**Bad Bug Book**

Foodborne Pathogenic Microorganisms and Natural Toxins

---

**Clostridium botulinum**

1. **Organism**

*Clostridium botulinum* is an anaerobic, Gram-positive, spore-forming rod that produces a potent neurotoxin. The spores are heat-resistant and can survive in foods that are incorrectly or minimally processed.

Seven types of botulinum are recognized (A, B, C, D, E, F and G), based on the antigenic specificity of the toxin produced by each strain. Types A, B, E and F cause human botulism. (Types C and D cause botulism in animals. Types C and E also cause botulism in birds. No outbreaks of type G have been reported.) Most strains produce only one type of toxin, but strains producing dual toxin types have been reported.

The organism and its spores are widely distributed in nature. They are found in both cultivated and forest soils; bottom sediments of streams, lakes, and coastal waters; in the intestinal tracts of fish and mammals; and in the gills and viscera of crabs and other shellfish.

(Another species of *Clostridium*, i.e., *perfringens*, causes foodborne illness, but does not cause botulism. It is addressed in another chapter.)

2. **Disease**

**Overview:** Botulism is a serious, sometimes fatal, disease caused by a potent neurotoxin formed during growth of *C. botulinum*. The infection results in flaccid paralysis of muscles, including those of the respiratory tract. Three major types of botulism are known, two of which will be discussed in this chapter: foodborne

---

**For Consumers: A Snapshot**

Not many people get botulism – the illness this bacterium causes – but when they do, it’s often deadly if *it’s not treated*, although some cases can be mild. A toxin produced by the bacterium causes the illness. The bacterium grows well in places with low oxygen, such as cans of food that became contaminated before being sealed. Often, there’s no visible sign that a food is contaminated, but sometimes a can is swollen. Most often, illnesses are due to home-canned foods that weren’t processed or cooked properly. Occasionally, canned foods sold in stores have caused botulism. Tiny amounts of the toxin can cause paralysis, including paralysis of the breathing muscles. With anti-toxin and other treatment, and the help of a “breathing machine,” the paralysis usually goes away within weeks or, in severe cases, months. Early symptoms start from 4 hours to 8 days after eating (although it’s usually 18 to 36 hours) and include double or blurred vision, drooping eyelids, slurred speech, swallowing problems, dry mouth, muscle weakness, constipation, and swollen abdomen. You can help protect yourself from botulism by following canning instructions and good hygiene *if you make home-canned foods and by boiling canned foods for 10 minutes before eating them, whether they’re home-made or store-bought.*

A special type of botulism, infant botulism, occurs when the bacterium “sets up housekeeping” in babies’ intestines and makes the toxin there, in the gut. Constipation is often the first sign. Other symptoms are dull face, weak sucking, weak cry, less movement, trouble swallowing, more drooling than usual, muscle weakness, and breathing problems. **Children under 1 year old should never be fed honey,** which has been linked to infant botulism (but not to adult botulism). It’s important to give early treatment with an anti-toxin made especially for infant botulism.
Botulism and infant botulism, which also is foodborne. The third type, wound botulism, is not foodborne and will not be covered extensively in this chapter.

Botulinum toxin causes flaccid paralysis by blocking motor nerve terminals at the neuromuscular junction. The flaccid paralysis progresses symmetrically downward, usually starting with the eyes and face, to the throat, chest, and extremities. When the diaphragm and chest muscles become fully involved, respiration is inhibited and, without intervention, death from asphyxia results.

**Foodborne botulism** is a severe type of food poisoning caused by ingestion of foods containing the toxin produced by *C. botulinum*. This type of botulism most often develops after consumption of improperly processed and inadequately cooked home-preserved foods. Home-canned or, occasionally, commercially produced foods have been involved in botulism outbreaks in the United States. Although the incidence of the disease is low, the disease is of considerable concern because of its high mortality rate if not treated immediately and properly.

**Infant botulism** is a serious illness caused by ingestion of *C. botulinum* spores that colonize and produce toxin in the intestinal tracts of infants (i.e., intestinal toxemia botulism).

**Wound botulism** is the rarest form of botulism and is discussed only briefly here, because it does not involve food. It results when *C. botulinum* colonizes in a wound and produces toxins, which reach other parts of the body via the bloodstream. Whereas foodborne botulism is limited to the amount of toxin ingested, *C. botulinum* in wounds produce toxin *in situ* (gas gangrene) until the pathogen is gone.

A fourth, “undetermined” category consists of adult cases in which a food or wound source cannot be identified. It has been suggested that some cases of botulism assigned to this category might result from intestinal colonization in adults, with *in vivo* production of toxin.

The medical literature suggests the existence of an adult form of botulism similar to infant botulism. In these cases, patients have had surgical alterations of the gastrointestinal tract and/or antibiotic therapy. It is proposed that these procedures may have altered the normal bacterial population of the gut and allowed *C. botulinum* to colonize the intestinal tract.

**Recommended treatment** for foodborne botulism includes early administration of botulinum antitoxin, available from the Centers for Disease Control and Prevention (CDC), and intensive supportive care, including mechanical breathing assistance. An antitoxin for infant botulism (Botulism Immune Globulin Intravenous, abbreviated BIG-IV) also is available and should be administered as early in the illness as possible. Antimicrobial therapy is not recommended, due to concerns about increased toxin release as a result of cell lysis.

- **Mortality:** The mortality rate is high if treatment is not immediately administered. The disease is generally fatal in 5% to 10% of cases.
- **Infective dose:** An extremely small amount—a few nanograms—of the toxin can cause illness.
**Onset:**

*Adult:* Usually 18 to 36 hours after ingesting food containing the toxin, although times have varied from 4 hours to 8 days.

*Infant:* Generally follows a period of normal development.

**Illness / complications:** See above.

**Symptoms:**

*Adult:* Initial symptoms may include double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, and muscle weakness. If the disease is not treated, symptoms may progress to paralysis of the arms, legs, trunk, and respiratory muscles.

Early signs of intoxication consist of marked lassitude, weakness and vertigo, usually followed by double vision and progressive difficulty in speaking and swallowing. Difficulty in breathing, weakness of other muscles, abdominal distention, and constipation may also be common symptoms.

*Infant:* Constipation after a period of normal development is often the first sign of infant botulism. This is followed by flat facial expression; poor feeding (weak sucking); weak cry; decreased movement; trouble swallowing, with excessive drooling; muscle weakness; and breathing problems.

**Duration:** Patients with severe cases that involve paralysis of the respiratory muscles may need mechanical ventilation and intensive care for weeks or months.

**Route of entry:** Oral, for foodborne infection. (Infection of wounds also occurs).

**Pathway:** Clinical presentation develops after a person ingests the pre-formed toxin, or if the organisms grow in the intestines or in wounds, followed by toxin release. The ingested botulinum toxin (an endopeptidase enzyme) blocks peripheral cholinergic neurotransmission at the neuromuscular junction and cholinergic autonomic nervous system. The toxin acts by binding presynaptically to high-affinity recognition sites on the cholinergic nerve terminals and decreasing the release of acetylcholine, causing a neuromuscular blocking effect. (This mechanism laid the foundation for development of the toxin as a therapeutic tool; e.g., when temporary inactivation of specific muscles is needed for therapeutic or cosmetic purposes.)

*C. botulinum* produces the toxin as a complex of proteins, among which is the neurotoxic moiety. The toxin is synthesized as a relatively inactive single-chain polypeptide with a molecular weight of ~150 kDa. It becomes an active toxin by selective proteolytic cleavage to yield the heavy and light chains that are linked by a single disulphide bond and non-covalent interactions. The toxin’s light chain is a Zn⁺⁺-containing endopeptidase that blocks acetylcholine-containing vesicles from fusing with the terminal membrane of the motor neuron, resulting in flaccid muscle paralysis.
3. Frequency

As noted, the incidence of the disease is low, but the mortality rate is high, if the disease is not treated immediately and properly. Some cases of botulism may go undiagnosed because symptoms are transient or mild or are misdiagnosed as Guillain-Barré syndrome.

![Chart showing reported cases of foodborne botulism in the U.S. 2001-2009]

Source: National Botulism Surveillance, Centers for Disease Control and Prevention

4. Sources

**General info:** The types of foods involved in botulism vary according to food preservation and cooking practices. Any food conducive to outgrowth and toxin production can be associated with botulism. This can occur when food processing allows spore survival and the food is not subsequently heated before consumption, to eliminate any live cells.

Almost any type of food that is not very acidic (pH above 4.6) can support growth and toxin production by *C. botulinum*. Salt concentration from 4% to 5% is needed for inhibition of its spores (especially regarding type E), with a 5% concentration completely inhibiting their growth. Salt concentrations slightly lower than those providing inhibition tend to extend spore outgrowth time at low temperatures.

A variety of foods, such as canned corn, peppers, green beans, soups, beets, asparagus, mushrooms, ripe olives, spinach, tuna fish, chicken and chicken livers, liver pate, luncheon meats, ham, sausage, stuffed eggplant, lobster, and smoked and salted fish have been associated with botulinum toxin.

**Infant botulism:** Of the various potential environmental sources, such as soil, cistern water, dust, and foods, honey is the one dietary reservoir of *C. botulinum* spores linked to infant botulism by both laboratory and epidemiologic studies. **Honey should not be fed to infants under 12 months of age.**

5. Target Populations

All people are believed to be susceptible to botulism.
6. Diagnosis

Although botulism can be diagnosed by clinical symptoms alone, differentiation from other diseases may be difficult. The most direct and effective way to confirm the clinical diagnosis of botulism in the laboratory is to demonstrate the presence of toxin in the serum or feces of the patient or in the food the patient consumed. Currently, the most sensitive and widely used method for detecting toxin is the mouse neutralization test. This test takes 48 hours. Culturing of specimens takes 5 to 7 days.

7. Food Analysis

Since botulism is foodborne and results from ingestion of preformed \textit{C. botulinum} toxin, determination of the source of an outbreak is based on detection and identification of toxin in the food involved. The most widely accepted method is the injection of extracts of the food into passively immunized mice (mouse neutralization test). The test takes 48 hours. This analysis is followed by culturing all suspect food in an enrichment medium, for detection and isolation of the causative organism.

8. Examples of Outbreaks

See CDC information on \textit{surveillance and investigation}.

9. Other Resources

\textit{Loci index for genome Clostridium botulinum} is available from GenBank.

CDC’s \textit{Emergency Preparedness and Response for Botulism}.