Germ Warfare

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**History of Biological Warfare**

Biological weapons include any organism (such as bacteria, viruses, or [fungi](http://www.emedicinehealth.com/script/main/art.asp?articlekey=24858)) or [toxin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5828) found in nature that can be used to kill or [injure](http://www.emedicinehealth.com/script/main/art.asp?articlekey=33836) people. (Toxins are poisonous compounds produced by organisms.)

The act of [bioterrorism](http://www.emedicinehealth.com/script/main/art.asp?articlekey=18548) can range from a simple hoax to the actual use of these biological weapons, also referred to as agents. A number of nations have or are seeking to acquire biological warfare agents, and there are concerns that terrorist groups or individuals may acquire the technologies and expertise to use these destructive agents. Biological agents may be used for an isolated assassination, as well as to cause incapacitation or death to thousands. If the environment is contaminated, a long-term threat to the population could be created.

History: The use of biological agents is not a new concept, and history is filled with examples of their use.

Attempts to use biological warfare agents date back to antiquity. Scythian archers infected their arrows by dipping them in decomposing bodies or in blood mixed with manure as far back as 400 BC. Persian, Greek, and Roman literature from 300 BC quotes examples of dead animals used to contaminate wells and other sources of water. In the Battle of Eurymedon in 190 BC, Hannibal won a naval victory over King Eumenes II of Pergamon by firing earthen vessels full of [venomous](http://www.emedicinehealth.com/script/main/art.asp?articlekey=40549) snakes into the enemy ships.

During the battle of Tortona in the 12th century AD, Barbarossa used the bodies of dead and decomposing soldiers to [poison](http://www.emedicinehealth.com/script/main/art.asp?articlekey=11890) wells. During the siege of Kaffa in the 14th century AD, the attacking Tatar forces hurled plague-infected corpses into the city in an attempt to cause an [epidemic](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3273) within enemy forces. This was repeated in 1710, when the Russians besieging Swedish forces at Reval in Estonia catapulted bodies of people who had died from [plague](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59375).

During the French and Indian War in the 18th century AD, British forces under the direction of Sir Jeffrey Amherst gave blankets that had been used by [smallpox](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59376) victims to the Native Americans in a plan to spread the disease.

Allegations were made during the American Civil War by both sides, but especially against the Confederate Army, of the attempted use of smallpox to cause disease among enemy forces.

Modern times: Biological warfare reached sophistication during the 1900s.

During World War I, the German Army developed [anthrax](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59372), [glanders](http://www.emedicinehealth.com/script/main/art.asp?articlekey=13712), [cholera](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6534), and a wheat [fungus](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3527) specifically for use as biological weapons. They allegedly spread plague in St. Petersburg, Russia, infected mules with glanders in Mesopotamia, and attempted to do the same with the horses of the French Cavalry.

The Geneva Protocol of 1925 was signed by 108 nations. This was the first multilateral agreement that extended prohibition of chemical agents to biological agents. Unfortunately, no method for verification of compliance was addressed.

During World War II, Japanese forces operated a secret biological warfare research facility (Unit 731) in Manchuria that carried out human experiments on prisoners. They exposed more than 3,000 victims to plague, anthrax, [syphilis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58878), and other agents in an attempt to develop and observe the disease. Some victims were executed or died from their infections. Autopsies were also performed for greater understanding of the effects on the human body.

In 1942, the United States formed the War Research Service. Anthrax and [botulinum toxin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=25769) initially were investigated for use as weapons. Sufficient quantities of botulinum toxin and anthrax were stockpiled by June 1944 to allow unlimited retaliation if the German forces first used biological agents. The British also tested anthrax bombs on Gruinard Island off the northwest coast of Scotland in 1942 and 1943 and then prepared and stockpiled anthrax-laced cattle cakes for the same reason.

The United States continued research on various offensive biological weapons during the 1950s and 1960s. From 1951-1954, harmless organisms were released off both coasts of the United States to demonstrate the vulnerability of American cities to biological attacks. This weakness was tested again in 1966 when a test [substance](http://www.emedicinehealth.com/script/main/art.asp?articlekey=25243) was released in the New York City subway system.

During the Vietnam War, Viet Cong guerrillas used needle-sharp punji sticks dipped in [feces](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3400) to cause severe infections after an enemy soldier had been stabbed.

In 1979, an accidental release of anthrax from a weapons facility in Sverdlovsk, USSR, killed at least 66 people. The Russian government claimed these deaths were due to infected meat and maintained this position until 1992, when Russian President Boris Yeltsin finally admitted to the accident.

**Bioterrorism and Biowarfare Today**

Bioterrorism and biowarfare today: A number of countries have continued offensive biological weapons research and use. Additionally, since the 1980s, terrorist organizations have become users of biological agents. Usually, these cases amount only to hoaxes. However, the following exceptions have been noted:

* + *In 1985, Iraq began an offensive biological weapons program producing anthrax, botulinum toxin, and* [*aflatoxin*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=10796)*. During Operation Desert Storm, the coalition of allied forces faced the threat of chemical and biological agents. Following the Persian Gulf War, Iraq disclosed that it had bombs, Scud missiles, 122-mm rockets, and artillery shells armed with botulinum toxin, anthrax, and aflatoxin. They also had spray tanks fitted to aircraft that could distribute agents over a specific target.*
  + *In September and October of 1984, 751 people were intentionally infected with* [*Salmonella*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6310)*, an agent that causes* [*food*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58866) [*poisoning*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58837)*, when followers of the Bhagwan Shree Rajneesh contaminated restaurant salad bars in Oregon.*
  + *In 1994, a Japanese sect of the Aum Shinrikyo cult attempted an aerosolized (sprayed into the air) release of anthrax from the tops of buildings in Tokyo.*
  + *In 1995, two members of a Minnesota militia group were convicted of possession of* [*ricin*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59134)*, which they had produced themselves for use in retaliation against local government officials.*
  + *In 1996, an Ohio man attempted to obtain* [*bubonic plague*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2544) *cultures through the mail.*
  + *In 2001, anthrax was delivered by mail to U.S. media and government offices. There were four deaths.*
  + *In December 2002, six terrorist suspects were arrested in Manchester, England; their apartment was serving as a "ricin laboratory." Among them was a 27-year-old chemist who was producing the toxin. Later, on Jan. 5, 2003, British police raided two residences around London and found traces of ricin, which led to an investigation of a possible Chechen separatist plan to attack the Russian embassy with the toxin; several arrests were made.*
  + *On Feb. 3, 2004, three U.S. Senate office buildings were closed after the toxin ricin was found in a mailroom that serves Senate Majority Leader Bill Frist's office.*

The threat that biological agents will be used on both military forces and civilian populations is now more likely than it was at any other point in history.

**How Biological Agents Are Delivered and Detected**

Although there are more than 1,200 biological agents that could be used to cause illness or death, relatively few possess the necessary characteristics to make them ideal candidates for biological warfare or terrorism agents. The ideal biological agents are relatively easy to acquire, process, and use. Only small amounts (on the order of pounds and often less) would be needed to kill or incapacitate hundreds of thousands of people in a metropolitan area. Biological warfare agents are easy to hide and difficult to detect or protect against. They are invisible, odorless, tasteless, and can be spread silently.

**Delivery**

Biological warfare agents can be disseminated in various ways.

Through the air by [aerosol](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2163) sprays: To be an effective biological weapon, airborne germs must be dispersed as fine particles. To be infected, a person must breathe a sufficient quantity of particles into the [lungs](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4209) to cause illness.

Used in explosives (artillery, missiles, detonated bombs): The use of an explosive device to deliver and spread biological agents is not as effective as the delivery by aerosol. This is because agents tend to be destroyed by the blast, typically leaving less than 5% of the agent capable of causing disease.

Put into food or water: Contamination of a city's water supplies requires an unrealistically large amount of an agent as well as introduction into the water after it passes through a regional treatment facility.

Absorbed through or injected into the skin: This method might be ideal for assassination, but is not likely to be used to cause mass casualties.

**Detection**

Biological agents could either be found in the environment using advanced detection devices or after specific testing or by a doctor reporting a medical [diagnosis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2979) of an illness caused by an agent. Animals may also be early victims and shouldn't be overlooked.

Early detection of a biological agent in the environment allows for early and specific treatment and time enough to treat others who were exposed with protective medications. Currently, the U.S. Department of Defense is evaluating devices to detect clouds of biological warfare agents in the air.

Doctors must be able to identify early victims and recognize patterns of disease. If unusual symptoms, a large numbers of people with symptoms, dead animals, or other inconsistent medical findings are noted, a biological warfare attack should be suspected. Doctors report these patterns to [public health](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5120) officials.

**Protective Measures**

Protective measures can be taken against biological warfare agents. These should be started early (if enough warning is received) but definitely once it is suspected that a biological agent has been used. To read more about protective clothing, see Equipment. Masks: Currently, available masks such as the military gas mask or high-efficiency particulate air ([HEPA](http://www.emedicinehealth.com/script/main/art.asp?articlekey=20218)) filter masks used for [tuberculosis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58881) exposure filter out most biological warfare particles delivered through the air. However, the face seals on ill-fitting masks often leak. For a mask to fit properly, it must be fitted to a person's face.

Clothing: Most biological agents in the air do not penetrate unbroken skin, and few organisms stick to skin or clothing. After an aerosol attack, the simple removal of clothing eliminates a great majority of surface contamination. Thorough showering with soap and water removes 99.99% of the few organisms that may be left on the victim's skin.

Medical protection: Health care professionals treating victims of biological warfare may not need special suits but should use latex gloves and take other precautions such as wearing gowns and masks with protective eye shields. Victims would be isolated in private rooms while receiving treatment.

[Antibiotics](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58694): Victims of biological warfare might be given antibiotics orally (pills) or through an IV, even before the specific agent is identified.

Vaccinations: Currently, protective vaccines (given as shots) are available for anthrax, Q fever, yellow fever, and smallpox. The widespread immunization of nonmilitary personnel has not been recommended by any governmental agency so far. Immune protection against ricin and staphylococcal toxins may also be possible in the near future.

**Anthrax Exposure Symptoms, Signs, and Diagnosis**

Anthrax bacteria occur worldwide. The United States Working Group on Civilian Biodefense and the Centers for Diseases Control and Prevention (CDC) have identified anthrax as one of a few biological agents capable of causing death and disease in sufficient numbers to cripple a developed region or urban setting. The organisms known as [*Bacillus anthracis*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=18820) may ordinarily produce disease in domesticated as well as wild animals such as goats, sheep, cattle, horses, and swine. Humans become infected by contact with infected animals or contaminated animal products. [Infection](http://www.emedicinehealth.com/script/main/art.asp?articlekey=12923) occurs mainly through the skin and rarely by [breathing](http://www.emedicinehealth.com/script/main/art.asp?articlekey=11056) spores or swallowing them. Spores exist in the soil and become active when the organisms in the carcass are exposed to air.

Apart from biological warfare, anthrax in humans is rare. In the United States, only 127 cases of anthrax appeared in the early years of the 20th century and dropped to about one per year during the 1990s.

***Signs and Symptoms***

Skin anthrax ([cutaneous](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2885)): Infection begins when the spores enter the skin through small [cuts](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2886) or abrasions. Spores then become active in the host (human or animal) and produce poisonous toxins. Swelling, [bleeding](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58961), and tissue death may occur at the site of infection.

More than 95% of the cases of anthrax involve the skin. After a person is exposed, the disease first appears in one to five days as a small pimple-looking [sore](http://www.emedicinehealth.com/script/main/art.asp?articlekey=40400) that progresses over the next one to two days to contain fluid filled with many organisms. The sore is usually painless, and it may have swelling around it. Sometimes the swelling affects a person's entire face or [limb](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4162).

Victims may have [fever](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3425), feel [tired](http://www.emedicinehealth.com/script/main/art.asp?articlekey=26113), and have a [headache](http://www.emedicinehealth.com/script/main/art.asp?articlekey=11396). Once the sore opens, it forms a black area of tissue. The black appearance of the tissue [injury](http://www.emedicinehealth.com/script/main/art.asp?articlekey=25495) gives anthrax its name from the Greek word *anthrakos*, meaning coal. After a period of two to three weeks, the black tissue separates, often leaving a scar. With adequate treatment, less than 1% of people infected with skin anthrax die.

Inhalation anthrax: In inhalation anthrax, the spores are inhaled into the lungs where they become active and multiply. There they produce massive bleeding and swelling inside the [chest](http://www.emedicinehealth.com/script/main/art.asp?articlekey=19270) cavity. The germs then can spread to the blood, leading to [shock](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59301) and [blood poisoning](http://www.emedicinehealth.com/script/main/art.asp?articlekey=7232), which may lead to death.

Historically known as wool sorter’s disease (because it affected people who work around sheep), inhalation anthrax can appear anywhere within one to six days, or as long as 60 days after exposure. Initial symptoms are general and can include headache, [tiredness](http://www.emedicinehealth.com/script/main/art.asp?articlekey=26114), body aches, and fever. The victim may have a nonproductive [cough](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2852) and mild [chest pain](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58673). These symptoms usually last for two to three days.

Some people show a short period of improvement. This is followed by the sudden [onset](http://www.emedicinehealth.com/script/main/art.asp?articlekey=31474) of increased trouble breathing, shortness of breath, bluish [skin color](http://www.emedicinehealth.com/script/main/art.asp?articlekey=25008), increased chest [pain](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4723), and [sweating](http://www.emedicinehealth.com/script/main/art.asp?articlekey=9299). Swelling of the chest and [neck](http://www.emedicinehealth.com/script/main/art.asp?articlekey=16929) may also occur. Shock and death may follow within 24-36 hours in most people with this type of infection.

Anthrax is not spread from person to person. Inhalation anthrax is the most likely form of disease to follow a military or terrorist attack. Such an attack likely will involve the aerosolized delivery of anthrax spores.

[Mouth](http://www.emedicinehealth.com/script/main/art.asp?articlekey=33422), [throat](http://www.emedicinehealth.com/script/main/art.asp?articlekey=53392), [GI tract](http://www.emedicinehealth.com/script/main/art.asp?articlekey=25977) (oropharyngeal and [gastrointestinal](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3555)): These cases result when someone eats infected meat that has not been cooked sufficiently. After an [incubation period](http://www.emedicinehealth.com/script/main/art.asp?articlekey=18956) of two to five days, victims with oropharyngeal disease develop a severe [sore throat](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58801) or sores in the mouth or on a tonsil. Fever and neck swelling may occur. The victim may have trouble breathing. GI anthrax begins with nonspecific symptoms of [nausea](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4510), vomiting, and fever. These are followed in most victims by severe [abdominal pain](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6139). The victim may also [vomit](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6005) blood and have [diarrhea](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59276).

***Diagnosis***

Doctors will perform various tests, especially if anthrax is suspected.

With skin anthrax, a [biopsy](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2466) is taken of the sore ([lesion](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4135)), and lab tests are performed to look at the organism under a [microscope](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4375) and confirm the diagnosis of anthrax.

The diagnosis of inhalation anthrax is difficult to make. A [chest X-ray](http://www.emedicinehealth.com/script/main/art.asp?articlekey=110395) may show certain signs in the chest cavity. A [CT scan](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58707) of the chest may be very helpful when there is suspected inhalational anthrax. Early in the process, when the chest X-ray is still normal, the CT scan may show pleural, pericardial, and mediastinal fluid collections, enlarged hemorrhagic mediastinal lymph nodes, and bronchial airway [edema](http://www.emedicinehealth.com/script/main/art.asp?articlekey=97830). Cultures (growing the bacteria in a lab and then examining them under a microscope) are minimally helpful in making the diagnosis. Blood tests may also be performed.

GI anthrax also is difficult to diagnose because the disease is rare and symptoms are not always obvious. Diagnosis usually is confirmed only if the victim has a history of eating contaminated meat in the setting of an outbreak. Once again, cultures generally are not helpful in making the diagnosis.

[Meningitis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=10375) ([brain swelling](http://www.emedicinehealth.com/script/main/art.asp?articlekey=30900)) from anthrax is difficult to distinguish from meningitis due to other causes. A [spinal tap](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58714) may be performed to look at the person's spinal fluid in identifying the organism.

The most useful microbiologic test is the standard [blood culture](http://www.emedicinehealth.com/script/main/art.asp?articlekey=7202), which is almost always positive in victims with anthrax throughout their bodies. Blood cultures should show growth in six to 24 hours and if the laboratory has been alerted to the possibility of anthrax, [biochemical](http://www.emedicinehealth.com/script/main/art.asp?articlekey=15510) testing should provide a preliminary diagnosis 12-24 hours later. However, if the laboratory has not been alerted to the possibility of anthrax, there is the chance that the organism may not be identified correctly.

Rapid diagnostic tests for anthrax and its [proteins](http://www.emedicinehealth.com/script/main/art.asp?articlekey=15380) include [polymerase chain reaction](http://www.emedicinehealth.com/script/main/art.asp?articlekey=151188) ([PCR](http://www.emedicinehealth.com/script/main/art.asp?articlekey=151188)), [enzyme-linked immunosorbent assay](http://www.emedicinehealth.com/script/main/art.asp?articlekey=9100) (ELISA), and direct fluorescent [antibody](http://www.emedicinehealth.com/script/main/art.asp?articlekey=19101) (DFA) testing. Currently, these tests are only available at national reference laboratories.

**Anthrax Exposure Treatment, Prevention, and Postexposure Prophylaxis**

***Treatment***

Inhalation anthrax: As previously stated because inhalation anthrax moves quickly throughout the body, doctors will begin [antibiotic](http://www.emedicinehealth.com/script/main/art.asp?articlekey=8121) treatment right away even before a firm diagnosis is made through lab testing.

[Ciprofloxacin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=102507) (Cipro), [doxycycline](http://www.emedicinehealth.com/script/main/art.asp?articlekey=101867) (Vibramycin), and [penicillin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=15277) are FDA-approved antibiotics for treatment of anthrax. Experts currently recommend ciprofloxacin or other drugs in the same class for adults who are assumed to have inhalation anthrax infection. Penicillin and doxycycline may be used once organism culture sensitivities are known.

Traditionally, ciprofloxacin and other antibiotics in that class are not recommended for use in children younger than 16-18 years of age because of a weak theoretical link to permanent [joint](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4074) disorders. Balancing these small risks against the risk of death and the possibility of infection with a resistant [strain](http://www.emedicinehealth.com/script/main/art.asp?articlekey=15255) of anthrax, experts recommend that ciprofloxacin nonetheless be given to children in appropriate doses.

Because there is a risk the infection will [recur](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5255), victims are treated with antibiotics for at least 60 days.

Skin anthrax: Treatment of skin anthrax with antibiotics generally prevents the disease from progressing to the entire body although the black tissue and scar continue to form. Although previous guidelines have suggested treating skin anthrax with seven to 10 days of [therapy](http://www.emedicinehealth.com/script/main/art.asp?articlekey=10897), recent recommendations suggest treatment for 60 days in the setting of bioterrorism, thus assuming the person may also have been exposed to inhalational anthrax.

In [pregnant](http://www.emedicinehealth.com/script/main/art.asp?articlekey=10695) women, experts recommend that ciprofloxacin be given after exposure as a preventive medication following exposure to an anthrax attack.

***Prevention***

A vaccination series to protect against anthrax consists of five IM doses administered at day 0, week 4, and months 6, 12, and 18, followed by annual boosters. The CDC does not recommend vaccination for the general public, health care workers, or even people working with animals. The only groups that are recommended to receive routine vaccination are military personnel and investigators and remediation workers who are likely to enter an area with *B. anthracis* spores.

***Postexposure Prophylaxis***

When unvaccinated people are exposed to anthrax, it is now recommended that they receive both antibiotics for 60 days and be vaccinated. The common antibiotics used for postexposure prophylaxis are ciprofloxacin and doxycycline. The vaccine is [Anthrax Vaccine](http://www.emedicinehealth.com/script/main/art.asp?articlekey=105870) Adsorbed (AVA), and it is given as three subcutaneous doses (administered at 0, 2, and 4 weeks postexposure). These recommendations are for everyone and include pregnant women and children (although the recommendation for children will be reviewed on an event by event basis). The government has stockpiles of drugs and vaccines available and can deliver them to an affected area very quickly.

**Plague**

Plague is another infection that can strike humans and animals. It is caused by the bacteria [*Yersinia pestis*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6058), which has been the cause of three great human pandemics in the sixth, 14th, and 20th centuries. Throughout history, the oriental rat flea has been largely responsible for spreading bubonic plague. After the flea bites an infected animal, the organisms can multiply inside the flea. When an infected flea attempts to bite again, it vomits clotted blood and bacteria into the victim's bloodstream and passes the infection on to the next victim, whether small mammal (usually rodent) or human.

Although the largest outbreaks of plague have been associated with the rat flea, all fleas should be considered dangerous in areas where plague may be found. The most important [vector](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5968) (a vector is an animal that can transmit the disease) in the United States is the most prevalent flea of [rock](http://www.emedicinehealth.com/script/main/art.asp?articlekey=13762) squirrels and California ground squirrels. The black rat has been most responsible worldwide for the continuing spread of plague in urban epidemics.

***Signs and Symptoms***

People infected with plague may suddenly develop high a fever, painful [lymph](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4212) nodes, and have bacteria in their blood. Some victims with the bubonic form of the disease may develop secondary [pneumonic plague](http://www.emedicinehealth.com/script/main/art.asp?articlekey=18882) (a disease similar to [pneumonia](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4962)). Plague is contagious, and when the victim [coughs](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58790), plague can spread. Pneumonic plague is the most severe form of the disease and if untreated, most people die.

As few as one to 10 organisms are enough to infect humans or other animals including rodents. During the early phase, the germs usually spread to lymph nodes near the bite, where swelling occurs. The infection then spreads to other organs such as the [spleen](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5531), [liver](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4179), lungs, skin, [mucous](http://www.emedicinehealth.com/script/main/art.asp?articlekey=10681) membranes, and later, the [brain](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2516).

In the United States, most victims with human plague have the bubonic form. If the organisms were used as a biological warfare agent, it most likely would be spread through the air and inhaled by victims. The result would be primary pneumonic plague (epidemic pneumonia). If fleas were used as carriers of disease, bubonic or septicemic (blood infection) plague would result.

Bubonic plague: [Swollen lymph nodes](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58853) (called [buboes](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2543)) develop one to eight days after exposure. Their appearance is associated with the onset of sudden fever, chills, and headache, which often are followed by nausea and vomiting several hours later. The buboes become visible within 24 hours and cause severe pain. Untreated, [septicemia](http://www.emedicinehealth.com/script/main/art.asp?articlekey=15917) (blood poisoning) develops in two to six days. Up to 15% of bubonic plague victims develop secondary pneumonic plague and thus can spread illness from person to person by coughing.

Septicemia plague: Septicemia plague may occur with bubonic plague. The signs and symptoms of primary septicemic plague include fever, chills, nausea, vomiting, and diarrhea. Later, bleeding in the skin may develop, hands and feet may lose [circulation](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2735), and tissue may die.

Pneumonic plague: Pneumonic plague may occur primarily from inhaling organisms in the air or from exposure to infected blood. Victims typically have a productive cough with blood-tinged [sputum](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5539) within 24 hours of [symptom](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5610) onset.

***Diagnosis***

The diagnosis of bubonic plague may be made if the victim has painful lymph glands and other common symptoms, especially if the victim has been exposed to rodents or fleas. But if the victim is not in an area where plague is present and symptoms are typical of other illnesses, the diagnosis may be difficult.

The doctor may view under a microscope a sample of sputum from a productive cough or the fluid from a swollen [lymph gland](http://www.emedicinehealth.com/script/main/art.asp?articlekey=22444).

Samples may grow in the laboratory and indicate plague within 48 hours and blood tests may also be performed.

***Treatment***

Victims of suspected plague will be isolated for the first 48 hours after treatment begins. If pneumonic plague is present, isolation may last for four more days. Since 1948, streptomycin has been the treatment of choice for plague but other antibiotics may be given.

If treated with antibiotics, buboes typically become smaller in 10-14 days and do not require drainage. Victims are unlikely to survive primary pneumonic plague if antibiotic therapy is not begun within 18 hours of the beginning of symptoms. Without treatment, 60% of people with bubonic plague die, and 100% with pneumonic and septicemic forms die.

***Prevention***

Fleas always must be targeted for destruction before the rodents, because killing rodents may release into the environment massive amounts of infected fleas, which will be hungry for a blood meal and, in the absence of rodents, the fleas will seek out any warm-blooded animal, including humans and infect them. Pesticides have been successful in getting rid of rats and other animal hosts. Public education about how plague spreads is an important part of prevention.

People who have been exposed to pneumonic plague and those who have been exposed to organisms in the air may be treated with antibiotics. Currently recommended antibiotics are streptomycin or gentamycin IM for 10 days, or until two days after the fever subsides. Alternative medications include doxycycline, ciprofloxacin, and chloramphenicol.

Contacts with victims who have bubonic plague do not need preventive medication. But people who were in the same environment as those who are infected may need preventive antibiotics. A previously FDA-approved plague vaccine is no longer manufactured. It was useful against the bubonic form of plague but not the more serious pneumonic (lung) form of plague, which is the kind most often expected in a terrorist incident. A new vaccine effective against all varieties of plague is under development.

Cholera

Cholera is an [acute](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2133) and potentially severe gastrointestinal disease ([stomach](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5560) and intestines) caused by the bacteria [*Vibrio cholerae*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6259). This agent has been investigated in the past as a biological weapon. Cholera does not spread easily from human to human, so it appears that major drinking water supplies would have to be profusely contaminated for this agent to be effective as a biological weapon.

Cholera normally can infect water or food that becomes contaminated by human [bowel](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2508) waste. The organism can survive for up to 24 hours in sewage and as long as six weeks in certain types of relatively impure water containing [organic](http://www.emedicinehealth.com/script/main/art.asp?articlekey=11780) matter. It can withstand freezing for three to four days, but it is killed readily by dry heat, steam, boiling, short-term exposure to ordinary disinfectants, and chlorination of water.

The toxin causes a person's intestines to create massive amounts of fluid that then produces thin, grayish brown diarrhea.

**Signs and Symptoms**

Depending on how many organisms a person drinks or eats, the illness could begin within 12-72 hours. The symptoms start suddenly with intestinal cramps and painless (rice-water appearing) diarrhea. Vomiting, feeling ill, and headache often accompany the diarrhea, especially early in the illness.

Fever is rare. If untreated, the disease generally lasts one to seven days. During the illness, the body loses great amounts of fluid, so it is important during recovery to replace fluids and balance [electrolytes](http://www.emedicinehealth.com/script/main/art.asp?articlekey=86874) (such as [sodium](http://www.emedicinehealth.com/script/main/art.asp?articlekey=9969) and [potassium](http://www.emedicinehealth.com/script/main/art.asp?articlekey=9970)).

Children may experience seizures and [cardiovascular](http://www.emedicinehealth.com/script/main/art.asp?articlekey=18311) imbalances severe enough to cause [heart](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3668) problems. The rapid loss of body fluids often leads to more severe illness. If not treated, up to half of children with cholera may die.

**Diagnosis**

The doctor may examine a sample of the [stool](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5564) under a microscope to confirm the diagnosis. Symptoms alone are usually enough to identify cholera.

**Treatment**

Fluids and electrolytes need to be replaced because the body has lost large amounts of fluids through the vomiting and diarrhea. Doctors may encourage the person to drink, but if someone continues to vomit or has frequent stools, an IV may be used to replace the fluid lost.

Antibiotics such as [tetracycline](http://www.emedicinehealth.com/script/main/art.asp?articlekey=101913) or doxycycline shorten the duration of diarrhea and reduce fluid losses. The antibiotics ciprofloxacin or [erythromycin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=102774) also may be used for a few days.

**Prevention**

There are two oral vaccines available; however, the CDC does not recommend their routine use, and in fact, did not use the vaccines during the most recent severe outbreak in Haiti after the 2010 earthquake. The vaccines require two doses, and it may be weeks before the person develops immunity. The CDC does not recommend the vaccines for routine travel prophylaxis.

Tularemia is an infection that can strike humans and animals. It is caused by the [bacterium](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2416) *Francisella tularensis*. The disease causes fever, localized skin or mucous membrane ulcerations, regional swelling of lymph glands, and occasionally pneumonia.

G.W. McCay discovered the disease in Tulare County, Calif., in 1911. The first confirmed case of human disease was reported in 1914. Edward Francis, who described transmission by deer flies via infected blood, coined the term *tularemia* in 1921. It has been considered an important biological warfare agent because it can infect many people if dispersed by the aerosol route.

Rabbits and [ticks](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59309) most commonly spread tularemia in North America. In other areas of the world, tularemia is transmitted by water rats and other aquatic animals.

The bacteria are usually introduced into the victim through breaks in the skin or through the mucous membranes of the eye, [respiratory](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5329) tract, or GI tract. Ten [virulent](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6912) organisms injected under the skin from a bite or 10-50 organisms breathed into the lungs can cause infection in humans. Hunters may contract this disease by trapping and skinning rabbits in some parts of the country.

***Signs and Symptoms***

Tularemia can be divided into two forms: the ulceroglandular (75% of cases) and typhoidal (25% of cases). Victims with the ulceroglandular type have sores on the skin or mucous membranes, large lymph nodes, or both. Those with typhoidal tularemia have smaller lymph nodes and no skin sores.

After three to six days, people with the ulceroglandular form of the disease develop a group of symptoms: fever, chills, headache, cough, and [muscle](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4464) aches. They may also have chest pain, vomiting, [joint pain](http://www.emedicinehealth.com/script/main/art.asp?articlekey=98445), sore throat, [abdominal](http://www.emedicinehealth.com/script/main/art.asp?articlekey=19269) pain, diarrhea, shortness of breath, [back pain](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59170), or neck stiffness.

A sore up to 1 inch across may appear on the skin in about 60% of people and is the most common sign of tularemia. If the bite associated with infection was from an animal carrying the disease, the sore is usually on the upper part of a person's body, such as on the arm. If the infection came from an insect bite, the sore might appear on the lower part of the body, such as on the [leg](http://www.emedicinehealth.com/script/main/art.asp?articlekey=8739).

Enlarged lymph nodes are seen in about 85% of victims and may be the initial or the only sign of infection. Although enlarged lymph nodes usually occur as single lesions, they may appear in groups. Enlarged lymph nodes may come and go and last for as long as three years. When swollen, they may be confused with buboes of bubonic plague.

Sore throat and other complications may occur in up to 25% of people with tularemia.

People with either type of tularemia may develop pneumonia. They may have a productive or nonproductive cough and possibly chest pain, shortness of breath, and vomit blood.

***Diagnosis***

Tularemia can be diagnosed by growing the bacteria in the laboratory from samples taken of blood, ulcers, sputum, and other body fluids. Blood tests may not be helpful.

***Treatment***

Victims with tularemia who do not receive appropriate antibiotics may have a prolonged illness with weakness and [weight loss](http://www.emedicinehealth.com/script/main/art.asp?articlekey=53393). Treated properly, very few people with tularemia die. A 14-day course of streptomycin is effective treatment for tularemia. [Gentamicin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=102964) is also effective. Although tetracycline and chloramphenicol have also been found effective, they are associated with significant [relapse](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5292) rates.

Although laboratory-related infections with this organism are common, human-to-human spread is unusual. Victims do not need to be isolated from others.

***Prevention***

An antibiotic given after exposure to tularemia is difficult, because the ideal drug, streptomycin, must be given by injection. Tetracycline is effective after exposure to an aerosol of tularemia if given within 24 hours of the exposure and taken for 14 days.

Although there exist a vaccine against Tularemia, the vaccine is not routinely available in the U.S., and the CDC does not recommend it for use patients already infected.

***Postexposure Prophylaxis***

In the event of a biological attack using *Francisella tularensis*, the recommendation is to treat exposed people who are not yet ill with 14 days of oral doxycycline or ciprofloxacin. The vaccine is not routinely used in postexposure management.

**Brucellosis**

[Brucellosis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=9305) is an infection of domesticated and wild animals that can be transmitted to humans. It is caused by an organism of the genus *Brucella*. The organism infects mainly cattle, sheep, goats, and other similar animals, causing death of developing fetuses and [genital](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3576) infection. Humans, who usually are infected incidentally by contact with infected animals, may develop numerous symptoms in addition to the usual ones of fever, general illness, and muscle pain.

The disease often becomes long-term and may return, even with appropriate treatment. The ease of transmission through the air suggests that these organisms may be useful in biological warfare.

Each of six different species may tend to infect certain animal species. Four are known to cause illness in humans. Animals may transmit organisms during a [miscarriage](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58750), at the time of slaughter, and in their milk. Brucellosis is rarely, if ever, transmitted from human to human.

Certain species can enter animal hosts through skin abrasions or cuts, the eye membranes, the respiratory tract, and the GI tract. Organisms grow rapidly and eventually go to the lymph nodes, liver, spleen, joints, kidneys, and [bone marrow](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2502).

***Signs and Symptoms***

Victims may have a fever or a long-term infection or just a local [inflammation](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3979). The disease may appear suddenly or develop slowly anywhere from three days to several weeks after exposure. Symptoms include fever, sweats, [fatigue](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58902), loss of appetite, and muscle or joint aches. [Depression](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58644), headache, and irritability occur frequently. In addition, infection of bones, joints, or the [genitourinary](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3579) tract may cause pain. Cough and chest pain also may be noted.

Symptoms often last three to six months and occasionally for longer than a year. Different species of the organism can cause different symptoms from skin sores to [low back pain](http://www.emedicinehealth.com/script/main/art.asp?articlekey=20587) to [liver disease](http://www.emedicinehealth.com/script/main/art.asp?articlekey=53394).

***Diagnosis***

The doctor will want to know about any exposure to animals, animal products, or environmental exposures in making the diagnosis. Military troops exposed to a biological attack and who have fever are likely candidates for this illness. Environmental samples may show the presence of this organism in the attack area. Laboratory tests and cultures of blood or body fluid samples including bone [marrow](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4286) may be performed.

***Treatment***

Therapy with a single drug has resulted in a high relapse rate, so a combination of antibiotics should be prescribed. A six-week course of doxycycline along with streptomycin for the first two weeks is effective in most adults with most forms of brucellosis.

***Prevention***

Animal handlers should wear appropriate protective clothing when working with infected animals. Meat should be well cooked, and milk should be pasteurized. Laboratory workers need to take appropriate cautions in handling the organism.

***Postexposure Prophylaxis***

In the event of a biological attack, the standard gas mask should protect adequately from airborne species. No commercially available vaccine exists for humans. If the exposure is considered high risk, the CDC recommends treating with doxycycline and [rifampin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=103470) for three weeks.

**Q Fever**

Q fever is a disease that also affects animals and humans. It is caused by the bacteria *Coxiella burnetii*. A spore like form of the organism is extremely resistant to heat, pressure, and many cleaning solutions. This allows the germs to live in the environment for long periods under harsh conditions. In [contrast](http://www.emedicinehealth.com/script/main/art.asp?articlekey=18238), the disease it causes in humans is usually not harmful, although it can be temporarily disabling. Even without treatment, most people recover.

The organism is extremely infectious. The potential of the organism as a biological warfare agent is related directly to its ability to infect people easily. A single organism is capable of producing infection and disease in humans. Different strains have been identified worldwide.

Humans have been infected most commonly by contact with domestic livestock, particularly goats, cattle, and sheep. The risk of infection is increased greatly if humans are exposed while these animals are giving birth to young. Large numbers of the germs may be released into the air as an animal gives birth. Survival of the organism on surfaces, such as straw, hay, or clothing, allows for transmission to other people who are not in direct contact with infected animals.

People can become infected by breathing the organisms.

***Signs and Symptoms***

Humans are the only hosts that commonly develop an illness as a result of the infection. The illness may begin within 10-40 days. There is no typical pattern of symptoms, and some people show none at all. Most people appear mildly to moderately ill.

Fever (can go up and down and last less than 13 days), chills, and headache are the most common signs and symptoms. Sweating, aches, fatigue, and loss of appetite are also common. Cough often occurs later in the illness. Chest pain occurs in a few people. Sometimes there is a [rash](http://www.emedicinehealth.com/script/main/art.asp?articlekey=101047). Other symptoms such as headache, facial pain, and hallucinations have been reported.

Sometimes problems in the lungs are seen on chest [X-rays](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58739). And some people may seem to have acute [hepatitis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3705) because of their liver involvement. Others may develop a heart condition called endocarditis.

***Diagnosis***

Blood tests may help in making the diagnosis of Q fever.

***Treatment***

The drug of choice for treatment of Q fever is doxycycline.

People with [chronic](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2728) Q fever who develop endocarditis may die, even with appropriate treatment.

***Prevention***

Although an effective vaccine (Q-Vax) is licensed in Australia, all Q fever vaccines used in the United States are under study. Q fever can be prevented by immunization.

***Postexposure Prophylaxis***

In the case of bioterror attack, postexposure prophylaxis is recommended using oral doxycycline.

**Smallpox**

[Variola](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6257) (the [virus](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5997) that causes smallpox) is the most notorious of the poxviruses. Smallpox was an important cause of illness and death in the developing world until recent times. In 1980, the [World Health Organization](http://www.emedicinehealth.com/script/main/art.asp?articlekey=11087) (WHO) declared that smallpox had been completely wiped out. The last case was noted in Somalia in 1977.

Variola represents a significant threat as a biological warfare agent. Variola is highly infectious and is associated with a high death rate and secondary spread. Currently, the majority of the U.S. population has no [immunity](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3908), vaccine is in short supply, and no effective treatment exists for the disease. Two WHO-approved and inspected repositories remain: One is at the [Centers for Disease Control and Prevention](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2664) in the United States and the other at Vector Laboratories in Russia. It is widely believed that clandestine stockpiles exist in other countries such as Iraq and North Korea.

Variola virus is highly infectious when released into the air. It is environmentally stable and can retain its ability to infect people for long periods. Infection through contaminated objects such as clothing is infrequent. After a person is exposed to aerosolized virus, the virus multiplies in the person's respiratory tract. After a period of seven to 17 days, variola is spread through the bloodstream to lymph nodes where it continues to multiply.

Variola then moves into smaller blood vessels near the surface of the skin where the inflammatory changes occur. The classic smallpox rash then begins. Two types of smallpox generally are recognized.

Variola major, the most severe form, may cause death in up to 30% of unvaccinated people who develop it (3% of people vaccinated people may also develop variola major).

Variola minor, a milder form of smallpox, produces death in 1% of unvaccinated people.

***Signs and Symptoms***

The symptoms of variola major occur after a seven- to 17-day incubation period. They begin acutely with high fever, headache, chills, aches, vomiting, abdominal pain, and back pain. During the initial phase, 15% of people develop [delirium](http://www.emedicinehealth.com/script/main/art.asp?articlekey=23364) (hallucinations), and 10% of light-skinned people may develop a fleeting rash.

After two to three days, the rash develops on the face, hands, and forearms and extends gradually to the trunk and lower part of the body. The sores progress all at once into fluid-filled sacs. The distribution of the rash is important in making the diagnosis of smallpox. A greater number of lesions will appear on the face [arms](http://www.emedicinehealth.com/script/main/art.asp?articlekey=26231) and legs compared to the trunk. People with smallpox are most infectious on days three through six after the fever begins. Virus is spread to others through coughing and sneezing or by direct contact.

With the milder form of smallpox, variola minor, the skin sores are similar but smaller and fewer in number. People are not as ill as those who have variola major.

***Diagnosis***

Most doctors have never seen a case of smallpox and may have difficulty diagnosing it. Other [viral](http://www.emedicinehealth.com/script/main/art.asp?articlekey=15037) illnesses with rash, such as [chickenpox](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58832) or [allergic](http://www.emedicinehealth.com/script/main/art.asp?articlekey=9597) [contact dermatitis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59362), can look similar. Smallpox is different from chickenpox because of the distribution of the lesions and because they are all at the same stage of development everywhere on the body. With chickenpox, sores may be forming while others are scabbing over.

The failure to recognize mild cases of smallpox in people with partial immunity permits rapid person-to-person transmission. Exposed people may shed virus through coughing without ever showing the signs and symptoms of the disease.

The doctor may look at scrapings of tissue under a microscope but will be unable to tell the difference between smallpox and [monkeypox](http://www.emedicinehealth.com/script/main/art.asp?articlekey=12416) or [cowpox](http://www.emedicinehealth.com/script/main/art.asp?articlekey=23596). Advanced PCR techniques have been developed and may provide for more accurate diagnosis in the near future.

***Treatment***

People with smallpox are usually isolated from people without smallpox for 17 days. Anyone exposed to either weaponized variola or people infected with smallpox must be vaccinated immediately; this may lessen or prevent the illness if done within four or five days of infection.

Treatment of smallpox is mainly to help relieve symptoms. The [antiviral agent](http://www.emedicinehealth.com/script/main/art.asp?articlekey=8146) [cidofovir](http://www.emedicinehealth.com/script/main/art.asp?articlekey=102501) may be effective in treating symptoms.

***Prevention***

[Smallpox vaccine](http://www.emedicinehealth.com/script/main/art.asp?articlekey=21693) is used to prevent people from getting smallpox. The vaccine is given as a type of shot, but a two-pronged needle is used to place the medication into the skin. This leaves a permanent scar, which many adults may still have from smallpox inoculations given to them when they were babies.

Once the shot is given, a small fluid-filled [pimple](http://www.emedicinehealth.com/script/main/art.asp?articlekey=33356) usually appears five to seven days later. A scab forms over the site during the next one to two weeks. Common side effects include low-grade fever and [swollen lymph glands](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58853). People with weakened immune systems should not have the smallpox vaccination. This includes people with [HIV](http://www.emedicinehealth.com/script/main/art.asp?articlekey=3769), anyone with a history of [eczema](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59364), and pregnant women.

***Postexposure Prophylaxis***

In the case of a bioterror attack, it is recommended that all people who were exposed be immunized using the vaccine as soon as possible, but at least within four days. Again, use of the vaccine is not recommended in people with skin diseases like eczema, immunocompromised individuals (like HIV), or in pregnant women.

**Monkeypox**

The monkeypox virus is a naturally occurring relative of variola, which is found in Africa. The first case of human monkeypox was identified in 1970, but fewer than 400 cases have been diagnosed since. Some concern exists that monkeypox may be weaponized, however, human monkeypox is not as potent as smallpox. Pneumonia due to monkeypox may cause death in about half of people who develop it.

**Arboviral Encephalitis**

The arboviral encephalitis with high fatality rates include Venezuelan equine [encephalitis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58863) (VEE) virus, western equine encephalitis (WEE) virus, and eastern equine encephalitis (EEE) virus. They are members of the Alphavirus genus and are regularly associated with encephalitis. These viruses were recovered from horses during the 1930s. VEE was isolated in the Guajira peninsula of Venezuela in 1930, WEE in the San Joaquin Valley of California in 1930, and EEE in Virginia and New Jersey in 1933. A more common, but milder arboviral disease, is West Nile, which is caused by a flavivirus.

Although natural infections with these viruses occur following bites from mosquitoes, the viruses are also highly infectious when spread through the air. If intentionally released as a small particle aerosol, this virus may be expected to infect a high percentage of people exposed within a few miles.

VEE virus has the capacity to produce epidemics. Outcomes are significantly worse for the very young and the very old. Up to 35% of people infected may die. WEE and EEE typically produce less severe and widespread disease but are associated with death rates as high as 50%-75% in those with severe illness.

***Signs and Symptoms***

VEE: After an incubation period of two to six days, people with VEE develop fevers, chills, headache, aches, sore throat, and [sensitivity](http://www.emedicinehealth.com/script/main/art.asp?articlekey=24599) to light (eyes). They may become mildly confused, have seizures or [paralysis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4765), or go into a [coma](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2803). For those who survive, their nervous system functions usually recover completely.

EEE: The incubation period for EEE varies from five to 15 days. Adults may have certain early symptoms up to 11 days before the onset of nervous system problems such as mild confusion, seizures, and paralysis. Signs and symptoms include fever, chills, vomiting, muscle rigidity, [lethargy](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4138), slight paralysis, excess salivation, and difficulty breathing. Children frequently develop swelling on their face and near their eyes. Up to 30% of survivors of severe disease have permanent nervous system problems such as seizures and various degrees of confusion ([dementia](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2940)).

WEE: The incubation period is five to 10 days. Most people have no symptoms, or they might develop a fever. Other symptoms include nausea, vomiting, headache, a stiff neck, and drowsiness. Up to 90% of victims younger than 1 year of age have seizures. Typically, adults recover completely. Children, especially newborns, may have lasting nervous system problems.

***Diagnosis***

Laboratory tests, including [nasal](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4504) swab samples, may show any of the three viruses.

***Treatment***

No specific treatment is available. Doctors will help control symptoms. For some people, that may include medications to control fever and seizures or help breathing.

***Prevention***

There are no commercially available vaccines against any of the arboviral encephalitis. They are experimental and only available for researchers who work with the virus.

**Viral Hemorrhagic Fevers**

Viral hemorrhagic fevers are caused by four families of viruses.

* [Arenaviridae](http://www.emedicinehealth.com/script/main/art.asp?articlekey=26656) (Lassa, Argentine, Bolivian, Brazilian, Venezuelan hemorrhagic fevers)
* Bunyaviridae (Rift Valley, Crimean-Congo, Hantaan)
* [Filoviridae](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6499) (Marburg, Ebola)
* [Flaviviridae](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6501) (Yellow, [Dengue](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6625), Kyasanur Forest, Omsk HFs)

The best known of the viral hemorrhagic fevers is Ebola virus. First recognized in Zaire in 1976, the virus has been linked to at least 20 outbreaks in Africa. Up to 92% of people who contract Ebola will die. A related virus was discovered in Reston, Va., in 1989 in association with an outbreak of illness among monkeys imported from the Philippines. No human cases occurred with this outbreak. In 2012, an outbreak of Ebola started in Uganda and now has spread to Democratic Republic of the Congo.

These viruses are each characterized by an acute generalized illness that includes feeling quite ill (flulike illness) with profound exhaustion and often associated [internal bleeding](http://www.emedicinehealth.com/script/main/art.asp?articlekey=13599). All agents are highly infectious via the aerosol route, and most are stable as respiratory aerosols. Thus, they possess characteristics that may make them attractive for use by terrorists.

The agents that produce [viral hemorrhagic fever](http://www.emedicinehealth.com/script/main/art.asp?articlekey=26706) are all simple [RNA](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5382) viruses. They are able to survive in blood for long periods, which means they can infect people who are around animals slaughtered domestically. These viruses are linked to the rodent or insect that helps to spread them, which helps in searching for a diagnosis.

The specific viral hemorrhagic fever that develops depends on many factors such as the strength of the virus, its strain, and the route of exposure.

***Signs and Symptoms***

All viral hemorrhagic fevers primarily target blood vessels. They damage the blood vessels and produce internal bleeding. Victims may have fever, aches, exhaustion, infected eyes, [low blood pressure](http://www.emedicinehealth.com/script/main/art.asp?articlekey=88489) to severe shock, and bleeding in tiny blood vessels such as in the eye. More severe cases will have serious problems with the nervous system, liver, and lungs.

Depending on the type of virus, symptoms can include [deafness](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6791), severe internal bleeding, [kidney](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4103) failure, rash, black (bloody) vomit, and other life-threatening symptoms.

***Diagnosis***

It is important for the doctor to know a person's travel history in making a diagnosis of viral hemorrhagic fever. These agents are linked tightly with their natural geographic area and the ecology of the species and vectors found in that specific locale. Victims often recall exposures to rodents ([Arenavirus](http://www.emedicinehealth.com/script/main/art.asp?articlekey=26655), [Hantavirus](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6408)), mosquitoes ([Rift Valley fever](http://www.emedicinehealth.com/script/main/art.asp?articlekey=14875) virus, yellow and [dengue fever](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6626) viruses), or even slaughtered horses (Rift [Valley fever](http://www.emedicinehealth.com/script/main/art.asp?articlekey=15211) virus, Crimean-Congo virus).

Laboratory tests may be helpful. Testing can be conducted at the [CDC](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2655) in Atlanta or the U.S. Army Medical Research Institute of Infectious Disease (USAMRIID) at Fort Detrick in Frederick, Md.

***Treatment***

Treatment for viral hemorrhagic fevers is largely directed at easing the discomfort of the symptoms. Victims benefit from being placed in a hospital setting immediately. Air transport is not advised. [Sedative](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5439) and pain-relieving medications are helpful, but [aspirin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2371) and similar drugs should not be given because of their tendency to make bleeding worse.

Doctors will also not usually use IV lines or catheters because of bleeding problems. The treatment for bleeding is controversial. Generally, mild bleeding is not usually treated, but severe bleeding requires appropriate replacement therapy (blood through an IV line).

Specific treatment with [ribavirin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=102581) has been used and is currently under investigation as a therapy for [Lassa fever](http://www.emedicinehealth.com/script/main/art.asp?articlekey=8061), hantavirus, Crimean-Congo, and Rift Valley fever. Treatment is most effective if begun within seven days. Ribavirin has poor activity against the filoviruses and flaviviruses.

***Prevention***

The only established and licensed virus-specific vaccine against any of these viruses is the [yellow fever](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6054) vaccine. It is mandatory for those traveling into areas of Africa and South America where the disease is commonly found. Current trials are underway for further vaccines and antibody therapies.

Staphylococcal Enterotoxin B

Staphylococcal enterotoxin B (SEB) is one of the best-studied and, therefore, best-understood toxins.

Staphylococcal enterotoxin is one of the most common causes of food poisoning. Nausea, vomiting, and diarrhea normally occur after someone eats or drinks contaminated food.

The toxin creates different symptoms when exposure is through the air in a biological warfare situation. Only a small, inhaled dose is necessary to harm people within 24 hours of inhalation.

**Signs and Symptoms**

After exposure, signs and symptoms begin in two to 12 hours. Mild-to-moderate exposure to SEB produces fever, chills, headache, nausea, vomiting, shortness of breath, chest pain, body aches, and a nonproductive cough. Severe exposures can lead to a [toxic shock](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5825)-type picture and even death. Depending on the severity of exposure, the illness may last three to 10 days.

**Diagnosis**

Diagnosis of SEB can be difficult. Laboratory tests and a chest [X-ray](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6032) may be performed. Nasal swabs may show the toxin for 12-24 hours after exposure.

**Treatment**

Doctors provide care to relieve symptoms. Close attention to [oxygenation](http://www.emedicinehealth.com/script/main/art.asp?articlekey=11807) and hydration are important. People with severe SEB may need help breathing with a [ventilator](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5983). Most victims are expected to do well after the initial phase, but the time to full recovery may be long.

**Prevention**

No approved human vaccine exists for SEB, although human trials are ongoing. Passive [immunotherapy](http://www.emedicinehealth.com/script/main/art.asp?articlekey=7824) agents have demonstrated some promise when given within four hours of exposure, but such therapy is still being tested.

**Ricin**

Ricin, a plant [protein](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6554) toxin derived from the beans of the castor plant, is one of the most toxic and easily produced of the plant toxins. Although the lethal [toxicity](http://www.emedicinehealth.com/script/main/art.asp?articlekey=34093) of ricin is about 1,000-fold less than botulinum toxin, the worldwide ready availability of castor beans and the ease with which the toxin can be produced give it significant potential as a biological weapon.

Since ancient times, more than 750 cases of ricin intoxication have been described. Ricin may have been used in the highly published killing of Bulgarian exile Georgi Markov in London in 1978. He was attacked with a device in an umbrella that implanted a ricin-containing pellet into his [thigh](http://www.emedicinehealth.com/script/main/art.asp?articlekey=8759).

***Signs and Symptoms***

The toxicity of ricin varies greatly with the way it is given. Ricin is extremely toxic to cells and acts by inhibiting protein [synthesis](http://www.emedicinehealth.com/script/main/art.asp?articlekey=15508). Inhalation exposure causes primarily breathing and lung problems. If eaten, ricin causes symptoms in the GI tract. If injected, the reaction takes place in that area.

Following inhalation exposure of ricin, toxicity is characterized by the sudden onset of nasal and throat congestion, nausea and vomiting, [itching](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4060) of the eyes, itching, and tightness in the chest. If exposure is significant, after 12-24 hours severe breathing problems may set in. In animal studies, death occurs 36-48 hours after severe exposure.

Ingestion of ricin is generally less toxic because it is not absorbed well and may degrade in the digestive tract. Out of 751 ingestions recorded, only 14 resulted in a death.

At low doses, injection exposures produce flulike symptoms, body aches, nausea, vomiting, and localized pain and swelling at the injection site. Severe exposure results in tissue death and GI bleeding, as well as widespread liver, spleen, and kidney problems.

***Diagnosis***

The diagnosis of ricin poisoning is made on the basis of symptoms and whether exposure was possible. In biological warfare, exposure is likely to occur by inhalation of a toxin aerosol.

Victims may have certain signs on a chest X-ray. The diagnosis can be confirmed by lab tests on samples from a nasal swab. Ricin can be identified for up to 24 hours after exposure.

***Treatment***

Treatment is mainly to relieve symptoms. If exposure was by inhalation, the person may need help breathing. Those who ingested the poison may need to have their stomachs pumped (gastric lavage), or they might be given [activated](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58704) [charcoal](http://www.emedicinehealth.com/script/main/art.asp?articlekey=101840) to soak up the material.

***Prevention***

Currently, no vaccine is available for ricin exposure. Test vaccines have proven effective in animals. Other drugs are being studied as well.

Botulinum Toxin

Botulinum toxins are the most deadly toxins known. Because botulinum toxin is so lethal and easy to manufacture and weaponize, it represents a credible threat as a biological warfare agent. When used in this manner, exposure is likely to occur following inhalation of aerosolized toxin or ingestion of food contaminated with the toxin or its microbial spores. Iraq admitted to active research on the offensive use of botulinum toxins and to weaponizing and deploying more than 100 munitions with botulinum toxin in 1995.

All seven subtypes (A-G) of botulinum toxin act in similar ways. The toxin produces similar effects whether ingested, inhaled, or via a wound. The time course and severity of illness vary with route of exposure and dose received. Symptom onset is slower after inhalation exposure.

**Signs and Symptoms**

Symptoms may occur hours to several days after exposure. Initial signs and symptoms include [blurred vision](http://www.emedicinehealth.com/script/main/art.asp?articlekey=26099), dilated pupils, [difficulty swallowing](http://www.emedicinehealth.com/script/main/art.asp?articlekey=110126), difficulty speaking, an altered voice, and muscle weakness. After 24-48 hours, muscle weakness and paralysis may cause the person to be unable to breathe. Varying degrees of [muscular](http://www.emedicinehealth.com/script/main/art.asp?articlekey=4468) weakness may occur.

**Diagnosis**

Paralysis may indicate the presence of this exposure. Laboratory tests generally are not helpful. Infection by inhalation can be diagnosed from nasal swabs up to 24 hours after exposure.

**Treatment**

The most serious [complication](http://www.emedicinehealth.com/script/main/art.asp?articlekey=25405) is [respiratory failure](http://www.emedicinehealth.com/script/main/art.asp?articlekey=10698). With attention to symptoms and help breathing, sometimes with a ventilator, death occurs in fewer than 5% of cases. For confirmed exposures, an [antitoxin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2289) is available from the CDC. This antitoxin has all of the disadvantages of horse [serum](http://www.emedicinehealth.com/script/main/art.asp?articlekey=5470) products, including the risks for shock and serum sickness. Skin testing is performed first by injecting a small amount of the antitoxin into the skin and then monitoring the person for 20 minutes.

**Prevention**

The only botulinum vaccine was discontinued by the CDC in 2011.

**Mycotoxins**

The trichothecene mycotoxins are highly toxic compounds produced by certain species of fungi. Because these mycotoxins can cause massive [organ](http://www.emedicinehealth.com/script/main/art.asp?articlekey=21288) damage, and because they are fairly easy to produce and can be dispersed by various methods (dusts, droplets, aerosols, smoke, rockets, artillery mines, portable sprays), mycotoxins have an excellent potential for weaponization.

Strong evidence suggests that trichothecenes ("yellow rain") have been used as a biological warfare agent in Southwest Asia and Afghanistan. From 1974-1981, numerous attacks resulted in a minimum of 6,310 deaths in Laos, 981 deaths in Cambodia, and 3,042 deaths in Afghanistan. When taken from [fungal](http://www.emedicinehealth.com/script/main/art.asp?articlekey=15039) cultures, the mycotoxins yield a yellow-brown liquid that evaporates into a yellow crystalline product (thus, the "yellow rain" appearance). These toxins require certain solutions and high heat to be completely inactivated.

***Signs and Symptoms***

After exposure to the mycotoxins, early symptoms begin within five minutes. Full effects take 60 minutes.

If skin exposure occurs, the skin [burns](http://www.emedicinehealth.com/script/main/art.asp?articlekey=58964), becomes tender, swollen, and blisters. In lethal cases, large areas of skin die and slough (fall off).

Respiratory exposure results in nasal itching, pain, sneezing, a [bloody nose](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6562), shortness of breath, [wheezing](http://www.emedicinehealth.com/script/main/art.asp?articlekey=9401), cough, and blood-tinged saliva and sputum.

If ingested, the person feels nausea and vomits, loses appetite, feels abdominal cramping, and has watery and/or bloody diarrhea.

Following entry into the eyes, pain, tearing, redness, and blurred vision occur.

[Systemic](http://www.emedicinehealth.com/script/main/art.asp?articlekey=25440) toxicity may occur and includes weakness, exhaustion, [dizziness](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59400), inability to coordinate muscles, heart problems, low or high temperature, diffuse bleeding, and low [blood pressure](http://www.emedicinehealth.com/script/main/art.asp?articlekey=2486). Death may occur within minutes to days depending on the dose and route of exposure.

***Diagnosis***

Diagnosis of an attack of trichothecene [mycotoxin](http://www.emedicinehealth.com/script/main/art.asp?articlekey=26613) depends on the symptoms and identifying the toxin from biological and environmental samples. Many people with these symptoms may report being in a yellow rain or smoke attack.

Initial laboratory tests are not always helpful. Currently, a rapid identification kit for any of the trichothecene mycotoxins does not exist. Gas-liquid chromatography has been used in the past with great success. However, chromatographic methods lack great sensitivity, and presently alternative methods of detection are under investigation.

***Treatment***

Treatment is mainly to help with symptoms. The immediate use of protective clothing and mask during a mycotoxin aerosol attack should prevent illness. If a soldier is unprotected during an attack, the outer clothing should be removed within four to six hours and decontaminated with 5% sodium hydroxide for six to 10 hours. The skin should be washed with copious amounts of soap and uncontaminated water. The eyes, if exposed, should be washed out with large amounts of normal [saline](http://www.emedicinehealth.com/script/main/art.asp?articlekey=16206) or sterile water. U.S. military personnel can use a skin decontamination kit effectively against most [chemical warfare](http://www.emedicinehealth.com/script/main/art.asp?articlekey=59373) agents, including the mycotoxins.

No specific therapy exists for a trichothecene exposure. After appropriate skin decontamination, victims of inhalation and oral exposures may be given super activated charcoal orally. Activated charcoal removes mycotoxins from the GI tract. Some victims may need help breathing with a ventilator. Early use of [steroids](http://www.emedicinehealth.com/script/main/art.asp?articlekey=98554) increases survival time by decreasing the primary injury and shock-like state that follows significant poisoning.

***Prevention***

No vaccine exists for trichothecene mycotoxin exposure.

**Synonyms and Keywords**

anthrax, [*Bacillus*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=10960) *anthracis,* inhalation anthrax, cutaneous anthrax, skin anthrax, plague, [*Yersinia*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6057)[*pestis*](http://www.emedicinehealth.com/script/main/art.asp?articlekey=8547)*,* bubonic plague, septicemic plague, pneumonic plague, cholera, [Vibrio](http://www.emedicinehealth.com/script/main/art.asp?articlekey=6258) cholerae*, tularemia*, *Francisella tularensis,* brucellosis, *Brucella,* Q fever, *Coxiella burnetii*, smallpox, variola major, variola minor, viral encephalitis, viral hemorrhagic fevers, staphylococcal enterotoxin B, SEB, ricin, botulinum toxin, trichothecene mycotoxins, yellow rain, mycotoxins, biological warfare, biological warfare agents, VEE, WEE, EEE, encephalitis, weaponization, bioterrorism, Hantavirus, Ebola, Ebola virus

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