CLINICAL SEQUELAE OF SNAKE BITE

A McKillop.

If Dr Sutherland has trouble being original I do not know what chance I have got, talking about snake bite. It is a bit like neurosurgical anaesthesia, speaking fourth after three other experts, a lot of repetition, probably about 5% panic and no idea what the end result is going to be.

It is my brief to describe the clinical conditions which should be anticipated when patients have been envenomated by Australian land snakes. Much of it has been said. The protocol for managing land snake envenomation developed by Dr Sutherland and his colleagues is well documented. No doubt due to the availability of information, expertise and anti-venom in Australia, it is possible to gain the impression in clinical practice that it is a very uncommon event for our patients to develop serious complications. It is these uncommon events that I shall be describing today.

Snake bitten people still die in Australia. Why is that? The short answer is that the major lesions in envenomation are neurological, haemostatic and cytoycotoxic and they can rapidly lead to either serious illness or death. Usually, appropriate first-aid, if applied, will delay systemic envenomation and its consequences, until medical expertise is available to manage them. Rarely, patients suffer intravenous envenomation or massive envenomation following multiple bites and even rapidly applied first-aid may not prevent systemic envenomation. Anaphylactic reactions may claim other lives. Perhaps most of these deaths are inevitable. The mistake of assuming that a snake is harmless has recently in Queensland caused a death because of belated presentation for medical care. The situation more tragic than all of these is that of an ill patient reaching medical care with no history of envenomation and the diagnosis not being made because it is not considered.

Major sequelae are rare if appropriate first-aid has been applied and appropriate antivenom given. If the incorrect anti-venom is given based on correct identification of a snake, or if larger than standard volumes of anti-venoms are not administered when indicated, or if there is a significant delay before administration of antivenom, or if antivenom is not given at all when indicated, then the instance of major sequelae is greatly increased.

To return to the uncommon yet, particularly to those working in intensive therapy, the ever present possibility of failing to diagnose envenomation in ill patients giving no history of snake bite. The bite episode may not have been noted, the lesion may be invisible or atypical or, particularly in children, be unreported. A 7 year old child was bitten three times on the foot by a Taipan. The child presented 36 hours after envenomation to the practitioner, not knowing he had been bitten, with a history of not being able to swallow his Vita-Brits. At this stage the presenting symptom was difficulty in breathing. It was decided that perhaps the child could have epiglottitis, so the child was taken to theatre and intubated for epiglottitis and the epiglottis was normal. A further search was made and the bites were found. These situations can occur.

How may these worrisome patients present? The triad of headache, nausea, and vomiting are common early symptoms of envenomated patients. The diagnosis of envenomation, probably should always be excluded in areas where envenomation may have occurred in such presentations. The recent onset of cranial nerve palsy particularly ptosis, diplopia and dysarthria, limb weakness or ataxia should direct attention to a possible toxic origin. Drowsiness or coma, usually secondary to respiratory insufficiency, may be misinterpreted if envenomation is not included in the differential diagnosis. Spontaneous haemorrhage from acute coagulopathy is a rare yet potential presenting symptom. Bruising and swelling of the bitten area may, and has, mimicked traumatic, inflammatory or infective lesions. A band-aid placed over the bite area on the foot, could easily lead a Casualty RMO astray in managing a patient to consider his illness due to a septic arthritis. Many conditions have, in the literature, been noted as being incorrectly diagnosed in patients suffering from snake bites. Venom detection kits should be part of our diagnostic work-up in such conditions if any possibility of envenomation exists.

What then should we anticipate in those patients who have a history of envenomation or potential envenomation? I will exclude anaphylactic and anaphylactoid reactions which have been mentioned by Dr Airey. The major systemic dysfunctions which our patients may develop, are neurological, haemostatic and renal. The physician attending the patient must remember these when faced with a case of multiple poisoning. Three or more toxic reactions or changes may occur simultaneously or consecutively. The resultant syndromes are ventilatory failure, coagulopathy and acute renal failure. Each may be fatal in its own right, or may set the scene for sepsis, circulatory failure or complications of therapy. Although venom of various species may show a predilection towards a particular lesion, in practice, any envenomated, or possibly envenomated, patient must be handled with multi-system vigilance.

In looking in more detail at these pathological processes, I would like to make some comments on the neurological lesion. Accepting, as an anaesthetist, that diaphragmatic and intercostal paralysis is a worrisome clinical event, following envenomation you must remember that the progressive neuro-muscular blocking actions of the venom can precipitate severe pulmonary complications much earlier. The respiratory morbidity will be exacerbated by failure to appreciate the contribution of upper airway obstruction, aspiration of oropharyngeal secretions and gastric contents to the clinical events of atelectasis and pulmonary soiling. The cranial and peripheral neurological impairment may be of insidious or dramatic onset and vary from transient weakness to complete and persistent paralysis. Careful and repeated observations of neurological and respiratory status, should continue until resolution of neurological symptomatology has occurred. It is a common clinical observation that once significant neurological impairment exists, the response to anti-venom may be quite unimpressive. The management of patients with progressive respiratory impairment is familiar to us all. The lateral position, frequent oropharyngeal suction,

supplementary oxygenation and cessation of oral intake are appropriate initial responses. Correct, adequate and early anti-venom administration may minimize further impairment but progression may occur despite such therapy. Early tracheal intubation and skilled ventilatory support will minimize respiratory morbidity and may be needed for several days, even a week or more, until ventilatory adequacy and pharyngeal reflexes have returned. Adequate nutrition should be maintained and narrow-bore enteral feeding is usually tolerated by these patients.

The haemostatic deficit is initiated by prothrombin conversion and subsequent fibrogen consumption and depletion. The coagulopathy can be life-threatening. Even in the absence of significant neuro-toxicity it is of particular importance in Tiger, Taipan, Black and Brown snake envenomation. Clinically the disorder may produce oozing from the wound site, venipuncture bleeding, epistaxis, gastro-intestinal, uterine or even intra-cranial haemorrhage. Although death directly attributable to haemorrhage is uncommon, the additional physiological stress placed upon renal and pulmonary function may be a serious consequence. A coagulation profile is of great value and should be performed early and repeated regularly, if it is abnormal or if clinical signs of envenomation persist. The expected abnormalities are prolongation of the whole blood clotting time, prolongation of the prothrombin time and thrombin time, decreased fibrogin, decrease in factor V and VIII and an elevated level of fibrin degeneration products. Although Australian snake venoms may act on platelets in vitro the effect in vivo is variable. Thrombocytopenia accompanying the above abnormalities suggests disseminated intravascular coagulopathy (DIC) which can occur in severe envenomation.

The correct initial response to severe abnormalities is to give further anti-venom which most often produces a clinical response within 12 hours. If despite this therapy the profile remains abnormal and bleeding is worrisome, component therapy may be necessary. There is a real danger of exacerbation of fibrinogen consumption if adequate anti-venom has not been given before fibrogen administration. Secondary fibrinolysis activated by intravascular coagulation frequently accompanies systemic envenomation. It is usually not severe enough of itself to produce serious haemorrhage. It can be readily corrected by the use of Epsilon Aminocaproic Acid (EACA) but in this may have no effect on the clinical state of the patient or on the parameters of defibrination. Animal studies strongly suggest that EACA may increase mortality by inducing widespread intravascular clotting.

Snake venom may produce haemolysis which may be detected by blood film examination, bilirubin elevation, the presence of free haemoglobin, and haemoglobinuria. Microangiopathic haemolytic anaemia has also been described following envenomation in Australia. This is thought to be due to red blood cell injury by fibrin deposition in the micro-circulation.

The cytotoxic nature of venom components is most obvious in its destruction of muscle cells. The patient may complain of muscular pain, muscular tenderness and weakness. Although little is described in clinical literature myocardial involvement is probably concurrent and may contribute to the tachydysrhythmias often seen in snake envenomation. Elevation of all CPK isoenzymes has been shown. This suggests myocardial injury in these patients. The urine may be dark from myoglobin but this should be distinguished from haemoglobinuria by laboratory assay. The most serious consequence of cell destruction is myoglobinaemia and its contribution to the deterioration of renal function which may occur following envenomation. Shock, DIC, haemolysis and the defibrination syndrome have also been incriminated in the appearance of acute renal failure. There maybe a direct nephrotoxic action of a venom component. Renal function, particularly when myolysis is detected, must be monitored carefully. The renal complications may be minimized by correcting dehydration and avoiding hypotension. Therapy includes intravenous hydration, colloid, and vasopressor therapy to maintain renal perfusion and perhaps the use of diuretics to maintain a good urine output. Dialysis may be needed despite this therapy. Acute tubular necrosis is the pathological lesion most often found in envenomation associated with acute renal failure.

Fortunately with effective first-aid, skilled anti-venom and supportive therapy these sequelae of snake bite are relatively uncommon. When they do occur their seriousness may be minimized by anticipation, early recognition and appropriate therapy.

We have been unable to obtain copies of two of the papers presented during this session. These were "Taipan snake bite: a case presentation" by Dr John Orton and "Anaphylaxis complicating snake bite and its treatment" by Dr Ian Airey.

PANEL DISCUSSION

The panel consisted of Drs S Sutherland, J Orton, I Airey and A McKillop.

Question
Can Dr Sutherland explain why Australian snakes are so venomous?

Dr S Sutherland
That is a question that is often raised. There is really no firm answer. The fangs on our snakes are quite small compared with overseas snakes. It seems that instead of developing big jaws and teeth and weak toxins Australian snakes have gone in for powerful toxins and weak teeth.

Question
Although the bandaging technique is of undoubted benefit and represents a huge advance in the management of snake bite, does Dr Sutherland think it is going to increase the incidence of local tissue damage at the bite site. Secondly, whether this form of treatment would be suitable for envenomation, or snake bite, where neurotoxicity is not a major problem?

Dr S Sutherland
By and large the Australian snake venoms do not cause tissue damage such as is caused by Rattlesnake venom, which is full of enzymes to digest the tissues. One worry is what is going to happen when venom is trapped in the tissues for a long time. Will there be necrosis? In some cases, particularly when Tiger snake venom has been kept trapped in the proximity of a blood vessel for five or six hours, an area of necrosis does develop. It may be only 1 cm by 1 cm or the area looks as though it may lose its viability. When that has happened it has only been around the puncture site. If it is a finger the damage only appears on one side of the finger, where the venom is, and does not appear on the other side. If an arterial tourniquet has been applied in that situation there is. quite symmetrical damage around the finger.

Why does this happen? The venom causes intravascular coagulation in all the little vessels in that area. One little boy had first aid on and he had quite a wide area of marked cyanosis when the crepe bandage was taken off. Next day it was all back to normal, with just little fang marks visible. There is a small risk from leaving venom trapped for a long time in the tissues, there may be tissue damage. It does not appear to be serious. It is certainly better than the patient being dead. It varies from one venom to another. For example a bite by a King Brown snake is perhaps the most painful of the snake bites, and it is more likely to cause tissue damage than any other of the snakes. It also puts the biggest volume in so one would expect tissue damage.

People who die from Rattlesnake bite generally die from shock because the whole limb blows up with extravasation of fluid. The central effects are pretty harmless. We did work with Rattlesnake venom and found that the first aid measure kept the venom static. There was some necrosis but it is better to get necrosis at the site of injection than of the whole limb. The most important thing was that with crepe bandages there was no oedema of the limb. Take off the crepe bandage and one could watch the oedema appear. We cannot tell the Americans or Indians what to do. However, we have published material on American venoms in America. There is quite a following in the States for our first aid treatment. It is certainly better than the old ones of using Bowie knives or shooting the finger off.

Question

What is the incidence of false negatives with the venom detection kit?

Dr S Sutherland
You get a false negative when there is no venom or too little in the sample. Even if the test is negative we treat the patient. By and large every time that someone has been sick and the fang marks have been swabbed the venom has been found.

Question

Have you any comment on the attempts by the persons who have been envenomated to bring the reptile with them. In my opinion it is a particularly stupid and dangerous thing to do. It might be then difficult to catch the animal and the staff in hospital are placed in danger.

A voice from the audience
I had an interesting experience in Darwin. A snake was sold to three chaps in the bar at a hotel. It only cost them $1.00. They let it bite them many times. Then we had three patients presenting at once at the hospital. One with gastrointestinal haemorrhage, in the next cubicle was a chap with a fractured jaw, who had collapsed and had broken it on the way to the hospital, and the third chap (this is true, because it was recorded in the papers), went to the labour ward to visit his wife and child taking the snake with him. He collapsed on the ground, lost the snake and the whole Obstetric Department had to be evacuated. The snake, a Western Brown snake, was found two weeks later under the Occupational Therapy Department.

Another voice from the audience
A patient presented to the PA Casualty one day and said he had been bitten by a snake. They asked what sort of snake was it? He replied “I don’t know”. They said, “Did you catch it?” He said, “Yes,” and put his hand into his pocket and pulled out the head of the snake. They asked, “How did you get the head?” He said, “I bit it off.” The casualty staff enquired why. His answer was “The snake bit me so I decided to bite it!”

The old chap had performed the old fashioned trick of sucking the bite. Can you tell me anything about the oral absorption of toxin?

Dr S Sutherland
With an Australian snake bite you would not be able to suck anything out. It is a deep injection and the injection site closes up when you suck. But you can eat snake venom quite happily because it is destroyed by the pepsin in your stomach. There is no problem there.

Question

How quickly do people recover from coagulation disorders?

Dr S Sutherland
The young seem to recover their fibrinogen level very quickly after antivenom, sometimes in a couple of hours. Older people sometimes seem to take much, much longer. There is some aspect of liver function here. With the older person who has got a severe coagulation defect, it is a good idea to correct this with fresh frozen plasma. We have had one death after a Brown snake envenomation. He had a cerebral haemorrhage, although he was not hypertensive at the time. In Hobart a little while back a man had a massive gastro-intestinal haemorrhage after a Tiger snake bite. These two events make me feel that it is not a bad idea, in the older person, to correct the defect.

Question

How did you track how well you have reversed the circulating venom? If the patient still had circulating venom you have not given enough antivenom. If you then give him fresh frozen plasma, you could, theoretically, be making things worse.

Dr S Sutherland
We always say give adequate antivenom before you correct blood coagulopathy. It is a good point. I think you have

just got to make sure that all your clinical investigations indicate that every other aspect is under control including the neurological side and that the only thing you are treating is the coagulation problem. Never give fresh whole blood to snake bite victims, that has happened a few times without antivenom having been given. The patient has died with gangrenous arms and legs. By and large, properly treated snake bite has a fairly smooth course. The correction of a coagulation defect is usually achieved with more antivenom. The trend now is to give more antivenom than is really necessary.

I would like to see antivenoms improved further in Australia. I saw a little boy two weeks ago who had to have a lot of antivenom. I was distressed to watch the delayed serum sickness he developed. A lot of antivenom that goes in, perhaps 95% of it, has no specific activity. So there is still a lot to be done.

Unknown speaker
In relation to the coagulopathy, I have not had a lot of clinical experience with this, but in the couple of patients that I have dealt with I have found that if you give the antivenom and then try to correct the coagulopathy by factor replacement, that can actually be a guide as to whether, in fact, you have given enough antivenom. If you have further evidence of coagulopathy give them more antivenom, then give them more fresh frozen plasma.

Question
I wanted to address a question that Dr John Orton raised. Give sufficient antivenom to reverse the coagulopathy and then often the neuromuscular effects become fixed. With a neuro-muscular effect when do you decide you have given enough antivenom?

Dr J Orton
The coagulopathy appears to be the more easily, the reversible component envenomation of it. The neuro-muscular blockade, particularly where there had been delay in establishing antivenom treatment, may becomes, and probably will with Taipan, irreversible. Obviously with neuromuscular problems the treatment is ventilation until they wear off. We should all know that. Could Dr Sutherland comment on using the degree of coagulopathy as a method of titrating the amount of antivenom required.

Dr S Sutherland
Normally after 24 hours all the venom has been absorbed from the bite site. If one did a post-mortem then one would not find very much venom at all at the bite site as the venom has been absorbed and gone to its target areas. It reaches its target areas via the blood stream. By and large one or two doses of antivenom will saturate all the target areas. We know that when the venom peaks in the serum, a lot comes out in the urine including some of the neurotoxins.

Once I had to give a talk at a large hospital. It is one of these hospitals that you go into and when you go to the "Enquiries" there is a notice "At lunch. Back at 1". The Superintendent, when finally I found him, said, "We only asked you to come out and give a talk because you have been making such a fuss about snake bites. We never get any cases." It was really a lovely welcome. I gave the talk and I had just got back to the Lab when the registrar in casualty at this hospital, who had not been to the talk, rang up in a panic because they had a case of snake bite. You never know when a snake is going to strike.

Question
I was involved once with a gentleman who was bitten by a Brown snake on his long saphenous vein. I am pretty certain there was a degree of direct intravascular injection of the venom. The chap that was with him said that about five minutes after the bite he started fitting. I eventually went to the medical evacuation of this guy. He was fitting quite severely. If you give to your animals direct intravascular injection does fitting occur? Or was this man's fitting related to hypoxia or inter-cerebral bleeding or epilepsy?

Dr S Sutherland
There have been a number of cases in humans where epilepsy has followed snake bite. We do not know why it happens, but there is always a massive amount of venom involved. There is often no history of epilepsy before the incident. It would be very hard to design an experiment in mice to see if epilepsy occurs. They are very sensitive to venom and before you could tell that they had epilepsy, they would be dead on the table.

Question
Could you give us a brief word about the long term effects? A couple of our patients have had neurological involvement and muscle weakness for many, many months. The ones that had the severe renal failure were a bit changed mentally afterwards.

Dr A McKillop
Headache is the most common persistent symptom after envenomation. Paresis of individual limbs has been described. Over-zealous tourniquet application may have been the cause. Whether there is a direct proteolytic injury to the nerves, I am not sure. Permanent injury to patients has been described in the Australian literature. In Western Australia three patients had persistent diminished renal function, when reviewed six to twelve months after the episode. Other patients have suffered cerebral injury, presumably part of the whole syndrome of hypoxia or hypotension.

Question
Could Dr Sutherland comment on direct proteolytic damage to nerves?

Dr S Sutherland
Direct nerve damage is uncommon. You will occasionally get it locally with massive envenomation. The patient has paraesthesia around the bite site with loss of motor power.

There are multiple targets where the venom is going to attack. A severe case generally takes three or four months to get back to normal. A lot of them lose quite a lot of weight. This generally relates to delay in treatment. If they get serum sickness they could be washed out for months. For example with cases of Funnel-web spider bite that survived before antivenom the patients often were weak and "run down" for months. By and large these envenomations do not do you much good!