INFORMATION PAPER

Military Vaccine Agency
1 March 2007

SUBJECT: Botulism and botulinum antitoxin

1. Purpose. To describe botulism and the antitoxin to treat it.

2. Facts.

a. Microbiology. Botulism is caused by an extremely potent neurotoxin produced by ***Clostridium botulinum,*** a spore-forming, rod-shaped bacterium commonly found in the soil. Botulinum toxin exists in 7 distinct, identifiable types given the letters A thru G. There are 3 forms of naturally occurring botulism: foodborne, wound, and infant. Inhalation botulism is a potential method for a bioterrorism attack, but does not occur naturally. All forms of botulism result from the toxin being absorbed into the bloodstream through the gut, lungs or a wound. Once the toxin enters the body it interferes with the chemical communication between nerves and muscles by blocking the chemical messenger acetylcholine.

b. Epidemiology. Botulism has a worldwide distribution. On average, 110 cases of botulism are reported annually in the United States. Two-thirds are infant botulism and one-third foodborne. Outbreaks occur when food products are improperly prepared or preserved, failing to destroy bacterial spores, allowing for renewed toxin production. No cases of waterborne botulism have ever been reported. Botulism is not transmissible from person to person. Symptoms begin within 6 hours to 2 weeks after exposure (often within 12-36 hours). People with botulism typically experience double or blurred vision, speaking and/or swallowing difficulties. If untreated, a progressive head to toe muscle paralysis (weakness) may occur. Death can result from respiratory or upper airway muscle paralysis. Modern medical therapies have reduced the numbers of deaths from foodborne botulism to approximately 6% of cases.

c. Vaccine. A licensed vaccine to prevent botulism is not available at this time. A pentavalent toxoid vaccine of *C. botulinum* toxin types A,B,C,D and E is only available as an Investigational New Drug (IND). It will likely remain under IND status, as efficacy testing in humans is not possible. At-risk laboratory workers are the primary recipients of the vaccine.

d. Antitoxin. Passive immunity is provided by the administration of equine (horse-derived) botulinum antitoxin following a diagnosis of botulism. The early administration of antitoxin is critical. Antitoxin does not reverse paralysis but arrests its progression. Several licensed antitoxin products are available in the U.S. A trivalent (types A, B, E) antitoxin is available through the Centers for Disease Control and Prevention (CDC) for cases of foodborne botulism. A licensed bivalent human intravenous antitoxin (types A and B) is available from the California Department of Health Services for treatment of infant botulism. Two “despeciated” equine heptavalent antitoxin preparations against all seven toxin-types are available under IND status. These “despeciated” antitoxins have had some of the non-essential horse protein removed to minimize potential allergic reactions. The original heptavalent preparation, developed at USAMRIID, and the newer commercial heptavalent IND product are available through USAMRIID or the CDC. The amount of neutralizing antibody in both the licensed and investigational equine antitoxins far exceeds the serum toxin concentrations found in foodborne botulism cases. Larger exposures, e.g., a BW attack, may require repeat doses.

e. Immunization. Equine antitoxin is supplied in single dose vials. It is administered by slow intravenous infusion, in accordance with an IND protocol, in both adults and children.

f. Cautions. Based on limited information, there is no evidence that the treatment of pregnant women, children, or immunocompromised individuals should vary from standard therapy. Administration of antitoxin may require skin testing with increasing doses of the antitoxin to determine an individual's sensitivity to horse protein prior to initiating treatment. Those who test positive will require a rapid desensitization procedure, preferably by an allergist, prior to receiving the full dose.

g. Adverse Events. Safety data on botulinum antitoxins is limited. Hypersensitivity reactions to horse proteins contained in the antitoxin remains the greatest concern. In studies of older antitoxin preparations, approximately 9% of recipients developed urticaria (hives), serum sickness (a delayed allergic reaction) or other hypersensitivity reactions. Anaphylaxis occurred in 2% of recipients. Similarly, in a study of 50 persons receiving heptavalent equine antitoxin 2% displayed serum sickness and 18% had mild reactions.

h. DoD Policy. Equine antitoxin is for the emergency treatment of suspected or confirmed cases of botulism and is administered under IND protocol.

3. References.

a. Arnon SS, et a. Botulinum toxin as a Biological weapon: Medical and Public Health Management. *Journal of the American Medical Association*.2001;285(8):1059-1070

b. CDC disease information. www.cdc.gov/doc.do/id/0900f3ec8027202b

c. USAMRIID's Medical Management of Biological Casualties Handbook 6th Ed. US Army Medical research Institute of Infectious Disease; 2005

d. Multiple resources assembled by the Military Vaccine Agency: www.vaccines.mil/botulism

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