species.
- ANTIVENOM:** CSL monovalent taipan antivenom or CSL polyvalent antivenom.

Death adders (*Acanthophis rugosus*, *Acanthophis laevis*)

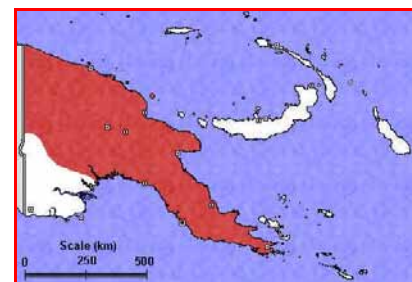
- DESCRIPTION:** Short, thickset snakes with large angular heads and raised supraocular scales that give the appearance of small horns. The tail is thin and ends in a soft ‘*spine-like*’ tip. Colour varies enormously and background body colour can vary from almost black to red, brown, yellow or light grey interspersed with alternate light and dark transverse bands which are most prominent when the snake is threatened. The labial scales are usually white with dark brown or black streaks. The belly is white, occasionally with darker spots.
- SCALATION:** Dorsal scales in 21-23 rows at mid-body; 110-135 ventrals; anal single; 36-60 subcaudals – anteriorly single, paired posteriorly. Dorsal scales of *Acanthophis laevis* are usually smooth, while those of *Acanthophis rugosus* are strongly keeled and look rough.
- BODY SIZE:** Average length is from 0.3-0.6 metre; maximum length is 1.1 metres.
- DISTRIBUTION:** Occurs in all of the mainland PNG Provinces and on closer islands such as Karkar, Yule, Daru and those in the mouth of the Fly River. Also found throughout West Papua and on Seram and the Aru islands.
- HABITAT:** Death adders occur in a wide range of habitats including lowland grasslands and savannahs, sago swamps, monsoonal forests, woodlands, rainforest, coffee, tea and cocoa plantations, village gardens, highland grasslands and other montane environments.
- These ground dwelling snakes do well in any area with an abundance of leaf litter, grass trash or other ground cover.
- DIET:** Predominantly small ground-dwelling lizards, frogs and occasionally small rodents or ground birds that are attracted to wriggling of the snake’s grub-like tail. The tail does not contain a poisonous sting.
- REPRODUCTION:** One of the very few viviparous venomous snakes in PNG which produce live-born young in litters of 8-12.
- ACTIVITY:** Generally nocturnal these snakes usually sit under cover during the day; often close to pathways along which small animals (and people) often travel. If disturbed (by the burning of grass for example) they may move around during the day.
- BEHAVIOUR:** Death adders are unique in their reliance on a ‘*sit and wait*’ ambush feeding strategy which means that they will remain motionless on the ground even when approached very closely. These inoffensive snakes become a significant snakebite threat because of this behaviour. While most snakes will flee from an approaching human, death adders rely on remaining motionless to avoid detection, but if touched will strike reflexively.
- MEDICAL IMPORTANCE:** Although considered responsible for only about 10% of serious snakebites in Central Province, death adders are the major cause of snakebites in northern PNG where they are the most commonly encountered venomous snake. (see CHAPTER 3 for venom data).
- ANTIVENOM:** CSL monovalent death adder antivenom or CSL polyvalent antivenom.



PAPUAN TAIPAN (*Oxyuranus scutellatus canni*) showing characteristic orange-red dorso-vertebral stripe. The very dark body colour of some snakes (smaller photograph) often results in this species being mistaken for a Papuan blacksnake (*Pseudechis papuanus*)



DEATH ADDERS (*Acanthophis* spp.) Note large angular head with raised supraocular scales over eyes. Also note thin tail with soft spine-like tip that is used as a lure to attract prey – has no poisonous sting.



NEW GUINEA SMALL-EYED SNAKE (*Micropechis ikaheka*) A fossorial burrowing snake that is often found living in plantation trash and husk piles on Cocoa plantations in northern Papua New Guinea.

New Guinea small-eyed snake (*Micropechis ikaheka*)

- DESCRIPTION:** This is a thick-bodied snake with an extremely variable colour pattern based on a greyish head and pale yellow, creamish or salmon coloured body with dark-tipped scale edges that give rise to broad dark bands from midbody to the end of the tail. Juvenile snakes are much more prominently marked than adults (see inset photograph previous page). In Madang Province the snake is often known as the ‘white snake’ due to its pale body colour.
- SCALATION:** Midbody dorsal scale rows are in 15 rows; ventrals number 178-225; the anal is divided as are 36-55 subcaudals under the tail.
- BODY SIZE:** Average length is from 1.2-1.4 metres; maximum length is 2.1 metres.
- DISTRIBUTION:** Recorded from northern Western Province (Kiunga to Star Mountains); and all of the Highland and New Guinea Provinces. Isolated records in Gulf and Central Provinces. Widely distributed in West Papua and the Aru Islands.
- HABITAT:** Lives in wet environments from sea level to over 1,500 metres. Common in monsoonal forests, lowland swamps and rainforests where it lives in ground debris. There are abundant regional populations in and around Cocoa plantations (especially Karkar Island) where the snake lives in old coconut husk piles.
- DIET:** Believed to be an opportunistic feeder, preying on a wide variety of small ground dwelling animals including lizards, rodents, frogs and particularly other snakes, including its own species.
- REPRODUCTION:** Nothing is currently known although juvenile snakes have been collected in the wild.
- ACTIVITY:** Although generally considered to be a ground dwelling largely nocturnal species, there is a single report from West Papua of a serious snakebite having been caused by a large *Micropechis ikaheka* that was caught in a bird trap high in a tree.
- During the dry season this snake is a common inhabitant of coconut husk piles, but appears to disperse during the wet season and may be encountered at night moving on the ground.
- BEHAVIOUR:** A shy snake until disturbed. If handled this snake is very aggressive and will bite readily, often chewing down hard and refusing to let go of its victim. Small specimens are very agile and surprisingly fast.
- The small eyes and smooth body scales are specific adaptations for foraging among ground debris and loose topsoil.
- MEDICAL IMPORTANCE:** This highly venomous snake is believed to account for only a small proportion of snakebites in the mainland Madang and Sepik regions, however one study found that approximately 40% of snakebites on Karkar Island could be attributed to bites by *Micropechis ikaheka* (see CHAPTER 3 for venom data).
- ANTIVENOM:** CSL polyvalent antivenom.

Papuan blacksnake (*Pseudechis papuanus*)

- DESCRIPTION:** As the name implies these snakes are typically gunmetal black both on the dorsal and ventral surfaces. The tip of the nose and the throat may be cream to yellow in colour. Rare brown-coloured specimens have also been recorded. This is a large heavy-bodied snake; the head is indistinct from the neck, unlike the Papuan taipan (*Oxyuranus scutellatus canni*) in which the head is clearly distinct from the slender neck.
- SCALATION:** There are 19 rows of dorsal scales; 220-230 ventrals; a divided anal scale and from 48-65 subcaudals (single anteriorly, but divided posteriorly).
- BODY SIZE:** Average length is from 1.2-1.7 metres; maximum length is 2.45 metres.
- DISTRIBUTION:** Specimens have been recorded in Milne Bay, Central, Gulf and Western Province, as well as in neighbouring southern West Papua. The current status of the species in Milne Bay and Central Provinces is unknown; very few specimens have been reported over the last 25 years, and no live or dead specimens have been positively identified in Central Province since 1992. The species is believed to be common in coastal areas of Gulf Province, but there are no identified specimens. Three snakes were collected near Kunini and Weam in Western Province in 2001, and the species is known to be common around Merauke in West Papua.
- HABITAT:** Coastal swamps and marshland, monsoonal forests, bamboo thickets and occasionally savannah woodland. Specimens have been found in rubber tree groves in the Abau district, and in rainforest around Veifa'a.
- DIET:** Opportunistic, but prefers frogs. One hypothesis for the apparent decline in numbers in Central Province is that the spread of the poisonous introduced cane toad (*Bufo marinus*) has resulted in regional extinction.
- REPRODUCTION:** Oviparous, producing clutches of 12-18 eggs.
- ACTIVITY:** This is a diurnal snake that is more likely to be encountered in daylight when it comes out of hiding to bask or hunt for food. In West Papua specimens have been collected in the early morning basking close to the edge of sago palm lined river banks. Specimens have been reported basking near the edges of forest thickets near Kukipi in Gulf Province. Ken Slater noted in the 1960's that these snakes were more likely to be seen during the late dry season.
- BEHAVIOUR:** Ken Slater, who collected many Papuan blacksnakes during the 1950's and 1960's for antivenom production, believed that it was a shy snake which almost always attempted to escape when disturbed, but noted that if provoked it would bite with minimal provocation.
- MEDICAL IMPORTANCE:** Lalloo et al (1995) determined by EIA that 4.2% of serious snakebites admitted to PMGH over a thirty month period were caused by this snake. (*For venom data see CHAPTER 3*).
- ANTIVENOM:** **CSL blacksnake antivenom or CSL polyvalent antivenom.**

Papuan mulga snake (*Pseudechis cf. australis*)

<u>DESCRIPTION:</u>	A small slender species that is typically light yellowish-tan to reddish-brown dorsally, with a creamish ventral surface. The head is short, broad and indistinct from the neck. When agitated the snake will flatten the body to make it appear larger to a potential enemy.
<u>SCALATION:</u>	Dorsal scales in 17 rows at midbody; 185-225 ventrals; anal divided with 48-60 subcaudals that are normally all single with last few paired.
<u>BODY SIZE:</u>	Average length is from 0.8-1.0 metre; maximum length is 1.3 metres.
<u>DISTRIBUTION:</u>	Only recorded near Bensbach and Weam in Western Province but possibly occurs further east on the Oriomo plateau. Common around the Etna Bay and Merauke districts in West Papua.
<u>HABITAT:</u>	Restricted to dry savannah and savannah woodlands where they hide among rocks, fallen timber and in animal burrows. Specimens have also been found near the periphery of wetlands where frogs are abundant.
<u>DIET:</u>	An opportunistic species that feeds on lizards, frogs, small rodents and ground birds. Australian specimens are known to be cannibalistic.
<u>REPRODUCTION:</u>	Oviparous; however nothing is currently known of clutch sizes or seasonal reproductive timing in Papuan specimens. In Australia specimens of <i>Pseudechis australis</i> reproduce in early spring through to mid-summer, with females depositing clutches of 6-18 eggs.
<u>ACTIVITY:</u>	A diurnal snake that may become nocturnal in very warm weather. Mulga snakes are often observed hunting during early to mid-morning or in the late afternoon. In Australia very closely related forms are commonly nocturnal in the tropics. In north-west Queensland and the Northern Territory these snakes may be found hunting for food well into the early hours of the morning; it seems reasonable to anticipate the same behaviour among Papuan specimens.
<u>BEHAVIOUR:</u>	The Papuan mulga snakes are much smaller and more slender than their Australian relatives, and it is possible that they actually represent a different species. Captive specimens are extremely nervous and flighty and have been noted to bite with little if any provocation.
<u>MEDICAL IMPORTANCE:</u>	There are no current records of bites by this snake in PNG; however, the venom of mulga snakes is highly toxic (<i>see</i> CHAPTER 3).
<u>ANTIVENOM:</u>	CSL blacksnake antivenom or CSL polyvalent antivenom.

New Guinea brown snake (*Pseudonaja cf. textilis*)

- DESCRIPTION:** A slender snake that may be tan to dark brown in colour dorsally with a cream to yellow belly that is speckled with greyish-brown spots. Juveniles have a black patch on the top of the head and a black bar across the nape of the neck; some also have up to 50 black cross bands that eventually fade with age.
- SCALATION:** Dorsal scales in 17 rows at midbody; 200-210 ventrals; anal divided; 45-75 paired subcaudals (although a few may be single anteriorly).
- BODY SIZE:** Average length is from 1.2-1.8 metres; maximum length is 2.15 metres.
- DISTRIBUTION:** Most common in Milne Bay and Oro Provinces. A handful of specimens have been recorded in Central Province. Common in West Papua near Merauke and also reported in Western Province near Weam.
- HABITAT:** Grasslands, savannah woodland and coastal heaths. Adapts well to areas of human settlement.
- DIET:** Very opportunistic, but primarily small lizards and rodents.
- REPRODUCTION:** Females lay eggs in clutches of up to 22 eggs in October-November.
- ACTIVITY:** Almost exclusively diurnal and unlikely to be seen at night. Brown snakes are very active foraging species that are often encountered moving around searching for food or shelter.
- BEHAVIOUR:** If approached this is a very aggressive snake that will defend itself with little encouragement. Brown snakes typically adopt a very characteristic defensive stance in which they lift the front third or more of the body high off the ground in a rigid 'S' shape and hiss violently while holding the mouth open. From this position the snake will make repeated lunges at an antagonist, and will strike several times. This defensive posture is often well remembered by people who experience it due to the similarity to the threat display of Asian cobras (*Naja* spp.)
- MEDICAL IMPORTANCE:** Lalloo et al (1995) reported that this species was responsible for 1.8% of the serious snakebites in their study within Central Province, and reported bites from Tapini, Goldie River, Kapari and 9-Mile. Although the venom is extremely toxic, both the yield and the fangs used to deliver it are small (*see* CHAPTER 3 for venom data).
- In Australia the brown snakes (*Pseudonaja* spp.) are the most common cause of serious snakebites, and particularly of fatal cases. The common brown snake (*Pseudonaja textilis*) is distributed throughout eastern Australia and is abundant even in the suburbs of cities like Melbourne, Sydney and Adelaide.
- ANTIVENOM:** **CSL brown snake antivenom or CSL polyvalent antivenom.**

Sea kraits (*Laticauda colubrina* and *Laticauda laticaudata*)

There are two species of banded sea krait that occur in Papua New Guinean waters; the yellow lipped sea krait (*Laticauda colubrina*) and the common sea krait (*Laticauda laticaudata*). Both of these snakes have alternating blue-grey and black bands around the body, and a laterally compressed tail for swimming. The average length is 1 metre with a maximum length of 1.5 metres. Unlike the true Hydrophiine sea snakes, the sea kraits have round bodies and are equally at home on land.

Both *L. colubrina* and *L. laticaudata* have been reported from Lion, Manubada and other inshore islands in Central Province, and from Samarai Island in Milne Bay Province. Both species are also recorded from the seas around Rabaul. *L. colubrina* has been recorded off Karkar Island and along the coast north of Madang. It occurs around Manus and Pigeon Islands, and has been recorded off Aitape.

Sea kraits typically emerge from the water at night and make their way ashore to rest and to reproduce. Female snakes lay eggs in clutches of 3-6 eggs.

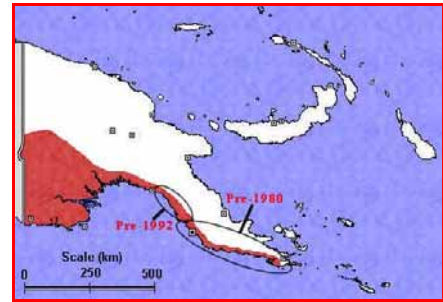
These two species are highly venomous, but generally considered to be of minor medical importance due to their docile nature and reluctance to bite even when handled.

True Sea Snakes (*Hydrophiine* species)

There are 20 species of true sea snake in the waters surrounding Papua New Guinea. The majority of these are inoffensive species and bites are uncommon. Several species are, however, commonly caught by fisherman and trawler operators, and these people are at risk of bites while separating the snakes from their catch. Two large species which are common in the waters off southern PNG; the olive sea snake (*Aipysurus laevis*) and the Stoke's sea snake (*Astrotia stokesii*) have been reported to cause serious envenomation, and have fangs that are moderately large. A third, smaller species, the spine-bellied sea snake (*Lapemis hardwicki*) is also capable of inflicting a serious bite.

Closer inshore, several species of sea snakes inhabit muddy coastal estuaries and sometimes travel long distances up coastal river systems. The beaked sea snakes (*Enhydrina schistosa*) and (*Enhydrina zweifeli*) have among the most toxic venoms of any snakes in the world, and one of these species is believed to have been responsible for at least one confirmed death in Ramu River. Other estuary-dwelling species from PNG including *Hydrophis elegans*, *Hydrophis ornatus* and *Lapemis hardwicki* have caused fatalities in South-East Asia and elsewhere.

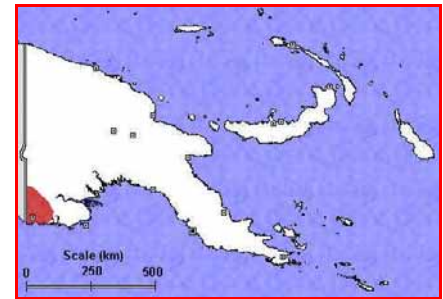
True sea snakes have tails and bodies that are laterally flattened, and most have great difficulty moving on dry land. Two exceptions are *Hydrelaps darwiniensis* and *Parahydrophis mertoni*, species that live on mudflats and have learned to move reasonably well out of the water. *H. darwiniensis* is recorded from the coast of Western Province. Most sea snakes average from 0.5-1.0 metre in length, however *Aipysurus laevis* can reach lengths of 2.3 metres; *Astrotia stokesii* grows to 1.8 metres and *Hydrophis elegans* can attain a maximum length of almost 2.5 metres. The inshore beaked sea snake *Enhydrina schistosa* grows to almost 1.5 metres in length.



PAPUAN BLACKSNAKE

(Pseudechis papuanus)

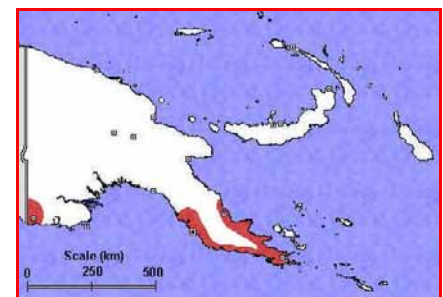
This species has been disappearing from the east of its range over the past 25 years. Snake shown has burn scarring.



PAPUAN MULGA SNAKE

(Pseudechis cf. australis)

Known from only a few specimens in the south-west of Western Province. The species may occur further east on the Oriomo plateau towards the mouth of the Fly River.



NEW GUINEA BROWN SNAKE

(Pseudonaja textilis)

Once considered to be an exotic import from Australia, it now seems likely that like other venomous species, the brown snake invaded PNG during the late Pleistocene via temporary land bridges.

Venomous Land Snake Distribution by Province

Western	Papuan taipan	Known only from south of Lake Murray & Balimo but possible further north
	Papuan blacksnake	
	Small-eyed snake	North of Lake Murray & Balimo
	Death adder	Widespread in whole Province
	Papuan mulga snake Brown snake	Weam and Bensbach districts
Gulf	Papuan taipan	East of Kerema; but possibly also lowland areas further west
	Papuan blacksnake	Probable in lowland regions
	Death adder	Widespread in whole Province
	Small-eyed snake	Kikori, Purari, Kerema, Omati
Central & NCD	Papuan taipan	Widespread in lowlands but not Yule Island
	Papuan blacksnake	Extremely rare but possibly in Mekeo, Yule Island and Abau
	Death adder	Widespread in whole Province
	Brown snake	Uncommon but widespread
	Small-eyed snake	Rare, but recorded from Dinawa, Koroko, Sogeri, Musgrave River
Milne Bay	Papuan taipan Papuan blacksnake	Southern coast to the west of Samarai Island
	Death adder	Few records
	Brown snake	Cape Vogel, Dogura, Menapi and Baiawa
	Small-eyed snake	Loani and Kwagira River
	Oro (Northern)	Death adder Small-eyed snake
Brown snake		Coastal: Embogo & Popondetta
Morobe		Death adder
	Small-eyed snake	Scattered records
Eastern Highlands	Death adder	Widespread in whole Province
	Small-eyed snake	Rare but reported from Aiyura
Simbu	Death adder	Common to altitudes of 1800 m
	Small-eyed snake	Tive plateau and Karimui
Southern Highlands	Death adder	Widespread in whole Province
	Small-eyed snake	Mt Sisa and Mt Bosavi

Venomous Land Snake Distribution by Province

Western Highlands	Death adder	Widespread in whole Province
Enga	Death adder	Widespread in whole Province
Sandaun	Death adder	Widespread in whole Province; a giant race occurs in the Sepik valley
	Small-eyed snake	Widespread in whole Province
East Sepik	Death adder	Widespread in whole Province
	Small-eyed snake	
Madang	Death adder	Widespread in whole Province
	Small-eyed snake	Widespread in whole Province and very common on Karkar Island
Manus		No highly venomous species
West New Britain		No highly venomous species
East New Britain		No highly venomous species
New Ireland		No highly venomous species
North Solomons		No highly venomous species

Important Footnotes to the Distribution Table

The table above is based upon available records of species and records of snakebites in which the species responsible has been reliably identified.

There are still many gaps in our knowledge of venomous snake distribution in Papua New Guinea. New distribution records may extend the ranges of some species, and it is also possible for venomous snakes to be translocated in shipments of freight and other goods.

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PHOTOGRAPHS: David Williams, Mark O'Shea, Richard Mastenbroek, Dr Wolfgang Wüster and the Queensland Museum.

ILLUSTRATIONS: Adapted from 'A Guide to the Snakes of Papua New Guinea' by Mark O'Shea and from 'Australian Snakes: A Natural History' by Richard Shine.

The composition and actions of Papua New Guinean snake venoms

David Williams and Ronelle Welton

Introduction

Snake venoms are complex mixtures of bioactive agents with diverse pharmacological activities against a wide range of physiological targets. Many of these agents are complex chemicals which have toxic effects upon the cells and cellular mechanisms that they target, and in some snakes the toxicity is sufficient to be extremely harmful to man. Understanding the composition and activities of different snake venoms forearms clinicians with a knowledge of the underlying physiological changes responsible for clinical envenomation syndromes. In some cases this knowledge may enable presumptive identification of the biting species and early selection of the most appropriate antivenom.

The biological roles of snake venoms

There are three natural uses for snake venom. The most obvious is the role of venom in subduing or killing other animals that the snake wants to eat. Snakes with toxic venom evolved in order to limit their exposure to the dangers that their own prey might present to them. If we consider that snakes already have a natural disadvantage through the lack of limbs with which to move, or to use for catching food, then the development of a venomous bite is a logical advantage. By quickly biting and injecting toxins into a prey animal, and then keeping a safe distance until the prey is immobilized or dead, snakes reduce the possibility that a prey animal (such as a large bush rat) might turn on them and use its own teeth to damage or kill the snake.

The second very important role of many types of venom is as an aid to the actual digestion of the prey that the snake kills and eats. Many of the toxins in snake venom are powerful hydrolysing agents that break down cellular tissue into more basic, easily absorbed and utilized nutrients. Snake venom myotoxins that break down muscle cells are one example of the types of toxin that can assist in the pre-digestion of food.

The role that brings snakes into so much conflict with humans, however, is the use of venom as a defensive tool against a snake's perceived enemies, and as a means of ensuring that the snake does not end up being eaten itself. Most snakes do not like to waste venom on their enemies, and this is the reason that its use is often reserved only for those occasions when the snake feels the most threatened or intimidated. Many snakes bite, but actually inject very little if any venom when they are defending themselves, and this is the reason that many people who are bitten by snakes do not become seriously ill.

The amount of venom that a snake uses when it bites is often determined by the reason for its use, and by other factors such as the temperament of the snake itself – some species are more

easily intimidated than others, and these species are most likely to inject venom when biting a potential enemy. Snakes that are hunting for food when they bite also tend to inject much more venom, than a snake that is defensive.

The difference between ‘venoms’ and ‘poisons’

There are no ‘poisonous’ snakes, but many snakes are ‘venomous’. The difference between being a ‘venomous’ snake as opposed to a ‘poisonous’ snake is related to the nature of venoms and poisons themselves.

Venoms are produced exclusively by animals, including spiders, scorpions, snakes, stingrays, stonefish, jellyfish, marine cone snails and invertebrates like ticks and centipedes. Venom is manufactured in specialized glands in the animal’s body, and each animal has a specific mechanism for delivering the venom into the body of the animal it is used against. In the case of snakes, spiders, ticks and centipedes this mechanism is through biting, while stingrays and stonefish used special spines on their bodies to inject venom as a form of defence. Marine cone snails produce tiny spear-like teeth that they fire at their prey from their mouths, and jellyfish have special cells, called nematocysts that evert a long sharp tube into the skin of prey through which venom is injected.

Poisons on the other hand are passively acquired toxins that are produced by either animals or plants as a means of defence. These organisms do not have an active mechanism through which the poison is delivered. Many species of frogs defend themselves against enemies and predators by producing poison in glands on or under the skin; if they are picked up or eaten, the poison comes in contact with the enemy and may either kill it (preventing it from eating any more frogs), or taste so unpleasant that the animal spits out the frog and learns never to try and eat the same type of frog again. Poisonous plants use the same type of principle. The toxins produce an unpleasant experience for the animal eating them, and results in the plant being avoided and left alone.

Venoms are typically mixtures of proteins or peptides, while poisons may be much more diverse types of chemicals including steroids, alkaloids, amines and other substances.

Snake venom evolution and diversity

Not all snake venoms are the same. Although it is believed that the venoms of all venomous snakes evolved from common biological ancestors many millions of years ago, the reality today is that nearly every species of snake has different venom, with different types of components and different types of activity against different types of cellular targets.

This is a very important concept to understand when treating snakebites. Different venoms produce different clinical effects, and may require different treatments, including different types of antivenoms.

The vast majority of the world’s 3,000 or so species of snakes belong to an evolutionary superfamily known as the Colubroidea, which includes all of the venomous species. Some of these snakes evolved specialized forms of saliva that served as aids to the digestion of food, and over time the glands producing this saliva diversified and developed further. Through a process of positive selection, proteins and peptides with specific toxic activity were conserved and retained. When these early snakes bit their prey the wounds made by their teeth allowed these toxic chemicals in their saliva to enter the bodies of the prey, speeding death and assisting in the breakdown of the food. This gave these snakes an important biological advantage that helped them to survive and colonize different environments.

Evolution also recognised that snakes with larger teeth made larger wounds in their prey, allowing more of the toxic saliva to enter, resulting in quick effects and even more success at obtaining food. Over millions of years three different large groups of snakes evolved very similar (but structurally different) teeth (*'fangs'*) and jawbones that aided the injection of toxins. As we discussed in the previous chapter, the most primitive of these groups evolved fangs at the rear of the mouth that allowed venom to seep into a wounded prey animal along slight grooves; more advanced snakes had fangs at the front of the mouth, and the most advanced evolved very large fangs that folded against the roof of the mouth when not in use – but which rotated forwards to enable downward stabbing bites that injected venom deep into the prey for maximum digestive effect.

The process of evolution means that while most snakes started their development of venom with an arsenal of common components (many toxins can today be used to study the evolutionary relationships of different snakes), over the millions of years in which the species have developed and evolved into those that we see today, their venoms have also diversified and evolved. Studies of the toxic saliva found in some of the species of colubrid snake that we traditionally assumed to have been non-venomous have actually found that these snakes possess toxins that are remarkably like the very potent neurotoxins present in some sea snakes and many of the highly venomous land snakes, and this information tells us a lot about the origins of venom.

Many factors influence venom evolution and diversity. The diet of a snake is one important factor. A species that feeds on mammals is likely to have venom that acts more effectively against mammals than against fish or frogs. Another factor is the ability of the prey to defend itself against the snake. If the prey animal is potentially dangerous to the snake, there is a much greater chance of this species having extremely potent venom that acts quickly and lethally, than would be the case if the prey animal was unable to mount an effective defence.

Activity of Papuan snake venoms

The venoms of the medically important Papua New Guinean snakes contain many different types of toxins that act against different physiological targets.

Despite this diversity it is possible to broadly classify many components on the basis of just a handful of medically important clinical effects. What is important to remember, however, is that these effects may be produced by different toxins using different mechanisms of action at the cellular level. This has very important implications for the treatment of snakebite.

The venom components of Papuan snakes include:

- (1) **Neurotoxins** – active against the nervous system
 - (a) Presynaptic neurotoxins
 - (b) Postsynaptic neurotoxins
- (2) **Haemotoxins** – affecting normal coagulation and haemostasis
 - (a) Procoagulants
 - (b) Anticoagulants
 - (c) Platelet toxins
- (3) **Myotoxins** – destructive enzymes that cause skeletal muscle degeneration

Snake venoms also contain toxins which produce a variety of less medically obvious effects.

Snake venom neurotoxins

Papua New Guinean snakes produce neurotoxicity using toxins that target both presynaptic and postsynaptic neuromuscular junction targets. Depending on the species of snake involved, there may be more than one toxin in the venom targeting the neuromuscular junction, and these may involve more than one mechanism, all with the common purpose of producing paralysis.

In order to understand how these toxins work, it is important to remember how the interface between the motor nerves and the skeletal muscle system operates (FIGURE 1):

- ? Nerve impulses generated by the body in response to either voluntary (i.e.: *a conscious decision to lift an arm*) or involuntary (i.e.: *the unconscious commands to relax and contract the diaphragm and other chest muscles that produces respiratory effort*) commands result in the depolarisation of nerve membranes.
- ? Depolarisation involves sodium (Na^+) and potassium (K^+) ions changing places across the nerve membrane via ion transport channels.
- ? At the axolemma of the nerve terminal this depolarisation opens calcium (Ca^{2+}) channels which produce the stimulus for the release of neurotransmitter, typically acetylcholine (ACh), from internal nerve cell structures known as presynaptic vesicles.
- ? The vesicles fuse with the nerve cell membrane allowing the acetylcholine inside to diffuse into the synaptic cleft.
- ? Acetylcholine binds to special protein complexes in the adjacent muscle cell membrane that are known as acetylcholine receptors (AChR), and in effect act like a key in a lock, opening the receptors to allow extracellular Ca^{2+} into the cell and K^+ to leave.
- ? This in turn activates the internal muscle cell components producing activation of the fibres, resulting in either contraction or relaxation.
- ? With its job finished, ACh dissociates from the AChR and is bound by another substance known as acetylcholinesterase (AChE) which breaks ACh down into acetate and choline.
- ? Acetate and choline are taken back up by the nerve cell, reconstituted to form more ACh and used to fill more vesicles so that the cycle can be repeated with the next impulse.

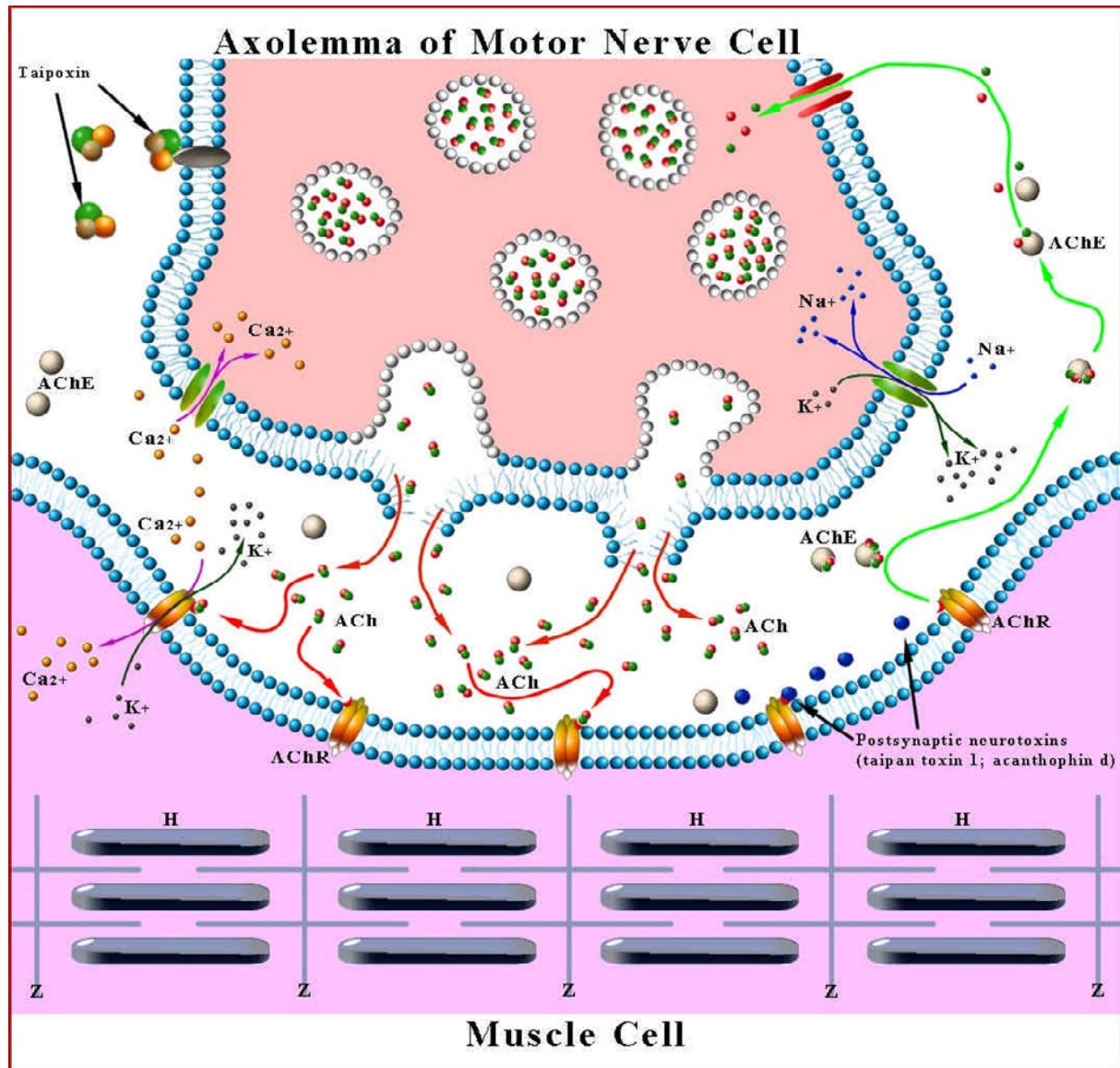
Snake venom neurotoxins break this cycle via several different mechanisms that have the same result: the ability of acetylcholine (ACh) to trigger muscle cell activation is interrupted and the muscle becomes paralysed.

In Papua New Guinean snakes this is achieved by two main types of toxin that can be categorised simply according to the location of the site upon which they exert their effects:

- ? Presynaptic neurotoxins that directly target sites on the nerve cell; and,
- ? Postsynaptic neurotoxins that target the acetylcholine receptor (AChR) to prevent the binding of acetylcholine (ACh).

Some species such as the Papuan taipan (*Oxyuranus scutellatus canni*) have both types of neurotoxin in their venom, while others like death adders (*Acanthophis* spp.) possess only postsynaptic neurotoxins.

Although these neurotoxins all aim to produce the same result – paralysis of the victim, the means by which this occurs differs in different snakes and these different mechanisms mean that while the visible and detectable effects in the snakebite patient are generally the same, the type of treatment needed and the risks to patients can be very different. This is just one of the reasons it is so important to know how the venoms of different species work.



KEY TO SYMBOLS













	Sodium (Na ⁺) Ions		Phospholipid-based cell membrane		Postsynaptic acetylcholine receptor (AChR) (Binds ACh, targeted by neurotoxins)
	Potassium (K ⁺) Ions		Presynaptic vesicle filled with ACh		Neuronal pentraxin-like protein complex (Cellular messenger, targeted by taipoxin)
	Calcium (Ca ²⁺) Ions		Na ⁺ /K ⁺ Ion Channel "Pump"		Presynaptic neurotoxin "Taipoxin" from Papuan taipan (<i>Oxyuranus scutellatus canni</i>)
	Acetylcholine (ACh) (Choline + Acetate)		Anticholinesterase (AChE) (Binds and dissociates ACh)		Postsynaptic neurotoxins, i.e: taipan toxin 1 (Papuan taipan) or acanthophin d (death adder)

FIGURE 1: Representation of a neuromuscular junction showing normal ion transport and acetylcholine (neurotransmitter) dispersal, dissociation and reuptake. The target sites of some snake venom presynaptic and postsynaptic neurotoxins are also shown. **Presynaptic:** The Papuan taipan (*Oxyuranus scutellatus canni*) toxin "taipoxin" is shown bound to presynaptic transmembrane protein complexes in the phospholipid cell wall of the neuronal axolemma; the consequence of binding is depletion of synaptic vesicles, cessation of acetylcholine release and physical destruction of the axolemma as a result of damage potentiated by massive Ca²⁺ influx into the neuron. **Postsynaptic:** Long-chain neurotoxins such as taipan toxin 1 (Papuan taipan; *Oxyuranus scutellatus canni*) or acanthophin d (Papuan death adder; *Acanthophis* spp) compete with acetylcholine for postsynaptic receptor binding sites; neurotransmission is blocked by competition, but is easily reversed with specific antivenom and anticholinesterase drugs.

NOTE: These are not the only neurotoxins that act against these targets; there are other toxins in both the same species and in other snakes that target presynaptic and postsynaptic binding sites.

In Papuan New Guinean snakes with presynaptic neurotoxicity, such as the Papuan taipan (*Oxyuranus scutellatus canni*), the toxins belong to a class of very diverse proteins known as phospholipases A₂ (PLA₂) that under normal circumstances are responsible for a number of cellular activities including signal transduction and phospholipid metabolism through their ability to catalyse the 2-acyl ester bonds of 3-sn-phosphoglycerides. Not all PLA₂ are toxic, and many occur naturally in humans. Non-toxic human pancreatic PLA₂ are in fact very similar to extremely toxic snake venom PLA₂.

The venom PLA₂ are very small in size compared to some of the toxins that target haemostasis. In the Australo-papuan elapids these toxins are typically 13-15 kDa and are polypeptides comprised of 118-120 amino acids linked by 7 disulphide bonds that contribute to their three dimensional shape, and hence to their activity. These PLA₂ possess both toxic catalytic activity and non-toxic enzymatic activities at different locations within their structure; this means that they can often have more than one type of action. Some PLA₂ also bind to common receptors that may be located on both nerve cells and muscle cells. The result is that in addition to being neurotoxic, they are also powerful myotoxins which destroy muscle.

While many of the presynaptic PLA₂ neurotoxins are basic (alkaline) single polypeptide chain toxins, the most toxic are multi-chain proteins, such as the three subunit PLA₂ 'taipoxin' from the venom of Australian coastal taipans (*Oxyuranus scutellatus scutellatus*) and Papuan taipans (*Oxyuranus scutellatus canni*), and 'paradoxin' from the inland taipan (*Oxyuranus microlepidotus*).

Postsynaptic neurotoxins that compete with ACh for AChR binding sites are a very diverse group that include some of the most primitive snake venom toxins. These very small polypeptides are usually 6-9 kDa in size with between 62-80 amino acids. Although some may be acidic, the majority are basic proteins. These postsynaptic neurotoxins typically target binding sites on the two subunits that form the pentameric acetylcholine receptor (AChR), and this prevents ACh from binding, thereby inhibiting the activation of the ion channel and the exchange of Ca²⁺ and K⁺ that potentiates muscle contraction and relaxation.

Snake venom haemotoxins

The evolutionary recruitment of toxins that are active against haemostasis and coagulation is common in many of the world's snakes. The integrity of the circulatory system is crucial to the maintenance of life, and therefore presents itself as a logical target for venom-based toxins.

Haemostasis is a delicate balance between the two opposing forces of clot formation and dissolution. Appropriate timely clotting is essential at the site of a wound in order to maintain hemostasis and to prevent traumatic blood loss; however, the factors that produce clotting have to remain inactive away from the site of the wound in order to prevent life-threatening thrombotic events such as stroke. In a healthy person this balance is well maintained by a series of interconnected sequential reactions involving the proteins that initiate both clot formation and clot breakdown. Different snake venom toxins interfere with some of the specific biochemical reactions within coagulation pathways that are designed to ensure this balance (FIGURE 2), and the result is that they can produce both coagulopathy and thrombosis depending upon the mechanism that is activated or inhibited by the toxin.

From a Papua New Guinean perspective, the most important coagulation mechanism that is disrupted by snake venom toxins is the conversion of the zymogen, prothrombin, by activated Factor X (Factor X_a) to thrombin, which in turn drives the conversion of soluble fibrinogen to

insoluble fibrin – the necessary element, in conjunction with Factor XIII_a, for successful clot formation. Under normal conditions, this reaction is localized to the site of a vascular injury such as a break in a blood vessel wall, and is enhanced by the presence of activated platelets and the rate-increasing activated Factor V (Factor V_a). The result is the production of a stable cross-linked fibrin clot that stops the loss of blood, enabling the underlying vessel wall to heal and regenerate. As the wound heals, the body’s fibrinolytic system converts plasminogen to plasmin via a fibrin bound tissue-type plasminogen-activating enzyme. Plasmin dissolves the fibrin clot, resulting in the production of fibrin degradation products – the clot remnants which are eventually completely reassimilated.

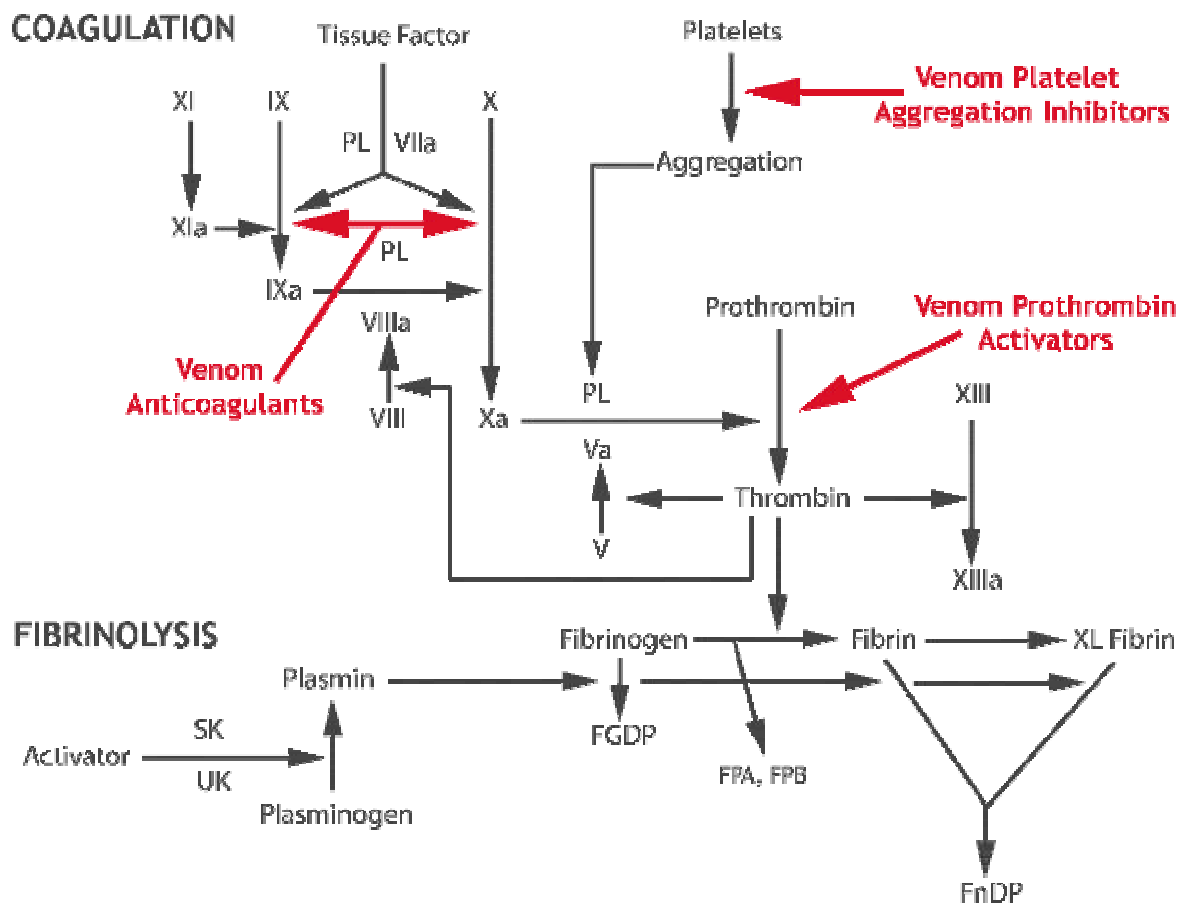


FIGURE 2: Simplified representation of coagulation and fibrinolytic pathways indicating the sites of action of the some important haemotoxic components in some Papua New Guinean snake venoms. Other toxins may also be present in PNG snake venoms that target additional reactions such as the conversion of plasminogen to plasmin, potentially inhibiting clot dissolution.

Procoagulants

There are four different classes of prothrombin-activating toxins that are defined by their need for circulating cofactors (i.e.: platelet phospholipids, Ca²⁺ and/or Factor V). These are not present in all snake venoms, however, and are notably absent from the venoms of Papua New Guinean death adders (*Acanthophis* spp.). The same is not true for the Papuan taipan (*Oxyuramus scutellatus canni*), whose venom contains the most medically significant toxin affecting coagulation in Papua New Guinean snakebite patients: a potent procoagulant that

converts prothrombin to thrombin in the presence of Ca^{2+} and circulating phospholipids without the need for Factor V (the toxins themselves contain a Factor V-like subunit). The consequence of abnormal prothrombin activation is a depletion of available fibrinogen resulting in consumption coagulopathy and incoagulable blood. Disseminated intravascular coagulopathy is the dominant clinical outcome and is the cause of the bleeding from mucosal membranes and venepuncture sites, prolonged clotting times and haematemesis.

Anticoagulants

The true anticoagulants bind Factor IX and Factor X and produce anticoagulation without concurrent fibrinolysis. These toxins are typically phospholipases A_2 and may also be involved in collagen-induced platelet aggregation. Bleeding may be a feature, but is usually not as significant as that seen following prothrombin activation by procoagulants.

Platelet Inhibitors & Activators

Platelets are abundant in blood and are small, discoid, phospholipid-rich entities with pivotal roles in maintenance of endothelial integrity and haemostasis. When blood vessel wall endothelium is damaged, platelets are immediately activated and will adhere and aggregate at the site of injury, effectively ‘plugging the leak’. Platelets also stimulate circulating coagulation factors in plasma, and subsequently provide the phospholipid substrate for the cleavage of thrombin from prothrombin by Factor X_a and Factor V_a .

There are a number of toxins that act as either inhibitors or activators of platelet aggregation, a key process in the formation of normal clots. Platelet aggregation inhibition can be the result of either monophasic or biphasic mechanisms, with the latter involving initial arachidonic acid-induced platelet aggregation, followed by inhibition. In Papua New Guinean snakes, the inhibition of platelet aggregation is induced by PLA_2 toxins which also have anticoagulant effects.

Snake venom-induced myotoxicity

Many neurotoxic phospholipases A_2 are also potent myotoxins that are destructive to skeletal muscle tissue. Venom-induced myonecrosis, involving disruption of the plasma membrane and disorganization of the myofibrils, can result in rhabdomyolysis and myoglobinuria arising from elevated serum myoglobin levels, as tissue damage progresses. Affected muscle tissue may become heavily infiltrated with phagocytic cells. Oedema and muscle pain may be accompanied by gross elevation of serum creatine kinase, lactate dehydrogenase and or isoenzyme levels.

The destruction, while extensive, falls short of damaging basal lamina and myogenic stem cells in the muscle, and this enables muscle tissue regeneration, although the process may take several weeks. Patients affected by myotoxicity are at considerable risk of renal impairment due to tubular necrosis arising from the infiltration of myoglobin and other myolytic metabolites into the kidney nephrules.

Patients suffering from rhabdomyolysis frequently develop clinically evident myoglobinuria and will pass discoloured urine. In severe cases the urine will be deep brown in colour, and if a sample is allowed to stand it may take on a striated appearance, appearing ‘stringy’. Many patients with myoglobinuria are mistakenly assumed to have haemoglobinuria, and it is important to distinguish between these two conditions as early as possible.

Venom Components of Medically Important Species

Papuan taipan (*Oxyuranus scutellatus canni*)

This species has the third most highly toxic snake venom in the world, with an experimental LD₅₀ (lethal dose that kills 50% of test animals) of a mere 0.05 mg/kg body weight.

What makes Papuan taipans even more dangerous to humans is that they also have the most highly developed venom delivery system of any Australo-papuan snake; the fangs are well forward on a partially mobile maxilla, are extremely large compared to other elapids (up to 1.2 cm), and the venom yield of up to 600 mg is the highest of any Papuan snake. Taipans use a lightning-fast ‘snap and release’ biting strategy and may inflict multiple bites in rapid succession, with increasing quantities of venom being injected with each subsequent bite.

Combined with the relative abundance of the species throughout southern PNG in areas of high human population, and its nervous, excitable temperament, this large reptile is possibly the most dangerous snake in the world to encounter. In Central province it has been shown to cause more than 80% of serious snakebites.

Taipan venom is a complex mixture of many toxins; however, the clinical effects are probably dominated by just a few, and in particular:

- ? *Taipoxin*: a lethal phospholipase A₂ toxin with irreversible presynaptic neurotoxicity and myotoxicity.
- ? *OS-2*: a presynaptic inhibitor of K⁺ transport that contributes to acetylcholine depletion by impairing vesicle recycling.
- ? *Taipan toxin 1*: a postsynaptic neurotoxin that competes with ACh for AChR binding sites on skeletal muscle cells, as well as several additional postsynaptic neurotoxins.
- ? *Oscutarin*: a powerful activator of prothrombin that produces rapid defibrination coagulopathy.
- ? *Taicatoxin*: a potent blocker of voltage-dependent myocardial Ca²⁺ channels and L-type Ca²⁺-dependent neuronal K⁺ channels in the brain.

Taipoxin, OS-2 and taipan-toxin 1

The severe neurotoxicity seen in taipan bite victims is a consequence of the destructive, irreversible neurotoxicity caused by taipoxin, in conjunction with additional neurotransmitter inhibition by taipan toxin 1 at the postsynaptic junction and the inhibition of acetylcholine vesicle recycling by OS-2.

Taipoxin is a multi-subunit neurotoxin that has an LD₅₀ of a just 2µg/kg (in other words; only 1/500th of 1 mg for each kg of the victim’s body weight!), and the toxin may comprise more than 17% of the total protein in the venom. Taipoxin has a molecular weight of 45.6 kDa and binds to the neuronal integral membrane proteins NPR, NP1, NP2 and TCBP49. These are believed to form a novel pathway for the uptake of taipoxin into the synapse. The toxin consists of three polypeptide components:

- ? a neurotoxic basic α-subunit of 119 amino acids with an LD₅₀ of 300 µg/kg;
- ? a neutral β-subunit of 118 amino acids that lacks both toxicity and enzymatic activity;
- ? a 133 amino acid acidic γ-subunit with 133 amino acid that enhances the toxicity of the α-subunit and is believed to act as both a chaperone and an orientating partner, ensuring that the toxin is presented properly to its target receptor.

Perhaps the most important difference between taipoxin and other snake venom neurotoxins in Papua New Guinean species is that taipoxin does not only prevent the transmission of nerve impulses across the neuromuscular junction, but, more importantly, produces catastrophic physical destruction of nerve terminals.

The consequence of this is that once taipoxin has bound to the axolemma of the nerve terminal, the subsequent physical damage cannot be treated with either antivenom or other drug therapies.

For a patient whose nervous system has been physically damaged in this way the prognosis for survival is greatly reduced, and while the use of mechanical ventilation is of value in maintaining respiration while the nerve terminals recover and regenerate, there are numerous potential problems that can hinder recovery.

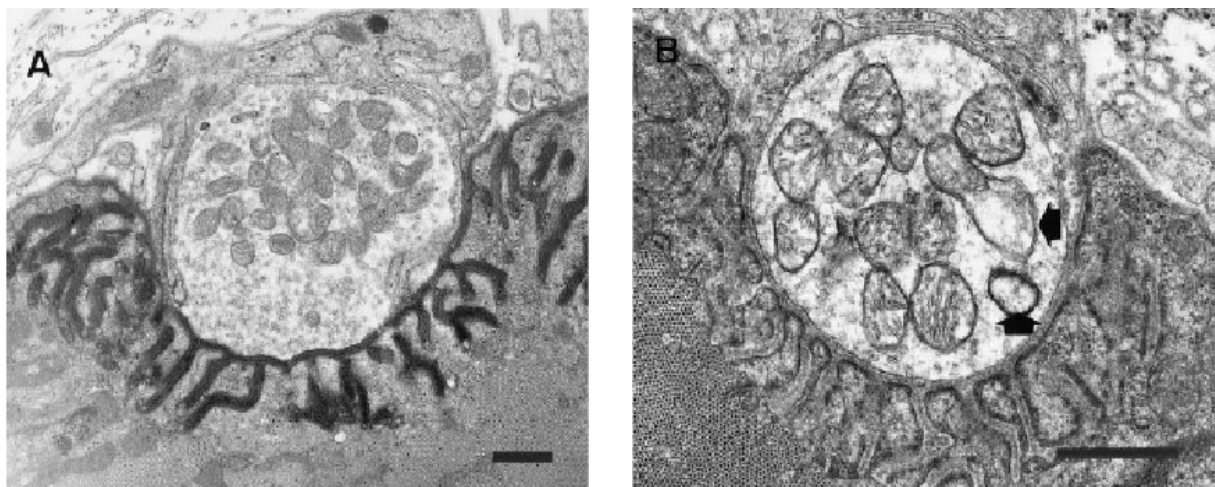


FIGURE 3: Damage to nerve terminals caused by exposure to the presynaptic snake venom neurotoxin taipoxin from the venom of the Papuan taipan (*Oxyuranus scutellatus canni*). **(A)** Normal neuromuscular junction on rat soleus muscle prior to exposure to taipoxin. **(B)** Rat soleus muscle neuromuscular junction one hour after the subcutaneous injection of 2 μ g of taipoxin into the anterolateral aspect of the rat hind limb. The large arrows show the loss of cristae and depleted presynaptic vesicles within the axolemma of the nerve terminal.

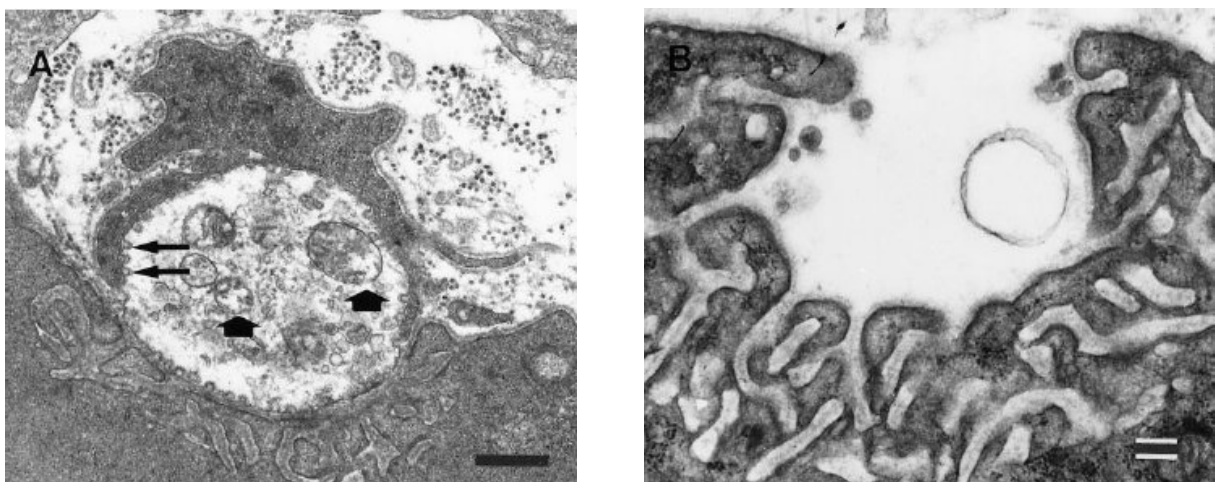


FIGURE 4: Damage to nerve terminals caused by exposure to the presynaptic snake venom neurotoxin taipoxin from the venom of the Papuan taipan (*Oxyuranus scutellatus canni*). **(A)** Rat soleus muscle neuromuscular junction 24 hours after exposure to taipoxin. Narrow arrows show the characteristic clathrin-coated ? shaped indentations on the nerve terminal membrane, while the larger arrows show damaged mitochondria. **(B)** The result is complete destruction of the nerve terminal.

SOURCE: HARRIS *et al* (2000)

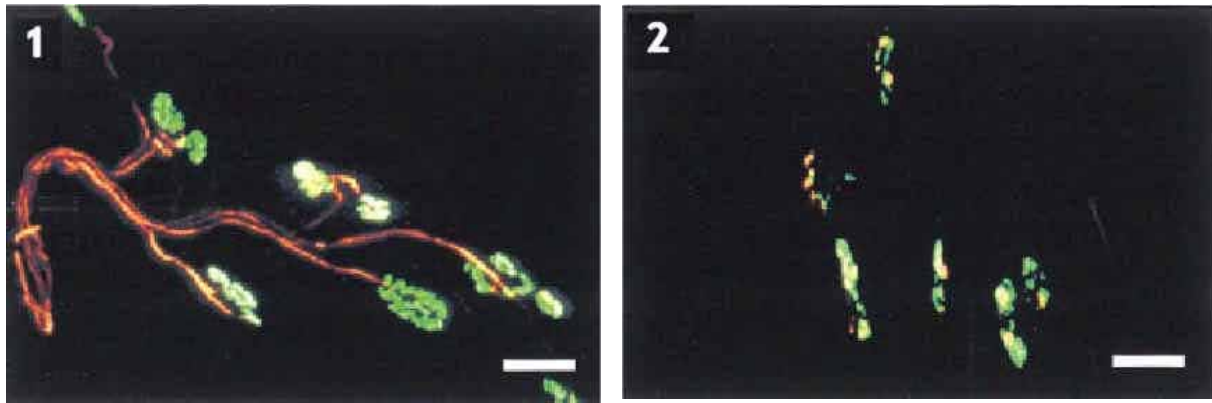


FIGURE 5: Nerve terminal damage caused by taipoxin, a presynaptic neurotoxin from Papuan taipan (*Oxyuramus scutellatus canni*) venom. Fluorescent antibody-labelled nerve fibre and fluorescein isothiocyanate-conjugated α -bungarotoxin-labelled acetylcholine receptors (AChR) are shown both **(1)** before and **(2)** after exposure to taipoxin. Loss of the nerve terminals is clearly seen in **(2)**.

SOURCE: HARRIS *et al* (2000)

Although there is still a lot to be learned about the actual mechanisms that produce the nerve terminal damage shown in figures 3-5, the sequence of events has been studied by Dr John Harris and his colleagues from the University of Newcastle in the United Kingdom; they determined that:

- ? within 1 hour of injection taipoxin produces depletion of ACh in synaptic vesicles and the emergence of clathrin-coated γ -shaped indentations at the synapse, as well as abnormalities in mitochondria and lysosomal structures;
- ? between 3-6 hours later the neuronal space may be completely empty of contents with significant mitochondrial damage, formation of large lysosome-like bodies, and invasion of junctional clefts with Schwann cell processes;
- ? at 24 hours more than 70% of muscle fibres are completely denervated; however junctional folds and segments of the plasma membrane may still be intact and numerous phagocytic cells are present;
- ? 88% of nerve terminals had regenerated and reinnervated within 5 days;
- ? total regeneration occurred within 28 days, although collateral innervation of the same fibres is common and was found to persist for more than 9 months.

It is worth noting that many of the patients who were ventilated in the Intensive Care Unit at Port Moresby General Hospital between 1992 and 2001 had a median ventilation duration of 4.5-5.0 days. This corresponds well to Dr John Harris' finding that reinnervation after the loss of nerve terminals following exposure to taipoxin occurred within 5 days.

In addition to its role as a presynaptic neurotoxin, taipoxin has also been shown to bind to integral membrane proteins on skeletal muscle cells and to produce clinically significant rhabdomyolysis. The basic α -subunit of taipoxin produces myonecrosis in both mammal and bird muscle fibres, and the myotoxicity is enhanced by the acidic taipoxin β -subunit. The myotoxicity is the result of the hydrolysis of muscle plasma membranes and disruption of myofibril structure. Muscle necrosis results and may progress for more than 48 hours before the damaged tissue begins to recover and regenerate from the surviving basal lamina.

Common clinical features of myonecrosis are oedema, myoglobinuria and elevated serum levels of myoglobin, creatine kinase, lactate dehydrogenase and other isoenzymes. New myotubes begin to form within 3 days and small immature fibres are present after 5 days. Regeneration is usually complete within 21 days.

Among the other neurotoxins that contribute to clinical neurotoxicity is a presynaptic polypeptide PLA₂ named OS-2 that appears to be involved in the early depletion of ACh from presynaptic vesicles. The mechanism involves loss of outward K⁺ ions transport from the nerve terminal due to putative K⁺ channel blockade by the toxin. Like taipoxin, OS-2 was also found to bind to specific myotubule membrane proteins, and is probably a contributor to myonecrosis.

Not content with preventing the release of ACh and then physically destroying the nerve terminals at the neuromuscular junctions, taipan venom also contains several non-PLA₂ postsynaptic neurotoxins that bind to the nicotinic AChR. Only a couple of these toxins have been described in the scientific literature, including taipan-toxin 1, a ‘short-chain’ neurotoxin with a molecular weight of 6-7 kDa and a strong similarity to many of the other basic postsynaptic neurotoxins that are found in other land and sea snake venoms. As previously explained, the postsynaptic neurotoxins do not produce physical damage to the tissues that they bind with, and rapidly dissociate from AChR when exposed to specific antivenoms.

Oscutarin

Clinical defibrination coagulopathy seen in victims of taipan envenoming is due to the rapid cleavage of prothrombin to meizothrombin by Oscutarin, a potent Group III activator of prothrombin that is dependent on Ca²⁺ and phospholipids, but is Factor V independent. This is one of the largest components in taipan venom, being comprised of two large (110 kDa and 80 kDa) subunits that closely resemble Factor V_a. These are tightly bound to two disulphide-bonded Factor X_a-like serine proteinases of 57 kDa that contain the glycine-rich active site.

Oscutarin cleaves prothrombin randomly at either the ARG273-THR274 (thrombin-producing) site or the ARG322-ILE323 (meizothrombin-producing) site. The presence of phospholipid-rich platelets accelerates the cleavage of prothrombin. Coagulopathy may develop within less than 1 hour after envenoming and can be detected and monitored readily using the 20WBCT test.

In addition to gross prolongation of the blood clotting time, the clinical features of coagulopathy may include bleeding of the gingival sulci and other mucous membranes, haematemesis (‘coffee-ground’ stained vomit), haemoptysis, epistaxis, menorrhagia, haematuria, venepuncture site bruising and bleeding, and local bite site bleeding.

Disseminated intravascular coagulopathy is a characteristic indication of envenomation by the Papuan taipan (*Oxyuranus scutellatus canni*).

Taicatoxin

Taicatoxin is a 52 kDa oligomeric toxin comprised of a 16 kDa α-subunit, 8 kDa β-subunit and four 7 kDa γ-subunits. The α-subunit is an extremely toxic PLA₂ that is essential to the activity of the complex. Taicatoxin was originally characterised as a specific voltage-dependent cardiac Ca²⁺ channel blocker, but further research demonstrated that it also blocks apamin-sensitive, small-conductance K⁺ channels on chromaffin cells and in the brain. This makes taicatoxin unique in being the first small-conductance K⁺ channel blocker to be described from snake venom.

Although it seems highly probable that this toxin might be one of the causes of some of the electrocardiographic disturbances (abnormalities in the ‘electrical conductance’ within the heart) seen in some victims of taipan envenoming, the actual clinical significance of the toxin remains unclear. Similarly, the potential effects on neurological function as a result of K⁺ channel blockade in brain tissue are unknown.

New Guinean death adders (*Acanthophis* spp.)

The death adders are the most widely distributed species-group of highly venomous snakes in PNG and Papua. As explained in Chapter 2, the group is in urgent need of comprehensive research, not just to determine exactly how many different species do occur, but also to examine their venoms for specific variations that may result in variable clinical presentations.

Despite their fearsome common name, death adders are generally inoffensive snakes, and bites typically only occur when the snake is either stepped upon or accidentally handled by an unwary victim. These small snakes are largely nocturnal and are responsible for the majority of serious snakebites that occur at night. In fact, it would be very true to say that the majority of bites by death adders could be prevented if people used torches or kerosene lamps when walking around at night and took care to watch where they placed their feet. Death adders very rarely strike higher than the ankle so wearing shoes is also a very good means of preventing bites.

Unlike Papuan taipans (*Oxyuranus scutellatus canni*), the venom of death adders does not contain activators of prothrombin, and as a consequence incoagulable blood is not a feature of death adder envenomation. This is a very important distinction between the clinical presentations of bites by these two very different types of venomous snake.

Death adder venoms are rich in a diversity of ‘short-chain’ and ‘long-chain’ postsynaptic neurotoxins that bind to nicotinic AChR in skeletal muscle and produce facial and bulbar paralysis. Among these are the ‘short-chain’ neurotoxins acanthophin a and toxin Aa-c, and the ‘long-chain’ neurotoxins acanthophin d, toxin Aa-b and toxin Aa-e, all from the Australian common death adder (*Acanthophis antarcticus*). A postsynaptic neurotoxin called acantoxin IVa from the Seram population of *Acanthophis laevis* has also been isolated and characterized. Postsynaptic neurotoxicity can be effectively reversed with antivenom.

One of these neurotoxins (toxin Aa-c) is a basic (alkaline) 6.7 kDa ‘short-chain’ neurotoxin comprised of 62 amino acid residues cross-linked by four structurally supportive disulphide bridges that shape the toxin into an acceptable ‘key’ for the AChR ‘lock’. Aa-c is very similar (‘homologous’) to the classic ‘three-fingered erabutoxins’ that are present in the venoms of the banded sea kraits (*Laticauda* spp.). The ‘long-chain’ neurotoxins in death adder venoms have molecular weights of 7.9-8.4 kDa, and comprise of 73-79 amino acid residues cross-linked by five disulphide bridges. Both the ‘short-chain’ and ‘long-chain’ neurotoxins compete with ACh for AChR binding sites and, once bound, these toxins prevent muscle contraction initiation, producing paralysis.

Several moderately toxic basic PLA₂ toxins which are presynaptically neurotoxic have recently been identified in death adder venoms, and were found to possess acceptor molecule recognition sites that enhance enzymatic activity once bound to their targets. These toxins may contribute to the potential myotoxicity in some death adder species. Research has shown that at least one race of New Guinean death adder (*Acanthophis rugosus*) from Papua possesses a PLA₂ toxin (Acanmyotoxin 1) capable of inducing *in vitro* myotoxicity.

While lacking prothrombin activators, death adder venoms have been found to contain several kunitz-type protease inhibitors of 6.6-7.2 kDa that may be potent inhibitors of coagulation factors. PLA₂ inhibitors of platelet aggregation known as acanthins are also present; however their activity is related more on enzyme isoelectric points than to PLA₂ enzymatic activity. These PLA₂ may be responsible for subclinical anticoagulant activity that prolongs PT and APTT *in vitro* without inducing fibrinogenolysis. There is however no clinical evidence of these activities.

New Guinean small-eyed snake (*Micropechis ikaheka*)

As is likely to be the case with the Papuan blacksnake (*Pseudechis papuanus*), the availability of live small-eyed snakes (*Micropechis ikaheka*) from wildlife dealers in Papua and Indonesia has resulted in the recent characterization of several major venom components by overseas researchers. The venom has strong neurotoxic, myotoxic, anticoagulant, platelet aggregation inhibiting and insulin-secretion stimulating activities. In patients bitten by this species neurotoxicity and myotoxicity appear to be the major clinical consequences.

Two cases in which patients had incoagulable blood have been attributed to powerful anticoagulant rather than procoagulant activity; however researchers in Singapore recently isolated Mikarin, a single-chain metalloproteinase of 47 kDa. Mikarin is unique compared to all other Australo-papuan snakes in being a Ca^{2+} -independent prothrombin activator, and is the first Group I prothrombin activator to be found in elapid venom.

A novel non-haemolytic, haemoglobinuria-inducing toxin (MiPLA-1), which is a 14 kDa, 124 amino acid residue PLA_2 , has been identified, and shown to also strongly inhibit collagen-induced platelet aggregation, as well as being potently myotoxic and anticoagulant. It has been suggested that this toxin might produce haemoglobinuria by causing kidney leakage via either a direct or indirect nephrotoxic mechanism. MiPLA-1 is unique among snake venom PLA_2 s in that it is one of only a few to possess a 'pancreatic loop' region which has a major role in toxin conformation and hydrolytic activity.

Several 'short-chain' and 'long-chain' postsynaptic neurotoxins with molecular weights between 6-8 kDa have also been isolated from *Micropechis ikaheka* venom. One of these, Mikatoxin, has been found to produce neuromuscular paralysis through irreversible nicotinic AChR antagonism. As well as these, an 11 kDa venom fraction containing a 'long-chain' neurotoxin also inhibited ADP-induced platelet aggregation. The anticoagulant activity of *Micropechis ikaheka* venom is underpinned by the presence of a 17 kDa PLA_2 toxin that inhibits both endothelial and platelet-induced procoagulation. Three additional PLA_2 toxins exhibit myotoxicity, anticoagulant activity and stimulate insulin secretion. While the myotoxicity and anticoagulant activity were induced by the enzymatic actions of the toxins, the stimulation of insulin secretion was independent of enzymatic activity.

Papuan blacksnake (*Pseudechis papuanus*)

Until very recently there was only 1 living specimen of this species in captivity anywhere in the world. As a consequence, very little is known about the actual venom composition of these rare, and possibly endangered, snakes. More specimens have become available during the last few years as a result of the wildlife trade in Papua, and a number of snakes are now held in collections in Europe and North America. Venom from Papuan blacksnakes is becoming available to researchers and during the next few years our knowledge may improve.

We do know that the main cause of death in experimental animals injected with Papuan blacksnake venom was cyanosis leading to sudden respiratory arrest, suggesting that neurotoxins are present. The venoms of other *Pseudechis* spp. have been shown to contain abundant PLA_2 toxins with neurotoxic, myotoxic and anticoagulant activity. Weak presynaptic PLA_2 neurotoxins are present in the venom of the Australian red-bellied black snake (*Pseudechis porphyriacus*), and that other species such as Collett's blacksnake (*Pseudechis colletti*) possess a potently myotoxic PLA_2 , as well as a phospholipase B with haemolytic and erythrolytic activities. This latter species is closely related to the Papuan blacksnake (*Pseudechis papuanus*), which has been shown to be haemorrhagic in rats, with a minimum haemorrhagic dose (MHD) of 46-60 $\mu\text{g}/\text{rat}$, suggesting that Papuan blacksnake

venom may contain a weak non-zinc metalloproteinase haemorrhagin. Papuan blacksnake venom has a subcutaneous LD₅₀ in experimental animals of 1.09 mg/kg and this is much less toxic than the 0.05 mg/kg subcutaneous LD₅₀ of Papuan taipans (*Oxyuranus scutellatus canni*).

A 15 kDa neutral PLA₂ isolated by British researchers from Papuan blacksnake venom is a potent monophasic platelet aggregation inhibitor with strong anticoagulant activity, but lacks fibrinolytic activity. Snakebite victims, who were shown to have been bitten by this species using laboratory tests, typically developed reversible neurotoxicity, and had thrombocytopenia, mild defibrination with fibrinolysis, spontaneous bleeding and prolonged prothrombin (PT) and activated partial thromboplastin (APTT) times, suggesting that other venom components affecting coagulation are present in this snake venom. Platelets exposed to the PLA₂ toxin identified by British researchers lost their normal discoid shape, formed membranous projections and developed microfilament disruptions that impaired their ability to aggregate. The same toxin also has moderate myotoxic activity of 546 U/ml. At high concentrations, whole venom from Papuan blacksnakes does have mild procoagulant (prothrombin activating) activity, but this was not sufficiently powerful enough to prevent the clotting of blood within 20 minutes in envenomed animals. The clinical experience with patients bitten by Papuan blacksnakes is that they respond better to antivenom than victims of Papuan taipan (*Oxyuranus scutellatus canni*) bites and appeared to recover much more quickly.

Papuan mulga snake (*Pseudechis cf. australis*)

Nothing is currently known about the venom of the mulga snake species that occurs in Papua and the south-western corner of Western Province, and there are definite records of bites by these snakes. Reports from herpetologists in Europe who have captive specimens that were collected in the Merauke district of Papua suggest that this is a pugnacious snake that will bite with little provocation.

It is probable that the venom is very similar to that of Australian mulga snakes (*Pseudechis australis*), and while this snake has venom that contains many different toxins, the dominant clinical outcome is typically massive rhabdomyolysis with myoglobinuria and possible acute renal failure. There are several potent PLA₂ myotoxins in the venom including mulgatoxin a and Pa-5. Pa-5 has an LD₅₀ of 0.25 mg/kg in laboratory mice while mulgatoxin a has an LD₅₀ of 200 mg/kg in mice when given intraperitoneally. The serum creatine kinase levels of patient bitten by mulga snakes may rapidly reach levels of over 300,000 IU/L (the normal range is less than 200 IU/L), and myoglobinuria (dark brown 'stringy' urine) may persist for several days producing a high risk of nephrotic necrosis and renal failure.

Mulga snake venom also contains several presynaptic and postsynaptic neurotoxins, but, from a clinical perspective, neurotoxicity is usually either minor or non-existent. The neurotoxins include several 13.5-14.0 kDa PLA₂ toxins and at least one 'short-chain' (toxin Pa-a) and one 'long-chain' (toxin Pa-1D) postsynaptic neurotoxin. The toxin Pa-1D was found to be non-lethal in experimental studies despite binding to nicotinic AChR.

There are no known procoagulant toxins in mulga snake venom, but there are a number of haemolytic PLA₂ and possibly PLB toxins that may produce haemoglobinuria (although this is very likely to be overshadowed by myoglobinuria). Australian mulga snake venom also contains true anticoagulant PLA₂ toxins and has been shown to produce prolongation in PT and APTT, without fibrinolysis. The presence of inhibitors of platelet aggregation is unclear; however, these are present in other *Pseudechis* venoms, including *Pseudechis papuanus* and may therefore also occur in this snake.

New Guinean brown snake (*Pseudonaja cf. textilis*)

The common brown snake (*Pseudonaja textilis*) from eastern Australia, to which these Papua New Guinean snakes are the most closely related, is an extremely venomous species that has been implicated as the cause of most of Australia's snakebites and snakebite deaths over the last few decades. Venom from the Papua New Guinean species (*Pseudonaja cf. textilis*) has not been specifically studied, but it is very likely that it contains many of the same toxins and has similar clinical effects.

The most clinically important components in brown snake venom appear to be the prothrombin activator textarin and the plasmin inhibitor textilinin. Disseminated intravascular coagulopathy is the dominant clinical effect, vastly overshadowing neurotoxicity. The spontaneous bleeding from gingival sulci, mucous membranes and other sites that is seen after brown snake (*Pseudonaja cf. textilis*) envenomation is much more prominent than that seen in Papuan taipan (*Oxyuranus scutellatus canni*) envenomation. Textarin is a large molecule with a molecular weight of approximately 200 kDa and an LD50 of 0.023 mg/kg in laboratory rats. Defibrination coagulopathy and drops in the levels of Factor V, Factor VIII, plasminogen and Protein C are reported. In Australia, some patients have had to be treated with as many as 25 ampoules of monovalent brown snake antivenom in order to restore normal coagulation. Deaths are often due to cerebral haemorrhage.

Despite the fact that neurotoxicity is often considered to be relatively minor after bites by brown snakes, the common brown snake (*Pseudonaja textilis*) produces the most lethal presynaptic neurotoxin known from any snake venom. This toxin, known as textilon, is a multi-subunit PLA₂ toxin with some similarity to taipoxin from the venom of the Papuan taipan (*Oxyuranus scutellatus canni*). Like taipoxin, it causes irreversible presynaptic neurotoxicity and structural damage to nerve terminals including mitochondrial and organelle destruction through phospholipid hydrolysis. Myotoxicity and myoglobinuria have not been reported in this species, but there is evidence that there may be a directly nephrotoxic compound, as some Australian patients have experienced acute tubular necrosis in the kidneys.

A common occurrence following brown snake bites is early sudden collapse and transient loss of consciousness that may be due to a brief episode of hypotension brought about by the presence of vasoactive amines or other components.

Sea Kraits (*Laticauda* spp.) and true sea snakes (*Hydrophiinae*)

Remarkably, despite there being many different species of sea snakes with diverse dietary preferences, different evolutionary lineages and widespread distribution, the venoms of these snakes are unique in their relative simplicity. Sea snake venoms are predominantly comprised of 'short-chain' and 'long-chain' postsynaptic neurotoxins, most of which share a unique 'three-fingered' structural backbone designed to optimise the interaction of the toxin with the nicotinic AChR. Erabutoxins found in the venoms of sea kraits (*Laticauda* spp.) are classic three-fingered toxins that strongly bind to AChR, and this is reversible with antivenom.

Many sea snakes have powerfully myotoxic venom PLA₂ toxins. The beaked sea snake (*Enhydrina schistosa*), which is implicated in most sea snake bite fatalities, has a potent myotoxin and renal failure is a common outcome. In addition to a number of PLA₂ toxins, this venom contains several postsynaptic neurotoxins including three enhydrotoxins. Bites by Stoke's sea snake (*Astrotia stokesii*) also produce extensive rhabdomyolysis and myoglobinuria. Lecithinases in some sea snake venoms may cause erythrolysis, and some species are also believed to have weak anticoagulants that may have clinical activity.

Summary Table: Venom components, clinical effects and antivenoms

<u>Species</u>	<u>Toxin types</u>	<u>Typical clinical effects</u>	<u>Effective antivenoms</u>
Papuan taipan (<i>Oxyuramus scutellatus canni</i>)	<ul style="list-style-type: none"> • Powerful procoagulant toxins • Irreversible, very destructive presynaptic neurotoxins • Postsynaptic neurotoxins • Myotoxic PLA₂ • Ca²⁺ channel toxins 	<ul style="list-style-type: none"> • Incoagulable blood (20WBCT > 20 min.) and spontaneous bleeding • Irreversible destructive neurotoxicity leading to sustained facial, bulbar and respiratory paralysis • Rhabdomyolysis and myoglobinuria • Electrocardiographic disturbances 	<p>CSL taipan or CSL polyvalent</p>
Death adders (<i>Acanthophis</i> spp.)	<ul style="list-style-type: none"> • Postsynaptic neurotoxins • Weak presynaptic neurotoxins • Weak anticoagulants • Possible myotoxins • Platelet aggregation inhibitors 	<ul style="list-style-type: none"> • Reversible postsynaptic neurotoxicity • Normal 20WBCT (i.e. <20 min.) 	<p>CSL death adder or CSL polyvalent</p>
Small-eyed snake (<i>Micropechis ikaheka</i>)	<ul style="list-style-type: none"> • Potent myotoxins • Postsynaptic neurotoxins • Platelet aggregation inhibitors • Haemotoxins (MiPLA₂) 	<ul style="list-style-type: none"> • Significant rhabdomyolysis with myoglobinuria and potential renal failure • Reversible postsynaptic neurotoxicity • Thrombocytopenia • Haemoglobinuria 	<p>CSL polyvalent</p>
Papuan blacksnake (<i>Pseudechis papuanus</i>)	<ul style="list-style-type: none"> • Presynaptic neurotoxins • Postsynaptic neurotoxins • Haemorrhagins • Platelet aggregation inhibitors 	<ul style="list-style-type: none"> • Reversible neurotoxicity • Incoagulable blood (20WBCT > 20 min.) • Haemoglobinuria • Possibly rhabdomyolysis/myoglobinuria 	<p>CSL blacksnake or CSL polyvalent</p>

Summary Table: Venom components, clinical effects and antivenoms (Continued)

<u>Species</u>	<u>Toxin types</u>	<u>Typical clinical effects</u>	<u>Effective antivenoms</u>
Papuan mulga snake (<i>Pseudechis cf. australis</i>)	<ul style="list-style-type: none"> • Powerful myotoxins • Weak presynaptic and postsynaptic neurotoxins • Anticoagulant PLA₂ toxins 	<ul style="list-style-type: none"> • Local pain, oedema and ecchymosis • Rhabdomyolysis, myoglobinuria and subsequent acute renal failure • Subclinical neurotoxicity • Possible spontaneous bleeding due to anticoagulants rather than procoagulants 	<p>CSL blacksnake or CSL polyvalent</p>
New Guinean brown snake (<i>Pseudonaja cf. textilis</i>)	<ul style="list-style-type: none"> • Dominant procoagulants • Irreversible and destructive presynaptic neurotoxin • Possible nephrotoxins • Plasmin inhibitors 	<ul style="list-style-type: none"> • Sudden brief loss of consciousness • Incoagulable blood (20WBCT >20 min.) • Significant spontaneous bleeding • Moderate neurotoxicity • Possible renal failure 	<p>CSL brown snake or CSL polyvalent</p>
Sea kraits (<i>Laticauda</i> spp.) True sea snakes (<i>Hydrophiinae</i>)	<ul style="list-style-type: none"> • Postsynaptic neurotoxins • Powerful myotoxins 	<ul style="list-style-type: none"> • Reversible neurotoxicity • Massive rhabdomyolysis/myoglobinuria and subsequent renal failure 	<p>CSL seasnake or CSL polyvalent</p>

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Symptoms and signs of snakebite in Papua New Guinea

Dr Simon Jensen

Introduction

This first clinical chapter will introduce the key features of bites and envenomation by Papuan snakes, which can be recognised as typical experienced symptoms and typical detectable signs.

The chapter will describe the common features of snakebite, as well as unique features that accompany envenomation by specific species of venomous snakes. It will explain what the signs and symptoms are, and what they mean. It will describe ways to classify symptoms and signs, and how to elicit different signs. The aim is to provide a clear understanding of the typical presentation features of the various snakebite syndromes in PNG, covering the various organ systems and tissues that may be affected.

It is important that you appreciate the difference between **snakebite** and **snakebite with envenomation**. Around 50% of people who are bitten by a snake are either bitten by a minimally- or non-venomous snake, or, are occasionally bitten, but not significantly envenomed, by a venomous snake. That is, a bite from a snake does not necessarily mean that evidence of envenomation will develop.

So, **snakebite** is simply that, a bite by a snake, with no implication about the presence of toxic effects, while **envenomation** (snakebite with envenomation) means that the patient experiences some direct effects from venom entering their lymphatic system and then into their bloodstream.

The **assessment** of a patient with possible or definite snakebite must include a **thorough**, but **focussed**:

- **History**, including the history of the bite and the subsequent symptoms,
- **Examination**, determining the vital signs and any signs of envenomation, and
- **Investigations** (which will depend on what tests are available at your health care facility).

This material is covered in more detail in Chapter 6 (*Patient Examination and Diagnosis*), which deals with all aspects of patient assessment, as well as the formation of a diagnosis and treatment strategy.

When assessing a patient after snakebite, you should be looking for not only symptoms and signs of envenomation, but also for evidence of:

- Secondary complications of envenomation; including,
- Any injury suffered during a collapse (not discussed in detail here); and,
- Any adverse effects of traditional first aid methods (such as tourniquet use and cutting the skin near the bite site, which will be discussed here).

What are symptoms? And what are signs?

Symptoms Are what the patient experiences and reports. Note that this will include the history given by relatives and friends, if the patient is unable to communicate with you.

Signs Are what you find on observation of the patient, and can demonstrate through examination.

Symptoms and signs may overlap. For example, the patient may report swelling, bleeding and tenderness at the bite site, features which you can also find on examination. They might also report having coughed up or vomited blood, which you might also observe.

Symptoms and signs of snakebite may be divided into categories such as

- non-specific and specific;
- early and late; or,
- local, regional and systemic.

This chapter will divide symptoms and signs into these categories, as well as looking at the individual organ systems affected in snakebite, and finally the typical presentation features of various snakebite syndromes in PNG.

By considering these different categories of symptoms and signs when you assess a snake-bitten patient, you will be able to be more thorough in your assessment, reduce the chance of omitting significant things, and be better able you to assess the progress of the patient and so provide better care for them.

You will need to **frequently reassess** the patient to look for these signs and symptoms as you **monitor their progress** and look for the development or progression of signs and symptoms of envenomation.

Non-specific and specific symptoms & signs

The majority of serious symptoms and signs of snakebite, especially those occurring within the first 24 hours after a bite, relate to the development of coagulopathy (causing easy bleeding and bruising) and neurotoxicity (causing muscle weakness). Significant cardiotoxicity may also occur (causing features such as collapse and cardiac rhythm disturbances).

Non-specific Symptoms and signs are those which may occur in other medical conditions, and which are not specific for snakebite, though those listed here do occur very frequently after snakebite, and strongly imply a degree of envenomation, when present.

Specific Symptoms and signs are those experienced particularly after snakebite with envenomation, and should make you think of snakebite when a patient presents as unwell, even when there is no clear history of a bite.

It is on the basis of such **specific signs**, that is, on the basis of objective evidence of **envenomation** that you will decide to give antivenom, if this is available where you work. The sooner you can give an appropriate type of antivenom, once a definite indication for its administration exists, the less likely the patient is to develop life-threatening direct effects and secondary complications of snakebite.

Some symptoms and signs may occur more frequently, and more quickly, in children than in adults, and may also be more prominent, or severe. This is due to their smaller size and weight relative to the venom load from a bite, and the fact that their skin is generally softer and thinner than an adult's, and perhaps allows quicker absorption of the venom components. For example, children are more likely to collapse soon after a bite, and with very small children, not yet old enough to talk, this might initially be the only clue to suggest snakebite. Children may also experience more abdominal pain and tenderness than adults, and on at least one documented occasion this has been incorrectly diagnosed as appendicitis, with tragic consequences.

Non-specific symptoms

1. Early symptoms

- Groin pain (in the case of a lower limb bite), axillary (armpit) pain (in the case of an upper limb bite – due to lymphadenitis, inflammation of lymph nodes there),
- Abdominal pain (may be due to abdominal lymphadenitis),
- Nausea, and sometimes vomiting (may be due to severe anxiety),
- Backache (when this occurs later it may be due to intramuscular or retroperitoneal bleeding),
- Headache (beware the early intracranial bleed – see below),
- Palpitations (may also be due to anxiety),

2. Later symptoms

- A changed voice, or slurred speech (dysarthria)
- Generalised weakness,
- Being unable to walk, stand or sit,
- Difficulty breathing (though this may be due to anxiety, in the absence of objective evidence of neurotoxicity),
- Blurred vision, or
- Dizziness (may also be due to hyperventilation).

These symptoms may occur after envenomation from any of the venomous, and possibly some minimally-venomous species, and will usually be present within an hour or two of the bite. They **do not** represent an indication for antivenom on their own. However when they do occur you should do a 20WBCT to check for early coagulopathy, which is a **clear** indication for antivenom.

Therefore, you must **always** ask about these symptoms, and **monitor their progress** as you **frequently reassess** the patient.

Note that there may sometimes be an element of symptom exaggeration due to the obvious anxiety-provoking circumstances in which the patient finds themselves, but you should try not to let this colour your assessment of the patient. On the other hand, you will be most unwise not to take a patient's complaints seriously.

Severe anxiety can cause tachypnoea (rapid breathing), tachycardia, dizziness, nausea and even vomiting or headache. There is some evidence that these symptoms are more common after death adder bites, so there may be some biochemical basis for them.

Specific symptoms

The following specific symptoms are indicative of snakebite envenomation:

- Early dizziness and collapse or “fainting”,
- Bite site symptoms of pain, bleeding, bruising, swelling or tenderness,
- Bruising distant from the bite site, especially at sites of minimal, or no, trauma,
- Bleeding from cuts, or abrasions,
- Bleeding from the gums, or spitting blood,
- Coughing or vomiting up blood,
- Heavy eyelids,
- Diplopia,
- Difficulty opening the mouth,
- A weak voice,
- Difficulty swallowing,
- Progressively increasing weakness, or
- Generalised muscular pain and tenderness, with or without weakness or dark urine.

Non-specific signs

These are signs that while commonly reported by those with snakebite envenomations are not necessarily specific for snakebite, such as:

- Tender, enlarged regional lymphadenopathy; and
- Abdominal tenderness.

In patients with abdominal tenderness there may be voluntary guarding, but this is not usually associated with rebound tenderness or rigidity (the presence of these two signs should make you think of causes of an acute abdomen such as appendicitis, ileal perforation, pelvic inflammatory disease, ectopic pregnancy or pancreatitis).

Specific signs

These are those which are typical of snakebite, and include:

- Obvious abnormal bleeding, such as from the gums, with spitting of blood;
- Ptosis (drooping eyelids), ophthalmoplegia (fixed eyeballs);
- Poor mouth-opening;
- A weak voice (or “thick speech”);
- Pooling of saliva in the mouth (prominent in death adder and taipan bites), or difficulty swallowing (dysphagia);
- Partial or complete respiratory paralysis, including a weak cough;
- Progressive weakness of the truncal muscles (the back and abdominal muscles) including an inability to stay sitting up (truncal ataxia);
- Progressive symmetric (i.e.: the same on both sides) limb weakness.

Local, regional and systemic symptoms & signs

Local symptoms and signs are those which occur at the bite site.

Symptoms may include:

- Pain;
- Swelling;
- Bruising and bleeding;

Signs include but are not limited to:

- Fang marks, which may be multiple and give an indication of multiple strikes (you may see nothing or there may be scratches or even a small laceration; or single or double puncture marks);
- Swelling, bruising, bleeding;
- Lacerations from scarification, and other effects of deleterious traditional first aid.

Regional symptoms and signs are those which occur in the bitten limb, distant from the actual bite site. They include the complications of tourniquet use, and include the symptoms of:

- Unilateral limb pain, swelling, and
- Regional lymph node pain,

Common regional signs include:

- Unilateral bruising, swelling or tenderness, mainly of the muscles, and
- Regional lymph node tenderness and enlargement (lymphadenopathy).

Systemic symptoms and signs include all those not listed above, and are an indication of systemic envenomation. They include symptoms and signs due to:

- Coagulopathy and other haematological effects;
- Neurotoxicity including CNS toxicity;
- Cardiotoxicity;
- Generalised myotoxicity; and,
- Renal effects (direct and secondary).

Organ system and tissue-specific symptoms & signs

(See also Chapter 3 – Composition of PNG snake venoms)

The results of laboratory testing will not be discussed here.

Cardiovascular effects

(See also Chapter 10)

According to Lalloo *et al* (1995) 23% of people bitten by the Papuan taipan (*Oxyuranus scutellatus canni*) experience early collapse with up to 5 minutes of unconsciousness. It is possible that this is due to a direct cardiotoxic effect of the venom, since this is sometimes preceded by dizziness. However, transient intravascular thrombosis of coronary arteries, such as has been suggested as a cause of the early (within the first hour) collapse in Australian brown snake envenomation is another possibility.

Other effects seen in taipan envenomation include sinus bradycardia (the venom contains taicatoxin, a calcium channel blocker) and septal T-wave inversion (Lalloo *et al*, 1995). Rapid supraventricular tachycardia's, such as atrial fibrillation has also been observed in a heavily envenomed patient (Jensen, *unpublished*). After taipan bites, hypertension, hypotension, and transient sinus tachycardia have also been reported.

Pulmonary oedema has also been observed, possibly due to either myocardial ischaemia or to renal failure. Other venom components may have cardiac effects, but these don't appear to be clinically important.

So you should ask about dizziness, palpitations and periods of collapse.

Additionally, patients who have lost a considerable amount of blood due to coagulopathy may be shocked, with a high pulse pressure (the difference between the systolic and diastolic pressures), increased heart rate and hypotension.

A full assessment of the cardiovascular system will involve measuring the heart rate and blood pressure, and noting peripheral perfusion (blood should return to the nail beds within 2 seconds when these are compressed for 2 seconds, then released), the presence of profuse haemorrhage, and performing an ECG.

Neurological effects

(See also Chapter 8)

PNG snake venoms contain both presynaptic and postsynaptic neurotoxins (*see Chapter 3 for details*). The post-synaptic toxins affect cholinergic receptors of muscle endplates to prevent acetylcholine binding, and hence the transmission of nervous impulses. This binding is reversible, and the weakness due to this binding usually resolves with 24-48 hours, or within a few hours (1-3) of administration of the appropriate antivenom. This is the case with death adder neurotoxins, and with a toxin found in taipan venom.

Presynaptic neurotoxins form the main neurologically-active component of taipan venom, and a clinically minor, though very toxic, component of brown snake venom. Nerve terminals are damaged to the extent that they, and the peripheral parts of the nerve, disappear completely within 24 hours. As a result of this damage, paralysis can take several days to a few weeks to recover, which is due to the time taken for the nerve endings to re-grow and for new connections to form with the muscle end-plates, depending on the timing of any antivenom therapy and the use of proven first aid measures, i.e.: pressure-immobilisation bandaging, limb splinting and patient immobilisation.

The first muscles affected are the smallest voluntary muscles, those of the eyelids and the external ocular muscles. Next affected are the larger facial muscles and bulbar (swallowing and speaking muscles), then the respiratory muscles (first the intercostals, then the accessory muscles of respiration – the sternomastoids and trapezius - and finally the diaphragm).

Although voluntary (skeletal) is the most obviously affected muscle type, the urinary retention that occurs in all paralysed patients suggests some smooth muscle involvement as well. This has yet to be clarified. Certainly, all require an **indwelling urinary catheter**, not only because they are unable to get up to go to the toilet, and because they invariably develop urinary retention, but also to monitor their renal perfusion and function and the appearance of gross haematuria or myoglobinuria.

One Papuan taipan toxin, taicatoxin, has an effect on certain brain cells, though the clinical significance of this is unknown. It may be one of the reasons for early dizziness and collapse with brief loss of consciousness seen in a significant proportion people bitten by this snake.

It is very important to realise that snake-bitten patients **do not** develop coma unless they have one of the following:

- Early collapse, and moderate or severe head injury as a result of their collapse,
- Intracerebral haemorrhage,
- Respiratory failure with cerebral hypoxia,
- Or some un-related condition, such as alcohol intoxication, or assault involving head injury.

Patients have often been left to 'sleep' only to be found either dead many hours later, or in respiratory failure with complete ptosis; so frequent reassessment to avoid missing this deterioration is vital. It can be very difficult to assess the responsiveness of a paralysed patient!

When assessing a patient for neurotoxic effects of snake venom, a thorough assessment would include testing the following (*this will be covered more in Chapter 6*):

1. All cranial nerves innervating voluntary muscles:

- *Nerves III, IV, VI* = eye movements, diplopia (external ocular muscles); eye-opening (eyelid elevation – assess the resting position, and the degree of elevation with attempted upward gaze = *III*);
- *Nerve V* = mouth-opening (masseter);
- *Nerves VII* = facial expression (upper and lower facial muscles – brow wrinkling, squeezing the eyes shut, smiling and showing the teeth, puffing out the cheeks);
- *Nerves IX, X* = speech, swallow, gag reflex, palatal movement (bulbar muscles);
- *Nerve XI* = shrugging shoulders, neck flexion and head rotation (sternomastoids, trapezius);
- *Nerve XII* = tongue protrusion (tongue muscles).

2. Muscles of respiration:

- *Intercostal muscles* = when these are paralysed there is little actual chest expansion with respiration and so-called paradoxical breathing is seen; that is, the upward movement of the abdominal muscles with inspiration;
- *Accessory muscles* = sternomastoids, trapezius; elevate clavicles to assist chest expansion; indicates respiratory distress;
- *Diaphragm* = the last to be paralysed; assess by looking at the degree of abdominal movement and the degree of air entry on auscultation.

A full respiratory assessment should also include determining the respiratory rate, the peripheral oxygen saturation, if possible, and the presence of cyanosis – a grave sign implying airway obstruction, large pulmonary aspiration or advanced respiratory failure, requiring urgent intubation and ventilatory support to prevent death.

Note that an anaemic patient might not develop cyanosis, since 50g/l of deoxygenated haemoglobin is required for this sign to be evident.

3. Truncal muscles:

- Can the patient sit up unaided, remain sitting up, or contract their abdominal muscles?

4. Upper and lower limb muscles

- There should be roughly symmetric weakness of the upper limb muscle groups; clear asymmetry suggests a diagnosis other than snakebite, such as a stroke;
- In the upper limbs, grip strength loss will be evident early on, since it depends partly on the small muscles of the hand;
- There will be some weakness of the muscles responsible for joint extension before this is apparent in the joint flexors, since the former are generally the weaker muscles;
- Deep tendon reflexes, such as the knee jerk and biceps jerk, will become less brisk and eventually be lost altogether, since they depend on normally-functioning neuromuscular junctions.

To monitor the progress of neurotoxicity, it is necessary only to follow the progression of a selection of these signs, which will be included on your snakebite assessment sheet.

Trismus is often reported in referral letters. However, true trismus, that is, spasm of the muscles of mastication (the chewing muscles), does **not** occur in snakebite, unless the patient is fitting due to a severe head injury suffered during a collapse, due to intracerebral bleeding, or to severe hypoxia secondary to pulmonary aspiration, airway obstruction or respiratory failure. (Exceptions to this would be when an unimmunised patient actually develops tetanus – *Clostridium tetani* infection - with true trismus, or when a patient has an unrelated medical condition such as severe hypoglycaemia or epilepsy, both resulting in seizures, and is not actually suffering from snakebite.) Trismus is being confused, most often, with facial muscle weakness and an inability to open the mouth widely, or with myolysis and painful mouth-opening.

Haematologic effects

(See Chapters 3 & 9)

Papua New Guinean snake venoms contain both procoagulants and anticoagulants, and information about these toxins is presented in Chapters 3 & 9. Haemolysis (erythrocytolysis) sometimes occurs, as does impairment of platelet function. Collapse soon after snakebite and especially in the first hour, maybe due to transient coronary or cerebral thrombosis due to the effects of the procoagulant components of the venom.

Extensive peripheral superficial venous thrombosis, without obvious subsequent embolisation has also been observed after Papuan taipan envenomation (Jensen, *unpublished*). The result of consumption of clotting factors, and to a lesser extent, the effect of anticoagulant components of venom and the effect on platelets, is bleeding. This is seen as:

- Bleeding from the bite site and/or bruising and swelling at the bite site;
- Bleeding from scarification sites;
- Bleeding from any subsequent of recent sites of injury (bruises, cuts and abrasions);
- Spontaneous subcutaneous bruising distant from the bite site;
- Bleeding gums and/or spitting of blood;
- Vomiting blood – haematemesis;
- Coughing up blood (haemoptysis) that may be torrential in someone with active pulmonary TB or a pulmonary tumour;
- Bleeding from i.v. or venepuncture sites: It is important to try to insert an i.v. cannula on the first attempt, and to take all blood samples from this site; many patients arrive at PMGH with multiple oozing sites of attempted and failed i.v. insertion;

- Oral or nasal bleeding due to mucosal injury during tracheal intubation, naso- or orogastric insertion, or suctioning, (take care to perform these procedures as atraumatically as possible); there may also be altered blood (dark brown) in the nasogastric drainage;
- Subconjunctival bleeding;
- Subglottic haematoma (under the tongue) may be an indication for intubation to prevent the development of airway obstruction;
- Microscopic or macroscopic haematuria (care with IDC insertion):
- Excessive menstrual losses;
- Retroplacental bleeding, causing abdominal pain or PV bleeding, in pregnancy;
- Retroperitoneal bleeding, causing back pain and ileus;
- Bloody diarrhoea, rectal bleeding or malaena (black stools);
- Intracranial bleeding, often leading to coma and death (mostly avoidable with prompt, appropriate and adequate antivenom therapy).

Ecchymosis (bruising) is more indicative of coagulation factor defects and deficits, while petechiae, very small subcutaneous bruises, such as are seen in Henoch-Schonlein purpura, are more indicative of platelet defects (either low because of DIC – disseminated intravascular coagulation - or due to functional impairment).

Remember that tetanus vaccination is effective up to 3 days after an injury, though complete protection is not obtained until after a full course of 3 vaccinations. Therefore, the patient with obvious coagulopathy should probably **not have** any intramuscular injections until after antivenom is given, and all medications that are required should be given intravenously, or orally.

Myotoxicity

(See Chapter 10)

Myotoxic venom components can cause massive lysis of skeletal muscle cells. This causes release of, most importantly, myoglobin, which can lead to acute renal tubular necrosis and renal failure (it has a directly toxic effect on the renal tubules). It also releases potassium, which can lead to cardiac rhythm disturbances. Not only does this lysis cause pain and swelling and tenderness of the associated muscles, there will be significant muscle weakness, and even respiratory failure. The muscles will usually repair over the next few weeks, provided the patient survives.

There may be concern about compartment syndrome. This is due to the swelling of muscles of the limbs, and subsequent increase in the pressure within that muscle compartment, which leads to impairment of sensory function of nerves passing distally, of impaired venous return from the limb, and eventually to impaired blood flow to the limb, leading to muscle necrosis and contractures. However, this has been shown, in snakebite, to be best managed conservatively, that is, without surgery, with a better eventual outcome.

Renal effects

(Chapter 10)

These include renal failure (both as a direct effect and as a secondary complication) and haematuria. Renal failure may be due to a number of different causes, depending on the snake involved and the clinical circumstances.

Causes of snake venom-related renal failure include:

- Myolysis resulting in myoglobinuria and renal tubular necrosis (myoglobin is directly toxic to the renal tubules; Papuan blacksnake, sea snakes, mulga and small-eyed snakes),
- Haemolysis, resulting in glomerular and tubular blockage (brown snakes and small-eyed snakes),
- Micro- and macro-vascular thrombosis (and possibly microangiopathic haemolytic anaemia (Papuan taipans, brown snakes),
- Direct nephrotoxic effects of venom components,
- Glomerular and tubular necrosis due to filtered fibrin degradation products (Papuan taipans, brown snakes)
- Renal cortical ischaemia due to shock secondary to blood loss,
- Renal cortical ischaemia due to respiratory failure and hypoxia +/- pulmonary aspiration.

Prolonged bladder outlet obstruction due to urinary retention may occasionally contribute to renal function impairment, in those who are brought to medical attention late, with advanced muscular weakness and respiratory failure. Coagulopathy is also frequently associated with microhaematuria, and occasionally gross haematuria. This is to be distinguished from the effect of extensive rhabdomyolysis, which causes smoky, then dark brown urine (possibly with white stranding).

Symptoms and signs of complications of snakebite

These are effects that are secondary to the primary effects of the snake venoms on the various tissues and organ systems.

Cardiac effects such as early intravascular thrombosis, due the procoagulant effects of venom, may result in early collapse, if the coronary arteries are involved, or if significant arrhythmias occur. Such early collapse can result in injury, such as cuts and abrasions, or head injury. Subsequent coagulopathy may result in significant bruising and bleeding, such as noted by Lalloo *et al* (1995) in a number of patients bitten by PNG taipans, and where a head injury has occurred the resultant intracerebral bleeding will be life-threatening.

Coagulopathy usually results in spontaneous haemorrhage, as well at sites of recent injury, and this may secondarily result in:

- Shock, with myocardial, renal or brain injury;
- Cerebral injury and death from various types of cerebral haemorrhage;
- Partial airway obstruction from haemorrhage in the neck musculature and under the tongue;
- Acute renal failure due to glomerular and tubular obstruction and necrosis due to fibrin degradation products (worsened by infusing clotting factors if there is un-neutralised venom still in the circulation);
- Compartment syndrome due to bleeding within the limb muscles; and
- Anaemia.

Neurotoxicity invariably causes in a degree of bulbar paralysis leading to an inability to swallow, and respiratory muscle paralysis leading to an inability to cough, both resulting in pulmonary aspiration of oral secretions, and occasionally of vomitus, or of food or oral fluids given to snakebite patients.

Paralysis of respiratory muscles results in respiratory failure, meaning that there is inadequate gas exchange, i.e.: oxygen uptake (oxygenation), and carbon dioxide excretion (ventilation).

This will result in tissue hypoxia and acidosis and eventually cause hypoxic organ damage, which is particularly serious when it occurs to:

- The brain, causing coma and possibly permanent neurological deficits,
- The myocardium, causing infarction, a degree of heart failure and possibly hypotension (shock);
- The renal cortex, causing acute and possibly chronic renal failure.

The mixed respiratory and metabolic (lactic) acidosis which results will further impair cardiac function, and CO₂ retention will exacerbate the raised intracranial pressure associated with any intracerebral bleeding, and possibly worsen bleeding, by causing cerebral vasodilatation.

Renal effects of envenomation may result in acute, leading to chronic, renal failure, which contributes to the late deaths of snakebite patients. This is especially to be anticipated when marked rhabdomyolysis is observed. Though this is amenable to peritoneal (and haemo-) dialysis, this treatment is generally not available in PNG at present. The signs of renal failure are usually apparent after a few days, and will include:

- Oliguria or anuria,
- Pulmonary oedema,
- Cardiac rhythm disturbances due to hyperkalaemia (monitor the QRS interval if you are unable to measure the serum K⁺).

Myotoxic venom components can cause massive lysis of muscle cells, as noted above. This causes release of, most importantly, myoglobin, which can lead to acute renal tubular necrosis and renal failure. It also releases potassium, which can lead to cardiac rhythm disturbances. Not only does this lysis cause pain and swelling and tenderness of the associated muscles, there will be significant muscle weakness, and even respiratory failure. The muscles will usually repair over the next few weeks, provided the patient survives.

Septicaemia may be the eventual result of:

- Tissue hypoxia (from respiratory failure and shock), leading to bone marrow depression;
- Pulmonary aspiration of oral bacteria leading to aspiration pneumonia; and
- Scarification near the bite site.

Septicaemia may lead to late death.

Symptoms & signs of complications of traditional first aid

(See Chapter 5 for more detail)

The most obvious complications of traditional first aid methods are that:

- They do not prevent the effects of venom
- They defer the use of proven first aid methods
- They often delay the patient seeking medical help, and the definitive treatment with antivenom.

Scarification (cutting the skin above the bite site) does not prevent the uptake of venom into the bloodstream, but does result in:

- Pain,
- Bleeding,
- Localised swelling,
- Later skin infection and scarring.

Tourniquet use causes limb pain, swelling, and tenderness distally, due initially to venous engorgement, and ischaemia later on causing hypoxic damage to the muscles distally, leading to compartment syndrome and even contractures. If the venom contains myotoxins, tourniquet use may worsen the muscle damage once the tourniquet is released, especially if antivenom is not available immediately. Herbal and other remedies taken orally may cause poisoning.

Envenomation Syndromes

The following is a summary of the observed effects of envenomation by the various PNG snakes. It should be noted that the non-specific symptoms of snakebite, especially abdominal pain +/- nausea and vomiting, regional lymphadenitis, and headache +/- backache, may occur after envenomation by any of these species.

Snake species	Common & predominant effects of snake venom	Occasional & minor effects of venom
Papuan taipan	Brief collapse Consumption coagulopathy Persistent destructive presynaptic neurotoxicity	Postsynaptic neurotoxicity Transient cardiotoxicity and ECG changes
New Guinea death adders	Postsynaptic neurotoxicity	Bite site pain
New Guinea small-eyed snake	Myolysis Postsynaptic neurotoxicity Acute renal failure	Thrombocytopenia Haemolysis
Papuan blacksnake	Postsynaptic neurotoxicity Myolysis Acute renal failure	Bite site symptoms Consumption coagulopathy Platelet effects
New Guinea brown snake	Brief loss of consciousness Consumption coagulopathy Mild-moderate presynaptic neurotoxicity	Other haemorrhagic effects Acute renal failure
Papuan mulga snake	Local pain and swelling, bruising Myolysis Acute renal failure	Anticoagulant effects Postsynaptic neurotoxicity
True sea snakes Sea kraits	Postsynaptic neurotoxicity Myolysis Acute renal failure	Minor coagulation defects Local swelling



Rubber tourniquet-induced local swelling in the calf of a Brown River man bitten by a Papuan taipan; the use of tourniquets is not recommended after snakebite (*See Chapter 5 for discussion*)

Summary

In summary, it is recommended that when you take a history and examine a patient who is known to have been, or may have been, bitten by a snake, you first determine the need for, then proceed immediately with, resuscitation of airway, breathing and circulation, if this is required. Then you should assess the local, then the regional, then the systemic symptoms and signs, ensuring that all organ systems likely to be involved are included.

Next, assess those symptoms and signs elicited to decide if the patient has features typical of snakebite or not, i.e.: if they have only non-specific symptoms and signs, or if they have some specific to snakebite. Try to decide if they are representative of a specific envenomation syndrome. Look for secondary complications of the snakebite.

You will be presented with an identification algorithm later in the handbook (Chapter 14) which will help you to work through this decision-making process.

First aid for snakebite in PNG

Benjamin Bal and David Williams

Introduction

Many victims of snakebite are not seen at an aid post or rural health centre until many hours after they were bitten by the snake. During this time the snake venom has been able to infiltrate their bodies and spread to reach many of the sites where the toxins exert their deadly effects. One of the factors that contribute to the poor outcomes, such as prolonged hospitalisation on expensive ventilators and high mortality rates that we see after snakebite in Papua New Guinea, is the fact that, by the time they present for treatment, many patients have already developed serious signs and symptoms of envenomation.

The majority of snakebite patients make no attempt at any form of first aid to slow the absorption and spread of the snake venom. Those who do often use potentially dangerous and/or completely ineffective first aid treatments that have no clinical benefits. The consequence is that, by the time the patient presents for treatment, they may already have developed irreversible neurotoxicity and other problems such as coagulopathy or myotoxicity. These are medical problems that challenge the abilities of even highly trained emergency physicians with the benefits of properly equipped high dependency and intensive care facilities at their disposal. In our rural PNG situations, where the resources and skills are far less developed, we face very serious difficulties in successfully treating such patients.

The use of correct first aid immediately after snakebite has the potential to significantly delay the development of systemic envenomation. This can improve the chances of survival a great deal. Unfortunately, very few snakebite patients arrive at an aid post, health centre or hospital with appropriately applied, correct first aid having been applied, although this is starting to change in some districts thanks to public education work by some health workers and snakebite researchers.

We as health workers must be proactive in the teaching of safe, efficacious snakebite first aid to the people in the communities that we serve if we want to reduce the burden that this very serious problem places on our medical and health resources, and more importantly, to save lives. Going out into our communities, into schools, marketplaces, and other places where people gather to teach them how to apply proper first aid after a snakebite, and how they should care for the patient before arrival at the health facility, should be an important part of our village and community health promotion efforts.

This chapter of the Handbook discusses some of the very different types of first aid that Papuan New Guinean people use to treat snakebites and explains why most of them are ineffective, unsafe or just plain dangerous. It will also explain the rationale and reasoning behind the current medically endorsed snakebite first aid technique; the use of simple compression bandages and immobilisation of the patient.

Important principles of first aid for snakebite

The most important things to remember about first aid are that the method used must be able to be applied with **SPEED**:

- **SAFE** It must not be harmful or cause injury to the patient.
- **PRACTICAL** It should be practical and appropriate to the situations in which it is most likely to be needed, and the materials should be easily accessible.
- **EFFECTIVE** It should be effective in reducing the risks of long term illness or death after snakebite.
- **EASY** The method should be easy to teach to unskilled users and should be easy to apply to the patient by unskilled users.
- **DISTINCTIVE** The method should be easily associated with the treatment of snakebite so that it is remembered by the people who may need to use it.

Unfortunately, many of the first aid methods that are commonly used to treat snakebites in Papua New Guinea do not meet all five of these important criteria. Some of the first aid ‘treatments’ administered by well-meaning friends and family members are actually more dangerous to the patient than the snakebite itself, while others based on local traditional beliefs, or the beliefs of outsiders, simply do not work at all.

Different types of first aid for snakebite

Many different types of first aid have been proposed for either delaying or preventing the activity of the injected snake venom. First aid treatments tend to be traditional and to have been handed down as a part of a local pharmacopeia over many generations. Many Papua New Guinean communities have their own local treatments for snakebite, and with the arrival in the country of outsiders of European, Asian and African descent, several new treatments, in the traditions of these newcomers, have been introduced.

Most Papua New Guinean snakebite treatments are offered as cures rather than as first aid, and these may include:

- The use of natural substances such as plants, fungi and animal materials.
- Reversing the effects of sorcery, witchcraft and curses placed on the victim by a living enemy or the spirit of a relative or other being.
- Bleeding the victim using a sharpened stick or blade, or cauterising with a heated knife.

In traditional Papua New Guinean culture, snakebite is often due to the spirits of dead ancestors who may have been angered by some wrongdoing of the victim, or it may be caused by an evil spirit or mythological entity such as the *ove-hahu* of the Elema people in Gulf province. The treatment of snakebites caused in these ways is often very spiritually based.

Colonial European settlers brought with them their own traditions for the treatment of snakebite which, while based more on the principles of medicine, also sometimes had their own elements of spiritual or supernatural involvement, often gained from colonial experience elsewhere in the world, such as in Africa or India. The ‘black stone’ brought to Papua New Guinea by early missionaries for instance, has been used widely in African cultures as a witchdoctors treatment for snakebites, but gained acceptance by religious workers who spread its use to other parts of the world. Other exotic treatments for snakebite have also been brought to PNG by immigrants and expatriate workers from Asia, India and Africa.

'Imported' first aid methods and treatments for snakebite include:

- Wound scarification (incising or excising the bite site) to remove venom by bleeding.
- Tourniquet and rope ligature use to delay systemic absorption of venom.
- Suction of venom from a wound either by mouth, vacuum pump, suction device or by 'cupping' with a heated glass container.
- The application of electrical current to the bitten area in the attempt to inactivate venom.
- Injecting the bite with potassium permanganate (Condy's crystals).
- Application of the Belgian 'black stone' to attempt to absorb venom from the bite site.
- The use of traditional 'Chinese' herbal remedies or 'snakebite pills'.
- Pressure immobilisation bandaging to delay venom uptake.

The actual efficacy of many of these techniques is extremely questionable. While some simply do not work, others are actually dangerous to the health and welfare of the snakebite patient.

Forms of first aid that are potentially dangerous

While any attempt at first aid that does not work, or which delays access to appropriate medical care, should be considered potentially harmful rather than helpful, there are some methods of first aid treatment that are commonly used which are potentially very dangerous to the health and safety of the patient:

Wound scarification

Up until the late 1970's it was commonly believed that wound scarification could be helpful in removing venom from the body of a victim of snakebite. It was believed that by bleeding the patient venom would be removed and the effects of the snakebite reduced.

Two basic techniques of scarification were in wide use in Australia, and were subsequently taught in PNG. These were the use of incision (cutting through the bite marks to promote bleeding) or excision (the pinching up of the skin around the bite and completely cutting out the piece of flesh). Although sterile scalpels or razor blades were the commonly suggested tools, the reality is that under actual field conditions people tend to be very ingenious and everything from broken glass, rusty pieces of tin cans, knives, wood-working chisels and gardening clippers have been used.

Incising or excising snakebite injuries is contraindicated by the following arguments:

- Many of the snakebites reported in PNG and elsewhere are caused by non-venomous snakes, and more harm is done by scarification than was caused by the actual snakebite.
- Venom is rarely injected directly into the bloodstream. In most cases it is injected into fat or muscle tissue and is taken up and spread by the lymphatic system. It is highly unlikely that venomous is effectively removed as a result of scarification.
- The powerful procoagulants in Papuan taipan (*Oxyuranus scutellatus canni*) and other PNG snake venoms produce severe consumption coagulopathy that can result in life-threatening haemorrhage. Cutting the bite site can result in serious blood loss that may be rapidly fatal.
- Serious local trauma to tendons, ligaments, blood vessels and musculature; people bitten by non-venomous snakes have suffered serious disfiguring injuries by having tendons cut during first aid. There is also a very high risk of secondary infection, including tetanus.

Tourniquet and ligature use

The use of tourniquets or improvised ligatures in the treatment of snakebite remains common throughout the world, despite overwhelming evidence that indicates that these techniques are both ineffective for practical use, and potentially dangerous.

In Papua New Guinea the use of tourniquets was often advocated in conjunction with wound scarification by the colonial Australian population who were accustomed to this technique at home. In rural PNG, tourniquets are still used quite commonly and are often fashioned from a variety of materials including string/rope, wire, strong grass strands, bicycle inner tubes and packing straps. Many are incorrectly applied to lower limbs where they have even less clinical benefit than correctly applied upper limb tourniquets.

Tourniquets and ligatures can play an important role in the control of blood loss, and are used in situations such as accidental amputation where catastrophic haemorrhage may lead to sudden death. Their use in the treatment of snakebite employs a different strategy; rather than attempting to control haemorrhage the principle has been to prevent or delay the return of presumably venom-containing venous blood from the periphery to the heart.

Using a tourniquet or rope ligature to severely restrict venous return is potentially dangerous and has limited efficacy in the treatment of snakebite. The major factors contraindicating the use of tourniquets are:

- Limited efficacy; correctly applied, a tourniquet is placed on a single-boned part of a limb (thigh or upper arm) but must be released briefly every 20-30 minutes in order to relieve the venous pressure differential – the problem of course is that once released any venom that has been taken up in the blood by diffusion from tissue will be rapidly delivered to the systemic circulation.
- Local tissue injury can result from the failure to release a tourniquet or ligature. Harmful metabolites and waste gases that would normally be removed by kidney filtration or gas exchange in the lungs become localised and in conjunction with tissue hypoxia can lead to ischemic necrosis, gangrene and the loss of limbs through subsequent amputation.
- Prolonged tourniquet use is extremely uncomfortable and can be very painful.

Injection with potassium permanganate solutions

Potassium permanganate (also called Condy's crystals) was a common inclusion in many snakebite treatment kits during the 20th century. The injection of a weak solution of the chemical directly into the snakebite wounds was believed to inactivate the venom based on laboratory *in vitro* experiments that suggested this to be the case.

Contraindications to potassium permanganate use include:

- Absence of clinical evidence to demonstrate effective *in vivo* snake venom inactivation.
- The caustic nature of potassium permanganate and evidence that indicates that it may have harmful necrotic effects on tissue.

Treatment with electrical current

Although the use of electricity to inactivate snake venom has been widely advocated in the Americas, its use in Papua New Guinea is uncommon. This is extremely fortunate, as in addition to strong medical and experimental evidence that shows electricity to have absolutely no effect on the toxicity of snake venoms, there is considerable danger of actual electrocution and death through the use of excessive electrical current.

Direct suction or the use of suction devices

Anyone who has ever seen an old Western movie on the television will have seen the hero who comes to the rescue of the pretty girl bitten by a rattlesnake by quickly cutting open the wound with his trusty Bowie knife and then proceeding to use his mouth to suck away the venom...

We can only hope that our hero has no small abrasions, ulcers or gingival injuries inside his mouth, because if this were to be the case the chances are that he himself would probably be the snake's second victim! He might also doom the young lady to potential sepsis by introducing oral bacteria into the blood stream while he is sucking away at her lacerated arm.

In addition to these potential risks, suction has been shown to remove very little of the injected venom, even when specially designed suction devices and 'venom extractors' are used. During the Australian administration of PNG it was common to use heated glass containers that were placed over the bite site to create a vacuum that was believed to draw venom out of the body. In reality, all that was usually removed was a little blood or serum.

In general, suction is contraindicated because:

- Venom absorption in the oral cavity of the first aid provider may result in there being two snakebite victims instead of just one.
- Oral bacteria can be transferred into the wound and may cause secondary infection.
- Suction is ineffective at removing all of the injected venom, and the local stimulation caused by the application of suction may actually enhance the absorption of venom into the systemic circulation.
- Local burns can be caused by applying very hot glass containers to bite sites without first cooling the mouth of the bottle or glass.

Forms of first aid that are clinically ineffective

The majority of other first aid techniques commonly used in PNG, while not directly dangerous to the patient, lack clinical efficacy and are likely to delay more appropriate treatment.

'Chinese snakebite pills' and other Asian medicines

Traditional Chinese medicine dates back many thousands of years, and there are many remedies based on natural Chinese pharmaceuticals that have been proven to have clinical benefit. This does not apply to all of the treatments offered by Chinese Herbalists and Pharmacists, and there is scant evidence to justify the use of Chinese snakebite cures. Many of the Chinese road construction workers who built the Bereina-Malalaua road in southern PNG were well supplied with these preparations and often gave them to local wantoks.

Among the substances that occasionally find their way into these 'medicines' are parts of certain snakes themselves, arthropods such as the *Wugong* (centipede), and various types of tree bark and other plants. Some of the plant materials in these medicines may themselves be potent toxins. Lobelia which is used in some Asian medicines to treat complaints such as asthma, kidney disease, cancer and snakebite is also very toxic and even quite small amounts can cause fatal overdoses. Preparations containing Echinacea, yellow dock, comfrey, white oak, valerian, senega snakeroot, garlic and many other herbal materials are often sold as 'snakebite pills'. Other than costing lots of money most of these 'medicines' are probably quite harmless; the real danger lies in the risk that the user may take them and remain at home, rather than taking steps to seek urgent medical attention at an aid post or health centre.

The Belgian ‘black stone’

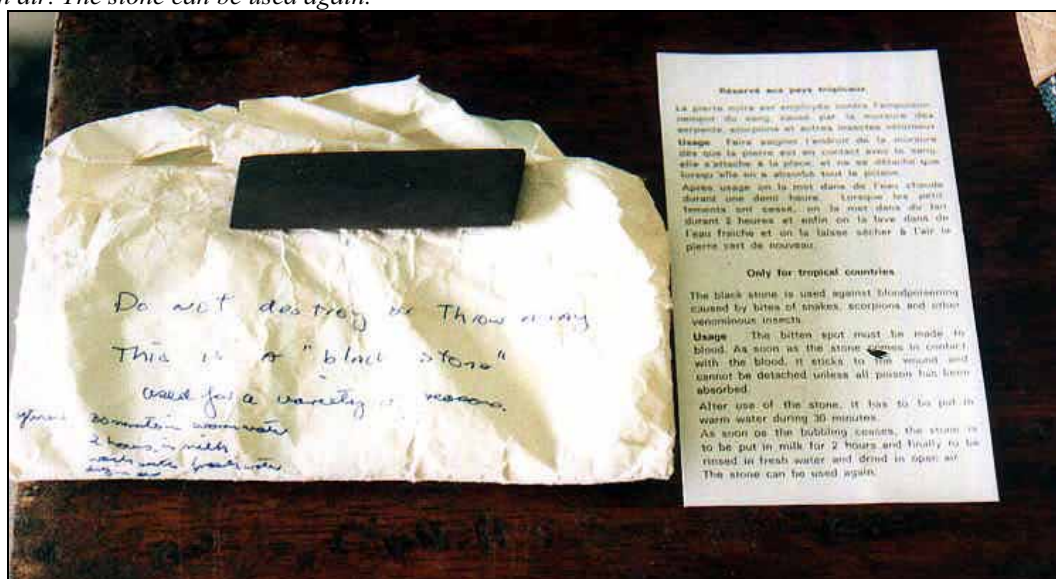
The ‘black stone’ is promoted more as a treatment for snakebite than a means of first aid. However, because it is often applied by non-medical personnel before actual medical care is sought or obtained, it is appropriate to discuss its use here.

It is generally accepted that the ‘black stone’ originated in parts of Africa where it was used widely by local healers and witchdoctors as a traditional cure for venomous snakebite. European (particularly Belgian) missionaries were the first to encounter its use, and, impressed by its apparent efficacy, they embraced its use and returned home convinced that the ‘black stone’ was the answer to all of their colonial snakebite problems.

‘Black stones’ tend to appear everywhere in the world that European missionaries established colonial Christian outposts. As well as their native Africa, they are common in South America, the Caribbean Islands and in parts of Asia and the South Pacific. In north-eastern Peru the use of the *Piedra negra* (‘Blackstone’) is even promoted in local medical treatment books, and instructions on its manufacture are provided to health workers. ‘Stones’ are actually nothing more than small rectangular pieces of fire-charred and blackened cow bone that are filed into the right shape and smoothed by rubbing.

Despite the fact that the ‘black stone’ can have very profound placebo effects in true believers, the reality is that it is little more than a cheap magic trick designed originally by African witchdoctors to part the snakebite victim from his or her riches in return for its use. The porous ‘stone’ sticks easily to drying clot (as most things do), and when immersed in water afterwards produces bubbles as air escapes from the small pores in the bone – giving the patient an impression that the ‘stone’ has special properties. The reality is that the ‘black stone’ has absolutely no ability whatsoever to cure the bite of a venomous snake (although it cures many people bitten by non-venomous snakes!) and it should not be used in preference to more appropriate first aid or obtaining medical treatment.

FIGURE 1: A traditional ‘black stone’ used in the treatment of snakebites in Papua New Guinea and many other parts of the developing world. The instructions for use read: “*The black stone is used against bloodpoisoning caused by bites of snakes, scorpions and other venomous (sic) insects. Usage – The bitten spot must be made to bleed. As soon as the stone comes in contact with the blood, it sticks to the wound and cannot be detached unless all poison has been absorbed. After use of the stone, it has to be put in warm water during 30 minutes. As soon as the bubbling ceases, the stone is to be put in milk for 2 hours and finally to be rinsed in fresh water and dried in open air. The stone can be used again.*”



Traditional PNG herbal treatments for snakebite

There are many different herbal and plant treatments for snakebite in use throughout Papua New Guinea and in many other traditional communities elsewhere in the world. Surprisingly, little is known about the efficacy and safety of preparations used in traditional treatments of snakebite, and without demonstrable clinical and experimental data, it is not appropriate to endorse the use of these compounds and substances as alternatives to the treatments that have been shown to work, such as antivenom.

As with the use of the 'black stone', the strong local beliefs in the curative effects of plant or herbal preparations may result in people delaying attempts to obtain proper medical treatment after snakebite, and such delays can prove fatal in the case of bites by highly venomous snakes if the traditional remedy is ineffectual.

Only time and careful scientific study will demonstrate whether any of the traditional snakebite treatments actually prove to be effective. In other parts of the world research has found that many of the plants used to treatment snakebites do actually contain chemicals with potentially therapeutic value. The drug atropine which comes from the deadly nightshade (*Atropa belladonna*) plant is a widely used medical treatment for poisoning that can be used in conjunction in anticholinesterase drugs (i.e.: neostigmine or edrophonium) in the treatment of postsynaptic neurotoxicity. Atropine helps to control the excessive oral secretions that can complicate bites by death adders (*Acanthophis* spp.) and Papuan taipans (*Oxyuramus scutellatus canni*), but does not provide an actual cure to snakebite. Several different species of plants such as false daisy (*Eclipta prostrata*) and the African plant *Schumanniphyton magnificum* have been shown to inhibit the activity of phospholipases A₂ (present in many snake venoms) and can also protect mitochondrial membranes in cells. A PLA₂ toxin from African saw scaled viper (*Echis carinatus*) venom was shown to react immunologically with an extract from the seeds of the velvet bean plant (*Mucuna pruriens*). In Brazil a chemical in *Harpalyce brasiliensis* a leguminous plant is used to treat snakebite by traditional healers and has been proven to have a combination of activities against myotoxic and proteolytic toxins through PLA₂ inhibition.

Not all plant or herb treatments have potential. In northern PNG materials from six different plant species that were being used locally as either topical or ingested treatments of snakebite were tested for specific activity but were found to contain no secondary metabolites that might offer medicinal benefits. A further problem that can arise is that, while some of these extracts may be able to produce a positive effect when used experimentally, the reality is that they may themselves be potent toxins that can have serious adverse effects if taken internally. This has been to be the case with at least one South American traditional cure, which, while neutralizing the haemorrhagic effects of snake venom, also inhibited the proliferation and activity of human lymphocytes.



Velvet bean (*Mucuna pruriens*) – occurs in PNG



Deadly nightshade (*Atropa belladonna*)

Correct first aid treatment for snakebite in PNG

The most appropriate and effective method for the treatment of snakebites by both terrestrial and marine species in Papua New Guinea is the **PRESSURE IMMOBILISATION BANDAGING** (PIB) technique, developed to treat Australian snakebites more than 25 years ago.

History of development

It is well known that many substances, including hormones and immune system proteins are transported around the body in the lymphatic system. Snake venom toxins are also transported from the periphery to the rest of the body via the lymphatic system, and a number of experiments have shown that venom proteins reach high concentrations in the regional lymph nodes (lymphadenopathy is a common early sign of envenomation).

Australian toxinologist and immunologist Professor Struan Sutherland conducted several important experiments at the Commonwealth Serum Laboratories during the late 1970's and was able to demonstrate that snake venom moved from the bite site to the systemic circulation by lymphatic transport.

Sutherland subsequently proposed that by applying direct compression to a bitten limb the low-pressure lymphatic vessels become occluded. In combination with immobilisation of the limb to prevent movement and remove the 'muscle pump' effect, it was shown that snake venom could be effectively sequestered at or near the site of the bite, effectively preventing the development of systemic envenomation. In 1978 Professor Sutherland published the results of his research in the British medical journal 'The Lancet'. The technique described was subsequently endorsed by several Australian medical bodies and is now the only officially approved first aid for Australian snakebites.

Safety and Efficacy

Pressure immobilisation bandaging (PIB) satisfies all of the **SPEED** criteria for the appropriate treatment of snake:

- **SAFE** The use of a broad elastic bandage to compress lymphatic vessels is safe to use for even extended periods of time without causing pain, discomfort, pain or the risk of ischemic injury. There have been cases in which correctly applied PIB has been left *in situ* for many hours on patients who were evacuated from remote areas without doing harm.
- **PRACTICAL** PIB is practical and appropriate to all situations in which it may need to be used. Bandages can be improvised from clothing, bedding or other easily obtained materials if commercially made elastic bandages are not available.
- **EFFECTIVE** There is significant clinical and experimental evidence to show that correctly applied PIB effectively reduces the risks of long term illness or death after snakebite, by restricting venom transport and delaying the development of systemic envenomation.
- **EASY** PIB has been successfully taught to millions of Australian men, women and even young children, and non-medical users can learn to apply PIB correctly with minimal training.
- **DISTINCTIVE** Through public education and training, PIB has become synonymous with the treatment of snakebite in Australia. Health workers should use health promotion to achieve the same result in PNG.

Immediate care of a snakebite patient

There are a number of important things to do when a person is bitten by a snake:

RETREAT to a safe distance from the snake.

CALM the patient, sit or lay them down and keep them still – given the reputation that Papua New Guinean snakes have, anxiety is to be expected, but panic must be avoided.

REMOVE rings, bracelets or other constrictive objects from the bitten limb – if swelling of the limb should occur these can cause serious injury by constriction.

APPLY a broad pressure bandage to the bitten limb as quickly as possible (see next page for illustrations) – if proper medical bandages are not available then any sort of flexible material can be used including clothing, towels or other material.

SPLINT the bitten limb with a stick, long bush knife, axe, shovel or broom handle, and be sure to bind the splint to the limb thoroughly so that no bending of the joint is possible.

GET HELP from friends, family or colleagues as quickly as possible.

TREAT all snakebites as potential medical emergencies, even if you think the snake might not be venomous – it is far better to be safe than sorry.

BE AWARE of the potential for sudden collapse and loss of consciousness – if the patient does become unconscious lay them over on the side of their body so that they do not choke or inhale vomit if they become sick.

GIVE only water if the person becomes thirsty.

TRANSPORT the patient to an aid post, health centre or hospital without delay – people who are treated for snakebite with antivenom within four hours of being bitten have the best chances of survival.

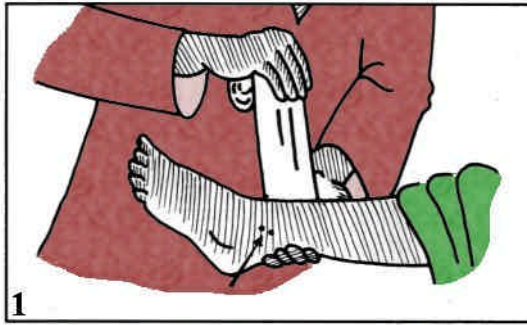
RESPECT traditional belief within reason – remember the priority is to get the patient to proper medical care as soon as possible. Be cautious about allowing anyone to give a patient any herbal medicine or other unknown drug; other practices such as applying ‘black stones’ (which do not work, but may help to calm an anxious patient and their relatives/friends) may be permissible after medical treatment has been commenced.

Things you should not do after snakebite

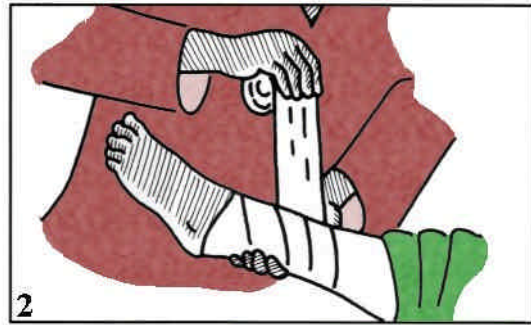
There are also things that should not be done after snakebite has occurred, and this includes the following:

- **DO NOT** attempt to catch, chase or kill the snake – this may result in another bite.
- **DO NOT** give the patient alcohol, tea, coffee or food.
- **DO NOT** give the patient any medicines except with the permission of a health worker or doctor – this includes traditional medicines.
- **DO NOT** elevate the bitten limb higher than the rest of the body.
- **DO NOT** wash the wound.
- **DO NOT** cut the wound by either incising or excising the bite site.
- **DO NOT** apply a tourniquet or rope ligature.
- **DO NOT** attempt to either suck the wound or use suction from any device.
- **DO NOT** apply ice to the bite site.
- **DO NOT** allow the snakebite patient to move at all – if they have to be taken to a place where transport can be arranged, make a stretcher from bush materials and carry them.

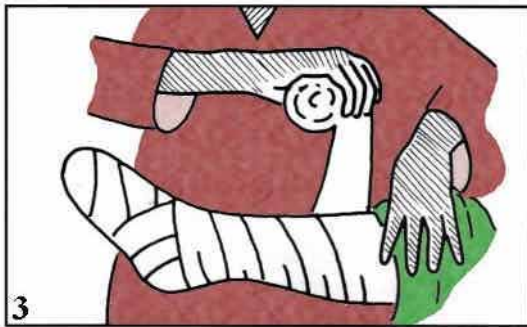
Application of Pressure Immobilisation Bandaging (PIB)



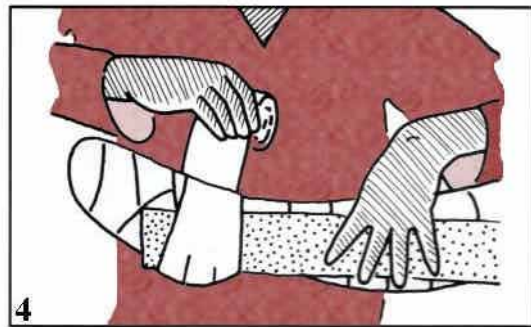
1 A broad elastic bandage is firmly applied directly over the site of the snakebite. Bandages can be improvised from any type of flexible material such as clothing or towels that have been torn into wide strips.



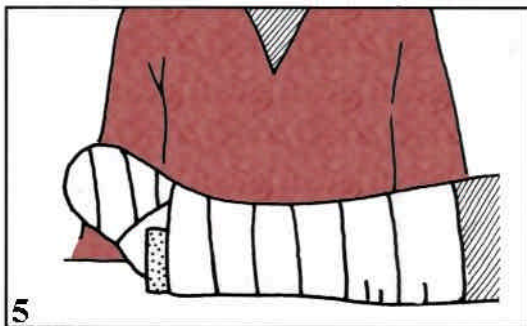
2 The bandage should be the same tightness as would be used to support a sprained wrist or ankle. Keep the patient calm and still. Do not remove clothing from the limb as the movement involved helps spread the venom.



3 Initially bandage from the site of the bite down to just before the toes or fingertips and then bandage as high up the limb as possible. This ensures that the bandage stays comfortable and can be left in place.



4 Use a rigid object such as part of a shovel handle, thick stick, rolled up newspaper or bush knife to make a split that can be bound to the sides of the limb in order to completely immobilise it.



5 Be sure to bind the split to the full length of the limb so that movement is completely restricted. If the patient is still able to bend the knee the split is not properly bound and the bandages will become ineffective due to the 'muscle pump' effect when the leg is bent or moved.



6 For bites to the hand or arm it is sufficient to splint the limb from the tips of the fingers to the elbow, and to then place the arm in a sling across the body in order to achieve immobilisation. This is more comfortable than splinting the whole arm, and means the patient is less likely to try to move the arm.

What to do if the bite is on the body, neck or head

Bites to the torso or to the head and neck are rare. The majority (about 70%) of snakebites occur on a lower limb, and most other bites (>25%) are on the hands or arms. This means that the method of pressure immobilisation bandaging (PIB) shown on the preceding page will be suitable for more than 95% of all snakebite cases.

If a person is unfortunate enough to be bitten on the body, or on the head or the neck, it is not practical to wrap them in a pressure bandage.

A firm pad of cloth should be used as a substitute for PIB to apply direct pressure over the site of the snakebite, and this pressure must be maintained until the person reaches medical care.

Is there any value in applying pressure immobilisation to a snakebite patient who was bitten several hours previously?

This is a potentially contentious issue.

There are strong reasons to believe that applying PIB to a person who presents at an aid post or health centres long after the actual bite occurred may have very little value, especially if the person has already walked a long distance and has definite signs and symptoms of envenomation. More value time may be wasted applying PIB instead of proceeding with the assessment, diagnosis and treatment of the patient.

The other side of the argument is that very little is known about the rate of absorption of snake venom in different types of body tissue. The thick calluses on the feet may delay absorption of some snake venom, and even a delayed pressure bandage might help sequester this venom until treatment has been commenced. In small rural aid posts or health centres that do not have antivenom stocks, the application of PIB, even after a considerable time has elapsed, may have some benefit, and if it does not delay the seeking of further treatment, then there may be no reason not to apply first aid.

Certainly, in the situation where antivenom treatment is not available locally and a medical transfer to another facility is needed, and where the patient is accompanied by anxious, frustrated or fearful friends and family, the application of a pressure bandage means that the health worker is being seen to be doing something positive for the patient. This can diffuse possibly difficult situations.

Removal of pressure immobilisation bandaging (PIB)

As a general rule it is not advisable to remove PIB from a snakebite patient until after they have arrived at a health centre or hospital which has supplies of appropriate antivenom, and they have been assessed and a plan of treatment commenced.

In a patient who has clear signs and symptoms of envenomation, or who has been tested using the 20WBCT or CSL venom detection kit and found to have been bitten by a venomous species, the ideal time to remove PIB is after the commencement of the antivenom infusion.

Removing the bandages quickly, and especially before antivenom therapy is commenced, may result in sudden deterioration. Bandages should be removed gradually over a 30-60 minute time frame and if a sudden worsening of the patient's condition does occur during this process then it may be advisable to stop removing the bandage any further until the patient has been reassessed.

The importance of teaching pressure immobilisation bandaging (PIB) and snakebite education to our communities

Snakebite is a very serious problem in many of our rural communities and even the people living in urban areas are not safe, because many snakes including the Papuan taipan (*Oxyuramus scutellatus canni*) are very good at learning to live close to humans.

The most important thing to remember about the use of pressure immobilisation bandaging is that if it is not applied until after the snakebite patient has walked for three hours to reach a health centre, it is most likely to be ineffective!

With this in mind one of the best things we can do in our communities is to conduct positive health promotion programs and to teach the correct use of pressure immobilisation bandaging (PIB) to as many people as possible. Such programs can involve visits to schools and vocational centres, timber camps and mining sites, village markets and other places where people congregate. Health centres can stock supplies of elastic bandages and sell them to the members of the public at a small overhead to cover freight costs.

Public education and health promotion programs about snakebite should not only address the proper use of pressure immobilisation (PIB), but can also be used to teach people about practical common sense ways to reduce their risks of snakebite, including:

Keeping long grass away from their homes and the places where children play.

Storing building materials like corrugated iron or timber up off the ground because snakes like to hide underneath objects on the ground, especially if they are overgrown by weeds and long grass.

If possible, wearing shoes or gumboots in the bush or when working in the garden.

Teaching their children not to go near snakes, and not to try and catch, chase or kill them.

Using a torch, kerosene light or candle light when walking around at night.

Learning to look down when walking and to watch for snakes on pathways and beside roads or on trails near water.

Learning to look carefully at where they put their hands when pulling vegetables out of the garden, when reaching in grass, or when collecting firewood.

We should also teach people that it is not safe to do things such as:

- Delaying seeking medical treatment after snakebite in favour of traditional medicine or other 'cures' that have no scientific basis.
- Put their hands into animal burrows or hollow logs without checking to be sure no snakes are inside first.
- Run through long grass or along bush paths and roads – most snakes will quickly crawl away at the approach of a person if they have enough time; a person running often treads on the snake before it has time to crawl away.

If we as health workers invest the time in providing this vital education to the people in the communities that we serve, the results will not come overnight. But, if we are consistent and persist in teaching as many people as possible how to be proactive and avoid snakebite, as well as how to use proper first aid when bites occur, then we will see change over time.

Papua New Guineans are keen and eager to learn about snakebite and it is our responsibility to teach them what they need to know to save their lives.

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Patient Assessment and Diagnosis

Dr Bill Nimorakiotakis, Dr Evelyn Lavu and Dr Simon Jensen

Introduction

The objective of this chapter is to teach the essentials of initial and ongoing patient assessment, diagnosis and monitoring. A practical standard protocol is presented that will provide the best possible model for correct diagnosis and hence the implementation of appropriate early treatment.

Many snakebite case histories lack clear patient histories. The history of the actual snakebite circumstances and the events occurring subsequently is usually incomplete.

There are also often deficiencies in the extent of the initial patient examination, in the subsequent interpretation of findings, and hence in the diagnosis. There is often confusion over the interpretation of symptoms and signs and the results of tests. As a result, antivenom might not be given when indicated, or given late, leading to more severe venom effects and secondary complications for the patient. For example, a positive 20WBCT (whole blood unclotted at 20 minutes) is sometimes ignored as a clear indication for antivenom, or the test is simply not performed at all.

Good, frequent, ongoing assessments and regular monitoring are also not always routine - though they should be - to monitor the progress of the patient. Patients are sometimes allowed to “sleep” for hours between examinations, when in fact they may have complete ptosis and severe neurotoxicity, and even coma from cerebral hypoxia. Standard measures such as GCS (Glasgow Coma Score – developed for use in the assessment and management of head injury) are not of great value.

As noted in Chapter 4, the **assessment** of a patient with possible or definite snakebite must include a thorough, but focussed:

- history, including the history of the bite and the subsequent symptoms,
- examination, determining the vital signs and any signs of envenomation, and complications of envenomation, and
- investigations (which will depend on what tests are available at your health care facility).

This chapter will look again at these aspects, in more detail than before. The importance of clear and complete patient histories is emphasised. It will end with a suggested diagnostic algorithm.

Ongoing assessment, critical to the safe management of snakebite patients, is discussed briefly here, and in more detail in Chapter 14 (*Management plans for snakebite patients*).

Assessment

History

The history is vital, as in the medical assessment of all conditions, and will give vital clues as to the possible, or likely, snake. It will also give you a good idea if the patient has already experienced symptoms likely to be ascribed to envenomation, and so alert you to look for specific signs of snakebite when you examine the patient, which would provide you with an acceptable indication for antivenom (for Indications for Antivenom, see Chapter 11).

The important aspects of the history are the timing of the snakebite, activity performed since and first aid employed, both traditional and modern, and the presence and absence of specific symptoms and signs.

Obtaining a history from envenomed patients can be difficult, especially if the patient has neurotoxic effects of envenomation, though there will usually be family members present to assist. Small children pose much the same problem when they have been bitten. However, beware that those present with the patient often guess aspects of the history so as not to disappoint the person questioning them.

A clear succinct history should include questions listed in the tables below. History-taking should include open-ended questions so as to not influence answers.

You must be sure to cover all types of symptoms and organ systems likely to be affected in snakebite. That is, you must ask about:

- local/bite site symptoms,
- regional symptoms
- systemic symptoms
- non-specific and specific symptoms

The follow are examples of the types of information needed.

Sample Snakebite Assessment and Admission Form

History

Patient name:		Village & district:	
Age:		Date:	
Sex:		Time:	

Snakebite Details:

Time of snakebite		Place where snakebite occurred, eg. home, garden	
Location, village, district		Activity being undertaken when bitten	

Description of the snake (length, girth, colouring, head, neck, body, tail)

--

Body site bitten		Number of strikes/bites	
------------------	--	-------------------------	--

Other snake behaviour, eg. chased patient, moved away slowly, held on when biting

--

Conditions, ie. wet, dry, swampy, long grass, roadside, village or bush track

--

Pre-hospital Care

Activity since snakebite, eg. ran, walked, carried, and for how far/how long	
Traditional first aid methods used – cutting (scarification), black stone, grass/bark or fabric tourniquet, other	
Modern first aid methods used – pressure bandaging, splinting, patient immobilisation	

Past medical history

Previous snakebite history if applicable

- approximate date of previous snakebite
- antivenom given/no. of ampoules
- any history of adverse antivenom reaction

History of atopy – asthma, eczema, hay fever

Medications

Drug and food allergies

Past and present medical problems including heart disease, lung disease, renal disease, bleeding tendency

Treatment already given elsewhere

Premedication

- adrenaline SC – 0.25mg (0.005 mg/kg)
- other drugs (such as promethazine, hydrocortisone)
- Antivenom (type, amount, time given after bite, time taken to give the infusion, time when infusion ended)
- Tetanus toxoid given
- Other medications given [IV fluids (type, amount), penicillin]
- Resolution of symptoms/signs since antivenom given
- Hospital contacted for advice or referral?
- Mode of transport to the hospital

Examination

Initial attention should be made to the patient’s Airway; Breathing and Circulation. Once you are happy with the above, a more focused examination should be conducted.

Vital signs:	Reading	Time	Time	Time	Time	Time	Time
Heart rate							
Blood pressure							
Respiratory rate							
Peripheral oxygen saturation							
Temperature							
Urine output							

Standard measures such as GCS (Glasgow Coma Score) are of limited value since a paralysed, **but awake**, patient may be unable to speak, eye-open or follow commands, but may be fully conscious. Subtle signs such as the patient complaining of blurred vision, early collapse, decrease in respiratory function or bleeding of the gums are of much more value.

Other Symptoms and signs

Local

- pain
- swelling
- bleeding, oozing

Bite site

- single or double puncture marks or scratch marks
- multiple punctures, likely to have more severe envenomation

Regional

- limb swelling
- painful/tender lymph nodes

Systemic:

- painful/tender muscles
- headache
- nausea/vomiting
- abdominal pain/tenderness

Neurotoxicity

- early collapse
- blurred vision
- cranial nerves: ptosis (a “sleepy/sleeping” patient); unable to look upwards ophthalmoplegia (“fixed eyeballs”); facial muscle weakness (expressionless face); poor mouth-opening (this is NOT trismus); poor tongue protrusion; pharyngeal muscle weakness (poor swallow, excessive saliva, pooling of oral secretions); laryngeal muscle weakness (weak or hoarse voice, “thick speech” ~ bulbar palsy)

Other Symptoms and signs (continued)

Neurotoxicity continued

- peripheral nerves: respiratory muscle weakness (breathless/dyspnoea, poor expansion, poor cough, weak voice, low SpO₂; diaphragm, intercostals)
- limb and truncal muscle function (eg. can't walk, sit): limb power; limb reflexes; abdominal muscle tone and power

Coagulopathy

- bleeding (bite site, gums, scarifications/lacerations, haemoptysis, haematemesis, spitting blood)
- 20WBCT positive (blood unclotted at 20 min.)

Differential diagnoses should be considered when snakebite cannot be confirmed as the cause of the patient symptoms. These might include:

- infection
- stroke
- myocardial infarction
- allergic reaction
- hypoglycaemia/hyperglycaemia
- drug overdose
- closed head injury

Focal neurological signs should prompt suspicion of either a complication of envenomation such as head injury, intracranial bleeding, or another diagnosis such as central nervous system infection, particularly Tb meningitis or cryptococcal abscess, stroke, CNS tumour, or hyperosmolar non-ketotic diabetic coma.

FIGURE 1: Some features of snakebite



Puncture wounds from snakebite on the upper thigh



Incoagulable blood



Patient with ptosis, and difficult tongue protrusion

Temporal relationship of signs and symptoms of snakebite

LESS THAN 1 HOUR AFTER THE BITE

- Transient hypotension associated with confusion or loss of consciousness
 - Transient or persistent blurring of the vision
 - Headache
 - Nausea, vomiting, abdominal pain
 - Coagulopathy (20WBCT or laboratory testing)
 - Regional lymphadenitis
-

1 TO 3 HOURS LATER

- Paresis/paralysis of cranial nerves – ptosis, double vision, (external) ophthalmoplegia, dysarthria, dysphonia, dysphagia, facial weakness
 - Haemorrhage from mucosal surfaces (coughing, spitting or vomiting blood) and needle punctures
 - Tachycardia, or bradycardia, hypotension or hypertension
 - Tachypnoea, shallow respirations
-

MORE THAN 3 HOURS LATER

- Paresis/paralysis of truncal and limb muscles
 - Paresis/paralysis of respiratory muscles, bradypnoea and respiratory failure
 - Rhabdomyolysis
 - Dark urine (due to myoglobinuria or haemoglobinuria)
 - Renal failure
 - Coma; possibly due to hypoxaemia or shock.
-

(Adapted from Dr G. Didei, Chapter 8)

Investigations

Bedside tests

There are a variety of fundamental and special diagnostic tests available. Most of these should also form part of your ongoing assessment and monitoring of patients after snakebite.

Blood tests:

- 20WBCT Test (see Chapter 9)

This is a simple effective test of envenomation, where whole blood is placed in a glass container/bottle and left untouched for 20 minutes out of direct sunlight, and then reassessed to see if it has clotted; if the blood has not clotted the patient has a coagulation problem and the likelihood of envenomation, is high (Positive Predictive Value 98.4%, Specificity 99.6% for the subsequent development of neurotoxicity).

- Blood Glucose level

This is a vital bedside test (using a hand-held glucometer) for any patient with a possibly altered conscious state (difficult to assess accurately in the paralysed patient), for diabetics, and for those who have been fitting; it should also be performed on every patient who requires resuscitation.

Respiratory function tests:

- A peak flow meter measures the peak expiratory flow rate (monitor regularly to see if there is a decreasing reading), which is a test of abdominal and intercostal muscle strength.
- An incentive spirometer, such as is used post-operatively to encourage inspiration, is a good way to assess diaphragmatic function; the patient sucks through a tube, and sees how far up a column they can suck each of 3 balls (this will be demonstrated in the course).
- A simple measure of respiratory function could be as simple as assessing the ability of the patient to blow up a balloon and noting any deterioration in the ability to do this (this is untested; it is important to use what you have available to you).

CSL Snake Venom Detection Kit:

- This immunoassay test is important in identifying which monovalent antivenom should be administered to the patient – which will neutralise the venom. (It must be noted it does not tell us exactly what species of snake has envenomed the patient.)
- A negative result does not indicate the patient is not envenomed and if there are clear features of envenomation, antivenom should not be withheld.

Urinalysis:

- Naked eye – haematuria and haemoglobinuria will appear red, while myoglobinuria will be evident as dark brown urine, which may develop white strands upon standing.
- Bedside assessment of urine is possible with a variety of dipsticks, to supplement the assessment of the naked eye. These note the presence of blood, haemoglobin (cannot distinguish this, normally, from myoglobin), protein, glucose, bilirubin, as well as pH (you should be aiming for a **pH of 7** in the treatment of rhabdomyolysis) and specific gravity (for example, a concentrated urine, with a high SG indicates not only well functioning kidneys, but inadequate hydration).

Laboratory tests

The relevance and availability of these tests in PNG is very variable, depending on the institution. Generally, little equipment is available for blood testing, and this is often broken down, there are no reagents, or there is no-one to run the tests. This is why the bedside tests are so important. However, when they can be performed, the following tests contribute significantly to the appropriate and precise management of a snakebite patient:

- blood film for malaria parasites
- renal function tests and electrolytes
- clotting studies INR/PT, APTT, ACT, D-dimer, X-FDP, fibrinogen for details of the coagulopathy
- creatine kinase for myolysis
- urinalysis for haemoglobin, myoglobin

Blood collection

Principles

Snake venom especially that of the taipan, affects the coagulation pathways and interferes with the normal clotting process. Disseminated intravascular coagulation (DIC) is also a complication of snakebites. The overall effects are reduced levels of coagulation factors, platelets and haemoglobin if there is significant bleeding or haemolysis. Patients may have established abnormal bleeding and anaemia upon presentation.

Kidney function and liver function may also be altered. The blood glucose should be checked, especially if the patient is comatose and has not been eating or drinking (this is particularly the case with small children, who have limited reserves of glycogen to make glucose for cells, and a limited ability to manufacture glucose from protein).

Materials required:

- 20 ml plastic syringe
- 22 or 23 gauge needle
- EDTA bottle (5 ml, pink top) or as provided your laboratory
- Citrate bottle (5 ml)
- 2 plain bottles (10-15 ml)
- Centrifuge (if unavailable, use 1 plain bottle with gel clot activator, though this type cannot be used for the 20WBCT)
- Blood glucose bottle (3 ml), if you do not have access to a bedside glucometer

Procedure

Blood is ideally collected from the antecubital vein, or through the newly-placed IV cannula, and the skin must be 'clean'. Swab this area well with 70% alcohol swab (e.g. isopropanol) once you have identified a good vein. Collect 10-20 ml of venous blood using a 19-21 gauge needle (or through the cannula) in adults and 23-25 gauge in young children, attached to a 20ml syringe. Remove the needle to avoid haemolysis before filling the bottles (unless you are using Vacutainers). Place 4.5 ml into your 5 ml citrate bottle (9:1 ratio) and mix well. Add 3-4 ml into the EDTA bottle and mix thoroughly. Add another 3 ml into the glucose bottle and mix this as well and the rest should go into the plain bottles. A drop of blood can be used to measure the venous glucose with a glucometer at the bedside (a cheaper and quicker method).

If you are in a hospital with a laboratory technician or technologists, all the separation and preparation is done by them. However if you are alone, the following should be done:

Serum and plasma separation

Serum is obtained from the blood sample in the plain bottle. Placing this sample in a 37°C water bath enhances the clotting process. Centrifuge for 15 minutes. Serum is the straw-coloured fluid which makes up the top layer above the red cells. If you do not have a centrifuge, a container with gel clot activator should have the same effect or alternatively leave it in 37°C water bath for 1-2 hours and then separate the serum.

Plasma, on the other hand, is obtained from centrifuging the citrate sample for 15 minutes at 4000 rpm in a standard bench centrifuge. Unfortunately there is no other alternative for achieving plasma apart from centrifugation. For the EDTA bottle, make a thin blood film and send this with the sample without any separation.

Storage and transport of samples

Heat destroys some of the contents of blood that are for analysis. Ideally, the tests should be done within 1-4 hours of specimen collection. However, in PNG, this is not possible in isolated health centres. Samples should be stored at 4°C, or the normal kitchen refrigerator, and transported in coolers or eskies to the nearest laboratory as soon as is practical, preferably with the patient.

Interpretation of results

If a patient's coagulation pathway is affected, the 20 minute whole blood clotting test (20WBCT), a sensitive and specific screening test for coagulopathy, which can be done at the bedside, should be positive (See 20WBCT Practical). The PT and APTT should be prolonged. The PT measures the activity of coagulation factors in the extrinsic pathway and common pathway (Factors II, VII, X, Fibrinogen, Fibrin), while the APTT measures the factors in intrinsic pathway and common pathway (Factors XII, XI, X, etc). Taipan venom, for example, contains a prothrombin activator (which is a component of the common pathway).

In DIC, there is both activation of micro-clot formation, and consumption of clotting factors and platelets (consumptive coagulopathy). Therefore, in this situation, the haemoglobin (Hb) level and platelet counts may be reduced, and the FDP level should be positive or raised.

These results should guide you in deciding what blood products can be given in such situations as coagulopathy and DIC, though they may be given **only** once enough antivenom has been given to neutralize **all** the circulating venom, and if the patient is bleeding heavily or is not making enough new coagulation factors.

Kidney and liver function: monitor these organs in snakebite patients, as they can be directly and indirectly adversely affected by venom components.

Hypoglycaemia should be prevented at all costs, especially in patients who are already comatose for another reason.

Urine collection

Like most urine samples, this should be collected as a midstream specimen, when possible. Otherwise, a catheter sample is adequate. Analysis should start from the gross appearance of the colour. The difficulty arises when a patient has red or tea-coloured urine which could be due to haematuria, haemoglobinuria or myoglobinuria.

Simple dipstick urinalysis can pick up haematuria (and proteinuria), but it cannot distinguish between red blood cells, haemoglobin (Hb) from lysed red cells, and myoglobin (Mb), from lysed skeletal muscle cells. Haematuria is confirmed by the presence of red cells on the slide examined by microscope made from deposits after spinning the urine down by centrifugation.

Mb is released if there is skeletal muscle damage, and can be measured by a sensitive and specific radio-immune assay. Spectrophotometry can be used to differentiate between Hb and Mb, although they have absorption spectra which are similar, but not identical. Unfortunately, in PNG the facilities to do such tests do not currently exist in public hospitals.

Haemoglobin is released into the circulation when there is intravascular haemolysis causing haemoglobinuria; this is rarely clinically important in envenomed patients.

Patient Monitoring and Reassessment

Patient reassessment and monitoring are critical in the care of snakebite patients. A patient with confusion or abdominal pain is much more obvious in your Emergency Department (A&E) than the person with snakebite who quietly develops respiratory paralysis. Relatives and friends should not be relied upon to alert staff to deterioration in the clinical state of their relative – they do not have the skills and knowledge to see subtle changes.

Patients who have been bitten by a snake should be kept in a central place in the department, and should not be left to quietly “sleep” in the corner.

It is critical that the vital signs (HR, BP, RR, SpO₂) and urine output (much easier to monitor with an IDC in place, though an asymptomatic, or minimally-symptomatic, patient does not need one) are assessed, and recorded, at least hourly for the first 24 hours after a snakebite, and that any abnormalities are acted upon. It might be unpleasant for a patient to be woken so frequently, but it is for their own potential benefit, and this must be explained to them.

Symptoms and signs can evolve slowly or rapidly depending on the snake and degree of envenomation. Repeated re-examination of the patient is required to see if new symptoms or signs develop. This might not be noted from simply performing hourly observations, so actual reassessment of clinical signs and investigations, such as cranial nerve function, respiratory function (eg. with an incentive spirometer), limb power and the 20WBCT will be necessary. This is the purpose of recording systems such as the Snakebite Observations sheet provided by the National Department of Health.

Treatment Overview

Dr Simon Jensen

Introduction

This chapter reviews the general principles and key issues associated with each aspect of the management of snakebite patients. The focus will be more on the rural setting with minimal resources, but some detail of advanced management will be mentioned. Further detail is presented in other chapters. It is hoped that the resources and capabilities of health care facilities, both in urban and in rural Papua New Guinea, will be developed and improved over the coming years; in such circumstances, such extra knowledge will come to be useful.

The emphasis will be on presenting an introduction to a practical, resource-appropriate model treatment strategy and plan for the management of snakebite for rural health centres. It is hoped that this will help you to develop a practical, resource-appropriate model for your particular health care facility. This will be discussed in more detail in Chapter 14.

In the 4 decades since the first snakebite research was carried out in PNG, and the first treatment and management guidelines were introduced by the National Department of Health of PNG, with the help of Campbell's work (1961-1969), a lot of new knowledge has been acquired. A large amount of research, laboratory and clinical, has been carried out in Australia, in PNG, and around the world, on Australian and Papua New Guinean snakes, which are clearly, and very closely, related. Much of this has been, and will be, discussed in other chapters. It is important that Papua New Guineans who are bitten by snakes benefit from this new knowledge; the course, which this Handbook accompanies, is one way of achieving this.

The most important achievement in improving the outcome for bitten patients throughout the world has been the development of **antivenoms**. Australia is one of the first countries to develop highly effective and safe antivenoms, for Australian snakes. Clinical experience and a limited amount of research has proven these to be effective in neutralising the venoms of most, if not all, venomous Papua New Guinean snakes, provided they are administered appropriately – that is the **correct antivenom** is given **early**, in the **required dose**, and with the **correct supportive care** given to the patient.

The second most important advance has been the development of an excellent method of first aid, **pressure immobilisation bandaging**, developed by Sutherland (1979). This has led to vast improvements in the survival of snakebite patients where it is used correctly, in combination with patient immobilisation, in Australia and for neurotoxic bites by elapid snakes in Africa. It is also highly appropriate in the mainland and islands of PNG and West Papua, but is rarely used, or used correctly; the use of traditional methods, or no first aid at all, is the norm.

This chapter will attempt to address many of the errors and misconceptions that accompany the management of bitten patients.

Firstly, priorities and objectives of treatment are discussed, and a general treatment and nursing strategy is presented. This is discussed in more detail in Chapter 14 (which discusses management plans for snakebite patients, the importance of having a specific, evidence-based plan, and the importance of consistency of such plans).

Secondly, a practical overview of treatment is presented. Specific treatments are introduced for the clinical effects of snakebite, and current controversies are discussed; more detail about most of these is given in the chapters specific to the particular clinical issues. And finally, the referral and transportation (disposition) of snakebite patients is discussed, and guidelines for these processes presented.

Priorities and Objectives

The priorities of treatment are to **maintain life and limb**, to prevent lasting significant morbidity (damage to the patient's organs and tissues), and to **do no harm** to the patient, by not administering unnecessary or incorrect treatments, or by delaying the correct treatment and referral. So, priority must be given to interventions which will make a difference to the patient's outcome, and in the correct order of priority.

With this in mind, staff caring for snakebite patients must make every effort to ensure that they are in a position to provide optimal management, within the limits of their clinical circumstances. This means

- replacing used stocks of consumable items,
- maintaining, and being careful with, vital equipment,
- ensuring their knowledge and skills are kept at a high level,
- knowing when to refer patients to a higher level facility and when to seek advice, and actually doing these things, when necessary.

Specifically, staff must ensure that they attend to the following needs of the patient:

- the institution of first aid on arrival, if possibly of value,
- appropriate early antivenom, where this is indicated,
- good airway management,
- good respiratory (ventilatory) support,
- dealing appropriately with bleeding and coagulopathy,
- dealing with the effects of myolysis,
- dealing with cardiac effects, and
- supportive care of all vital functions, including hydration, and renal function monitoring.

General Treatment and Nursing Strategy

Essentially, this part of the care of snakebite patients is about basic supportive and nursing care. It overlaps with the monitoring and frequent reassessment of patients that should be performed as well. The **treatment** of a patient with possible or definite snakebite must include **concurrent** (at the same time):

- applying pressure-immobilisation bandaging, and splinting, where indicated,
- checking the **vital signs**:
 - heart rate (HR),
 - blood pressure (BP),
 - respiratory rate (RR),
 - peripheral oxygen saturation (SpO₂),
 - temperature (T),
- instituting **monitoring** (depending on availability – ECG, oximetry), and frequently recording and **acting on** the vital signs,
- resuscitating the patient with respect to:
 - **Airway,**
 - **Breathing,**
 - **Circulation,**

followed by:

- supportive care
 - proper patient positioning,
 - regular gentle suctioning (whether the patient is intubated or not)
 - oxygen as required,
 - IV fluids,
 - an indwelling urinary catheter, in the patient with respiratory muscle weakness, to prevent urinary retention, monitor urine output, and watch for a change in urine colour (suggesting haematuria or myoglobinuria),
 - care of potential pressure areas,
 - reassurance of patient and relatives (often neglected),
- specific, or definitive, treatments, as outlined below, including
 - antivenom,
 - airway management and intubation if required,
 - possibly the use of atropine to dry secretions if unable to intubate,
 - oxygen,
 - treatment of shock,
 - treatment of coagulopathy,
 - treatment of the complications of rhabdomyolysis and managing pain,
 - treatment of primary and secondary cardiac effects of envenomation,
 - antibiotic treatment and tetanus vaccination, where and when indicated,
 - wound care,
- ongoing monitoring and recording (hourly) of
 - vital signs,
 - secretions,
 - respiratory effort,
 - urine output (volume and colour),
- frequent (hourly at first) reassessments (re-examination); this is best performed using pre-formatted Snakebite Observation sheets such as that provided by the NDoH).

Specific Treatments

This section specifically discusses controversial treatments, and outlines the essentials of treatment in each of the major areas.

Snakebite happens to children as well as to adults. It is critical that children are given the correct, weight-calculated dose for all medications, except for antivenom, which is the same dose as for adults (though it should be diluted in a smaller, weight-based volume of fluid).

Controversial and Unsupported Therapies

The following therapies are controversial. For some, there is no proven benefit and no research base to support their use.

For others, their use has been traditional, and though they might not have been reported to be detrimental to patients, there are clear reasons why they can be. For yet others, some recent research guides us a little about their use and usefulness.

- The routine use of promethazine for premedication – which may be harmful (see below).
- The routine use of hydrocortisone for premedication – often no benefit (see below).
- The routine use of penicillin – benefit in only a few circumstances (see below).
- The use of adrenaline premedication – often omitted or given in an inappropriate way (see below).
- The routine use of IV fluids (see below).
- The use of sedative drugs in the anxious, bitten patient (see below).

With each of these therapies, and considering the resource-limited environment in which each of you works, the time, money, syringes, and needles used to administer them, and the drugs themselves, could often be more usefully be used for other patients with other conditions.

Traditional First Aid Methods

The vast majority of traditional first aid methods are totally ineffective in preventing venom entering the circulation; in fact, many are harmful, and this is discussed in more detail in Chapters 4 & 5. You should be looking for complications of these when assessing a snakebite patient, as outlined in Chapter 5.

Potential benefit

- Little, other than potentially allaying anxiety, which may have a small effect in delaying the entry of the venom into the circulation.

Potential harm

- Failure to use effective first aid, and hence no impediment to the development of toxic effects from the venom.
- Delay in seeking definitive medical care (antivenom, in the case of the patient envenomed by a dangerous snake).
- Muscle ischaemia and necrosis from tourniquet use.
- Burns from hot vessels.
- Toxicity from oral herbal preparations and snakebite pills.

Promethazine

Potential benefit

- There is a quoted benefit in reducing the incidence and severity of antivenom reactions (but this is unsupported by published data). It may have been appropriate a few decades ago, when the antivenoms produced were much less pure, and reactions to them were common. The current reaction rate in Australia, without premedication, is low. It is, however, probably of benefit when given in the case of an allergic reaction, once it has occurred.
- It may reduce airway (oral and bronchial) secretions, due to its mild anticholinergic effect, and delay the onset pulmonary aspiration (atropine would be more effective).

Potential harm

- Giving it can distract and delay staff from giving life-saving antivenom.
- It may cause hypotension, particularly in a patient who is already
 - hypoxic from respiratory failure,
 - volume depleted from vomiting or haemorrhage,
 - anaemic from haemorrhage,
 - suffering adverse cardiac effects from venom components, such as tachycardia.
- It will cause sedation in an otherwise unwell patient, by
 - its known antihistaminic and anticholinergic effects, (worsening conscious state in a patient where this is already impaired for some reason),
 - worsening respiratory function in a patient with neurotoxicity and causing hypoxia,
 - worsening pre-existing hypotension to the point where cerebral circulation is impaired,
 - being given in an excessive dose (particularly when given to children).

Hydrocortisone

Potential benefits

- It is not proven to reduce the incidence of antivenom reactions, particularly if given immediately before the antivenom, though there is a quoted (but unsupported by published data) benefit in reducing the incidence and severity of antivenom reactions, except in special circumstances. It may have been appropriate a few decades ago, when the antivenoms produced were much less pure, and reactions to them were common. The current reaction rate in Australia, without premedication, is low. It is, however, probably of benefit when given in the case of an allergic reaction, once it has occurred.
- It may be of benefit when given 30-60 minutes before antivenom, in the patient who has received the same antivenom before (either as a monovalent antivenom or as polyvalent antivenom). However, health care workers administering antivenom in this, and in all circumstances, must be alert and ready to treat any allergic reactions, which can still occur, even with premedication with steroid.
- It may reduce the incidence of allergic reactions in atopic people, i.e.: those with asthma, eczema, hay fever or multiple food or drug allergies.

Potential harm

- It has no significant adverse effects other than distracting staff from giving necessary treatments, such as early antivenom.

Penicillin

Potential benefits

- If there is established infection, a wound with a foreign body or that is grossly contaminated, penicillin will potentially be a suitable antibiotic.

Potential harm

- Allergic reactions to penicillin do occur. Care should be taken to ensure any antibiotic is given only after a previous history of drug allergy has been sought.
- The administration of an unnecessary drug can delay the administration of antivenom, and so increase the chance of significant complications such as worsening respiratory failure.

Intravenous Fluids

Potential benefits

- shock
- persistent vomiting
- the administration of antivenom
- for maintenance of hydration when nil by mouth because of respiratory failure or intubation, or because of an altered conscious state
- treatment of renal impairment and maintenance of urine output in myoglobinuria

Potential Harm

- when administering it delays the administration of antivenom
- the presence of an altered conscious state due to intracerebral haemorrhage – excessive IV fluid administration can further increase intracranial pressure
- can worsen respiratory function in the patient with severe renal failure pulmonary oedema (a risk in the severely oliguric and anuric patient)
- multiple failed attempts to insert an IV line at rural health centres is often noted at PMGH; these patients rarely appear to have needed the fluid, and the many attempts have caused them discomfort; the sites often subsequently become multiple sites of bleeding once a coagulopathy develops.
- may worsen a coagulopathy by further diluting low levels of clotting factors and platelets.

The specific treatments that do potentially provide significant benefit for the patient are listed below, and most are discussed in detail in subsequent chapters.

First Aid

Health care workers should teach this to the population in the area from which they draw their patients. It is a way they can help people to help themselves. They should also teach people how to AVOID snakebite (discussed in Chapter 5). Then they should note the results of their education efforts: are people presenting more promptly after snakebite, and more often with correct first aid having been applied? Have they been teaching proper first aid in a way that people can understand?

The first aid method taught in this course, and in Chapter 5, is proven to be of great benefit for delaying the onset of toxicity from elapid snakes, such as those found in Australia and Papua New Guinea. This Pressure Immobilisation Bandaging method, which essentially prevents the flow of venom components through the lymphatic system back to the heart, and thence to the blood circulation, from where it moves on to the various organs to exert its observed effects.

The following is a summary of the essential aspects of the recommended first aid:

- Move away from the snake; do not attempt to chase it away, to catch it or to kill it, but note its characteristics, if possible.
- The bitten person should sit or lie down.
- Those with them should try to calm them – they will be very anxious.
- Do not interfere with the bite site at all. Do not apply a tourniquet or other traditional first aid to the limb.
- Pressure immobilisation bandaging should be applied to the entire limb, ideally with elastic (“crepe”) bandages as described previously.
- A splint should also be applied to the entire limb to prevent movement at knee and ankle, or at the elbow and wrist joints.
- If the bitten part is not on a limb, place a large pad over the wound and bandage this firmly in place.
- Do not allow the patient to walk or move unnecessarily.
- Transport the patient, by carrying or by vehicle, to the nearest health care facility where either the patient can be assessed and antivenom given, or to a place from where they can be urgently transported to such a place.
- Do not remove the first aid until the person is in a health care facility where antivenom is available, the correct antivenom chosen and ready to give.
- If a patient arrives at a health care facility soon after a bite (within 3 hours), the late application of pressure-immobilisation bandaging may be beneficial.

Antivenom

This is covered in depth in Chapter 11; only the essentials are covered here.

Premedication

Adrenaline

Potential benefits

- There is proven benefit from premedication with adrenaline in reducing the incidence and severity of antivenom reactions. It must be given by the correct route (subcutaneously, SC) and in the correct dose, or it will be either less effective or harmful, as with any medication given for any reason; further adrenaline should be available at the bedside.
- In hospitals, if the patient is in the care of senior staff, it may be appropriate to give no adrenaline, but to have an adrenaline infusion (6 mg in 1000ml 0.9% saline = 6 µg/ml) ready to give if needed starting at 1.0 ml/min. (or, alternatively, 6 mg in 100 ml starting at 0.1 ml/min.), i.e.: 6µg/min., and titrate upwards as required monitoring HR, BP & ECG.

Potential Harm

- There is clear evidence that adrenaline given intravenously increases the risk of hypertension, and therefore of bleeding, particularly intracranial bleeding, in coagulopathic patients, and deaths have occurred as a result. It is, therefore, no longer recommended in Australia.
- Adrenaline given intramuscularly can cause hypertension; this route is not recommended when giving it as a premedicant, though this route is accepted for the treatment of moderate to severe allergic reactions to antivenom, as is very cautious IV administration (0.5-1.0 µ/kg boluses initially); it can cause significant intramuscular haematoma, and be painful, and perhaps erratically absorbed, in patients with extensive myolysis.

Hydrocortisone

Based on the limited available evidence, this course recommends that this is given to the following people, ideally 30-60 minutes before antivenom, though it should not delay the administration of the antivenom:

- those with a previous history of antivenom administration,
- those working extensively with horses,
- atopic individuals (asthma, hayfever, eczema, nasal polyps),
- those with multiple food or drug allergies, or a previous life-threatening allergic reaction,
- those receiving multiple doses of antivenom,
- possibly those receiving polyvalent antivenom.

Indications for antivenom

(As in Chapter 12)

The indications for antivenom are specific symptoms or signs such as

- early collapse,
- cranial nerve weakness,
- abnormal bleeding,
- generalised muscular pain and tenderness,
- grossly discoloured urine (red or dark brown), or the pathology test results of
- incoagulable blood, by the whole blood clotting test (20WBCT),
- a grossly elevated serum creatine kinase level,
- haematuria, haemoglobinuria or myoglobinuria, or
- a positive SVDK test on a urine sample in the presence of non-specific or specific symptoms or signs of envenomation.

Selection of the most appropriate antivenom

This will be discussed elsewhere. *(See Chapter 11)*

Dosage and administration

In general, all patients require at least one ampoule of antivenom. The use of half ampoules is strongly discouraged, since the antivenom in one ampoule is apparently equivalent to the venom yield expressed in an average 'milking'. Experience in Australia has shown that people often require more than one, and up to 3 (except in the case of the western brown snake, where up to 25 ampoules has been needed to fully neutralise the venom effects). Children receive the same dose as adults, but diluted in a weight-adjusted volume of crystalloid.

Serum Sickness

This is a syndrome of rash, arthralgia, fever, lymphadenopathy, and a 'flu-like illness, and other less common symptoms such as headache, pleuritis, pericarditis, nephritis. It is due the deposition of immune complexes (venom-antivenom) in tissues. It occurs predictably 5-10 days after the administration of the antivenom, and may last a week.

Both the incidence and the severity of delayed serum sickness may be reduced by the having the patient take prednisone, at a dose of 50 mg (adult), or 1 mg/kg (child), once daily for five days after the administration of the antivenom. This is recommended after polyvalent antivenom, and after multiple doses of monovalent antivenom.

Treatment of Paralysis and Neurotoxicity

(See also Chapter 8)

The most important point in the care of the patient with neurotoxicity is that people die because of airway obstruction and aspiration before they would have died because of a lack of respiratory effort. This is particularly the case for patients with relatively healthy lungs. Those with co-morbidities will succumb sooner. Either way, they die a slow, hypoxic death that is both readily **preventable**, from good first aid, early appropriate antivenom, and good airway management and ventilatory support; it is not something that they can do anything about themselves, because all voluntary muscle is paralysed.

The treatment of neurotoxicity includes the following:

- Correct first aid, applied early.
- Rapid transport to the nearest antivenom supply with someone capable of correctly prescribing it.
- Appropriate patient positioning.
- Gentle oropharyngeal suction.
- Use of regular atropine to reduce oropharyngeal secretions, if intubation not possible.
- Supplemental oxygen to balance the reduced respiratory effort.
- The use of upper airway devices (Guedel, nasopharyngeal airways).
- Endotracheal intubation.
- Assisted or controlled ventilation.

Anticholinesterase drugs

(See Chapter 12)

The use of long-acting anticholinesterase drugs such as neostigmine can reverse the post-synaptic neurotoxicity of death adder venom. It has been used alone, with prolonged first aid, and as an adjunct to antivenom when this is in short supply. The unwanted muscarinic effects (bradycardia, salivation, sweating) are controlled with the use of atropine.

Treatment of Coagulation Disturbances

(See Chapter 9)

This has been fraught with misconceptions in the past. These are dealt with in Chapter 9. Essentially, the treatment for coagulopathy (a persistently positive 20WBCT or ongoing bleeding) is more antivenom. Only when adequate antivenom has been given (1-3 ampoules) and the patient has liver function impairment, or is bleeding heavily, should FFP and other blood products containing clotting factors be given.

Administering clotting factors when there is un-neutralised venom in the circulation will only lead to further clot formation, risking worsening organ dysfunction and further depletion of remaining clotting factors, and hence worsening of bleeding.

Additionally, the patient with frank unilateral pulmonary haemorrhage may need intubation, with the ETT passed into the other lung (the cuff in the other main bronchus), to secure oxygenation and prevent contamination of the opposite lung with blood.

Treatment of Rhabdomyolysis

(Chapter 10)

This centres around the maintenance of an alkaline urine, and a high urine output (2 ml/kg/hr), to reduce the toxic effects of filtered myoglobin on the renal tubules.

The aim is to reduce the severity of renal impairment that results. This is the primary cause of death in a number of patients admitted with snakebite.

Hyperkalaemia is another potentially dangerous effect of extensive myolysis, often made worse by renal impairment and subsequent metabolic acidosis. The most significant effects are cardiac, with ECG changes, bradycardias and ventricular tachycardia's, the effects of increasing levels. Aggressive treatment is warranted, as detailed in Chapter 10.

Compartment syndrome, where muscular blood supply is impaired by massive swelling of the muscles in that compartment, can lead to permanent injury, though the normal result of myolysis is complete recovery. Surgical intervention should be discouraged, since overseas experience has shown that this worsens the long-term outcome.

The final notable effect of extensive myolysis is pain. This should be treated first with paracetamol and codeine, and the addition of morphine only when maximal doses are being given regularly. Non-steroidal anti-inflammatory drugs are contraindicated because of the risks of worsened coagulopathy, and causing gastric bleeding and worsening of renal impairment.

Treatment of Cardiovascular Effects

(Chapter 10)

These rarely require active treatment. The exceptions are

- Hypotension, without significant blood loss; give IV crystalloid and monitor its effect.
- Severe bradycardia (less than 35 bpm), due to conduction and AV or SA nodal effects, may respond to the cautious administration of atropine. Note that the BP is not a reliable indicator of peripheral perfusion in bradycardia, and peripheral warmth and capillary return may be a better guide. Beware the child with a bradycardia – in children and infants this immediately precedes cardiac arrest due to hypoxia or volume loss. Also look for hypoxia due to respiratory failure in adults, as a cause of bradycardia.
- Hyperkalaemia, as above.

Conduction defects, dysrhythmias (tachycardia's and bradycardia's), and ST-segment changes may respond to a further dose of antivenom.

Treatment of Renal Effects

(See Chapter 10)

This is essentially the same as for the treatment of rhabdomyolysis. In the absence of significant myolysis, a urine output of around 1 ml/kg/hr should be the goal, to ensure that adequate hydration is being achieved, and to ensure excretion of venom components and venom-antivenom complexes.

Renal function may also be threatened by

- hypoxia, from airway obstruction, pulmonary aspiration, respiratory failure,
- hypotension, from any cause,
- severe anaemia,
- the effect of procoagulant toxins (DIC and intravascular thrombosis),
- direct nephrotoxic effects,
- delayed serum sickness and the glomerular deposition of immune complexes,

and these should be avoided or anticipated, and treated, where possible.

Treatment of Infections

(See Chapter 10)

Prophylactic antibiotics

This has been discussed above.

Antibiotics are only advised in the case of gross wound contamination, imbedded foreign bodies (remove them!), and established wound infection. Additionally, when pulmonary aspiration leads to a clinical pneumonia, broad spectrum antibiotic cover, including gram negative and anaerobic cover, is advisable.

Referral and transport of snakebite patients

Patient referral

Many snakebite patients are managed quite satisfactorily in rural centres, and generally only those patients who have developed significantly complications are sent to a larger centre for more specialised care. Generally this will be somewhere where there is a specialist physician, anaesthetist or paediatrician.

Sometimes, though, patients are referred on because of a lack of antivenom; this is very unfortunate because of the negative effects this has on patient care:

- greatly delayed antivenom administration,
- secondary increase in complications from envenomation,
- serious dangers of transporting an envenomed patient over long distances, often by road, often without a nursing or medical escort, and often by PMV,
- potential loss of one staff member who acts as escort,
- inconvenience and cost for the family.

It is vital that staff know when to refer patients to a higher level facility and when to seek advice, and that they actually do these things, when necessary.

Requests for advice should be sought in the event that the staff dealing with the patient are unable to decide what to do next for a patient; this advice may be sought from

- the senior medical person at that facility,
- a senior medical officer at the provincial hospital,
- the senior medical officer on duty in the Emergency Department at PMGH, or
- the consultant emergency physician at PMGH.

Patient Transport

The general principle of transporting a patient is that the standard of care should not drop from referring hospital to transport, transport to receiving hospital. While this is potentially difficult, the principle exists for the patient's best interest, and every effort should be made to sustain minimum standard of care during patient transfer that doesn't seriously compromise the safety of the patient.

While it is occasionally possible for aerial retrieval of patients from isolated areas, this is not at all to be relied upon and it tends only to be available during daylight hours. Therefore, the only option is land transport, which is also often not possible, due to the state of the roads, or to the lack, or poor repair, of the local "ambulance". PMV is often the only option, and people in smaller communities have walked long distances to reach a PMV stop, only to have none stop because they already had a full load; patients have died on the side of the road waiting for a PMV, and clearly this mode of transport cannot be relied upon.

The very unfortunate reality is that many patients die en route to hospital, or soon after arrival at the facility. There are a number of reasons for this:

- Staff "accompanying" the patient often sit in the front of the pickup, while the patient is in the back with the relatives, where the staff member cannot check on them.
- Accompanying staff bring no drugs or resuscitation equipment with them on the transport.
- The patient is generally transported without any oxygen, or upper or lower airway device to maintain the airway; suction is certainly not carried.
- The patient, who often hasn't received antivenom, frequently develops life-threatening airway obstruction, pulmonary aspiration or respiratory failure en route.

If a staff member is going to accompany a patient, they should consider the following issues:

- Patient ready
 - family aware and available to also accompany the patient,
 - stable, and any ongoing treatment can be carried out in the transport vehicle (better to be intubated before transport, than during transport),
 - antivenom given, if indicated and available,
 - first aid applied, if indicated, and traditional first aid removed,
 - Any IV line well-secured.
- Staff member ready
 - capable of dealing with any likely problems with the patient en route,
 - personal items.
- Drugs and equipment ready
 - oxygen (enough for the journey),
 - resuscitation drugs and equipment (OP and NP airways, portable suction device, atropine, intubation equipment, Ambu-bag, IV fluid, adrenaline, morphine, diazepam); the facility that refers a lot of unwell or unstable patients should consider developing a Transport Bag for just this purpose.
- Communication complete
 - shift covered,
 - receiving hospital aware,
 - referral letter, results and x-rays with patient.

What to teach families if no staff member can accompany the patient:

- patient positioning
 - sitting up if still breathing reasonably well, and clearing secretions;
 - left or right lateral if there is pooling of secretions;
 - keep them in this position the entire journey, including when carrying them into the hospital;
- basic airway manoeuvres – chin lift and jaw thrust;
- insertion of the Guedels airway – if not tolerated or required at the time of patient departure; consider the nasopharyngeal airway as a good alternative;
- not feeding or giving oral fluid to the patient during the trip if there is any risk that their ability to protect their airway will become compromised en route;
- IV line care (if the decision is made that the patient needs to continue with this en route).

The family must also be given to take and give to the receiving hospital, a detailed letter, or a complete copy of the patient's notes for that admission, detailing the following:

- the bite history,
- initial and subsequent examination findings,
- the results and times of investigations,
- details and timing of any treatment,
- response to treatment,
- other progress,
- ongoing concerns and reasons for referral.

They should also bring any CXR, and the snake, if caught (only to PMGH, where DNA will be taken for research purposes; otherwise it should be kept in methylated spirits for later collection, the date and site of collection noted on the container).

The referring professional should note his/her name clearly on the letter, with a contact telephone number or radio frequency, so that they might receive feedback about their patient.

Clinical assessment and treatment of neurotoxicity

Dr Gertrude Didei

Overview

Neurotoxicity is the major clinical consequence of all venomous snakebites in Papua New Guinea and a major contributor to fatal outcomes.

Mechanism of neurotoxicity & implications for envenomed patients

Neurotoxins can either be presynaptic or postsynaptic. Some snake venoms contain both presynaptic and postsynaptic neurotoxins. Presynaptic neurotoxins are difficult to reverse, whereas postsynaptic neurotoxicity can be reversed with anticholinesterase drugs such as neostigmine.

The neurotoxins interfere with transmission of nerve impulses from nerve endings to muscles. This occurs at the neuromuscular junction (NMJ). The presynaptic neurotoxins probably act by interfering with the release of acetylcholine (ACh), while the postsynaptic neurotoxins interfere with the action of acetylcholine, as has been explained elsewhere in this Handbook.

Neuromuscular junction (NMJ) and neurotransmission

Acetylcholine is the neurotransmitter at the NMJ which allows normal muscle activity to occur (see **FIGURE 1** – Neuromuscular junction).

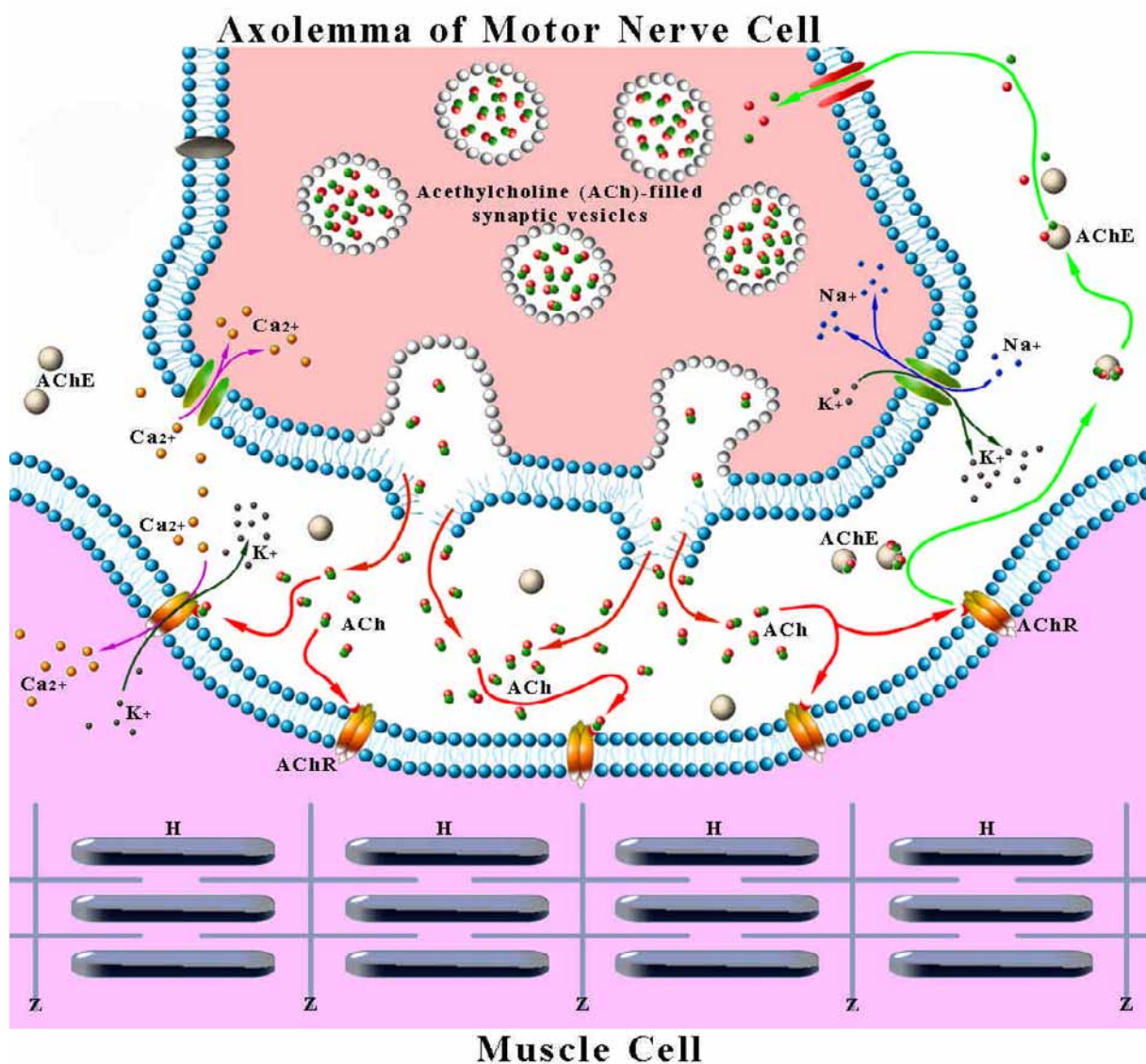
The nerve impulse arriving at the end of the motor neuron increases the permeability of the phospholipid membrane to calcium. This causes an increase in exocytosis of acetylcholine vesicles in the synaptic cleft. Acetylcholine diffuses across the synaptic cleft to bind with the acetylcholine receptors on the muscle membrane. Binding of acetylcholine to these receptors opens up the sodium-potassium pump in the muscle membrane and allows sodium to enter the muscle cell membrane. The influx of sodium into the cell produces a decrease in potential outside the muscle membrane and an increase in potential on the inside. As a result, an electrical impulse known as depolarisation potential is produced. The decrease in the potential outside also depolarises adjacent muscle membranes to their firing levels.

Postsynaptic neurotoxins competitively bind to acetylcholine receptors on ion channels in the phospholipid membrane of motor muscle cells, preventing acetylcholine from binding. This prevents depolarisation and the muscle remains paralysed. Anticholinesterases can be used to treat postsynaptic neurotoxicity because they inhibit neurotransmitter recycling and enable acetylcholine to remain in the synaptic cleft longer, increasing neurotransmitter binding to unblocked receptors, and producing depolarisation.

Presynaptic neurotoxicity is more difficult to treat because the toxins bind to transmembrane proteins on the motor neurons and not only inhibit acetylcholine release by blocking exocytosis of the synaptic vesicles, but also cause extensive physical damage to the nerve ending itself, perhaps through uncontrolled calcium influx into the neuronal cytoplasm, as has been detailed in Chapter 3. Other presynaptic neurotoxins inhibit outward potassium ion (K^+) transport, which in turn inhibits the actual recycling of the synaptic vesicles.

Impairment of neurotransmission by snake venom toxins predominates in the skeletal musculature rather than in smooth or cardiac muscle. There is evidence that does suggest, however, that some snake venom toxins may also exert effects on ion transport in the myocardium which can lead to arrhythmias and other myocardial conduction problems. Vasoactive toxins that affect endothelial cells in blood vessel walls may also have a role in hypotensive syndromes seen after some snakebites.

FIGURE 1: Neuromuscular junction showing the processes of synaptic vesicle exocytosis, acetylcholine (ACh) binding to receptors on the motor muscle, and dissociation of acetylcholine by acetylcholinesterase (AChE), followed by re-uptake of acetate and choline by the motor neuron. These processes provide many potential physiological target sites for snake venom neurotoxins; presynaptic neurotoxins affect the motor nerve ending, while postsynaptic neurotoxins affect the ability of acetylcholine to bind to the motor muscle receptors (nAChR).



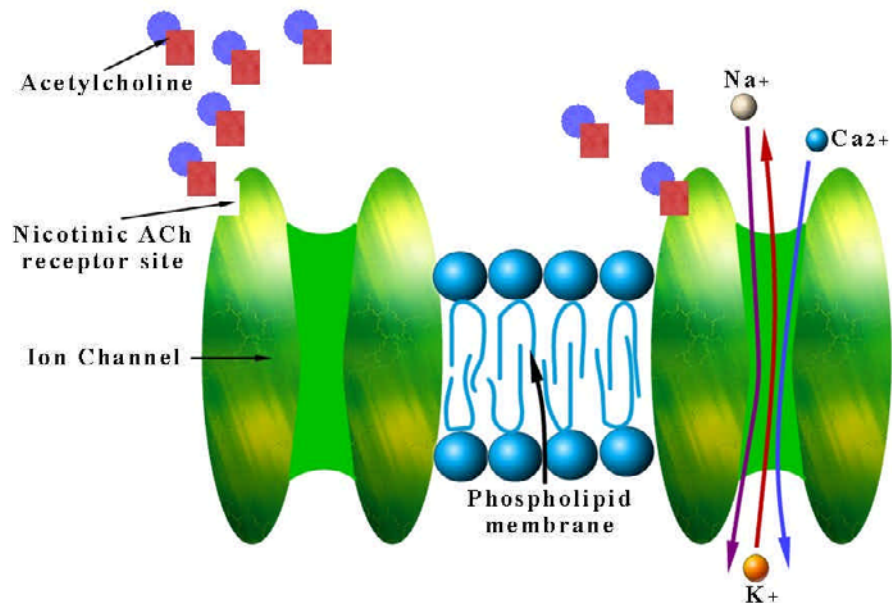


FIGURE 2: Schematic of motor muscle ion channel containing the nicotinic acetylcholine receptor (nAChR); when acetylcholine (AChR) binds to the nAChR, the ion channel is opened, allowing ions such as sodium (Na^+) and calcium (Ca^{2+}) into the cell, while potassium (K^+) is able to leave the cell and enter the extracellular space.

Assessment and Recognition of Neurotoxicity

Bites are relatively painless (with the exception of mulga snakes, and possibly the Papuan blacksnake) and may be unnoticed. Paired fang marks are usually evident, but sometimes only scratches or single puncture wounds are found. Papua New Guinean snakes do not cause extensive damage to local tissues. There may be mild swelling and slight bleeding from the bite site.

Symptoms and signs of envenomation

Not all possible symptoms or signs occur in a particular case; in some cases, one symptom or sign may predominate, while in most cases there is a mixture (see **TABLE 1**).

The earliest symptoms and signs of neurotoxicity typically involve the cranial nerves affecting the ability to control both the major and minor facial muscles. Ptosis is generally the first clinical indication of neurotoxicity and involves paralysis of the muscles responsible for opening the eyelids. Relatives and friends of a snakebite victim, and even health care workers, may often interpret ptosis as ‘tiredness’ or ‘sleepiness’.

In a patient with a history of suspected snakebite, early ptosis is an important early indication for the administration of appropriate antivenom and should not be ignored.

Additional symptoms of neurotoxicity may include blurred vision, double vision (diplopia), slurred speech (dysarthria), difficulty in swallowing (dysphagia) and shortness of breath or difficulty breathing (dyspnoea).

On examination, the following are important clinical signs of neurotoxicity: inability to open the eyes (ptosis), fixed gaze and inability to move eyeballs (ophthalmoplegia), dysphonia, dysphagia, dysarthria, impaired ability to protrude tongue, dyspnoea, tachypnoea, limb weakness (reduced hand grip is a sign), loss of deep tendon reflexes, abdominal breathing and, in severe cases, cyanosis caused by insufficient oxygenation of the blood.

TABLE 1: Course of progressive onset of major systemic symptoms and signs of untreated envenomation. In cases of massive envenomation, or bites in children, a critical illness may develop in minutes rather than in hours.

LESS THAN 1 HOUR AFTER THE BITE

- Headache
- Nausea, vomiting, abdominal pain
- Transient hypotension associated with confusion or loss of consciousness
- Coagulopathy (20WBCT or laboratory testing)
- Regional lymphadenitis

1 TO 3 HOURS LATER

- Paresis/paralysis of cranial nerves – ptosis, double vision, external ophthalmoplegia, dysarthria, dysphonia, dysphagia, facial weakness
- Haemorrhage from mucosal surfaces and needle punctures
- Tachycardia, hypotension, tachypnoea, shallow respirations

MORE THAN 3 HOURS LATER

- Paresis/paralysis of truncal and limb muscles
- Paresis/paralysis of respiratory muscles and respiratory failure
- Rhabdomyolysis
- Dark urine (due to either myoglobinuria or haemoglobinuria)
- Renal failure
- Coma; possibly due to hypoxaemia and shock. Shock may result from intracranial haemorrhage or coagulopathy



FIGURE 3: Ptosis in a patient with suspected Papuan taipan (*Oxyuranus scutellatus canni*) envenomation.

Note that despite the brow furrowing caused by the patient as she attempts to open her eyes, she is completely unable to do so.

Ptosis is a very important early sign of developing systemic envenomation and should be assessed with care; a common error is to mistakenly assume that a person with ptosis is tired or sleepy.

The person should be asked to attempt to open their eyes as wide as possible, and if unable to do so then antivenom should be given without delay, especially if the 20WBCT was positive.

Many patients with ptosis also have a varying degree of ophthalmoplegia (the paralysis of the muscles which allow the eyes to move in vertical, horizontal or diagonal planes), and you can assess this sign by asking the patient to use their eyes to follow finger movements through the sphere of vision while they keep their heads facing forward.

General Treatment Strategy

Before discussing specific treatment strategies for dealing with issues related to neurotoxicity such as respiratory support and airway protection, a general overview of some other patient management considerations is helpful:

1. Allay anxiety and fear

- Reassurance.
- Sedation – this can be achieved with use of diazepam i.v, or via an orogastric tube, but only in the intubated patient, since this may remove what respiratory drive they have left.

2. Analgesics and antipyretics

- Paracetamol suppositories or crushed tablets via orogastric tube.
- Aspirin, particularly, but also other non-steroidal anti-inflammatory analgesics, should be avoided in the case of snakebite where coagulopathy may occur, or is already present.

3. Nutrition

- Insert an orogastric or nasogastric tube for feeds and medication (ideally inserted at the time of intubation), but take great care not to cause mucosal damage if there is concurrent coagulopathy.
- Regular 3-4 hourly blood glucose checks and giving glucose-containing iv fluids when needed.

4. Bowel and bladder care

- Prophylaxis against stress ulcers – cimetidine i.v. or via enteral feeding tube.
- Insert an indwelling urinary catheter for monitoring of renal functions as well as for checking for blood, blood pigments and myoglobin.

5. General care of an unconscious patient

- Hourly monitoring of vitals – pulse, blood pressure, temperature, respiratory pattern and rate, level of consciousness, pulse oximetry and urine output.
- Hourly snakebite observations.
- Regular gentle suctioning of secretions in the mouth and the oropharynx, and of the endotracheal tube if the patient is intubated (don't pass the catheter beyond the end of the tube).
- Care of pressure areas by regular changing of position and massaging (gently) of pressure points; application of soft padding over these areas.
- Limb and chest physiotherapy for those who are heavily envenomed.

6. Oxygen therapy

- Supplementary oxygen should be given to every patient with respiratory failure, pulmonary aspiration or shock.

7. Antibiotic cover

- This is not required unless the patient has clear skin infection or pneumonia; the use to “prevent” infection will simply select more resistant organisms to colonise the patient's wounds. However, local wound care, after antivenom has been given, is required.

8. Intravenous fluids

- These are given for shock, to replace fluid losses and for maintenance requirements.

9. Laboratory investigations

- FBE, UEC's, fibrin degradation products and clotting times.
- Blood grouping and cross-matching (unless there is clearly no coagulopathy).
- Chest x-ray if there are signs of chest infection, or after intubation of the trachea.
- Arterial blood gas analysis – in those centres with this facility; it is vital, as it not only assists in patient management, but also helps save the cost of oxygen.

Management of patients with respiratory difficulties

Airway maintenance

- Pooling of secretions (saliva), difficulty in swallowing, slurring of speech and hoarseness of voice are early signs that the airway is compromised. Therefore, it is important that suction apparatus and oxygen delivery equipment are readily available at the bedside.
- Insertion of Guedel airway may not be tolerated at this stage, unless the gag reflex has been abolished.
- Intubation of the trachea is indicated when there is marked pooling of saliva, the gag reflex is disappearing, when peripheral oxygen saturations are falling, below 90% despite oxygen, or when the patient presents with cyanosis or in respiratory arrest. They are likely to allow fairly easy laryngoscopy and intubation of the trachea.
- The use of diazepam to facilitate intubation should be used with caution, since it does little to improve intubating conditions (i.e.: make it easier for you to perform), and has a slow onset of action, but may completely remove the patient's respiratory drive before you have secured the airway. Morphine is a better drug for this, or better still, use the 2 drugs together and be prepared to manually ventilate the patient for a while once intubated. The use of suxamethonium, as well, will produce the best conditions for intubation, if you are trained in its use.
- **REMEMBER:** If you are not confident to intubate, then **do not sedate** the patient and **do not try to intubate**.
- Keep the endotracheal tube sterile at all times; otherwise you risk introducing bacteria into the lungs and causing pneumonia or tracheitis.
- Do not forcefully perform laryngoscopy or intubation. This causes pain for the patient. It also causes mucosal injury and the consequent bleeding, if coagulopathy is present, will further compromise the airway and respiration. The stimulation may also cause bronchospasm, laryngospasm, severe bradycardia (all via vagal nerve stimulation) or ventricular arrhythmias, which can each kill the patient quite quickly.
- When you intubate, someone should be providing cricoid pressure, to prevent vomiting, and should monitor the pulse continuously throughout the procedure.
- If the patient resists laryngoscopy, then he or she still has the ability to maintain their own airway, for now.
- If you are unable to intubate, use the Guedel airway and a non-rebreathing, or a Hudson, mask with supplementary oxygen.
- If you have managed to intubate the patient, you must always give supplementary oxygen, since the patient will almost always need it.

- ETT insertion should be followed by very gentle orogastric or nasogastric tube insertion to empty the stomach, thus making ventilation easier and reducing the risk of reflux of gastric contents.

Assisted ventilation strategies in rural health centres

- Guedel/nasal airway with Ambu-bag and mask ventilation may be appropriate, but be aware that this can inflate the stomach with air if not done very carefully, and hence increase the risk of reflux of gastric contents, or vomiting, and pulmonary aspiration.
- Perform laryngoscopy and intubation (if you are appropriately trained), then assist ventilation with an Ambu-bag, as discussed above.
- Do not leave the intubated patient breathing through the Ambu-bag with very low flows of oxygen (less than 4 litres/minute), since their minute volume (respiratory rate times the volume of each breath) may be higher than this and they will essentially be suffocating. If you have a limited oxygen supply, it is better to use a T-piece, or to administer oxygen via a fine suction catheter that has been placed inside the endotracheal tube (ETT) with its tip not beyond the end of the ETT.
- If you are assisting the patient's ventilation, or are fully manually ventilating them with the Ambu-bag, you will need enough oxygen flow to refill the bag after each time you have squeezed it.
- Do not leave an intubated patient with relatives or untrained staff ventilating, or assist-ventilating, a patient for long periods without frequently checking that they are performing it correctly, that the ETT is still in the correct position, and that the patient's vital signs are stable and okay.
- Oxygen must be administered during assisted ventilation.
- Transport of the patient to the nearest hospital with facilities to provide ventilation must be a high priority.

Assisted ventilation strategies in urban hospitals

- Intubate and assist ventilation with Ambu-bag and mask, or a T-piece breathing circuit.
- Attach to a mechanical ventilator. The mode of ventilation depends on the respiratory drive/function of the patient. Generally two common modes are used:
 - ? Synchronized intermittent mandatory ventilation (SIMV)
 - ? Controlled mechanical ventilation (CMV)
- Sometimes patients who have normal respiratory drive, but have pulmonary oedema or pulmonary aspiration, are ventilated in the continuous positive airway pressure (CPAP) mode.

Complications of various interventions

A number of different complications can arise during efforts to maintain ventilation, depending on the particular technique that is being employed:

1. Guedel/nasal airway with bag and mask ventilation

- Increased risk of regurgitation and aspiration.
- Trauma to mucosal surfaces of the oropharynx and nasopharynx.
- Damage to teeth by forceful insertion of a Guedel airway.

2. Bag and mask ventilation via endotracheal tube

- Trauma to soft tissues of the mouth, oropharynx and trachea and to teeth. These are complications that often occur during laryngoscopy and intubation. Therefore care must be taken during this procedure. These complications are usually a result of inexperience and anxiety.
- Spontaneously breathing patients can rebreathe their own expired gases if inappropriately managed. Increased levels of CO₂ initially cause hypotension due to vasodilation, then later hypertension, tachycardia and CO₂ narcosis. The CO₂ narcosis can be mistaken for deepening of neurotoxicity and therefore not treated. The patient will eventually develop a coma.
- Breathing dry gases, since the normal humidifying system (nose) is bypassed. As a result there may be crust formation in the airways which can cause blockages.
- Over-inflation of the lungs may increase the risk of ruptures of the alveoli and bullae formation, causing pneumothorax.
- Under-inflation of lungs can precipitate collapse of the alveoli.

FIGURE 4: Patient with presumed Papuan taipan (*Oxyuranus scutellatus canni*) envenomation being maintained on a ventilator due to a loss of respiratory effort.



3. Assisted ventilation with mechanical ventilators

- Increased risk of transmission of infection during suctioning and the use of a breathing circuit.
- Breathing of dry gases.
- Trauma to tracheal mucosa from over inflation of endotracheal tube cuff and prolonged intubation may result in tracheal mucosal ischaemia and finally fibrosis and stenosis.
- Unequal distribution of gases and blood flow to the lung tissues (ventilation-perfusion mismatch). The alveoli on the top (i.e.: proximal in relation to gravity) are better oxygenated than those distally, which in turn are better perfused. Normally this mismatch is not so significant, but in ventilated patients this difference is increased.
- Increased risk of rupture or collapse of alveoli with over inflation or under inflation respectively.
- Increased intrathoracic pressure exerting external pressure on the major vessels such as the inferior and superior vena cava, thereby reducing venous return to the heart and eventually reduced cardiac output.

Reversal of neurotoxicity with antivenom

In Papua New Guinea the selection of antivenom has typically been a decision that is made on the basis of one or more of the following:

1. An identification of the snake responsible by the patient or by those who were with the patient at the time of the bite.
2. A good description of the snake by the patient or those who were with the patient at the time of the bite.
3. The availability or otherwise of antivenoms.
4. The clinical presentation of the patient.

Unfortunately, the reality is that identifications made by patients/others are extremely prone to error, and especially prone to the common misconception that bites by large snakes are caused by ‘Papuan (Pap) blacks’, a potentially lethal error if CSL blacksnake antivenom is then given erroneously to the victim of a much more dangerous Papuan taipan (*Oxyuranus scutellatus canni*).

Good descriptions of the snake can be helpful, **but always consider them with caution:**

- Large ‘dark-coloured snakes with red stripes on the back’ are Papuan taipans (*Oxyuranus scutellatus canni*), but **REMEMBER** the reddish dorsal stripe of the taipan may not always be seen by the patient, and failure to report it does not mean the snake was not a Papuan taipan.
- ‘Small snakes with triangle-shaped heads’ and short, ‘sharp’ tails may be death adders (*Acanthophis* spp.).
- In northern and highland provinces, a large ‘white snake’ or a ‘pale snake with a dark head’ is almost certainly a small-eyed snake (*Micropechis ikaheka*).
- **REMEMBER:** ‘black snakes’, whether big or small, are not necessarily genuine Papuan blacksnakes (*Pseudechis papuanus*) – there are several black or dark-coloured snakes (including taipans) that are commonly mistaken for Papuan blacksnakes.

The most important way of identifying the species responsible for a particular case of snakebite is to obtain a thorough history from the patient that includes a careful and accurate assessment of both the reported symptoms and observed signs. The clinical examination will provide you with reliable information upon which to make management decisions, including the selection of antivenom. Combined with knowledge of which species of snakes occur in your region, and what the effects of their venoms may be, it is possible to make sound presumptive identifications of the species responsible. (See also Chapter 11 page 11.8)

The 20WBCT should be used to determine if a coagulopathy exists, and if blood remains unclotted at 20 minutes and the bite occurred in Milne Bay, Central, Gulf or Western province, a diagnosis of envenoming by the Papuan taipan (*Oxyuranus scutellatus canni*) is extremely likely.

REMEMBER: The earliest possible administration of antivenom significantly reduces the risks of airway compromise and respiratory failure.

A further consideration is the cost and availability of antivenom. In many cases the high cost will affect which antivenoms are available, and in Papua New Guinea it is usual to give only a single ampoule of antivenom because of high costs. Further information on the procedures for the administration of antivenom is given in detail in Chapter 11 of this Handbook.

Limitations of Antivenom

Antivenom is generally very effective in the reversal of postsynaptic neurotoxicity produced by species such as death adders (*Acanthophis* spp.) and can produce remarkable improvement in the clinical situation within a short period of time for some patients.

The same cannot be said for the reversal of presynaptic neurotoxicity caused by the bites of snakes like the Papuan taipan (*Oxyuranus scutellatus canni*). Clinical experience shows that unless antivenom is given within 4 hours of a bite by this species the majority (70%) of patients will continue to deteriorate and will require intubation and ventilation. In victims of taipan bites who present late for treatment and have well established neurotoxicity, the reality is that while antivenom is of value in correcting coagulation disturbances, it is very unlikely to reverse the neurotoxicity even if given in multiple doses. Protection of the airway and planning for the necessity to provide prolonged ventilation should be important priorities.

Ancillary Drug Interventions

Anticholinesterases

Neostigmine is the only anticholinesterase that has been used for snakebite in PNG, although there are other anticholinesterase drugs available. Neostigmine inactivates the enzyme acetylcholinesterase (AChE) which is responsible for breaking down acetylcholine (ACh). As a result, ACh accumulates in the synaptic cleft, producing increased binding to receptors, and resulting in depolarisation and muscle action.

Dosage: adults 1.25-2.5mg, children 0.05-0.07mg/kg, slow iv, repeated 2-4 hourly if initial improvement in motor function is observed.

Atropine must be given in conjunction with neostigmine to counteract unwanted side effects of neostigmine, which can include bradycardia, increased salivation and sweating (See Chapter 12 for more detailed information on anticholinesterase therapy).

Dosage: adults 0.6-1.2mg, children 0.02mg/kg, slow iv, repeated approximately 6-hourly, depending on the reappearance of excessive salivation or sweating.

The Assessment and Treatment of Coagulopathy

Dr Antony Chenhall and David Williams

Introduction

Many snake venoms contain toxins which interfere with normal haemostasis and the targets of venom haemotoxins are as diverse as the enzymatic coagulation reactions themselves.

The role of haemostasis is to successfully maintain the integrity of the circulation by ensuring that the processes of clot formation and clot degradation remain in equilibrium at all times. Both of these pathways involve step-wise biochemical reactions that activate inactive blood clotting factors in an ordered sequence that leads to either the production of a viable blood clot at the site of a breach in the circulatory system such as a cut or scratch, or the breakdown and removal of that same clot once the underlying tissue has begun to heal.

Snake venoms that interfere with these sequential reaction pathways have the ability to seriously compromise the haemostatic integrity and to cause life-threatening haemorrhage.

An early coagulopathy is an absolute indication for the administration of antivenom in a patient suspected as having been bitten by a venomous snake in Papua New Guinea.

Coagulation disturbances have been documented following the bites of three common highly venomous snakes: Papuan taipans (*Oxyuranus scutellatus canni*), Papuan blacksnakes (*Pseudechis papuanus*) and small-eyed snakes (*Micropechis ikaheka*). They are also a prominent feature in bites by brown snakes (*Pseudonaja textilis*). Slight subclinical changes in haemostasis have been seen after bites by death adders (*Acanthophis* spp.), but these are not likely to be clinically significant.

In southern Papua New Guinea, where the Papuan taipan (*Oxyuranus scutellatus canni*) may be responsible for more than 80% of the serious snakebites, coagulopathy is common and may be severe. Venom from this snake converts prothrombin to thrombin in the presence of Ca^{2+} and circulating phospholipids in a Factor V-independent reaction. Systemic prothrombin activation causes depletion of available fibrinogen resulting in consumption coagulopathy and incoagulable blood. Disseminated intravascular coagulopathy results, and bleeding may occur from mucosal membranes, bite wounds, minor cuts or grazes, and venepuncture sites.

In the Milne Bay, Central, Gulf and Western provinces it is extremely likely that a person who presents with incoagulable blood has been bitten by a Papuan taipan (*Oxyuranus scutellatus canni*), and the early detection of this abnormality and recognition of its clinical significance is crucial to successfully treating bites by this extremely venomous snake.

This chapter briefly describes the major mechanisms of snake venom-induced coagulopathy, outlines the diagnosis and assessment of resultant haemostatic disturbances, and explains the process of clinical treatment and management.

Mechanisms of snake venom coagulation disturbances

The majority of coagulation disturbances observed in victims of snakebite in Papua New Guinea are due to either of the following:

Prothrombin activation

The conversion of the zymogen prothrombin to active thrombin enables soluble fibrinogen to be, in turn, converted into insoluble fibrin which provides the essential matrix for the formation of a viable blood clot at the site of an injury.

Prothrombin activation is tightly regulated, but may be seriously compromised by snake venoms procoagulant toxins, which are able to catalyse the cleavage of prothrombin to thrombin in the presence of phospholipid-rich platelets and circulating Ca^{2+} ions. Under normal conditions, this reaction is driven by Factor X_a , and another blood clotting enzyme (Factor V_a) is needed in order to optimise the reaction rate. However, some snakes, including the Papuan taipan (*Oxyuranus scutellatus canni*), have developed toxins that mimic both Factor X_a and Factor V_a , effectively substituting themselves for the natural factors.

Venom-induced activation of prothrombin results in uncontrolled, excessive thrombin production, leading to a disseminated intravascular coagulopathy (DIC) that involves:

- Systematic conversion of fibrinogen to fibrin.
- Activation of Factor XIII to Factor XIII_a , required for formation of cross-linked fibrin clots.
- Excessive consumption of fibrinogen, prothrombin, platelets and clotting factors.
- Activation of fibrinolysis by endothelial cell-secreted plasminogen activators.
- Alpha_2 antiplasmin consumption, leading to overabundant plasmin availability and the degradation of both fibrinogen and fibrin.
- Failure of haemostasis, with overwhelming defibrination, producing incoagulable blood and a pronounced bleeding diathesis.

Incoagulable blood (hypofibrinogenaemia) leads to bleeding from a variety of sites including:

- Gingival sulci,
- Gastrointestinal mucosa,
- Nasal mucosa,
- Venepuncture sites,
- Minor cuts, scratches or grazes including the bite site,
- Uterine membranes,
- Capillaries in the eyes, lungs, and brain.

It is important to note that consumption coagulopathy results in critical depletion of clotting factors, through their use as substrates and cofactors for venom-induced thrombin production. Also that, in the absence of venom neutralisation by antivenom, the replacement of these depleted clotting factors with FFP, cryoprecipitate or other blood products is very likely to promote further defibrination and hypofibrinogenaemia. Blood products **should not be used** until circulating venom has been neutralised with appropriate antivenom, except in cases of severe, immediately life-threatening haemorrhage.

Platelet function alteration

Platelets are small, disc-shaped, non-nucleated blood components that have phospholipid-rich plasma membranes that serve as the substrates for several important haemostatic processes, including the activation of prothrombin by both direct and indirect means.

Platelets are activated in response to haemostatic disruption, and will adhere and aggregate at injury sites where they act as temporary plugs, and stimulate coagulation factors in plasma to activate mechanisms in clotting pathways. Inhibitors of platelet aggregation can lead to true anticoagulation in which the normal pathways to prothrombin activation and fibrin clot formation are effectively disrupted, resulting in incoagulable blood.

There are inhibitors of platelet aggregation in the venoms of Papua New Guinea snakes that can produce anticoagulant effects (bleeding tendencies) without defibrination. From a clinical perspective, the haemostatic effects of these toxins are usually less severe than those produced by prothrombin activation. The venoms of the Papuan blacksnake (*Pseudechis papuanus*), small-eyed snake (*Micropechis ikaheka*) and death adders (*Acanthophis* spp.) have all been found to contain inhibitors of platelet aggregation.

Assessment and recognition of coagulopathy

Coagulation disturbances often develop rapidly after envenomation, and may be pronounced some time before the first symptoms or signs of neurotoxicity become apparent.

Recognising coagulopathy at the earliest possible time point can aid in the identification of the biting species and enable antivenom to be administered without delay. Coagulopathy in a person with suspected snakebite is an **absolute indication for antivenom**.

The 20WBCT (20 minute whole blood clotting test)

The 20WBCT (20 minute whole blood clotting test) should be performed on **ALL PATIENTS** with suspected snakebite in Papua New Guinea immediately after presentation at an aid post, health centre or hospital.

Equipment

- Latex gloves and 70% alcohol wipes.
- New, sterile needle and disposable syringe.
- Clean, dry glass bottle or sample vial.
- A watch or clock.

Procedure

1. Wearing gloves, swab the site carefully and perform venepuncture to collect 2 ml of fresh venous blood from an appropriate venepuncture site, such as the antecubital vein, or from the IV cannula, if you decide to insert one.
2. Carefully transfer the blood to the glass container and place the sample where it will not be disturbed and **do not touch it** for a minimum of 20 minutes.
3. Dispose of used sharps appropriately.
4. After 20 minutes, tilt the glass vial/bottle gently over onto its side and observe whether or not a functional clot has formed.
5. Record the result on the observation chart **clearly** as either ‘clotted at 20 minutes’ or ‘unclotted at 20 minutes’

Appearance of the blood at 20 minutes

- If the blood is incoagulable after 20 minutes, it will appear to have a ‘watery’ consistency and this is regarded as a **positive** test result.
- Clotted blood will ‘clump’ in the bottom of the glass vial as a ‘jellylike’ consistency and this is regarded as a **negative** test result.

Rationale and interpretation of the 20WBCT result

- If the blood is incoagulable after 20 minutes, the patient has a 98.4% chance of developing neurotoxicity if the bite is not treated with appropriate antivenom immediately.
- A patient with incoagulable blood after 20 minutes has hypofibrinogenaemia resulting from a consumption coagulopathy (DIC) and should receive appropriate antivenom as soon as possible.
- In Milne Bay, Central, Gulf and Western provinces, a **positive** 20WBCT strongly indicates a presumptive identification of envenomation by the Papuan taipan (*Oxyuranus scutellatus canni*), and either CSL taipan antivenom or CSL polyvalent antivenom should be administered.
- In other provinces a **positive** 20WBCT suggests either brown snake (*Pseudonaja cf. textilis*) or small-eyed snake (*Micropechis ikaheka*) envenomation, and CSL polyvalent antivenom should be administered.
- A **negative** test (clotting blood at 20 minutes) does not mean that a venomous snakebite has not occurred. The patient should continue to be observed hourly for a minimum of 24 hours and the 20WBCT should be repeated after six (6) hours.

Repetition of the test

- The 20WBCT can be used to assess the neutralization of circulating venom with antivenom, and should be **repeated six (6) hours** after the administration of antivenom.
- A positive 20WBCT (ie. the blood is not clotted after 20 minutes) six hours or more after antivenom administration indicates that circulating snake venom has not been fully neutralised and that more antivenom may be required.

Important considerations for proper use of the 20WBCT

- **Always** take appropriate precautions when drawing blood and handling blood, and take care with sharps to avoid needle-stick injury.
- **Use only clean dry glass tubes:** plastic tubes are not suitable and will not give a proper result. Do not use glass bottles washed with detergent, as their ability to activate clotting will be reduced.
- **Be patient!** Do not tilt or shake the tube during the 20 minute ‘clotting interval’: disturbing the sample will only delay clot formation and this can cause false-positive results that invalidate the test.
- **Do not** draw blood from the same limb in which an intravenous line has been established, unless you have first stopped the infusion for at least 10-15 minutes.
- **Take care** when drawing blood to minimise the risk of haematoma or bleeding from the venepuncture site afterwards.
- **Record** both the time the 20WBCT was carried out and the results of the test itself on the snakebite observation chart **each time** that it is performed on the patient.

Other tests of coagulation status

The following specific tests of coagulation status are typically only available in larger hospitals with functional pathology facilities:

1. Prothrombin Time (PT)

- Measures the function of clotting factors involved in the extrinsic and common pathway mechanisms of the coagulation cascade (i.e. Factors II, VII, X, fibrinogen and fibrin).
- Normal range for is 12-16 seconds.
- In patients with snake venom-induced DIC or anticoagulation, the PT will be prolonged, and can be greater than 150-180 seconds.

2. Activated Partial Thromboplastin Time (APTT)

- Measures the function of clotting factors involved in the intrinsic and common pathway mechanisms of the coagulation cascade (i.e. Factors X, XI, XII, XIII etc).
- Normal range is 25-47 seconds.
- In patients with snake venom-induced DIC or anticoagulation, the APTT will be prolonged, in some cases grossly so (i.e. >300 sec).

3. Fibrinogen Level

- Normal range is 1.5-4.5 g/L.
- In a patient with a DIC involving defibrination, the fibrinogen level will be critically below these ranges, and is often undetectable.
- Depletion of fibrinogen is not seen in bites by species with anticoagulant venoms.

4. Fibrin-degradation Products (FDP)

- Normal range is <10 µg/ml.
- In a patient with a DIC involving defibrination, the FDP may be extremely high.
- FDP levels are not typically elevated in bites by snakes with anticoagulant venoms.

5. Platelet Counts

- Normal range is $150-500 \times 10^9/L$.
- A range of $50-100 \times 10^9/L$ indicates mild to moderate thrombocytopenia.
- $< 50 \times 10^9/L$ suggests severe thrombocytopenia.

6. White Cells Counts

- Normal range is $4,000-11,000 \times 10^6/L$.
- Following snakebites the WBC may be higher than $30,000 \times 10^6/L$.

In a patient with a positive 20WBCT, a prolonged PT and APTT, with depleted fibrinogen and elevated FDP levels, confirms a disseminated intravascular coagulopathy involving defibrination, as would be seen after Papuan taipan (*Oxyuranus scutellatus canni*) envenomation.

In a patient with a positive 20WBCT, a prolonged PT and APTT, but normal fibrinogen and FDP levels, the coagulation disturbance is one of anticoagulation and probably due to a bite by either a Papuan blacksnake (*Pseudechis papuanus*) or a small-eyed snake (*Micropechis ikaheka*).



FIGURE 1: 20WBCT (20 minute whole blood clotting test) in a severely envenomed patient bitten by a Papuan taipan (*Oxyuranus scutellatus canni*). When drawing blood ensure that **(a)** gloves are worn, **(b)** precautions against needle-stick injury are taken (including proper sharps disposal), **(c)** a clean, dry glass container is available at the bedside, **(d)** venepuncture is performed with consideration to minimising subsequent bleeding or ecchymosis at the site, and **(e)** if drawing from the same limb that has been used for intravenous line access, turn off the IV for 10-15 minutes prior to the venepuncture to avoid contaminating or diluting the blood sample. Once drawn, place 2 ml of blood in the glass container and **allow it to stand undisturbed for 20 minutes** before determining the test outcome as either **(1)** ‘clotted at 20 minutes’ or **(2)** ‘unclotted at 20 minutes’.

Symptoms and clinical signs of coagulation disturbances

The commonly reported **symptoms** of abnormal coagulation are:

- Unabated bleeding from the bite site,
- Bleeding from the sites of minor cuts, scratches or grazes, including those that can occur if the patient collapses and loses consciousness after the bite,
- Spitting or vomiting of blood,
- Bleeding from the gums and the nose.

Clinical **signs** of coagulopathy include:

- A positive 20WBCT (the blood is unclotted at 20 minutes),
- Bite site or venepuncture ecchymoses,
- Haematemesis,
- Haemoptysis,
- Epistaxis,
- Haematuria,
- Haemoglobinuria,
- Menorrhagia (at any age) or retroplacental bleeding (pregnant women),
- Retinal or subconjunctival haemorrhage,
- Bloody diarrhoea or per rectal bleeding or malaena,
- Prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT),
- Fibrinogenaemia and grossly elevated FDP levels,
- Thrombocytopenia,
- Intracranial bleeding (may appear like a stroke; leading to coma and death).

Monitoring of haemostasis in rural health centres

Rural health centres in Papua New Guinea do not generally have access to the resources of pathology clinics in urban centres, and cost means that even in urban hospitals many laboratory tests are either unavailable or uneconomical on the basis of cost.

The most important non-laboratory means of monitoring the haemostatic integrity of a patient with suspected envenomation in a rural aid post or health centre is to properly perform the 20WBCT to determine whether or not the blood of the patient is coagulable, both upon admission and over the time that the patient remains under care.

In a rural environment the 20WBCT, therefore, has two critical roles:

- **As a specific and absolute indication for administration of appropriate antivenom** in a patient suspected of having been bitten by a venomous snake;
- **As a simple, rapid and effective test** of the coagulation status of the patient.

An appropriate simple plan for the use of the 20WBCT in the management of snakebite would be to:

1. Perform a 20WBCT on all suspected snakebite patients immediately upon presentation.
2. If the 20WBCT is positive (blood is unclotted at 20 minutes):
 - ? Administer appropriate antivenom without delay.
 - ? Wait six (6) hours before repeating the 20WBCT to assess coagulability.
 - ? If the patient continues to demonstrate frank bleeding, more antivenom may be needed within 1-2 hours of the first ampoule (the 20WBCT can be repeated to confirm the presence of persistent coagulopathy).
 - ? If the 20WBCT is still positive after 6 hours, consider giving more of the appropriate antivenom.
3. If the 20WBCT is negative (blood is clotted at 20 minutes) and the bite occurred <2 hours previously:
 - ? Wait one (1) hour and repeat the 20WBCT.
 - ? Observe hourly for signs of envenomation over 24 hours and repeat the 20WBCT after a further six (6) hours.
 - ? If signs of envenomation develop, treat with the appropriate antivenom.
4. Repeat the 20WBCT every six (6) hours after any antivenom until the result of the test is negative, i.e.: the blood shows some clot formation at 20 minutes, and there is no evidence of bleeding.

In conjunction with using repeated 20WBCTs to assess whether or not the blood is clotting, and if antivenom has restored haemostasis, it is also important to:

- Maintain strict hourly observation and assessment of the patient in accordance with a treatment and nursing plan.
- Ensure that both the signs that are present, and the signs that are not present at each examination are recorded on the patient's observation and treatment chart, because this sequential process will tell you whether the patient is improving or deteriorating.

- Monitor blood pressure, heart rate, respiratory rate and depth (and peripheral oxygen saturations, if possible) hourly; temperature can be measured 4-hourly.
- Minimise the risk of bleeding and ecchymoses at venepuncture sites by considering the use of a second i.v. cannula (inserted in the opposite arm) to draw blood samples.
- Treat shock with IV fluid (normal saline, Hartmanns, or colloid).

Treatment Strategies

Disseminated intravascular coagulopathy (DIC), involving defibrination and consumption of clotting factors, is the most commonly encountered disturbance of haemostasis following snakebite in Papua New Guinea.

In Milne Bay, Central, Gulf and Western provinces, the most common cause of snakebite-related DIC with defibrination is the Papuan taipan (*Oxyuranus scutellatus canni*).

Reversal of coagulation disturbances with antivenom

The **first and most important step** in the treatment of coagulopathy after snakebite is the earliest possible administration of the most appropriate antivenom.

The selection and use of antivenom is discussed in detail in Chapter 11.

Antivenom is necessary in order to neutralise the toxins that catalyse the enzymatic reactions of the coagulation pathways that produce catastrophic thrombin overproduction, defibrination and clotting factor consumption. Until the toxins responsible for coagulopathy are neutralised, the patient remains at significant risk of haemorrhage.

Use of FFP and other blood products

Blood products such as fresh frozen plasma (FFP), cryoprecipitate and fresh whole blood **should not be used** to treat snake venom-induced blood loss **until after** coagulation is restored with the administration of appropriate antivenom.

Administration of FFP and other blood products to a patient with un-neutralised circulating snake venom toxins is potentially dangerous because:

- The addition of new clotting factors provides new substrates and cofactors for use in the uncontrolled overproduction of thrombin.
- It increases the degree of fibrinolysis and contributes to worsening of the coagulation defect rather than its repair.

The only circumstances under which FFP, or any other blood product, should be given are:

- **After antivenom administration** has been shown to have neutralised the circulating haemostatic toxins and where bleeding has stopped but circulating clotting factor levels are slow to rise back to normal levels, perhaps as a result of impaired liver function, or protein malnutrition.
- In cases that involve severe spontaneous bleeding where antivenom has already been given, but the immediate bleeding tendency is life threatening.

Remember: If you give FFP or other blood products to a patient who has not received enough antivenom to neutralise the circulating procoagulant toxins, you potentially contribute to a worsening of the coagulopathy rather than an improvement!

Treating other effects of envenomation

Dr Kenny Limbo Aaron, David Williams and Dr Simon Jensen

Introduction

Papuan taipans (*Oxyuranus scutellatus canni*), death adders (*Acanthophis* spp.) and Papuan blacksnakes (*Pseudechis papuanus*) are the most dangerous snakes along the Papuan coastline. Although the Papuan blacksnake is rare, the Papuan taipan is very common in parts of Milne Bay, Central, Gulf and Western provinces, and is the commonest venomous snake implicated in cases of snakebite. Deaths adders are widespread throughout mainland Papua New Guinea. The small-eyed snake (*Micropechis ikaheka*), brown snake (*Pseudonaja cf. textilis*) and mulga snake (*Pseudechis cf. australis*) are also considered dangerous, but the incidence of bites by these snakes is not high and we know relatively little about them because not many studies have been done on these snakes in Papua New Guinea. Therefore, this section will mostly cover the effects of bites associated with the first three snakes. We will discuss the following effects:

1. Myocardial effects.
2. Rhabdomyolysis (muscle necrosis).
3. Acute renal failure.
4. Haematological effects.

We know that Papuan taipan (*Oxyuranus scutellatus canni*) venom contains other toxins apart from the major components, responsible for neurotoxicity and bleeding problems (coagulopathy). While death adder (*Acanthophis* spp.) venom is not known to cause any bleeding abnormalities, it may have other toxins, which may or may not be clinically significant; because there has been little research on PNG snake venoms, there is nothing much available in the current literature. The Papuan black (*Pseudechis papuanus*) has toxins causing neurotoxicity and a weak coagulopathy, which is associated more with platelet inhibition and anticoagulation than with thrombin activation and fibrinolysis.

Myocardial Effects

Symptoms and signs of myocardial effects

Rural health centres that lack the ability to monitor cardiac function by ECG monitoring or recording will not be able to detect some specific myocardial problems. It is important, however, to recognise some basic changes in cardiac function:

Bradycardia

The normal range for resting heart rate for an adult is 55-75 beats per minute (bpm). Generally speaking, a resting heart rate of less than 45-50bpm indicates bradycardia. The resting heart rate of a patient depends on the following factors:

- Age – faster in children and infants; faster again in older adults after middle age.

- Fitness – the resting heart rate is lower in fitter individuals.
- Co-morbidities (as below).

Moderate to severe bradycardia in an adult is indicated by a rate of less than 35 bpm (under 50bpm for a child, 80bpm for an infant). It is not necessarily a problem on its own, unless the peripheral perfusion is affected (end-organ perfusion), the blood pressure is low, or there is a clear conduction defect.

Tachycardia

A resting heart rate of more than 80 beats per minute indicates tachycardia in an otherwise well adult. Sinus tachycardia is common in snakebite patients, especially after Papuan taipan (*Oxyuranus scutellatus canni*) bite, and may be over 120bpm. Other contributing factors are:

- Anxiety.
- Co-morbidities – many acute and chronic medical conditions affect the resting heart rate; previous myocardial infarction, rheumatic heart disease and other valve disease; severe pulmonary disease, such as bronchiectasis, extensive pulmonary Tb, chronic obstructive lung disease; anaemia; dehydration from diarrhoea and vomiting; febrile illness and infections, eg. malaria, pneumonia; pregnancy.

Hypertension

The normal range for blood pressure for an adult is

- Systolic 100-130
- Diastolic 60-80

The exact pressure will depend on factors such as:

- Co-morbidities (as above).
- Age – lower in younger individuals.
- Sex – lower in women (SBP of 90 is considered normal in a young woman).
- Pregnancy – BP lower, especially in the second trimester.

A systolic blood pressure of more than 140-150/90 implies mild hypertension, 170-180/100 moderate hypertension, 200+/120 severe.

Hypotension

A diastolic pressure below 90 mmHg indicates hypotension, and in more severe cases the diastolic pressure can be less than 50 mmHg.

Electrocardiographic Findings

The commonest reported abnormal ECG findings are septal T-wave inversion, sinus bradycardia, atrioventricular block and other conduction defects. These are especially associated with bites by Papuan taipans (*Oxyuranus scutellatus canni*). Most venomous snakes in PNG may have myotoxic venom components capable of causing myocardial cell damage, but studies done have been inconclusive. The creatinine phosphokinase (CK) enzyme levels are high in some patients, but this is more likely to be due to rhabdomyolysis (skeletal muscle damage) than to myocardial damage. The cardiac enzyme troponin T, however, is a cardio-specific enzyme, which is released when heart muscle cells are damaged. It would seem likely that appreciable increases in the blood level of this enzyme would be indicative of

myocardial venom effects. However, serological studies from those patients with ECG abnormalities have shown no consistent relationship between troponin T and ECG changes.

There are some concepts put forward to explain the ECG changes seen in snakebite patients, but none of these have been universally accepted:

- Directly acting cardiotoxins (such as the myocardial Ca^{2+} channel blocker, taicatoxin) in venom causing myocardial damage and suppression of myocardial function.
- Myotoxins causing rhabdomyolysis and myocardial damage.
- Coronary vasospasm leading to myocardial ischaemia.
- Coronary artery thrombosis, especially in patients with a consumption coagulopathy, leading to coronary occlusion.
- Haemorrhagin (a toxin) causing myocardial haemorrhage.
- Electrolytes abnormalities causing electrical changes.
- Severe hypotension and/or respiratory failure causing hypoxia, leading to coronary insufficiency.
- Cardiac autonomic nervous supply disturbance.

A myotoxin (mulgatoxin) from the Australian mulga snake (*Pseudechis australis*) is known to cause both rhabdomyolysis and myocardial damage. A very closely related variant of this species occurs in Western province and neighbouring Papua. Papuan taipan (*Oxyuranus scutellatus canni*) venom does contain a potent voltage-dependent Ca^{2+} channel blocker (taicatoxin) that is specific to myocardial VDCC's as well as Ca^{2+} -dependent K^+ channels in brain tissue. Whether or not this toxin is actually responsible for some of the electrocardiographic changes seen in taipan bite patients is unclear. Death adder (*Acanthophis* spp) venoms are unlikely to contain a similar toxin, but phospholipase A2 toxins are present in death adder venom, and the diversity of targets that these toxins have means that it is possible some might, one day, be found to cause myocardial effects.

Most experts believe that the ECG changes seen especially in patients bitten by taipans may be related to the toxin causing myocardial function suppression rather than direct damage. As explained above it may also be related to the actions of taicatoxin (calcium channel blocker) in taipan venom or to an abnormal autonomic nervous response to the general pathophysiology. The current belief is that taipan venom causes no direct myocardial damage.

Jensen (unpublished case) noted that a 35 year old man, who presented in respiratory failure more than 16 hours after a Papuan taipan (*Oxyuranus scutellatus canni*) bite, had an irregular, narrow complex (supraventricular) tachycardia of up to 140bpm, possibly atrial fibrillation, with a blood pressure in the normal range, and without apparent ST segment changes (no 12-lead ECG was available). This persisted after intubation, with satisfactory oxygenation and ventilation, opiate analgesia and sedation, and an initial ampoule of CSL polyvalent antivenom. A second dose, this time of CSL taipan antivenom, led to a fairly prompt reduction in the heart rate; within 1 hour he was in sinus rhythm at around 80bpm and remained so thereafter. No CK results are available because of a reagent shortage.

Treatment considerations

Rural health centres are not equipped to deal with serious electrocardiographic disturbances and patients with severe detectable rate and rhythm disturbances should be referred to a larger hospital, such as PMGH in Port Moresby, for treatment and monitoring.

Shock and hypovolaemic disturbances should be treated with appropriate IV fluids, preferably crystalloid (normal saline or Hartmanns), with urine output monitoring and central venous pressure monitoring if possible, if there is co-existent renal failure or other serious complication of envenoming.

Patients with marked bradycardia, especially with associated poor peripheral perfusion (can occur with a normal blood pressure) or hypotension can be treated with atropine (0.02 – 0.05 mg/kg children; 0.3 - 3 mg adults). If persistent after IV fluid resuscitation, inotropic drugs such as dopamine may be useful for hypotension (also useful for bradycardic patients who do not respond to atropine), and vasodilators such as hydralazine or GTN might be useful for treating hypertension (though it is seldom severe, or persistent, enough to warrant intervention).

Rhabdomyolysis

Mulga snakes (*Pseudechis cf. australis*) and the small-eyed snake (*Micropechis ikaheka*) have specific myotoxins that cause rhabdomyolysis. In other species, phospholipase A₂ toxins have been long associated with rhabdomyolysis, leading to varying degrees of myoglobinuria, tubular necrosis of the kidneys and acute renal failure.

Rhabdomyolysis has been reported after bites by Papuan taipans (*Oxyuramus scutellatus canni*), and should be expected after bites by Papuan blacksnakes (*Pseudechis papuanus*). Although a species of death adder (*Acanthophis* spp.) from the highlands of Papua has been shown to produce a myotoxin (Acanmyotoxin 1), clinical myotoxicity has not yet been reported among patients bitten by death adders in Papua New Guinea.

Muscle cells contain a pigment called myoglobin that is similar to haemoglobin, although not the same functionally or structurally. This pigment is released from damaged muscle in large quantities and can cause indirect nephrotoxicity and renal tubular damage by blocking kidney nephrons, leading to acute renal failure via acute tubular necrosis, as well as having direct tubular toxicity. Acute renal failure is a common complication in snakebite patients admitted to PMGH.

Elevated creatinine phosphokinase (another enzyme liberated from inside damaged muscle cells) is elevated in many snakebite patients and is a clear indication that some muscle damage is present. There are also variants of this enzyme liberated when the myocardium is damaged, and without knowing exactly which isoenzyme variant is being released, this can lead to confusion over whether or not the damage is skeletomuscular or myocardial in nature. If troponin T levels are normal in the presence of elevated CK, then rhabdomyolysis is the likely cause.

What is the clinical importance of rhabdomyolysis in snakebite patients?

1. Rhabdomyolysis causes myoglobinaemia and myoglobinuria, resulting in kidney damage that leads to a degree of acute renal failure – a potentially life-threatening condition.
2. Electrolyte abnormalities also occur and these can have very serious, mainly cardiac effects.
3. Massive muscle necrosis can occur and may be debilitating, prolonging recovery, which is however, eventual.

Symptoms of Rhabdomyolysis

- Generalized muscle pain or tenderness ('aching muscles') is usually reported by the patient within 3-4 hours of the snakebite. In the case of the Papuan blacksnake (*Pseudechis papuanus*) there may also be bite site pain.
- Weakness of the limbs (care that this might indicate a degree of neurotoxicity, so check for ptosis as well).
- Complaints of discoloured urine.
- There may also be bilateral renal angle pain.

Signs of Rhabdomyolysis

From a practical perspective, the following may be the only detectable signs:

- Discoloured dark brown urine (often described as being 'Coca cola coloured') that may appear 'stringy' if left to stand; will test positive for blood on the urine dipstick, with no red cells seen in the urine on microscopy (unless there is co-existent coagulopathy).
- Proteinuria (measured by 'dipstick').
- Hyperkalaemia (elevated serum potassium level), with ECG changes if the level rises over 7 mmol/l – tall, peaked T-waves and a prolongation of the QRS duration beyond 0.12 s; progresses to SA node and AV node impairment with bradycardias or life-threatening ventricular dysrhythmias as the level rises much further.
- Fluid imbalance: a significant reduction in urine output when there is adequate fluid input (by IV or by mouth), blood pressure and oxygenation, may be indicative of renal impairment.

Laboratory findings

Many of the important tests for rhabdomyolysis are unavailable in PNG at the present time, and certainly in rural health centres, definitive tests are not available. If tests are available, the following indicate rhabdomyolysis:

- Elevated creatine phosphokinase (CK) levels (levels > 250 IU/L)
- Elevated serum creatinine levels (an increase > 0.2 mmol/L)
- Elevated serum myoglobin (levels > 80 ng/ml)
- Elevated aspartate transaminase (AST) (levels >50 IU/L)

Treatment

The most important treatment of snake venom-induced rhabdomyolysis is the neutralisation of the circulating toxins with appropriate antivenom.

Very little other treatment is possible in a rural health centres, although it is important to:

- Maintain proper fluid load and hydration, but avoid fluid overload, which can lead to pulmonary oedema, even without co-existent renal failure (this may be indicated if a patient receiving high volumes of fluids becomes breathless); up to 1000 ml/hr for the first 4 hours, then reduce to a level that gives the required urine output.
- Maintain a urine pH>7 (this may be on your urine dipsticks), since myoglobin is more toxic at a lower pH; 50 mmol/hr for the first hour, then 30 mmol/hr; beware that this can worsen hypocalcaemia, resulting in abdominal pain, skeletal muscle fasciculations,

convulsions, and ECG changes (prolonged QT interval) due to severe hypocalcaemia in patients whose underlying cause of renal impairment is rhabdomyolysis.

- If fluid replacement (and blood pressure and oxygenation) is adequate, but moderate to severe renal impairment is present (oliguric urine output < 0.5 ml/kg/hour) give 40 mg frusemide over 2-3 minutes. If urine output does not improve to at least 40 ml/hour, then give a second dose of 100 mg over 20 minutes; a third dose of 200 mg over 40 minutes may be given if there is certainty about the adequacy of the fluid status of the patient, but persistent oliguria, or the patient is likely to have pulmonary oedema (and not pulmonary aspiration). Ideally the urine output should be maintained at 2 ml/kg/hour.
- If frusemide does not improve urine output, then a **single dose** of 200 ml of 20% mannitol IV over 20 minutes may be given. It is important that you **do not give more than one dose** of mannitol, as this can precipitate dangerous fluid electrolyte imbalances once it causes a diuresis.

Additional considerations

In Papua New Guinea, an observation of dark coloured urine is often interpreted as haematuria or haemoglobinuria, when myoglobinuria is more likely. There are no dipstick tests that distinguish directly between haemoglobinuria and myoglobinuria; however, if muscle weakness, pain or tenderness is reported, then myoglobinuria is the more likely diagnosis.

In facilities with a microscope, haematuria (red cells in the urine) can be confirmed by examination of a centrifuged sample under the microscope.

It is important to understand that patients with profound rhabdomyolysis may take many weeks to recover their muscle strength, and that while physiotherapy during the course of the myolysis can be extremely painful, physiotherapy during recovery is important to healing.

Acute Renal Failure

Acute renal failure with electrolyte imbalance is a major cause of morbidity and prolonged hospital stay in snakebite patients. In fact, a high percentage of snakebite patients develop renal failure, with some requiring peritoneal dialysis. Snake venoms can induce renal failure in several ways:

- Direct nephrotoxicity: venom can directly damage the renal glomeruli and tubules, and patients develop acute tubular necrosis and renal failure.
- Myoglobinuria, as discussed above, can also cause acute renal failure.
- Immune-mediated renal damage, especially by the humoral mechanism, is also possible.
- Pre-hospital renal failure is likely in those patients who are kept in the rural health centres on a nil-by-mouth regime without intravenous fluids, and also in those who develop renal insufficiency secondary to prolonged hypotension or hypoxia. Snakebite patients need good hydration in order to maintain an optimal urine output and renal function. Snake venom toxins are also cleared from the body in urine, so a higher output may help to remove circulating toxins.
- In those patients with a severe coagulopathy (defibrination syndrome or DIC), fibrin strands and fibrin degradation product (FDP) deposition in glomeruli, or thrombosis of renal vessels, can cause renal failure.

Acute renal failure is a serious, potentially life-threatening condition. In the study of snakebite mortality that was conducted among patients admitted to the PMGH ICU between January

1992 and December 2001, renal failure was a direct cause of death in 10% of the cases, and was a contributing factor in another 16.7% of fatalities.

Patients with moderate to severe renal failure need urgent medical care in a high dependency or intensive care facility, and patients who develop signs and symptoms of renal failure in a rural health centre should be transported to a larger hospital as soon as possible.

Symptoms and signs of developing renal failure

In a rural health centre setting, where there are no laboratory facilities, the diagnosis of renal impairment is seldom straightforward. The following symptoms may indicate a developing renal insufficiency:

- A greatly reduced urine output despite adequate hydration, oxygenation and blood pressure and the use of an IDC. A satisfactory output is >35-45 ml/hour; if the output drops to < 0.5 ml/kg/hr, this indicates oliguric renal impairment. Anuria is a complete lack of urine production, and therefore a very serious condition.
- Development of a syndrome of clinical uraemia featuring:
 - ? hiccups;
 - ? nausea and vomiting;
 - ? drowsiness;
 - ? confusion;
 - ? coma;
 - ? muscle twitching, 'flapping' tremor or convulsions;
 - ? pericardial friction rub or evidence of a pericardial effusion;
 - ? development of fluid overload;
 - ? symptoms suggestive of hyperkalaemia, such as arrhythmias.
- Hypovolaemia: defined by postural hypotension (a reduction in BP upon standing; supine hypotension comes later), cool peripheries, sunken eyeballs (especially children), dryness of the mucosal tissues, loss of skin turgor and 'empty' neck veins.

Treatment in a rural health centre

A patient who is developing renal failure needs to be evacuated to a larger medical facility as a matter of priority.

There are some steps that can be taken at the health centre that may be helpful:

- Fluid challenge: Give 1-2 litres of isotonic (normal) saline over 1-2 hours with close observation of their BP, jugular venous pressure and respiratory rate. Stop the challenge if the vertical height of jugular venous pulsation reaches 6-8 cm above the sternal angle, with the patient reclining at 45 degrees, or if respiratory distress develops.
- After the fluid challenge, continue to maintain an adequate fluid load and hydration, but **avoid fluid overload**, which can lead to pulmonary oedema and other serious complications (this may be indicated by breathlessness in a patient receiving a large volume of fluids).
- Correct hyperkalaemia: bradycardia (or rapid tachycardia) and/or shortness of breath – implies respiratory compensation for a metabolic acidosis, which is usually accompanied by hyperkalemia; there may also be accompanying pulmonary oedema; the following medications should be given/commenced in this order:
 - ? 10 ml of 10% calcium gluconate IV over 2 minutes, while monitoring heart rate and rhythm; this dose can be repeated up to 3 times every 30-60 minutes.

- ? 50 ml of 50% dextrose, with 10 units of soluble insulin (may not be required in the patient who does not have diabetes), IV over 1 hour; monitor the blood sugar hourly for the next 4 hours.
- ? 1 ml/kg (1 mmol/kg) of 8.4% sodium bicarbonate given **slowly** over 30 minutes, but be cautious as this may cause abdominal pain, skeletal muscle fasciculations, convulsions, and ECG changes (prolonged QT interval) due to severe hypocalcaemia in patients whose underlying cause of renal impairment is rhabdomyolysis.
- ? Salbutamol, 5-20 mg nebulised (or by Ventolin inhaler).
- ? Increase the IV fluid load (provided the patient is making SOME urine), accompanied by IV frusemide (40-80 mg IV over 5-20 minutes).
- ? Rectal or oral sodium resonium resin will be required (10-15 g tds).
- ? Stop any K⁺-containing medications or infusions, and restrict dietary intake of K⁺ (eg. bananas); stop K⁺-sparing diuretics.
- If fluid replacement (and blood pressure and oxygenation) is adequate, but moderate to severe renal impairment is present (oliguric urine output < 0.5 ml/kg/hour) give 40mg frusemide over 2-3 minutes. If urine output does not improve to at least 40 ml/hour, then give a second dose of 100mg over 20 minutes; a third dose of 200 mg over 40 minutes may be given if there is certainty about the adequacy of the fluid status of the patient, but persistent oliguria, or the patient is likely to have pulmonary oedema (and not pulmonary aspiration). Ideally the urine output should be maintained at 1-2 ml/kg/hour.
- If frusemide does not improve urine output, then a **single dose** of 200 ml of 20% mannitol IV over 20 minutes may be given. It is important that you do not give more than one dose of mannitol as this can precipitate dangerous fluid electrolyte imbalances once a diuresis occurs.

Haematological Effects

Coagulopathy and neurotoxicity are the most common pathophysiological changes seen in most snakebite patients in Papua New Guinea, and they are covered widely in this Handbook by other authors. Apart from coagulopathy, snake venoms may also cause other pathophysiological changes in the blood and blood vessels:

1. Haemolysis (breakdown of red blood cells).
 - (a) Microangiopathic haemolysis: Destruction of red blood cells in the microvasculature (capillaries and arterioles) due to a change in their shape and size brought about by venom components. Prothrombin activation and fibrinolysis, common in Papuan taipan envenomation, leads to accumulation of fibrin degradation products (FDP). The deposition of fibrin strands in small vessels can contribute to haemolysis by catching red cells as they pass.
 - (b) Direct attack on the red blood cell phospholipid bilayer, leading to cell damage and haemolysis. Sphero-echinocytic changes in red cell morphology have been observed after a taipan bite in Australia and may be due to either phospholipase A₂ or phospholipase B.

Haemolysis is evident by a falling haemoglobin level, increased bilirubin level and haemoglobinuria.

2. Platelet abnormalities:
 - (a) Vascular endothelial damage, leading to microthrombosis and platelet consumption, may occur after the bites by some Papua New Guinean snakes.

- (b) Most patients have a normal platelet count, but if they continue to bleed, this may suggest that some component of the venom toxin is suppressing the normal function of the platelets. Platelet dysfunction is a common concomitant finding in snakebite patients with coagulopathy.
- (c) Thrombocytopenia, due to platelet aggregation inhibition and persistent bleeding, may occur in some snakebite patients many hours after a bite, and may be first noticed when the patient experiences epistaxis.

Treatment issues

The issue of using blood products in the treatment of coagulopathy is dealt with in Chapter 9.

Heparin and antifibrinolytic drugs have no place in the treatment of coagulopathy in Papua New Guinea. Heparin may precipitate further bleeding and must not be used.

Local effects of snakebites

The majority of patients with snakebite experience few if any local effects from the bite itself.

Local pain

Local pain has been reported after bites by death adders (*Acanthophis* spp.) and is a particular feature of bites by blacksnakes (*Pseudechis* spp.) in Australia, although it is poorly documented in Papuan blacksnake (*Pseudechis papuanus*) envenomation. Local pain and swelling has been reported after envenomation by the small-eyed snake (*Micropechis ikaheka*).

If necessary, pain management should be dealt with cautiously. Sedatives or other agents that affect consciousness should be avoided if possible. If pain medication is considered necessary then consider:

- Paracetamol suppositories or crushed tablets via an orogastric tube.
- Codeine.

Non-steroidal anti-inflammatory analgesics, especially aspirin, should be avoided in the case of snakebite where coagulopathy may occur, or is already present.

Local tissue effects

Some degree of swelling, oedema, and ecchymoses may be present after the bites of Papua New Guinean snakes. Bruising to the bite site may be either the result of the trauma caused by the bite itself, especially if the snake was large. Small-eyed snakes (*Micropechis ikaheka*) may bite and grip the victim for some time before either letting go, or being kicked free. In these cases the bite site bruising may be distinctive.

Early coagulopathy may also result in local ecchymoses at the bite site, but is often associated with oozing of blood from the punctures. Mild to moderate localised swelling may cause discomfort that can be best managed with paracetamol, elevation and cold packs.

Most snake venom related swelling or oedema should subside within 5-7 days without requiring further treatment. In a few cases more significant local injury may occur, including the formation of haemorrhagic bullae containing lysed cells and blood. This has been seen after bites by Australian species of blacksnake (*Pseudechis* spp.) and may therefore also occur

after bites by either Papuan blacksnakes (*Pseudechis papuanus*) or New Guinean mulga snakes (*Pseudechis cf. australis*).

Local swelling and oedema may also result from ischaemic injury caused by the prolonged use of homemade tourniquets from materials such as rubber tyre inner-tubes, grass fronds, rope or electrical wire. Very severe cases of ischaemic injury can lead to amputation.



FIGURE 1: Local swelling, ecchymoses and haemorrhagic bullae after the bite of a 30 centimetre spotted blacksnake (*Pseudechis guttatus*) from Australia. It is possible that similar local injury could result from bites by Papuan blacksnakes (*Pseudechis papuanus*) or New Guinean mulga snakes (*Pseudechis cf. australis*). Treatment of this case involved surgical debridement of tissue

Secondary infection and sepsis

Clinical infection at a bite site is rarely present by the time a patient presents for medical attention. However, there is a tradition in PNG of giving every snakebite patient, and, in fact, every patient with trauma (sometimes even with blunt trauma), penicillin, and sometimes chloramphenicol as well. This may be in the form of a stat dose, or ongoing treatment for several days until someone notices and decides to cancel the order.

Various theories have been presented as to why this tradition exists. While there might be some sympathy for hope that this helps to prevent a subclinical infection developing into a clinical one (this is an animal bite, after all), there seems to be no research to support this. It is perhaps more likely is that there will be selective growth of resistant organisms. Certainly the excessive use of any antibiotic in the past, around the world, has led to the development of

antibiotic resistance. Similarly, there seems to be little logic, and no research, to support the idea that a single dose of penicillin will help to prevent the development of tetanus infection, though a tetanus vaccination soon after the bite might do so. Tetanus infection develops after germination of infecting spores, which are not sensitive to penicillin. Another adverse result of giving antibiotics unnecessarily is that the time, syringe, needle and dose of antibiotic are not being used for another patient who might stand to benefit from them more.

There are some special circumstances in which antibiotic therapy should be considered in snakebite:

- Established cellulitis around the bite site.
- A retained foreign body, eg. a fang, imbedded in the skin, indicating a deeper inoculation.
- Early collapse with a compound fracture, or a large laceration.
- Aspiration pneumonia (pulmonary aspiration with a fever).

Ideally, suitable microbiological samples should be obtained for culture before antibiotic therapy is commenced. If antibiotics are given, they should be given intravenously (or orally or via the NGT), not intramuscularly, especially when the patient is known to have a coagulopathy.

As with any wound, local wound care is **very** important in the prevention of infection, which is due not only to introduced bacteria, but also to local skin flora. This care should probably be delayed in the snakebite patient until they are at a facility where they can be given, and have been given, antivenom, where this is indicated. The basis for this assertion is that local cleaning may release more venom into the circulation; pressure bandaging should certainly not be removed to clean a wound.

Once it has been established that a patient has not been envenomed, or has been given the correct antivenom, and any coagulopathy has begun to resolve, the wound may be cleaned with saline, all foreign material removed, and Betadine applied to the skin of the immediate area. The wound will generally not need dressing, provided the patient maintains cleanliness of the area for the next few days. This procedure is very effective in preventing wound infections in other types of wound, and there is no reason to believe that it would not be applicable to snakebite as well. However, its efficacy compared to no wound care at all, which is the norm in PNG, has not yet been formally studied.

If a patient has not had a full tetanus vaccination course, and suffers snakebite, or any other trauma resulting in a break in the skin, they should receive a booster. If the person has never received the vaccination, they should be encouraged to have a full 3-dose course, with the subsequent doses being at 6 weeks and 6 months after the first.

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The role and use of antivenom in Papua New Guinea

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Introduction

Although antivenoms were first developed in France in 1894, Australia only starting using them in the 1930's and in PNG they were not available for routine use until the 1960's. During the early 1960's, PNG snakebite patients who developed paralysis often received up to four ampoules each^{1,2}. Since then antivenom use has become more frugal as antivenom costs have increased, although in the 1980's and early 1990's the majority of patients received at least one ampoule^{3,4}.

Our recent studies at PMGH indicate that the treatment focus has switched from high antivenom availability and usage with lower rates of ventilation, to one of low antivenom availability and consequent high rates of ventilation. This is despite clear evidence that snakebite deaths in PNG may be prevented by more widespread availability of antivenom⁵. Regrettably, PNG is not alone in the shortage of antivenom supplies, an international problem that is particularly acute in the Indo-Pacific⁶⁻⁸. This chapter will discuss the use of antivenom and highlight ways in which scarce supplies can be used most effectively.

As explained in Chapter 2 only six of the venomous snakes described in the PNG/Solomon Island archipelago are considered potentially lethal. Antivenom produced in Australia by CSL Ltd is the only specific treatment for envenomation by these venomous snakes. The decision to use antivenom should be based on the patient's history, examination and pathologic findings, and the type of antivenom used will depend on geographic, clinical and pathologic factors. Antivenom is only indicated if there is clear evidence of systemic envenomation, and it should be given by the intravenous route.

Initial recommended doses of antivenom are based on the average venom yields from each of the snakes concerned. There is evidence that these doses may be insufficient to reverse coagulopathy associated with the bites of several venomous snakes, notably the brown snake and the taipan. Larger initial doses should be considered if there is evidence of severe envenomation (multiple bites, rapidly progressive symptoms, large snakes) and the earlier it is given the better. Children should receive exactly the same dose as adults.

As antivenoms are animal products, acute and delayed adverse reactions (anaphylaxis and serum sickness) can occur and premedication should be considered. The patient should be monitored for their response to antivenom and multiple doses may be required. Other treatments such as clotting factor replacement, supplemental oxygen and, sometimes, mechanical ventilation may be indicated. All patients should receive appropriate tetanus prophylaxis and consideration should be given to antibiotic prophylaxis if the bite wound is contaminated.

Anticholinesterase inhibitors such as neostigmine and edrophonium might also be useful in the diagnosis and emergency management of death adder envenomation. When antivenom supply is limited, there may be some therapeutic value in the prolonged use of pressure-immobilisation bandaging for death adder bites.

Recent Snakebite Studies at PMGH

Together with Kenny Aaron and Gertrude Didei, we recently examined mortality and morbidity records at PMGH, and found that snakebite places a greater burden on PMGH ICU ventilators than all other conditions combined, and that the duration of dependency in cases of snakebite was significantly longer, undoubtedly adding to treatment costs. So far as the authors are aware, this represents the highest proportional ventilator load yet reported for snakebite in any hospital globally.

The second major finding related to the worsening outcomes for paediatric snakebite inpatients. A study of snakebite in children during the 1980's found that only 29.6% of children admitted to the PMGH ICU with envenomation required intubation; 91% received antivenom; and the case fatality rate was 7.7%⁹. In contrast 85.4% of children admitted to the ICU in this study were intubated and ventilated; antivenom use was only documented for 50% of the paediatric fatalities; and the paediatric case fatality rate was 14.6%. Ventilation was also a key feature in the management of the adult ICU admissions (See Chapter 13).

Increased reliance on ventilation may be a consequence of inadequate antivenom supplies due to rising costs influenced partly by the floating of the Kina, and its subsequent devaluation against the Australian Dollar^{6,7,10} (Table 1). The cost issue is even more extreme when considering direct antivenom purchases from Port Moresby pharmacies by individuals, when PMGH stocks have been depleted. Purchasing of less expensive monovalent antivenoms, in combination with appropriate diagnostic use of the simple 20WBCT and CSL's Venom Detection Kit (VDK), should not only generate significant unit cost savings, but also result in increased stock availability. It is hoped that this course will facilitate improved use of scarce antivenom based on more rational purchasing and prescribing habits.

Previous studies have found that delays in the administration of antivenom significantly increased the necessity to intubate snakebite patients at PMGH^{4,11}. Patients who received antivenom within four hours post-bite were:

- Three times less likely to require intubation;
- Exhibited more rapid resolution of neurotoxicity; and,
- Had shorter hospital stays.

Unfortunately, despite the fact that many cases in our study arrived at a health facility, either a peripheral clinic or PMGH itself, within four hours of the bite, very few received antivenom within that period (Table 2).

Despite clear guidelines for appropriate antivenom administration, their relevance becomes questionable in the absence of adequate antivenom supplies, and consequently antivenom is often reserved for moribund patients, or only partial ampoules given and its use may be delayed until significant deterioration has occurred^{12,13}. Given the concern about intracranial haemorrhage in the context of a bleeding diathesis, use of products such as fresh frozen plasma might appear reasonable. Blood products are, however, scarce, expensive and their value in the treatment of snakebite coagulopathy is unclear and potentially hazardous. Moreover, previous studies have demonstrated that systemic bleeding generally resolves rapidly after administration of appropriate amounts of specific antivenom⁴.

TABLE 1: The cost of antivenom purchased in PNG (1985-2003): comparison of prices (per ampoule) for CSL polyvalent and taipan antivenoms to the PNG Department of Health. Costs are given in PNG Kina (K) with equivalent Australian Dollar (A\$) prices (at effective K/A\$ exchange rates).

Year	Type Of Antivenom			
	<i>CSL Polyvalent</i>		<i>CSL Taipan</i>	
	K	A\$	K	A\$
1985 ¹⁰	212	300	173	245
1987 ¹⁰	367	580	352	556
1992	803	1180	730	1073
1995	1739	1758	1604	1620
1998	2352	1811	2338	1800
2000	2960	1835	1740	1079
2003	3575	1833	3075	1577

TABLE 2: Time of use of antivenom in the 60 fatal cases of snakebite treated at PMGH 1/1/92 – 31/12/01. This compares the time of arrival of patients at either a primary health clinic or Port Moresby General Hospital with the number of each subset who received antivenom at those times. Note that most patients who arrived in either the hospital or clinic within 4 hours of snakebite did not receive antivenom within those 4 hours.

<i>Time Post-bite (Hours)</i>	Clinic Records (n=29)		PMGH Records (n=60)	
	<i>No. of Patients</i>	<i>No. Given Antivenom</i>	<i>No. of Patients</i>	<i>No. Given Antivenom</i>
<4	24	1	19	2
4-10	4	1	22	10
>10	1	2	19	16
Total	29	4	60	28

Hospital care of snakebite patients

General/ supportive care

Once the patient reaches hospital, initial management consists of venous cannulation and resuscitation if required. Where possible, a careful history and examination should be undertaken with reference to the features of envenomation described above, as well as previous envenomations and allergies to antivenom or to horse serum. This will assist in diagnosis and aid decision-making with respect to definitive treatment, and is covered in more detail elsewhere in these notes. Samples for venom detection and for pathology testing should be obtained, and an attempt made to identify the genus of snake, if possible (see below).

When an intravenous line is *in situ* and antivenom and resuscitation facilities, including adrenaline, are assembled, then first aid measures may be removed. If the patient has not developed any symptoms or signs of envenomation, nor any indication of coagulopathy or myolysis on blood taken 4-6 hours after the removal of first aid (or after the bite if no first aid was used) then the patient has probably not sustained a significant envenomation, although delayed onset of symptoms (especially neurotoxicity) up to 24 hours after bites have been described. Overnight observation is desirable, especially if the patient comes from a remote area.

Ideally, envenomed patients should be admitted to hospital and observed for a period of at least 24 hours, depending on the clinical circumstances. Regular (i.e.: at least hourly) neurological observations should be performed and basic pathology studies (such as 20WBCT and Multistix urine tests for blood or protein) repeated regularly to monitor progression of the illness. The 20WBCT should be repeated as discussed in Chapter 9. After circulating antivenom has been neutralised, it may be several (4-6) hours before reconstitution of plasma clotting factors has occurred sufficiently to return clotting times towards normal. A lack of improvement in clotting times on retesting may therefore represent insufficient antivenom or insufficient time before re-testing. Improvement in clotting times may represent the efficacy of antivenom, or the natural history of the disease. Worsening of coagulopathy on testing, however, is an indication that circulating procoagulants remain un-neutralised, and that further antivenom is required.

The potential therapeutic value of pressure-immobilisation bandaging

Several studies suggest that there may be some therapeutic value in the prolonged use of pressure-immobilisation bandaging. Dr Struan Sutherland, who developed the technique in the late 1970's, noted that the monkeys who received this type of first aid for experimental tiger snake envenomation generally developed a less severe coagulopathy. In addition funnel-web spider venom-induced neurotoxicity was abrogated by pressure-immobilisation first-aid¹⁴. Building on these observations, Dr John Oakley, an Australian GP working at Rumginae Hospital in Western Province, examined the outcome of patients given prolonged PIB after death adder bites¹⁵. His retrospective, uncontrolled study suggested that prolonged use of PIB, followed by graded cautious release, was effective at managing most cases of death adder envenomation.

In John Oakley's study, which was conducted between 1994 and 1999, 44 patients with unequivocal signs of envenomation were all managed with pressure bandaging, strict bed rest and close observation. The bandages were kept in place for at least 24 hours and the graded release commenced when there were no longer signs of envenomation. Three cases (7%) required antivenom for severe central muscle weakness and there were no deaths. It is also

important to note that no significant local complications occurred as a consequence of the prolonged bandaging. Whilst not strictly comparable, from a series of 18 definite death adder envenomations managed at PMGH between 1990 and 1992, 13 (72.2%) received antivenom and 5 (27.7%) required intubation and ventilation¹⁶.

Thus, if antivenom is limited, prolonged use of pressure-immobilisation first-aid may help to reduce the severity of the neurotoxicity after death adder envenomation. Note that it is critically important to get pressure applied just right. It has to be firm, but not uncomfortable and should cover almost the entire limb – leaving enough space to regularly test capillary return to the toes or fingers. The place of the prolonged use of this technique after other PNG snakebites is less clear. This is because, generally speaking, local tissue damage due to the venom is least likely after death adder bites than after taipan, black snake and small-eyed snakebite.

Adjunctive Therapies

Other treatments such as analgesia (avoid sedating agents such as morphine if possible), plasma volume expanders and fresh frozen plasma may be required; but **blood products should only be given after antivenom** has been used and the coagulopathy has been arrested.

In severe envenomations resulting in respiratory compromise, supplemental oxygen and, sometimes, mechanical ventilation, are indicated. Incipient renal failure may be treated with volume replacement and diuretics, but dialysis may occasionally be required, particularly in cases where treatment has been delayed. Hyperkalaemia secondary to rhabdomyolysis may be treated with calcium, insulin and glucose, salbutamol, frusemide and IV fluids, and resonium.

All patients should receive appropriate tetanus prophylaxis (after resolution of coagulopathy) and consideration should be given to antibiotic prophylaxis if the bite wound is contaminated. Rarely, the snake's fangs may break and become embedded in the wound, acting as a foreign body and a nidus for infection. Crystalline penicillin is the first-line of treatment in such cases¹².

Anticholinesterases

(See Chapter 12)

Antivenom

Antivenom is the only specific treatment for effective bites by venomous PNG snakes. In Australia, prior to the availability of antivenom, death ensued in approximately 90% of taipan envenomations. The decision to use antivenom should be based on the patient's history, examination and pathologic findings, and the type of antivenom used will depend on geographic, clinical and pathologic factors as described above.

Indications for antivenom

Antivenom is indicated if there is specific evidence of **systemic envenomation**.

Such evidence includes specific symptoms or signs such as collapse, cranial nerve weakness, abnormal bleeding, generalised muscular pain and tenderness, or grossly discoloured urine (red or dark brown). Laboratory investigations consistent with systemic envenomation include incoagulable blood in whole blood clotting test (20WBCT)²¹, a grossly elevated serum creatine kinase level, haematuria, haemoglobinuria or myoglobinuria, or a positive SVDK test

on a urine sample in the presence of non-specific or specific symptoms or signs of envenomation.

If pressure-immobilisation first aid is in place, symptoms or signs of envenomation, including laboratory signs, may only become apparent when first aid measures are removed.

Puncture marks, and lymphadenopathy and other non-specific symptoms and signs of envenomation are not indications *per se*, for antivenom, as these can occur in bites from non-venomous snakes, or in cases where little or no venom is injected. Similarly, a positive SVDK result (see below) from a bite site is not in itself an indication for antivenom, as venom may be present on the skin or clothing, but not in sufficient quantity in the circulation to cause systemic envenomation. A positive SVDK result from a urine sample is an indication that venom is present in the circulation and that antivenom is indicated.

If the blood remains incoagulable (20WBCT positive) 6 hours after the first dose, a second dose of antivenom is indicated.

TABLE 3: Non-specific and specific signs of probable envenomation in approximate order of occurrence; these must be present in conjunction with a history of actual or suspected snakebite.*

Type	Indication
Neurotoxic signs and symptoms	Early – [1-3 hours] cranial nerve signs: such as droopy eyelids, double vision, reduced or paralysed eye movements, difficulty with swallowing, talking and tongue protrusion Late – [>3hrs] limb and respiratory muscle paralysis leading to respiratory failure
Haemostatic abnormality	Spontaneous bleeding from wound, gums, mouth, nose, vomitus, rectum/stool and urinary tract or evidence of non-clotting blood via the WBCT20
Cardiovascular abnormality	Shock, hypotension, cardiac failure, pulmonary oedema, arrhythmias and ECG abnormalities
Depressed consciousness	Including confusion and coma
Generalised rhabdomyolysis	Muscle aches and pains, red, brown, black or ‘Coca-cola’ urine
Likely renal failure	Uraemia, hypercreatininaemia, oliguria, and acidosis

* Adapted from:

Warrell, DA. (1990) Treatment of Snakebite in the Asia-Pacific region: a personal view. In: Gopalakrishnakone, P, Chou, LM. *Snakes of Medical Importance (Asia-Pacific Region)*, Venom and Toxin Research Group, National University of Singapore,
Warrell DA & Lalloo DG. (1996) Snakebite and its treatment in PNG, In: O’Shea M. 1996. *A guide to the snakes of Papua New Guinea*. Independent Publishing, Port Moresby, p23-30.

The **indications for antivenom are**, thus, specific symptoms or signs such as

- early collapse,
- cranial nerve weakness,
- abnormal bleeding,
- generalised muscular pain and tenderness,
- grossly discoloured urine (red or dark brown),

or the pathology test results of

- incoagulable blood, by the whole blood clotting test (20WBCT)²¹,
- a grossly elevated serum creatine kinase level,
- haematuria, haemoglobinuria or myoglobinuria, or
- a positive SVDK test on a urine sample in the presence of non-specific or specific symptoms or signs of envenomation.

Choice of Antivenom

Selecting the correct antivenom is crucial to the successful treatment of envenomation. Monovalent antivenoms are much less expensive than polyvalent antivenom, and are associated with a reduced risk of adverse antivenom reactions. Their disadvantage, however, is that they are only intended for use against the bites of a particular species, rather than all species (which is the advantage of polyvalent antivenom). Unless the precise identity of snake responsible for the envenomation can be confirmed, the use of monovalent antivenom can be hazardous.

If the identity of the snake cannot be determined, then the appropriate antivenom to use, in all circumstances, is CSL polyvalent antivenom.

There are ways in which the choice of antivenom can be narrowed down and two methods are discussed here.

Snake Identification

The difficulties of identifying snakes have been discussed in detail in Chapter 2.

Identification of the offending snake will aid in the choice of the appropriate antivenom and alert clinicians to particular features characteristic of envenomation by that species of snake. In many cases a snakebite victim will not have seen the snake, or only glimpsed it briefly as it fled after the bite. An identification of a snake made by a patient, or those accompanying them, should be treated with scepticism, although a clear description of the offending animal (such as describing a “blacksnake with a red back”: Papuan taipan) may assist you in narrowing the possibilities.

Even seemingly experienced snake handlers can misidentify some snakes. Identifications by the general public or by hospital staff are frequently unreliable, and a formal identification by a professional herpetologist is the ideal approach, but seldom available in Papua New Guinea.

It is possible to use of some basic information about the snakebite to make a presumptive identification with enough confidence to make prudent antivenom choices (*see algorithm table on next page*). For example, it is possible to split Papua New Guinea into three broad regions on the basis of the number of highly venomous snakes which occur naturally in

particular provinces, and then combine this knowledge with the clinical signs of envenoming that are present in order to select appropriate antivenom.

Algorithms, such as the simple one offered here, **must to be used with care**:

- You must ensure that the 20WBCT was properly performed to ensure a valid test result of either ‘positive’ or ‘negative’ for incoagulable blood.
- Any description obtained must be offered without prodding or suggesting answers, ie. ask only open-ended questions. For example, do not ask a patient/relative “*Did the snake have a red back*”, just ask “*What did the snake look like?*”.
- Ensure that the clinical signs have been properly elucidated, and use signs that you have observed or elicited, rather than less reliable symptoms reported by the patient/relative.
- Record the answers you reach for each question in the algorithm to ensure that the decision-making process is clear to you and to others who treat the patient.

Use the algorithm cautiously, and if you still have doubts, select the general purpose CSL polyvalent antivenom.

Presumptive selection of appropriate antivenoms

The following algorithm uses information about the snakebite in order to enable conservative selection of an antivenom product. This technique of antivenom selection is evidence-based, but should be used with care. *If you are in doubt about the identity of the snake after using this algorithm, and if it is available, you should use CSL polyvalent antivenom.*

1. Where in PNG did the bite occur?

- | | |
|---|---------|
| (a) MBAY, ORO, CENT, NCD, GULF, WEST? | Go to 2 |
| (b) MOR, SIM, E.HIGH, S.HIGH, W.HIGH, ENGA, SAND, E.SEP, MAD? | Go to 4 |
| (c) MAN, WNB, ENB, N.IRE, N.SOL? | Go to 6 |

2. What was the result of the 20WBCT?

- | | |
|--|---------|
| (a) Positive test (unclotted at 20 min.) | Go to 3 |
| (b) Negative test (clotted at 20 min.) | Go to 4 |

3. Was there a description of the snake that referred to it having “a red stripe on the back” or being a “blacksnake with a red back”?

- | | |
|---------|---|
| (a) Yes | CSL taipan antivenom
(Papuan taipan) |
| (b) No | CSL polyvalent antivenom
(Papuan blacksnake, brown snake or small-eyed snake) |

4. Are there observed or elicited signs of ptosis, diplopia, or other neurotoxicity?

- | | |
|---------|--|
| (a) Yes | Go to 5 |
| (b) No | Observe and reassess the patient hourly for 24 hours |

5. Is there generalised muscle pain, muscle tenderness or dark coloured urine?

- | | |
|---------|---|
| (a) Yes | CSL polyvalent antivenom
(Small-eyed snake) |
| (b) No | CSL death adder antivenom
(death adder) |

6. Did the bite occur in the ocean, close to the ocean foreshore or in a coastal river?

- | | |
|---------|---|
| (a) Yes | CSL seasnake antivenom
(Sea krait or true seasnake) |
| (b) No | Go to 4 |

Snake Venom Detection Kits

(See also Appendix: CSL Snake Venom Detection Kits)

Australia and Papua New Guinea are the only countries in the world that have potential access to commercially available snake venom detection kits. At the moment, these kits are not being used in Papua New Guinea, however this may change soon.

The introduction of snake venom detection kits (SVDK) will provide a major improvement in the ability to choose the most appropriate antivenoms. This will have several advantages including:

- Significantly reducing the costs of treating many snakebites.
- Increasing the purchasing power of health authorities so that more vials of appropriate antivenoms are available without necessarily spending more money.
- Improving the prognosis for patients through greater antivenom availability.
- Greater specificity and potentially reduced risks of adverse serum reactions.

SDVKs consist of a rapid two-step enzyme immunoassay in which wells are coated with antibodies to the major Australian snake venom groups. Venom from a bite site swab or a urine sample will react with the antibodies in one specific well, resulting in a colour change indicating the snake group involved. This information is used to help select the type of snake antivenom that may be required. Note that the primary purpose of the venom detection kit is not to decide whether envenomation has occurred (i.e.: whether antivenom is indicated), but to help to choose the appropriate antivenom if required:

- A positive SVDK result is not, in itself, an indication for antivenom.
- Venom detected at the bite site may be present in insufficient quantity in the circulation to cause significant illness.
- Venom detected in a urine sample indicates that venom is present in the circulation and that the indicated antivenom is the correct one to be given.
- A negative SVDK result does not mean that envenomation has not occurred; the venom may have been washed off or diluted at the bite site, or may not have reached the urine, but still be present in the circulation.

Bite site swabs are considered to be the most reliable sample for use with venom detection kits. Venom may also be obtained from clothing, or even from the fangs of the dead snake. Note that very high concentrations of venom in the sample may cause false positives, with multiple test wells turning blue, either simultaneously or sequentially. If this occurs, the sample should be diluted tenfold and the test repeated. Blood and urine samples may also be used in the venom detection kit, but are less reliable than bite site swabs. Urine, in particular, may be used if there has been some delay in presentation, if no bite site can be identified, or it has been washed. Blood (serum) is the least reliable.

The kit has 'built-in' positive and negative controls that need to be checked to validate the test results. In addition, after the final wash, the test wells need to be continuously observed for the **first well to turn blue**. Snake Venom Detection Kit results should be used in conjunction with other information (such as clinical presentation, knowledge of snakes in the geographic area, identification of snakes brought to hospital with the patient) to determine which antivenom to use if the patient is significantly envenomed.

If a reliable identification cannot be made, then polyvalent snake antivenom (or the appropriate combination of monovalent antivenoms for the locality) should be used.

Antivenoms for PNG snakes

At present only 6 of the 25 species of terrestrial elapids described in the PNG/Solomon Island archipelago are considered potentially lethal²¹ – the antivenom requirements for these major groups, together with sea snakes, are discussed in more detail below. However, it should be noted that there are a variety of other snake species of potential medical importance.

Firstly, the bite of non-venomous snakes may be confused with those of venomous species. Non-venomous species (See Chapter 2) include the tree and water pythons, ground and tree boas and file snakes. As the bitten patient may develop the non-specific symptoms of anxiety, breathlessness, dizziness, headache, nausea or vomiting, it can be difficult to exclude envenomation. Hence, even if the bite of a non-venomous snake is suspected, such cases should be managed as for a venomous snakebite until proved otherwise. Attention should, therefore, be paid to the specific indications for snake antivenom to avoid unnecessary antivenom use. Note that any animal (or human!) bite may be complicated by infection. This is an uncommon problem after snakebite in Australia but may be more frequent in PNG. This issue is discussed further in adjunctive therapies section above.

Secondly, a variety of species, classified as ‘mildly venomous rear-fanged snakes’, may cause troublesome local effects or pose a significant hazard in very young children. These include the mangrove, mud, water and cat (tree) snakes. It is unknown whether CSL antivenoms have any value in treating such cases, but as they are primarily arboreal or semi-aquatic species, significant bites are unlikely.

The third group, representing potentially dangerous ‘front-fanged terrestrial’ venomous snakes, includes many very poorly researched species. Some of these are known to be quite dangerous and others are suspected to be. This includes New Guinea forest snakes, the brown headed snake, the Solomon’s and Bougainvillean coral snakes, the Solomon’s small-eyed snake, the Australian small-eyed snake, the New Guinea crowned snake and Papuan whip snakes. In the absence of information about the VDK reactivity of these venoms and in cases of definite envenomation from one of these snakes (i.e.: satisfying one of other of the indications for antivenom described above, it is recommended that CSL polyvalent antivenom be given.

The following highly venomous snakes (*See Chapter 2 for further detail*) are capable of causing human deaths. The bites of any of these snakes can be treated with **CSL polyvalent antivenom**, although the monovalent antivenoms shown below are not only effective but much more cost efficient, and should be used if the identification is reliable and the particular monovalent antivenom is available:

Papuan Taipan (*Oxyuranus scutellatus canni*)

This nervous and highly venomous snake is only found in southern PNG from Milne Bay to Western province (including Daru Island). It also occurs in the Merauke region of Irian Jaya. It is the longest venomous snake in PNG and has the most efficient bite. The clinical syndrome includes neurotoxicity, coagulopathy and rhabdomyolysis. Prior to the development of antivenom, effective bites from taipans were almost invariably fatal. Papuan taipan venom is neutralised with **CSL Australian taipan antivenom** if given early after a bite, but antivenom efficacy declines as neurotoxicity becomes established. The reasons for this reduction in antivenom efficacy have been discussed at length in Chapter 3, and relate to the physiological nerve damage caused by the toxins, rather than actual inability of the antivenom to neutralise the venom itself.

Death adders (*Genus Acanthophis*)

The death adders are found throughout PNG to an altitude of 1800m as well as on Manam and Karkar islands in Madang Province, the island of Geelvinck Bay and those west of Vogelkop in Irian Jaya. They are readily identified by their short, squat, viperine appearance. They are ambush predators, and unlike most snakes, will not necessarily retreat from humans. They may therefore be trodden on or disturbed by the unwary, and bite defensively. The venom contains predominantly postsynaptic neurotoxins, with some mild anticoagulant and possibly myolytic activity (the latter two characteristics are not seen with most Australian death adders). At least one case of renal failure has been described after a PNG death adder bite. This venom's neurotoxicity is readily reversed with **CSL death adder antivenom**.

The Blacksnakes (*Pseudechis papuanus* and *Pseudechis cf. australis*)

Mulga snakes (*Pseudechis australis*) (also known as king brown snakes) are the largest venomous snakes in Australia and may reach 3 metres in length; however the New Guinean race is much smaller and rarely attains 1.3 metres. Large Australian specimens have had the highest recorded venom outputs of any snake. This species is only known from the far south-western corner of Western province and from adjoining southern Papua, but may eventually be found further east on the Oriomo plateau. The name "king brown" snake may lead to confusion and to the incorrect use of brown snake antivenom, and is therefore best avoided. The Papuan black snake (*Pseudechis papuanus*) is an uncommon cause of snakebite, and the species is rarely encountered. Its conservation status in the eastern two-thirds of southern PNG is unknown. No live or recently dead specimens have been collected in Central province since the early 1990's. Mulga snake and Papuan blacksnake venoms contain neurotoxins, myotoxins and mild anticoagulants that are neutralised by **CSL black snake antivenom**.

Brown snakes (*Pseudonaja cf. textilis*)

The eastern brown snake (*Pseudonaja cf. textilis*) has been recorded from Western, Central, Milne Bay and Oro Provinces of PNG, and from southern Papua. Bites are very uncommon and this is in marked contrast to Australia where brown snakes are responsible for the majority of snakebites and snakebite deaths. Coagulation disturbance is common in brown snakebites, but there exists the potential for significant neurotoxicity. Myolysis is not a feature of brown snake envenomation, although renal failure may ensue putatively as a result of direct nephrotoxicity. The possibility of direct cardiotoxicity has also been suggested, as several brown snakebite deaths have been associated with early cardiovascular collapse, but this is more likely due to the venom procoagulants causing temporary coronary artery blockage by thrombosis. The venom is neutralised by **CSL brown snake antivenom**, although recent Australian experience is that multiple ampoules may be needed in cases of profound coagulopathy.

The New Guinean small-eyed snake (*Micropechis ikaheka*)

The PNG small-eyed snake is distributed widely throughout PNG and neighbouring Irian Jaya at altitudes of 0–1500 m^{21,22}. It is also found on Karkar Island in Madang Province and on the islands of Geelvinck Bay and those west of Vogelkop in Irian Jaya. Although the species has been implicated in human deaths and serious illness, reports of bites are few²²⁻²⁵ and, in some cases, identification of the snake was unverified²³⁻²⁵. In one recent series²² of 11 cases with two fatalities, reliable attribution of bites to *M. ikaheka* was made by enzyme immunoassay of serum, bite site swabs and urine from victims. In these cases, typical symptoms of envenomation included neurotoxicity, generalised myalgia, spontaneous haemorrhage,

incoagulable blood and passage of dark urine. One of the victims who died had hypotension associated with untreated respiratory paralysis.

The New Guinean small-eyed snake (*Micropechis ikaheka*) is not related to the Australian small-eyed Snake (*Rhinoplocephalus nigrescens*). Although no specific antivenom exists for the bite of the New Guinean small-eyed snake *Micropechis ikaheka*, there are reports of some patients who appear to have benefited from treatment with CSL polyvalent antivenom, but not CSL death adder antivenom²². These observations are consistent with our recent *in vitro* and *in vivo* neutralisation studies²⁷ that found that CSL polyvalent antivenom and to a lesser extent, CSL Blacksnake antivenom, could neutralise this venom's toxicity. *In vitro* immunoreactivity tests suggest that the monovalent blacksnake antivenom component is the most active of the five monovalent components of CSL polyvalent antivenom. At this stage, **CSL polyvalent antivenom** is recommended as the antivenom of choice for New Guinean small-eyed snake envenomation.

Sea snakes (Family *Hydrophiinae* & *Laticaudidae*)

At least 20 species of sea snakes have been recorded in PNG waters, both coastal and estuarine. All sea snakes are dangerously venomous, with neurotoxicity and myolysis, leading to renal failure, being the major features. The bite itself is not particularly painful, and may go unnoticed, distinguishing it from envenomation by stinging fishes or jellyfish, both of which cause immediate, and often excruciating, pain. Bites may occur whilst swimming, on the beach or during fishing activities, as sea snakes may be caught in nets and bite when handled. It is rarely encountered as a medical problem in PNG and supplies of sea snake antivenom are very limited. Envenomation should be treated with **CSL sea snake antivenom**, but if this is not available, then CSL polyvalent antivenom may be useful. In the case of the latter, two (2) ampoules should be given initially.

Administration of antivenoms

Where there is clinical evidence of systemic envenomation, the most appropriate available antivenom should be administered as soon as possible. If the appropriate antivenom is not on hand, it will be necessary to either:

1. Obtain the appropriate antivenom from the closest source (perhaps a nearby health centre or hospital) or,
2. Transport the patient without delay to another health centre or to a hospital that does have stock of the appropriate antivenom.

Giving the wrong antivenom simply because it is the only one available may do more harm to the patient, and should be avoided. There have been a number of deaths in Papua New Guinea that were the result of patients having been administered the incorrect antivenom on the basis of misidentification by the bitten person or their relatives. This commonly occurs when health centre staff accept a claim that the snake responsible was a 'Papuan black' and give CSL Blacksnake antivenom, when in reality the species that caused the bite was a Papuan taipan.

Route of administration

Snake antivenoms are given by the intravenous route. Antivenoms that are given intravenously should be diluted in at least 100ml of either normal saline, 5% dextrose, or Hartmann's solution immediately prior to administration. If giving CSL polyvalent antivenom it is advisable to dilute 1 in 10 for adults, or 1 in 5 for children (to avoid fluid overload).

Premedication

Adrenaline

In rural health centres patients should be premedicated with subcutaneous adrenaline prior to the intravenous administration of antivenom.

Dosage: Adults: 0.25 mg subcutaneously
 Children: 0.005 mg/kg subcutaneously

Adrenaline premedication should never be given intravenously. This is to avoid hypertension in the coagulopathic patient with the potential for bleeding, as this has been documented to cause deaths from intracerebral bleeding. Similarly, it should not be administered intramuscularly, as this may also lead to hypertension, as well as to haematoma formation in the presence of coagulopathy.

Additional adrenaline should also be drawn up into a syringe and kept on hand for immediate use in the event of an early adverse antivenom reaction (see below).

Antihistamines and hydrocortisone

Although both antihistamine (typically Phenergan - promethazine) and hydrocortisone are traditionally used in the premedication of patients prior to antivenom administration, their use in Australia has now been widely discontinued.

There is no current proven benefit to giving either antihistamine or hydrocortisone as premedication before antivenom use. They do have a role in the treatment of allergy and this is discussed later.

Antivenom dosages

The following table gives the initial monovalent antivenom dosages for the bites of Papua New Guinean snakes. Additional doses may be required, so use this table as a guide only:

TABLE 4: Initial doses of antivenoms for snake bites. Use this information when the snake has been positively identified by SVDK, for example. Severe envenomation may require more than one dose of antivenom. Dosage for children is the same as that for adults. *If the snake is unidentified, use CSL polyvalent antivenom.*

Snake	Appropriate Antivenom	Initial Dose
PNG small-eyed snake (<i>Micropechis ikaheka</i>)	Polyvalent antivenom	1 vial
Papuan death adder (<i>Acanthophis spp.</i>)	Death adder antivenom	6,000 units (1 vial)
Papuan Taipan (<i>Oxyuranus scutellatus canni</i>)	Taipan antivenom	12,000 units (1 vial)
Eastern Brown snake (<i>Pseudonaja textilis</i>)	Brown snake antivenom	1,000 units (1 vial)
Papuan Black snake (<i>Pseudechis papuanus</i>)	Black snake antivenom	18,000 units (1 vial)
King brown (Mulga snake) (<i>Pseudechis australis</i>)	Black snake antivenom	18,000 units (1 vial)
Sea snake (multiple species)	Sea snake antivenom, or Polyvalent antivenom	1,000 units (1 vial)

One ampoule of CSL polyvalent snake antivenom (Australia/Papua New Guinea) contains:

Tiger snake antivenom	3,000 units	Taipan antivenom	12,000 units
Brown snake antivenom	1,000 units	Black snake antivenom	18,000 units
Death Adder antivenom	6,000 units		

Note: If stored at 2-8°C, antivenoms have a shelf life of three years; but they should not be frozen.

The initial doses of antivenom shown in Table 4 are based on the average venom yields from each of the snakes concerned. There is evidence, however, that these doses may be insufficient to reverse coagulopathy associated with the bites of several venomous species, notably the brown snake (*Pseudonaja cf. textilis*) and the Papuan taipan (*Oxyuranus scutellatus canni*). Larger initial doses should be considered if there is evidence of severe envenomation (multiple bites, rapidly progressive symptoms, description of large snakes).

The dose of antivenom for children should not be reduced according to their weight, since the amount of venom injected by the snake is independent of patient body size. Patients should be monitored for their response to antivenom, and additional antivenom may be required (See Table 3 for indications for repeated doses of antivenom).

Note: The antivenom requirements of patients will vary considerably. Some patients with minimal envenoming will require no antivenom, while more severely envenomed patients may require multiple doses of antivenom. Detailed information is packaged with the individual antivenoms.

Rate of administration

Administer the whole dose of antivenom (the contents of the entire vial) and diluent over a period of 30-60 minutes.

Early adverse antivenom reactions

Antivenoms are foreign proteins, and it is possible for a patient to experience a reaction to antivenom administration that can range from mild to severe. According to the manufacturer, adverse reactions to antivenoms can include:

Type of reaction	Frequency	Conditions
Hypersensitivity & skin	Common	Urticaria Rash Welts or local swellings Hypotension Bronchospasm
	Uncommon	Anaphylaxis Angioedema
Neurological	Common	Headache
Musculoskeletal	Uncommon	Arthralgia Myalgia
Gastrointestinal	Uncommon	Abdominal pain Vomiting
Cardiovascular	Uncommon	Chest pain Cyanosis
General	Common	Pyrexia
	Uncommon	Pain at the infusion site

If the patient reacts to the antivenom, the rate may need to be slowed or the infusion ceased temporarily. If the reaction is more severe, then treatment with adrenaline, antihistamines, corticosteroids, plasma volume expanders and β -agonists should be undertaken as required.

Skin testing for allergy to antivenom is not recommended, as it is unreliable and may delay urgent therapy. The decision to recommence antivenom should always be based on the clinical state of the patient. Special care needs to be taken if the patient has a known allergy to equine (horse) serum or to antivenom. Antivenom should not be withheld from these people; however it is important to have adrenaline and other drugs at hand in case they are needed, and to be in a situation where resuscitation and airway protection are immediately possible.

Issues surrounding the use of premedication

The issue of premedication has been controversial, and until recently, definitive evidence for its efficacy had been lacking. A randomised, double-blind, placebo controlled trial of the efficacy of low dose subcutaneous adrenaline to prevent acute adverse reactions to snake antivenom in Sri Lanka demonstrated a four-fold reduction in such reactions. No adverse reactions (such as intracranial haemorrhages) were observed in the premedicated patients²⁸. This study strongly suggests the efficacy and safety of low dose subcutaneous adrenaline.

Despite this good evidence, there are conflicting opinions about the role of adrenaline as a premedication before giving antivenoms. In Australia's toxinology textbook²⁹, Drs Struan Sutherland and James Tibballs considered the evidence available up to 2001 and concluded that "*premedication with subcutaneous adrenaline is recommended (0.25 mg for an adult, 0.005 mg/kg for a child) before antivenom therapy*". In contrast, in a recent review, Dr Bart Currie concluded: "*with the very low rate of severe reactions to antivenom seen in Australia . . . and the ability of emergency medicine physicians to adequately manage reactions that may occur, a policy of withholding premedication but always having adrenaline drawn up and ready is now recommended by many authorities and is policy in the Northern Territory*"³⁰. In the middle is Australia's antivenom manufacturer, CSL Limited (Product information: ANG/Polyvalent snake antivenom, 2000): "*Some authorities have advocated premedication with subcutaneous adrenaline and intravenous antihistamine, particularly in those patients who are known to be at risk, but such use is controversial*". Readers should consult the references for further details of the respective arguments and the history and evolution of the manufacturer's recommendations^{31,32}.

Although it is likely that well staffed major hospitals can, if it is recognized early, readily and rapidly manage antivenom reactions, such events can be severe, progressive and are not necessarily remediable³³. Therefore, it is the small rural centres, with more limited staffing and facilities, that may benefit most from the apparent efficacy of adrenaline premedication^{28,29,32}. If any premedication is to be given, currently the best evidence is that it should be **subcutaneous** adrenaline²⁸.

Thus, premedication with subcutaneous adrenaline is especially recommended prior to the intravenous administration of antivenoms in smaller centres. Adults should receive 0.25 mg of adrenaline by the **subcutaneous route** (0.005 mg/kg SC for a child).

Adrenaline premedication should never be given intravenously.

This is in order to avoid hypertension in the coagulopathic patient with the potential for bleeding. Similarly, it should not be administered intramuscularly, as this may also lead to hypertension, as well as to haematoma formation in the presence of coagulopathy. Alternatively, a treatment dose of adrenaline should be drawn up in a syringe ready for use (1 in 1000 – see anaphylaxis section below).

The traditional role of antihistamines in premedication is less clear. On one hand a recent, well conducted, but underpowered, study from Sri Lanka³⁴ documented a reduction in mild-to-moderate acute reactions to antivenom with an antihistamine bolus in conjunction with a hydrocortisone infusion. However, with respect to the clinically important endpoints of moderate and severe reactions, there was insufficient power in this study to confirm a trend toward fewer reactions in the hydrocortisone-containing regimens. This study is in contrast to a previous study from Brazil that failed to demonstrate any difference in early antivenom reactions with prophylactic promethazine alone³⁵.

Adverse reactions to antivenom

Acute adverse reactions and/or anaphylaxis

Snake antivenoms are derived from antibodies of immunized animals; in the case of CSL snake antivenoms, the animals are horses. The rates of reactions to antivenoms appear to vary with the species of antibody origin, the extent of enzymatic digestion of the antibody molecules, the presence of molecular aggregates and the total protein content of the product^{36,37}. It has been presumed that most acute reactions relate to the extent of complement activation from Fc receptor binding^{37,38}, with improvements in quality having largely resulted from enhancements in antivenom processing³⁶.

The antivenoms made in Australia by CSL Ltd, which are also used in Papua New Guinea, are amongst the safest in the world. The acute reaction rates to these antivenoms are reported as 10% in the absence of premedication³¹ and 4.6% with premedication³². Three cases (3.8%) of delayed serum sickness were reported from 79 adequately followed up patients in one study³². A more recent survey of returned (but not followed up) antivenom usage report forms found a total of 14 adverse reactions (6%) to antivenom from 232 snakebite cases over 46 months. These figures probably underestimate the true adverse reaction rate to Australian antivenoms, but nonetheless compare favourably with figures from overseas, where adverse reactions to antivenoms have been reported in up to 80% of patients.

Many patients, even those with a past history of reaction to equine proteins, such as snake handlers, have had minimal or no problems with repeat antivenom therapy after premedication. All antivenoms however, contain foreign proteins (CSL snake antivenoms are comprised of approximately 17% equine IgG), and the possibility of allergic reactions, including life-threatening anaphylaxis, should always be considered. This is especially so if the patient has allergic/atopic disease (asthma, hay fever or eczema), if they have a history of prior exposure to equine serum (eg. anti-tetanus serum or antivenom for a previous snakebite), or have been given multiple doses of antivenom, especially if this was polyvalent antivenom.

Facilities should be available for dealing with complications such as anaphylaxis before the administration of antivenoms. The patient should be monitored closely for acute reactions (most occur within the first 30 minutes after starting antivenom administration). These signs include generalised feelings of anxiety, warmth, itching, progressive erythematous or urticarial rash, oedema of face/neck/soft tissues, vomiting, wheeze and shortness of breath, fever, hypotension, collapse and other evidence of shock. Adrenaline (*See next page for dosages and injection routes*) is the immediate treatment of choice for anaphylactic and anaphylactoid reactions, in conjunction with cessation of antivenom administration, oxygen by face mask, bronchodilators, H₁ receptor blockers, fluid replacement and corticosteroids.

Once the episode has been treated antivenom administration can be cautiously recommenced.

Adrenaline dosages for adverse serum reactions or anaphylaxis

The following initial doses of adrenaline should be given by the intramuscular route (IM).

Adrenaline concentration	Patient weight/age	Dosage
1 in 1,000	Small adults (< 50 kgs)	0.25 ml IM
	Average adults (50-100 kgs)	0.5 ml IM
	Large adults (> 100 kgs)	0.75 ml IM
1 in 10,000	Children (< 25 kgs)	10 µg/kg up to 250 µg IM

Only if there is little or no response to the initial dose should the same amount (diluted to 1 in 10,000) be given slowly via an intravenous line. It is important to establish radio contact with a consultant at PMGH while treatment with adrenaline is being undertaken and to seek qualified advice specific to the particular reaction that has occurred.

Serum Sickness

Serum sickness, due to the deposition of immune complexes, is a recognized complication of the administration of foreign protein solutions such as antivenoms. Symptoms include fever, rash, arthralgia, lymphadenopathy and a flu-like illness. Serum sickness following the administration of Australian antivenoms was reported in 3 out of a total of 70 cases in one series, although this is may be an underestimate due to loss to follow up of some patients.

Serum sickness typically **occurs between 5-10 days after antivenom** has been administered.

The possibility of serum sickness, and the usual symptoms and signs, should be discussed with the patient prior to discharge, so that it may be recognized and treated early. If a large amount of antivenom (i.e. polyvalent antivenom or multiple doses of monovalent antivenom) was given, then corticosteroid treatment should be considered. This may also be advisable if the patient has a past history of exposure to equine protein.

Both the incidence and severity of delayed serum sickness may be reduced by the having the patient take prednisone, at a dose of 50 mg (adult), or 1 mg/kg (child) for five days after the administration of the antivenom.

Quantity of antivenoms to be held by hospitals

The following is a suggested guide to the minimum amounts of antivenoms that should be held by health centres and hospitals at all times.

Regional Hospitals

1. Adequate antivenom to treat **six (6) to eight (8) serious cases** of envenomation by the major venomous snake species found in that province, i.e. a minimum of twelve (12) to sixteen (16) vials of appropriate relevant monovalent antivenoms; and
2. Eight (8) ampoules of polyvalent antivenom that should be held for the treatment of cases in which the snake has not been positively identified.

Urban Clinics and Rural Health Centres

The ability of clinics and health centres to maintain stocks of antivenom depends entirely on whether or not adequate cold chain storage is available and can be maintained. The shelf life of antivenom is three years when stored protected from light at between 2⁰C to 8⁰C. Antivenom must not be frozen.

1. Adequate antivenom to treat **two (2) serious cases** of envenomation by the major venomous snake species found in that region, i.e. a minimum of four (4) vials of appropriate relevant monovalent antivenom; and,
2. Four (4) ampoules of polyvalent antivenom that should be held for the treatment of cases in which the snake has not been positively identified.

Rural health centres that treat large numbers of snakebites each year should stock the same minimum quantities as large regional hospitals.

In areas where snakebite is infrequent and where there is **reasonable timely access** to a larger health centre or hospital, it may not be necessary for all small centres to stock antivenom. In these circumstances there should, however, be a clear medical evacuation strategy for transferring a snakebite patient to the larger centre for treatment with minimal delay.

All health centres and hospitals should have clear procedures for replacing antivenom stock as and when it is used from the appropriate Area Medical Store.

Provincial Antivenom Requirements

The medically important snake species in Papua New Guinea have natural distributions that vary from one type of snake to another. While some species are widespread and common throughout that distribution, other types of snakes may only be found in some parts of the country, and may not be common throughout those places (*See Chapter 2 for more information on individual species*).

Antivenoms are extremely expensive and it is prudent to conserve resources by planning for the most appropriate distribution and use of antivenoms, according to which species of venomous snake occur in particular parts of Papua New Guinea. Until the introduction of snake venom detection kits across PNG makes it possible to select monovalent antivenoms for all envenomations, the Provincial antivenom stocking recommendations made on the following two pages which are based on the current scientific knowledge of the natural distribution of Papua New Guinea snakes, and should be used as a basis for stocking antivenom and supplying it to health centres and hospitals in each province.

Recommended antivenoms for snakebites in PNG Provinces

This chart recommends appropriate antivenoms for each of the provinces throughout Papua New Guinea. The chart can be used in conjunction with the antivenom selection algorithm on page 11.8 to choose the antivenoms in the absence of SVDK testing.

Province	Native Species	Antivenoms Needed
Western	Papuan taipan	CSL taipan antivenom
	Death adder	CSL death adder antivenom
	Papuan blacksnake	CSL polyvalent antivenom
	Papuan mulga snake	
	Small-eyed snake	
Brown snake		
Gulf	Papuan taipan	CSL taipan antivenom
	Death adder	CSL death adder antivenom
	Papuan blacksnake	CSL polyvalent antivenom
	Small-eyed snake	
Central & NCD	Papuan taipan	CSL taipan antivenom
	Death adder	CSL death adder antivenom
	Papuan blacksnake	CSL polyvalent antivenom
	Brown snake	
	Small-eyed snake	
Milne Bay	Papuan taipan	CSL taipan antivenom
	Death adder	CSL death adder antivenom
	Papuan blacksnake	CSL polyvalent antivenom
	Brown snake	
	Small-eyed snake	
Oro (Northern)	Death adder	CSL death adder antivenom
	Small-eyed snake	CSL polyvalent antivenom
	Brown snake	
Morobe	Death adder	CSL death adder antivenom
	Small-eyed snake	CSL polyvalent antivenom
Eastern Highlands	Death adder	CSL death adder antivenom
	Small-eyed snake	CSL polyvalent antivenom
Simbu	Death adder	CSL death adder antivenom
	Small-eyed snake	CSL polyvalent antivenom
Southern Highlands	Death adder	CSL death adder antivenom
	Small-eyed snake	CSL polyvalent antivenom

Recommended antivenoms for snakebites in PNG Provinces

This chart recommends appropriate antivenoms for each of the provinces throughout Papua New Guinea. The chart can be used in conjunction with the antivenom selection algorithm on page 11.8 to choose the antivenoms in the absence of SVDK testing.

Province	Native Species	Antivenoms Needed
Western Highlands	Death adder	CSL death adder antivenom
Enga	Death adder	CSL death adder antivenom
Sandaun	Death adder	CSL death adder antivenom
	Small-eyed snake	CSL polyvalent antivenom
East Sepik	Death adder	CSL death adder antivenom
	Small-eyed snake	CSL polyvalent antivenom
Madang	Death adder	CSL death adder antivenom
	Small-eyed snake	CSL polyvalent antivenom
Manus		CSL Sea snake antivenom
West New Britain		CSL Sea snake antivenom
East New Britain		CSL Sea snake antivenom
New Ireland		CSL Sea snake antivenom
North Solomons		CSL Sea snake antivenom

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The use of anticholinesterase therapy

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Introduction

Postsynaptic neurotoxins compete with the acetylcholine (ACh) that is released from nerve terminals at the neuromuscular junction for available nicotinic ACh receptor sites on adjacent skeletal muscle cell synaptic clefts. The binding of these types of toxins to the receptor prevents acetylcholine from depolarising the muscle, producing paralysis. Unlike the extremely destructive paralysis that is caused by phospholipase A₂ presynaptic neurotoxins, postsynaptic snake venom neurotoxins tend to be reversible. This means that once bound by antivenom, these toxins dissociate from the receptor binding site and nerve impulse conduction resumes. This resumption may be either rapid or gradual, depending upon the individual toxins and their respective binding affinities. Rapid early responses to antivenom with varying degrees of persistent residual neurotoxicity have been documented.

Acetylcholine, once discharged from the presynaptic vesicles in the axolemma of the nerve terminal, is rapidly bound by acetylcholinesterase; this breaks down the acetylcholine into its component parts, choline and acetate. These are then taken back up into the nerve terminal and recycled to produce new acetylcholine molecules. This process of release, breakdown and reuptake continues to take place in the presence of postsynaptic neurotoxicity even though there the blockade of the binding site by the toxin prevents acetylcholine from accomplishing its job of depolarising the muscle and initiating contraction or relaxation. The result is that even though postsynaptic paralysis is present, the nerve continues producing neurotransmitter, which only fails to accomplish the task of initiating movement because of excessive competition for binding sites caused by the presence of the toxins.

The reality is that, in each synapse, there are large numbers of receptors for acetylcholine, but the short life of the molecule (before it is split back into acetate and choline by acetylcholinesterase) prevents it from finding unaffected receptors and activating the muscle. This opens a unique window for potential non-antivenom intervention in postsynaptic paralysis induced by snake venom neurotoxins. Anticholinesterases are drugs that inhibit the process of acetylcholine breakdown and reuptake. These drugs allow acetylcholine to remain in the synaptic for considerably longer than they would ordinarily, and this prolonged presence gives acetylcholine greater opportunity to bind to unblocked nicotinic ACh receptor sites on the muscle cell.

The result can be a limited improvement in neuromuscular function and restoration of normal physiological function. Patients who have been treated with anticholinesterases after the bites of death adders (*Acanthophis* spp.) in Papua New Guinea have experienced improvements that were measurable and functional. Co-administration of anticholinesterase with antivenom to death adder victims has been shown to reduce the time to resolution of neurotoxicity, and even when given without antivenom, anticholinesterases have the potential to improve the neuromuscular function of the envenomed patient.

Clinical evidence of efficacy

Laloo et al (1996) observed that in patients treated concomitantly with antivenom and the anticholinesterase drug neostigmine (0.45 mg) (with 0.6 mg atropine) that the recovery of neuromuscular effort was significant. One patient who had been intubated experienced recovery of respiratory effort sufficient to enable extubation within 2 hours of administration:

CASE REPORT (from Laloo *et al*, 1996)

A seven-year-old girl was bitten on the right instep by a 34-cm-long death adder close to a stream where she had been drinking. The snake was killed, and she was taken to a local health centre where a compression bandage was applied. When she arrived at the hospital, 3.5 h after the bite, she was complaining of pain in the right groin and had been vomiting. Symptoms of neurotoxicity, heavy eyelids and difficulty in swallowing, had started about an hour and a half after the bite and she was beginning to have difficulty in breathing. On examination, there was tenderness but no swelling over two fang marks and she had tender lymph nodes in the groin. She had moderate ptosis, a partial ophthalmoplegia, and had developed pooling of secretions because of difficulty in swallowing. Respiratory efforts were weak and involved the diaphragm only. The whole blood clotting time was normal. She was immediately intubated and ventilated by hand. One ampoule of death adder antivenom was infused over 20 min, and she was given 0.45 mg neostigmine and 0.6 mg atropine intravenously. Over the following 2 h, there was a distinct improvement in the level of respiratory effort and the patient was extubated. Mild ptosis persisted, but 14 h after admission to hospital, all signs of neurotoxicity had disappeared and the patient made an uneventful recovery.

In another case reported by Hudson (1988) a 20 year-old man bitten by a death adder (*Acanthophis* spp.) had rapid resolution of most neurotoxicity within 2 hours after antivenom therapy, but had persistent ptosis. Treatment with atropine (0.6 mg) and an anticholinesterase drug, edrophonium (10 mg) resulted in clear improvement.

According to Little *et al* (2000), a patient bitten by a death adder (*Acanthophis antarcticus*) in Australia had significant improvement in lung expansion after treatment with neostigmine (1 mg) and atropine (0.6 mg) that was sustained in duration. Further treatment with 2.5 mg neostigmine and 1.2 mg atropine effectively resolved neurotoxicity altogether. Currie *et al* (1998) treated a Papua New Guinea man who had ptosis, difficulty swallowing and speaking, and respiratory difficulty after a death adder bite with 2.5 mg neostigmine and 1.2 mg atropine. The previous symptoms resolved very rapidly (within 5 minutes).

Limitations of acetylcholinesterase therapy

Anticholinesterase drugs have no value in the treatment of presynaptic neurotoxicity, such as that caused by Papuan taipans (*Oxyuranus scutellatus canni*). There is also no evidence at the present time to suggest that they have clinical value in treating the bites of Papuan blacksnakes (*Pseudechis papuanus*), mulga snakes (*Pseudechis cf. australis*), small-eyed snakes (*Micropechis ikaheka*) or brown snakes (*Pseudonaja cf. textilis*).

Anticholinesterases may suffice to improve muscle power in death adder (*Acanthophis* spp.) bites, and the effects may only be transient. Obviously, in the context of significant neuromuscular blockade with respiratory failure, these drugs are no substitute for antivenom therapy and mechanical ventilation.

The use of anticholinesterases is only justified in the treatment of known death adder bites, and preferably as an adjunct treatment with antivenom.

Contraindications to use

You should **not use** anticholinesterase drugs if any of the following apply:

- There is a positive 20WBCT (incoagulable blood).
- The patient has spontaneous bleeding and the 20WBCT has not been done.
- The patient describes a snake larger than 1 metre in length.
- The patient describes a snake with a ‘*red stripe on the back*’ or a ‘*blacksnake with a red back*’.
- The patient describes a ‘*white snake*’, or a ‘*pale snake with a dark head*’.
- Previous allergy to the drug.

Assessment of suitability

A useful gauge of whether a patient with neurotoxic envenoming might benefit from anticholinesterase therapy is to try the “Tensilon test”, using the short-acting anticholinesterase drug edrophonium chloride:

1. Administer atropine sulphate (0.5-1.0 mg for adults, 20 µg/kg for children) IV, then;
2. Edrophonium chloride (10 mg in adults, 0.10 mg/kg in children) by slow IV injection; or, by first giving 20% as a test dose, followed by the remainder 1 minute later;
3. Look for signs of improving muscle power after 10 minutes.

If improvement occurs, then administer and maintain **neostigmine** (much longer-acting):

Dosage: adults 1.25-2.5 mg, children 50-70 µg/kg/dose, by slow IVI, repeated every 2-4 hours whilst weakness remains, if an initial improvement in motor function is observed.

When moderate to large doses of neostigmine, such as this, are given, **atropine** must be given to counteract the unwanted muscarinic side effects of neostigmine, which include bradycardia, increased salivation and sweating:

Dosage: adults 0.6-1.2mg, children 0.02mg/kg, by slow IVI, repeated approximately 6-hourly, depending on the reappearance of excessive salivation or sweating and on the continued use of neostigmine.

Neostigmine is the only anticholinesterase that has been used for snakebite in PNG, although there are other anticholinesterase drugs available. Clearly, if the patient is already intubated and ventilated, this test is only helpful in deciding whether to give death adder monovalent antivenom – in that setting further neostigmine is not required, except on the odd occasion, as above, when there is persistent ptosis, or other neurological deficit, several hours after dose of death adder antivenom.

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Managing the respiratory effects of snake envenomation

Dr Antony Chenhall

General principles of respiratory management

In general the aim of respiratory management is to maintain adequate gas exchange. That is, absorption of oxygen and removal of carbon dioxide.

This requires:

- A patent (and protected) airway.
- Ventilation (moving air).
- Functioning alveoli.
- Perfusion of (blood flow to) alveoli.

In the envenomed patient, the respiratory problems are airway and/or ventilation problems:

- Progressive deterioration in conscious state leading to upper airway obstruction.
- Progressive deterioration of muscle strength leading to hypoventilation.
- Pulmonary aspiration of saliva or vomitus (due to not protecting their airway).

In snake envenomed patient, the aim of respiratory management is to maintain adequate ventilation and to prevent respiratory complications until definitive treatment for the underlying problem can occur, and their muscle power has returned to near normal.

In managing these patients, it is important to **do the basics well**.

In this chapter we will cover:

- Non-invasive airway management.
- Manual ventilation.
- Invasive airway management.
- Mechanical ventilation.

Non-invasive airway management

We first need to assess the patient's airway. Are they maintaining their airway? Are they protecting their airway?

It is important to continually reassess the airway, as the natural history is for progressive deterioration. We need to ensure that the airway is both patent and protected.

Is the airway patent?

- Rise and fall of the chest.
- Feel for air movement.
- 'Misting' in the oxygen mask.
- A 'rocking boat' pattern (alternate elevation of the chest then the abdominal wall) means attempted ventilation against an upper airway obstruction.
- Lack of air movement may be due to airway obstruction, or hypoventilation.

Airway patency can be maintained using

- Body Posture:
 - Left or right lateral.
- Simple airway manoeuvres:
 - Jaw thrust.
 - Chin lift.
- Simple upper airway devices, eg. Guedel airway, nasopharyngeal airway.

Is the airway protected?

- Absent gag reflex – airway not protected.
- GCS <9 – airway not protected.

If the patient is not protecting their airway, endotracheal intubation should be performed. If this is not possible, or not available, then the patient should be nursed in the left lateral position with suction available. They require 1:1 nursing and should be suctioned immediately if there are any secretions/vomit in the oropharynx. The obstructed airway that is being managed in a non invasive manner is NOT secure and needs continual monitoring and reassessment.

Manual ventilation

1. Expired air resuscitation "mouth to mouth".

- $FiO_2 \sim 16\%$.
- Technically difficult.
- Tiring, especially if single operator.

2. Bag/Valve/Mask.

- Can use room air ($FiO_2 \sim 21\%$) or supplemental O_2 .
- For envenomed patients with normal lungs, supplemental O_2 is less likely to be necessary. Adequate ventilation is **VERY** important.
- If using supplemental O_2 , the reservoir bag is important.

- Considerations:
 - Bag
 - ~ Rate (breaths/minute) x tidal volume (volume of each breath) = minute ventilation (minute volume).
 - ~ Rate 12/min. x volume ~500ml = 5-6 litres/min. (average adult).
 - ~ Rate 15–25/min. x 8 ml/kg tidal volume (child or infant).
 - ~ Bag volume varies with brand and size (neonatal, paediatric, adult).
 - Mask
 - ~ Size
 - ~ Seal
 - ~ Airway maintenance
 - Use upper airway devices – Guedel/oropharyngeal.
 - Simple airway manoeuvres – jaw thrust, chin lift.

Bag valve mask ventilation is a skill that requires hands-on practice.

A very important part of the skill is continuously monitoring the effectiveness of the ventilation and appropriately modifying the technique. If the way that you are trying to bag/valve/mask ventilate the patient is not working, then you need to change something; for example, mask size, hand grip, jaw manoeuvre, or by adding an airway device.

Invasive airway management

This section of the chapter covers techniques where equipment is placed into the laryngopharynx and lower in the airway. It is not intended as a comprehensive course in how to intubate, but as a discussion of how to use various airway management techniques with envenomed patients. The practical skills component will be covered in the practical session.

1. Endotracheal intubation

- Advantages:
 - Both maintains and protects the airway (with the cuff in the trachea).
 - Relatively secure.
 - Allows for mechanical ventilation.
- Disadvantages:
 - Technical skill and equipment is required and is not always available.
 - In some cases it may be technically very difficult.
 - Patient must be adequately sedated to tolerate the tube.
 - The procedure is associated with some complications.
- Indications:
 - Patient is not protecting their airway.
 - Marked pooling of secretions.
 - $\text{PaO}_2 < 60\text{mmHg}$ or $\text{PaCO}_2 > 60\text{mmHg}$ despite best available non-invasive respiratory support.
 - Cyanosis.
 - Apnoea (the patient is not breathing).

Envenomed patients will require intubation if they become too drowsy (due to hypoxia, intracranial bleeding, or the use of sedative agents) to adequately maintain and protect their airway, or if they develop respiratory muscle paralysis to the extent that they are

unable to make sufficient respiratory effort. They will not be adequately fasted, and may be nauseated and vomiting, and so will require a rapid sequence intubation to reduce the risk of pulmonary aspiration. The respiratory state of envenomed patients will, generally, deteriorate gradually. Once it becomes apparent that the patient is going to require intubation (**before** they deteriorate to the point that they need immediate intubation), the patient can be intubated ‘semi-electively’. Equipment is prepared and checked and personnel assembled so that the intubation occurs in a planned, orderly and controlled manner.

Rapid sequence intubation

- Everything checked, worked and at hand.
- Pre-calculated drug doses.
- Fast-acting muscle relaxant (suxamethonium).
- Pre-oxygenation.
- Introducer pre-loaded (if available).
- Suction at hand.
- Cricoid pressure.
- **ALWAYS** check and confirm ETT tube position.
- Secure tube.

2. Laryngeal mask airways (and combitubes)

These are devices that sit in the oropharynx and provide a maintained and relatively secure airway but do not protect the airway in the same way as an ETT, especially if using positive pressure ventilation.

They work by delivering air into the laryngopharynx, which they hold open. They require relatively normal anatomy to work effectively. Depending on their design, they may have a ‘cuff’ in the oesophagus to discourage aspiration but as the oesophagus is an easily distensible tube this will not always be effective. None of these devices have a cuff in the trachea.

Since none of them protect against aspiration (especially for a patient who is being positive-pressure ventilated), when it comes to the management of envenomed patients, they are a “second best” alternative to an endotracheal tube.

They may have a limited role where endotracheal intubation is not possible and the patient’s airway is not able to be maintained by other means; but, it must be remembered that these patients are still at risk of aspiration, which may be hidden by the airway device, and they need to be closely monitored for this.

3. Mechanical ventilation

The aim of ventilation in envenomed patients is to provide adequate gas exchange until the envenomation can be definitively treated and the patient has recovered. Unless they have co-morbidities (eg. COAD), or have already sustained complications (aspiration), envenomed patients should have normal lungs and be easy to ventilate, since their problem is with their weak respiratory and bulbar muscles.

Types of ventilators/modes of ventilation.

There are many different brands and models of ventilators and the different terminology they use can become confusing when really they are all doing the same job. There are only a limited number of parameters that can be manipulated.

All ventilators provide Positive Pressure Ventilation (PPV). They do this by either pushing a set volume of air into the patient over a set time (volume-driven ventilators) or by applying a set positive pressure to the patient for a set time (pressure-driven ventilators). Some transport ventilators (eg. Oxylog 2000) only operate as volume-driven ventilators, while others can run in volume- or in pressure-driven modes.

With a volume-driven ventilator, the pressures achieved will depend on the patient's lung compliance as well as the volumes and times set. In this situation airway pressures (peak and mean) should be measured to see that they are not too high.

With a pressure-driven ventilator, the tidal and minute volumes will depend on the patient's lung compliance as well as on the pressures and times set. In this situation, the tidal and minute volumes should be measured to see that they are appropriate for the situation.

Whether using a pressure- or a volume-driven ventilation mode, the aim should be to ventilate the patient with the lowest pressures that achieve adequate tidal volume (and minute ventilation).

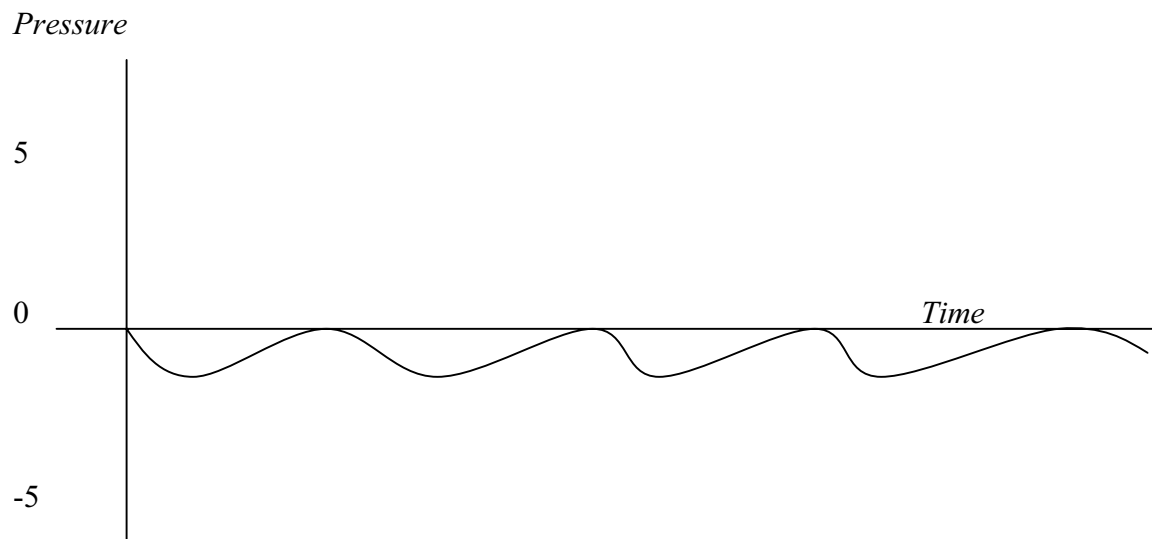
The breath rate (breaths per minute) must be set. Whether the 'breaths' are delivered in a volume- or a pressure-driven fashion, they can be either 'mandatory' or 'triggered'. Mandatory breaths are delivered at a set frequency, regardless of the patient's respiratory effort. This mode is useful if the patient is not making any respiratory effort. Triggered breaths are triggered by the patient's respiratory effort. This mode is good for keeping the ventilator 'co-ordinated' with the patient, and it is very important that the sensitivity of the trigger is appropriate to the amount of respiratory effort the patient is making. Some ventilators allow a combination of 'triggered' and 'mandatory' breaths to be used.

The amount of time that is spent in inspiration and expiration can also be set, and this is often expressed as the inspired: expired (I:E) ratio.

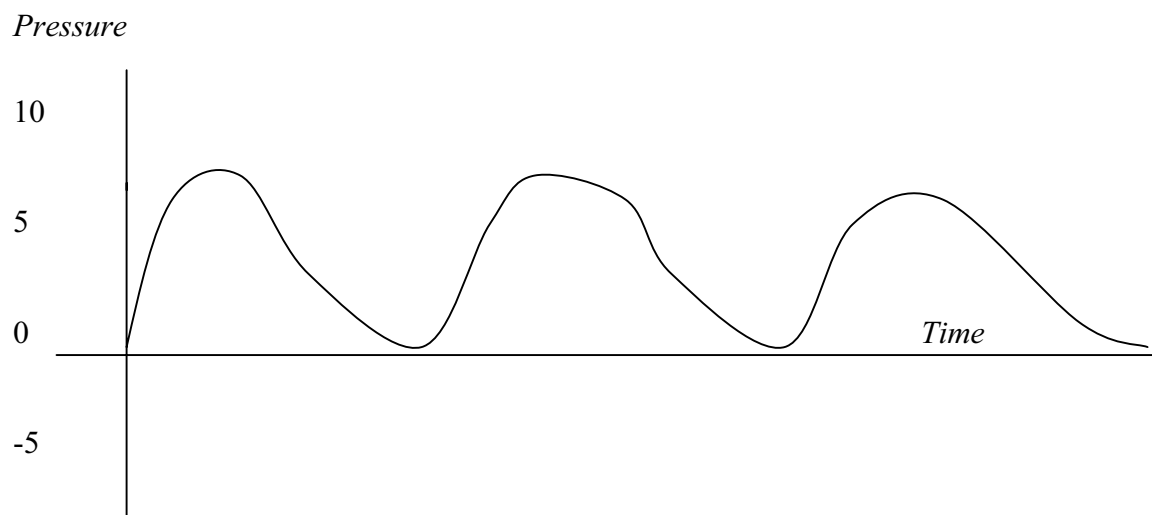
In addition to the number and way that breaths are delivered, it is important to consider the 'resting' pressure in the circuit between breaths, the end expiratory pressure. This pressure can be kept above atmospheric pressure either by the ventilator itself, or by using an expiratory valve in the circuit. This pressure is called PEEP (positive end expiratory pressure). Increasing the PEEP increases the end expiratory volume of the lung, which may make more alveoli available for gas exchange, by keeping them inflated.

The following diagrams show pressure changes in the lung with normal breathing, positive pressure ventilation and the addition of PEEP.

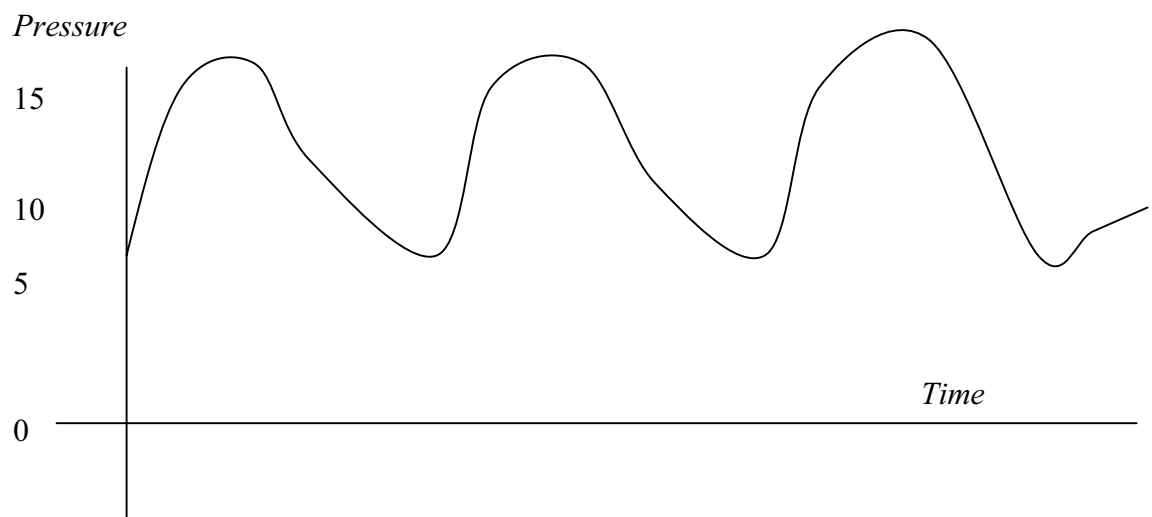
Normal Breathing



Positive Pressure Ventilation



PEEP (5cm H2O)



Initially the ventilation settings need to be chosen based on the patient's size and clinical problem. For this discussion it will be assumed that envenomed patients have normal lungs. A tidal volume (70-80ml/kg) and a rate (12/minute) are chosen, and the minute ventilation (volume) determined. The I:E ratio should be 1:2. Start with an FiO₂ of 100% until the patient's requirements are established. Some envenomed patients may have co-morbidities that will require more specialised ventilation techniques (eg. COAD).

Then, look at the effect of the ventilator settings chosen for the patient and make appropriate adjustments, as necessary:

- Check that the pressures (mean and peak) are not too high.
- Check a blood gas.
 - Is the PaO₂ adequate (should the FiO₂ be reduced or increased)?
 - Is the PaCO₂ acceptable (should the minute ventilation be increased or decreased)?

Close monitoring and continual, appropriate adjustment of ventilator settings is at least as important as the initial settings.

During mechanical ventilation, it is important that the patient is kept comfortable with adequate analgesia and sedation, and is paralysed if indicated. It is also important to ensure that all tubing is very **secure** and that a disconnection alarm is used.

Unless envenomed patients are treated **early** with appropriate antivenom, they are likely to require ventilation for several days (median 13 hours for a death adder envenomation, 88 hours for a taipan envenomation; Laloo *et al*, 1995).

Consideration of the problems associated with long-term ventilation of patients needs to start from day one. This includes consideration of pressure care, eye care, fluids and electrolytes, and nutritional needs.

As the envenomed patient begins to recover, they will gradually be able to take on more of the respiratory work from the ventilator. The exact weaning method will vary according to the ventilator modes available.

It is **very** important to ensure that the patient is not extubated, or is allowed to extubate themselves (many deaths in hospital have occurred this way; McGain *et al*, 2004) until they are able to protect and maintain their airway and exhibit sufficient respiratory effort.

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Management plans for snakebite patients

Dr Simon Jensen and David Williams

Introduction

Snakebite emergencies are usually unexpected sudden events in which critical decision-making at the right time points can have an enormous impact on whether or not the patient survives or dies. Snakebite can represent a serious challenge to the skills and resources of even the best staffed and resourced emergency departments in major developed countries. In an environment such as rural PNG these challenges are hugely magnified by the very basic conditions of most rural health centres and clinics. The success of treatment depends very largely on being able to meet each snakebite emergency with a consistent, practical approach that addresses the important clinical issues as early as possible in a proactive manner.

This chapter therefore deals with the issue of establishing clear plans for the consistent assessment, treatment and referral of all snakebite patients. In the absence of a clear specific, evidence-based plan snakebite patients tend to be managed very poorly, and the outcomes may be catastrophic. Poor initial clinical assessments are often accompanied by irregular reassessment, and proper patient monitoring is sometimes absent altogether. This is often because staff are unsure about what to do, either because of lack of information and knowledge; because of incorrect information; or because of confusion over the interpretation and application of standard management guidelines. In the urgency of the moment, staff may also be distracted by peripheral issues such as having to deal with large numbers of frustrated, worried relatives and wantoks. Without a plan of management there is no systematic approach and important clinical events may be overlooked or not recognised until it is too late.

One approach that can be used to overcome these problems and to bring order and consistency to the management of all snakebite patients is to develop and use clinically relevant, evidence based treatment algorithms. Accurate algorithms for the assessment and diagnosis are invaluable for maintaining consistency, and chapter will show you two different algorithmic approaches:

- (a) An algorithm for the selection of the most appropriate antivenoms based on clinical features of envenomation, snake species distribution and species traits; and,
- (b) Regional treatment plan algorithms that go slightly beyond that proposed in (a) by giving direction to the basic process of antivenom therapy, patient re-evaluation and monitoring.

To get the most out of these algorithmic methods you will need to carefully and thoroughly examine and assess patients, and ensure that your clinical decisions are always based on the evidence you obtain from the patient examinations and from the use of diagnostic tests such as the 20WBCT and the CSL snake venom detection kit (if it is available to you). The algorithms are intended as the basis of management plans which are both appropriate to the

available resources in your institution, while at the same time ensuring a certain minimum standard of care, and which address key problem areas with current treatment methods. To be effective access to algorithms needs to be extended to all of the staff who may be responsible for the treatment of a patient during any time of the day or night. All of these staff need to be taught how to understand and use the algorithms, and this implies that all of the staff need to have a consistent knowledge of the processes of patient assessment and diagnosis, and of the procedure for instituting treatment.

This implies the concept of operational consistency.

Operational consistency means that all of the staff in a health centre, aid post or hospital (and even within an organization such as the Department of Health) take the same consistent approach to a particular issue; in this case the process of assessing, diagnosing and treating patients with real or suspected snakebite.

Every patient who presents with real or suspected snakebite should be:

- Triaged on arrival according to resuscitation status
 - checking vital signs: heart rate (HR), blood pressure (BP), respiratory rate (RR), peripheral oxygen saturation (SpO₂), and temperature (T);
 - resuscitating the patient with respect to **Airway, Breathing and Circulation**;
 - instituting monitoring (depending on availability – ECG, oximetry).
- supportive care: proper patient positioning, oxygen as required, IV fluids, an indwelling urinary catheter (in the patient with respiratory muscle weakness).
- Examined for the same signs of envenomation, for example:
 - All patients should have a 20WBCT performed as soon after arrival at the health centre as possible to determine whether or no blood is clotting normally;
 - All patients should be assessed for the presence of signs that indicate neurotoxicity, such as cranial nerve paralysis (i.e.: ptosis, diplopia, dysphagia and other signs)
- Assessed on the results of the examination and any diagnostic tests in the same manner, for example:
 - Non-clotting blood should always be interpreted as an indication for antivenom being given without delay
- Treated appropriately on the basis of clinical assessment:
 - appropriate adequate antivenom if indicated;
 - secondary therapies on the basis of clinical need and justification.
- Monitored and reassessed in the same way.

The priorities of treatment are to **maintain life and limb**, and to prevent lasting significant morbidity (damage to the patient's organs and tissues), and to **do no harm** to the patient, by not administering unnecessary or incorrect treatments, or by delaying the correct treatment and referral. So priority must be given to interventions which will make a difference to the patient's outcome, and in the correct order of priority.

With this in mind, staff caring for snakebite patients must make every effort to ensure that they are in a position to provide optimal management within the limits of their clinical circumstances. This means replacing used stock, maintaining and being careful with, vital equipment, and ensuring their knowledge is kept at a high level.

Inconsistencies in management protocols frequently contribute to poor outcomes. Internally consistent protocols should provide a reliable basis for decision-making, but all staff involved in the management of snakebite patients must be aware of the locally agreed protocols for the

management of snakebite. This will greatly reduce errors in management which have previously lead to patient deaths. A consistent approach to snakebite management that is evidence-based, easy to follow, and easy to implement also has the important function of helping to protect inexperienced staff from making errors of judgement that might lead to adverse patient outcomes and the resultant difficulties with the patient's wantoks.

The management of snakebite must be based on good evidence and proven scientific facts, for the safety of the patient. Unproven therapies should not be used in a health care facility.

Standard Management Algorithms

The following algorithms are designed to provide an elementary guide to planned patient management and should only ever be used to make clinical decisions if the exact conditions of the algorithm are met. In conjunction with the algorithms you should always:

- Ensure that the clinical signs have been properly elucidated, and use signs that you have observed or elicited directly yourself rather than less reliable symptoms reported by the patient/relative.
- Record the answers you reach for each question in the algorithm on the patient record to ensure that the decision making process is clear to you and to others who treat the patient.
- You must ensure that the 20WBCT was properly performed to ensure a valid test result of either 'positive' or 'negative' for incoagulable blood.
- Any description obtained must be offered without prodding or suggesting answers, i.e.: ask only open-ended questions. For example; do not ask a patient/relative "*Did the snake have a red back*", just ask them "*What did the snake look like?*" The reason for this is that people are often very eager to be able to help, and if you ask them a question that suggests the type of answer you want (i.e.: did the snake have a red back) they will often say 'yes' if it they do not know, simply to try and be helpful.
- The algorithm will only work if you follow all of the steps in the process, all of the time, with all patients who have either real or suspected snakebite.

Use the algorithm cautiously, and if you still have doubts, select the general purpose CSL polyvalent antivenom.

There are two types of algorithms on the next four pages:

Snake Identification Algorithm

This enables you to ask and answer a series of questions that will give you an indication of the most likely species responsible for snakebite. This enables you to make an informed choice of antivenom in the absence of being able to use a CSL snake venom detection kit test.

This algorithm can be used in the case of snakebite in any province of Papua New Guinea.

Regional Snakebite Management Algorithms

There are three regional snakebite management algorithms that are each specific to one particular group of provinces. These are diagnosis and treatment plan guides.

Be certain that you use the correct algorithm for the province in which the snakebite occurred; even if the patient is referred to a Central province hospital from a health centre in the Sepik, you still need to use the algorithm designed for Sepik snakebites

Snake Identification Algorithm

Can be used at any location throughout Papua New Guinea to help select antivenom

1. Whereabouts in PNG did the bite occur?

- | | |
|---|---------|
| (a) MBAY, ORO, CENT, NCD, GULF, WEST? | Go to 2 |
| (b) MOR, SIM, E.HIGH, S.HIGH, W.HIGH, ENGA, SAND, E.SEP, MAD? | Go to 4 |
| (c) MAN, WNB, ENB, N.IRE, N.SOL? | Go to 7 |

2. What was the result of the 20WBCT for incoagulable blood?

- | | |
|--------------------------------------|---------|
| (a) Positive test (20WBCT > 20 min.) | Go to 3 |
| (b) Negative test (20WBCT < 20 min.) | Go to 4 |

3. Was there a description of the snake that referred to it having “a red stripe on the back” or being a “blacksnake with a red back”?

- | | |
|---------|--|
| (a) Yes | Papuan taipan (<i>Oxyuranus scutellatus canni</i>)
CSL taipan or CSL polyvalent antivenom is recommended |
| (b) No | Perform a Snake Venom Detection Kit Test (SVDK) or if unavailable, CSL polyvalent antivenom is recommended |

4. Are there observed or elicited signs of ptosis, diplopia, or other neurotoxicity?

- | | |
|---------|--|
| (a) Yes | Go to 5 |
| (b) No | Observe and reassess the patient hourly for 24 hours |

5. Is there generalised muscle pain, muscle tenderness or dark coloured urine?

- | | |
|---------|---|
| (a) Yes | Go to 6 |
| (b) No | Death adder (<i>Acanthophis</i> spp.)
CSL death adder antivenom is recommended |

6. Is there a description of the snake as being:

- | | |
|---|--|
| (a) ‘a white snake’ or a ‘pale snake with a dark head’? | Small-eyed snake (<i>Micropechis ikaheka</i>)
CSL polyvalent antivenom is recommended |
| (b) ‘a black snake’ or a ‘Papuan black’? | Papuan blacksnake (<i>Pseudechis papuanus</i>)
CSL blacksnake antivenom is recommended |
| (c) There was no description | Perform a Snake Venom Detection Kit Test (SVDK) or if unavailable, CSL polyvalent antivenom is recommended |

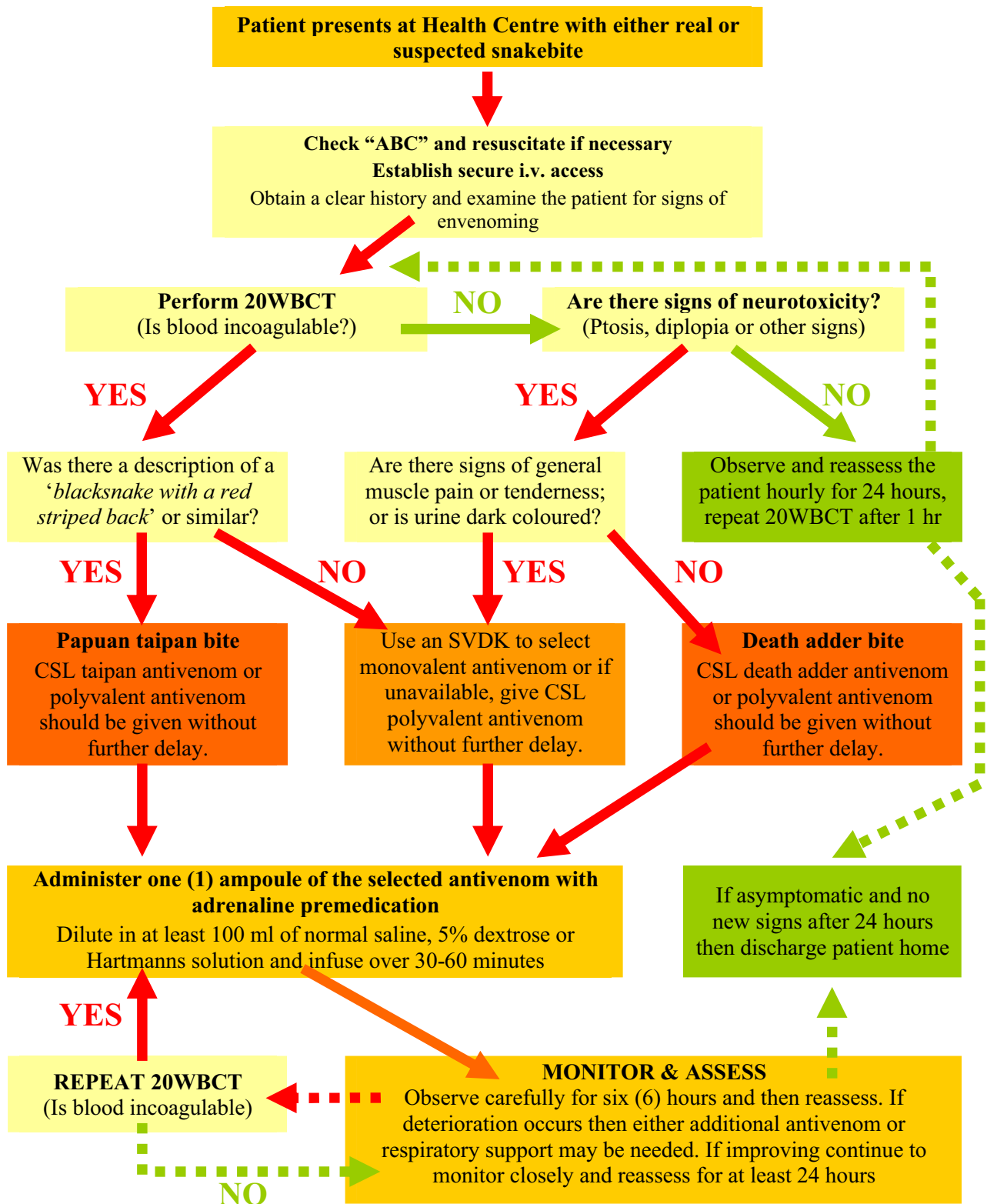
7. Did the bite occur in the ocean, close to the ocean foreshore or in a coastal river?

- | | |
|---------|--|
| (d) Yes | CSL seasnake antivenom
(Sea krait or true seasnake) |
| (e) No | Perform a Snake Venom Detection Kit Test (SVDK) or if unavailable, CSL polyvalent antivenom is recommended |

This algorithm should be used with caution; if available a SVDK test is preferable.

Snakebite Management Algorithm

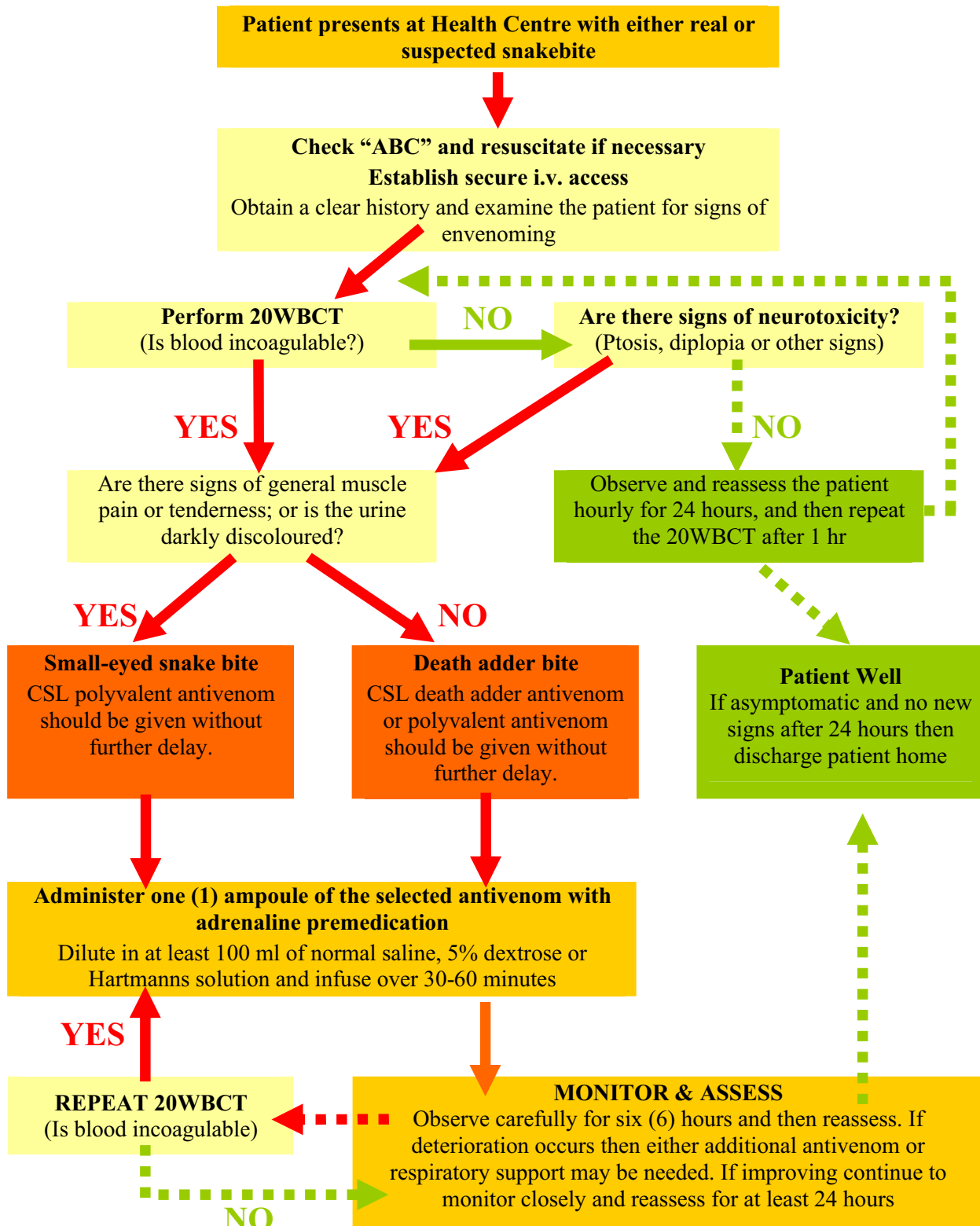
For Oro, Milne Bay, Central, NCD, Gulf and Western Provinces



Use this algorithm as a guide only: if respiratory distress develops after antivenom has been given then it is **imperative** that the airway be protected and steps taken to secure ventilatory support (i.e.: urgent referral to PMGH or another hospital with ventilation equipment)

Snakebite Management Algorithm

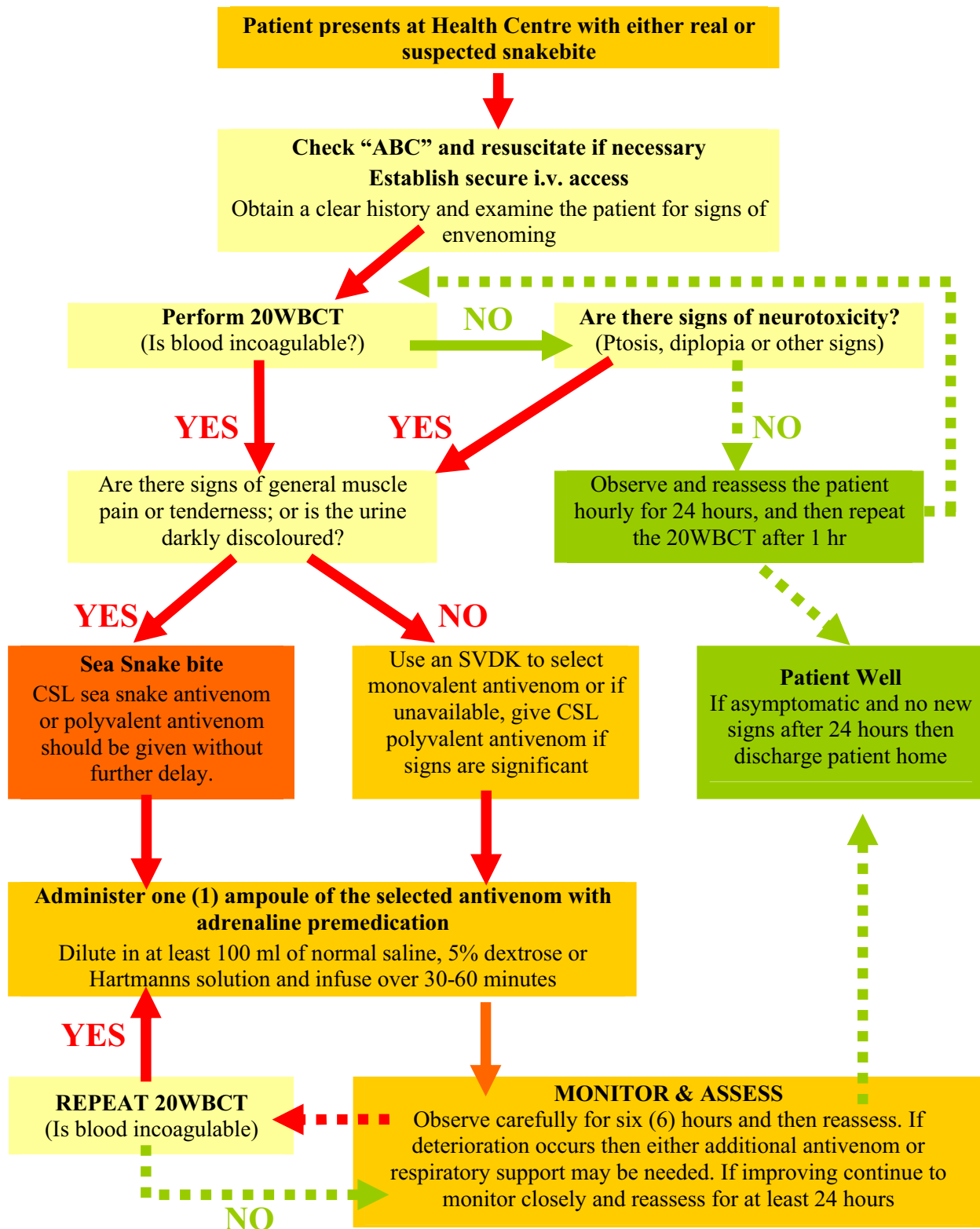
For Morobe, Simbu, Eastern Highlands, Southern Highlands, Western Highlands, Enga, Sandaun, East Sepik and Madang Provinces



Use this algorithm as a guide only: if respiratory distress develops after antivenom has been given then it is **imperative** that the airway be protected and steps taken to secure ventilatory support (i.e.: urgent referral to PMGH or another hospital with ventilation equipment)

Snakebite Management Algorithm

For Manus, West & East New Britain, New Ireland & North Solomons Provinces



Use this algorithm as a guide only: if respiratory distress develops after antivenom has been given then it is **imperative** that the airway be protected and steps taken to secure ventilatory support (i.e.: urgent referral to PMGH or another hospital with ventilation equipment)

Standard patient administration

In addition to ensuring that patients are clinically managed in a consistent and logical manner with emphasis on elicited evidence and careful assessment and diagnosis, it is also important to ensure that the process of patient administration is dealt with consistently.

This involves ensuring that the history and treatment of the patient are correctly recorded in an appropriate fashion, and that patients are nursed appropriately. It can also be taken to include having a clear plan in place for what you will do if a patient needs to be referred to another health centre or to a larger hospital for treatment.

Record keeping

A snakebite observation and assessment chart needs to be maintained for every patient as a record of the not only the symptoms and signs that are present and the treatment that was given, but also of the process by which the patients were treated, and their subsequent progress until an outcome was reached.

There are several variations of the standard snakebite observation chart that was first drawn up over 40 years ago. Some of the things on these charts may no longer be current. For example: tracheostomy is no longer usual in treating snakebite.

Regardless of what type of form (if any) that you use it is very important to obtain information about and record the following:

- Name, sex and age of the patient.
- Where they live.
- Who is their next-of-kin (closest relative who may be contacted).
- Where they were referred from (if applicable).
- At what place they were when they were bitten, including the :
 - Time of the bite.
 - Place name of the location where the bite took place.
 - Circumstances through which they came to be bitten (i.e.: what activity were they engaged in, such as gardening, hunting, walking in the bush etc.).
- What first aid was attempted if any, and in the case of a pressure bandage; whether or not it was effectively applied (i.e.: is the bandage still firmly in place or is it loose).
- Additional history of the snakebite:
 - The description of the snake if it was seen.
 - The number of times the person was bitten.
 - Symptoms which the patient reports as having occurred since the snakebite.
- What did the person do after being bitten and before coming to the health centre.
- Record the results of the patient examination:
 - Record the results of the 20WBCT.
 - If it is available record the results of the CSL snake venom detection kit test.
 - Results of the physical examination.
- Record the use of any algorithmic decision-making process – explain how you reached the decision by listing the steps you have followed in the algorithm.
- Record the diagnosis.
- Record the plan of treatment that you propose to follow as a result of the diagnosis reached.

- Record the hourly monitoring of the patient and the process of reassessment that takes place after the initial treatment phase.
- Record patient vital signs and bodily functions (as described elsewhere, including urine output and toilet).
- Nursing staff should also record their observations of the patient and keep a clear record of abnormal signs (they should also record when and to whom these are reported).
- A record of all drugs and medicines given to the patient, including the time given, the route of administration, and dosage.
- The reasons for referral of the patient to another centre should this become necessary (you should keep a copy of the referral letter if this is possible, otherwise make a summary of your reasons in the patient file).
- A summary of the outcome of the snakebite:
 - The final formal diagnosis at the time of discharge or death
 - The date of discharge or death
 - A summary of the patient's condition at the time of discharge
 - In the case of a death from snakebite a summary of the reasons that contributed to the death (i.e.: respiratory failure, intracerebral haemorrhage etc.).

Nursing considerations

After the initial assessment, diagnosis and treatment phase of snakebite management it is essential that the subsequent nursing of the patient be consistent and that the nursing staff are appropriately trained and able to identify abnormalities as and when they occur, and then bring these to the attention of the person responsible for treatment (i.e.: the OIC of the health centre or aid post, or the treating physician or health extension officer).

There have been cases where a patient who initially responded very well to primary treatment after snakebite has subsequently deteriorated and died during the nursing phase of care because the staff were not adequately able to identify the early signs of deterioration, or neglected to inform the OIC or HEO (sometimes nurses are reluctant to disturb this person at night, and wait until the following morning before alerting anyone to the problem: by this time the patient may be in a very serious and possibly terminal condition).

As part of the planning for the management of snakebite it is therefore essential that nursing staff be properly briefed and taught how to recognise signs of deterioration in a patient. This can be accomplished by:

- Developing a written set of instructions for nursing officers which clearly indicates what the potential signs of trouble in a snakebite patient may be;
- Providing a set of written values for measurements such as heart rate, respiration rate and pattern, blood pressure, temperature etc, that tell them when to become concerned;
- Give clear instructions regarding the need for immediate notification of deteriorating condition;
- Providing ongoing training to nursing officers so that their level of knowledge and awareness is improved;
- Encourage nursing officers to record their patient observations in the patient records.

FIGURE 1: Example of a snakebite observation sheet used for recording history, assessment, diagnosis, treatment and outcome information.

Date:/...../.....
Time: am/pm

DEPARTMENT OF HEALTH
Suspected Snakebite Observation Sheet

Health Centre:
Patient No.:

Patient Name:	Age: yrs	Sex: M / F
Referred from:	Examined By:	

Section A: About the Injury

Time of Bite:	am/pm	Location (Place Name):
Bite Site (Hand? Foot?):	Activity when bitten?:	
Other Comments:		

* Please include any description of the biting snake here, along with a general description of the circumstances leading to the bite. Attach additional pages if necessary.

Section B: Assessment & Treatment Recommendation

First Aid	Yes / No	Description:
Assessment:		
Treatment:		

Section C: Medication

	Adrenaline	Antihistamine	Hydrocortisone	Antivenom	Other
Time Given					
Name (Type):					
Initial Dosage:					
Route:					
Time Given					
Name (Type):					
Further Dose:					
Route:					

Section D: Outcome

Admit to Ward:	Yes / No	Time / Date:am/pm,/...../.....
Referred to:		Time / Date:am/pm,/...../.....
Outcome:		

Time	Pulse	Respiration	Blood Pressure	Temperature	Headache	Cland Tenderness	Abdominal Pain	Frosts	Eyeballs Fixed	Speech Thick	Mouth Open > 1"	Secretions Pooling in Pharynx	Respiratory Problems	Tachycardia or Inubation	Bleeding at Site	20 Minute WBC	Urinaytic Albumin/Blood

Patient Transport

The general principle of transporting a patient is that the standard of care should not drop from referring hospital to transport to receiving hospital. While this is potentially difficult, the principle is for the patient's best interest, and every effort should be made to sustain minimum standard of care during patient transfer that doesn't seriously compromise the safety of the patient.

While it is occasionally possible for aerial retrieval of patients from isolated areas, this is not at all to be relied upon and it tends only to be available during daylight hours. Therefore, the only option is land transport, which is often not possible, due to the state of roads, or to the lack, or poor repair, of the local "ambulance". PMV transport is often the only option, and people in smaller communities have walked long distances to reach a PMV stop, only to have none stop because they already had a full load; patients have died on the side of the road waiting for a PMV, and clearly this mode of transport cannot be relied upon.

The very unfortunate reality is that many patients die en route to hospital, or soon after arrival at the facility. There are a number of reasons for this:

- Staff "*accompanying*" the patient often sit in the front of the utility or 4WD vehicle, while the patient is in the back with the relatives, where the staff member cannot check on them.
- Accompanying staff bring no drugs or resuscitation equipment with them on the transport.
- The patient is generally transported without any oxygen or upper or lower airway device to maintain the airway; suction is certainly not carried.
- The patient is often poorly positioned in such a way that airway obstruction is likely to occur as nervous control of musculature declines.
- The patient, who often hasn't received antivenom, frequently develops life-threatening airway obstruction, pulmonary aspiration or respiratory failure en route.

If a staff member is going to accompany a patient, they should consider the following factors (already discussed in detail in Chapter 7):

- Patient ready
- Staff member ready
- Drugs and equipment ready
- Communication complete

What to teach families if no staff member can accompany the patient (See also Chapter 7):

- Patient positioning
- insertion of the Guedels airway – if not tolerated or required at the time of patient departure; consider the nasopharyngeal airway as a good alternative
- not feeding or giving oral fluid to the patient during the trip if there is any risk that their ability to protect their airway will become compromised en route.

The family must also be given a detailed letter, or a complete copy of the patient's notes for that admission (*as per Chapter 7*)

Summary

The best chance that a person has for survival after a snakebite is to be admitted to a health centre or hospital where they are treated in a consistent manner by staff who are well trained and who adhere to an organised evidence-based management plan, rather than being treated in a disorganised or disjointed manner as and when their condition worsens.

The key elements of successful management are:

- Attend to resuscitation needs early.
- Properly assess and diagnose each patient in a consistent manner.
- Use the 20WBCT for all patients as soon as they arrive at the health facility.
- Be proactive: know what the specific signs of envenomation are, and institute antivenom therapy as soon as possible using appropriate antivenom.
- Carefully monitor and reassess all patients according to a systematic management plan.
- Keep careful, thorough records.
- Nurse the patient well.
- Transport in the best manner possible with appropriate precautions if referral is necessary.

CSL Snake Venom Detection Kits

Tim Carroll

Introduction

The snake venom detection kit (SVDK) is produced specifically to identify the presence and type of snake venom. The kit is designed for use in cases of suspected snakebite by different types of snakes which occur naturally in Australia, Papua New Guinea or Papua.

It is very practical in design, giving results which relate directly to the most appropriate antivenom to use. Being able to select and use an appropriate monovalent antivenom has a number of advantages:

- Less volume of antivenom is required to neutralise the bite, which is safer for the patient.
- It is significantly cheaper to treat the bite and more effective.
- It minimises the chance of not having enough polyvalent to neutralise the bite

SVDKs can also reduce the time it takes to reach a decision to give antivenom and this has definite advantages in term of potentially improving the prognosis for each patient.



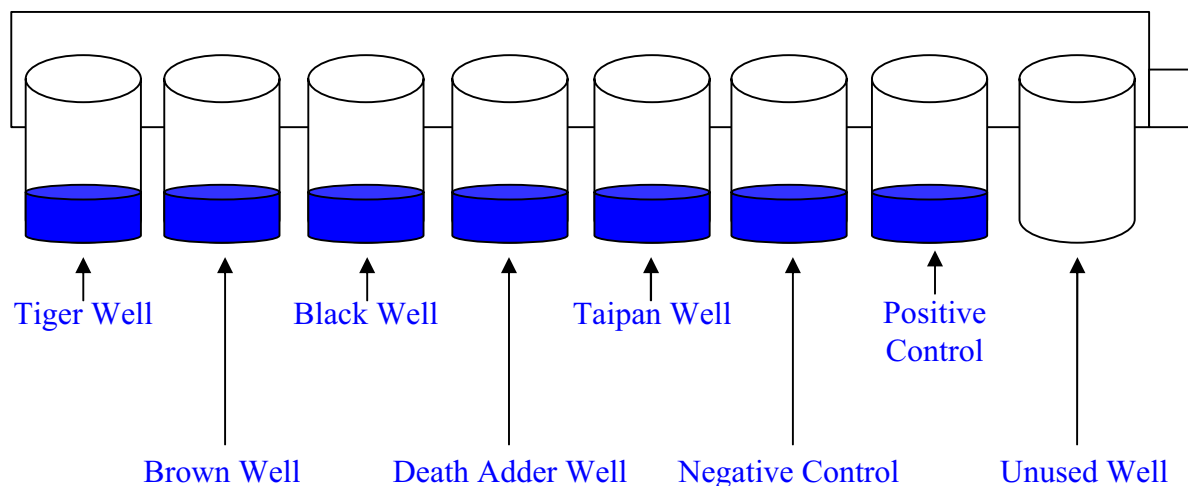
What is the SVDK? And what is it made with?

The SVDK is a commercially produced diagnostic tool that can help clinicians and health workers to make the right decisions about the most appropriate type of antivenom to administer to a person who has been bitten and envenomed by a venomous snake.

The basis of the SVDK is a rapid, freeze dried, sandwich enzyme immunoassay (EIA) that uses antibodies specific to five different snake venom immunotypes:

- Australian tiger snake group
- Brown snake group
- Blacksnake group
- Death adder group
- Taipan group

Each test in the kit (there are 3 tests per kit) consists of a flat-bottomed plastic, 8 well microtitre strip that clips into a provided holder. Seven of the eight wells have a dry blue substance in them (the 8th is left blank). There are five wells that are each specific to a particular snake immunotypes, in addition to a positive control and a negative control well (*See below*).



The wells are made of plastic that under the right conditions can bind antibodies to its surface. For each of the five wells CSL Biosciences manufactures a pair of antibodies specific for each of the five snake immunotypes. They match the five monovalent antivenoms (although the test antibodies are produced from rabbits, as the horse antibodies do not work well in this system). Each of the five wells are coated with a polyclonal antibody against a different snake, this is unmodified and called the primary antibody. This primary antibody is “glued” to the plastic.

The conjugate for each of the antibodies has an enzyme (in this case peroxidase) bound to it and is added to each well. This conjugate antibody is left unattached, and not bound to the plastic surface. Each well has the appropriate pair of antibodies added, for example Anti-Tiger to the first well, Anti-Brown to the second well, Anti-Black to the third well, and so on....

The seven wells are then freeze dried, leaving a blue powder in each of the wells.

What does the SVDK test?

SVDKs test for the presence of one of the five snake venom immunotypes. Correctly used they give a positive result if venom from one of the immunotypes is present in the test sample and enable an informed choice of appropriate antivenom in the event that the person from whom the sample was taken develops envenomation.

What types of samples are tested?

The best type of sample for testing in most situations is a swab from the bite site of the patient. The test is very sensitive to even the smallest nanogram quantities of venom, and even a bite site that has been washed may still yield a positive result.

If the patient already has symptoms and signs of systemic envenomation, then venom may be present in the urine, and this is then a useful alternative for sampling, especially if you are not sure where the actual bite occurred on the body.

Blood is not usually a good sample to test.

Proteins in the plasma can cause non-specific binding which increases the likelihood of an incorrect result, and for this reason special procedures are necessary in order to test blood.

How are the samples obtained?

There are four ways in which to obtain a sample for testing in the SVDK:

1. Bite site swabs

- Locate the bite site (if there is first aid in place, cut off the bandage over the bite site to gain access). Make sure no-one washes the site.
- Take one of the cotton bud swab sticks provided in the kit and an unused “Yellow Sample Diluent” bottle. Unscrew the cap off the bottle, revealing the dropper cap. Lever this off, using a fingernail and put it to one side.
- Put the swab stick into the sample diluent bottle and thoroughly moisten it.
- Rotate and rub the moistened sample stick vigorously over the bite site and adjacent skin, to pick up venom on the skin around the bite and from just beneath the surface of the bite marks.
- Place the swab stick back in the “Yellow Sample Diluent” bottle and twirl it around, to get the venom off the stick and into the solution, then remove the swab stick and replace the dropper cap.



2. Urine

- Collect a urine sample from the patient (remember that retention may be a problem in snakebite patients, so an IDC may need to be inserted in order to obtain a flow of urine).
- Take an unused yellow-capped “Yellow Sample Diluent” bottle. Unscrew the cap off the bottle, revealing the dropper cap. Lever this off, using a fingernail and put it to one side.
- Transfer some of the urine into the “Yellow Sample Diluent” bottle (one or two drops of urine is sufficient).
- Replace the dropper cap onto the “Yellow Sample Diluent”.

3. Affected Clothing or Bandage Sample

- A sample from the bandage, clothing or bite cover may be used. Snip off a portion that looks to have blood or tissue exudate and put in a Yellow Sample Diluent bottle.

4. Blood

- Heparinised whole blood may be used and should be mixed into the “Yellow Sample Diluent”.
- This should be considered as a last resort sample in the event that no other sample can be found.

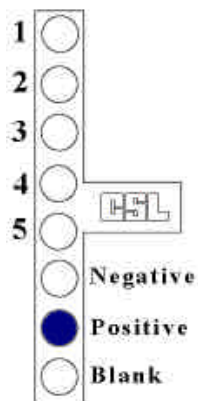
Note: The SVDK is a very sensitive test and can detect even minute quantities of snake venom: as little as 10 to 20 ng per ml (nanograms per millilitre).

How is the actual test carried out?

- Open a pack containing a set of test wells (silver-like pack), remove the enclosed set of 8 joined wells and place them in the holder. There is a lug at one end to enable easy placement in the right orientation.
- Remove the cover from the wells.
- Place two (2) drops of the sample in your “Yellow Sample Diluent” bottle into each individual well.
- Leave the wells to stand for ten (10) minutes in a safe place where they cannot be accidentally spilt or thrown away.
- Gently wash all the wells under gently running water seven (7) times*, then invert and gently tap-out excess water on absorbent paper (don't try to dry the inside of the wells with anything!).
- Now add one (1) drop from the “Peroxide” reagent bottle to each of the wells.
- Next add one (1) drop from the “Chromagen” reagent bottle to each of the wells.
- Place the wells on a white background (a sheet of white paper will do) and let them stand and incubate for ten (10) minutes while you must watch them carefully to see which wells change colour, and in what order.
- There should be blue colour development in well 7 (positive control well) usually within only 2-3 minutes.
- There should be no colour change in well 6 (negative control well).
- If venom from one of the five snake venom immunotypes was present in your sample, then a colour change in one of the well 1 to 5 will indicate the presence of snake venom.
- The number of the well (between 1 and 5) changing colour first indicates the type of snake venom and corresponding appropriate CSL monovalent antivenom.
- If no venom is detected then there will be no colour change in wells 1 to 5.
- **REMEMBER:** You have to watch carefully and record which of the five venom wells changes colour first – this is the correct test result and indicates both the type of venom present and the best choice of monovalent antivenom.
- Over time other wells will also change colour, ignore these.
- After you have finished the test, put the two reagent tubes, the white plastic well holder, instructions, unused swab sticks and well packets back in the box and then in the fridge.

* Blood is not a recommended sample to use in an envenomed human patient, but if blood is used then you will need to wash the wells fifteen (15) times instead of just seven (7) times.

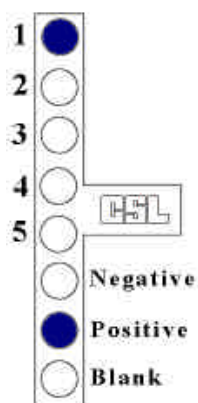
Interpreting the results of the SVDK



Only well 7 positive

No snake venom detected in the sample.

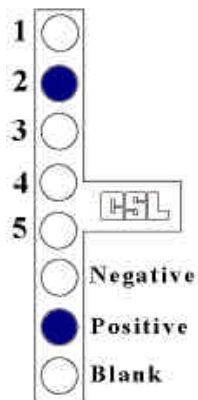
This result does not mean however that a venomous snakebite has not occurred. Observe the patient hourly for at least 24 hours and retest if symptoms or signs of envenomation occur.



Wells 7 and 1 positive

A colour change in well 1 means that the snake species has a venom that belongs in the Australian ‘tiger snake’ immunotype.

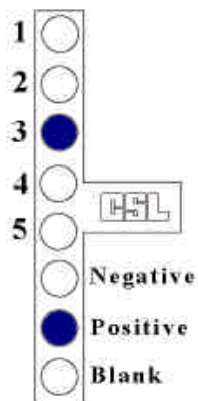
CSL tiger snake or CSL polyvalent antivenoms would be appropriate if systemic envenomation is present.



Wells 7 and 2 positive

Brown snake (*Pseudonaja cf. textilis*) venom is present in the sample.

CSL brown snake antivenom is recommended.

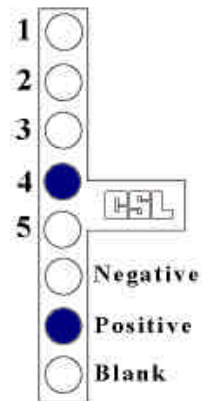


Wells 7 and 3 positive

Papuan blacksnake (*Pseudechis papuanus*) or mulga snake (*Pseudechis cf. australis*) venom is present in the sample.

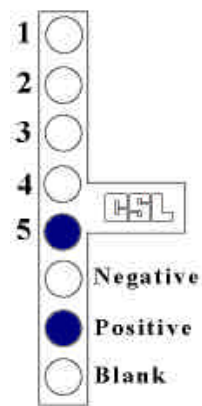
CSL blacksnake antivenom is recommended.

Interpreting the results of the SVDK



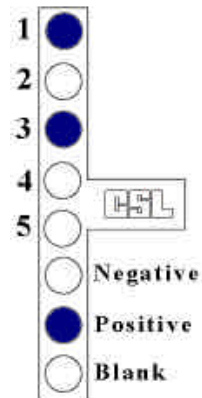
Wells 7 and 5 positive

Death adder (*Acanthophis* spp.) venom is present in the sample.
CSL death adder antivenom is recommended.



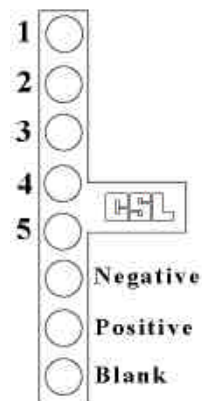
Wells 7 and 5 positive

Papuan taipan (*Oxyuranus scutellatus canni*) venom is present in the sample.
CSL taipan antivenom is recommended.



Wells 1, 3 and 7 positive

This result is sometimes seen after bites by some blacksnakes (*Pseudechis* spp.) and by some other Australian species.
CSL blacksnake or CSL polyvalent antivenom recommended.



No wells positive

Indicates that the kit has failed: retest with a new kit.

Interpretation notes and warnings

Always remember that a positive result for venom from the bite site does not mean the patient has been significantly envenomed.

A positive SVDK from the bite site is not an indication to give antivenom. It is an indication of the type of antivenom to give if, on clinical or laboratory grounds, the patient needs antivenom therapy.

A positive SVDK from a urine sample is an indication to give antivenom because it shows that venom from that type of snake is present in the circulation of the patient: in most cases the patient will have symptoms and signs of envenomation if urine is positive for venom.

Sea snake venoms are not reliably detected with the SVDK.

There may be some species of non-lethal venomous snakes (i.e.: small species of elapid snake whose bites are not usually clinically significant) that may sometimes give positive results in the SVDK because of their venoms contain toxins that correspond to immunotype groups. Bites from whipsnakes are examples of this phenomenon.

If the SVDK gives a positive result for a non-lethal venomous snake, the indicated antivenom will have some effect on that particular venom, and can be used if symptoms and signs become severe enough to cause concern for the patient.

WARNING: Any sample introduced into the kit must be in the “Yellow Sample Diluent”

- Most useful sample usually bite site, followed by urine
- Ensure that the specimen and the Yellow Sample Diluent are well mixed by inverting several times
- Blood may cause non-specific results in the assay

WARNING: The most common technical mistake made in SVDK use is insufficient washing

- Washing is performed a minimum of 7 times and 15 times for blood samples
- A 'flick' is used to remove the washing fluid from the wells
- Tap out the strip on blotting paper or tissue between each wash
- Wash more rather than less

WARNING: The colour reaction observation must be performed as per the instructions

- Colour development must be observed continuously for 10 minutes after addition of Peroxide and Chromogen
- The first well to show colour development being diagnostic
- Large concentrations of venom in the sample may cause rapid colour development and more than one blue well at 10 minutes
- Reactions should not be interpreted after 10 minutes

WARNING: Users may be confused when more than one well develops colour

- This is entirely normal and is due to natural cross-reactions in Australian snake venoms
- Many Australian snakes have common venom components detectable with the SVDK
- Example is the well characterised cross-reactivity between King Brown Snake and Tiger Snake (See Product Insert or Technical Information Booklet for details)

Storage of SVDKs

SVDKs should be stored in refrigerated conditions between 2-8°C and should also be protected from light. If the kit is frozen or heated the performance of the test strip and the reagents can not be guaranteed, and may cause erroneous results.

It is strongly recommended by CSL that kits outside of their expiry should not be used; the performance of the test strip and the reagents can not be guaranteed and may cause erroneous results.

Glossary of medical terms

The following is a glossary (list of definitions) of some of the medical terms used in this Handbook.

Accessory muscles	Muscles other than the diaphragm which are involved in respiration, especially the intercostals and the external neck muscles
Anaphylactic	Severe allergic reaction characterised by hypotension and swelling of upper airway tissues; may also involve wheeze and rash; mediated by mast cell degranulation and histamine release.
Anaphylactoid	Similar to an anaphylactic reaction but not mediated by mast cell degranulation; usually less severe.
Antecubital	The anterior surface of the cubital fossae, (ie. The flexor surface of the elbow).
Anuria	No output of urine
Assessment	History, examination and investigations.
Bradycardia	Heart rate less than 50 beats per minute.
Bulbar	Related to the cranial nerves 9 and 10 (eg. Bulbar palsy).
Cardiotoxicity	Toxicity effecting the tissues of the heart.
Coagulopathy	Failure of the blood to clot due to an absence or dysfunction of clotting factors or platelets.
Coma	Decreased conscious state to the point of being non-responsive to stimuli.
Compartment syndrome	Loss of blood supply to a limb when the pressure within a compartment of a limb (compartment enclosed by strong fascia eg. Peroneal compartment of leg) is greater than the venous blood pressure. This can occur with any injury involving significant swelling, such as a burn or a snakebite.
Cranial nerves	Those nerves that have their origin directly from the brain, rather than the spinal cord; numbered 1-12.
Diplopia	Double vision; occurs when the eyes are not looking in exactly the same direction, usually due to nerve or muscle problems with eye movement.
Disseminated intravascular coagulation (DIC)	Coagulopathy due to the consumption of clotting factors and platelets; a process causing clotting factors to be consumed in a generalised, disorganised fashion, not involving useful clot formation.
Dysarthria	Difficulty speaking due to problems with the muscles of the mouth or pharynx (weakness, poor coordination).
Dysphagia	Difficulty swallowing
Dysphonia	A quiet, altered voice.
Dyspnoea	Difficulty breathing; respiratory distress.

Envenomation	In the setting of snakebite, this means that toxin has entered the patient's body and they are showing symptoms or signs.
Gag reflex	A reflex whereby stimulus of the pharynx causes the glottis to close over the laryngeal opening, lost in coma and in generalised paralysis.
Haematemesis	Vomiting blood; either bright red, indicating torrential bleeding, or dark brown ("coffee grounds") due to alteration of blood in the stomach by the stomach acid.
Haemoglobinemia	Haemoglobin in the blood (in the serum, due to breakdown of red blood cells).
Haemoglobinuria	Haemoglobin in the urine.
Haemoptysis	Coughing up blood.
Haemorrhage	Bleeding.
Hypertension	Increased blood pressure.
Hypotension	Low blood pressure.
Inspiration	Breathing in.
Intercostal muscles	The muscles that lie between the ribs, are not used in usual quiet breathing, but can be used as accessory muscles of inspiration and expiration
Intracranial	Inside the skull.
Lymphadenitis	Inflammation of lymph nodes.
Lymphadenopathy	Enlargement of lymph nodes.
Malaena	Stools containing, or composed of, altered blood; blood from the upper GI tract that has been altered by digestive processes (not fresh blood).
Management	Specific treatments and general supportive treatments aimed at improving or curing a condition; communication about the patient (referral) and disposition (where they are sent for care).
Menorrhagia	Heavy menstrual bleeding.
Minute volume	The volume of air that is breathed (and out) in one minute.
Myoglobinuria	The presence of muscle breakdown products in the urine.
Myolysis	Muscle cell damage/breakdown.
Myotoxicity	Toxicity to (skeletal) muscle.
Neurotoxicity	Toxicity to nerves/the nervous system
Ocular	Involving the eye
Oedema	The collection of fluid within tissues.
Oliguria	A condition of markedly reduced urine output.
Ophthalmoplegia (external)	Paralysis of the external muscles of the eye.
Oxygenation	The delivery of oxygen, either to a patient, or to their tissues.
Palpitations	Awareness of the heart beat; may be regular or irregular, usually faster, and possibly stronger, than normal.
Paralysis	A complete loss of the function of a muscle or muscles; can be either neurological or muscular in origin.

Paresis	Weakness (a partial paralysis).
Procoagulant	Factor that increases the propensity of blood to clot.
Protrusion	Sticking out.
Ptosis	Paralysis of the muscles of the eye lid, leading to drooping of the upper lid(s), and a reduced ability to look upwards.
Pulmonary	Related to the lungs or respiratory system.
Rectal bleeding	Bright red (fresh) bleeding from the rectum.
Renal	Pertaining to the kidneys.
Respiratory	Related to the lungs or respiratory system.
Rhabdomyolysis	A clinical syndrome in which there is massive muscle breakdown; involves myoglobinaemia (myoglobin – the major muscle protein, and potassium ions leaking into the blood), myoglobinuria (myoglobin in the urine) and the deposition of myoglobin in the kidneys leading to acute renal failure.
Signs	Objective signs found on physical examination.
Sternomastoid	An anterior muscle of the neck that can be used as an accessory muscle of respiration.
Symptoms	Subjective complaints found on history-taking.
Tachycardia	An increased heart rate, greater than 100 beats per minute.
Tachypnoea	An increased respiratory rate, greater than 20 per minute (for adults).
Tidal volume	The volume of air moved in one breath.
Trapezius	A posterior muscle of the neck that can be used as an accessory muscle of respiration.
Trismus	Spasm of the muscles of the jaw.
Truncal	Related to the trunk, i.e.: The truncal muscles are the muscles of the trunk.
Ventilation	The movement of air in and out of the lungs; allows for the absorption of oxygen and the exhalation of carbon dioxide; is can be spontaneous or artificial (eg. Positive pressure ventilation).