SPUMS SCIENTIFIC MEETING 1983

SEA SNAKE ENVENOMATION

Chris Acott

On my first dive in the central Queensland area I noticed a very large sea snake swimming between my legs. Unfortunately I had not been warned about the sea snake population in the area.

SEA SNAKES

Physiology

Sea snakes are recognised by their flattened paddle-like tails. They grow to variable lengths, some can be more than 2 metres long.

They are mainly fish eaters, and are usually bottom feeders. However, the Pelarmis platurus is pelagic (ie. a surface feeder). They are preyed upon by sea eagles, sharks (especially the Tiger shark) and even by seals.

Lacking the ability to regulate their own body temperature, they are often found sunning themselves on the surface. This will only elevate their body temperature slightly. They cannot breed or survive in water below 20°C, hence their distribution in tropical and sub-tropical waters.

They can excrete only hypotonic or isotonic urine as their kidneys lack the ability to concentrate it. Their skin is impermeable to salt. A salt gland is located at the base of the tongue. It secretes salt into the mouth which is washed away.

They have one lung which extends backwards into the abdominal cavity. This lung is divided into 3 sections. The 2 front parts are rich in blood vessels, while the posterior section is not functional as a gas exchanger but as an air storage organ. They are capable of diving to depths of 100 metres. Their maximal submergence (voluntary) time is 2 hours. However they usually dive to 20-40 metres and stay submerged for 60-90 minutes. Anaerobic metabolism is only used in emergency situations. Upon surfacing the operculum covering the nostrils opens and allows the reptile to breathe. They usually take only one breath at the surface and then dive again.

Sea snakes have a breathing tachycardia and not an apnoeic diving bradycardia. The sea snake is normally bradycardic. An increase in the pulse rate is seen as the animal surfaces. The breathing tachycardia increases the perfusion of the lung during ventilation. This tachycardia has been noted to begin 15 seconds before the animal surfaces and starts to breathe. It is not semantics to talk of a breathing tachycardia or an apnoeic diving bradycardia. A diving bradycardia husbands oxygen for the vital organs.

The sea snake's skin is also unique. It has a respiratory function. Not only is a third of the snake's oxygen requirement taken up during a dive via the skin, but carbon dioxide and nitrogen are eliminated. Most of the CO_2 produced during a dive is eliminated via the skin and not during expiration at the surface.

The cardiovascular system is also very interesting. They only have one ventricle which is incompletely divided. During a dive there is an increase in the pulmonary vascular resistance. This increases their right to left shunt. Hence blood is shunted away from the pulmonary bed to the skin. This decreases nitrogen uptake and increases nitrogen excretion. In this way they avoid decompression sickness.

Evolution

The evolution of the sea snakes is interesting and still clouded in uncertainty. The Elapidae, the most significant group of land snakes, have given rise to marine forms on two different occasions. These are the Laticaudiae (sea kraits) and the Hydrophilae (true sea snakes). Both are venomous to man.

The sea kraits lay their eggs on the shore, and also rest in crevices amongst rocks on land. Their nostrils are placed laterally and they have broad overlapping ventral (belly) scales which allow land movement.

The Hydrophilae, however, are purely aquatic. They lay their eggs at sea. They have central nostrils covered by an operculum. They have poor land locomotion because they lack the ventral scales.

There are other aquatic snakes, however these occur in fresh or brackish water, are not fully marine and are generally not venomous.

The strong evolutionary links between the Tiger snake and the Hydrophilae are important especially when considering which antivenom to use. This is discussed later. Tiger snakes are nearly always found near water, be it rivers, lakes or dams. Their front fangs are medium sized in comparison to their head size, which is very similar to the Hydrophilae.

Distribution

Distribution of the Hydrophilae (true sea snakes) is generally confined to tropical and sub-tropical regions of the Indian and Pacific areas. The most widely spread of all the species is the Pelarmis platurus (yellow bellied sea snake).

Local distribution of a particular species around any reef is patchy, and is probably due to seasonal shifts which determine winds, currents and food supplies.

Normally sea snakes inhabit sea water, usually around estuaries, especially in the rainy season. However they can live in fresh water and captured ones have been kept alive in tap water. Some species of Enhydrina schistosa have been found in fresh water lakes of Cambodia, while other species have been found in fresh water in the Philippines.

Attacks on man

Statistics of attacks and their subsequent fatal or non fatal outcome are difficult to obtain. There are probably

thousands of attacks each year, usually against fishermen in South East Asia. Superstition there forbids anyone talking about attacks. Both Reid (in Malaya) and Barme (in Vietnam) found that once bitten, the victim disappeared and it was impossible to learn from his companions what became of him. Apparently it is believed that the King of Snakes and the Genie of the Sea rule the sea snakes. Anybody who talked about attacks or the victims was liable for reprisals from one of the king's other subjects.

Contrary to public opinion, there have probably been two deaths in Australia from sea snake envenomation. My reference here is Prof H Heatwole, who has made an extensive study of Australian sea snakes.

Generally sea snakes from non-reef habitats are aggressive and responsible for many human deaths. These attacks occur against fishermen who handle the snakes that have been caught in their nets.

In contrast the species from the Australian reefs are relatively inoffensive and only very rarely attack when provoked. Catching, restraining or striking them may convert curious behaviour into an aggressive attack. Stay clear when they are feeding, or if you see them swimming in pairs, as this usually indicates that they may be mating. Treat them with respect and handle them gently if you have to. Commonsense often prevents trauma, both to you and to the snake.

The Bite

The bite is usually painless. Victims hardly realize that they have been bitten. At the most they may feel a sting. There is no local swelling, ecchymosis or abnormal bleeding. My patient noticed a slight sting. However, rarely, some victims may develop some hypaesthesia, then localized anaesthesia and numbness spreading to adjacent areas.

Defensive bites rarely release venom. Large amounts of venom may be milked from the snake shortly afterwards. In the envenomating bite most venom appears to be released at the first bite, very little on the second, and none on the third. However, the Astrotia stokesii (Stoke's sea snake) can inject large amounts of venom in each of 7 successive attacks. After their venom stores have been depleted it take 7 days for them to be replenished.

Sea snakes can open their jaws wide enough to inflict a good bite. Their fangs are fixed, usually of small size and are hidden in folds of mucous membrane. The fangs are fragile and often break off and remain in the wound. The fangs are not usually long enough to penetrate the average wet suit, except for Astrotia stokesii and Aipyrsus laevii.

Clinical Course

This can be very variable as these two cases from Queensland show.

On the Australia day holiday weekend 1983, a 19 year old youth noticed a stinging sensation on his left foot. He looked down and saw a sea snake wrapped around his ankle. From his description it was probably an Emydocephalus annulatus. There were no signs of envenomation when the first aid pressure bandage was removed.

In 1981 Dr H Mercer, a paediatrician at the Royal Brisbane Hospital, published a report in the Medical Journal of Australia of an incident in October 1979. A 2 year old girl started screaming while playing in the water at the beach of the central Queensland resort of Yeppoon which is 40 km from Rockhampton. Her mother noticed a snake wrapped around her daughter's left ankle. The snake then swam off towards two teenage boys, who later killed it and brought it to the Yeppoon hospital. Using her hands as a tourniquet around the child's calf the mother rushed her to the nearest ambulance station. At this stage the child was quite settled and was claiming that a snake had bitten her. The mother released her grip when she reached the ambulance station and within 30 seconds the child became drowsy and developed ptosis. While being rushed to Yeppoon hospital she began vomiting and respiratory distress became obvious. On arrival at Yeppoon hospital, 20 minutes after being bitten and 4 minutes after the onset of symptoms, the patient was unconscious, cyanosed and had tonic movements of her limbs. She required intubation 40 minutes after being bitten. There were multiple fang marks and serrated edge lacerations on her foot. The snake was identified as Astrotia stokesii. The child survived.

Reid pioneered the study of sea snake envenomation while working in Malaya in the 1950s and 1960s. Nearly all his work was with victims of the Enhydrina schistosa. He documented 101 cases and found that 68% of victims were not envenomated. This has subsequently been substantiated by other workers. Fifty per cent of the envenomated patients died, while the remaining victims took up to 2 months to recover. All fatalities were due to respiratory failure, renal failure and hyperkalaemia. Even after the antivenom was available patients still died, all from hyperkalaemia. The antivenom used was against the venom of Enhydrina schistosa. Reid found that the antivenom could be used up to 2 days following envenomation with a successful outcome.

Haemodialysis has also been successfully used in the management of envenomated victims. Sitprija et al in Thailand reported, "*The treatment with dialysis are comparable to those victims who received the specific antivenom. Haemodialysis appears to be a lifesaving procedure for sea snake poisoning and constitutes an alternative treatment, especially in hospitals where sea snake antivenom is not available. Venoms from all the Hydrophilae are not dialysable, their molecular weight being greater than 9,000, so one assumes that the hyperkalaemia was the main factor causing the muscular weakness and respiratory failure.*" Reading the reports showed the response was quite dramatic.

Reid developed a "2 hour rule". This differentiated envenomated cases into "serious" (or potentially fatal) and "non serious cases". This 2 hour rule still applies, however, it can only be applied to victims who have had no first aid measures, such as a pressure bandage and immobilization, performed. Once the measures have been discontinued,

the 2 hour rule comes into effect. Serious envenomation was indicated by:- myalgic pains, especially in the neck muscles, trismus, prosis, opthalmoplegia, red-black urine (myoglobinuria), leucocytosis >20,000. It is interesting to note there is no mention of joint pain. The development of myoglobinuria was an important index of the expected morbidity. For each day of myoglobinuria there would be one week of illness.

In serious cases death would usually occur between 12-24 hours but it could occur as early as 8 hours or as late as 48 hours.

Reading the case histories shows how respiratory and ventilator care has advanced in the past 20 years.

SNAKE VENOMS

All snake venoms contain a diverse array of toxic substances which are only now being elucidated. They are all proteins. Short chained toxins consist of 60-62 amino acid residues. Medium length toxins consist of 66 amino acid residues. Long chain toxins consist of 71-74 amino acid residues. They are characterized by potent specific toxins which act on the victim usually at sites distant from the actual bite.

Broadly the venoms can contain:-

1. Neurotoxins
2. Myotoxins
3. Cardiotoxins. The role of cardiotoxins in envenomation by Australian snakes remains unresolved. Kellaway noted that the venoms of the Copperhead Red Bellied Black snake has a weak cardiotoxic action. The cardiotoxic properties irreversibly reduce the resting membrane potential. There is an increase in the QT interval. Some of the venoms cause the release of histamine SRS or indirectly cause their release by forming lysolecithin which in turn damages the cells causing the release of these substances.
4. Haematologically active components.
    a. Coagulation disturbances are caused either by the formation of autoprothrombin, formation of thrombin, or the formation of fibrin. Most Australian snakes cause the conversion of prothrombin to thrombin.
    b. Haemolysins. Some of the venoms have a strong haemolytic action (black snake) while some are weakly haemolytic (brown snakes). The action is either a direct one on the red blood cells or an indirect one converting lecithin to lysolecithin which then causes haemolysis.
5. Other enzymes that cause local damage, anticoagulation, the release of kinins, local tissue damage and necroses.

Sea Snake Venoms

Sea snake venoms are interesting. Fish and mice are susceptible, but the reef eel is not. Broadly they have either neurotoxic properties, or myolytic properties, or a combination of both. Usually one particular property dominates the clinical picture, from the neurotoxic properties of the Astrotia stokesii to the myolytic activity of the Enhydrina schistosia.

The lethal activity of 23 species sea snake venoms have been reported. There are probably about 50 different species of Hydrophilae. Nearly all the venoms act on neuromuscular transmission, the majority being post-synaptic. According to Professor Heatwole the following are the main species seen in Australian waters, Pelamis platurus, Astrotia stokesii, Emydocephalus annulatus, Aipyrsus laevis, Aipyrsus dudoisii. The venoms of Astrotia stokesii, Aipyrsus laevis and Pelamis platurus are all neurotoxic, while the venom of the Aipyrsus dubosii has not been studied extensively. Emydocephalus annulatus is not considered dangerous to man. Enhydrina schistosia venom has been extensively studied in different regions. It is possible that geographical variations in venom composition may occur. The Australian distribution of Enhydrina schistosia is uncertain. It is found from the Gulf of Iran through the waters of the Far East to as far south as Rockhampton.

Neurotoxins

These act at two sites.

1. Presynaptic. Typically cause a progressive-neuromuscular paralysis. This paralysis is preceded by a latent period. During this period spontaneous transmitter release is increased, as evidenced by an increase in miniature endplate potentials. At the time of paralysis there is a marked reduction in the number of vesicles due to hydrolytic phospholipase activity with a wide variation in the size and shape of the remaining vesicles. There is also damage to the mitochondria and other intracellular organelles storing calcium, thereby increasing the amount of free ionized calcium which decrease the amount available for synaptic transmission.

2. Post-synaptic. These toxins bind to and inhibit the function of the acetyl choline receptors. The rest of the molecule probably blocks many other receptor by its sheer size. No ultrastructural changes are produced.

Myolytic properties

Reid pioneered the work on sea snake venoms, particularly the venom of the Enhydrina schistosia. He found this caused muscle destruction, sometimes extensively, with the release of myoglobin causing myoglobinanaemia and myoglobinuria, which can lead to acute tubular necrosis.

ANTIVENOMS

Workers in 1967 found in vitro cross neutralization between the majority of land snake venoms and Enhydrina schistosia antivenom. Further work by Baxter and Gallichio demonstrated, in vitro, that Tiger snake antivenom was

more effective than Enhydrina schistosia antivenom in the neutralization of the 9 species of sea snake venoms they tested. However, they found that it was not as effective in neutralizing the venoms from Enhydrina schistosia, Laticaudata semifasciata and Hydrophis major. One would not encounter these frequently in Australian waters. Baxter and Gallichio suggested where these species and Lapemis hardwickii are encountered Enhydrina schistosia antivenom is the antivenom of choice, while in other areas of the Pacific Tiger snake antivenom is preferable. However in vitro neutralization is more efficient than in vivo, and clinically the pattern seen is not always the one which is reflected by the in vitro results.

TREATMENT

First Aid

First aid measures are as for any other snake envenomation. Apply a pressure bandage and immobilize.

One wonders whether a wet suit would provide adequate pressure to prevent venom spread. Probably it would, but this has to be confirmed. A pressure bandage should be applied to the site as soon as possible. If the wet suit is to be removed, ensure that the affected area is kept immobilized and that the pressure bandage is continued up the limb, ie. cut the wet suit off. It appears that both pressure of at least 50 mm Hg, and immobilization are the important aspects of preventing venom spread.

Antivenoms

Dr S Sutherland recommends the use of CSL's Sea Snake Antivenom for the Australian region and if this is not available then Tiger snake antivenom. Failing this polyvalent antivenom could be used. CSL's Sea Snake Antivenom now contains both Tiger snake antivenom and Enhydrina schistosia antivenom. It is a refined pepsin digested immunoglobulin. Each ampoule contains 1000 units. The antivenom is obtained from horses that are immunized against both Enhydrina schistosia and Tiger snakes. The exact content of Tiger snake antivenom in the preparation is not known.

One has the choice of antivenom, either Sea Snake Antivenom, Tiger snake antivenom or the polyvalent antivenom. The polyvalent antivenom contains antivenom to all the Australian land snakes, and includes 3,000 units of Tiger snake antivenom. Antivenoms are not cheap. Sea snake (1,000 units) costs $99.87 per ampoule, Tiger snake (3,000 units) costs $18.87 and Polyvalent costs $200.00 per ampoule.

The initial dose recommended by CSL is 1,000 units of sea snake antivenom, the contents of one ampoule or 12,000 units of Tiger snake antivenom, the contents of 4 ampoules. The equivalent dose is 4 ampoules of polyvalent antivenom at a cost of $800.00!

Reid advocates that for seriously envenomated cases a stat dose of 3,000 units of sea snake antivenom be used. There may be a need to use up to 10,000 units. For non-serious cases he suggests 1,000 units stat and up to 3,000 units in all. I feel attention should be paid to his 2 hour rule, so I think the advice on the leaflet from CSL is a little misleading.

The cost involved for using 10,000 units of sea snake antivenom and its equivalent in Tiger snake or polyvalent antivenom is Sea snake $998.70, Tiger snake $754.80, polyvalent $8000. Polyvalent antivenom is a last resort, not only from the cost effective point of view, but there is considerable risk of delayed serum sickness from its use. In practice from my experience, when one is considering what antivenom to use one may be left with no other alternative than to use a combination of all of them. Experience is the best teacher, so now at the Rockhampton Base Hospital we keep between 6 and 10 ampoules of sea snake antivenom, and 12 ampoules of Tiger snake antivenom. This is considered enough to cover any emergency. However, other hospitals may not have the luxury of having so much sea snake antivenom available.

PUBLICATIONS CONSULTED

Barme, M. Venomous Sea Snakes. Venomous Animals and their venoms. Acad. Press. 1968, Vol. 1: 285-308.

Baxter and Gallichio H. Cross neutralization by Tiger snake antivenom and sea snake antivenom against several sea snakes. Toxicon. 1974; 12: 273-275.

CSL. Leaflet with Sea snake antivenom and Tiger snake antivenom.

Heatwole H. Sea snake Attack Myth or menace. Skin diving in Australia and New Zealand. 1978; 8(1): 40-45.

Heatwole, H. Sea Snakes. Oceans. 1979; 1(3): 126-131.

Heatwole, H. Seal predation on a sea snake. Herpeto Fauna. 1980; 11: 24.

Heatwole, H. Adaptations of Marine Snakes. American Scientist. Sept. 1978; 66: 594-604.

Heatwole H, Minton SA, Taylor R, Taylor, V. Underwater observation of sea snake behaviour. Records of the Australian Museum, 1978; 31(18): 737-761.

Heatwole H and Seymour R. Pulmonary and cutaneous oxygen uptake in sea snakes and File snakes. Comp. Biochemical Physiol. 1975; 51: 399-405.

Kaire, G. Sea snake antivenom. Med. J. Aust. 31 Oct 1964: 729.

Mercer H, McGill JJ and Ibrahim R. Envenomation by a sea snake in Queensland. Med. J. Aust. 7 Feb 1981: 130-132.

Minton, S. Paraspecific protection by Elapid and sea snake antivenoms. Toxicon. 1967; 5: 47-55.

Pickwell GV. Sea Snakes in Vietnam and South east Asia. Handbook of Dangerous Marine Animals to field personnel. Dec 1972: 5-25.

Pickwell GV. Venomous Sea Snakes. Fauna. July/ August 1972; 4: 17-32.

Pickwell GV, Vick JA, Shipman WH and Grenan MM. Production, Toxicity and Preliminary pharmacology of venom from the Sea Snake, Pelamis Platurus. Marine Tech. Society Food and Drugs from the Sea. 1972: 247-265.

Reid HA. Myoglobinuria and Sea Snake Bite Poisoning. Brit. Med. J. 6 May 1961: 1284-1289.

Reid HA. Antivenom in Sea Snake poisoning. Lancet. 15 March 1975: 622-623.

Reid HA. Sea Snake Antivenom: Successful trial. Brit. Med. J. 1 Sept 1962: 576-579.

Reid HA. Diagnosis, prognosis and treatment of Sea Snake Bite. Lancet. 19 Aug 1961: 399-402.

Reid HA and Marsden AT. Pathology of Sea Snake poisoning. Brit. Med. J. 6 May 1961: 1290-1293.

Sitprija V, Sribhibhadh R and Benyajati C. Haemodialysis in poisoning by sea snake venom. Brit. Med. J. 24 July 1971: 218-219.

Sutherland S. Hydrophiilae. Sea snakes. Australian animal toxins. Oxford University Press. 1983: 159.

Tamiya N. Sea snake venoms and toxins. The Biology of Sea snakes ed. Dunson, 1975: 385-415.

Tamiya N and Maeda N. Neurotoxins of Australian Sea Snakes. Neurotoxins; Fundamentals and clinical advances. 1979: 95-101.

White J. Ophidian envenomation. A South Australian Perspective. Records of Adelaide Children's Hospital. 1980-81; 12(3): 311-421.

THE UNDERSEA MEDICAL SOCIETY MEETING JUNE 1983, ST JOVITE, CANADA

Jim Lloyd

The meeting was actually the eighth symposium on underwater physiology sponsored by the Undersea Medical Society (UMS). Although I am not a physiologist it happened that I was in Canada at the time.

The meeting was very interesting if a little bit high powered. They seemed to concentrate mostly on events occurring below 500 metres and that does not have much relevance to the Federal Police Diving School. The meeting was held at St Jovite in the Province of Quebec, La Belle Province I should call it as it is now a unilingual province. Luckily we were allowed to speak English at this particular conference. Some of the delegates from out of Canada, in fact most of them, were most surprised to find this venue was 80 km from Montreal and a $50.00 taxi fare from either of the airports. Most of us knew that Grey Rocks Inn was a well known ski resort. Being primarily a ski resort there was no air conditioning in the rooms so it was rather unfortunate that summer came early in Canada this year. The daytime temperatures were 35°C dropping to 22°C overnight. It was very hard to turn off the central heating in the rooms. However, there were plenty of distractions, golf, tennis, sailing, water skiing, horseback riding, you name it, they could provide it. There were the biggest mosquitoes not in captivity and an abundance of biting black flies.

The organisation went off very smoothly except for one little hiccup. No programme had been issued to anybody before they actually arrived on the spot and then we found that the scientific programme did not start until the second day. This was alright for those who were just there for a tax free holiday, but rather upsetting for those who had juggled very tight schedules to get there on time.

The meeting was entirely devoted to poster sessions. This was apparently a new departure for the UMS and they are not going to repeat it. The format of each session was a half hour review of the subject by an invited speaker, then an hour session in the poster room followed by a half hour discussion. Sixty four papers were presented in this way.

The only formal lectures were the introduction and the keynote session, and one formal lecture which was the Kronheim Memorial Lecture. Apart from this, the only relief from the posters was a film that Peter Bennett put on of the Atlantis Four Dive

The poster format was really rather annoying both to the delegates and to the presenters. The invited review at the beginning of each session was supposed to give an introduction to the posters themselves, so that everyone would be nicely primed by the time they got into the poster room. Unfortunately the quality of the reviews varied considerably from a mere paraphrase of the printed abstract, which themselves varied considerably in quality, to a half hour dissertation on the reviewer's own work, completely ignoring the other papers in the session. The poster room was not nearly big enough for the numbers present and the advantage went to tall delegates with hypermetropia. The shorter delegates like Dennis Walder and myself had problems.

The paper presenters also found themselves having to stand by their production and repeat the same speech over and over again to small groups of constantly changing people. There was a general agreement that they could have said all that they wanted to say much better in a ten minute lecturette, to the whole group. This would have got through the same amount of material in the same time. The discussion sessions were also pretty barren because those who really wanted to discuss a paper already had done so with the presenter in the poster room. The only thing that can be said in favour of this method of presentation is that it does tend to keep people awake.

There was an official welcome to Canada by a Canadian delegate, who read a message from the Governor General of Canada, who is a very keen diver and was unfortunately not able to attend, although he would have liked to be there. There were also a few words from the Lieutenant Governor of Quebec which were of course in French and an opening address by John Hallenbeck, the outgoing President of the