

Botulinum Toxins as a Bioterrorist Agent

Agent: The bacillus *Clostridium botulinum* may produce any of seven neurotoxins (Types A-G). Botulinum toxins may be aerosolized or used to sabotage food supplies.

Disease: Botulism

Incubation Period: 1-5 days

Signs/Symptoms: A history of simultaneous onset of cranial nerve palsies and descending paralysis in a group of individuals may alert healthcare providers to the diagnosis of botulism. Fever is absent, neurologic manifestations are symmetric, patient remains responsive, heart rate is normal or slow in the absence of hypotension, and sensory deficits do not occur (except for blurred vision). Inhaled botulinum toxins produce a clinical picture similar to that of classic foodborne botulism, although the time of onset of paralytic symptoms may actually be longer than that for foodborne cases. Initial symptoms include ptosis, generalized weakness, lassitude, and dizziness. Diminished salivation with extreme dryness of the mouth may contribute to a sore throat. With the progression of the disease, more severe motor symptoms begin to appear. Diplopia, dysphonia, dysarthria, and dysphagia occur. This is followed by a symmetric, descending, progressive weakness of the extremities along with weakness of the respiratory muscles. Other symptoms may include nausea and vomiting. The patient is alert, oriented, and afebrile. Additional neurologic findings may include a diminished gag reflex, facial paresis, tongue weakness, and nystagmus. Respiratory failure due to paralysis of respiratory muscles is the most serious complication and, generally, the cause of death.

Diagnosis:

Differential Diagnosis: Cases might be confused with myasthenia gravis or Lambert-Eaton myasthenic syndrome, but these conditions are rarely fulminant and lack autonomic features. Guillain-Barré syndrome and other acute inflammatory polyneuropathies are similar but rarely begin with cranial nerve dysfunction. Tick paralysis can be excluded by careful examination since the tick should still be attached. Polio patients generally present with fever and asymmetric flaccid paralysis. Magnesium intoxication, diphtheria, organophosphate poisoning, and brain stem infarction may sometimes be confused with botulism.

Diagnostic Tests: Mouse bioassay is the most sensitive test to detect toxin in patient specimens but may take several days to complete. Survivors do not generally develop an antibody response due to the small amount of toxin necessary to cause death. The organism can be isolated from food or stool. Demonstration of toxin in isolates, serum, stool, vomitus, gastric aspirates, food, or respiratory secretions is possible. Toxin may possibly be identified in nasal swabs up to 72 hours after inhalational exposure.

Electromyography results show diminished action potential after single supramaximal stimulus and facilitation with repetitive stimuli at 20-50/second; nerve conduction is normal.

At least 10ml of serum and 10g of stool are required for toxin typing. Blood for serum should be collected in tiger-top (SST) or red-top tubes. Specimens must be kept cold (2-8°C) or frozen.

Food samples may be submitted for toxin detection and or isolation of organism. A minimum 25g sample of each food to be tested should be submitted. Food samples must be sent on cold packs rather than wet or dry ice. Unopened suspect canned food samples can be sent at ambient temperature.

All specimens should be sent to the **Oregon State Public Health Laboratory** (OSPHL) immediately. Confirmation of toxin in stool or foods may take up to 4-10 days. Contact Acute and Communicable Disease Prevention (ACDP) at (503) 731-4024, 800 NE Oregon—Suite 772, Portland, OR 97232 and The Oregon State Public Health Laboratory at (503) 229-5882, 1717 SW Tenth Avenue, Portland, OR 97201 prior to sending samples.

Supportive Tests: Routine testing is of little value in diagnosis. The cerebrospinal fluid is normal in botulism and myasthenia gravis; protein may be elevated in Guillain-Barré syndrome. The Tensilon[®] test will be negative in botulism and Guillain-Barré syndrome, positive in myasthenia gravis.

Treatment: Supportive care and prolonged nursing may be necessary. Suspected cases should be monitored for respiratory compromise using forced expiratory volume (FEV's). Intubation and ventilatory assistance may be required for respiratory failure. Tracheostomy may be required. Botulinum antitoxin (equine origin) has been used in cases of foodborne botulism. Antitoxin may be effective in aerosol exposure, sometimes even after onset symptoms. Skin test for sensitivity to horse serum is necessary before equine antitoxin administration. **NOTE:**

botulinum anti-toxin is only available through OHD, (503) 731-4024, (503) 731-4030, nights, weekends, and holidays.

Infection Control: Standard precautions should be practiced, but isolation is not required. The toxin is not dermally active, and secondary aerosols from patients are not a hazard. Boiling for 5-10 minutes destroys the toxin. Surfaces may be decontaminated with 0.5% sodium hypochlorite solution (1 part household bleach added to 9 parts water) and/or soap and water.

Report: Immediately report any suspect cases to your local health department or the Oregon Health Division at (503) 731-4024 during working hours (8:00 am to 5:00 pm Monday through Friday) or (503) 731-4030 nights, weekends and holidays.

Adapted with permission from the Texas Department of Health