Health, Seniors and Active Living

Public Health and Primary Health Care
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Re: Botulism Case Management

Section 8.1 *Management of Cases* has been updated to clarify information on:

Acquisition of botulinum antitoxin:

- Botulinum antitoxin may be ordered by an Infectious Diseases specialist or by the local Medical Officer of Health http://www.gov.mb.ca/health/publichealth/contactlist.html through the provincial vaccine warehouse at 204-948-1333 or Toll-free 1-855-683-3306 during regular business hours or at 204-805-4096 after hours. After regular hours, the Medical Officer of Health on call may be contacted at 204-788-8666. Patient follow-up may be required as per Health Canada regulations for Special Access products http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/index-eng.php.

Dosing of botulinum antitoxin:

- Botulinum antitoxin dosing is product specific. **Clinicians must refer to the specific product monograph(s) for the botulinum antitoxin prior to ordering and using the product to ensure correct dosing is used.** Links to the product monograph(s) of the botulinum antitoxin product(s) currently available in Manitoba can be found on the Communicable Disease Control Protocol Manual website: http://www.gov.mb.ca/health/publichealth/cdc/protocol/index.html below the Botulism protocol. Consultation with the Medical Officer of Health (204-788-8666) is highly recommended.

Please refer also to pages 6 and 7 of this protocol for the updated information.

Sincerely,

"Original Signed By"

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Botulism

Manitoba
Public Health Branch

1. Case Definition

1.1 Foodborne Botulism:

Confirmed Case: Clinical illness[1] with laboratory confirmation of intoxication including at least one of:

- Detection of botulinum toxin in serum, stool or food that was consumed by patient;

OR

- Isolation of *Clostridium botulinum* from stool (1).

Probable Case: Clinical illness[1] without laboratory confirmation, but with an indication that the client ate the same suspect food as an individual who was culture positive for *C. botulinum* or from whom botulinum toxin was detected in serum, stool or gastric aspirate (1).

1.2 Wound Botulism: Clinical illness[2] with laboratory confirmation including at least one of:

- Detection of botulinum toxin in serum;

OR

- Isolation of *C. botulinum* from a wound

AND

- Presence of a freshly infected wound in the two weeks before symptoms and no history of consumption of food known to be contaminated with *C. botulinum* (1).

1.3 Infant Botulism: Clinical illness[3] compatible with botulism in a person less than one year of age with laboratory confirmation including at least one of:

- Detection of botulinum toxin in stool or serum;

OR

- Isolation of *C. botulinum* from the patient's stool at autopsy (1).

1.4 Intestinal/Colonization Botulism: Clinical signs and symptoms compatible with botulism in a patient aged ≥ 1 year with severely compromised gastrointestinal tract functioning (i.e., abnormal bowel) due to various diseases, such as colitis, or intestinal bypass procedures, or in association with other conditions that may create local or widespread disruption in the normal intestinal flora and:

- Detection of botulinum toxin in stool or serum

OR

- Isolation of *C. botulinum* from the patient's stool or at autopsy (1).

2. Reporting Requirements

Laboratory:

- All positive laboratory results for *C. botulinum* or its toxin are reportable to the Public Health Surveillance Unit by secure fax (204-948-3044). A phone report must be made to a Medical Officer of Health at 204-788-8666 on the **same day** the result is obtained, **in addition** to the standard surveillance reporting by fax.

- Manitoba clinical laboratories are required to submit residual specimens or isolate sub-cultures from individuals who tested positive for *C. botulinum* or its toxin to Cadham Provincial Laboratory (CPL) as soon as possible (within 48 hours of report). Submitting laboratories must notify CPL of the shipment PRIOR to submission.

[1] Characterized by blurred vision, dry mouth and difficulty swallowing and speaking. Descending and symmetric paralysis may progress rapidly, often requiring respiratory support.
[2] Characterized by diplopia, blurred vision and bulbar weakness. Symmetric paralysis may progress rapidly.
[3] Characterized by constipation, loss of appetite, weakness, altered cry and loss of head control.

- *C. botulinum* or its toxin in commercial food products should be reported to the Canadian Food Inspection Agency (CFIA) at 1-204-797-4501or via e-mail at MBARC@inspection.gc.ca . The phone number is operational from 8:00 a.m. until 11:00 p.m. seven days a week, and the email account is monitored during the same time period.

Health Care Professional:

- Probable (clinical) cases of botulism are reportable to the Public Health Surveillance Unit by telephone (204-788-6736) during regular hours (8:30 a.m. to 4:30 p.m.) AND by secure fax (204-948-3044) on the **same day** that they are identified. After hours telephone reporting is to the Medical Officer of Health on call at (204-788-8666). The *Clinical Notification of Reportable Diseases and Conditions* form (http://www.gov.mb.ca/health/publichealth/cdc/protocol/form13.pdf) should be used for fax reporting.
- Cooperation in Public Health investigations is appreciated.

Regional Public Health or First Nations Inuit Health Branch (FNIHB):

- Once the case has been referred to Regional Public Health or FNIHB, the *Communicable Disease Control Investigation Form* (www.gov.mb.ca/health/publichealth/cdc/protocol/form2.pdf) should be completed and returned to the Public Health Surveillance Unit by secure fax (204-948-3044).

3. Clinical Presentation/Natural History

Four distinct naturally occurring forms of human botulism have been recognized and all forms are associated with an acute, afebrile, symmetric, descending flaccid paralysis (2, 3). The symptoms of botulism are caused by the toxin produced by *C. botulinum* and vary with the type of toxin produced rather than the site of its production (4). Typical clinical symptoms of all forms of botulism are a result of muscle paralysis from affected cranial nerves. These include double vision and dilated pupils, slurred speech, dry mouth, difficulty in swallowing and speaking and facial paralysis (5). As the disease progresses, paralysis of the limbs and respiratory dysfunction becomes apparent (5). Untreated, botulism may result in respiratory failure and death (6). With prompt attention and supportive care, the mortality rate for botulism ranges from less than 5% to 8% (4). Recovery often takes weeks to months (7) and is dependent upon the amount of toxin ingested and to a lesser extent the type of toxin (5). Type A toxin tends to cause longer lasting disease than types B and E (5).

3.1 Foodborne Botulism: Foodborne botulism is a severe intoxication resulting from ingestion of preformed botulinum toxin present in contaminated food (2). Symptoms begin 12 to 36 hours after ingestion (2). There is no fever and no loss of consciousness (2). In addition to the general signs of botulism, gastrointestinal symptoms including nausea, vomiting, constipation and abdominal swelling and less commonly diarrhea may occur (2, 5).

3.2 Wound Botulism: Wound botulism results when *C. botulinum* contaminates traumatized tissue, germinates, multiplies and produces toxin in the wound which is absorbed systemically (3).The symptoms are similar to foodborne botulism but take four to 14 days to develop (2).

Fever may be present and reflects wound infection rather than botulism (8).

3.3 Infant Botulism: Ingested *C. botulinum* spores germinate in the infant intestine to produce bacteria that release toxin (2). Colonization of infants is believed to occur because normal bowel flora that would compete with *C. botulinum* has not been fully established (9). It is the most common form of botulism (2). Infant botulism has a wide spectrum of clinical severity, ranging from mild illness with gradual onset (2) to sudden infant death caused by rapidly progressing botulism (3). The classic presentation begins with constipation followed by decreased movement, loss of facial expression, poor feeding, weak cry, diminished gag reflex, ocular palsies, loss of head control and progressive descending generalized weakness and hypotonia (3). The mortality rate for infant botulism is < 1% (4).

3.4 Intestinal/Colonization Botulism:

A syndrome similar to infant botulism (adult intestinal toxemia botulism) has been rarely observed in immunocompromised adults, those using antimicrobials, or those with some anatomical or functional bowel abnormality (2). The symptoms are similar to those of foodborne botulism (10).

3.5 Other Presentations: Inhalational botulism does not occur naturally but can result from inhalation of aerosolized neurotoxin (e.g., laboratory setting) (2). The clinical features are similar to other forms of botulism (8). Iatrogenic botulism resulting from accidental injection of the botulism neurotoxin into the systemic circulation instead of the intended therapeutic locus (e.g., cosmetic procedure, chronic pain treatment) has been reported (2, 4).

4. Etiology

Botulism is caused by toxins produced by the spore-forming bacterium *C. botulinum* (2, 5). Of the recognized subtypes of clostridial neurotoxins, only types A, B, E and rarely type F have been documented to cause human illness (2). Less frequently, cases involving type E toxin produced by *Clostridium butyricum* and type F toxin produced by *Clostridium barati* have been reported (11). *Clostridium botulinum* strains A, B, E and F have been associated with foodborne intoxications. Type E botulism is associated with the consumption of improperly prepared foods of aquatic origin, either fresh water or marine (12, 13). The toxins are absorbed from the intestine, spread to the peripheral nerves blocking the transmission of impulse (14). Cases of infant botulism are usually caused by toxin types A and B (3).

5. Epidemiology

5.1 Reservoir: Spores are found in soil worldwide, marine sediments, some agricultural products (e.g., honey), the intestinal tracts of some animals including fish (2), and household dust (15). Botulinum toxin retains much of its activity in untreated water and beverages for up to 70 days; water treatment processes inactivate the toxin (2). Growth of *C. botulinum* and production of toxin is favoured in canned food products with low-acid, low-salt, low-sugar and low oxygen content (2, 9). Home-canned vegetables, fruit and fish products are now the most common sources of botulism (4). Modern industrial canning was developed expressly for killing *C. botulinum* spores (9).

5.2 Transmission: Foodborne botulism occurs after ingestion of food containing preformed botulinum toxin not heated sufficiently to inactivate the toxin (2, 3, 16, 17). Botulinum toxin is produced in food contaminated with spores of *C. botulinum* preserved or stored improperly under anaerobic conditions that permit germination, multiplication and toxin production (3). Foodborne botulism has often been caused by home-canned foods with low acid content, such as

asparagus, green beans, beets or corn (8). Other sources have included chopped garlic in oil, chilli peppers, tomatoes, and home-canned or fermented fish (8). Commercially prepared foods have also been implicated (2). Vacuum packed hot-smoked fish is a known risk food for type E botulism (12). Consumption of ungutted salted fish products such as fesikh is a risk for botulism (18). Outbreaks have resulted from baked potatoes being consumed after cooking in foil wrap and subsequent storage at room temperature for several days (19).

Wound botulism results from dirt containing *C. botulinum* spores getting into the wound (2). Injection of contaminated black tar heroin has been associated with cases of wound botulism (3). Intestinal botulism (infant or adult intestinal toxemia) arises from ingestion of *C. botulinum* spores that germinate in the colon, rather than through ingestion of preformed toxin (2). Ingestion of honey has been implicated in many cases of infant botulism but the source of contamination is frequently unknown (11).

Cases have been associated with the clinical use of unlicensed preparations of botulinum toxin (6). Inhalation botulism has only been documented in the laboratory following inhalation of the aerosolized toxin (2). However, attempts have been made to use botulism toxin (dispersed through the aerosol route) as a bioweapon (20). Terrorist use of botulinum toxin might also be manifested as deliberate contamination of food (20). Botulism is not transmitted from person-to-person (3). Neither *C. botulinum* spores nor its toxins can be absorbed through intact skin (9, 11).

5.3 Occurrence:

General: *C. botulinum* spores occur in soils and dust worldwide. A high incidence of botulism cases have been reported from the Republic of Georgia, Poland, China, Russia, Kyrgyzstan and Alaskan Eskimos and Canadian Inuit (5). Japan, Italy, Portugal, Germany, France, and the former Yugoslavia have also reported relatively high numbers of cases (5). The largest reported outbreak in Thailand in 2006 was attributed to home-prepared bamboo shoots and affected 209 people, with no deaths (2). Most countries have not yet reported cases of infant botulism suggesting that infant botulism is under recognized, underreported or both (21). Wound botulism has occurred among injection drug users in some parts of Europe and North America (2).

The majority of recent global cases were reported by the United States of America (U.S.), with approximately 50% of cases in California (2). Wound botulism is increasing in the U.S. and occurs almost exclusively among injection drug users (9). In 2010, 112 laboratory-confirmed cases of botulism were reported to U. S. Centers for Disease Control and Prevention (22). Foodborne botulism accounted for 9 cases (8%), infant botulism for 85 (76%), wound botulism for 17 (15%), and botulism of unknown or other etiology for 1 case (<1%) (22). Alaska's foodborne botulism rate (27% of U.S. foodborne botulism cases) exceeds those in any other state and is among the highest in the world (13).

Canada: Preliminary data indicates that there were 1 (foodborne), 14 (infant), 13 (wound) and 11 (unknown) cases of botulism reported nationally for 2005-2008 (23). On average, for 2000-2008, approximately two cases per year were reported in children less than one year of age (23).

Manitoba: There has been one case of botulism reported to Manitoba Health since 1992.

5.4 Incubation Period:

Foodborne Botulism: Neurological symptoms usually appear within12-36 hours of ingesting contaminated food (2), with a range from six hours to eight days after ingestion (3).

Wound Botulism: The incubation period is four to 14 days from the time of injury until the onset of symptoms (3).

Infant Botulism: The incubation period is estimated to be three to 30 days after exposure to spore-forming organisms (3).

Inhalation Botulism: The incubation period is thought to range from 12-80 hours after exposure (2).

5.5 Host Susceptibility: Susceptibility is universal (2). Infants under one year of age and adults who are immunocompromised or with bowel problems leading to abnormal gastrointestinal flora are more susceptible to infant/intestinal botulism (2). Botulism cases do not develop immunity to botulinum toxin (3). Recurrent foodborne botulism has been documented (13), and recurrent wound botulism has been documented among injection drug users (7).

5.6 Period of Communicability: No secondary person-to-person transmission has been recorded (2).

6. Diagnosis

Initially, diagnosis is based on the clinical presentation and history. Consult Cadham Provincial Laboratory (CPL) (204-945-7184) as soon as possible if botulism is suspected. CPL will provide direction on the collection and transportation of clinical samples. Blood samples should be taken BEFORE administering antitoxin. Public Health Inspectors (204-945-0911) will provide direction on the collection and submission of food samples (consumed by the patient) to the appropriate environmental testing laboratory.

Definitive diagnosis by laboratory methods is typically difficult to obtain. Collection of serum within the first 24 hours of symptoms, before administration of antitoxin, is best. Nucleic acid testing and ELISA methods are available for botulism diagnosis, but gold standard testing with culture and with the mouse bioassay are still the best methods for definitive diagnosis.

Foodborne Botulism: Demonstration of botulinum toxin in serum, stool, gastric aspirate or incriminated food; or by culture of *C. botulinum* from gastric aspirate or stool. Identification of organisms in a suspected food is helpful but not diagnostic as botulinum spores are ubiquitous; the presence of toxin in a suspected contaminated food source is more significant.

Wound Botulism: Toxin identified in serum or by positive culture from wound exudate, swab or tissue sample.

Infant or Intestinal/Colonization Botulism: Identification of *C. botulinum* organisms and/or toxin in patient's feces or in autopsy specimens. Toxin is not usually detected in the sera of patients.

Confirmation of the clinical diagnosis should be done in consultation with a neurologist.

7. Key Investigations for Public Health Response

Suspicion of a single case of botulism requires immediate investigation to determine if a common source outbreak has occurred.

Foodborne Botulism:

- Initiate food history investigation early in symptomatic patients as the symptoms may compromise the patient's ability to communicate as the disease progresses (9). Consumption of home-preserved foods should be particularly considered to identify the source of the toxin. *C. botulinum* may or may not cause container lids to bulge and the contents to have "off-odours", and other contaminants can also cause these. Nonproteolytic strains (Type

E) even when growing in meat, fish and other high protein foods, do not produce spoilage characteristics (14).

- Contact Public Health Inspectors (PHIs) at 204-945-0911 to assist with recovering all suspected food for appropriate testing and disposal. Foods suspected of being responsible for botulism case(s) should be refrigerated until they are collected by PHIs and tested.
- Any required food recalls are handled through the CFIA with assistance from local public health inspectors.
- Identify other individuals who may have ingested the potential source food.
- Collect sera/stool specimens from patients and others exposed to the same source but not ill as appropriate. Forward patient specimens with relevant clinical history immediately to Cadham Provincial Laboratory (CPL) before administration of antitoxin. CPL should be phoned ahead of specimen submission (204-945-7184) as specimens are forwarded on to a reference laboratory.

Wound Botulism:

- Obtain history of trauma and injection drug use, particularly use of black tar heroin.
- Identify other individuals who may have been exposed to the same source.

Infant Botulism:

- Determine food history, especially history of honey consumption.
- Identify other individuals who may have been exposed to the same source.

8. Control

8.1 Management of Cases:

- Persons with botulism require immediate treatment with antitoxin (as indicated below under "Treatment"), ideally < 24 hours after onset of symptoms (9), to limit the progression of paralysis (3).
- **Treatment must not await laboratory confirmation.** Serum should be collected to identify the specific toxin **before** antitoxin is administered, but antitoxin should not be withheld pending test results (2).
- The antitoxins are produced in horses; therefore, hypersensitivity reactions are possible. Testing for hypersensitivity to horse sera or antitoxin may be undertaken prior to antitoxin administration (3, 9).
- Arrange immediate access to an intensive care unit so respiratory failure can be anticipated and managed promptly (2).
- Botulinum antitoxin dosing is product specific. **Clinicians must refer to the specific product monograph(s) for the botulinum antitoxin prior to ordering and using the product to ensure correct dosing is used.** Links to the product monograph(s) of the botulinum antitoxin product(s) currently available in Manitoba can be found on the Communicable Disease Control Protocol Manual website: http://www.gov.mb.ca/health/publichealth/cdc/protocol/index.html below the Botulism protocol. Consultation with the Medical Officer of Health (204-788-8666) is highly recommended.

Treatment:

Foodborne Botulism or Intestinal/Colonization Botulism:

- Intravenous administration of a botulinum antitoxin as soon as possible is routine treatment (2).

Wound Botulism:

- Penicillin or metronidazole should be given to patients with wound botulism following antitoxin administration (as described above under *Foodborne Botulism*) (3, 4).
- The wound should be débrided even if it appears to be healing well (4, 11).

Acquisition of Antitoxin:

- Botulinum antitoxin may be ordered by an Infectious Diseases specialist or by the local Medical Officer of Health http://www.gov.mb.ca/health/publichealth/contactlist.html through the provincial vaccine warehouse at 204-948-1333 or Toll-free 1-855-683-3306 during regular business hours or at 204-805-4096 after hours. After regular hours, the Medical Officer of Health on call may be contacted at 204-788-8666. Patient follow-up may be required as per Health Canada regulations for Special Access products http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/index-eng.php.

Infant Botulism:

- Human-derived antitoxin (BabyBIG®) is indicated for the treatment of infant botulism caused by type A or type B *Clostridium botulinum*. It is only available through Health Canada's Special Access Program (SAP) (http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/index-eng.php). Equine-derived antitoxin is generally not recommended for infant botulism (3), because of the potential risk of anaphylaxis, serum sickness or the sensitization of the infant to horse antigen (11).
- Antimicrobial therapy is not indicated to treat infant botulism (3).
- Refer to California Department of Health Services Infant Botulism Prevention Programme at: http://www.infantbotulism.org/

Public Health/Infection Control Measures:

- Routine Practices in health care as per Manitoba Health's *Routine Practices and Additional Precautions: Preventing the Transmission of Infection in Health Care* available at (http://www.gov.mb.ca/health/publichealth/cdc/docs/ipc/rpap.pdf).

8.2 Management of Contacts:

- Individuals in direct contact with cases of botulism do not require treatment or follow-up as the disease is not transmitted from person-to-person.
- Prophylactic equine antitoxin is not recommended for asymptomatic people who have ingested a food known to contain botulinum toxin (3).
- Persons known to have eaten the incriminated food should be kept under close medical observation for signs and symptoms of the disease, with antitoxin administered at the first signs of illness (3, 4, 20). Management of these clients should be done in conjunction with an internist.

8.3 Management of Outbreaks:

Due to the severity and rarity of botulism, a single confirmed case constitutes an outbreak.

- Outbreaks should be investigated to identify a common source of infection and

prevent further exposure to that source. The extent of outbreak investigations will depend upon the number of cases, the likely source of contamination and other factors. However, the source is frequently not identified.

- Refer to the *Enteric Illness Protocol* for foodborne outbreaks available at: www.gov.mb.ca/health/publichealth/cdc/protocol/enteric.pdf .
- Public notification should occur. The level of notification will usually be at the discretion of regional Public Health and/or provincial Public Health for local outbreaks but may be at the discretion of the Federal Government for nationally linked foodborne outbreaks as per *Canada's Foodborne Illness Outbreak Response Protocol (FIORP) 2010: To guide a multijurisdictional response* available at: www.phac-aspc.gc.ca/zoono/fiorp-pritioa/index-eng.php
- Cases and contacts should be managed as recommended in this protocol.
- A deliberate release of toxin (i.e., bioterrorist activity) should be suspected if there is:
    - An outbreak of a large number of cases of acute flaccid paralysis with prominent bulbar palsies;
    - An outbreak with an unusual botulinum toxin type (i.e., type C, D, F or G or type E toxin not acquired from an aquatic food);
    - An outbreak with a common geographic factor among cases (e.g., airport, work location) but without a common dietary exposure (i.e., features suggestive of an aerosol attack);
    - Multiple simultaneous outbreaks with no common source (20).

For bioterrorist threats or suspected bioterrorist activity, the police should be contacted at 911 (24 hours) as well as the Office of Disaster Management Duty Officer at: 204-793-1632 (24 hours).

8.4 Preventive Measures:

- *C. botulinum* toxin is destroyed by boiling food/water for 5 minutes or longer or heating at 90°C for 15 minutes; heating to 115°C will inactivate spores (14).
- Honey (even pasteurized honey) should not be given to children younger than 12 months of age (2, 3, 24). Refer to California Department of Health Services Infant Botulism Prevention Programme at: http://www.infantbotulism.org/
- Inactivation of bacterial spores in heat-sterilized or canned products and inhibition of growth in all other products (2). Refer to Health Canada's Food Safety Tips for Home Canning available at: http://www.hc-sc.gc.ca/fn-an/securit/kitchen-cuisine/food-canning-conserve-aliment-eng.php .
- Refrigeration of foods to prevent bacterial growth and formation of toxin (2).
- Not eating food from dented, bulging or leaking home or commercially-canned food or food that is discoloured or has a foul smell (24, 25).
- Not using aluminum foil to wrap potatoes or other vegetables for baking unless they will be cooked and eaten immediately or unwrapped and refrigerated once they are cooked (19, 24).
- Continued efforts to reduce injection drug use and to educate current users on the infectious and other risks associated with illicit drug use, e.g. bloodborne infections, anthrax and botulism (7).
- Addition of thermal treatment or acidification step to the manufacturing

process for refrigerated low-acid juices (e.g., carrot juice), to decrease the risk of *C. botulinum* contamination should any breaches in refrigeration occur (17).

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