

Plague Etiology

*Peste, Black Death,
Bubonic Plague, Pneumonic Plague,
Septicemic Plague, Pestis Minor*

Last Updated: Jan. 2004

Plague results from infection by *Yersinia pestis*, a non-motile, facultatively intracellular, Gram negative rod (family Enterobacteriaceae).

Geographic Distribution

Plague is seen in parts of North and South America, Africa, the Middle East, Central and Southeast Asia and Indonesia. Foci of infection are found in the former Soviet Union. This disease does not occur in Europe, Australia or Japan.

Transmission

Plague is usually spread between rodents or humans by the bites of infected fleas. Vectors include a variety of rodent fleas, particularly the oriental rat flea (*Xenopsylla cheopis*). In the U.S., the most common vector is *Oropsylla montana*, a flea often found on California ground squirrels, rock squirrels, and sometimes other rodents including prairie dogs. Human fleas (*Pulex irritans*) may also carry *Y. pestis*. *Y. pestis* is also present in the tissues and body fluids of infected animals; these bacteria can be transmitted directly through mucous membranes and broken skin. Aerosols from people or animals with the pneumonic form are infectious and animals may transmit bacteria in bites. Carnivores often become infected when they eat diseased rodents.

In the wild, *Y. pestis* is maintained in cycles between wild rodents and fleas; sporadic cases occur in humans and domestic animals when they come into contact with infected animals or fleas. Infection of rodents in urban areas, particularly the Roof rat or Norway rat, can result in epizootic and epidemic plague in humans. Direct person-to-person transmission can occur in pneumonic plague.

Y. pestis can survive for long periods of time in organic material; it may remain viable for up to 100 days in blood and for as long as 9 months in human bodies. Infectious bacteria can also be found in water, moist soil and grains for several weeks. *Y. pestis* is not resistant to desiccation or heat: it is destroyed by exposure to 55°C for 15 minutes or several hours in sunlight.

Disinfection

Y. pestis is susceptible to a number of disinfectants including 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, formaldehyde and iodine-based and phenolic disinfectants. It can also be inactivated by moist heat (121° C for at least 15 min) or dry heat (160–170° C for at least 1 hour).

Infections in Humans

Incubation Period

The incubation period for pneumonic plague is 1 to 3 days. The symptoms of bubonic plague appear after 2 to 6 days.

Clinical Signs

Three major forms of plague are seen in humans: bubonic plague, septicemic plague, pneumonic plague.

Bubonic plague appears acutely; the initial symptoms may include fever, headache, malaise and myalgia. Vomiting, nausea, abdominal pain, hepatomegaly and splenomegaly are sometimes seen. Patients with bubonic plague typically develop an infected, swollen, and very painful draining lymph node, called a bubo; the bubo is often one of the femoral or inguinal lymph nodes. Other lymph nodes, or multiple nodes, may also be involved. In some cases, a pustule, vesicle, eschar or papule occurs at the site of the flea bite.

Bubonic plague can develop into septicemic plague. Bacteremia is present in most cases of bubonic plague but the symptoms of septicemia – including high fever, chills, malaise, nausea, vomiting, abdominal pain, diarrhea and hypotension – do not always develop. Meningitis is relatively rare; it occurs in approximately 6% of people with the septicemic or pneumonic forms. Thromboses in blood vessels can cause necrosis and



**Institute for International
Cooperation in Animal Biologics**
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine



IOWA STATE UNIVERSITY®

**Center for Food
Security and Public Health**
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294-7189
FAX: (515) 294-8259
E-mail: cfsph@iastate.edu
Web: <http://www.cfsph.iastate.edu>

gangrene of the extremities or disseminated intravascular coagulation (DIC).

Pneumonic plague occurs after inhalation of bacteria or after blood-borne spread to the lungs. Pneumonic plague is expected to be the predominant form in a bioterrorist attack. The symptoms of pneumonic plague develop acutely and include high fever, chills, headache, myalgia and malaise. Nausea, vomiting, diarrhea and abdominal pain may be seen. Within 24 hours, a cough with bloody sputum develops; the sputum contains only specks of blood at first but eventually becomes foamy and pink or red. Cervical buboes occur rarely. Pneumonic plague is rapidly fatal, with dyspnea, stridor and cyanosis ending in respiratory failure and circulatory collapse.

Pestis minor is a benign form of bubonic plague, usually seen only in regions where plague is endemic. Pestis minor is characterized by fever, lymphadenitis, headache and prostration. These symptoms resolve spontaneously within a week.

Communicability

In the United States, person-to-person transmission of bubonic plague has not occurred since 1924; however, person-to-person transmission is seen in epidemics in some countries. Pneumonic plague can be highly contagious, particularly under crowded conditions

Diagnostic Tests

A presumptive diagnosis can be made by identifying the characteristic organisms in sputum, blood, lymph node (bubo) aspirates or cerebrospinal fluid; *Y. pestis* is a Gram negative, non-motile, facultative intracellular coccobacillus with bipolar staining. Organisms can be identified by immunofluorescence. Immunoassays can also detect *Y. pestis* antigens in serum. Polymerase chain reaction (PCR) assays are used in research. Bacteriophage typing can be helpful in tracing outbreaks.

Plague can also be diagnosed by isolation of *Y. pestis*. Organisms can be recovered from sputum, blood or aspirates of lymph nodes and may be cultured on ordinary media including blood agar, MacConkey agar or infusion broth. Automated systems may misidentify this bacterium, as it grows slowly and biochemical reactions may be delayed. Guinea pig inoculation can also be used.

Serology is occasionally helpful. A fourfold rise in titer is diagnostic. Latex agglutination is most often used, but passive hemagglutination tests and complement fixation are also available.

Treatment and Vaccination

Antibiotics are effective in the early stages of bubonic or pneumonic plague; in pneumonic plague, their efficacy is often limited after 24 hours. Buboes are occasionally drained but usually resolve with antibiotic treatment.

Vaccines may be available for people with occupational risk factors; these vaccines are not wholly protective, particularly against the pneumonic form. A whole cell vaccine was marketed until November 1998 but appears to have been taken off the market. A new vaccine is in development and may be more effective against both forms of plague.

Morbidity and Mortality

The mortality rate is approximately 50 to 60% for untreated bubonic plague and nearly 100% for untreated pneumonic plague. The pneumonic form is often fatal within 48 hours after it becomes symptomatic. Early treatment reduces the mortality rate to less than 5%; however, treatment for the pneumonic form must be started during the first 24 hours after symptoms begin.

Worldwide, approximately 1,000 to 2,000 cases of plague are seen annually; epidemics occur regularly in Africa and Asia. Sporadic cases also occur in North and South America after exposure to wild rodents and fleas. In the United States, approximately 18 cases of plague were seen yearly during the 1980s; the mortality rate for these cases was approximately 14%.

Infections in Animals

Species Affected

More than 200 species of mammals can be infected with *Y. pestis*. Rodents are the reservoir hosts. Many rodents, including prairie dogs, chipmunks, wood rats, ground squirrels, deer mice and voles suffer occasional epidemics or maintain the virus in natural cycles. Rock squirrels and the California ground squirrel are often the sources of human infections in the United States. Rats are usually the carriers for epidemics in humans. Rabbits, wild carnivores, domestic cats and dogs can develop plague when they are exposed to infected rodents or their fleas; among carnivores, cats are particularly susceptible.

Incubation Period

Clinical signs can develop within 3–4 days in experimentally infected cats.

Clinical Signs

Asymptomatic infections and mild illness are typical in some reservoir hosts. Wild carnivores including coyotes, skunks and raccoons can also seroconvert without clinical disease. Other animals may have fever, lymphadenitis, abscesses in internal organs, or sudden death from sepsis.

In cats, clinical signs can include fever, anorexia, dehydration and depression. Infected cats may develop enlarged lymph nodes near the site of infection: the submandibular or cervical lymph nodes are most often involved. Infected lymph nodes can develop abscesses, ulcerate and drain. Swellings may also be seen around the

head, neck and eyes. Sneezing, hemoptysis, incoordination, quadriplegia, necrotic tonsillitis and symptoms of pneumonia may occur.

Dogs seem to be relatively resistant to plague and animals may seroconvert without symptoms. High fevers and lymphadenopathy, with occasional deaths, have also been seen. Ten experimentally infected dogs developed a fever and other signs of illness but recovered spontaneously during the next week.

Communicability

Yes. Bacteria can be transmitted in aerosols, by direct contact with tissues and body fluids, and in bites. Infected fleas can transmit bacteria for months.

Diagnostic Tests

Plague can be diagnosed by isolation of *Y. pestis*; bacteria may be found in blood, nasal swabs, lymph node aspirates, transtracheal aspirates and tissue samples. If neurologic signs are present, cerebrospinal fluid (CSF) may yield bacteria. *Y. pestis* is a Gram negative, non-motile, facultative intracellular coccobacillus with bipolar staining. The organism can be identified by immunofluorescence or antigen-capture enzyme linked immunosorbent assays (ELISAs).

Organisms can also be cultured; *Y. pestis* will grow on ordinary media including blood agar, MacConkey agar or infusion broth. Automated systems may misidentify this bacterium, as it grows slowly and biochemical reactions may be delayed. Guinea pig inoculation can also be used. A rise in titer in paired serum samples is diagnostic, if the animal survives; the latex hemagglutination and passive hemagglutination tests (PHA) are often used.

Treatment and Vaccination

Early treatment with antibiotics can be successful.

Morbidity and Mortality

In endemic areas, many rodents – including chipmunks, wood rats, ground squirrels, deer mice and voles – suffer occasional epidemics. Mortality in some rodent species can be high; infections are fatal in nearly 100% of prairie dogs. Between outbreaks, bacteria seem to cycle in reservoir populations without causing high mortality.

The mortality rate is 50% in cats fed plague-infected mice; sick cats may die within 1 to 2 days or after several weeks. Dogs, coyotes, raccoons, skunks and other carnivores often seroconvert without symptoms; clinical infections and deaths are relatively rare in these species. Ten experimentally infected dogs recovered spontaneously.

Post-Mortem Lesions

Post mortem lesions vary with the type of infection. Signs can include lymphadenopathy, bacterial pneumonia with lung hemorrhages, and necrosis in the liver, spleen and other internal organs.

Internet Resources

Centers for Disease Control and Prevention (CDC) Plague Pages
<http://www.bt.cdc.gov/agent/plague/index.asp>

Material Safety Data Sheets–
 Canadian Laboratory Center for Disease Control
<http://www.hc-sc.gc.ca/pphb-dgsp/msds-ftss/index.html#menu>

Medical Microbiology
<http://www.gsbs.utmb.edu/microbook>

The Merck Manual
<http://www.merck.com/pubs/mmanual/>

The Merck Veterinary Manual
<http://www.merckvetmanual.com/mvm/index.jsp>

USAMRIID's Medical Management of
 Biological Casualties Handbook
<http://www.vnh.org/BIOCASU/toc.html>

References

- Biberstein, E.L. and J. Holzworth. "Bacterial Diseases. Plague." In *Diseases of the Cat*. Edited by J. Holzworth. Philadelphia, PA: W.B. Saunders, 1987, p. 294; 660.
- Collins, F.M. "Pasteurella, Yersinia, and Francisella." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 20 November 2002 <<http://www.gsbs.utmb.edu/microbook/ch029.htm>>.
- "Bacterial infections caused by Gram-negative bacilli. Enterobacteriaceae." In *The Merck Manual*, 17th ed. Edited by M.H. Beers and R. Berkow. Whitehouse Station, NJ: Merck and Co., 1999. 8 Nov 2002 <<http://www.merck.com/pubs/mmanual/section13/chapter157/157d.htm>>.
- Butler, T. In *Zoonoses*. Edited by S.R. Palmer, E.J.L. Soulsby and D.I.H Simpson. New York: Oxford University Press, 1998, pp. 286–292.
- "Control of Communicable Diseases." Edited by J. Chin. American Public Health Association, 2000, pp.532–535.
- "Information on plague." *Centers for Disease Control and Prevention (CDC)*, June 2001. 19 Nov 2002 <<http://www.cdc.gov/ncidod/dvbid/plague/info.htm>>.
- Macy, D.W. "Plague." In *Infectious Diseases of the Dog and Cat*. Edited by C.E. Greene. Philadelphia: W.B. Saunders, 1998, pp. 295–300.
- Macy, D.W. "Plague." In *Current Veterinary Therapy X. Small Animal Practice*. Edited by R.W. Kirk and J.D. Bonagura. Philadelphia: W.B. Saunders, 1989, pp. 1088–91.

- “Material Safety Data Sheet –*Yersinia pestis*.”
Canadian Laboratory Centre for Disease Control,
March 2001. 20 November 2002 <<http://www.hc-sc.gc.ca/pphb-dgsp/msds-ftss/msds169e.html>>.
- “Plague.” In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 19 Nov 2002 <<http://www.vnh.org/BIOCASU/9.html>>.
- “Plague.” In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 485–6.