Botulism Foodborne Disease: A Review

Vinayak M Gaware¹, Kiran B Kotade², Ramdas T Dolas³, Kiran B Dhamak¹, Sachin B Somawanshi³ and Vikrant K Nikam³

¹Department of Pharmaceutical Chemistry, College of Pharmacy Chincholi, Sinnar, Nashik, M.S(India)
²Department of Pharmacology, College of Pharmacy Chincholi, Sinnar, Nashik, M.S(India)
³Department of Pharmaceutics, College of Pharmacy Chincholi, Sinnar, Nashik, M.S(India)

ABSTRACT
Botulism is a lethal disease also known as botulinus intoxication is a rare but serious paralytic illness caused by botulinum toxin, which is produced by the bacterium Clostridium botulinum under anaerobic conditions. The toxin enters the body in one of four ways: by colonization of the digestive tract by the bacterium in children or adults, by ingestion of toxin from foods or by contamination of a wound by the bacterium and leads to paralysis that typically starts with the muscles of the face and then spreads towards the limbs. In severe forms, it leads to paralysis of the breathing muscles and causes respiratory failure. In view of this life-threatening complication, all suspected cases of botulism are treated as medical emergencies and public health officials are usually involved to prevent further cases from the same source. In the present review knowledge of botulism, its epidemiology, mechanism of disease, its signs and symptoms, types, clinical features, diagnosis, treatment and vaccination has been focused. This ailment occurs worldwide, afflicts human of all age groups from infants to elderly people. Botulism is a rare yet potentially common form of food poisoning that can be fatal.

Keywords: Botox, Botulism, Clostridium botulinum, Paralysis.

INTRODUCTION

Botulism (Latin, botulus, "sausage") also known as botulinus intoxication is a rare but serious paralytic illness caused by botulinum toxin, which is produced by the bacterium Clostridium botulinum under anaerobic conditions. The toxin enters the body in one of four ways: by
colonization of the digestive tract by the bacterium in children (infant botulism) or adults (adult intestinal toxemia), by ingestion of toxin from foods (foodborne botulism) or by contamination of a wound by the bacterium (wound botulism). All forms lead to paralysis that typically starts with the muscles of the face and then spreads towards the limbs.[1] In severe forms, it leads to paralysis of the breathing muscles and causes respiratory failure. In view of this life-threatening complication, all suspected cases of botulism are treated as medical emergencies and public health officials are usually involved to prevent further cases from the same source.[2] Botulism can be prevented by killing the spores by cooking at 121 °C (250 °F) for 3 minutes or providing conditions that prevent the spores from growing. Additional precautions for infants include not feeding them honey [3].

History
Although laboratory confirmation is necessary for a definitive diagnosis, clinical presentation, patient history and physical examination (particularly neurologic exam) can be used as strong indicators for the presence of botulism. Due to the delay in laboratory confirmation and the necessity of treatment prior to the binding of the toxin to neurons, antitoxin should be empirically begun in patients with highly suggestive presentations [4]. Place special attention on eliciting a complete patient history, including the following:

- History of foods eaten and any ill contacts that eat the same foods.
- History of intravenous drug abuse (especially "skin popping")
- Recent surgery or trauma
- Gastrointestinal problems or intestinal bypass surgery

Epidemiology
Between 1990 and 2000, the Centers for Disease Control reported 263 individual 'cases' from 160 foodborne botulism 'events' in the United States with a case-fatality rate of 4%. Thirty-nine percent (103 cases and 58 events) occurred in Alaska, all of which were attributable to traditional Alaska Native foods. In the lower 49 states, home-canned food was implicated in 70 (91%) events with Asparagus being the worst culprit. Two restaurant-associated outbreaks affected 25 persons. The median number of cases per year was 23 (range 17–43), the median number of events per year was 14 (range 9–24). The highest incidence rates occurred in Alaska, Idaho, Washington and Oregon. All other states had an incidence rate of 1 case per ten million people or less.[5] The number of cases of foodborne and infant botulism has changed little in recent years, but wound botulism has increased because of the use of black tar heroin, especially in California.[6]

Types of Botulism [7, 8, 9]
There are three main kinds of botulism, which are categorized by the way in which the disease is acquired:
- Food-borne botulism is caused by eating foods that contain the botulinum neurotoxin.
- Wound botulism is caused by neurotoxin produced from a wound that is infected with the bacteria Clostridium botulinum.
- Infant botulism occurs when an infant consumes the spores of the botulinum bacteria. The bacteria then grow in the intestines and release the neurotoxin.
Three other kinds of botulism have been described but are seen rarely. The first is adult intestinal colonization that is seen in older children and adults with abnormal bowels. Only rarely does intestinal infection with the *Clostridium botulinum* bacteria occur in adults. Typically, the adult form of this intestinal botulism is related to abdominal surgical procedures. The second kind (injection botulism) is seen in patients injected with inappropriately high amounts of therapeutic neurotoxin (for example, BOTOX, Dysport, Myobloc), while the third kind (inhalation botulism) has occurred in laboratory personnel who work with the neurotoxins. All six kinds of botulism are potentially fatal.

- In addition, strains of *C botulinum* have been classified into 4 groups based on their phenotypic characteristics and DNA homology.
  - Group I organisms are proteolytic and produce toxins A, B, or F.
  - Group II is nonproteolytic and can make toxins B, E, or F.
  - Group III organisms produce toxins C or D.
  - Group IV organisms, now identified as *Clostridium argentinense*, produce toxin type G, which has not been shown to cause neuroparalytic illness but has been associated with sudden death in Switzerland.

**Mode of Acquisition**

Four main modes of entry for the toxin are known. The most common form in Western countries is *infant botulism*. This occurs in small children who are colonized with the bacterium during the early stages of their life. The bacterium then releases the toxin into the intestine, which is absorbed into the bloodstream. While the consumption of honey during the first year of life has been identified as a risk factor for infant botulism, it is only a factor in a fifth of all cases.[10] The adult form of infant botulism is termed *adult intestinal toxemia* and is exceedingly rare.[11] Foodborne botulism results from contaminated foodstuffs in which *C. botulinum* spores have been allowed to germinate in anaerobic conditions. This typically occurs in home-canned food substances and fermented uncooked dishes. Given that multiple people often consume food from the same source, it is common for more than a single person to be affected simultaneously. It takes 3–5 days for the symptoms to become apparent. *Wound botulism* results from the contamination of a wound with the bacteria, which then secrete the toxin into the bloodstream. This has become more common in intravenous drug users since the 1990s, especially people using black tar heroin and those injecting heroin into the skin rather than the veins.[12] Isolated cases of botulism have been described after inhalation by laboratory workers and after cosmetic use of inappropriate strengths of Botox.

**Aetiology** [13, 14]

- Disease caused mostly be type A, B and E exotoxin
- Spores are moderately resistant to heat (i.e. they withstand boiling for several hours
- Vast majority food-bourne. Outbreaks largely due to home-preserved vegetables (type A), meat (B) or fish (E)
- Other high risk foods include low acid fruit and condiments
- Wound botulism (rare) due to contamination of wound with soil containing type A or B organisms
- Chronic IV drug abusers at risk
Mechanism

_C. botulinum_ is an anaerobic, Gram positive, spore-forming rod. Botulin toxin is one of the most powerful known toxins: about one microgram is lethal to humans. It acts by blocking nerve function and leads to respiratory and musculoskeletal paralysis[15]. In all cases illness is caused by the toxin made by _C. botulinum_, not by the bacterium itself. The pattern of damage occurs because the toxin affects nerves that are firing more often. Specifically, the toxin acts by blocking the production or release of acetylcholine at synapses and neuromuscular junctions. Death occurs due to respiratory failure [16].

Figure 1: Illustrates The Basis of The Potency of Botulinum Toxin

The Toxin Is A Zinc Proteinase That Cleaves 1 or More of The Fusion Proteins By Which Neuronal Vesicles Release Acetylcholine Into The Neuromuscular Junction.
Pathophysiology [17, 18]
- Exotoxin absorbed in gut and carried to cholinergic nerves at NMJ, post ganglionic nerve endings and autonomic ganglia to which it binds irreversibly
- Toxin enters nerve endings and interferes with ACh release

Clinical Features [19, 20, 21]
- Usually 3 day incubation after ingestion of toxin. Range 12h-16 days
- GI symptoms (food-borne botulism only): nausea, vomiting, abdo pain, diarrhoea or constipation
- Ocular symptoms: blurred vision, mydriasis, diplopia, ptosis
- Dry mouth
- Dysphasia
- Impaired gag, facial and tongue weakness
- Generalized weakness. Progresses in a symmetrical descending fashion. Reflexes normal/decreased
- Severe cases: respiratory insufficiency and flaccid weakness of limbs

Laboratory Studies [22, 23, 24]
Laboratory confirmation
- Before treatment with antitoxin, obtain 10-15 mL of serum, 25-50 g of feces and possibly 25-50 mL of fluid from gastric aspiration. Collect and refrigerate similar quantities of suspected food samples for testing. In constipated patients, a gentle saline enema may be required to obtain fecal specimens.
- Label each specimen container with the patient's name, specimen type, date of collection and medications being received and send it to a state health department-approved reference laboratory in insulated cold packs. Contact your local health department for specific instructions.
- Confirmation of the organism and/or toxin and toxin typing is obtained in almost 75% of cases. Early cases are more likely to be diagnosed by toxin assay, whereas later ones are more likely to have a positive culture. Laboratory confirmation of toxin presence is via a mouse bioassay and identification of the toxin type is performed by a mouse toxin neutralization test.

Food-borne botulism
- For food-borne botulism, toxin is found in serum samples 39% of the time and in stools 24% of the time.
- Organisms are found in cultures of stool samples 55% of the time.
- Stool cultures generally are more sensitive than toxin detection for specimens obtained later (>3 d post ingestion) in the course of illness.

Infant botulism
- In patients whom infant botulism is suspected, stools and enema fluids (with minimal water added to limit dilution of toxin) are the specimens of choice, as serum is only rarely toxin positive.
- One also may wish to culture possible sources of clostridia, such as honey or house dust.
Wound botulism
- Wound botulism may be identified by detection of toxin in serum or by culture of wound specimens.

Adult colonization botulism
- Organisms may be detected in stool and toxin in serum for up to 119 days following the onset of symptoms.

New methods of detection
- In vitro methods of detection, including polymerase chain reaction-based detection of clostridial genes and ELISA identification of toxin, but these methods are not widely available outside of research institutions.

Signs and Symptoms
The classic symptoms of botulism include double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth and muscle weakness. Constipation may occur. The doctor’s examination may reveal that the gag reflex and the deep tendon reflexes like the knee-jerk reflex are decreased or absent [25]. Infants with botulism appear lethargic, weak and floppy, feed poorly, become constipated and have a weak cry and poor muscle tone. In infants, constipation is often the first symptom to occur. These are all symptoms of the muscle paralysis that is caused by the bacterial neurotoxin. If untreated, these symptoms may progress to cause paralysis in various parts of the body, often seen as a descending paralysis of the arms, legs, trunk and breathing muscles [26].

Investigations [27, 28]
- Detection of toxin in patient or food
- CSF normal apart from mild elevation of CSF protein in a few cases
- Edrophonium test -ve although transient less impressive responses may be seen in botulism patients
- ECG: may be minor conduction disturbances and non-specific T wave and ST changes
- Nerve conduction normal
- EMG: presynaptic block in affected muscles in only 1/3
- Detection of Cl botulinum in stool considered confirmatory

Complications
Infant botulism has no long-term side effects, but can be complicated by nosocomial adverse events. The case fatality rate is less than 1% for hospitalized infants with botulism. Botulism can result in death due to respiratory failure. However, in the past 50 years, the proportion of patients with botulism who die has fallen from about 50% to 8% due to improved supportive care. A patient with severe botulism may require a breathing machine as well as intensive medical and nursing care for several months. Patients who survive an episode of botulism poisoning may have fatigue and shortness of breath for years and long-term therapy may be needed to aid their recovery [28].

Prevention
Food-borne botulism has often come from improperly prepared home-canned foods such as asparagus, green beans, beets and corn. However, there have been outbreaks of botulism from more unusual sources such as chopped garlic in oil, agave nectar, chili peppers, broccoli,
tomatoes, tomato sauce, improperly handled baked potatoes wrapped in aluminum foil and home-canned or fermented fish. People who do home canning should follow strict hygienic procedures to prevent or kill *Clostridium* bacteria, their spores and neutralize its neurotoxin [29]. Oils that are infused with garlic or herbs should be refrigerated. Potatoes that have been baked while wrapped in aluminum foil should be kept hot until served or refrigerated. Bacon should be cooked well since bacon preservatives (salts), which inhibit clostridial spores, have been reduced to have less salt. Because botulism neurotoxin is destroyed by high temperatures (85 degrees C for five minutes), people who eat home-canned foods should consider boiling the food for 10 minutes before eating it to help ensure that the food is safe to consume. Bulging cans or abnormal-smelling preserved foods should be discarded. Do not taste-test them or attempt to boil the food. Because honey can contain spores of *Clostridium botulinum* and this has been a source of infection for infants, children less than 12 months old should not be fed honey. Honey is relatively safe for people 1 year of age and older. Wound botulism can be prevented by promptly seeking medical care for infected wounds or skin cuts and avoiding injectable street drugs [30].

Treatment

Most infant botulism patients require supportive care in a hospital setting. The only drug currently available to treat infant botulism is Botulism Immune Globulin Intravenous-Human (BIG-IV or BabyBIG). BabyBIG was developed by the Infant Botulism Treatment and Prevention Program at the California Department of Public Health [31]. The respiratory failure and paralysis that occur with severe botulism may require a patient to be on a ventilator for weeks, plus intensive medical and nursing care. After several weeks, the paralysis slowly improves. If diagnosed early, foodborne and wound botulism can be treated by inducing passive immunity with a horse-derived antitoxin, which blocks the action of toxin circulating in the blood.[11] This can prevent patients from worsening, but recovery still takes many weeks. Physicians may try to remove contaminated food still in the gut by inducing vomiting or by using enemas. Wounds should be treated, usually surgically, to remove the source of the toxin-producing bacteria [32]. Good supportive care in a hospital is the mainstay of therapy for all forms of botulism. Furthermore each case of food-borne botulism is a potential public health emergency in that it is necessary to identify the source of the outbreak and ensure that all persons who have been exposed to the toxin have been identified and that no contaminated food remains [33]. There are two primary Botulinum Antitoxins available for treatment of wound and foodborne botulism. Trivalent (A,B,E) Botulinum Antitoxin is derived from equine sources utilizing whole antibodies (Fab & Fc portions). This antitoxin is available from the local health department via the CDC. The second antitoxin is heptavalent (A,B,C,D,E,F,G) Botulinum Antitoxin which is derived from "despeciated" equine IgG antibodies which have had the Fc portion cleaved off leaving the F(ab')2 portions. This is a less immunogenic antitoxin that is effective against all known strains of botulism where not contraindicated. [34]

Vaccination

Vaccine development for the major human types of botulism neurotoxin is currently being investigated, but there is no vaccine commercially available or approved for public use by the FDA. However, in the United States, an investigational pentavalent (against neurotoxins A, B, C, D and E) botulinum toxoid vaccine can be distributed by the CDC for laboratory workers at high risk of exposure to botulinum toxin and by the military for protection of troops against attack. Unfortunately, it takes several months to induce immunity. In 2009, a new research finding with
molecules that mimic botulism toxin binding sites may provide another method to block toxin from binding to nerve tissues, but this approach is only in the research phase of development. The herb milk thistle has been suggested by alternative medicine proponents (mainly in Europe) to treat food poisoning (especially mushroom poisoning) and to help detoxify the liver. There is no good data on its use in preventing or treating botulism [35].

CONCLUSION

Botulism, although rare, can present in multiple forms. The history and physical examination are essential to making the diagnosis. The signs and symptoms usually include constipation, weakness, hypotonia, cranial nerve abnormalities, and often respiratory depression. Loss of airway control or respiratory failure from diaphragmatic weakness is insidious. Treatment is supportive. Hospitalizations are often prolonged, but regardless of the severity of disease, the outcome is usually complete recovery. Botulism a food borne disease is still a very rare condition, yet when it does occur; it requires a full range of potential public health emergency.

REFERENCES


