Plague

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

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Importance

Plague is an important zoonotic bacterial disease, and a cause of significant mortality in wild rodents and rabbits. In some animals such as prairie dogs, outbreaks may kill nearly all of the animals in a colony. Sporadic cases also occur in other wild and domesticated mammals, particularly felids. Infections in animals can be transmitted to humans, resulting in life-threatening disease. Pneumonic plague, which is a particularly deadly form of the disease, is usually fatal if antibiotics are not started very soon after the symptoms appear. Bubonic plague, the most common form, is less fulminant, but also has a high mortality rate if left untreated.

At least three major plague pandemics have been seen in human populations. The Justinian plague occurred in the Mediterranean region in the 6th century AD and caused an estimated 100 million deaths, and the Black Death killed a third of the European population beginning in the 14th century. The most recent pandemic, which began in China in the late 1800s, spread worldwide and caused an estimated 12 million fatalities by 1930. The organisms that caused these three pandemics still exist in wild animal reservoirs in parts of the world, and occasionally spill over from these reservoirs to affect people or other animals. More than a thousand human cases and 100 to 200 deaths are reported annually to the World Health Organization (WHO), and many additional cases are probably not diagnosed. Most outbreaks occur in Asia and Africa, but sporadic cases and outbreaks can be seen in any endemic region. Plague may reoccur after a long period when the disease seems to disappear; recent outbreaks in India, Indonesia and Zambia followed quiescent periods of 30 to 50 years. An additional concern is that the agent of plague has been identified as a potential biological weapon.

Etiology

Plague results from infection by *Yersinia pestis*, a Gram negative bacillus in the family Enterobacteriaceae. Only one serotype is recognized. *Y. pestis* can be divided into three biovars: Antiqua, Medievalis, and Orientalis. The Antiqua strains are more variable than isolates in the other two biovars. Other classification schemes have also been proposed, and some recent analyses classify isolates using genetic markers.

There are three principal forms of plague, defined mainly by the syndrome in humans. Bubonic plague is the most common form, and usually results from the inoculation of *Y. pestis* into the skin. Patients with bubonic plague typically develop a swollen and very painful draining lymph node, called a bubo, in addition to other clinical signs. Pneumonic plague occurs after the inhalation of bacteria (primary pneumonic plague) or after blood–borne spread to the lungs (secondary pneumonic plague). The third form, septicemic plague, may occur without obvious involvement of the lymph nodes (primary septicemic plague) or as the result of dissemination of the other two forms.

Recent evidence suggests that attenuated strains of *Y. pestis* used in research might be virulent in some circumstances. One of these strains (*Y. pestis* KIM) caused fatal septicemic plague in a researcher who was an insulin-dependent diabetic and also had evidence of hereditary hemochromatosis. There is some evidence that hemochromatosis might have been a predisposing factor, possibly by providing iron deposits this organism was able to exploit. Immunosuppression from the diabetes might also have played a role.

Species Affected

Rodents and lagomorphs are the most important host species for plague. These animals are infested with fleas that can transmit *Y. pestis*, and develop bacteremia high enough to infect those fleas. Infections have been documented in more than 200 species and subspecies of rodents. Significant rodent hosts include prairie dogs (*Cynomys* spp.), ground squirrels/ susliks (*Spermophilus* spp.), antelope ground squirrels (*Ammospermophilus* spp.), chipmunks (*Tamias* spp.), rats (*Rattus* spp.), wood rats (*Neotoma* spp.). mice (*Peromyscus* spp.), Siberian marmots (*Marmota sibirica*), voles (*Microtus* spp.), jerboas, and some gerbils (*Rhombomys opimus* and

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Meriones spp.). The principal rodent hosts vary with the geographic region. Pikas *(Ochotona* spp.), which are lagomorphs, are also important hosts in Asia.

Many other species of mammals also become infected, but the majority are incidental hosts. Some species are more likely to develop clinical signs than others. Felids seem to be particularly susceptible to plague; fatal disease has been reported in housecats and wild cats including bobcats (*Lynx rufus*) and mountain lions (*Puma concolor*). Black-footed ferrets (*Mustela nigripes*) are also very susceptible. Infrequent cases of plague have been described in ungulates including camels (*Camelus bactrianus* and *Camelus dromedarius*), various species of deer, pronghorn antelope (*Antilocapra americana*), at least one llama, and goats. *Y. pestis* infections have also been reported in dogs, coyotes (*Canis latrans*), foxes, badgers, skunks and nonhuman primates.

Zoonotic potential

Humans are susceptible to infection with *Y. pestis* as incidental hosts, and are not involved in the natural cycle of this organism outside epidemics.

Geographic Distribution

Y. pestis can be found in parts of Africa, the Middle East, Asia, and North and South America, as well as Madagascar. The distribution of this organism is patchy. In North America, *Y. pestis* occurs in the western third of the continent, from British Columbia and Alberta, Canada to Mexico, and as far east as Dallas and the western borders of Kansas, Nebraska, Oklahoma and South Dakota. In South America, active foci have been identified mainly in Brazil and the Andes mountain region of Bolivia, Peru and Ecuador. In Asia, plague has been reported from areas in the former U.S.S.R. east through China, and south to Southwest and Southeast Asia. In Africa, this disease occurs primarily in the eastern and southern regions, but foci are also found in the west and north. Plague is not endemic in Europe or Oceania.

The distribution of each biovar varies. The Antiqua biovar occurs in Africa and Central Asia, and the Medievalis biovar seems to be found mainly in Central Asia (however, one isolate was reported in northern Africa). The Orientalis biovar can be found in most regions where plague occurs.

Transmission

Plague is usually transmitted by the bites of infected fleas. More than 30 species of fleas are capable of transmitting *Y. pestis*, but they vary in their efficiency as vectors. The oriental rat flea, *Xenopsylla cheopis*, is a particularly effective biological vector. Other species of rodent fleas are also important in transmission. Dog and cat fleas (*Ctenocephalides* spp) can be infected, but are poor vectors compared to species such as *X. cheopis*. Human fleas (*Pulex irritans*) can also carry *Y. pestis*. Fleas are usually short-lived; however, some may survive for several months, or even a year or more, in rodent burrows after their hosts have died. During epizootics, there is a high risk that fleas leaving dead animals will bite species they do not usually infest, such as humans. Other arthropods have also been proposed as potential vectors. *Y. pestis* has been detected in human lice during outbreaks in people, and lice were able to transmit the infection between rabbits in the laboratory. Ticks have been suggested as possible mechanical vectors in some countries.

Direct transmission can also occur between animals or people, but the importance of this route varies with the form of the disease. *Y. pestis* is present in tissues, draining lesions and some body fluids, and these bacteria may enter the body through mucous membranes and broken skin. Person-to-person spread of bubonic plague seems to be rare or nonexistent, though theoretically possible. In contrast, people or animals with the pneumonic form may transmit *Y. pestis* in respiratory droplets. In humans, this occurs most readily in crowded, poorly ventilated conditions. Pnuemonic plague is most contagious during its final stages, when the number of bacteria in the sputum increases. In the earlier stages, transmission does not seem to occur as readily.

Animals, including cats, can transmit bacteria in bites. Carnivores and omnivores, including humans, may also be infected by eating tissues from infected animals. In camels and other herbivores, this might occur when dead rodents or their excretions contaminate the animal's feed. At present, there is little information about the survival and growth of *Y. pestis* in food products. In one study, an attenuated *Y. pestis* strain (*Y. pestis* KIM5) was able to persist without growth in raw meat (ground pork) for at least 2 months at 4°C, and to grow in this product at 10-30°C.

Y. pestis can be transmitted on fomites at least for short periods; however, its long-term survival in the environment, particularly in soil, is still poorly understood. This organism is not resistant to desiccation or heat, and on surfaces such as glass and steel, it usually persists for less than 72 hours. However, it is reported to 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. Viable *Y. pestis* was recently found after 24 days in soil that had been contaminated by the blood of a dead mountain lion. In the laboratory, this organism can survive for many months, and possibly years, in autoclaved soil, and for long periods in water. Rodents have been infected experimentally by burrowing in or running over recently contaminated soil, but whether this is an important maintenance mechanism for plague remains to be determined.

Epidemiology

In the wild, *Y. pestis* seems to be maintained in cycles between wild rodents or lagomorphs (e.g., pikas) and fleas. Periodically, these animals experience epizootics, increasing the risk of transmission to other species. What

triggers these epizootics, and how *Y. pestis* persists during interepizootic periods, is poorly understood. Whether this organism circulates in its epizootic hosts between outbreaks, or in a different 'maintenance' host, is controversial.

Sporadic cases of plague occur in people who are exposed to tissues from wild animals, or to their fleas. Domesticated animals can act as 'bridges' that carry *Y. pestis* closer to humans. These animals may become infected themselves, or they can simply act as temporary hosts for infected fleas. Infection of rodents in urban areas, particularly rats, can result in epidemic plague in humans. The importance of different transmission routes during human epidemics (e.g., aerosols, or transmission via ectoparasites) is still incompletely understood.

Human infections

Most human cases are associated with wild rodents or lagomorphs, but other species have also been involved. Among domesticated animals, cats seem to be most likely to transmit plague to humans. Unusually, a recent case of primary pneumonic plague in China, which then spread to 11 human contacts, was attributed to close contact with a severely ill, *Y. pestis* (Antiqua biovar) infected dog. One study suggested that extended contact with dogs may increase the risk of plague, possibly by bringing infected rodent fleas into the household. Small outbreaks have also been reported in people who ate uncooked tissues from infected hosts (e.g., uncooked camel liver or guinea pig flesh). A few human cases have been attributed to contact with wild animals including bobcats, coyotes, mountain lions, foxes and badgers. In these cases, it may sometimes be difficult to determine whether the organism was acquired directly from an animal or from infected fleas.

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 [250° F] for at least 15 minutes) or dry heat (160-170° C [320-338°F] for at least 1 hour).

Infections in Animals

Incubation Period

Clinical signs usually develop within 1 to 4 days in cats. Few cases have been reported in other species.

Clinical Signs

The three principal forms of plague - bubonic plague, septicemic plague and pneumonic plague - seem to occur in animals as well as humans; however, plague should be a consideration in any animal with a systemic infection and a history of potential exposure in an endemic area.

Most cats infected with *Y. pestis* develop the bubonic form. This form is usually characterized by fever, anorexia and lethargy, with an enlarged lymph node (bubo) near the site of inoculation. Many cats are probably infected by ingestion, and the submandibular lymph nodes are most often involved. The affected lymph node may develop abscesses, ulcerate and drain. Some cats also have cellulitis, abscesses at sites other than lymph nodes, mouth lesions including ulcers, or necrotic tonsillitis. Vomiting, diarrhea, ocular discharges, dehydration and weight loss have been reported. Bubonic plague can progress to septicemic plague, with typical signs of sepsis. Disseminated intravascular coagulation (DIC) and/or respiratory distress may be seen. Primary septicemic plague, without a bubo, has also been reported in cats. Pneumonic plague can develop in cats with bubonic or septicemic plague, and is characterized by respiratory signs including dyspnea and hemoptysis. Neurological signs such as incoordination have been reported in some infected cats. Studies in experimentally infected cats and serological surveys suggest that some animals might have mild or asymptomatic infections after exposure.

Dogs seem less likely to become ill than cats, and subclinical infections may be more common. Only rare descriptions of plague in naturally infected dogs have been published: the clinical signs included fever, lethargy, submandibular lymphadenitis, lesions in the mouth and coughing. Two recent, linked cases in China were characterized by prostration, anorexia, and severe coughing and vomiting with blood in the nose and mouth, and death within a few days. Experimentally infected dogs inoculated by the subcutaneous or oral routes developed a fever and other signs of illness, but recovered spontaneously during the next week. However, two dogs exposed via aerosols died.

In rodents, the outcome varies from subclinical infection or mild illness to severe, rapidly fatal disease. Epizootics with high mortality rates are reported among some rodents and lagomorphs. Infections in other wild animals are poorly understood. Infected mountain lions, bobcats, coyotes, foxes and other animals have occasionally been found dead. Fever and lethargy, without bacteremia, were reported in experimentally infected raccoons in one study. In another experiment, neither fever nor deaths were seen in this species, or in coyotes and striped skunks infected by the oral route. Whether individual susceptibility or other factors (e.g., dose or route of exposure, or underlying illness) affect the outcome in these species is not known.

Occasional cases of plague have been reported in domesticated or wild ungulates. Ocular plague, characterized by keratoconjunctivitis, endophthalmitis and panophthalmitis, has been documented in mule deer (*Odocoileus hemionus*) and black-tailed deer (*Odocoileus hemionus columbianus*). Septicemia and pneumonia have also been seen in mule deer, either with or without ocular

signs. Overall, plague is not reported to be an important cause of morbidity and mortality in this species. Goats and camels can become ill and die, and a death was reported in a llama in New Mexico. Clinical cases have not been reported in the literature in cattle, horses or pigs.

Post Mortem Lesions

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In cats, necrotic foci may be found in the liver, spleen, lungs and other internal organs. The liver may be pale and the spleen enlarged. Affected lymph nodes can be markedly swollen, with necrosuppurative inflammation, edema and hemorrhages. Diffuse interstitial pneumonia, focal congestion, abscesses and hemorrhages may be found in the lungs.

In wild animals, reported lesions have included hemorrhagic buboes and splenomegaly in some acute cases, or caseous buboes and necrotic lesions in the spleen, liver and lungs when the disease progresses more slowly. Keratoconjunctivitis, endophthalmitis and panophthalmitis, as well as septicemic lesions, pneumonia and lymphadenitis have been reported in deer.

Diagnostic Tests

A presumptive diagnosis can be made by identifying the characteristic organisms in clinical samples such as lymph node (bubo) aspirates or swabs of draining lesions. Some types of samples, such as lymph nodes, may contain a relatively homogenous population of bacteria. *Y. pestis* is a Gram negative, facultative intracellular coccobacillus or bacillus with bipolar staining. Bipolar staining is particularly evident when Wright-Giemsa or Wayson stains are used. Bacteria in clinical samples can be identified by immunofluorescence. Rapid immunoassays can also be used to detect *Y. pestis* antigens in clinical samples, and PCR may be used to identify nucleic acids. *Y. pestis* can sometimes be detected by PCR or other techniques in fleas collected from the animal.

Plague can also be diagnosed by isolating *Y. pestis* from blood, nasal/oral swabs, lymph node aspirates, swabs of draining lesions, transtracheal aspirates and/or tissue samples including the liver, spleen, lungs and affected lymph nodes. Specimens for culture should be collected before antibiotics are started. *Y. pestis* will grow on ordinary media including blood agar, MacConkey agar, nutrient agar or brain-heart infusion broth. *Yersinia*-specific CIN agar can also be used; this medium is particularly helpful with contaminated samples. *Y. pestis* can be identified with routine biochemical tests and other methods. It should be kept in mind that automated systems may misidentify this bacterium, as it grows slowly and biochemical reactions may be delayed. A specific bacteriophage that lyses only *Y. pestis* and not *Y. pseudotuberculosis* is used as a rapid diagnostic test in reference laboratories. Although animal assays are generally discouraged if there are other alternatives, *Y. pestis* may also be recovered in laboratory animals such as mice, particularly when the sample is contaminated with other organisms.

Serology using paired serum samples can be helpful. A single sample, together with consistent clinical signs, may also be supportive. Various serological tests including latex hemagglutination and passive hemagglutination may be available.

Treatment

Early treatment with antibiotics can be successful. Some antibiotics that have been used to treat plague in animals include streptomycin, gentamicin, doxycycline, tetracycline and chloramphenicol. Drug availability may vary with the country.

Control

Disease reporting

Veterinarians who encounter or suspect a case of plague should follow their national and/or local guidelines for disease reporting. In endemic areas, prompt reporting helps prevent exposure of other animals and humans. In addition to any other state reporting requirements, all suspected cases of animal or human plague in the U.S. should be reported to the local or state public health department. The state public health laboratory or U.S. Centers for Disease Control (CDC) laboratory should be contacted before collecting or shipping samples.

Prevention

A good flea control program should be established for dogs and cats, and they should be kept from eating tissues from animals that may be infected. Allowing animals to hunt or roam increases the risk of infection in endemic areas. Animals that become ill should be examined by a veterinarian. Barrier precautions are necessary during examination and treatment, and suspected cases are isolated. The most stringent measures are needed before antibiotics are begun and during the initial stages of treatment. Personal protective equipment (PPE) may include gloves, surgical masks to prevent droplet infection, protective clothing, and eye protection if splashes or sprays are expected. Excellent hygiene should be practiced.

Vaccination has been used to protect endangered black-footed ferrets, which are highly susceptible to plague, during epizootics. Vaccines (in food bait) were also given to prairie dogs, which are the food source for these ferrets, and prairie dog burrows were dusted with an insecticide. Vaccines have been tested in other wildlife species susceptible to plague, and they might be promising for controlling *Y. pestis* in rodents near human environments. Vaccines are not currently available for domesticated animals.

Morbidity and Mortality

In endemic areas, epizootics occur periodically in susceptible rodents and lagomorphs. Resistance to plague differs between rodent species, and the percentage of individuals that survive *Y. pestis* infection can vary. The

mortality rate in some species can approach 100%. Between epizootics, plague persists in wild animals without causing high mortality. Populations that live in endemic areas may be more resistant than those outside these regions.

Among domesticated animals, cats seem to be particularly susceptible to plague. One study reported that the mortality rate was 14% in housecats with bubonic plague, 70% in cats with septicemic plague (or cases that were not classified into a form), and 83% in the pneumonic form. In experimentally infected cats with bubonic plague, the case fatality rate can be as high as 60% if the disease is left untreated. Subclinical infections also seem to occur. Surveillance has reported antibodies in healthy cats, and some cats have survived experimental infections. In one study, 20 of 25 cats inoculated by ingestion or subcutaneous inoculation became ill, but three cats seroconverted without clinical signs. Dogs do not seem to be as susceptible to plague as cats. Ten experimentally infected dogs that were inoculated by subcutaneous or oral inoculation experienced only a brief illness and recovered on their own. However, severe illness is possible. Two dogs infected by aerosols died, and fatal cases of plague have been reported rarely in naturally infected dogs.

Serological evidence suggests that wild carnivores are frequently exposed to *Y. pestis*, probably through hunting. Fatal cases of plague have been reported in large cats including bobcats and mountain lions. A recent survey from the western U.S. found that 2% of apparently healthy bobcats and mountain lions in California, and 21% to 46% of these animals in different regions of Colorado, had antibodies to *Y. pestis*. Seroprevalence rates of 13-14% in raccoons and coyotes, and 55% in badgers, have also been reported. Endangered black-footed ferrets (*M. nigripes*) are very susceptible to plague, and have a high mortality rate. In contrast, experimentally infected domesticated ferrets (*Mustela putorius furo*) and Siberian polecats (*M. eversmanni*) did not become ill.

Infections in Humans

Incubation Period

Pneumonic plague develops rapidly, within 1 to 4 days. The incubation period for bubonic plague is 1 to 10 days, but in most cases, the symptoms usually appear in 2 to 5 days.

Clinical Signs

Bubonic plague is the most common form of plague in humans. It begins with the sudden onset of high fever, chills, headache, malaise and myalgia. Dizziness, nausea and vomiting may also be seen, in addition to an infected, swollen and very painful draining lymph node (the bubo). Although it can occur anywhere, the bubo is often one of the femoral or inguinal lymph nodes. In some cases, a pustule, vesicle, eschar or papule may be found at the site of the flea bite; however, this is often absent or missed. People who become infected by ingestion can develop severe pharyngitis and tonsillitis, with swelling of a submandibular lymph node and the neck. Vomiting, diarrhea and abdominal pain may also be seen. In a recent outbreak linked to eating undercooked camel meat, gastrointestinal signs without prominent pharyngeal signs were the primary syndrome. If it is not treated, bubonic plague often progresses to septicemia and/or secondary pneumonia.

Approximately 10-25% of human plague cases are characterized by primary septicemia. In addition to high fever and other signs in common with bubonic plague, this form has signs of sepsis, but there may be no obvious involvement of the lymph nodes. Epistaxis, hematuria petechiae, DIC and neurological signs may also be seen, and the course of the disease can be rapid, with multiorgan failure. Secondary septicemia is similar, but results from disseminated bubonic plague. Meningitis is a relatively rare form of plague; it occurs in approximately 6% of people with the septicemic or pneumonic forms.

Pneumonic plague occurs after the inhalation of bacteria or after blood–borne spread to the lungs. The symptoms of pneumonic plague develop acutely and include high fever, chills, headache (often severe), myalgia, malaise and an increased respiratory rate. Within 24 hours, a cough develops; it is initially dry but becomes productive, then bloodstained and/or purulent. The sputum contains only specks of blood at first but eventually becomes foamy and pink or red from blood. 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 among people in regions where plague is common. Pestis minor is characterized by fever, lymphadenitis, headache and prostration, which resolve spontaneously within a week.

Diagnostic Tests

A presumptive diagnosis can be made, as for animals, by identifying the characteristic organisms in sputum, bronchial/tracheal washings, blood, lymph node (bubo) aspirates, cerebrospinal fluid (CSF) or postmortem tissue samples. Rapid immunoassays employed with human samples include an F1 antigen test used in Africa.

Plague can also be diagnosed by isolating *Y. pestis*. Organisms may be recovered from respiratory secretions, blood and/or aspirates of affected lymph nodes, depending on the form of the disease, as well as from lungs and other tissues postmortem. Organisms are usually present in blood only during septicemia; however, bacteria are sometimes released intermittently from lymph nodes into the blood, and a series of blood samples collected 10-30 minutes apart may be diagnostic. Specimens for culture should be collected before antibiotics are started.

Serology is occasionally helpful. Serological tests include ELISAs, passive hemagglutination, hemagglutination-inhibition, latex agglutination and complement fixation. A fourfold rise in titer is diagnostic.

Treatment

Antibiotics are effective for the treatment of plague; however, their efficacy in the pneumonic form is often limited if the symptoms have been present for more than 20 hours. Buboes are occasionally drained but usually resolve with antibiotic treatment. Although antibiotic resistant strains of *Y. pestis* have been detected, they seem to be rare. In a recent study, no resistant *Y. pestis* was found among approximately 400 isolates from the Americas, Asia and Africa, including nearly 300 organisms isolated between 1995 and 2009.

Control

In endemic areas, rodents should be controlled around human homes, workplaces and recreational areas. Buildings should be rodent-proofed, and access to food sources should be prevented. Brush, rock piles, junk and cluttered firewood should not be allowed to accumulate, as they may provide nesting places for rodents. Campers and hikers should not approach rodents or their carcasses, and should avoid sleeping beside rodent burrows. Prevention methods for pets (see Animal section) can help keep them from becoming infected or carrying infected fleas into the home. Game meat, as well as tissues from domesticated animals that might be infected, should be cooked thoroughly if they are eaten (however, eating tissues from sick animals is not recommended). Die-offs of rodents or lagomorphs should be reported.

Personal protective equipment (PPE) should be worn when handling animals if there is any risk that they might be infected. More stringent precautions are necessary when pneumonic plague is suspected or higher risk procedures such as necropsies are performed. Good hygiene, including frequent hand washing, should be practiced. Insect repellents can also be applied to clothing and skin if exposure to rodent fleas is expected. Specific recommendations for protective measures are available from the CDC and other groups (see Internet Resources, below).

In endemic regions, rodents that host *Y. pestis* may be monitored and/or controlled. Concurrent insecticidal treatment is often necessary when hosts die or are killed, as fleas leave the carcasses to seek new hosts. People who have been exposed to *Y. pestis* are treated prophylactically with antibiotics. Good infection control procedures, including the use of disposable surgical masks, are used to prevent transmission from patients with pneumonic plague.

Human vaccines may be used in some countries or high risk groups, but there are concerns about their safety and efficacy, and their availability is limited. Efforts to create safe and effective human vaccines, as well as vaccine baits to reduce environmental load, are areas of current research.

Morbidity and Mortality

Y. pestis is endemic in populations of wild rodents and lagomorphs, and occasionally spills over to affect people or other animals. Worldwide, approximately 1,000 to 2,000 human cases of plague and 100 to 200 deaths are currently reported annually to the World Health Organization (decreased from a high of 5,000 cases in 1997). The exact number of plague cases is, however, uncertain. Some reported cases are not laboratory confirmed, and conversely, many cases are probably not diagnosed. Most outbreaks occur in Asia and Africa, but sporadic cases and outbreaks can be seen in any endemic region. On average, fewer than 20 cases of plague are reported annually in the U.S., but up to 40 cases have been reported in some years. Plague may reoccur after a long period when the disease seems to disappear; recent outbreaks in India, Indonesia and Zambia followed quiescent periods of 30 to 50 years.

Bubonic plague accounts for 80–95% of the cases seen worldwide. Without treatment, the case fatality rate for this form is estimated to be 40-70%; some sources suggest it may be as high as 90%. The availability of treatment lowers the case fatality rate in bubonic or septicemic plague to approximately 5–15%. Untreated pneumonic or septicemic plague is almost always fatal, often within a few days. If appropriate treatment is given very soon after the onset of symptoms, most people survive; however, the narrow window for treatment means that the case fatality rate for the pneumonic form remains greater than 50%.

Internet Resources

Centers for Disease Control and Prevention (CDC) Plague
http://www.cdc.gov/plague/

eMedicine.com
http://emedicine.medscape.com/article/967495-overview

Public Health Agency of Canada. Pathogen Safety Data Sheets
http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php

The Merck Manual
http://www.merckmanuals.com/professional/index.html

The Merck Veterinary Manual
http://www.merckmanuals.com/

United States Geological Survey. National Wildlife Health Center. Sylvatic Plague
http://www.nwhc.usgs.gov/disease_information/sylvatic_plague/

University of Alberta. Some Potential Microbiological Hazards for Field Workers
http://www.biology.ualberta.ca/courses/zool224/?Page=700

World Health Organization (WHO). Plague
http://www.who.int/csr/disease/plague/en/

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References

Fatal laboratory-acquired infection with an attenuated *Yersinia pestis* strain - Chicago, Illinois, 2009. MMWR Morb Mortal Wkly Rep. 2011;60(7):201-5.

Acha PN, Szyfres B [Pan American Health Organization (PAHO)]. Zoonoses and communicable diseases common to man and animals. Volume 1. Bacterioses and mycoses. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Plague; 207-18.

Aiello SE, Moses SA, editors. The Merck veterinary manual [online]. Whitehouse Station, NJ: Merck and Co; 2012. Plague. Available at: http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/51900.htm. Accessed 16 September 2013.

Ayyadurai S, Sebbane F, Raoult D, Drancourt M. Body lice, *Yersinia pestis* orientalis, and black death. Emerg Infect Dis. 2010;16(5):892-3.

Ayyadurai S, Houhamdi L, Lepidi H, Nappez C, Raoult D, Drancourt M. Long-term persistence of virulent *Yersinia pestis* in soil. Microbiology. 2008;154(Pt 9):2865-71.

Bevins SN, Tracey JA, Franklin SP, Schmit VL, Macmillan ML et al. Wild felids as hosts for human plague, Western United States.Emerg Infect Dis. 2009;15(12):2021-4.

Bhaduri S, Phillips JG. Growth of a pYV-bearing *Yersinia pestis* KIM5 in retail raw ground pork. Foodborne Pathog Dis. 2013;10(5):467-71.

Biberstein EL, Holzworth J. Bacterial diseases. Plague. In: Holzworth J, editor. Diseases of the cat. Philadelphia, PA: W.B. Saunders; 1987. p. 294, 660.

Bin Saeed AA, Al-Hamdan NA, Fontaine RE. Plague from eating raw camel liver. Emerg Infect Dis. 2005;11(9):1456-7.

Butler T. Plague gives surprises in the first decade of the 21st century in the United States and worldwide. Am J Trop Med Hyg. 2013;89(4):788-93.

Butler T. Yersiniosis and plague. In: Palmer SR, Soulsby EJL, Simpson DIH, editors. Zoonoses. New York: Oxford University Press; 1998. p. 281–93.

Cabanel N, Leclercq A, Chenal-Francisque V, Annajar B, Rajerison M, Bekkhoucha S, Bertherat E, Carniel E. Plague outbreak in Libya, 2009, unrelated to plague in Algeria. Emerg Infect Dis. 2013;19(2):230-6.

Centers for Disease Control and Prevention (CDC). Plague [Web site]. CDC; 2013 Jun. Available at: http://www.cdc.gov/plague/ Accessed 16 September 2013.

Collins FM. *Pasteurella*, *Yersinia*, and *Francisella*. In: Baron S., editor. Medical microbiology. 4th ed. New York: Churchill Livingstone; 1996. Available at: http://www.ncbi.nlm.nih.gov/books/NBK7798/* Accessed 20 Nov 2002.

Dhawan VK. Plague. eMedicine.com; 2013 Aug. Available at: http://emedicine.medscape.com/article/967495-overview. Accessed Sept 2013..

Drancourt M, Houhamdi L, Raoult D. *Yersinia pestis* as a telluric, human ectoparasite-borne organism. Lancet Infect Dis. 2006;6(4):234-41.

Edmunds DR, Williams ES, O'Toole D, Mills KW, Boerger-et al. Ocular plague (*Yersinia pestis*) in mule deer (*Odocoileus hemionus*) from Wyoming and Oregon. J Wildl Dis. 2008;44(4):983-7.

Eisen RJ, Gage KL. Adaptive strategies of *Yersinia pestis* to persist during inter-epizootic and epizootic periods. Vet Res. 2009;40(2):1.

Eisen RJ, Petersen JM, Higgins CL, Wong D, Levy CE et al. Persistence of *Yersinia pestis* in soil under natural conditions. Emerg Infect Dis. 2008;14(6):941-3.

Frank KM, Schneewind O, Shieh WJ. Investigation of a researcher's death due to septicemic plague. N Engl J Med. 2011;364(26):2563-4.

Gage KL, Kosoy MY. Natural history of plague: perspectives from more than a century of research. Annu Rev Entomol. 2005;50:505-28.

Galimand M, Carniel E, Courvalin P. Resistance of *Yersinia pestis* to antimicrobial agents. Antimicrob Agents Chemother. 2006;50(10):3233-6.

Gould LH, Pape J, Ettestad P, Griffith KS, Mead PS. Dog-associated risk factors for human plague. Zoonoses Public Health. 2008;55(8-10):448-54.

Harbeck M, Seifert L, Hänsch S, Wagner DM, Birdsell D et al. *Yersinia pestis* DNA from skeletal remains from the 6(th) century AD reveals insights into Justinianic Plague.PLoS Pathog. 2013;9(5):e1003349.

Hinckley AF, Biggerstaff BJ, Griffith KS, Mead PS. Transmission dynamics of primary pneumonic plague in the USA. Epidemiol Infect. 2012;140(3):554-60.

Houhamdi L, Lepidi H, Drancourt M, Raoult D. Experimental model to evaluate the human body louse as a vector of plague.J Infect Dis. 2006;194(11):1589-96.

Kool JL.Risk of person-to-person transmission of pneumonic plague. Clin Infect Dis. 2005;40(8):1166-72.

Kortepeter M, Christopher G, Cieslak T, Culpepper R, Darling Ret al., editors. Medical management of biological casualties handbook [online]. 4th ed. United States Department of Defense; 2001. Plague.Available at: http://www.dhhr.wv.gov/oeps/disease/Documents/USAMRIID_BlueBook.pdf . Accessed 19 Nov 2002.

Leslie T, Whitehouse CA, Yingst S, Baldwin C, Kakar F et al. Outbreak of gastroenteritis caused by *Yersinia pestis* in Afghanistan. Epidemiol Infect. 2011;139(5):728-35.

Macy DW. Plague. In: Greene CE, editor. Infectious diseases of the dog and cat. Philadelphia: W.B. Saunders; 1998. p. 295–300.

Macy DW. Plague. In: Kirk RW, Bonagura JD. Current veterinary therapy X. Small animal practice. Philadelphia: WB Saunders; 1989. p. 1088–91.

Neerinckx S, Bertherat E, Leirs H. Human plague occurrences in Africa: an overview from 1877 to 2008.10. Trans R Soc Trop Med Hyg. 2010;104(2):97-103.

Orloski KA, Lathrop SL. Plague: a veterinary perspective. J Am Vet Med Assoc. 2003;222(4):444-8..

Piarroux R, Abedi AA, Shako JC, Kebela B, Karhemere S et al. Plague epidemics and lice, Democratic Republic of the Congo Emerg Infect Dis. 2013;19(3):505-6.

Porter RS, Kaplan JL, editors. The Merck Manual [online]. . Whitehouse Station, NJ: Merck and Co.; 2009. Plague and other *Yersinia* infections. Available at: http://www.merckmanuals.com/professional/infectious_diseases/gram-negative_bacilli/plague_and_other_yersinia_infections.html#v1007213. Accessed Sept 2013.

Prentice MB, Rahalison L. Plague. Lancet. 2007;369(9568):1196-207.

Public Health Agency of Canada. Material Safety Data Sheet – *Yersinia pestis*. Office of Laboratory Security; 2001 Mar. Available at: http://www.phac-aspc.gc.ca/msds-ftss/msds169e-eng.php. Accessed 16 September 2013..

Ratsitorahina M, Rabarijaona L, Chanteau S, Boisier P. Seroepidemiology of human plague in the Madagascar highlands. Trop Med Int Health. 2000;5(2):94-8.

Rocke TE, Pussini N, Smith SR, Williamson J, Powell B, Osorio JE. Consumption of baits containing raccoon pox-based plague vaccines protects black-tailed prairie dogs (*Cynomys ludovicianus*). Vector Borne Zoonotic Dis. 2010;10(1):53-8.

Salkeld DJ, Stapp P. Seroprevalence rates and transmission of plague (*Yersinia pestis*) in mammalian carnivores. Vector Borne Zoonotic Dis. 2006;6(3):231-9.

Stenseth NC, Atshabar BB, Begon M, Belmain SR, Bertherat E et al. Plague: past, present, and future. PLoS Med. 2008;5(1):e3.

St Romain K, Tripp DW, Salkeld DJ, Antolin MF. Duration of plague (*Yersinia pestis*) outbreaks in black-tailed prairie dog (*Cynomys ludovicianus*) colonies of northern Colorado. Ecohealth. 2013 Sep 21. [Epub ahead of print]

Sun W, Roland K, Curtiss R 3rd. Developing live vaccines against plague. J Infect Dev Ctries. 2011;5(9):614-27.

Tourdjman M, Ibraheem M, Brett M, Debess E, Progulske B et al. Misidentification of *Yersinia pestis* by automated systems, resulting in delayed diagnoses of human plague infections--Oregon and New Mexico, 2010-2011.Clin Infect Dis. 2012;55(7):e58-60.

United States Geological Survey (USGS). National Wildlife Health Center. Sylvatic plague immunization in black-footed ferrets and prairie dogs. USGS; 2008 Oct. Available at: http://www.nwhc.usgs.gov/disease_information/sylvatic_plague/index.jsp. Accessed 7 Oct 2009.

Urich SK, Chalcraft L, Schriefer ME, Yockey BM, Petersen JM. Lack of antimicrobial resistance in *Yersinia pestis* isolates from 17 countries in the Americas, Africa, and Asia. Antimicrob Agents Chemother. 2012;56(1):555-8.

Wang H, Cui Y, Wang Z, Wang X, Guo Z et al. A dog-associated primary pneumonic plague in Qinghai Province, China. Clin Infect Dis. 2011;52(2):185-90.

Williams ES, Thorne ET, Quan TJ, Anderson SL. Experimental infection of domestic ferrets (*Mustela putorius furo*) and Siberian polecats (*Mustela eversmanni*) with *Yersinia pestis*. J Wildl Dis. 1991;27(3):441-5.

Wolfe LL, Shenk TM, Powell B, Rocke TE. Assessment of a recombinant F1-V fusion protein vaccine intended to protect Canada lynx (*Lynx canadensis*) from plague. J Wildl Dis. 2011;47(4):888-92.

Wong D, Wild MA, Walburger MA, Higgins CL, Callahan M et al.. Primary pneumonic plague contracted from a mountain lion carcass. Clin Infect Dis. 2009;49(3):33-8.

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