Factsheet

Botulinum Toxin (Botulism)

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Background

Botulism is a serious but rare paralytic illness caused by neurotoxins (botulinum toxin) produced by the common bacterium, *Clostridium botulinum*, which is found throughout the world in soil and ocean sediment. Normally, the bacterium exists in the environment as a dormant spore; however, in low oxygen (anaerobic) environments such as in canned foods, deep wounds, or the intestinal tract, the spores germinate into active bacteria, multiply, and produce toxin.[1] *C. botulinum* produces 7 types of toxins (A through G), which are among the most potent toxins known. Types A, B, E, and F can cause botulism infection in humans; types C, D, and E cause illness in other animal species.[2] Despite their toxicity, *C. botulinum* toxins A and B have been developed for various therapeutic utilities based on their ability to minimize muscle tension.[3]

There are 3 types of naturally occurring botulism, each resulting from absorption of botulinum toxin into the bloodstream:

- **Foodborne botulism** is caused by ingestion of food or drink containing botulinum toxin. Often this occurs when preserved foods that are contaminated with *C. botulinum* are not adequately sterilized. The bacterium produces toxin while growing in the anaerobic interior of the container. Foodborne botulism also could result from intentional contamination of the food supply.
- **Wound botulism** is the result of a deep, contaminated wound. *C. botulinum* can multiply and produce botulinum toxin in the anaerobic center of the wound, which is then absorbed into the bloodstream. Wound botulism has become more prevalent in recent years among people who inject drugs.
- **Infant/Intestinal botulism** is the result of eating food contaminated with *C. botulinum* spores that then go on to produce botulinum toxin in the intestine. Intestinal botulism primarily affects infants. A healthy adult can consume a small number of *C. botulinum* spores without becoming sick. Because honey can contain *C. botulinum* spores, it should be avoided for children younger than 12 months of age.[1]

Botulism also can result from biological attack, laboratory accident, or clinical usage. **Inhalational botulism** results from inhaling aerosolized botulinum toxin. It could only result from an intentional aerosol release or a laboratory/industrial accident.[2] **Iatrogenic botulism** can occur if too much botulinum toxin is injected during therapeutic applications.[1]

Approximately 100–250 cases of botulism occur each year in the United States. In 2018, 242 cases were reported to the CDC, the most recent year with published figures.[4] Most cases of naturally occurring botulism are infant (intestinal) botulism, with 67% of cases reporting in 2018 falling into this category. The largest botulism outbreak in the US 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.[5]

Botulism as a Biological Weapon

Botulinum toxins pose a major threat as biological weapons:

- They are extremely potent and lethal.
- Some of the toxins are relatively easy to produce and transport.
- People with botulism require prolonged intensive hospital 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. Several countries developed botulinum toxin as aerosol weapons in the past.[6] Animal models suggest that inhaling 0.7-0.9 µg of aerosolized botulinum toxin would be enough to kill a standard weight person (70 kg or 154 lbs).[7] The release of aerosolized botulinum toxin likely would result in an outbreak of acute flaccid paralysis (sudden, profound muscle weakness) among persons in the same geographic area who have had no obvious common dietary exposure.

Bioterrorism involving deliberate contamination of food with botulinum toxin would produce similar symptoms, but there would be a connection to a common food source. Initially, there are few clues to help distinguish between an intentional and a naturally occurring foodborne botulism outbreak (see "The History of Bioterrorism: Botulism," a short video from the Centers for Disease Control and Prevention [CDC], https://www.youtube.com/watch?v=Af15UzpsoWs.)

Transmission

Botulism is not transmitted from person to person.[2]

Infection Control Measures

No special precautions are needed for botulism patients who have been exposed to the naturally occurring toxin. As with all patients, however, standard precautions should be followed. If aerosolized exposure is suspected, additional precautions are needed. Clothing and other personal items of the patient should be removed and bagged, and the patient should be decontaminated immediately. (See CDC Isolation Precautions Guidelines, https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html)[2, 6]

Illness

Symptoms of botulism are not caused by the *C. botulinum* bacteria but by the toxin it produces. The initial diagnosis of botulism is based on clinical signs and symptoms. Confirmatory testing is available at the CDC and some local and state laboratories, but the specialized tests needed to confirm a diagnosis of botulism can take days to complete.[1] 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.[6]

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 3 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 flaccid paralysis, which begins in the muscles of the head and neck and progresses to 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.

Botulism is frequently misdiagnosed as Guillain-Barré syndrome, stroke, or other diseases of the central nervous system. Difficulty swallowing, loss of the protective gag reflex, and paralysis of the respiratory muscles may require endotracheal intubation for airway protection and mechanical ventilation.

Botulism poisoning does not cause fever. Patients typically are fully alert and aware of their situation. Although the patient's muscles may be paralyzed, they can still feel pain, temperature, and touch. Without treatment, death results from airway obstruction (paralysis of pharyngeal and upper airway muscles) and respiratory failure (paralysis of diaphragm and accessory breathing muscles).

Recovery from paralysis due to botulism requires the regrowth of motor nerve endings and can take weeks to months. Muscle fatigue and shortness of breath can persist for years.[1,2,6]

Clinical Uses

Botulinum toxins A and B can be used therapeutically and cosmetically in a very dilute form for a variety of ailments, all of which derive use from the toxins' ability to minimize muscle tension. FDA-approved uses include treatment of chronic migraine, cervical dystonia, blepharospasm, strabismus, hyperhidrosis, urinary incontinence, and hemifacial spasms. Other off-label uses include chronic pain conditions, cosmetics, and TMJ dysfunction, among others. Practitioners inject the toxin into distinct muscles in the affected area, with results that last about 3-6 months based on use and dosage.[3]

Treatment and Prophylaxis

There is no post-exposure prophylaxis available for persons exposed to botulinum toxin. A toxoid vaccine against the toxin exists but the CDC discontinued the vaccine program in 2011 due to low efficiency. Additionally, as therapeutic and cosmetic uses of botulinum toxin have increased, plans for large-scale vaccination against the toxin have decreased.[6]

For symptomatic individuals, botulinum antitoxin is available in limited supply. Such patients should be treated as quickly as possible. Timely administration of antitoxin minimizes further nerve damage by the toxin, but it cannot reverse paralysis that has already occurred. Antibiotics are of no use, except in the case of wound botulism and then only as an adjunct to surgical wound care.

Botulism patients require supportive therapy, which may include mechanical ventilation, administration of nutrition via feeding tube, and treatment of secondary infections.[1,2,8,9]

Countermeasures

Botulism Antitoxin Heptavalent (BAT), an antitoxin produced by Emergent BioSolutions, contains antibodies to the 7 botulinum toxin types.[10] BAT has been purchased for US Strategic National Stockpile.[11]

In 2003, the FDA approved human botulinum immune globulin (BabyBIG) for the treatment of infant botulism.[12]

Diagnostics

Because testing for botulinum toxin is time consuming, diagnosis is heavily dependent on clinical presentation and examination. If a clinician suspects botulism, antitoxin treatment and supportive therapy should start right away. Laboratory confirmation of a botulism diagnosis should confirm clinical diagnoses.[1,2]

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See also:

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