

BOTULISM

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Botulism is a severe illness affecting primarily the nervous system (neuroparalytic disorder) caused by the botulinum toxin produced by *Clostridium botulinum*. Botulism can be classified into the following categories: foodborne, infant, wound and undetermined.

The botulinum toxins are a group of seven related neurotoxins produced by the bacillus *Clostridium botulinum*. Botulism and tetanus toxins are very similar in structure and function, but differ dramatically in their clinical effects because they target different cells in the nervous system.

Botulinum toxins are the most lethal toxins known. For type A toxin, the toxic dose is estimated at 0.001 mcg/kg; the lethal dose for a 70-kg person by the oral route is estimated at 70 mcg, by the inhalational route 0.80 to 0.90 mcg and by the intravenous route 0.09 to 0.15 mcg. The toxins are identified by neutralization with type-specific antitoxin; minor cross-neutralization between types C and D and between types E and F has been observed. The toxins are produced by vegetative cells (ie, germination of spores), and released by cell lysis. Some toxins are fully activated by the bacteria that produce them (proteolytic strains of type A, B and F), and some require exogenous proteolytic activation (types E and non-proteolytic types B and F). Botulinum toxins are colorless, odorless and presumably tasteless. The toxins are inactivated by heating (>85°C for 5 minutes).

Toxins are differentiated according to their antigenic differences: types A to G. Human botulism is almost always caused by neurotoxins A, B, E and F. Type A botulism is found most commonly in the West and type B is more common in the East. Type E is associated with fish. Types C and D are associated primarily with botulism in birds and mammals. Almost all cases of infant botulism are caused by types A and B.

Botulinum toxin A produced longer paralysis than botulinum toxin B, consistent with human observations.

- For type A, duration of paralysis was exponentially related to toxin dose; the paralysis time doubled with every 25% increase of the toxin concentration.
- For type B, the duration of paralysis was linear relative to the toxin dose.
- Types C and D cause natural disease in birds, horses and cattle; strains that produce these types reside in the intestinal tract of certain animals. Contaminated silage has been reported to cause botulism outbreaks among cattle.
- Type E toxin had the shortest duration of action, but unlike the other two toxins, the dose of toxin did not influence recovery time.
- Toxin type G has never clearly been shown to cause human disease.

Aerosolized particles of toxin are approximately 0.1 to 0.3 micrometers in size. In the event of an intentional release of botulinum toxin, the causative organisms may, or may not be present

These toxins could be delivered by aerosol. When inhaled, these toxins produce a clinical picture very similar to foodborne intoxication. However, the botulinum toxin is so inherently toxic that this characteristic does not limit its potential as a biological weapon.

Exposure to botulinum toxin occurs through the following mechanisms (toxin is not absorbed through intact skin):

- Ingestion of preformed toxin
- Inhalation of preformed toxin
- Local production of toxin by *C. botulinum* organisms in the gastrointestinal tract
- Local production of toxin by *C. botulinum* organisms in devitalized tissue at the site of a wound

Epidemiology

Food botulism is caused by the ingestion of a preformed toxin in contaminated food. The toxin is produced when the bacteria grow in food that has been improperly preserved or stored under anaerobic conditions. Most poisonings in the U.S. are due to home-canned vegetables and fruits. Botulinum spores are often present in the environment; therefore identification of the organism in food is not necessarily diagnostic.

Not all foodborne botulism results from ingestion of improperly prepared home-canned food as demonstrated by restaurant-associated outbreaks from foods such as patty-melts, potato salad and aluminum foil-wrapped baked potatoes. The word “botulism” comes from the Latin word *botulus*, or sausage.

The following steps are necessary for a food item to cause botulism:

- The food item must be contaminated with *C. botulinum* spores, which are normally found in soil.
- The spores must survive food preservation methods.
- Adequate conditions for spore germination and neurotoxin production must be present
- The food must not be reheated adequately (>85°C for 5 minutes) to inactivate the heat-labile toxin before the food is consumed.
- Generally, adequate conditions for germination and neurotoxin production include the following:
 - An anaerobic environment
 - Non-acidic pH (generally 4.6 to 4.8; pockets of different pH may be present within a single food source and allow toxin to be produced in a food that overall has an acidic pH)
 - Minimum temperature of 10°C (the optimum temperature for growth of proteolytic strains is close to 35°C; some non-proteolytic strains of types B, E and F can produce toxin at refrigeration temperatures [3°C to 4°C])
 - Availability of water with limited solute concentration

Infant botulism: In contrast to classical foodborne botulism, which is intoxication due to ingestion of preformed botulinum toxin, infant botulism occurs after infants eat spore contaminated food. The spores grow in the intestines and then release the toxin in the body. The infant’s large intestine vulnerability to spore germination and toxin production is not yet understood. Honey is the one identified and avoidable source of botulinum spores. By a process of exclusion (testing over the years of hundreds of foods, beverages and other items placed in infants' mouths with negative results), it was concluded that most infant botulism patients acquired their spores by swallowing microscopic dust particles that carry the spores. In most cases the precise source is not identified. Honey has been identified as one vehicle and should not be given to children under one year of age.

Botulism is not transmitted from person to person. *C. botulinum* spores are found throughout the world in soil samples and marine sediment.

Wound botulism:

C. botulinum is a natural contaminant of soil throughout the United States. Wound botulism has been recognized with increasing frequency among injecting drug users. Wound botulism in drug abusers can be misdiagnosed as drug intoxication. It should be considered in injecting drug users who present with dysarthria and dysphagia. Wound botulism may occur following traumatic injury to an extremity, such as a compound fracture, laceration, puncture wound, gunshot wound, severe abrasion ("road rash"), or crush

injury. Sinusitis associated with intranasal cocaine use has been the source of wound botulism in a few cases.

A few cases have occurred postoperatively (usually following intra-abdominal procedures), and in one case, an abscessed tooth was the source of *C. botulinum* infection.

Adult Intestinal Toxemia Botulism:

The pathogenesis of intestinal botulism in adults is similar to that of infant botulism. Disease is caused by ingestion of *C. botulinum* spores, with subsequent colonization of the gastrointestinal tract. Spores germinate and produce toxin, which is then absorbed into the circulation. Only a few cases have been recognized and most have occurred postoperatively or in adults with underlying pathology of the gastrointestinal tract such as Crohn's disease.

Iatrogenic Botulism:

Iatrogenic botulism is caused inadvertently by injection of botulinum toxin for therapeutic or cosmetic reasons. Four cases of iatrogenic botulism occurred in December, 2004 in Florida following cosmetic injection with a botulinum toxin that was not approved for use in humans. The injections contained much higher concentrations of botulinum toxin than the FDA-approved product Botox®. A research firm in Arizona sold the raw botulinum toxin to healthcare practitioners as a Botox® substitute.

Botulinum Toxin as a Biological Weapon: Past efforts to weaponize botulinum toxin include the following:

- The United States produced botulinum toxin as a potential biological weapon beginning in World War II; however, the U.S. offensive biological weapons program ended after the 1972 Biological and Toxin Weapons Convention (BTWC).
- The former Soviet Union conducted research on use of botulinum toxin as a biological weapon as late as the early 1990s, despite having signed the BTWC.
- At the time of the Gulf War, Iraq had produced 19,000 L of concentrated botulinum toxin, some of which was loaded into military weapons.
- The Japanese cult Aum Shinrikyo attempted to use aerosolized botulinum toxin in Japanese cities on at least three occasions between 1990 and 1995. Fortunately, these efforts were not successful.
- The two most likely mechanisms for use of botulinum toxin as a terrorist weapon include deliberate contamination of food or beverages, or via an aerosol release.

Because food products are often widely distributed, contamination of a commercially produced food or beverage product could result in a high number of casualties and fatalities across the country. In addition, such a bioterrorist act would produce severe civic disruption, economic loss and social anxiety. Any food or beverage item that is not heat-processed at 85°C (185°F) for five minutes prior to consumption or is potentially contaminated following sufficient temperature processing must be considered a possible vehicle for botulinum toxin. For example, typical temperatures employed for pasteurization of commercially available beverage products will not sufficiently denature all botulinum toxin in the product. Mathematical modeling suggests that one gram of botulinum toxin added to commercially distributed milk consumed by 568,000 people could result in 100,000 cases of botulism. Ten grams of toxin added to the same quantity of milk could result in over 500,000 cases in the exposed population.

An aerosol release could also lead to high numbers of casualties, although the event would be more localized. Experts have estimated that one gram of aerosolized botulinum toxin could kill up to 1.5 million people (see References: Shapiro 1997). Aerosolized particles of botulinum toxin are approximately 0.1 to 0.3 μm in size.

Although contamination of a water supply is feasible, this approach is unlikely since a large amount of toxin would be needed to initially contaminate water. In general, deliberated contamination of water with potential bioterrorism agents may not be very effective for the following reasons: dilution of the agent in a large body of water; direct inactivation from chlorine or other disinfectants; nonspecific inactivation by other mechanisms (such as hydrolysis, sunlight, or microbes); filtration; the relatively small amount of water that is

actually ingested from the source. Botulinum toxin is naturally inactivated in fresh water within three to six days and toxin is rapidly (within 20 minutes) inactivated by standard potable water treatment. A 2005 study found that two of seven small-scale water purification devices tested were able to effectively eliminate botulinum toxin from water. Those based on filtration (pore size 0.2 to 0.4 mcm) or irradiation from a UV-lamp (254 nm) failed to remove the toxin from inoculated water. Reverse osmosis and experimental sand filtration effectively eliminated the toxin.

The following features of a botulism outbreak would suggest deliberate toxin release:

- An outbreak involving a larger number of cases than previous outbreaks
- An outbreak caused by an unusual toxin type (ie, C, D, F, or G) or an outbreak involving type E toxin without an apparent aquatic source
- Multiple simultaneous outbreaks with, or without an apparent source
- For aerosol release, cases would not have a common food exposure but would have been in a common geographic location during the week before symptom onset

The usual incubation period is:

- for foodborne botulism 12 to 36 hours (range, 6 hours to 10 days)
- for wound botulism, 4 to 14 days between the time of injury and the onset of symptoms
- for infant botulism, the incubation period is estimated at 3 to 30 days from the time of exposure to spore-containing honey or other food.

Clinical Description

Botulinum neurotoxins predominantly affect the peripheral neuromuscular junction and autonomic synapses, and its effects are primarily manifested as weakness. It is NOT associated with mental status or sensory changes.

Except for infant botulism, onset of symptoms occurs abruptly within a few hours or evolves gradually over several days. Botulism is an acute, afebrile symmetric, descending, flaccid paralysis. Fatigue, dizziness, dysphagia, dysarthria, diplopia, dry mouth, dyspnea, ptosis, ophthalmoparesis, tongue weakness and facial muscle paresis are early findings seen in more than 75% of cases. Progressive muscular involvement leading to respiratory failure ensues

Symptoms and Signs in Patients with the Common Types of Human Botulism

	Type A (%)	Type B (%)	Type E (%)
<i>Neurologic Signs and Symptoms</i>			
Dysphagia	96	97	82
Dry Mouth	83	100	93
Diplopia	90	92	39
Dysarthria	100	69	50
Upper Extremity Weakness	86	64	NA
Lower Extremity Weakness	76	64	NA
Blurred Vision	100	42	91
Dyspnea	91	34	88
Paresthesias	20	12	NA

	Type A (%)	Type B (%)	Type E (%)
<i>Gastrointestinal Signs and Symptoms</i>			
Constipation	73	73	52
Nausea	73	57	84
Vomiting	70	50	96
Abdominal Cramps	33	46	NA
Diarrhea	35	8	39
<i>Miscellaneous Symptoms</i>			
Fatigue	92	69	84
Sore Throat	75	39	38
Dizziness	86	30	63
<i>Neurological Findings</i>			
Ptosis	96	55	46
Diminished Gag Reflex	81	54	NA
Ophthalmoparesis	87	46	NA
Facial Paresis	84	48	NA
Tongue Weakness	91	31	66
Pupils Fixed or Dilated	33	56	75
Nystagmus	44	4	NA
Upper Extremity Weakness	91	62	NA
Lower Extremity Weakness	82	59	NA
Ataxia	24	13	NA
DTRs Diminished or Absent	54	29	NA
DTRs Hyperactive	12	0	NA
<i>Initial Mental Status</i>			
Alert	88	93	27
Lethargic	4	4	73
Obtunded	8	4	0

Infant botulism occurs in infants younger than six months of age. The disease infant botulism is first suspected based on clinical features of the infant patient (12 months of age or younger). Symptoms such as:

- poor feeding
- droopy eyelids
- constipation
- lethargy

- bulbar palsies, hypotonia, weakness and loss of head control

The spectrum of disease ranges from mild (eg, constipation, slow feeding) to rapidly progressive (eg, apnea, sudden infant death).

Accordingly, it is necessary for prompt laboratory analysis to be performed to establish the diagnosis. Prompt laboratory diagnosis of infant botulism is helpful for patient management and will rule-out the possibility of fatal degenerative neuromuscular diseases.

Wound botulism lacks the prodromal gastrointestinal disorder of the foodborne form, but it is otherwise similar in signs and symptoms.

The most prominent electromyographic finding is an incremental increase of evoked muscle potentials at high-frequency nerve stimulation (20 to 50 Hz). In addition, a characteristic pattern of brief, small-amplitude, overly abundant motor action potentials can be seen.

Differential diagnosis:

Myasthenia gravis and the Eaton-Lambert myasthenic syndrome (LEMS) may be somewhat similar to botulism but are rarely fulminant and lack autonomic features. An edrophonium test may be considered, but an improvement in strength is not pathognomonic of myasthenia gravis, and has been reported in botulism. Tick paralysis is excluded by a careful physical examination, because the Dermacentor tick will still be attached.

Classic acute inflammatory demyelinating polyneuropathy (AIPN; Guillain-Barré syndrome) frequently begins with sensory complaints, rapidly becomes areflexic, rarely begins with cranial nerve dysfunction and does not alter pupillary reactivity. Botulism patients do not become areflexic until the affected muscle group is completely paralyzed.

Patients with polio are febrile on presentation and have asymmetrical weakness.

Magnesium intoxication looks like botulism.

Laboratory Tests

1- A toxin neutralization bioassay in mice is used to identify botulinum toxin in serum, stool, or suspect foods. To increase the likelihood of diagnosis, both serum and stool should be obtained from all persons with suspected botulism.

In infant and wound botulism, the diagnosis is a two step process:

- 1-Demonstrate *C.botulinum* organisms
- 2-Demonstrate the presence of toxin in feces, wound exudate or tissue samples.

The toxin has been demonstrated in serum in approximately one percent of infants with botulism. In foodborne cases, serum specimens collected more than three days after ingestion of toxin usually are negative, at which time stool and gastric aspirates are the best diagnostic specimens for culture. Since obtaining a stool specimen may be difficult because of constipation, an enema using sterile nonbacteriostatic water can be given.

Enriched and selective media are used to culture *C.botulinum* from stool and foods. *C. botulinum* is a large, usually gram-positive, strictly anaerobic bacillus that forms a subterminal spore.

The reporting source may request the assistance of the health department in sending specimens (stool and blood) to the Centers for Disease Control and Prevention (CDC) for testing. Consult the Infectious Disease Epidemiology Section on guidelines/ requirements for accepting specimens and the appropriate handling of them.

Stool and blood specimens must be sent to the Central Laboratory in New Orleans to be forwarded to the CDC. Stool specimens (1 to 2 g) are to be collected in a clean container (no preservatives), and kept refrigerated. Serum specimens (at least 1 cc) are to be collected in a red-topped tube and either spun down and sera sent or the whole blood sent refrigerated.

Stool for infant botulism:

The specimen required for the definitive diagnosis of infant botulism is stool or enema. The best container to collect, store and submit fecal specimens in is a sterile urine container with a tight, screw-capped lid. ***Do not use*** containers containing fixatives such as those used for ovum and parasite collection. If passed stool is difficult to obtain due to constipation, an attempt to collect stool in the rectal vault should be made by ***gentle*** digital examination by the team member with the smallest fifth finger. If no stool can be obtained digitally, do not wait for a spontaneous bowel movement. Instead, please follow the enema collection procedure outlined below.

*Important: Note that glycerin suppositories yield an unsatisfactory specimen and **should not be used**. The procedure described below will yield the best specimen for diagnostic purposes.*

Enema Collection Procedure

1. Attach a 12 to 16 French red rubber (Robinson) catheter to a tapered, catheter-tip syringe.
2. Trim catheter tip to enlarge hole.
3. Lubricate the catheter tip with petroleum jelly or equivalent and insert into distal colon.
4. The volume of sterile, ***non-bacteriostatic*** water to use should be a bedside clinical decision based on the patient's body mass.
5. Inject ***up to*** 30 ml of sterile, ***non-bacteriostatic*** water slowly into distal colon and maintain catheter in rectum. Please note that a ***minimum volume of 5 ml*** is required to enable the most accurate diagnostic analysis.
6. Wait approximately 3 minutes and then draw enema effluent into the syringe.
7. Have an assistant hold a sterile urine container under the anus during this time to collect any expelled material.
8. Expel all fluid collected in the syringe into the same sterile urine container.
9. Tightly seal the lid. Properly label the container with patient's name, date and time of collection.
10. If more than 5 ml of water is retained in the colon, exert gentle pressure onto left lower abdomen (with your hand or with infant's knee to abdomen) to aid in excretion and to minimize intestinal absorption of water.
11. Send the enema specimen to your laboratory with an order to keep it refrigerated and to expedite shipment to the appropriate botulism diagnostic laboratory.

Retain all subsequent stool specimens and have your laboratory store them in their refrigerator until a diagnosis has been established by the appropriate laboratory. Please do not send ***extra*** stool specimens unless requested. For California only - please contact 510-231-7676 with any questions regarding specimen collection, requirements or submission. For all other states, please contact your state health department. Thank you.

Storage for shipping of stool or enema samples:

All fecal specimens (stool or enema) collected for infant botulism testing require refrigeration only. Do not freeze them.

2- A PCR test is used for the detection of the gene for botulinum toxin, not the toxin itself and ought to be able to report the specific toxin type involved here. The assay, however, cannot measure whether the toxin is expressed. The usual toxin assay is a mouse bioassay, which by neutralization analysis can also indicate the specific toxin involved.

3-Serology is not very useful for diagnosis, as small amounts of toxin are involved and survivors rarely develop antibodies. The mouse protection bioassay (MPB) is currently considered the "gold standard" for detecting antibodies against botulinum toxin A (BTX-A). A recently developed immunoprecipitation assay (IPA) compares favorably with MPB. Serologic tests are available from several laboratories (NorthWest Pacific Laboratories, Berkeley, CA).

Summary Guidelines for specimen collection and shipment

1. Specimen collection

Suspected foodborne botulism cases

- Suitable materials for examination are: serum, feces, vomitus, gastric contents and suspected foods
- Serum samples must be taken before antitoxin treatment
- Ideally, 15 ml of serum should be obtained (without anticoagulant)
- Ideally, 10 g to 20 g of feces should be collected
- Foods should be left in their original containers or placed in sterile unbreakable containers
- Empty containers with remnants of suspected foods can also be examined
- We do not test unopened commercial products, except with permission from regulatory authorities (Food and Drug Administration (FDA)/United States Department of Agriculture (USDA))

Suspected wound botulism cases

- Suitable material for examination are; serum, tissue, feces

Suspected infant botulism cases

- Suitable specimens: stool, rectal swabs (it is not necessary to collect serum samples from infant botulism cases, according to the recommendations from the Infant Botulism Treatment and Prevention Program)
- Ideally, 10 g to 20 g of feces should be collected
- Potential sources (honey, opened formula, etc.) can also be examined

2. Specimen shipment

- Specimens should be maintained at 4°C and should be sent with cold packs
- CDC form 50.34 with **State Department of Health and Hospital phone and fax numbers** should accompany the package
- If CDC form 50.34 is not available, please provide **State Department of Health and Hospital phone and fax numbers and patient's name, onset date and birthdate**
- Send the package to:
STAT (Attn: Botulism Lab)
Centers for Disease Control and Prevention
1600 Clifton Rd. NE
Atlanta, GA. 30333
- Package must have proper labeling for biological hazards
- Packages may arrive on weekends
- Notify our laboratory as soon as possible that you are sending specimens (e-mail is fine, Cluquez@cdc.gov)

Surveillance

Botulism is a class A reportable condition (to be reported in 24 hours).

Case Definition

A case of food-borne botulism is defined as:

1. An illness characterized by clinical manifestations relating to the nervous system (ptosis, blurred or double vision, dry mouth and sore throat are usually the first symptoms followed by descending paralysis) that is laboratory confirmed
2. Or a clinically compatible illness that occurs in a person who ingested the same food as someone with laboratory confirmed botulism.

A case of infant botulism is defined as a syndrome compatible with botulism in a person less than one year of age and detection of botulinum toxin in serum or *C. botulinum* organisms in the patient's stool.

A case of botulism is confirmed:

1. By identifying the specific toxin in serum or stool, or
2. Rarely, by culturing *C. botulinum* from a wound in a clinical case.

A case of infant botulism is confirmed by:

1. Identification of *Clostridium botulinum* spores in stool specimens.
2. Identification of botulinum toxin in serum or stool specimens.

Case investigation

The purpose of the investigation is:

- to identify sources of contaminated food,
 - to identify other individuals who shared the suspected food,
 - to identify clusters related to a possible bioterrorism event.
- Because of the serious nature of this disease and the difficulty of diagnosing, the notification of the case would come from a major hospital or medical center.
 - Upon receipt of a report of botulism, contact the physician and/or hospital to confirm the diagnosis. (See Laboratory Tests).
 - An immediate concern would be to determine the source of the toxin. Check recent food history of ill individuals and recover all suspected foods for appropriate testing.
 - Suspicion of a single case of botulism should immediately raise the question of a group outbreak involving a family or others who may have shared a common food or have been associated with a cluster event.

Case Management - Treatment

1- Adult: Adults with botulism are treated with an antitoxin derived from horse serum distributed by CDC. Treatment with Botulism Immune Globulin (BIG) should be started as early in the illness as possible and **should not be delayed while awaiting laboratory confirmation.**

A new heptavalent botulinum antitoxin (HBAT, Cangene Corporation) is available through a CDC-sponsored Food and Drug Administration (FDA) Investigational New Drug (IND) protocol. HBAT replaces a licensed bivalent botulinum antitoxin AB and an investigational monovalent botulinum antitoxin E (BAT-AB and BAT-E, Sanofi Pasteur) with expiration of these products on *March 12, 2010*. As of *March 13, 2010*, HBAT became the only botulinum antitoxin available in the United States for naturally occurring non-infant botulism. Botulinum antitoxin for treatment of naturally occurring non-infant botulism is available only from the CDC. The transition to HBAT ensures uninterrupted availability of antitoxin. BabyBIG (botulism immune globulin) remains available for infant botulism through the California Infant Botulism Treatment and Prevention Program (1). BabyBIG is an orphan drug that consists of human-derived botulism antitoxin antibodies and is approved by the FDA for the treatment of infant botulism types A and B.

HBAT contains equine-derived antibody to the seven known botulinum toxin types (A--G) with the following nominal potency values: 7,500 U anti-A; 5,500 U anti-B; 5,000 U anti-C; 1,000 U anti-D; 8,500 U anti-E; 5,000 U anti-F; and 1,000 U anti-G. HBAT is composed of less than 2% intact immunoglobulin G (IgG) and $\geq 90\%$ Fab and F(ab')₂ immunoglobulin fragments; these fragments are created by the enzymatic

cleavage and removal of Fc immunoglobulin components in a process sometimes referred to as despeciation. Fab and F(ab')₂ fragments are cleared from circulation more rapidly than intact IgG (2), and repeat HBAT dosing might be indicated for some wound or intestinal colonization patients if in situ botulinum toxin production continues after clearance of antitoxin.

The HBAT FDA IND treatment protocol includes specific, detailed instructions for intravenous administration of antitoxin and return of required paperwork to CDC. Health-care providers should report suspected botulism cases immediately to their state health department; all states maintain 24-hour telephone services for reporting of botulism and other public health emergencies. Additional emergency consultation is available from the CDC botulism duty officer via the CDC Emergency Operations Center, telephone, 770-488-7100 (3). Additional information regarding CDC's botulism treatment program is available at website <http://www.bt.cdc.gov/agent/botulism>.

To obtain antitoxin call directly the CDC. A CDC staff member will ask questions to determine whether antitoxin therapy is indicated
Primary number: 770-488-7100 CDC Emergency Operations Center and ask for the Botulism Officer In Charge
Alternate numbers: 404-639-2206 during workdays, or 404-639-2888 other times

Attached are the forms that will be used by CDC to determine whether antitoxin is indicated. Do not fill out the forms. Do not send them to the Office of Public Health (OPH) prior to obtaining CDC approval.

Once the CDC approval is obtained, fill out the forms and send them with the sample to the OPH central laboratory.

2-Infant botulism: Human botulism antitoxin is the drug recommended for infants, not adult antitoxin. BabyBIG[®], Botulism Immune Globulin Intravenous (Human) (BIG-IV), is an orphan drug that consists of human-derived botulism antitoxin antibodies that is approved by the U.S. Food and Drug Administration for the treatment of infant botulism types A and B. It is available through the Infant Botulism Treatment and Prevention Program in Berkeley, CA. Baby Big neutralizes toxin types A, B, C, D and E before they bind to nerve endings. Baby BIG is active up to four months after injection against A and B. Although many infants recover with supportive care, BabyBIG cuts a hospital stay in half.

Baby BIG is only available through the California Department of Health which holds a license on the drug. Call the Infant Botulism Treatment and Prevention Program in Berkeley, CA at (510) 217-4449 (24 hours a day). The fee for obtaining the drug is \$45,000 (forty-five thousand dollars) payable within five days. Extensive paperwork needs to be filled out and can be obtained by phone request.

The product is a solvent-detergent-treated, sterile, lyophilized powder of immunoglobulin G (IgG), stabilized with 5% sucrose and 1% albumin (human). It contains no preservative. The purified immunoglobulin is derived from pooled adult plasma from persons immunized with pentavalent botulinum toxoid who were selected for their high titers of neutralizing antibody against botulinum neurotoxins type A and B. All donors were tested and found negative for antibodies against the human immunodeficiency virus and the hepatitis B and hepatitis C viruses. The pooled plasma was fractionated by cold ethanol precipitation of the proteins according to the Cohn/Oncley method, modified to yield a product suitable for intravenous administration.

To obtain BabyBIG[®] for a patient with suspected infant botulism, the patient's physician must first contact the Infant Botulism Treatment and Prevention Program (IBTPP) on-call physician at (510) 231-7600 to review the indications for such treatment. As a guide for obtaining BabyBIG[®], inquiring physicians should use read IBTPP's internal programmatic checklist as a guide to follow that contains the necessary steps IBTPP must take necessary to release BabyBIG[®] to a hospital.

The infant should have good to full recovery of muscle strength and tone before immunizations resume. In addition, live-virus vaccines (i.e., measles, mumps, rubella and varicella) need to be delayed until five months after BabyBIG[®] treatment because the antibodies in BabyBIG[®] may interfere with the effectiveness

of the vaccine. Because these vaccines are normally first given at one year of age, this consideration will affect only those infant botulism patients seven months of age or older at onset.

Prognosis: In the absence of serious hospital-acquired complications, no. The prognosis for infant botulism patients is for full and complete recovery. Recovery results from regrowth of the nerve endings that then are able to signal the muscles to contract. Botulinum toxin does not penetrate into the brain and so infant botulism patients retain all the intelligence, athletic ability, musical ability, sense of humor and orneriness with which they were born.

Prevention

When a food item has been identified by epidemiologic evidence or laboratory tests, immediate recall of the product is necessary. This will be done by the Infectious Disease Epidemiology Section working in conjunction with the CDC and/or the FDA.

Education to improve home-canning methods should be promoted, but cases also may be restaurant-acquired. Use of a pressure cooker (at 116°C = 240.8°F) is necessary to kill spores of *C. botulinum*. Boiling for ten minutes will destroy the toxin. Time-temperature-pressure requirements vary with the product being heated. In addition, food containers that appear to bulge may contain gas produced by *C. botulinum* and should be discarded. Other foods that appear to be spoiled should not be tasted.

The only known prevention measure for infant botulism is to avoid feeding honey to infants twelve months of age or younger. Breastfeeding may slow the onset of illness if it develops.

Hospital precaution and isolation: Standard precautions.