**Botulism**

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### Case Definition

**Confused Case**

**Foodborne Botulism**

Clinical illness\(^{(A)}\) with laboratory confirmation of intoxication:

- Detection of botulinum toxin in serum, stool, gastric aspirate or food\(^{(B)}\)
- Isolation of *Clostridium (C.) botulinum* from stool or gastric aspirate

**OR**

Clinical illness\(^{(A)}\) and indication the client ate the same suspect food\(^{(B)}\) as an individual with laboratory confirmed botulism.

**Wound Botulism**

Presence of a freshly infected wound in the two weeks before symptoms and no evidence of consumption of food contaminated with *C. botulinum* with laboratory confirmation of infection:

- Detection of botulinum toxin in serum
- Isolation of *C. botulinum* from a wound.

**Infant Botulism**

Laboratory confirmation with symptoms compatible with botulism in a person less than one year of age\(^{(C)}\):

- Detection of botulinum toxin in stool or serum
- Isolation of *C. botulinum* from the patient’s stool, or at autopsy.

\(^{(A)}\) Clinical illness is characterized by diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

\(^{(B)}\) **Foodborne** – identification of organisms in a suspected food is helpful but not diagnostic because botulinum spores are ubiquitous. Therefore, the presence of toxin in a suspected contaminated food source is more significant.

\(^{(C)}\) Clinical illness in infants is characterized by constipation, loss of appetite, weakness, altered cry and loss of head control.

*Denotes potential bioterrorism agent.*
Colonization Botulism
Laboratory confirmation with symptoms compatible with botulism in a patient aged greater than or equal to one year with severely compromised gastrointestinal tract functioning (i.e., abnormal bowel) due to various diseases such as colitis, intestinal bypass procedures or in association with other conditions that may create local or widespread disruption in the normal intestinal flora.
- Detection of botulinum toxin in stool or serum
OR
- Isolation of \( C. \ botulinum \) from the patient’s stool, or at autopsy.

Probable Case

Foodborne
Clinical illness\(^{(D)}\) and consumption of a suspect food item\(^{(E)}\) in the incubation period (12–48 hours).

Suspect Case

Foodborne
Clinical illness\(^{(D)}\) in a person without laboratory confirmed infection or an epidemiological link.

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\(^{(D)}\) Clinical illness is characterized by diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

\(^{(E)}\) Foodborne – identification of organisms in a suspected food is helpful but not diagnostic because botulinum spores are ubiquitous. Therefore, the presence of toxin in a suspected contaminated food source is more significant.
Reporting Requirements

1. **Physicians/Health Practitioners and others**
   Physicians, health practitioners and others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed, probable and suspect cases in the prescribed form by the Fastest Means Possible (FMP).

2. **Laboratories**
   All laboratories shall report all positive laboratory results by the FMP to the MOH (or designate) of the zone and the Chief Medical Officer of Health (CMOH) (or designate).

3. **Alberta Health Services and First Nations and Inuit Health Branch**
   - The MOH (or designate) of the zone where the case currently resides shall notify the CMOH (or designate) by FMP of all confirmed, probable and suspect cases.
   - The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all confirmed, probable and suspect cases to the CMOH (or designate) within one week of notification and the final NDR (amendment) within two weeks of notification.
   - For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by FMP:
     - name,
     - date of birth,
     - out-of-province health care number,
     - out-of-province address and phone number,
     - positive laboratory report, and
     - other relevant clinical / epidemiological information.

4. **Additional Reporting Requirements**
   - **Canadian Food Inspection Agency (CFIA):** In the event of a confirmed or suspect case of botulism related to a food product the Alberta Regional Recall Coordinator for CFIA should be notified immediately by the MOH (or designate). During 8:00 am to 4:00 pm call 403-292-4650. For all after hour incidents call pager 403-661-7505. (Personal communication [e-mail March 31, 2008] George Mach acting Regional Recall Coordinator for CFIA).
   - **Botulism Reference Service for Canada.** The Botulism Reference Service for Canada assists with alerting responsible agencies when a commercial food source is suspected. Contact information is available at: http://www.hc-sc.gc.ca/sr-sr/activ/micro/botulism-eng.php

**NOTE:** Treatment, investigation and laboratory follow-up (on clinical and food samples) for suspected cases of botulism constitutes a public health emergency.(1)
Etiology (1-5)
Toxins produced by *Clostridium botulinum*, a spore-forming obligate anaerobic bacillus, cause botulism. Only a few nanograms of the toxin can cause illness. Human botulism is primarily caused by the strains of *C. botulinum* that produce toxin types A, B and E. Strains of *C. baratii*, which produce type F toxin and *C. butyricum* which produce type E toxin, have also been implicated in human botulism.

Type G has been isolated from soil and autopsy specimens but an etiologic role has not been established. Most cases of infant botulism have been caused by type A or B.

Botulinum toxin is considered the most potent lethal substance known to man.

Conditions that promote germination and growth of *C. botulinum* spores include absence of oxygen (anaerobic conditions), low acidity (pH > 4.6), temperatures > 4ºC, and high moisture content.

Clinical Presentation (6-13)
The classic presentation is that of a person who develops acute, bilateral cranial neuropathies along with symmetrical descending weakness. The following are cardinal features present in botulism cases:

- fever is absent (unless a complicating infection occurs);
- the neurologic manifestations are symmetrical;
- the patient remains responsive;
- the heart rate is normal or slow in the absence of hypotension; and
- sensory deficits do not occur (except for blurred vision).

There are four naturally occurring forms of botulism – foodborne (the classic form), wound, infant and adult intestinal toxemia botulism. In addition, two forms of botulism that have also been found and are not naturally occurring are:

- **inhalation botulism**, which is a result of inhaling aerosolized botulism neurotoxin and
- **iatrogenic botulism**, which can result from accidental injection of the botulism neurotoxin into the systemic circulation instead of the intended therapeutic location.

**Foodborne botulism** results from the ingestion of preformed toxin present in contaminated food. Symptoms usually develop between 12 and 36 hours after toxin ingestion. The initial complaints may be gastrointestinal and can include nausea, vomiting, abdominal cramps or diarrhea. Constipation is more likely to occur after the onset of neurologic symptoms. Dry mouth, blurred vision, and diplopia are the earliest neurologic symptoms. Lower cranial nerve dysfunction manifests as: dysphasia (difficulty speaking), dysarthria (difficulty articulating), and hypoglossal (tongue) weakness. Symmetric weakness then descends to the upper extremities, the trunk, and the lower extremities. Respiratory dysfunction may require ventilation. Autonomic problems may also include: alterations in resting heart rate, loss of responsiveness to hypotension or postural change, hypothermia, and urinary retention. Recovery may not begin for up to 100 days and may take months to conclude. With critical care management, the death rate is about 14%.

**Wound botulism** lacks the prodromal gastrointestinal symptoms of the foodborne form, but is otherwise similar in presentation. Fever, if present, reflects wound infection rather than botulism. *C. botulinum* infection may also produce skin abscesses.

Botulism has also been reported in individuals with sinusitis as a result of cocaine inhalation. The reported incubation period varies from 4 – 14 days. The case fatality rate for wound botulism is approximately 15%.
Infant botulism: Is generally the most common form of botulism and affects infants under one year of age, with the majority of cases occurring between six weeks and six months old. Ingested spores germinate in the intestine, where they produce bacteria which then reproduce in the gut and release toxin. Clinical symptoms start with constipation and may include loss of appetite, weakness, altered cry, weak suck, drooling and a significant loss of head control. The illness has a wide spectrum of clinical severity, ranging from mild illness with gradual onset (that never requires hospitalization) to sudden infant death. Progression is more severe in infants that are younger than two months old.

Upper airway obstruction may be the initial sign, and is the major indication for intubation. In severe cases, the condition progresses to include cranial neuropathies and respiratory weakness, with respiratory failure occurring in about 50% of diagnosed cases. The condition progresses for 1–2 weeks, and then stabilizes for another 2–3 weeks before recovery starts. Relapses of infant botulism may occur.(13)

Adult intestinal toxemia botulism: similar to infant botulism, is relatively rare. It affects adults who have altered GI anatomy and microflora (i.e., intestinal surgery, inflammatory bowel disease, and with exposure to microbial agents).

Botulinum toxin A (BTA) (BOTOX) is available for cosmetic and therapeutic use and in its licensed form has rarely been associated with cases of botulism; however, dysphagia and other symptoms of neuromuscular impairment have been reported after the therapeutic use of botulinum A toxin.

There are reports of cases of botulism associated with the inappropriate use of cosmetic BTA injection (14).

The mortality rate in Canada for all types of Botulism is about 14%.

Diagnosis(6;14;15)
Botulism diagnosis is based primarily on clinical presentation and should be suspected in a person with acute onset of gastrointestinal, autonomic (such as dry mouth or difficulty focusing eyes), and cranial-nerve dysfunction (diplopia, dysarthria, dysphagia). The diagnosis is even more likely if the patient has recently eaten home-canned foods or if family members/companions who have shared the same meals are similarly ill.

Specimens should be obtained and sent in consultation with the Microbiologist on call at the ProvLab. Please see the ProvLab “Guide to services” for specimen collection at: www.provlab.ab.ca/guide-to-services.pdf. Testing of samples for suspect cases of botulism will be coordinated through the MOH (or designate). Most specimens collected (food and clinical) are sent by the ProvLab to the Botulism Reference Laboratory in Ottawa, Ontario.

Electromyography (EMG) studies may be useful in establishing the diagnosis of botulism. EMG may be helpful if distinguishing botulism from myasthenia gravis and Guillain-Barre’s syndrome, diseases that botulism often mimics closely. This test is very uncomfortable, and should not be requested unless botulism is a serious consideration.

Laboratory evaluation includes anaerobic cultures and toxin assays of serum, stool, and the implicated food if available. Cases caught early are more likely to be diagnosed by the toxin assay, whereas those studied later in the disease are more likely to have a positive culture than a positive toxin assay. The most sensitive test for toxin remains the mouse bioassay. Toxin excretion may
continue up to one month after the onset of illness, and stool cultures may remain positive for a similar period.

**Epidemiology** (3;16-27)

**Reservoir**
Botulism spores are ubiquitous in soil worldwide. They are frequently recovered from agricultural products, including honey. Spores are also found in marine sediments and in the intestinal tract of animals and fish.

**Transmission**

**Foodborne botulism.** Toxin production due to improperly processed, canned, low-acid or alkaline foods, in pasteurized and lightly cured foods held without refrigeration, especially in airtight packaging, is the causative agent for foodborne botulism. Newer varieties of certain garden foods such as tomatoes, formerly considered too acidic to support growth of *C. botulinum*, may no longer be low-hazard foods for home canning. Most poisonings in North America are due to home-canned vegetable and fruits. Meat is an infrequent vehicle. In Europe, most cases are due to consumption of sausages and smoked or preserved meats, and in Japan, to seafood. Changes in the epidemiology of botulism have emerged in the past few decades. Recently identified modes of transmission include: homemade salsa, uneviscerated fish, baked potatoes sealed in aluminum foil, cheese sauce, improperly handled commercial potpies, sautéed onions, minced garlic in oil, home-prepared pickled eggs and home-prepared fermented tofu. Type E outbreaks are usually related to fish, seafood, and meat from marine mammals. Type E toxin can be produced slowly at temperatures as low as 3ºC (37.4ºF), which is lower than that of ordinary refrigeration.

**Wound botulism** occurs when *C. botulinum* contaminates a wound and is accompanied by anaerobic conditions that allow for *in-vivo* toxin production in the wound.

Historically, the primary cause of wound botulism was due to soil contamination from a penetrating trauma or crush injury. But in the past decade, parenteral drug abuse related cases have surpassed those related to trauma. Most cases of wound botulism are associated with the intramuscular or subcutaneous injection of (contaminated) black tar heroin as well as sinusitis in those who snort cocaine.

**Infant botulism** results from the ingestion of botulinum spores that then germinate in the intestinal tract and produce toxin, rather than by ingestion of preformed toxin.

The infant's intestinal flora is thought to be particularly permissive for the germination of spores, which leads to the production of toxin. Although the source of ingestion in most cases is unknown it is thought that the spores are acquired from environmental sources in which botulinum spore counts are high. Possible sources of spores for infant botulism are multiple, including foods and dust. Persuasive evidence that links infant botulism to corn syrups or other syrups is lacking. Random sampling of honey shows that less than 5% of honey products produced in Canada contain the bacteria spores. (27)

**Adult intestinal toxemia botulism:** Intestinal botulism, although rare, can also occur in older children and adults after intestinal surgery, in the presence of inflammatory bowel disease and with exposure to antimicrobial agents.
**Alberta Health**  
**Public Health Disease Management Guidelines**  
**Botulism**

**Inhalation botulism** has occurred in laboratory workers. Studies in monkeys indicate that, if aerosolized, the toxin can also be absorbed through the lungs but incubation period may be slightly longer than that for foodborne.(26)

**Iatrogenic botulism** occurs from accidental injection of the botulism neurotoxin into the systemic circulation.

**Incubation Period**  
**Foodborne and Inhalation Botulism**  
- Neurological symptoms appear within 12 – 36 hours (range is six hours to eight days) after toxin ingestion. Generally, the shorter the incubation period, the more severe the disease and the higher the case fatality rate.

**Wound Botulism**  
- Usually 4 – 14 days from the time of injury until the onset of symptoms.

**Infant Botulism**  
- The incubation period is estimated at 3 – 30 days from the time of exposure to the spore-containing substance.

**Period of Communicability**  
No instance of secondary person-to-person transmission has been documented despite excretion of *C. botulinum* toxin and organisms in the feces of infant, colonization and foodborne botulism patients.

**Host Susceptibility**  
Susceptibility is general. Adults with special bowel problems leading to unusual gastrointestinal flora (or with a flora unintentionally altered by antibiotic treatment for other purposes) may be susceptible to colonization botulism. Injection drug users (IDUs) who intentionally or accidentally inject subcutaneously or intramuscularly have been vulnerable to infection. Immunity to botulism toxin does not develop even following severe disease.

In one study, looking at multiple cases of infant botulism, being breast fed was associated with a significantly older age at onset of illness.(28)

**Occurrence**  
**General** (3;5;24;28-30)  
Worldwide outbreaks occur where food products are prepared or preserved by methods that do not destroy the spores and permit toxin formation. Cases rarely result from contaminated commercially processed products. Outbreaks have occurred from contamination through cans damaged after processing. In the United States in 2004, there were 16 laboratory-confirmed cases with an age range of 23 – 91 years old. Almost half of the cases of foodborne botulism are caused by toxin type A; the remaining cases are almost equally divided between toxins E and B.

In the UK, a total of 134 suspected cases of wound botulism have been reported since 2000. In 2006, there were 22 suspect cases of wound botulism reported. Nine were laboratory confirmed. As with previous years the majority were male. However, the average age of 40 years is older than in previous years. All reported cases of wound botulism in the UK have been among IDUs. The primary routes of injection cited are the muscle (“muscle popping”)
and subcutaneous tissue (“skin popping”). Wound botulism in IDUs has also been reported in Switzerland and Norway.

Approximately 80% of cases of wound botulism are caused by type A and 20% are by toxin type B. In 2004, the United States reported 30 lab-confirmed cases of wound botulism with ages ranging from 23 – 57 years.

Cases of infant botulism have been reported worldwide. It is the most common form of botulism in North America. The actual incidence and distribution of infant botulism is unknown because physician awareness is limited. Almost all patients hospitalized with infant botulism have been between the age of two weeks and one year with the majority being less than six months of age. Cases of infant botulism have occurred in all major racial and ethnic groups. From 1973 through 1996 there were 1,444 cases of infant botulism reported to Centres for Disease Control and Prevention (CDC). In 2004, there were 87 lab-confirmed cases of infant botulism in the US. The age range was six days to 61 weeks old. These cases are divided equally between type A and type B toxins. Some studies suggest that it may be the cause of up to 5% of cases of sudden infant death syndrome (SIDS).

**Canada** (1;31-35)
Since first being reported in 1933, foodborne botulism remains a rare disease that primarily affects the First Nations and Inuit people. Over the last few years, most of the cases have occurred in rural or remote areas and have been linked to fermented salmon roe (“stink eggs” or “gink”) in British Columbia as well as fermented sea mammal meat and improperly stored meat among the Inuit. Other traditional foods, such as smoked salmon, are known to cause illness and death.

In 2001, there were eight cases reported (two in British Columbia, one in North West Territories, four in Quebec, and one in the Yukon). Ages range from: two cases age 0 – 4, three cases age 40 – 59, and three cases age 60+ years.

In 2002 there were 10 cases reported (one in Alberta, one in British Columbia, one in Ontario and seven in Quebec) with ages: two cases age 0 – 4 years, one case age 15 – 19, one case age 25 – 29, three cases age 30 – 39, one case age 40 – 59 years and two cases age 60+.

In 2003, of the six cases reported, two were in Ontario, and four were from Quebec, two cases were infants, one case age 30 – 39 and three cases age 60+.

Of the seven cases reported in 2004, two were from Ontario and five cases were from Quebec; one case age 40 – 59 and the remaining six cases were age 60+.

The source(s) for all the cases largely remain unknown.

A published review of outbreaks from 1919 to 1973 documents that two-thirds of the 62 outbreaks reported involved Inuit and West Coast Aboriginal people. Type E toxin is most commonly seen in foodborne cases in Canada. Infant botulism is rare in Canada with only seven cases reported since 1979. The source is rarely identified.

**Alberta** (35)
From 1985 to 2007 there have been eleven reported cases of botulism in Alberta. Three were reported in 1985, one in 1986, one in 1993, one in 1996, one in 1999, one in 2002, one in 2006 and two in 2007. Half of the cases were reported in infants. The source of illness was
usually not identified by laboratory confirmation but foodborne transmission was suspected in most of the cases.

Key Investigation (32;36)
- Contact the Microbiologist-On-Call at the ProvLab for information on collection and transportation of both food and clinical specimens.
- Notification of a suspicion of a single case of botulism constitutes a public health emergency and may herald the beginning of a larger outbreak.
- Investigation of a suspect case of botulism includes a search for other possible cases, identification of suspect food exposures, and diagnostic testing of both cases and foods as needed.
- Efforts to locate persons exposed to the same suspect food may lead to early diagnosis and/or instituting an emergency product recall.

Foodborne Botulism
- Involve environmental/public health inspectors and CFIA.
- Collect food samples and forward to the laboratory for toxin analysis.
- Take a detailed food history of those who are ill, especially foods consumed within the last two or three days. Include consumption of home-preserved foods and traditionally prepared foods. Even theoretically unlikely foods should be considered. *C. botulinum* may or may not cause container lids to bulge and the contents to have “off-odours.” Other contaminants can also cause cans or bottle lids to bulge.
- Collect clinical samples (sera, gastric aspirates and stool) from patients and, when indicated, from others exposed but not ill and forward immediately, with relevant clinical history, to the ProvLab before administration of antitoxin.
- Identify individuals who may have been exposed to the same source.

Infant Botulism
- Investigate source, in particular, history of honey consumption.
- Identify individuals who may have been exposed to the same source.

Wound Botulism
- Contact the physician to determine the possible source of infection.
- Determine if history of trauma, or IDU and if possible forward sample of drug for testing.
- Identify individuals who may have been exposed to the same source.

Control (3;26;36-45)
Management of a Case
- Persons with botulism require immediate emergency medical treatment. Treatment must not await laboratory confirmation.
- Hand washing and other routine practices are indicated.

Treatment of a Case (3;26;36-48)
- Botulism antitoxin and immune globulin are not approved for sale in Canada and are currently only available via Health Canada’s Special Access Programme (SAP).
- Requests for any of these SAP products require the submission of a SAP request form which is reviewed expeditiously by SAP staff.
- Botulism Antitoxin (BAT) and Botulism Immune Globulin Intravenous (Baby BIG-IV®) use must be approved and accessed via the Office of the Chief Medical Officer of Health (OCMOH). See Annex B: General Botulism Antitoxin (BAT) Guidelines and Annex D: General Baby Botulism Immune Globulin Guidelines.
- Treatment focus for wound and foodborne botulism is early administration of the botulism antitoxin/immune globulin with immediate access to an intensive care setting should ventilatory support be required. Giving antitoxin within 24 hours has been shown to decrease need for and duration of mechanical ventilation.(38).
- Antibiotics do not improve the course of the disease. Aminoglycosides and tetracyclines (which can impair neuron calcium entry), have been shown to worsen infant botulism. Thus, it is recommended that antibiotics only be used to treat secondary infections.(48)

**Wound Botulism**
- Administration of antitoxin as per the product monograph and Annex B: General Botulism Antitoxin (BAT) Guidelines.
- The wound should be debrided and/or drainage established.
- Appropriate antibiotics (benzyl penicillin or metronidazole) should be administered.
- The best results are obtained when very large doses of antitoxin are given early in the disease process to provide the body with excess circulating antitoxin.
- Other treatment considerations include enemas, laxatives and other cathartics. If ingestion was recent, may induce vomiting and/or gastric lavage.

**Management of Contacts** (37;42;47)
Botulism is not passed person to person, therefore, direct contacts of the index case do not require follow-up.
- Those who are known to have consumed the suspected food should be purged with a cathartic, given gastric lavage and high enemas, and kept under close medical observation.
- Providing immunoprophylaxis for asymptomatic individuals strongly suspected of foodborne exposure is recommended. This decision should be weighed carefully due to the risk of adverse effects and sensitization to horse serum.
- If antitoxin is required, it should be given within 1 – 2 days of ingestion of the suspect food.

**General Preventive Measures** (26;31;33;49;50)
- Methods to control botulism should focus on the inhibition of bacterial growth and toxin production. Manufacturers of commercially canned low acid foods use strict thermal processes which are designed to destroy spores of *C. botulinum*.
- The CFIA administers and enforces 13 Acts governing food safety and food inspection within Canada and at its borders.
- Search for any remaining food from the same source that may be similarly contaminated and submit for laboratory examination.
  - The implicated food(s) should be detoxified by boiling before discarding or the containers broken and buried deeply in soil to prevent ingestion by animals.
- Contaminated utensils should be sterilized by boiling or by chlorine disinfection to de-activate any remaining toxins.
- Usual sanitary disposal of feces/diaper from infant cases.
- Educate the public about safe handling of food. For example:
  - Do not use food from damaged or bulging containers. These containers should be returned unopened to the vendor.
O Foods with off-odours and unusual tastes should not be eaten or ‘taste-tested’.
O Proper storage is one of the keys to food safety. Refrigeration slows down most bacterial growth. Encourage people to check the temperature of their fridge on a regular basis with a refrigerator thermometer. Set the refrigerator at or below 4°C (40°F). Don’t overload the fridge - cool air must circulate freely to keep food properly chilled. After grocery shopping, immediately refrigerate or freeze foods as indicated on the label.
O Storing food in non-airtight containers and at 4°C or lower will prevent growth of the bacterium.
O Boil and stir home-canned foods (for at least 10 minutes) to destroy botulinum toxins.
O Take precautions with home-prepared foods stored in oil (e.g., vegetables, herbs and spices). If these products are prepared using fresh ingredients, they must be kept refrigerated (below 4°C) and for no more than 10 days.
O If the above products are purchased from fairs, farmer’s markets, roadside stands or have been received as a gift, and prepared more than a week ago, discard them.
O Avoid feeding honey to infants (even pasteurized).
O Provide information to Aboriginal groups regarding food preparation traditions that pose a risk of botulism.
O Promote research to evaluate the safety of traditionally prepared (high-risk) foods, and to identify the precise conditions under which botulinum toxin will be present or absent. (33) Areas to emphasize might include:
   ▪ the importance of refrigeration with home-canning methods,
   ▪ heating food to temperatures high enough to kill the botulism toxin, and
   ▪ keep aging meats such as whale, seal or walrus in a cool place (below 4°C), in containers that allow air in and, if aged in oil, keep in a cool place and stir frequently to allow the meat to be in contact with air.
O Where wound botulism occurs in IDUs, educate them regarding safe injection practices:(51)
   ▪ Do NOT inject into muscle or under the skin.
   ▪ Decrease the amount of citric acid used to dissolve the drug. Too much citric acid damages the tissues under the skin leaving them susceptible to bacterial growth.
   ▪ Studies have shown that when cocaine is mixed with heroin and when injected at the same site it gives bacteria a better chance to grow so, inject different drugs at different sites on the body.
   ▪ Teach IDUs signs and symptoms of infection(s) and to seek physician help especially if infection seems different than ones had in the past.
O Laboratory safety (51)
   ▪ Botulism requires biosafety level 3 practices.
   ▪ Refer to the current PHAC Laboratory Safety Guidelines at: www.phac-aspc.gc.ca/publicat/lbg-ldmbl-04/index.html
Annex A: Process for the Approval and Release of Botulism Antitoxin
(Updated September 2015)

Physician identifies suspect case and reports to Zone Medical Officer of Health (MOH)

Arrange 3-way phone call with Alberta Health OCMOH (on-call pager) and Physician to discuss clinical findings, diagnosis and eligibility

Approved

Not Approved

Withdraw Request

OCMOH/designate arranges for release of antitoxin to hospital pharmacy care of attending physician

Physician provides BAT to client

OCMOH/designate completes SAP "FORM B" to ensure necessary replacement of provincial antitoxin stock

FOLLOW UP BY PHYSICIAN

Complete and return "FORM C" to CMOH/Director Immunization Team within 7 days of BAT use

ANNEX B: General Botulism Antitoxin (BAT) Guidelines
Please read Product Monograph and the Alberta Immunization Policy for detailed instructions regarding dosage and administration for the product supplied.

Indications for Use
- Botulism Antitoxin (BAT) is used for the treatment of botulism.
- For infant botulism see Annex C: Process for the Approval and Release of Baby Botulism Immune Globulin Intravenous (Human) – BabyBIG-IV®.

General Description
- BAT is made from horse (equine) serum and has as its main side effects hypersensitivity, anaphylaxis and serum sickness.

Botulism Antitoxin (BAT) General Use Guidelines
- Access to and shipment of BAT is facilitated by the Director, Immunization Team at Alberta Health.
- It is shipped under strict cold-chain management from the Provincial Vaccine Depot (PVD) to the facility pharmacy.
- All shipments of BAT will have a Health Canada’s Special Access Program (SAP) “Form C” (Patient follow-up form) accompanying it. This form must be completed by the MOH (or designate) and sent back to the CMOH/Director Immunization Team.
- The CMOH will contact the SAP for urgent delivery of more vials if required.
- Delivery will occur by the most rapid mode of transport available.
- If the BAT is not used, the product can be shipped (maintaining cold-chain) back to the PVD.
- Serum should be collected to identify the specific toxin before antitoxin is administered; however the administration of antitoxin should not be withheld pending test results.
- Approximately 9% of people treated with equine antitoxin experience some degree of hypersensitivity to equine serum but severe reactions are rare.

Precautions:
- Consultation with an infectious disease specialist should be done prior to the administration of BAT.
- Sensitivity testing and desensitization may be required depending on the product that is used. See individual product monograph for details.
- Conduct a thorough history of asthma, hay fever, and sensitivity/distress in presence of horses, previous doses of horse serum (i.e., Diphtheria Antitoxin, BAT, anti-snake venom).
  - These persons may develop serious anaphylactic-like reactions especially if previous doses were administered intravenously.(3)

NOTE: The product that is currently available through the SAP (as of September 2015) is Botulism Antitoxin Behring (Novartis). The product monograph is available at: www.lba.admin.ch/internet/lba/de/home/themen/armeeapotheke/0/a-c.parsys.1838.downloadList.21149.DownloadFile.tmp/professionalinformationbotulismusantitoxinbehringe.pdf

NOTE: This product is subject to change without notice and be replaced with another BAT product accessed through the SAP.
ANNEX C: Process for the Approval and Release of Baby Botulism Immune Globulin Intravenous (Human) – BabyBIG-IV®
(Updated September 2015)

BabyBIG® is not approved for use in Canada and is not stocked in Alberta.

Physician identifies suspect case and reports to Alberta Health Services (AHS) Zone Medical Officer of Health (MOH)

AHS Zone MOH

Arrange 3-way phone call with Alberta Health OCMOH (on-call pager) and Physician to discuss clinical findings, diagnosis and eligibility
OCMOW: 780-638-3630
RAAPID On Call Numbers*: 403-944-4486

Place request to Health Canada by completing and faxing (1-613-941-3194)
Health Canada’s Special Access Programme (SAP) FORM A*
(See below)

Call the California Department of Health Infant Botulism Treatment and Prevention Program (IBTPP) On Call Physician to order BabyBIG® at: 1-510-231-7600

Follow-up with phone call to SAP office at: 613-941-2108 Extension 2

Health Canada will provide a Letter of Authorization (LOA) to the California Department of Public Health with a copy sent to the attending Physician

Place request to Health Canada

Physician provides BabyBIG® to client

Contact Hospital Pharmacy to notify them of impending delivery of BabyBIG®

Print and complete the Invoice and Purchase agreement for BabyBIG® accessed at: www.infantbotulism.org
PLEASE NOTE INSTRUCTIONS BELOW

AHS Zone MOH will send Invoice and Purchase agreement for BabyBIG® to Alberta Health for payment:
Fax: 780-422-6663 or Email: health.imm@gov.ab.ca

PHYSICIAN and TEAM to complete the following:

Follow-up by physician

Complete and return FORM C** (see below) to CMOH/Director Immunization Team within 7 days of BabyBIG® use

Completion of Invoice and Purchase Agreement for BabyBIG® (Page 7) – Authorized Official of the Purchasing Institution – Any Authorized Official may sign ‘on behalf of’ the CEO or CFO. This may be an Executive Director, Administrator on Call or a Senior Operating Officer. BabyBIG® still requires the Name and Title of the Authorized Official (CEO or CFO) along with the signatory’s name and title.

*Special Access Program Form A: www.hc-sc.gc.ca/dhp-mps/acces/drugs-droges/sapf1_pasf1-eng.php
** Special Access Program Form C: www.hc-sc.gc.ca/dhp-mps/acces/drugs-droges/sapf3_pasf3-eng.php
California Department of Health: www.infantbotulism.org
ANNEX D: General Baby Botulism Immune Globulin (Baby BIG-IV®) Guidelines

Please read Product monograph and the Alberta Immunization Policy for detailed instructions regarding dosage and administration.

Indications for Use: Infant (Intestinal) Botulism (46)
- Meticulous supportive care is essential.
- Equine derived botulinum antitoxin is not used in infants because of the sensitization and anaphylaxis hazard. Human IG (Baby BIG-IV®) is available in the United States (California) and can be accessed via the OCMOH.
  - Prompt treatment with BabyBIG-IV® is safe and effective in shortening length of hospital stay and severity of illness.

Contraindications
- Do not use in infants with a prior history of severe reaction to other human IG preparations.
- Do not use in infants with selective IgA deficiency that have anti-IgA antibodies to IgA.

Baby Immune Globulin General Use Guidelines (Baby BIG-IV®) (41;43;46)
- For use in patients one year of age and younger.
- A human IG preparation containing IgG antibodies from pooled donors.
- Contains titres against type A & B toxin.

Other information
- BabyBIG® does not reverse symptoms of botulism but rather prevents disease progression by binding circulating toxin.
- In infants exposed (but not yet symptomatic) BabyBIG® is expected to provide a protective level of neutralizing antibodies for 6 months.
- As with other human globulin preparations, immune response to live-virus vaccines (e.g., MMR, MMRV) may be altered, therefore, vaccination with live virus vaccines should be deferred until approximately five months after administration of BabyBIG®.
References


(47) Instituto Butantan. Antibotulinum Serum Type AB and Antibotulinum Serum Type E. 2008. Sao Paulo, Brazil.

