



Complete Summary

GUIDELINE TITLE

(1) Botulinum toxin as a biological weapon: medical and public health management. (2) Botulinum toxin as a biological weapon. (Addendum)

BIBLIOGRAPHIC SOURCE(S)

Arnon SS, Schechter R, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Fine AD, Hauer J, Layton M, Lillibridge S, Osterholm MT, O'Toole T, Parker G, Perl TM, Russell PK, Swerdlow DL, Tonat K. Botulinum toxin as a biological weapon. In: Henderson DA, Inglesby TV, O'Toole T, editor(s). Bioterrorism : guidelines for medical and public health management. Chicago (IL): American Medical Association; 2002. p. 141-65. [109 references]

Arnon SS, Schechter R, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Fine AD, Hauer J, Layton M, Lillibridge S, Osterholm MT, O'Toole T, Parker G, Perl TM, Russell PK, Swerdlow DL, Tonat K. Botulinum toxin as a biological weapon: medical and public health management. JAMA 2001 Feb 28;285(8):1059-70. [106 references]

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Exposure to or infection with the botulinum toxin (*Clostridium botulinum*)

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Infectious Diseases
Internal Medicine
Pathology
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Clinical Laboratory Personnel
Hospitals
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To develop consensus-based recommendations for measures to be taken by medical and public health professionals following the use of botulinum as a biological weapon against a civilian population

TARGET POPULATION

Adults, pregnant women, children and immunosuppressed persons exposed to or infected with botulinum toxin as a biological weapon

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis and Differential Diagnosis

1. Assessment of clinical findings and epidemiological features
2. History of travel, activity, and diet
3. Immediate notification of local public health department and hospital epidemiologist to coordinate shipment of therapeutic antitoxin, laboratory diagnostic testing, and epidemiological investigation
4. Collection and refrigeration of serum, stool, gastric aspirate, vomitus, and suspect foods for diagnostic testing of botulism with the mouse bioassay
5. Diagnostic procedures to exclude botulism as the cause of paralysis (e.g., electromyogram with repetitive nerve stimulation at 20 to 50 Hz, cerebrospinal fluid analysis, imaging of the brain, spine, and chest)

Management/Treatment/Post-Exposure Prophylaxis

1. Supportive care as needed (e.g., feeding by enteral tube or parenteral nutrition, intensive care, mechanical ventilation, treatment of secondary

- infections, monitoring of respiratory functioning, reverse Trendelenburg positioning)
2. Passive immunization with equine antitoxin: licensed trivalent antitoxin; investigational heptavalent (ABCDEFG) antitoxin
 3. Selected use of Botulism Immune Globulin Intravenous (Human) (an investigational product, California Department of Health Services, Berkeley)

Note: Preexposure immunization for the general population was discussed but not recommended.

Decontamination

Infection Control

1. Standard hospital precautions

MAJOR OUTCOMES CONSIDERED

Therapeutic efficacy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The OLDMEDLINE and MEDLINE databases were queried for all articles published between January 1960 and March 1999 that contained words referring to biological warfare (bioterrorism, biowarfare, terrorism, war, warfare, and weapon) in combination with terms related to *Clostridium botulinum* (bacillus, botulin, botulinal, botulinum, botulinus, botulism, clostridia, clostridial, and *Clostridium*). The articles identified in the databases were fully reviewed. In addition, published and unpublished articles, books, monographs, and special reports in the primary authors' collections were reviewed. Additional MEDLINE searches were conducted through April 2000 during the review and revisions of the consensus statement.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The first draft of the working group's consensus statement was a synthesis of information obtained in the formal evidence-gathering process. The working group convened to review the first draft in May 1999. Working group members reviewed subsequent drafts and suggested additional revisions. The final statement incorporates all relevant evidence obtained in the literature search in conjunction with final consensus recommendations supported by all working group members.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

One external reviewer is acknowledged in the guideline document for his participation in the consensus process.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): In 2002 the Center for Civilian Biodefense Strategies added information to its 1999 guideline pertaining to the following topics:

1. Production of monoclonal antibodies that neutralize botulinum toxin
2. Changes in the availability of licensed equine botulinum antitoxin
3. Economic impact of an aerosolized botulinum toxin attack on a civilian population in Canada
4. Unusual modes of dissemination

Information from the 2002 addendum appears at the end of this field. The recommendations from the 1999 guideline, slightly modified to match their presentation in the 2002 document, are presented first.

1999 Guideline Recommendations

Bioterrorism Considerations

Any outbreak of botulism should bring to mind the possibility of bioterrorism, but certain features would be particularly suggestive (see below).

Features of an Outbreak That Would Suggest a Deliberate Release of Botulinum Toxin:

- Outbreak of a large number of cases of acute flaccid paralysis with prominent bulbar palsies
- Outbreak with an unusual botulinum toxin type (i.e., type C, D, F, or G, or type E toxin not acquired from an aquatic food)
- Outbreak with a common geographic factor among cases (e.g., airport, work location) but without a common dietary exposure (i.e., features suggestive of an aerosol attack)
- Multiple simultaneous outbreaks with no common source

Note: A careful travel and activity history, as well as dietary history, should be taken in any suspected botulism outbreak. Patients should also be asked if they know of other persons with similar symptoms. See the 2002 addendum at the end of the "Major Recommendations" section for additional information about modes of dissemination.

The availability and speed of air transportation mandate that a careful travel and activity history, as well as a careful dietary history, be taken. Patients should also be asked whether they know of other persons with similar symptoms. Absence of a common dietary exposure among temporally clustered patients should suggest the possibility of inhalational botulism.

Diagnosis and Differential Diagnosis

Clinical diagnosis of botulism is confirmed by specialized laboratory testing that often requires days to complete. Routine laboratory test results are usually unremarkable. Therefore, clinical diagnosis is the foundation for early recognition of and response to a bioterrorist attack with botulinum toxin.

Any case of suspected botulism represents a potential public health emergency because of the possibility that a contaminated food remains available to others or that botulinum toxin has been deliberately released. In these settings, prompt intervention by civil authorities is needed to prevent additional cases. Consequently, clinicians caring for patients with suspected botulism should notify their local public health department and hospital epidemiologist immediately to coordinate shipment of therapeutic antitoxin, laboratory diagnostic testing, and epidemiological investigation (see below). In most jurisdictions of the United States, botulism suspected on clinical grounds alone by law must be reported immediately by telephone to local public health authorities. The attending clinician needs to be both prompt and persistent in accomplishing this notification.

Clinicians Caring for Patients With Suspected Botulism Should Immediately Contact Their:

1. Hospital epidemiologist or infection control practitioner
2. Local or state health departments

Consult your local telephone operator; the telephone directory under "government listings," or the Internet at: <http://www.cdc.gov/other.htm#states> or <http://www.astho.org/state.html>.

If the local and state health departments are unavailable, contact the [Centers for Disease Control and Prevention](#), (404) 639-2206; (404) 639-2888 (after hours).

Differential Diagnosis

Botulism is frequently misdiagnosed, most often as a polyradiculoneuropathy (Guillain-Barré or Miller-Fisher syndrome), myasthenia gravis, or a disease of the central nervous system (for a list of selected mimics and misdiagnoses of botulism, see Table 3 in the original guideline document). In the United States, botulism is more likely than Guillain-Barré syndrome, intoxication, or poliomyelitis to cause a cluster of cases of acute flaccid paralysis. Botulism differs from other flaccid paralyzes in its prominent cranial nerve palsies disproportionate to milder weakness and hypotonia below the neck, in its symmetry, and in its absence of sensory nerve damage.

Diagnostic Testing

At present, laboratory diagnostic testing for botulism in the United States is available only at the Centers for Disease Control and Prevention (CDC) and approximately 20 state and municipal public health laboratories. The laboratory should be consulted prospectively about specimen collection and processing. Samples used in diagnosis of botulism include serum (≥ 30 mL of blood in "tiger"-top or red-top tubes from adults, less from children), stool, gastric aspirate, and, if available, vomitus and suspect foods. Serum samples must be obtained before therapy with antitoxin, which nullifies the diagnostic mouse bioassay. An enema may be required to obtain an adequate fecal sample if the patient is constipated. Sterile water should be used for this procedure because saline enema solution can confound the mouse bioassay. Gastric aspirates and, perhaps, stool may be useful for detecting inhaled aerosolized botulinum toxin released in a bioterrorist attack. A list of the patient's medications should accompany the diagnostic samples

because anticholinesterases, such as pyridostigmine bromide, and other medicines that are toxic to mice can be dialyzed from samples before testing. All samples should be kept refrigerated after collection.

The standard laboratory diagnostic test for clinical specimens and foods is the mouse bioassay, in which type-specific antitoxin protects mice against any botulinum toxin present in the sample. The mouse bioassay can detect as little as 0.03 ng of botulinum toxin and usually yields results in 1 to 2 days (range, 6-96 hours). Fecal and gastric specimens also are cultured anaerobically, with results typically available in 7 to 10 days (range, 5-21 days). Toxin production by culture isolates is confirmed by the mouse bioassay.

An electromyogram with repetitive nerve stimulation at 20 to 50 Hz can sometimes distinguish between causes of acute flaccid paralysis. The characteristic electromyographic findings of botulism include normal nerve conduction velocity, normal sensory nerve function, a pattern of brief, small-amplitude motor potentials, and, most distinctively, an incremental response (facilitation) to repetitive stimulation often seen only at 50 Hz. Immediate access to electrophysiological studies may be difficult to obtain in an outbreak of botulism.

Additional diagnostic procedures may be useful in rapidly excluding botulism as the cause of paralysis (see Table 3 in the original guideline document). Cerebrospinal fluid (CSF) is unchanged in botulism but is abnormal in many central nervous system diseases. Although the cerebrospinal fluid protein level eventually is elevated in Guillain-Barré syndrome, it may be normal early in illness. Imaging of the brain, spine, and chest may reveal hemorrhage, inflammation, or neoplasm. A test dose of edrophonium chloride briefly reverses paralytic symptoms in many patients with myasthenia gravis and, reportedly, in some with botulism. A close inspection of the skin, especially the scalp, may reveal an attached tick that is causing paralysis. Other tests that require days for results include stool culture for *Campylobacter jejuni* as a precipitant of Guillain-Barré syndrome and assays for the autoantibodies that cause myasthenia gravis, Lambert-Eaton syndrome, and Guillain-Barré syndrome.

Foods suspected of being contaminated should be refrigerated until retrieval by public health personnel. The US Food and Drug Administration and the US Department of Agriculture can assist other public health laboratories with testing of suspect foods by using methods similar to those applied to clinical samples.

Therapy

Therapy for botulism consists of supportive care and passive immunization with equine antitoxin. Optimal use of botulinum antitoxin requires early suspicion of botulism. Timely administration of passive neutralizing antibody will minimize subsequent nerve damage and severity of disease but will not reverse existent paralysis. Antitoxin should be given to patients with neurologic signs of botulism as soon as possible after clinical diagnosis. Treatment should not be delayed for microbiological testing. Antitoxin may be withheld at the time of diagnosis if it is certain that the patient is improving from maximal paralysis.

In the United States, botulinum antitoxin is available from the Centers for Disease Control and Prevention (CDC) via state and local health departments. The components of the formerly licensed trivalent antitoxin that contained neutralizing antibodies against botulinum toxin types A, B, and E (the most common causes of human botulism) have been reformulated into a licensed bivalent (AB) product and an investigational monovalent anti-E product (see addendum at the end of the original guideline document). If another toxin type was intentionally disseminated, patients could potentially be treated with an investigational heptavalent (ABCDEFG) antitoxin held by the US Army. However, the time required for correct toxin typing and subsequent administration of heptavalent antitoxin would decrease the utility of this product in an outbreak. See the 2002 addendum at the end of the "Major Recommendations" section for additional information about availability of antitoxin and production of monoclonal antibodies to neutralize botulinum toxin.

The dose and safety precautions for equine botulinum antitoxin have changed over time. Clinicians should review the package insert with public health authorities before using antitoxin. At present, the dose of licensed botulinum antitoxin is a single 10-mL vial per patient, diluted 1:10 in 0.9% saline solution, administered by slow intravenous infusion. One vial provides between 5500 and 8500 IU of each type-specific antitoxin. The amount of neutralizing antibody in both the licensed and the investigational equine antitoxins far exceeds the highest serum toxin levels found in foodborne botulism patients, and additional doses are usually not required. If a patient has been exposed to an unnaturally large amount of botulinum toxin as a biological weapon, the adequacy of neutralization by antitoxin can be confirmed by retesting serum for toxin after treatment.

There are few published data on the safety of botulinum antitoxins. To screen for hypersensitivity, patients are given small challenge doses of equine antitoxin before receiving a full dose. Patients responding to challenge with a substantial wheal and flare may be desensitized over 3 to 4 hours before additional antitoxin is given. During the infusion of antitoxin, diphenhydramine and epinephrine should be on hand for rapid administration in case of adverse reaction. Although both equine antitoxins have been partially despeciated by enzymatic cleavage of the allogenic Fc region, each contains a small residual of intact antibody that may sensitize recipients to additional doses.

Botulism patients require supportive care that often includes feeding by enteral tube or parenteral nutrition, intensive care, mechanical ventilation, and treatment of secondary infections. Patients with suspected botulism should be closely monitored for impending respiratory failure. In nonventilated infants with botulism, a reverse Trendelenburg positioning with cervical vertebral support has been helpful, but applicability of this positioning to adults with botulism remains untested. This tilted, flat-body positioning with neck support may improve ventilation by reducing entry of oral secretions into the airway and by suspending more of the weight of the abdominal viscera from the diaphragm, thereby improving respiratory excursion (see Figure 4 in the original guideline document). In contrast, placing a botulism patient in a supine or semirecumbent position (trunk flexed 45° at the waist) may impede respiratory excursion and airway clearance, especially if the patient is obese. The desired angle of the reverse Trendelenburg position is 20° to 25°.

Botulism patients should be assessed for adequacy of gag and cough reflexes, control of oropharyngeal secretions, oxygen saturation, vital capacity, and inspiratory force. Airway obstruction or aspiration usually precedes hypoventilation in botulism. When respiratory function deteriorates, controlled, anticipatory intubation is indicated. The proportion of patients with botulism who require mechanical ventilation has varied from 20% in a foodborne outbreak to more than 60% in infant botulism. In a large outbreak of botulism, the need for mechanical ventilators, critical care beds, and skilled personnel might quickly exceed local capacity and persist for weeks or months. Development of a reserve stockpile of mechanical ventilators in the United States is under way and will require a complement of staff trained in their use.

Antibiotics have no known direct effect on botulinum toxin. However, secondary infections acquired during botulism often require antibiotic therapy. Aminoglycoside antibiotics and clindamycin are contraindicated because of their ability to exacerbate neuromuscular blockade. Standard treatments for detoxification, such as activated charcoal, may be given before antitoxin becomes available, but there are no data regarding their effectiveness in human botulism.

Special Populations

Based on limited information, there is no indication that treatment of children, pregnant women, and immunocompromised persons with botulism should differ from standard therapy. Despite the risks of immediate hypersensitivity and sensitization to equine proteins, both children and pregnant women have received equine antitoxin without apparent short-term adverse effects. The risks to fetuses of exposure to equine antitoxin are unknown. Treatment with human-derived neutralizing antibody would decrease the risk of allergic reactions posed by equine botulinum antitoxin, but use of the investigational product, Botulism Immune Globulin Intravenous (Human) (California Department of Health Services, Berkeley), is limited to suspected cases of infant botulism.

Prophylaxis

Botulism can be prevented by the presence of neutralizing antibody in the bloodstream. Immediate immunity can be provided by passive administration of equine botulinum antitoxin or by specific human hyperimmune globulin, while endogenous immunity can be induced by immunization with botulinum toxoid.

Use of antitoxin for postexposure prophylaxis is limited by its scarcity and its reactogenicity. Because of the risks of equine antitoxin therapy, it is less certain how best to care for persons who may have been exposed to botulinum toxin but who are not yet ill. In a balance between avoiding the potential adverse effects of equine antitoxin and needing to rapidly neutralize toxin, it is current practice in foodborne botulism outbreaks to closely monitor persons who may have been exposed to botulinum toxin and to treat them promptly with antitoxin at the first signs of illness. To facilitate distribution of scarce antitoxin following the intentional use of botulinum toxin, asymptomatic persons who are believed to have been exposed should remain under close medical observation and, if feasible, near critical care services.

In the United States, an investigational pentavalent (ABCDE) botulinum toxoid is distributed by the Centers for Disease Control and Prevention for laboratory workers at high risk of exposure to botulinum toxin and by the military for protection of troops against attack. A recombinant vaccine is also in development. The pentavalent toxoid has been used for more than 30 years to immunize more than 3000 laboratory workers in many countries. Immunization of the population with botulinum toxoid could in theory eliminate the hazard posed by botulinum toxins A through E. However, mass immunization is neither feasible nor desirable for reasons that include scarcity of the toxoid, rarity of natural disease, and elimination of the potential therapeutic benefits of medicinal botulinum toxin. Accordingly, preexposure immunization currently is neither recommended nor available to the general population. Botulinum toxoid induces immunity over several months and, so, is ineffective as postexposure prophylaxis.

Decontamination

Despite its extreme potency, botulinum toxin is easily destroyed. Heating to an internal temperature of 85°C for at least 5 minutes will detoxify contaminated food or drink. All foods suspected of contamination should be promptly removed from potential consumers and submitted to public health authorities for testing.

Persistence of aerosolized botulinum toxin at a site of deliberate release is determined by atmospheric conditions and the particle size of the aerosol. Extremes of temperature and humidity will degrade the toxin, while fine aerosols will eventually dissipate into the atmosphere. Depending on the weather, aerosolized toxin has been estimated to decay at between less than 1% to 4% per minute. At a decay rate of 1% per minute, substantial inactivation (≥ 13 logs) of toxin occurs by 2 days after aerosolization.

Recognition of a covert release of finely aerosolized botulinum toxin would probably occur too late to prevent additional exposures. When exposure is anticipated, some protection may be conferred by covering the mouth and nose with clothing such as an undershirt, shirt, scarf, or handkerchief. In contrast with mucosal surfaces, intact skin is impermeable to botulinum toxin.

After exposure to botulinum toxin, clothing and skin should be washed with soap and water. Contaminated objects or surfaces should be cleaned with 0.1% hypochlorite bleach solution if they cannot be avoided for the hours to days required for natural degradation.

Infection Control

Medical personnel caring for patients with suspected botulism should use standard precautions. Patients with suspected botulism do not need to be isolated, but those with flaccid paralysis from suspected meningitis require droplet precautions.

2002 Addendum

1. Production of monoclonal antibodies that neutralize botulinum toxin. Two recent publications describe potent recombinant human and murine monoclonal antibodies that neutralize type A botulinum toxin, which were

- made by using phage display technology. A combination of three human-compatible monoclonal antibodies that bind to heavy-chain epitopes neutralized 4×10^5 mouse LD₅₀s of toxin. In a separate investigation, a single murine antibody that bound to a heavy-chain epitope neutralized 10^4 mouse LD₅₀s. The development of these recombinant antibodies establishes the "proof of concept" needed to make a supply of high-potency, fully human heptavalent (A-G) botulinum antitoxin sufficient to defend both civilian and military populations. However, before beginning large-scale production of a recombinant human heptavalent antitoxin, the most efficacious neutralizing epitopes on both toxin heavy and light chains need to be established.
2. Changes in availability of licensed equine botulinum antitoxin. The use of equine antitoxin to treat the common types of human botulism has become more complicated because of a change in its formulation. The components of the former trivalent (ABE) licensed antitoxin mixture have been reformulated into a licensed bivalent (AB) product and an investigational monovalent anti-E product. Efforts to license the anti-E antitoxin are under way. Both antitoxin products may be given to cases when type E botulinum toxin is suspected but test results are pending. The US government also maintains limited stocks of an investigational equine heptavalent (A-G) antitoxin product for use in emergency situations.
 3. Economic impact of an aerosolized botulinum toxin attack on a civilian population in Canada. The cost of such an attack on a suburban population with aerosolized botulinum toxin was conservatively estimated to be \$8.6 billion (Canadian) per 100 000 persons exposed. This figure computes to \$86 000 (Canadian) per person exposed, or equivalently, to \$57 000 (US) per person exposed and \$114 000 per person ill. The model that produced these figures used the following assumptions: 100 000 persons were exposed for 2 hours, half of whom became paralyzed. The case-fatality ratio was 60% in patients who could not be provided with both antitoxin and mechanical ventilation and was 30% in patients who could be provided with both. At 48 hours a supply of ventilators and antitoxin adequate for all patients surviving to that point had become available. Although the case-fatality ratios used in this analysis are higher than recent US experience, their use probably resulted in a lower overall cost estimate because fewer patients would have survived to need prolonged mechanical ventilation and intensive care hospitalization.
 4. Unusual modes of dissemination. The transmission of weaponized anthrax spores via letter in the US postal system in September and October 2001 demonstrates that terrorists may utilize unconventional methods or vehicles to spread a bioweapon such as botulinum toxin. In addition, more than one agent may be released at the same time or in the same vehicle. The possibility underscores the need for new rapid diagnostic assays. When confronted with epidemiologically or clinically perplexing situations, medical and public health personnel should consider atypical routes and vehicles of dissemination of one or more bioweapon agents.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Diagnostic and management recommendations in the setting of a biological botulinum attack are consensus recommendations of the Working Group based on the best available evidence (see also "Qualifying Statements" and "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved diagnosis, management and containment of botulism following a bioterrorist attack

POTENTIAL HARMS

There are few published data on the safety of botulinum antitoxins. From 1967 to 1977, when the recommended dose was larger than today, approximately 9% of recipients of equine botulinum antitoxin in the United States displayed urticaria, serum sickness, or other reactions suggestive of hypersensitivity. Anaphylaxis occurred within 10 minutes of receiving antitoxin in 2% of recipients. When the US Army's investigational heptavalent antitoxin was given to 50 individuals in a large Egyptian outbreak of type E foodborne botulism in 1991, 1 recipient (2%) displayed serum sickness, and 9 (18%) had mild reactions.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Although standard treatments for detoxification, such as activated charcoal, may be given before antitoxin becomes available, there are no data regarding their effectiveness in human botulism.
- In some instances, the indications, dosages, and other information in this article are not consistent with current approved labeling by the US Food and Drug Administration (FDA). The recommendations on use of drugs and vaccine for uses not approved by the FDA do not represent the official views of the FDA nor of any of the federal agencies whose scientists participated in these discussions. Unlabeled uses of the products recommended are noted in the sections of the original guideline document in which these products are discussed. Where unlabeled uses are indicated, information used as the basis for the recommendation is discussed.
- The views, opinions, assertions, and findings contained herein are those of the authors and should not be construed as official US Department of Defense or US Department of Army positions, policies, or decisions unless so designated by other documentation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Safety
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Arnon SS, Schechter R, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Fine AD, Hauer J, Layton M, Lillibridge S, Osterholm MT, O'Toole T, Parker G, Perl TM, Russell PK, Swerdlow DL, Tonat K. Botulinum toxin as a biological weapon. In: Henderson DA, Inglesby TV, O'Toole T, editor(s). Bioterrorism : guidelines for medical and public health management. Chicago (IL): American Medical Association; 2002. p. 141-65. [109 references]

Arnon SS, Schechter R, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Fine AD, Hauer J, Layton M, Lillibridge S, Osterholm MT, O'Toole T, Parker G, Perl TM, Russell PK, Swerdlow DL, Tonat K. Botulinum toxin as a biological weapon: medical and public health management. JAMA 2001 Feb 28;285(8):1059-70. [106 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Feb 28 (addendum published 2002)

GUIDELINE DEVELOPER(S)

Center for Biosecurity - Academic Institution

GUIDELINE DEVELOPER COMMENT

The working group included 23 representatives from academic, government, and private institutions with expertise in public health, emergency management, and clinical medicine, including:

- Infant Botulism Treatment and Prevention Program and Viral and Rickettsial Diseases Laboratory, California Department of Health Services, Berkeley
- Center for Civilian Biodefense Strategies, Johns Hopkins University School of Medicine
- US Army Medical Research Institute of Infectious Diseases
- Bureau of Communicable Disease, New York City Health Department
- Science Applications International Corp
- Centers for Disease Control and Prevention
- Infection Control Advisory Network Inc.
- Office of Emergency Preparedness, Department of Health and Human Services

SOURCE(S) OF FUNDING

Funding for this study primarily was provided by each participant's institution or agency. The Johns Hopkins Center for Civilian Biodefense Strategies provided travel funds for 6 members of the group.

GUIDELINE COMMITTEE

Working Group on Civilian Biodefense

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors of the Original Guideline: Stephen S. Arnon, MD; Robert Schechter, MD; Thomas V. Inglesby, MD; Donald A. Henderson, MD, MPH; John G. Bartlett, MD; Michael S. Ascher, MD; Edward Eitzen, MD, MPH; Anne D. Fine, MD; Jerome Hauer, MPH; Marcelle Layton, MD; Scott Lillibridge, MD; Michael T. Osterholm, PhD, MPH; Tara O'Toole, MD, MPH; Gerald Parker, PhD, DVM; Trish M. Perl, MD, MSc; Philip K. Russell, MD; David L. Swerdlow, MD; Kevin Tonat, PhD, MPH; for the Working Group on Civilian Biodefense

Ex Officio Participants in the Working Group on Civilian Biodefense: George Counts, MD; Margaret Hamburg, MD; Stuart Nightingale, MD; Robert Knouss, MD; and Brian Malkin

Addendum Authors: Stephen S. Arnon, MD and Robert Schechter, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies of the original guideline: Available from the Journal of the American Medical Association Web site.

Full text available in:

- [HTML Format](#)
- [Portable Document Format \(PDF\)](#)

Print copies of the addended guideline: Available from the American Medical Association (AMA) Press by calling (800)621-8335 or by visiting www.amapress.com. Product Number: OP405502.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on November 1, 2001. The summary was updated by ECRI on February 12, 2003.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is copyrighted 2001 by the American Medical Association.

© 1998-2004 National Guideline Clearinghouse

Date Modified: 11/1/2004



