American Red Cross Scientific Advisory Council

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Scientific Advisory Council
Scientific Review
Jellyfish Stings

Questions to be addressed:
In adults and children who sustain a sting/envenomation from a jellyfish in coastal or territorial water of the United States, does the application of vinegar, baking soda, sea water, cold packs, heat, topical steroids or other preparations designed to treat jellyfish stings, compared to each other or to no intervention, reduce symptoms of pain, redness, or allergic reactions

Introduction/Overview:
Stings from jellyfish are common, particularly during summer months when vacationers flock to beaches on the east and gulf coasts. Fortunately, most stings from jellyfish in US waters only cause pain, with little risk for allergic reactions or death.

The current American Red Cross First Aid Manual provides information about jellyfish stings and treatment that includes advice to first remove any tentacles to prevent further stinging, then "irrigate the injured part with large amounts of vinegar as soon as possible for at least 30 seconds" and if vinegar is not available, to use a baking soda slurry. For Bluebottle or Portuguese Man-of-war stings, ocean water is recommended instead of vinegar." These actions are thought to deactivate the stinging nematocysts. Following this, the manual states, "Once the stinging action is stopped and tentacles removed, care for pain by hot-water immersion. Have the person take a hot shower if possible for at least 20 minutes. The water temperature should be as hot as can be tolerated (non-scalding) or about 113° F if the temperature can be measured."
The International Life Saving Federation has also published a Medical Position Statement on Marine Envenomation, 1/12/2000. This position statement advises 1) prevention of further stinging by removing tentacles, then using a baking soda paste for stings by sea nettles (*Chrysaora* species), or vinegar for 30 seconds for box jellyfish stings followed by compression/immobilization bandaging for major stings. Second, pain is controlled by application or ice or cold packs. It was noted that hot water stops the pain from the Hawaiian box jellyfish, *Carybdea alata* and that no other treatments should be used. The most recent included study referenced for this position statement is 1996.

This review sought to examine any new scientific literature in regards to first aid for jellyfish stings, with an emphasis on species found in coastal and territorial waters of the United States. Because the specific species of jellyfish may not be identifiable during treatment, we looked first at which species are most commonly identified in Hawaiian and Coastal Pacific, Gulf, Atlantic and Caribbean waters. Next, we performed literature searches that included limitations to US and territorial waters. Two reviewers independently reviewed titles or abstracts to determine eligibility for inclusion and after a consensus was met, the included studies were reviewed for quality of evidence and interventions, comparison (if any), outcomes and jellyfish species evaluated. Results have been broken down by geographic location for individuals sustaining a jellyfish sting.

Search Strategy and Literature Search Performed

Answer all questions and complete PRISMA flow sheet below
Key Words Used

First:Search ((((("Cnidarian Venoms"[Mesh]) OR "Scyphozoa"[Mesh]) OR "Cubozoa"[Mesh]) OR "Hydrozoa"[Mesh])) OR (jellyfish OR Portuguese man of war OR bluebottle OR marine Envenomation OR physalia utriculus
AND
Search (((stings OR Envenomation OR nematocysts OR deactivation))) OR ("Bites and Stings"[Mesh])

Second: #1 Search (("Scyphozoa"[Mesh] OR "Cnidarian Venoms"[Mesh] OR "Cubozoa"[Mesh])) OR ((jellyfish OR portuguese man of war OR bluebottle OR marine envenomation OR physalia utriculus))
AND
#2 Search (("United States"[Mesh]) OR "United States Virgin Islands"[Mesh]) OR "Puerto Rico"[Mesh] OR "United States" OR "United States Virgin Islands" OR "Puerto Rico" or Virgin Islands or (Florida Keys)

#3 Search (("First Aid"[Mesh] OR (vinegar OR baking soda OR meat tenderizer OR hydrocortisone cream OR ice packs OR hot packs OR hot water OR diphenhydramine OR ammonium OR topical agent*)

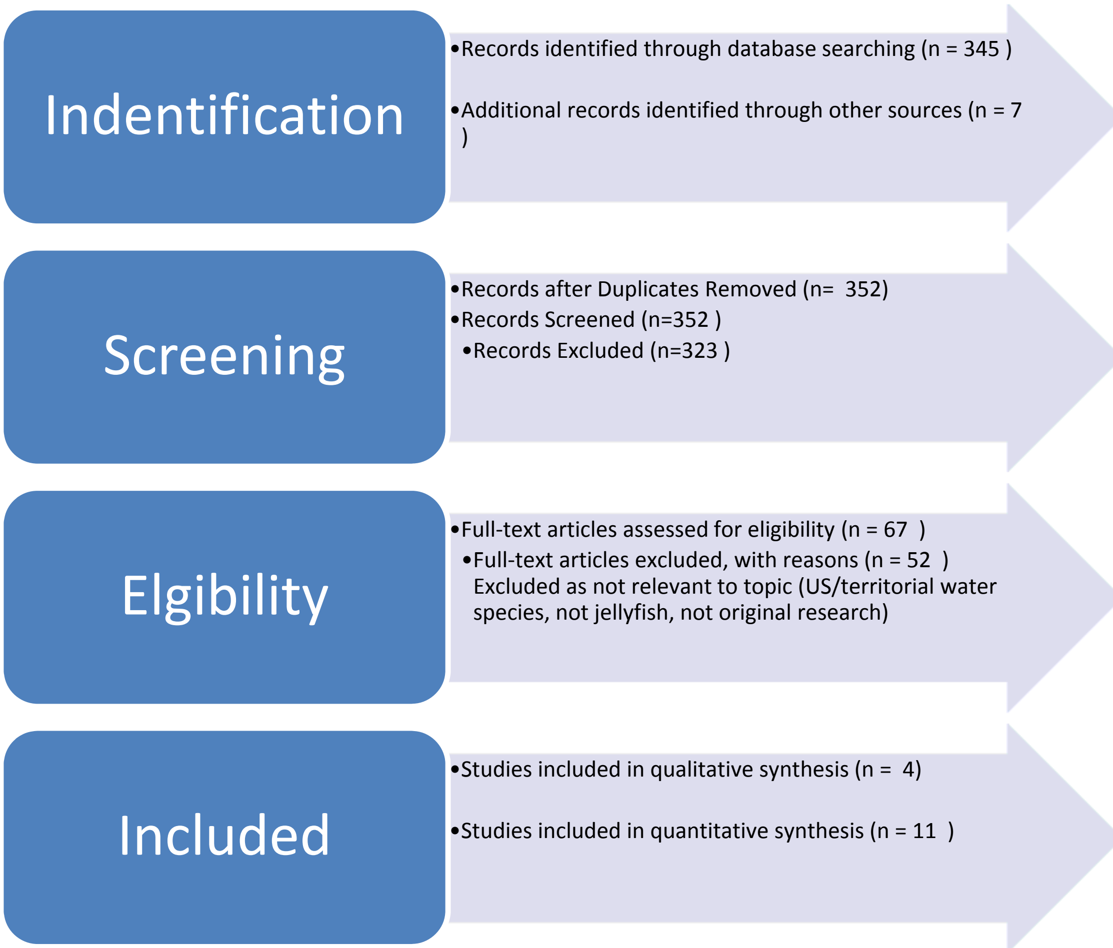
Inclusion Criteria (time period, type of articles and journals, language, methodology)

Publication date from 1995/01/01 to 2015/12/31; RCTs, Case series, bench studies, Systematic reviews, position papers
1955 to present; RCTs, case series, bench research, Guidelines from other organizations. USA Coastal and territorial waters (Atlantic, Pacific, Gulf, Caribbean, Hawaii)

Exclusion Criteria (only human studies, foreign language, etc…)
Human; adults and children, English only

Databases Searched and Additional Methods Used (references of articles, texts, contact with authors, etc...)

References from included studies reviewed; attempted contact with authors, attended presentations at Toxicology meeting, internet search of marine science organizations for epidemiology



Studies included for final review for data analysis:

Title	Author(s)	Journal	Vol	Issue
What is the most effective treatment for relieving the pain of a jellyfish sting?	Ostermayer, D. G. and Koyfman, A.	Ann Emerg Med	65	4
Nematocyst discharge in Pelagia noctiluca (Cnidaria, Scyphozoa) oral arms can be affected by lidocaine, ethanol, ammonia and acetic acid	Morabito, R., Marino, A., Dossena, S. and Spada, G. la	Toxicon	83	
Interventions for the symptoms and signs resulting from jellyfish stings	Li, L., McGee, R. G., Isbister, G. and Webster, A. C.	Cochrane Database Syst Rev	12	
Evidence-based treatment of jellyfish stings in North America and Hawaii	Ward, N. T., Darracq, M. A., Tomaszewski, C. and Clark, R. F.	Ann Emerg Med	60	4

Epidemiology of jellyfish stings presented to an American urban emergency department	Ping, J. and Onizuka, N.	Hawaii Med J	70	10
Evaluation of the effects of various chemicals on discharge of and pain caused by jellyfish nematocysts	Birsa, L. M., Verity, P. G. and Lee, R. F.	Comp Biochem Physiol C Toxicol Pharmacol	151	4
Cnidarian (coelenterate) envenomations in Hawai'i improve following heat application	Yoshimoto, C. M. and Yanagihara, A. A.	Trans R Soc Trop Med Hyg	96	3
A randomized paired comparison trial of cutaneous treatments for acute jellyfish (Carybdea alata) stings	Nomura, J. T., Sato, R. L., Ahern, R. M., Snow, J. L., Kuwaye, T. T. and Yamamoto, L. G.	Am J Emerg Med	20	7
Box jellyfish (Carybdea alata) in Waikiki: their influx cycle plus the analgesic effect of hot and cold packs on their stings to swimmers at the beach: a randomized, placebo-controlled, clinical trial	Thomas, C. S., Scott, S. A., Galanis, D. J. and Goto, R. S.	Hawaii Med J	60	4
Box jellyfish (Carybdea alata) in Waikiki. The analgesic effect of sting-aid, Adolph's meat tenderizer and fresh water on their stings: a double-blinded, randomized, placebo-controlled clinical trial	Thomas, C. S., Scott, S. A., Galanis, D. J. and Goto, R. S.	Hawaii Med J	60	8
A randomised controlled trial of hot water (45 degrees C) immersion versus ice packs for pain relief in bluebottle stings	Loten, C., Stokes, B., Worsley, D., Seymour, J. E., Jiang, S. and Isbister, G. K.	Med J Aust	184	7
Treatment of physalia envenomation	Turner B	Med J Aust	2	
In vitro eval of nematocyst discharge	Burnett JW 1983	Southern Medical Journal	76	7
Florida jellyfish	Lopez EA	Clinical Toxicology	38	5
Hot water immersion treatment for lion’s mane jellyfish stings in Scandinavia	Knudsen K, Agren S	Clinical Toxicology	54	4

Scientific Foundation:
Provide a summary of the science and other documents reviewed including biases and limitations which may be present. Include values and preferences if applicable (such as while the evidence was low were very concerned about the risk of… or while evidence was low the potential benefit was great in the setting of low to no risk…). Describe any environment or personnel decisions, opinions or considerations (such as this may not be appropriate for general first aid but would apply to wilderness first aid or while not appropriate for lay responders would be needed for emergency medical responders,…)

Background
Jellyfish, or 'jellies' are free-swimming marine animals that belong to the phylum Cnidaria, subphylum Medusozoa, and are found in every ocean. Frequently referred to as Cnidarians, they typically have an umbrella shaped bell and stinging tentacles used to capture prey and capable in some species of delivering a painful sting to humans, most commonly through inadvertent contact. In the United States and territorial waters, reports of jellyfish envenomation are from Gulf, Atlantic, Pacific (Hawaii) and Caribbean (i.e. Puerto Rico/US Virgin Islands) waters.

The phylogenetics of jellyfish are complex and evolving. The four major classes include **Schyphozoa** ('true' jellyfish, e.g. Lion's Mane or *Cyanea capillata*, *Chrysaora quinquecirrha* or Atlantic sea nettle, Pacific sea nettle and purple striped jelly), **Cubozoa** (box jellyfish, e.g., *Carybdeidae alata* and *Carukia barnesi* [Irukanji Syndrome] and *Chironex fleckerii* [Sea Wasp]), **Hydrozoa** (order Siphonophorae, including *Physalia physalis*) and ***Staurozoa*** (stalked jellyfish).

The Extent of the Problem
Jellyfish sting through a specialized cell in their tentacle, the cnidocyst (or nematocyst). Symptoms of envenomation in humans vary with the species but can range from a mild sting to agonizing pain and systemic symptoms. Anaphylaxis can occur. Stings are most common during summer months when beaches and coastal waters are invaded by vacationers. The National Science Foundation estimates that about 500,000 people are annually stung by jellyfish in the Chesapeake Bay and about 200,000 people are annually stung by jellyfish in Florida. Fortunately, fatalities are rare. There have been reports of as many as 800 box jellyfish stings per day at a single beach in Hawaii (1). Most stings cause a local reaction that do not require care in an emergency department. For example, a survey of jellyfish stings in Hawaii found only 116 cases seen in the ED over 8 years (2).

Despite the potential toxicity and adverse effects of cnidarian stings, this review found the literature on treatment and epidemiology of jellyfish to be limited and contradictory, with treatment results varying with the class and family of Cnidaria involved. Jellyfish are often clear or are submerged and not visible, thus, the type of jellyfish may not be readily identified. Therefore, jellyfish envenomation care may be directed at the type of jellyfish most commonly encountered in a geographic area, particularly with 'blooms' in their population. This review attempted to first identify reports of jellyfish envenomation or blooms by geographical region in US and territorial waters. Jellyfish populations, however, are dependent on ocean currents and there are reports of 'invasive' jellyfish in the US, such as the White Spotted Jellyfish (*Phyllorhiza punctata*) -native to Australia and the Philippines – which are felt to have 'hitchhiked' on ocean vessels (3). Consequently, the types of jellyfish found in US and territorial waters are subject to change and epidemiologic studies are warranted, such as through the Jellyfish Data Initiative (JeDI) and JellyWatch.org. JellyWatch.org allows member of the public to upload reports and photographs to their website, which can be of benefit for warning others of periodic risks. To determine the relative frequency of jellyfish in US Territorial waters, reports to the JellyWatch.org site were reviewed along with any epidemiologic studies and websites reporting sightings.

Distribution of Jellyfish in the US and Territorial Waters

Hawaii

In the Pacific Ocean surrounding Hawaii, the most common cnidarian stings are due to the box jellyfish (Carybdea alata) and Portuguese Man-of-war (Physalia physalis) (3) .

Pacific Coast

Fortunately, the vast majority of jellies found on the Pacific Coast are nonvenomous. The Pacific Sea Nettle, ***Chrysaora fuscescens*** is found widely on the Pacific coast but has a relatively mild sting in humans. A box jelly, *Carybdea marsupialis* can be occasionally found off Southern California in the late summer or fall. This species lacks a potent sting, especially compared to the notorious sea wasp of Australia, *Chironex fleckeri* which is responsible for hundreds of fatal stings.

Gulf of Mexico

According to the National Science Foundation, the most abundant species of jellyfish in the Gulf are the sea nettle and moon jellyfish, which typically swarm during summer months (4). The Portuguese Man O'War, *Physalia Physalis*, is also commonly reported in the Gulf. The Portuguese Man O' War, *Physalia physalis*, is a jelly from the class Siphonophore. These animals are a colony of minute organisms (zooids). A gas-filled float or bladder resembling a purple or blue bottle provides buoyancy, and long blue/purple tentacles trail the float. The species is given the common name 'blue bottle' to distinguish it from the more widely distributed and larger *Physalia physalis*, the Portuguese Man-of war. The species are told apart by the size of the float (six inches compared to twelve) and by having a single versus several long fishing tentacles. No fatalities from envenomation are recorded for *P. utriculus*, in contrast to the larger Man-of- war' War. Portuguese Man-of-wars have been reported frequently in the Gulf Coast waters and in the Atlantic as far north as Delaware and NY. The first reported fatalities from this animal occurred on the Florida Atlantic coast in 1987 (6,7)

Atlantic Coast

Chrysaora quinquecirrha, the common Atlantic Sea Nettle, can be found along the entire US east coast and particularly in the Chesapeake Bay and is responsible for thousands of stings each summer.

There are about 50 species of box jellies, which belong to the class Cubozoa and are primarily found in tropical waters (8) . The box jelly, *Carybdea marsupialis* is occasionally found in the Atlantic ocean and has been reported as far north as Delaware and NY (http://jellieszone.com/cubozoa/).

Carukia barnesi, a tiny (2 cm tall) cubozoan, is also found in Australia and its venom is responsible for causing Irukanji Suyndrome, which is associated with severe muscle spasms, breathing difficulty, vomiting, tachycardia and hypertension. While *Carukia barnesi* has not been identified in US waters, an Irukanji-like condition has been reported following jellyfish envenomations in the Florida Keys (9).

Physalia physalis (Portuguese Man-of-war) is also reported along the southern Florida Atlantic Coast and can be carried by the Gulf Stream as far north as NJ or NY.

Puerto Rico/USVI

Moon jellies (*Aurelia aurita)* are commonly found in the tropical waters surrounding Puerto Rico and the USVI. These jellies have a short tentacle with a relatively mild, irritating sting. Box jellyfish have also been reported in these waters and are reported to cause more severe, painful stings or allergic reactions (personal communication, VISAR Virgin Gorda).

Traditional First Aid

The severity of a sting from a jellyfish varies with the type of jellyfish, but may range from a mild irritation to severe, agonizing pain, rash, symptoms of allergic reaction, or rarely, Irukanji Syndrome. A host of home remedies have been tried for jellyfish, with varying results. Studies have conflicting results, often because the interventions are performed on different classes of jellies and issues of heterogenicity.

For a person who is stung by an unknown jellyfish, initial first aid should begin with an assessment of signs or symptoms of shock or cardiac arrest. 9-1-1 should be contacted immediately if there is suspected shock, and CPR initiated for the rare case of cardiac arrest following a sting.

For other stings, care is directed first at inactivating the stinging nematocysts, followed by removal of tentacles and treatment for pain. This review evaluated studies looking at the inactivation or nematocysts and treatment for pain.

RESULTS

In 2002, **Nomura** et al performed a randomized controlled trial with 25 participants in which ***Alatina (Carybdea) alata*** caught in **Hawaiian waters** were used to inflict stings on study volunteers. Tentacles from the captured jellyfish were cut and applied to each forearm of the subjects until pain occurred. Each subject was treated with hot fresh water immersion (i) (40-41° C) or with either 5% acetic acid (c) or papain meat tenderizer paste (c) (Adolph's meat tenderizer). The arm receiving the hot water treatment was randomized for each subject. Pain following treatment was then rated on a 100 mm VAS over 20 minutes. This study provided very low quality evidence, downgraded for risk of bias and indirectness. This study found a mean difference in VAS at 4 minutes and 20 minutes of 11 mm and 16 mm, respectively, between patients treated with hot water vs acetic acid/papain meat tenderizer comparators. In this study not enough information was given to differentiate between the acetic acid/papain meat tenderizer comparators. No other control was used. The authors concluded that hot water application provided a clinically significant reduction in pain.

In April of **2001, Thomas**, et al conducted a randomized trial studying the effect of hot pack (i)(Kwik-Heat 110° F) versus cold packs (i) (Kwik-Kold 42° F) in the treatment of self-presenting victims of jellyfish stings to lifeguard stations in Waikiki Beach **Hawaii.** All patients were treated with vinegar dousing and then subjects were randomized to hot pack (i), cold pack (i) or control (depleted pack). Blinding was not performed. Subjects recorded pain on a 100 mm VAS over 15 minutes; 127 subjects were available for analysis, however there was significant attrition over time. The jellyfish were **likely *Alatina (Carybdea) alata*** as correlated with lunar cycle. This study provided low quality evidence and was downgraded due to inadequate blinding and significant participant drop out. In this study, hot pack (i) versus control (depleted heat pack) produced a mean difference in pain relief VAS at 5, 10, 15 min of 6.4 mm (95% CI 5.8-7.0), 10.7 mm (95% CI 9.59-11.81), and 3.2 mm (95% CI -0.85-7.25), respectively. Cold pack (i) versus control (depleted cold pack) produced a mean difference in pain relief VAS at 5, 10, 15 min of 4.9 mm (95%CI 4.29-5.51), 2 mm (95% CI 0.83-3.17), and -7.7 mm (95% CI -11.04-(-4.36)), respectively. When hot pack (i) was compared with cold pack (c) pain relief VAS at 5, 10, 15 min revealed a mean difference of 1.5 mm (95% CI 0.90-2.10), 8.7 mm (95% CI 7.54-9.86), and 10.9 mm (95% CI 7.27-14.53), respectively. When researchers evaluated cessation of pain, hot pack (i) versus control (depleted heat pack) produced a relative risk of 0.7154 (95% CI 0.3951-1.255); cold pack (i) versus control (depleted cold pack) produced a relative risk of 0.8780 (95% CI 0.4631-1.6649); hot pack (i) versus cold pack (c) produced a relative risk of 0.8148 (95% CI 0.4673-1.4207). While hot packs showed a statistically significant reduction in pain at 5 and 10 minutes, authors of this study did not feel that this reached clinical significance and concluded that due to the minimal clinical improvement in pain relief, neither heat nor cold pack should be applied as first aid.

Yoshimoto et al conducted an observational study in 2002 with a retrospective chart review of 32 cases analyzing the efficacy of heat application (i) (hot shower or hot compress) versus analgesic (c) or benzodiazepine (c) in relieving pain. The study was conducting using data from a single health care facility **in Hawaii**, and the species of jellyfish involved with **likely predominantly *Alatina (Carybdea) alata* or *Physalia spp.*** After cases were identified using ICD-9 codes, researches evaluated for signs of clinical improvement in pain within 20 minutes of receiving either heat treatment or an intravenous medication (recorded as an analgesic or benzodiazepine). This study provided very low quality evidence and was downgraded for imprecision and limitations of the retrospective design. An odds ratio of 11.5 (95% CI 1.007-131.28) was obtained for pain relief for heat application versus analgesics. An odds ratio of 23.0 (95% CI 1.40-378.90) was obtained for pain relief in heat application versus benzodiazepines. The number of patients treated with benzodiazepines or analgesics was extremely small at 7 total. The temperature of the heat therapy was not recorded. The authors of this study recognized the limitations of the retrospective design, but were encouraged by the results and suggested that prospective studies be done to confirm the results.

In **August of 2001, Thomas** et al studied the efficacy of fresh water, seawater, Sting-Aid (aluminum sulfate) and Aldolph's meat tenderizer (papain) in the treatment of self-presenting victims of jellyfish stings to lifeguard stations in Waikiki Beach **Hawaii.** Stings were likely due to ***Alatina (Carybdea) alata*** or ***Physalia spp*** based on location and moon phase. All patients were treated with vinegar dousing and then subjects were randomized to treatment group. Subjects recorded pain on a 100 mm VAS over 15 minutes; 62 subjects were available for analysis. This data was low quality evidence downgraded for significant participant drop out and selection bias (had to come to lifeguard stand). Adoph's meat tenderizer (papain) (i) versus control (sea water) produced mean difference in pain relief VAS at 0, 5, 10 min of -1.9 mm (95% CI -3.99-1.39), -8.8 mm (95% CI -13.36-(-4.24)), and -3.4 mm (95% CI -13.4-6.6), respectively. Fresh water (i) versus control (sea water) produced mean difference in pain relief VAS at 0, 5, 10 min of -3.7 mm (95% CI -6.01-1.39), -6.4 mm (95% CI -9.94-(-2.86)), and -5.5 mm (95% CI -14.18-3.18), respectively. Sting-Aid (alum) (i) versus control (sea water) produced mean difference in pain relief VAS at 0, 5, 10 min of 1 mm (95% CI -1.79-3.79), -7.2 mm (95% CI -11.40-(-3.00)), and -2.4 mm (95% CI -5.54-10.34), respectively. The authors of this study suggest flushing the area of the sting with fresh or salt water but do not recommend papain or alum as a treatment.

Loten et al, in 2006, published a randomized controlled trial enrolling 96 participants with an observed or suspected **blue bottle (*Physalia spp.* (Australian - likely *utriculus*))** stings which were randomized to hot water immersion (45° C) (i) versus ice pack (-4˚ C) (c). Participants were recruited from self-presenters to two life guard first aid stations in Newcastle Australia. Participants were eligible if they had an observed or suspected bluebottle sting. They were randomized to intervention or control and then asked to rate their pain on a 100 mm VAS over 20 minutes. Neither subjects nor investigators were blinded. The study was stopped early due to interim analysis of 20 min VAS score showing a statistically significant clinically relevant reduction in pain with hot water. This study provided very low quality of evidence due to possible allocation bias (unequal baseline pain scores), selection bias (had to come to lifeguard stand), and that it was unblinded. The endpoint of a clinically important reduction in pain at 10 min showed a relative risk of 0.6015 (95% CI 0.3671-0.9854) hot water versus cold pack. A clinically important reduction in pain at 20 min had a relative risk of 0.3757 (95% CI 0.2407-0.5863) hot water versus cold pack. There was no control group in this study. The authors of this study recommend that hot water immersion be included in the first aid treatment of jellyfish sting.

In 1980, Turner et al enrolled 20 participants in a randomized controlled trial that used cut ***Physalia spp*** tentacles to evaluate four different solutions on the pain relief. The forearm of the subjects was divided into four quadrants and 2-3 cm of cut tentacle was applied for 2 minutes. Salt water (c) was used in one quadrant as a control. In the other four quadrants one of the following agents was applied to each quadrant: methylated spirits (i), vinegar (i), and Stingose (i). Treatment area was randomly rotated between the agents. After treatment, subjects were asked rank each quadrant from most painful to least painful. This study provided very low quality of evidence evaluating the efficacy of four first aid agents in providing pain relieve in ***Physalia spp***. (**Australian - likely *utriculus***) stings. This study was downgraded for indirectness and imprecision. Cut tentacles were applied both forearms of the participants who judged which provide the "most relief." Vinegar (i) versus salt water (c) gave a relative risk in pain reduction of 2.7778 (95% CI 1.4177-5.4428). Stingose (i) versus salt water (c) provided a relative risk of 2.111 (95% CI 1.0502-4.2845). Methylated spirits (i) versus salt water (c) showed a relative risk 0.111 (95% CI 0.0145-0.8500). The authors recommended not using methylated spirits in the treatment of bluebottle stings and suggested that vinegar is lightly more efficacious than Stingose.

In 2016, Knudson publish a trial in abstract form that enrolled 18 patients in a study evaluating the efficacy of hot water immersion versus topical lidocaine on stings from **lion's mane jellyfish (*Cyanea capillata*)** tentacles. This study provided low quality evidence due to lack of blinding and indirectness. Cut tentacles were applied to each ankle of the subject and one ankle was the randomized to receive 5% topical lidocaine treatment (c) and the other hot water immersion (i) at 45° C. 100 mm VAS scores were collected regarding pain and itching, respectively, before treatment and at 30 minutes, 60 minutes and 24 hours post treatment. Pre-treatment VAS was 18 mm regarding pain and 34 mm regarding itching. Following treatment, VAS regarding pain for hot water immersion was5 mm and for lidocaine was 13 mm at 30 minutes ($p<0.05$). The author's concluded that while both lidocaine and hot water immersion are effective in reducing symptoms after contact with a lion's mane jellyfish, hot water immersion appears to be more effective for treatment of pain and itching.

Lopez et al published an abstract in 2000 based out of the Florida Poison Information Center – Miami in which callers to the poison center (either patients or health care providers) were randomized to receive instruction on hot water immersion (i) (110° F) or ice packs (c) for pain relief of jellyfish stings. Twenty-seven subjects with jellyfish stings were enrolled in the study, likely with stings **from south Florida coastal waters**. Three patients (2 from hot water, 1 from ice pack) were excluded for unspecified protocol violations. This study provided low quality of evidence, downgraded for a lack of blinding and selection bias. Participants were randomized to hot water or a cold pack on alternating days. The 3 patients that failed to obtain pain relief with ice packs were crossed over and experienced pain relief with hot water immersion. Participants receiving hot water treatment had a relative risk of 1.600 (95% CI 0.8722-2.9351) for pain relief compared to those with ice pack therapy. In this study no control group was present. The author's concluded that hot water was more effective than ice packs for analgesia following jellyfish sting.

In **2013 a Cochran review** was completed to evaluate the literature on the worldwide treatment of jellyfish stings. The review found 7 trials with 435 patients which were primarily conducted in Hawaii and Australia. The primarily species involved were ***Physalia*, *Carukia* and *Alatina* (*Carybdea*) *alata*** jellyfish. These were found to be low quality studies with a high risk of bias. A wide range of interventions were employed in these studies. This review suggested that heat appears to be effective for ***Physalia*** stings based on one study but did not extrapolate this finding to other jellyfish.

In 2015 Ostermayer and Koyman further reviewed the data of the 7 randomized studies from the Cochran review. The authors extracted the data and synthesized risk ratios for reduction in pain by at least 50% on a VAS after **bluebottle stings**, comparing hot water to ice packs at 10 and 20 min. At 10 minutes, 26/49 subjects treated with hot water and 15/47 treated with ice packs experience at least 50% reduction , giving a risk ratio of 1.7 (95% CI 1.0-2.7) for pain relief. Number needed to treat was 4.7 (95% CI 2.5-54.4). At 20 min 39/45 subjects treated with hot water and 14/43 treated with ice packs experience at least 50% reduction , giving a risk ratio of 2.7 (95% CI 1.7-4.2) for pain relief. Number needed to treat was 1.8 (95% CI 1.4-2.7).

In 2012, Ward et al performed a systematic review of evidence evaluating treatments of envenomations by North American and Hawaiian jellyfish. This review also evaluated a variety of treatments over a variety of clinical scenario and relies on low quality studies. The authors concluded that the application of vinegar may not be ideal in general jellyfish envenomation as it may cause exacerbation of envenomation in species other than ***Physalia***. The authors suggested that hot water or topical lidocaine may be more beneficial. If the envenomation is determined to be from a ***Physalia*** species, then vinegar may be beneficial.

Birsa et al conducted an experimental study in 2010 involving microscopic examination of cut ***Physalia physalis*** **(Portuguese man-of-war)** and ***Chrysaora quinquecirrha*** **(Sea nettle)** tentacles to evaluate for nematocyst discharge following application of various solutions traditionally used in first aid for jellyfish stings. Solutions tested included salt water (28 ppt), acetic acid (5%), ammonia (20%), meat tenderizer (bromelain 10%), urea (50%), ethanol (70%), sodium bicarbonate (10%) and lidocaine (4%). Acetic acid, ethanol, ammonia and bromelain (meat tenderizer) suspensions resulted in immediate nematocyst discharge. Meat tenderizer caused the most discharges in ***P. physalis*** tentacles while ammonia caused the most in ***C. quinquercirrha***. Little or no discharge occurred after the addition of seawater, lidocaine or sodium bicarbonate solutions. Lidocaine also inhibited nematocysts discharge after subsequent exposure to acetic acid, ethanol, ammonia or bromelain. In a subsequent study, two of the authors exposed the each of their inner forearms to either ***Chrysaora quinquecirrha*** (**sea nettle**) or ***Chiropsalmus quadrumanus*** (**sea wasp**) tentacles. Treatment solutions included lidocaine (15%, 10%, 5%, 3%, 1%), benzocaine (5, 10% in ethanol), ethanol (70%), acetic acid (5%), or ammonia (20%)] to one of the arms with the control of no treatment being the opposite arm. Lidocaine concentrations of 10 and 15% produced immediate relief; 4 and 5% solutions produced relief after approximately 1 min, while 1, 2 and 3% solutions required 10 to 20 min provide noticeable relief. Benzocaine provided some relief but took 10 or more min. Higher concentrations of lidocaine also resulted in fewer areas of redness. Areas of skin redness were observed after treatment with benzocaine, acetic acid, or ethanol in contact with jellyfish tentacles. This data was deemed to be very low quality evidence due to indirectness, and imprecision. The authors concluded that lidocaine both inhibits nematocyst discharge and provides pain relief due to its anesthetic effect.

Table 2
Quantitation of discharged nematocysts after a treatment of suspensions of jellyfish tentacles with various chemicals. For 2 of the studies there was addition of lidocaine to tentacle suspension, followed in 1 min. by addition of acetic acid or ammonia.

Chemical	Number of discharged nematocysts (number/mm ± standard deviation)	
	Chrysaoroa quinquecirrha (sea nettle)	*Physalis physalis* (Portuguese man-of-war)
Ethanol (70%)	66 ± 14	53 ± 26
Ammonia (20%)	80 ± 16	80 ± 5
Meat tenderizer (10%) (Bromelain)	29 ± 10	112 ± 16
Acetic acid (5%)	5 ± 11	100
Seawater	0	0
Urea (10%)	0	0
Lidoocaine (4%)	0	0
Lidocaine (4%) followed by addition of acetic acid	0	0
Lidocaine (4%) followed by addition of ammonia	0	0

Table 3
Relative relief of jellyfish sting pain intensity after application of various traditionally used chemicals and by the anesthetics, benzocaine or lidocaine. See Methods and materials for concentrations, sources, and experimental protocols.

Chemical	Pain intensity after application of chemical	
	Chiropsalmus quadrumanus (Sea Wasp)	*Chrysaoma quinquecirrha* (Sea Nettle)
Control (seawater)	0	0
Control (deionized water)	0	0
Lidocaine (5%)	-	-
Lidocaine (10%)	–	–
Lidocaine (15%)	—	—
Benzocaine (5%)	-	N
Benzocaine (10%)	-	N
Ammonia (20%)	+	+
Acetic Acid (5%)	+	+
Ethanol	+	+
Bromelain = Meat tenderizer	0	0

"0" = no apparent change in sting intensity or duration of pain. "+" = exacerbation of pain intensity. "-" = noticeable alleviation of pain intensity and duration. "–" = further reduction in pain alleviation. "—" = maximum observed reduction in pain of jellyfish stings. N = no test with the chemical.

In 1983, Burnett et al studied the effects of various first aid agents on nematocyst discharge of the sea nettle (***Chrysaora quinquecirrha*) and Portuguese man-of-war (*Physalia physalis*) tentacles**. This study provided very low quality evidence, downgraded due to indirectness. Cut tentacles were placed in a Petri dish and washed with salt water. Solutions tested included Stingose, Little Darling-Sudsy ammonia, Clorox bleach (sodium hypochlorite), Adolph's meat tenderizer, Bactine, lidocaine, Witch Hazel, Arm and Hammer Baking Soda, Campho Phenique, Cream Corn Starch, Regina Red Wine Vinegar, Right Guard deodorant, acetone, 20% aluminum chloride, glycerol, 33% and 100% ethanol, 70% isopropyl alcohol, sodium hydroxide, magnesium chloride, 0.1% and 1.0 % papain, and formalin 4% and 40%. Results were poorly classified by the authors. Regarding the sea nettle tentacles, acetone, Clorox and ammonia caused nematocyst discharge. Stingose, Adolph's meat tenderizer and papain inhibited nematocyst discharge. Baking soda prevented nematocyst discharge induced by vinegar or ammonia. Magnesium chloride did not inhibit chemically stimulated nematocysts. In regards to Portuguese man-of-war tentacles, Clorox and 0.1N sodium hydroxide resulted in nematocyst discharge. Vinegar appeared to be the best solution to block nematocyst discharge by either Clorox or sodium hydroxide. The authors concluded that Clorox, acetone or vinegar should not be used for sea nettle stings. They recommend baking soda for sea nettle stings and vinegar for Portuguese Man-of-war stings.

Morabito et al in 2014 conducted an experimental study comparing the effect of lidocaine, ethanol, ammonia, acetic acid and sodium bicarbonate on ***Pelagia noctiluca*** stings. In this study, cut ***P. noctiluca*** tentacles were incubated in artificial salt water containing chemosensitizing agents in the presence or absence of either 1% v/v lidocaine, 70% v/v ethanol, 20% v/v ammonia, or 5% v/v acetic acid. After incubation, mechanical stimulation was applied, and nematocyst discharge was quantified. To evaluate whether the discharge modulation was reversible, tentacles treated with 1% v/v lidocaine were then washed with artificial salt water then exposed to a chemosensitizer compound and mechanically stimulated by a non-vibrating test probe. Simultaneous treatment with 1% lidocaine 70% v/v ethanol, 20% v/v ammonia or 5% v/v acetic acid and chemosensitizers produced a significant decrease in discharge response ($p < 0.001$). In this study artificial salt water did not induce nematocyst discharge. This study provided very low quality evidence due to indirectness. The authors concluded that lidocaine, ethanol, ammonia and acetic acid are highly effective in reducing the in situ discharge response.

Table 1
Number of discharged nematocysts in oral arms of *Pelagia noctiluca* following combined chemical-mechanical stimulation with different chemosensitizer compounds and a non-vibrating test probe. Control experiments are performed by mechanical stimulation of oral arms without exposure to chemosensitizers. $^{*}p < 0.05$ *vs* control as determined by one-way analysis of variance (ANOVA), followed by Bonferroni's post-hoc test, $n = 20$.

Number of discharged nematocysts	
Control	4.69 ± 0.6
10^{-3} M NANA	$33.5 \pm 1.5^{*}$
10^{-3} M NAGA	$39.85 \pm 0.6^{*}$
10^{-3} M Glutamate	$35.83 \pm 1.2^{*}$
10^{-3} M Artherenol	$38.12 \pm 0.7^{*}$
10^{-3} M Carbachol	$41.57 \pm 0.9^{*}$
10^{-3} M Cysteine	$26.75 \pm 0.3^{*}$
10^{-3} M Glycine	$47.52 \pm 0.5^{*}$
10^{-3} M Arginine	$28.17 \pm 1.07^{*}$
10^{-3} M Albumin	$20.75 \pm 1.14^{*}$
10^{-3} M Mucin	$24.05 \pm 0.31^{*}$
1% v/v Lidocaine	5.93 ± 1.04
70%v/v Ethanol	2.63 ± 0.3
20% v/v Ammonia	2.00 ± 0.2
10% w/v Sodium bicarbonate	$17.62 \pm 0.8^{*}$
5% v/v Acetic acid	1.49 ± 0.4

R. Morabito et al. / Toxicon 83 (2014) 52-58 55

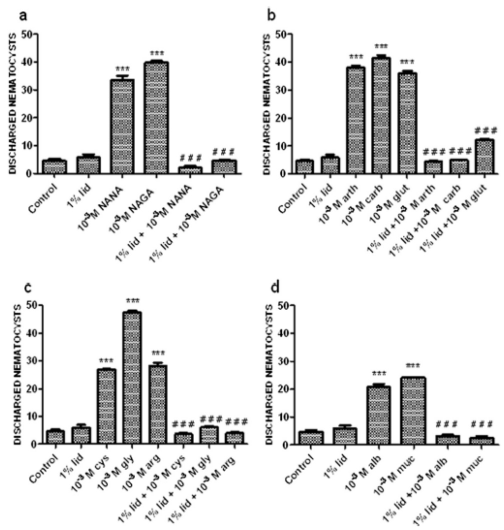


Fig. 1. Number of nematocysts discharged under mechanical stimulus (control) and after a chemico-mechanical stimulation by incubation of oral arms with, alternatively, **a)** 1% v/v lidocaine, and 10^{-3} M NANA, 10^{-3} M NAGA, alone (data are taken from Table 1) or combined; **b)** 1% v/v lidocaine, and 10^{-3} M artherenol, 10^{-3} M carbachol, 10^{-3} M glutamate, alone (data are taken from Table 1) or combined; **c)** 1% v/v lidocaine, and 10^{-3} M cysteine, 10^{-3} M glycine, 10^{-3} M arginine, alone (data are taken from Table 1) or combined; **d)** 1% v/v lidocaine, and 10^{-3} M albumin, 10^{-3} M mucin, alone (data are taken from Table 1) or combined. $^{***}p < 0.001$ significant *vs* control, $n = 20$; $^{\#\#\#}p < 0.001$ significant *vs* NANA and NAGA (a), *vs* artherenol, carbachol, glutamate (b), *vs* cysteine, glycine, arginine (c), *vs* albumin, mucin (d), $n = 20$.

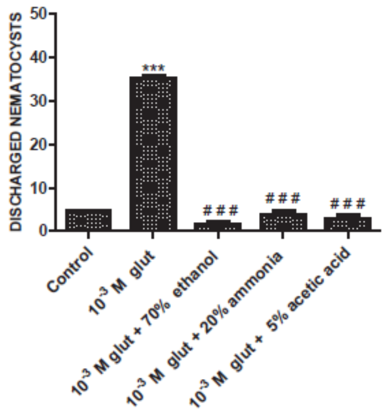


Fig. 3. Number of nematocysts discharged following a mechanical stimulus (control) and after a chemico-mechanical stimulation by incubation of oral arms with, alternatively, 10^{-3} M glutamate, 70% ethanol, 20% ammonia, 5% acetic acid. $^{***}p < 0.001$ *vs* control, ###$p < 0.001$ significant *vs* glutamate $n = 20$. Data of control and 10^{-3} M glutamate are taken from Table 1.

Please end this section with a summary of your final evidence integration and the rationale for the guideline, recommendation and/or option. Describe any mismatches between the evidence and your final guideline, recommendation and/or option.

Data regarding the first aid treatment of jellyfish envenomation is limited. Studies favor the use of heat over analgesics, ice/cold packs, acetic acid or papain. While studies reach a statistical significance, numbers are small and there is some question over clinical significance. Acetic acid showed varied resulted and in some species may increase nematocyst discharge. In addition, there is some evidence that lidocaine may both inhibit nematocyst discharge and provide pain relief from jellyfish stings. There is some evidence that cold packs may provide minimal relief over placebo.

Recommendations and Strength (using table below):
The strength of all recommendations and conclusions is related to the scientific evidence upon which they are based. All recommendations therefore derive from critical review of the available literature and the strength of their design, standard reference material, textbooks, and expert opinion. All recommendations are weighted based upon the source and strength of the scientific evidence and are classified into one of three groups – Standards, Guidelines, or Options.
Standards represent the strongest recommendations and have a high degree of scientific certainty. These recommendations result from strong evidence obtained from well designed, prospective, randomized controlled studies.
Guidelines provide a moderate degree of scientific certainty and are based on less robust evidence such as non-randomized cohort studies, case-control studies, or retrospective observational studies.
Options result from all other evidence, publications, expert opinion, etc. and are the least compelling in terms of scientific evidence.

Jellyfish envenomation in North America may be painful but is rarely life threatening. Often the species of jellyfish causing the envenomation is unknown making the need for universal treatment recommendations necessary. In the treatment of jellyfish envenomation there are two important concepts: inhibiting further nematocyst discharge and subsequent pain relief. During envenomation the tentacle may break off the body and remain adhered to this victim. In addition, there is the concept that even if the tentacle no longer remains, undischarged nematocysts may remain on the skin and further physical or chemical stimulus may result in discharge of the remaining nematocyst, worsening envenomation.

Acetic acid (vinegar) has traditionally been applied to inhibit further nematocyst discharge, but the studies providing evidence for its efficacy in different species, and even in the same species, is limited and often contradictory. Although Turner indicates that acetic acid was more beneficial than a commercial sting aid and salt water, Birsa suggests that acetic acid may stimulate nematocyst discharge in *Physalia spp*. Birsa also found that acetic acid appeared to cause more nematocyst discharge in relation to salt water for *Chrysaora quinquecirrha* (Sea nettle). Burnett, however, reported that acetic acid blocked further neumatocyst discharge from other chemical agents. Morabito suggests that for *Pelagia noctiluca* acetic acid reduced nematocyst discharge. Due to the variability of this evidence it is difficult to continue to recommend acetic acid as the type of jellyfish involved in the sting is often unknown. In addition, it is unknown how many undischarged nematocysts remain on the victims skin after contact with the jellyfish and whether or not this treatment is clinically useful.

Studies in Hawaiian waters suggest that hot water and hot packs are more efficacious in relieving pain than acetic acid, analgesics/benzodiazepines and cold packs. This includes evidence for *Physalia* spp. and *Alatina* (*Carybdea*) *alata* provided by Thomas, Nomura and Yoshimoto. Loten also found that hot water was better than ice pack for *Physalia spp*. for producing pain relief. Salt water does not appear to induce nematocyst discharge and would therefore be safe for irrigation.

In US coastal Atlantic waters Lopez found that hot packs performed better than cold packs in relieving pain following jellyfish stings in Florida waters. Heat seems to be efficacious in *Physalia spp*., whereas acetic acid may cause nematocyst discharge (Birsa). Acetic acid may also induce some nematocyst discharge in the sea nettle (Birsa, Burnet). Lidocaine does appear to inhibit nematocyst discharge in both *Physalia physalis* and *Chrysaora quinquecirrha* (sea nettle). Salt water does not appear to induce nematocyst discharge.

The only data found regarding continental North American Pacific waters is regarding the Lion's Mane jellyfish. One small study found that heat immersion was more efficacious at relieving pain and itching than lidocaine (Knudsen).

In US coastal waters jellyfish envenomation can rarely be life threatening and can be caused by direct venom effect or allergic reaction. Following jellyfish envenomation ABC's should be assessed. For signs of shock the patient should be placed in the supine position.

In Hawaiian waters, remove any remaining tentacles with a blunt object to avoid further stings. Rinse the affected area with sea water and follow by application of hot water or hot pack (approximately 106-113°F). If a hot pack is not available a cold pack can be used to attempt to relieve the pain.

In costal Atlantic waters, remove any remaining tentacles with a blunt object to avoid further stings. Rinse the affected area with sea water. If topical lidocaine is available, this can be applied to inhibit further nematocyst discharge and provide pain relief. This should be followed by application of hot water or hot pack (approximately 106-113°F). If a hot pack is not available a cold pack can be used to attempt to relieve the pain.

In US coastal pacific waters it would be reasonable to treat as for Hawaiian waters. Remove any remaining tentacles with a blunt object to avoid further stings. Rinse the affected area with sea water and follow by application of hot water or hot pack (approximately 106-113°F). If a hot pack is not available a cold pack can be used to attempt to relieve the pain.

It should be noted that the general recommendations below are not presented in order of care, but based on level of evidence/degree of certainty.

Standards:

- Assess for loss of responsiveness, signs of shock or anaphylaxis and call 9-1-1 if present. Begin CPR as indicated.
- Following removal of remaining tentacles, use hot water immersion/irrigation or apply a hot pack to relieve pain. The temperature of the water or hot pack should be ~106-113° F, or as hot as tolerated (not scalding), for 20 minutes or until pain is relieved.

Guidelines:

- Gently lift or scrape off any remaining tentacles with a blunt object, such as a sea shell, and/or rinsing the affected area with sea water.
- Vinegar (acetic acid) is not recommended for most jellyfish stings in US coastal waters.

Options:

- Topical lidocaine cream or gel may be of benefit for pain control
- If hot packs or hot water are not available, it is reasonable to apply a cold pack

Knowledge Gaps and Future Research:

- What is the optimal temperature and mode of delivery for heat therapy?
- What is the role of topical lidocaine in the treatment of jellyfish envenomation?

Implications for ARC Programs:

The biggest changes is that in the new recommendations vinegar will be de-emphasized and baking soda will no longer be recommended. Following removal of the tentacle the area will be flushed with sea water and topical lidocaine can be applied with available. While heat was recommended in the prior recommendations, it will become the primary treatment in the new recommendations. Hot water immersion or irrigation with water from 106-113ºF will be preferred as there is the most evidence for this method, however, chemical heat packs can be used if water is not available. Cold packs will also be and option if heat is not available as there is some evidence it may improve pain.

American Red Cross
Scientific Advisory Council
Scientific Review
Jellyfish Stings

Summary of Key Articles/Literature Found and Level of Evidence/Bibliography:

(Please fill in the following table for articles that were used to create your recommendations and/or guidelines. For references please us the American Medical Association Manual of Style and please only use abbreviations for journal names as listed in index medicus)

Author(s)	Full Citation	Summary of Article (provide a brief summary of what the article adds to this review including which question(s) it supports, refutes or is neutral)	Methodology	Bias Assess ment	Indirectness/ Imprecision/ Inconsistency	Key results and magnitude of results	Support, Neutral or Oppose Question	Level of Evidence (Using table below)	Quality of study (excellent, good, fair or poor) and why
Ward NT, Darracq MA, Tomaszewski C, Clark RF	Evidence-based treatment of jellyfish stings in North America and	Systematic review of evidence evaluating treatments of envenomati	A systematic review studies related to North American and Hawaiian jellyfish stings.	Significant risk of bias.		The authors concluded that the application of vinegar may not be ideal in	Supports the use of heat therapy and lidocaine for	1a	Good – based on low quality studies with low numbers of participants

	Hawaii. Ann Emerg Med. 2012 Oct;60(4):399-414. doi: 10.1016/j.annemergmed.2012.04.010. Epub 2012 Jun 6.	ons by North American and Hawaiian jellyfish	This review also evaluated a variety of treatments over a variety of clinical scenario and relies on low quality studies.			general jellyfish envenomation as it may cause exacerbation of envenomation in species other than Physalia. The authors suggested that hot water or topical lidocaine may be more beneficial. If the envenomation is determined to be from a *Physalia* species, then vinegar may be beneficial.	jellyfish stings. Suggests that vinegar may be beneficial for *Physalia* stings.		and multiple different treatments used.
Li L, McGee RG, Isbister G,	Interventions for the symptoms and signs resulting	A Cochran review to evaluate the literature	The review found 7 trials with 435 patients which were primarily	Significant risk of bias		This review suggested that heat appears to be effective for	Supports the use to heat therapy for the	1a	Good – based on low quality studies with low

Webster AC	from jellyfish stings. Cochrane Database Syst Rev. 2013 Dec 9;(12):CD009688. doi: 10.1002/14651858.CD009688.pub2.	on the worldwide treatment of jellyfish stings.	conducted in Hawaii and Australia. The primarily species involved were *Physalia*, *Carukia* and *Alatina (Carybdea) alata* jellyfish . A wide range of interventions were employed in these studies			*Physalia* stings based on one study but did not extrapolate this finding to other jellyfish.	treatment of jellyfish envenomation.		numbers of participants and multiple different treatments used.
Thomas CS, Scott SA, Galanis DJ, Goto RS.	Box jellyfish (*Carybdea alata*) in Waikiki. The analgesic effect of sting-aid, Adolph's meat tenderizer and fresh water on their stings: a double-blinded, randomized, placebo-	A randomized trial studying the effect of hot pack (Kwik-Heat 110° F) versus cold packs (Kwik-Kold 42° F) in the treatment of self-presenting victims of	All patients were treated with vinegar dousing and then subjects were randomized to hot pack (i), cold pack (i) or control (depleted pack). Blinding was not performed The jellyfish were likely *Alatina*	Significant bias		Hot pack versus control produced a mean difference in pain relief VAS at 5, 10, 15 min of 6.4 mm (95% CI 5.8-7.0), 10.7 mm (95% CI 9.59-11.81), and 3.2 mm (95% CI -0.85-7.25), respectively.	Provided some evidence that heat therapy is superior to both control and cold packs in the treatment of Hawaiian jellyfish envenomation.	1a	Good. Significant subject drop out. Researchers attempted blinding. Selection bias of those presenting to the lifeguard station.

	controlled clinical trial. Hawaii Med J. 2001 Aug;60(8):205-7, 210.	jellyfish stings to lifeguard stations in Waikiki Beach Hawaii.	*(Carybdea) alata* as correlated with lunar cycle.. Subjects recorded pain on a 100 mm VAS over 15 minutes; 127 subjects were available for analysis, however there was significant attrition over time.			Cold pack versus control produced a mean difference in pain relief VAS at 5, 10, 15 min of 4.9 mm (95%CI 4.29-5.51), 2 mm (95% CI 0.83-3.17), and -7.7 mm (95% CI -11.04-(-4.36)), respectively. When hot pack was compared with cold pack pain relief VAS at 5, 10, 15 min revealed a mean difference of 1.5 mm (95% CI 0.90-2.10), 8.7 mm (95% CI 7.54-9.86),			

						and 10.9 mm (95% CI 7.27-14.53), respectively. When researchers evaluated cessation of pain, hot pack versus control) produced a relative risk of 0.7154 (95% CI 0.3951-1.255); cold pack versus control produced a relative risk of 0.8780 (95% CI 0.4631-1.6649); hot pack versus cold pack produced a relative risk of 0.8148 (95% CI 0.4673-1.4207).			

Nomura JT, Sato RL, Ahern RM, Snow JL, Kuwaye TT, Yamamoto LG	A randomized paired comparison trial of cutaneous treatments for acute jellyfish (*Carybdea alata*) stings. Am J Emerg Med. 2002 Nov;20(7):624-6.	A randomized controlled trial with 25 participants in which *Alatina (Carybdea) alata* caught in Hawaiian waters were used to inflict stings on study volunteer. . Subjects were treated with hot water immersion, acetic acid or papain.	Each subject was treated with hot fresh water immersion (40-41° C) or with either 5% acetic acid or papain meat tenderizer paste (Adolph's meat tenderizer). The arm receiving the hot water treatment was randomized for each subject. Pain following treatment was then rated on a 100 mm VAS over 20 minutes.	Significant risk of bias	Indirectness	There was a mean difference in VAS at 4 minutes and 20 minutes of 11.2 mm and 16 mm, respectively, between patients treated with hot water vs acetic acid/papain meat tenderizer comparators. In this study not enough information was given to differentiate between the acetic acid/papain meat tenderizer comparators.	This study provides evidence for the use of heat therapy over either papain meat tenderizer or acetic acid.	1b	Fair. Small number of patients. No control group was used. No blinding
Knudsen K, Agren S	Hot water immersion treatment for lion's mane	Randomized trial evaluating the use of	Cut lion's mane jellyfish (*Cyanea capillata*)	Significant risk of bias	Indirectness	100 mm VAS scores were collected	This study provided evidence that both	1b	Fair. Unblinded, indirect No control

	jellyfish stings in Scandinavia. Clinical Toxicology. 2016;54(4):512	lidocaine versus hot water immersion in the treatment of lion's mane jellyfish enevenomation.	tentacles were applied to each ankle of the subject and one ankle was the randomized to receive 5% topical lidocaine treatment (c) and the other hot water immersion (i) at 45 C.			regarding pain and itching, respectively, before treatment and at 30 minutes, 60 minutes and 24 hours post treatment. Pre-treatment VAS was 18 mm regarding pain and 34 mm regarding itching. Following treatment, VAS regarding pain for hot water immersion was5 mm and for lidocaine was 15 mm at 30 minutes ($p<0.05$).	lidocaine and hot water immersion reduce symptoms after contact with a lion's mane jellyfish. , Hot water immersion appears to be more effective for treatment of pain and itching.		group was used.

Loten C, Stokes B, Worsley D, Seymour JE, Jiang S, Isbister GK	A randomized controlled trial of hot water (45 degrees C) immersion versus ice packs for pain relief in bluebottle stings. Med J Aust. 2006 Apr 3;184(7):329-33.	A randomized controlled trial enrolling 96 participants with an observed or suspected blue bottle (*Physalia spp.* (Australian - likely *utriculus*)) stings	Participants were recruited from self-presenters to two life guard first aid stations in Newcastle Australia and were suspected to have a bluebottle sting. Subjects. were randomized to hot water immersion (45° C) (i) versus ice pack (-4° C) (c). Subjects were asked to rate their pain on a 10 cm VAS over 20 minutes	Risk of bias		The study was stopped early due to interim analysis of 20 min VAS score showing a statistically significant clinically relevant reduction in pain with hot water.	This study provides evidence of the efficacy of heat therapy over cold therapy in the treatment of bluebottle stings.	1b	Fair. Selection bias of those presenting to the lifeguard station. No control used. Not blinded.
Lopez EA, Weisman RS, Bernstein J.	A prospective study of the acute therapy of jellyfish envenomatio ns. Clinical	A poison center study in Florida evaluating the use of hot water	Callers to the poison center (either patients of health care providers) were randomized to	Signific ant risk of bias		Participants receiving hot water treatment had a relative risk of 1.600 (95% CI	This study provides evidence that hot water therapy is more	1b	Fair. Significant selection bias. Unblinded. no control group.

	Toxicology. 2000;38(5):503-582	versus ice packs in the treatment of jellyfish stings.	receive instruction on hot water immersion (110° F) or ice packs for pain relief of jellyfish stings. Participants were randomized to hot water or a cold pack on alternating days. 27 subjects were enrolled in the study.			0.8722-2.9351) for pain relief compared to those with ice pack therapy	efficacious in relieving pain that ice packs in the treatment of Florida Jellyfish envenomations.		
Birsa LM, Verity PG, Lee RF	Evaluation of the effects of various chemicals on discharge of and pain caused by jellyfish nematocysts. Comp Biochem Physiol C Toxicol Pharmacol. 2010	An experimental study in 2010 involving microscopic examination of cut *Physalia physalis* (Portuguese man-of-war) and *Chrysaora*	Solutions tested included salt water (28 ppt), acetic acid (5%), ammonia (20%), meat tenderizer (bromelain 10%), urea (50%), ethanol (70%), sodium bicarbonate (10%) and lidocaine (4%).	Significant risk of bias	Indirectness, imprecision	Meat tenderizer caused the most discharges in *P. physalis* tentacles while ammonia caused the most in *C. quinquercirrha*. Little or no discharge occurred	Supports the use of lidocaine for inhibiting nematocyst discharge and providing pain relief in jellyfish sting. Suggests that acetic	2a	Fair. The human study only used two subjects and had significant bias. The in vitro study provided only indirect evidence.

	May;151(4):426-30. doi: 10.1016/j.cbpc.2010.01.007. Epub 2010 Jan 29.	*quinquecirrha* (Sea nettle) tentacles to evaluate for nematocyst discharge following application of various solutions traditionally used in first aid for jellyfish stings. Authors also exposed the each of their inner forearms to either *Chrysaora quinquecirrha* (sea nettle) or *Chiropsalmus quadrumanus* (sea wasp)	Acetic acid, ethanol, ammonia and bromelain (meat tenderizer) suspensions resulted in immediate nematocyst discharge.			after the addition of seawater, lidocaine or sodium bicarbonate solutions. Lidocaine also inhibited nematocysts discharge after subsequent exposure to acetic acid, ethanol, ammonia or bromelain. In the second part of the study, lidocaine concentrations of 10 and 15% produced immediate relief; 4 and 5% solutions produced relief after approximately 1 min,	acid may cause nematocyst discharge in *Physalia physalis* and to a lesser degrees in *Chysaora quinquecirrha*.		

		tentacles amnmd studies the effects of lidocaine (15%, 10%, 5%, 3%, 1%), benzocaine (5, 10% in ethanol), ethanol (70%), acetic acid (5%), or ammonia (20%)].				while 1, 2 and 3% solutions required 10 to 20 min provide noticeable relief. Benzocaine provided some relief but took 10 or more min. Higher concentrations of lidocaine also resulted in fewer areas of redness. Areas of skin redness were observed after treatment with benzocaine, acetic acid, or ethanol in contact with jellyfish tentacles.			

Yoshimoto CM, Yanagihara AA	Cnidarian (coelenterate) envenomations in Hawai'i improve following heat application. Trans R Soc Trop Med Hyg. 2002 May-Jun;96(3):300-3.	A retrospective chart review of patients with the diagnosis of jellyfish sings presenting to one hospital in Hawaii. Evaluated heat therapy versus treatment with nezodiazepines or analgesics.	The study was conducting using data from a single health care facility in Hawaii, and the species of jellyfish involved with likely predominantly *Alatina (Carybdea) alata* or *Physalia* spp. After cases were identified using ICD-9 codes, researches evaluated for signs of clinical improvement in pain within 20 minutes of receiving either heat treatment or an intravenous medication (recorded as an	Significant bias	Imprecision	An odds ratio of 11.5 (95% CI 1.007-131.28) was obtained for pain relief for heat application versus analgesics. An odds ratio of 23.0 (95% CI 1.40-378.90) was obtained for pain relief in heat application versus benzodiazepines	Supports the use of heat therapy over benzodiazepines or analgesics in jellyfish envenomation.	2b	Fair. Small number of patients. No control group. Retrospective design. On 7 patients were treated with benzodiazepines or analgesics.

			analgesic or benzodiazepine).						
Ostermayer DG, Koyfman A	What is the most effective treatment for relieving the pain of a jellyfish sting? Ann Emerg Med. 2015;65(4):432-433.	This was a small article reworking some of the data from the 2013 Cochran review.	The authors reviewed the data of these 7 randomized studies from the Cochran review. The authors extracted the data and synthesized risk ratios for reduction in pain by at least 50% on a VAS after bluebottle stings, comparing hot water to ice packs at 10 and 20 min.	Significant bias		At 10 minutes, 26/49 subjects treated with hot water and 15/47 treated with ice packs experience at least 50% reduction , giving a risk ratio of 1.7 (95% CI 1.0-2.7) for pain relief. Number needed to treat was 4.7 (95% CI 2.5-54.4). At 20 min 39/45 subjects treated with hot water and 14/43 treated with ice packs experience at	Supports the use of heat in the treatment of jellyfish stings over the use of ice.	3e	Fair – based on low quality studies with low numbers of participants. The only comparison was between heat and ice. .

						least 50% reduction , giving a risk ratio of 2.7 (95% CI 1.7-4.2) for pain relief. Number needed to treat was 1.8 (95% CI 1.4-2.7).			
Thomas CS, Scott SA, Galanis DJ, Goto RS	Box jellyfish (Carybdea alata) in Waikiki: their influx cycle plus the analgesic effect of hot and cold packs on their stings to swimmers at the beach: a randomized, placebo-controlled, clinical trial. Hawaii Med J. 2001 Apr;60(4):100-7.	A randomized trial efficacy of fresh water, seawater, Sting-Aid (aluminum sulfate) and Aldolph's meat tenderizer (papain) in the treatment of self-presenting victims of jellyfish stings to lifeguard	Due to the location and phase of the moon, stings were likely due to *Alatina (Carybdea) alata* or *Physalia spp*. All patients were treated with vinegar dousing and then subjects were randomized to treatment group. Subjects recorded pain on a 100 mm	Significant selection bias		62 subjects were available for analysis. Adolph's meat tenderizer (papain) versus control (sea water) produced mean difference in pain relief VAS at 0, 5, 10 min of -1.9 mm (95% CI -3.99-1.39), -8.8 mm (95% CI	This study suggests that papain and alum as not useful in the treatment of Hawaiian jellyfish stings.	1b	Fair. All patients were treated with vinegar prior to the other experimental therapies. There was significant drop out during the treatment phase.

		stations in Waikiki Beach Hawaii.	VAS over 15 minutes; 62 subjects were available for analysis			-13.36-(-4.24)), and -3.4 mm (95% CI -13.4-6.6), respectively. Fresh water versus control (sea water) produced mean difference in pain relief VAS at 0, 5, 10 min of -3.7 mm (95% CI -6.01-1.39), -6.4 mm (95% CI -9.94-(-2.86)), and -5.5 mm (95% CI -14.18-3.18), respectively. Sting-Aid (alum) versus control (sea water) produced mean difference in			

						pain relief VAS at 0, 5, 10 min of 1 mm (95% CI -1.79-3.79), -7.2 mm (95% CI -11.40-(-3.00)), and -2.4 mm (95% CI -5.54-10.34), respectively.			
Turner B, Sullivan P	Disarming the bluebottle: treatment of Physalia envenomation. Med J Aust. 1980 Oct 4;2(7):394-5.	A randomized controlled trial that used cut *Physalia spp* tentacles to evaluate four different solutions on the pain relief	The forearm of each subjects was divided into four quadrants and 2-3 cm of cut tentacle was applied for 2 minutes. Salt water was used in one quadrant as a control. In the other four quadrants one of the following agents was applied to each quadrant: methylated	Risk of significant bias	Imprecision and indirectness	Vinegar versus salt water gave a relative risk in pain reduction of 2.7778 (95% CI 1.4177-5.4428). Stingose versus salt water provided a relative risk of 2.111 (95% CI 1.0502-4.2845). Methylated spirits versus salt water	This study supported the use of vinegar and Stingose in comparison to salt water in the treatment of bluebottle envenomations.	1b	Fair. Use a cut tentacle. Unsure of blinding. Using all comparators at once may make it difficult to distinguish between them.

			spirits, vinegar, and Stingose. Treatment area was randomly rotated between the agents. After treatment, subjects were asked rank each quadrant from most painful to least painful			showed a relative risk 0.111 (95% CI 0.0145-0.8500).			
Morabito R, Marino A, Dossena S, La Spada G.	Nematocyst discharge in Pelagia noctiluca (Cnidaria, Scyphozoa) oral arms can be affected by lidocaine, ethanol, ammonia and acetic acid. Toxicon. 2014 Jun;83:52-8. doi: 10.1016/j.toxicon.2014.03.	Experimental study comparing the effect of lidocaine, ethanol, ammonia, acetic acid and sodium bicarbonate on *Pelagia noctiluca* stings.	In this study, cut *P. noctiluca* tentacles were incubated in artificial salt water containing chemosensitizing agents in the presence or absence of either 1% v/v lidocaine, 70% v/v ethanol, 20% v/v ammonia, or 5% v/v acetic acid. After	Significant risk of bias	Indirectness	Simultaneous treatment with 1% lidocaine 70% v/v ethanol, 20% v/v ammonia or 5% v/v acetic acid in the presence of chemosensitizers produced a significant decrease in discharge response ($p < 0.001$). In	Supports certain traditional treatments for jellyfish envenomation.	4	Fair - in situ study. Both chemical and mechanical stimuli usded to incite nematocyst discharge.

	002. Epub 2014 Mar 15.		incubation, mechanical stimulation was applied, and nematocyst discharge was quantified. To evaluate whether the discharge modulation was reversible, tentacles treated with 1% v/v lidocaine were then washed with artificial salt water then exposed to a chemosensitizer compound and mechanically stimulated by a non-vibrating test probe.			this study artificial salt water did not induce nematocyst discharge. This study suggests that lidocaine, ethanol, ammonia and acetic acid are effective in reducing the in situ discharge response in P. noctiluca nematocysts. .			
Burnett JW	In vitro eval of nematocyst discharge. Southern	An experimental study that evaluated	Clorox bleach (sodium hypochlorite), Adolph's meat tenderizer,		Indirectness.	Results were poorly classified by the authors. Regarding	This study provided evidence that vinegar	4	Fair. Indirect evidence. Results were

	Medical Journal. 1983;76(7):870-872	the effects of various first aid agents on nematocyst discharge of the sea nettle (*Chrysaora quinquecirrha*) and Portuguese man-of-war (*Physalia physalis*) tentacles	Bactine, lidocaine, Witch Hazel, Arm and Hammer Baking Soda, Campho Phenique, Cream Corn Starch, Regina Red Wine Vinegar, Right Guard deodorant, acetone, 20% aluminum chloride, glycerol, 33% and 100% ethanol, 70% isopropyl alcohol, sodium hydroxide, magnesium chloride, 0.1% and 1.0 % papain, and formalin 4% and 40%.			the sea nettle tentacles, acetone, Clorox and ammonia caused nematocyst discharge. Stingose, Adolph's meat tenderizer and papain inhibited nematocyst discharge. Baking soda prevented nematocyst discharge induced by vinegar or ammonia. Magnesium chloride did not inhibit chemically stimulated nematocysts. In regards to Portuguese man-of-war tentacles,	may induce nematocyst discharge in *Chysaora quinquecirrha* stings, but may reduce nematocyst discharge in physalia physalia stings.		poorly described.

						Clorox and 0.1N sodium hydroxide resulted in nematocyst discharge. Vinegar appeared to be the best solution to block nematocyst discharge by either Clorox or sodium hydroxide			
Ping J, Onizuka N.	Epidemiology of jellyfish stings presented to an American urban emergency department. Hawaii Med J. 2011 Oct;70(10):217-9.	Epidemiologic study that provides evidence for the types of jellyfish envenomations seen in Hawaii.						5	

<u>Additional References (Background, Epidemiology):</u>

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Level of Evidence	**Definitions (See manuscript for full details)**
Level 1a	**Experimental and Population based studies** - population based, randomized prospective studies or meta-analyses of multiple higher evidence studies with substantial effects
Level 1b	**Smaller Experimental and Epidemiological studies** - Large non-population based epidemiological studies or randomized prospective studies with smaller or less significant effects
Level 2a	**Prospective Observational Analytical** - Controlled, non-randomized, cohort studies
Level 2b	**Retrospective/Historical Observational Analytical** - non-randomized, cohort or case-control studies
Level 3a	**Large Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 3b	**Small Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 4	**Animal studies or mechanical model studies**
Level 5	**Peer-reviewed Articles** - state of the art articles, review articles, organizational statements or guidelines, editorials, or consensus statements

Level 6	**<u>Non-peer reviewed published opinions -</u>** such as textbook statements, official organizational publications, guidelines and policy statements which are not peer reviewed and consensus statements
Level 7	**<u>Rational conjecture</u>** (common sense); common practices accepted before evidence-based guidelines
Level 1-6E	**<u>Extrapolations</u>** from existing data collected for other purposes, theoretical analyses which is on-point with question being asked. Modifier E applied because extrapolated but ranked based on type of study.