Botulism

A. Agent:
Botulism is an intoxication caused by ingestion or other exposure to a neurotoxin produced by the anaerobic, Gram-positive, spore-forming bacterium *Clostridium botulinum*[1]. Because *C. botulinum* is a spore former, it can survive indefinitely under essentially any environmental condition[1-2]. The toxin is produced as the bacteria are multiplying[1-2]. There are seven types of botulinum toxin, designated A-G[2]. Types A, B, and E are the most common sources of human disease[2]. F is very rare, and C and D are not known to cause human illness[2]. The toxin is heat-labile and can be inactivated by boiling for ten minutes[1].

B. Clinical Description:
Botulism is characterized by neurologic symptoms that may include: dysphagia (trouble swallowing), dry mouth, diplopia (double vision), and dysarthria (changes in speech) (the "4 D's") [1-3]. Ptosis (drooping eyelids) and weakness, reflecting a descending (progresses downward), symmetrical flaccid paralysis that starts with the facial muscles are also characteristic symptoms[1-2]. The patient is usually mentally alert[1]. Neurologic symptoms may be preceded or accompanied by mild GI disturbance such as constipation, vomiting, or diarrhea[1]. Respiratory distress often occurs when the muscles that assist with breathing are compromised[1,3].

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)[1].

- Differential Diagnosis:
  For adults[1,3]: Guillain-Barre syndrome, myasthenia gravis, cerebrovascular accident (CVA), bacterial/chemical food poisoning, tick paralysis, chemical intoxication, mushroom poisoning, poliomyelitis, psychiatric illness.
  For infants[1,3]: disorders that produce generalized depression of central nervous system, including septicemia, meningitis, metabolic disturbances and intoxications. Also acute polyneuropathies.

C. Reservoirs:
C. botulinum spores are common in soil and elsewhere in the environment[1].

D. Mode of Transmission:
Epidemiologically, cases fall into one of four categories[1]:

Foodborne Botulism - Caused by ingestion of preformed toxin. Typically implicated foods have been low acid, home-canned foods that had not been heated adequately during canning. In recent years, however, a growing proportion of implicated foods have been "ethnic" delicacies prepared in traditional methods, such as fermented fish heads (among Alaska Natives). In some instances commercial products have been implicated, usually after some breakdown in standard canning procedures has occurred. 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 (several cases in Arizona have been due to improperly cooked/handled potatoes);
- Among Alaska Natives, "traditional" foods including fermented whale blubber, salmon heads, salmon eggs, and other delicacies.

Infant Botulism (Infants < 1 year) - The most common form of botulism.
- 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 the infant's large intestines.
- Most cases occur in infants <3 months old (almost always <6 months old).
- According to CDC - as many as 5% of SIDS cases may be infant botulism.

Wound Botulism - The toxin is produced *in situ* and disseminated in the blood.
- Results from a local *C. botulinum* infection in devitalized tissue at a wound site, where semi-anaerobic conditions are obtained.
- Often reported in drug users, especially injectors of "black-tar" heroin.

Inhalational Botulism - Does not occur naturally.
- To date, the only human cases have been the result of inadvertent inhalation of toxin by laboratory workers.
- Toxin can be absorbed through the lung and it is believed that if botulinum toxin were to be used as a bioweapon, it would be by this route.

E. Incubation Period[1-2]:

Foodborne Botulism - variable; 12 hours to several days, usually 12-48 hours. A short incubation is associated with more severe disease.

Infant Botulism - incubation period is unknown, since the precise time of ingestion often cannot be determined. It is estimated to be 3 to 30 days from the time of ingestion of spores.

Wound Botulism - Typically from 4 to 14 days.

Inhalational Botulism - thought to be 12-36 hours after inhalation, but may take several days after exposure to low doses of toxin.

F. Period of Communicability[1]:

Botulism is not communicable from person to person.

G. Susceptibility and Resistance[1]:

Anyone is susceptible to *C. botulinum* as it is naturally occurring in our environment.

H. Treatment[1-2]:

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:

Foodborne Botulism

- Botulinum antitoxin can halt the progression of symptoms caused by absorbed toxin if given promptly after exposure, but does not cure any damage that may have occurred.
- Antitoxin therapy should never be delayed pending laboratory confirmation of the diagnosis.
- The heptavalent (anti-A-G) antitoxin (also known as HBAT) is purified from horse serum (most common reported side effects include headache, nausea, and localized skin reaction including itching and hives).
- CDC controls the distribution of botulinum antitoxin, which is stocked at U.S. Public Health Service Quarantine Stations throughout the country. Any healthcare provider considering antitoxin use must consult first with their local health department. The local health department will then contact the Arizona Department of Health Services Infectious Disease Epidemiology staff (602-364-3676; after hours answering service: 480-303-1919).
- ADHS staff will contact CDC EOC (770-488-7100) – Ask for the On-Call Botulism Person to provide pertinent information and have CDC confer with the attending physician about ultimate release of antitoxin.

Infant Botulism

- Most infants do well on supportive care; however, they may need weeks of hospitalization and mechanical ventilation.
- A human-derived hyper-immune globulin (BIG-IV, or "BabyBIG") approved by FDA for treatment of infant botulism types A and B.
- BabyBIG can be obtained from the Infant Botulism Treatment and Prevention Program (IBTPP) (24 hour: 510-231-7600). Any healthcare provider considering BabyBIG can call IBTPP and do not need to discuss with the local health department or ADHS beforehand.
- Additional information about infant botulism is available at http://www.infantbotulism.org.

Wound Botulism

- Wound botulism is treated with heptavalent botulinum antitoxin. Antitoxin should be administered as for foodborne botulism (see above). Antimicrobial therapy may also be warranted for wound care.
- Debridement of the wound is indicated to remove devascularized tissue that provides the anaerobic conditions required for growth of *C. botulinum*.

Disease Management

I. Clinical Case Definition[4]:

Foodborne Botulism - Ingestion of botulinum toxin results in an illness of variable severity. Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

Infant Botulism - An illness of infants, characterized by constipation, poor feeding, and "failure to thrive" that may be followed by progressive weakness, impaired respiration, and death.

Wound Botulism - An illness resulting from toxin produced by *Clostridium botulinum* that has infected a wound. Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

Other Botulism - Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

J. Laboratory Criteria for Diagnosis[2]:

Foodborne Botulism

- Detection of botulinum toxin in serum, stool, or patient's food, OR
- Isolation of *Clostridium botulinum* from stool

Infant Botulism

- Detection of botulinum toxin in stool or serum, OR
- Isolation of *Clostridium botulinum* from stool

Wound Botulism

- Detection of botulinum toxin in serum, OR
- Isolation of *Clostridium botulinum* from wound

Other Botulism

- Detection of botulinum toxin in clinical specimen, OR
- Isolation of *Clostridium botulinum* from clinical specimen

Case Classification	
Confirmed	Foodborne Botulism - A clinically compatible case that is laboratory confirmed or that occurs among persons who ate the same food as persons with laboratory confirmed botulism. Infant Botulism - A clinically compatible case that is laboratory-confirmed, occurring among children aged less than 1 year. Wound Botulism - A clinically compatible illness that is laboratory confirmed in a patient who has no suspected exposure to contaminated food and who has either a history of a fresh, contaminated wound during the 2 weeks before onset of symptoms, or a history of injection drug use within the 2 weeks before onset of symptoms. Other Botulism - An illness clinically compatible with botulism that is laboratory confirmed among patients ≥1 year of age without histories of ingestion of suspect food and without wounds.
Probable	Foodborne Botulism - A clinically compatible case with an epidemiologic link to a suspect food item (e.g. home-canned foods within the previous 48 hours). Wound Botulism - A clinically compatible case in a patient who has no suspected exposure to contaminated food and who has either a history of a fresh, contaminated wound during the 2 weeks before onset of symptoms, or a history of injection drug use within the 2 weeks before onset of symptoms.

K. Classification of Import Status:

N/A

L. Laboratory Testing:

Approval for botulism testing must be obtained from the ADHS Office of Infectious Disease Services prior to submission (call: 602-364-3676; after hours answering service: 480-303-1919). ADHS will contact CDC for further assistance. No testing can occur without treatment.

Sample collection guidelines can be found here.

After receiving approval for testing, properly labeled specimens should be submitted to the Arizona State Public Health Laboratory (see the Guide to Laboratory Services for additional information: http://www.azdhs.gov/lab/documents/microbiology/lab-guide.pdf). Testing for botulism in clinical samples (culture and toxin identification) is performed at the CDC in Atlanta, GA. With prior approval, food samples can be tested at CDC.

TYPE	SPECIMEN	TRANSPORT
Infant Botulism	-Stool for culture and toxin – 10 to 20 grams (or as much as possible); If an enema is needed, use sterile non-bacteriostatic water -Rectal swab -Food or other potential sources for toxin and culture	All specimens should be kept at refrigerated temperatures during storage and shipment. Shipment should contain ice or cool packs.
Foodborne Botulism (Adult)	-Serum – 5 to 15 mL without anticoagulant -Stool – 10 to 20 grams; If an enema is needed, use sterile non-bacteriostatic water -Vomitus -Gastric contents -Remainder of suspected food.	
Wound Botulism	-Serum – 5 to 15 mL -Debrided tissue, exudate or swab samples from wound. -Stool 10 to 20 grams (to rule out foodborne botulism)	

M. Assessing Laboratory Results:
The State Laboratory will notify the submitting agency and the Office of Infectious Disease Services with results of the botulism testing as soon as they are available.

N. Outbreak Definition:
An outbreak is at least one case of confirmed botulism with evidence of transmission occurring within Arizona.

Investigation Guidelines

O. Time Frame:
Report all high suspect cases to ADHS OIDS Epidemiology, within 24 hours of initial report (ideally as soon as diagnosis is suspected).

- Case should be entered into MEDSIS within 24 hours.
- Outbreaks should be entered into MEDSIS Outbreak Module within 24 hours.

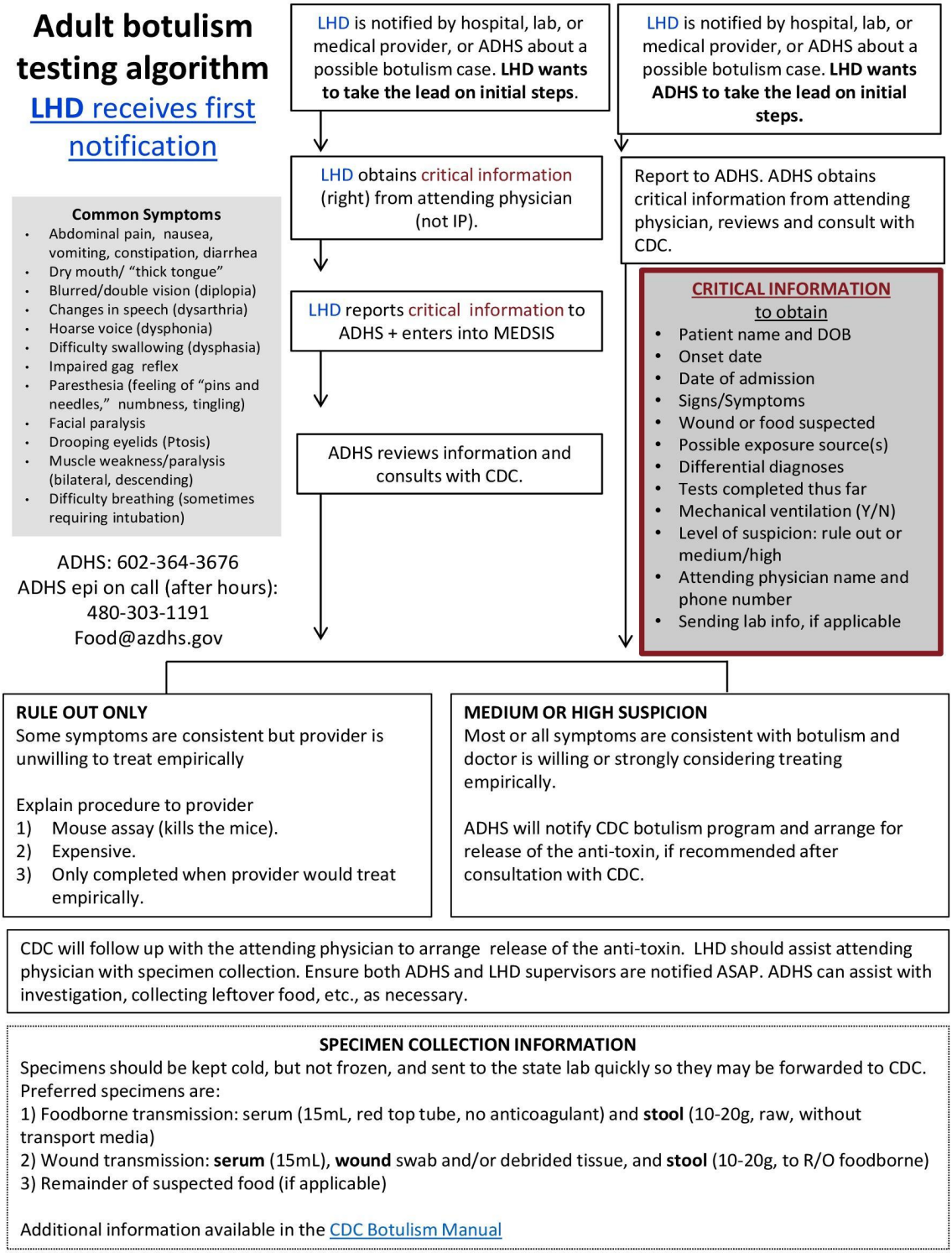
Investigational activities should begin immediately!

P. Forms:

- ADHS Adult Botulism Investigation Form: https://azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/adult-botulism.pdf

- ADHS Infant Botulism Investigation Form: https://azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/infant-botulism.pdf

Testing algorithm:



Suspected Infant botulism algorithm

1. Public health is notified by hospital, lab, or medical provider, or ADHS about a possible infant botulism case.

2. Obtain critical information (right).

3. Direct attending physician to contact the **Infant Botulism Treatment and Prevention Program**.

4. Provide a notification email to county and AHDS managers, food@azdhs.gov and other necessary individuals with critical information. The county is responsible for creating a case in MEDSIS and providing it to ADHS.

5. Provide guidance to the attending physician regarding sample collection. Samples will be sent to the state lab (ASPHL) and tested at CDC. Ensure samples are accompanied by the laboratory submission form.

CRITICAL INFORMATION

- Patient name and DOB
- Onset date
- Date of admission
- Signs/Symptoms
- Possible exposure source(s)
- Differential diagnoses
- Tests completed thus far
- Mechanical ventilation (Y/N)
- Attending physician name and phone number
- Sending lab info, if applicable

Infant Botulism Treatment and Prevention Program
(510) 231-7600
Infantbotulism.org

ADHS: 602-364-3676
ADHS epi on call (after hours): 480-303-1191
Food@azdhs.gov

COMMON SYMPTOMS

- Muscle weakness (poor head control, "floppy")
- Altered/feeble cry
- Trouble swallowing
- Poor suckling/eating
- Constipation (typically the first symptom)/diarrhea
- Irritable
- Loss of facial expression
- Drooling/pooling of saliva
- Fever
- Difficulty breathing
- Ptosis (drooping eyelids)
- Pupils: sluggish/dilated
- Somnolent

SPECIMEN COLLECTION INFORMATION

Specimens should be kept cold, but not frozen, and sent to the state lab quickly so they may be forwarded to CDC. Please direct provider to **collect stool.**

The stool sample should be raw and placed into a sterile urine container with a tight, screw-capped lid. Do not use fixatives or preservatives.

If stool collection is not possible, perform an enema using non-bacteriostatic water. Glycerin suppositories should not be used. For more detailed instructions, see here.

Additional information available at infantbotulism.org.

Q. Investigation Steps:

Inform Program Manager as soon as possible regarding a suspect case.

The investigation steps below are intended for a local health jurisdiction. If the investigation is ADHS led, please refer to the ADHS on-call manual and ADHS-specific algorithm.

Confirm Diagnosis

- Obtain information that supports clinical findings in the case definition and information on the progression of clinical illness, including:
  - Counties will need to provide the following information to ADHS, which will be shared with the on call botulism doctor at CDC to evaluate the need for botulism anti-toxin:
    - Patient name and DOB
    - Onset date
    - Date of admission
    - Signs/Symptoms
    - Possible exposure source(s)
    - Differential diagnoses
    - Tests completed thus far
    - Mechanical ventilation (Y/N)
    - Level of suspicion: rule out or medium/high
    - Attending physician name and phone number(s)
  - Request medical records that include patient's admission notes, history and physical exam findings, progress and consultation notes, lab report(s), neurologic exam findings, any testing performed (and results), complications, and a discharge summary, if available.
  - Hospitalized patients should be treated with standard precautions.
- If provider is interested in pursuing testing and treatment, call ADHS (602-364-3676 or 480-303-1919 for after-hours service) with case information (see above). ADHS will consult with CDC on-call botulism doctor. If warranted, CDC will speak directly with the clinician to conduct an assessment and determine need for release of anti-toxin.
- If botulism testing is approved, work with provider to coordinate appropriate specimen collection and transport to Arizona State Public Health Laboratory. Remind the provider and submitting lab that specimens must be appropriately labeled in order to be tested.
  - Notify ASPHL of specimen arrival and that it is approved for testing. Please notify labreceiving@azdhs.gov, making sure to CC food@azdhs.gov.
  - Botulism testing is performed at the CDC. ASPHL will forward approved specimens to CDC for testing.
- Send summary email to local and ADHS staff and program managers as soon as possible, even if testing is not approved.

Conduct Case Investigation

- Interview the case and/or other close contacts to determine source, risk factors and transmission settings.
- Collect information as specified on the Communicable Disease Report and investigation forms (see section P for links to these forms).
  - For adults, focus on the incubation period of 7 days prior to illness onset.
  - For infants, consider exposures since child's birth.

Adult Botulism Specimen Collection and Testing

All testing for botulism must be arranged through public health. Testing cannot occur without treatment.

ADHS PREPAREDNESS

Collection

Stool and **serum** should be collected for **all** cases.

Collect additional samples if wound botulism is suspected.

SERUM

15ml serum (without anticoagulant), 5ml minimum.

(red top tube)

STOOL

10 to 20g raw stool. If an enema is needed, use sterile non-bacteriostatic water.

(sterile cup)

WOUND

Debrided tissue or wound swab in anaerobic media.

(Port-A-Cul tubes or vials. Cultured tissue also acceptable)

Shipping

Each specimen requires an ASPHL **submission form**.

Ship and maintain specimens at **4°C.**

TO: ASPHL
250 N. 17th Ave
Phoenix, AZ 85007

Testing and Results

Testing for botulism is conducted at **CDC** in Atlanta.

Preliminary results are typically available in one week.
Final results are reported within three weeks.

To finalize the case, complete a Clinical Outcome Report and fax to both CDC and ADHS.

Arizona Department of Health Services (ADHS)
(p) 602-364-3676 (f) 602-364-3199

Arizona State Public Health Laboratory (ASPHL)
(p) 602-542-1190 (f) 602-364-0758

Foodborne Botulism

- 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. Identify the following products that were consumed in the week prior to onset of symptoms:
  - Home-canned, vacuum-packed, or traditionally preserved foods. 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, that some cases may develop symptoms several days after the index case). Identify and collect all remaining jars of the home-canned foods.
  - Commercially canned or vacuum-packed foods or mishandled commercial products; such products are rarely implicated. For implicated foods, determine the brand, manufacturer, package size, lot number, and place and date of purchase. If this product is highly suspected as source of contamination, share information with ADHS Food Safety Program Manager for additional follow up.
  - Preserved or traditionally prepared fish and marine products.
  - Items stored in oil (ie: onions, garlic) or foil (baked potatoes).
  - Sausage; preserved or traditionally preserved meats, and inadequately refrigerated meats.
  - In prison setting: consider prison brew (pruno or hooch), especially if made with baked potatoes.
  - With the identification of more than one case of botulism without a likely source of exposure, consider the possibility of intentional exposure through deliberately contaminated food. Interview the case and others who may be able to provide information about possible exposures such as locations where food and water were consumed, particularly at gatherings and public events.
- When a commercial product is implicated, see below.
- Complete the Adult Botulism Investigation Form.
- Ensure the provider completes the Clinical Outcome Report form, faxing a copy to CDC (404-639-2205 ATTN: Botulism Surveillance) and ADHS (602-364-3199).

Infant Botulism

- Complete the Infant Botulism Reporting Form.
- No public health follow-up is required. Provide education and counseling as needed.
  - Honey is not recommended for children under 1 year of age as it can be contaminated with botulism spores.

Wound Botulism

- Ask the patient about illicit injection drug use, including type of drugs used and how the drugs are used (i.e., injected into veins, injected into tissues, snorted, etc). In addition to drug use, interview regarding potential foodborne exposures.
- Complete the Adult Botulism Investigation Form.
- Once foodborne illness is ruled out, no public health follow-up is required unless there is reason to suspect drug contamination.

Inhalational Botulism

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

Identify Potentially Exposed Persons

- Obtain the name, address, and telephone number of every person who may have eaten the suspected food item.
- Obtain the name, address, and telephone number of every person who may have the suspect home-processed food in his or her possession.
- Obtain the organization name, contact telephone number, and attendance lists (particularly e-mail or telephone lists) for every suspected gathering, public event, or other shared environmental exposure.

Conduct Contact Investigation

- Locate additional cases and/or contacts.
  - Consider ill contacts that shared exposure of consuming potentially contaminated item(s).
- Follow-up symptomatic contacts as suspect cases.

Foodborne Botulism - If reachable within six hours of exposure, other persons who have eaten implicated food should be purged and given gastric lavage to remove any unabsorbed toxin. Persons who have eaten the implicated food should be monitored for signs of botulism at least twice daily for three days, and instructed to seek medical care immediately should symptoms develop.

Wound Botulism - When possible, provide education to risk groups and to healthcare providers serving them regarding typical symptoms of botulism and the importance of rapid diagnosis and treatment. Potential routes for education include needle exchange programs and urban hospital emergency departments.

Control Measures

- Medical personnel caring for patients with suspected botulism should use standard precautions[3].
  - Patients with suspected botulism do not need to be isolated[3].
- If meningitis is suspected in a patient with flaccid paralysis, medical personnel should use droplet precautions.
- Heating to an internal temperature of 85°C for at least 5 minutes will detoxify contaminated food or drink.
- When inhalational exposure is anticipated, some protection may be conferred by covering the mouth and nose with clothing such as an undershirt, shirt, scarf, or handkerchief.
  - In contrast with mucosal surfaces, intact skin is impermeable to botulinum toxin.
- After exposure to botulinum toxin, clothing and skin should be washed with soap and water.
  - Contaminated objects or surfaces should be cleaned with 0.1% hypochlorite bleach solution if they cannot be avoided for the hours to days required for natural degradation.

Environmental Consideration

- Restaurant is implicated: conduct an immediate inspection to identify home canned or mishandled product in the facility. Collect specimens as needed.
- Commercial product is implicated, IMMEDIATELY notify ADHS Office of Infectious Disease Services Program Manager. If an environmental exposure is suspected, review with ADHS Epidemiology Program Manager and Food Safety Manager for assistance with sampling and coordination with relevant internal and outside agencies (FDA, USDA, CDC, etc).

Notifications

Be sure to include both local and state partners in communications regarding the investigation.[2] At a minimum, this should include manager and epidemiology staff from the local jurisdiction where the case resides, ADHS state epidemiologist, OIDS program manager, and foodborne disease epidemiologist.

R. Outbreak Guidelines:

With the identification of more than one case of botulism without an obvious source of exposure, consider the possibility of a contaminated commercial food product. In such situations, call ADHS IMMEDIATELY at 602-364-3676 or 480-303-1919 for after-hours service.

The cases will need to be extensively interviewed to identify possible exposures such as locations where food and water were consumed, particularly at gatherings and public events.

S. Special Situations:

Bioterrorism Potential[1-2]:
C. botulinum toxin has been classified as a possible agent of bioterrorism because it is extremely potent and lethal. The toxin is also easy to produce and transport, and affected individuals often need extensive and prolonged intensive care. Dissemination through aerosol or food would be the most likely mode of spread. Aerosol dissemination could cause many cases in a geographic area. Therefore, inhalational botulism produced by an act of bioterrorism should be considered for 2 or more botulism cases linked temporally and geographically but without a likely common foodborne or drug exposure.

In such situations, contact OIDS Program Manager or Office Chief IMMEDIATELY at 602-364-3676. The cases should be extensively interviewed to identify possible exposures such as gatherings, public events, specific geographic locations, large buildings, shopping areas, and public transportation.

- Inform ADHS Preparedness Bureau immediately!
- Inform Law Enforcement immediately (FBI, ACTIC)!
- Follow steps outlined in the *Criminal and Epidemiological Investigation Handbook* on how to conduct a joint Epi and Law Enforcement Investigation.

Additional Information & Resources

Arizona Regulations/Statutes Related to Infectious Disease:
https://apps.azsos.gov/public_services/title_09/9-06.pdf

Centers for Disease Control and Prevention: Botulism in the United States, 1899-1996. Handbook for Epidemiologists, Clinicians, and Laboratory Workers, Atlanta, GA. CDC, 1998:
https://www.cdc.gov/botulism/pdf/bot-manual.pdf

CDC Botulism Surveillance:
http://www.cdc.gov/nationalsurveillance/botulism-surveillance.html

CDC Botulism General Information: https://www.cdc.gov/botulism/

Washington State Department of Health, Botulism Guidelines (July 2014):
http://www.doh.wa.gov/Portals/1/Documents/5100/420-047-Guideline-Botulism.pdf

For additional information and/or questions concerning isolate submission, and laboratory supplies:

- Arizona Department of Health Services (ADHS) State Public Health Laboratory (ASPHL), located at 250 N 17th Avenue, Phoenix, AZ 85007, Ph: 602-542-1188, Fax: 602-542-0760. http://www.azdhs.gov/lab/documents/microbiology/lab-guide.pdf

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