Botulism

An overview of the disease

Updated 22.12.2008
Botulism milestones

- 1793  Human outbreak linked to sausages (Germany)
- 1870  Disease named “botulism” - *botulus* = "sausage“ (Latin)
- 1895  Organism isolated
- 1944  Toxin isolated
- 1949  Identification that toxin blocks neuromuscular transmission
- 1973  Animal experiments
- 1980  Therapeutic usage - treatment of strabismus
- 1989  BOTOX (botulinum toxin, therapeutic usage) is approved in the United States for treatment of specific conditions
C. Botulinum

- Worldwide distribution
  - *Clostridium* spores are found in soil
  - High mortality rate unless identified and treated early

- **Epidemiology**
  
  **Ireland**
  - Rare, between 1998-2007 only 1 case notified
  - 3 cases in injection drug users reported in 2002 (wound botulism became notifiable 1st Jan 2004)

  **EU**
  - UK -6 food borne outbreaks between 1987 and 2005, >130 wound botulism cases between 2000-2007
  - Food-borne botulism commoner in Italy, Germany and Baltic States

  **USA**
  - ~145 cases/year; 15% food borne, 65% infant botulism, 20% wound
**C. Botulinum characteristics**

- Nerve toxin produced by the bacterium *Clostridium botulinum*
  - One of the most powerful toxins known to man – tiny infectious dose
- A medical and Public Health emergency
- 7 types of botulism toxin (A-G)
  - Types A, B, E and F cause human illness
- Anaerobic, gram positive, rod-shaped bacteria
- Spores
  - Can remain dormant for 30 years or more
  - Spores resistant to heat and UV light
- Toxin is inactivated by heat
  - Cooking at 80°C for 10 minutes or longer
Clostridium botulinum

Photomicrograph of *C. botulinum* stained with Gentian violet.

Picture courtesy of CDC
Photomicrograph of *C. botulinum* type A viewed, Gram stain

Picture courtesy of CDC/ Dr. George Lombard
Botulism food poisoning

These are *Clostridium botulinum* Type E colonies displaying an opaque zone grown on a 48hr egg yolk agar plate; Mag. 1.9X.

Picture courtesy of CDC/ Dr. Holdeman
Botulism food poisoning

These are *Clostridium botulinum* Type A colonies, Strain 2, grown on a 48hr blood agar plate

Picture courtesy of CDC/ Dr. Holdeman
**Clostridium botulinum**

- 7 types of botulism A through G, based on the antigenic properties of the toxin produced
  - toxins A, B, E and F  Humans
  - toxins C and D  Birds, mammals
  - toxin G  Soil isolate in Argentina, but no disease reported
- Type B predominates in Europe and the US, east of the Rockies. The more severe Type A is commoner west of the Rockies
Categories of Botulism

- **Food borne botulism**
  - foods containing botulism toxin
- **Intestinal botulism (infant and child/adult)**
  - Ingested spores of *C. botulinum* germinate and produce toxin in intestines
  - Uncommon in adults
- **Wound botulism**
  - *C. botulinum* spores germinate in the wound and release toxin
- **Inhalation botulism**
  - Aerosolised toxin is inhaled
  - Usually does not occur naturally (has been reported in cocaine users)
  - Potential for use as a bioterrorist agent
Botulism – development and progression of disease

- Suspected Botulism is a medical emergency
- Incubation period
  - food borne: 4 hours-8 days
  - wound: 4-14 days
  - Shorter incubation period associated with higher ingested dose and more severe disease
- Toxin enters bloodstream
  - Binds to peripheral cholinergic nerve endings
  - Inhibits release of acetylcholine, preventing muscles from contracting
- Symmetrical, descending paralysis
  - begins with cranial nerves, progresses peripherally
Schematic representation of the action of botulinum toxin (BT) on a neuromuscular junction


Ach not released
## Symptoms

Motor loss cranial → peripheral + cholinergic effects

<table>
<thead>
<tr>
<th>Gastrointestinal*</th>
<th>Neurologic</th>
<th>Miscellaneous</th>
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</thead>
<tbody>
<tr>
<td>• Nausea</td>
<td>• Blurred/double vision</td>
<td>• Fatigue</td>
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<tr>
<td>• Diarrhoea (early)</td>
<td>• Difficulty swallowing, dry mouth</td>
<td>• Sore throat</td>
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<td>• Constipation (late)</td>
<td>• Muscle weakness</td>
<td>• dizziness</td>
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<td>• Abdominal cramps</td>
<td>• Drooping eyelids</td>
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<tr>
<td>• Vomiting</td>
<td>• Slurred speech</td>
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<td>• Difficulty breathing</td>
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*for food borne illness
Physical findings*

- Ptosis
- Extra-ocular muscle weakness
- Facial nerve dysfunction
- Hypoactive gag reflex
- Tongue weakness
- Pupils fixed or dilated
- Extremity weakness
  - Symmetric
  - Proximal to distal
  - Descending pattern
- Nystagmus
- Hypoactive deep tendon reflexes

Botulism – clinical course (cont.)

• Respiratory muscle involvement
  – many cases require mechanical ventilation when voluntary and involuntary muscles (diaphragm) affected
  – Sudden deterioration may occur

• Complications
  – related to prolonged ventilator support, secondary bacterial infection and prolonged paralysis/weakness
  – Death
Infant botulism

Picture courtesy of CDC
Botulism Differential Diagnoses

Requires high index of suspicion*

- Guillain-Barré syndrome
- Myasthenia gravis
- Stroke
- Lambert-Eaton syndrome
- Intoxication with organophosphates, atropine, carbon monoxide, opiates, alcohol
- Paralytic fish poisoning

*Differs from other causes of flaccid paralysis:
  - Cranial nerve palsies are disproportionately more profound than peripheral weakness/hypotonia
  - Absence of sensory nerve damage
Possible Case of Botulism – Action

• Suspected Botulism is a **Public Health** emergency
• Immediate notification
  – Call local HSE Department of Public Health immediately if a case of botulism is suspected
• Laboratory confirmation
  – Obtain serum sample for toxin testing
  – Isolation of *C. botulinum* from wound
• Treat with anti-toxin
• Full epidemiological investigation
  – Enhanced surveillance undertake and investigation
Botulism Clinical Treatment

• Antitoxin supply and administration
  – Contact Medical officer, Cherry Orchard Hospital; Tel:01 620 6000 who authorises delivery of anti-toxin
  – Anti-toxin administration should NOT BE DELAYED pending microbiology/toxin testing results
  – Turnaround times for reliable negative results can be up to one week
  – Hospital pharmacy should be informed of request

• Elimination
  – Induced vomiting, high enemas (food borne)
  – Antibiotics for wound botulism, debridement if needed

• Supportive Care
  – Mechanical ventilation, parenteral nutrition, rehabilitation
Botulism Antitoxin

- **Antitoxin**
  - Can be procured from HSE
    - Authorised by Medical Officer, Cherry Orchard Hospital
    - Stored and distributed through National Cold Chain, National Immunisation Office (NIO) when stocks available
    - Emergency stock available from Novartis Germany on named patient basis within 24 hours of request
  - Unlicensed product
    - For use on named patient basis
- For treatment of most common forms of botulism
Botulism Antitoxin (cont.)

- Does not reverse current paralysis, but may limit progression and prevent nerve damage if administered early

- Hypersensitivity to antitoxin
  - 9% of people experience some hypersensitivity to equine anti-toxin
Botulism Infection Control

- Botulism cannot be transmitted person-to-person

- Standard precautions should be taken when caring for botulism patients
Botulism Laboratory Procedures

- Toxin neutralization mouse bioassay
  - serum, stool, gastric aspirate, suspect foods

- Isolation of *C. botulinum* or toxin
  - Faeces (food borne or intestinal), wound, tissue
Wound botulism

• Avoid use of illegal drugs
• If using drugs
  – is your supply safe? Is your equipment sterile?
• Promptly seek medical care for infected wounds
• Seek medical attention if develop any of signs or symptoms of botulism
Food borne botulism

– Typically low acid content e.g.
  • Canned green beans, spinach, mushrooms, and beets;
  • Fish, including canned tuna, fermented, smoked and salted fish;
  • Meat products, especially ham but also chicken and sausage

– Also
  • Chopped garlic in oil, tomatoes, carrot juice, improperly handled baked potatoes
Preventing food borne botulism

- Follow strict hygienic procedures to reduce contamination of foods
- Refrigerate oils infused with garlic/herbs
- Baked potatoes (wrapped in aluminum foil) should be kept hot until served or refrigerated
- Boil canned food for 10 minutes before eating
- Don’t give honey to children less than 12 months of age
Botulism Vaccine

- Not available in Ireland- concerns about its effectiveness and adverse event profile
- In the U.S.
  - a toxoid vaccine (antigen types A, B, C, D, and E) is available for laboratory workers at high risk of exposure
Documented outbreaks

• Food borne
  – Canned soups - USA, 1971
  – Chili Sauce - USA, 2007
  – Fermented foods - Eskimo population (frequent)
  – Yoghurt - Turkey, 2005
  – Carrot juice - USA, 2006
  – Bamboo shoots - Thailand, 2006
Documented outbreaks (cont.)

• Wound botulism
  – Mainly injection drug users (heroin)
References

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• Centers for Disease Control (CDC)  
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