

Fact Sheet

Bacillus anthracis (Anthrax)

Background

Anthrax is a disease caused by the bacterium *Bacillus anthracis*. This bacterium exists in nature in two forms: as an active growing cell (called the vegetative form) or as a dormant spore. The spores are very hardy and tolerant to extremes of temperature, humidity, and ultraviolet light. They can survive for long periods of time (even decades) in the environment without nutrients or water. When a spore enters a mammal host, the internal environment of the host—rich in water, sugars and amino acids—induces that spore to germinate into a vegetative cell that leads to disease.

In nature, anthrax primarily affects herbivorous mammals such as cattle, sheep, and goats.¹ According to the World Health Organization (WHO), anthrax is enzootic in animal populations 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. Outbreaks in animals also occur sporadically in other countries around the world. Human cases of anthrax are much less frequent.²

There are 4 forms of naturally occurring human anthrax infection:

- **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 covered by a black scab (eschar). Cutaneous anthrax accounts for approximately 95% of all reported human anthrax cases. Cutaneous anthrax could also occur as a result of an aerosol attack.
- **Gastrointestinal anthrax** typically occurs as a result of eating the meat of animals infected with *B. anthracis*. The intestinal tract, mouth, or throat (oropharyngeal anthrax) may be infected.¹ GI anthrax is normally thought to occur as a result of ingestion of vegetative bacteria rather than spores; therefore, GI anthrax is not expected to result from exposure to aerosolized spores.
- **Inhalational anthrax** is the result of breathing *B. anthracis* spores into the lungs. Inhalational infection is the form of anthrax that would be of most concern following an intentional aerosol attack with *B. anthracis*.
- **Injection related anthrax** is a newly recognized entity. A number of cases have occurred recently in Europe in intravenous drug users. This is believed to be caused by injecting heroin that is contaminated with material containing *B. anthracis* spores.³

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, *B. anthracis* was developed by several countries as part of their biological weapons (BW) programs. Autonomous groups have also demonstrated intent to use *B. anthracis* 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 In 1993, the Japanese cult, Aum Shinrikyo, sprayed aerosols containing *B. anthracis* several times in attempted terrorist attacks in Tokyo. Fortunately, the material they used turned out to be ineffective, and consequently no one was sickened.⁵ Most notably, in October 2001, anthrax attacks were perpetrated in the U.S. via the mail, when 7 envelopes containing *B. anthracis* spores were sent through the U.S. postal system (4 were recovered). Twenty-two cases of anthrax resulted (11 inhalational, 11 cutaneous), and 5 people died from inhalational anthrax. In 2009, the FBI closed its investigation into the origin of the attacks concluding that Dr. Bruce Ivins, an anthrax researcher at U.S. Army Medical Research Institute of Infectious Diseases had perpetrated the attack.⁶ However, Dr. Ivins committed suicide before charges could be filed; therefore, the case was never tried. Other organizations have questioned the FBI's conclusion.⁷

Several factors contribute to concern about the potential use of *B. anthracis* 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 hardiness of anthrax spores in the environment may make anthrax aerosol dissemination more effective than many other potential agents.
- Untreated inhalational anthrax has a high fatality rate.
- Antibiotic-resistant strains of *B. anthracis* exist in nature and could be used in an intentional release.
- Anthrax has been used in the past as a biological weapon.¹

An 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 *B. anthracis* over Washington, DC, making such an attack as lethal as a hydrogen bomb.⁸ (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>.)

Diagnosis

The diagnosis of naturally occurring anthrax should be considered if there are symptoms and signs consistent with the disease and a history of contact with sick animals or animal skins, or travel to an area where anthrax is endemic. The expected hallmark of the use of an anthrax weapon would be a sudden surge of patients presenting with symptoms of severe pneumonia and sepsis. The physical signs of cutaneous anthrax are often quite characteristic if the clinician is attuned of them. The radiographic signs of inhalational anthrax may also be quite distinct in a patient with a clinical presentation consistent with the diagnosis.

Clinical Presentation of Anthrax¹

Anthrax Infection	Incubation Period	Signs and Symptoms	Lethality
Inhalational	Ranges from as little as 2 days following exposure to spores to as long as 6 to 8 weeks after exposure	Initial symptoms are fever, headache, and muscle aches. If untreated, the disease progresses to shortness of breath, chest discomfort, shock, and death. Meningitis may complicate the clinical course. Chest imaging reveals widening of the mediastinum, enlargement of and bleeding into lymph nodes, and bloody fluid collections around the lungs.	Historical data suggest that the case fatality rate of untreated inhalational anthrax may be as high as 90%. With appropriate treatment, a fatality rate of approximately 50% or less may be expected.
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 a painless ulcer covered by a black scab. Often there is marked swelling around the ulcer.	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: Symptoms are 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 and vomiting. 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. ¹⁰
Injection related	1-2 days after injection	Inflammation or abscess at the injection site sometimes progressing to cellulitis or necrotizing fasciitis. Some patients progress to sepsis without extensive local infection	Of 14 reported cases, 7 patients died despite aggressive medical therapy.

B. anthracis grows quickly and easily in routine culture. In addition, there are a number of rapid diagnostic tests for identifying anthrax at reference laboratories, but none is available widely in ordinary hospital laboratories.¹

Transmission

Humans may contract anthrax following contact with infected animals or contaminated animal products, or by breathing in aerosolized 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, levofloxacin, doxycycline, and penicillin are currently the

only FDA-approved antibiotics for the treatment of anthrax, other antibiotics would be effective as well.⁸ 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. Naturally occurring cutaneous anthrax is typically treated with antibiotics for 7 to 10 days. However, in an aerosol bioterrorism attack, patients with cutaneous anthrax may also have had an inhalational exposure that could lead to coincident inhalational anthrax; therefore, it is recommended that patients with either cutaneous or inhalational anthrax in the setting of bioterrorism continue antibiotic therapy for 60 days.⁹

Prophylaxis

Post-exposure prophylaxis should begin immediately in persons suspected of exposure to *B. anthracis* 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. 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.⁹

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). However, the extent to which re-aerosolized spores are infectious is not known. Re-aerosolization depends on a number of variables:

- Concentration of spores present,
- Type of surface where spores land, and
- 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.¹¹

Countermeasures

Vaccine

BioThrax[®] Anthrax Vaccine Absorbed (AVA) is produced by Emergent BioSolutions, Inc., and is the only anthrax vaccine licensed by the FDA. While it is not FDA-approved 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 5-dose series is required for immunization, with annual boosters.¹²

SparVax[™] is a recombinant protective (rPA) anthrax vaccine made by PharmAthene, Inc., 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 nonhuman primates against lethal aerosol anthrax spore challenge.¹³

Antitoxin

Anthrax Immune Globulin (AIG) antitoxin is a therapy derived from the plasma of individuals previously immunized with the anthrax vaccine. This investigational product consists of antibody directed against the anthrax protective antigen. Patients already presenting with symptoms of anthrax infection may be treated with AIG in addition to antibiotic therapy. AIG has been purchased for the CDC's Strategic National Stockpile and may be released for use in an emergency.¹⁴

Raxibacumab (ABthrax), a human monoclonal protective antigen-targeted antibody developed by Human Genome Sciences (HGS), targets anthrax toxins after they have been released by anthrax bacteria, when antibiotics might not be effective.¹⁵

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. <http://jama.ama-assn.org/content/287/17/2236.full?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=anthrax+consensus&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT>. Accessed September 20, 2011.
2. World Health Organization. Anthrax in humans and animals-4th ed 2008. http://www.who.int/csr/resources/publications/anthrax_webs.pdf. Accessed September 20, 2011.
3. Ramsay CN, Stirling A, Smith J, et al. An outbreak of infection with *Bacillus anthracis* in injecting drug users in Scotland. *Euro Surveill*. 2010;15(2):pii=19465. <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19465>. Accessed September 20, 2011.

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 September 20, 2011.
5. Danzig R, Sageman M, Leighton T, et al. Aum Shinrikyo: Insights Into How Terrorists Develop Biological and Chemical Weapons. Center for New American Security. 2011. <http://www.cnas.org/node/6703>. Accessed September 20, 2011.
6. Justice Department and FBI announce formal conclusion of investigation into 2001 anthrax attacks [news release]. Washington, DC: U.S. Department of Justice; February 19, 2010. <http://www.justice.gov/opa/pr/2010/February/10-nsd-166.html>. Accessed September 20, 2011.
7. Committee on Review of the Scientific Approaches Used During the FBI's Investigation of the 2001 *Bacillus Anthracis* Mailings; National Research Council. *Review of the Scientific Approaches Used During the FBI's Investigation of the 2001 Anthrax Letters*. The National Academies of Science. 2011. http://www.nap.edu/catalog.php?record_id=13098. Accessed September 20, 2011.
8. 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.
9. Stern E, Uhde K, Shadomy S, Messonnier N. Conference report on public health and clinical guidelines for anthrax. *Emerg Inf Dis* 2008;14(4) http://wwwnc.cdc.gov/eid/article/14/4/07-0969_article.htm. Accessed September 20, 2011.
10. Martin GJ, Friedlander AM. *Bacillus anthracis* (anthrax). In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010.
11. Occupational Safety and Health Administration Anthrax eTool, U.S. Department of Labor: <http://www.osha.gov/SLTC/etools/anthrax/decon.html>. Accessed September 20, 2011.
12. Emergent BioSolutions. Biothrax webpage. <http://biothrax.com>. Accessed September 20, 2011.
13. PharmAthene. SparVax webpage. <http://www.pharmathene.com/product-portfolio/sparvax-rpa-anthrax-vaccine>. Accessed September 20, 2011.
14. Gotten F. Project BioShield: Appropriations, Acquisitions, and Policy Implementation Issues for Congress. Congressional Research Service. June 11, 2007. <http://www.fas.org/sgp/crs/terror/RL33907.pdf>. Accessed September 20, 2011.
15. Human Genome Sciences. Raxibacumab webpage. <http://www.hgsi.com/abthrax-raxibacumab.html>. Accessed September 20, 2011.

See Also

Anthrax information Web page. Centers for Disease Control and Prevention, Emergency Preparedness and Response. <http://www.bt.cdc.gov/agent/anthrax/>. Accessed September 20, 2011

Anthrax Web page. National Institute of Allergy and Infectious Disease, National Institutes of Health. <http://www.niaid.nih.gov/topics/anthrax/Pages/default.aspx>. Accessed September 20, 2011

Visual Dx: Visual clinical decision support software. <http://www.logicalimages.com/resourcesBTAgents.htm>. Accessed September 20, 2011

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