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TOXINS OF SOME VENOMOUS SEA CREATURES

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A great many sea creatures possess venoms with which they immobilize, kill and tenderize their prey, with which they defend themselves or which they passively accumulate by feeding on smaller species. Human envenomation is seldom, if ever, a result of unprovoked offensive action on a sea creature's part and is much more commonly a result of accidental contact.

A recent review (1) recorded 68 known species found in Australasian waters which possess neurotoxins (that is, toxins which produce their effect by acting on the nervous system and often result in paralysis) but of these very few are capable of injecting enough toxin into an adult human to produce important effects let alone muscle paralysis. There are, however, a few species which produce a high proportion of all serious and sometimes lethal envenomations and these will be mentioned individually below.

This brief review looks at the way in which some of the venoms produce their clinical effects, the characteristics of envenomation by creatures whose toxins may be lethal to man and concludes by examining factors which combine to determine the effects of envenomation.

For a thoroughly comprehensive treatment of these subjects, there is no source better than the newly published Australian Animal Toxins by Straun K Sutherland (published Oxford University Press, 1983; price $100.00). This is well illustrated and eminently readable. Unfortunately, the price is a disincentive to purchase!

HOW TOXINS WORK

The detailed characterization of toxins from marine creatures is a continuing process and new information appears each year. Our present understanding of these chemicals is, at best, incomplete and there may be many more modes of action than we currently recognize. The classification below is not exhaustive but covers most of the important ways toxins may affect us.

TABLE 1

TYPES OF TOXIC RESPONSES
TO THE VENOMS OF SEA CREATURES

Allergy - immediate - anaphylactic response
- delayed

Neuro- (or myo-) toxicity often resulting in paralysis or disturbance of feeling

Impairment of Functions of the Blood eg. clotting or the ability of red cells to carry oxygen

Tissue Digestion breakdown of muscle or other tissues, often with the release of substances producing their own damage in turn

Pain

Allergic and Allergy-Like Responses

Allergy occurs when the injected venom contains a (normally) protein substance (antigen) to which the body makes, or has already made, an antibody. The antigen and antibody recognize each other, react together and may cause, as an immediate result of the interaction, the release of powerful substances from some of the body's own cells which in the extreme can lead to a profound fall in blood pressure and severe, sometimes life-threatening narrowing of the air passages with swelling of other tissues. This immediate hypersensitivity reaction is called anaphylaxis and may account for the stories of occasional envenomations resulting in very rapid death, although in general, these are poorly described.

A longer term allergic response occurring in weeks rather than minutes may lead to the laying down of antigen-antibody complex in tissues, and particularly in small blood vessels, and thereby impairing the functions of those tissues - a delayed hypersensitivity reaction. There is some presumptive evidence that this may occasionally occur after envenomation

However, many marine creatures possess venoms which contain the chemical, histamine. and other substances which can directly release histamine from the cells of the human body which contain it. As histamine is released during an allergic reaction, the

injection or release of histamine mimics a hypersensitivity response and may have the same consequences. The same fall in blood pressure and narrowing of the air passages that may occur in immediate hypersensitivity can be reproduced by injection of histamine, while minor envenomations confined to the skin (eg. the stings of many marine species) produce characteristic weals - raised areas which itch - are normally painless but which commonly become infected when bacteria are introduced to the area during scratching. Similar weals can be reproduced simply by injecting small amounts of histamine into normal skin.

Nerve and Muscle Toxicity

It is not surprising that slowly moving sea creatures need to immobilize their prey and have toxins which rapidly cause paralysis. What is surprising is the variety of toxins that exist which act at many different points in human nerve and/or muscle to produce this effect.

Each voluntary muscle in our body possesses a particular nerve running to it which transmits information from the brain by way of small electrical currents which pass rapidly down the nerve - the nerve impulse. At the nerve endings, the current induces the release of a chemical, acetylcholine, which moves rapidly out of the nerve and on to a specialized part of the muscle surface where it reacts with a receptor molecule. This reaction leads to muscle contraction.

The electrical current which passes down the nerve is associated with the movement into the nerve of sodium and calcium ions and the outward flux of potassium. Restoration of the nerve to its resting state is accompanied by the pumping out of sodium ions and inward movement of potassium. Interrupt this whole sequence at any point and paralysis results.

These concepts are illustrated in Figures 1 and 2 which also show the probable main sites of action of some important toxins. For example, tetrodotoxin, identified as a major toxin from the blue ringed octopus, Hapalochlaena maculosa, only in 1978 (2), is known to block the sodium channels in nerves and thereby prevent the passage of the electrical current. It is possible that the cardiac poison of Chironex fleckerii, the box jellyfish or sea wasp, may act at the same site. However, the venoms of many sea snakes contain erabutoxins, a group of toxins which interfere with the linkage of acetylcholine with its receptor. By contrast, worm- and fish-eating conus shells appear to produce a myotoxin, ie. a substance acting directly on muscle without interfering with nerve function. The end-result of all these toxins is paralysis but the intimate mechanism differs.

Impairment of Functions of the Blood

The two most important reactions of injected toxins on the blood itself are the stimulation of blood

FIGURE 1

ESTABLISHED AND POSSIBLE SITES OF ACTION OF NEUROTOXINS FOUND IN VENOMOUS SEA-CREATURES

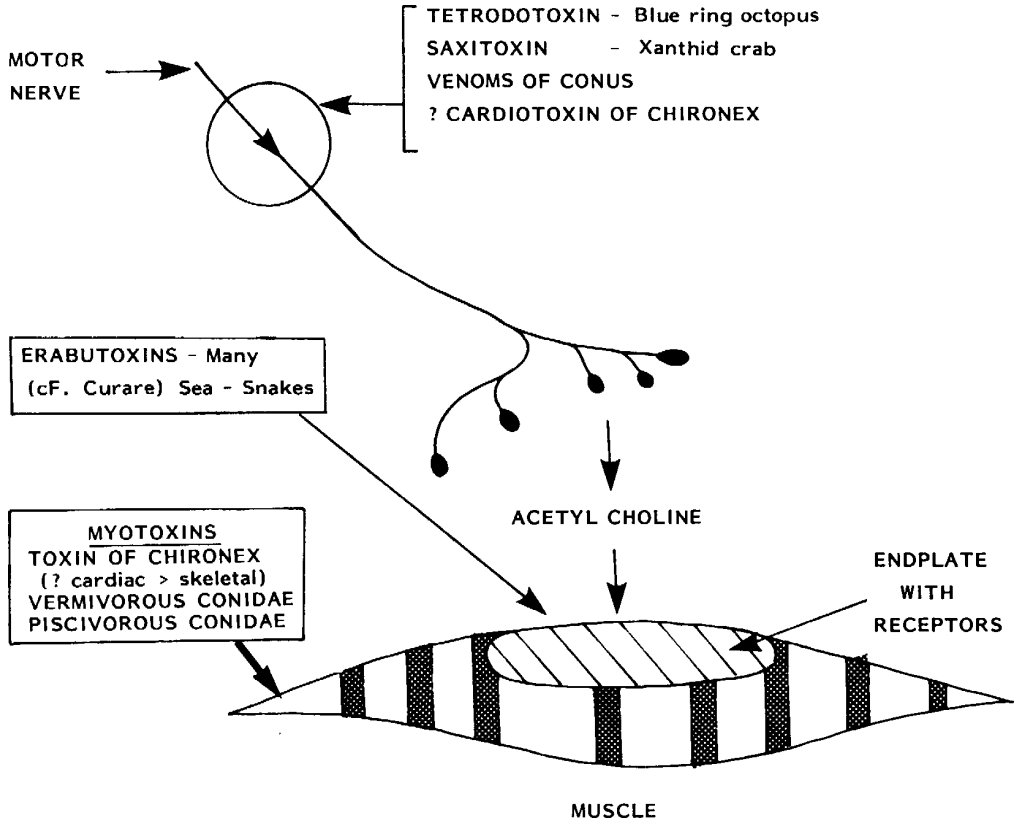
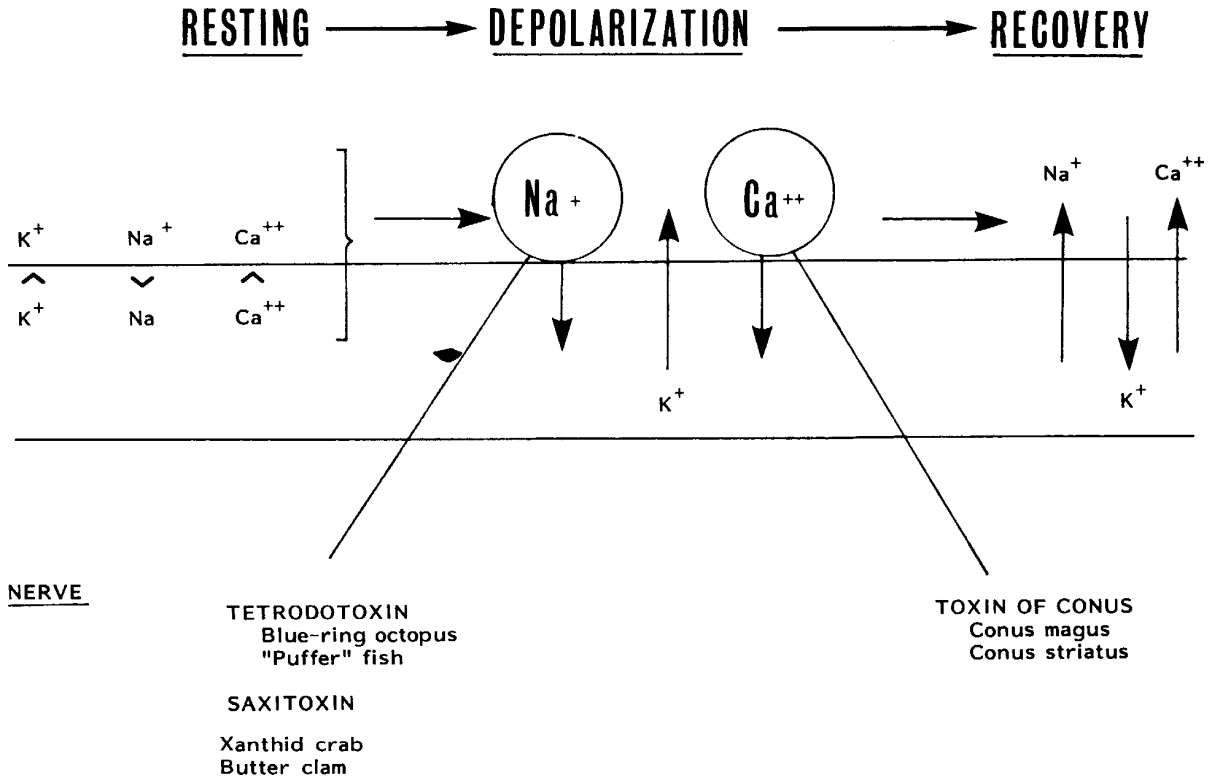


FIGURE 2
SITES OF ACTION OF NEUROTOXINS WHICH BLOCKTHE TRANSPORT OF SODIUM OR CALCIUM IONS



These blocks interfere with nerve depolarization with consequent paralysis. The figure represents a nerve axon during the resting phase, the phase of depolarization and the phase of recovery.

coagulation and the breakdown of the cell membrane of the red blood cells (haemolysis). Both of these actions are well recognized and prominent effects of envenomation by, for example, many land snakes but are also a feature of bites or stings by some marine species though seldom giving rise to serious clinical effects.

Effects on coagulation promote the conversion of circulating fibrinogen to fibrin which is laid down in smaller blood vessels. Blood platelets adhere to the fibrin deposits, red cells are damaged in their passage through the deformed blood vessels and fibrin, broken down by circulating natural enzymes, produces degradation products which are readily detectable in blood and urine and have anti-coagulant properties of their own. The clinical result is a patient, commonly bleeding from many sites, who has low plasma fibrinogen, low platelet count, many abnormal red cells in the circulation and sometimes impaired small vessel function particularly in the kidney. Ironically, but logically, the treatment includes the administration of heparin, another anticoagulant which, by activating anti-thrombin III, inhibits the conversion of fibrinogen to fibrin which is catalysed by thrombin and encouraged by the toxin.

Haemolysis or, red cell breakdown, may occur as a secondary event to the coagulation process described above. Alternatively, some creatures (sea snakes, box jellyfish) do possess a specific haemolysin, a toxin which damages the red cell envelope ultimately disrupting it and leading to loss of contents. Records suggest that this, though commonly present in envenomation is rarely an important aspect of the total clinical picture.

Tissue Digestion

Again, it is not surprising that creatures which have immobilized their prey using a neurotoxin also possess enzymes capable of producing tissue digestion as the first stage in incorporating the captured species into their own body tissues. Many creatures, therefore, inject as part of their venom these enzymes which may cause tissue destruction of differing magnitude in man. Stings from the tentacles of box jellyfish are not only extremely painful but also set up severe reactions in the skin which may lead to skin necrosis and ultimately severe scarring as a result of the healing process. Perhaps the most spectacular example of tissue digestion, however, is afforded by the sting of the stone fish which initially is invariably extremely painful, but, in the absence of antivenene, progresses over a period of two or three days, to produce quite massive tissue loss usually in the foot as the dorsal spines of this fish commonly penetrate the sole of the foot of the unwary. Many of the clinical records of envenomation by stone fish describe a short and extremely painful course of pain, prostration and even of local paralysis (the species possesses a

neurotoxin) followed by a prolonged period in hospital during which tissue death followed by reconstructive surgery is a common feature. An interesting aspect of this form of toxin is that it nearly always to act locally in contrast, for example, to neurotoxins which clearly may be transported through the body, presumably via the circulation, and produce paralysing effects at sites away from the point of envenomation itself.

Pain

In the course of the past ten years our concepts of the mechanisms of production of pain in the body have been clarified considerably by the discovery of new pain pathways within the nervous system and by the realization that many substances normally present in the body may, if present in abnormal amounts, induce pain. Substance P, a small polypeptide, bradykinin and several of the prostaglandins may be concerned with the normal transmission of pain and certainly increasing quantities of prostaglandins and bradykinin at a site of inflammation may be the main mediators of the pain associated with that condition. It has not been possible to identify with any certainty the pain producing toxins within many of the venoms of sea creatures but certain species apparently inject bradykinin and some related peptides have been postulated as a cause of severe pain in some envenomations. Perhaps the severest pain ever encountered in envenomation result from the venoms of the stone fish and the box jelly fish. There are many accounts of normally stoical people becoming delirious with pain following envenomation although not necessarily suffering any of the life-threatening consequences of the other toxins injected by the animal. It is perhaps most important to recognize that the pain following a bite or sting is not a good marker of the possible adverse consequences of the envenomation representing, as it does, the reaction to one or at most a few chemicals injected which in themselves have no lethal potential. The bite of many sea snakes and of the blue ringed octopus may be so innocuous as to occasion little notice. Nevertheless, envenomation with lethal quantities of toxin may occur. Equally, the severe pain resulting from exposure to the sting of the sea wasp may not necessarily be associated with the introduction of large quantities of the toxin acting on the cardiovascular system.

One further point needs to be made about these different forms of toxin. The time course for the development of symptoms following envenomation may be very different for each form of toxin. Anaphylaxis is virtually immediate, neuromuscular paralysis takes seldom more than 30 to 40 minutes to become apparent, whereas changes in the function of the blood may require 24 to 48 hours to be fully developed and tissue damage will occur over a period of days. Furthermore, not all of the effects of envenomation are directly related to the toxins injected. Tissue digestion will release substances, eg. myoglobin, which may produce their own secondary effects. In the case of muscle breakdown and the release of myoglobin, renal failure may follow a few days after the initial damage has been done to the muscle itself.

SPECIES WITH POTENTIALLY LETHAL VENOMS

Relatively few creatures have the capacity to cause fatal envenomation in man and some of the factors determining outcome are discussed in the final paragraph of this article. However, it is clear that four species stand out from all others as the most dangerous. Well-attested deaths have occurred following stinging by the box jellyfish/sea wasp which frequents particularly the tropical waters around our coasts, deaths have occurred in otherwise very healthy people bitten by the blue ringed octopus and occasional fatalities have followed the injection of venom from stone fish or from envenomation by various members of the genus Conus. Both the stone fish and sea wasp commonly produce painful envenomations and there is little doubt that the victim needs urgent attention. However, in the case of the blue ringed octopus, and to a lesser extent, the Conus, the puncture may be relatively painless and the first symptoms developed may be those of progressive paralysis. An awareness of what may have happened in these circumstances should alert divers to the possible need for support of respiration and urgent transfer to hospital.

INGESTED TOXINS

Not all poisonings by venomous sea creatures occur as a direct result of injection of toxin into the victim. Many forms of puffer fish contain large quantities of tetrodotoxin in their livers and eating these fish may result in fatal poisoning. Remarkably, cooking the creatures seems to offer little protection and the toxins appear to be heat stable.

DETERMINANTS OF THE EFFECTS OF ENVENOMATION

It is practically impossible to predict the likely outcome after a bite or sting from a venomous sea creature. Many variables will determine the outcome including the amount of venom injected (which may in turn depend upon the season of the year), the route of envenomation (as symptoms are much more likely to occur early after intravenous injection or injection into a very vascular area), the size of the victim (as a little venom goes a long way in a small person) and, of course, the state of health of the person envenomated. It is clear that a large amount of venom injected into a small person whose health is already compromised in some way is more likely to produce serious illness than a small amount injected into a large and healthy person.

The adequacy of immediate treatment may be a major determinant of outcome, however. While antivenenes

are available for stone fish and sea wasp stings and for some at least of the venoms of the many Conus species, no antivenene is available for the bite of a blue ringed octopus. Clearly, the envenomation is likely to occur a long way from a handy store of antivenenes so first aid measures and a recognition of the potential severity of the problem will determine the outcome. It is clear from many reports in the literature that the wearing of protective clothing will afford much protection from jelly fish of all sorts, that the use of acetic acid to remove intact tentacles or portions of tentacles is at least as effective, and much cheaper, than the use of proprietary solutions and that rapid transport of the victim to hospital where appropriate observation can be undertaken is mandatory. For most forms and consequences of envenomation there is plenty of time to initiate appropriate measures away from the marine environment. In the case of rapidly progressing paralysis however, such as follows the bite of a blue ringed octopus, it is clear that the early recognition of symptoms of muscle weakness coupled with the ability to maintain respiration by, if necessary, mouth to mouth resuscitation should prevent the tragic deaths which have occurred. All the evidence points to complete recovery being possible if support of ventilation can be provided for a period of a few hours. (3)

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REPRINTING OF ARTICLES

SPEAKING PERSONALLY: RECOGNITION AND MANAGEMENT OF APPREHENSION IN RESORT DIVERS

Steve Hills

First some background to these observations. For the last one and a half years I have been employed at a dive shop in Port Vila, Vanuatu as an instructor/guide for visiting tourist divers (mostly Aussies or Kiwis). We dived two or three times every day under ideal tropical conditions of warm (21°-27°C), clear (average 25 metres) water, although depths sometimes necessarily reached a maximum of 37-38 metres on some of the excellent wrecks. Average depths however were commonly shallower than 20 metres. Decompression dives were avoided. The group of divers assembled on the boat on any one day would typically be a mixed bunch ranging from visiting instructors through divers with no formal qualifications but many years of actual experience eg. abalone divers, to recently certified novices and also the very rusty, but qualified diver. On occasions when circumstances permitted there would also be student divers on the dive or holiday makers attempting the openwater segment of their one-day introductory scuba course, following their morning pool and theory session.

This daily "pot-pourri" of scuba divers presenting themselves at the dive store would be screened, to the best of our ability, for the suitability of the proposed diver.

Of necessity, incidents will occur in this type of daily routine where certified divers are completely unknown to us and the diving conditions are normally quite different to what they are used to, and were trained under. To date our safety record has only been blemished once - a Japanese honeymooner jumped out of a tree and fractured his ankle! (So as not to lose face however, he assured everyone as to his good health, donned his fins and then completed his dive!)

However, it is the almost daily occurrence of small incidents that did not turn into accidents that should be of concern. Because the regularity of these incidents is sufficient to fuel daily staff post mortems as to the success, or otherwise of each dive, we now recognise that a problem exists, and one which if not treated correctly, could lead to a fatality.

Many of these 'incidents' concern apprehension or panic. This condition may manifest itself in a variety of conflicting ways, making early detection not always possible. Apprehension always precedes panic and has been observed in one or more of the following behaviour patterns, by afflicted divers:

- inability to absorb information from a dive plan;
- prolonged questioning about proposed dive;