

***Bacillus anthracis* (Anthrax)**

Background

Anthrax is a disease caused by the bacterium *Bacillus anthracis*. This bacterium exists in nature in two forms: vegetative and spore. A spore is a tough, dormant form that persists for long periods of time (even years or decades) in the environment. When it enters a human or animal host, both of which provide an environment rich in sugars and amino acids, an anthrax spore becomes a vegetative cell that leads to disease.

In nature, anthrax primarily affects herbivorous mammals such as cattle, sheep, goats, and wild animals.^{1,2} According to the World Health Organization (WHO), anthrax is endemic to animals in much of sub-Saharan Africa and Asia, as well as in some southern European countries, parts of the Americas, and some regions in Australia. Epidemics in animals also occur sporadically in other countries around the world. Human infection with anthrax occurs less frequently.³

There are three forms of naturally occurring human anthrax infection:

- **Inhalational anthrax** is the result of breathing *B. anthracis* spores into the lungs. Inhalational infection is the form of the disease that would be of most concern following an intentional aerosol attack with *B. anthracis*.
- **Cutaneous anthrax** is the result of spores entering the body through small breaks in the skin. This form of the disease is characterized by a sore at the point of infection that develops into a painless ulcer known as a black eschar. Cutaneous anthrax disease could also occur as a result of an aerosol attack.
- **Gastrointestinal anthrax** occurs as a result of eating food (typically meat) contaminated with *B. anthracis*. With GI anthrax, the intestinal tract may be infected, or the mouth or throat (oropharyngeal anthrax).²

Anthrax as a Biological Weapon

Anthrax is currently considered one of the most serious bioterrorism threats. Beginning in the second half of the 20th Century, anthrax was developed by several countries (including the Soviet Union and the United States) as part of their biological weapons (BW) programs. Since that time, the U.S., Russia, and many other countries have discontinued offensive BW programs. However, some programs still may be in operation.^{1,2}

Autonomous groups have also demonstrated an intent to use anthrax in acts of terrorism. For example, as evidenced in a March 10, 2007, Department of Defense transcript of the Tribunal Hearing of Khalid Sheikh Muhammad, Al Qaeda leadership has shown interest in and has worked to develop anthrax and other biological weapons.⁴ Most notably, in October 2001, anthrax attacks were perpetrated in the U.S. via the mail, when seven envelopes containing *B. anthracis* spores were sent through the U.S. postal system (4 were recovered). All of the letters were presumed to have been mailed from Trenton, New Jersey. Twenty-two cases of anthrax resulted (11 inhalational, 11 cutaneous), and 5 people died from inhalational anthrax. In the summer of 2008, the investigation into the origin of the attacks focused on Dr. Bruce Ivins, an anthrax researcher at USAMRIID. However, he committed suicide before charges could be filed. (See Transcript of Amerithrax Investigation Press Conference, August 8, 2008, <http://www.usdoj.gov/opa/pr/2008/August/08-opa-697.html>)

A number of factors contribute to concern about the use of anthrax as a biological weapon:

- There is widespread availability of *B. anthracis* in microbe banks around the world
- There is widespread natural availability of *B. anthracis* in endemic areas
- There is evidence that techniques for mass production and aerosol dissemination of anthrax have been developed
- The robustness of anthrax spores in the environment make anthrax easier to weaponize for aerosol dissemination
- Untreated inhalational anthrax has a high fatality rate
- Anthrax has a very low infectious dose: based on animal data, estimates of infectivity via the respiratory route suggest that as few as 1 to 3 spores may cause infection
- Antibiotic-resistant strains of *B. anthracis* exist in nature and may be used in an intentional release
- Anthrax has been used recently as a biological weapon.²

A 1970 analysis by the WHO (updated in 2004) concluded that the release of aerosolized anthrax upwind of a population of 5,000,000 could lead to an estimated 250,000 casualties, of whom as many as 100,000 could be expected to die.⁵

A later analysis in 1993 by the Office of Technology Assessment of the U.S. Congress estimated that 130,000 to 3 million deaths could occur following the release of 100 kilograms of aerosolized anthrax over Washington, DC, making such an attack as lethal as a hydrogen bomb.⁶ (See “The History of Bioterrorism: Anthrax,” a short video from the Centers for Disease Control and Prevention [CDC]: <http://emergency.cdc.gov/training/historyofbt/02anthrax.asp>)

Signs and Symptoms

Diagnosis of anthrax is based on clinical presentation of symptoms, confirmed by laboratory testing. There are a number of rapid diagnostic tests for identifying anthrax at reference laboratories, but none is available widely. The first sign of a bioterrorist attack with anthrax most likely would be a sudden surge of patients presenting with symptoms of severe pneumonia and sepsis at hospitals and doctors’ offices.¹

Transmission

Humans may contract anthrax following contact with infected animals or contaminated animal products or by breathing in an aerosolized form of the bacteria following the intentional release of anthrax spores. Anthrax is *not* transmitted from person to person.¹

Infection Control Measures

Because anthrax is not passed from person to person, it is not necessary to take airborne or droplet precautions when in close proximity to an infected individual, and there is no need to provide prophylaxis to close contacts of an infected patient.¹

Treatment

Early antibiotic treatment of anthrax is vital, as delay decreases a victim’s chance for survival. Although ciprofloxacin, doxycycline, and penicillin are currently the only FDA-approved antibiotics for the treatment of anthrax, it is believed that other antibiotics would be effective as well.⁷ In an emergency, public health authorities will make recommendations for treatment based on laboratory susceptibility testing. A regimen containing ciprofloxacin or doxycycline is recommended as first line treatment until susceptibility information is available. Combination therapy with additional antibiotics is recommended for treatment of both inhalational and cutaneous anthrax. Cutaneous anthrax is typically treated with antibiotics for 7 to 10 days. However, according to the *MMWR* from October 26, 2001, in a bioterrorism attack, the “risk of simultaneous aerosol exposure” may be elevated, and it is recommended that patients with either cutaneous or inhalational anthrax continue antibiotic therapy for 60 days.⁷

Clinical Presentation of Anthrax^{1,2}

Anthrax Infection	Incubation Period	Signs and Symptoms	Lethality
Inhalational	Ranges from as little as 2 days following exposure to spores to 6 to 8 weeks after exposure	Initial symptoms are fever, headache, and muscle aches. If untreated, the disease progresses to shortness of breath, fatigue, chest discomfort, shock, and death. Meningitis may complicate the clinical course. Chest imaging reveals a widening of the mediastinum (the area between the lungs that contain the large vessels, heart, trachea, esophagus, bronchi, and lymph nodes).	Historical data suggest that if appropriate antibiotics are not started before development of symptoms, the mortality rate may be greater than 90%. However, in the U.S. anthrax attacks of 2001, 45% of persons with inhalational anthrax died despite supportive therapy.
Cutaneous	Range of 1 to 12 days following exposure; incubation period is typically closer to 1 day	The first symptom is a small sore at the point of infection that develops into a blister and later into an ulcer known as a black eschar. This ulcer is painless and has a depressed, black center.	Approximately 20% of persons with cutaneous anthrax may die if not treated with appropriate antibiotics. With appropriate antibiotic treatment, the death rate is approximately 1%.
Gastrointestinal	Typically 1 to 6 days following exposure	Oropharyngeal: Fever, ulcers in the back of the mouth and throat, severe sore throat, difficulty swallowing, and lymph node and neck swelling Intestinal: Initial symptoms are nausea, vomiting, and malaise. The disease may progress rapidly to bloody diarrhea, abdominal pain, and shock.	Without antibiotic treatment, gastrointestinal anthrax results in the death of more than 40% of affected persons.

Prophylaxis

Post-exposure prophylaxis should begin immediately in persons deemed exposed to anthrax spores, and should not be delayed until symptoms emerge. If susceptibility of the *B. anthracis* strain is unknown, initial therapy with ciprofloxacin or doxycycline is recommended for adults and children, or levofloxacin for adults. Once started, antibiotic therapy should be continued for 60 days post-exposure if used alone, or for at least 30 days post-exposure if used in combination with vaccine, which can also be used for post-exposure prophylaxis. A 3-dose post-exposure anthrax vaccine regimen (at 0 weeks, 2 weeks, and 4 weeks) is recommended by the CDC, in conjunction with antibiotics.⁸

Decontamination

The greatest risk of anthrax infection occurs during the period when spores are first aerosolized (primary aerosolization). After this primary period, *B. anthracis* spores will settle on the ground and other surfaces, possibly in high concentrations, at which point there is a risk that *B. anthracis* may become airborne again (secondary aerosolization). Re-aerosolization depends on a number of variables:

- Concentration of spores present
- Type of surface where spores land
- Type of movement in the area that could disturb spores (ie, wind, foot traffic, indoor air movement/ventilation, etc.).¹

Surfaces should be decontaminated to help eliminate the risk of secondary aerosolization, and this should be done in coordination with local health, public health, and environmental authorities. (See Occupational Safety and Health Administration Anthrax eTool, U.S. Department of Labor: <http://www.osha.gov/SLTC/etools/anthrax/decon.html>)

Countermeasures

Vaccine

Biothrax[®] Anthrax vaccine adsorbed (AVA) is produced by Emergent Biosolutions and is the only anthrax vaccine licensed by the FDA. While it is not for post-exposure use, the Advisory Committee on Immunization Practices (ACIP) has issued a provisional recommendation for a 3-dose treatment in post-exposure settings under an Investigational New Drug (IND) or potentially under an emergency use authorization (EUA).

AVA is a cell-free filtrate made from cultures of a strain of anthrax not capable of causing disease. A five-dose series is required for immunization, with booster shots annually. According to a 2007 GAO report, the Strategic National Stockpile (SNS) held 10 million doses of Biothrax. Emergent Biosolutions was under contract to deliver 18.75 million doses

by September 2010 and secured another contract to deliver 14.5 million more doses to the SNS by late 2011. The shelf life of Biothrax is 4 years.

SparVax[™] is a recombinant protective (rPA) anthrax vaccine made by PharmAthene that requires only 3 doses to induce protective immunity. Phase I and Phase II trials have been completed; in preclinical testing, SparVax protected rabbits and non-human primates against lethal aerosol anthrax spore challenge. In December 2009, the Department of Health and Human Services canceled its request for proposals for rPA vaccines because it did not believe that developers could have the product ready for licensure within 8 years; however, PharmAthene continues to advance its rPA work on an existing contract with HHS.

Antibiotics

There are enough antibiotics in the SNS to treat more than 40 million people.

Antitoxin

Anthrax Immune Globulin (AIG) antitoxin is a therapy derived from the plasma of individuals previously immunized with the anthrax vaccine. Patients already presenting with symptoms of anthrax infection can be treated with AIG. Cangene Corporation, a Canadian company, has delivered 10,000 doses of AIG to the SNS. Emergent Biosolutions also has an AIG product under development.

Raxibacumab (ABthrax), a human monoclonal antibody developed by Human Genome Sciences (HGS), targets anthrax toxins after they have been released by anthrax bacteria, when antibiotics might not be effective. HGS has already delivered an initial 20,000 doses of Raxibacumab to the SNS and has begun delivery on second order of 45,000 doses. Delivery to the U.S. government is to be completed by the end of 2012. However, after HGS requested FDA certification for Raxibacumab, the FDA questioned the efficacy of the drug, and in November 2009, withheld approval.

Anthim[™] is an anthrax anti-toxin developed by Elusys Therapeutics, Inc., that is indicated for pre- and post- exposure prophylaxis as well as treatment of active inhalational anthrax disease. This high-affinity deimmunized monoclonal antibody targets anthrax toxin protective antigen and neutralizes the toxin before it interacts with target cells. The therapy received fast track and orphan drug status from the FDA, is in late stage development, and has entered into a manufacturing agreement with Lonza Sales AG.

Valortim[®] is an anthrax antitoxin developed by Medarex and PharmAthene designed to protect against inhalational anthrax. This fully human monoclonal antibody protects cells from the damaging effects of anthrax toxins by targeting anthrax

protective antigen. It can provide protection even after toxins have attached to a cell. In preclinical studies on rabbits and non-human primates, Valortim[®] was effective pre- and post-

exposure. Medarex has completed a Phase I clinical trial and has entered into an agreement with PharmAthene to jointly complete clinical development and commercialize Valortim.[®]

References

1. Inglesby TV, O'Toole T, Henderson DA, et al., for the Working Group on Civilian Biodefense. Anthrax as a biological weapon, 2002: updated recommendations for management. *JAMA*. 2002;287:2236-225.
2. Inglesby TV, Henderson DA, Bartlett JG, et al., for the Working Group on Civilian Biodefense. Anthrax as a biological weapon: medical and public health management. *JAMA*. 1999;281:1735-1745.
3. Anthrax fact sheet. World Health Organization (WHO) October 2001. <http://www.who.int/mediacentre/factsheets/fs264/en>. Accessed September 10, 2007.
4. Verbatim transcript of combatant status review tribunal hearing for ISN 10024. Department of Defense. (pg. 17) http://www.defenselink.mil/news/transcript_ISN10024.pdf. Accessed October 31, 2007.
5. Health aspects of chemical and biological weapons, 1st edition. World Health Organization, United Nations. 1970. <http://www.who.int/csr/delibepidemics/biochem1stenglish/en/index.html>. Accessed September 25, 2007.
6. Office of Technology Assessment, U.S. Congress. *Proliferation of Weapons of Mass Destruction*. Washington, DC: U.S. Government Printing Office. 1993;53-55. Publication OTA-ISC-559.
7. Update: investigation of bioterrorism-related anthrax and interim guidelines for exposure management and antimicrobial therapy, October 2001. *MMWR*. October 26, 2001;50(42):909-919.
8. Anthrax Q&A: preventive therapy. U.S. Centers for Disease Control and Prevention. Last Modified March 25, 2005. <http://www.bt.cdc.gov/agent/anthrax/faq/preventive.asp>. Accessed October 31, 2007.
9. Emergent BioSolutions completes first delivery of BioThrax[®] (anthrax vaccine adsorbed) to the Department of Health and Human Services under new contract [news release]. Rockville, MD: Emergent BioSolutions; October 2, 2007.
10. Government Accountability Office. *Project BioShield: Actions Needed to Avoid Repeating Past Problems with Procuring New Anthrax Vaccine and Managing the Stockpile of Licensed Vaccine*. GAO Report to Congressional Requesters. October 23, 2007. <http://www.gao.gov/new.items/d0888.pdf>. Accessed October 31, 2007.
11. Borio L, Gronvall GK. Anthrax countermeasures: current status and future needs. *Biosecurity Bioterrorism*. 2005;3(2).
12. Statement of Gerald W. Parker, Principal Deputy to the Assistant Secretary Office of Public Health Emergency Preparedness U.S. Department of Health and Human Services on *Anthrax Preparedness: HHS Progress* before Committee on Government Reform Subcommittee on National Security, Emerging Threats, and International Relations. 109th Congress. May 9, 2006. <http://www.hhs.gov/asl/testify/t060509a.html>. Accessed October 31, 2007.
13. U.S. government agrees to purchase ABthrax[™] from Human Genome Sciences for the Strategic National Stockpile [news release]. Rockville, MD: Human Genome Sciences; June 20, 2006.
14. Anthrax Immune Globulin (AIG) – therapeutic product candidate Web page. Emergent BioSolutions. <http://www.emergentbiosolutions.com/AIG>. Accessed October 31, 2007.

See Also

Amerithrax fact sheet. Federal Bureau of Investigation (FBI), September 2006. http://www.fbi.gov/anthrax/amerithrax_factsheet.htm. Accessed October 2007.

Anthrax information Web page. Centers for Disease Control and Prevention, Emergency Preparedness and Response. <http://web.archive.org/web/20051222222657/www.bt.cdc.gov/agent/anthrax/index.asp>. Accessed October 10, 2007.

Deitch S. House committee concerned about timeline for acquisition of anthrax countermeasures. *Biosecurity Briefing*. September 14, 2007. http://www.upmc-biosecurity.org/website/biosecurity_briefing/archive/countmeasr_dev/content/2007/2007-09-14-housecomtimeanthraxcounter.html. Accessed September 21, 2007.

Anthrax Web page. National Institute of Allergy and Infectious Disease, National Institutes of Health. December 2005. <http://www.niaid.nih.gov/factsheets/anthrax.htm>. Accessed October 10, 2007.

Visual Dx: Visual clinical decision support software. <http://www.logicalimages.com/resourcesBTAgents.htm>. Accessed October 11, 2007.

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