Treating Influenza continued

Finally, a recent study by Hayden analyzed 1,559 healthy, non-immunized patients who were treated either with placebo or oseltamivir for six weeks.[10] At the end of the six week period, 4.8% of the placebo group had laboratory confirmed flu compared with only 1.2% of the oseltamivir group. Additional studies are on-going analyzing both treatment efficacy as well as the profinitive effects of the neuraminidase inhibitors.

The decision by the EM physician on whether to prescribe one of the newer neuraminidase inhibitors should be individualized to the patient and the likelihood of actually having influenza A or B, and potential benefit that may occur. Advantages for prescribing these agents include a significant reduction in illness severity as well as reducing total illness duration. The elderly and high-risk patients also have decreased secondary complications of influenza when treated with these agents.

Disadvantages include potential side effects and costs. However, many patients are willing to pay $50 to have a less severe bout of the flu. Side effects include: 1) potential bronchospasm with inhaled zanamivir and, 2) nausea, vomiting and headache from oseltamivir. The bronchospasm associated with zanamivir has received attention from the national media. Until more data is available, physicians should not prescribe zanamivir to patients prone to bronchospasm.

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TOPICS IN TOXICOLOGY

CIGUATERA FISH POISONING

Troy M. Falck, M.D.
Jeffrey R. Suchard, M.D.
Division of Emergency Medicine
University of California-Irvine Medical Center
Orange, CA

Ciguatera poisoning is the most common foodborne illness related to fish consumption both within the United States and worldwide.[1] Ciguatera is found in a broad global belt within 35 degrees of latitude of the equator. Around the U.S., ciguatera is endemic in the Caribbean region, Mexico, Florida, Hawaii and other Pacific island territories. Since ciguatera is not a reportable public health disease, its epidemiology is not completely understood. Nevertheless, large common source epidemics have been described, including a recent series of 25 cases in Southern California Emergency Departments.[2] In Southern Florida, data suggest an annual incidence of five cases of ciguatera poisoning per 10,000 people, while the incidence rates in the South Pacific range up to 600 cases per 10,000.[3] Worldwide, it is estimated that over 25,000 people are affected by ciguatera fish poisoning annually.[4] Within California, local fish carry low risk, even those caught off of the Baja coast; whereas, higher risk fish imported from tropical waters might be found in any restaurant.

Ciguatera is an icthyosarcotoxicosis: food poisoning by the ingestion of toxin-contaminated fish meat. *Gambierdiscus toxicus* is the single-cell dinoflagellate that is responsible for the disease. It is believed that the presence of specific bacteria, phagocytized by the dinoflagellate, is required to synthesize ciguatoxin. *G. toxicus* attaches itself to dead coral surfaces and algae, and the toxins are passed up the food chain from small herbivorous fish to large carnivorous fish to larger predatory fish, and finally to man. The toxin load becomes concentrated as it moves up the food chain, although fish harboring the toxin do not appear to suffer ill effects. The proliferation of *G. toxicus* appears to be related to disturbances if the reef ecosystem. Toxic fish are more often found on the windward side of tropical islands where wave energy and storm damage are greater. Storms, floods, tidal waves, and man-made processes such as anchoring, mining, dredging, and military bombing all appear to increase proliferation of the organism.

Over 400 species of fish are associated with ciguatera poisoning. In the U.S., the greatest risk comes from consumption of grouper, red snapper, barracuda and jacks. Large, bottom-feeding, reef-dwelling fish caught in shallow water carry the greatest risk of contamination. Affected fish can not be identified by inspection, taste, smell or texture. Several non-specific methods for detecting contaminated fish are employed in Pacific island cultures, such as rubbing the fish liver on the gums or tasting the slime of the fish's eye. If a tingling sensation occurs, the fish is considered toxic. Others feed the fish to domestic animals and observe how they react.

Ciguatoxin is one of the most potent toxins known, with an LD_{50} estimated at 20 ng/kg.[4] Ciguatoxin is a heat-stable, lipid-soluble polyether that is not inactivated by cooking, freezing, drying, salting, smoking or marinating.[5] The toxin opens and prolongs the activated state of voltage-gated sodium channels in cell membranes. In neural tissue, this increase in sodium permeability results in a prolonged refractory period and a supernormal period of excitability.[4]

Ciguatera Fish Poisoning continued

Clinical manifestations vary depending on the amount and parts of the fish eaten, fish species and size.[5] Eating the viscera, liver, or brain of affected fish usually results in more serious toxicity because of higher toxin concentrations in these tissues. Symptom onset is generally within 6 hours. Patients will usually present to the ED with prominent gastrointestinal (GI) symptoms, including nausea, vomiting or diarrhea, and less often with hypersalivation and abdominal pain.

The most distinctive and persistent features of ciguatera fish poisoning relate to neurotoxicity. Typical neurologic complaints include circumoral and extremity numbness and tingling, and pruritus. A reversal of hot and cold temperature sensation is essentially pathognomonic for ciguatera poisoning;[7] victims may experience a hot shower as bitterly cold, or a cool drink as burning hot. Cranial nerve dysfunction has also been reported. Cardiovascular effects are rare, but usually consist of hypotension and bradycardia when they occur. In Australia, an association has been reported between ciguatoxin-positive blood specimens and chronic fatigue syndrome.[8] Reports also exist of women with exacerbation of symptoms during menses or in association with sexual intercourse, and men with severe penile shaft pain during erection.[9]

The toxin can be stored in adipose tissue for several years and symptoms may recur during periods of stress, weight loss, and excessive alcohol use. The median duration of illness is two to three weeks. A chronic phase of the disease has been reported where recovery may take years. Chronicity has been associated with worse symptom severity, a longer latency period, and a longer duration of peak symptoms. The mortality rate for ciguatera poisoning is estimated at 0.1% of cases, with death resulting from cardiac or respiratory failure.

Ciguatera may potentially be confused with scombroid fish poisoning, since both may present to the ED with prominent gastrointestinal distress after consumption of fish. Scombroid generally occurs from ingesting dark-fleshed fish that have been improperly handled. If not kept properly chilled, bacteria may proliferate and decarboxylate histidine in the muscle to histamine. Ingestion of excess histamine causes GI distress and flushing, which can resemble an allergic reaction. Scombroid does not, however, cause prominent neurotoxic effects, and ciguatera does not cause intense flushing.[4] At triage in the ED, it may also be possible to confuse the symptoms of ciguatera with more ordinary staphylococcal food poisoning, or indeed even with acute anxiety. A brief history of recent food consumption should be able to discriminate between such patients, although it is likely in non-endemic areas that a patient with ciguatera poisoning could be asked to wait several hours to be seen in a busy ED.

With the increasing prevalence of imported fish and travel by patients, ciguatera should be considered whether illness occurs in endemic areas or not. A history of ingesting marine fish in conjunction with the onset of characteristic gastrointestinal and neurologic effects is sufficient to make the clinical diagnosis. Specific assays to detect ciguatoxin exist, but are not widely available.

Medical management is supportive. Most cases of ciguatera are self-limited. If the patient presents soon after ingestion of the fish, gastrointestinal decontamination with activated charcoal and/or lavage should be considered. More severe or rapidly-progressing cases may require IV fluids, cardiac and respiratory support. Mannitol is the drug of choice for acute ciguatera fish poisoning. The dose is 1 g/kg IV given over 30 minutes. Mannitol's mechanism of action is not fully understood. Mannitol is an effective scavenger of hydroxyl groups, which are plentiful on ciguatoxin. The osmotic diuretic effect may enhance renal toxin clearance. Mannitol may also alter neurotoxic effects by shrinking edematous axons. Symptomatic therapy may consist of antiemetics, antidiarrheals, analgesics, and antipruritics.

As with other toxic ingestions, prevention is key. Avoid eating grouper, snapper and jacks in endemic regions, and never eat barracuda or moray eel. Avoid any fish considered to be harmful by the local population, and avoid the liver, gonads, head and viscera from any marine fish.

CIGUATERA AT-A-GLANCE

Symptoms	**Gastrointestinal**: diarrhea, nausea, vomiting, abdominal pain **Neurologic**: paresthesias, temperature reversal Cardiovascular: bradycardia, hypotension Musculoskeletal: arthralgias, myalgias
Diagnosis	Mostly clinical Ciguatera assay available
Prevention	**Avoid high-risk fish**: barracuda, snapper, jacks, grouper, moray eel, mullets, wrasses, parrotfishes
Treatment	Consider GI decontamination Supportive care IV **mannitol** for moderate to severe cases

See page 11 for assay information.

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