Plague
Investigative Guidelines
October 2021

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To identify the source of infection and determine risk of transmission to others.
2. To determine whether the source of infection is a major public health concern (e.g., intentional release of the organism, increased human exposure due to wildlife epizootics, etc.) and to stop transmission from such a source.
3. To identify other cases, facilitate treatment and in the case of pneumonic plague, prevent person-to-person spread.

1.2 Laboratory and Physician Reporting Requirements

Laboratories and physicians are required to report any suspect plague case **immediately (day or night)** to the local health department or to Oregon Public Health Division (OPHD). **Laboratories must send isolates suspected of being *Yersinia pestis* or other *Yersinia* species to the Oregon State Public Health Laboratory (OSPHL) for confirmation.** (OAR 333-018-0018, [1,2])

1.3 Local Health Department Reporting and Follow-Up Responsibilities

1. Report all confirmed, presumptive and suspect cases of plague (see definitions below) to OPHD **immediately (day or night)** at 971-673-1111.
2. Begin follow-up investigation immediately. Use the CDC Plague Case Investigation Report (CDC 56.37 (E)), available through a link on the *Basics* tab for Plague cases in Orpheus or at: www.cdc.gov/plague/resources/plaguecasereportform.pdf .

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

Yersinia pestis is an aerobic, non-spore-forming, gram-negative, non-motile coccobacillus. With certain stains (Geimsa or Wright), it may exhibit bipolar staining, giving it a characteristic “safety pin” appearance. *Y. pestis* can be viable for weeks under moist conditions. At near-freezing temperatures or within soil, it can be viable for months to years. However, sunlight and heat readily kill the organism, and on common environmental surfaces, it becomes non-viable within 48 hours.

2.2 Description of Illness

Yersinia pestis infection in humans occurs in three primary clinical forms:

1. Bubonic Plague

   Bubonic plague accounts for more than 80% of the plague cases in the United States and, if untreated, has a case-fatality rate of 50 to 60%. Bubonic plague results from the bite of an infected flea or contamination of an open skin lesion with plague-infected material. After an incubation period of 2 to 6 days, patients typically experience a sudden onset of fever, shaking chills, malaise, and pain in the affected regional lymph nodes. Symptoms progress rapidly, with development of lymphadenitis, which becomes very painful. These swollen lymph nodes are known as buboes. Untreated bubonic plague can progress to septicemic or secondary pneumonic plague.

2. Septicemic Plague

   Primary septicemic plague accounts for about 1% of plague cases in the United States and has a case-fatality rate of 50%. Buboes are not seen in primary septicemic plague, making diagnosis more difficult. Septicemic plague can also develop secondary to bubonic plague. Patients may develop endotoxic shock, disseminated intravascular coagulation (DIC), multisystem organ failure, acute respiratory distress syndrome (ARDS), mental confusion, and death. Hemorrhage and tissue necrosis may be seen with DIC.

3. Pneumonic Plague

   Though primary pneumonic plague is rare in the United States, it can arise as a complication of the septicemic or bubonic forms, affecting as many as one in ten people with these conditions. The case-fatality rate of untreated pneumonic plague approaches 100 percent. With prompt treatment, it is about 50 percent. This is the form that would likely be seen in the event of an intentional aerosol release. Onset is typically abrupt, with fever, chills, headache, malaise and muscle aches, followed by cough and rapidly progressive shortness of breath, with the production of bloody sputum, stridor, and cyanosis, often terminating in respiratory failure, circulatory collapse, and death.

   Meningeal and pharyngeal plague have also been described.

2.3 Reservoirs

Wild rodents are the natural reservoir of *Y. pestis.* Feeding fleas transmit the organism, maintaining the disease in the wild rodent population. In the United States, the major reservoir species include the prairie dog *Cynomys gunnisoni* and the rock squirrel *Spermophilus variegatus*. The most important reservoir on the Pacific Coast is the California ground squirrel *Spermophilus beecheyi*. Others include chipmunks, the California vole, and the golden-mantled ground squirrel *Spermophilus lateralis*.

Infection from the wild reservoir can spill over into peri-domestic and commensal (domestic) rodents that are more susceptible to the disease and are important in transmitting the disease to humans.

2.4 Sources and Routes of Transmission

1. Flea bites

   The most common means of transmission to humans is through bites from fleas infected with *Y. pestis*. Fleas become infected by feeding on plague-infected rodents and can remain infective for months.

2. Infected animals

   Handling tissues of infected animals is also a source of human infection.

   Natural infection in domestic cats has been reported and is believed to be due to consumption of infected rodents. Cats have been a source of human infection in some instances, especially in the Southwestern United States, where plague is enzootic. Transmission from infected cats to humans has resulted from direct contact, bites, scratches, (rarely) droplet transmission from respiratory secretions, and from bites by plague-infected fleas carried by cats.

3. Infected humans

   Person-to-person transmission occurs from patients with pneumonic plague through respiratory droplet spread. Individuals with bubonic plague are communicable when buboes or other cutaneous lesions are draining.

4. Intentional Dissemination

   Intentional dissemination of plague would most likely occur as an aerosol release of the organism, resulting in pneumonic plague. Individuals who develop pneumonic plague would then be a source of person-to-person transmission.

2.5 Incubation Period

1. Bubonic plague — 2 to 6 days.
2. Primary septicemic plague — 2 to 6 days.
3. Primary pneumonic plague — 1 to 6 days (usually 2 to 4 days).

2.6 Period of Communicability

1. Bubonic –- Transmission through contact may occur as long as buboes are draining. Contact precautions are indicated.
2. Septicemic –- Not typically transmissible in absence of one of the other forms.
3. Pneumonic –- Patients should be assumed to be contagious from the onset of respiratory symptoms. Contact and droplet precautions are required until completion of 48 hours of appropriate antibiotic therapy, with a favorable clinical response.

2.7 Treatment and Prophylaxis

1. Treatment

   Information about treatment of plague is available on CDC's website: www.cdc.gov/plague/healthcare/clinicians.html

2. Prophylaxis

   People with the following exposures in the prior 6 days should receive preventive antibiotics:

   - Close contact (<2 meters) with pneumonic plague patients without recommended respiratory protection,
   - Exposure to a suspected plague-containing aerosol,
   - Likely exposure to *Y. pestis*-infected fleas,
   - Direct contact with drainage from the buboe of a plague-infected patient,
   - Direct contact with bodily fluids or tissues of a *Y. pestis*-infected mammal, or
   - Laboratory exposure to known, plague-infected materials without recommended precautions.

   Duration of post-exposure prophylaxis to prevent plague infection: 7 days.

   Please refer to: www.cdc.gov/plague/healthcare/clinicians.html ; for up-to-date treatment and prophylaxis recommendations.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

Rapid testing is not widely available for diagnosing plague. Initial diagnosis is typically based on clinical suspicion. Clinical laboratories should refer to and follow the American Society for Microbiology (ASM) Sentinel Clinical Laboratory Guidelines for the presumptive identification testing procedures: www.asm.org/Articles/Policy/Laboratory-Response-Network-LRN-Sentinel-Level-C

Confirmatory testing must be performed by a Laboratory Response Network (LRN) Reference Lab such as the OSPHL, however, to meet the confirmed case definition below.

3.1 Laboratory Criteria for Diagnosis

1. **Confirmed Case**

   - Isolation of *Y. pestis* from a clinical specimen and confirmed by LRN Reference Lab procedures, or
   - Fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen.

2. **Presumptive Case**

   - 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 prior plague infection; or
   - Detection of *Yersinia pestis*-specific DNA by polymerase chain reaction (PCR), or antigens, including F1 antigen, in a clinical specimen by direct fluorescent antibody assay (DFA) or immunohistochemical assay (IHC). PCR and DFA tests are conducted at LRN Reference Labs.

3.2 Epidemiological Linkage

1. Person that is epidemiologically linked to a person or animals with confirmatory laboratory evidence within the prior two weeks;
2. 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; or
3. A person who lives in or has traveled within two weeks of illness onset to a geographically localized area with confirmed plague epizootic activity in fleas or animals, as determined by the relevant local authorities

3.3 Case Classification

1. **Confirmed Case**

   - A clinically compatible case with confirmatory laboratory results, or
   - A clinically compatible case with presumptive laboratory results *and* epidemiologic linkage

2. **Presumptive Case**

   A clinically compatible case with presumptive laboratory results, without epidemiologic linkage in the absence of an alternative diagnosis

3. **Suspected Case**

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

3.4 Services Available at the Oregon State Public Health Laboratory (OSPHL)

Contact ACDP Epi on-call and OSPHL (503-693-4100) prior to specimen shipment.

The OSPHL can perform rapid molecular presumptive and confirmatory testing using standard LRN Reference Laboratory procedures for microbiological and biochemical identification of *Y. pestis* to confirm direct clinical specimens or isolates submitted by clinical laboratories. For specimen submission information, please review the OSPHL Lab Test Menu at www.healthoregon.org/labtests.

Submission of isolates is strongly preferred. In rare circumstances, the OSPHL can accept direct clinical specimens for *Y. pestis* confirmation. Please consult with the OSPHL if this is needed.

If needed, OSPHL can arrange for serology at CDC. For antibody testing, please refer to the CDC instructions for submitting *Y. pestis* serology specimens: www.cdc.gov/laboratory/specimen-submission/detail.html?CDCTestCode=CDC-10419. Specimens to be tested by CDC should be sent to the OSPHL, who will forward the specimens to CDC.

4. CASE INVESTIGATION

Interview the case and others who may be able to provide pertinent information, using the CDC *Plague Case Investigation Report* (CDC 56.37 5-85) available in Orpheus or at: www.cdc.gov/plague/resources/PlagueCaseReportForm.pdf

For possible intentional aerosol release (bioterrorist event), see *Section 6* below.

4.1 Confirm the Diagnosis

1. Review clinical presentation and available laboratory results.
2. Confirmatory testing by the OSPHL or another reference laboratory is required.
3. Facilitate shipment of relevant laboratory specimens to OSPHL if not yet done.

4.2 Identify Source of Infection

For the 6 days prior to onset, obtain history of:

- bites by fleas;
- contact with wild or commensal rodents;
- direct contact with a "sick" cat (holding, petting, being bitten or scratched);
- contact with anyone with confirmed, presumptive or suspect plague;
- travel to plague enzootic areas (e.g., South Central Oregon, New Mexico, Arizona, Colorado, Utah, or California);
- any work in a microbiology lab;
- exact whereabouts of cases with pneumonic plague during the 6 days prior to onset of symptoms.

4.3 Identify Other Potentially Exposed People

Identify and contact people who may have had the same exposures as the case. Identify and contact any acquaintances or household members with similar illnesses. Asymptomatic people having household, hospital or other close contact (<2 meters) with symptomatic pneumonic plague cases in the prior 6 days (or other exposures listed in Section 2.7 [2], above) should receive post-exposure antibiotic prophylaxis for 7 days and be watched for fever and cough. (See *Model Standing Order for Antimicrobial Prophylaxis in the Setting of Exposure to Yersinia pestis Aerosol or to a Patient with Pneumonic Plague*, available at: https://public.health.oregon.gov/PreventionWellness/VaccinesImmunization/ImmunizationProviderResources/Documents/SOPneuPlague.pdf .)

4.4 Environmental Evaluation

1. If the source of infection appears to be wild rodents, inform the public of the risk of and how to avoid contact with potentially plague-infected rodents.
2. If the source appears to be contact with plague-infected commensal rodents or domestic cats, this is likely due to spill-over from a wild rodent population, and further investigation of the animal source is warranted.

5. CONTROLLING FURTHER SPREAD

5.1 Environmental and Infection Control

1. Reduce risk of flea bites through flea and rodent control.
2. In the face of an epizootic, insecticides should be employed before or at the same time as rodenticides, but never after, as fleas abandon dead animals in search of new hosts, including humans.
3. Reduce direct contact with potentially infective tissues and exudates by wearing gloves when hunting and handling wildlife or dead animals.
4. Reduce exposure to patients with pneumonic plague by:
   - using Droplet Precautions in addition to Standard Precautions (see below);
   - avoiding unnecessary close contact with pneumonic plague patients until at least 48 hours after initiation of antibiotic therapy;
   - cohorting multiple cases.

5.2 Education

Educate the public regarding:

- location of plague enzootic areas,
- modes of human and domestic animal exposure and how to avoid them,
- the importance of commensal rodent and flea control, and
- wearing gloves when handling wildlife.

5.3 Isolation and Work or Day Care Restrictions

1. Standard precautions should be applied to management of all suspected plague patients.
2. In addition, droplet precautions should be observed in management of patients with pneumonic plague and should be continued until completion of 48 hours of effective antimicrobial therapy with a favorable clinical response. Descriptions of isolation precautions are available in Section IIIb of HICPAC Isolation Precautions; www.cdc.gov/hicpac/2007ip/2007ip_part3.html .

5.4 Case Follow-up

Anyone with suspect, presumptive, and confirmed plague should be under medical care to ensure effective therapy can be started in a timely fashion.

5.5 Protection of Contacts

All close contacts of confirmed, presumptive or suspected cases with pneumonic plague, including medical personnel who were not using appropriate infection precautions, should be provided with chemoprophylaxis, as should contacts with other exposures listed in Section 2.7 [2], above. (See standing orders at: https://public.health.oregon.gov/PreventionWellness/VaccinesImmunization/ImmunizationProviderResources/Documents/SOPneuPlague.pdf .)

5.6 Environmental Measures

Vector identification and control is key. *Yersinia pestis* does not form spores and does not survive long on common environmental surfaces. (See section 2.1, above.) In the case of an intentional aerosol release, the organism will have dissipated long before the first case of pneumonic plague occurs.

6. MANAGING SPECIAL SITUATIONS

6.1 Bioterrorist Event

Yersinia pestis is classified as a "Category A" bioterrorism agent because it can be easily disseminated by aerosol, can be transmitted from person to person (pneumonic plague) and has the capacity to cause severe illness and death. An intentional release (bioterrorist event) should be suspected if unusual clusters of pneumonia are seen in otherwise healthy individuals or in people in areas of buildings with common ventilation systems. Call OPHD (971-673-1111) **immediately, day or night,** if plague is suspected.

REFERENCES

1. CDC Emergency Preparedness and Response. National Center for Preparedness, Detection, and Control of Infectious Diseases. Plague, Information for Health Professionals. Accessed 4 December 2018.
2. Inglesby TV, Dennis DT, Henderson DA. et al. Plague as a biological weapon: medical and public health management. JAMA. 2000;283:2281-2290.
3. Nelson CA et al. Antimicrobial Treatment and Prophylaxis of Plague: Recommendations for Naturally Acquired Infections and Bioterrorism Response. MMWR 2021; RR 70(3):1-27; Accessed: 6 October 2021
4. Heymann DL (Ed.). Control of communicable diseases manual (20th ed.). Washington, DC: American Public Health Association; 2015

UPDATE LOG

October 2021. Minor edits for clarity. Links and references updated. (Leman, Nickla)

January 2020. Updated links as needed. Update Section 3 Case Definition, Diagnosis, and Laboratory Services to reflect new CSTE case definition. (Leman, OSPHL staff)

Dec. 2018. Updated links and lab section, minor edits. (Leman, OSPHL staff)

July 2016. Updated sec. 2.2. on epidemiology of pneumonic plague. Clarified Sec. 2.6. Period of Communicability. Removed section on treatment and prophylaxis, and added link to existing standing orders for Plague prophylaxis. Updated case definition to 2009 CSTE position statement 09-ID-52. Added Section 4.1 Confirm the Diagnosis and clarified other information in Case Investigation section. References added. (Ryff, Leman)

June 2004. Created.