Botulism

As a Bioterrorism Agent
Botulism History

- Germany (1793) earliest recorded human outbreak
- Organism isolated in 1895
- Mortality rate of 5-50%; long recovery period
- Weaponized by several nations including the U.S., Japan, and Soviet Union, beginning in the 1930’s
- Iraq (1980’s) produced 19,000 L of concentrated botulism toxin
- Japan (1990’s) Aum Shinrikyo cult
What Makes Botulism Toxin a Good Weapon?

• Botulism toxin is the most poisonous substance known
• High lethality: 1 aerosolized gram could potentially kill 1 million people
• Isolated fairly easily from soil
• Could be released as an aerosol or as a contaminant in the food supply
• Expensive, long-term care needed for recovery
Botulism Microbiology

- Toxin produced by the bacterium *Clostridium botulinum*
- Anaerobic, gram positive, rod-shaped bacteria
- Bacteria are 0.5 to 2.0 mcm in width and 1.6 to 22.0 mcm in length
- Create spores that can remain dormant for 30 years or more
- Spores extremely resistant to environmental stressors, such as heat and UV light

*C. botulinum*
Clostridium botulinum

- 7 types of botulism A through G, based on the antigenic properties of the toxin produced
  - toxins A, B, E and F cause illness in humans
  - toxins C and D cause illness in birds and mammals
  - toxin G
Categories of Botulism

- **Foodborne botulism**
  - caused by eating foods that contain botulism toxin

- **Intestinal botulism (infant and child/adult)**
  - caused by ingesting spores of the bacteria which germinate and produce toxin in the intestines

- **Wound botulism**
  - C. botulinum spores germinate in the wound

- **Inhalation botulism**
  - Aerosolized toxin is inhaled
  - does not occur naturally and may be indicative of bioterrorism
Botulism Pathogenesis

- Incubation period
  - ingestion: unknown
  - foodborne: 6 hours-8 days
  - wound: 4-14 days
  - inhalation: (estimated) 24-36 hours
- Toxin enters bloodstream from mucosal surface or wound
- Binds to peripheral cholinergic nerve endings
- Inhibits release of acetylcholine, preventing muscles from contracting
- Symmetrical, descending paralysis occurs beginning with cranial nerves and progressing downward
Botulism Pathogenesis (cont.)

- Can result from airway obstruction or paralysis of respiratory muscles
- Secondary complications related to prolonged ventilatory support and intensive care
Botulism Toxin Mechanism

A Normal Neurotransmitter Release
- SNARE Proteins Form Complex
- Vesicle and Terminal Membranes Fuse
- Neurotransmitter Released
- Acetylcholine Released
- Acetylcholine Receptor
- Muscle Fiber Contracts

B Exposure to Botulinum Toxin
- Botulinum Toxin Endocytosed
- Light Chain Cleaves Specific SNARE Proteins
- SNARE Complex Does Not Form
- Membranes Do Not Fuse
- Neurotransmitter Not Released
- Muscle Fiber Paralyzed
Botulism Clinical Presentation

• Classic symptoms of botulism poisoning include:
  – blurred/double vision
  – muscle weakness
  – drooping eyelids
  – slurred speech
  – difficulty swallowing
  – patient is afebrile and alert

• Infants with botulism will present with:
  – weak cry
  – poor feeding
  – constipation
  – poor muscle tone, “floppy” baby syndrome
Possible Case of Botulism

- Call MDH immediately (24/7) at 612-676-5414 or 1-877-676-5414 if a case of botulism is suspected.
Botulism Clinical Treatment

- Antitoxin administration

- Supportive Care
  - mechanical ventilation
  - body positioning
  - parenteral nutrition

- Elimination
  - Induced vomiting
  - High enemas
Tightly Rolled Cloth for Cervical Support

Bumpers to Prevent Downward Sliding

Rigid Mattress Support

Tilt
Botulism Transmission

- Home-canned goods (foodborne)
  - particularly low-acid foods such as asparagus, beets, and corn

- Honey (ingestion)
  - can contain *C. botulinum* spores
  - not recommended for infants <12 months old

- Crush injuries, injection drug use (wound)
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
  – feces, wound, tissue
Botulism Antitoxin

- Equine antitoxin
  - Trivalent and bivalent antitoxins available through the CDC
  - Licensed trivalent antitoxin neutralizes type A, B, and E botulism toxins
  - Effective in the treatment of foodborne, intestinal, and wound botulism
  - Effectiveness for inhalation botulism has not been proven
  - Does not reverse current paralysis, but may limit progression and prevent nerve damage if administered early
Botulism Antitoxin (cont.)

- Hypersensitivity to equine antitoxin
  - 9% of people experience some hypersensitivity
Botulism Differential Diagnoses

- Guillain-Barré syndrome
- Myasthenia gravis
- Stroke
- Tick paralysis
- Lambert-Eaton syndrome
- Psychiatric illness
- Poliomyelitis
- Diabetic Complications
- Drug intoxication
- CNS infection
- Overexertion
Botulism Vaccine

- A toxoid vaccine (antigen types A, B, C, D, and E) is available for laboratory workers at high risk of exposure
- Limited supplies of this vaccine available
Therapeutic Uses of Botulism Toxin

- Focal dystonias - involuntary, sustained, or spasmodic patterned muscle activity
- Spasticity - velocity-dependent increase in muscle tone
- Nondystonic disorders of involuntary muscle activity
- Strabismus (disorder of conjugate eye movement) and nystagmus
- Disorders of localized muscle spasms and pain
- Smooth muscle hyperactive disorders
- Cosmetic use
- Sweating disorders