



Developed in cooperation with ASHP Advantage

Disclaimer:

Information is accurate as of print date, December 1, 2006.

The information presented herein reflects the opinions of the authors. It should not be interpreted as an official policy of ASHP or as an endorsement of any product.

Because of ongoing research and improvements in technology, the information and its application contained in this chart are constantly evolving and are subject to the professional judgment and interpretation of the practitioner due to the uniqueness of a clinical situation. The authors and the ASHP Research and Education Foundation have made reasonable efforts to ensure the accuracy and appropriateness of the information presented in this document. However, any user of this information is advised that the authors and the ASHP Research and Education Foundation are not responsible for the continued currency of the information, for any errors or omissions, and/or for any consequences arising from the use of the information in the document in any and all practice settings. Any reader of this document is cautioned that the ASHP Research and Education Foundation makes no representation, guarantee or warranty, express or implied as to the accuracy and/or appropriateness of the information contained in this document and specifically disclaims any liability to any party for the accuracy and/or completeness of the material or for any damages arising out of the use or non-use of any of the information contained in this document.

©2007, American Society of Health-System Pharmacists Research and Education Foundation. All rights reserved.

ASHP is a service mark of the American Society of Health-System Pharmacists, Inc.; registered to the U.S. Patent and Trademark Office.

POCKET REFERENCE

Treatments for Biological and Chemical Terrorism Agents

Check www.ashpfoundation.org for more information and updates.

Produced by:
ASHP Research and Education Foundation



Supported by an educational grant from Baxter



Treatments for Common Chemical Terrorism Agents

AGENT NAME	COMMON CLINICAL EFFECTS	ANTIDOTE OR PRIMARY TREATMENT	MEDICATION DOSE AND ADMINISTRATION	HIGH PRIORITY MONITORING PARAMETERS
NERVE AGENTS (e.g., Sarin, Tabun, Soman, VX, pesticides)	Cholinergic <u>Muscarinic</u> • Secretions (oral, bronchial, dermal) • Diarrhea/vomiting • Miosis • Bradycardia <u>Nicotinic</u> • Weakness • Muscle fasciculations In moderate to severe poisoning the patient may develop profound respiratory difficulty, coma and seizures.	Atropine Pralidoxime (2-PAM) Diazepam	<u>*Atropine (Muscarinic Effects)</u> • Children 0.05-0.1 mg/kg IV or IM • Adults 2-5 mg IV or IM <u>*Pralidoxime (Nicotinic Effects)</u> • Children 20-40 mg/kg IV • Adults 1-2 gm IV Administer over 15-30 minutes. <i>*Both are available for IM injection as part of the Mark 1 Autoinjector (atropine 2 mg and pralidoxime 600 mg)</i> <u>Diazepam (Seizures)</u> • Children 0.2-0.5 mg/kg IV or IM • Adults 5-10 mg IV or IM Repeat every 5-10 minutes as needed to control seizures.	Pupil size should not be used to monitor the effectiveness of therapy. Decreased secretions and restoration of cardiovascular and respiratory homeostasis are the best indicators of success following atropine administration. Cessation of muscular fasciculations is an indicator of pralidoxime effectiveness. Some patients may require additional doses of these medications for initial stabilization or for maintenance therapy.
CYANIDE (e.g., KCN, NaCN, HCN)	• Insidious onset to rapid collapse • Headache, fatigue, agitation, confusion • Hypertension → hypotension, dysrhythmias • Metabolic acidosis • Nausea, vomiting • Seizures • CV arrest	Cyanide Antidote Kit • Amyl nitrite • Sodium nitrite • Sodium thiosulfate Hydroxocobalamin* <i>*Hydroxocobalamin was being considered for approval by the FDA at the time of this printing.</i>	<u>Cyanide Antidote Kit</u> • Amyl nitrite—inhaler 30 seconds of every minute while IV access is being obtained. • Sodium nitrite <u>Children</u> —0.15–0.33 ml/kg IV <u>Adults</u> —300 mg IV Administer over 5-15 minutes. • Sodium thiosulfate <u>Children</u> —1.65 ml/kg of a 25% solution <u>Adults</u> —12.5 gm IV Administer over at least 10 minutes. <u>Hydroxocobalamin*</u> • Children—70mg/kg IV-off-label, unapproved • Adults—5 gm IV Administer over 30 minutes.	Nitrite administration may cause hypotension. Nitrites may produce elevated methemoglobin concentrations which could be a co-morbid factor in patients with pre-existing CV disease. If the terrorism event involves smoke inhalation, carbon monoxide (CO) poisoning may be present. The concurrent use of nitrites in a CO poisoned patients is a relative contraindication. The sole use of sodium thiosulfate should be considered. Hydroxocobalamin therapy may cause transient hypertension. Hydroxocobalamin will cause pink to red discoloration of the skin and urine and persist for several days.
NITROGEN MUSTARD	• Mucous membrane irritation-ocular and respiratory • Respiratory difficulty • Dermal irritation-initially a sunburn-like appearance • Blister formation-small blisters may coalesce to form very large blisters	No antidote	Supportive care, decontamination of affected areas and burn therapy for affected skin.	Protect the airway and prevent microbial infection of affected areas.
CHLORINE & PHOSGENE	• Mucous membrane irritation—ocular and respiratory • Respiratory difficulty—coughing, choking • Dermal irritation	No antidote	Supportive care and decontamination of affected areas.	Protect the airway, maintain oxygenation, anticipate bronchospasm and delayed pulmonary edema.

For 24/7 assistance in the emergency management of an actual or suspected chemical terrorism exposure, contact a Regional Poison Information Center at 1-800-222-1222.

Edward P. Krenzelo, PharmD, FAAC, DABAT
Director, Pittsburgh Poison Center,
University of Pittsburgh Medical Center
Professor of Pharmacy and Pediatrics, University of Pittsburgh
Pittsburgh, Pennsylvania

Treatments for Bioterrorism Category A Agents (Adults)

Agent	Common Clinical Effects	Treatment (symptomatic)	Post-exposure Prophylaxis (prevention)	Vaccination ¹	Comments
Anthrax (<i>Bacillus anthracis</i>)	<p>Based on route of exposure:</p> <p>Inhalational Anthrax Myalgias, fever, dysphagia, headache and cough (can mimic a common cold). Symptoms can progress to shortness of breath, hypoxia, respiratory failure and shock.</p> <p>Cutaneous Anthrax Pruritic macular/papular rash that evolves to vesicles and necrotic ulcers. Blackened eschar will develop (often painless). Can also develop fever, myalgias and lymphadenopathy</p> <p>Intestinal Anthrax Sore throat, nausea, vomiting, bloody diarrhea and lymphadenopathy</p>	<p>Duration: 60 days</p> <p>Life-threatening (inhalational, systemic or serious cutaneous)</p> <p>Ciprofloxacin 400 mg IV q12h or Doxycycline 200 mg IV, then 100 mg IV q12h or Levofloxacin 500-750 mg IV daily or Gatifloxacin 400 mg IV daily</p> <p>plus 1-2 additional: ampicillin, chloramphenicol, clindamycin, imipenem, linezolid, meropenem, macrolide, penicillin, rifampin, vancomycin</p> <p>Supportive therapy (aggressive and early) for shock, fluid volume deficit, and adequacy of airway may be indicated</p>	<p>Duration: minimum of 60 days after last exposure</p> <p>Ciprofloxacin 500 mg PO q12h or Doxycycline 100 mg PO q12h or Levofloxacin 500 mg PO daily or Gatifloxacin 400 mg PO daily</p>	<p>Pre-exposure prophylaxis: Anthrax Vaccine Adsorbed 0.5ml SC at 0, 2, 4 wks, 6, 12, 18 mos with annual booster, as indicated</p> <p>Post-exposure prophylaxis: Anthrax Vaccine Adsorbed 0.5ml SC at 0, 2, 4 wks post-exposure (IND³).</p> <p>Vaccine is not readily available to general public and mass vaccination is not practical.</p>	<p>Pregnancy and immunocompromised: same recommendations.</p> <p>Cutaneous anthrax treatment: fluoroquinolone or doxycycline for 60 days.</p> <p>Modify antimicrobials (treatment and post-exposure prophylaxis) as indicated by susceptibility testing.</p> <p>Treatment: change from IV to PO when clinically appropriate. Consultation with ID specialist advised.</p>
Botulinum toxins (<i>Clostridium botulinum</i>)	Fatigue, weakness and vertigo, followed by blurred vision and progressive difficulty in speaking and swallowing. Other common symptoms: difficulty in breathing, weakness of other muscles, abdominal distention, and constipation.	<p>Type-specific antitoxin administered per product insert; usual dose: 10ml vial (diluted 1:10 in 0.9% saline) slow IV infusion</p> <p>Risk of anaphylaxis to equine antigens requires skin test +/- desensitization before antitoxin administration.</p>	None; observe/monitor for signs and symptoms	Pentavalent toxoid vaccine (A-E) for high risk individuals; pre-exposure prophylaxis (IND ³).	<p>Antitoxins may also cause serum sickness.</p> <p>Antitoxin comes with diluent and information about skin testing and desensitization.</p>
Plague (<i>Yersinia pestis</i>)	<p>Bubonic Plague Chills, fever, myalgias, arthralgias, headache, weakness, tenderness/pain in affected lymph node (femoral, inguinal, axillary, etc.), bubo formation</p> <p>Septicemic Plague Absence of typical bubo; nausea, vomiting, diarrhea, then rapid, fulminant septic shock, DIC, bleeding into skin and other organs</p> <p>Pneumonic Plague Fever, chills, myalgias, headache, weakness, cough, chest pain, hemoptysis, rapidly progressive respiratory failure</p>	<p>Duration: 10 days or until afebrile for 2-3 days, whichever is longer</p> <p>Plague pneumonia: Streptomycin 15 mg/kg (max. 1 g) IM q12h or Gentamicin 2 mg/kg load, 1.7 mg/kg IV/IM q8h (or 5 mg/kg once daily) or Ciprofloxacin, Levofloxacin, Gatifloxacin or Doxycycline IV (see doses under anthrax section) or Chloramphenicol 25 mg/kg IV q6h</p> <p>Plague meningitis: Chloramphenicol IV 25 mg/kg load, then 12.5 mg/kg q6h</p>	<p>Duration: 7 days after last exposure</p> <p>Ciprofloxacin 500 mg PO q12h or Doxycycline 100 mg PO q12h or Levofloxacin 500 mg PO daily or Gatifloxacin 400 mg PO daily</p> <p>Alternatives: Chloramphenicol 25 mg/kg PO q6h or Tetracycline 500 mg PO q6h</p>	<p>Former vaccine no longer available.</p> <p>New vaccine under development.</p>	<p>Treatment with doxycycline may need longer duration of therapy (10-14 days.)</p> <p>Adjust aminoglycoside dose for renal function; optimal dosing should be determined by blood concentrations.</p>
Small pox (<i>Variola major</i>)	Initial symptoms: fever, malaise, headache, backache, sometimes vomiting, and occasionally mental confusion. Later rash emerges in mouth, then spreads to face, arms and legs (including hands and feet), and to the rest of the body. Initial rash: raised bumps filled with a thick fluid, often with a depression in the center.	Supportive care! Cidofovir (IND ³): <i>in vitro</i> data only.	<p>Commence mass vaccination</p> <p>Vaccinia vaccine effective in preventing or ameliorating infection if given within 96 hours of exposure.</p> <p>Vaccinia immune globulin (VIG) 100 mg/kg (2 ml/kg) IV (within 3 days of exposure; best within 24 hrs.)</p> <p>Limited info with VIG ± vaccine for post-exposure.</p>	<p>Review contraindications and precautions prior to smallpox vaccination (refer to most recent ACIP recommendations.)</p> <p>VIG is indicated for certain vaccine complications and vaccinia exposures in immunocompromised persons (www.cdc.gov)</p> <p>VIGIM-IND³ VIGIV-licensed; peds and elderly-IND³</p>	<p>VIGIV infusion: 1 ml/kg/hr for 30 min. then 2 ml/kg/hr for 30 min. then 3 ml/kg/hr for remainder.</p> <p>Ribavirin- treatment option (<i>in vitro</i> data only)</p>
Tularemia (<i>Francisella tularensis</i>)	<p>Aerosol dissemination Sudden fever, chills, headaches, muscle aches, joint pain, dry cough, progressive weakness, and pneumonia.</p> <p>Other routes of exposure Ulcers on the skin or mouth, swollen and painful lymph glands, swollen and painful eyes, and a sore throat.</p>	<p>Duration: streptomycin, gentamicin or fluoroquinolone: 10-14 days; Doxycycline or chloramphenicol: 14-21 days</p> <p>Streptomycin 1 gm IM q12h or Gentamicin 5 mg/kg IV/IM daily or Ciprofloxacin, Levofloxacin or Gatifloxacin IV daily or Doxycycline 100 mg IV q12h or Chloramphenicol 15 mg/kg IV q6h</p>	<p>Duration: 14 days after last exposure</p> <p>Ciprofloxacin 500 mg PO q12h or Doxycycline 100 mg PO q12h or Levofloxacin 500 mg PO daily or Gatifloxacin 400 mg PO daily</p>	<p>Former vaccine no longer available.</p> <p>New vaccine under development.</p>	N/A
Viral hemorrhagic fevers* (<i>filoviruses, arenaviruses, bunyaviruses</i>)	<p>Based on route of exposure and particular organism involved.</p> <p>Myalgias, fever, headache, nausea, vomiting, abdominal pain, dizziness with progression to shock and multifocal bleeding. Clinical findings may include: conjunctival suffusion, petechiae, jaundice, orthostatic hypotension and hemoconcentration.</p>	<p>Duration of therapy: 10 days Empiric treatment with ribavirin before identification may be appropriate.</p> <p>Arenavirus or bunyaviruses: Ribavirin (IND³) 30 mg/kg IV load, then 16 mg/kg IV q6h x 4 days then, 8 mg/kg IV q8h x 6 days</p> <p>Filoviruses: Supportive care</p>	<p>High risk contacts (arenavirus or bunyavirus): Ribavirin PO 500 mg q6h x 7 days</p> <p>Observe/monitor for signs and symptoms of illness.</p>	<p>Yellow Fever vaccine only VHF vaccine available.</p>	<p>Supportive care: fluids (watch pulmonary edema), vasopressors, APAP (for fever.)</p> <p>Contraindicated: IM injections, NSAIDs/ASA and anticoagulants. Ribavirin: pregnancy category X.</p> <p>Ribavirin may have activity against West Nile Virus (flavivirus).</p>

1. Currently no vaccines commercially available to the general public; 2. SNS- Strategic National Stockpile program (CDC)- availability of drugs may change in future;
3. IND- investigational new drug *Filoviruses: Ebola, Marburg; Arenaviruses: Lassa Fever, Machupo, Junin, Guanarito, Sabia; Bunyaviruses: Rift Valley Fever, Congo-Crimean hemorrhagic fever, hantaviruses; Flaviviruses: Yellow fever, Dengue, Omsk hemorrhagic fever, Kyansur Forest disease, West Nile Virus.

References

- Brouillard JE et al. Antibiotic selection and resistance issues with fluoroquinolones and doxycycline against bioterrorism agents. *Pharmacotherapy*. 2006;26:3-14.
- Centers for Disease Control and Prevention [Internet]. Accessed 2006 Oct. Available from <http://www.bt.cdc.gov>
- Clinical Pharmacology [Internet]. Tampa, FL: Gold Standard; 2006 [accessed 2006 Oct]. Available from <http://www.clinicalpharmacology.com>
- JAMA Consensus Statements:
 - Inglesby TV et al. Anthrax as a biological weapon, 2002. Update recommendations for management. *JAMA*. 2002;287:2236-52.
 - Arnon SS et al. Botulinum toxin as a biological weapon. *JAMA*. 2001; 285:1059-70.
 - Inglesby TV. Plague as a biological weapon. *JAMA*. 2000;283:2281-90.
 - Henderson DA. Smallpox as a biological weapon. *JAMA*. 1999;282:2127-37.
 - Dennis DT et al. Tularemia as a biological weapon. *JAMA*. 2001;285:2763-73.
 - Borio L et al. Hemorrhagic fever viruses as biological weapons. *JAMA*. 2002;287:2391-2405.
- USAMRIID Medical Management of Biological Casualties Handbook. Fifth edition. August 2004. (www.usamriid.army.mil/education/bluebook.htm)

Colleen M. Terriff, Pharm.D.
Clinical Associate Professor
Washington State University College of Pharmacy
Deaconess Medical Center
Spokane, Washington

Check www.ashpfoundation.org for more information and updates.