(and severe scorpionfish) envenomation are made in Australia by the Commonwealth Serum Laboratories (CSL; 45 Poplar Road, Parkville, Victoria, Australia 3052; *www.csl.com.au*; 61-3-9389-1911). When administering the box jellyfish antivenom, time is of the essence. For cardiac or respiratory decompensation, give a minimum of one ampoule and up to six ampoules consecutively IV, preferably in a 1:10 dilution with normal saline. For stonefish (or severe scorpionfish) envenomation, give one ampoule of specific antivenom IM for every one or two punctures, to a maximum of three ampoules.

MARINE POISONINGS

CIGUATERA

Epidemiology and Pathogenesis Ciguatera poisoning is the most common nonbacterial food poisoning associated with fish in the United States; most U.S. cases occur in Florida and Hawaii, although, with transportation of imported fish nationwide, all clinicians need to be aware of ciguatera. The poisoning almost exclusively involves tropical and semitropical marine coral reef fish common in the Indian Ocean, the South Pacific, and the Caribbean Sea. Global estimates predict that 20,000–50,000 people may be affected by this poisoning each year. More than 400 different fish have been associated with ciguatera toxicity, but 75% of poisonings involve the reef-dwelling barracuda, snapper, jack, or grouper. Ciguatera toxin is created by warm-water ocean reef microalgae of the genus *Gambierdiscus toxicus*, whose consumption by grazing fish allows the toxin to bioaccumulate in the food chain. Three major ciguatoxins are found in the flesh and viscera of ciguateric fish: CTX-1, -2, and -3. Recent research suggests that CTX-1 activates astrocytes and astroglia. In addition, TRPV1, a nonselective cation channel expressed in nociceptive neurons, may play a role in the neurologic disturbances unique to ciguatera poisoning. Most, if not all, ciguatoxins are unaffected by freeze-drying, heat, cold, and gastric acid. None of the toxins affects the odor, color, or taste of fish. Cooking methods may alter the relative concentrations of the various toxins.

Clinical Manifestations The onset of symptoms may come within 15–30 min of ingestion and typically takes place within 2–6 h. Symptoms increase in severity over the ensuing 4–6 h. Most victims develop symptoms within 12 h of ingestion, and virtually all are afflicted within 24 h. The more than 150 signs and symptoms reported include those shown in Table 474-3. Diarrhea, vomiting, and abdominal pain usually develop 3–6 h after ingestion of a ciguatoxic fish. Symptoms may persist for 48 h and then generally resolve (even without treatment). A pathognomonic symptom is the reversal of hot and cold tactile perception, which develops in some persons after 3–5 days and may last for months. More severe reactions tend to occur in persons previously stricken with the disease. Persons who have ingested parrotfish (scaritoxin) may develop classic ciguatera poisoning as well as a "second-phase" syndrome (after 5–10 days' delay) of disequilibrium with locomotor ataxia, dysmetria, and resting or kinetic tremor. This syndrome may persist for 2–6 weeks.

TABLE 474-3 REPRESENTATIVE SIGNS AND SYMPTOMS OF CIGUATERA POISONING

System	Signs/Symptoms
Gastrointestinal	Abdominal pain, nausea, vomiting, diarrhea
Neurologic	Paresthesias, pruritus, tongue and throat numbness or burning, sensation of "carbonation" during swallowing, odontalgia or dental dysesthesias, dysphagia, tremor, fasciculations, athetosis, meningismus, aphonia, ataxia, vertigo, pain and weakness in the lower extremities, visual blurring, transient blindness, hyporeflexia, seizures, coma
Dermatologic	Conjunctivitis, maculopapular rash, skin vesiculations, dermatographism
Cardiovascular	Bradycardia, heart block, hypotension, central respiratory failure[a]
Other	Chills, dysuria, dyspnea, dyspareunia, weakness, fatigue, nasal congestion and dryness, insomnia, sialorrhea, diaphoresis, headache, arthralgias, myalgias

[a]Tachycardia and hypertension may occur after potentially severe transient bradycardia and hypotension. Death is rare.

Diagnosis The differential diagnosis of ciguatera includes paralytic shellfish poisoning, eosinophilic meningitis, type E botulism, organophosphate insecticide poisoning, tetrodotoxin poisoning, and psychogenic hyperventilation. At present, the diagnosis of ciguatera poisoning is made on clinical grounds because no routinely used laboratory test detects ciguatoxin in human blood. Liquid chromatography–mass spectrometry is available for ciguatoxins but is of limited clinical value because most health care institutions do not have the equipment needed to perform the test. A ciguatoxin enzyme immunoassay or radioimmunoassay may be used to test small portions of the suspected fish, but even these tests may not detect the very small amount of toxin (0.1 ppb) necessary to render fish flesh toxic. A newer neuroblastoma assay may be sufficiently sensitive to detect small amounts of toxin but is not readily available for clinical use.

TREATMENT CIGUATERA POISONING

Therapy is supportive and based on symptoms. Nausea and vomiting may be controlled with an antiemetic such as ondansetron (4–8 mg IV). Syrup of ipecac and activated charcoal are not recommended for ciguatera poisoning. Hypotension may require the administration of IV crystalloid and, in rare cases, a pressor drug. Bradyarrhythmias that lead to cardiac insufficiency and hypotension generally respond well to atropine (0.5 mg IV, up to 2 mg). Goal-directed combination cardiovascular fluid and pressor therapy may be required. Cool showers or the administration of hydroxyzine (25 mg PO every 6–8 h) may relieve pruritus. Amitriptyline (25 mg PO twice a day) reportedly alleviates pruritus and dysesthesias. In three cases unresponsive to amitriptyline, tocainide has appeared to be efficacious. Nifedipine has been used to treat headache and poor circulation in order to prevent hypotension, but only after the initial acute phase of the poisoning has passed. IV infusion of mannitol may be beneficial in moderate or severe cases in fluid-repleted patients, particularly for the relief of distressing neurologic or cardiovascular symptoms, although the efficacy of this therapy has been challenged and has not been definitively proved. The infusion is rendered initially as 1 g/kg per day over 45–60 min during the acute phase (days 1–5). If symptoms improve, a second dose may be given within 3–4 h and a third dose may be administered the next day. Care must be taken to avoid dehydration in a treated patient. The mechanism of the benefit against ciguatera intoxication is perhaps hyperosmotic water-drawing action, which reverses ciguatoxin-induced Schwann cell edema. Mannitol may also act in some fashion as a "hydroxyl scavenger" or may competitively inhibit ciguatoxin at the cell membrane.

During recovery from ciguatera poisoning, the victim should exclude the following from the diet for 6 months: fish (fresh or preserved), fish sauces, shellfish, shellfish sauces, alcoholic beverages, nuts, and nut oils. Consumption of fish in ciguatera-endemic regions should be avoided. All oversized fish of any predacious reef species should be suspected of harboring ciguatoxin. Neither moray eels nor the viscera of tropical marine fish should ever be eaten.

DIARRHETIC SHELLFISH POISONING

Diarrhetic shellfish poisoning occurs with consumption of shellfish producing diarrheal illness. The first suspected incident, which occurred in the Netherlands in 1961, was followed by outbreaks in Japan, the United Kingdom, and (most recently) China. The causative agents are the lipophilic compound okadaic acid and the dinophysistoxins, which inhibit serine and threonine protein phosphatases, with consequent protein accumulation and continued secretion of fluid in intestinal cells leading to diarrhea. Shellfish acquire these toxins by feeding on dinoflagellates, particularly of the genera *Dinophysis* and *Prorocentrum*.

Symptoms include diarrhea, nausea, vomiting, abdominal pain, and chills. Onset occurs within 30 min to 12 h. The illness is usually