Botulism

Investigative Guideline

May 2022

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To assist in the diagnosis and treatment of potential cases and facilitate prompt administration of antitoxin when indicated.
2. To classify reported cases as foodborne, intestinal (infant or adult), wound, iatrogenic, or inhalational botulism. (See §2.4. Inhalational "bot" should be considered the result of bioterrorism until proven otherwise.)
3. For foodborne botulism, to identify contaminated food and to prevent others from eating it.
4. For foodborne botulism, to identify and assure the proper evaluation and care of other persons who may be at immediate risk of illness because they have already eaten the implicated food.

1.2 Laboratory and Physician Reporting Requirements

Any suspected botulism case should be reported **immediately, day or night** (within minutes) to local health departments, or, if they are unreachable, to Oregon Public Health Division (PHD).

1.3 Local Health Department Reporting and Follow-Up Responsibilities

Any suspected case of botulism is a **medical emergency**. Foodborne or inhalational botulism require immediate investigation. Thus, it is critical to determine what kind of illness you are dealing with. See §2.4 (Modes of Transmission).

1. Report all confirmed, presumptive, and suspect cases (see definitions below) to PHD (971-673-1111) **within minutes** of initial physician or lab report.
2. Begin follow-up investigation immediately. Use the PHD *Botulism Reporting Form* https://public.health.oregon.gov/DiseasesConditions/CommunicableDisease/ReportingCommunicableDisease/ReportingForms/Documents/botulism.pdf to collect information about demographics, clinical presentation, risk factors, and, if foodborne or injection drug-related wound botulism is suspected, others who might be at risk. Once you have basic information, contact the PHD on-call epi. Send a copy of the completed form to PHD within seven days of initial report.

3. Consult with PHD epidemiologists about the need for botulism antitoxin therapy and assist with logistic arrangements as necessary.
4. For foodborne botulism, work with PHD to investigate possible sources, identify other people who might have been exposed, submit patient and food specimens to the appropriate laboratory and, within 24 hours of receiving the case report, complete steps to prevent others from eating suspect foods.

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent and Toxin

Botulism is an intoxication caused by ingestion or other exposure to a toxin produced by the anaerobic Gram-positive bacillus *Clostridium botulinum*. *C. botulinum* is a spore former, which means that it can survive indefinitely under essentially any environmental conditions—even boiling. Bacterial growth, however, (as opposed to spore survival) occurs only under anaerobic conditions and low acidity (generally pH>4). The higher temperatures (>120.5°C/250.5°F) that can be achieved under pressure (e.g., in an autoclave or *properly functioning* home pressure cooker) are sufficient to kill even spores.

The toxin itself is produced as the bacteria are multiplying. There are seven types of botulinum toxin, designated A– G. Types A, B, and E are the most common sources of human disease. F and G are very rare, and C and D are not known to cause human illness. The toxin is heat-labile, and (in contrast to, say, staphylococcal enterotoxin) can be inactivated by boiling for ten minutes.

2.2 Description of Illness

Botulism is a neurological disease caused by exposure to botulinum toxin.

Botulism is characterized by neurologic symptoms that may include dysphagia, dry mouth, diplopia, and dysarthria (the "4 D's"). Blurred vision, ptosis (drooping eyelids), and weakness, reflecting a descending, symmetrical flaccid paralysis that starts with the facial muscles and progresses downward, are also characteristic symptoms. The patient is usually mentally alert. Neurologic symptoms may be preceded or accompanied by mild gastrointestinal disturbance such as constipation, vomiting, or diarrhea. The severity of symptoms and the rate of progression are highly variable, depending on dose and other factors.
Respiratory distress may ensue if the muscles of breathing are compromised. In severe cases, patients may survive only after months on a ventilator.

The first sign in infants is often constipation, followed by lethargy, listlessness, difficulty feeding (weak or absent sucking response), a weak cry, ptosis, and generalized weakness (the “floppy baby” syndrome).

2.3 Reservoirs

C. botulinum spores are common in soil and elsewhere in the environment.

2.4 Modes of Transmission

Epidemiologically, cases fall into one of five categories. Although all types are potentially fatal and demand aggressive medical care, foodborne, inhalational, and epidemic wound botulism require immediate public health action.

Foodborne Botulism: Foodborne botulism is caused by ingestion of pre-formed toxin. Typically, implicated foods have been low acid, home-canned foods that had not been heated adequately during canning. Rarely, commercial products are implicated, usually after some breakdown in standard canning procedures. Examples of implicated foods include:

- home-canned asparagus, beans, and other vegetables (including low-acid tomatoes), usually canned by the water-bath method;
- fish that has been improperly canned, dried, or stored;
- sausage or other prepared meats that are improperly processed (inadequate sodium nitrite) and improperly stored;
- chopped garlic in oil, fried onions, and baked potatoes in foil;
- among Alaska Natives, traditional foods including fermented whale blubber, salmon heads, salmon eggs, and other delicacies.

Intestinal Botulism

- Infant: By far the most common form of botulism, infant “bot” occurs when *C. botulinum* spores, ingested in food or soil, germinate in a gut that does not have mature flora, leading to an intestinal infection. Botulinum toxin is then produced *in situ*. Most cases occur in infants <6 months old (and usually <3 months old). As many as 5% of SIDS cases may be infant botulism.

- Adult: This form of botulism rarely occurs. As with infant botulism, toxin is produced in the colonized intestine of the individual. It occurs in adults with a history of abdominal surgery, gastrointestinal tract abnormalities, Crohn’s disease, or recent treatment with antibiotics.

Wound Botulism: Wound botulism results from a local *C. botulinum* infection in devitalized tissue at a wound site, where semi-anaerobic conditions develop. As with intestinal bot, the toxin is produced *in situ* and disseminated in the blood. Wound botulism has been rare, but increasingly reported, especially in injectors of "black-tar" heroin.

Inhalational Botulism: Inhalational botulism does not occur naturally. There have been only three reported cases in humans world-wide. Studies done with monkeys have shown that the toxin can be absorbed through the lung. It is believed that if botulinum toxin were to be used as a bioweapon, it would be by this route.

Iatrogenic Botulism from cosmetic botulinum toxin injection: Very rare, but it’s been reported.

2.5 Incubation Period

- Foodborne Botulism: Variable: ranges from less than half a day to a week or more, usually 12–36 hours. A short incubation is associated with larger toxin exposure and, typically, more severe disease.
- Intestinal Botulism: Incubation period is unknown.
- Wound Botulism: Up to several days.
- Inhalational Botulism: Thought to be 12 –36 hours after inhalation but may take several days after exposure to low doses of toxin.

2.6 Period of Communicability

Not communicable.

2.7 Treatment

All patients require close monitoring of ventilatory status, and aggressive supportive therapy is required in severe cases. Some patients have recovered completely after months on a ventilator. Additional therapies depend on the type of botulism and are outlined below. CDC has also published evidence-based diagnostic and treatment guidelines.

Foodborne Botulism: Botulinum antitoxin can halt the progression of symptoms caused by absorbed toxin if given promptly after exposure. **Antitoxin therapy should never be delayed pending laboratory confirmation of the diagnosis.** The heptavalent (anti A -G) antitoxin (licensed by FDA in 2013) is purified from horse serum, and then "de-speciated". Consequently, there is less potential for allergic reactions or "serum sickness" compared with earlier antitoxin. However, premedication with corticosteroids and antihistamines is recommended in patients with the following relative contraindications:

- Any known or documented allergies to horse serum (observation of adverse events after treatment with any product containing horse serum).
- History of hypersensitivity to blood products derived from an equine source.

CDC controls the distribution of botulinum antitoxin, which is stocked at U.S. Public Health Service Quarantine Stations throughout the country. (For Oregon, the regional station is at Sea-Tac Airport in Seattle.) Any physician considering antitoxin use must consult first with PHD Communicable Disease staff. Day or night, call 971-673-1111 and ask for the on-call epidemiologist. [***Note:*** CDC is most likely to release antitoxin when compatible neurological findings are present on exam. Probe for that when talking with clinicians.] We, in turn, will communicate with CDC, who will arrange for delivery of antitoxin to an Oregon airport. From there, it is the treating team's responsibility to get it to the patient. In general, we will connect federal Quarantine officials with the hospital pharmacist, who arranges for the pickup.

It's unlikely that clinicians would be calling you about antitoxin dosing, but if they do: First, refer them to the package insert. Second, it that doesn't provide enough information, call us.

Intestinal Botulism

- Infants: Most infants do well with supportive care, with or without cathartics or penicillin to try to eliminate intestinal infection by *C. botulinum*; the heptavalent antitoxin is not indicated. A human-derived hyper immune globulin (BIG-IV or "Baby BIG") is approved by FDA for treatment of infants. Though the cost is substantial (in the tens of thousands of dollars) its use may be cost-effective. A randomized, double-blinded, placebo-controlled trial of BIG-IV found a 3-week reduction in the mean length of hospital stay and a reduction in the mean hospital charges of $88,600 per patient treated. Baby BIG can be obtained from the California Department of Health Care Services by calling their 24-hour number at 510- 231-7600.
- Adults: Horse-derived antitoxin is used to treat adult intestinal botulism. More than one dose of antitoxin may be required

Wound botulism: Debridement of the wound is indicated to remove de-vascularized tissue that provides the anaerobic conditions required for growth of *C. botulinum*. Antitoxin should be administered as for foodborne botulism. Antimicrobial therapy may also be warranted.

3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

3.1 Confirmed Case Definition

Confirmation requires identification of botulinum toxin in serum or stool and is not always possible. Completion of the tests may take several days to 2 weeks or more. Treatment, including consideration of antitoxin use, should never wait for laboratory confirmation.

3.2 Presumptive Case Definition

A presumptive case is someone with a compatible illness who has been exposed to the same suspected source as a confirmed case.

3.3 Suspect Case Definition

Anyone with compatible illness of unknown etiology.

3.4 Services Available at the Oregon State Public Health Laboratory (OSPHL)

OSPHL does not test for botulinum toxin. Clinical laboratories should send specimens directly to CDC for testing to avoid delay in submission. **Testing must be approved beforehand by an OPHD epidemiologist.**

Each specimen must be accompanied by a separate CDC 50.34 specimen submission form with all required fields completed. OSPHL staff can walk the clinical lab through completion of this form, as needed. ACDP staff will alert OSPHL when testing is approved. The form and other information about specimen submission is also available at: https://www.cdc.gov/botulism/botulism-specimen.html#:~:text=CDC%20offers%20laboratory%20confirmation%20of,laboratories%20and%20other%20federal%20agencies .

The following specimens should be collected as indicated for the situation. Specimens should be collected as early in the course of illness as possible, and *serum must be collected before administration of antitoxin.*

- Foodborne botulism (adult): Collect 5-15 mL serum (without anti-coagulant) and at least 10g stool. Enema (with sterile non-bacteriostatic water) and food are accepted. Although not ideal, gastric contents may also be submitted.

- Wound botulism: serum (without anti-coagulant), debrided tissue, swab from wounds, stool (only if foodborne is also suspected).

- Infant botulism: at least 10g stool is preferred. Enema (with sterile non-bacteriostatic water) and rectal swabs are also accepted. Potential sources (honey, opened formula, etc.) may also be submitted.

Stool collection may be difficult because patients are often constipated. In a pinch, as little as 5 g (5 mL) of stool is enough to test, but ideally, encourage clinicians to get 10 g of stool (a volume at least the size of a walnut). **Note: Stool specimens must be received by the CDC Lab within 72 hours of collection. Otherwise, they will be rejected.**

When open containers of suspected foods can be tracked down, send whatever is left of each of the suspected food items. Check with the OPHD epi before sending unopened containers. (Usually not necessary, but you never know…) Containers should be placed individually into leakproof bags and double bagged prior to shipping. CDC won't test unopened commercial products unless approved by FDA/USDA.

All specimens must be kept refrigerated (*not frozen*) during storage and transport. (Please use frozen cold packs.) Specimens must be properly packaged using guidelines for shipping and packaging of Category B diagnostic specimens. Use absorbent material around the primary leakproof container. *Note:* CDC won't accept routine shipments on weekends or holidays.

Please notify the submitting hospital or laboratory that if botulism is identified they are required to contribute to the CDC's Select Agent Form 4. Consider obtaining a contact at the facility to help with this process. Individuals with knowledge of the facility-level specimen handling processes will be most appropriate, rather than an individual clinician.

4. ROUTINE CASE INVESTIGATION

The nature of follow-up depends on the suspected mode of transmission. No botulism investigation is "routine."

Note: CDC currently wants its staff to collect a bunch of clinical and risk exposure information themselves about antitoxin recipients. We have included a case report form on our website at: *https://public.health.oregon.gov/DiseasesConditions/CommunicableDisease/ReportingCommunicableDisease/ReportingForms/Documents/botulism.pdf*

This will get you what you need to enter cases into Orpheus. We will request a copy of the Botulism Case Report Form completed by CDC and attach it to the Case in Orpheus, it could be useful in completing the Orpheus case investigation data fields.

4.1 Foodborne Botulism

1. Identify the Source of Intoxication.

Interview the case and others who may be able to provide pertinent information about foods eaten. A home visit is strongly recommended when home-canned foods are implicated, or if the source is not readily apparent. **Note: In Camara v. Municipal Court of the City and County of San Francisco, the U.S. Supreme Court ruled that health inspections of living quarters, conducted without consent of the occupant, require a search warrant.** In light of this, if you can't get consent from the owner, you'll probably need to arrange for a warrant with a judge in your jurisdiction. (This isn't something that comes up often. If you have questions, give us a call.)

- Identify all home-canned foods eaten during the week prior to onset of symptoms. The most suspect foods are those that were eaten less than two days before onset, those that are low in acid (vegetables, fish, and meat), and those that were not eaten by other persons who remain well. (Keep in mind, however, that some cases may develop symptoms several days after the index case.) Identify and collect all remaining jars of the home-canned foods.
- Identify all commercially canned foods eaten during the week prior to onset of illness. For implicated foods, determine the brand, manufacturer, package size, lot number, and place and date of purchase (see §5B).
- Identify all sausage and other preserved meats eaten during the week prior to onset of illness.
  - Meat products that have not been adequately refrigerated should also be suspected as a source.
  - Identify all preserved fish eaten during the week before onset of symptoms.
- Identify all items stored in oil (e.g., onions, garlic) or foil (e.g., baked potatoes)

2. Identify Potentially Exposed Persons

- Obtain the name, address, and telephone number of every person who might have eaten the suspected food item.
- Obtain the name, address, and telephone number of every person who might have the suspect home-processed food in his or her possession.
- When a commercial product is implicated, see §5.2.

4.2 Intestinal Botulism (Infant Botulism)

No epidemiological follow-up is required. Consider testing of infant formula if this is part of the infant's diet. Provide education and counseling as needed.

4.3 Wound Botulism, Intestinal (Adult) Botulism, and Iatrogenic Botulism

Once foodborne illness is ruled out, no public health follow-up is required, unless a cluster of illness suggests a widespread exposure to contaminated drugs. If you suspect this, give us a call.

4.4 Inhalational Botulism

1. Identify Source of Intoxication. Interview the case and others who might be able to provide pertinent information about possible exposures. Ask about public events recently attended.
2. Identify Potentially Exposed Persons. Obtain the name, address, and phone number of every person who might have been exposed.

5. CONTROLLING FURTHER SPREAD (FOODBORNE BOTULISM ONLY)

5.1 Home Canned Food Implicated

1. If reachable within six hours of exposure, others who have eaten implicated food should be purged and given gastric lavage to remove any unabsorbed toxin. They should be monitored for signs of botulism at least twice daily for three days and instructed to seek medical care immediately should symptoms develop.
2. Any opened, implicated home-canned food should be sent to OSPHL for testing, which will be done if clinical specimens are positive. Remaining suspect canned goods should be destroyed. Avoid any contact with the contents; this is toxic stuff! To avoid endangering trash haulers or others, these foods should be boiled for 10 minutes before discarding. Any containers should be likewise boiled. Botulinum toxin can also be deactivated by mixing the contaminated product in a 1:10 dilution of household bleach for 20 minutes or more.
3. The person who prepared the home-canned food should be thoroughly instructed in proper canning techniques. The OSU Extension Service is a good resource for canning information. Their website is: http://extension.oregonstate.edu/fch/food-preservation

5.2 Commercial Products Implicated

When a commercial product is implicated as the source of intoxication, the OPHD Epi on-call should be notified immediately. OPHD will coordinate follow-up with relevant outside agencies (FDA, USDA, CDC, etc.). Again, any leftover, suspect food should be sent to OSPHL.

6. MANAGING SPECIAL SITUATIONS

Clostridium botulinum toxin has been classified as a possible agent of bioterrorism because it is phenomenally potent and lethal (considered the most toxic compound, by weight, known). It is also easy to produce and transport, and affected individuals often need extensive and prolonged intensive care. It is believed that aerosol dissemination would be the most likely mode of intentional spread.

Aerosol dissemination could produce many cases in a geographic area. Therefore, inhalational botulism produced by an intentional release should be considered for any clusters of botulism where food cannot be implicated. Call the PHD Epi on-call immediately (971-673-1111), day or night.

UPDATE LOG

May 2022. Laboratory section updated to reflect new procedure for direct submission of specimens to CDC (Leman, Cavanaugh, Frieder, Humphrey-King).

April 2022. Minor edits. Added guidance about probing for physical findings when talking with clinicians requesting antitoxin. (Leman)

May 2021. Added link to CDC Clinical Guidelines for Diagnosis and Treatment of Botulism, 2021. Noted that OHA routinely uploads to Orpheus a case report form from CDC to aid LPHAs in completing botulism case investigations. Updated laboratory section (Leman, Cavanaugh, Frieder, Humphrey-King)

March 2019. Changed Section 3.4 to reflect that, beginning in March, botulism testing will be don at CDC. Minor edits. (Leman)

August 2018 Updated info. on stool specimen collection, in accordance with OSPHL guidance. Section 2.7, added sentence describing how to address questions regarding antitoxin dosage. Section 5.1.2, added bleach immersion as an option to neutralize botulinum toxin in contaminated products. Minor edits for clarity. (Leman)

December 2015. Guideline placed in new template. (Leslie Byster)

September 2014. Included information on need for warrant prior to environmental inspection of a home if consent cannot be obtained. Links updated. Minor wording revisions. (Leman)

April 2013. Incorporated info. on heptavalent botulism antitoxin, including removal of requirement for skin testing before administration. Revised and updated section on laboratory services available through OSPHL and specimen requirements. Updated language on collection and testing of suspect food items. Minor word changes elsewhere. Updated *Case Report Form*. (Leman)

September 2010. Based on recent literature review, added consideration of formula testing in setting of infant botulism when formula is part of infant's diet. Updated information on use of Baby-Big in setting of infant botulism. Updated PHD contact numbers. (Richard Leman)