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CIGUATERA POISONING

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Etiology

The condition is caused by eating fish containing toxins produced by the benthic dinoflagellate *Gambierdiscus toxicus*, a one-celled plantlike organism that occurs as a film on corals (usually dead coral) and seagrass in tropical waters worldwide. Gambiertoxins (produced by *G. toxicus*) contains a chemical precursor, which is converted to ciguatoxin in the livers of herbivorous fish. These polyether toxins are lipid soluble, they are passed on and concentrated in the muscles of large predatory fish such as groupers, snappers, jacks, mackerel, triggerfish, barracuda and shark which eat the small fish (Barracuda, black grouper, blackfin snapper, cubera snapper, dog snapper, greater amberjack, hogfish, horse-eye jack, king mackerel and yellowfin grouper have been known to carry ciguatoxins). These toxins are cumulative; they become progressively concentrated as they move up the food chain from small fish to large fish that eat them and reach high concentrations in large predatory tropical reef fish. The dinoflagellates reach high abundance in seasons when the sea contains large quantities of nutrients, such as during the wet season and after periods of disturbance such as those caused by cyclones and harbour dredging. Fish that live in oceans between latitude 35° N and 35° S have caused the disease. More than 400 species of fish can be vectors of ciguatoxin, but a small number of species are repeatedly toxic.

More than twenty precursor gambiertoxins and ciguatoxins have been identified in the dinoflagellate *Gambierdiscus toxicus* and in herbivorous and carnivorous fish. Ciguatoxin as a sodium channel agonist: it activates sodium channels and cause membrane instability and excitability. The toxins become more polar by oxidative metabolism as they move up the food chain. The level of ciguatoxin in fish that causes human illness varies. The Pacific ciguatoxin (P-CTX-1) causes poisoning at levels=0.1 µg/kg in flesh of carnivorous fish, such as those mentioned above. The main Caribbean ciguatoxin (C-CTX-1) is less polar and 10 times less toxic than P-CTX-1. The pathogenic dose for humans is 23-230 µg and usual regulatory tolerance is that it must not be detected in a product. The 50% lethal dose in mice is 0.45 µg/kg when injected intraperitoneally.

Ciguatoxins are odorless, colorless and tasteless and cannot be eliminated or reduced by cooking or freezing.

Epidemiology

Ciguatera-endemic U.S. states and territories include Hawaii, Florida, Puerto Rico, Guam, the U.S. Virgin Islands, American Samoa and the Commonwealth of Northern Mariana Islands.

Under-diagnosis and under-reporting (especially in endemic areas such as the Caribbean) make it difficult to know the true worldwide incidence of the 'Marine Toxin Diseases'. Ciguatera is a substantial cause of morbidity in areas where ciguatera is endemic. Approximately 5-70 cases per 10,000 population are estimated to occur each year. Because of difficulties confirming cases and the absence of a reliable assay for human exposure, the number of cases reported to health departments is estimated at 2-10% of the actual number of cases in the United States. Outbreaks of ciguatera are limited in distribution and time and are usually very localized. In St. Thomas, a household survey estimated that 4.4% of all households suffered from Ciguatera annually (at least 2640 persons per year or an annual incidence of 600 cases per year); in Puerto Rico, 7% of the residents have experienced at least one episode of Ciguatera in their lifetime.

The attack rate has been reported to be 73%-100% with ingestion of contaminated fish, without any apparent age-related susceptibility.

Acute fatality, usually due to respiratory failure, circulatory collapse or arrhythmias, ranges from 0.1% to 12% of reported cases; presently in the Pacific, the mortality is less than 1%. Lethality is usually seen with ingestion of the most toxic parts of fish (ie. the liver, viscera, roe and other organs).

Expanding geographic distribution:

Ciguatoxic fish such as barracuda and amberjack migrate seasonally; therefore, they can acquire the toxin in one region and transport it to another. Migration of barracuda from south Florida waters and the Caribbean to South Carolina waters has been documented by the South Carolina Department of Natural Resources cooperative Marine Game Fish Tagging Program; migration of barracuda from Florida to Texas waters has been documented by Fish Trackers, Inc., a volunteer fish-tagging organization that catches, tags and releases certain fish species.

The number of oil rigs in Gulf Coast waters is increasing, providing new habitats for *Gambierdiscus* species and the reef fish that feed on them. In addition, the oil rigs are popular sport-fishing sites and are being considered for experimental fish farming, increasing the likelihood that humans will be exposed to ciguatoxic fish. In the western Gulf of Mexico, these structures already are becoming habitats for hard coral reefs, which in turn provide a surface for algae growth.

The temperatures of the northern Caribbean and extreme southeastern Gulf of Mexico have been predicted to increase 4.5°F-6.3°F (2.5°C-3.5°C) during the twenty-first century, with

greater temperature increases in higher latitudes. Higher temperatures favor *G. toxicus* growth and are likely to alter fish migration patterns.

Incubation period:

Symptoms most commonly begin within 2-6 hours, gastro-intestinal symptoms within 2 to 30 hours, neurological symptoms within 3 hours and cardiovascular dysfunction in 1 to 3 days.

Clinical Manifestation

Ciguatera fish poisoning is characterized by:

- 1- Gastrointestinal symptoms such as nausea, vomiting, diarrhea cramps
- 2- Neurological symptoms: weakness, paresthesias (tingling), severe pruritus (itching), tooth pain or the feeling that teeth are loose, pain on urination, and blurred vision. Patients may experience reversal of temperature sensation in their mouth (hot surfaces feeling cold and cold, hot), unusual taste sensations, nightmares, or hallucinations.
- 3- Common nonspecific symptoms include excessive sweating, headache, and muscle aches. Ciguatera often is associated with signs of cardiovascular dysfunction, such as hypotension, bradycardia (slowed heartbeat), or arrhythmia (irregular heartbeat).

Chronic symptoms: Complete recovery usually occurs within a few weeks (usually 1 to 4 weeks), but neurological symptoms can recur periodically. The symptoms of Ciguatera poisoning, especially the paresthesias and weakness, can persist in varying severity for weeks to months after the acute illness. Chronic ciguatera can also present as a psychiatric disorder of general malaise, depression, headaches, muscular aches and peculiar feelings in extremities for several weeks.

It is reported that those with chronic symptoms seem to have recurrences of their symptoms with the ingestion of fish (regardless of type), ethanol, caffeine and nuts 3 to 6 months from initial ingestion. Ciguatera poisoning is rarely fatal.

Variability: The clinical picture may be variable among individuals, even with the same food source, different ethnic groups, and possibly with different types of fish and/or geographic location. It appears that ciguatera from consumption of carnivore fish species may be more toxic than that from consumption of herbivores due to biotransformation of the toxin. In Polynesia, Ciguatera is dominated and initiated by neurological symptoms (90% of patients report paresthesias and dysesthesia), while reports from the Caribbean suggest that Ciguatera initially presents acutely as a gastroenteritis often with associated cardiovascular symptoms, with the gradual onset and dominance of neurological symptoms over the first 24 hours.

Diagnostic Tests

Diagnosis is usually based on the presence of characteristic symptoms in a patient with a recent history of fish ingestion (especially those mentioned above).

The Food and Drug Administration has developed some tests to detect this toxin in serum and urine. The presence of ciguatera in fish samples saved from a meal can be confirmed through laboratory testing (i.e., high-performance liquid chromatography and mass spectrometry). In addition, no proven screening test exists for detecting ciguatera in fish before they are distributed and eaten.

Treatment

In case of a suspected ciguatera fish poisoning, consult a medical doctor. Many physicians are not familiar with ciguatera in particular in areas where this toxin is not endemic. Doctors are often at a loss to explain these symptoms and ciguatera poisoning is frequently misdiagnosed as Multiple Sclerosis.

There is no single specific remedy for the treatment of ciguatera fish poisoning. The most successful management of the disease has been accomplished by supportive and symptomatic treatment. Intravenous mannitol has been suggested for the treatment of severe ciguatera poisoning when given within the first 48-72 hours from ingestion. But some studies show that there is no difference if the patient is given mannitol or normal saline, when trying to relieve symptoms at 24 hours.

Control measures

Persons living in or traveling to ciguatera-endemic areas should keep the following in mind:

- Normal household cooking (e.g. boiling, steaming, frying) will not reduce or eliminate the toxin. The ciguatera toxin is very heat-stable.
- Avoid eating the head, viscera, or roe of any reef fish
- Avoid consuming large, predatory reef fish, especially barracuda. Avoid eating fish caught at sites known to be ciguateric. The local population knows which species are ciguateric in their area.

- Physicians everywhere who treat patients with gastrointestinal or neurological symptoms after eating large, predatory fish should consider a diagnosis of ciguatera. There appears to be sensitivity to certain foods (i.e. ingestion of fish (regardless of type), ethanol, caffeine and nuts) after ciguatera poisoning and these should be avoided for 3 to 6 months after the illnesses. There is no immunity to this illness and recurrences of actual ciguatera in the same individual appear to be worse than the initial illness.

Investigation:

- Try to obtain portions of the meal and in particular the fish to assist in confirming the diagnosis. These portions should be packaged and frozen for any subsequent analysis.
- Collect information on the persons affected by ciguatera (see following form).

CIGUATERA TOXIN QUESTIONNAIRE

Date of interview: ___ / ___ / ___

DEMOGRAPHICS

1. Name: _____

2. Address: _____

3. Phone: _____

4. Age: ___ (years)

5. Sex: ___ Male ___ Female

6. Did you get sick after eating at the English turn country club? Yes No

ILLNESS INFORMATION:

7. Date and time of symptom onset

_____ Don't know/Can't remember

Date: ___ / ___ / ___ Time: ___ : ___

Symptoms	Yes	No	Don't know
Fever	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Chills	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Increased (sweating)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weak/shaky	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Watery eyes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Itching	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Skin rash	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Shortness of breath	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Burning on urination	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Diarrhea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Abdominal pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nausea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vomiting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Increased salivation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Dizzy/vertigo	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Headache	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Light headed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Visual changes/disturbances	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Stiff neck	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bad or metallic taste	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tooth pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Reversal of hot & cold sensations	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Numbness or tingling around the mouth	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Numbness or tingling in your legs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Numbness or tingling in your arms	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other numbness (paresthesia) Specify:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
General body aches	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Joint pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weakness in the legs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pain in the legs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weakness in the arms	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pain in the arms	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other (specify):	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

9. Did you seek medical care for this illness episode?
 ___ Yes ___ No ___ Don't know/can't remember

9b. If yes, where did you go
 ___ Private physician Name: _____
 ___ Hospital ED Name: _____
 ___ Poison Control Center
 ___ Other

9c. What treatments were you given? _____

EXPOSURE INFORMATION:

10. Can you tell me the date and time the fish was eaten?

____ Don't know/Can't remember

Date: ____ / ____ / ____ Time: ____ : ____

11. Did you share this fish with anyone else?

__ Yes __ No __ Don't know/Can't remember

Name: _____

Contact information: _____

Name: _____

Contact information: _____

Name: _____

Contact information: _____

12. Can you tell me what type of fish made you ill?

____ Don't know what type of fish was eaten

Fish: _____