

## Fact Sheet

## Botulinum toxin (Botulism)

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Unless otherwise noted, all information presented in this article is derived from the following two sources:

1. Arnon SS, Schechter R, Inglesby TV, et al., for the Working Group on Civilian Biodefense. Botulinum toxin as a biological weapon: medical and public health management. *JAMA*. 2001;285(8):1059-70.
2. Bossi P, Tegnell A, Baka A, et al. Bichat guidelines for the clinical management of botulism and bioterrorism related botulism. *Euro Surveillance*. 2004;9(12): Epublish.

### Background

Botulism is a serious, but rare, paralytic illness caused by botulinum toxin, a product of the *Clostridium botulinum* bacteria. Botulinum toxin is the most poisonous substance known. In nature, *C. botulinum*, which produces seven types of toxin (A through G), is found in soil and ocean sediment.

There are three clinical presentations associated with naturally-occurring botulism; each results from absorption of botulinum toxin into the bloodstream:

- **Foodborne botulism** is caused by ingestion of food or drink already contaminated with botulinum toxin. Heat inactivates the toxin, so food can become contaminated if it is not heated or is inadequately heated. Foodborne botulism can also result from intentional contamination of food.
- **Wound botulism** is the result of a wound infection. *C. botulinum* can multiply and produce botulinum toxin in the wound, which then may be absorbed into the bloodstream. Wound botulism has become more prevalent in recent years among intravenous drug users.
- **Infant/Intestinal botulism** is the result of production of botulinum toxin in the intestine after eating food contaminated with *C. botulinum* spores. Intestinal botulism primarily affects infants, but can affect adults as well. Because honey can contain *C. botulinum* spores, it should be avoided in children under 12 months of age.

Inhalational botulism is a manmade form of disease that results from inhaling aerosolized botulinum toxin.

Fewer than 200 cases of botulism occur each year in the United States. A healthy adult can consume a small number of *C. botulinum* spores without becoming sick. Most cases of naturally occurring botulism are either foodborne or infant (intestinal) botulism, typically due to eating contaminated food. The largest botulism outbreak in the U.S. in the past century occurred in 1977, when 59 people became ill from poorly preserved jalapeño peppers. Many types of food have been associated with botulism in past outbreaks.

### Botulism as a Biological Weapon

Botulinum toxins pose a major threat as biological weapons:

- The amount of toxin needed to cause disease (infectious dose) is very small
- They are extremely potent and lethal
- Some of the toxins are relatively easy to produce and transport
- People exposed to botulinum toxin will potentially require prolonged intensive care.

A deliberate release of botulinum toxin could be in the form of an aerosolized weapon or contamination of the food or water supply with *C. botulinum* or botulinum toxin. Animal models suggest that inhaling 0.7-0.9 µg of aerosolized botulinum toxin would be enough to kill a person weighing 154 lbs. Exposure to a covert release of aerosolized botulinum toxin could result in outbreaks of acute flaccid paralysis (rapid onset of weakness, which can include weakness of the muscles involved in breathing and swallowing) with no accompanying fever in persons in the same geographic region without the expected common dietary exposure. Other than similar geography among patients, there would be few clues to help distinguish a deliberate contamination from a naturally occurring foodborne botulism outbreak. In addition, botulism is frequently misdiagnosed as Guillain-Barré syndrome, stroke, or other diseases of the central nervous system. (See “The History of Bioterrorism: Botulism,” a short video from the Centers For Disease Control and Prevention [CDC], available at <http://www.bt.cdc.gov/training/historyofbt/05botulism.asp>)

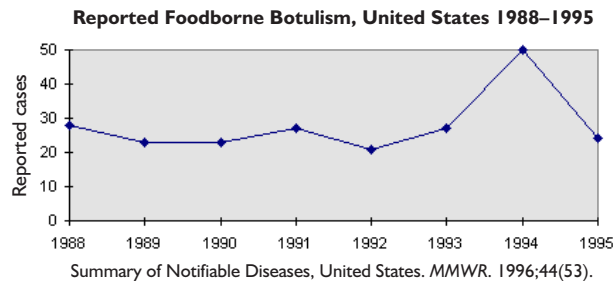
Countries that are suspected or known to have developed botulism as a weapon include Canada, France, Iran, Iraq, North Korea, South Africa, Syria, UK and the U.S. A CIA document about Iraq’s weapons of mass destruction programs reports that after the 1991 Gulf War, Iraq acknowledged having produced thousands of liters of concentrated botulinum toxin, loading the toxin into weapons, and conducting open-air testing with botulinum toxin.

## Transmission

Botulism and botulinum toxin are **not** contagious and are not transmitted from person to person.

## Infection Control Measures

For botulism patients in the hospital, standard precautions should be followed. Medical personnel should wear gloves, gowns, and masks. (See CDC Isolation Precautions Guidelines: [http://www.cdc.gov/ncidod/dhqp/gl\\_isolation.html](http://www.cdc.gov/ncidod/dhqp/gl_isolation.html).)



Source: FDA's *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook: Clostridium botulinum* (available at <http://www.cfsan.fda.gov/~mow/chap2.html>).

## Signs and Symptoms

Symptoms of botulism are not caused by the *C. botulinum* bacteria but by the toxin it produces. Diagnosis is based on clinical presentation of symptoms in the patient. Testing is available at the CDC and some local and state laboratories, but the specialized tests to confirm a diagnosis of botulism can take days to complete. In the case of a bioterrorist attack with botulinum toxin, clinical diagnosis will be the basis for medical response, and treatment should be started without waiting for laboratory confirmation of disease.

Symptoms are similar for all types of botulism, but the severity of illness and the time it takes for symptoms to appear can vary widely, in part depending on the amount and type of toxin absorbed. Symptoms of foodborne botulism usually appear within 12 to 72 hours after ingestion, but may begin anywhere from 2 hours to 8 days after eating contaminated food. The three known cases of inhalational botulism, which occurred after a laboratory accident, caused symptoms approximately 72 hours after exposure. The amount of aerosolized toxin inhaled in these cases is unknown.

Botulism causes progressive paralysis, which begins in the muscles of the head and neck. Affected muscles are left flaccid. If untreated, paralysis can affect the muscles of the trunk and extremities. Initial symptoms of botulism poisoning include difficulty seeing, speaking, and/or swallowing. Sagging eyelids, double vision, and blurred vision are common. Difficulty

swallowing and the loss of the protective gag reflex may require intubation for airway protection and mechanical ventilation.

Botulism poisoning does not cause fever in patients unless a secondary infection is present. Patients typically are fully alert and aware of their situation. Although a patient's muscles may be paralyzed, patients can still feel pain, temperature, and touch in the affected areas, and experience no changes in sense or cognition. Without treatment, death results from airway obstruction (paralysis of pharyngeal and upper airway muscles) and breathing difficulties (paralysis of diaphragm and accessory breathing muscles).

Recovery from paralysis can take weeks to months, and requires the growth of new motor nerve endings. Fatigue and shortness of breath can persist for years.

## Treatment and Prophylaxis

There is no post-exposure prophylaxis available for persons believed to have been exposed to botulinum toxin. For treatment, botulinum antitoxin is available in limited supply and is reserved for symptomatic individuals, who should be treated as quickly as possible given the severity of botulism poisoning. Timely administration of antitoxin minimizes further nerve damage and severity of disease, but cannot reverse paralysis that has already occurred. Antibiotics are not required, except in the case of wound botulism.

Botulism patients require supportive therapy, which may include mechanical ventilation, administration of nutrition via feeding tube, and treatment of secondary infections. Supply of botulism toxoid vaccine is limited, and because it helps build immunity to botulism over several months, it would not be effective for rapid post-exposure prophylaxis after a bioterrorist attack.

## Countermeasures

- **Antitoxin:** There are two licensed botulinum antitoxins available in the U.S.: The CDC Drug Service has botulism antitoxin A/B (sanofi aventis) and heptavalent botulism antitoxin (Cangene); the Strategic National Stockpile (SNS) has initial batches of 200,000 doses of heptavalent botulism antitoxin from Cangene, purchased by the U.S. Department of Health and Human Services. Antitoxin is stored at CDC quarantine stations located in major airports around the nation and in SNS locations; the use of these stockpiles must be requested by a state or local health department for suspected or confirmed cases of botulism poisoning.
- **Vaccine:** In the U.S., an investigational vaccine, a pentavalent botulinum toxoid (originally produced by the Michigan Department of Public Health and now owned

by Emergent BioSolutions), has been used to vaccinate high-risk laboratory workers and military personnel. This vaccine is no longer in production, supply is limited, and it is neither recommended for nor available to the general public. According to the Emergent BioSolutions website, HHS has sought to acquire up to 10 million doses of a trivalent vaccine, and DoD contracted with a company in 1997 to deliver botulism vaccine for the military. Bivalent vaccines are also being developed, but have yet to be licensed or acquired for the stockpile. (See <http://www.emergentbiosolutions.com/rBOT/>)

- **Diagnostics:** Because testing for botulinum toxin is time-consuming, future development is focused on rapid diagnosis/detection. Rapid point-of-care diagnostic tools for botulism are considered high priorities for the HHS Public Health Emergency Countermeasure Enterprise (PHEMCE). According to the PHEMCE Implementation Plan, development and acquisition of rapid diagnostics are slated for 2009 to 2013.

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### See Also

Arnon SS, Schechter R, Inglesby TV, et al., for the Working Group on Civilian Biodefense. Botulinum toxin as a biological weapon: medical and public health management. *JAMA*. 2001;285(8):1059-1070.

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