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Botulism

Surveillance and Investigation Protocol

West Virginia Department of HEALTH

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I. ABOUT THE DISEASE

A. Clinical Presentation

All forms of human botulism display virtually identical neurological signs. Botulism is an acute, afebrile, symmetric, descending flaccid paralysis that always begins in bulbar musculature. It is not possible to have botulism without having multiple cranial nerve palsies.

Patients with botulism typically present with difficulty seeing, speaking, and/or swallowing. Prominent neurologic findings in all forms of botulism include ptosis (drooping of eyelids), blurred vision, often enlarged or sluggishly reactive pupils, and the "4 Ds" (diplopia, dysarthria, dysphonia, and dysphagia). The mouth may appear dry and the pharynx injected because of peripheral parasympathetic cholinergic blockade. Sensory changes are not observed except for infrequent circumoral and peripheral paresthesias from hyperventilation as the patient becomes frightened by onset of paralysis.

As paralysis extends beyond bulbar musculature, loss of head control, hypotonia, and generalized weakness become prominent. Dysphagia (difficulty swallowing) and loss of the protective gag reflex may require intubation and mechanical ventilation. Deep tendon reflexes may be present initially but diminish or disappear in the ensuing days, and constipation may occur. In untreated persons, death results from airway obstruction (pharyngeal and upper airway muscle paralysis) and inadequate tidal volume (diaphragmatic and accessory respiratory muscle paralysis).

In foodborne botulism, neurological signs may be preceded by abdominal cramps, nausea, vomiting, constipation or diarrhea. Disease manifestations are similar regardless of botulinum toxin type. However, the extent and pace of paralysis may vary considerably among patients. Some patients may be mildly affected while others may be so paralyzed that they appear comatose and require months of ventilatory support. The rapidity of onset and the severity of paralysis depend on the amount of toxin absorbed into the circulation. The toxin does not penetrate brain parenchyma, so patients are not confused or obtunded. However, they often appear lethargic and have communication difficulties because of bulbar palsies.

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B. Etiologic Agent

Botulism is caused by toxins produced by *Clostridium botulinum*, a gram-positive, spore forming rod. *C. botulinum* spores can survive indefinitely under essentially any environmental conditions--even boiling. Spore germination resulting in bacterial growth and toxin production occurs only in low oxygen, non-acidic conditions. Botulinum toxins are temperature sensitive and are inactivated by heating to 85C (185F) for 5 minutes. However, in order to kill *C. botulinum* spores, higher temperatures (>120C or 250F) which are achieved under pressure (e.g., in an autoclave or a properly functioning home pressure cooker) are required.

Botulinum toxin is produced as the bacteria are multiplying. There are 7 types of botulinum toxin, designated by the letters A-G. Only types A, B, E, and rarely F are known to cause human disease. Most cases of infant botulism have been caused by Type A or B. Type E outbreaks are usually related to fish, seafood and meat from marine animals. Type G has been isolated from soil and autopsy specimens but an etiologic role in botulism has not been established.

Botulinum toxins are the most potent toxins known to exist. A few nanograms of the toxin can cause illness. The toxin is heat-labile and can be inactivated by boiling.

C. Reservoir

C. botulinum spores are widely distributed in nature and are commonly found in soil worldwide, in agricultural products, the intestines of animals, and in the gills and viscera of fish.

D. Incubation Period

Symptoms of foodborne botulism usually begin within 12-72 hours but could be seen as early as 2 hours and as late as 8 days after ingesting the toxin. The time of onset of inhalational botulism cannot be stated with certainty because so few cases are known. The three known human cases of inhalational botulism had onset of symptoms approximately 72 hours after exposure to an unknown but probably small amount of re-aerosolized toxin.

E. Mode of Transmission

1. Foodborne Botulism

Foodborne botulism is caused by ingestion of preformed toxin in foods. Typically, implicated foods have been low acid, home-canned foods that were not heated adequately during canning. A growing

proportion of implicated foods have been cultural delicacies prepared by traditional methods, such as fermented fish heads (among Alaska Natives). Rarely, commercial products are implicated, usually after some breakdown in standard canning procedures. Examples of implicated foods include:

a. Home-canned asparagus, beans, and other vegetables (including low-acid tomatoes), usually canned by the water-bath method;
b. Fish that has been improperly canned, dried, and/or stored;
c. Sausage or other prepared meats that are improperly processed (inadequate sodium nitrite) and improperly stored;
d. Commercially processed canned chili sauce; chopped garlic in oil;
e. Baked potatoes in foil;
f. Among Alaska Natives, traditional foods including fermented whale blubber, salmon heads, salmon eggs, and other delicacies.

2. Intestinal or 'Infant' Botulism

The most common form of botulism is infant botulism. It occurs when *C. botulinum* spores, ingested in food or soil, germinate in a gut that does not have a mature flora. Botulinum toxin is then produced by the bacteria growing in the intestine. Most cases occur in infants <3 months old. Adult cases of intestinal botulism have very rarely been reported, in adults with gastrointestinal illness that may predispose to enteric colonization.

3. Wound Botulism

Wound botulism results from a local *C. botulinum* infection of damaged tissue at a wound site, with low oxygen conditions. As with intestinal botulism, the toxin is produced in situ and disseminated in the blood. Wound botulism is the rarest form of naturally occurring botulism. It is most commonly associated with people who inject "black tar" heroin.

4. Inhalational Botulism

Inhalational botulism is not a naturally occurring disease and is only known to occur through deliberate aerosolization of pre-formed botulinum toxin.

5. Iatrogenic Botulism

Iatrogenic botulism is due to overdose of botulinum toxin injected for cosmetic or therapeutic purpose.

F. Period of Communicability

There is no person-to-person transmission of botulism.

II. DISEASE CONTROL AND PREVENTION

A. Disease Control Objectives

To identify and investigate case/s and outbreak/s at the earliest possible time, so that control measures can be instituted rapidly.

B. Disease Prevention Objectives

Prevent cases of botulism by educating the general public about the causes and prevention of:
1. Foodborne botulism, (e.g. use of commercially canned goods and adequate home canning techniques).

2. Infant botulism, (e.g., appropriate feeding of infants).

3. Wound botulism (e.g. needle use, appropriate wound care).

Preventive Interventions

1. Effective processing and preparation of commercially canned and preserved foods can prevent this disease.

2. Educate the public on the proper use of all canned goods. Botulinum toxin is destroyed by high temperatures. Persons who eat home-canned foods should consider boiling the food for 10 minutes before eating it to ensure safety. Instructions on safe home canning can be obtained from the county extension services or from the US Department of Agriculture.

3. Children less than 12 months old should not be fed honey. Honey is safe for persons 1 year of age and older.

4. Wound botulism can be prevented by promptly seeking medical care for infected wounds and not using injectable street drugs.

5. In the event of an intentional aerosolization of *C. botulinum*, proper personal protective equipment, including clothing and respirator use, must be employed by all personnel entering a *C. botulinum* exposure zone. Only experienced and fully equipped personnel should enter the

exposure zone until safety can be assured.

6. Botulinum toxin degrades rapidly in the environment with substantial degradation occurring by 2 days after aerosolization. Contaminated surfaces should be cleansed with 0.1% hypochlorite bleach solution if they cannot be avoided for the hours to days required for natural degradation.

C. Disease Treatment

The mortality and sequelae associated with botulism have diminished with contemporary therapy. Despite this increase in survival, the paralysis of botulism can persist for weeks to months with concurrent requirements for fluid and nutritional support, assisted ventilation, and treatment of complications. The mainstays of therapy are meticulous intensive care unit support, with mechanical ventilation if needed, and administration of antitoxin. Timely antitoxin administration may arrest the progression of paralysis and decrease the duration of illness.

For cases of foodborne, wound, or iatrogenic botulinum, antitoxin is available from the CDC via state and local health departments (LHD). The heptavalent botulinum antitoxin (HBAT) contains equine-derived antibody to the seven known botulinum toxin types (A-G). Confirmatory lab results can take 10 to 12 weeks turnaround from CDC, so the antitoxin should be administered as soon as the diagnosis is suspected and before confirmatory laboratory results are available. Antitoxin will prevent further paralysis but will not reverse existing neurological defects.

Infant botulism is treated with BabyBIG®, Botulism Immune Globulin Intravenous (Human) (BIG-IV) and is available through the Infant Botulism Treatment and Prevention Program (IBTPP) of the California Department of Public Health by calling telephone number (510) 231-7600. BIG-IV is approved by the U.S. Food and Drug Administration for the treatment of infant botulism types A and B, and a controlled trial demonstrated reduction in hospitalization from 5.7 to 2.6 weeks in infants receiving BIG-IV compared to controls.

III. DISEASE INVESTIGATION

A. Criteria for Case Ascertainment

A toxin neutralization bioassay in mice is used to detect botulinum toxin in stool, serum, gastric aspirate, or suspect foods. Stool is the preferred specimen. Testing cannot be done by clinical laboratories and must be coordinated through public health. Call the local health department or West Virginia Department of Health Epidemiologist on-call at (304) 558-5358, ext. 2 to arrange for testing.

B. Case Definition and Case Classification (2011)

1. Foodborne Botulism

Clinical Description: An illness of variable severity. Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

Laboratory Criteria: Detection of botulinum toxin in serum, stool, or patient's food, OR Isolation of *Clostridium botulinum* from stool.

CASE CLASSIFICATION

Probable: A clinically compatible case with an epidemiologic link (e.g., ingestion of a home- canned food within the previous 48 hours)

Confirmed: A clinically compatible case that is laboratory confirmed or that occurs among persons who ate the same food as persons who have laboratory-confirmed botulism

2. Infant Botulism

Clinical Description: An illness of infants, characterized by constipation, poor feeding, and "failure to thrive" that may be followed by progressive weakness, impaired respiration, and death

Laboratory Criteria: Detection of botulinum toxin in stool or serum, OR Isolation of Clostridium botulinum from stool

CASE CLASSIFICATION

Confirmed: A clinically compatible case that is laboratory-confirmed, occurring in a child aged less than 1 year.

3. Wound Botulism

Clinical Description: An illness resulting from toxin produced by *C. botulinum* that has infected a wound. Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

4. Botulism, other

Clinical Description: An illness of variable severity. Common symptoms are diplopia, blurred vision,

and bulbar weakness. Symmetric paralysis may progress rapidly.

Laboratory Criteria: Detection of botulinum toxin in clinical specimen, OR isolation of *C. botulinum* from clinical specimen.

CASE CLASSIFICATION

Confirmed: A clinically compatible case that is laboratory-confirmed in a patient aged greater than or equal to 1 year who has no history of ingestion of suspect food and has no wounds

C. Health Care Provider Responsibilities

1. Report suspected and confirmed cases of botulism to the local health department immediately. State and local public health agencies will coordinate with the CDC to procure antitoxin for cases of foodborne and wound botulism; and with the California Department of Public Health to procure botulinum immune globulin for infant botulism.

Note: Do NOT wait for laboratory confirmation to contact the health department and arrange for antitoxin. The decision to administer antitoxin must be made on clinical presentation. Antitoxin must be administered early in the course of illness to lessen the chance of severe outcomes.

2. Coordinate with the state public health laboratory (WV Office of Laboratory Services or OLS) to obtain laboratory specimens to confirm cases of botulism. All specimen submissions to the CDC should be sent through OLS.

3. Provide the necessary clinical information to the LHD for completion of the West Virginia Electronic Disease Surveillance System (WVEDSS) Botulism Investigation Form.

4. Use standard precautions with botulism patients.

D. Laboratory Responsibilities

1. Coordinate closely with clinicians, the LHD, and the Division of Communicable Disease Epidemiology (DCDE) to ensure timely and correct specimen collection, storage, form submission, and shipping/transportation of the specimen to the CDC lab. CDC specimen instructions are available at https://www.cdc.gov/laboratory/specimen-submission/detail.html?CDCTestCode=CDC-10132

2. Report suspected and confirmed cases of botulism immediately to the LHD by phone. Refer requests for testing immediately to the LHD or DCDE at (304) 558-5358 ext. 2.

E. Local Health Responsibilities

1. Prior to the occurrence of a botulism case:

   a. Educate employees about employee health: Botulism is NOT transmitted from one person to another. It is transmitted by ingestion of contaminated food or by inhalation (in a BT event). In a BT event, the environment could be contaminated with botulinum toxin; however, the toxin degrades rapidly (e.g., within 2 days) depending on weather conditions. Nonetheless, untrained personnel should NOT enter a presumed contaminated site until cleared by the appropriate (state or federal) agencies.

   b. Assemble and train a bioterrorism (BT) epidemiologic response team: Periodically train and pre-drill individuals on the team in their respective responsibilities during an outbreak.

2. Educate healthcare providers and the public on the recognition and diagnosis of botulism.

3. Educate providers and laboratories to immediately report suspected botulism infections to the LHD in the patient's county of residence.

4. When a suspected case of botulism is reported, the LHD should contact the WV Department of Health Epi On-Call at (304) 558-5358, ext. 2. Do not wait for lab confirmation to contact the state.

   a. Treatment: On many cases the healthcare provider has already contacted IBTPP or the CDC. If not, for foodborne or wound botulism, the Epi on-call will coordinate with the CDC and the attending physician to request release of botulinum antitoxin. In the case of infant botulism, the Epi on-call will contact the *Infant Botulism Treatment and Prevention Program* for release of infant botulism immune globulin.

   b. Laboratory diagnosis: All submissions to the CDC should be coordinated through OLS. The DCDE will coordinate with clinical provider(s) and OLS for information on laboratory confirmation.

   c. Outbreak investigation: In the event of an outbreak (>1 case of botulism), the WV Dept. of Health will assist local health with the investigation and coordinate with partners.

5. Preliminary investigation and triage: Once the connections have been made to obtain the needed antitoxin, the steps to investigation of a reported case of botulism are:

   a. Confirm the diagnosis. Review the case definition and determine if the case meets the case

definition.

b. Do a preliminary epidemiological investigation. Using the case report form, interview the case or a family member to identify risk factors for foodborne botulism, wound botulism or infant botulism.
c. Collect clinical laboratory specimens: Collaborate with DCDE and the healthcare provider to obtain specimens for confirmatory testing.
d. **IF A SUSPECT FOOD IS IDENTIFIED, SEIZE FOOD SAMPLES IMMEDIATELY** especially if the food is commercially distributed. It is an emergency to confirm or rule out the food item as a source. Consult with DCDE and OLS about testing immediately.
e. If the source is not obvious or if there is more than one case. Contact DCDE for assistance in completing a more detailed epidemiological investigation.

6. Most cases identified are sporadic, however if preliminary investigation suggests an outbreak or a suspect or confirmed BT event:

a. Consult DCDE immediately. Anticipate the need to collaborate with local, state and federal officials. For a BT event, collaboration with FBI will be necessary.

F. State Health Responsibilities

1. Facilitate communication between the attending physician and appropriate agency to determine the necessity for the release of antitoxin for reported botulism cases. (CDC for foodborne or wound botulism and the IBTPP for infant botulism.) For non-infant cases call CDC's Clinical Botulism Service at (770) 488-7100. For infant cases call the Infant Botulism Treatment and Prevention Program at (510) 231-7600.

2. Immediately (within 4 hours) notify the CDC Emergency Operations Center (EOC) of any case of foodborne botulism, clusters or outbreaks of infant botulism, intentional or suspected intentional release, or any case of unknown etiology.

a. If collaboration with the CDC confirms a potential case based on clinical presentation, immediately facilitate communication with OLS to ensure appropriate specimen collection for testing. All submissions to the CDC should be coordinated through OLS at (304) 558-3530. The same phone number is to be used for after-hours reporting.

3. Promptly complete the report of botulism to the CDC through WVEDSS.

4. Provide technical expertise and consultation on surveillance, investigation, control measures and

prevention of botulism.

5. Assist local health jurisdictions in obtaining the knowledge and resources necessary for investigation of a botulism outbreak.

G. Outbreak Recognition and Investigation

Historically, the majority of botulism cases have been traced to home-processed foods such as home-canned vegetables, fruits, and meat products. Previous outbreaks have been associated with commercially canned or processed products such as chili sauce, carrot juice, garlic in oil, and inadequately eviscerated fish. In 2011, an outbreak occurred among inmates of a prison facility after consumption of an illicit homemade alcohol known as pruno. The principal ingredients are fruit, sugar, and water, but many items including root vegetables, are sometimes added, depending on the availability of foods in prison. A baked potato saved from a meal served weeks earlier and added to the pruno was the suspected source of *C. botulinum*.

Outbreak recognition and investigation requires timely and complete epidemiological investigation (risk factors, food history, history of exposures, etc.) paired with timely and complete laboratory investigation. A careful travel history and activity history, as well as dietary history, should be obtained in any suspected botulism outbreak. Patients should be asked if they know of other persons with similar symptoms.

An outbreak of botulism with the following characteristics should raise suspicion of a bioterrorist event:

1. Outbreak of a large number of cases of acute flaccid paralysis with prominent bulbar palsies.

2. Outbreak of an unusual botulinum toxin type (i.e. type C, D, F, or G, or type E toxin).

3. Outbreak with a common geographic factor among cases (e.g. airport, work location) but without a common dietary exposure (i.e., features suggestive aerosol attack).

4. Multiple simultaneous outbreaks with no common source.

5. If preliminary investigation suggests an outbreak or a suspect or confirmed BT event, proceed as follows:

   a. Anticipate the need to collaborate with local, state, and federal officials.

b. Case Finding:

i. Develop a working case definition: Develop a working case definition for the outbreak investigation. After the outbreak has been identified, a working case definition may be considered as follows: 1) a confirmed case of botulism (according to the CDC definition), 2) a clinically confirmed case of botulism after laboratory confirmation of exposure to *C. botulinum* or botulinum toxin, or 3) a clinically confirmed case of botulism while laboratory confirmation of *C. botulinum* is pending, and the individual is epidemiologically-linked to a previous confirmed case.

ii. Begin enhanced passive surveillance: Immediately begin enhanced passive surveillance as needed with healthcare providers and laboratories in the county.

1. Educate health care providers and the public in the recognition and diagnosis of botulism.

2. Educate providers and laboratories to immediately report possible botulism infections that meet the 'working case definition' to the LHD in the patient's county of residence.

iii. Prepare for active surveillance: If necessary, alert the regional epidemiologist and be prepared to expand active surveillance throughout the region, e.g., interview providers and patients, and review/abstract patient records.

iv. Confirm new cases: Receive and screen reports of suspected cases and confirm new cases.

v. Develop line list of cases: Develop a line listing of all clinically and laboratory confirmed cases. Use the line list to manage the work related to the outbreak. Record information on:

1. Case ID number (use this number to link to other databases)
2. Name
3. Age, date of birth
4. Location (hospital, clinic, home)
5. Date and time of onset of symptoms
6. Classification of case (confirmed, pending, ruled out, suspected, clinically confirmed, and laboratory confirmed)
7. Laboratory confirmation status (confirmed, negative, pending)

8. Status of clinical information (complete or incomplete), and
9. Status of exposure information (complete or incomplete).

vi. Maintain a current line listing of cases as new information becomes available.

c. Assist with development of a risk factor/exposure data base: For large outbreaks, this activity requires the leadership of an epidemiologist experienced in outbreak investigation and study design. The basic steps are:

i. Perform descriptive epidemiology to guide hypothesis generation.

ii. Perform detailed open-ended interviews with a sample of 8-10 ill persons to further develop hypotheses. Use the WVEDSS form, modified as appropriate to guide the open-ended inquiry.

iii. Design and implement appropriate epidemiologic, laboratory, and environmental studies to test, confirm, and refine hypotheses.

iv. Establish control measures as guided by the results of the investigation and continue surveillance to evaluate the effectiveness of control measures.

1. Eliminate any continuing source of exposure. Botulism is a major public health emergency. Any implicated commercial food item must be removed from circulation immediately.

2. Identify exposed population:

a) Definition of an exposed individual: An exposed individual will be a person who shared or possibly shared airspace that was contaminated by C. Botulinum, or ingested contaminated food or water.

b) Develop a line list of all persons possibly exposed. Record each person's exposure risk based upon contact or proximity to exposure.

c) Surveillance of exposed population: Assure that all exposed individuals are contacted within 24 hours. For large populations, alert the public through media announcements. Conduct surveillance of all exposed individuals for 8 days.

3. Prevention and control:

   a) Management of exposed persons: Because of the short incubation period, exposed individuals should be kept under surveillance and treated with antitoxin when botulism symptoms are first identified.

   b) Treatment of Cases: Recommend to the State Health Officer that cases should be treated with antitoxin according to current guidelines (See treatment section).

IV. DISEASE SURVEILLANCE

A. Public Health Significance

Botulism is a very serious but rare illness. Three forms of naturally occurring human botulism exist: foodborne, wound, and infant botulism. All forms result from absorption of botulinum toxin into the circulation from either a mucosal surface (gut, lung) or a wound. Wound botulism and infant botulism are infectious diseases that result from production of botulinum toxin by *C. botulinum* either in damaged tissue or in the intestinal lumen, respectively. Neither would result from intentional use of botulinum toxin. Foodborne botulism could occur from intentional or unintentional exposure, while inhalational botulism is only known to occur by intentional exposure. Iatrogenic botulism resulting from an over dosage of botulinum toxin administered for cosmetic purposes has also been reported.

Historically, the majority of botulism cases have been traced to home-processed foods such as home-canned vegetables, fruits, and meat products. Outbreaks have been associated with commercially canned or processed products such as chili sauce, carrot juice, foil wrapped baked potatoes held at room temperature, sautéed onions, garlic in oil, inadequately eviscerated fish, yogurt, cream cheese and jarred peanuts.

With recognition of the threat posed by bioterrorism, public health officials must also be prepared to recognize botulism outbreaks due to intentional causes. Botulism was first weaponized in the mid-20th century and could be disseminated by airborne or foodborne routes. The cause of a botulism outbreak should be carefully and quickly determined by thorough epidemiologic and law enforcement investigation.

B. Disease Surveillance Objectives

To identify and characterize case/s of botulism at the earliest possible time to prevent more cases.

C. Surveillance Indicators

1. Time from diagnosis to notification of public health.
2. Proportion of investigations with complete demographic information.
3. Proportion of cases with known laboratory confirmation.
4. Proportion of cases with complete risk factor investigation.
5. Proportion of cases severity information (e.g. death, sequelae).

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