Food Safety Digest

World Health Organization

November 2020

Department of Food Safety and Zoonoses

# Ciguatera poisoning

## Ciguatera poisoning is a consequence of eating contaminated seafood

Ciguatera poisoning affects people after they have eaten certain seafood, primarily fish, which contains the poison ciguatoxin. The poison is produced by microscopic algae known as dinoflagellates that are found in shallow coastal waters on the surfaces of seaweeds and other marine plants such as corals. Herbivorous fish that browse on the plants consume the dinoflagellates. These fish can then in turn be consumed by carnivorous fish. In this way, the toxin moves up the food chain, becoming more and more concentrated each time a larger fish eats a smaller fish. Other marine animals such as sea urchins and snails may also become contaminated with the toxin, but are less important than fish in terms of ciguatera poisoning.

Knowledge about the global burden of disease is rather limited. Ciguatera poisoning (CP) is known to be underreported as doctors are often unaware of the obligation to report it, but also because CP is very often not correctly diagnosed. However, it is thought that 50 000–500 000 people each year are affected by the condition. In regions where the poison-producing dinoflagellates grow, such as the Pacific islands, estimates are that up to 10 per cent of the local population is affected each year.

## Ciguatera poisoning is now a global problem and is affected by climate change

CP is endemic between latitudes $35^0$ N and $35^0$ S, and is especially known from the South Pacific, Indian Ocean and Caribbean regions. While the toxins are produced in tropical and subtropical waters, CP has become global due to the international seafood trade and travel. Intoxication has been reported in many geographical areas in which the toxin-producing dinoflagellates cannot be found; for example, in Europe, the European Rapid Alert System for Food and Feed has issued eight alerts for ciguatoxins in the past few years, stemming from chilled and frozen fish imported from other continents.

Water temperature is a main factor that drives the growth, distribution and abundance of CP-associated dinoflagellates; global warming is facilitating their expansion, although in some areas the water is becoming warm enough to depress their growth. The conditions under which dinoflagellates produce the toxin, and produce algal ‘blooms’, are not yet clearly understood, but such blooms can follow extreme weather events such as hurricanes, floods and droughts, as well as man-made impacts such as pollution, destructive fishing practices and damage to coral reefs.

## Ciguatera poisons of many different types are found in many different types of fish

CP has been known for centuries, but it was only in 1977 that the causative organism (the dinoflagellate) was described. Different dinoflagellates produce different types of ciguatoxin (CTX), and these accumulate through the food chain, becoming more toxic as they are modified or metabolized in the fish.

The toxins accumulate most highly in the visceral tissues and flesh of fish. More than 425 species of fish have been linked to CP cases; they include high-valued commercial species such as barracuda, grouper, snapper, wrasse, moray eel and parrotfish. The toxicity of fish can be, amongst other things, dependent on the species, size, seasonal variations, water temperature and location.

Photo of barracuda specie

## Ciguatera poisoning causes many different types of symptom

More than 175 symptoms have been reported for CP. Acute symptoms appear within 48 hours after consumption and are observed in almost all organ systems – gastrointestinal, cardiovascular and neurological. They include e.g. fatigue, any kind of pain, nausea, vomiting, diarrhoea, low blood pressure, and heart rhythm disorder. While most symptoms are unspecific and could also hint towards other food poisoning, a classic symptom for CP is cold allodynia – the sensation that cold things feel hot to the touch.

In at least 20 per cent of CP-affected persons, symptoms persist for months or years after the initial poisoning; they are characterized by neurological, neuropsychiatric and systemic symptoms. These chronic symptoms include seizures, depression, anxiety, and memory disturbances.

Symptoms may also recur from time to time, for months or years. Recurrence can be triggered by certain foods (e.g. alcohol, nuts, dairy products, fish, meat), by behavioural (e.g. intense physical activity, fatigue) or other external (e.g. sun exposure) factors.

While the fatality rate of CP may exceed 10 per cent in some contexts, it is overall estimated to be less than 0.5 per cent. Death due to CTX exposure often follows cardiovascular and/or complications of the central nervous system.

## Ciguatera poisoning is difficult to diagnose correctly

Since none of the symptoms reported for CP are specific to the disease, patients must meet several criteria to be diagnosed with CP:

- Exposure criteria: patient has consumed marine fish known to be associated with CP prior to the onset of symptoms.
- Clinical criteria: patient presents described neurological symptoms, especially cold allodynia, within 48 hours after a meal. These symptoms might be preceded or accompanied by gastrointestinal and/or cardiovascular symptoms.

The diagnosis is strengthened by:

- Laboratory criteria: testing in a laboratory confirms CTX to be present in fish left over from the meal.
- Epidemiological criteria: symptoms appear in the context of an outbreak.

## Ciguatera poisoning is treated by managing symptoms

As there are no specific treatments for CP, symptom-managing medications are used. Mannitol is commonly administered quickly after the onset of neurological symptoms; however, its efficacy in treating CP remains controversial. Symptom-managing medications are used to e.g. depress muscle spasms, change the heart rate, prevent vomiting and diarrhoea, alleviate depression, rehydrate the patient, treat allergies, relieve pain, lower blood pressure.

Traditional remedies have been reported; however, their efficacy remains to be demonstrated in clinical trials. In the Indo-Pacific and West Indies endemic regions, 90 different herbal remedies such as *Heliotropium foertherianum*, *Euphorbia hirta*, *Rosmarinus* spp., *Vitex* spp. as well as castor oil and carapat oil have been used.

## Ciguatoxins are detected using a two-step approach

Ciguatoxins are difficult to detect and quantify: they are odourless, tasteless, heat stable, and present at very low levels in contaminated seafood. Although a number of detection methods are available, none are yet validated and there is no consensus worldwide on their use. A two-step approach to detection is recommended: first screening, and then confirming.

The screening methods normally used are based on measuring the death of cultured nerve cells, the most widely used being the N2a assay which is based on mouse neuroblastoma cells, and the fluorescent receptor-binding assay based on rat brain synaptosomes. Recently, a highly sensitive immunological assay for CTXs was developed – a direct sandwich enzyme-linked immunosorbent assay based on multiple antibodies, which is however specific only for CTXs found in the Pacific region.

A good method for confirmation is liquid chromatography coupled with mass spectrometry. The use of mass spectrometry allows the profiling of CTXs in algal and environmental samples as well as in seafood (fish, bivalves, sea urchins, starfish, gastropods).

Traditional methods for detecting CTXs in fish (e.g. feeding a piece of fish to a dog or cat, observing the avoidance of toxic fish by flies or ants) may have potential but their validity has yet to be confirmed, and ethical concerns about animal testing may be pertinent.

When possible, it is important to screen and confirm the presence of toxins in the local species of poison-producing dinoflagellates (*Gambierdiscus and Fukuyoa* spp.) as the abundance and toxin profiles of these can significantly impact the toxin profiles in surrounding fish. Optical microscopy can be used to screen for the species, and scanning electron microscopy and molecular techniques such as sequencing or polymerase chain reaction can be used to confirm the species. Sampled dinoflagellates can be evaluated for the presence of CTXs using the methods mentioned above. Another approach is to screen for the presence of the toxin in water, by utilizing the passive adsorption of CTXs to some known resins.

## Controlling ciguatera poisoning: restricting the size of fish in the market

In the absence of a rapid, cost-effective and reliable screening test for CTXs, many countries impose restrictions on the size of fish entering the commercial market, as older and larger fish are more likely to be contaminated with higher levels of CTXs.
For high-risk species, the range of maximum size allowed varies from, for example, 3 kg for coral rockcod to 10 kg for mackerel.

## Controlling ciguatera poisoning: monitoring toxicity

Control measures vary according to the local dinoflagellate profiles, implicated fish species, food habits, and often with the season.

Monitoring the algal populations will help address seasonal variations in CP. For monitoring fish, the target species associated with CP in each area can be selected, according to the seafoods that contain CTXs and are commonly consumed by people in the region. Species of fish that stay within a small area for their whole life are selected.

As most tropical fish are territorial, areas with toxicity usually remain toxic while the areas without toxicity usually remain safe. Local people may know which areas are safe and which may be toxic, and this knowledge can be used for monitoring.

## Controlling ciguatera poisoning: setting good practices

In some parts of the world fish are eaten whole, and good practices include developing guidance about what parts of the fish should not be eaten. Visceral organs, eggs, heads, eyes and bones should be avoided, as these tissues can contain high levels of CTXs and should be removed prior to consumption.

As fish flesh may become contaminated with visceral tissue during handling, good practices include providing guidance on the disposal of ciguatoxic fish, fish heads and viscera.

Good practices also include informing the consumer through public outreach programmes about the potential risks posed by consuming fish heads and viscera, and some invertebrates. Raising awareness is an important part of the risk management options, and risk communication needs to be tailored to the local situation regarding the consumption and trade of specific fish.

A potential problem in monitoring and CP prevention is the mislabelling of fish species. To allow trade from endemic areas, good practices include ensuring that seafood products are labelled accurately.

## Controlling ciguatera poisoning: reporting, regulating and warning early

Some countries or regions use reporting systems to quickly detect and warn about outbreaks. For example, in the United States of America, cases are reported to the surveillance system of the Centers for Disease Control and Prevention. In the European Union, the Rapid Alert System for Food and Feed provides alerts to food safety agencies and consumers. In French Polynesia, the Institut Louis Malardé provides information and issues alerts about CP.

Regulatory authorities set a maximum permitted level for toxins, based on toxicological data obtained in laboratory tests. Above this level, seafood must be banned from the market. Both the United States Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA) have proposed a fish CTX maximum concentration of 0.01 µg/kg CTX1B as being unlikely to elicit symptoms of CP.

Fish and water (dinoflagellate) samples can be regularly screened for CTXs to elicit early warnings on ciguatoxic fish.