

Cnidarian (coelenterate) envenomations in Hawai'i improve following heat application

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Abstract

A retrospective review of medical records from 113 patients with cnidarian stings in western O'ahu, Hawai'i, was conducted for the 5-year period 1994–98. The most common clinical feature was acute local pain, but cases of anaphylaxis or anaphylactoid syndrome and a persistent or delayed local cutaneous syndrome were also documented. Six cases resembled the Irukandji syndrome described from northern Australia, characterized by severe pain and signs of catecholamine excess, including muscle cramping, elevated blood pressure, diaphoresis, and tremor. Treatment with heat application, usually by means of a whole-body hot shower, appeared to provide better clinical improvement than parenteral analgesics or tranquilizers, particularly in patients with the Irukandji-like syndrome. The heat sensitivity of one or more of the *Carybdea alata* venom components might account for the effect of heat treatment. Prospective, randomized, controlled clinical trials should be performed to assess heat treatment for cnidarian envenomation.

Keywords: cnidaria, *Carybdea*, coelenterates, jellyfish, envenoming, stings, Hawaii, Irukandji syndrome, treatment, USA

Introduction

Marine cnidaria (particularly the Hawaiian box jellyfish *Carybdea alata* and Portuguese man-of-war *Physalia* sp.) injure thousands of people annually in Hawai'i by envenoming (stinging). Lifeguards on the island of O'ahu alone estimated treating about 800 stings by *Carybdea* sp. and 6500 stings by *Physalia* sp. during 1994, with about 90% of stings on the leeward coasts thought to be caused by *Carybdea* (THOMAS & SCOTT, 1997, pp. 18–19, 59). Although there have been no reported fatalities due to these envenomings in Hawai'i, they cause considerable morbidity, often requiring medical care.

Despite the abundance of cnidarian envenomations in Hawai'i and globally (FENNER & WILLIAMSON, 1996), treatment recommendations are largely based on anecdotal evidence, small case series (HARTWICK *et al.*, 1980), uncontrolled treatment protocols (EXTON *et al.*, 1989), and in-vitro laboratory studies of nematocyst discharge (HARTWICK *et al.*, 1980; FENNER & WILLIAMSON, 1987). Current suggestions for treating *Carybdea* stings in Hawai'i include vinegar dousing, removal of tentacles, and topical ice packs for pain relief; for *Physalia* stings, a salt or fresh-water rinse to remove tentacle fragments and ice for pain relief are recommended (THOMAS & SCOTT, 1997, pp. 21–23, 62–64).

The fortuitous observation that a hot shower was associated with prompt relief of cnidarian sting pain encouraged the emergency department (ED) staff of the Wai'anae Coast Comprehensive Health Center (WCCHC) to use this treatment for other patients. A retrospective medical record review for patients receiving medical care at WCCHC was conducted to evaluate the efficacy of hot showers or other treatments.

Methods

WCCHC is the largest health care facility on the western or leeward coast of the island of O'ahu, Hawai'i, an area of intensive ocean-related activity including swimming, surfing, diving, and fishing. Summaries of all medical encounters with the International Classification of Diseases, 9th edition (ICD-9) codes 989.5 (toxic effect of venom) or E905.6 (poisoning and toxic reactions caused by venomous marine animals and plants), from 1 January 1994, through 31 Decem-

ber 1998, were reviewed to identify cases compatible with cnidarian sting injuries. A case was defined as a medical encounter in which the patient reported either a jellyfish sting, or a marine sting, with no other identified source. Data on demographic information, environmental circumstances, type and extent of injury, treatment, and outcome were extracted from the full medical records.

Cases were further classified according to the type of envenoming syndrome. An acute local reaction was defined as immediate local pain, itching, or swelling without systemic symptoms or signs. Anaphylaxis was broadly defined as a generalized cutaneous syndrome or angio-oedema or bronchospasm, recognizing that some cases may actually be non-IgE-mediated anaphylactoid syndrome. The 'Irukandji' syndrome has been described from Australia (BARNES, 1964; FENNER *et al.*, 1986; LITTLE & MULCAHY, 1998), and was defined for this study as severe pain or muscle cramps, with one or more signs consistent with catecholamine excess (diaphoreses, tremor, vomiting, elevated blood pressure). A persistent or delayed local reaction was defined as local cutaneous pain or itching, one or more days after injury.

Improvement was defined as reported relief of pain or of other symptoms and signs of envenoming including itching, regional neurological symptoms, anaphylaxis/anaphylactoid syndrome, Irukandji-like syndrome and/or mild systemic symptoms. Improvement was considered to be associated with a particular treatment when it occurred within 20 min following that treatment (for heat treatment or intravenous medication), when it occurred before a subsequent treatment was administered, or when the medical record indicated that it followed a specific treatment. If multiple treatments were given in close temporal proximity, the association of a specific treatment with improvement was considered indeterminate and was not analysed.

The 2-tailed Fisher exact test was used to compare the outcomes of pairs of treatments, calculated by Version 6 of the EpiInfo software program (DEAN *et al.*, 1994). Confidentiality of the medical records was assured and the study was approved by the Human Research Committee and the Board of Directors of the WCCHC.

Results

The computer-based search of WCCHC medical records yielded 1113 individual cases with ICD-9 codes of 989.5 or E905.6 between 1 January 1994 and 31 December 1998; 172 cases were identified as cnidarian

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stings, and an additional 5 were marine-acquired stings probably due to cnidaria (no identified contact with fish, sea urchin, or coral), for a total of 177 stings.

Of the 177 definite or probable cnidarian stings, the original medical records were obtained for 113 (63.8%); other records were generally in archival storage. The age of patients ranged from 15 months to 49 years, with a median of 17 years. Twenty three (20.4%) of the patients were female, 90 (79.6%) were male.

Cnidarian stings were more common during the summer months, June through September (126/177), and on the 8th–10th days following the full moon (26/113) consistent with the pattern of shoreline appearance of *C. alata* along the leeward coast of O'ahu (Landy Blair, Ocean Safety and Lifeguard Service O'ahu, Hawai'i, USA, unpublished observations).

Most of the cases presented with immediate pain and/or itching localized to the sting site(s) (Table 1). Regional pain or numbness was sometimes associated with the local pain. Six cases had an illness resembling the Irukandji syndrome; clinical features are detailed in Table 2.

Heat treatment was used in 60 cases, 53 by means of a whole-body hot shower and 7 by localized hot packs or hot wet compresses. Of the cases treated with heat, records of 42% (25/60) contained sufficient outcome information to be analysed for results of treatment (Table 3). Parenteral analgesics were used in 15 cases and included meperidine, butorphanol, morphine sulphate, and ketorolac, with or without hydroxyzine or promethazine; an oral analgesic (paracetamol) was used in one case. Parenteral lorazepam (a benzodiazepine) was used in 5 cases. The percentage of analysable cases was 25% (4/16) for analgesic treatment, 60% (3/5) for parenteral benzodiazepines (Table 3).

For overall treatment of cnidarian stings, heat was superior to parenteral analgesics (odds ratio [OR] = 11.5, $P = 0.08$), particularly if the analysis is restricted to hot shower treatment (OR = 22.0, $P = 0.0485$). For treatment of the Irukandji-like syndrome, heat again appeared to be superior to analgesics (OR undefined, $P = 0.40$) or benzodiazepines (OR undefined, $P = 0.10$). All 4 episodes in which analgesics or benzodiazepines failed to provide relief were cases of Irukandji-like syndrome. There was no difference in outcome between heat and analgesics for acute local pain, nor between heat and the combination of epinephrine plus antihistamines for anaphylaxis/anaphylactoid syndrome ($P = 1.0$, data not shown).

In 10 cases, the duration of a hot shower and outcome were recorded (Table 3, footnote). None of the patients was hospitalized; there were no deaths.

Discussion

The various clinical presentations observed among the victims in this series have previously been described for cnidarian envenoming elsewhere (AUERBACH,

1995; BURNETT & CALTON, 1987a; BURNETT, 1991). The most serious Hawai'i cases involved anaphylaxis or an Irukandji-like syndrome.

Irukandji syndrome has been described from cases in northern Australia and was associated with the sting of a small cubozoan, *Carukia barnesi* (FENNER *et al.*, 1986). It was postulated (FENNER *et al.*, 1988) that this syndrome was present in Hawai'i, based on a case with abdominal and low-back pain (KIZER, 1984). However, the cases in the present study (Table 2) resemble the classically described Irukandji syndrome even more closely. *Carukia* sp. have not been reported from Hawai'i; it is not known whether other cnidarians such as *Carybdea* sp. may also cause this disorder. As in classic Irukandji syndrome, muscle cramping, back spasm, tremor and/or diaphoreses were observed within 1 h of the sting, in the patient cases summarized in Table 2. Thus, regardless of the aetiology, it appears that Irukandji syndrome or a very similar disorder occurs in Hawai'i.

Symptomatic treatment was frequently employed in this series, particularly antihistamines and analgesics. Virtually none of the cases treated with antihistamines had outcome information, precluding useful comparison with other treatments. This may have been because antihistamines were often given after clinical improvement, upon discharge from the ED, with no further period of observation.

Heat treatment (generally in the form of a whole-body hot shower, administered within 2 h of the sting) was most often (in 92% of cases) associated with relief of pain, agitation, dyspnoea, or markedly elevated blood pressure. Although this treatment appears superior to analgesics or benzodiazepines, the large number of unanalysable cases renders any conclusions tentative.

Outcomes were better after hot showers than after focal hot packs (Table 3), although few cases were treated with the latter. If the benefit of heat treatment depends on the amount of heat transferred to the dermal site of venom deposition, then it may be relevant that the skin surface temperature attained by a 44°C hot-water irrigation (42.2°C after 10 s) is greater than that attained by a topical sodium thiosulphate hot pack (39.6°C peaking at 2.5 min) (P. Bjorkman, unpublished observations at the WCCCH ED). Thus, it appears that hot showers would transfer a greater quantity of heat than hot packs [c.f., the same phenomenon underlying the use of a circulating hot water bath for external rewarming of hypothermia victims (DANZL *et al.*, 1995)]. Further support for the dermal heat hypothesis comes from the duration of the hot shower. The only case in which a hot shower reportedly failed to provide relief was one with 10 min of treatment, the briefest recorded duration (Table 3, footnote).

There is limited information from other investigators on the effects of heat treatment for cnidarian stings. PECA *et al.* (1997) found that soaking the affected part in warm salty water (8 cases) was associated with the resolution of pain from *Carybdea marsupialis* stings from the Italian Adriatic. AUERBACH (1995) mentions (without citation) the reported benefit of a hot shower among 'beach patrol members'. In contrast, BURNETT (1989, 1991) found that hot-water immersion for an experimental *Physalia* (Atlantic specimen) sting resulted in proximal lymphatic dilatation and erythema, but no relief of pain. This single case has been the basis for warnings against heat treatment (STEIN *et al.*, 1989; BURNETT, 1991; FENNER *et al.*, 1993; AUERBACH, 1995).

There is a report of clinical deterioration following fresh-water application in an apparent *Chironex fleckeri* sting (BARNES, 1966), and some authors proscribe it (BURNETT *et al.*, 1987; AUERBACH, 1991; HOLMES, 1996). However, it is difficult to interpret this case report, because the same patient rapidly improved after

Table 1. Cnidarian envenomation syndromes at Wai'anae, Hawai'i, 1994–98 ($n = 113$)

Presentation signs and symptoms	Number of cases
Local pain and/or itching	59
Local pain with regional neurological symptom	3
Anaphylaxis/anaphylactoid syndrome	11
Irukandji-like syndrome	6
Mild systemic symptoms	7
Persistent/delayed cutaneous syndrome	21
Other	2
Unclassifiable	4

Table 2. Characteristics of Irukandji-like syndrome cases at Wai'anae, Hawai'i, 1994–98 (n = 6)

Case A.	Stung on chest, intense pain, shaking. P, 110; RR, 22; BP, 160/106
Case B.	Stung on R arm, back pain and spasm, throat pain, diaphoresis, shaking. P, 100; RR, 20; BP, 150/120
Case C.	Stung on torso, severe pain, shortness of breath with rapid shallow breathing, marked agitation, combativeness, diaphoresis. P, 170; RR, 40; BP, 132/86
Case D.	Stung on L axillary area, severe pain, violent agitation, diaphoresis. P, 98; RR, 30; BP, 136/61
Case E.	Stung on L shoulder and R ankle, muscle cramping, chest and abdominal pain. P, 106; RR, 26; BP, 121/104
Case F.	Stung on L arm and L thigh, severe pain, increase of cough, tremor. P, 118; RR, 20; BP, 226/110

P, pulse (beats/min); RR, respiration rate (breaths/min); BP, blood pressure (mmHg); R, right; L, left.

Table 3. Outcomes of treatments of cnidarian envenoming at Wai'anae, Hawai'i, 1994–98

Treatment	Relief	No relief
Any form of heat	23	2
Hot shower	22	1
Hot pack/compress	1	1
Analgesics	2	2
Benzodiazepines	1	2

Among persons treated with a hot shower, the outcome (relief/no relief) according to duration of shower was: 10 min, 3/1; 15 min, 4/0; 20 min, 2/0; duration not recorded, 13/0.

the application of alcohol (BARNES, 1966), which may provoke nematocyst firing *in vitro*. Several investigators have found no evidence of nematocyst discharge caused by fresh water (EXTON, 1988; FENNER *et al.*, 1993). In the present series, fresh-water hot showers were used without clinical evidence of increased envenoming or other adverse effects.

Cnidarian venoms are complex, generally consisting of multiple components that vary according to the species of organism (BURNETT & CALTON, 1987b). *C. fleckeri* venom has attracted the greatest research attention. This crude venom extract loses its lethal and haemolytic activities after a 10-min treatment at 50°C (BAXTER & MARR, 1969). Heating at 42°C for 5 min (but not at 40°C for 20 min) abolishes another biological activity, that causing contraction of striated muscle (ENDEAN & HENDERSON, 1969). Further, heating to 60°C for 30 min blocks cytotoxic effects of crude venom from both *C. fleckeri* and *Chrysaora quinquecirrha* (BURNETT *et al.*, 1996).

There is limited published information about other cnidarian venoms. A haemolytic fraction of *Carybdea marsupialis* venom was inactivated by heat, but there was no testing at a temperature suitable for human treatment (ROTTINI *et al.*, 1995). Similarly, Atlantic *Physalia* crude venom is inactivated by heating to 60°C for 5 min (LANE, 1960), although some factors are heat stable (BURNETT & CALTON, 1977).

Laboratory studies in progress at the University of Hawai'i have found that, as with many other characterized cnidarian venoms (BURNETT & CALTON, 1987b; ROTTINI *et al.*, 1995; GUSMANI *et al.*, 1997), *Carybdea alata* venom is profoundly haemolytic *in vitro* (CHUNG *et al.*, 2000). Pre-incubation of the *C. alata* crude venom at 45°C for 30 min decreased its haemolytic activity by 95%. The inhibitory effect was increased at higher concentrations, relative to untreated or 4°C pretreated crude venom (A. A. Yanagihara, unpublished observations). This experimental evidence suggests that at least the haemolytic component(s) of *C. alata* venom is heat sensitive. There is a striking similarity with the case of fish envenoming, in which there are heat-sensitive venom components and a heat-based treatment (KIZER, 1985; AUERBACH, 1995).

Precautions should be observed in the use of heat treatment in patients to avoid thermal injury, to exer-

cise good clinical judgement in placing patients in a setting where monitoring and resuscitation are difficult, and to consider potential contraindications to heat stress [extremes of age, cardiovascular disease, hyperthyroidism, the use of many drugs, and certain other conditions (DANZL, 1988)]. It may be prudent to avoid excessive heat stress by using a focal hot shower to the affected body part when possible, but this has not been studied.

The limitations of this study include its retrospective nature, an unrepresentative study population (people seeking medical care for stings), the absence of a randomized control group, and the restricted medical record availability. Another limitation is the large number of medical records lacking details on circumstances, treatment sequence, and outcome, yielding a small number of analysable cases for several of the treatments.

Nevertheless, the findings on heat, specifically, hot-shower treatment of cnidarian stings in Hawai'i are very encouraging. There is a constellation of circumstantial evidence suggesting that such treatment may be beneficial for both the common acute local-pain syndrome as well as the uncommon Irukandji-like syndrome, and that a greater transfer of heat to an envenomed site is more beneficial, within the limits of physiological tolerance. Furthermore, heat application was not reported deleterious in 60 treatments in this series.

Prospective controlled clinical trials of heat treatment for cnidarian envenomings are warranted. One such trial of beachside treatment in Hawai'i is currently in progress, using hot packs as a heat source (C. Thomas and S. Scott, personal communication). A study evaluating whole-body or partial-body hot showers would also be valuable. Other studies in progress are attempting to characterize the biochemical properties of cnidarian venoms in Hawai'i, which may yield further insights into specific clinical management. If validated in prospective trials, hot-shower treatment would offer a simple and widely available method of managing these common marine injuries.

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Addendum

A randomized controlled trial (mentioned in the last paragraph of the above text) has recently been published on beachside treatment of stings probably caused by the Hawaiian box jellyfish (*Carybdea* sp.) (THOMAS *et al.*, 2001a). Following vinegar dousing, the use of topical chemical hot packs was associated with greater temporary (10 min) pain relief than topical chemical cold packs or control (ambient temperature) packs, although the degree of pain relief was of marginal clinical significance. Note should be made that the subjects of that Waikiki study (sting victims who sought assistance from a lifeguard at the beach) may differ from the Wai'anae study population (sting victims who sought emergency department care). In addition, there may be significant differences between hot pack application and a hot shower in the skin temperature attained and the duration of heat application (see Discussion above). A companion article (THOMAS *et al.*, 2001b) found no difference in pain relief between the application of sea water, fresh water, aluminium sulphate and detergent, or papain solution following vinegar dousing.

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