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. Photo: 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.

Slide 3

The Organism

Slide 4

Yersinia pestis

- Family Enterobacteriaceae
  - Gram negative coccobacillus, pleomorphic
  - Aerobic, facultative anaerobic, and facultative intracellular
- Several plasmids and virulence factors
  - F1, murine exotoxin, LPS endotoxin, coagulase, pesticin, plasminogen activator

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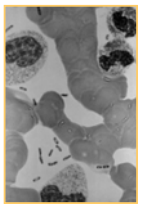
Yersinia pestis, the causative agent of plague, is in the Family Enterobacteriaceae. It is a pleomorphic, Gram negative coccobacillus which is aerobic, facultatively anaerobic and a facultative intracellular pathogen. *Yersinia pestis* has several plasmids (110 and 9.5 kbp plamids) and virulence factors (F1, Murine exotoxin, LPS endotoxin, coagulase, pesticin, plasminogen activator).

Slide 5

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 is able to survive for up to one hour (depending on conditions) when released into air. This could increase it threat and aid in its dispersal as a potential bioterrorism weapon. Photo: Wayson stain of blood shows the characteristic bipolar "safety pin" appearance of *Yersinia pestis*. From CDC.

Slide 6

History

Slide 7

Brief History of Plague

- 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 a very rich past and long history. Throughout history, plague has caused several outbreaks (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. It 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. Soon after plaque spread to the rest of Europe. During this time Venice instituted a 40-day period of detainment for docking ships, which gave us what is now known as the "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 the 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 of our 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" being an early sign to appear on the skin (perhaps the ulcer that commonly appears around a flea bite wound infected with *Y. pestis*); "a pocket full of posies" being the use of flower petals as a means of warding off the stench and infection of a plague victim; "ashes, ashes" meaning dust to dust; then "all fall down" for victims who were falling down dead.

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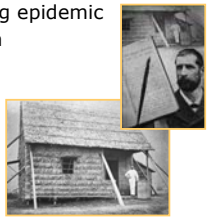
Discovery

- 1894: Hong Kong epidemic
- Alexandre Yersin
  - Gram negative
  - Bacillus
- 1896
  - Developed antiserum



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An outbreak in Hong Kong in 1894 attracted the attention of Alexandre Yersin, who was on leave from his job from the Pasteur Institute, and went to investigate. The Hong Kong port was quarantined shortly after the first plague victims were diagnosed. Shibasaburo Kitasato, celebrated collaborator of Robert Koch and Emil von Behring, arrived with a large team of Japanese scientists on June 12. Three days later, Yersin, a bacteriologist, almost unknown arrived from Indochina arrived. Kitasato identified a gram positive bacteria, while Yersin a gram negative. In 1896, Yersin developed an antiserum that saved the life of an 18 year old Chinese student. Eventually it turned out that Yersin had found the agent (a gram negative bacillus) responsible for plague. Bottom photo: 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*. Image from CDC.

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United States

- 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. It entered the U.S. via Hawaii in the early 1900's. Plague spread from the rats from ships to indigenous, sylvatic wild rodents throughout the western U.S. Currently it 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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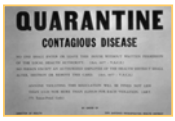
Plague as a Disease



- Class 1 quarantinable disease (WHO)
- CDC Division of Quarantine
- Reportable disease

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Today, the World Health Organization lists plague as a Class 1 quarantinable disease. This allows for detention and inspection of any vehicle or passenger originating from an area where a plague epidemic is in progress. It is also a disease (one of several) that personnel of 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 (78%)
- Direct animal contact (20%)
  - Tissues, body fluids, scratches, bites
  - Enters through break in skin
- Aerosol (2%)
- Human cases
  - April-November (93%)
  - Increased activity of fleas and hosts

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Transmission can occur via three main routes. Transmission from a flea bite is most common. For the period 1970-1995 (284 out of 341 cases), 78% of cases were acquired via flea bite. Direct contact of animals accounted for 20%, and aerosol transmission 2%. People (hunters especially) can be directly infected by handling the tissues of infected animals, for example rodents, rabbits or wild carnivores (coyotes, badgers, mountain lion, bobcat, etc.) that prey on these animals. Plague has been transmitted by bites or scratches of infected animals, but this is rare. The bacteria enter when there is a break in the skin. 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. Ninety-three percent of human cases in the U.S. occur during this period.

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Flea Vectors

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

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Fleas (Order Siphonaptera) are able to live off their host for weeks to months. Host specificity of fleas varies and most will feed temporarily on other host(s). Many species have been found to transmit plague. Host burden may vary with season. The flea most often responsible for human cases, *Oropsylla montana* (ground squirrel flea), is the flea most commonly found on rock squirrels, California ground squirrels and also 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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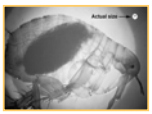
Flea Transmission

- ≤27°C (80°F)
  - Blood clots in gut of flea
  - *Y. pestis* trapped
  - Transmission occurs more readily
- ≥27°C
  - Blood clot in gut of flea dissolves
  - Organism passes through
  - Transmission less likely



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The flea plays the most significant role in plague transmission, but successful transmission from the flea depends upon ambient temperature. 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°C (80.6°F) or less, the blood clots in the flea gut due to a coagulase enzyme that inhibits the enzymes that would break down the clot. 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 back out, carrying *Yersinia pestis* with it. It enters the wound produced by the flea bite and infects the host.

When temperatures are above 27°C (80.6°F) transmission is reduced because the coagulase is not produced, thereby allowing enzymes in the flea gut 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° 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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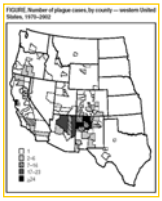
Slide 17

Where Are Cases Found?

- 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, but it is most often associated with human cases in the Southwest. Between 10 and 20 people in the rural Southwestern U.S. acquire plague from flea or rodent bites (usually prairie dogs), and about one in seven of these will die from the disease. 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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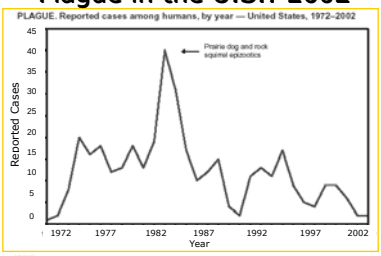
Plague in the U.S.: 2002



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This graph depicts the number of reported human cases of plague in the United States from 1972-2002. During 1988-2002, a total of 112 human cases were reported to the CDC from 11 western states. In 2002 there were only 2 human cases reported, and both were in travelers in New York City who had acquired the infection in New Mexico. Since 1983 almost all plague cases have been contracted in New Mexico (50%), Colorado (17%), Arizona (11%), and California (11%). The spike in the number of cases in 1983 corresponds to the prairie dog and rock squirrel epizootics, in which there was an increased number of infections transmitted to humans. Data from the Summary of Notifiable Diseases 2002, CDC website.

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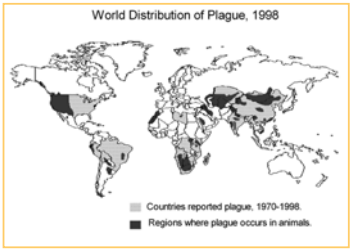

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Globally, plague is found in Africa, Asia, South America and the US. It has not been reported in Australia or Western Europe. Worldwide, a total of 18,739 cases of plague in humans were reported to WHO from 20 countries during 1980–1994. On average 1,000-3,000 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.

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Epidemiology in Nature

- Sylvatic (wild)
- Urban (domestic)
- Reservoirs
  - Rock squirrels
  - Ground squirrels
  - Prairie dogs
  - Mice, Voles
  - Others

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There are two epidemiologic divisions (or distributions) 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 photo: Image is of *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 photo: A spotted ground squirrel (*S. spilosoma)*, can be a carrier of *Y. pestis* vector fleas. From CDC.

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Sylvatic Plague

- Enzootic
  - Steady level in rodent populations
  - Low death rates
- Epizootic
  - Large die-offs ➔ fleas change hosts
  - Amplifying hosts
    - Prairie dog, ground squirrels, rock squirrels, woodrats, chipmunks
  - Expansion into human occupied areas
  - Greatest threat to humans

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There are two types of sylvatic (wild form) plague. Many different species of rodents and fleas contribute. Rodents may share burrows and overlap territory; fleas can then be easily transferred among rodent populations. Most rodents die readily from infection of plague. In the **enzootic cycle**, plague is present at low, steady levels (maintenance) within a rodent population in a rodent-to-flea cycle. This is achieved by 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. The true maintenance reservoirs of plague are not fully known. **Epizootic plague** results in a large die off of rodents at which time the rodent fleas seek out a new host and create a large burden on the new host. Many rodent species, especially prairie dogs, serve as amplifying hosts for this level of plague. This is also the greatest threat to humans as rodents and fleas invade into human occupied areas. This leads to urban (domestic) plague. Epizootic sylvatic plague is more likely to result in human infection when there is spillover into urban areas and when people intrude into a wilderness area experiencing an epizootic.

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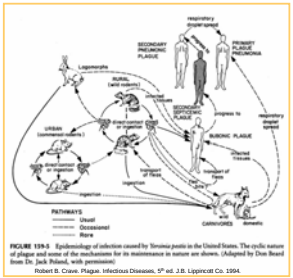

FIGURE 139-1 Epidemiology of infection caused by *Yersinia pestis* in the United States. The cyclic nature of plague and some of the mechanisms for its maintenance in nature are shown. (Adapted by Don Beard from Dr. Jack Poland, with permission)

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

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The full picture of the epidemiology of plague. Note the Urban and Wild (Rural) cycles of transmission.

Slide 23

Urban Plague

- Infected fleas or rodents move to urban area
- Commensal (domestic) rodents infected
  - Roof rat, Norway rat
- Rapid die off
- Fleas seek new host
  - Domestic cats or humans
- Poverty, filth, homelessness

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Urban (domestic) plague occurs when the infected fleas and/or rodents move into urban areas. Influx can also occur when there is significant development and expansion into wilderness areas (i.e., interface building that borders a city and outlying wilderness), as is seen in some parts of the Southwest. The epizootics may cause high mortality in commensal (domestic) rat populations, thereby 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 become infected with plague (i.e., hunting rodents) or transport rodent fleas into the home, thereby exposing their owners. Poverty, filth, and homelessness all contribute to urban plague transmission. Photo: 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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Disease in Humans

Slide 25

Human Disease

- Continuum of illness
  - Bubonic
  - Septicemic
  - Pneumonic
    - Primary
    - Secondary

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Plague is continuum of illness, progressing from one form to the next if left untreated. In humans there are three forms of disease: Bubonic, septicemic, and pneumonic. Bubonic accounts for 80-90% 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

- 80-90% of cases
- Incubation: 2-6 days
- Clinical signs
  - Fever, malaise, chills, headache
  - Bubo: swollen, painful lymph node
  - ± vomiting, abdominal pain, nausea, petechiae
- Mortality (untreated): 50-60%

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Bubonic plague is the most common form and accounts for roughly 80% of cases. The incubation period is 2-6 days. Signs and symptoms include fever, malaise, chills, headache, and very swollen, painful lymph nodes (called "bubo"). Vomiting, abdominal pain, nausea, and petechiae may also occur. Without treatment 50-60% of bubonic cases are fatal. Photo: Enlarged axiallary lymph node - "bubo" (black circle), commonly seen with bubonic plague. From CDC.

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Septicemic Plague

- Systemic spread
- Clinical signs
  - Similar to bubonic, plus
  - Prostration, circulatory collapse, septic shock, organ failure, hemorrhage, DIC
  - Necrosis of extremities
    - Microthrombi blocking capillaries
- Mortality (untreated): 100%

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Septicemic plague occurs when the bacteria enter the bloodstream and are dispersed throughout the body. This phase follows bubonic in most cases, but not all people will develop buboes. In addition to the above signs, prostration, circulatory collapse, septic shock, organ failure, hemorrhage, disseminated intravascular coagulation, and necrosis of extremities can be seen (this is often seen 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. Photo: 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: 1-6 days
- Primary - *Y. pestis* inhaled
- Secondary - septicemic form spreads
- Clinical signs
  - Fever, chills, headache, septicemia
  - Respiratory distress, hemoptysis
- Person-to-person possible

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Pneumonic is the least common form but the most fatal. Primary pneumonic plague occurs when *Y. pestis* inhaled and the bacteria gain direct access to the lungs. Primary pneumonic plague has a very rapid incubation period of 1-6 days. If septicemic plague is left untreated, it progresses to pneumonic plague (secondary pneumonic plague). A person with secondary pneumonic plague who coughs upon another person will transmit plague in an aerosol and infect that person with a primary pneumonic infection. 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 receive **within 24 hours** after the onset of symptoms, otherwise they are unlikely to survive. The use of plague as an aerosol in a bioterrorist attack will result in a very rapid course of illness and potential person-to-person spread.

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Diagnosis

- Isolation of organism
- Fourfold rise in antibody titer
- Single titer of >1:128
- Differential diagnoses
  - Tularemia
  - Hantavirus
  - *Streptococcus*
  - *Staphylococcus aureus*

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A **confirmed** case of plague in people is found by either 1) isolation of *Y. pestis* from clinical specimen or culture is lysed by bacteriophage, 2) fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen by agglutination test, or 3) a single serum specimen tested by agglutination has a titer of >1:128 and the patient has no known previous plague exposure or vaccination history.
A **suspect** case of plague meets the following criteria: 1) clinical symptoms compatible with plague, 2) small, gram-negative and/or bipolar staining coccobacilli seen on smear from affected tissues [lymph node for bubonic; blood for septicemic; tracheal wash for pneumonic.
A **presumptive** case is when one or both of the following are met: detection of F1 antigen in a clinical specimen by fluorescent assay and/or elevated serum antibody titer (>1:10) F1 antigen (without documented fourfold or greater change) by agglutination test in a patient with no history of plague vaccination. Samples for culture should be taken prior to the starting antibiotic therapy.

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Treatment

- With early treatment – Survival ~100%
- Supportive
- Antibiotics
  - Aminoglycosides
    - Streptomycin, kanamycin
  - 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 100% fatal. Currently about 14% (1 in 7) of all plague cases in the U.S. are fatal. Fatalities in the U.S. are often linked to delay in seeking medical care or misdiagnosis. 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. Differential diagnoses include tularemia, Hantaviral pulmonary syndrome, *Streptococcus,* and *Staphylococcus aureus.*

Slide 31

Human Case

- 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 (NYC). They both became ill and sought medical care in a NYC 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, who 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 husbands diagnosis). She recovered without complications.

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Importance of Case

- NMDPH and CDC investigation
  - Trapped rodents and fleas around home
  - *Y. pestis* isolated
- Importance
  - Plague out of endemic area
    - Should raise suspicions
  - 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 the *Y. pestis* isolated from the male patient. Any time plague is suspected or diagnosed out of it endemic area (southwestern U.S.), suspicions should be raised about the source of the infection. In this case, the patients were both had come from the endemic area (New Mexico). What if they had been from Michigan?? This case also emphasizes the importance of early detection and diagnosis. This is important not only for patient care but also for implementation of any isolation or precautionary measures that may need to be implemented. [Case from MMWR 2003;52(31):725-728].

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Animals and Plague

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Slide 34

Animals

- Many found serologically positive
  - Bears, bobcats, badgers, fox, ringtails, skunks, Mountain lion, deer, African elephant, African buffalo, camel, coyote, more …
- Rodents
  - Most die readily from infection
- Farm animals and dogs
  - Very resistant to disease
  - May be incubating at time of slaughter
    - Human risk

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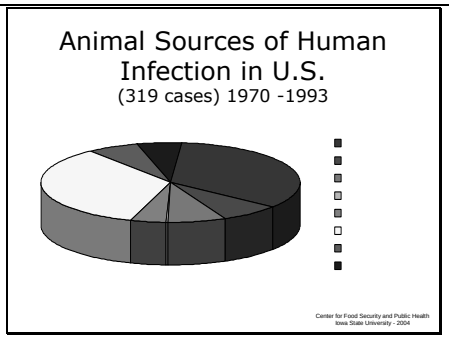
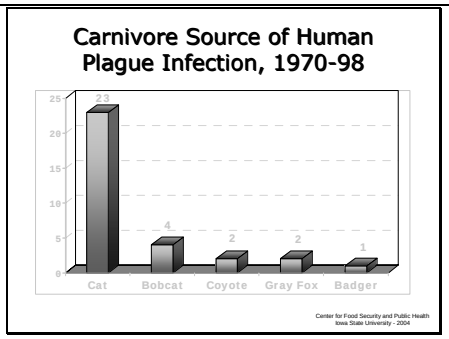
Although many mammals have been found to be serologically positive for plague, canine and farm animals appear to be very resistant to disease. Most rodents die readily from infection. People involved in trapping and skinning wild carnivores, especially bobcats, should be extremely cautious about exposure to *Y. pestis* vectors. Goats, camels, and possibly sheep may be incubating plague at the time of slaughter and have, historically, caused human illness when the contaminated meat has been consumed. Photo: Bobcat.

Slide 35



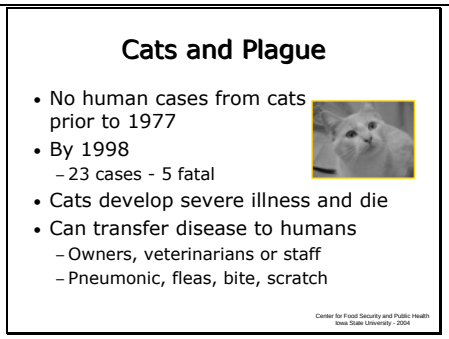
This pie chart depicts the most common animal sources for human infection for 1970-1993. Carnivores include cats, coyotes, badgers, and others. Rock squirrels and California ground squirrels are the most common source of infection. Rock squirrels account for roughly 41% of all human cases in the U.S.

Slide 36



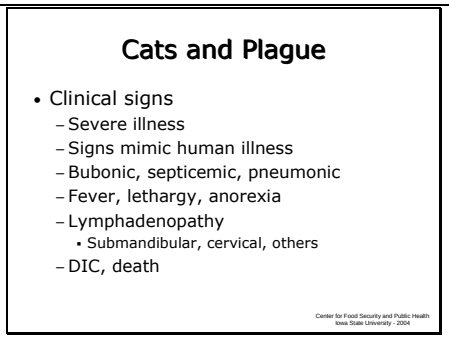
Transmission from animals to people can be either by respiratory aerosol, as seen with domestic cats, or the direct contact with infected tissues of other carnivores, bites, or scratches. Number of human cases attributed to: Cats (23) Bobcat (4) Coyote (2) Gray Fox (2) Badger (1). Carnivores can also 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.

Slide 37



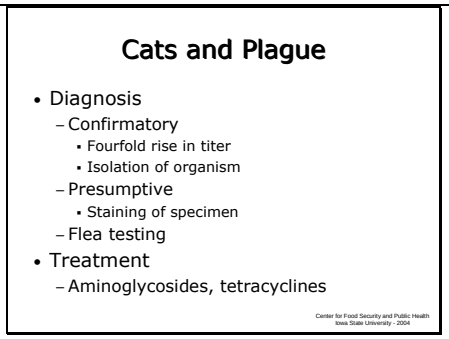
Prior to 1977, no reported cases of plague in humans were acquired from domestic cats. However by 1998, 23 human cases developed from domestic cat exposure. Five of these cases proved to be fatal. Four cases occurred in veterinarians, and two in veterinary staff. The outdoor domestic cat can be infected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

Slide 38



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.

Slide 39



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. Samples for culture should be taken prior to the start of antibiotics. Presumptive diagnosis by fluorescent or Gram's staining of bubo aspirate, lesion exudate, pharyngeal swab, or tissue sample. The 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.

Slide 40

Cats: 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 affects 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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Cat to Human Case

- 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 appear ance 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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Case

- Improved, fever continued for 8 days
- Buboes incised & drained on day 13
- Released on day 16
- History
  - Grandfather shot rabbits
    - Fed to cats and dogs
  - Boy took one cat home
    - Bit and scratched him
    - Cat later died of plague

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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 I 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 cats infection could not be determined, but its wild rabbit meal on Aug. 31 was suspected."
Slide 43	**Dogs and Plague** • Rarely show signs – Fever, lethargy, oral lesions, lymph node lesions • May seroconvert • May carry infected fleas • Diagnosis and treatment – Same as cats • Sentinels  Center for Food Security and Public Health Iowa State University - 2004	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.
Slide 44	Prevention and Control	
Slide 45	**Prevention and Control** • Isolate infected animals – Limit number of people in contact – Personal protection ▪ Surgical mask, gloves, eye protection • Flea control – Dogs and cats ▪ Spring to fall – Premise Center for Food Security and Public Health Iowa State University - 2004	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 mask, 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, premise treatments can also be used to kill fleas brought into the house or yard if needed.
Slide 46	**Prevention and Control** • Prevent roaming or hunting of pets • Rodent control – Eliminate rodent habitat around home ▪ Brush, food sources, firewood, junk – Undertaken only after insecticide use • Insect repellents for skin & clothes • Insecticide use in epizootic areas Center for Food Security and Public Health Iowa State University - 2004	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.

Slide 48

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 prevention and control techniques is vital to preventing cases from occurring. Educating people on the routes of transmission and the risk will go a long way toward prevention. Two-three weeks of antibiotics (tetracyclines or sulfonamides) may be given to people during a plague outbreak. Prophylactic antibiotics may also be given by a physician to a person 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.

A formalin-inactivated vaccine was licensed for use in the United States at one time. This vaccine (plague vaccine, USP) was manufactured by Cutter Biologicals (a division of Miles Laboratories, Inc.), then Greer Laboratories, Inc. This vaccine has been discontinued and 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. Researchers have not determined whether vaccination protects against infectious droplets or aerosols generated in laboratories or against exposure to infectious respiratory droplets from patients who have pneumonic plague.

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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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So what is your role? 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. Educate 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 and avoid risky activities.

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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
    - 80,000-100,000 hospitalized
    - 500,000 secondary cases
  - Up to 100,000 deaths total

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, 80,000-100,000 of which would require hospitalization and 36,000 of which 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 Information

- 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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Acknowledgments

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