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Botulism – Guide for Healthcare Professionals

January 2019

Bureau of Microbial Hazards
Food Directorate
Health Products and Food Branch

Canada

Healthcare workers should notify local and/or provincial public health authorities when a case of botulism is suspected. The *Botulism - Guide for Healthcare Professionals* document is intended primarily for use by healthcare workers and facilities/organizations providing healthcare including pharmacies, hospitals, long-term care facilities, community-based healthcare service providers and pre-hospital emergency services.

Contact Information
Botulism Reference Service for Canada:
Office (613) 957-0902, Laboratory (613) 957-0885, After-hours (613) 296-1139

Please ship samples by courier to:

Botulism Reference Service – Dr. John Austin
Health Canada, Banting Research Centre
251 Sir Frederick Banting Driveway,
Tunney's Pasture
Ottawa, Ontario K1A 0K9

Special Access Programme: (613) 941-2108

Botulism is a rare neuroparalytic disease caused by a neurotoxin that is produced by the bacterium *Clostridium botulinum*. Botulism develops if a person ingests the toxin or if the organism grows in the intestines or wounds and toxin is released. There are four main forms of botulism: Foodborne, Infant, Adult Intestinal Colonization and Wound.

Foodborne Botulism results from the ingestion of preformed neurotoxin in food or drink. In foodborne botulism, symptoms generally begin 12 to 36 hours after eating contaminated food, but can also occur as early as six hours or as late as 10 days. Symptoms may initially include vomiting and/or diarrhea and are followed by one or more of: ptosis (drooping of eyelids), visual disturbance, dilated and fixed pupils, dysphagia (difficulty in swallowing), dry mouth and dysphonia (difficulty speaking). These symptoms may extend to a descending symmetrical flaccid paralysis in an alert afebrile person. Constipation is a common symptom later in presentation. The case-fatality rate is approximately 5%.

Infant Botulism affects infants under the age of one with most cases occurring between six weeks and six months old. This form of botulism results from ingestion of spores that germinate in the intestine and produce bacteria that release toxin. Clinical symptoms start with constipation and may include loss of appetite, generalized weakness, weak cry, weak suck, ptosis, sluggishly reactive pupils, disconjugate gaze, blunted facial expression, drooling, decreased anal sphincter tone, hypotonia and a significant loss of head control.

Adult Intestinal Colonization Botulism results when *C. botulinum* germinates and produces toxin in the digestive system. This form of botulism affects adults who have altered gastrointestinal anatomy and microflora (i.e., intestinal surgery, inflammatory bowel disease, and with exposure to microbial agents).The symptoms observed are similar to foodborne botulism.

Laboratory Confirmation

Laboratory confirmation of foodborne botulism is made by demonstration of botulinum toxin in serum, stool, gastric aspirate or incriminated food, or isolation of *C. botulinum* from stool or gastric aspirate. Identification of organisms in a suspected food is helpful but not diagnostic because *C. botulinum* spores are ubiquitous in the environment. Individuals may be diagnosed with foodborne botulism if they consumed a food item linked to a laboratory confirmed botulism case. The diagnosis of intestinal botulism is established by identification of *C. botulinum* organisms and/or toxin in a patient's feces over an extended period of several days or weeks, combined with the lack of a toxic food. Wound botulism is diagnosed by evidence of a wound combined with detection of toxin in serum or isolation of *C. botulinum* from a wound culture. Differential diagnoses of botulism include Guillain-Barré syndrome, stroke, and myasthenia gravis.

Federal Support

The management of a suspected botulism case involves healthcare professionals, and provincial and federal public health officials. The federal management involves Health Canada's Botulism Reference Service (BRS) for Canada and the Health Canada Special Access Programme (SAP).

The BRS for Canada, established in 1974, provides the following support:

- Assists physicians and Provincial Departments of Health when botulism is suspected;
- Examines suspect foods and clinical specimens submitted for analysis;
- Rapidly alerts responsible agencies when commercial foods are involved;
- Maintains reference cultures of *C. botulinum*; and
- Liaises with centres that have similar interests and responsibilities in Canada and abroad.

The SAP considers requests for non-marketed drugs from practitioners treating patients with serious and/or life-threatening conditions when conventional therapies have failed, are unsuitable, or unavailable. The SAP authorizes a manufacturer to sell a drug that cannot otherwise be sold or distributed in Canada.

Both the BRS and SAP are involved in suspected cases of botulism as they are responsible for testing samples and approving the release of botulism antitoxin. The procedure for healthcare workers and facilities/organizations providing healthcare, however, varies between provinces. Please check with the office of the Chief Medical Officer of Health for the provincial reporting requirements.

Laboratory Investigation

The following provides information on submitting laboratory specimens to the BRS in Ottawa. A member of the BRS should be called immediately, day or night, when a case of botulism is suspected to:

- Discuss the clinical presentation of the suspect case of botulism in order to support the diagnosis; and
- Make arrangements for transporting suspect food and clinical specimens to Ottawa for laboratory analysis.

Clinical specimens must be obtained prior to administrating botulism antitoxin. Food samples may be leftovers or unopened containers. For commercial foods, retrieve the label, the manufacturer's lot number, codes embossed on the can or package, etc.

Suitable clinical specimens for analyses include:

- Faecal samples (approximately 10g);
- Enema fluid;
- Gastric contents (adjusted to approximately pH 6.0 with 1N NaOH, if possible);
- Serum (from 20 ml of blood collected before administration of antitoxin); and
- For suspected infant botulism, the essential material for analysis is the infant's faeces. As constipation is a common symptom, the soiled parts of diapers, a rectal swab, 2 ml of serum or a combination of samples may be submitted if necessary.

After collecting the sample, but prior to shipping, ensure the sample is kept in a refrigerator at 4°C. Ship specimens in a watertight primary receptacle, in a watertight secondary container, with sufficient absorbent material between the two containers to absorb the entire contents of the primary receptacle[1]. The preferred method of preserving the material is by cooling rather than freezing (i.e., by including commercial cooling packs in the parcel). After the specimen is shipped, inform BRS of the expected delivery time.

Botulism Antitoxin

Botulism antitoxin and immune globulin are not approved for sale in Canada and are currently only available via the SAP. At this time, only three products are considered for access through the SAP:

- BAT® [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine)] made by Emergent BioSolutions Canada Inc. (formerly Cangene Corporation); and

[1] Samples that may contain botulinum neurotoxin and/or viable organisms (including spores) should be shipped using the Transportation of Dangerous Goods instruction TC-125-1B.

- BabyBIG®, Botulism Immune Globulin Intravenous (Human) (BIG-IV) for pediatric patients under the age of one year, accessed from the Infant Botulism Treatment and Prevention Program (IBTPP) at the California Department of Public Health (CDPH).

The heptavalent product is kept on hand throughout the country, either at a provincial depot or by the Public Health Agency of Canada's National Emergency Stockpile System (NESS).

For infant botulism cases up to the age of one, BabyBIG® will need to be requested on a per patient basis from the California Department of Health Services Infant Botulism Treatment and Prevention Program at (510) 231-7600.

The producers of BabyBIG® do not permit pre-orders of their product; therefore, the requesting physician must also submit a request with the SAP to gain access:

- The physician must complete a SAP request form, FORM A, which is available at: https://www.canada.ca/en/health-canada/services/drugs-health-products/special-access/drugs.html and fax it immediately to (613) 941-3194. To avoid delays, all sections of the form must be completed accurately and it is **recommended** to follow-up with a phone call to the SAP office at (613) 941-2108.
- If a case presents on a weeknight, weekend or holiday, the SAP on-call officer can be reached by telephone at (613) 941-2108 (press 0). The requesting physician should be prepared to provide the information from the form to the on-call officer and then follow-up on the next business day with a copy the completed form. The SAP will authorize the California Department of Health Services to ship BabyBIG® to the hospital.

The SAP will then authorize the California Department of Health Services to ship the BabyBIG® to the hospital.

References

Ontario - Ministry of Health and Long-Term Care Staff, Public Health Division

Canada's Food-borne Illness Outbreak Response Protocol (FIORP) 2010: To guide a multi-jurisdictional response