وزارة الصحة
Ministry of Health

Comprehensive Botulism poisoning Management Protocol in acute care settings: Guidelines for Diagnosis, Treatment, and Supportive Care

Version 1.1 (April 28, 2024)

Disclaimer: this is a living guidance that is subjected to change as more evidence accumulates. It will be updated regularly and whenever needed. The guidance should be used to assist healthcare practitioners in the management of Botulism according to the best available and current evidence and it's not intended to replace clinical judgement but rather to complement it.

I. Background

Botulism is a rare but serious paralytic illness caused by a nerve toxin produced by the bacterium Clostridium botulinum. The disease can manifest in three main forms: food-borne, wound, and infant botulism. The rapid identification and treatment are critical to prevent respiratory failure and other severe complications.

II. Aim & Scope

- **To provide clinical practice guidelines** for managing patients with botulism in Critical care.
- **To standardize and optimize the use of antitoxins** and supportive treatments.
- **To maximize patient recovery** and minimize length of stay through effective management protocols.

III. Targeted Population

Patients diagnosed with or suspected to have botulism presenting with respiratory failure or neurological compromise requiring intensive care.

IV. Targeted End Users and Setup

- **End Users:** Critical care staff, emergency medicine staff, neurologists, and respiratory therapists, psychologist clinical pharmacist and physiotherapist.

- **Setup:** Critical care departments, emergency departments, and neurology units.

V. Conflict of Interest

None.

VI. Funding

None.

VII. Methodology

The protocol is based on the latest recommendations from the Centers for Disease Control and Prevention (CDC), expert opinions, and peer-reviewed literature, adapted to align with local resources and healthcare standards. The protocol was reviewed by adult critical care leaders in all MOH directorates and health clusters.

VIII. Clinical Types

- **Food-borne botulism**
  - caused by ingestion of preformed botulinum neurotoxin in food contaminated by *Clostridium botulinum.*
  - Home-canned, -preserved, or -fermented foods are a major source.
- **Infant (intestinal) botulism**
  - is caused by absorption of neurotoxin produced by bacteria colonizing the intestines of infants < 1 year old.
  - The lack of fully established normal bowel flora at this age is thought to permit colonization with *C. botulinum.*
  - About 20% of cases are associated with consuming raw honey
  - , which less commonly occurs in adults with anatomic or functional abnormalities of the intestinal tract.
- **Wound botulism**
  - caused by contamination of a wound with *C. botulinum* spores.

IX. Clinical Presentation

- **Food-borne Botulism:**
  Symptoms typically start 12 to 36 hours after toxin ingestion but can range from a few hours to two weeks. Early symptoms often include nausea, vomiting, abdominal pain, and diarrhoea, which may precede or accompany cranial nerve weakness or palsies and descending flaccid paralysis.
  Dry mouth, blurred vision, and diplopia are usually the earliest Neurological symptoms, followed by dysphonia, dysarthria, dysphagia, and peripheral muscle weakness. The paralysis usually progresses from the upper body muscles to the lower limbs and may advance to respiratory muscles, causing breathing difficulties and potentially respiratory failure.
  Intensivist should be vigilant before diagnosing brain death in these condition as Botulism can mimic brain death and locked in syndrome.
- **Wound Botulism:**
  Similar to food-borne botulism in its progression but differs in three key aspects: gastrointestinal symptoms are usually absent, the incubation period is more extended (around ten days), and about half of the cases exhibit fever and leukocytosis due to a secondary bacterial infection, unlike in
- **Infant Botulism:**
  Infants typically present with constipation and poor feeding. This presentation is followed by progressive hypotonia and weakness. Loss of deep tendon reflexes appears to occur more commonly in type B infection. Cranial nerve dysfunction is manifested by decreased gag and suck, diminished range of eye movement, pupillary paralysis, and ptosis. Autonomic signs include decreased tearing and salivation, fluctuating heart rate and blood pressure, and flushed skin.

X. Case Definition

Type	Case Definition	Criteria for suspected Case	Criteria for Confirmed Case
Food-borne	Clinically compatible syndrome **Common symptoms are:** diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.	Clinically compatible syndrome + epidemiologic link	Clinically compatible syndrome + any of: - Laboratory confirmation. - Case among others with confirmed botulism from the same foods. - Detection of botulinum neurotoxin in serum, stool, or patient's food. - Culture of Clostridium botulinum from stool.
Wound	Clinically compatible syndrome with a specific history	Clinically compatible syndrome + no contaminated food exposure + history of contaminated wound or injection drug use within two weeks of symptom onset	Clinically compatible syndrome that meets the epidemiologic criteria + one of the following - Detection of botulinum neurotoxin in serum - Culture of C. botulinum from wound
Infant	Clinically compatible syndrome in a child < 1 year old	Clinically compatible syndrome + detection of botulinum neurotoxin in serum or stool, or culture of C. botulinum from stool	

Clinical evidence of food-borne botulism includes blurred vision, dry mouth, difficulty swallowing and speaking, and descending symmetric paralysis that may progress rapidly.

Notification:

If the emergency department has not yet reported a suspected case of botulism, it should be reported immediately to public health authority or call 1937.

XI. Management:

1. **Admission:**

Patients displaying clinical signs, symptoms, or a history suggestive of botulism could be admitted to the hospital and closely monitored for any signs of worsening weakness and respiratory failure. Patient should be admitted to critical care if meeting the ICU admission criteria. https://www.moh.gov.sa/en/Ministry/MediaCenter/Publications/Documents/Adult-ICU-Triage-Admission-and-Discharge-Criteria.pdf

2. **Antidote:**

- **Heptavalent Botulinum antitoxin (BAT)** is the primary treatment for botulism and should be administered promptly once a clinical diagnosis is suspected. If there is a high clinical suspicion of botulism, antitoxin should be given immediately without waiting for diagnostic test results. Its effectiveness is likely diminished for those who have progressed to complete paralysis, especially if symptoms have been present for more than seven days.

- **There are two types** of antitoxin for botulism treatment:

  - **BAT (Botulism Antitoxin Heptavalent)** is suitable for all age groups, including infants, mainly when botulism is not caused by type A or B toxins. This is the antidote for food borne and wound botulism.
  - **BabyBIG®**: Derived from human plasma, this antitoxin is only used for treating only infants with botulism caused by types A and B toxins.

BAT (Botulism Antitoxin Heptavalent):

Timing:

Antitoxin (BAT) should be given as early as possible as soon as presumptive clinical diagnosis of botulism is made, and it should not be delayed until laboratory confirmation.

BAT should be administered even if the patient progresses to complete paralysis and requires ventilation as long as patient symptoms started less than 7 days ago.

Antitoxin (BAT) must not be given as a prophylaxis in patients without symptoms according to case definition.

Dosing:

- **Adults:**
- In Adults, administer 1 single-use vial diluted 1:10 in NS via IV infusion starting at rate of 0.5 mL/min; may double rate every 30 minutes, if tolerated; MAX infusion rate 2 mL/min; MAX dose, 1 vial. Do not administer a second dose as it is not beneficial, please contact public health authority if you believe a second dose is needed.

- **Pediatrics (1-17 years)**:
- (10 to 14 kg) Administer 20% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every

30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min

- (15 to 19 kg) Administer 30% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every 30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min
- (20 to 24 kg) Administer 40% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every 30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min
- (25 to 29 kg) Administer 50% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every 30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min
- (30 to 34 kg) Administer 60% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every 30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min
- (35 to 39 kg) Administer 65% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every 30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min
- (40 to 44 kg) Administer 70% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every 30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min
- (45 to 49 kg) Administer 75% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every 30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min
- (50 to 54 kg) Administer 80% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every 30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min
- (55 kg or greater) Administer 1 single-use vial diluted 1:10 in NS via IV infusion starting at rate of 0.5 mL/min; may double rate every 30 minutes, if tolerated; MAX infusion rate 2 mL/min; MAX dose, 1 vial

- **Infant botulism: Human Botulism Immune Globulin (BIG-IV, BabyBIG):** (Younger than 1 year) Administer 10% of 1 vial diluted 1:10 in NS via IV infusion starting at rate of 0.01 mL/kg/min; may increase rate by 0.01 mL/kg/min every 30 minutes if tolerated; MAX infusion rate 0.03 mL/kg/min or adult infusion rate of 2 mL/min

3. **Respiratory Support:**
    - **Monitoring for respiratory function** is crucial in patients with botulism due to the high risk of respiratory failure, the primary cause of death in these cases. Monitoring measures include respiratory rate, pulse oximetry, and blood gases. It is important to note that signs such as desaturation or labored breathing might only appear shortly before the respiratory collapse. Facial paralysis may mask signs of distress; therefore, clinicians must be vigilant as patients may not exhibit hypoxia until advanced stages of respiratory failure.
    - **Serial measurements** of Forced Vital Capacity (FVC) are essential. Patients with an **FVC of less than 20 ml/kg** may require respiratory support. Additionally, if available, repeated measurements of static inspiratory pressure (Pimax) can help predict imminent respiratory failure; a **Pimax less than 15-20% and/or those whose vital capacity falls below 30 percent of the predicted value** indicate a likely need for mechanical ventilation, (table1).
    - **Continuously monitor** oxygen saturation and carbon dioxide levels using pulse oximetry and capnography, respectively. If capnography is unavailable, perform arterial blood gas analysis every 4 hours initially.
    - **Pregnant patients** might be at increased risk for respiratory failure because of decreased functional residual lung capacity, diaphragmatic rise, increased oxygen consumption, and increased intra-abdominal pressure.

4. **Neurologic Monitoring:**
    - Frequency: Every 1 hour for the first 24 hours post-diagnosis, then every 2 hours for the next 24 hours, followed by a reassessment phase. Intensivists should be notified if patient develops any warning sign (table2).
    - Assessments: Conduct comprehensive neurological exams to assess muscle strength, reflexes, and sensory function. Special attention should be paid to changes or progression in neurological symptoms or signs (table2).
    - Electrophysiological Monitoring: Utilize electromyography (EMG) and nerve conduction studies to monitor the extent and progression of nerve involvement. These should be performed initially as a baseline and subsequently as needed.
    - Cranial Nerve Assessment: Specifically assess cranial nerves impacting swallowing, vision, and facial movements, which are commonly affected in botulism cases.

5. **Supportive measures:**
    - **Feeding:**
      Tube feeding can be utilized for nutritional support if there's no ileus or once the ileus has resolved. Oral feeding should be gradually reintroduced under specific conditions, including stable respiratory status without mechanical ventilation, verified swallowing safety through appropriate studies, and complete resolution of ileus.

    - **Medication to Avoid:**
      Certain medications can exacerbate symptoms of paralysis and should be used cautiously. These include antimicrobials and antibiotics, particularly aminoglycosides, magnesium, monoamine

oxidase inhibitors, calcium channel blockers, and neuromuscular blocking agents (contraindicated).

- **Psychosocial Support:**
  Patients with botulism are often cognitively intact but may struggle to communicate due to paralysis. Therefore, they may require additional psychosocial support and alternative methods of communication with caregivers. Intensivist and bedside nurse should communicate with the patient regularly even if they are in coma, intubated or has no motor activities.
- **Physiotherapy:**
  Early physiotherapy is encouraged in all patients if no contraindications.

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XII. References:

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Table 1 Predictors for respiratory failure.

Parameter	Significance	
Forced Vital Capacity (FVC)	<20 ml/kg	These parameters may show changes late, observe for clinical signs of distress, and consider intubation early.
Negative inspiratory force NIF	<-30	
Vital Capacity	>30% reduction from baseline	

Table 2 Warning signs

Warning sign "when the nurse should notify physician":
Any rapid and substantial muscle weakness, such as the inability to lift elbows or head, or diplopia.
Facial muscle weakness, difficulty with swallowing, or changes in speech quality.
Respiratory distress signals like rapid, shallow breathing or paradoxical breathing patterns.
Neurological changes such as mental clouding or somnolence.
Signs of autonomic dysfunction, including significant fluctuations in heart rate or blood pressure.

Figure 1 Algorithm for Food-borne botulism.