http://www.emedicine.com/emerg/topic100.htm

Background: Ciguatera poisoning is the most common nonbacterial, fish-borne poisoning in the United States. It is caused by consumption of reef fish that feed on certain dinoflagellates (ie, algae) associated with coral reef systems. At least 5 types of ciguatoxin have been identified and are noted to accumulate in larger and older fish higher up the food chain. Ciguatera poisoning has been a significant concern in tropical areas for centuries and generally is believed to be confined to coral reef fish in water between the latitudes of 35 degrees N and 35 degrees S. In the modern era of world travel and rapid transportation, many warm-water fish are available commercially in markets throughout the world, and cases of ciguatera poisoning may be seen in any location.

Pathophysiology: Gambierdiscus toxicus is the dinoflagellate most notably responsible for production of ciguatoxin, although other species have been identified more recently. Over 400 species of fish have been implicated in ciguatera poisoning, starting with herbivores and then climbing up the food chain to the larger carnivorous fish.

Species of fish most frequently implicated include groupers, amberjack, red snappers, eel, sea bass, barracuda, and Spanish mackerel. Fish larger than 2 kg contain significant amounts of toxin and readily produce toxic effects when ingested. Although not completely reliable, an immunoassay and mouse biologic assay are available for detection of ciguatoxin in affected fish. Ciguatoxin and other similar toxins are heat stable and lipid soluble; they are unaffected by temperature, gastric acid, or cooking method. Presence of toxin does not affect odor, color, or taste of the fish.

Ciguatoxin produces toxic effects by activation of voltage-dependent sodium channels, resulting in hyperexcitability, decreased conduction, and prolonged refractoriness. Effects are most pronounced on neuronal, cardiac, and GI tissues.

Frequency:

In the US: Most ciguatera outbreaks in the United States occur in Hawaii and Florida, although tourists may develop symptoms after returning home. Global marketing of tropical fish has been responsible for sporadic cases reported across the United States mainland.
Internationally: Annually, an estimated 50,000 cases of ciguatera poisoning occur worldwide; however, this poisoning is difficult to track and is thought to be underreported. Ciguatera poisoning is endemic in Australia, the Caribbean, and the South Pacific islands. No doubt exists that ciguatera has had a substantial economic impact on many of the Third World countries where it is endemic.

Mortality/Morbidity: Ciguatera poisoning seldom is lethal. Typical mortality rate is 0.1%, although rates as high as 20% have been reported. Death usually is attributed to cardiovascular depression, respiratory paralysis, or hypovolemic shock.

Race: Several reports note that patients of similar ethnic backgrounds tend to share common symptom groupings.

Age: Children appear to be affected more severely and are involved more often in life-threatening cases.

History: Currently, ciguatera poisoning is a clinical diagnosis based upon a constellation of symptoms temporally related to ingestion of suspect fish products. Onset of symptoms may be within 15 minutes or as late as 24 hours (rarely) after ingestion of the toxin. Generally, symptoms are noted within 6-12 hours after ingestion of tropical reef fish. Symptoms increase in frequency and severity over the subsequent 4-6 hours. Reported symptoms are numerous but commonly affect 3 major organ systems: GI, neurologic, and cardiovascular.

GI symptoms often are the first to appear, may last 1-2 days, and include the following:
Abdominal pain
Nausea
Vomiting
Diarrhea
Neurologic symptoms usually are multiple, varied, and, at times, bizarre. Symptoms may begin within a few hours to 3 days after the meal, can last several months, and include the following:
Lingual and circumoral paresthesias
Painful paresthesias of extremities
Paradoxical temperature reversal (eg, cold objects feel hot and hot objects feel cold); a classic finding, but occurs in only one third of patients
Dental pain (teeth feel loose)
Pruritus
Arthralgias
Myalgias
Weakness
Ataxia, vertigo
Respiratory paralysis
Coma
Cardiovascular symptoms are less common but can be severe. They usually resolve within 2-5 days. Patients may experience weakness and dizziness from bradycardia and hypotension.

Other features include dyspnea, sweating, salivation, chills, neck stiffness, and pruritus.
Physical:

Dehydration from GI losses is a common finding.
Neurologic findings are extremely variable, from mild to life threatening.
Cardiovascular findings include bradycardia and hypotension. Signs of shock may be observed. Hypotension results from the following:
Fluid loss
Bradycardia
Peripheral vasodilation
Myocardial depression
Causes: Ingestion of sufficient quantities of fish with accumulated ciguatoxin produces this syndrome. DIFFERENTIALS Section 4 of 9
Author Information Introduction Clinical Differentials Workup Treatment Medication Follow-up Bibliography

Aeromedical Transport
Shock, Septic
Sinus Bradycardia
Snake Envenomations, Cobra
Snake Envenomations, Coral
Snake Envenomations, Sea
Stroke, Ischemic
Toxicity, Antidysrhythmic
Toxicity, Arsenic
Toxicity, Beta-blocker
Toxicity, Calcium Channel Blocker
Toxicity, Carbamazepine
Toxicity, Disulfiram
Toxicity, Isoniazid
Toxicity, Lithium
Toxicity, Mercury
Toxicity, Mushroom - Amatoxin
Toxicity, Mushroom - Disulfiramlike Toxins
Toxicity, Mushroom - Gyromitra Toxin
Toxicity, Organophosphate and Carbamate
Toxicity, Phenytoin
Toxicity, Scombroid
Toxicity, Tetrodotoxin

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Patient Education
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Lab Studies:

All routine laboratory tests are nonspecific for ciguatera poisoning but may reflect volume depletion from fluid losses. Mild creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) elevations, if present, reflect muscle tissue breakdown. Currently, home products are available to detect ciguatoxin in fish at the time of preparation. Reliability of these products in the hands of the consumer has not been validated.

Other companies are developing similar products for detection of ciguatoxin in human blood (eg, Hawaii Chemtect at 626-568-8606).

TREATMENT Section 6 of 9

Emergency Department Care:

Treatment of ciguatera poisoning is largely supportive and symptom driven.
GI decontamination with activated charcoal may be of value if performed within 3-4 hours of ingestion. Avoid syrup of ipecac because of its potential to worsen fluid losses.
Orogastric lavage is not recommended; it is not of proven benefit for ciguatera poisoning, and risks of this procedure are likely to outweigh benefits.
Antiemetics may control nausea and vomiting.
Cool showers and antihistamines have been recommended to relieve pruritus.
Manage hypotension with volume replacement. Pressor agents rarely are needed.
Bradyarrhythmias respond well to atropine.

MEDICATION Section 7 of 9

Medications used to treat ciguatera poisoning include (1) neurologic agents, (2) serotonin-norepinephrine re-uptake inhibitors, (3) antihistamines, (4) analgesics, (5) antipyretics, and (6) anti-inflammatories.

Drug Category: Diuretics, osmotic -- These agents are used empirically to treat neurologic symptoms associated with ciguatera poisoning.Drug Name
Mannitol (Osmitrol, Resectisol) -- Osmotic diuretic that has become mainstay of acute treatment in recent years. Mechanism of action unknown, but diminishes dramatically or prevents neurologic symptoms associated with ciguatera poisoning. Most effective when given early in course of treatment, but somewhat effective even after several days of symptoms. Neurologic symptoms often decrease within minutes of treatment and may resolve completely within 2 days.
Adult Dose 1 g/kg IV of 20% solution over 30 min; not to exceed 50 g
Pediatric Dose 0.25-1 g/kg IV or 60 g/m 2 IV administered over 2-6 h
Contraindications Documented hypersensitivity, anuria, severe pulmonary congestion, progressive renal damage, severe dehydration, active intracranial bleeding, and progressive heart failure
Interactions None reported
Pregnancy B - Usually safe but benefits must outweigh the risks.

Precautions Assure adequate hydration status is attained prior to giving mannitol; monitor for fluid/electrolyte imbalance; solutions may crystallize if cooled
Drug Category: Serotonin/norepinephrine reuptake inhibitors -- These agents have central and peripheral anticholinergic effects, as well as sedative effects, and block the active reuptake of norepinephrine and serotonin.Drug Name
Amitriptyline (Elavil) -- Reported to relieve pruritus and dysesthesias, may act by blocking fast sodium channels that have been activated by ciguatoxin. Most effective for chronic neurologic symptoms that often follow ciguatera poisoning.
Adult Dose 25-50 mg PO bid; start at 25 mg PO bid
Pediatric Dose 1-5 mg/kg PO qd or divided bid
Contraindications Documented hypersensitivity; MAOIs in past 14 d; history of seizures, cardiac arrhythmias, glaucoma, urinary retention
Interactions May cause cardiotoxicity (via sodium channel blockade) when used concurrently with type IA, IC, or III antiarrhythmics; phenobarbital may decrease effects; coadministration with CYP2D6 enzyme system inhibitors (eg, cimetidine, quinidine) may increase levels; inhibits hypotensive effects of guanethidine; may interact with thyroid medications, alcohol, CNS depressants, barbiturates, and disulfiram
Pregnancy C - Safety for use during pregnancy has not been established.
Precautions Caution in cardiac disease, elderly patients, and renal or hepatic impairment
Drug Category: Analgesics -- These agents are used symptomatically to provide pain relief.Drug Name
Acetaminophen/paracetamol (Tylenol/Panadol) -- Extremely useful in treatment of headaches.
Adult Dose 325-500 mg PO q4-6h prn; not to exceed 4000 mg/d
Pediatric Dose 10-15 mg/kg/dose PO q6h prn
Contraindications Documented hypersensitivity
Interactions Rifampin can reduce analgesic effects; coadministration with barbiturates, carbamazepine, hydantoins, or isoniazid may increase hepatotoxicity
Pregnancy A - Safe in pregnancy
Precautions Hepatotoxicity possible in chronic alcoholics following various dose levels; severe or recurrent pain or high or continued fever may indicate serious illness; contained in many OTC products, and combined use with these products may result in cumulative doses exceeding recommended maximum
Drug Name
Indomethacin (Indocin) -- Relieves myalgias and arthralgias.
Adult Dose 75 mg PO qd
Pediatric Dose 1.25-2.5 mg/kg/d PO divided tid/qid
Contraindications Documented hypersensitivity; active GI bleed; previous peptic ulcer disease is a relative contraindication
Interactions Coadministration with aspirin increases risk of inducing serious NSAID-related adverse effects; probenecid may increase concentrations and, possibly, toxicity; may decrease effect of hydralazine, captopril, and beta-blockers; may decrease diuretic effects of furosemide and thiazides; may increase PT in patients taking anticoagulants (instruct patients to watch for signs of bleeding); may increase risk of methotrexate toxicity; may increase phenytoin levels
Pregnancy C - Safety for use during pregnancy has not been established.

Precautions Category D in third trimester of pregnancy; acute renal insufficiency, hyperkalemia, hyponatremia, interstitial nephritis, and renal papillary necrosis may occur; increases risk of acute renal failure in patients with preexisting renal disease or compromised renal perfusion; reversible leukopenia may occur (discontinue if persistent leukopenia, granulocytopenia, or thrombocytopenia)
Drug Category: Antihistamines -- These agents are used to reduce pruritus (itching).Drug Name
Cyproheptadine (Periactin) -- Antihistamine-antiserotonergic agent; reported to ameliorate pruritus.
Adult Dose 4 mg PO bid/tid; not to exceed 0.5 mg/kg/d
Pediatric Dose <2 years: Not established
2-6 years: 2 mg PO bid/tid; not to exceed 0.25 mg/kg/d
7-14 years: 4 mg PO bid/tid; not to exceed 0.25 mg/kg/d
Contraindications Documented hypersensitivity, newborns or infants
Interactions Potentiates effects of CNS depressants; MAOIs may prolong and intensify anticholinergic and sedative effects
Pregnancy B - Usually safe but benefits must outweigh the risks.
Precautions Caution in patients with predisposition to urinary retention, history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, or hypertension; may thicken bronchial secretions caused by anticholinergic properties and may inhibit expectoration and sinus drainage
Drug Name
Diphenhydramine (Benadryl, Benylin) -- For relief of symptoms caused by release of histamine in pruritus.
Adult Dose 25-50 mg PO/IV/IM q4-6h
Pediatric Dose 5 mg/kg/d divided q4-6h
Contraindications Documented hypersensitivity
Interactions Potentiates effect of CNS depressants; because of alcohol content, do not give syrup form to patient taking medications that can cause disulfiramlike reactions
Pregnancy B - Usually safe but benefits must outweigh the risks.
Precautions Avoid in first trimester; unsafe when breastfeeding; may exacerbate angle-closure glaucoma, hyperthyroidism, peptic ulcer, and urinary tract obstruction
Drug Name
Hydroxyzine (Atarax, Vistaril) -- Antagonizes H1 receptors in periphery. May suppress histamine activity in subcortical region of CNS. Has antipruritic effects.
Adult Dose 0.5-1 mg/kg or 25-100 mg PO/IM qd/qid
Pediatric Dose Not recommended
Contraindications Documented hypersensitivity
Interactions Alcohol or other CNS depressants may cause CNS depression
Pregnancy C - Safety for use during pregnancy has not been established.
Precautions Avoid when breastfeeding; associated with clinical exacerbations of porphyria (may not be safe for porphyric patients); ECG abnormalities (alterations in T waves) may occur; may cause drowsiness
FOLLOW-UP Section 8 of 9
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Further Outpatient Care:

During the recovery period, victims of ciguatera poisoning should avoid ingesting any of the following, which cause an exacerbation of symptoms:
Any fish products
Shellfish products
Alcoholic beverages
Nuts
Nut oils
Opiates and barbiturates also may exacerbate symptoms and are not recommended.
Deterrence/Prevention:

Avoiding consumption of tropical reef fish is the only true method of prevention. Although this method is not practical in all circumstances, the following can decrease the incidence of ciguatoxin poisoning:
Avoiding ingestion of fish larger than 2-3 kg that are at the top of the food chain
Avoiding all visceral organ and gonad meat (where ciguatoxin is concentrated)
Prognosis:

Excellent

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