Botulism in the United States

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Abstract

Botulism is a rare public health emergency, serious life-threatening neuroparalytic disease caused by antigenically distinct, heat labile, protein neurotoxin produced *Clostridium botulinum*, *Clostridium butyricum*, and *Clostridium baratii* bacteria. Five kinds of botulism naturally occurring forms of the disease include food-borne, wound, infant, intestinal and other or undetermined. Other disease forms are unintentional or iatrogenic acquired following toxin injection for therapeutic or cosmetic purposes and exposure as a result of an intentional act of terrorism either by aerosolization through absorption through mucous membranes or broken skin or distributed on food items (Sobel, 2005). Since 1973 the Centers for Disease Control and Prevention (CDC) has maintained for cases of botulism in the United States the National Botulism Surveillance System. Data published yearly from 2001 to 2011 in the Botulism Surveillance Summary adds to a total of 1,548 confirmed cases of botulism, with a mean and median of 140 cases, coefficient of variation 0.13 and standard deviation 17.6. Botulinum neurotoxin (BoNT) is considered the most potent lethal substance known. The only available treatment for botulism is administration of the heptavalent botulinum antitoxin (HBAT) to block the action of the circulating toxin in the blood. Many cases of botulism are preventable except for infant botulism since the spores of the causative organism are widely distributed in the soil affecting the immature immune infant’s system causing intestinal colonization.
Introduction

Botulism has probably affected humans since the beginning of time. Food consumption leading to death was not realized in ancient times. The earliest notion of the paralytic disease after consumption of certain foods and eventually death was in the 10th century when food laws imposed by Emperor Leo VI Byzantium (886-911) prohibited blood sausage manufacturing and applied fines and penalties if the edict was violated (Erbguth, 2004). Documentation of food poisoning did not take place until late in the 18th century. Sausage poisoning outbreak providing well documented signs and presentation of the intoxication occurred in the village of Wilbad in Württemberg, Germany involving 13 cases and 6 deaths which were concluded to be caused by either prussic acid or possibly an organic poison (Erbguth, 2004). It was not until 1820 when more outbreaks affected Württemberg again that Justinus Kerner, a poet and medical officer, published observations and theories on the lethal poisoning caused after consumption of smoked sausages. Kerner’s publication included clinical observations describing symptoms, autopsy reports, experimental work of sausage extracts fed to mammals, birds, and other animals, hypothesis on the toxin’s action, prevention, treatment, and even suggestions on using the toxin for therapeutic applications (Erbguth, 2008).

The food poisoning was then named “Kerner’s disease”. The name eventually was changed to botulism meaning sausage from the Latin *botulus*. Recovery of the botulism toxin producing bacterial was achieved in 1985 by Pierre Marie Van Ermengen, a microbiologist, after an outbreak in Ellezelles, Belgium who gave the bacteria the current name *Clostridium botulinum* (Erbguth, 2004). Eventually, in 1904 it was found that the toxin was not just formed in sausages and meats, but due to a botulism outbreak involving canned white beans it was found that the strain of the organisms producing this toxin was distinctly different from the previous one.
recovered. In 1919 Georgina Burke at Stanford University designated the toxins as type A and type B (Erbguth, 2008).

Botulinum neurotoxin (BoNT) is very lethal, therefore, intensive surveillance and control measures are mandated in the U.S. The Centers for Disease Control and Prevention (CDC) in partnership with the Council of State and Territorial Epidemiologists (CSTE) has maintained the National Botulism Surveillance System since 1973 for both laboratory confirmed and suspected probable cases of botulism. Laboratories report all confirmed cases of botulism which fit the CSTE case definition. Data are collected by the system and monitored to detect early outbreaks from all fifty states and the District of Columbia (CDC, 2012). The reports from all the states must include case demographics, clinical information, laboratory, and epidemiological finding: age, sex, race, ethnicity, case outcome, transmission, testing methods, toxin type, and the infectious vehicle (CDC, 2012). The average total number of botulism cases reported in the U.S. annually are 145 cases. The median annual reports of botulism are 22 foodborne cases or approximately 15 percent, 29 cases or 20 percent wound botulism, and 94 infant botulism cases or approximately 65 percent (CDC, 2011).

*Clostridium botulinum* has the ability to form heat resistant spores that survive preservation methods and may require temperatures higher than boiling to be destroyed. The occurrence worldwide of sporadic cases, family, and general outbreaks are associated with preparation and preservation of foods that do not destroy the spores and allow toxin production (CDC, 2012). Rare cases are associated with commercially processed foods and canning. The U.S.A reports most of the cases occurring globally with California reporting half of the cases (Heymann, 2004). Foodborne botulism as indicated by the aforementioned annual data is rare, but consumption of the implicated contaminated food if not identified rapidly may expose many people to BoNT and
cause many deaths, therefore, its suspicion represents a medical and public health emergency (CDC, 2012). Foodborne botulism required rapid recognition by physicians and demands effective communication between clinicians and public health epidemiologists and experts of suspected cases in order to provide a rapid response from health care personnel and testing laboratories.

**Causative Agent**

*Clostridium botulinum* and strains of *Clostridium butyricum* and *Clostridium baratii* produce botulinum toxin with similar pharmacological activity, but diverse in serological properties. Seven toxin types A, B, C, D, E, F, and G are produced by different strains (Winn, et al., 2006). *Clostridium botulinum* produces toxins A, B, E, and F which cause human disease; type A is the most common and type F the least common. *Clostridium botulinum* also produces types C and D which cause disease in birds and animals, toxin production is phage mediated. *Clostridium butyricum* produces toxin type E and *Clostridium baratii* toxin F. *Clostridium argentinense* produces type G have been isolated from autopsy samples of sudden death individuals, however role in disease is unclear, toxin production is plasmid mediated (CDC, 2011 and Winn et al., 2006). Botulinum neurotoxin (BoNT) is a dipeptide chain, Zinc-containing metalloprotease with a 100-kd “heavy chain” joined by a single disulfide bond to a 50-kd “light” chain. The toxins are distinguished by neutralization of biological activity with type specific antisera (A-G) by mouse bioassay (Shapiro, Hathaway, and Swerdlow, 1998 and Dassey & Bolivar, 2012).

The organism is an anaerobic, spore forming, gram positive bacilli. The spores are found in the soil worldwide recovered from agricultural products, honey, marine sediment, and the intestinal tract of animals including fish (Heymann, 2004). All antigenic botulinum toxin types act
primarily by binding to synaptic vesicles of nerves, preventing the release of acetylcholine at the peripheral nerve endings resulting in flaccid, descending paralysis. The paralysis begin with bilateral impairment of the cranial nerves resulting in descending paralysis of the face, eyelids, head, throat, continuing to the thorax, diaphragm and extremities last. Patients die of respiratory paralysis unless proper intensive care is provided with a mechanical ventilation. Dead may also result from secondary pneumonia (Winn, et al., 2006). The toxin lethal human dose for BoNT type A is estimated to be between 100 – 1,000 ng equivalent to 5,000 to 50,000 mouse lethal injected dose (MLD). Food implicated in cases of foodborne botulism have contained as high as 10,000 MLD/gram. Some culture supernatants of Clostridium botulinum contain over 1million MLD/ml. Clostridium botulinum grows under anaerobic, low salt, low acid, and low water activity, it is inhibited by temperature <4°C or >121°C and pH < 4.5. The spores are inactivated by autoclaving at 121°C under pressure of 15-20 lb/in². BoNT is destroyed by heating at greater than 85°C for 5 minutes (Shapiro, Hathaway, and Swerdlow, 1998 and Dassey & Bolivar, 2012). Five kinds of botulism naturally occurring forms of the disease include 1) food-borne; resulting from the ingestion of preformed toxin in contaminated food, 2) wound which is the rarest form; results from toxin production in vivo after Clostridium botulinum has multiplied in an infected wound, 3) infant botulism, is the most common; it results from in vivo multiplication of the bacterial organism with production of the neurotoxin within the gut of the infant; 4) Intestinal colonization of child or adult caused by colonization of the gastrointestinal tract by Clostridium botulinum or C. baratii after surgery or illness that may predispose for enteric colonization (Shapiro, Hathaway, and Swerdlow, 1998), and 5) classification undetermined include cases on persons greater than 12 months of age in whom no food or wound source of Clostridium botulinum can be implicated (Winn, et al., 2006). Other disease forms are unintentional or
iatrogenic acquired following toxin injection for therapeutic or cosmetic purposes and intentional as the result of an act of terrorism either by aerosolization through absorption through mucous membranes or broken skin or distributed on food items (CDC, 2010).

**Clinical Aspects of Disease**

Rapid and accurate clinical assessment of the case to diagnose botulism is essential to manage the disease. Case history must be carefully collected to make sure botulism is not misdiagnosed. According to LAC-DPH (2012) a high index of suspicion is required to make an accurate diagnosis based mainly on epidemiological evidence of potential exposure. It is imperative that the epidemiology investigator ask detailed questions as soon as possible before symptoms progress. Questions should encompass consumption of home- canned foods, knowledge of other persons with similar symptoms, recent travel to Alaska or consumption of fermented Native American fish, whale, seal or walrus, history of intravenous drug use such as cocaine or black tar heroin, and the presence of any abscess, infected wound or deep skin puncture (Alaska H&SS, 2013). Source of exposure would be lacking in the case of a bioterrorism attack. Botulism may be underdiagnosed since cases occur singly, and even in outbreaks the initial case may be missed and not diagnosed until after death when clusters of botulism are reported and investigated by public health practitioners (Shapiro, Hathaway, and Swerdlow, 1998).

The incubation period of botulism depends on the dose ingested if the route is consumption of contaminated food. Symptoms may take from 2 hours to 10 days to appear, but usually 12-72 hours (Winn, et al., 2006). The clinical symptoms are salient involving gastrointestinal, urinary, neurologic, and muscular systems. The person would complain of a combination of three of more of the following gastrointestinal, urinary, neurological, and muscular symptoms: nausea, vomit,
diarrhea, abdominal pain, urinary retention, dry mouth, blurry vision, double vision (diplopia),
dilated or unreactive pupils, hoarse voice (dysphonia), difficulty swallowing (dysphagia),
difficulty articulating words (dysarthria), dropping eyelids (ptosis), descending, symmetrical
skeletal muscle weakness, afebrile, with normal mental status even though communication may
be impaired (LAC-DPH, 2012).
Based primarily on clinical presentation initial diagnosis of botulism is made. Initial
gastrointestinal manifestation of botulism is not enough to suspect botulism unless neurological
symptoms are observed. Progressive descending paralysis accompanied with muscle weakness,
fatigue, and gasping lead clinicians to suspect botulism. Differential diagnosis must be
performed to rule out presentation of other conditions such as stroke, diphtheria, mushroom
poisoning, gastroenteritis, tick paralysis, chemical intoxication, medication reaction, psychiatric
illness, Guillain-Barre syndrome, Myasthenia Gravis, paralytic shellfish poisoning, and
poliomyelitis (CDC, 20122 and Alaska H&SS, 2013). Once diagnosis of botulism is considered
authorization for specific confirmatory testing at the CDC or designated public health laboratory
is granted and the antitoxin is released upon consultation with public the health physician.
Laboratory confirmation of botulism diagnosis consists in detection of the BoNT in the serum
and/ or stool of the patient if foodborne botulism suspected. Serum sample must be collected
before antitoxin treatment is given to be able to demonstrate presence of the BoNT. The gold
standard assay for BoNT confirmation is the mouse neutralization bioassay which detects
functionally active BoNT in serum and sample extract present as little as 10 – 30 pg (LAC-DPH,
2012). Detection of the toxin depends on the amount of circulation toxin and time elapsed from
presentation of symptoms to testing. The assay is labor and time consuming and may take up to 4
days for results to be available (Winn, 2006). When Clostridium botulinum is recovered from
microbiological culture of stool or wound sample, real time PCR testing of Clostridia for the presence BoNT A, B, C, D, E, F, and G of the botulinum toxin gene is available at the CDC and designated state and local public health laboratories. Enzyme linked immuno-sorbert assays (ELISA) testing of the implicated food sample or environment matrix provides presumptive A, B, E, or F BoNT presence with sensitivity to < 10 pg, requires no animal testing, and results can be obtained within 5 hours (Shapiro, Hathaway, and Swerdlow, 1998 and Dassey & Bolivar, 2012). Evolving diagnostic testing only available at the CDC and very few public health and commercial laboratories include Matrix Assisted Laser Desorption/Ionization- Time of Flight (MALDI-TOF) mass spectrometry (MS) capable of detecting and differentiating botulinum toxins A, B, E, and F at concentrations starting from 5pg/ml in clinical, food, and environmental samples (Sobel, 2005 and Dassey & Bolivar, 2012).

Antitoxin administration is the only therapy available for botulism. Treatment is never dependent on results of specific botulism toxin tests. The only source of therapeutic antitoxin is CDC. The antitoxin is stocked for rapid release in locations around the country (Maslanka, 2004) including LAX and Alaska. The botulinum antitoxin currently used is an investigational heptavalent antitoxin to replace long term used licensed botulinum antitoxin AB and investigational botulinum antitoxin E (Sobel, 2005). The botulinum antitoxin is most effective when given early in the course of the illness. The antitoxin neutralizes only circulating toxin and does not reverse neurological symptoms, the slow muscular and motor recovery is due to regrowth of nerve endings. The circulating life of the antitoxin is 5-8 days, rarely a second dose is needed and 9% of patients have reported a hypersensitivity reaction (Shapiro, Hathaway, and Swerdlow, 1998). Administration of the antitoxin in a timely manner, providing supportive care, and intensive care support improvements have contributed to decrease in mortality rates to drop to approximately
6%. The most serious complication is respiratory failure due to respiratory muscles paralysis which is the most common cause of death (LAC-DPH, 2012).

**Epidemiology**

Humans are affected by five forms of clinical botulism which include food-borne botulism, wound botulism, infant intestinal colonization or infant botulism, adult intestinal colonization, and other or undetermined. Other botulism forms are unintentional or iatrogenic acquired following toxin injection for therapeutic or cosmetic purposes and exposure as a result of an intentional act of terrorism either by aerosolization through absorption through mucous membranes or broken skin or distributed on food items (Sobel, 2005). From 2001 to 2011 in the United States 1,548 confirmed cases of botulinum were reported to the National Enteric Disease Surveillance System (CDC, 2012). A comparison on the reported cases from the year 2001 and a decade later, the year 2011 shows an overall decrease in the number of cases reported. In 2001 a total of 169 cases of intoxication with BoNT were reported to CDC compared to a total of 140 confirmed total cases reported in 2011. In 2001 the total number of foodborne cases was 33; the three top states with most number of foodborne cases reported in 2001 were Texas (16) followed by Alaska (9), and California (4). In 2011 only 20 foodborne cases were reported; Utah 8 cases, Alaska 5 cases, and 1 case each in California, Arizona, Georgia, New York City, Ohio, Oklahoma, and Oregon. In 2001 the median age was 46 years, while in 2011 the median age was 42 years. Toxin A accounted for most of the cases (CDC, 2012).

The following epidemic curves illustrate botulism cases in the USA 2006-2010 (Figure 1), botulism cases in the USA & CA and deaths (Figure 2), 2006-2010, and botulinum cases
(excluding infant botulism) by toxin type and route in Los Angeles County 2000-2012 (Figure 3) (Dassey & Bolivar, 2012).

Botulism Cases in the USA 2006-2010

Figure 1

Botulism Cases in the USA & CA and Deaths

Figure 2

Botulinum Cases by Toxin Type and Route in Los Angeles County 2000-2012

Figure 3
Foodborne botulism case definition is defined as 1) probable: clinically compatible case with epidemiological link such as ingestion of home-canned food within previous 48 hours and 2) confirmed: clinically compatible case that is laboratory confirmed or that occurs among persons who ate the same food as persons who have laboratory-confirmed botulism (Dassey & Bolivar, 2012). The laboratory criteria for diagnosis is detection of botulinum toxin in serum, stool, or patient’s food, or isolation of *Clostridium botulinum* from stool. Incubation is dependent on quantity and rate of absorption of BoNT which can be as early as 2-8 hours after a meal consumption, typical incubation is 12-72 hours when gastrointestinal symptoms occur. Mild cases of foodborne botulism may not be detected. Foodborne vehicles most common implicated are homemade or processed foods: low acid with a pH > 4.6 (Sobel, 2005). Many types of food have been associated with outbreaks of foodborne botulism; the most commonly implicated foods in the United States are vegetables. Documented cases and outbreaks have been caused by baked potatoes in foil left at room temperature, garlic in oil, sautéed onions in butter sauce, pot pie, and canned chili. In Alaska, traditional preparation methods for fish, whale and seal regularly cause outbreaks, usually due to type E toxin. Outbreaks associated with commercial products have been rare, most recently Castleberry canned chili in 2007. There was just reported in November 2012 a major outbreak in an Arizona prison attributed to “pruno” (Maslanka, 2004). A botulism case from drinking prison made illicit alcohol in Utah affected 12 inmates. Pruno is made of fruit, sugar, and water with addition sometimes of vegetables. Depending of the availability of foods in prison vegetable roots are added. In this case a leftover baked potato added to the fermenting pruno was the suspected the source of incriminated *Clostridium botulinum* spores vehicle that contaminated the drink (MMWR, 2012).
Approximately 25% of all the cases of botulism reported annually in the US are foodborne botulism with men and women affected equally. Geographic distribution include mainly five states California, Washington, Colorado, Oregon, and Alaska where more than half of all outbreaks occur since 1950 (CDC, 2006). Alaska Native population have a distinctive public health problem associated with native fermented foods which has been addressed with the development of culturally appropriate educational materials to include safer food preparation, avoidance of fermentation in plastic or glass containers, traditional fermentation processes, boiling native foods, hand-washing, and discarding of suspicious foods (Maslanka, 2004).

Among Alaska Natives the average incidence of foodborne botulism is 10.7 cases per 100,000 population which indicate an increase in the number of cases when compared to 3.5 cases per 100,000 population during 1950-1954 due most likely to recognition of cases (Alaska H&SS, 2013). The intoxication is not common in children, the mean average in age is 43 years. The most frequent type of botulinum toxin in Alaska is type E accounting for 82% of the outbreaks and responsible for 79% of the cases and 84% of the deaths. Outbreaks occur mainly from June to September (Alaska H&SS, 2013). The Alaska environment especially the beach soil has shown to contain moderate amounts of Clostridium botulinum spores. Alaska salmon have been found to be intrinsically contaminated with type E Clostridium botulinum spores. In a past studies conducted about 1% of salmon varieties; pink, chum, chinok, and sockeye from Southeastern Alaska, Bristol Bay, the Yukon River, and Kodiak the salmon gills were found to have BoNT type E toxin. Samples from various sites from beach soil, marine mammals, ocean water and sediments were also found to be contaminated with the same botulinum type toxin (Alaska H&SS, 2013). Most of the rest of the states in the United States approximately half of the cases are caused by BoNT type A, with the rest of the cases involving BoNT type E and BoNT type B divided in almost equal numbers (CDC, 2011).
Alaska Native foods, home-canned foods, and restaurant associated outbreaks remain the main cause of foodborne outbreaks in the United States. Outbreak reporting of suspected botulism cases must be reported immediately to the local or state public health department without laboratory confirmation to avoid consumption of toxin contaminated food and numbers of persons exposed to the BoNT. Medical epidemiologist at the CDC and in all state public health departments provide consultation and advice 24 hours a day regarding questions on diagnosis, specimen collection and treatment (LAC-DPH, 2012 and Alaska H&SS, 2013). Steps in a botulism outbreak investigation would consist of: 1) physician or health care provider suspecting a case reports to the public health department, 2) Clinical presentation is discussed and if suspicion is confirmed an investigation is started as soon as possible, 3) The investigating epidemiologist contacts or visits the patient to determine possible sources of exposure, 4) the extent of the outbreak is determined based on questions of suspected food consumption and symptoms, 5) Evaluation of similar cases are evaluated at health care facilities in the area of initial suspected case and asymptomatic exposed individuals are advise to seek immediate medical care if symptoms develop, 6) Recommendation are made by the epidemiologist no consumption of implicated food item (s) pending on laboratory confirmatory findings, 7) Food and clinical samples are collected from the affected cases and shipped to the designated health public health testing laboratory, and 8) laboratory results are disseminated to remove any implicated food (Alaska H&SS, 2013).

Upon diagnosis of botulism the patient is injected with a vial of concentrated heptavalent antitoxin containing more than 100 fold greater that needed for treating the highest level of circulating botulinum neurotoxin ever detected at the CDC (Alaska H&SS, 2013). Patient’s neurological and muscular systems deterioration may continue in about a third of the diagnosed
cases, therefore, close monitoring must be provided after treatment. Completely paralyzed patients are fully aware and recall after recovery of the events that took place. Recovery of respiratory functions is experienced by most cases rather rapidly with complete resolution of muscular strength within one to two months (LAC-DPH, 2012).

The following epidemic curves illustrate the foodborne botulism cases in the U.S.A. for the period 2006-2016 (Figure 4), foodborne botulism cases in the U.S.A and California cases for the same time period (Figure 5), foodborne botulism cases in the U.S.A and California and type A cases during the period 2006-2010 (Figure 6), and foodborne and unknown botulism cases by toxin type in Los Angeles County for the period 2000-2012 (Figure 7) obtained from epidemiological available data at the CDC and at the Los Angeles Public Department of Public Health Acute Communicable Disease and Control Section of Epidemiology. (Dassey & Bolivar, 2012).

Botulism Cases in the U.S.A. 2006-2016

![Figure 4](path/to/image1.png)

Foodborne Botulism Cases in the U.S.A and California 2006-2010

![Figure 5](path/to/image2.png)
Figure 5

Foodborne Botulism Cases in the U.S.A and California and Type A Cases, 2006-2010

Figure 6

Foodborne and Unknown Botulism Cases by Toxin Type in Los Angeles County 2000-2012

Figure 7

According to the data captured on the epi curves, an increased number of cases were reported in the United States and CA in 2007. In the Los Angeles County the numbers of botulism cases
increased last year (2012) having the highest number of cases reported over a decade. BoNT type A has caused all of the reported cases since 2001.

According to the CDC (2006) an average of 30 to 40 cases of wound botulism is reported annually in the U.S.A with infected patient median age 41 years with a range of 23-58 years, gender 77% males and 23% females. In 2011 out of 140 confirmed cases of botulism 13 cases were reported from California 9 cases, Washington 2 cases, Colorado 1 case, and Texas 1 case also. BoNT type A accounted for 100% of the cases. Use of illicit drugs is the vehicle of transmission associated mainly with needle puncture. 11 of the 13 cases were associated with black-tar heroin injection drug use, one case occurred through a wound sustained in a motorcycle accident and one was associated with a face wound caused by an accidental skin puncture by bark. The median incubation period in trauma cases was 7 days with a range of 4 to 21 days (CDC, 2012).

In a study conducted by Yuan et al (2011) during 1993 and 2006 there were 25 laboratory confirmed cases of recurrent wound botulism of which 94% were male from ages ranging 32 to 61 years old. Wound botulism most common presentation include the presence of a wound with symptoms of double vision, speech, respiratory, and swallowing difficulty. In wound botulism there is no gastrointestinal involvement. The BoNT involved in wound botulism are type A in 80% and type B in 20% of the cases (LAC-DPH). As more cases of wound botulism have become epidemic in California among injection drug users recurring case are bound to happen which must alert physicians to timely diagnose and quickly provide antitoxin administration and supportive care. Wound botulism was first reported in 1951 mainly associated with contaminated post-surgery wounds and traumatic skin and tissue injury wounds. Wound botulism epidemics
among injection drug users have been reported since 1994 in California associated with “skin popping” black tar heroin used in the Western US. (Yuan, et al (2011).

Wound botulism case definition classification are 1) Confirmed: clinically compatible case that is laboratory confirmed in a patient who has no suspected exposure to contaminated food and who has a history of a fresh, contaminated wound during the 2 weeks before onset of symptoms, or a history of injection drug use within the 2 weeks before onset of symptoms and 2) Probable: a clinically compatible case in a patient who has no suspected exposure to contaminated food and who has either a history of fresh, contaminated wound during the 2 weeks before onset of symptoms, or a history of injection drug use within the 2 weeks before onset of symptoms (Dassey & Bolivar, 2012). Laboratory criteria for diagnosis of wound botulinum is the detection of BoNT in serum, or isolation of Clostridium botulinum from wound (LAC-DPH, 2012).

The two following epidemiologic curve and depict the incidence of wound botulism case in California from the time period 1951 to 1998 recent epidemic in heroin injectors and the cumulative wound botulism in injection drug users in the United States (Werner, et al., 2000).
Wound botulism (WB) cases in the U.S.A. from 2006 to 2010, WB cases in U.S.A. and California, WB cases in U.S.A. and California and percentage of Type A in the same time period, as well as WB cases by toxin type in Los Angeles County from 2000-2012 are illustrated in the epidemic curved in Figures 8 to 11 as follow:

Wound Botulism Cases, U.S.A. 2006-2010
Wound Botulism Cases in U.S.A. & California 2006-2010

Wound Botulism Cases in U.S.A & California and % of Type A Cases, 2006-2010

Wound Botulism Cases by toxin Type in Los Angeles County, 2000-2012
Infant botulism is the most common form of botulism reported in the United States is infant intestinal botulism. The BoNT involved in all cases of infant botulism are 50% type A and 50% type B (LAC-DPH, 2012). Infant botulism results from the consumption of Clostridium botulinum spores followed by subsequent intestinal colonization and toxin production which differs from foodborne botulism where the formed toxin is present in the contaminated food item (Alaska H&SS, 2013). Constipation of the baby is the first symptom, followed by muscular weakness, lethargy, poor feeding, floppy head where progression to more severe disease if not treated. According to CDC (2006) the incidence of infant botulism is an average of 110 cases reported annually in the US constituting 70% of all botulism cases. In 2011 there were 102 reported confirmed cases of infant botulism from 27 states. 40% (41) of the cases were attributed to BoNT type A, 59% (60) to BoNT type B, and 1% was caused by BoNT type Ba. The median age was 17 weeks of age with a range of 2-50 weeks. Males constituted 55% of the cases and no deaths were reported (CDC, 2012).

In 1976 infant botulism was recognized being now the most reported from of botulism since 1980. The disease is sporadic and presents no epidemic potential. Infant botulism hospitalized infants are mostly of higher birth weight, from older Caucasian mothers with higher education levels who breastfeed, with history of normal delivery and no congenital abnormalities (CDC, 2006). Distribution of documented cluster have occurred in the Eastern U.S.A. and in the West rural and small towns. The vehicle of transmission is still unclear with majority of the cases associated with corn syrup and honey. *Clostridium botulinum* spores in the environment such as soil, construction in the vicinity, dust, and windy areas may also be causes of intestinal colonization (CDC, 2006). *Clostridium botulinum* toxin presence demonstrated in the stool
supported by stool culture positive for the organism is diagnostic of infant botulism. The BoNT is usually not found in the infant’s serum (Alaska H&SS, 2013).

Infant botulism is treated with BabyBIG®, Botulism Immune Globulin Intravenous (Human) (BIG-IV), 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 from the California Department of Public Health, Infant Botulism Treatment and Prevention Program, http://www.infantbotulism.org/ at 510-231-7600 (LAC-DPH, 2012). The following epidemic curve illustrates the confirmed infant botulism cases in the U.S.A. and California for the period 2006-2010 (Dassey & Bolivar, 2012).

Infant Botulism Cases in the U.S.A. & CA, 2006-2010

Botulism other or undetermined cause, case definition classification is confirmed; a clinically compatible case that is laboratory-confirmed in a patient aged greater than or equal to 1 year who has no history of ingestion of suspect food and has no wounds. The laboratory criteria for diagnosis consist of detection of botulism toxin in clinical specimen, or isolation of Clostridium botulinum from clinical specimen (LAC-DPH, 2012). According to CDC (2012) botulism surveillance summary report in the year 2011 out of a total 140 cases 5 cases of unknown etiology were reported from 3 cases from California, one case from Arizona, and one case from
New York. All 5 cases were confirmed BoNT type A of which two deaths were reported, median age 74 years with a range of 27-79 in which 3 cases or 60% were male.

Iatrogenic botulism is one example a non-foodborne, non-wound type of disease. Purified botulinum toxin has been historically used to treat various medical conditions strabismus, cervical dystonia, torticollis, blepharospasm, and achalasia. Therapeutic dose use in medical treatment do not cause botulism, but it is estimated from documented cases that the patient use at least 10 times the recommended dose (Shapiro, Hathaway, and Swerdlow, 1998). Botulism toxins have proven effect in treating several neuromuscular conditions which opens the door to accidents and misuse such as intravenous injection leading to systemic toxicity. For example, some clinicians are unaware that Botox – using type A toxin, is not bioequivalent to Myobloc, which uses type B toxin. This has led to overdosing when switching from one product to the other in patients who are being treated over the long term and develop antibodies against one or the other toxin if the dosage is not adjusted properly (Wenhaum, 2008). Illegal use of botulinum toxin by unlicensed and unscrupulous persons caused serious consequences in Florida several years ago when laboratory-grade toxin was injected, rather than adequately diluted toxin caused 4 cases of botulism (LAC-DPH, 2012 and Dassey, 2012).

Botulinum toxin is a possible weapon of bioterrorism. The threat of botulism toxin being used as a weapon of mass destruction is more than theoretical. Records show that significant research was conducted on this subject, including in the United States, which ceased all biological weapons research in 1970. The Japanese terrorist group Aum Shinrikyo cult attempted poisoning at least three times from 1950 to 1955 from Japanese soil collected in Northern Japan. The attacks failed probably due to poor microbiology skills, faulty and deficient aerosol generator, or internal group sabotage (Wenhaum, 2008). Presently it is believed that several
countries maintain stockpiles of botulism toxin for offensive purposes (Dassey & Bolivar, 2012). According to Shapiro, Hathaway, and Swerdlow (1998) countries have included BoNT in their offensive weapons program. Botulism toxin is relatively easy to produce and highly lethal in small quantities which makes it attractive to use to develop it as a bioweapon. During the Persian Gulf War in 1995 Iraq revealed to have prepared 11,200 liters of botulinum toxin and loaded into specially designed missile warheads. Features that suggest deliberate release of BoNT would be indicated by outbreak of a large number of cases of acute flaccid paralysis with prominent bulbar paralysis. Such outbreak would have certain unusual characteristics: an unusual botulinum toxin type C, D, F, G, or type E not acquired from an aquatic food, a common geographic factor such airport or work location, but without a common dietary exposure, and may present multiple simultaneous outbreaks with no common source (CDC, 2011).

Botulism caused by a bioterrorism attack either by aerosolized exposure or the enteric route by food or water contamination would entail treatment of the victims with supportive care and rapid provision of mechanical ventilators. First responders may have to manually intubation and ventilation. Since the only pharmacological treatment is administration of the antitoxin stockpiles will have to be quickly mobilized to the affected area in order to reduce mortality rate. Without antitoxin administration within 24 to 48 hours after exposure of inhalation the toxin is very lethal even if adequate ventilation is provided. The botulinum toxoid vaccine is available for high risk groups such as laboratory staff handling the toxin regularly that work with botulism specimens and military personnel. The vaccine does not elicit life-long immunity and in order to provide effective protection must be administered months before exposure (CDC, 2011).
Prevention and Control

According to CDC (2010) many cases of botulism in the United States are preventable. In foodborne botulism good practices in food preparation and preservation, hygiene, and proper hand-washing are essential in order to achieve inactivation of the bacterial spores and reduce the risk of contamination. Recommended instructions provided by the US Department of Agriculture on safe home canning include the use of pressure cookers and canners. Consumers of home-canned food are advised to boil the food for at least ten minutes before eating it to assure destruction of any BoNT present. Reducing food contamination of Clostridium botulinum spores and prevention of toxin production in canned foods are two strategies to control food borne botulism as is the early recognition and identification of botulism cases. Educating food and canned foods preparers on properly food handling and preservation as well as health care providers to recognize and report promptly have shown effectiveness in limiting the adverse effects of botulism intoxication (Heymann, 2004). In Alaska education efforts on careful food consumption, and medical follow up with rapid epidemiological investigation of suspicious illness with gastrointestinal and neurological symptoms have produced good results. Cases are rapidly identified, provided with supportive care and administration of BoNT antitoxin which is available in both rural and urban hospitals (Alaska H&SS, 2013).

Wound botulism prevention include seeking medical care promptly after noticing an infected wound and no use of injectable street drugs. Infant botulism in the majority of the cases are not preventable since Clostridium botulinum spores are found in the dust and soil, therefore, spores may be present on the environment, air, carpets, floor, and even on the surfaces of countertops after cleaning. Children under twelve months should not eat honey or any foods that may contain
honey or corn syrup (CDC, 2010). Proper hand-wash can never be overstated especially after handling soiled diapers.

Control of patient, contacts, and the immediate environment recommended by Heymann, D. (2004) include: Immediate reporting to local authorities by phone, hand washing after handling soiled materials, concurrent disinfection by boiling implicated food before discarding or breaking the container and burying it in the soil to prevent animal exposure, removing any remaining toxin by boiling or heat sterilization of contaminated utensils or bleach disinfection, and sanitary disposal of diapers. There are no control measures for simple direct contact. Purging with cathartics, gastric lavage and enemas should be performed on those persons who have eaten the implicated food as well as close medical monitoring.

Contact with affected persons since person to person botulism transmission does not happen pose no risk. Epidemic measures are basically keeping eyes and ears open to single suspicious cases as possible root of an outbreak involving a family, restaurant, or commercial product linked to a common food (Heymann, 2004). Any confirmed BoNT contaminated food item calls for immediate recall, search of people potentially exposed, and removal of any remaining incriminated food. Commercial products distributed nationally and internationally may require multiple agencies combined efforts to recover the food items and laboratory tested (Heymann, 2004). Measures in the case of a deliberate use of BoNT entails suspicion of even a single case with no history of improperly preserved food, rapid investigation, proper reporting, and quick intervention treatment by administration of the heptavalent BoNT antitoxin. Strong surveillance and an effective bioterrorism response and preparedness plan in place are the most efficient ways to counteract a potential attack via air, water, or food supply towards both humans and animals.
Summary

Botulism, derived from the word “botulus” meaning sausage, is a life threatening paralytic disease caused by a neurotoxin produced in the majority of reported confirmed cases by *Clostridium botulinum* and to a lesser extent by *Clostridium butyricum*, and *Clostridium baratii* bacteria. The organism spores are ubiquitously found in soil. There are seven botulinum neurotoxins BoNT; A, B, C, D, E, F, and G, described as the most poisonous substances known to humankind. BoNT causes illness via irreversible blockade of the chemical acetylcholine released at the nerve endings leading to acute descending flaccid paralysis that may lead to death, typically due to respiratory failure, if not diagnosed in time. Botulism spores may be present on a variety of foods including in prepackaged foods and root of vegetables. If foods are not properly prepared hygienically, sterilized during canning, heated above boiling, or pressure cooked under certain environmental conditions such as anaerobic, low salt and sugar content, low acidity, and unrefrigerated, these spores can germinate, leading to bacterial growth and production of BoNT. Botulism cases reported annually average 110 cases of which 25% are foodborne botulism, 70% are infant botulism, between 30% and 40% is wound botulism, and 1% adult intestinal colonization botulism. West of the Mississippi river BoNT type A botulism is most common, while BoNT type B botulism is most common in the states East of the Mississippi river, and BoNT type E botulism outbreaks occurs in Alaska associated with preserved salmon and other ocean preserved fish products. Prompt recognition of botulism by well-trained health care clinicians and rapid communication with public health practitioners is essential to expedite release of the antitoxins from CDC stations, initiate investigation by epidemiologists, and prevent additional cases from occurring. Due to botulism lethal human dose of only 100-1,000 ng it is also a potential weapon of bioterrorism.
References


Los Angeles County Department of Public Health (2012). Terrorism Agent Information and Treatment Guidelines for Clinicians and Hospitals: Botulism.


