

## *Yersinia pestis* (Plague)

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Unless otherwise noted, all information presented in this article is derived from Inglesby TV, Dennis DT, Henderson DA, et al., for the Working Group on Civilian Biodefense. Plague as a biological weapon: medical and public health management. *JAMA*. 2000;283(17):2281-2290.

### Background

Plague is an infectious disease caused by *Yersinia pestis*, a naturally occurring bacterium found primarily in wild rodents. Plague has been the cause of three of the great pandemics of the modern era—in the mid-6th century, the mid-14th century (known as the Black Death), and the early 20th century.

Three forms of naturally-occurring plague infection exist:

- **Pneumonic plague** is the result of *Y. pestis* infection of the lungs. Primary pneumonic plague would be the expected form of disease following an aerosol attack with *Y. pestis*. Secondary pneumonic plague may occur if bubonic or septicemic plague goes untreated and the plague bacteria are allowed to spread to the lungs.
- **Bubonic plague** is the most common form of naturally occurring plague, typically acquired through the bite of an infected flea. Bubonic plague is characterized primarily by swollen, tender lymph nodes (called buboes).
- **Septicemic plague** is the result of plague bacteria multiplying in the blood and disseminating throughout the body. Septicemic plague usually occurs as a result of untreated bubonic or pneumonic plague.

Plague is recognized by public health experts as a re-emerging infectious disease. Worldwide incidence has reached approximately 2,000 to 3,000 reported cases each year. For example, according to the WHO fact sheet on plague, the worldwide reported incidence in 2003 was 2,118 cases with 182 deaths (see Plague: Overview. Fact sheet revised February 2005. WHO. <http://www.who.int/mediacentre/factsheets/fs267/en/>). The disease is endemic in rodent populations in much of Southern Asia, parts of Africa, and the Americas. According to the CDC, approximately 5 to 15 naturally occurring human cases of plague are reported in the United States each year, usually in rural areas of the Southwest (e.g., New Mexico, California, Colorado, and Texas). Advances in living conditions, public health, and antibiotic therapy make future natural plague pandemics improbable, but plague outbreaks following an attack with a biological weapon do pose a serious risk.

### Plague as a Biological Weapon

Plague is currently considered to be one of the most serious bioterrorism threats to the human population. In the 1950s and 1960s, the U.S. and Soviet biological weapons programs developed techniques to aerosolize *Y. pestis*. Aerosol dissemination of bacteria would cause a primary pneumonic plague outbreak in the exposed population, an otherwise uncommon, highly lethal, and contagious form of plague.

A number of following factors contribute to concern over the use of plague as a biological weapon:

- There is widespread availability of *Y. pestis* in microbe banks around the world
- There is widespread natural availability of the *Y. pestis* bacteria in endemic areas
- Reports indicate that techniques for mass production and aerosol dissemination of *Y. pestis* have been developed
- The fatality rate of pneumonic plague in untreated cases is extremely high
- Plague has the potential for secondary spread from person to person following an attack
- *Y. pestis* can be disseminated in aerosol form with relative ease
- Plague has a low infectious dose: based on animal data, estimates of infectivity via the respiratory route vary from 100 to 20,000 organisms
- Antibiotic resistant strains of *Y. pestis* exist in nature

A 1970 World Health Organization (WHO) assessment asserted that in a worst-case scenario a dissemination of 50 kg of *Y. pestis* in an aerosol cloud over a city of 5 million might result in 150,000 cases of pneumonic plague. Of those, 80,000 to 100,000 cases would require hospitalization, and 36,000 victims would be expected to die. (See “The History of Bioterrorism: Plague,” a short video from the CDC, available at <http://www.bt.cdc.gov/training/historyofbt/03plague.asp>)

## Signs and Symptoms

Diagnosis of plague is based on clinical presentation of symptoms and confirmed by laboratory testing, which usually takes 24 to 48 hours. There are no widely available rapid diagnostic tests for plague. The first sign of a bioterrorist attack with plague would most likely be a sudden surge of patients presenting at hospitals and doctors' offices with symptoms of severe pneumonia and sepsis.

## Transmission

Fleas are natural vectors (carriers) of *Y. pestis*, and the bacteria are typically transmitted to and among rodents via flea bite. Humans may contract plague through a flea bite or by handling an infected animal or breathing in an aerosolized form of the bacteria.

Neither bubonic or septicemic plague are known to spread directly from person to person. However, pneumonic plague does spread from person to person through respiratory droplets over short distances.

## Infection Control Measures

The Centers for Disease Control and Prevention (CDC) recommends that individuals suspected of having pneumonic plague be placed in isolation, with respiratory droplet precautions, and monitored for symptoms for the first 48 hours of antibiotic treatment. Those with confirmed pneumonic plague should remain in isolation under droplet precautions until all laboratory cultures are negative, indicating that disease

has run its course. Standard respiratory droplet precautions should also be taken by individuals in close contact with patients with confirmed or suspected pneumonic plague. Contacts of patients with plague should be identified for surveillance purposes, and any contacts who develop plague should be placed in isolation.

## Treatment and Prophylaxis

Early antibiotic therapy is recommended for persons deemed exposed to or infected with plague. Tetracyclines (e.g., doxycycline), fluoroquinolones (e.g., ciprofloxacin), and aminoglycosides (e.g., streptomycin, although not widely available, and gentamicin) are all antibiotics that have been used for post-exposure prophylaxis and treatment of plague. Specific treatment recommendations following a biological attack with plague will depend on several factors, including antibiotic susceptibility of the strain.

Antibiotic treatment should be initiated within 24 hours for patients showing symptoms of pneumonic infection, and should be continued for 10 days. Prophylactic antibiotics may be administered to protect people who have had known direct contact with infected patients, and should be continued for 7 days. People with suspected exposure to pneumonic plague should be placed under surveillance and monitored for symptoms. If symptoms develop, antibiotic therapy should be initiated immediately and continued for 10 days. In addition to antibiotic prophylaxis, people with established ongoing exposure to a patient with pneumonic plague should use standard respiratory droplet precautions.

## Clinical Presentation of Plague

Plague Infection	Incubation Period	Signs and Symptoms	Lethality
Pneumonic	2 to 4 days (range 1 to 6 days) after exposure	The first signs are fever, cough, muscle aches, and headache, with progression to chest pain, difficulty breathing, and hemoptysis (coughing blood). Nausea, vomiting, and abdominal pain might also occur.	Pneumonic plague is highly lethal when untreated or when antibiotic treatment is started more than 24 hours after the onset of symptoms. Untreated, the fatality rate of pneumonic plague approaches 100%.
Bubonic	1 to 8 days following exposure to an infected animal or sustaining a flea bite	Sudden onset of fever, chills, weakness, headache, and buboes will occur, typically followed by nausea and vomiting. The bubo is an extremely painful bump resulting from a swollen, tender lymph node, usually in the groin, armpit, or neck.	Without prompt treatment, or if left untreated, bubonic plague has a fatality rate of 50% to 60%.
Septicemic	Untreated, bubonic or pneumonic plague may develop into septicemic infection 2 to 6 days after initial symptoms appear.	Fever, chills, abdominal pain, nausea, vomiting, diarrhea. Later, this infection may lead to coagulation problems and gangrene of the extremities.	Without prompt treatment, or if left untreated, the fatality rate of septicemic plague approaches 100%.

## Countermeasures

A vaccine for plague is not currently available for civilian use in the United States. A U.S. licensed vaccine exists but it is no longer commercially available. This vaccine has some efficacy in preventing or lessening the severity of bubonic disease in a pre-exposure setting; however, it has not been shown to be effective in preventing pneumonic plague.

Research and development efforts for both an attenuated live vaccine and a subunit vaccine that protects against pneumonic plague are ongoing. A phase 2 clinical study of Dynport Vaccine Company's rF1V vaccine has been completed and research into other vaccines is underway.

Additionally, a number of promising new antibiotics and intervention strategies have yet to be fully explored experimentally.

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## See Also

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