Plague

Signs and Symptoms	• **Bubonic:** >80% of U.S. cases; abrupt fever, headache, chills, weakness, and swollen, tender and painful lymph node(s) or buboes • **Septicemic:** Fever, chills, extreme weakness, and abdominal pain; progress to shock, disseminated intravascular coagulation (DIC), multiple organ failure, mental confusion, gangrenous extremities • **Pneumonic:** Acute fever, chills, headache, weakness, and myalgias, hemoptysis, shortness of breath, pneumonia, circulatory collapse; primary (inhalation) or secondary (spread in blood with bubonic or septic plague) • **Pharyngeal:** pharyngitis and cervical lymphadenitis		
Incubation	Bubonic 2–6 days, pneumonic plague 1–3 days		
Case classification	**Clinical criteria**: acute fever with disease manifested in one of above clinical forms **Epi linkage:** linked to confirmed person or animal case or travel to area with confirmed plague epizootic activity in fleas or animals		
	Confirmed: Clinically consistent with *Y. pestis* isolation or ≥4-fold change in *Y. pestis* F1 antigen titer; or with presumptive lab evidence and epi linkage	**Probable:** Clinically consistent with elevated titer to *Y. pestis* F1 antigen in absence prior plague vaccination or F1 antigen in a clinical specimen by DFA, IHC, or PCR and no epi linkage	**Suspect:** Clinically consistent with no laboratory results with epi linkage, or lab results without clinical information
Differential diagnosis	Varies by form; mononucleosis, viral or bacterial sore throat, cat-scratch fever, tularemia, sepsis, bacterial or viral pneumonia, mycobacterial infection, influenza, hantavirus		
Treatment	Appropriate antibiotics and supportive care. Case fatality rate 8-10%.		
Duration	Varies by form; pneumonic plague can be droplet spread		
Exposure	Reservoirs: wild rodents (sagebrush vole, ground squirrel in Washington); pets with fleas. Exposure by flea bite (bubonic, septicemic); handling animal (pneumonic, pharyngeal); ingestion (pharyngeal); droplet exposure from human case (pneumonic).		
Laboratory testing	LHJ and CDE arrange testing for individual cases or confirm isolates • Washington State Public Health Laboratories (PHL) can culture or confirm isolates • **Best specimens**: **isolate in screw-top slant; sputum; tissue (2+ grams in sterile container, moisten with saline); NP swabs (one dry, one in transport medium)** *Specimen shipping (Section 4):* Keep isolate at **ambient temperature**, other specimens **cold** according to PHL requirements: https://doh.wa.gov/sites/default/files/legacy/Documents/5230//302-018-BioterrorismSpecimen.pdf. Ship specimens according to PHL requirements: https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu • Specimen Collection and Submission Instructions https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-Yersinia-pestis-V1.pdf		
Public health actions **URGENT**	Immediately report to CDE any suspected or laboratory positive cases • Identify risk exposure: in plague-endemic area; flea bite; contact with wild rodents or wild animal; direct contact with a sick cat or dog; contact with confirmed, probable or suspected case of pneumonic plague; work in microbiology laboratory • Identify close contacts or others potentially exposed (household, hospital, lab) and evaluate, if symptomatic arrange testing, if asymptomatic educate about symptoms and arrange post-exposure antibiotic prophylaxis and monitoring for fever and cough for 14 days: https://www.cdc.gov/plague/healthcare/clinicians.html • Consider environmental evaluation *Infection Control:* standard precautions; droplet precautions for pneumonic plague until 48 hours of antibiotic treatment		

Plague

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To assist in the diagnosis and treatment of cases.
2. To identify potentially exposed close contacts, health care workers, and laboratory personnel and to provide counseling.
3. To identify sources of transmission (e.g., wild rodents or other animals) and to prevent further transmission from such sources.
4. To raise suspicion of a possible bioterrorism event if there is no natural exposure source.

B. Legal Reporting Requirements

1. Health care providers and Health care facilities: *immediately* notifiable to **local health jurisdiction**.
2. Laboratories: *immediately* notifiable to **local health jurisdiction**; submission required – presumptive positive isolate or if no isolate specimen associated with presumptive positive result, within 2 business days.
3. Veterinarians: animal cases notifiable to Washington State Department of Agriculture. See: https://app.leg.wa.gov/WAC/default.aspx?cite=16-70
4. Local health jurisdictions: **Suspected and confirmed cases are immediately notifiable** to the Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE) (206-418-5500 or 1-877-539-4344).

C. Local Health Jurisdiction Investigation Responsibilities

1. **If bioterrorism is suspected, immediately report the case to DOH: 1-877-539-4344.**
2. Facilitate the transport of specimens to Washington State Public Health Laboratories for confirmatory testing.
3. Educate potentially exposed persons about signs and symptoms of disease; recommend antibiotic prophylaxis as needed.
4. Report all *suspected, probable* and *confirmed* cases to CDE (definition below). Complete a report form https://www.doh.wa.gov/Portals/1/Documents/5100/210-058-ReportForm-Plague.pdf and enter in the Washington Disease Reporting System (WDRS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Plague is caused by *Yersinia pestis*, a non-spore-forming, non-motile Gram-negative coccobacillus with a characteristic "safety pin" appearance due to bipolar staining. *Y. pestis* is viable for weeks in moist conditions and may survive an hour in the air, but is killed by sunlight or heat. It is naturally maintained in an enzootic cycle involving fleas and the rodent hosts on which they feed.

B. Description of Illness

Yersinia pestis infection in humans occurs as four main clinical forms depending on route of transmission. Additional rare forms of plague include meningeal and cutaneous. Overall about 11% of plague cases in the United States are fatal.

1. Bubonic Plague

The bubonic form accounts for over 80% of plague cases in the United States. Patients typically experience a sudden onset of fever, headache, chills, and weakness, and one or more swollen, tender and painful lymph nodes. This form is usually the result of an infected flea bite. Symptoms progress rapidly, with development of lymphadenitis, which becomes very painful. The bacteria multiply in the lymph node closest to where the bacteria entered the human body. These swollen lymph nodes are known as buboes, which are typically found in the inguinal (groin) region, but also the axillary (armpit) or cervical (neck) region. Untreated bubonic plague can progress to cause septicemic or secondary pneumonic plague. Rarely, it progresses to meningitis.

2. Septicemic Plague

The primary septicemic form occurs in about 10% of plague cases in the United States. Diagnosis can be difficult because buboes are not seen in primary septicemic plague. Septicemic plague can be secondary to bubonic plague. Fever, chills, extreme weakness, and abdominal pain are common. Patients may progress to endotoxic-shock, disseminated intravascular coagulation (DIC), multiple organ failure, acute respiratory distress syndrome (ARDS), mental confusion, gangrenous extremities (black plague), and death. This form results from bites of infected fleas or from handling an infected animal.

3. Pneumonic Plague

About 3% of plague patients in the United States develop primary pneumonic plague. Secondary pneumonic plague can also result from the spread of *Y. pestis* to the lungs in patients with untreated bubonic or septicemic infection. Primary pneumonic plague results from inhaling infectious droplets in the air. Pneumonic plague causes acute onset of fever, chills, headache, weakness, and myalgias, followed within 24 hours by cough with bloody sputum. The pneumonia progresses rapidly, resulting in dyspnea, stridor, and cyanosis, terminating in respiratory failure, circulatory collapse, and death. Pneumonic plague is the most serious form of the disease and is the only form of plague that can be spread from person to person (by infectious droplets).

4. Pharyngeal

Sore throat and cervical lymphadenitis from exposure to larger infectious droplets or ingestion of infected tissues.

C. Plague in Washington State

Plague infections of animals occur in the state, mainly in eastern counties but also in western Washington. Statewide serologic sampling of 8,921 wild carnivores between 1975 and 2015 showed 2.5% seropositivity (DOH summary: https://www.doh.wa.gov/Portals/1/Documents/Pubs/333-401.pdf) indicating the presence of infected wild rodents. However, sampling during 2003-2014 found only a single positive coyote (0.11%), indicating possible decrease in infected rodent populations over

time. Human plague infections are extremely rare, the last report was an animal trapper exposed while skinning a bobcat in Yakima County in 1984. In Oregon, one person was diagnosed with plague in 2015.

Nationally, plague occurs mainly in southwestern states with an average of 7 cases annually.

D. Vectors and Reservoirs

Wild rodents (especially squirrels, prairie dogs, other burrowing rodents) are the reservoir of *Y. pestis* which is transmitted by fleas. In eastern Washington the sagebrush vole is the major reservoir; ground squirrels are competent reservoirs in the south central Cascades. *Y. pestis* can spread from rodents to other wildlife, domestic animals, and humans.

E. Modes of Transmission

1. Flea Bites

The most common means of transmission to humans is through bites from fleas infected with *Y. pestis*. During plague epizootics, many rodents die, causing fleas to seek other sources of blood. Fleas can remain infective for months. People or animals in places where rodents have recently died from plague are at risk of infection from flea bites.

2. Infected Animals

Handling tissues or bodily fluids of infected rodents or other animals can cause human infection. Cats and dogs that become infected (due to eating infected rodents or bites by their fleas) have been sources of human infection through direct contact, bites and scratches, bringing home plague-infected fleas that bite humans, or respiratory droplets from animals with pneumonic plague. A recent outbreak of human pneumonic plague in Colorado was associated with dog-to-human transmission.
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6416a1.htm

3. Infected Humans

Person-to-person transmission occurs from patients with pneumonic plague through respiratory droplet spread. Individuals with bubonic plague are infectious when buboes or other cutaneous lesions are draining. Typically, transmission requires direct and close contact with the person infected with plague.

4. Intentional Dissemination

Intentional dissemination of plague would most likely occur as an aerosol release of the organism, resulting in pneumonic plague. Because of this route of exposure, exposed persons would likely develop primary pneumonic plague and would then be a potential source of person-to-person transmission.

F. Incubation Period

Generally, the incubation period for plague is 1–7 days with bubonic plague occurring 2–6 days and primary pneumonic plague occurring 1–3 days after an exposure.

G. Period of Communicability

Patients with pneumonic plague are communicable at the onset of symptoms. The infection generates an intense cough reflex, which readily disperses respiratory droplets

capable of exposing close contacts. Patients with pneumonic plague are infectious until completion of at least 48 hours of appropriate antibiotic therapy.

Exudates from buboes contain viable *Y. pestis* organisms and patients with draining buboes are communicable until lesions are surgically excised or heal.

H. Treatment

Treatment includes prompt therapy with appropriate antibiotics and supportive care.

3. CASE DEFINITIONS

A. Clinical Description

An illness characterized by acute onset of fever as reported by the patient or healthcare provider with or without one or more of the following specific clinical manifestations:

- Regional lymphadenitis (bubonic plague)
- Septicemia (septicemic plague)
- Pneumonia (pneumonic plague)
- Pharyngitis and cervical lymphadenitis (pharyngeal plague)

B. Laboratory Criteria for Diagnosis

1. Presumptive*:
    - Elevated serum antibody titer(s) to *Yersinia pestis* fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination or
    - Detection of *Yersinia pestis* specific DNA or antigens, including F1 antigen, in a clinical specimen by direct fluorescent antibody assay (DFA), immunohistochemical assay (IHC), or polymerase chain reaction (PCR)
2. Confirmatory:
    - Isolation of *Y. pestis* from a clinical specimen with culture identification validated by a secondary assay (e.g., bacteriophage lysis assay, direct fluorescent antibody assay) or
    - Fourfold or greater change in paired serum antibody titer to *Y. pestis* F1 antigen

* Other laboratory tests, including rapid bedside tests, are in use in some low resourced international settings but are not recommended as laboratory evidence of plague infection in the United States.

C. Exposure

Criteria for epidemiologic linkage are dependent upon exposure, which may include:

- Epidemiologic linkage to a person or animals with confirmatory laboratory evidence within the prior two weeks
- Close contact with a confirmed pneumonic plague case, including, but not limited to, presence within two meters of a person with active cough due to pneumonic plague

- Residence in or travel to a geographically-localized area with confirmed plague epizootic activity in fleas or animals within two weeks of illness onset

D. Case Definition (2020)

Suspect:

- A clinically compatible case with epidemiologic linkage without laboratory evidence, OR
- Confirmed or presumptive laboratory evidence without any associated clinical information

Probable:

- A clinically compatible case with presumptive laboratory evidence without epidemiologic linkage in absence of an alternative diagnosis

Confirmed:

- A clinically compatible case with confirmatory laboratory evidence, OR
- A clinically-compatible case with presumptive laboratory evidence AND epidemiologic linkage

Serial or subsequent plague infections in one individual should only be counted if there is a new epidemiologically-compatible exposure and new onset of symptoms.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

Yersinia pestis can be isolated from a variety of bodily fluids and tissues including bubo aspirates, blood, and tracheal/bronchial washings for bubonic, septicemic, and pneumonic forms, respectively. Specimens intended for culture should be taken **before** initiation of antibiotic treatment. Microbiology laboratory personnel should be alerted when *Y. pestis* is suspected, as laboratory acquired cases of plague have been reported. **Confirmatory laboratory testing must be performed by a reference laboratory such as the Washington State Public Health Laboratories.** If cultures do not detect the organism, serologic testing can be used to diagnose plague. Bipolar staining may be seen (Gram, Wright, Giemsa, or Wayson stain).

B. Tests Available at the Washington State Department of Health Public Health Laboratories (PHL)

PHL provide identification of *Y. pestis* from pure isolates as well as culturing of clinical specimens. Serologic tests are not performed at PHL but will be forwarded to the CDC for testing. PHL also perform rapid diagnostic testing in suspected bioterrorism situations. Contact Office of Communicable Disease Epidemiology (CDE) for approval prior to collection and shipment of specimens.

Note that PHL require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

C. Specimen Collection (and Shipping)

Consult CDE prior to specimen preparation and shipment (206-418-5500). For details of specimen requirements and appropriate shipping procedures for *Y. pestis* see: https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-Yersinia-pestis-V1.pdf
Keep isolate at **ambient temperature**, other specimens **cold** according to PHL requirements: https://doh.wa.gov/sites/default/files/legacy/Documents/5230//302-018-BioterrorismSpecimen.pdf. Ship specimens according to PHL requirements: https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu

Serology: Obtain one serum specimen as early in the illness as possible and a second sample 1 to 4 months after antibiotic therapy has ceased. Refrigerate specimens and transported cold. Avoid repeated freeze-thaw cycles.

5. ROUTINE CASE INVESTIGATION

Interview the case or others who may be able to provide pertinent information.

A. Evaluate the Diagnosis

Review the clinical presentation and laboratory results. **Confirmatory laboratory testing should be performed by a reference laboratory such as Washington State Public Health Laboratories (PHL).** Facilitate submission of specimens to PHL for confirmation. For sporadic cases proceed with investigation after preliminary or confirmatory laboratory results are available. During an outbreak event or a potential bioterrorism situation, start investigation before laboratory results are available if needed.

B. Identify Potential Sources of Infection

Review clinical presentation and history to determine appropriate potential exposures (i.e., bubonic presentation would indicate most likely flea bite or animal carcass exposure; pneumonic presentation would indicate inhalation exposure). Investigate possible exposures during the period 1 to 7 days before onset, including a history of:

1. Travel to plague endemic areas (e.g., New Mexico, Arizona, Colorado, California, or parts of Washington or Oregon known to have plague activity);
2. Bites by fleas;
3. Contact with wild or commensal rodents or hunting/skinning wild animals;
4. Direct contact with a sick cat or dog (holding, petting, being bitten or scratched);
5. Contact with individuals with confirmed, probable or suspected pneumonic plague;
6. Work in microbiology laboratory.

C. Identify Close Contacts or Others Potentially Exposed to the Patient

1. Identify persons having household, hospital or other close contact with persons with pneumonic plague and educate them of symptoms of illness to facilitate diagnosis.
2. Identify laboratory workers and health care providers exposed to specimens or laboratory isolates and educate them of symptoms of illness to facilitate diagnosis.

   Persons having household, hospital or other close contact with pneumonic plague cases, or direct contact with infected bodily fluids or tissues (including from infected animals)

should receive post-exposure antibiotic prophylaxis and be monitored for fever and cough for 14 days. See: https://www.cdc.gov/plague/healthcare/clinicians.html.

Guidelines for post-exposure prophylaxis are outlined here: https://www.cdc.gov/plague/healthcare/clinicians.html

D. Identify Potentially Exposed Persons

1. Identify and contact persons who participated with the case in any of the activities listed above. If any contacts are ill, inform them (or their physician) of possible exposure, in order to facilitate proper diagnosis and therapy.

E. Environmental Evaluation

1. If the source of infection appears to be wild rodents, the public should be informed of the risk of and how to avoid contact with potentially plague infected rodent populations.
2. If the source appears to be contact with plague-infected commensal rodents (i.e., rodent living in close association to humans, such as urban rats and pet rodents) or domestic cats, it can be assumed that this is due to spill over from a wild rodent population, and further investigation of the animal source is warranted.

F. Infection Control Recommendations/Case Management

1. Pneumonic plague: Droplet precautions are indicated for all patients until at least 48 hours after appropriate therapy has been initiated.
2. Bubonic plague: Hospitalized patients should be cared for using standard precautions.

6. MANAGING SPECIAL SITUATIONS

A. Bioterrorist Event

Yersinia pestis is classified as a bioterrorism "category A" agent (of greatest concern) because it can be easily disseminated by aerosol, be transmitted from person to person (pneumonic plague) and cause severe illness and death. Suspect an intentional release (bioterrorist event) if unusual clusters of pneumonia occur in persons who are otherwise healthy or are in common buildings. **If plague is suspected immediately call Office of Communicable Disease Epidemiology (1-877-539-4344 or 206-418-5500).**

In event of a biological attack, antibiotic prophylaxis may be recommended for a suspected or known exposure to *Y. pestis*. For more information, see Recommendations of the Working Group on Civilian Biodefense, JAMA.2000;283;2281-90.

7. ROUTINE PREVENTION

A. Immunization Recommendations

There is currently no commercially available vaccine against plague in the United States.

B. Routine Prevention

1. **Avoid contact with sick or dead wild animals.** Wear gloves if handling dead animals. When skinning wild game keep gloves away from eyes and other mucous membranes. Thoroughly wash hands after handling wild game carcasses. Wild game meat should be cooked “well done” (to at least 74°C/165°F).

2. **Rodent-proof your home.** 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.
3. **Prevent your pets from contracting fleas.** Use flea-control products and don't allow pets to wander unsupervised. Ask your veterinarian for recommended flea-control brands and guidelines.
4. **Take precautions when outdoors.** Closely supervise your children and pets when spending time outside in areas with large rodent populations. Use insect repellent on your skin and clothing.
5. **If you suspect you have plague, consult a health care provider as soon as possible.**

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UPDATES

January 2011: Legal Reporting Requirements section revised to reflect the 2011 Notifiable Conditions Rule revision.

September 2013: Reviewed, updated links

October 2015: Reviewed, updated links

December 2017: Front page added, general updates

December 2019: Updated case definition to 2020 revision, routine review.
December 2022: For 2023 WAC revision combined provider and facility reporting requirement, updated laboratory submission (Section 1B)

December 2023: For 2024 WAC revision updated laboratory submission.