

Travel Medicine

Seafood Poisoning

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Introduction

The incidence of seafood poisoning, as a subset of food poisoning, is increasing. In the United States, fish, shellfish, and other marine organisms are responsible for at least 1 in 6 food poisoning outbreaks with a known etiology, and for 15% of the deaths associated with these particular outbreaks. In other parts of the world, the impact of seafood poisoning is even greater. From 1971-1990, seafood was the single most important vehicle in food poisoning outbreaks in Korea (32%) and Japan (22%). Therefore, international travelers are at particular risk for seafood poisoning.

As with general food poisoning, seafood poisonings share the following epidemiologic characteristics: ingestion as the primary route of exposure, a wide variety of etiologies (bacterial, viral, parasitic, and toxin), significant under-reporting, and an apparently increasing incidence in human populations. Seafood poisonings also have a similar approach to treatment, diagnosis and prevention as general food poisoning episodes, with some specific exceptions.

General Epidemiologic Issues of Seafood Poisoning

Seafood poisonings, as with most foodborne diseases, are under-diagnosed and under-reported. They tend to occur in disease clusters due to both cultural eating habits (ie. eating in families) and commerce (ie eating in restaurants). Meanwhile seafood consumption is increasing worldwide.

As with other foodborne pathogens, the internationalization of the food supply -- over 50% of the commercial seafood eaten in the U.S. is imported -- has greatly facilitated the transmission of seafood pathogens. National and international commerce allows for the rapid and wide geographic spread of contaminated seafood. Examples range from cholera on international airplanes to Norwalk-like gastroenteritis in 5 different states associated with the same contaminated collection site. The pathogenic organisms themselves can cross national and international boundaries, as seen with the spread of bacterial and dinoflagellate species through the dumping of ballast and bilge water from international shipping.

Seafood poisoning has certain transmission mechanisms in common with all foodborne illness. One is improper food handling. In 1992, the Centers for Disease Control and Prevention (CDC) reported contributing factors for foodborne outbreaks including: improper holding temperatures (62%), inadequate cooking (29%), contaminated equipment (18%), food from unsafe source (7%), and poor personal hygiene (29%). For seafood as for other types of food, the relative importance of restaurant and other commercial establishments versus private food sources in the epidemiology of food poisoning is unclear. In the US, 20% of the seafood consumed is derived from recreational and/or subsistence fishing outside most public health controls. A further

global problem with all foodborne illness outbreaks is that, in non-endemic areas, medical personnel will often not recognize the illness or know of reporting requirements, further clouding the true epidemiologic picture due to significant under-reporting.

Seafood poisoning also varies etiologically by vehicle or transvector. In the United States during the period 1983-92, fish was the transvector for scombroid and ciguatoxin, while shellfish was the transvector for Norwalk-like viruses, paralytic shellfish poisoning, *Vibrio* species, and hepatitis A virus.

Different ethnic subpopulations also have different seafood consumption and preparation patterns. For example, many southeast Asian and south American groups traditionally eat raw fish, while northern Europeans consume fish preserved by pickling. These cultural differences have important implications for prevention and control. Health warnings that are not culturally targeted and in the appropriate language may not reach these ethnic subpopulations. In addition, many populations, including ethnic subpopulations, believe that the consumption of raw seafood is healthier and/or has aphrodisiac properties (as with raw oysters or fugu/pufferfish) .

In addition to the transmission mechanisms it shares with other foodborne illnesses, seafood poisoning has unique modes of transmission related to the marine environment. Discharge of treated and untreated human fecal material, other sewage, and industrial wastes into estuaries and coastal waters is extremely common, even in developed nations. The coastal waters of the U.S. receive more than 30,000 million liters of municipal sewage each day. Viruses can settle out of the water column and attach to sands, clays, aquatic life forms, and sediments, accumulating in the loose layer over the compact bottom sediment. This layer can be easily resuspended after storms, dredging or even boating; tidal currents can then transport these resuspended viruses to distant waters.

Shellfish, especially the filter feeding bivalve mollusks (oysters, scallops, mussels, clams, cockles) live in estuarine areas and obtain their food by filtering large amounts of water. A wide variety of organisms and toxins pathogenic to humans can accumulate in the shellfish alimentary tract, especially if the filtered water is contaminated by sewage or chemical pollutants. After contamination, it can take hours to weeks of filtering in uncontaminated water before these pathogenic organisms are removed. Since the alimentary tract of these bivalves forms the major edible portion for humans, these mollusks can serve as extremely effective vehicles for a wide range of organisms and toxins pathogenic to humans. The other commonly consumed group of shellfish is the crustaceans (e.g. shrimp, crab, and lobsters). Although not filter feeders, they can acquire surface contamination from contaminated water.

General Medical Management of Seafood Poisonings

In general, the approach to the medical management of seafood poisoning does not differ significantly from that of any food poisoning. In acute disease situations, the emphasis is

on assessing and symptomatically treating the patient; the exact etiology of the seafood poisoning is important for only a few etiologies from the point of view of particular treatment options. In the chronic disease situation, the correct diagnosis of seafood poisoning can prevent an expensive and invasive work up of the patient. In both cases, but especially acute illness, reporting of suspected seafood poisoning outbreaks to public health authorities can prevent additional cases of poisoning, as well as lead to appropriate diagnosis in already exposed persons.

Treatment of Seafood Poisonings
<p>Acute Illness:</p> <ol style="list-style-type: none"> 1. Assess the patient for fluid and electrolyte status; 2. Stabilize patient for fluid and electrolyte status; 3. Collect diagnostic samples: food, stool, vomitus, blood, urine, biopsy, (store extra samples if possible for future analyses); 4. Take History, physical examination; 5. Institute specific medical interventions if precise etiology known; 6. Report illness to public health authority including possible additional cases; 7. Follow up patient and evaluate for possible chronic sequelae; 8. Recommend preventative measures.
<p>Chronic Illness:</p> <ol style="list-style-type: none"> 1. Take History, physical examination; 2. Collect diagnostic samples: food, stool, vomitus, blood, urine, biopsy, (store extra samples if possible for future analyses); 3. Institute specific medical interventions if precise etiology known; 4. Report illness to public health authority including possible additional cases; 5. Follow up patient for possible chronic sequelae; 6. Recommend preventative measures.

Specific Seafood Pathogens (see Table 1)

Bacteria

Traditionally, the most frequently reported seafood poisoning outbreaks have been associated with bacteria. Although increased sophistication of laboratory testing now implicates viral origin, new bacteria-associated seafood poisonings are appearing due to increasing worldwide seafood consumption by sensitive subpopulations.

Vibrios

Vibrios are natural inhabitants of marine environments. Pathogenic marine *Vibrio* species, especially *V. cholerae*, *V. parahaemolyticus*, and *V. vulnificus*, most commonly cause disease when they are ingested in raw shellfish and, less commonly, in fish (47, 48). Many

Vibrio species are not associated with fecal contamination, so the use of fecal coliform counts as clean water indicators does not ensure that water or seafood beds are free of pathogenic vibrios (3).

Cholera, caused by the toxin-producing *V. cholerae*, can be a severe infection with mortality rates as high as 50%, but is more commonly an asymptomatic infection. Seafood is the most common vehicle of outbreaks. The infection can be acquired through fecal contamination of food by a person who is ill or an asymptomatic carrier; through seafood harvested in a sewage contaminated area; or through seafood gathered in natural environmental reservoirs of *V. cholerae*. Nevertheless, epidemiologic studies have shown that unhygienic food handling in the home or on the street are the most common sources of seafoodborne cholera (37, 49).

Cholera has the potential for rapid international spread, as evidenced by the seven pandemics since 1817, including the recent Peruvian epidemic. In a particularly dramatic example of the potential for spread of disease through international travel, 75 people developed cholera after taking an airplane flight from Latin America to California during which they consumed a cold seafood salad plate from Lima, Peru (38-40). In another example of international spread, shellfish beds in the U.S. have been contaminated with *V. cholerae* transported in the bilge and ballast of ships arriving from Latin America (37, 43). *V. parahaemolyticus* is associated with the consumption of inadequately cooked or refrigerated crustaceans and fish (36). In Japan, up to 50% of reported foodborne outbreaks have been caused by *V. parahaemolyticus*; in Guam, the risk of laboratory confirmed *V. parahaemolyticus* food poisoning was highly associated with recent seafood consumption, especially fish (OR=37.59, CI 8.30-220.2).

In the U.S., *V. vulnificus* is rare outside the Gulf of Mexico coast states, but relatively common in these states; Florida recorded 141 cases during the period 1981-93. This organism can be associated with mortality as high as 50% in persons who are immunocompromised or have liver disease; the risk of oyster-related *V. vulnificus* infection is 80 times greater in adults with a history of liver disease or who have chronic alcoholism (2, 26, 46, 48-50). The risk of infection from eating oysters is highest in the months April through October, when more than 90% of raw oyster-associated *V. vulnificus* infections occur (51). Florida and other states laws require restaurants that serve raw oysters to post warnings about the danger of consuming raw oysters. Although not directly seafood consumption, *V. vulnificus* also can cause wound infections in persons who go wading or swimming in contaminated waters. In Florida, during the period 1981 through 1993, one-third of the 141 *V. vulnificus* infections were wound infections occur (51).

Listeria

In New Zealand and elsewhere, *Listeria monocytogenes*, found on the external surfaces of fresh and frozen fish as well as in the processing plant environment, has been implicated in several seafoodborne outbreaks of listeriosis. These outbreaks have included perinatal infections associated with transmission from infected mothers, who may be asymptomatic

(52, 53). There has been a wide range of seafood transvectors associated with these reported listeriosis outbreaks, from raw fish and shellfish to ready-to-eat (but insufficiently processed) cooked shrimp and crabmeat, and smoked mussels.

Salmonella

Salmonella and *Aeromonas* species are frequent contaminants of raw fish and shellfish, especially if the seafood has had prolonged exposure to elevated temperatures. The risk of transmission is higher for shellfish than for fish because shellfish often are refrigerated for many days without obvious spoilage and then eaten raw (30, 54). As with *Vibrio* infections, persons who are elderly, immunocompromised or very young are at greater risk for more severe gastroenteritis after infection with *Aeromonas*, especially enteropathogenic strains.

Other

A wide spectrum of bacterial species has been cultured from shellfish and fish without definitive etiologic connections to seafood poisoning outbreaks (53-57). Some of these organisms, like *Aeromonas*, are part of the normal flora of the seafood. Others are more likely introduced by unhygienic human handling; enterotoxigenic *Escherichia coli*, the common pathogen of travelers' diarrhea, and *Staphylococcus aureus* have both been detected on seafood (54-58).

Future threats

International trade in feral-harvested seafood and increasingly in aquaculture seafood products has facilitated the introduction of pathogens into new geographic areas, as well as into seafood and human communities (31). For example, *Salmonella agona* was first introduced to Europe following the importation of Peruvian fishmeal, with subsequent rapid spread into other food products, producing an increase in human outbreaks. Furthermore, the intensive use of antibiotics in the aquaculture industry, leading to antibiotic accumulation in seafood tissues, increases the potential for development of multiply-resistant bacteria (59, 60).

Viruses

As discussed above, shellfish harvested in waters contaminated with raw or inadequately treated sewage are extremely efficient transvectors of seafood pathogens because the shellfish filter the water as they feed, concentrating the pathogens (1, 2, 30, 61). Refrigeration paradoxically increases the pathogens' geographic range, permitting transport of apparently healthy shellfish to many geographic areas, thus extending and prolonging outbreaks. Inadequate procedures for tracing and recall of contaminated seafood also serve to extend outbreaks (17, 18, 27).

Small round structured (Norwalk-like) viruses (SRSVs)

In the period 1978-87, approximately a third of seafood outbreaks in the U.S. and two-thirds of cases were associated with consumption of raw molluscan shellfish, according to

CDC and Food and Drug Administration records (2). In the majority of these cases, the pathogens were small round structured viruses (SRSVs) (26, 30, 46).

SRSVs, or Norwalk-like viruses, are classified as caliciviruses and are common causes of outbreaks of gastrointestinal illness in the United States. Because the infectious dose is small, cooking the shellfish does not reliably eliminate the risk of contracting gastroenteritis. For example, in an outbreak of Norwalk-like gastroenteritis in North Carolina following consumption of oysters at church suppers, the attack rate (56%) did not differ based on whether the oysters were eaten raw or steamed for at least 12 minutes. Outbreaks of Norwalk-like gastroenteritis have been reported after grilling, stewing, steaming, and frying the shellfish (26, 27, 62). Furthermore, routine water quality tests from the areas of contaminated shellfish collection were within normal limits, demonstrating that fecal coliform monitoring is inadequate protection for SRSV contamination (27, 63).

Hepatitis A

The proportion of hepatitis A cases in the U.S. that are attributable to foodborne or waterborne outbreaks is small (7.5% in the period 1983-9) (46). Nevertheless, the most common cause of these outbreaks is the consumption of raw or inadequately prepared shellfish taken from sewage contaminated waters (36, 45, 64, 65). As with other seafood-related pathogens such as *V. cholerae*, seafood poisoning with hepatitis A has been associated with significant geographic spread due to seafood export patterns. For example, an outbreak of hepatitis A after consumption of raw oysters from Florida resulted in cases in 5 different states, including Hawaii (41).

Parasites

Consumption of raw and inadequately cooked seafood, especially in certain ethnic subpopulations, is associated with parasitic infections, particularly with anisakids and cestodes (2, 36). Correct food preparation and handling will eliminate the majority of these diseases.

Anasikiasis

Anasikiasis is a rare nematode (roundworm) infection acquired through the consumption of raw fish (especially cod, herring, mackerel and salmon) and cephalopods (such as squid). Traditionally associated with Asian cultures, because of changing consumption patterns anasikiasis is now reported in Europe and the US, although rarely (66, 67). Although often asymptomatic, patients can present with eosinophilia, abdominal discomfort, invasion, or hemorrhage due to burrowing of the worm, as well as granulomatous reaction and frank allergic reactions (36, 46, 67). A similar disease associated with the helminth *Gnathostoma* has been reported in Southeast Asia, and the Middle East.

Diphyllobothriasis

Diphyllobothriasis or fish tapeworm disease was traditionally associated with gefilte fish preparation by Jewish women; although often asymptomatic, megaloblastic anemia

(secondary to vitamin B₁₂ deficiency) and eosinophilia are classic findings. Approximately 10% of people in Scandinavia are reportedly infected with *Diphyllobothrium*. Although usually associated with freshwater fish consumption, *Diphyllobothriasis* has been reported with the ingestion of raw Pacific salmon (36, 68).

Allergies

Seafood allergies include true food allergy (i.e. Type I IgE-mediated hypersensitivity) and food intolerance (ie. non-immunologic hypersensitivity) (69, 70). It is estimated that 3% of 3 year old Finnish children are allergic to fish and the prevalence of fish allergy is close to 1/1000 in the general Norwegian population (69). In a study in Spain of 3034 persons over 14 years seen as outpatients in an allergy unit, skin testing and/or RAST testing found 30 (0.98%) persons with a possible food allergy, with 14.9% related to seafood (especially shellfish) and 4.2% to fish. Symptoms ranged from acute cutaneous disorders to gastrointestinal complaints to respiratory symptoms (71). In South Africa, among 105 persons with suspected fish allergy, adverse reactions were reported with shellfish (prawns (46.7%), crayfish (43.8%), abalone (35.2%), and black mussels (33.3%), and with fish (hake (24.8%), yellowtail (21.9%), salmon (15.2%), and mackerel (15.2%); these reports were confirmed by double-blind, placebo controlled, food challenge (69).

Allergic reactions, ranging from urticaria to anaphylaxis, have been reported after consumption of seafood with parasitic or certain natural toxin (i.e. scombroid) contamination. Allergic reactions after seafood ingestion have been reported even with negative skin test to fish or shellfish; these are often associated with parasitic infestation or exposure and specific allergic reaction, rather than seafood associated allergy. In particular, chronic intermittent allergic reactions type I and/or III with eosinophilia have been reported after the consumption of Anisakidae-parasitized fish. The ingestion of even safely cooked but Anisakidae-parasitized fish has lead to allergic reactions with IgE-mediated sensitization (66, 67, 72).

Toxins

The marine environment contains a variety of chemicals, both natural and manmade, that can be acutely and/or chronically toxic to humans if ingested in large enough quantities. Unfortunately, the marine organisms that humans prefer as food tend to concentrate toxins through a process known as bioaccumulation. Many of the fish that humans eat are at the top of the marine food chain; that is, they are predators (salmon) or even predators of predators (sharks). Toxins from the smaller organisms these predators eat accumulate in the predators' tissues, particularly if the toxins are lipophilic, and often reach levels high enough to cause acute or chronic disease in humans. The largest and oldest fish of each species contain the most toxin, and also tend to be the most desired by seafood consumers. Molluscan shellfish, also prized as a food source, are filter feeders, concentrating natural and chemical toxins indiscriminately (2, 46, 73, 74). Often the toxins that marine organisms accumulate have no obvious health effects on the fish and shellfish, thus they remain

available for capture for human consumption, and they appear healthy and appetizing to the consumer.

Among the diseases caused by natural toxins, only scombroid, botulism, ciguatera, PSP and tetrodotoxin (fugu) are required to be reported to the CDC (1). Individual states may require reporting of other diseases (26). Therefore, as with all the seafoodborne diseases, under-reporting is a major epidemiologic issue.

Bacterial

The seafood diseases caused by bacterial toxins generally are associated with improper food preparation, handling and storage. Scombroid is probably the most commonly reported fish-associated illness in the U.S. (1, 3, 36, 69, 70, 75). It is often mistakenly diagnosed as fish allergy because the symptoms resemble an IgE-mediated reaction and respond rapidly to antihistamines. Scombroid actually is caused by bacterial overgrowth associated with inadequate fish storage, especially of fish in the Scombroidae family (i.e. tuna, mackerel, and jacks) as well as mahi-mahi or dolphin fish, bluefish, and sardines. The surface bacteria (e.g. halophilic *Vibrio* spp, *Proteus*, *Klebsiella*, *Enterobacteriaceae*) decarboxylate the histidine present naturally in dark meat fish to produce high levels of histamine, optimally when the temperature is between 20°C to 30°C. The phenomenon occurs with consumption of fresh and canned fish.

The bacteria *Clostridium botulinum* type E is most prevalent in fresh water and marine environments. The bacteria produce botulism toxin E on smoked fish, fish eggs, and unviscerated and salted whitefish. The majority of the cases are associated with inadequate canning procedures. Although smoking or light cooking may not kill the bacterial spores, the toxin is heat labile. The toxin produces an acute gastroenteritis followed by cranial nerve dysfunction and symmetrical descending weakness. Although rare, this disease is occasionally seen among ethnic minority communities and with home canned fish (2, 35, 36, 70).

Staphylococcus aureus elaborates an enterotoxin on improperly stored seafood, especially if the fish is garnished with cream sauces or mayonnaise (70).

Marine

The marine toxin diseases are caused by myriad natural toxins produced by minute organisms called dinoflagellates and diatoms. These phytoplankton are part of the base of the marine food web and are ubiquitous in the marine world (76). Humans are most often exposed through consumption of fish and shellfish that accumulate these toxins. The toxins, small non-peptides, are some of the most powerful natural substances known; ciguatoxin is toxic to humans in a total body dose of 70 nanograms. Because these toxins are tasteless, odorless, and heat and acid stable, normal screening and food preparation procedures will not prevent intoxication if the fish or shellfish is contaminated (42, 77).

The marine toxin diseases are categorized into two groups based on their primary

transvectors. Shellfish harbor the toxins that produce paralytic shellfish poisoning (PSP), neurotoxic shellfish poisoning (NSP), diarrhetic shellfish poisoning (DSP), and amnesic shellfish poisoning (ASP). Fish carry the toxins responsible for ciguatera poisoning and tetrodotoxin (fugu or pufferfish) poisoning. The shellfish-associated diseases generally occur in association with algal blooms or "red tides," which may be characterized by patches of discolored water and dead or dying fish. The fish-associated diseases are more localized to specific reef areas (ciguatera poisoning) and fish (fugu poisoning).

Under-diagnosis and under-reporting, especially in endemic areas, make it difficult to know the true worldwide incidence of the marine toxin diseases. For example, it is believed that ciguatera affects at least 50,000 - 100,000 people per year who live in or visit tropical and subtropical areas, but there is significant under-reporting of this relatively common marine toxin disease in endemic areas. (16, 42).

The primary target of marine toxins is the neurologic system, although affected individuals usually present with a wide range of symptoms, resulting in a confusing clinical picture. Gastrointestinal symptoms begin minutes to hours after eating contaminated seafood. In the case of PSP, fugu, and ciguatera, accompanying acute respiratory distress may be fatal within hours. Ciguatera and ASP may also produce debilitating chronic neurologic symptoms lasting months to years. Chronic disease (neurologic, immunologic, etc) associated with the marine toxins is an area of active scientific research.

In the past, these illnesses have been highly localized to endemic island and coastal communities. With increasing worldwide seafood consumption and trade, as well as international tourism, these diseases are expanding beyond their traditional geographic boundaries. One side effect has been the high costs of diagnosis and treatment of disease in traditionally non-endemic areas. In Canada, with an estimated 1000 cases per year related to tourism and food importation, the average medical cost per case is \$2470 (78, 79).

In addition to increased worldwide seafood consumption, other anthropogenic factors may have helped spread the dinoflagellates and their toxins. Human-assisted transportation of the dinoflagellates or their cysts occurs in spat cultivation (young bivalve shellfish sold commercially to global markets for aquaculture) and dumping of ship ballast water. In response, new international regulations will require ships to purge ballast water in the open ocean prior to docking (43). Human-generated environmental changes, such as reef destruction and eutrophication, also may help explain the apparent increase in human marine toxin disease as well as the increase in red tides reported worldwide.

Global climate changes, which some suggest are linked to human activities, also may help explain the apparent global increase of algal blooms as well as the appearance of new marine toxin diseases like pfiesteria (31, 77, 80-82). There is even new research connecting red tides to cholera outbreaks since cephalopods carrying *V. cholerae* feed on marine algal blooms; thus these algal blooms can lead to cholera dissemination and outbreaks

associated with increasingly frequent monsoon flooding (81).

Paralytic Shellfish Poisoning (PSP):

Classic PSP symptoms include paresthesias of the mouth and extremities, frequently accompanied by gastrointestinal symptoms, within minutes to hours after eating. The disease occurs worldwide. Although often associated with a red tide or algal bloom, significant epidemics of PSP can occur in humans in the absence of a known red tide, as discussed in Box 2 with the Guatemalan PSP epidemic of 1987 (28). The dinoflagellates associated with PSP produce at least 12 toxins that are heat and acid stable; saxitoxin was the first characterized and the best understood (42).

In a population-based study in Alaska after 5 local outbreaks of PSP, 70% of the 170 people interviewed had eaten shellfish gathered from the same area and 13% reported symptoms consistent with at least one episode of PSP (83). The case fatality rate was about 8.5-9.5% in two large series; the 1987 Guatemalan outbreak on the Pacific coast had a case fatality rate of 14% overall, but 50% in young children, who may be more sensitive to PSP toxins. Access to emergency medical services in acute cases is crucial to survival. Chronic health effects have not been studied (28).

Neurotoxic Shellfish Poisoning (NSP):

Red tides that occur off the Florida coasts are associated with two distinct clinical syndromes depending on the route of exposure. Ingestion of contaminated shellfish (and less commonly contaminated fish) causes gastroenteritis and neurologic symptoms similar to but less severe than those associated with PSP. Inhalation of toxins, predominantly brevetoxin, from the seaspray associated with the red tide and accompanying fish kills causes an upper respiratory syndrome in humans and other mammals (42). The classic causative organism, *Gymnodinium breve*, is a dinoflagellate restricted to the Gulf of Mexico and the Caribbean waters, although similar species occur throughout the world (84).

NSP was first identified by Walker in 1844 on the west coast of Florida. Since then, NSP has been reported from the Gulf of Mexico (including the coasts of Texas, Alabama and Mississippi), the east coast of Florida, and the North Carolina coast, as well as northern Spain, the eastern Mediterranean, Japan, and New Zealand. Recent prolonged NSP red tides in the Gulf of Mexico have been associated with die-offs of endangered manatees as well as respiratory problems among humans (26, 85). Fish feed harvested from red tide-contaminated areas also has been blamed for fish kills in the aquaculture industry.

Diarrheic Shellfish Poisoning (DSP):

The first cases of DSP were reported from the Netherlands in the 1960s, followed by similar reports in the late 1970s from Japan. Since then, more than 1300 cases have been reported from Japan, with the peak season from April to September. Other outbreaks have been reported in Europe and South America as well as the Far East (42).

The causative organisms are the marine dinoflagellates *Dinophysis*. These dinoflagellates are widely distributed, but do not always form red tides. They produce at least nine different toxins consisting of okadaic acid and its derivatives. Because okadaic acid is a potent animal carcinogen, the issue of chronic disease from DSP poisoning needs to be addressed in humans (42, 86).

Amnesiac Shellfish Poisoning (ASP):

First recognized in an outbreak on Prince Edward Island in Canada in 1987, this syndrome produces nausea, vomiting, severe headache, abdominal cramps and diarrhea within 15 minutes to 38 hours of eating mussels, accompanied in about 25% of cases by acute memory loss. The 1987 outbreak, associated with consumption of mussels, produced 153 cases and 4 deaths. Some persons with ASP develop apparently permanent neurologic deficits, especially dementia. The toxin responsible is domoic acid, elaborated by the pennate diatom, *Nitzschia pungens*. It has been suggested that the index bloom of the diatom may have been related to fertilizer run-off from extensive tobacco farming in the area (42, 87). The organism later was identified as a continuing problem among seabirds and shellfish in Washington State and Oregon.

Ciguatera Fish Poisoning:

Ciguatera is the most common foodborne illness caused by a marine toxin. Its most distinguishing symptom is temperature reversal (hot coffee tastes cold, ice cream tastes hot). It is caused by the consumption of reef fish that have fed on organisms contaminated with *Gambierdiscus toxicus* and other reef-dwelling dinoflagellates. Ciguatera has been reported since ancient times and occurs in tropical and subtropical areas around the world, with epicenters in the Caribbean and the Indo-Pacific islands. It is not associated with red tides.

Ciguatera is another of the seafood related diseases that have spread geographically because of tourism, and national and international commerce (42, 77). For example, a single amberjack from a dealer in Key West (Florida), sold to 2 restaurants and 2 grocery stores, resulted in at least 20 ciguatera cases in at least 2 states (88). An estimated 10,000 to 50,000 people per year who live in or visit tropical and subtropical areas develop ciguatera poisoning. The CDC and others estimate that only 2-10% of cases is actually reported in the United States.

Human impact on the environment may also have played a role in the spread of ciguatera.

Disturbances of coral reefs by military and other human activities stimulates rapid recolonization by *G. toxicus*, which appears to grow better after disturbance than under normal conditions (77).

Ciguatera has had a measurable social and economic impact in endemic regions. Because the toxin is so widespread among reef fish, and because it cannot be detected by smell or taste or destroyed by cooking, populations in several endemic areas have abandoned local

fish as a food source. Lewis (1986) found that ciguatera in the South Pacific caused depression of both the local and exporting fishing industries and tourism, and had an indirect affect on human health due to avoidance of fresh fish consumption (89)

Pufferfish Poisoning/ Fugu:

Pufferfish poisoning or tetrodotoxin intoxication (fugu) produces symptoms similar to PSP, with case fatality rates as high as 60%. Tetrodotoxin poisoning is found worldwide, associated predominantly with the ingestion of pufferfish. Fugu poisoning was known to the ancient Chinese as early as 2800 BC.

Unlike diseases caused by marine toxins, fugu poisoning is not due to dinoflagellates. The toxin, tetrodotoxin, is found in the order of fish known as Tetraodontiformes, especially in the family Tetraodontidae (pufferfish). Marine bacteria colonize the gut and skin mucosal layers of the puffer following infection, and produce persistent levels of tetrodotoxin which the fish sequesters in gonads, liver, and, to a lesser extent, muscle (42, 77).

The most toxic pufferfish are found along the coasts of China and Japan, where they are considered a delicacy and are eaten only after preparation by specially trained chefs. In Japan, where the seafood is known as fugu, 60 poisonings were reported in the 1974-79 period, with 20 deaths. About 50% of fatal food poisonings in Japan each year are due to eating fugu; cases are more common among men than women, probably related to eating habits. Cases have been reported in Europe associated with the mislabeling of imported fish, and elsewhere in the world due to ignorance of the toxic potential of the pufferfish. Thus, fugu is a very circumscribed public health problem with a high mortality. Chronic health effects have not been studied (42).

Other Natural Marine Toxins

Numerous other types of poisoning are associated with the consumption of a wide variety of fish and shellfish. However, at present these poisonings have very restricted geographic and race-ethnic population distributions. These include a pseudo-allergic reaction after eating Japanese Callista during the spawning season to hallucinatory fish poisoning after eating mullet in the tropical Pacific and Indian Oceans to hypervitaminosis A and neurologic disorders after consuming shark contaminated with unknown toxins (70, 75, 77). In addition, consumption of edible red algae *Aogonori* in Japan has been associated with acute foodborne illness and death (90). As with the other seafood diseases, international seafood commerce, as well as tourism, may change the geographic and population profiles of these illnesses in the future.

Chemical Toxins

Humans, through their industrial activities, liberate mercury and other heavy metals from the earth and send them into the seas, where they bioaccumulate through the food chain and come back to humans in the form of contaminated seafood. Manmade chemicals and chemical byproducts such as polychlorodibenzo-p-dioxins (PCDDs) and polychlorinated biphenyls (PCBs), many of them lipophilic and nondegradable, follow the same pathways

and are consumed by humans. Infants and fetuses are at particular risk because many of these substances are incorporated into breast milk and cross the placenta (74, 91).

Evaluating the impact of these toxins requires a thorough understanding of the ecotoxicology of pollutants. For example, arsenic bioconcentrates in shellfish. Nevertheless, years of research have revealed that little of the organic arsenic accumulated by humans from consumption of seafood is converted into toxic inorganic arsenic. Therefore, seafood containing arsenic represents a low risk to human consumers (92, 93).

Traditionally, it was believed that many chemical toxins contaminated the marine environment through single source polluters such as specific industries. One extreme example of single source pollution was the epidemic of chronic neurologic disease that occurred when the people of Minimata, Japan consumed fish contaminated with a methylmercury effluent from a local chloralkali plant (94). Other examples include highly visible marine oil spills that can force closure of shellfish beds and fish spawning areas for years. For example, after the Braer oil spill in the Shetlands, the sediment of the traditional herring spawning beds rose from a background oil level of 50 ppb to 100-350 ppb (95).

However, in recent years, more global sources of pollution have been recognized. For example, many freshwater and marine fish have become contaminated with methylmercury not from industrial point sources but via a complex exposure pathway originating in global burning of fossil fuel that produced inorganic mercury as a byproduct (33, 74, 96). Atmospheric and oceanic currents then spread this mercury to distant sites. Persistent contaminants such as the heavy metals and the organochlorines have been found in the Arctic food chain and in biological sampling of Arctic natives (74). Even radioactive materials can be bioconcentrated in seafood. Radioactive waste dumping, atmospheric fallout, leaks from spent reactors, and runoff from contaminated rivers have led to measurable radioactivity in seafood found in some Arctic regions (97).

Pesticide residues increasingly are being found in seafood. This is probably due to agricultural runoff and the lipophilic properties of many pesticides that cause them to bioaccumulate in both the seafood and the human consumer. In 1993, in the Food and Drug Administration (FDA) residue monitoring program, 15.8% of 444 imported fish/shellfish samples analyzed for pesticide residues were above regulatory levels; by comparison, only 3.3% of 2261 imported fruits were above regulatory levels during the same sampling time period (98).

Long term exposure to relatively low levels of these chemical contaminants through seafood ingestion may be important in the etiology of immune diseases and cancer. Multiple myeloma, a relatively rare and deadly form of B-cell neoplasm, has been associated with the consumption of fish contaminated with dioxins (possible immunogens) in Baltic Sea fishers and Alaskan natives (99). Recent research points to the increased sensitivity of children, infants and fetuses to heavy metals and pesticides, especially to bioaccumulated neurotoxins, which may lead to dramatic lowering of these allowable

residue levels in seafood and other foods the future (91, 100).

Prevention

Primary disease prevention, the goal of public health, reduces the incidence of disease by preventing human infection (11-13, 22). Secondary and tertiary prevention seek to reduce, respectively, the duration of and complications from disease. Of the three approaches, primary prevention is almost always the most effective, from both economic and public health standpoints, although it may not always be possible. Primary prevention of seafood poisoning has two foci: the environment in which the seafood grows and is processed, and the people who prepare and eat the seafood.

Environmental

After a large outbreak of typhoid fever was traced to contaminated shellfish, in 1925 the U.S. Public Health Service established the Interstate Shellfish Sanitation Program (ISSP) to ensure that contaminated shellfish do not reach the retail market (17, 45).

Recommendations to prevent shellfish contamination included sewage control, limiting shellfish harvests to areas with clean water based on fecal coliform counts, and tagging all boxes of shellfish to indicate harvest location and date. Because fecal coliform counts are not sensitive to the presence of many *Vibrio* species and of Norwalk-like viruses, this has led to a shift from the wastewater-associated bacterial outbreaks to outbreaks involving wastewater-derived viral pathogens and bacteria of environmental origin (101-103).

More recently, in the wake of a 1998 Texas outbreak of *V. parahaemolyticus*, the ISSP has adopted new standards that call for the sampling of shellfish meat in growing areas associated with illnesses caused by *V. parahaemolyticus*.

The recent passage of the National Food Safety Initiative is a significant primary prevention intervention that includes the following seafood safety initiatives (104):

- § Required seafood testing for pathogens and toxins as soon as it has left the hands of the fisher;
- § increased personnel, epidemiologic, and laboratory resources devoted to surveillance programs;
- § implementation of a Hazard Analysis and Critical Control Point (HACCP) approach to seafood processing. HACCP rules require food industries to design and implement preventive measures that identify points where contamination is likely to occur and implement controls to prevent it.

Epidemiologic evaluation will be very important in the future to determine the implementation and efficacy of these programs.

Education

In surveys in Florida and elsewhere, from 17% to 25% of the adult population reported

eating raw clams and oysters in the preceding year (51, 104). These data suggest the need for targeted food safety messages to educate consumers about the dangers of seafoodborne illnesses, especially sensitive subpopulations such as the immunosuppressed, elderly and children. The health care providers of these sensitive subpopulations need to be aware of the potential dangers of seafood consumption. In addition, food processors and food service workers need information about proper food handling procedures for each step of the process from the marine environment to the consumer's plate. Finally, the seafood testing information, as well as food handling and storage procedures, needs to be communicated back to the fisher and the seafood industry to seek out and provide safer seafood.

Conclusions

Seafoodborne poisonings, both acute and chronic, are under-reported, but are probably increasing in incidence and geographic spread. In particular, there has been very little research into chronic disease associated with seafood poisoning. Furthermore, subpopulations, both race-ethnic and immunosuppressed, may be at increased risk for seafood diseases. Although primary prevention is the most desirable, the continual emergence of new seafoodborne diseases signifies that active disease surveillance will always be necessary. Finally, although required by the Food Safety Act in the US, reliance on the testing of food will never be enough since such testing must always be targeted and it will not be possible to test for new or different pathogens and toxins in all seafood prior to human consumption. Therefore, education with regard to seafood safety (particularly issues such as the consumption of raw seafood and the importance of sanitation) will remain important (3, 41).

The education of health care providers and public health officials in traditionally non-endemic areas is necessary concerning the diagnosis and the importance of official reporting of imported Aexotic@ or emerging seafood diseases (40). Targeted groups should be international travelers (both workers and tourists), recent emigrants, certain ethnic subpopulations, and immunosuppressed individuals. In addition, education and cooperation of the seafood industry concerning the risks of the seafoodborne poisonings as well as primary and secondary prevention programs are necessary for these programs to function effectively (11-13, 22). There should also be cooperative exploration of new and inexpensive technologies such as seafood irradiation between international and national health agencies, and the seafood industry (4, 105).

Given the high reported prevalence of disease with multiple etiologies associated with the consumption of raw or inadequately cooked seafood, thorough cooking of all seafood is a basic recommendation (55, 64). This is particularly true for persons who are immunocompromised and/or suffering from liver disease (2, 52, 106), although not a complete panacea (for example, some viruses have high virulence, and many toxins cannot be removed by cooking) (27, 62). Furthermore, it is critical that the necessary time and temperature studies be done with seafood to determine the degree of cooking that will

denature a virus such as SRSV. It is also important to communicate the dangers of raw seafood consumption to ethnic subpopulations, using culturally sensitive and appropriate language (33-35). In addition, laboratory and epidemiologic evaluation of possibly protective culturally acceptable practices such as adding acidic substances (i.e. lemon juice in the Latin American marinated seafood dish of Ceviche against *Vibrio cholera*) should also be explored (14, 15, 37, 38). Alternative technologies such as the use of naturally occurring bacteria in seafood with antagonistic activity towards pathogens such as *Listeria* are being tested (53).

Good sanitation, including facilities for human waste disposal and for proper hand washing with soap, are important to protect food and water supplies. Furthermore, education should be focused on the dangers of human fecal waste near drinking, agricultural or aquacultural water supplies to prevent the contamination of irrigation and run-off waters (37). Educational efforts targeting food handlers (both at home and in the street), food handling and preparation to both prevent fecal contamination, as well as maintain food integrity without spoilage or bacterial overgrowth, should be undertaken (37, 49, 55). Even food storage should be emphasized; for example, in Hong Kong, cholera may have been spread through the consumption of fish kept in tanks with contaminated water from polluted water (47).

As seen in several seafoodborne outbreaks discussed above, national and international commerce can lead to the rapid, wide and prolonged spread of contaminated seafood with multiple resultant disease outbreaks (1, 17, 27, 37, 38, 40, 41). Fecal coliform counts are a good initial screen for water contamination by fecal material, but are inadequate in the case of some bacteria and even more so for many pathogenic viruses and both natural and chemical toxins. New laboratory techniques such as PCR will lead to better diagnosis, tracing and ultimately prevention of seafood poisonings (3, 17, 18).

Todd and Harwig (1996) recommend a risk analysis approach for seafood that have the following characteristics: widely consumed, international sources (both feral and aquaculture), associated with emerging diseases, and potentially produced under unsanitary conditions (30). They emphasize the importance of integrating this risk assessment approach into HACCP system to more accurately determine the hazards and control of seafood processes. They particularly recommend focusing on potentially unsafe preparation and consumption practices (such as raw or smoked seafood), since these processes are known to increase risk of disease. Additional recommendations include economic data collection and presentation to evaluate both the impact and cost effectiveness of intervention programs, as well as of present seafood practices (15, 30, 53, 59). Thus, epidemiology will necessarily play an active role in evaluating the impact of seafood poisonings and their prevention-interventions in the future.

Bibliography

Centers for Disease Control (CDC). (1996). Surveillance for Foodborne Disease Outbreaks C United States, 1988-1992. *M. M. W. R.*, 45:SS-5.

Ahmed, F. E. (1993). Issues in fishery products safety in the United States. *Env. Tox. Water Quality*, 8:141-152.

Lipp, E. K., Rose, J. B. (1997). The role of seafood in foodborne diseases in the United States of America. *Rev. Sci. Tech.*, 16(2):620-640.

Todd, E. (1994). Surveillance of foodborne disease. In *Foodborne Disease Handbook*. Y.H. Hui, J.R. Gorham, K.D. Murrell, D.O. Cliver, eds. Marcel Dekker Inc, New York, pp. 461-536.

Motarjemi, Y., Moy, G., Reilly, A., Kaferstein, F.K. (1988). Food Safety. In *International Occupational and Environmental Medicine*. J.A. Herzstein, W.B. Bunn, L.E. Fleming, M. Harrington, J. Jeyaratnam, I.R. Gardner. Mosby, St. Louis, Missouri, 1998. Pp. 602-619.

Fleming LE, Katz D, Hammond R, Bean JA. (in press) The Epidemiology of Seafood Poisonings. In:

Fleming, L. E., Bean, J. A., Baden, D. G. (1995). Epidemiology of Toxic Marine Phytoplankton. In *UNESCO-IOC Manual on Harmful Marine Phytoplankton #33*. G. M. Hallegraeff, D.A.N. Anderson, A.D. Cembella, eds. UNESCO, Paris.

McDonnell, S., Kirkland, K.B., Hlady, W.G., et al. (1997). Failure of cooking to prevent shellfish-associated viral gastroenteritis. *Arch Int Med.*, 157:111-116.

Todd, E.C.D., Harwig, J. (1996). Microbial risk analysis of food in Canada. *J. Food Protection*, Suppl: 10-18.

Todd, E.C.D. (1994). Emerging diseases associated with seafood toxins and other water-borne agents. *Annals N.Y. Acad. Sci.*, 740:77-94.

Eastaugh, J., Shephard, S. (1989). Infectious and toxic syndromes from fish and shellfish consumption. *Arch. Intern. Med.*, 149:1735-1740.

Eberhart-Phillips, J., Besser, R.E., Tormey, M.P. et al. (1996). An outbreak of cholera from food served on an international aircraft. *Epidemiol. Inf.* 116(1):9-13.

Baden, D., Fleming, L. E., Bean, J. A. (1995). Marine Toxins. In *Handbook of Clinical Neurology: Intoxications of the Nervous System Part II. Natural Toxins and Drugs*. F. A.

- deWolff, F., ed. Elsevier Press, Amsterdam, Netherlands, pp. 141-175.
- Moreno Ancillo, A., Caballero, M.T., Cabanas, R., et al. (1997). Allergic reactions to *Anisakis simplex* parasitizing seafood. *Ann. Allergy Asthma Immunol.*, 79:246-250.
- Bouree, P., Paugam, A., Petithory, J.-C. (1995). Anisakidosis: report of 25 cases and review of the literature. *Comp Immun Microbiol Infect. Dis.*, 18(2):75-84.
- Ayotte, P., Dewailly, E., Bruneau, S., Careau, S., Vezina, A. (1995). Arctic air pollution and human health: what effects should be expected? *Sci. Tot. Env.*, 160/161:529-537.
- Lange, W.R., Snyder, F.R., Fudala, P.J. (1992). Travel and Ciguatera Fish Poisoning. *Arch. Int. Med.*, 152, 2049-53.
- Epstein, P. R., Ford, T.E., Colwell, R.R. (1994). Marine ecosystems. In: *Health and Climate Change*. P.R. Epstein, D. Sharp, eds. The Lancet Ltd, London. pp. 14-17.
- Tester, P.A.(1994). Harmful marine phytoplankton and shellfish toxicity. *Annals N.Y. Acad. Sci.*, 740:69-77.
- Anon. (1994). Food and Drug Administration Pesticide Residue Monitoring: 1993. *J. Ass. Official Anal. Chemists Int.*, 77(5):161A-185A.
- Food and Drug Administration hp. May 1997. online. available: vm.cfsan.fda.gov/~dms/fsreport.html.

Table 1. Reported Seafood Poisoning Outbreaks by Etiology

Etiology	Seafood vehicle/ transvector	Clinical Presentation
<i>Bacterial:</i>		
Salmonella (typhi, paratyphi)	Molluscs	Septicemia
Vibrio (cholerae, parahaemolyticus, mimicus, hollisae, fluvialis, vulnificus)	Molluscs, Crustaceans, Fish	Gastroenteritis, Septicemia (at risk immuno-compromised, liver disease)
	Molluscs	Gastroenteritis
Camphylobacter	Molluscs	Gastroenteritis
Aeromonas hydrophila, veronii sobria, caviae	Shellfish, seafood	Gastroenteritis (at risk immuno-compromised)
Bacillus cereus	Shellfish	Gastroenteritis
Edwardsiella tarda	Shellfish	Gastroenteritis
E. coli (including enterotoxigenic)	Shellfish, Seafood	Gastroenteritis
Listeria monocytogenes	Seafood	Listeriosis
<i>Viral:</i>		
Hepatitis A	Molluscs	Hepatitis
Small Round Structured Viruses, Norwalk- Like Viruses (Norwalk, Cockle, Snow Mountain, Calicivirus)	Shellfish	Gastroenteritis
Rotavirus	Shellfish	Gastroenteritis
Astrovirus	Shellfish	Gastroenteritis
<i>Parasitic:</i>		

Anisakis	Fish (raw) herring, cod, whiting, haddock, salmon	Abdominal discomfort, Eosinophilia, Allergy
Gnathostoma	Fish	Abdominal discomfort, Eosinophilia, Allergy, Eosinophilic Meningitis
Diphyllobothrium Latum	Fish (raw) Gefilte fish, Salmon	Gastroenteritis, Anemia (B ₁₂), Eosinophilia
Giardia lamblia	Salmon	Giardiasis
Nanophyetus salmincola	Fish (raw) Steelhead trout	Gastroenteritis, Eosinophilia
Heterophes	Fish (raw) Asian and Nile	Gastroenteritis
Eustrongylides	Fish (raw)	Peritonitis
<i>Toxins (natural):</i>		
Scombrototoxin	Fish	Scombroid
Botulism Toxin E (Clostridium botulinum)	Fish	Botulism
Enterotoxin (Staphylococcus aureus)	Seafood	Gastroenteritis
Saxitoxin (Dinoflagellate)	Molluscs	Paralytic Shellfish Poisoning (PSP)
Brevetoxin (Dinoflagellate)	Molluscs	
Okadaic Acid (Dinoflagellate)	Molluscs	Diarrheic Shellfish Poisoning (DSP)
Domoic Acid (Diatom)	Molluscs	Amnesiac Shellfish Poisoning(ASP)
Tetrodotoxin (?Bacteria)	Pufferfish	Fugu/Pufferfish Poisoning
Ciguatoxin (Dinoflagellate)	Reef fish	Ciguatera Fish Poisoning

<i>Toxins (other):</i>		
Heavy metals:		
Mercury	Fish	Methylmercury Poisoning
Other:		
Polychlorinated Biphenyls (PCBs), Organochlorines	Fish	?Cancer, ?Neurotoxicity, ?Immunotoxicity, ?Reproductive Toxicity
Radioactive waste, Radionucleotides	Seafood	Unknown, ?Cancer