

CLINICAL ASPECTS OF ENVENOMATION BY MARINE ANIMALS

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ABSTRACT

Certain marine envenomation deaths are not as common as once believed, although 5 jellyfish species have been shown to cause many human deaths each year, most of these being in the Indo-Pacific region. Other marine animals proven to have caused deaths - but in fewer numbers - are: some species of spiny fish (including stingrays, weever fish, catfish, scorpionfish and stonefish), molluscs (cone shells and blue-ringed octopus) and sea snakes.

Clinical management is specific for each type of envenomation, and first aid includes varied treatments such as cardio-pulmonary resuscitation, compression/immobilisation bandaging, prevention of further envenomation, and local analgesia in the form of hot or cold therapy. Medical treatments may include advanced life support, systemic analgesia, antivenom administration, specific drug therapy and management of both systemic and regional vascular problems. As venoms of many of these creatures are antigenic specific antivenoms have now been developed for the management of envenomation by *Chironex fleckeri* Box-jellyfish, sea snakes and stonefish. There is a need to develop antivenom for the treatment of envenomation by other marine animals, including stingray and Irukandji jellyfish.

INTRODUCTION

Marine animals may cause death and severe morbidity by envenomation - the introduction of a venom into the tissues of its prey by some puncturing or traumatising apparatus, including teeth, spines, barbs or miniature 'harpoons' such as nematocysts, the stinging cells of jellyfish); first aid and medical treatments are necessarily diverse. Marine animals also cause a huge range of poisoning including ciguatera (tropical fish poisoning), paralytic shellfish poisoning and pufferfish poisoning.

The initial response to any marine envenomation is the safety of the rescuer and rescued, followed by the prevention of further envenomation. Because the first aid treatment is species specific, it often causes confusion with first aiders; medical treatments are similarly diverse.

Marine envenomation may be broadly divided into three types: envenomation by jellyfish with their micro-harpoons (nematocysts); envenomation by bites, including sea snakes and blue-ringed octopus and cone shell (with its envenoming proboscis); and envenomation by penetrating spines.

ENVENOMATION BY JELLYFISH

Method of envenomation

The tentacles of all jellyfish causing envenomation contain millions of tiny stinging cells called nematocysts. These act like mini-harpoons, with their thread tubes penetrating the integument of the victim and injecting multiple small amounts of venom. The outer surface of the bell of some jellyfish may also contain nematocysts capable of envenomation (e.g. *Carukia barnesi* - the Irukandji), but this is less common. Because nematocyst numbers are so large, and the venom is often injected over a large area of the victims skin, it is rapidly absorbed. Recent research has also shown that the microscopic thread tubes, which have venom present on the outside of the injecting thread, actually transfix some smaller blood vessels in the dermis giving an effective intra-venous injection (Endean 1988). This makes envenomation even more rapid and deaths have occurred on the beach within minutes after massive envenomation.

Jellyfish antivenom

Chirodropids (multi-tentacled box jellyfish) are the élite, the most advanced of the jellyfish world. However, despite many studies, the action of their venom is still not fully understood. There are difficulties associated with venom retrieval and isolation, the thermolability of venom components and their propensity to aggregate and disaggregate and adhere to equipment surfaces (Othman & Burnett 1990). Fortunately, despite this, *Chironex fleckeri* antivenom was produced by the Commonwealth Serum Laboratories (CSL) Australia in 1970 (Sutherland 1983). The antivenom is made using hyperimmunised sheep, and reactions are rare, unlike snake antivenoms (based on horse antisera). In over 20 years use of *Chironex fleckeri* antivenom only one documented adverse reaction has occurred, being a mild generalised rash 20 minutes after antivenom administration (Sutherland 1992). Because of this safety record, surf lifesavers were taught how, and when, to administer *Chironex* antivenom in the acute envenomation on the beach. They held it for 12 years in Surf Clubs in tropical Queensland, but for financial reasons, as it was never used, it was withdrawn, and Ambulance Officers were taught administration. Ambulance Officers have administered *Chironex* antivenom on a number of occasions on the beach, at least 3 of which may have been life-saving (Fenner *et al* 1989a; Beadnell *et al* 1992).

Deaths from jellyfish envenomation

Chironex fleckeri, the north Australian box-jellyfish, has caused 63 documented deaths in Australia since 1883 when records were first kept. Deaths have occurred within minutes of massive envenomation, with the victim in agonising pain until rapid unconsciousness and death supervene. In major stings the venom may affect the heart, causing it to stop in asystole (Lumley *et al* 1988); the respiratory system, causing respiratory failure (Fenner *et al* 1989a; Beadnell *et al* 1992); and the skin, causing severe skin damage and subsequent permanent scarring.

Chiropsalmus quadrigatus is a close relative of *Chironex*. Recent work by Rifkin (unpublished observations 1994) suggests that, because of species identification, it is difficult to claim deaths in the Indo-Pacific as being due to just one species, but *Chiropsalmus quadrigatus* has historically been held responsible for many deaths each year in this region, and probably for thousands over the centuries. Deaths seem to occur frequently in the Philippines (Cleland & Southcott 1956) with estimates between 20-50 per year (based on the author's personal travels and investigations, 1986). This figure has been confirmed more recently (Cornelius 1994, unpublished observations; Heegar 1994, unpublished observations). Past investigations (Cleland & Southcott 1965), and more recent investigations by the authors have now confirmed human deaths in Malaya, Borneo, and Indo-China (old names), Papua New Guinea, Sabah, Brunei, and even Japan (Okinawa). Another chirodropid, *Chiropsalmus quadrumanus* caused the death of a young boy in Texas, USA in June 1990 (Bengston *et al* 1991). Other chirodropid species with a similar nematocyst armament are present on the west coast of tropical Africa, and the tropical Indian Ocean. Although there is no documented proof of any human death, there probably has. Envenomation effects would be similar to *Chironex* as their nematocysts are alike, and comparison of venoms between *Chironex* and *Chiropsalmus quadrigatus* has shown they are similar (Keen 1971).

Stomolophus nomurai is a large jellyfish in the Yellow Sea on the east coast of China. Little is currently known about the jellyfish itself, but it has caused 8 documented deaths in the waters around Qingdao (Zhang Mingliang 1992). The victim suffers severe, localised skin pain, and may develop limb muscle cramps. In some large envenomations, pulmonary oedema occurs 1-4 hours after the initial sting and may cause death.

Physalia physalis is actually a siphonophore, and not a jellyfish. However, it has nematocysts and stings like a jellyfish, and is easiest considered as one. It has now caused 3 deaths from cardio-pulmonary collapse, in south eastern United States (Stein *et al* 1989; Burnett & Gable 1989), and also causes serious morbidity.

Serious morbidity from jellyfish envenomation

Serious morbidity occurs with envenomation by a number of jellyfish species. Often, some 30 minutes after initial envenomation, a number of systemic symptoms called the 'Irukandji syndrome' may develop (see below). Jellyfish species causing this include: *Carukia barnesi* (the 'Irukandji') - mainly in Australia; *Physalia physalis* - in most tropical, or sub-tropical oceans; *Stomolophus nomurai* - in the Yellow Sea, China; 'Morbakka' a large, unnamed carybdeid (4 tentacled box-jellyfish) - mainly in Australia; and *Gonionemus vertens* (and possibly *G. Oshoro*), a small hydroid in the Sea of Japan.

Signs and symptoms of jellyfish envenomation

With most jellyfish stings there is immediate skin pain. Stings from chirodroids are excruciating, with the victim frequently screaming in pain. The sting leaves marks which look, and feel, like the skin has been burnt, or scourged; blistering occurs quickly, followed by skin death within hours. Care should be taken to carefully observe the victims breathing and pulse as a 'noisy' patient who suddenly becomes quiet and 'cooperative' might be lapsing into unconsciousness.

In contrast, the Irukandji syndrome typically consists of the onset of severe low back pain, starting some 5-40 (usually 30) minutes after the original envenomation, which is usually a minor skin sting, and difficult to see.

This back pain is quickly followed by severe muscle cramps in all four limbs, the abdomen and chest (causing painful breathing). Further symptoms developing may include: profuse, localised or generalised sweating; pilo-erection (skin hairs 'standing on end') - again, localised or generalised, and possibly related or unrelated to the sting area; severe anxiety and 'wretchedness'; pallor, even grey-coloured skin; severe headache; nausea, occasionally with intractable vomiting; increased respiratory rate, often with painful, 'sighing' respiration; oliguria - a combination of hypovolaemia (sweating / vomiting) and vasoconstriction affecting the renal vasculature; tachycardia - often fast and irregular with ventricular extra-systoles (Flecker 1952). The victim feels absolutely dreadful, often with a feeling of 'impending doom' (a thought that may be shared by the attending first aider!); the victims are producing symptoms similar to excess catecholamine release, as experienced in adrenal medullary excess (e.g. pheochromocytoma). Similar symptoms are also caused by scorpion stings (Freire-Maia & Campos 1987), and Funnel-web spider envenomation (Sutherland 1983) - also caused by the excessive release of catecholamines into the bloodstream.

More severe symptoms reported in recent years have been hypertension, with systemic blood pressure reaching up to 280/150 mm Hg in previously normotensive individuals (Fenner *et al* 1986); cerebral oedema with unconsciousness (Heazlewood 1992 unpublished observations) and severe cardio-pulmonary decompensation with acute pulmonary oedema. This usually occurs some 15-18 hours post-envenomation (Fenner *et al* 1988; Martin & Audley 1990), although it has occurred within two hours in some recent cases (Fenner 1994, unpublished observations). Fenner *et al* (1988) demonstrated a (toxic) global cardiac dilatation, but could not exclude a pulmonary membranous contribution with 'leaky lungs', whereas Martin & Audley (1990) felt the oedema in their patient was due to massive alpha-adrenergic stimulation.

First aid for jellyfish envenomation

First aid for jellyfish stings is species specific, but in serious envenomation with an unconscious victim, resuscitation takes precedence. Prevention of further envenomation, particularly if sufficient help is available may be life saving; remaining adherent tentacles should preferably have their nematocysts deactivated to prevent further discharge and envenomation. Usually, remaining tentacular material is only present with chirodroid envenomation, and original work by Hartwick *et al* (1980) proved vinegar (4-6% acetic acid in water) totally inhibited further discharge of nematocysts in *Chironex fleckeri* envenomation after 30 seconds dousing. This has been shown to occur in all other chirodroids tested so far (Fenner 1991). No other substances need be used to prevent further envenomation, as few other jellyfish leave remaining tentacles on the skin. If fresh tentacles are present, they can be washed off with seawater, or picked off by the first-aider (the thickened pads of the fingers prevent envenomation of the rescuer). Although this stretching of the tentacle causes some nematocyst discharge, it is more important to remove the tentacles to prevent continuous further envenomation, and allow the first-aider to treat the envenomated area.

Pain relief is usually achieved with the application of cold - either with specific cold packs (as used in sporting injuries) or ice, wrapped in a cloth and applied to the stung area for up to 15 minutes, then repeated as often as necessary. This controls pain in over 90% of skin pain (Exton *et al* 1989), and even eases the savage skin pain of a chirodroid sting, although taking longer to achieve (Fenner *et al* 1992). Other important first aid measures, particularly with major chirodroid stings are the use of compression/immobilisation bandaging (see below) (Fenner *et al* 1989a; Beadnell *et al* 1992). Although this misses any minor, direct intravascular injection of venom, it helps reduce absorption of the larger amount of venom deposited locally in tissues.

In north Queensland the Ambulance carry specific *Chironex* antivenom, which has proved very effective when used on the beach, before actual transport to hospital (Fenner *et al* 1989a; Beadnell *et al* 1992). No other antivenom is available for jellyfish envenomation. Ambulances carry inhaled analgesia, including entenox (50% nitrous oxide and 50% oxygen), and penthrane, but these have only mild benefit in envenomations treated by the authors to date.

Medical management of jellyfish envenomation

Medical treatment in the conscious patient must deal with remaining, severe local skin pain. In chirodripid envenomation it has been shown that *Chironex* antivenom gives excellent pain relief (Williamson *et al* 1984; Beadnell *et al* 1992) - no explanation can be given for this. Skin pain from other jellyfish stings, or the severe backache and muscle cramps of the Irukandji syndrome needs intravenous narcotics; localised pain may respond well to regional nerve block. In severe envenomation life support may be necessary for respiratory or cardiac arrest, and/or specific drug therapy for pulmonary oedema, hypo- or hypertension, and heart failure.

A less-common, but serious complication in some jellyfish stings, is peripheral arterial spasm and compartment syndrome threatening limb viability (Williamson *et al* 1988). Circulatory compromise should be aggressively treated medically, or by surgical decompression. Rehydration, maintenance of good fluid balance and the administration of 100% oxygen are essential, and anticoagulation, vasodilators (such as papaverine), prostaglandin_E and antiplatelet aggregation agents (i.e. prostacyclin) may be necessary; many of these treatments have proved ineffective in the past. Hyperbaric oxygen therapy may be useful (Williamson *et al* 1988).

The severe muscle cramps of the Irukandji syndrome usually only respond to intravenous narcotics, and the symptoms of catecholamine excess respond well to α -receptor blockade. Current treatment is phentolamine intravenously as a 5mg bolus dose, followed by increments of 5-10mg until the hypertension and other symptoms of excessive catecholamine release have settled. To date, few other α -receptor blockers have been tried, but nifedipine will be trialed in the future. B-blockers should be avoided at all costs as they recently precipitated circulatory collapse and acute renal failure (Carney - personal communication 1994).

As with any wound, antibiotics need to be considered, bearing in mind that many micro-organisms in the sea including the Flavobacteria, are inherently resistant to the aminoglycosides, the extended-spectrum cephalosporins, and the tetracyclines, but are susceptible to co-trimoxazole and quinolones (eg. ciprofloxacin). Less serious infections can be treated with orally administered doxycycline or co-trimoxazole. Quinolones (ciprofloxacin, etc) are active against most bacteria, but the efficacy of these drugs in the treatment of marine wound infections is largely unknown (Aueurbach *et al* 1987; Ashdown 1994, unpublished information). Anti-tetanus prophylaxis should not be forgotten!

Prevention of jellyfish envenomation

In Australia tourists are encouraged to avoid swimming in hot summer months in tropical water, or to swim at beaches patrolled by surf lifesavers and wear protective clothing - especially 'stinger-suits'. These are lycra suits covering the arms, body and trunk to minimise contact area - the majority of stings occur on the lower limbs with less than 2% occurring on the head or face (Fenner *et al* 1993b). Purpose-built, large 'stinger-resistant' nets designed to keep out *Chironex* are present at some beaches, but their use is restricted at beaches with a large tidal range, or flat, sandy beaches with a low beach profile as the nets have to be moved in and out with the tide to prevent jellyfish access.

ENVENOMATION BY MARINE ANIMALS THAT 'BITE'

Method of envenomation

Included into this broad group are sea snakes, which inject venom through specialised hollow teeth attached to venom glands; the blue-ringed octopus with a beak connected to salivary glands containing venom; and the cone shell, where envenomation occurs via a single radular tooth on its proboscis, which is attached to the venom gland.

Venom

Sea Snake: The bites are usually solitary, although repeated separate strikes have been recorded. As with other snakebites, sea snakes may bite but fail to inject venom or enough venom to cause any significant clinical effect (Reid & Lim 1957; Sutherland 1983) and so clinical symptoms are uncommon. Overall, about 80% of bites do not cause envenomation, or cause only minor systemic disturbance (Reid 1975). Sea snake venom has neurotoxic and myotoxic properties and either one of these particular properties may dominate the clinical presentation.

Sea snake antivenom was developed by Commonwealth Serum Laboratories (CSL), Australia (Sutherland 1983) by hyperimmunising horses with *Enhydrina schistosa* (the beaked sea snake) venom; it is also effective against other sea snake venoms (Sutherland 1983). CSL tiger snake (*Notechis scutatus*) antivenom can also be used, but is only recommended if sea snake antivenom is not available. Several ampoules of tiger snake antivenom are required to be equivalent to an ampoule of sea snake antivenom - with the commensurate increase in risk of delayed serum sickness with the larger volumes. As with all snake antivenoms sea snake antivenom should be given intravenously over 30 minutes, and diluted 1:10 with a crystalloid solution (Sutherland 1983).

Blue-ringed octopus: The bite is commonly painless or not noticed (Sutherland 1983) - not every bite results in symptoms of envenomation, but deaths, as well as near deaths are well documented (Sutherland 1983). The venom is a salivary toxin with a complex composition, including tetrodotoxin and hapalotoxin of great biological interest.

Deaths from envenomation bites

Sea snakes: deaths have occurred in India, Burma, Malaysia, Indonesia (Reid & Lim 1957; Halstead 1988), Okinawa, Japan, in 1989 (Tomihara 1993 unpublished observations), and Oman in 1991 (Victor 1994 unpublished observations). Reid & Lim (1957) recorded 41 fatal bites from 144 known sea snake bites in Malaysia; estimates of fatality rates have been reported at 3% (Reid 1956).

Blue-ringed octopus: two deaths have occurred in Australia (Sutherland & Lane 1969), and one in Singapore (Williamson 1987). Death occurs from respiratory paralysis unless expired air resuscitation is commenced - when a successful outcome is probable (Williamson 1985).

Cone shells: the authors have confirmed 9 deaths, although Kohn (1963) claims 18 - all occurring only in the Indo-Pacific region. Deaths occur from respiratory paralysis, and like the blue-ringed octopus, are probably preventable using efficient expired air resuscitation. One victim's breathing returned to normal after 4 hours of artificial resuscitation (Sutherland 1985).

Signs and symptoms of marine bites

Sea snakes: signs of envenoming may occur between 30 minutes and 3.5 hours (Reid 1961) unless compression / immobilisation bandaging has been applied (see first aid). Generalised muscle aches and pains and weakness are usually the first symptoms with nausea, vomiting, dizziness, dry throat, shallow breathing and rapid pulse. The muscle pain causes a marked reluctance to move, and may be confused with paralysis. If myotoxins are present, myoglobinuria occurs some 3-6 hours after envenoming and plasma creatine kinase (CPK) will be elevated (Sutherland 1983), indicating muscle necrosis. Secondary renal damage may occur as a result of the myoglobinuria (Zimmerman & Heatwole 1987) causing hyperkalaemic and death. Neurotoxins may cause rapid paralysis after the bite, with progressive blurred vision, ptosis, drooling, inability to swallow, dysarthria, and respiratory distress (Acott 1983).

Blue-ringed octopus: The first sign of serious envenomation may occur within 10 minutes, with onset of progressive muscle weakness, speech and respiratory difficulty, dysphagia and visual disturbance (Flecker & Cotton 1955). Nausea and vomiting may occur, and collapse from muscle weakness soon

occurs with unconsciousness and death in the absence of effective resuscitation. Autonomic effects of the toxin may give fixed, dilated pupils, suggesting actual death. However, the victim may be conscious and aware, whilst unable to breathe, hearing everything that goes on around whilst being resuscitated (Williamson 1985)!

Cone shell: A sharp pain is usually felt at the site of penetration of the radula tooth. The envenomated area may blanch, or develop a bluish tinge, and is followed by numbness and local swelling. In serious envenomation, muscular weakness and incoordination develop, and swallowing, speech and vision may be affected. Respiratory paralysis may occur (Sutherland 1983), and death ensues unless effective resuscitation is commenced.

First aid treatment for marine bites

Prevention of Increased Envenomation

As a large amount of venom is injected into one site with consequent slower venom absorption, there is usually sufficient time for first aid treatment before the onset of symptoms. The immediate treatment is the application of a compression / immobilisation bandage. This is a broad, elastic bandage applied directly over the envenomated area, then extended to cover the whole limb using the same pressure as for a sprained ankle. This effectively compresses the underlying capillaries and lymphatic returns. As it does not compress the arteries or deep veins, it can be left *in situ* indefinitely. The patient's limb is then preferably immobilised with external splints, or splinted to the other limb. The splinting helps prevent any 'muscle-pump' effect. Expired air resuscitation or cardio-pulmonary resuscitation may be necessary (Williamson *et al* 1984).

Medical treatment of marine bites

Antivenom is available for sea snake envenomation, if symptoms and/or signs develop. Advanced life support may be necessary, as may analgesia. Further symptoms described above are managed in the same way as land snake envenomation.

Prevention of marine bites

Envenomation from both cone shells and blue-ringed octopus has only been reported in persons handling the animals out of water. Avoid touching the blue-ringed octopus, and cone shells should only be collected by experienced shellers wearing sturdy gloves and avoiding the pointed end of the shell (although the proboscis in some species may be able to reach all areas!). Sea snakes are not usually aggressive, and should be avoided if possible. They are very inquisitive, especially with divers, and should be treated gently, and with respect.

ENVENOMATION BY VENOMOUS SPINY FISH

Method of envenomation

All the fish in the following sections have spines that are either covered in venom, or are connected to venom sacs so venom can be injected; each will be covered individually.

Venoms of spiny fish

Stonefish (*Synanceja*) sp.: have 13 dorsal spines that are defensive, and not used for capture of food. Paired venom glands are attached to each spine and when the spine is pushed down (e.g. a human foot treading on the fish) the spine penetrates the skin, and acts like an injector, forcing venom into the wound. Although no deaths have occurred to date in Australia, antivenom, made from horse serum, has been developed by CSL Australia to deal with the serious morbidity (Wiener 1959).

Stingray: has a tail, which contains at least 1, but up to 6 barbs, each being covered in a sheath bathed in venom. When the large pectoral fins and stimulated (e.g. a human standing on them), the tail whips forwards, driving the barb into the victim where the barb sheath ruptures, releasing venom into the surrounding tissue. This venom may cause systemic symptoms, and is capable of local muscle and tissue necrosis (Fenner *et al* 1989b).

Spiny Fish: There are many species of fish with (defensive) venomous spines. These include weeverfish, catfish, zebrafish, scorpionfish ("butterfly cod"), chinaman, and "happy moments".

Deaths from marine bites

Stonefish: Deaths from stonefish are much rarer than previously believed with just 3 documented - one in the Seychelles and one in Mozambique (Smith JLB. 1957), and the third in Japan who "fell down and drowned" after envenomation on the foot in 40cm of water (Araki & Tomihara 1990 unpublished observations).

Stingray: Nine deaths have been reported (Fenner *et al* 1989b). At least two were from exsanguination after the barb punctured a major blood vessel; two penetrated the heart, one causing instant death, the other causing death 5 days later from cardiac tamponade, after chemical myocardial muscle necrosis secondary to the penetrating stingray barb (Fenner *et al* 1989b); one died later from tetanus. The cause of death in the others was not ascertained, as permission for post-mortem was refused (Russel *et al* 1958).

Spiny fish: There is poor documentation on actual 'envenomation' deaths, but the following are reported in the literature:

1. Weeverfish - deaths are reported in Europe and Africa (Evans 1943; Halstead & Modglin 1958; Russell & Emery 1960; Skeie 1962), but at least 3 were secondary septicaemia (Russell 1965).
2. Catfish - Texas (McKinstry 1993) - death occurred in a diabetic, 9 days after envenomation. Halstead (1988) reports deaths, but gives no details.
3. Zebrafish, Scorpionfish (Butterfly Cod) - Philippines deaths are reported (Herre 1952). Halstead (1988) lists 5 deaths, but again gives no details.

Signs and symptoms of marine bites

Stonefish: Envenomation is fairly common. Sutherland (1983) reported 265 cases in the years 1965-1981, with a further 21 cases reported in the years 1970-1991 (Fenner *et al* 1993b). The pain is excruciating, with the victim usually quite distraught. Muscle weakness and some degree of paralysis may develop in the affected limb, with the victim in various stages of shock.

Stingray: Envenomation is common, with one series of 100 cases being described (Fenner *et al* 1989b). Severe local pain may occur, although not as severe as stonefish envenomation. Venom and tissue remaining from the torn integumentary sheath (around the barb) often cause infection that is difficult to clear, sometimes taking up to a year to subside, and occasionally resulting in localised osteomyelitis (Fenner *et al* 1989b).

Spiny fish: The main problem is localised pain, with few systemic symptoms.

First aid treatment of marine bites

The envenomated part is placed in water, as hot as can be tolerated - the rescuer should first test the water, or the victim tests it with another limb!

Medical treatment of marine bites

Local anaesthetic can be injected around the area, or a nerve block performed to reduce local pain. Antivenom (for stonefish) is also very effective for the pain, or if further symptoms develop (Sutherland 1983). Intravenous opiates may also be necessary. The wound area is X-rayed to exclude remaining foreign material, and then carefully cleaned under local or general anaesthetic to remove any remaining venom, or pieces of barb. It is then allowed to heal by primary intention, and not stitched. Antibiotics are usually necessary, and selected as suggested above. Tetanus prophylaxis is essential.

Prevention of marine bites

Don't touch fish with venomous barbs!

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