SNAKE VENOMS

A/Prof Goh Lee Gan

INTRODUCTION

The best way to avoid being bitten by a venomous snake is simply to leave it alone.

Joseph Slowinski

This quotation comes from the last sentence of an article in the California Wild (Slowinski, 2000)[1] on venomous snakes written by the late Joseph Slowinski, an up-and-coming herpetologist who was the Assistant Curator of the California Academy of Sciences, a year before he died of a snakebite from a multi-banded krait (*Bulgaris multicintus*) in the remote part of northern Myanmar. He was on his 11th expedition to Myanmar to study its snakes and reptiles there when on the morning of the 11 September 2001, he casually picked up a pencil thin, foot long snake that had bitten a team member the day before to study it. He realised it was venomous but not before he was bitten. There was no pain. He died of neurotoxin effects 30 hours later despite his colleagues' best efforts to keep him alive by rescue breathing – a sombre truth of his quotation.

Snakebites invoke fear and panic of death from envenomation. Fortunately, the majority of bites are from non-venomous bites and only 10-20% of bites end up with envenomation or ophitoxaemia. Many ineffective ways of first aid have been described. The method of pressure-immobilisation first aid first developed by Professor Struan Sutherland in the 1970s has a scientific proof that it works (Sutherland, 1981)[2]. It is the method adopted by the Australian Resuscitation Council, the Royal Australasian College of Surgeons and the Australian and New Zealand College of Anaesthetists as the effective method of first aid against envenomation.

It is important for us to update ourselves on the truth about snakes and their bites. For this, we need to thank the herpetologists - people who have an interest to study snakes and do research on them so that we know how to deal with their bites.

Countries rich in venomous snakes are the Indian subcontinent, Myanmar and Australia. What is important to say is that snakes generally attack only when provoked e.g. being handled or trodden upon. The latter is likely to happen in the tropics after the rains when snakes are flushed out of their habitat and come face-to-face with man. In America, deaths are mainly in snake handlers. The mistaken notion that snakes should be eliminated result in snake hunts when some become snakebite victims as the snakes strike back in self-defence. The availability of anti-snake venoms has reduced the number of deaths in those with ophitoxaemia.

It is also important to remember that a killed snake can still bite and kill. There are instances on record wherein a recently killed snake and even those with severed heads have ejected venom into those handling them. Ban on handling and extreme caution in transportation which is usually advocated for killed snakes (Warrel, 1996)[3].

VENOMOUS SNAKES

Of the 2500-3000 species of snakes distributed world-wide, about 500 are venomous (Matthew JL, and Gera T, 2000)[4]. Venomous snakes belong to one of the four families namely, the Elapidae, Hydrophidae, Viperidae and the Colubridae. Snake venoms have been classified as neurotoxic, coagulopathic, and myotoxic and these are respectively the result of the envenomation

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predominantly from the elapids, the vipers and the sea snakes. The colubrids cause a slow coagulopathy.

The distinction is not always so straightforward. Elapid bites can also produce symptoms typical of viperid bites, and many viperid bites result in neurotoxic symptoms. One generalization that can be made is that elapids are more toxic than viperids. The neurotoxic proteins they have evolved are extremely effective at bringing about death with minimal disturbance to the body. Viperid venoms, on the other hand, are messy – tearing apart tissues and literally melting cells. So an elapid venom is more likely to kill a person, but will leave a far prettier corpse (Slowinski, 2000)[1].

Elapidae

The Elapidae are exemplified by the cobra and the kraits. In Singapore, we have the king cobra and the banded krait. In Australia, there are the brown snakes and taipans. In Mexico and the United States there are the coral snakes, which are so-called because they are brightly coloured. In Singapore, we also have the blue coral snake.

Venoms from elapid snakes kill via proteins called neurotoxins, which disable muscle contractions and bring about paralysis. These neurotoxins cause peripheral paralysis by competitively binding to postsynaptic nicotinic acetylcholine receptors at the neuromuscular junction. Death from elapid bites generally result from asphyxiation because the diaphragm can no longer contract. They can also cause death by sudden cardiac muscle spasm.

Viperidae

The snakes in the Viperidae family are the vipers. In the Indian subcontinent, this family is represented by the Russell's viper (*Daboia rusellii*), pit viper and saw-scaled viper *(Echis carinatae)*. In the United States, we have the rattlesnakes, copperheads, and water moccasins. In Singapore, we have the shore pit-viper, the Sumatran viper and the Wragler's pit-viper.

Viperid venoms contain an abundance of protein-degrading enzymes called proteases, which produce extensive local swelling and necrosis, and blood loss from cardiovascular damage complicated by coagulopathy, or disruption of the blood clotting system. Death from viperid bites is generally caused by a collapse of blood pressure.

Hydrophidae

These are the sea snakes. They are toxic but seldom bite, even if roughly handled. The clinically relevant toxins in sea snake venom are neurotoxins and myotoxins Their potent myotoxins account for the significant muscle necrosis, with consequent myoglobinemia and hyperkalemia that may occur following envenomation. Sea snake venom does not affect blood coagulation to a significant degree. Sea snakes are closely related to Australian elapids; some paraspecificity exists between sea snake antivenom and Australian elapid antivenom.

Colubridae

The snakes in the Colubridae family should be considered venomous. The venom causes a slow coagulopathy and can be lethal. They include the African boomslang and twig snake and the Southeast Asian red-necked keelback. The latter is in fact kept as pets.

The mistaken sense of security has resulted in deaths before people become wiser. Joseph Slowinski had this to say about the colubrids (Slowinski, 2000)[1]: "*Although it had long been*

understood that some colubrids are venomous, the potential threat posed to human life by these species was not really taken seriously until two of the most prominent herpetologists of the twentieth century found out the hard way that some colubrids can inflict fatal bites. Karl Schmidt of the Field Museum of Natural History in Chicago died after suffering a bite from an African boomslang in 1957. And in 1975 a bite from an African twig snake killed German herpetologist Robert Mertens. Neither man sought medical help at the time, largely because the lack of severe symptoms early on led each to underestimate the gravity of his condition.

These unfortunate incidents drove home the point in the herpetological community that at least some colubrids should be treated with extreme caution. But which ones, other than boomslangs and twig snakes? We don't really know, although we think that at least 25 percent of colubrid species are venomous. But we have little idea how dangerous they are. Unlike the front-fanged elapids and viperids, the venomous colubrids are rear-fanged snakes, which must hang on and chew when they bite to inject any venom. Further, many venomous colubrids are docile and reluctant to bite, even when picked up.

I suspect that several other colubrid species will turn out to be lethally toxic to humans. Several years ago, a beautiful Asian snake, the red-necked keelback (Rhabdophis subminiata), was commonly sold into the pet trade as harmless, until one fatal and several near-fatal bites occurred to people handling them. In fatal bites by the toxic colubrids, the venom acts in the following insidious way. Initially, the venom proteins promote massive blood clotting, which leads to headaches, dizziness, and vomiting. This subsides after a day or so, and the victim begins to feel better. But the victim is actually dying. The person's clotting protein has been used up, and can no longer plug leaks in the circulatory system. An autopsy of Karl Schmidt revealed that, even as he prepared to go back to work, he had been hemorrhaging from small leaks all over his body. People tend to categorize snakes as either venomous or harmless, but, as colubrids demonstrate, the reality is a continuum, from completely harmless, to mildly venomous, to deadly."

A report in the SMJ (Seow, 2000)[5] of such a snakebite in a 21-year-old student presented to the A & E Department in Tan Tock Seng Hospital two days after he was bitten on his left middle finger by his pet snake reiterated what Slowinski related, except the Singapore victim was more fortunate. This snake had held onto the student for 2 minutes.

Subsequently, he developed a swelling of his right knee, haemoptysis and bleeding from his gums and skin. On admission, his fibrinogen level was undetectable and the D-Dimer was 2 eg/mL. He remained in DIVC for the next 14 days. Consequently, he developed gross haematuria as well as haemorrhage in the right iliopsoas muscle. The latter resulted in weakness of his right leg, probably due to compression neuropathy. His haemoglobin level dropped from 15.5 gm to 8.8 gm. He was given 59 bags of fresh frozen plasma, 76 bags of cryoprecipitate and 2 units of packed red cells during hospitalisation. He was able to ambulate upon discharge although he had not regained full power in his right hip. On his last review, his general condition had improved and his fibrinogen level had risen to 2.5 gm/L. The take home message of the authors was the red-necked keelback be considered a dangerous animal and the public be discouraged from keeping it as a pet.

DANGER AND DEATH FROM SNAKEBITES

Danger from snakes depends on more than just the toxicity of its venom. Many sea snakes have very toxic venoms, but almost never bite, even when handled roughly. On the other hand, the vipers are notorious for their readiness to bite humans. One such species is the Russell's viper of India and Southeast Asia, which kills many people. One herpetologist, the late Slowinski's testimony of its aggressiveness is graphic, "*I have watched an angry Russell's viper in Myanmar striking wildly at anyone or anything that came near it*."

Main killers

Around the world, the elapids and vipers are the main venomous snakes that cause mortality or morbidity. Reliable figures do not exist, but elapids and viperids together may kill between 10,000 to 50,000 people a year worldwide. On an average – cobras and sea snakes result in about 10% mortality – ranging from 5-15 hours following bite. Vipers have a more variable mortality rate of 1-15% and generally more delayed (up to 48 hours).

Clinical features and outcomes are not as simple to predict because every bite does not result in complete envenomation. Morbidity and mortality resulting from snake-bite envenomation also depend on the species of snake involved, since the estimated "fatal dose" of venom varies with species.

The vast majority of these deaths occur in the tropics, where, for reasons not understood, venomous snakes tend to have more toxic venoms, and where people come into contact with snakes more frequently. Epidemics of snakebite following floods owing to human and snake populations getting concentrated together have been noted in Pakistan, India and Bangladesh. In the United States, where snakebites generally cause fewer than five deaths a year, many bites happen to people who handle snakes (Slowinski)[1].

India. In India, of the 52 poisonous species there, the majority of bites and consequent mortality is attributable to 5 species, three of which belong to the Elapidae family viz. *Ophiophagus hannah* (king cobra), *Naja Naja* (common cobra), *Bungarus caeruleus* (krait) and the remaining two are Russell's viper (*Daboia rusellii*), and saw-scaled viper. *(Echis carinatae)*.

In the Indian setting, almost two-thirds of bites are attributed to saw-scaled viper (as high as 95% in some areas like Jammu), about one fourth to Russell's viper and smaller proportions to cobra and kraits (Saini et al, 1984)[6].

Nepal. There are 14 venomous species in Nepal. These include pit vipers (5 species), Russell's viper, kraits (3 species), coral snake and 3 species of cobra including the king cobra (Bhetwal et al, 1998)[7].

Sri Lanka. In Sri Lanka, *Daboia russellii* accounts for 40% of bites and *Naja naja* for another 35% (Silva de A, 1981)[8].

Myanmar. Daboia russellii alone accounts for 70% bites in Myanmar (Aung-Khin, 1980)[9].

Australia. Of all the cases of snakebites in Australia, only 2-3 fatalities occur per year. About 3000 bites occur per year in Australia from all species of snakes, 500 of which require antivenin. As many as 60% of fatalities from snake envenomations may be attributed to the brown snake. Approximately 30% of brown snakebites cause systemic envenomation; 60% of bites with systemic involvement produce altered mental status, loss of

consciousness, or seizures; and approximately 33% of these present with defibrination syndrome (Chun & Cheng, 2001)[10].

EPIDEMIOLOGY OF SNAKEBITE

The predominance of male victims suggests a special risk of outdoor activity. The high incidence of snakebite between the early hours of the morning to midnight corresponds well with the period of maximum outdoor activity observed in most studies. The incidence of snakebite shows a distinct seasonal pattern closely related to rainfall and temperature which compels the reptiles to come out of their shelter (Hansdak et al, 1998)[11]. A large number of bites occur in fields, most individuals are unable to spot the snake due to tall grass and crops. The observation that the most frequent site of bite is the lower extremity suggests that in most cases the snake is inadvertently trodden upon.

Among the host factors, people involved in occupations and/or lifestyles requiring movement in dense undergrowth or undeveloped land, are the worst affected. These include farmers, herders and hunters and workers on development sites. Paul reported an incidence of 7-15 percent in children less than10 years. For obvious reasons, bites are maximal in lower limbs (about two thirds) (Warrel, 1996)[3] with 40 percent occurring in the feet alone.

CLINICAL MANIFESTATIONS

Fear and panic

The most common and earliest symptom following snakebite (poisonous or non poisonous) is fright, particularly of rapid and unpleasant death. Fear may cause transient pallor, sweating and vomiting.

Bite marks

A venomous snakebite may have classical paired fang marks, but this is not the most common picture. Often there are just a few lacerations or scratches, and sometimes these may be painless or go unnoticed. A row of bite marks, if present suggests a non-venomous bite.

LOCAL MANIFESTATIONS OF ENVENOMATION

Pain and numbness

Not all venomous snakebites are painful. The bite site can be painless if it is an elapid bite. Tingling and numbness over the tongue, mouth and scalp and paraesthesia around the wound occur mostly in viper bites.

Bruising, bleed and local swelling

Local bleeding including petechial and/or purpuric rash is seen most commonly in bites from the viper family. Major bleeding disturbances are seen with the American Western diamondback rattlesnake.

A graphic account of such a bite is given by Slowinski (Slowinski, 2000)[1]: "*The snake seizes the opportunity to plunge its two fangs into the man's forearm. Within seconds the venom molecules begin to destroy tissue around the wound. The forearm quickly swells and becomes black and purple; the pain is intense. But these are only the first, localized symptoms. As the blood spreads the toxins around the body, the venom molecules attack the circulatory system: destroying red blood cells, punching holes in the blood vessels, and interfering with blood clotting. Twelve hours after the bite, large, blood-filled blisters appear all over the arm. As blood continues to leak out through perforated vessels, the blood pressure drops precipitously.*" Fortunately, with antivenin treatment the man survived.

Major bleeding disturbances are rare with Australian snakes, although the development of coagulopathies and a DIVC-like picture are relatively common. Thromboctopaenia and haemolysis may occur. Watch for haematuria, haemoptysis, haematemesis, low bowel haemmorrhage, menorrhagia or haemoglobinuria, and remember that about 20% of patients who die after snakebite have cerebral haemmorrhages.

Lymphadenopathy

Regional lymphadenopathy may be marked, even with non-venomous snakebites, and is not by itself an indication for the administration of antivenom. It may contribute to abdominal pain in children.

SYSTEMIC MANIFESTATIONS OF ENVENOMATION

The time onset of poisoning is similar in different species. Cobra produces symptoms as early as 5 minutes or as late as 10 hours after the bite. Vipers take slightly longer – the mean duration of onset being 20 minutes. However, symptoms may be delayed for several hours. Sea snakebites almost always produce myotoxic features within 2 hours, so that they are reliably excluded if no symptoms are evident within this period.

Neurotoxic features

These are typically seen in a bite from cobra, kraits and coral snakes. Neurotoxic features are a result of selective d-tubocurarine like neuro-muscular blockade which results in flaccid paralysis of muscles. Cobra venom is however 15-40 times more potent than tubocurarine.

Paralysis, when it occurs, usually commences with cranial nerves, then skeletal muscle, then the muscles of respiration. In small children or with highly venomous snakebites, it may happen much more quickly. Ptosis is the earliest neuroparalytic manifestation followed closely by opthalmoplegia. Paralysis then progresses to involve muscles of palate, jaw, tongue, larynx, neck and muscles of deglutition-but not strictly in that order. Generally, muscles innervated by cranial nerves are involved earlier. However, pupils are reactive to light until terminal stages. Muscles of chest are involved relatively late with diaphragm being the most resistant. This accounts for the respiratory paralysis, which is often terminal.

Reflex activity is generally not affected in ophitoxaemia and deep tendon jerks are preserved until late stages.

Onset of coma is variable, however several cases of cobra bite progress to coma within 2 hours of bite. Symptoms that portend paralysis include repeated vomiting, blurred vision, paraesthesiae around the mouth, hyperacusis, headache, dizziness, vertigo and signs of autonomic hyperactivity.

Cardiotoxic features

Cardiotoxic features include bradycardia, hypotension and ECG changes. Cardiotoxicity occurs in about 25% viperine bites and includes rate, rhythm and blood pressure fluctuations. In addition, sudden cardiac standstill may also occur owing to hyperkalemic arrest. Tetanic contraction of heart following a large dose of cobra venom has been documented in vivo and in vitro.

Coagulopathic features

Snake venoms cause haemostatic defects by a number of different mechanisms. Some cause activation of intravascular coagulation and result in consumption coagulopathy. Notable in this

group is *Daboia russelli* which has procoagulant activating factors V and X. Diamondback rattlesnake venom causes defibrinogenation by activating endogenous fibrinolytic system. Besides direct effects on the coagulation cascade, venoms also can cause qualitative and quantitative defects in platelet function.

In India and Sri Lanka, Russell's viper envenomation is often associated with massive intravascular haemolysis. Haematological changes – both local as well as systemic – are some of the commonest features of snakebite poisoning. Bleeding may occur from multiple sites including gums, GIT (haematemesis and melaena), urinary tract, injection sites and even as multiple petechiae and purpurae. Subarachnoid haemorrhages were documented in 5 of 200 cases in Saini's series of patients in Jammu region (Saini, 1984)[6]. In addition, cerebral haemorrhage and extradural haematoma have also been reported.

Myotoxic features

Muscular aches worsen with movement and usually begin in the bitten extremity and neck 30-60 minutes after envenomation are typically seen with sea snakebites. Muscle necrosis may also result in myoglobinuria.

Renal failure

Almost every species of snake can cause renal failure. It is fairly common following Russell's viper bite and is a major cause of death (Myint-Lwin et al, 1985)[12]. In a series of 40 viper bites, renal failure was documented in about a third (Vijeth et al, 1997)[13]. The extent of renal abnormality in them correlated well with the degree of coagulation defect. However, in a majority, renal defects persisted for several days after the coagulation abnormalities normalized, suggesting that multiple factors are involved in venom induced acute renal failure.

Acute deterioration and death

Brown snakebites are common in Australia, even apparently trivial ones have been associated with acute deterioration over a five minute period leading to death. This may occur as soon as 30 minutes to an hour after the original bite. Acute, severe cardiac depression may be the mechanism for sudden death.

Confusion and loss of consciousness

Snakebite should always be considered in any case of unexpected confusion or loss of consciousness following outdoor activities in a snake country e.g. in Australia.

Toxemia without bite

Naja nigricollis (spitting cobra) is a species which can eject venom with considerable accuracy even from a distance of 6-12 feet (Warrel, 1996)[3]. The exact range and target of this snake's venom is a matter of considerable debate among herpetologists. Most are in agreement that the venom is aimed at the victim's eyes resulting in conjunctivitis and corneal ulceration. The latter may be deep enough to cause anterior uveitis and hypopyon. There are patients who have required enucleation of both eyes following a vicious attack by the spitting cobra. Besides the local manifestation, a dull headache persisting beyond 72 hours is a common feature. Spitting cobra is an exotic species since even the king cobra does not eject venom in this manner.

Long term effects of venomous snakebites

In most cases of venomous bites, swelling and oedema resolve within 2 to 3 weeks. However, they

may occasionally persist up to 3 months. In exceptional circumstances, they may also be permanent. There are records which suggest that coagulation disturbances and neurotoxicity may persist beyond 3 weeks. Necrosis of the local tissue, resultant gangrene and the consequent cosmetic defects are obvious long term effects of ophitoxaemia (Reid, 1983)[14].

Necrosis is typical of bites by the African spitting cobras (*Naja nigricollis, Naja mossambica, Naja pallida*, and *Naja katiensis*), *Naja atra* (the Chinese cobra), *Naja kaouthia* (monocellate cobra), and *Naja sumatrana* (Sumatran spitting cobra). Although the venoms of these cobras contain neurotoxins, necrosis is often the chief or only manifestation of envenoming in humans.

Snakebites With No Manifestations

The most obvious explanation for a confirmed snakebite but no clinical manifestations is bite by a non-poisonous species. However, it is well documented that a large number of poisonous species also often do not cause symptoms. In Saini's study of 200 cases in Jammu region in India, in which only 117 showed symptom/sign of envenomation (Saini, 1984)[6].

From the relatively low frequency of poisoning following snakebites, it has been suggested that snakes on the defensive when biting humans seldom inject much venom. Other possible explanations include a bite without release of venom (dry bite). In a study of 40 bites by snakes which were captured and identified as poisonous, about one- third showed no clinical or laboratory evidence of systemic envenoming suggesting a high incidence of dry bites (Silveria PV and Nishioka, C de A, 1995)[15].

There are also cases wherein venom is spewed into the victim's body as the snake attempts to bite, thereby reducing the overall quantity of venom in the blood stream. Almost 30% of cobra bites are "superficial" with minimal envenomation. Other protective factors include the layers of clothing or boot leather through which the snake sometimes strikes.

APPROACH TO AN INDIVIDUAL ALLEGEDLY BITTEN BY A SNAKE

In a patient presenting with history suggestive of snake-bite, it is important to address the following questions.

1. Is it actually a snakebite?

Non-poisonous snakes generally leave a row of tooth impressions, but not fangs marks. However, it is advocated that too much stress should not be laid on this rather variable feature. Venomous snakes may not all leave fang marks if the bite is a glancing bite, or clothing or shoes prevent both the fangs from sinking into the body.

2. Could it be anything else?

Russell contends that the marks left by snakes may be so variable as to make it difficult to distinguish from bites of rats, mice, cats and even lizards. They may also be confused with insect and scorpion bites/stings. Scratches or penetration by thorns or cactus may also leave marks like those of fangs; all these may be accompanied by local changes further compounding the problem of correct diagnosis.

3. Is it likely to be a poisonous species?

There is no simple, reliable method to distinguish poisonous from non-poisonous

species. Poisonous species generally have fangs but these may be very small in elapids and not easily visible in vipers. Tails are usually not compressed and belly scales are small in non-venomous species – all of which are opposite in poisonous species. Short of identifying the offending reptile, the only way to determine the poisonous nature of a species is to watch for features of envenomation, namely, local changes and/or systemic features.

4. Which species is involved?

Among the commonest poisonous species seen in Singapore, the cobra is easiest to identify owing to a mental picture well entrenched in most peoples' minds. It has a hood bearing a single or double spectacle shaped mark on its dorsal aspect. A white band in the region where the body touches the hood is another identifying feature. In general, elapidae have relatively short, fixed front fangs; as do the Hydrophidae.

Russell's viper is identified by its flat, triangular head with a white 'V' shaped mark and three rows of diamond-shaped black or brown spots along the back. The fangs of vipers are long, curved, hinged, front fangs, which have a closed venom channel, giving them a structure akin to a hypodermic needle. Besides these, there are several other differentiating characteristics among the poisonous snakes, which are of more interest to an expert than medical personnel.

LABORATORY AIDS IN OPHITOXAEMIA

Laboratory tests are useful for monitoring, prognosticating victims of ophitoxaemia, as well as determining stages of intervention. Recently emphasis is being laid on the value of immuno-enzymatic tests to identify the offending species accurately.

Haematological changes. Haematological changes include anaemia, leucocytosis and thrombocytopenia. In addition, peripheral smear may show evidence of haemolysis, particularly in viperine bites.

Coagulopathies. Deranged coagulant activity manifested by prolonged clotting time and prothrombin time may also be evident. The quality of clot formed may be a better indicator of coagulation capability than the actual time required for formation, since clot lysis has been observed in several patients who had normal clotting time. Hypofibrinogenemia may also be evident. CSF haemorrhage has been documented in a minority of victims.

Electrolyte and blood gas changes. Hyperkalaemia and hypoxemia with respiratory acidosis, especially with neuroparalysis may be present.

Urine abnormalities and renal changes. Urine examination could reveal haematuria, proteinuria, haemoglobinuria or myoglobinuria. In cases of ARF, all features of azotemia are also present.

ECG changes. ECG changes are generally non-specific and include alterations in rhythm (predominantly bradycardia) and atrioventricular block with ST segment elevation or depression. T wave inversion and QT prolongation have also been noted. Tall T waves in lead V2 and patterns suggestive of acute anterior wall infarction have

been reported as well. In addition, cases who develop hyperkalaemia manifest typical changes of this electrolyte disturbance.

MANAGEMENT OF OPHITOXAEMIA

First aid

The lymphatic system is responsible for systemic spread of most venoms. This can be reduced by the application of a firm bandage (as firm as you would put on a sprained ankle) over a folded pad placed over the bitten area. While firm, it should not be so tight that it stops blood flow to the limb or to congest the veins. The bitten area should be immobolised to reduce movement and the victim instructed to stay still in order to delay systemic spread of the venom. These findings were from the research done by Struan Sutherland in the 1970s and reported in medical journals (Sutherland, 1981)[2]. This "pressure-immobilisation" technique is currently recommended by the Australian Resuscitation Council, the Royal Australasian College of Surgeons and the Australian and New Zealand College of Anaesthetists.

If the bandages and splint have been applied correctly, they will be comfortable and may be left on for several hours. They should not be taken off until the patient has reached medical care. The treating doctor will decide when to remove the bandages. If a significant amount of venom has been injected, it may move into the blood stream very quickly when the bandages are removed. They should be left in position until appropriate antivenom and resuscitation equipment have been assembled. Bandages may be quickly reapplied if clinical deterioration occurs, and left on until antivenom therapy has been effective.

Technique

Start bandaging directly over the bitten area, ensuing that the pressure over the bite is firm and even. Do not take off any clothing as this will in the process cause movement and assist spread of the venom. If you have enough bandage you can extend towards more central parts of the body, to delay spread of any venom that has already started to move centrally. A pressure dressing should be applied even if the bite is on the victim's trunk or torso.

Immobility is best attained by application of a splint or sling, using a bandage or whatever to hand to absolutely minimise all limb movement, reassurance and immobilisation (eg, putting the patient on a stretcher). Where possible, bring transportation to the patient (rather then vice versa). Don't allow the victim to walk or move a limb. Walking should be prevented.

Bite in the arm

Bandage as much of the arm as possible, starting at the fingers. Use a splint to the elbow. Use a sling to immobilise the arm. Do no restrict chest movement. Keep the patient still.

Bite in problem areas

Bites to the head, neck, and back are a special problem – firm pressure should be applied locally if possible.

What should not be done

DO NOT cut or excise the bitten area. DO NOT apply an arterial tourniquet. (Arterial tourniquets, which cut off the circulation to the limb, are potentially dangerous and are no longer recommended for any type of bite or sting in Australia. DO NOT wash the bitten area if snake identification is to be attempted with venom detection kits. Removal of the bandage will be

associated with rapid systemic spread. Hence ALWAYS wait until the patient is in a fully-equipped medical treatment area before bandage removal is attempted.

Medical Management

The Australian experience is that only 1 in 20 snakebites require active emergency treatment or the administration of antivenom. Medical management depends on the degree of systemic envenomation and the type of venom.

Critically ill patients

These are patients with hypotension and having respiratory difficulties.

- Maintain immobilisation, splint and bandage until the situation is under control
- Support airway, breathing and circulation. Intubate and ventilate with 100% oxygen if airway or assisted respiration fail
- Intravenous adrenaline should be given only for life threatening hypotension or anaphylaxis – its use has been associated with cerebral haemorrhage
- Give antivenom immediately if available. Repeat antivenom as clinically indicated
- Volume expansion may be necessary
- Severe coagulation disturbances, electrolyte abnormalities, and muscle damage leading to acute renal failure are likely and should be looked for
- General management as for less seriously ill patients as well (see below).

In cases of bleeding, replacement with fresh whole blood is ideal. Fresh frozen plasma and fibrinogen are not recommended. Volume expanders including plasma and blood are recommended in shock, but not crystalloids. Persistent shock may require inotrope support under CVP monitoring. Early mechanical ventilation is advocated in respiratory failure though dramatic responses have also been observed with edrophonium followed by neostigmine. Cases of acute renal failure generally respond to conservative management. Occasionally peritoneal dialysis may be necessary. In cases of DIVC, use of heparin should be weighed against risk of bleeding and hence caution is advocated.

Less seriously ill patients

These are patients with no signs of systemic spread

- Admit to ICU for non-invasive monitoring, strict bedrest and full head injury observations (wake hourly)
- Leave bandages in place
- Obtain appropriate antivenoms and venom detection kit
- Obtain intravenous access
- Take blood for group and X-match, coagulation screen (including fibrinogen levels, and tests for DIVC), full blood count, electrolytes and calcium, creatinine kinase and arterial blood gases. Perform ECG. Repeat at appropriate intervals
- Collect urine for microscopy to detect haematuria and for free protein, haemoglobin and myoglobin measurement. Record urine output. Freeze the first sample for venom detection
- Draw up adrenaline, antihistamine, and steroids in case of anaphylaxis to antivenom
- When ready, cut a hole over the wound site, inspect and take swabs for use with the venom detection kit
- Once the results of the venom detection kit

are known, slowly and progressively remove the bandages. Don't rush. Watch closely for systemic symptoms of envenomation. *If systemic symptoms ensue:* re-apply bandages and give antivenom as clinically indicated.

Follow-on management

Beyond the immediate hospital management, there is a need to monitor the patient, to detect and correct the systemic effects of envenomation.

- Ensure the patient is well hydrated (to reduce the risk of acute renal failure due to rhabdomyolysis)
- Repeat blood tests, ECG, etc at clinically relevant intervals
- Correct abnormal coagulation; look out for disseminated intravascular coagulation
- Correct hypotension, if present, with volume expansion and vasopressors (exclude occult bleeding)
- Watch for development of renal failure – monitor urine output and composition.
- Tetanus prophylaxis is recommended
- Analgesia and sedation where needed but be cautious.

Usually, if there are no signs of envenomation four hours after removal of the bandages, and if repeat blood tests taken at that time are normal, then it is probable that significant envenomation has not occurred. If laboratory tests are not available, 12 to 24 hours is a reasonable period of observation.

Use of antivenin

Antivenins are prepared by immunizing horses with venom from poisonous snakes and extracting the serum and purifying it. Antivenins or antivenins may be species specific (monovalent) or effective against several species (polyvalent). Monovalent antivenin is ideal, but the cost and non-availability, besides the difficulty of accurately identifying the offending species, makes its use less common.

Indications for use. There are specific indications for use of antivenin. Every bite, even if by poisonous species does not merit its use. This caution against the empirical use of antivenin is due to the risk of hypersensitivity reactions. Antivenin is indicated only if serious manifestations of envenomation are evident, namely: coma, neurotoxicity, hypotension, shock, bleeding, DIVC, acute renal failure, rhabdomyolysis and ECG changes. In the absence of these systemic manifestations, swelling involving more than half the affected limb, extensive bruising or blistering and progression of the local lesions within 30-60 minutes are other indications.

Dose. Conventionally 50 ml (5 vials) are infused for mild manifestations like local swelling with or without lymphadenopathy, purpura or ecchymosis. Moderate envenomation defined by presence of coagulation defects or bradycardia or mild systemic manifestations, merits the use of 100 ml (10 vials). 150 ml (15 vials) is infused in severe cases, which includes rapid progression of systemic features, DIVC, encephalopathy and paralysis.

Administration. The freeze dried powder is reconstituted with 10 ml of injection water or saline or dextrose. A test dose is administered on one forearm with 0.02 ml of 1:10 solution intradermally. Similar volume of saline in the other

forearm serves as control. Appearance of erythema or wheal greater than 10 mm within 30 min is taken as a positive test. In this event, desensitization is advised starting with 0.01 ml of 1:100 solution and increasing concentration gradually at intervals of 15 minutes till 1.0 ml subcutaneous can be given by 2 hours. Infusion is started at 20 ml/kg per hour initially and slowed down later. Antivenin is administered by the intravenous route.

Timing. Best effects are observed within four hours of bite. It has been noted to be effective in symptomatic patients even when administered up to 48 hours after bite.

Response. Response to infusion of antivenin is often dramatic with comatose patients sitting up and talking coherently within minutes of administration. Normalization of blood pressure is another early response. Within 15 to 30 minutes, bleeding stops though coagulation disturbances may take up to 6 hours to normalize. Neurotoxicity improves from the first 30 minutes but may require 24 to 48 hours for full recovery.

Reactions. Hypersensitivity reactions including the full range of anaphylactic reactions may occur in 3-4% of cases, usually within 10 to 180 minutes after starting infusion. These usually respond to conventional management including adrenaline, anti-histamines and corticosteroids.

If an antivenom is administered, ALWAYS advise the patient of the possibility of delayed serum sickness (up to 14 days later). This is characterised by fever, rash, generalised lymphadenopathy, aching joints and renal impairment. The likelihood of developing this depends on the volume of antivenin required. It occurs in about 10% of patients who are given polyvalent antivenins. Treatment with steroids is usually all that is needed.

TAKE HOME MESSAGES

The following take home messages help to rationalize our approach to snakebites and their venoms:

- Venomous snakes often do not attack unless provoked, so leave them alone.
- The propensity to bite varies with the species. Sea snakes are very toxic but seldom bite even when roughly handled. Vipers are aggressive and tend to bite.
- In the event of a snakebite, the presence of symptoms of envenomation like tingling, numbness or bleeding manifestations clearly indicate some haste in getting the patient to medical attention is indicated.
- For the rest, it is no harm to apply the pressure-immobilisation method as first aid unless one is quite sure the snake is harmless. A pressure bandaging-immobilisation first aid using the method of Prof Sutherland and adoped by the Australian Resuscitation Council helps to slow down systemic envenomation if the bite was truly venomous. The bandaging pressure to achieve is like that used in bandaging a sprained ankle. It should be firm bandaging but comfortable and can be left for some hours.
- Thankfully, some 80% of bites from venomous snakes are dry bites containing no venom. Anyway, if uncertain, it is better to apply pressure bandage rather than not.

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