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Botulism – Guide for Healthcare Professionals

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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:
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Greg Sanders, Laboratory Technician (office (613) 957-0885)
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Special Access Programme: (613) 941-2108

Botulism is a neuroparalytic disease caused by a neurotoxin that is produced by the bacterium *Clostridium botulinum*. Botulism develops if a person ingests the toxin (or rarely, if the toxin is inhaled or injected) 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. 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 5-10%.

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.

Wound Botulism results when a wound becomes infected with *C. botulinum* and toxin is produced. This form of botulism exhibits similar symptoms as foodborne botulism (except there is no vomiting and/or diarrhea). The presence of a wound is also useful to note.

Mode of Transmission
Foodborne botulism is a severe intoxication resulting from ingestion of preformed toxin present in contaminated food. Intestinal botulism results from ingestion of *C. botulinum* spores that germinate in the colon, rather than by ingestion of preformed toxin. Wound botulism cases may result from contamination of wounds by soil or gravel, or injection of illicit intravenous drugs.

Botulinum toxins could be used in bioterrorism. Although the greatest threat may be via aerosol use, the more common threat may be via deliberate contamination of food.

Incubation Period
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. The incubation period for wound botulism is longer, averaging about 10 days. The incubation period for intestinal colonization botulism is unknown.

Diagnosis
The Botulism Reference Service for Canada conducts the laboratory investigation. Diagnosis 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 positive 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 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 provides access to non-marketed drugs for practitioners treating patients with serious 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 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.

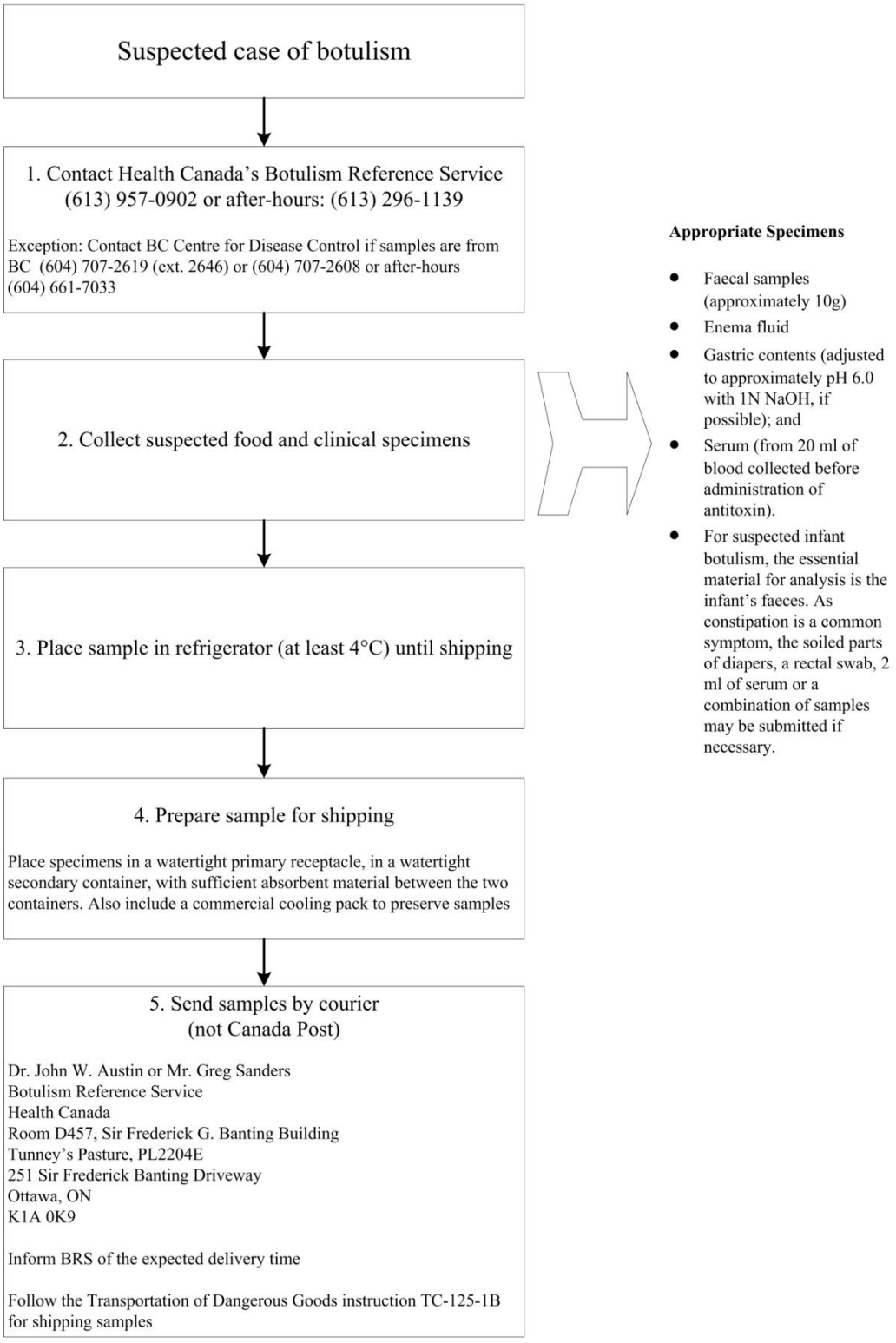
Suitable clinical specimens for analyses include:

- 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 that sample is kept in the 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. In urgent cases, the parcels are picked up immediately upon arrival, usually at the airport.

[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.

Figure 1: The Process for Sending Samples to the BRS Laboratory



Botulism Antitoxin

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

- Novartis trivalent Types ABE;
- BabyBIG®, Botulism Immune Globulin Intravenous (Human) (BIG-IV) for pediatric patients under the age of 1, accessed from the Infant Botulism Treatment and Prevention Program (IBTPP) at the California Department of Public Health (CDPH);
- NP-018 (heptavalent) Types A to G from Cangene Corporation; and
- Botulism antitoxin Type AB and Type E; accessed from the Butantan Institute in Brazil.

The antitoxin administered, except for infant botulism, depends on the supplies available from the province or the Public Health Agency of Canada's National Emergency Stockpile System. Requests for any of these products require the submission of a SAP request form which is reviewed expeditiously by SAP staff. For a copy of the request forms please refer to the SAP website.

For infant botulism cases, obtain infant botulism antitoxin. BabyBIG® is a human-derived botulism antitoxin used in the treatment of infant botulism for babies up to one year of age. For additional information on BabyBIG®, contact the Infant Botulism Treatment and Prevention Program at (510) 231-7600.

The producers of BabyBIG® do not permit pre-orders of their product; therefore, the attending physician must place a request with Health Canada for the SAP to gain access.

- The physician must complete the Special Access Request Form and fax it to the SAP immediately (fax: (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 the 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 attending physician should be prepared to provide the information required on the Special Access Request Form to the on-call officer and then follow-up on the next business day with a copy the completed form.

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

References

British Columbia Centre for Disease Control (2010). Chapter 1: Management of specific diseases- Botulism.

Ontario Ministry of Health and Long-Term Care Staff, Public Health Division (2012). Botulism.

Public Health Agency of Canada (2010). Canada's Foodborne Illness Outbreak Response Protocol (FIORP) 2010: To guide a multi-jurisdictional response.

Acknowledgements

This guide was developed using the Ontario Botulism – Guide for Healthcare Professionals.