

Background

Anthrax is a disease caused by the bacterium *Bacillus anthracis*. This bacterium exists in nature in 2 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 also could occur because of an intentional aerosol attack with *B. anthracis*.
- **Gastrointestinal (GI) anthrax** typically occurs due to eating the meat of animals infected with *B. anthracis*. The intestinal tract, mouth, or throat (oropharyngeal anthrax) may be infected.³ GI anthrax is normally thought to occur as a result of ingesting 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 is of most concern following an intentional aerosol attack with *B. anthracis*.
- **Injection-related anthrax** is a newly recognized route of infection. Several cases have occurred among injection drug users in Europe. The infection is believed to be caused by injecting heroin that is contaminated with material containing *B. anthracis* spores.⁴

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.⁵

Autonomous groups also have demonstrated intent to use *B. anthracis* in acts of terrorism. For example, as evidenced in a March 10, 2007, US 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.⁶ In 1993, the Japanese cult Aum

Shinrikyo sprayed aerosols containing *B. anthracis* several times in attempted terrorist attacks in Tokyo. Fortunately, the material used turned out to be ineffective, and consequently no one was sickened.⁷ Most notably, in October 2001, anthrax attacks were perpetrated in the US via mail, when 7 envelopes containing *B. anthracis* spores were sent through the US 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 the US Army Medical Research Institute of Infectious Diseases had perpetrated the attack.⁸ Dr. Ivins committed suicide before charges could be filed, and the case was never tried. Other organizations have questioned the FBI's conclusion.⁹

Several factors contribute to concern about the potential use of *B. anthracis* as a biological weapon:

- *B. anthracis* is widely available in microbe banks around the world
- *B. anthracis* is widely available naturally in endemic areas
- Evidence suggests techniques for mass production and aerosol dissemination of anthrax have been developed
- Anthrax spores' hardiness in the environment may make its aerosol dissemination more effective than 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 weapon¹⁰

A 1993 analysis conducted by the Office of Technology Assessment of the US 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.¹¹ (See "The History of Bioterrorism: Anthrax," a short video from the US Centers for Disease Control and Prevention [CDC], <https://www.youtube.com/watch?v=CmtLYQKT21I>.)

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 symptoms of anthrax—both the physical signs of cutaneous anthrax and the radiographic signs of inhalational anthrax—are often quite characteristic if the clinician is attuned and clinical presentation is consistent with the diagnosis. Thorough evaluation may be required, however, as several differential diagnoses are possible in the case of each form of anthrax infection.⁴ The expected hallmark of the use of an aerosolized anthrax weapon would be a sudden surge of patients presenting with symptoms of severe pneumonia and sepsis.

B. anthracis grows quickly and easily in routine culture. In addition, there are several rapid diagnostic tests for identifying anthrax at reference laboratories, but none are available widely in ordinary hospital laboratories.³



Transmission

Humans may contract anthrax following contact with infected animals or contaminated animal products, or by breathing in aerosolized spores. Anthrax is *not* contagious, meaning it cannot be transmitted from person to person like influenza or common cold viruses.¹

Infection Control Measures

Though anthrax is not contagious, few cases of person-to-person transmission have resulted from contact with discharges from cutaneous lesions, and therefore standard barrier isolation precautions are recommended for hospitalized patients with all forms of anthrax infection. There are no data to support the use of use of high-efficiency particulate air filter masks or other measures to provide protection from airborne or droplet transmission when in close proximity to an infected individual. Additionally, there is no need to provide prophylaxis to close contacts of an infected patient.³

Treatment

Early antibiotic treatment of anthrax is vital, as delay decreases an infected person's chance for survival. Many antibiotics can be used to treat anthrax infection; the CDC recommends broad coverage with IV ciprofloxacin or doxycycline and at least 2 other antibiotics.⁴ In an emergency, public health authorities will make recommendations for treatment based on laboratory susceptibility testing. Antibiotic therapy may be coupled with antitoxin treatment. There are 3 FDA-approved antitoxins that are available: two monoclonal antibodies called raxibacumab (Abthrax) and obiltoxaximab (Anthim), and a polyclonal antibody called Anthrasil. These are given via injection or IV and can be used for the treatment of inhalational anthrax.^{12, 13} 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.⁴

Clinical Presentation of Anthrax⁴

Anthrax Infection	Incubation Period	Signs and Symptoms	Lethality
Inhalational	Ranges from as few 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.	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.



Anthrax Infection	Incubation Period	Signs and Symptoms	Lethality
		Chest imaging reveals widening of the mediastinum, enlargement of and bleeding into lymph nodes, and bloody fluid collections around the lungs.	
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 reported cases, 30% of patients died despite aggressive medical therapy.

Post-Exposure Prophylaxis

Post-exposure prophylaxis should begin immediately in persons suspected of exposure to *B. anthracis* and should not be delayed until symptoms emerge. If susceptibility of the *B. anthracis* strain is unknown, initial therapy with the antibiotic ciprofloxacin or doxycycline is recommended for adults and children. Once started, antibiotic therapy should be continued for 60 days post-exposure. In conjunction with antibiotics, a 3-dose post-exposure anthrax vaccine regimen (at 0 weeks, 2 weeks, and 4 weeks) is recommended by the CDC. Antitoxins also can be used for prophylaxis in special circumstances.⁴

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 several 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.).³

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.¹⁴

Countermeasures

Vaccine

BioThrax® Anthrax Vaccine Adsorbed (AVA) is produced by Emergent BioSolutions, Inc., and is the only anthrax vaccine licensed by the FDA. BioThrax® is approved for pre-exposure prophylaxis of disease in persons aged 18-65 years at high risk of exposure to anthrax and for post-exposure prophylaxis following suspected or confirmed anthrax exposure in conjunction with antibiotic treatment. AVA is a cell-free filtrate made from cultures of a strain of anthrax not capable of causing disease. As pre-exposure prophylaxis, a 5-dose series is required for immunization, with annual boosters. When used as post-exposure prophylaxis, a 3-dose series is required at 0 weeks, 2 weeks, and 4 weeks after exposure.¹⁵

Antitoxin

There are currently 3 FDA-approved antitoxins available for treatment of inhalational anthrax: obiltoximab (Anthim), raxibacumab (Abthrax), and anthrax immune globulin (Anthraxil).¹³ Anthim is a monoclonal antibody injection that neutralizes the toxin and can be used in combination with antibiotic therapy after anthrax exposure.¹⁶ Abthrax is another monoclonal antibody injection that is used to treat inhalational anthrax infection, in combination with antibiotic therapy.¹⁸ Anthrasil is administered intravenously and can be used with antibiotics to treat inhalational anthrax. This antitoxin is manufactured from the plasma of anthrax-vaccinated individuals and leverages their antibodies to neutralize anthrax toxins.¹⁷ Antitoxins are important tools used in conjunction with antibiotic treatment, as they neutralize the toxins that have already been released in the body by the bacteria, while the antibiotics target the bacteria themselves.^{16, 17, 18}

Anthim has been purchased by the US Department of Health and Human Services (HHS) to be held in the Strategic National Stockpile, to be deployed in case of an anthrax emergency.¹⁹



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See also:

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