Botulinum Toxin Exposure Medical Response Guidance for the University of Wisconsin-Madison

1.0 Instructions: Information in this guidance is meant to inform both laboratory staff and health professionals about the risks and treatment in the event of an infectious agent exposure. In using this guidance, please consider that multiple routes of exposure may occur in a lab and that organism strains will sometimes be genetically modified to incorporate traits such as antimicrobial resistance. Research protocols and other available guidance such as Health Canada material safety data sheets will be provided as supporting information when available. It should be assumed that when exposures do occur, that the healthcare provider will be provided with information about the specific organism and strain involved, route of exposure, inoculum concentration, and victim vaccination and serological status, when available. This document was developed by UW Occupational Medicine in consultation with the UW Division of Infectious Disease. The information provided below is intended to provide guidance for treating physicians. Treatment and evaluation plans should be individualized to the patient based on the patient’s symptoms, exposure risk, and underlying health status.

If there are any questions about this document, please contact University Health Services, Occupational Medicine at 265-5610.

2.0 Signs and Symptoms of Infection: Describe signs and symptoms associated with the agent.

Naturally occurring botulism in adults is typically foodborne and associated with ingestion of food contaminated with preformed botulinum toxin. Botulinum toxin is produced by the bacterium Clostridium botulinum, C. baratii, and C. butyricum. Botulinum toxin serotypes A,B,E F, and G are associated with naturally occurring human illness.

Laboratory associated botulism can be associated with any of the 7 serotypes (A to G). Botulism develops when preformed toxin is released into the circulation following exposure, with routes of exposure including inhalation, mucous membrane exposure, skin break exposure, or injection. Exposure to the Clostridium neurotoxin producing species itself does not produce botulism. It is the neurotoxin, and not the organism itself, that causes botulism. In immune-compromised individuals, exposure to Clostridium spores in wounds or via the GI tract can lead to infection, toxin production, and subsequent clinical botulism.

Clinical botulism presents several hours to days after exposure to botulinum neurotoxin. Cases typically present with abrupt onset of blurred vision, double vision, drooping eyelids, dry mouth and difficulty with swallowing and speaking. A descending, symmetrical flaccid paralysis follows. This can progress to generalized muscle weakness and respiratory failure. Muscle weakness typically presents in the following order: head control, then upper extremities, then respiratory muscles, then lower extremity weakness. Fever is absent.
GI symptoms including nausea, vomiting, diarrhea, constipation, and cramping only present with food related botulism and are not relevant to laboratory acquired cases unless there has been hand to mouth exposure.

3.0 Infectivity - Describe infective dose, relevant exposure routes (considering laboratory use), incubation period and potential severity of infection.

Botulinum neurotoxin is one of the most toxic neuroproteins known. Injection or respiratory inhalation of less than one microgram (ug) can cause severe incapacitation or death. (The dose for equivalent effects from ingestion, the traditional route of exposure to botulinum toxin, is 70 ug.) The severity of clinical botulism varies with the toxin type, purity, dose and route of exposure.

Routes of laboratory exposure to botulinum toxin include aerosol exposure (particularly during centrifugation), needlesticks, or exposure of broken or lacerated skin to BoNT protein. Botulinum neurotoxin is not thought to penetrate intact skin but can be absorbed across mucous membranes. Cases of laboratory acquired botulism have been reported after necropsy work on animals previously exposed to aerosolized botulinum neurotoxin, perhaps from exposure to the animal fur.

Clostridia species or its spores can be stable for weeks to years in food products, clinical samples and environmental samples. Botulinum neurotoxin has been shown to retain its toxicity for long periods of time in a variety of frozen foods or products. The toxin itself is readily inactivated by heating.

Clinical botulism has a latency period of several hours to days between exposure to the toxin or toxin producing organism and development of symptoms. Injection, inhalation and skin break associated botulism cases typically present with neurologic symptoms 12 – 72 hours after exposure. Onset of symptoms may be significantly shorter following parenteral exposure to large amounts of toxin.

4.0 Description of First Aid - Provide an overview of first aid treatment of exposures considering that multiple routes of exposure could occur (needlestick, aerosol, eye, skin and ingestion).

For laboratory contact exposure to skin, immediate and thorough washing of exposed skin surfaces with soap and water for 15 minutes is recommended.

Needlesticks should be immediately bled out for 15 minutes under lukewarm water in the nearest sink, followed by bandaging.

For associated splashes or injuries to the eyes or mucous membranes, flush, preferably in an eye wash station, for 15 minutes.
5.0 Urgency of Medical Care- Describe how soon medical attention should be sought, i.e. is an ER visit necessary, a visit to University Health Services, or simply schedule a visit with a personal physician.

All exposures, after initial first aide, should be immediately reported to UW-Madison RO or ARO's (Responsible Official or Alternate Responsible Official) and PI. RO/ARO's can be reached at their direct office numbers or through the UW-Madison Police Department at 262-2957 or by dialing 9-1-1. RO/ARO will contact UW Infectious Disease to arrange for appropriate medical attention and notify UHS Occupational Medicine (608-262-5610 or 608-252-0955).”

6.0 Description of Medical Response- Provide an overview for clinical treatment of exposures to the agent considering that multiple routes of exposure could occur (needlestick, aerosol, eye, skin and ingestion) and that strains of agents will vary and sometimes include antimicrobial resistance.

An equine antitoxin product is available from CDC for treatment of patients with the symptoms of botulism. Because of risks inherent in equine products, actual treatment is limited to symptomatic botulism and not recommended for exposure only. Early recognition of symptoms and initiation of treatment is essential.

Screening for early symptoms is focused on the following physical findings: VITAL signs, particularly the respiratory rate; HEENT including checking for double vision, blurred vision, eyelid drooping, dilated pupils, slowed extra-ocular movements, slurred speech, difficulty swallowing, and dry mouth; LUNGS including respiratory excursions and depth of inspiration / expiration; NEUROLOGIC including motor strength, decreased gag reflex, deep tendon reflexes.

Follow-up visits should be scheduled for 24-48 hours and at 3 days for all potential exposures.

Toxin assays of serum can confirm the diagnosis of botulism but treatment is neither based on serum results nor delayed while awaiting the results. Treatment is based on symptom presentation only.

An antidote is available for symptomatic cases following exposure to toxin and should be given as soon as possible following symptom development or following significant exposures. The antitoxin is obtained through the state health dept (608-267-7422 or 608-267-9003) and obtained from CDC stockpiles at O’Hare airport. The CDC number for contact is 770-488-7100.

Patients with any symptom development or with significant exposures will be hospitalized and managed by UW Infectious Disease. Treatment for cases of botulism includes both antitoxin and supportive care.
7.0 Description of Medical Surveillance- Describe the advisability of medical surveillance strategies (in particular baseline and annual serology) for those working with the agent. If doing so would likely improve the identification, diagnosis or treatment of exposures, please indicate so.

There is no routine surveillance for individuals working with botulinum toxin. The CDC investigational vaccine for exposure to botulinum toxin has been withdrawn from the market and there are currently no other vaccines available. There are also no available tests to check for titers in individuals previously vaccinated with the CDC vaccine.

8.0 Considerations for Infection Control- Describe any special precautions required to prevent the further spread of infection. Include precautions for the healthcare, workplace, and home setting.

Clinical Botulism in healthy adults develops from exposure to botulinum neurotoxin, not from exposure to the clostridium organism or spores themselves. It is not transmissible person to person.

9.0 Reporting- Describe any public health or federal regulatory reporting requirements. Include the timing and mechanism for reporting.

Public Health: Confirmed or suspect cases of disease are Category I, immediately reportable by telephone or fax to the patient’s local health officer. In addition to the immediate report, within 24 hours, complete and submit a case report electronically through the Wisconsin Electronic Disease Surveillance System (WEDSS), by mail, fax, or other means.

Exposure or potential exposure to any select agent strains will be reported to the state health department communicable disease section by the Responsible Official at 608-267-9003 (7:45 AM-4:30 PM) or through the 24 hour WI health department clinical emergency contact number 608-258-0099 (after hours). The CDC Division of Select Agents and Toxins will also be notified by the Responsible Official.

Antitoxin is obtained through state health departments from CDC stockpiles at O’Hare airport. The CDC 24/7 number for contact is 770-488-7100.

10.0 References:

11.0 Document Revisions

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<td>Changed to new format; additional edits</td>
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