Slide 1

Plague

Slide 2

Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control

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In today's presentation we will cover information regarding the organism that causes plague and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects, and clinical signs seen in humans and animals. Finally, we will address prevention and control measures that can be taken.

Image: Plague, although of great historical importance, is still of concern in some parts of the world, as reflected in this Newsweek cover from October 10, 1994. This story covered the outbreak of plague in India.

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The Organism

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Yersinia pestis

- Family Enterobacteriaceae
  - Gram negative
  - Pleomorphic coccobacillus
  - Aerobic, facultatively anaerobic, facultatively intracellular
- One serotype
  - Three biovars
- Multiple plasmids and virulence factors

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Yersinia pestis, the causative agent of plague, is a pleomorphic, gram negative coccobacillus in the family Enterobacteriaceae. It is an aerobic, facultatively anaerobic, and facultatively intracellular pathogen. Only one serotype is recognized. *Y. pestis* can be divided into three biovars: Antiqua, Medievalis, and Orientalis. *Yersinia pestis* has multiple plasmids (110 and 9.5 kbp plasmids) and virulence factors (F1, Murine exotoxin, LPS endotoxin, coagulase, pesticin, plasminogen activator).

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Yersinia pestis

- Destroyed by
  - Sunlight
  - Desiccation
- Survival
  - 1 hour in air
  - Briefly in soil
  - 1 week in soft tissue
  - Years when frozen

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Yersinia pestis is easily destroyed by sunlight and drying. However, it can survive briefly in the soil and longer in frozen or soft tissues. Additionally, it can survive for up to one hour (depending on conditions) when released into air. This could increase its threat and aid in its dispersal as a potential bioterrorism weapon.

Image: Wayson stain of blood shows the characteristic bipolar "safety pin" appearance of *Yersinia pestis*. From CDC.

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History

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History

- 540-590 AD: Justinian's pandemic
  - 10,000 deaths per day
  - Fall of the Roman Empire
- 1346~1400: Black Death pandemic
  - Quarantine
  - 1/3 of European population died
  - Fall of the feudal system
- 1665: Great Plague of London

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Plague has played a long and important role throughout history. It has caused several pandemics and epidemics which have led to large numbers of deaths. Justinian's Constantinople pandemic lasted from 540 AD to 590 AD and resulted in approximately 10,000 deaths per day at its height. Plague also contributed greatly to the fall of the Roman Empire. In the 14th century, plague was carried from outbreaks in India and China to Italy by merchants returning home. During this time, Venice instituted a 40-day period of detainment for docking ships, which gave us what is now known as "quarantine." Despite these efforts, plague quickly spread throughout all of Europe. Over 1/3 of the European population died during the "Black Death pandemic." The decline in population aided in the fall of the feudal system of government. Another important plague epidemic occurred in 1665. Although limited to England, it killed approximately 100,000 (of the 500,000) inhabitants of London. During this outbreak, some modern public health practices were initiated (i.e., disease reporting, closing up of homes).

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"Ring Around The Rosy
A Pocket Full Of Posies
Ashes, Ashes
All Fall Down"

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It is thought that this nursery rhyme has origins from plague. "Ring" refers to an early clinical sign that appears on the skin (perhaps the ulcer that commonly appears around a flea bite wound infected with *Y. pestis*); "a pocket full of posies" refers to the use of flower petals as a means of warding off the stench and infection of a plague victim; "ashes, ashes" refers to dust to dust; and "all fall down" refers to victims who were falling down dead.

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Discovery

- 1894: Hong Kong
- Alexandre Yersin
  - Identified Gram negative bacillus
- 1896
  - Developed antiserum

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The causative agent of plague was first isolated following an 1894 outbreak in Hong Kong. Alexandre Yersin, an unknown bacteriologist, isolated a gram negative organism while celebrated Japanese scientists isolated a gram positive organism. In 1896, Yersin developed an antiserum that saved the life of an 18 year-old Chinese student. Eventually, it was accepted that Yersin had found the agent (a gram negative bacillus) responsible for plague.

Image: Dr. Alexandre Yersin in Front of the National Quarantine Station, Shanghai Station, 1936. This was the laboratory building in Shanghai, China where Dr. Yersin first isolated and described in detail, *Pasteurella pestis*, the old term used for *Yersinia pestis*. From CDC.

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History: U.S.

- 1899: Hawaii
  - From ship rats to sylvatic rodents
  - Spread throughout the western U.S.
- 1924: Los Angeles
  - Last person-to-person case
  - 32 pneumonic cases; 31 deaths
- Currently established in southwest

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The U.S. has not been immune to the influence of plague. In the late 1800s, plague was first identified in Hawaii. Later, ships brought rats carrying plague to the western U.S., and indigenous, wild rodents became infected. Currently, plague is permanently and enzootically established in the southwestern U.S. The last documented person-to-person transmission of plague occurred during the 1924 outbreak in Los Angeles, California. During this outbreak, 32 pneumonic cases were reported with 31 resulting in death.

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Plague as a Disease

- CDC Division of Quarantine
- Reportable disease in the U.S.
- All U.S. cases reported to the WHO

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Plague is a disease that the CDC Division of Quarantine are empowered to apprehend, detain, medically examine or conditionally release a suspect having this illness. Plague in humans is a reportable disease, and in many states plague in animals is also reportable. The U.S. Public Health Service requires that all cases of suspected plague be reported immediately to local and state health departments and that the diagnosis be confirmed by CDC. As required by the International Health Regulations, CDC reports all U.S. plague cases to the World Health Organization.

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Transmission

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Transmission

- Flea bite
- Direct animal contact
  - Tissues, body fluids, scratches, bites
  - Enters through break in skin
- Aerosol
- Human cases
  - April through November
  - Increased activity of fleas and hosts

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Transmission can occur via three main routes, however, flea bites are most common. Direct transmission can occur between animals or animals and people. *Y. pestis* is present in tissues, draining lesions, and some body fluids (depending on the form of the disease); these bacteria can be transmitted through mucous membranes and broken skin. People (hunters especially) can be directly infected by handling the tissues of infected animals. Plague has also been transmitted by bites or scratches of infected animals, but this is rare. People or animals with the pneumonic form of plague may transmit *Y. pestis* in respiratory droplets. In humans, transmission by inhalation is most common in crowded, poorly ventilated conditions. *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. Human cases of plague typically occur in April through November, when fleas and their hosts are most active and people are more likely to be outdoors.

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Flea Vectors

- Can live off host for months
- Many species can serve as vector
- *Oropsylla montana*
  - Rock squirrels, California ground squirrels, prairie dogs
  - Most important flea vector in U.S.
- *Xenopsylla cheopis*
  - Epidemics in Asia, Africa, South America

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More than 30 species of fleas are capable of transmitting *Y. pestis*, but they vary in their efficiency as vectors. Fleas (order Siphonaptera) are able to live off their host for weeks to months. Host specificity of fleas varies, and most fleas will feed temporarily on other host(s). The flea most often responsible for human cases, *Oropsylla montana* (ground squirrel flea), is commonly found on rock squirrels, California ground squirrels, and prairie dogs. It is the most important flea vector in the U.S. and will readily feed on humans when its normal host is absent, unlike most prairie dog fleas. *Xenopsylla cheopis* (oriental rat flea) is the primary vector of plague in most large plague epidemics in Asia, Africa, and South America.

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Flea Transmission

- ≤27°C (80°F)
  - Blood clots in gut of flea
  - *Y. pestis* trapped
  - Clotted blood regurgitated
  - Enters wound from flea bite
- ≥27°C
  - Blood clot in gut of flea dissolves
  - *Y. pes*tis passes through

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Successful transmission from the flea depends upon ambient temperature, because temperature affects the degree of blood clotting in the gut of the flea. After a flea takes a blood meal from a host, the blood enters the flea's stomach. When temperatures are roughly 27^{o}C (80.6^{o}F) or less, blood clots in the flea gut due to a coagulase enzyme. As a result, *Yersinia* bacteria are trapped in the clot and multiply. When the flea tries to feed during this time, new blood cannot pass the blockage and is therefore regurgitated, carrying *Yersinia pestis* with it. It enters the wound produced by the flea bite and infects the host. When temperatures are above 27^{o}C (80.6^{o}F), coagulase is not produced; enzymes in the flea gut are able to dissolve the blood clot. *Y.* pestis is not maintained for long periods in the gut or regurgitated into flea bite wounds. Epidemics of plague tend to decrease as temperatures rise above 27^{o} C.

Image: 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. From CDC.

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Epidemiology

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Distribution: U.S.

- Southwest (87%)
  - Northern New Mexico
  - Southern Colorado
  - Northern Arizona
  - California
- 1925-1964
  - ~2 cases/yr
- Since 1970
  - ~13 cases/yr

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Plague has been found in wild animals and their fleas in approximately 17 states. Human cases are most often found in the Southwest. The black and solid dark blue zones on the map indicate areas with the largest number of plague cases in the US. From 1925-1964, 41 human cases of plague were reported in the U.S. (an average of 2 cases per year), and since 1924 there has been no person-to-person infection in the U.S. Since 1970, there has been an average of about 13 cases per year.

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This graph depicts the number of reported human cases of plague in the United States from 1972-2002. From 1988-2002, 112 human cases were reported to the CDC from 11 western states. The spike in 1983 corresponds with prairie dog and rock squirrel epizootics. Since then, almost all plague cases have been contracted in New Mexico (50%), Colorado (17%), Arizona (11%), and California (11%). In recent years, the incidence of plague has remained low in the U.S.; in 2008, 3 cases occurred.

Data from the MMWR Summary of Notifiable Diseases 2002, 2008.

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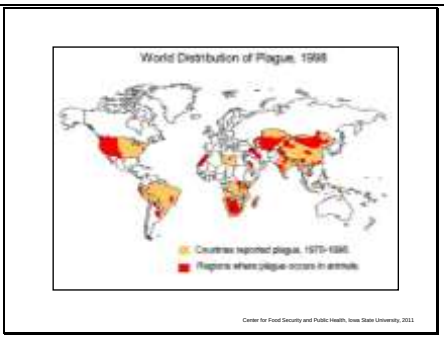
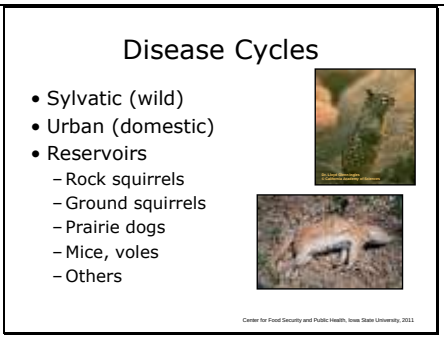


Globally, plague is found in Africa, Asia, South America, and the U.S. Worldwide, a total of 18,739 cases of plague in humans were reported to WHO from 20 countries during 1980 to 1994. On average 1,000 to 3,000 human cases of plague occur each year worldwide. Over the past decade, 76% of the cases and 81% of the deaths were reported from Africa.

Slide 20



There are two cycles of plague: the sylvatic (wild form) and the urban (domestic form). The main reservoirs for plague in the U.S. are wild rodents--primarily rock squirrels, ground squirrels, prairie dogs, or similar types of rodents. The epidemiology is very complex and varies between continents and within each country.

Top image: *Spermophilus beecheyi*, the California ground squirrel. Rock squirrels and California ground squirrels are very important epizootic hosts and their fleas are commonly associated with transmission to humans. Bottom image: A spotted ground squirrel (*S. spilosoma)*, can be a carrier of *Y. pestis* vector fleas. From CDC.

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In the wild, plague may be present at low, steady levels within a rodent population and maintained in a rodent-flea cycle. Known as enzootic plague, this occurs in a limited number and species of rodents, among which there are very low death rates due to plague. Mice and voles are probably significant enzootic reservoirs. Susceptibility of rodents to plague varies from region to region and the true maintenance reservoirs of plague are not fully known.

Periodically, rodents experience epizootics, increasing the risk of plague transmission to other species. Epizootic plague causes increased rodent mortality. Rodent fleas may seek out new hosts, and many rodent species, especially prairie dogs, serve as amplifying hosts. Epizootic plague is the greatest threat to humans as we invade rodent and flea occupied areas.

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Urban Plague

- Infected fleas or rodents move into urban areas
- Domestic rodents infected
  - High rodent mortality
- Fleas seek new host
  - Domestic cats or humans
- Associated with poverty in humans

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Urban (domestic) plague occurs when infected fleas and/or rodents move into urban areas. Influx may be related to significant development and expansion into wilderness areas (i.e., interface building that borders a city and outlying wilderness). Epizootics may cause high mortality in domestic-rat populations, forcing infected fleas to seek alternative hosts, including humans or domestic cats. Domestic cats in homes bordering wilderness areas pose a significant threat to humans because they may transmit plague to their owners. Conditions related to poverty are linked to urban plague transmission.

Image: The white-throated woodrat (*Neotoma albigula)* is a proven carrier of plague vector fleas. All woodrat species are quick to occupy and construct nests in human habitations or outbuildings within their range, thereby bringing vector fleas into close contact with humans and their pets. From CDC.

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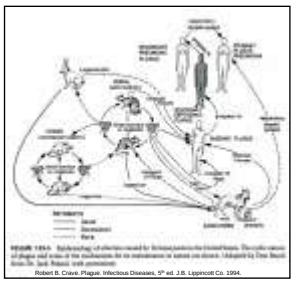

Robert B. Craive. Plague. Infectious Diseases, 5th ed. J.B. Lippincott Co. 1994.

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This graphic depicts the full picture of the epidemiology of plague. Note the urban and wild (rural) cycles of transmission.

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Disease in Humans

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Human Disease

- Three major forms of plague
  - Bubonic
  - Septicemic
  - Pneumonic
    - Primary
    - Secondary

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Three major forms of plague are seen in humans: bubonic plague, septicemic plague and pneumonic plague. All three are acute diseases. Bubonic accounts for 80 to 90% of cases in the U.S. In the United States during 1947–1977, approximately 10% of plague patients presented with septicemic plague; approximately 50% of these persons died as a result of disease

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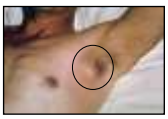
Bubonic Plague

- Most common form
  - ~80% of cases
- Incubation
  - 2 to 6 days
- Clinical signs
  - Fever, malaise, chills, headache
  - Bubo: swollen, painful lymph node
- Mortality (untreated): 50-60%



Bubonic plague is the most common form and accounts for roughly 80% of cases. The incubation period is 2 to 6 days. Signs and symptoms include fever, malaise, chills, headache, and very swollen, painful lymph nodes (called "buboes"). Vomiting, abdominal pain, nausea, and petechiae may also occur. Without treatment 50 to 60% of bubonic cases are fatal.

Image: Enlarged axillary lymph node - "bubo" (black circle), commonly seen with bubonic plague. From CDC.

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Septicemic Plague

- Primary or secondary
- Rapid onset
- Clinical signs
  - Signs of sepsis ± bubo
  - Necrosis of extremities
    - Microthrombi block capillaries
    - "Black Death"
- Mortality (untreated): 100%

Approximately 10 to 25% of 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, disseminated intravascular coagulation (DIC) and neurological signs may also be seen, and the course of the disease can be rapid. Secondary septicemia is similar, but results from disseminated bubonic plague. Necrosis of the extremities can be seen (often in the finger tips, tip of the nose, and toes) and is the result of microthrombi blocking capillaries and the circulation to these areas. Without treatment 100% of septicemic cases are fatal.

Image: Extremity necrosis due to the microthrombi in the septicemic form of plague. This is why it was called the "Black Death" in early history.

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Pneumonic Plague

- Incubation: 1 to 6 days
- Primary—*Y. pestis* inhaled
- Secondary—septicemic form spreads
- Clinical signs
  - Fever, chills, headache, septicemia
  - Respiratory distress, hemoptysis
- Person-to-person possible
- Potential use as bioweapon

Pneumonic is the least common but most fatal form of plague. Primary pneumonic plague occurs when *Y. pestis is* inhaled and bacteria gain direct access to the lungs. Primary pneumonic plague has a very rapid incubation period of 1 to 6 days. If septicemic plague is left untreated, it may progress to secondary pneumonic plague. Symptoms include fever, chills, headache, septicemia, respiratory distress and hemoptysis. Pneumonic plague is the only form of plague that can be transmitted person-to-person, but usually requires direct or close contact with the ill person or animal. Treatment for this form must be received within 24 hours after the onset of symptoms, otherwise, survival is unlikely. Person-to-person transmission and the rapid course of illness make plague a potential bioweapon.

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Diagnosis

- Identification of organism
- Serology
- Isolation of organism
- Differential diagnoses
  - Tularemia
  - Hantavirus
  - *Streptococcus*
  - *Staphylococcus aureus*

Plague may be presumptively diagnosed by identification of the organism in clinical samples (blood, lymph node, sputum, etc.). Rapid immunoassays can also detect antigens from this organism in clinical samples, and polymerase chain reaction (PCR) assays may be used to detect nucleic acids. In addition, plague can 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. Serology is also useful for diagnosis. Serological tests include enzyme-linked immunosorbent assays (ELISAs), passive hemagglutination, hemagglutination-inhibition, latex agglutination and complement fixation. A fourfold rise in titer is diagnostic. Differential diagnoses include: tularemia, hantavirus, streptococcal infection, and staphylococcal infection.

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Treatment

- Early treatment, survival ~100%
- Supportive care
- Antibiotics
  - Aminoglycosides
  - Doxycycline, tetracycline, chloramphenicol
  - Penicillins and cephalosporins are NOT effective

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Treatment of plague requires prompt antibiotic treatment and supportive therapy. Without treatment most forms of plague are fatal; fatalities in the U.S. are often linked to delay in seeking medical care or misdiagnosis. Currently, about 14% of all plague cases in the U.S. result in death. Penicillins and cephalosporins are not effective in treating plague. Prophylactic antibiotics should be administered to persons who have had close exposure (i.e., within 6.5 feet [2 meters]) to persons suspected of having pneumonic plague. Persons who have not had such exposure are unlikely to become infected, but should be monitored closely.

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Case Report

- New York, 2002
  - Married couple from New Mexico
  - Fever, unilateral inguinal adenopathy
  - Bubonic plague diagnosed
  - Antibiotic treatment
  - Deteriorated (septicemic spread)
  - Sent to ICU
  - Recovered after 6 weeks

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On November 1, 2002, a 53-year old man and his 47-year old wife traveled from Santa Fe County, New Mexico, to New York City. They both became ill and sought medical care in an emergency room on November 5. The man reported two days of fever, fatigue, and painful unilateral inguinal swelling. WBC was elevated and he had thrombocytopenia. A blood culture grew *Y. pestis* and revealed bipolar gram-negative rods with a "safety pin" appearance. Plague was diagnosed. The patient received gentamicin, doxycycline, cirpofloxacin, vancomycin and activated protein C. The patient's condition deteriorated and he was admitted to ICU in shock with septicemic plague. After 6 weeks in ICU, he recovered and was discharged to a long-term-care rehabilitation facility. His wife also presented to the ER on November 5, with fever, fatigue, myalgia and unilateral inguinal swelling. Her WBC and platelets were within normal limits. She was treated with antibiotics and presumed to have plague (based on husband's diagnosis). She recovered without complications.

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Case Report: Importance

- NMDPH and CDC investigation
  - Trapped rodents and fleas around home
  - *Y. pestis* isolated
- Importance
  - Plague outside of endemic area
    - Should raise suspicion
  - Prompt detection important

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The New Mexico Department of Public Health and the Centers for Disease Control and Prevention investigated the couple's New Mexico property. Trapped rodents and their fleas were tested (pulsed-field gel electrophoresis) for *Y. pestis*, and were found to be indistinguishable from *Y. pestis* isolated from the male patient. Any time plague is suspected or diagnosed out of its endemic area (southwestern U.S.), suspicion should be raised about the source of the infection. In this case, the patients had come from the endemic area. This case also emphasized early detection and diagnosis, which is important not only for patient care but for implementation of precautionary measures needed to limit the spread of disease.

Case from MMWR 2003;52(31):725-728.

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Disease in Animals

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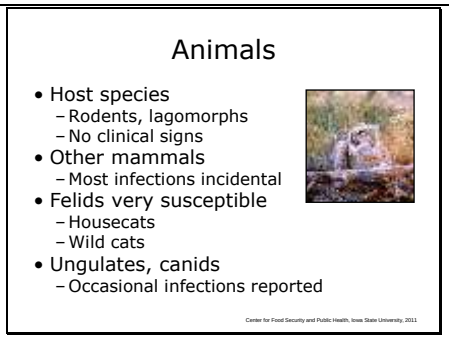

Rodents and lagomorphs are the most important host species for plague. Infections have been documented in more than 200 species and subspecies of rodents. In the U.S., significant hosts include prairie dogs, ground squirrels, antelope ground squirrels, chipmunks, woodrats, and mice in the southwestern states, and ground squirrels, chipmunks, and woodrats in Pacific coast states. 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 and mountain lions. Infrequent cases of plague have been described in ungulates including camels, various species of deer, prong-horn antelope, llamas and goats. *Y. pestis* infections have also been reported in dogs, coyotes, foxes, badgers, skunks and nonhuman primates.

Image: Bobcat.

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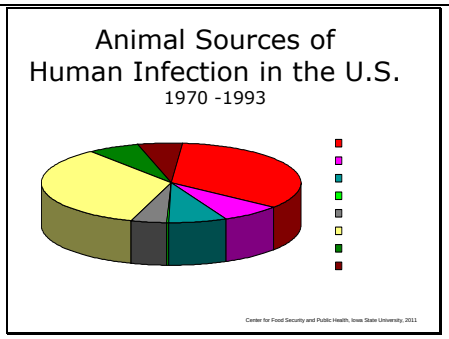

This chart depicts the most common animal sources for human infection for 1970-1993. Carnivores include cats, coyotes, badgers, and others. Rock squirrels and California ground squirrels are the most common source of infection. Rock squirrels account for roughly 41% of all human cases in the U.S.

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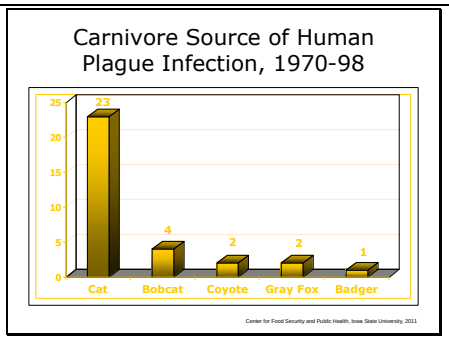

Transmission from animals to people can be either by aerosol, as seen with domestic cats, or direct contact with infected tissues of other carnivores, bites, or scratches. Number of human cases attributed to: Cats (23) Bobcat (4) Coyote (2) Gray Fox (2) Badger (1). Carnivores can also contribute to the transfer of infected fleas from one geographic area to another, such as when a coyote might walk from one region to another.

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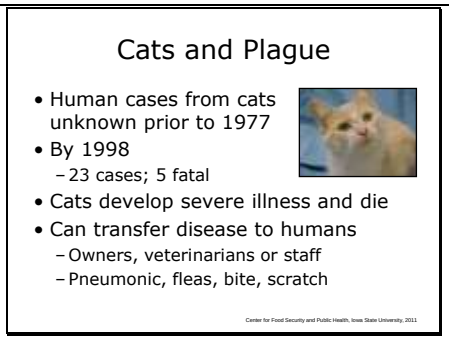

Prior to 1977, no reported cases of plague in humans were acquired from domestic cats. However, by 1998, 23 human cases developed from domestic cat exposure. Five of these cases proved to be fatal. Four cases occurred in veterinarians and two in veterinary staff. The outdoor domestic cat can be infected by eating infected rodents or acquiring infected rodent fleas. They expose their owners to the infected flea or respiratory aerosol when coughing. Cats can develop serious illness and die from plague. Rare cases of bite or scratch transmission of plague from cats to people have been documented.

Image: Courtesy of DB Weddle.

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Cats and Plague

- Clinical signs
  - Severe illness
  - Signs mimic human illness
  - Bubonic, septicemic, pneumonic
  - Fever, lethargy, anorexia
  - Lymphadenopathy
    - Submandibular, cervical, others
  - DIC, death

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After a cat has eaten an infected rodent, the submandibular and cervical lymph nodes may become enlarged. Other lymph nodes can also become swollen. Fever, anorexia, and lethargy are very common in cats with plague.

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Cats and Plague: Experimental Infection

- 16 cats
  - Each fed a plague infected mouse
  - All showed illness by day 3-4
  - Lymphadenopathy by days 4-6
- 6 cats died (37.5%)
- 75%
  - Blood culture positive
  - Culture positive throat/oral cavity

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In an experimental study of the effects of plague on cats, 16 healthy cats were divided into four groups of four cats each. To simulate natural exposure to plague, each cat was offered a 6-week-old laboratory mouse that had died of *Y. pestis* (strain NM77 _B) infection. Six cats (38%) died of experimental plague infection. The mean time to death following ingestion of the infective mouse was 5.7 days (range 4-9 days). All showed clinical signs of illness and depression by day 4. All had swollen, palpable nodes in submandibular, sublingual, and/or tonsillar regions evident by days 4-6. All demonstrated fever, which peaked at about the 3rd day. Blood was culture positive for *Y. pestis* in 12 cats (75%), some as early as two days after eating the mouse. Also in 12 of the 16 cats, *Y. pestis* was cultured from the throat or oral cavity.

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Case Report: Cat to Human

- New Mexico, 1977
  - 6 yr. old boy
- September 6
  - Fever, chills, vomiting, bilateral axillary pain
  - Insect bites & scratches on arms
  - Hospitalized with delirium
- September 8
  - Needle aspirate of lymph node
    - Positive on staining and FA for plague
  - IV antibiotics

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"On Sept 6, 1977, a 6-year-old boy who lived in Valencia County, New Mexico, had onset of fever (39.5 C), chills, vomiting, and bilateral axillary pain. He was examined by a physician, who diagnosed a viral syndrome and prescribed erythromycin. Later that day the child was admitted to a hospital; with body temperature of >40 C and delirium. On Sept 7, he had not improved despite IV and was transferred to a referral hospital, where admission findings included body temperature of 40.2 C and a total WBC count of 17,400/mm3, with 57% segmented neutrophils and 31% band neutrophils. He had multiple abrasions, scratches, and insect bites (attributed to mosquitoes) on both arms and painful bilateral nonfluctuant axillary lymphadenopathy. Intravenous cefazolin therapy was instituted after blood, throat, and CSF cultures had been obtained. Several hours later, the cefazolin was discontinued, and IV chloramphenicol therapy was initiated.

On Sept 8, needle aspiration of the right axillary lymph node yielded a serous fluid containing gram negative bacterial rods that had a bipolar appearance with Wayson's stain. The bacteria were fluorescent antibody test-positive. Based on a presumptive, laboratory diagnosis of plague, streptomycin was added to the continuing chloramphenicol therapy. Forty-eight hours later, *Yersinia pestis* was isolated from the admission blood specimen and from the serous fluid aspirated from the axillary lymph node. Slight clinical improvement was noted approximately 1 day after the initiation of specific therapy, but the patient remained febrile until Sept 16. Streptomycin was discontinued on Sept 15, and the chloramphenicol was stopped on Sept 17."

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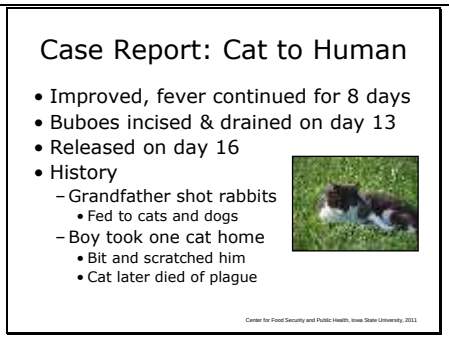

"Bilateral axillary pain and swelling continued, and the buboes had become fluctuant. On Sept 19, the buboes were incised and drained. Prior to surgery, the patient was placed on an oral treatment regimen with chloramphenicol, which was continued until Sept 25. The patient remained afebrile and had a marked decrease in axillary pain within 24 hours after surgery. *Yersinia pestis* was not isolated from the purulent bubo material, although fluorescent antibody test-positive organisms were in the pus. The patient was discharged on Sept 22, after 15 days of hospitalization. When he was examined on Sept 25, the incision sites were healing well, and he had returned to his full activity pattern. On Oct. 15, no remaining axillary adenopathy or tenderness was noted.

Epidemiologic investigation revealed that the patient lived with his parents in a mobile home. Few rodents were found in the vicinity, and the patient had had no exposure to dead animals. On Sept 3, he and his family had visited his grandparents, who lived on a nearby farm. The grandfather periodically shot rabbits in the immediate area and fed them to his 20 to 30 cats and 4 dogs. He had last done this on Aug. 31. The patient took one of the cats home with him on Sept 3. The cat climbed a tree and the patient retrieved it, sustaining scratches of both hands and forearms and a minor bite on the left hand in the process. The cat subsequently appeared ill, stayed in its box, and was returned to the grandparents on Sept 4. It disappeared on Sept 5 and was later found dead under a woodpile; culture of its bone marrow yielded *Y. pestis*. The source of the cat's infection could not be determined, but its wild rabbit meal on Aug. 31 was suspected."

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Dogs do not readily develop illness and do not die from plague. Signs in dogs might include: fever, lethargy, lesions of the oral cavity or purulent lesions of the lymph nodes. Dogs will develop antibodies when exposed to plague and can be used as sentinels for plague activity in a geographic area.

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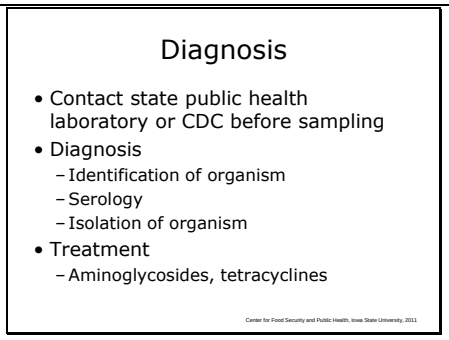

In the U.S., plague diagnosis is usually carried out by state public health laboratories or the CDC. These laboratories should be contacted before collecting samples. Plague is a serious zoonotic disease; samples should be collected, handled and shipped with all appropriate precautions, including appropriate personal protective equipment (PPE) during their collection.

Presumptive diagnosis is by fluorescent or Gram's staining of bubo aspirate, lesion exudate, pharyngeal swab, or tissue sample. Rapid immunoassays can also be used to detect *Y. pestis* antigens in clinical samples, and PCR may be used to identify nucleic acids. Confirmatory diagnosis is by bacterial isolation or fourfold rise in titer in serum collected 10-14 days apart. Culturing should be done by laboratories and not veterinarians in practice. Testing of fleas from the animal or the immediate environment may also be done by laboratories, but is not the

method of choice for diagnosing individual animals. Treatment with aminoglycosides is best in cats (and dogs if needed) that are showing signs, but tetracycline may also be adequate in cases that have not progressed to severe disease.

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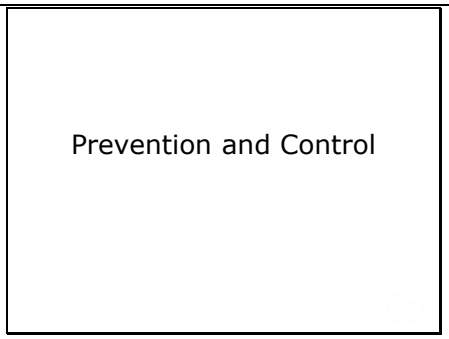
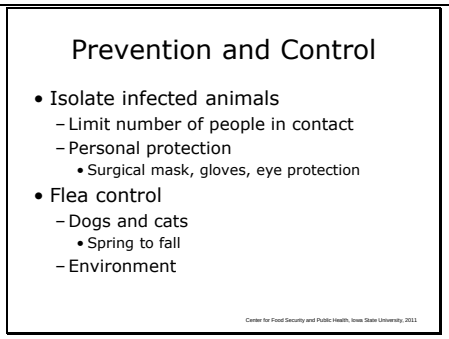


Slide 45



All animals suspected of having plague should be isolated. People working with plague patients (human or animal) should use barrier protection to prevent becoming infected. This includes using masks, gloves, and eye protection. Veterinarians working closely with pneumonic plague patients might consider prophylactic use of antibiotics as prescribed by their physician. If you live in areas where rodent plague occurs, treat pet dogs and cats for flea control regularly and do not allow these animals to roam freely. In addition, premises treatments can also be used to kill fleas brought into the house or yard if needed.

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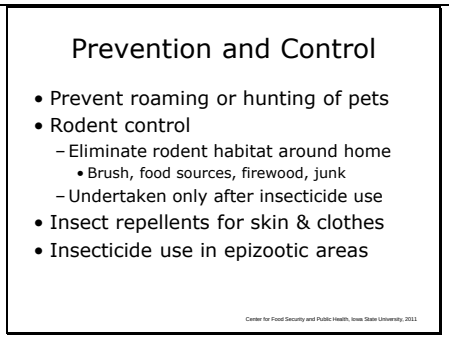

Cats and dogs should not be allowed to roam freely or hunt, especially rodents and rabbits. Outdoor cats in the Southwest U.S. should be considered at risk. It is important to remove food sources used by rodents and make homes, buildings, warehouses, or feed sheds rodent-proof. Eliminate sources of food and nesting places for rodents around homes, work places, and recreation areas; remove brush, rock piles, junk, cluttered firewood, and potential food supplies, such as pet and wild animal food. Applying chemicals that kill fleas and rodents is effective but should usually be done by trained professionals. Health authorities may use appropriate chemicals to kill fleas at selected sites during animal plague outbreaks. Killing or trapping rodents should follow the use of insecticides to kill fleas, otherwise, fleas will begin searching for a new host and may bite humans. Rats that inhabit ships and docks should also be controlled by trained professionals who can inspect and, if necessary, fumigate cargoes. Applying DEET to skin and clothing (permethrin may also be used on clothes) can help prevent flea bites and should be used if a person is outdoors in a plague enzootic area, or planning to enter an area experiencing a plague outbreak among rodent wildlife (epizootic). DEET should not be used on pets.

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Images from CDC. Left: Worker sprays insecticide powder into burrow to kill fleas. Top image: Man infusing a rodent burrow with insecticide powder. Bottom image: Permethrin-treated cotton is collected by rodents and brought back to their nests. Cotton treated with 0.5% Permethrin is collected by rodents to take back to their nests to kill fleas, preventing the transmission of Bubonic Plague & Colorado Tick Fever by such fleas and ticks to other rodents and people.

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Prevention and Control

- Public health education
- Prophylactic antibiotics
  - Plague outbreak/flea bites
  - Handled infected animal
  - Close contact with plague case
- Vaccine
  - Live and killed developed
  - No longer available in the U.S.

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Educating the veterinary and human medical communities and the general public on the previously mentioned transmission methods and prevention and control techniques is vital to prevention. In addition, prophylactic treatment of exposed persons should be considered. Two-three week courses of antibiotics (tetracyclines or sulfonamides) may be given to people during a plague outbreak, as well as to those who are bitten by fleas in a known plague outbreak or who have handled an animal known to be infected with plague. They should also be given when a person has close contact with a person or animal (less than 2 meters away) with suspected pneumonic plague. At one time a vaccine was licensed for use in the United States; however, it is no longer available. The efficacy of the inactivated plague vaccine in humans has not been measured in controlled studies. Completion of such studies in the United States is unlikely because of the low incidence of plague in this country.

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Prevention and Awareness

- Report suspected animal cases
  - State health department
  - State veterinarian
  - Animals may serve as sentinels
- Education of clients and public
  - Risks, transmission, prevention
- Take precautions in enzootic and epizootic areas

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As a veterinarian, you should report any animal/rodent deaths suspected to be due to plague to your state or local health department and your state veterinarian. Animals may show signs before people, thereby serving as sentinels, and help to mitigate human illness. Educating clients and the general public on clinical signs, transmission, and risk that animals pose for plague is very important for prevention and control. Precautions should be taken when visiting plague endemic areas.

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Plague as a Biological Weapon

- 1970 WHO estimate
  - 50 kg agent on city of 5 million
    - 150,000 pneumonic cases
      - 36,000 deaths
    - 80,000 to 100,000 hospitalized
    - 500,000 secondary cases
  - Up to 100,000 deaths total

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A 1970 World Health Organization assessment asserted that 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 would require hospitalization and 36,000 would be expected to die. When secondary cases and their resulting deaths are included, the total mortality may rise to 100,000.

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Additional Resources

- World Organization for Animal Health (OIE)
  - www.oie.int
- U.S. Department of Agriculture (USDA)
  - www.aphis.usda.gov
- Center for Food Security and Public Health
  - www.cfsph.iastate.edu
- USAHA Foreign Animal Diseases ("The Gray Book")
  - www.usaha.org/pubs/fad.pdf

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Additional Resources

- CDC - Division of Vector-borne Infectious Diseases
  - www.cdc.gov/ncidod/dvbid/index.htm
- CDC - Plague information
  - www.bt.cdc.gov/agent/plague/index.asp

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Acknowledgments

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