BOTULISM: ETIOLOGY, CLINICAL PRESENTATION, TREATMENT, AND PREVENTION

Turdiyev Tuymurod O'tkir o'g'li
Email:turdiyevtuymurod92@gmail.com
https://orcid.org/0009-0003-5191-7927
Bukhara State Medical Institute
named after Abu Ali Ibn Sino, Uzbekistan,
Bukhara city. A.Navoiy street 1
Tel:+998(65) 223-00-50 e-mail: mail.bsmi.uz

Botulism is a severe disease that leads to flaccid paralysis, caused by the botulinum neurotoxin, commonly known as botulinum toxin. This toxin is produced by anaerobic bacteria of the Clostridium genus, primarily Clostridium botulinum, and in rare cases, C. butyricum and C. baratii. There are seven serotypes of botulinum toxin (A–G), but the most pathogenic for humans are types A, B, and E, with type F being involved in rare cases. Other serotypes predominantly affect animals and birds, also causing flaccid paralysis. Most Clostridium strains synthesize only one type of neurotoxin. Despite differences between serotypes (A, B, E, and F), their pathogenic mechanism of action in the human body remains identical. Botulism is not transmitted from person to person. Infection occurs through the consumption of contaminated food, and more rarely, through inhalation of the toxin or its entry into the body through other means. The disease may also develop when C. botulinum colonizes the intestine or infects wound surfaces, leading to local toxin production and subsequent systemic spread.

Historical Aspects, Toxicological Characteristics, and Medical Applications of Botulism

The first documented cases of botulism were recorded in 1735 and were associated with the consumption of contaminated German sausage, leading to acute food poisoning. In 1870, the German physician Müller proposed the term "botulism," derived from the Latin word for sausage (botulus). Clostridium bacteria were first identified in 1895, and their neurotoxin was isolated by Dr. Edward Schantz in 1944. Experiments conducted in 1949–1950 established that botulinum toxin type A (BoNT-A) blocks the release of acetylcholine at neuromuscular synapses, leading to impaired neuromuscular transmission. Botulinum toxins are among the most toxic substances known to humanity. Due to their high toxicity, they are considered potential biological weapons, yet they also have extensive medical applications. In 1980, Dr. Alan B. Scott first used botulinum toxin to treat strabismus (crossed eyes). In December 1989, the U.S. Food and Drug Administration (FDA) approved BoNT-A (marketed as "Botox") for the treatment of strabismus, blepharospasm, and

hemifacial spasm in children. In 2002, the FDA sanctioned its use in cosmetic dermatology for wrinkle correction and aesthetic enhancement. Over the following years, the scope of botulinum toxin applications expanded to include the treatment of hyperhidrosis (excessive sweating) and various neurological disorders. Clinical cases of botulism continue to be recorded in the 21st century. In 2017, at least ten patients were hospitalized with botulism after consuming contaminated nacho cheese sauce purchased from a gas station near Sacramento, California, USA. Due to the resulting paralysis, the affected individuals required prolonged intensive care treatment lasting at least three weeks. This outbreak was associated with a suspected fatality.

Etiological Factors of Botulism

Botulism develops as a result of exposure to neurotoxins produced by bacteria of the Clostridium genus, primarily Clostridium botulinum, and, less commonly, C. butyricum and C. baratii. These neurotoxins inhibit the release of acetylcholine at presynaptic nerve terminals, leading to impaired neuromuscular transmission and the development of characteristic symptoms of the disease.

Risk Factors for Developing Botulism

The primary cause of botulism is the consumption of food containing Clostridium spores, vegetative bacterial forms, or botulinum toxin due to improper thermal processing or inadequate storage conditions. The main risk factors include:

- **Consumption of canned foods**, particularly homemade products such as meat, fish, and vegetable preserves (e.g., tomatoes, fish). If sterilization is insufficient, anaerobic storage conditions promote the growth of Clostridium botulinum and toxin production.
- **Honey consumption by infants**. Honey can contain C. botulinum spores, which, upon entering the gastrointestinal tract of infants under 12 months old, may lead to infant botulism. Due to this risk, the WHO and pediatric associations advise against giving honey to children under one year old.
- **Wound contamination**. If bacterial spores enter open wounds (e.g., through contact with soil or fecal contamination), the pathogen may multiply and produce botulinum toxin, causing wound botulism.
- **Intravenous drug use**. Individuals who use injectable drugs are at risk of wound botulism due to the use of non-sterile instruments and potential infection.
- **Laboratory exposure**. Individuals working with botulinum neurotoxins in laboratory settings face a risk of inhalational infection.

Classification of Botulism

Depending on the mechanism of infection, botulism is classified into three main forms:

1. **Foodborne botulism** – develops due to the consumption of food containing botulinum toxin. This is the most common form of the disease, associated with food poisoning.

2. **Wound botulism** – occurs when Clostridium botulinum infects open wounds, leading to in situ toxin production.

3. **Infant botulism** – results from the colonization of the intestines by C. botulinum in infants, leading to local neurotoxin production.

In addition to these classic forms, three rarer types of botulism are also recognized:

4. **Intestinal botulism in adults** – observed in patients with gut microbiota imbalances (e.g., due to surgery or prolonged antibiotic therapy), creating favorable conditions for C. botulinum colonization and toxin production.

5. **Injection botulism** – occurs in patients receiving excessive doses of botulinum toxins for cosmetic or therapeutic purposes (e.g., Botox, Dysport, Myobloc).

6. **Inhalational botulism** – found in individuals working in laboratories handling aerosolized forms of botulinum toxin.

All forms of botulism can lead to life-threatening respiratory failure and require urgent medical intervention.

Botulism: Severity and Toxicity of Botulinum Neurotoxin

Botulinum neurotoxin (BoNT) is one of the most potent and lethal biological agents known to modern science. The estimated lethal dose for humans is approximately 1 nanogram per kilogram of body weight, making it one of the most toxic substances in nature. Experts estimate that 1 gram of botulinum toxin could theoretically cause fatal outcomes in 1 million people. Due to its extreme toxicity and minimal effective dose, botulinum toxin is considered a potential biological weapon, posing a bioterrorism threat. It can be dispersed in aerosol form or used to deliberately contaminate food products and water sources. All forms of botulism—foodborne, wound, infant, intestinal, inhalational, and injection-related—pose an immediate threat to life and require urgent medical attention. Botulinum toxin is rapidly absorbed in the gastrointestinal tract, explaining the high risk of intoxication even from consuming small amounts of contaminated food. Symptoms can range from mild neurological disturbances to severe paralysis of respiratory muscles, which, if left untreated, leads to fatal outcomes.

Botulinum Neurotoxin: Mechanism of Action and Clinical Manifestations of Botulism

Effects of Botulinum Toxin on the Body

Botulinum neurotoxin (BoNT) exerts a paralytic effect on the nervous system by blocking the release of acetylcholine at synapses, leading to muscle contraction failure. Once the toxin enters nerve cells, it disrupts neuromuscular transmission, which is the primary cause of paralysis in botulism. If the damaged nerve endings are unable to regenerate lost axons and form new synaptic connections, paralysis may become irreversible. This explains why recovery from botulism is a prolonged

process. At the same time, this property of botulinum toxin makes it effective in cosmetic and therapeutic applications, providing long-lasting effects when used in medical treatments.

Characteristics of the Botulism Pathogen (Clostridium botulinum)

Clostridium botulinum is an anaerobic, spore-forming, Gram-positive rod-shaped bacterium that is widely found in the environment. It can exist in the form of spores, remaining inactive until it encounters favorable conditions for growth and toxin production (absence of oxygen, low acidity, optimal temperature, and humidity). There are seven known serotypes of botulinum toxin (A, B, C, D, E, F, G), but only serotypes A, B, E, and F are pathogenic to humans.

Prevalence of Botulism

Due to modern sterilization methods and improved food preservation technologies, the incidence of botulism has significantly decreased. Approximately 1,000 cases of botulism are reported worldwide each year, with the majority linked to the consumption of contaminated homemade canned foods.

In the United States, around 110 cases of botulism are recorded annually, distributed as follows:

- **25%** – foodborne botulism
- **72%** – infant botulism
- **3%** – wound botulism

Most outbreaks of foodborne botulism are associated with the consumption of contaminated canned products. In recent years, there has been a decline in the frequency of cases due to strict sanitary and hygiene regulations.

Clinical Manifestations of Botulism

Main Neurological Symptoms of Botulism:

- Diplopia (double vision)
- Blurred vision
- Ptosis (drooping eyelids)
- Dysarthria (speech impairment)
- Dysphagia (difficulty swallowing)
- Xerostomia (dry mouth)
- Muscle weakness progressing to flaccid paralysis

Additional Symptoms May Include:

- Dizziness
- Fatigue
- Constipation
- Abdominal discomfort or pain
- Nausea and vomiting
- Hypersalivation
- Urinary dysfunction

- Decreased or absent reflexes
- Progressive muscle weakness
- Paralysis of respiratory muscles

During a physical examination, a doctor may detect hyporeflexia or areflexia, which are key diagnostic criteria for botulism.

Characteristics of Infant Botulism

In infants, the disease manifests as lethargy, decreased muscle tone, weak sucking reflex, poor appetite, and constipation. Constipation is often the first clinical sign of infection. Botulism is a life-threatening condition, and without timely treatment, it can lead to generalized paralysis, including respiratory failure, making it one of the most severe bacterial infections.

Botulism: Incubation Period, Diagnosis, Treatment, Complications, and Prevention

Incubation Period of Botulism

In foodborne botulism, clinical symptoms typically develop within **18–36 hours** after consuming contaminated food. However, the latent period can vary between **6 hours and 10 days**, depending on the dose of the toxin and individual susceptibility.

Medical Specialists Involved in the Diagnosis and Treatment of Botulism

In addition to primary care physicians, the following specialists may be involved in the diagnosis and treatment of botulism:

- **Neurologists** (due to nervous system involvement)
- **Infectious disease specialists** (for differential diagnosis and specific therapy)
- **Pediatricians** (for infant botulism cases)

Diagnostic Methods for Botulism

The diagnosis of botulism is based on **medical history, clinical presentation, and laboratory methods**.

Clinical Examination

A clinical examination helps to suspect botulism; however, its symptoms may resemble **stroke, Guillain-Barré syndrome, myasthenia gravis,** and other neurological disorders. To rule out these conditions, additional tests are performed:

- **Neuroimaging (CT or MRI of the brain)** – to exclude stroke.
- **Cerebrospinal fluid analysis (lumbar puncture)** – to rule out inflammatory processes.
- **Electromyography (EMG)** – to detect characteristic neuromuscular transmission disorders.
- **Tensilon test (edrophonium test)** – to exclude myasthenia gravis.

Laboratory Diagnosis

The most specific diagnostic method is the **detection of botulinum toxin** in **blood, urine, gastric contents, or stool**.

A **biological test using laboratory animals ("mouse bioassay")** is used to confirm the presence of the toxin:

1. Blood or stool samples from the patient are injected into two laboratory mice.
2. One of the mice is pretreated with an antitoxin.
3. If botulinum toxin is present, the untreated mouse dies, while the one receiving the antitoxin survives.

This method helps differentiate botulism from other infections, such as **salmonellosis or Escherichia coli (E. coli) infections**.

Treatment of Botulism

Early diagnosis helps minimize the consequences of the disease through **specific anti-botulinum serum** and **supportive therapy**.

Antitoxin Therapy

- For **foodborne and wound botulism**, a **trivalent antitoxin** (against serotypes A, B, E) is administered.
- In military and emergency situations, a **heptavalent antitoxin** (against serotypes A, B, C, D, E, F, G) may be used.
- **The antitoxin neutralizes circulating toxin** but does not reverse existing neurological symptoms.

Toxin Elimination

- In **foodborne botulism**, **gastric lavage** and **enemas** are performed to remove undigested toxin.
- In **wound botulism**, **surgical debridement** of infected tissue may be necessary.
- **Antibiotics** (penicillin, metronidazole) are recommended **only for wound botulism**.

Supportive Therapy

- **Mechanical ventilation (MV)** may be required in severe cases due to respiratory muscle paralysis.
- **Intravenous fluid therapy** helps maintain electrolyte balance and hydration.

What Should Not Be Done?

- **Laxatives containing magnesium, citrate, or sulfates** should be avoided, as they enhance toxicity.
- **Antibiotics should not be used in foodborne botulism**, as bacterial destruction in the intestines can increase toxin release.

Complications of Botulism

The primary complication is **respiratory failure**, which can be fatal without timely medical intervention.

Mortality Rate

- Before the introduction of **antitoxin therapy**, mortality reached **50%**.

- Modern treatment methods have reduced the fatality rate to **3–5%**.
- **Full recovery** may take **several months to a year**, and some patients experience **chronic fatigue and shortness of breath**.

Prevention of Botulism

Foodborne Botulism

- Follow **sanitary guidelines** when home canning.
- Heat canned foods to **85°C for 5 minutes** before consumption to inactivate the toxin.
- Avoid **swollen cans** or foods with an **unpleasant odor**.

Infant Botulism

- **Do not give honey to infants under 1 year old**, as it may contain C. botulinum spores.

Wound Botulism

- Properly **clean and treat wounds** and seek medical attention if necessary.

References:

1. O‘zbekiston Milliy Ensiklopediyasi (Uzbek National Encyclopedia). Volume 1. Tashkent, 2000.
2. Shovakhobov Sh. "Fundamentals of Infectious Diseases and Epidemiology." Tashkent, 1997.
3. Shopulatov J. "Fundamentals of Veterinary Medicine." Tashkent, 1993.
4. Online Sources:
1. Botulism – Wikipedia (in Uzbek)
2. Botulism – Mymedic.uz
3. Botulism: A Deadly Danger – Sanepid.uz
4. About Botulism Disease – Sanepid Navoiy