

Micro Morphs

Male *Xenopsylla cheopis* (oriental rat flea) engorged with blood. This flea is the primary vector of plague in most large plague epidemics in Asia, Africa, and South America. Both male and female fleas can transmit the infection.



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Laboratory Professionals: Exceptional People – Exceptional Work

Yersinia pestis and Plague

From the Center for Disease Control and Prevention website
Public Health Preparedness and Response

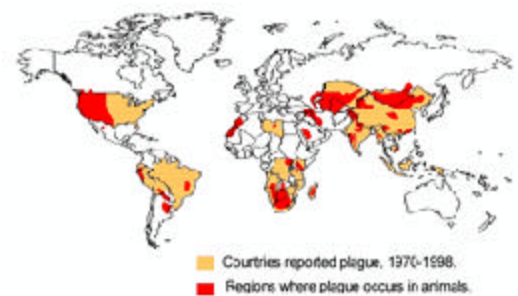
Introduction

Plague is an infectious disease of animals and humans caused by a bacterium named *Yersinia pestis*. People usually get plague from being bitten by a rodent flea that is carrying the plague bacterium or by handling an infected animal. Millions of people in Europe died from plague in the Middle Ages, when human homes and places of work were inhabited by flea-infested rats. Today, modern antibiotics are effective against plague, but if an infected person is not treated promptly, the disease is likely to cause illness or death.

Risks

Wild rodents in certain areas around the world are infected with plague. Outbreaks in people still occur in rural communities or in cities. They are usually associated with infected rats and rat fleas that live in the home. In the United States, the last urban plague epidemic occurred in Los Angeles in 1924-25. Since then, human plague in the United States has occurred as mostly scattered cases in rural areas (an average of 10 to 15 persons each year). Globally, the World Health Organization reports 1,000 to 3,000 cases of plague every year. In North America, plague is found in certain animals and their fleas from the Pacific Coast to the Great Plains, and from southwestern Canada to Mexico. Most human cases in the United States occur in two regions: 1) northern New Mexico, northern Arizona, and southern Colorado; and 2) California, southern Oregon, and far western Nevada. Plague also exists in Africa, Asia, and South America (see map).

World Distribution of Plague, 1998



Epidemics of plague in humans usually involve house rats and their fleas. Rat-borne epidemics continue to occur in some developing countries, particularly in rural areas. The last rat-borne epidemic in the United States occurred in Los Angeles in 1924-25. Since then, all human plague cases in the U.S. have been sporadic cases acquired from wild rodents or their fleas or from direct contact with plague-infected animals.

Rock squirrels and their fleas are the most frequent sources of human infection in the southwestern states. For the Pacific states, the California ground squirrel and its fleas are the most common source. Many other rodent species, for instance, prairie dogs, wood rats, chipmunks, and other ground squirrels and their fleas, suffer plague outbreaks and some of these occasionally serve as sources of human infection. Deer mice and voles are thought to maintain the disease in animal populations but are less important as sources of human infection. Other less frequent sources of infection include wild rabbits, and wild carnivores that pick up their infections from wild rodent outbreaks.

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***Yersinia pestis* and plague fact sheet cont'd.....**

Domestic cats (and sometimes dogs) are readily infected by fleas or from eating infected wild rodents. Cats may serve as a source of infection to persons exposed to them. Pets may also bring plague-infected fleas into the home.

Between outbreaks, the plague bacterium is believed to circulate within populations of certain species of rodents without causing excessive mortality. Such groups of infected animals serve as silent, longterm reservoirs of infection.

How Is Plague Transmitted?

Plague is transmitted from animal to animal and from animal to human by the bites of infective fleas. Less frequently, the organism enters through a break in the skin by direct contact with tissue or body fluids of a plague-infected animal, for instance, in the process of skinning a rabbit or other animal. Plague is also transmitted by inhaling infected droplets expelled by coughing, by a person or animal, especially domestic cats, with pneumonic plague. Transmission of plague from person to person is uncommon and has not been observed in the United States since 1924 but does occur as an important factor in plague epidemics in some developing countries.

Diagnosis

The pathognomic sign of plague is a very painful, usually swollen, and often hot-to-the touch lymph node, called a bubo. This finding, accompanied with fever, extreme exhaustion, and a history of possible exposure to rodents, rodent fleas, wild rabbits, or sick or dead carnivores should lead to suspicion of plague.

Onset of bubonic plague is usually 2 to 6 days after a person is exposed. Initial manifestations include fever, headache, and general illness, followed by the development of painful, swollen regional lymph nodes. Occasionally, buboes cannot be detected for a day or so after the onset of other symptoms. The disease progresses rapidly and the bacteria can invade the bloodstream, producing severe illness, called plague septicemia.

Once a human is infected, a progressive and potentially fatal illness generally results unless specific antibiotic therapy is given. Progression leads to blood infection and, finally, to lung infection. The infection of the lung is termed *plague pneumonia*, and it can be transmitted to others through the expulsion of infective respiratory droplets by coughing. The incubation period of primary pneumonic plague is 1 to 3 days and is characterized by development of an overwhelming pneumonia with high fever, cough, bloody sputum, and chills. For plague pneumonia patients, the death rate is over 50%.



Swollen lymph glands termed "buboes" caused by plague bacteria (bubonic plague). CDC website.

Treatment Information

As soon as a diagnosis of suspected plague is made, the patient should be isolated, and local and state health departments should be notified. Confirmatory laboratory work should be initiated, including blood cultures and examination of lymph node specimens if possible. Drug therapy should begin as soon as possible after the laboratory specimens are taken. The drugs of choice are streptomycin or gentamycin, but a number of other antibiotics are also effective. Those individuals closely associated with the patient, particularly in cases with pneumonia, should be traced, identified, and evaluated. Contacts of pneumonic plague patients should be placed under observation or given preventive antibiotic therapy, depending on the degree and timing of contact. It is a U.S. Public Health Service requirement that all suspected plague cases be reported to local and state health departments and the diagnosis confirmed by the CDC. As required by the International Health Regulations, CDC reports all U.S. plague cases to the World Health Organization.

Prevention

Plague will probably continue to exist in its many localized geographic areas around the world, and plague outbreaks in wild rodent hosts will continue to occur. Attempts to eliminate wild rodent plague are costly and futile. Therefore, primary preventive measures are directed toward reducing the threat of infection in humans in high risk areas through three techniques -- environmental management, public health education, and preventive drug therapy.

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Yersinia pestis and plague fact sheet cont'd.....

Environmental Management

Epidemic plague is best prevented by controlling rat populations in both urban and rural areas. This goal has been reached in the cities, towns, and villages of most developed countries. It has not been achieved in either the rural or urban areas of many developing countries where the threat of epidemic plague continues to exist. Control of plague in such situations requires two things: 1) close surveillance for human plague cases, and for plague in rodents, and 2) the use of an effective insecticide to control rodent fleas when human plague cases and rodent outbreaks occur.

Public Health Education

In regions such as the American West where plague is widespread in wild rodents, the greatest threat is to people living, working, or playing in areas where the infection is active. Public health education of citizens and the medical community should include information on the following plague prevention measures:

- Eliminating food and shelter for rodents in and around homes, work places, and recreation areas by making buildings rodent-proof, and by removing brush, rock piles, junk, and food sources (such as pet food), from properties.
- Surveillance for plague activity in rodent populations by public health workers or by citizens reporting rodents found sick or dead to local health departments.
- Use of appropriate and licensed insecticides to kill fleas during wild animal plague outbreaks to reduce the risk to humans.
- Treatment of pets (dogs and cats) for flea control once each week.

Preventive Drug Therapy

Antibiotics may be taken in the event of exposure to the bites of wild rodent fleas during an outbreak or to the tissues or fluids of a plague-infected animal. Preventive therapy is also recommended in the event of close exposure to another person or to a pet animal with suspected plague pneumonia. For preventive drug therapy, the preferred antibiotics are the tetracyclines, chloramphenicol, or one of the effective sulfonamides.

Vaccines

The plague vaccine is no longer commercially available in the United States.



Wayson stain of *Yersinia pestis*. Note the characteristic "safety pin" appearance of the bacteria. CDC website

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Laboratory Test Criteria for Diagnosis of Plague

From the Center for Disease Control and Prevention website

Human specimens:

Appropriate specimens should be examined for evidence of plague if a person resides in, or has a recent travel history to, plague-infected areas; has been bitten by fleas; and presents with symptoms suggestive of plague (fever, lymphadenopathy). Specimens should be obtained from appropriate sites for isolating the bacteria. The preferred specimen for microscopic examination and isolation from a bubonic case is material from the affected bubo, which should contain numerous organisms. Blood cultures should be taken whenever possible. Organisms may be seen in blood smears if the patient is septicemic, while blood smears taken from suspected bubonic plague patients are usually negative for bacteria. Bacteria may be intermittently released from affected lymph nodes into the bloodstream; therefore, a series of blood specimens taken 10-30 minutes apart may be productive in the isolation of *Y. pestis*. Sputum/throat smears taken from pneumonic plague patients may contain too many other organisms to be of diagnostic value if only Wayson stain is used; these smears should be stained as well with the more specific fluorescent-antibody (FA) test. Bronchial/tracheal washing should be taken from suspected pneumonic plague patients; throat specimens are not ideal for isolation of plague since they often contain many other bacteria that can mask the presence of plague.

In cases where live organisms are unculturable, e.g., in specimens taken postmortem, lymphoid tissues, lung and bone marrow samples may yield evidence of plague infection by FA test or by detection of *Y. pestis* DNA.

Specimens intended for culture should be taken **before** initiation of antibiotic treatment. Specimens are inoculated on general laboratory media and into laboratory mice for isolation; a thin smear is made from the remaining materials for examination by fluorescent microscopy. If a specimen is suspected to contain mixed flora, passage of the material through laboratory mice will increase the likelihood of recovery of a pure *Y. pestis* culture. Plague bacilli express a unique diagnostic envelope glycoprotein called the Fraction 1 (F1) antigen or capsular antigen at >33°C; this unique envelope antigen is the primary target antigen used for plague diagnostic FA and antibody tests. Plague bacilli are susceptible to lysis by a specific bacteriophage at both 25°C and 37°C. Plague bacilli are relatively inactive by standard enteric biochemical reactions; therefore, identification by biochemical profiles should be used as a supplemental diagnostic test. If a patient has been treated with a static antibiotic (e.g., tetracycline) for more than 4 days, bacterial cultures should be incubated for more than 5 days to give organisms a chance to recover. In case cultures yield negative results, serologic testing is advised. One serum specimen should be taken as early in the illness as possible to be followed by a second sample 1-4 months after antibiotic therapy has ceased.

SUSPECTED PLAGUE SHOULD BE CONSIDERED IF THE FOLLOWING CONDITIONS ARE MET:

Clinical symptoms that are compatible with plague, i. e., fever and lymphadenopathy in a person who resides in or recently traveled to a plague-endemic area.

If small gram-negative and/or bipolar-staining coccobacilli are seen on a smear taken from affected tissues, e.g.:

- Bubo (bubonic plague)
- Blood (septicemic plague)
- Tracheal/lung aspirate (pneumonic plague)

PRESUMPTIVE PLAGUE SHOULD BE CONSIDERED WHEN ONE OR BOTH OF THE FOLLOWING CONDITIONS ARE MET:

If immunofluorescence stain of smear or material is positive for the presence of *Yersinia pestis* F1 antigen.

If only a single serum specimen is tested and the anti-F1 antigen titer by agglutination is >1:10.*

CONFIRMED PLAGUE IS DIAGNOSED IF ONE OF THE FOLLOWING CONDITIONS IS MET:

If a culture isolated is lysed by specific bacteriophage.

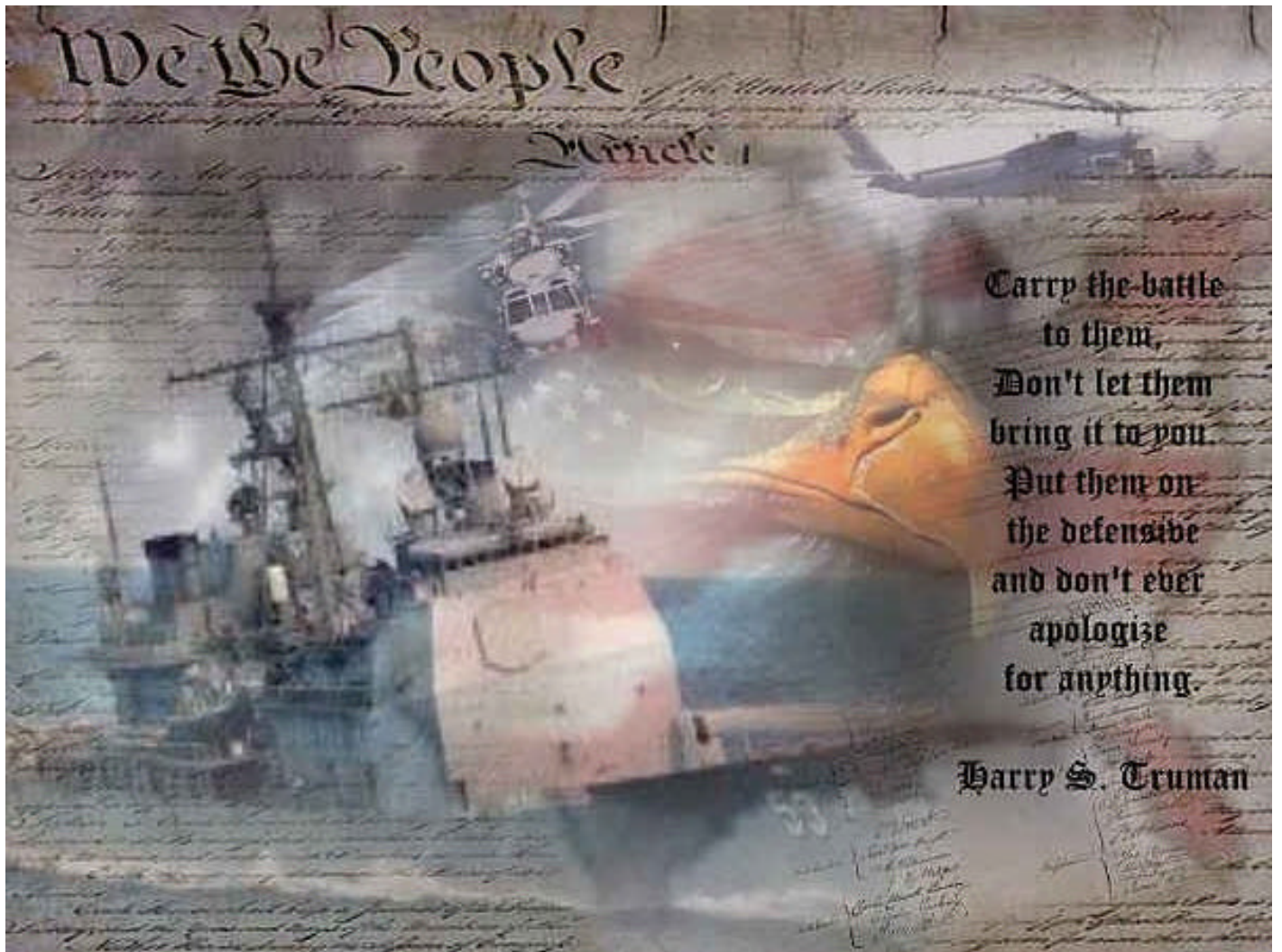
If two serum specimens demonstrate a four fold anti-F1 antigen titer difference by agglutination testing.*

If a single serum specimen tested by agglutination has a titer of >1:128 and the patient has no known previous plague exposure or vaccination history.*

*Agglutination testing must be shown to be specific to *Y. pestis* F1 antigen by hemagglutination inhibition.

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