Unusual Cnidarian Envenomations

37

Özgür Deniz Tezcan

Abstract

This chapter is a collection of unusual cnidarian envenomations. Cnidarian envenomations are common all around the world. According to the World Register of Marine Species database, there are 10,762 accepted cnidarian species and about 100 of these are considered harmful to humans. There is a great diversity of cnidarian envenomations. At one end of the spectum, there are serious envenomations, such as that of *Chironex fleckeri*, which can kill a man in minutes; while at the other end, there are minor conditions, such as an annoying itch. While the more serious or frequent envenomations are well-studied, others are rarely reported and poorly studied. Only a fraction of cnidarian toxins have been identified and throughly investigated. Rare cnidarian envenomations, such as fulminant hepatitis, autonomous nervous system dysfunction, or stroke are not only interesting, but they also provide a wider perspective to cnidarian toxicology. Here, there is a total of 65 cases. The cases are grouped according to the clinical outcomes and underlying physiopathology. To facilitate our understanding of these unusual and sometimes bizarre envenomations, some physiopathological data is also included with each group.

Keywords

Unusual cnidaria envenomation • Seastroke • Guillan-Barre • Neuropathy • Mononeuritis multiplex • Autonomic neuropathy • Priapizm • Dysphonia • Amnesia • Myocardial infarction • Tako-tsubo • Renal failure • Fulminant hepatitis • Mondor's disease • Palytoxin • Anaphylaxis • Dermographism

37.1 Introduction

Cnidaria is one of the oldest animal phylums. They have existed since the Cambrian period (541 million years ago). The *sine qua non* of cnidaria is the toxic organelle, nematocyst. Nematocyst is one of the most complex intracellular secretion products. The diversity of cnidarian toxins is immense. The venom encapsulated in the nematocyst is a complex mixture of polypeptides, proteins, purines, quaternary ammonium compounds, biogenic amines, and betaines. These toxins may induce necrotic, hemolytic, neurotoxic, cardiotoxic, nephrotoxic, hepatotoxic reactions, or hypersensitivity reactions (type I or type IV). On the cellular level, cnidarian toxins act through three basic mechanisms: pore formation, sodium channels, and potassium channels. Their action on calcium channels is controversial.

Observations suggest that overfishing, eutrophication, climate change, translocations, and habitat modifications will cause more frequent jellyfish blooms. Cnidarian toxins are considered to be a rich source for the development of new drugs or biomedical materials. The risk of more severe jellyfish blooms and hopes for new drug discoveries are the main motives underlying the growth of interest in cnidarian toxins.

Even today, the area of cnidarian toxicology may still be defined as *terra incognita*. In the conclusion of her detailed

Ö.D. Tezcan (✉)
Koç University Hospital, Davutpaşa Caddesi No:4 Topkapı, 34010 Istanbul, Turkey
e-mail: otezcan@kuh.ku.edu.tr

S. Goffredo, Z. Dubinsky (eds.), *The Cnidaria, Past, Present and Future*, DOI 10.1007/978-3-319-31305-4_37

review, Frazao et al. (2012) states, "*the venom from each species of cnidarians is supposed to contain around 100 compounds, but not more than 1 % is currently known even in the better studied species*". There are many reasons for this.

Cnidarian toxicology is not an easy area to study. For the clinician, it is hard to identify an envenomation which has happened underwater. Most of the victims don't even see the responsible organism. Only a fraction of the victims seek medical advice, and even the most interesting cases are rarely reported. The work of the toxicologist is even harder, and the difficulties begin with specimen collection. Laborious venom extraction, instability and inconsistency of the toxins, variation of the toxin composition of an organism's venom in different stages of its life cycle, and the difference between the toxin composition of the same species in different geographic localisations adds to this difficulty.

37.2 Neurotoxicity

The rapid paralysis of prey is vital for fragile, slow moving cnidaria. This makes neurotoxins the most important component of the venom. Neurotoxins act on voltage-gated ion channels, which are critical to normal neuromuscular transmission. Disruption of the voltage-gated ion channels can lead to rapid paralysis, which is why they are excellent targets for venomous organisms. In humans, cnidarian neurotoxins may cause direct toxicity (local or systemic), autonomic nervous system dysfunctions, or immune-mediated neuropathies.

37.2.1 Seastroke

Meyer (1993) reported three previously healthy young male patients who suffered brain stem infarction while swimming off the southeastern North Carolina coastline between the years 1990 and 1992. He called the condition "seastroke". These cases are unique, as none had a predisposing factor for a stroke, and the only probable offender was an unidentified neurotoxin.

The first case was a 15-year-old boy. After swimming in the ocean for 30–45 min, he experienced severe dizziness. He complained of a sting, feeling strange, and a mild headache. He began to laugh, cry and moan, and started sweating profusely. He experienced seizure-type activity, and lapsed in and out of consciousness. Initial cranial computerized tomography (CT) and cerebrospinal fluid examination, cervical spine films, electroencephalography and bloodwork were all normal. The drug screen was negative. Brain magnetic resonance imaging (MRI) showed a hyper-intensive spot within the central pontine region. The cerebral arteries which supply the area were all open. The patient remained intellectually unimpaired. In retrospect, the patient definitely remembered stepping on something in the sea 30–45 min before the onset of the symptoms. With his own words, it was "sort of rough and prickly; I wouldn't have remembered it, but it surprised me and caused an eerie feeling."

The second case was a 13-year-old boy who was playing in the shallow surf off Topsail Beach. He told his brother that something had stung him on the arm. He left the water and, approximately 30 min later, he was found by his father: alert but unable to move, paralyzed from the neck down. CT, lumbar puncture, cerebral arteriogram, roentgenograms of chest and cervical spine, and echocardiogram were normal. Three days later, he was transferred to a university center. Brain MRI showed "evidence of edema and abnormal enhancement within the cervical cord and lower medulla, consistent with myelitis. Infraction could not be excluded." After 9 weeks hospitalization, the patient was still ventilator dependent. He was transferred to a spinal rehabilitation center.

The third case was a 39-year-old man. While swimming off Wrightsville Beach, he experienced a sudden onset of severe dizziness and imbalance. His wife reported that he staggered out of the water, vomited, nearly passed out, and complained of severe dizziness. The patient was observed in the emergency department for 5 h. CT, lumbar puncture, and bloodwork were normal. As soon as he was well enough to walk on his own, he was discharged. Two days later, he experienced swallowing difficulty. A barium swallow study showed an inappropriate swallowing mechanism and poor motor function. MRI showed an abnormal signal in the inferior and posterior aspect of each cerebellar hemisphere extending on the left, involving the inferior lateral aspect of the medulla, suggesting ischemic infarcts. In retrospect, the patient remembered stepping on an object in the ocean that he describes "like seaweed; it was very quick, like when you get bit by a crab, but it didn't hurt, it didn't faze me." His symptoms came on within minutes of stepping on the object.

There is no information on whether any investigation was conducted to identify the causative organism in the area.

37.2.2 Peripheric Neuropathies

Cnidaria may induce peripheric neuropathies in three ways: autoimmune mechanism, direct toxicity, and indirect injury. Cnidarian toxins may trigger a cascade of immune reactions, which may end up as an autoimmune disorder, such as Guillain-Barre syndrome or mononeuritis multiplex. Direct toxicity is caused by the damage of a cnidarian toxin on a nerve underlying a sting site. Indirect injury is caused by mechanical factors, such as edema or inflammation, in the adjacent tissues caused by the sting.

37.2.2.1 Guillain-Barre

Guillain-Barre syndrome is an autoimmune disease which causes ascending polyneuropathy. The main symptom is muscle weakness, starting in the feet and hands, and progressing towards the trunk. Some subtypes can also affect sensation or pain. Guillain-Barre syndrome is usually triggered by an infection. The autoimmune process damages the myelin sheets of peripheral nerves leading to the blockage of signal transmission.

Pang and Schwartz (1993) reported a 39-year-old man who had multiple jellyfish stings over both legs on the north coast of Majorca. The victim described the jellyfish as red, palm-sized, and translucent.

One week later, a tingling sensation started in both heels. The following week, the tingling spread to his hands and he developed mild proximal muscle weakness in all limbs. He was unable to work as a van driver. Over the next 2 months, there was a general improvement in his symptoms. He had minimal proximal muscle weakness in the legs and mildly diminished sensation to light touch in a glove-and-stocking distribution. He also had an unsteady gait. All tendon reflexes were absent, except for a barely elicitable left knee jerk. Position and vibration sense were intact. Nerve conduction studies showed a prominent demyelinating neuropathy with conduction block.

The second case was reported by Devere (2011). The victim was a 66 year old woman who was stung by a jellyfish while swimming in the Atlantic Ocean off Charleston, South Carolina. She felt a stinging sensation on her right thigh and she saw a jellyfish in the water. A red rash arose in the same area. The sting and rash improved in 4 days.

Ten days after the sting, she developed severe low back pain radiating to the right thigh. In 24 h, progressive numbness, muscle weakness, burning and tingling pain began in all extremities. Her neuromuscular symptoms peaked 1 month after the onset. In her neurological examination: muscle strength in biceps, triceps, wrist extensors, finger flexors, quadriceps, and distal leg muscles were reduced to 3/5 (Medical Research Council scale); reflexes were absent; and she had hyperesthesia and decreased vibration/position senses in a glove-and-stocking distribution. Hip and shoulder muscles were normal. The nerve conduction studies 4 months after onset revealed sensory motor polyneuropathy compatible with demyelination.

Ten months after onset, the muscle strength, position and vibration senses were normal, and nerve conduction studies proved that there was continued improvement. After 4 years, her neurologist contacted her and heard that she was fine, and the only thing left was minimal numbness in the first two fingers of both hands and middle toes of both feet.

37.2.2.2 Mononeuritis Multiplex

Mononeuritis multiplex is a painful asymmetric peripheral neuropathy in at least two separate nerve areas. One of the mononeuritis multiplex cases was reported by Filling-Katz (1984). The patient was a 25-year-old man who was stung by a jellyfish across the right forearm off the coast of Norfolk, Virginia. At the time of injury, Physalia and Cyanea species were present in the region. Erythematous wheals developed immediately, and "purple blotches" developed progressively at the site of contact. Next morning, he woke up with weakness and numbness in the right hand and wrist, nausea, vomiting, generalized myalgias, sore throat, and low grade fever. While the weakness in his right hand started improving after a week, he noticed acute diffuse weakness, this time in his left hand and arm and a feeling of numbness extending to his elbow. His neurologic examination of the right and left upper extremity showed sensory and motor dysfunctions. The electromyography showed denervation at the right radial and left radial, ulnar, axillary nerves. The patient improved slowly and the electromyography made 2.5 months later showed re-innervation of the muscles.

There are other cases reported by Burnett et al. (1994). The first case was an experienced underwater photographer who lay on a corallimorpharia while photographing reef fish. Although he was wearing a thick lycra "skin suit", he realised a non-painful irritation on his left arm and knee. Shortly after his second dive, he observed itchy papillo-erythematous lesions over his left knee, elbow, and shoulder. That evening, muscle weakness developed in his left arm. Two days later, he woke up from his night sleep with back pain which worsened with movement. His left arm was noticeably weak. The paresthesia on his arm developed during sleep, but dispersed on walking and moving the arm. Six weeks later, he returned to normal vigorous diving activity, slept normally, and had full arm movement. Twelve weeks later, he recovered completely.

The second case was a healthy 20-year-old woman who was stung by an undefined jellyfish on her right arm and hand. She felt instant pain and came to the shore to receive first aid. Her arm swelled up immediately, and she had extreme pain at the sting site. She felt shortness of breath. Over the next few hours, she noticed numbness, paresthesia, and cooling of the distal right arm together with nausea and faintness. She developed pain on her trunk and became agitated. Pain, paresthesia, coolness, numbness and muscular weakness progressed. The neurological examination after 5 weeks showed considerable weakness in the dorsiflexors of the right hand and arm, profound weakness of the opponens pollicis muscle, and mild weakness in the interossei muscles and decreased sensation in the right median and radial nerve distribution areas. Over the next 4 months, the patient's condition improved spontaneously without residual damage.

Another case was reported from southern Florida, by Moats (1992). A 52-year-old woman touched a fire coral (*Millepora sp*.) with her right wrist. She experienced a local burning sensation for 2–3 days followed by general weakness and high fever (39 °C). In 6 weeks, she developed weakness and difficulty moving her right shoulder and arm. Winging of the right scapula was detected, and electromyography showed delayed latency of the right long thoracic nerve. After 8 months, the symptoms disappeared with a physical therapy programe.

37.2.2.3 Acute Peripheric Neuropathy

Peel and Kandler (1990) reported an 18-year-old female who was stung on her right wrist off the coast of Penang. An urticarial rash developed immediately and it was followed by painful swelling of the forearm. She noticed progressive numbness and difficulty in moving her fingers. By the third day, there was little active movement of the fingers, accompanied by complete anesthesia distal to the wrist. Nerve conduction studies carried out in Singapore showed that sensory action potentials could not be recorded from the ulnar, median or radial nerves. When the patient returned to England 2 weeks later, there was no clinical improvement. The findings implied a combination of degeneration and conduction block. Ten months after the sting, she had made a complete clinical recovery, apart from minimal sensory loss.

The second case was reported by Laing and Harrison (1991). A 21-year-old British student, who was on a hockey tour in Thailand, was stung by *C. fleckeri* on his back and right arm. On return to the shore, he developed wheezing and generalized edema. He was treated in the local hospital for anaphylaxis. After some days, his systemic illness improved, but he was left with right ulnar nerve palsy. His examination showed incomplete autonomous, sensory and motor weakness in the ulnar nerve distribution. Surgical exploration of the elbow was carried out to rule out a possible compression. The surgeons observed that the ulnar nerve was free in the ulnar tunnel, but the nerve was edematous and the adjacent muscles were ischemic.

There are two possible explanations for this case. Although the first explanation for this case is direct damage of *C. Fleckeri* toxins on the ulnar nerve segment, a second explanation could be derived from the surgeon's observation of "adjacent muscle ischaemia". It is known that cnidarian toxins may induce local vascular spasms. A local ischemic event may well damage the nerves crossing through the affected area.

37.2.3 Autonomic Nervous System Toxicity

The autonomic nervous system controls the visceral functions (digestion, perspiration, respiratory rate, heart rate, blood pressure, urination, etc.), unconsciously and involuntarily. It is diffused throughout the body with many interconnected centers and ganglions. The system keeps its balance with the help of two counteracting mechanisms: the sympathetic nervous system and the parasympathetic nervous system. While the sympathetic nervous system is responsible for the "*fight or flight*" response, the parasympathetic nervous system is responsible for the "*feed and breed*" and "*rest and digest*" responses.

37.2.3.1 Parasympathetic Dysautonomia

A reversible dysautonomia case after a *Chironex fleckeri* sting was reported by Chand and Selliah (1984). The victim was a 52-year-old fisherman who presented with acute abdominal distension and urinary retention. He was stung by a large (0.3 m wide, 1 m long), white-colored jellyfish while wading in the sea. He felt a sudden pain in both of his thighs. In a few minutes, he developed dyspnea, cough, wheezing, palpitations, and profuse lacrimation that lasted 30 min. Two hours later, his abdomen started bloating and he could not pass urine. Physical examination of the patient revealed linear purple vesicular sting marks on both thighs, abdominal distension, and urinary bladder distension 4 cm above the pubic bone. Direct x-ray of the abdomen showed gas distension in the large intestine. Bladder function returned to normal after 2 days and he improved enough to take oral food after 4 days. He lost nocturnal erection for a week after the sting. He recovered totally in the space of a week.

37.2.3.2 Urinary Incontinence and Biliary Dyskinesia

Burnett (2006) reported a 16-year-old girl who was stung on her abdomen by Chrysaora fuscescens while surfing. She developed biliary dyskinesia and urinary incontinence. The morning after the jellyfish contact, she started to complain of a burning sensation and cramps in the right upper quadrant. Eating exacerbated the symptoms. Tests revealed a healthy liver and a non-functioning gallbladder. The second main complaint was urinary incontinence. Urological examination showed inhibited detrusor contractions with urge incontinence.

The abdominal pains persisted. Ten weeks later, the gallbladder had to be removed surgically. The intraoperative cholangiogram documented rapid free flow of bile into the duodenum. The pathological examination of the gallbladder was compatible with biliary dyskinesia. After the operation, the abdominal pain resolved completely. The urinary incontinence resolved with the help of remedial bladder exercises.

Although there are some case reports concerning autonomic dysfunctions after cnidarian envenomations, this case is especially interesting, because two completely different organs, conducted by different parts of the autonomic nervous system, were affected.

37.2.3.3 Ileus

Digestion, (from regulation of the peristaltic movements, to the secretion of the digestive enzymes) is controlled by the enteric nervous system. Although the enteric nervous system can operate independently, it receives innervation from the parasympathetic and sympathetic nervous systems. Ileus is a condition when the gastrointestinal passage stops, either because of mechanical (stricture or occlusion) or neurological (paralytic) causes. Paralytic ileus is the loss of normal propulsive ability of the gastrointestinal tract (peristalsis) which causes bloating, abdominal pain, and vomiting.

A 31-year-old man from Medan, Sumatra, with paralytic ileus was reported by Ponampalam (2002). The patient picked up and handled a large jelly like mass while he was on a beach. While handling the mass, he felt a sharp pain in his left forearm. He noticed a linear urticarial lesion in that area. Within half an hour, he started to feel general weakness, joint pains, and lethargy. Abdominal distension followed shortly after. When he was admitted into Singapore General Hospital, 24 h after the incident, he had a distended abdomen, vomiting, and no bowel sounds. "Paralytic ileus", was diagnosed. Blood chemistry and abdominal radiography confirmed the diagnosis. He received conservative, supportive treatment and the intestines gained normal function after 4 days without any complication. Another case from India was reported by Das et al. (2002).

Some of the cnidarian toxins which affect intestinal motility are caissarone, reported by Cooper et al. (1995), pCrTX from the jellyfish *Carybdea rastonii*, reported by Nagase et al. (1987), and toxin II from *Anemonia sulcata* reported by Tazieff-Dapierre et al. (1977).

37.2.3.4 Priapism

Priapism is a medical condition characterized by erection of the penis and not returning to the flaccid state for more than 4 h, despite the absence of physical or psychological stimulation. Vascular, endocrine, and neurological factors may mediate priapism. Penile tumescence is determined by the balance between mediators of contraction (by norepinephrine) and relaxation (by nitric oxide, vasoactive intestinal peptide, and prostanoids) of the corpus cavernosum's vascular smooth muscles. Fenner and Carney (1999) and Nickson et al. (2009) reported cases of priapism caused by Irukandji syndrome.

Nickson et al. (2010) suggests that priapism caused by C. barnesi envenomation could be mediated by a neural sodium channel activator that releases nitric oxide.

37.2.3.5 Blurred Vision

Burnett and Burnett (1990) reported a 17-year-old patient who was stung on the knee by *Linuche unguiculata* in Nassau, The Bahamas. Three hours after the sting she developed nausea, dizziness, sweating, faintness, and feeling very hot in a cool room. At the same time, she realized that she could not focus on distant objects. She said, "Everything looked grey and blurred". The blurred vision continued for 8 days.

Accomodation reflex which maintains focusing on near or distant objects is controlled by the parasympathetic nervous system. Although most of the patient's symptoms can be attributable to systemic autonomic nervous system toxicity, the long-lasting and prominent symptom was confined to the eye, which was far away from the sting site.

37.2.4 Other Neurological Disorders

37.2.4.1 Dysphonia

Burnett (2005) reported a dysphonia case from Ft Lauderdale, Florida. The patient, who was a fit 20-year-old man, felt a sudden stinging irritation in his mouth after swimming through a swarm of small Physalia physalis medusae. When he returned to the companion boat, he realized he could not talk properly. He could make sounds and mumble, but no words. This lasted 30–45 min. While standing on the boat, he noticed a stinging, linear, papular eruption on his left pectoral and anterior deltoid areas. The condition was interpreted as toxin-induced paralysis of tongue muscles and lingual nerves.

Burnett et al. (1996) mention three other patients who had temporary loss of voice in their renowned book, *Venomous and Poisonous Marine Animals*. The patients were stung by unidentified jellyfish in the waters off Hua Hin, near Bangkok. Two weeks after being stung, two Thai and one American scuba diver developed aphonia for 3–4 days.

An explanation for these cases could be a super selective neurotoxin affecting a specific ion channel which is only found at the neuromuscular junction of the laryngeal muscles. A similar mechanism could also explain the biliary dyskinesia with urinary incontinence case and the blurred vision case. Until such toxins and ion channels are demonstrated, these cases will retain their mystery.

37.2.4.2 Coma and Death

Rhodactis howesii, a sea anemone-like corallimorph, is known to be cooked and eaten by the Samoans without any health hazard. But when eaten raw, it is known to cause fatal envenomations. Martin (1960) described this unusual envenomation from Pago Pago, capital of American Samoa. The envenomations started shortly after ingestion, with stupor that lasted 8–36 h. During this period, knee jerk and pupillary light reflexes were absent, but blood pressure and pulse rate stayed normal. After this period, patients went into a prolonged shock and eventually died of pulmonary edema.

37.2.4.3 Memory Impairment

Williamson et al. (1996) described a 49-year-old healthy man who had temporary memory impairment after contact with anemones. While he was collecting mussels from Hokimai Bay, Kawau Island, New Zealand, his chest came into contact with numerous small anemones. Within minutes, he developed a painful rash, swelling, and burning on his chest. He felt dizzy, weak, and hot. In the next 24 h, hemorrhagic vesicles erupted on his chest, and over the following days, he could not sleep or concentrate, and he felt dizzy and nauseated. For 4 weeks, he had memory impairment and muscle incoordination that restrained him from his professional work.

37.3 Cardiovascular Disorders

37.3.1 Cardiac Complications

37.3.1.1 Myocardial Infarction

Salam et al. (2003) reported a 45-year-old professional diver who developed myocardial infarction shortly after a jellyfish sting. The patient was stung by an unidentified jellyfish in the Gulf Sea, Qatar. Four hours after the contact, he started to feel chest pain. Twenty-two hours after contact, the patient presented to the hospital, distressed, diaphoretic and in pain. He was mildly hyperthermic (37 °C), tachypneic (20/min), and he had an erythematous area (10×5 cm) on his left forearm (site of contact). The electrocardiogram (ECG) and blood chemistry results suggested an acute myocardial infarction. The patient received routine thrombolytic and supportive treatment in the coronary care unit. The coronary angiography, which was made on the fourth day of his treatment, showed normal coronary arteries and hypokinetic right ventricle. The conclusion of the authors was a toxin-induced coronary vasoconstriction.

Konya and Elliott (1996) showed that the toxin from anemone *Tealia felina* produced marked reduction in the coronary flow (82 %) in the rat heart. Their findings showed that the toxin had a marked and irreversible constrictor action on coronary circulation. Elliott and Konya (1984) had previously shown that the venom extract was a potent vasoconstrictor of the isolated mesenteric artery. Lee et al. (1985) showed that equinatoxin, from *Actinia equina*, also produced coronary vasoconstriction.

37.3.1.2 Tako-Tsubo Cardiomyopathy

Tako-tsubo cardiomyopathy takes its name from a Japanese octopus fishing-pot, "takotsubo". It is characterized by acute chest pain, electrocardiographic changes which mimic an acute myocardial infarction, ballooning of the apical left ventricle, and absence of significant stenosis on the coronary arteries. It is known to be triggered by severe psychological stress and catecholamine discharge (Akashi et al. 2008).

Bianchi et al. (2011) reported the case of a patient who developed Takotsubo cardiomyopathy after a *Pelagia noctiluca sting*. The patient was a 53-year-old woman, swimming off the Calabrian coast of Italy, who was stung on her right forearm. She rushed to the shore and lost consciousness due to pulseless electrical activity. The lifeguard resuscitated her successfully. When the patient arrived at the emergency room, she had chest pain and the ECG showed signs of acute myocardial infarction. Echocardiogram showed apical akinesia with severe left ventricular dysfunction. She received thrombolytic treatment.

After successful thrombolysis, the chest pain and the ECG signs should improve. In this woman's case, none of these happened, as a result, an urgent coronary angiography was performed. The coronary angiography showed that there was no stenosis in the coronary arteries, but ejection fraction was low, and there was an aneurism in the left ventricle. She received supportive treatment. After 7 days, she was discharged from the hospital with improved EF and completely asymptomatic.

A similar case was reported from the far north of Queensland, Australia, by Tiong (2009). The 26-year-old diver was admitted to a local hospital following a jellyfish sting on his body. The description of the jellyfish was similar to that of Carukia barnesi. On admission to hospital, he developed symptoms consistent with Irukandji syndrome (pain, restlessness, agitation, palpitation). His serial ECGs revealed persistent generalized hyper-acute T waves. His Troponin I peaked at 5.5 μg 14 h after the sting. The serial echocardiograms showed mid-ballooning stress cardiomyopathy with poor mid-regional wall motions. The apex was spared. No invasive cardiac investigation was performed. This was the first documented case of mid-ventricular stress cardiomyopathy induced by jellyfish sting.

37.3.1.3 Heart Muscle Injury

Troponin I is used as a highly specific diagnostic marker for myocardial infarction and heart muscle death. Raised levels indicate cardiac muscle damage. In the medical literature, there are few reports of elevated troponin levels after jellyfish stings.

McD Taylor et al. (2002) reported a case with persistent cardiovascular symptoms and raised troponin levels after an unknown jellyfish sting. The 34-year-old female tourist was stung while snorkeling in 12 m of water on the outer portion of the Great Barrier Reef in North Queensland in April 2000. Shortly after seeing a jellyfish, she experienced intense burning pain in the right arm, leg, and flank, followed by dysphoria, anxiety, stomach cramps, vomiting, chest pain, dyspnea, and hyperventilation. When the patient arrived at

the hospital 3.5 h after the sting, her ECG showed non-specific T wave flattening and her cardiac troponin I level was high (12.4 μg/L). The echocardiogram was normal. Three days after the sting, the patient was transferred to a hospital in Melbourne with continuing symptoms. Troponin I elevation persisted for 2 weeks. The patient was discharged from the hospital still symptomatic with breathlessness, chest tightness, weakness, and fatigue, but over 5 months there was gradual improvement of symptoms. The most persistent symptoms were occasional chest pains and anxiety which remained for 17 months post-sting.

Little et al. (2001) reported another case in which the patient came into contact with an unidentified jellyfish off the Great Barrier Reef. The patient had initially normal troponin I levels (3.5 h post-sting) which peaked to 72 mg/L within the next 10 days. The patient developed left ventricular dysfunction and reduced ejection fraction 6 h after the sting.

37.3.2 Vascular Complications

Cnidarian envenomations may cause vascular complications. El Khatib and Al Basti (2000) reported a case who had ischaemia in her hand after a jellyfish sting in the Gulf Sea. The 15-year-old girl got stung by an unidentified jellyfish. She presented a few hours after the incident with skin eruption and erythema on the dorsum of her left hand. The index and middle fingers were swollen, cold, and cyanosed. The patient complained of numbness, pain, and itching in the area. Eighteen hours later, despite the anticoagulant and steroid treatments, the symptoms got worse. Surgical treatment was planned and fasciotomies were performed on the mid-ulnar and mid-radial aspects of the index and middle fingers. An immediate relief of ischemia was observed during the surgery.

Wiliamson et al. (1988) reported three jellyfish envenomation cases which caused impaired circulation of the stung limb from the Indian Ocean and the Andaman Sea. Distal arterial pulses were absent and there was regional cyanosis, suggesting the threat of distal gangrene. None of the patients had a previous history of vascular disease. Two patients underwent surgical fasciotomy, and surgical exploration was performed in one patient. The affected arterial segment appeared to be under the actual sting site. One of the patients was seriously and permanently handicapped with bilateral upper limb numbness and paresis, one had permanent sensory loss, while the third made an uneventful recovery.

37.3.2.1 Irukandji-Like Syndrome

Irukandji syndrome is characterized by abdominal pain, backache, vomiting, neuralgia, delayed systemic effects, and, cardiotoxicity. It is caused by *Carukia barnesi*. The envenomation sets of cathecolamine-like effects, ECG changes, troponin I elevation, hypertensive crisis, systolic dysfunction, or segmental hypokinesis of myocardium, and pulmonary edema. In Huynh et al.'s (2003) series, 22 % of the patients had evidence of myocardial injury.

The classical Irukandji syndrome is caused by Carukia barnesi; however, some cases with a similar clinical profile were reported from different locations. This entity is named as "Irukandji-like syndrome". Little et al. (2006) reported *Alatina nr mordens*, *Malo maxina*, *Carybdea alata* and *Carybdea xaymacana* as other cubozoan jellyfish which can cause this complex syndrome.

Grady and Burnett (2003) reported three US military combat divers who suffered from Irukandji-like syndrome during their diving exercises in Fleming Bay, off Key West, Florida. All cadets were in excellent physical condition before their dives. Envenomations happened during night dives in shallow water (10 ft). The patients experienced a stinging sensation, which was followed by extreme pain and spasm in the lower back. About 20 min later, cough and dyspnea started. They received basic first aid with 5 % acetic acid, according to the first aid instructions of the navy. They were found to be mildly hypertensive and tachycardic. Two of the patients experienced headache, cough, salivation, lacrimation, abdominal cramping, nausea, vomiting, anxiety, restlessness and severe muscle pain, and cramps in major muscle groups. One of the patient's blood chemistry revealed mild myoglobinemia and raised cardiac enzymes. The third patient's symptoms were less severe. Most symptoms resolved after 4 h with supportive, symptomatic treatment. This was the first report of Irukandji-like syndrome from US coastal waters.

37.3.2.2 Fatal Irukandji Syndrome

The first death from Irukandji syndrome was reported by Fenner and Hadok (2002). The victim was a 58-year-old tourist from the UK who was stung on the face and chest soon after he entered shallow water at a beach on Hamilton Island, Queensland, Australia. He did not see the creature, but he said, "something has got me," to his wife. Over 20 min, he developed muscle pains, cramps, sweating, anxiety, and nausea. He presented to the resort doctor. He was hypertensive (260/160) and tachycardic (142/min). Forty-five minutes after the sting, his condition suddenly deteriorated and he became unresponsive. A provisional diagnosis of cerebrovascular accident was made and an urgent transfer to a mainland hospital was requested. When the medical flight team arrived, the patient was unconscious with fixed dilated pupils. When he arrived at Mackay Base Hospital, brain CT showed an 8×5×7 cm hemorrhage centered on the basal ganglia, causing 1 cm midline shift. The hemorrhage was not considered salvageable by the neurosurgeon. The next day, the patient's pupils remained fixed and dilated, and brain death was confirmed.

37.4 Other Unusual Envenomations

37.4.1 Renal Complications

37.4.1.1 Acute Renal Failure

Guess et al. (1982) reported a Portuguese mano'war sting which caused acute renal failure in a 4-year-old girl. The envenomation caused a hemolytic reaction which led to the renal injury. In the same year, a similar case was reported by Spielman et al. (1982). Deekajorndech et al. (2004) reported a 7-year-old boy who developed acute renal failure following a jellyfish sting. The patient came into contact with the unidentified jellyfish at the Pattaya Beach, Thailand, 3 days before hospitalization. He developed hemoglobinuria and the renal biopsy revealed acute tubular necrosis.

Mizuno et al. (2000) reported an acute renal failure case after contact with the anemone, *Phyllodiscus semoni*. The 27-year-old man accidentally touched the anemone with his right arm while snorkeling in the Sulu Sea around Cebu Island. When the patient was admitted to the hospital, he had severe dermatitis on his right arm and signs of acute renal failure. The renal failure improved with supportive treatment. The renal biopsy revealed acute tubular necrosis.

P. semoni is found in the Western Pacific ocean. It is known as the "sea wasp anemone" in Japan. It is known to induce severe dermatitis. Nagai et al. (2002) identified three different toxins (PsTX-20A, PsTX-60A and PsTX60B) in the venom of *P. semoni*. Mizuno and colleagues identified another toxin (PsTx115), and carried on searching for the toxin which induced renal failure. They showed that the toxin bound directly to the glomeruli and induced endothelial injury in the glomeruli extending into the glomerular epithelial cells. The reaction was an acute thrombotic microangiopathy with complement activation and decreased membrane complement regulatory protein expression in rat glomeruli (Mizuno et al. 2007, 2012). Mizuno and colleagues' studies started with an unusual envenomation case and extended to the identification of the causative toxin and the nephrotoxicity mechanism. Their work deserves admiration.

37.4.1.2 Nephrotic Syndrome

Prasad et al. (2006) reported a 45-year-old woman who developed nephrotic syndrome after contact with *Milepora sp*. The renal biopsy showed minimal change disease.

37.4.2 Hepatic Complications

A fatal hepatotoxicity after contact with an anemone was reported by Garcia et al. (1994). The 28-year-old diver touched an anemone while free-diving in 6–10 m deep waters of St. Thomas, Virgin Islands. Ten to fifteen minutes after the contact, vesicular eruption and severe pain developed on his back and arms. He was admitted to a local hospital and followed for 24 h. After discharge he became progressively weak and lethargic. He was admitted to the hospital again, this time with jaundice and elevated liver enzymes. His condition deteriorated and after 5 days, he was intubated and transferred to Jackson Memorial Hospital in Miami, Florida. Four days after the transfer, he received liver and kidney transplants. His liver biopsy showed massive necrosis with peripheral lobular regeneration. The kidneys showed mild tubular necrosis. The patient's dive partner identified an anemone from *Condylactis sp*. The patient's serum was positive in 1:450 dilution against *Condylactis sp*.

Burnett (1992) reported another case from Florida who had elevated liver enzymes for 16 days after a presumed cnidarian sting. The serum of this patient was tested for *Condylactis sp*. antigens and found them to be similar to the other patient.

There are a number of studies which demonstrated the hepatotoxic effects of cnidarian toxins. Muhvick et al. (1991) encountered hepatic injury in rats injected by *Chrysaora quinquecirrha* venom while studying the effects of two antidotes (hyperbaric oxygen and verapamil). Wang et al. (2013) injected *Cyanea capillata* tentacle extracts into the rats and demonstrated destruction in the lobular structure, severe coagulation necrosis, extensive hemorrhage in the liver, as well as a dose-dependent increase of the liver enzymes. Ramkumar et al. (2012) observed occlusion of central veins with hemolyzed blood and vacuolation with pleomorphic nuclear material in the liver of mice which were injected with *Anthopleura asiatica* venom intraperitoneally. Houck et al. (1996) investigated the toxicity of *Chrysaora quinquecirrha* venom on cultured liver cells of rats and found that the hepatotoxin acted through Ca channels and that there was a large inter-animal variability. They also found that the hepatocytes cultured from old rats were more vulnerable to toxicity.

Some of the cnidarian hepatotoxicities could be related to complement activation. Ishikawa et al. (2004), who worked with *Chrysaora quinquecirrha* venom, found that the venom could induce complement activation, suggesting a role of complement activation in the tissue damage secondary to jellyfish stings.

37.4.3 Others

37.4.3.1 Gastrointestinal Bleeding

Fenner et al. (2010) reported a 40-year-old British diver who felt a sharp pain on the back of his head while ascending from a recreational dive near Pattaya in 2008. The burning

pain was very severe. On the boat, he developed nausea and started vomiting. He had abdominal cramps, shivering, headache, dizziness, chest tightness, and dyspnea. For a short while he fell unconscious. Three hours after the sting, the patient arrived at the hospital. He was hypertensive and still had abdominal cramps. After 18 h, he was discharged from the hospital with partial resolution of symptoms. Four hours after discharge, his abdominal cramps relapsed and he started vomiting blood. He returned to the hospital and his complaints settled with spasmolytic, anti-emetic, narcotic analgesic, and proton pump inhibitor treatments.

37.4.3.2 Pancreatitis and Pneumonia

Nickson et al. (2009) mention a 10-year-old girl who experienced pancreatitis, pneumonia, and ileus after jellyfish contact. There is not much detail except she was hospitalized for 11 days.

37.4.3.3 Mondor's Disease

Mondor's disease is a rare condition which causes superficial venous thrombophlebitis of the breast and anterior chest wall. Although it is usually benign and self-limiting, it is rarely associated with malignancy.

Ingram et al. (1992) reported two cases who developed Mondor's disease after a jellyfish sting. The first case, who was a 30-year-old woman, had a jellyfish sting while swimming off Rottnest Island, Western Australia. One week after the sting, a palpable 5–8 cm linear indentation developed in the breast. The second case who was a 50-year-old woman presented with a palpable cord extending from the nipple to the axilla. There were some visible marks from a jellyfish sting in the area. She reported as being stung by a jellyfish a month before.

37.4.3.4 Palytoxin Related Envenomations

Not all cnidarian envenomations take place in the sea. The ocean aquariums have brought the risk of cnidarian envenomation into homes.

Palytoxin is a powerful toxin found in soft corals or dynoflagellates. According to Moore and Scheuer (1971) and Khoo (2002), it is 60 times more potent than tetrodotoxin and 113 times more potent than stonustoxin of stonefish, with an intravenous LD50 (mice) of 0.15 mcg/kg. Intoxication with palytoxin can induce myalgias, weakness, neuromuscular dysfunction, wheezing, respiratory distress, hemolysis, and cardiac conduction abnormalities. Palytoxin may also cause Haff disease, which is characterized by massive rhabdomyolysis.

The first palytoxin intoxication from an aquarium tank case was reported from Europe by Hoffman et al. (2008). The patient was a 32-year-old man who was admitted to the emergency department of the University Hospital of Heidelberg, Germany. He had cut three fingers of his right hand while cleaning his sea aquarium which inhabited some zoanthid colonies. Two hours after the cut, shivering, myalgia, and general weakness appeared in all extremities. About 16 h later, he had collapsed in his workplace, exhibiting dizziness, speech disturbance, and glassy eyes. The palytoxin assay in the zoanthid colonies in the aquarium (*Parazoanthus sp*. and *Palythoa sp*.) was positive for *Parazoanthus sp*.

Another case was reported by Snoeks and Veenstra (2012) from the Netherlands. A family got intoxicated in their house by the soft coral in their ocean aquarium. The aquarium was getting invaded by the soft corals And to get rid of the invading coral, the father poured boiling water in the tank. This produced an offensive smelling fume. The 36-year-old man, his wife, and their 10 year old twins found themselves in an emergency department with nausea, headache, shivering, a metallic taste in their mouth, severe muscle cramps, hypotension, and high fever. The symptoms started right after they inhaled the offensive smelling steam coming out of the aquarium tank.

A third paper was published in 2013, this time from New York. Sud et al. (2013) reported six cases who were intoxicated by palytoxin vapor. The first case was a 32-year-old man who was trying to clean the mucous secretions of the *Palythoa* coral by boiling water. When he arrived at the emergency department he was tachycardic (120/min), tachypneic (24/min), and he was wheezing at chest oscultation.

The other cases mentioned in the paper were from another incident. A professional fish tank cleaner, the owner of the tank, the owner's wife and two children were intoxicated by palytoxin vapour. The tank cleaner poured boiling water over *Palythoa* coral. The man who inhaled the vapor developed shortness of breath almost instantly. The tank owner who was near the tank during the cleaning procedure developed a dry cough shortly after exposure. He presented to the emergency department 8 h later, when his cough got worse and he developed chills, myalgia, and fatigue. The wife of the patient also had similar symptoms, and paresthesia in both upper extremities. Their 3-year-old boy developed a dry cough, vomiting, and extreme fatigue. Their 2-month-old baby, who had been further away from the tank, was asymptomatic and had normal findings in the emergency department.

37.5 Hypersensitivity

The physiopathological mechanisms of hypersensitivity reactions and envenomations are completely different. In the case of hypersensitivities, the complex mixture of nematocyst constituents that enter the human skin sets off a complicated system of cytokine interactions. The symptoms are not direct actions of toxins.

The key cellular mediators of hypersensitivity are keratinocytes, mast cells, tissue macrophages, and dendritic cells.

Mast cells are the most potent drivers of inflammation. According to Tibals et al. (2011), cnidarian stings may activate mast cells in three ways. Primary envenomation may activate mast cells directly by porins or secretagogues (bioactive lipids, amines) in the venom; components of the nematocyst tubule or venom may activate innate or pattern recognition receptors on mast cells; physical changes (hypoosmolarity, acidification, reactive oxygen species) at the sting site may activate mast cells.

Cnidarian stings may induce type I or type IV hypersensitivity reactions. Type I hypersensitivity reactions can range from simple urticaria to lethal anaphylaxis. In this kind of hypersensitivity, an antigen stimulate the production of specific IgE antibodies and these bind to mast cells and basophils, producing a sensitized state against the antigen. Re-exposure to the same antigen results in degranulation of active mediators like histamine, prostaglandin, and leukotriene. These mediators produce vasodilatation, smooth muscle spasm, and leucocyte extravasation; causing an acute, sometimes life threatening reaction.

Type IV (delayed) hypersensitivity reactions develop days or weeks after the sting. This is a cell mediated response. Activated CD8+ T cells destroy target cells on contact and activated macrophages produce hydrolytic enzymes.

37.5.1 Anaphylaxis

Anaphylaxis is a severe, type I hypersensitivity reaction. It is characterized by fatal edema, low blood pressure, and rash. Anaphylaxis was discovered during the studies on anemone toxins. The French biologists, Portier and Ricket (1902), were investigating the toxicity of jellyfish in the early 1900s. After demonstrating the dose-related toxicity of *Physalia physalis*, they sought to demonstrate the same phenomenon with anemones. The toxin from the anemone proved to be less potent. But when they used the same animals again, they observed that a much smaller second dose was enough to kill them. They named this phenomenon anaphylaxis; in contrast to phylaxis (protection). This accurate observation provided the first insight into type I allergic reactions and brought them a Nobel Prize in 1913.

There are few reports of anaphylaxis caused by cnidaria. One of these was reported by Garcia Bara et al. (2006). The 34-year-old underwater swimmer with an allergic medical history (mite allergy with rhinitis, and asthma) came into contact with anemone *Actinia equina*. In a few minutes he developed local edema and papules at the affected skin area, followed by generalized flushing, dyspnea, hypotension, and he finally lost consciousness. When he arrived in the emergency room, he was under cardiopulmonary arrest. Fortunately, the resuscitative efforts were successful, and after only 24 h, he was discharged from the hospital with complete resolution of symptoms.

In this patient, a detailed allergy work-up was performed to find the triggering antigen. It was known that the patient had contact with anemones with minor symptoms before. The skin prick test was positive for mites and strongly positive for *Ac. equine* anemone. Gel electrophoresis for *Ac. equina* and *A. viridis*, which are prevalent anemones in the region, revealed a common 14.4 kDa band and the IgE immunoblotting with the patient's serum revealed an IgE binding band for this common 14.4 kDa protein. The conclusion was an IgE-mediated sensitization to *Ac. equina* and in vitro cross reactivity for another anemone (*A. viridis*).

Another case who had an anaphylactic reaction after contact with anemone was reported by Nagata et al. (2006). The 24-year-old man, working in an aquarium shop, presented to an emergency department with dyspnea and systemic urticaria. Before the incident, (at about 10 o'clock) he had started cleaning an aquarium tank in which there were many dead and decomposed Haddon's carpet anemones (*Stichodactyla haddoni*). At about 12 o'clock, he developed systemic eruptions and shortness of breath. When the patient presented to the hospital at 12:30, he was in visible distress and he had a cold sweat. There was marked urticaria on his face, trunk, and extremities, and he was drowsy. His physical examination revealed tachycardia (pulse: 116/min), hypotension (blood pressure 60 mmHg systolic) and wheezing. The patient received subcutaneous epinephrine, intravenous methyl prednisolone, dopamine infusion, and oxygen inhalation which improved his condition. The patient stated that several months before, he had been exposed to anemones and noticed local urticaria. The detailed allergy work-up of the patient and Western blotting with the homogenate of the sea anemones revealed specific IgE-mediated reaction against an 86 kDa anemone protein.

There are two cases of anaphylaxis caused by ingestion of jellyfish. The first of these was reported by Imamura et al. (2013). A 32-year-old female developed wheals, oral stinging sensation, dyspnea, hypotension, nausea, vomiting, and abdominal pain after eating salt-preserved jellyfish. As the patient was a surfer and frequently stung by jellyfish, the authors speculated that she could have been sensitized through the previous skin contacts.

The other case was reported by Inomata and colleagues (2014). The 45-year-old man presented with two episodes of anaphylactic reaction after eating jellyfish salad. He had a medical history of asthma and food allergies to natto (soybeans fermented by *Bacillus subtilis*), crab, and shrimp. In both instances, 2 h after the ingestion of jellyfish, he developed dyspnea, chest tightness, abdominal cramps, palpita-

tions, vomiting, dizziness, headache, and loss of consciousness. Interestingly, poly-gamma-glutamic acid, which is the major allergen of natto, is also found in cnidarian nematocyst capsules. The authors mention that 10 out of 12 natto allergy cases in their hospital were surfers who were frequently stung by jellyfish and speculate that their sensitization against natto could have been mediated by cnidarian stings.

37.5.2 Delayed Hypersensitivity Reactions

Nobody would expect a rash 1 week after a jellyfish contact. That was exactly what happened to a 57-year-old woman who returned from a trip to the Red Sea. Veraldi and Carrera (2000) reported a case who developed widespread papulonodular eruption, itching, and burning pain 1 week after contact with a shoal of unidentified jellyfish. At the time of contact, she did not have any symptoms. She claimed she had previous contacts with jellyfish during other trips to exotic seaside resorts. A histopathological examination revealed some necrotic keratinocytes in the upper and middermis, edema, and predominately perivascular and periadnexal lymphohistiocytic infiltrate with numerous neutrophils and eosinophils. The patient was treated with antihistamine and steroid, which resulted in the rapid disappearance of pruritus and burning symptoms, but the cutaneous lesions persisted for 3 weeks.

Another delayed hypersensitivity reaction was reported by Miracco et al. (2001). The 56-year-old woman was injured by coral while snorkeling off the coast of Saudi Arabia. She had an acute urticarial reaction which disappeared in 4 days with topical steroid treatment. But after 1 month, streaks of red papules appeared in the same area. The biopsy taken from the area revealed features similar to those of pityriasis lichenoides and persistent insect bite reaction. Daily topical corticosteroid application gave some symptomatic relief but it took 4 months for the skin lesions to clear completely. Some residual hyper-pigmentation remained.

An even more surprising case was reported by Rallis and Limas (2007) from Greece. A 4-year-old girl was referred to a dermatology clinic in Athens with recurrent dermatitis after a jellyfish sting. She had no previous allergies or other disease. The patient came into contact with a jellyfish on her left shoulder and cheek. She was initially treated with topical steroids and oral amoxicillin. However, the lesions reappeared after 15 days, and a second relapse followed within 1 month. Within 5 months, the child had nine relapses at gradually increasing intervals. The relapses always involved the sites of the primary lesions and consisted of erythematous, pseudo-vesicular, urticarial papules with mild edema. The biopsy taken after the second relapse revealed spongiotic vesiculation, dermal edema, and perivascular lymphohistiocytic infiltration. A search for nematocyst tubules was negative. 0.1 % tacrolimus ointment was used to control the relapses with partial success.

37.5.3 Dermographism

Dermographism is a skin disorder in which the skin gets raised and inflamed, like an urticarial rash, when scratched, rubbed, or stroked. Dermographism has simple or symptomatic forms. While simple dermographism has no apparent cause, symptomatic dermographism is linked to a cause, such as infection or medication. Wu et al. (2006) reported a coral induced symptomatic dermographism case. The 23-year-old perfectly healthy woman who had no personal or familial allergic condition presented to a dermatologist with pruritic hives appearing 5 min after she scratched her skin. The only unusual thing she could remember was a coral injury which happened 2 weeks ago. She cut her left foot on a coral, while scuba diving in the Florida Keys, which resulted in edema in the area. Her dermatologist prescribed a medium strength topical steroid and the wound was healed with scarring after 7 days without any complication.

37.6 Discussion

This chapter is a collection of unusual cnidarian envenomations in the medical literature. The diversity of these cases should remind us of the complexity of cnidarian envenomations and the variety of cnidarian toxins. We should be alarmed, as the oceans are transforming to be better habitats for most cnidaria, and activities, such as shipping and ballast water transfer, have facilitated the inoculation of alien species to distant seas more than ever (Richardson et al. 2009). Cnidaria can threaten human activities in the sea with their wide range of staggering envenomation syndromes, making it a potential public health care problem. The medical community's awareness of the unpredictable nature of cnidarian envenomations is an important issue. Cases in this chapter are plotted on a world map in Fig. 37.1. Distribution of the cases suggest a zone with better awareness against cnidarian envenomations. It could be hypothesized that there should be similar cases round the globe in tropical, subtropical and temperate zones which have not been diagnosed or reported.

With the current sum of knowledge, only some of these rare conditions can be explained. For others, such as the sea-

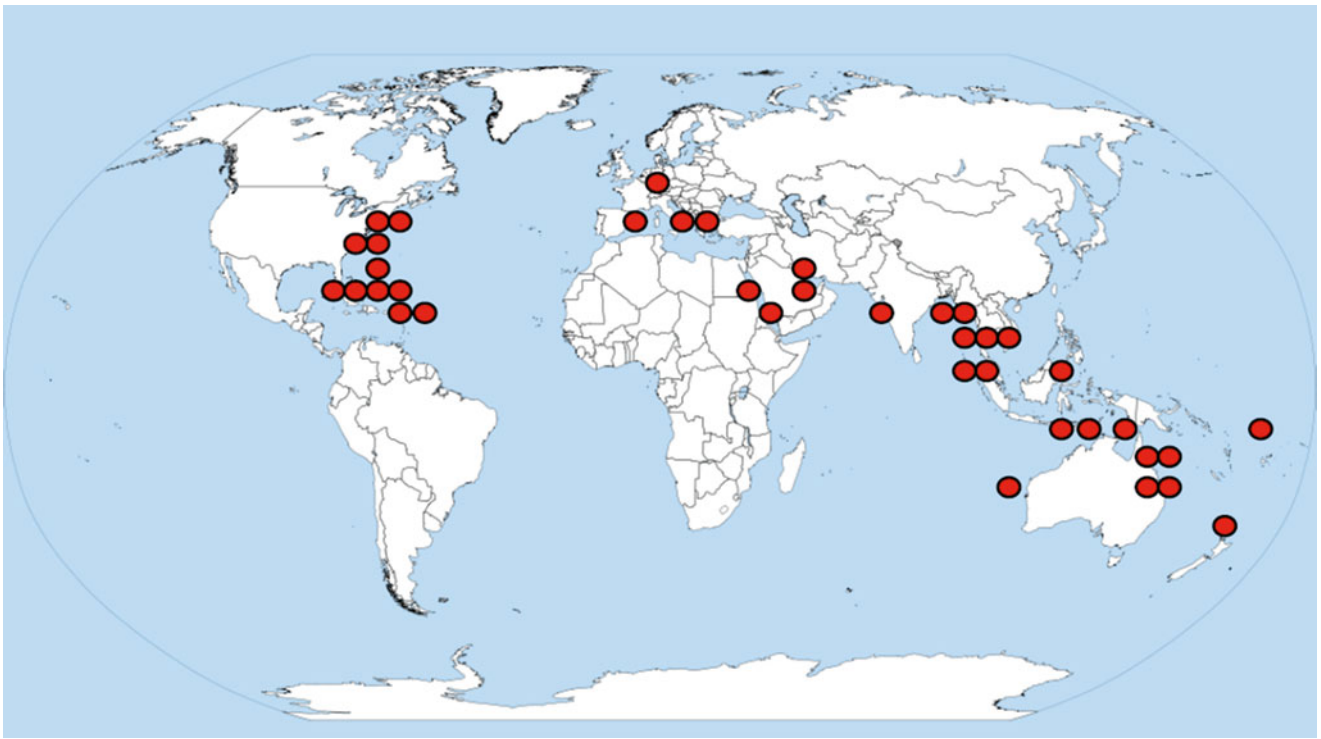

Fig. 37.1 Distribution of unusual cnidarian envenomations around the globe

stroke cases, there is still a dearth of sufficient data. Cnidaria are a rich source of bioactive compounds, making it an interesting and potentially beneficial area. As a result, both the number of scientists dealing with cnidarian toxins, and the annual number of studies being published is increasing, which should one day be able to provide data to enlighten these enigmatic cases.

References

Akashi YJ, Goldstein DS, Barbaro G, Ueyama T (2008) Takotsubo cardiomyopathy: a new form of acute reversible heart failure. Circulation 118:2754–2762

Bianchi R, Torella D, Spaccarotella, Mongiardo A, Indolfi C (2011) Mediterranean jellyfish sting-induced Tako-Tsubo cardiomyopathy. Eur Heart J 32:18

Burnett JW (1992) Human injuries following jellyfish stings. Md Med J 41:509–513

Burnett JW (2005) Dysphonia: a new addition to jellyfish envenomation syndromes. Wilderness Environ Med 16:117–118

Burnett JW (2006) Prolonged urinary incontinence and biliary dyskinesia following abdominal contact with jelyfish tentacles. Wilderness Environ Med 17:180–186

Burnett HW, Burnett JW (1990) Prolonged blurred vision following coelenterate envenomation. Toxicon 28:731–733

Burnett JW, Williamson J, Fenner P (1994) Mononeuritis multiplex after coelenterate sting, Med J Aust 161:320–322

Burnett JW, Rifkin J, Williamson J (1996) Cnidarian envenomation. In: Williamson JA, Fenner PJ, Burnett JW, Rifkin JF (eds) Venomous and poisonous marine animals. University of New South Wales Press, Sydney, pp 174–179

Chand RP, Selliah K (1984) Reversible parasympathetic dysautonomia following stinging attributed to the box jelly fish (*Chironex fleckeri*). Aust N Z J Med 14:673–675

Cooper RA, de Freitas JC, Porreca F, Eisenhour CM, Lucas R, Huxtable RJ (1995) The sea anemone purine, caissarone: adenosine receptor antagonism. Toxicon 33:1025–1031

Das MK, Das AK, Das Gupta S, Hazra SC (2002) Poisonous jellyfish contact and paralytic ileus. J Assoc Physicians India 50:1329

Deekajorndech T, Kingwatanakul P, Wananukul S (2004) Acute renal failure in a child with jellyfish contact dermatitis. J Med Assoc Thai 87(Suppl 2):S294

Devere R (2011) Guillain-Barre syndrome after a jellyfish sting. J Clin Neuromuscul Dis 12:227–230

El Khatib HA, Al Basti HB (2000) Finger ischemia following a jellyfish sting: a surgical approach. Qatar Med J 9:64–65

Elliott RC, Konya RS (1984) Vasoconstrictor effects of extract IV on rat mesenteric vessels. Proc IXth Int Congr Pharmac 633

Fenner PJ, Carney I (1999) The Irukandji syndrome: a devastating syndrome caused by a North Australian jellyfish. Aust Fam Phys 28:1131–1137

Fenner PJ, Hadok JC (2002) Fatal envenomation by jellyfish causing Irukandji syndrome. Med J Aust 177:362–363

Fenner PJ, Lippmann J, Gershwin LA (2010) Fatal and nonfatal severe jellyfish stings in Thai waters. J Travel Med 17:133–138

Filling-Katz MR (1984) Mononeuritis multiplex following jellyfish stings. Ann Neurol 15:213

Frazao B, Vasconcelos V, Antunes A (2012) Sea anemone (cnidaria, anthazoa, actinaria) toxins: an overview. Mar Drugs 10:1812–1851

Garcia Bara MT, Iriarte P, Pineda F (2006) Allergy to *Actinia equina* and *Anemonia viridis*. Allergy 61:1151–1152

Garcia PJ, Schein RM, Burnett JW (1994) Fulminant hepatic failure from a sea anemone sting. Ann Int Med 120:665–666
Grady JD, Burnett JW (2003) Irukandji-like syndrome in south Florida divers. Ann Emerg Med 42:763–766
Guess HA, Saviteer PL, Morris CR (1982) Hemolysis and acute renal failure following a Portuguese man-o-war sting. Pediatrics 70:979–981
Hoffman K, Hermanns-Clausen M, Buhl C et al (2008) A case of palytoxin poisoning due to contact with zoanthid corals through skin injury. Toxicon 51:1535–1537
Houck HE, Lipsky MM, Marzella L, Burnett JV (1996) Toxicity of sea nettle fishing tentacle nematocyst venom in cultured rat hepatocytes. Toxicon 34:771–778
Huynh TT, Seymour J, Pereira P et al (2003) Severity of Irukandji syndrome and nematocyst identification from skin scrapings. Med J Aust 178:38–41
Imamura K, Tsuruta D, Tsuchisaka A et al (2013) Anaphylaxis caused by ingestion of jellyfish. Eur J Dermatol 23:392–395
Ingram DM, Sheiner HJ, Ginsberg AM (1992) Mondor's disease of the breast resulting from a jellyfish sting. Med J Aust 157:836–837
Inomata N, Chin K, Aihara M (2014) Anaphylaxis caused by ingesting jellyfish in a subject with fermented soybean allergy: possibility of epicutanous sensitization to poly-gamma-glutamic acid by jellyfish stings. J Dermatol 41:752–753
Ishikawa T, Vucenik I, Shamsuddin A, Niculescu F, Burnett JW (2004) Two new actions of sea nettle (*Chrysaora quinquecirrha*) nematocyst venom: studies on the mechanism of actions on complement activation and on the central nervous system. Toxicon 44:895–899
Khoo HE (2002) Bioactive proteins from stonefish venom. Clin Exp Pharmacol Physiol 29:802–806
Konya RS, Elliott RC (1996) The coronary vasoconstrictor action of extract IV from the dahlia sea anemone *Tealina felina* L. Toxicon 34:277–282
Laing JH, Harrison DH (1991) Envenomation by the box-jellyfish – an unusual cause of ulnar nerve palsy. J R Soc Med 84:115–116
Lee CY, Lee SY, Chen YM (1985) Coronary vasospasm as the primary cause of death due to equinatoxin a toxic protein fron *Actinia equina*. Toxicon 23:586
Little M, Mulcahy RF, Wenck DJ (2001) Life threatening cardiac failure in a healthy young female with Irukandji syndrome. Anesth Intensive Care 29:178–180
Little M, Pereira P, Carrette T, Seymour J (2006) Jellyfish responsible for Irukandji syndrome. QJM 99:425–427
Martin EJ (1960) Observations on the toxic sea anemone *Rhodactis howesii* (Coelenterata). Pac Sci 14:403–407
McD Taylor D, Pereira P, Seymour J, Winkel KD (2002) A sting from an unknown jellyfish species associated with persistent symptoms and raised troponin I levels. Emerg Med 14:175–180
Meyer PK (1993) Seastroke: a new entity? South Med J 86:777–779
Miracco C, Lalinga AV, Sbano P, Rubegni P, Romano C (2001) Delayed skin reaction to Red Sea coral injury showing superficial granulomas and atypical CD30 positive lymphocytes: report of a case. Br J Dermatol 145:849–851
Mizuno M, Nishikawa K, Yuzawa Y et al (2000) Acute renal failure after a sea anemone sting. Am J Kidney Dis 36:E10
Mizuno M, Nozaki M, Morine N et al (2007) A protein toxin from the sea anemone *Phyllodiscus semoni* targets the kidney and causes a severe renal injury with predominant glomerular endothelial damage. Am J Pathol 171:402–414
Mizuno M, Ito Y, Morgan BP (2012) Exploiting the nephrotoxic effects of venom from the sea anemone, *Phyllodiscus semoni*, to create a hemolytic uremic syndrome model in the rat. Mar Drugs 10:1582–1604
Moats WE (1992) Fire coral envenomation. J Wilderness Med 3:284–287
Moore RE, Scheuer PJ (1971) Palytoxin: a new marine toxin from a coelenterate. Science 172:495–498
Muhvick K, Sengottuvelu S, Manson PN, Myers RA, Burnett JW, Marzella L (1991) Pathophysiology of sea nettle (*Chrysaora quinquecirrha*), envenomation in a rat model and the effects of hyperbaric oxygen and verapamil treatment. Toxicon 29:856–866
Nagai H, Oshiro N, Takuwa-Kuroda K, Iwanaga S, Nozaki M, Nakajima T (2002) Novel proteinaceous toxins from the nematocyst venom of the Okinawan sea anemone *Phyllodiscus semoni* Kwietniewski. Biochem Biophys Res Commun 294:760–763
Nagase H, Karaki H, Ozaki H, Urakawa N, Azuma H, Nakajima H (1987) Contractile and relaxant effects of jellyfish toxin on the vascular and intestinal tissues. Comp Biochem Physiol C 86:411–414
Nagata K, Hide M, Tanaka T et al (2006) Anaphylactic shock caused by exposure to sea anemones. Allergol Int 55:181–184
Nickson CP, Waugh EB, Jacups SP, Currie BJ (2009) Irukandji syndrome case series from Australia's tropical northern territory. Ann Emerg Med 54:395–403
Nickson CP, Curie BJ, Fenner PJ (2010) Priapizm and Irukandji syndrome. Ann Emerg Med 55:581
Pang KA, Schwartz MS (1993) Guillain-Barre syndrome following jellyfish stings (*Pelagia noctiluca*). J Neurol Neurosurg Psychiatry 56:1133–1137
Peel N, Kandler R (1990) Localized neuropath following jellyfish sting. Postgrad Med J 66:953–954
Ponampalam R (2002) An unusual case of paralytic ileus after jellyfish envenomation. Emerg Med J 19:357–358
Portier MM, Ricket C (1902) De l'action anaphylactique de certains venins. C R Soc Biol 54:170–172
Prasad GV, Vincent L, Hamilton R, Lim K (2006) Minimal change disease in association with fire coral (*milepora sp*.) exposure. Am J Kidney Dis 47:e15–e16
Rallis E, Limas C (2007) Recurrent dermatitis after solitary envenomation by jellyfish partially responded to tacrolimus ointment 0.1%. J Eur Acad Dermatol Venereol 21:1287–1288
Ramkumar S, Arun Sudhagar A, Venkateshvaran K (2012) Bioactivity of venom extracted from the sea anemone *Anthapleura aciatica* (Cnidaria: Anthazoa): toxicity and histopathological studies. Int J Fish Aquacult 4:71–76
Richardson AJ, Bakun A, Hays GC, Gibbons MJ (2009) The jellyfish joyride: causes, consequences and management responses to a more gelatinous future. Trends Ecol Evol 24:312–322
Salam AM, Albinali HA, Gehani AA, Al Suwaidi J (2003) Acute myocardial infarction in a professional diver after jellyfish sting. Mayo Clin Proc 78:1557–1560
Snoeks L, Veenstra J (2012) Family with fever after cleaning a sea aquarium. Ned Tijdschr Geneeskd 156:A4200
Spielman FJ, Bowe EA, Watson CB, Klein EF Jr (1982) Acute renal failure as a result of *Physalia physalis* sting. South Med J 75:1425–1426
Sud P, Su MK, Greller HA, Majlesi N, Gupta A (2013) Case series: inhaled coral vapour – toxicity in a tank. J Med Toxicol 9:282–286
Tazieff-Dapierre F, Choucavy M, Goudou D (1977) The effect of toxin II isolated from sea anemones (*Anemonia sulcata*) on the isolated guinea pig ileum. C R Acad Sci Hedb Seances Acad Sci D 284:1465–1468
Tibals J, Yanagihara AA, Turner HC, Winkel K (2011) Immunologic and toxicological responses to jellyfish stings. Inflamm Allergy Drug Targets 10:438–446
Tiong K (2009) Irukandji syndrome, catecholamines, and midventricular stress cardiomyopathy. Eur J Echocardiogr 10:334–336

Veraldi S, Carrera C (2000) Delayed cutaneous reaction to jellyfish. Int J Dermatol 39:28–29

Wang B, Zhang L, Zheng J et al (2013) Multiple organ dysfunction: a delayed envenomation syndrome caused by tentacle extract from the jellyfish *Cyanea capillata*. Toxicon 61:54–61

Wiliamson JA, Burnett JW, Fenner PJ, Hach-WunderleV HLY, Adiga KM (1988) Acute regional vascular insuficiency after jelyfish envenomation. Med J Aust 149:698–701

Williamson JA, Fenner PJ, Burnett JW (1996) Stop press. In: Williamson JA, Fenner PJ, Burnett JW, Rifkin JF (eds) Venomous and poisonous marine animals. University of New South Wales Press, Sydney, pp 448–449

Wu JJ, Huang DB, Murase JE, Weinstein GD (2006) Dermographism secondary to trauma from a coral reef. J Eur Acad Dermatol Venereol 20:1337–1338