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1.0 AUTHORITY

BC Public Health Act (2008). Available at
http://www.leg.bc.ca/38th4th/3rd_read/gov23-3.htm

2.0 GOAL

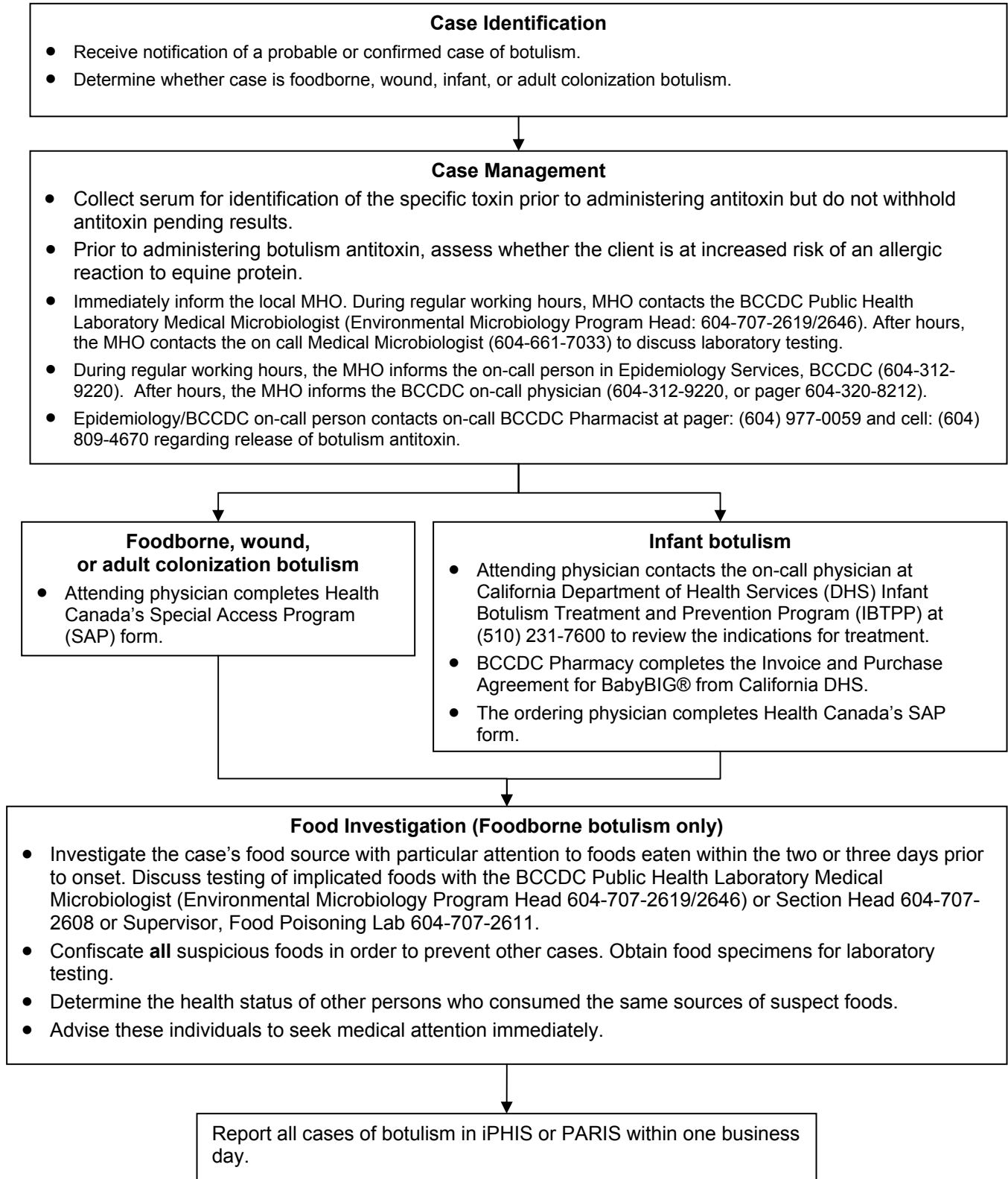
To prevent serious medical complications associated with botulism.

This will be accomplished by:

- Rapid availability of antitoxin,
- Laboratory processes for testing of appropriate specimens,
- Prompt confiscation of food(s) felt to be implicated, especially foods eaten within the last two to three days,
- Medical consideration of other possible causes that could produce a similar symptomatology, and
- Meticulous supportive care, particularly respiratory and nutritional.

3.0 BOTULISM FLOW CHART

The flow chart describes public health actions to be taken when notified of a case of botulism.



4.0 CASE IDENTIFICATION
4.1 Confirm the diagnosis

Surveillance	Definition	Reportable
Foodborne botulism		
Confirmed case	Laboratory confirmation of intoxication with clinical evidence❶: <ul style="list-style-type: none"> • Detection of botulinum toxin in serum, stool, gastric aspirate or food <li style="text-align: center;">OR • Isolation of <i>C. botulinum</i> from stool or gastric aspirate <li style="text-align: center;">OR Clinical evidence❶ and indication that the client ate the same suspect food as an individual with laboratory-confirmed botulism.	Yes
Probable case	Clinical evidence❶ AND Consumption of a suspect food item in the incubation period (12 – 48 hours)	Yes
Wound botulism		
Confirmed case	Laboratory confirmation of infection: <ul style="list-style-type: none"> • Detection of botulinum toxin in serum <li style="text-align: center;">OR • Isolation of <i>C. botulinum</i> from a wound <li style="text-align: center;">AND Presence of freshly infected wound in the 2 weeks before symptoms and no evidence of consumption of food contaminated with <i>C. botulinum</i>	Yes
Infant botulism		
Confirmed case	Laboratory confirmation with symptoms compatible with botulism❷ in a person < one year of age: <ul style="list-style-type: none"> • Detection of botulinum toxin in stool or serum <li style="text-align: center;">OR • Isolation of <i>C. botulinum</i> from the patient's stool, or at autopsy 	Yes
Adult colonization botulism		
Confirmed case	Laboratory confirmation with symptoms compatible with botulism❶ in a patient ≥ one 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: <ul style="list-style-type: none"> • Detection of botulinum toxin in stool or serum <li style="text-align: center;">OR • Isolation of <i>C. botulinum</i> from the patient's stool, or at autopsy 	Yes

❶Clinical evidence of foodborne botulism includes: blurred vision; dry mouth and difficulty swallowing and speaking; and descending symmetric paralysis that may progress rapidly.

❷Clinical evidence of infant botulism includes: constipation; loss of appetite; altered cry; and loss of head control.

5.0 CASE MANAGEMENT

5.1 Notification

When botulism is suspected, immediately inform the local Medical Health Officer.

During regular working hours, the MHO should first contact the BCCDC Public Health Laboratory Medical Microbiologist (Environmental Microbiology Program Head: 604-707-2619/2646). After hours, the MHO should contact the on call Medical Microbiologist (604-661-7033) to discuss laboratory testing.

During regular work hours, the MHO should next inform the on-call clinical person in Epidemiology Services, BCCDC (604-312-9220). After hours, the MHO should inform the BCCDC on-call physician (604-312-9220, or pager 604-320-8212). Notification of the on-call person is important as there may be further public health actions, or notifications required due to the severity of the disease and others potentially at risk.

The Epidemiology/BCCDC on-call person should contact the on-call BCCDC Pharmacist at pager: (604) 977-0059 and cell: (604) 809-4670 regarding release of botulism antitoxin.

If the on-call BCCDC Pharmacist is called first, Pharmacy should notify the Epidemiology/BCCDC on-call person. Pharmacy is to seek authorization for the release of botulism antitoxin from the Epidemiology/BCCDC on-call person.

5.2 Laboratory investigation

The MHO, or other ordering physician, should discuss testing with the BCCDC Public Health Laboratory Medical Microbiologist to ensure ordering of mice for the bioassay as well as adequate and rapid shipment of specimens to the Environmental Microbiology Program (Indicate Botulism Testing, STAT and “Attention: Dr. Isaac-Renton/J. Fung” on all associated requisitions; http://www.phsa.ca/NR/rdonlyres/6FED827E-0989-4933-9529-B59AE0DE2431/0/FoodPoisoningForm_PartB_Requisition.pdf).

Collect the following specimens: (*= preferred specimen):

- **Foodborne botulism**
 - 15 cc of serum for toxin bioassay (within 3 days of ingestion of suspect food)*
 - 25 - 50 gm of stool for culture and toxin bioassay*
 - 100 gm of vomitus or gastric aspirate for culture and toxin bioassay
 - 200 gm of suspect foods for culture and toxin bioassay

-
- **Wound botulism**
 - wound exudate for culture*
 - 15 cc serum for toxin bioassay

 - **Infant botulism**
 - at least 25 gm of stool for culture and toxin bioassay (may need to pool small samples and/or do high enema)*
 - 200gm of suspect food
 - 15 cc of serum for toxin bioassay (toxin rarely found in serum in infant cases)

 - **Adult colonization botulism**
 - At least 25 gm of stool for culture and toxin bioassay
 - 15 cc of serum for toxin bioassay

 - **Fatal case**
 - autopsy material (especially liver and contents of gut), at least 100gm

In some situations, other specimens may be collected and tested (e.g., food or environmental specimens in cases of infant botulism). Further information on botulism testing is available in the BCCDC Public Health Microbiology and Reference Laboratory Guide to Programs and Services available at <http://www.phsa.ca/NR/rdonlyres/D632D356-8E8F-4917-BC3D-463EB5F8A14B/0/GuidetoProgramServices.pdf>.

5.3 Treatment

Collect serum for identification of specific toxin prior to administering antitoxin.

Initiate treatment with antitoxin as soon as possible. Do not wait for lab confirmation if clinical suspicion is strong.

A limited supply of botulism antitoxin is kept on-site at BCCDC Pharmacy and in some remote locations in the Northern Health Authority. Two products are currently available (i.e., Botulism Antitoxin Behring (Novartis) and Instituto Butantan botulinum antitoxin). The BCCDC/Epidemiology on-call person and the BCCDC pharmacist will determine which product will be distributed.

Note: All formulations of botulism antitoxin require approval through Health Canada's Special Access Program (SAP) for release and use. The SAP can be reached at phone: (613) 941-2108, fax: (613) 941-3194.

This reporting to Health Canada may be completed retrospectively if the product is released from a local depot (e.g., BCCDC).

The prescribing physician must complete Health Canada's SAP form available at:
http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-droques/index_e.html

If wound botulism: debride wound, establish drainage, and give antibiotics.

Antitoxin cannot reverse the effects of the disease but can prevent further paralysis. Antibiotics are not effective against toxins but may be used to treat secondary infections.

5.3.1 Botulism Antitoxin Behring (for individuals \geq 1year)

The following information is taken from the product monograph. Refer to the product monograph for further dosage and administration details.

Botulism Antitoxin Behring is an equine-derived Fermo-Serum®.

It is supplied as a 250 mL bottle containing antitoxin against *C. botulinum* types:

- Type A 750 I.U./mL
- Type B 500 I.U./mL
- Type E 50 I.U./mL

Adults and children \geq 1 year of age receive the same dose:

- Initial dose 500 mL
- Another 250 mL may be indicated 4 – 6 hours later, depending on the clinical findings.

Prior to administering Botulism Antitoxin Behring, assess whether the client is at increased risk of an allergic reaction to equine protein (i.e., history of previous allergic reaction to equine protein, history of repeated use of antitoxin products). Increased risk of allergic reaction is **not** a contraindication to administration of botulism antitoxin. Consider concurrent administration of a medication to treat anaphylactic shock.

Infuse 250 mL within 30 minutes (while monitoring for any allergic reactions), and another 250 mL as continuous drip infusion.❶

❶ Dr. Berthold Bruckhoff, Novartis Germany (personal communication, June 17, 2010).

5.3.2 Instituto Butantan botulinum antitoxin (for individuals \geq 1year)

The following information is taken from the product monograph. Refer to the product monograph for further dosage and administration details.

Equine-derived botulism antitoxin is supplied in two separate vials: a vial containing bivalent A/B and a vial containing monovalent E.

Bivalent A/B (each 20mL ampoule contains 7500 IU of type A and 5500 IU of type B): one ampoule diluted in 0.9% saline in a 1:10 dilution for intravenous infusion.

A second dose may be required.

Monovalent E (each 20 mL ampoule contains 8500 IU of type E): one ampoule diluted in 0.9% saline in a 1:10 dilution for intravenous infusion. A second dose may be required.

5.3.3 Botulism Immune Globulin, IV (BIG-IV); (BabyBIG®)

Human-derived botulism immune globulin (BabyBIG®) is indicated in infant botulism cases caused by type A or B, the neurotoxins most implicated in infant botulism. BabyBIG® is indicated only in persons less than one year of age. Safety and efficacy have not been tested in other age groups. In infants, equine botulinum antitoxin is not given because of the risk of anaphylaxis.

Botulism immune globulin is derived from pooled adult plasma from persons immunized with pentavalent botulinum toxoid who have high titres of antibody against neurotoxins type A and B. In laboratory-confirmed infant botulism cases, BabyBIG® neutralizes circulating A and B toxins and so decreases the duration of hospitalization, mechanical ventilation, and tube feedings.

Treatment **should not** be delayed while awaiting laboratory confirmation.

BabyBIG® dose is 2.0 mL/kg (100 mg/kg), given as a single intravenous infusion. The product monograph for BabyBIG® is available at http://www.infantbotulism.org/babybig_package_insert.pdf.

Note: BabyBIG® is not a licensed product in Canada. For more information about infant botulism, refer to <http://www.infantbotulism.org/>.

There is no Canadian or BC depot of this product. Product is obtained through the on-call physician with the Infant Botulism Treatment and Prevention Program (IBTPP), California Department of Health Services (DHS).

The patient's physician must first contact the on call physician at DHS, available 24 hours, 7 days a week, year round, at (510) 231-7600, IBTPP to review the indications for treatment. BCCDC Pharmacy Services must facilitate the completion of the Invoice and Purchase Agreement (IPA) with the prescribing physician.

The use of an unlicensed product in Canada requires approval through Health Canada's Special Access Program (SAP). The prescribing physician must complete Health Canada's SAP form available at: http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-droques/index_e.html.

The attending physician can also transfer the patient to the closest US hospital that has the capability to administer BabyBIG®.

Antibiotics are not recommended in the treatment of infant botulism. Lysis of *C. botulinum* theoretically could increase the amount of toxin available for absorption. Aminoglycoside agents potentiate the paralytic effects of the toxin and should be avoided.

The antibodies present in BabyBIG® may interfere with the infant's response to live vaccines. For more information regarding the recommended interval between receipt of BabyBIG® and administration of live vaccines, refer to the BC Communicable Disease Control Manual, Chapter 2, Section VII available at http://www.bccdc.ca/NR/rdonlyres/CD9F6894-8373-469C-9F8A-6B27F76418D9/0/SectionVII_BiologicalProducts_Jan05.pdf.

5.4 Isolation of the case

Standard precautions are recommended.

6.0 OUTBREAK MANAGEMENT

In foodborne botulism, one case is considered an outbreak.

Early ascertainment and notification of the BCCDC of the potential for more cases is needed in order to secure sufficient inventory of antitoxin. The provincial supply is sufficient only for sporadic cases.

Search for potential food sources, collect for testing, and discard any remaining suspect foods.

Conduct active case finding for other people who may have eaten the suspect food. No isolation or quarantine of cases is necessary.

The Botulism Follow-Up Form may be used to assist with outbreak management. The form is available at http://www.bccdc.ca/NR/rdonlyres/0F77E474-2E3C-4E65-A412-49B4F5A90E20/0/Epid_Form_Botulism_20090609.pdf.

7.0 FOOD SOURCE INVESTIGATION (FOODBORNE BOTULISM ONLY)

Investigate the case's food source with particular attention to foods eaten within the two or three days prior to symptom onset.

Discuss testing of implicated foods with the Environmental Microbiology Lab Section Head or Supervisor, Food Poisoning Lab (604-707-2611/2608). If it is after regular working hours, contact the on call BCCDC Laboratory Medical Microbiologist (604-661-7033).

Confiscate **all** suspicious foods in order to prevent other cases. Home preserved food should be the prime suspect until ruled out.

Use gloves when confiscating food.

In a case of infant botulism, ingestion of honey, corn syrup, or other baby foods should be ruled out as the source of illness.

Obtain food specimens for laboratory testing after consultation with the BCCDC Public Health Laboratory (Environmental Microbiology: 604-707-2611/2608). When collecting food specimens, collect 200gm of each of the suspect foods for culture and toxin bioassay.

Determine the health status of other household members and other individuals who may have shared the same sources of suspected food.

Advise other contacts of the suspected food to seek medical attention immediately.

8.0 MANAGEMENT OF OTHER PERSONS WHO CONSUMED THE SAME SOURCES OF SUSPECT FOODS

People who are known to have eaten from incriminated food should be purged with cathartics, given gastric lavage and high enema. **Note:** these measures should not be used for infant botulism.

Ensure these people are kept under close medical supervision.

Educate regarding safe practices in food preparation and home canning methods.

Despite excretion of *C. botulinum* toxin and organisms at high levels in the feces of infant and adult colonization botulism patients for weeks to months after onset of illness, no instance of secondary person to person transmission has been documented. Hence, quarantine is not required.

8.1 Immunoprophylaxis of other persons who consumed the same sources of suspect foods

Immunoprophylaxis may be considered for asymptomatic people who have consumed probable or confirmed botulism-contaminated food.

The decision to provide immunoprophylaxis should be weighed carefully in view of the risk of adverse effects and sensitization to horse serum.

If antitoxin is given, it should preferably be given within 1-2 days of ingestion of the suspect food at the following doses:

- **Botulism Antitoxin Behring:**
 - Initial dose 500 mL.
 - Another 250 mL may be indicated 4 – 6 hours later, depending on the clinical findings.
- **Instituto Butantan botulinum antitoxin:**
 - Bivalent A/B: 1500 to 7500 IU of type A and 1100 to 5500 IU of type B diluted in 0.9% saline in a 1:10 dilution for intravenous infusion. The dose depends on the quantity of food consumed. A second dose may be required.
 - Monovalent E: 1600 to 8500 IU of type E diluted in 0.9% saline in a 1:10 dilution for intravenous infusion. The dose depends on the quantity of food consumed. A second dose may be required.

Refer to the product monograph for dosage and administration details.

No immunoprophylaxis is necessary for direct contacts of a case of botulism as botulism is not transmitted from person-to-person.

9.0 REPORTING

Report the case to BCCDC immediately (the same day) to arrange the shipment of antitoxin. Report the case(s) of botulism in iPHIS or PARIS within one business day.

The physician prescribing botulism antitoxin or BabyBIG® must complete Health Canada's Special Access Program form available at:

http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-droques/index_e.html

Complete the BC Botulism Follow Up Form available at http://www.bccdc.ca/NR/rdonlyres/0F77E474-2E3C-4E65-A412-49B4F5A90E20/0/Epid_Form_Botulism_20090609.pdf.

10.0 CLINICAL DESCRIPTION

Botulism is a severe neuroparalytic disorder caused by toxins A through F produced by *Clostridium botulinum*. Types A, B, E, and rarely F cause human botulism. There are four clinical forms of botulism: foodborne, wound, infant, and adult colonization. The site of toxin production is different for each of the forms but all share the symmetrical descending flaccid paralysis that results from botulinum neurotoxin. No immunity develops even following severe disease.

Foodborne botulism: This is a severe intoxication resulting from ingestion of preformed toxin present in contaminated food.

Acute bilateral cranial nerve impairment and descending weakness or paralysis characterizes the illness. Visual difficulty (blurred or double vision), dysphagia and dry mouth are often the first complaints. These symptoms may extend to a symmetrical flaccid paralysis in a paradoxically alert person. Vomiting and constipation or diarrhea may be present initially. Fever is absent unless a complicating infection occurs. The case-fatality rate is 5% - 10%. Recovery may take months.

Wound botulism: This form occurs when botulism spores get into an open wound and reproduce in an anaerobic environment. Symptoms are similar to the foodborne form but may take up to 2 weeks to appear. Clinical illness is characterized by double or blurred vision and bulbar weakness. Symmetric paralysis may progress rapidly.

Infant botulism: This form occurs when botulism spores are ingested and produce bacteria that reproduce in the gut and release toxin. It affects infants younger than one year of age. It is preceded by or begins with constipation and is manifested as lethargy, poor feeding, weak cry, diminished gag reflex, ptosis and ocular palsies, and progressive descending generalized weakness and hypotonia. Respiratory arrest and death can occur.

Adult colonization botulism: This form affects older children and adults who have altered GI anatomy or function and microflora which allows the germination of ingested *C. botulinum* spores. It is very rarely encountered. Clinical presentation is similar to foodborne botulism. Recurring symptoms and relapse during antitoxin treatment may be observed due to ongoing intraluminal production of toxin.

10.1 Modes of transmission

Foodborne botulism is transmitted by the ingestion of improperly prepared, stored or cooked food containing the toxin.

The foods most often implicated are canned food (vegetables and fruits), home preserved foods, smoked fish, and seal meat.

Wound botulism results from contamination of traumatized tissue by *C. botulinum* that grows in the wound and produces toxin locally. It occurs almost exclusively among injection drug users, particularly users of black tar heroin through “skin-popping” (i.e., injection of the black tar heroin into tissues, as opposed to veins).

Infant and adult colonization botulism result from ingestion of spores that germinate and produce toxin in the gut. Ingestion of honey is a known risk factor for infant botulism but probably only accounts for a proportion of cases. Ingestion of contaminated soil in an environment where soil is being disturbed may also be a risk factor.

Inhalational (through intentional or accidental release) and iatrogenic (through therapeutic uses) botulism can also occur, but extremely rarely.

10.2 Incubation periods

Foodborne botulism: neurologic symptoms usually appear within 12-36 hours, but may range from 6 hours to 8 days. The shorter the incubation period, the more severe the disease and the higher the case-fatality rate.

Wound botulism: onset of symptoms usually occurs 4-14 days after injury.

Infant botulism: cannot be determined for most cases but believed to be 3-30 days from the time of exposure to the spore-containing material.

Adult colonization botulism: unknown since the precise time of spore ingestion is often unknown.

11.0 EPIDEMIOLOGY

There were no cases of botulism reported in BC in 2008 or 2009.

Between 1998 and 2007, there were 6 cases of botulism reported in BC. Three were in infants and three, in adults. The latest case was reported in an infant in October 2007.

12.0 REFERENCES

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