Botulism

Botulism

Causative bacterium: ***Clostridium botulinum*** **neurotoxin**

- *C. botulinum* is an anaerobic, gram-positive, spore-forming rod that produces a neurotoxin (BoNT).
  - The bacterium and its spores are widely distributed in nature (soils, wetland sediments, GI tracts of fish and mammals and gills/viscera of crabs and other shellfish).
  - 7 Types (A to G) distinguished by the antigenic characteristics of the neurotoxins they produce.
    - Types A, B and E are the primary cause of human botulism.
    - Type F rarely identified as cause of human botulism
    - Types C & D cause most cases in animals

- *C. butyricum*-like and *C. baratii*-like species have been reported to rarely produce BoNT types E and F.

Case definition

There are 4 naturally occurring forms of botulism (foodborne, wound, infant and adult intestinal toxemia) and 2 other forms (inhalation and iatrogenic).

Foodborne

- *Confirmed*: a clinically compatible illness that is laboratory confirmed or that occurs among persons who ate the same food as persons who have laboratory-confirmed botulism.
  Laboratory criteria for diagnosis
  - Detection of botulinum toxin in serum, stool, or patient's food, or
  - Isolation of *Clostridium botulinum* from stool
- *Probable*: a clinically compatible illness with an epidemiologic link (e.g., ingestion of a home-canned food within the previous 48 hours)

Identification of C. botulinum in food source may be helpful, but not diagnostic because botulinum spores are ubiquitous. However, the presence of BoNT in a food can be used to implicate it as a source.

Intestinal (formerly Infant)

- *Confirmed*: a clinically compatible illness that is laboratory-confirmed, occurring in a child aged less than 1 year
  Laboratory criteria for diagnosis
  - Detection of botulinum toxin in serum or stool or
  - Isolation of *Clostridium botulinum* from stool

Wound

- *Confirmed*: a clinically compatible illness that is laboratory confirmed in a patient who has no suspected exposure to contaminated food and who has 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

Laboratory criteria for diagnosis

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

- *Probable*: a clinically compatible illness 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

Adult Intestinal Toxemia

- *Confirmed*: a clinically compatible illness 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

Laboratory criteria for diagnosis

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

Signs and symptoms

Foodborne botulism: Early signs often include GI upset preceding or accompanying neurological symptoms such as the following:

- Dryness of mouth
- Blurred vision
- Double vision
- Afebrile
- Voice impairment
- Dysphagia
- Symmetric, descending muscle weakness
- Respiratory failure

Infant botulism: Clinical signs may progress over hours, but usually occur over 1-4 days and include:

- Constipation
- Listlessness
- Lethargy
- Afebrile
- Altered cry
- Poor feeding
- Pooled oral secretions
- Loss of head control (aka Floppy Baby Syndrome)

See http://www.infantbotulism.org/ for more detailed descriptions.

Wound or Adult Intestinal botulism: Clinical signs will be consistent with those abnormal neurological signs observed with foodborne botulism (see above).

Other significant diagnostic findings:

- Mental status and sensory abilities of patient remain unchanged, because BoNT specifically disrupts muscle function by inhibiting the release of acetylcholine at myoneural junctions.
- Presumptive diagnosis made on the basis of patient history and clinical signs.

Transmission

Transmission primarily occurs via consumption of foods contaminated with the bacterium and/or BoNT. Inhalation, injection and contact are less common routes of transmission.

Incubation period: 6 hrs to 10 days for foodborne botulism, with onset of clinical signs usually occurring between 18 and 36 hrs after ingestion of BoNT. May be longer for infant botulism where bacterium colonizes the intestinal tract prior to producing toxin.

Period of communicability: Person to person transmission does not occur. However, remnants of the food source may pose a continued hazard to others.

Asymptomatic carriage: None reported

Priority for local public health response

It is imperative that a physician suspecting botulism in a patient immediately be put in contact with CDES staff to facilitate the required consultation with the CDC or the Infant Botulism Prevention Program at the California Department of Public Health in order to acquire anti-toxin. Physicians may initially by-pass LPHD when seeking a CDC consult. See the section below on "Roles and Responsibilities" for phone numbers to obtain anti-toxin.

*It is the responsibility of the clinician **and** the diagnosing laboratory to report a case of botulism **by telephone** to local and/or state public health officials as soon as possible. Reporting via the Wisconsin Electronic Disease Surveillance System (WEDSS) is not sufficient notification.*

** Response steps 1 and 2 may be completed directly by physician or medical facility ICP.

1. Ascertain clinical history of patient and how presumptive diagnosis was made. Using the Screening Worksheet (see Appendix A or EpiNet Manual) determine or confirm:
    - Clinical signs and symptoms
    - Date of illness onset
    - Physician name and direct contact information.
2. **Report by phone immediately** (per Health Code, HFS 145) all potential cases of botulism to the Wisconsin Communicable Disease Epidemiology Section (CDES).
    - General number for CDES staff during weekdays: **(608) 267-9003**
    - Emergency number for on-call CDES staff after hours and on weekends: **(608) 258-0099** (This number is for local health departments and clinical practitioners only, not for the general public.)
3. Following CDC determination of case status, LPHD staff will be contacted by CDES to conduct the case investigation.
    - Identification of potentially contaminated food source is critical to prevent additional cases. Interview patient or their contact as soon as possible. Interview may need to be performed in hospital setting. Obtain a complete 10 day food history with a focus on home-canned foods
    - Secure all implicated food products. Instructions for submitting food specimens will be provided by CDES.
        - Promptly contact CDES staff with suspect food information.
    - Complete Botulism Screening Worksheet and Acute & Communicable Disease Case Report (F 44151).
4. Enhance surveillance for additional cases:
    - With foodborne cases, rapidly investigate suspect cases and contact others having consumed suspect food source within the past 10 days.
    - Alert physicians in area of case.

Contact investigation

Person-to-person transmission of botulism does not occur.

Foodborne: Obtain list of contacts that may have consumed suspected food sources of BoNT within the past 10 days. Provide contacts with disease recognition information and need for immediate medical attention if symptoms occur. Severity and progression of illness is linked to amount of BoNT consumed.

Wound botulism: If injection drug use is implicated, attempt to identify other users of the implicated drug. Use of mass media may be considered.

Botulism outbreaks associated with a commercial product will involve mobilizing multiple agencies such as WDATCP, FDA, FSIS and CDC.

Chemotherapeutic agents

Foodborne, Wound and Adult Intestinal botulism cases require immediate treatment with a polyvalent (equine type AB or ABE) antitoxin available through CDC. Clinical specimens should be collected prior to administering antitoxin. Antitoxin should not be withheld pending test results.

Prophylactic use of the antitoxin is not recommended in most cases.

Infant botulism is treated with BabyBIG®, Botulism Immune Globulin Intravenous (Human) (BIG-IV), which consists of human-derived botulism antitoxin antibodies and is approved by the U.S. Food and Drug Administration for the treatment of infant botulism types A and B.

Proper Name: Botulism Immune Globulin Intravenous (Human)
Tradename: BabyBIG
Manufacturer: California Department of Health Services, License #1622

Roles and Responsibilities during a case of Botulism

BoNT is a Category 1 Select Agent/Toxin. In non-infant cases where the source is not readily evident, a bioterrorism event should be considered and appropriate actions taken. The following steps describe how to respond to cases NOT associated with an intentional exposure.

Wisconsin Communicable Disease Epidemiology Section (CDES)

1. Facilitate consult between the physician and CDC or the Infant Botulism Prevention Program at the California Department of Public Health to acquire antitoxin.
   a. Complete the Botulism Screening Worksheet (Appendix A).
   b. Infant botulism: Contact *Infant Botulism Treatment and Prevention Program* at the California Department of Public Health **(510) 231-7600**.
   c. Foodborne, Wound or Adult Intestinal botulism: Contact CDC **(770) 488-7100.**

2. Contact Minnesota Infectious Disease Epidemiology Prevention and Control to request approval to test clinical and environmental specimens at the MDH Clinical Lab. Provide completed Botulism Screening Worksheet.

   MN Infectious Disease Epi (24/7): (651) 201-5414 or (877) 676-5414
   MN Clinical Laboratory: (651) 201-5253

   - Provide physician or specimen collecting facility with collection and shipping instructions and forms for MDHCL (**Appendix B**).
     - http://www.health.state.mn.us/divs/phl/clin/gts/testsc.html#cbottoxin
   - Collect clinical specimens before administering anti-toxin.
   - WSLH can forward specimens to MDH Lab if needed.

3. If a commercial product is implicated as the source, immediately contact DATCP, CDC, and other response agencies as indicated by product type.
4. Coordinate investigations of clinical cases
5. Update and provide case data to CDC.
6. If multiple cases, review disease incident data to investigate potential links.

Local Health Department (LHD)

See *Priority for Local Public Health Response* on page 3

MN Dept of Public Health Clinical Laboratory

1. Perform *Clostridium* Culture and Toxin Neutralization Assay.
2. Report results to submitting laboratory/clinic and CDES.
3. Report identification of BoNT or *C. botulinum* to CDCP Select Agent office.

General number for CDES staff during weekdays: **(608) 267-9003**

Emergency number for on-call CDES staff after hours and on weekends: **(608) 258-0099**
(Emergency number is for local health departments and clinical practitioners only, not for the public.)

References

Center for Disease Control and Prevention, NCEZID, Botulism Technical Information available at: http://www.cdc.gov/nczved/divisions/dfbmd/diseases/botulism/technical.html

Centers for Disease Control and Prevention: Botulism in the United States, 1899-1996. Handbook for Epidemiologists, Clinicians, and Laboratory Workers, Atlanta, GA. CDCP, 1998.

Snyder, JW, ed. Sentinel level clinical microbiology laboratory guidelines for suspected agents of bioterrorism and emerging infectious diseases – Botulinum Toxin. Am. Soc. of Micro, 2003. Available at: http://www.asm.org/index.php/policy/sentinel-level-clinical-microbiology-laboratory-guidelines.html

MN Department of Health. Clinical Laboratory Guide to Services. Available at: http://www.health.state.mn.us/divs/phl/clin/gts/

Infant Botulism Treatment and Prevention Program. Division of Communicable Disease Control, CA Dept of Public Health. http://www.infantbotulism.org/

APPENDIX A

DEPARTMENT OF HEALTH SERVICES
Division of Public Health

STATE OF WISCONSIN
(608) 267-9003

Botulism Testing Request
Screening Worksheet

Patient Information

Patient's Name (Last) (First) (M.I.)	Date of Birth (mm/dd/yyyy)	Age	Gender Male / Female
Patient's Address City State Zip Code			
County of Residence	Home Telephone ( )	Work or Cell Telephone ( )	
Occupation or School, Day Care	Patient's Parent/ Guardian if patient is a minor		

Exposure Information (non-infant cases)

Does patient have a history of consuming home canned food products?	Y	N	U	If yes, date & time consumed:
If yes, what food(s) and how were they prepared?				
Does patient have a history of a fresh, contaminated wound or injection drug use during past 2 weeks?	Y	N	U	If yes, describe
Has patient consumed _____ product?	Y	N	U	If yes, date & time consumed:

Clinical Information

Hospital or Clinic providing care	Hospitalized? Yes / No / Unk	Admission Date (mm/dd/yyyy)
Physician's Name	Office Telephone ( )	Pager / Cell Telephone ( )

Symptoms: Onset of illness (date & time of first symptoms)

Non-Infant (Foodborne, Wound, other)	Y	N	U		Y	N	U
Descending paralysis				Difficulty breathing			
Double Vision				Muscle weakness			
Blurred Vision				Dizziness			
Drooping eyelids				Nausea			
Slurred speech				Abdominal cramps			
Dry mouth				Vomiting			
Difficulty swallowing				Diarrhea			
				Fever (highest temp. _____)			
Infant Botulism	Y	N	U		Y	N	U
Constipation				Poor feeding			
Lethargic				Pooled oral secretions			
Weakness				Poor muscle tone (especially in neck)			
Drooping eyelids				Descending paralysis			
Altered or weak cry				Fever (highest temp._____)			

Clinical Diagnostic Tests Which of the following tests have already been performed?	Y	N	Pending	Result(s)
CSF examination				CSF protein _____ mgm% WBC total
Electromyography (EMG)				BSAP noted?
Brain scan				
Tensilon test				

Treatment Has anti-toxin been requested or given?	☐ Requested Date:	☐ Given Date:	Has patient been Intubated? Yes / No Date:

Please fax completed worksheet to WDPH-CDES epidemiologist using secure fax: 608-261-4976.

Communicable Diseases & Epidemiology Section
Revised December 2011

APPENDIX B

Minnesota Department of Health Clinical Laboratory

Clostridium botulinum - Detection in Clinical and Environmental Samples and Food

Methodology: Culture
Restrictions: Contact Infectious Disease Epidemiology Prevention and Control at (651) 201-5414 or (877) 676-5414 before requesting this test.
Fee Sticker: Not required
Specimen: See collection requirements below or online at Specimen Requirements
Shipping: See shipping requirements below or online at Specimen Requirements
Turnaround: Within 10 working days of specimen receipt

This disease must be reported to MDH as required by State Rule 4605.7040

Note: This organism has been designated as a Select Agent (Select Agent Regulation, 42 CFR, 73, Final Rule). Special handling criteria apply. Please contact the laboratory for special instructions.

Clostridium botulinum - Identification/Confirmation of Referred Isolate

Methodology: Biochemical testing, Toxin testing
Restrictions: None
Fee Sticker: Not required
Specimen: Actively growing pure culture on suitable medium
Shipping: Ship at room temperature.
Turnaround: Not available

This disease must be reported to MDH as required by State Rule 4605.7040

***Clostridium botulinum* toxin** - Detection in Clinical and Environmental Samples and Food

Methodology: Toxin Neutralization Assay
Restrictions: Contact Infectious Disease Epidemiology Prevention and Control at (651) 201-5414 or (877) 676-5414 before requesting this test.
Fee Sticker: Not required
Specimen: See Specimen Requirements
Shipping: See Specimen Requirements
Turnaround: Within 5 working days of specimen receipt

This disease must be reported to MDH as required by State Rule 4605.7040

Source: http://www.health.state.mn.us/divs/phl/clin/gts/testsc.html#cbottoxin on 09/08/11

Minnesota Department of Health

Collection and Transport of Samples for Botulism Testing

Suspected Foodborne Botulism

Acceptable Specimens	Required Volume/Comments	Toxin Assay (T) or Culture (C) Performed
Serum (Priority Sample Type)	5 ml (less results in incomplete testing)	T
Gastric contents	20 ml, anaerobic transport system	T, C
Vomitus	20 ml, anaerobic transport system	T, C
Stool	25-50 g (walnut-size) collected before anti-toxin treatment.	T, C
Sterile water enema	Collect using a minimal amount of water, before anti-toxin treatment.	T, C
Implicated consumed food – commercial or home-prepared	Leave foods in their original containers, if possible, or transfer to sterile, leak-proof containers. Empty containers with remnants of food are acceptable.	T, C
Unopened home-prepared food from the batch consumed by the patient	Leave foods in their original containers.	T, C
Unopened commercial products	Products are referred immediately to the FDA.	T, C

Suspected Infant Botulism

Acceptable Specimens	Required Volume/Comments	Toxin Assay (T) or Culture (C) Performed
Stool (Priority Sample Type)	25-50 g (walnut-size) collected before anti-toxin treatment.	T, C
Sterile water enema	Collect using a minimal amount of water, before anti-toxin treatment.	T, C
Serum	3 ml (0.5 ml will allow screening but incomplete testing)	T
Rectal Swab	More useful for culture than toxin detection.	C
Potential Sources	Include honey, opened formula (Unopened commercial products are referred to the FDA.), other foods/liquids fed to the infant. Environmental sampling is discouraged.	C

Suspected Wound Botulism

Acceptable Specimens	Required Volume/Comments	Toxin Assay (T) or Culture (C) Performed
Serum (Priority Sample Type)	5 ml (less results in incomplete testing)	T
Wound swab	Anaerobic transport system	C
Tissue or exudate	Anaerobic transport system	C
Stool	To rule out foodborne botulism. Collect as above	T,C

Suspected Intentional Toxin Release

Acceptable Specimens	Required Volume/Comments	Toxin Assay (T) or Culture (C) Performed
Clinical material	Serum, stool, sterile water enema as above.	T
Food	As above.	T
Environmental swabs	Send in individual clean, dry containers	T

Shipping Requirements

Notify the laboratory in advance (651-201-5253).

- Collect and transport clinical samples in sterile, leak-proof containers.
- Leave foods in their original containers, if possible, or place in sterile leak-proof, unbreakable containers. Place each container in a separate sealed plastic bag to prevent cross-contamination during shipping. Label completely.
- Ship by the most rapid means available.
- Store and ship specimens in anaerobic transport systems at room temperature.
- Store and ship all other specimens at 4ºC.
- Freezing should be avoided as it decreases recovery of C. botulinum and may decrease toxin activity. However, if a delay of more than several days cannot be avoided, freeze samples for storage and ship frozen.

Source: http://www.health.state.mn.us/divs/phl/clin/gts/appendixd.html on 09/08/11

Address & Parking Information

Guidelines for Referring Biomedical Material MDH Clinical Laboratory

US Postal Service Address:
Minnesota Department of Health
Public Health Laboratory Division
P.O. Box 64899
St. Paul, MN 55164-0899

Courier Service Address:
Minnesota Department of Health
Public Health Laboratory Division
601 Robert Street North
St. Paul, MN 55155

Shipping guidelines for Select Agents found at http://www.asm.org/index.php/policy/sentinel-level-clinical-microbiology-laboratory-guidelines.html

Important Contacts	Phone Numbers
General Lab Receptionist	651-201-5200
Fax Number	651-201-5514
Enterics Laboratory	651-201-5048
Epidemiology (24 hour)	651-201-5414
Epidemiology (24 hour - toll free)	877-676-5414
Emergency Preparedness & Response	651-201-5582
Microbiology Laboratory	651-201-5073
MN Laboratory System (MLS) www.health.state.mn.us/mls	651-201-5581
Molecular Epidemiology Laboratory	651-201-5257
Mycobacteriology Laboratory	651-201-5053
Rabies Laboratory	651-201-5254
Sexually Transmitted Disease Laboratory	651-201-5246
Specimen Receiving, Shipping and Packaging	651-201-4953
Virology Laboratory	651-201-5248