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## IMMUNOLOGY AND JELLYFISH VENOMS

John Williamson

Jellyfish envenomation is a worldwide occurrence, producing effects ranging from mild local skin irritation<sup>1</sup> to rapid endotoxic<sup>2</sup> or less commonly, anaphylactic death.<sup>3</sup>

### **TOXIC REACTIONS**

Jellyfish venoms are complex mixtures of polypeptides and enzymes, structurally akin to the venoms of snakes, insects and spiders, that are pathogenic to man by toxic or antigenic mechanisms. That the principal clinical reactions to jellyfish envenomation appear to be toxic, rather than allergic, is suggested by the following evidence:

- (a) no immune resistance has so far been reported
- (b) repeated stings cause no difference in symptoms
- (c) venom injections into different mammals induce similar clinical results

Most human toxic reactions are also characterised by a direct correlation between the total venom dose (ie. size of the sting) and the severity of the clinical effects. Such toxic reactions include:

- immediate skin pain with tentacle contact
- acute inflammatory skin reactions, up to actual skin death and scarring
- localised and regional tissue oedema
- regional lymphadenopathy
- muscle pains
- vomiting
- breathing distress

impairment of consciousness

respiratory failure

Other severe documented effects that have been labelled as toxic are:

gangrene

haemolysis

renal failure

myocardial failure

Modern immunological research techniques are beautifully applicable to the study of both the toxic and allergic mechanisms of jellyfish venoms. The techniques include:

skin biopsy

immunofluorescence

radioallergosorbent test (RAST)

enzyme-linked immunosorbent assay (ELISA)

immunochromatography using monoclonal antibodies

Using such techniques, the following information has been revealed to date:

1. Partially purified extracts from the venoms of Hair Jelly (*Cyanea capillata*), Portuguese Man-O-War (*Physalia physalis*), Sea Nettle (*Chrysaora quinquecirrha*) and the Northern Australian Box jellyfish (*Chironex fleckeri*) have demonstrated cardiotoxicity to spontaneously beating cultured chick cardiocytes.<sup>4,5</sup>
2. The cardiotoxic components of venoms from *Physalia physalis*, *Chrysaora quinquecirrha* and *Chironex fleckeri* have their actions significantly intercepted by the presence of the calcium antagonist verapamil.<sup>6,7</sup>
3. The composition of some jellyfish venoms may alter with the climactic seasons of a single year.<sup>8,9</sup>
4. Several common world jellyfish venoms (*Chrysaora*, *Physalia* and *Pelagia noctiluca* (Mauve Stinger)) generate antibodies in humans that exhibit some cross-reactivity; further, it appears that the venoms of *Chrysaora* and *Physalia*, the brown recluse spider (*Loxosceles reclusa*), and purified cholera toxin all share common antigenic sites.<sup>9,10</sup>

### **ALLERGIC REACTIONS**

It is of interest that the scientific study of allergic disease actually began with the use of coelenterate protein,<sup>11</sup> when Pertier and Richer in 1902 induced anaphylaxis in dogs with injections of coelenterate venoms. Despite this early clue, over the ensuing decades repeated documentation and apparent contradiction occurred concerning so-called "harmless" jellyfish stings from different parts of the world, and the "unexpected" systemic nature, severity, and/or persistence of the clinical effects. It was really only with the demonstration in the serum of stung patients, of immune-specific and cross-reacting antibodies to *Chrysaora* and *Physalia* venoms taken from the Atlantic Ocean, in 1980, 1981 and 1983,<sup>12,13,14</sup> that the allergenic potential of jellyfish venoms was given

scientific objectivity. Finally, the rare but potentially fatal anaphylactic reaction to a jellyfish sting (probably *Pelagia noctiluca* from the Eastern Mediterranean Sea) was first adequately documented in 1985.<sup>3</sup>

In common with many other allergen sources, jellyfish venoms can be described as multi-allergenic systems, containing several of perhaps many allergenic macromolecules. It is now clear that the visible, in particular cutaneous, response to jellyfish envenomation may on occasions be allergic in nature. The differential diagnosis of such a response from the more toxic one is necessary for its effective management.

Allergic reactions to jellyfish stings may vary widely in their clinical presentation:

#### Cutaneous Reactions (erythema and/or urticaria)

may be

local or generalised,  
immediate or delayed (days to weeks),  
persistent or recurrent,  
occurring at the sting site, or at sites distant from  
the primary sting.

They may be with or without

exaggerated local oedema  
itching,  
clear watery discharge  
vesicle formation.

#### Generalised Hypersensitivity (extracutaneous and/or anaphylactic)

include

fever, sweating, chills,  
diarrhoea,  
nausea,  
tachycardia,  
hypotension,  
difficulty with respiration,  
loss of consciousness.

Some clues have been obtained from studies, so far confined to either venom extracts or human envenomation from American Sea Nettle (*Chrysaora quinquecirrha*), the Atlantic Portuguese Man-O' war (*Physalia physalis*), the Eastern Mediterranean Mauve Stinger (*Pelagia noctiluca*), and the Cabbagehead Jellyfish (*Stomolophus meleagris*),<sup>10</sup> of patients who have exhibited allergic reactions of either a cutaneous, extracutaneous or anaphylactoid nature to jellyfish envenomation, and whose sera have been examined.

- A. Both specific and cross-reacting IgG and IgE antibodies to these venoms have been detected in the patients' sera.<sup>15</sup>
- B. The sera from patients exhibiting the more severe reactions contain higher specific IgG and IgE antibody levels.<sup>14</sup>
- C. Detectable antibody levels were not influenced by the number of stings sustained by the individual.<sup>14</sup>

- D. Elevated levels of these immunoglobulin antibodies may persist for up to 5 years, at least.<sup>15</sup>
- E. Increased histamine release from venom-challenged basophil cells taken from a seriously sensitised patient, has been documented. There was strong evidence that this was specific IgE-antibody mediated.<sup>3</sup>
- F. Recent work supports the hypotheses that T cell function may be important in the pathogenesis of at least cutaneous lesions, following coelenterate envenomation.<sup>16</sup>

In this regard it is noteworthy that experimentally purified, so-called 'lethal', extracts of several jellyfish venoms are more powerfully antigenic, and curiously no case of serum sickness after jellyfish envenomation, either by natural tentacle contact or by ingestion, has been reported to date.<sup>17</sup>

As has been pointed out in the literature previously,<sup>3,18</sup> beta-adrenergic blocking drugs have the potential to increase the severity of an anaphylactic reaction; this is pertinent in view of the current widespread use of such drugs.

#### **FUTURE DEVELOPMENTS**

Further similar analysis of Chironex venom, the introduction into this research approach of the venoms of *Chiropsalmus quadrigatus*, *Carukia barnesi* (Irukandji), and other Carybdeid medusae, and the study of the skin, sera and blood collected from selected patients in this (and other) countries affected by a jellyfish problem, can be expected to shed further light on the subject. The tools to study the nature and prevalence of both toxic and allergic jellyfish sting reactions are now available and on theoretical grounds at least, the development of preventative immunotherapy is entirely feasible. There is strong indication for such an approach, given the ubiquitous and expanding association of man with the sea.

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## THE MANAGEMENT OF STINGS BY JELLYFISH, OTHER THAN CHIRONEX

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The term cubomedusan, simply translated, means box shaped jellyfish. There are so many box shaped jellyfishes that the deadly North Australian box jellyfish should always be referred to by its generic name of *Chironex*. This would then save any confusion from the terms box jellyfish or stingers, so loosely used by North Queenslanders for the deadly *Chironex fleckeri*. There have been recent problems with the Irukandji (*Carukia barnesi*) and the Morbakka, both of which are box jellyfish.

All types of jellyfish are derived from the Phylum Coelenterata and the biological classification for cubomedusans discussed in this article is presented on the next page.

Cubomedusans can also be simply classified as those with only four tentacles, ie. having only one tentacle per pedalius (corner) and those with many tentacles at each corner.

### PREVENTION OF MARINE STINGS

The wearing of protective clothing helps to give protection against any sting. The new and popular "stinger suits" are ideally suited as the thickness prevents the thread tube, through which the venom is injected from the nematocyst, or stinging capsule, coming close enough to the skin to be able to puncture it to sufficient depth to reach underlying blood or lymph vessels.<sup>1</sup>

In the same way two pairs of pantihose, as used to be worn by northern lifesavers is just as effective although perhaps not as aesthetic! One pair is used normally, with the feet cut out (otherwise they fill with sand!) and the others are worn upside down with a head hole cut in the crutch and the arms fit into the legs of the pantihose.

### TREATMENT OF MARINE STINGS

Vinegar has been proven to prevent further firing of nematocysts on remaining adherent tentacles of most species, particularly the life-threatening ones such as *Chironex*.<sup>2</sup> It does not inactivate the nematocysts of *Cyanea* (hair jelly) or *Chrysaora* (Sea nettle which is found in the USA). As *Pelagia* (the little mauve stinger) is similar to these two species, vinegar may well be of little use in the treatment of its stings also.

Note that vinegar, when used as treatment for *Chironex fleckeri*, the North Australian box jellyfish, or any other painful jellyfish sting **DOES NOT HELP PAIN**. It only prevents more nematocysts firing off and so possibly causing further envenomation.<sup>2</sup>

### FOUR TENTACLED CUBOMEDUSANS

#### IRUKANDJI (*Carukia barnesi*)

This stinger is very much in the news recently as there have been many reported cases, far more than usual.