CHAPTER 33

Food Poisoning: Toxic Syndromes

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Once away from home, travelers are especially vulnerable to food-borne illness since with regard to food, they rely on the sourcing, processing, and culinary skills of others. Toxic syndromes due to food poisoning may occur after ingestion of foods that have been inadequately cooked, stored, or preserved. Knowledge of common food associations and clinical syndromes can help travelers to select safe foods or prompt them to seek help if they are stricken. Humans become intoxicated in two ways: after ingesting pre-formed toxins produced by bacteria present in the foods or by ingesting bacterial forms that proliferate in the gut and produce enterotoxins that are absorbed within the small intestine (the latter mechanism is also called a "toxical infection"). The bacteria commonly recognized as causes of food poisoning are ubiquitous in the environment and include *Clostridium perfringens*, *Staphylococcus aureus*, *Bacillus cereus*, and *Clostridium botulinum* (types A, B, and E).

Disease caused by pre-formed enterotoxins of *S. aureus* and *B. cereus* typically present as acute gastrointestinal illness. *C. perfringens* type A food poisoning also presents as acute gastrointestinal illness, but enterotoxin production occurs in the host following ingestion of the bacteria. Pigbel or necrotizing enteritis is a serious illness caused by *C. perfringens* type C. Botulism occurs when foods contain pre-formed toxins produced by *C. botulinum*; however, the clinical presentation usually involves neurological rather than gastrointestinal symptoms. Infant botulism is similar to *C. perfringens* in that toxin is produced after ingestion of contaminated food when *C. botulinum* spores germinate to produce bacteria that release intraluminal toxin during vegetative multiplication in the gut.

Table 33.1 summarizes the agents of food poisoning, including the incubation periods, clinical syndromes, and characteristic food associations. Websites providing reports of major outbreaks and information on food safety are given in **Table 33.2**.

FOOD POISONING PRESENTING AS GASTROINTESTINAL ILLNESS

The onset of symptoms is usually within hours after ingestion of contaminated food. In mild cases of food poisoning, vomiting, diarrhea, and abdominal cramping may be of short duration and resolve before the afflicted person seeks medical attention.

Etiology

C. perfringens type A infection has been identified as a common cause of food-borne disease in industrialized countries and is a leading cause of food poisoning cases in the United States, responsible for approximately 10% of food-borne illness associated with a known pathogen. *C. perfringens* spores germinate during cooking in stews, soups, gravies, and other meat or poultry dishes, and then if the food is allowed to cool at room temperature for a prolonged period (e.g., 12-14 hours) the *C. perfringens* bacteria proliferate. After ingestion, the actively growing (vegetative stage) bacteria multiply and then sporulate in the small intestine.

TABLE 33.1 Common Pathogens Causing Food Poisoning

Pathogen	Incubation	Characteristic Foods	Major Symptoms	Pathophysiology
Clostridium perfringens	6-24 h	Meat, poultry	Cramping abdominal pain,[a] diarrhea; vomiting and fever uncommon	Enterotoxin formed in vivo
Staphylococcus aureus	30 min to 8 h; usually 2-4 h	Creamy desserts, custards, salads, chopped hams, meats, baked goods	Vomiting,[a] cramping abdominal pain, diarrhea	Preformed enterotoxin
Bacillus cereus (emetic syndrome)	1-6 h	Rice, vegetables, meat ("fried rice syndrome")	Vomiting,[a] diarrhea; fever uncommon	? Preformed enterotoxin
Bacillus cereus (diarrheal syndrome)	6-24 h	Custards, cereals, puddings, sauces, meat loaf	Diarrhea[a], abdominal cramps, and vomiting; fever uncommon	? Preformed enterotoxin similar to ETEC LT toxin
Clostridium botulinum	2 h to 8 days; usually 12-48 h	Types A and B: improperly canned or preserved (pickled, cured, smoked) meats and vegetables; type E: smoked or preserved fish	Diplopia,[a] blurred vision,[a] photophobia[a]; dysphonia, dysarthria, weakness of tongue; nausea and vomiting; symmetric descending paralysis of motor and respiratory muscles that may progress rapidly	Preformed toxin

[a]Major distinguishing symptoms.
Adapted from: CDC-EIS, 2003. Compendium of Acute Foodborne and Waterborne Diseases. http://www.cdc.gov (accessed July 9, 2009).
ETEC, Enterotoxigenic *Escherichia coli*; *LT,* heat-labile.

TABLE 33.2 Web Sites for Food Safety and Outbreak Information

Centers for Disease Control and Prevention	http://www.cdc.gov/foodsafety http://www.cdc.gov/botulism
US Dept. of Agriculture Food Safety and Inspection Service	http://www.fsis.usda.gov
US Food and Drug Administration	http://www.cfsan.fda.gov
World Health Organization, Regional Food Safety Newsletter	http://www.who.int

C. perfringens bacteria entering the sporulation stage produce enterotoxin, which is then absorbed by the host.

Rare cases of fatal adult necrotizing enterocolitis have been reported in association with food-borne *C. perfringens* type A infections. Cases reported included previously healthy adults, although some reported cases had drug-induced constipation and fecal impaction that may have led to prolonged exposure of the colonic mucosal tissue to *C. perfringens* type A toxins and contributed to the development of illness.

S. aureus strains producing enterotoxin are usually inoculated from hands of infected human carriers into proteinaceous food products (e.g., creamy desserts and pastries, salads, meats) served or stored at room or refrigerator temperatures, conditions allowing staphylococcal proliferation and toxin production. Staphylococcal enterotoxins (A, B, C, D, and E) are relatively heat stable, so subsequent cooking of contaminated foods will not necessarily destroy them.

B. cereus is a ubiquitous soil bacterium present on rice, vegetables, and some meats. The illness ensuing from ingestion of *B. cereus*-contaminated food has been given the nickname "fried rice syndrome", as ingestion of fried rice was associated with the first recognized outbreaks. The ingredients and the cooking technique for this dish are especially conducive to illness-producing situations when fried rice is stored for prolonged periods at room temperature after cooking. The heat of cooking stimulates the *B. cereus* spores to germinate, and bacterial proliferation takes place in the food at room temperature, liberating enterotoxins. Flash cooking or brief reheating of the contaminated food before serving is not sufficient to inactivate the toxin nor kill the bacteria.

A short-incubation syndrome, with onset 2-9 hours after ingestion, is associated with the pre-formed toxin in the food. There is a long-incubation syndrome, with onset 6-14 hours after ingestion of contaminated food, associated with toxin elaborated by *B. cereus* bacteria proliferating within the gastrointestinal tract.

Diagnosis

A gastrointestinal illness characterized by a relatively rapid onset of symptoms after eating, and limited to 1 or 2 days, is likely to be food poisoning. Cramping abdominal pain is the hallmark of food poisoning caused by *C. perfringens*, and severe vomiting is the hallmark of food poisoning caused by *S. aureus*. *B. cereus* has two toxins, one causing a gastrointestinal illness with prominent vomiting (like *S. aureus* toxin) and one causing watery diarrhea (like the heat-labile toxin of enterotoxigenic *E. coli*). The diagnosis can be best confirmed if some of the original questionable food is available for laboratory testing. Laboratory testing of patient stool specimens, vomitus, and serum is laborious and is customarily performed by state public health department laboratories during large outbreaks. Commercially available enterotoxin kits available for *B. perfringens*, *S. aureus*, and *B. cereus* allow for rapid diagnosis, often before culture results are available.

Treatment

Antibiotics are of no known value in food poisoning, since onset of symptoms is related to a certain level of the given enterotoxin being present in the gut; once formed, the toxin can exert its biologic effect independently of the continued viability of the bacterial source.

Treatment is directed toward symptomatic relief of the nausea and vomiting and replacement of fluids and electrolytes lost in watery stools and emesis. Oral rehydration is described in Chapter 8. Rarely, nausea, vomiting, and diarrhea will be so severe that parenteral rehydration is necessary. Infants, the elderly, and the debilitated are most susceptible to complications from common food poisoning.

PIGBEL

Pigbel is a form of necrotizing enterocolitis (enteritis necroticans) caused by *C. perfringens* type C endemic in the Papua New Guinea highlands. The *C. perfringens* bacteria are ingested in contaminated pork and other foods and appear to colonize the intestinal tract of up to 70% of normal villagers.

Rapid intestinal proliferation of *C. perfringens* with production of β toxin follows ingestion of meat and/or other high-protein foods. If a person has inadequate levels of proteases, the β toxin cannot be destroyed and causes necrotizing enterocolitis. Children appear to be especially susceptible to pigbel owing to low levels of intestinal proteases associated with a chronic protein-deficient diet and a low level of immunity to β toxin. A staple of the village diet is sweet potato, which contains trypsin inhibitors and contributes to the problem.

In most cases, cytopathic intestinal damage from β toxin occurs early during *C. perfringens* proliferation. Symptoms of necrotizing enterocolitis (fever, abdominal pain, intestinal obstruction) may not be manifested until several days later, too late for neutralization of β toxin by administration of exogenous antitoxin to ameliorate the clinical course. A pigbel vaccine (Wellcome Labs) employing *C. perfringens* type C β toxoid appeared to offer protection among recipients in trials in the Papua New Guinea highlands, and the incidence of the disease dramatically decreased after vaccine programs during the 1980s. Sporadic cases still occur in Papua New Guinea, and cases of enteritis necroticans have been reported from poor communities in diverse geographic locations in Africa, Central and South America, the western Pacific, and Asia where poor food hygiene coupled with conditions of protein deprivation, staple diets containing trypsin inhibitors, and intermittent meat feasting set the stage for development of disease.

BOTULISM

C. botulinum bacteria produce extremely potent nerve toxins that humans are exposed to through ingestion of improperly preserved food or by absorption of the toxins from *C. botulinum*–contaminated wounds. Patients with botulism develop severe muscle weakness that starts in the head and progresses to the rest of the body, eventually resulting in complete loss of muscle function and the inability to breathe. Cases of food-borne botulism have been associated with a variety of foods, including home-canned foods (especially low-acid foods such as vegetables) and lightly preserved foods such as fermented, salted, or smoked fish and meat products. The foods implicated differ among countries and reflect regional and cultural differences in eating habits and food preservation techniques. Occasionally, commercially canned foods are implicated in botulism outbreaks. Examples of foods associated with botulism outbreaks are low-acid preserved vegetables such as green beans, spinach, mushrooms, beets, potatoes, and bamboo shoots; fish, including canned tuna; and meat products, such as ham, chicken, and sausage.

Etiology

The spore form of *C. botulinum* is commonly found in soils, aquatic sediments, and fish. The spores are heat resistant, but after a heat shock or other stimulus, the spores can germinate and the vegetative-state bacteria will proliferate under anaerobic conditions at a relatively high pH (>4.6), producing toxin. Of the eight immunologically distinct types of *C. botulinum* toxin, types A and B are responsible for most reported cases of food-borne disease, and type E has been associated with smoked fish. Types Cα, Cβ, and D have been isolated from animals, and types F and G are rarely isolated from human cases.

Clinical Presentation

Blurred vision, dysphagia, and dysarthria are common presenting complaints, rather than gastrointestinal symptoms. Symmetric cranial nerve palsies and descending flaccid paralysis of motor and autonomic nerves are the hallmarks of botulism. As the disease progresses, consciousness is maintained and there is no fever. Other causes of neurologic dysfunction that mimic botulism, such as stroke, the Guillain-Barré syndrome, and myasthenia gravis, must be considered and ruled out.

Diagnosis

The diagnosis of botulism is extremely tricky owing to the great variation in time between ingestion of the contaminated food and the onset of diagnostic symptoms. The usual incubation period is 12-48 hours, but symptoms may develop within 2 hours after the ingestion

or appear more than a week afterward. A careful food history should be obtained for up to the 2 weeks prior to the development of illness. The presumptive diagnosis is made based on the development of compatible clinical findings, history of exposure to one of the suspect foods, and the elimination of other possible causes of the illness.

Diagnosis of botulism can be confirmed if the suspected food is still available. Toxin in the serum or feces of stricken patients can be detected by bioassay in laboratory animals. The most sensitive and widely accepted assay method for detection of botulinum neurotoxin is the mouse bioassay, which takes 4 days to complete. Rapid and sensitive in vitro detection methods are under development but are not yet available.

Treatment

In illness caused by *C. botulinum* toxin, prompt administration of polyvalent equine antitoxin is indicated as soon as possible after the clinical diagnosis has been made, although respiratory support for severe respiratory muscle weakness may be the most important critical intervention. In 2013, the Food and Drug Administration licensed Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G)-(Equine)(Calgene), which can neutralize all seven of the botulinum nerve toxin serotypes known to cause botulism. Botulism antitoxin (BAT) is distributed in the United States through the Centers for Disease Control and Prevention (CDC) Drug Service. BAT is administered through slow intravenous infusion, which may take several hours; common side effects may include headache, fever, chills, rash, itching, and nausea. The horse serum components of BAT can rarely induce an anaphylactic reaction in the recipient or a delayed hypersensitivity reaction (serum sickness). When providing care to a patient with the presumed diagnosis of botulism, clinicians should contact the CDC to obtain BAT, for guidance on management and treatment, and for assistance with outbreak management, depending on the circumstances of the reported exposure.

Outbreak Management

In identified source outbreaks, contact tracing and publicity through the public health departments may help to prevent additional cases of illness and death. One reported outbreak of botulism in travelers was associated with food served at a restaurant and proved difficult to trace because of the widespread dispersion of the cases in two countries after the common food source was ingested.

An outbreak of botulism associated with home-canned bamboo shoots in northern Thailand in March 2006 illustrated some of the challenges of providing a medical response to a large outbreak. Botulism caused illness in 209 persons, required hospitalization of 134, and required mechanical ventilation in 42. Supplies of *Botulinum* antitoxin sufficient to treat 90 patients (103 vials) eventually were obtained from multiple international donors and commercial sources, but a lack of a pre-arranged emergency plan for global mobilization of the antitoxin resulted in delays of 5-9 days to acquire and deliver the product. There were no deaths in this outbreak, and the ability of Thai authorities to mobilize 42 ventilators and staff to manage the most severely affected patients probably prevented significant mortality in this outbreak, given the unavoidable delay in acquiring the antitoxin.

National and international agencies (CDC in Atlanta, National Laboratory in London, National Institute of Infectious Diseases in Tokyo, World Health Organization in Geneva, etc.) are the best sources for information about available supplies of *Botulinum* antitoxin, but there is no formal predefined protocol for global mobilization of the antitoxin at the time of writing.

Prevention of Botulism

Cooking foods at high temperatures will inactivate the toxin: boiling at 212°F (100°C) for 10 minutes or heating at 176°F (80°C) for 30 minutes. However, the *C. botulinum* spores can survive heating at 212°F (100°C) for several hours. Occasionally, ingested spores will proliferate in the human gastrointestinal tract and liberate enterotoxin that is absorbed by the host, causing symptoms. This latter mechanism is thought to account for long-incubation botulism and for infant botulism.

INFANT BOTULISM

This condition usually occurs in infants <6 months of age and results from inadvertent ingestion of *C. botulinum* spores, which germinate in the gut, proliferate, and release toxin. Infants with this condition may present with clinical symptoms of constipation, loss of appetite, weakness, altered cry, and loss of head control. Prevention consists of appropriate sterilization of homemade infant formulas. Raw honey contains spores of *C. botulinum*, and mothers are cautioned to not feed raw honey to their infants.

ADVICE TO TRAVELERS

Travelers are at special risk of food-borne illnesses including food poisoning because of increased exposure to foods prepared outside the home under unknown conditions of preparation and storage. Common advice for prevention of all food-borne illnesses includes selecting food that is freshly prepared, thoroughly cooked, and served piping hot or within 1 hour of preparation. For safety, chicken should be cooked to a temperature above 165°F (74°C), pork above 155°F (68°C), and ground beef above 155°F (68°C): rare or pink meat or poultry should not be consumed. The new instant-read digital food thermometers may be useful for checking the internal temperature of cooked meats and casseroles. Pre-cooked foods served warm or served from chafing dishes should be reheated to over 150°F (66°C) and held at that temperature. Pre-cooked foods served at room temperature, cold foods served in all-day buffets, and baked goods with creamy fillings should be avoided when possible during travel in less-developed areas. Cold foods and leftovers should be refrigerated below 45°F (7°C) until serving. Fermented, salted, or smoked fish and meat products should be avoided in general during travel, unless known to be obtained from reliable sources. Careful selection of food is the only way to avoid food poisoning, as the contaminated food may appear, taste, and smell like safe edible food.

FURTHER RESOURCES

Centers for Disease Control and Prevention, 2009. *Clostridium perfringens* infection among inmates at a county jail—Wisconsin, August 2008. MMWR 58, 138–141.

A macaroni and beef casserole from a commercial food supplier served for dinner to inmates at a county jail was identified as the most probable cause of nausea, vomiting, and diarrhea among more than 100 inmates. C. perfringens *enterotoxin was present in submitted stool specimens and* C. perfringens *was isolated from a sample of the casserole. Improper food handling, cooking, storage, and reheating of the pre-cooked food were the most probable causes of the food contamination.*

Centers for Disease Control and Prevention, 2013. Outbreak of staphylococcal food poisoning from a military unit lunch party—United States, July 2012. MMWR 62, 1026–1028.

A detailed report of the epidemiologic investigation of 22 cases of staphylococcal intoxication associated with improperly prepared and stored food at a lunch party at a military base. Isolation of S. aureus *and staphylococcal enterotoxin A in the chicken, sausage, and rice casserole confirmed the diagnosis. Commercially available toxin detection kits for* S. aureus *and* B. cereus *are approved to directly test food samples; the test kit for* C. perfringens *enterotoxin is approved only for testing stool specimens.*

Centers for Disease Control and Prevention (CDC), 2015. Surveillance for Foodborne Disease Outbreaks, United States, 2013, Annual Report. US Department of Health and Human Services, CDC, Atlanta, Georgia.

Of approximately 48 million cases of food-borne illnesses per year in the United States, 9.4 million are caused by known pathogens. Food-borne disease outbreaks for the year 2013 are reported by pathogen, food item, where consumed (home, restaurant, institution), and state, and whether hospitalization was required.

Scallon, E., Hoekstra, R.M., Angulo, F.J., et al., 2011. Foodborne illness acquired in the United States—major pathogens. Emerg. Infect. Dis. 17, 7–15.

Analysis and summary of US data from 2005 to 2008. An average of around 1 million cases per year of domestically acquired food-borne illness were caused by C. perfringens, *approximately 250,000 cases by* S. aureus, *and 63,000 cases by* B. cereus. *There were 55 cases of* C. botulinum. *For comparison, nontyphoidal*

Salmonella *spp. accounted for just over 1 million cases per year. The complexities and challenges of food-borne illness surveillance in the United States are discussed. Data from resource-limited countries are likely to be less complete.*

Sobel, J., Mixter, C.G., Kohe, P., et al., 2005. Necrotizing enterocolitis associated with *Clostridium perfringens* type A in previously health North American adults. J. Am. Coll. Surg. 201, 48–56.
C. perfringens *type A infections may be an unsuspected etiology in adult necrotizing enterocolitis.*

Ungchusak, K., Chunsuttiwat, S., Braden, C.R., et al., 2007. The need for global planned mobilization of essential medicine: lessons from a massive Thai botulism outbreak. Available at <http://www.who.int/bulletin/volumes/85/3/06-39545> (accessed July 26, 2015).
Rapid mobilization of botulism antitoxin for use in a massive international botulism outbreak presented many challenges.