

Plague!

PROTOCOL CHECKLIST

- Contact provider
- Notify the Division of Disease Control, Bureau of Epidemiology (DCBE) immediately upon notification of potential bioterrorism events and for additional assistance in patient management (850-245-4401).
- Notify the Florida Department of Health (FDOH) Bureau of Public Health Laboratories (BPHL) to arrange for confirmatory testing or to facilitate further testing at the Centers for Disease Control and Prevention (CDC).
Detection of a suspected case is considered a **PUBLIC HEALTH EMERGENCY.**
- Enter available information into Merlin upon receipt of initial report
- Review background on disease, case definition, and laboratory testing
- Ensure patient is placed in isolation upon suspected diagnosis
- Review disease facts for the different presentations of the disease (bubonic, septicemic, pneumonic, pharyngeal)
 - Modes of transmission
 - Incubation period
 - Symptoms
- Interview patient
 - Ask about exposure to relevant risk factors
 - Travel to an area with known plague or plague risk
 - Contact with ill person, known plague patient or someone who has died in past week
 - Known contact with infected rodents or fleas of infected animals, handling infected animals
 - Exposure to tick infested domestic cats and dogs, sick pets or pets who brought home dead animals
 - Occupational exposure such as hunting, trapping, farming, or laboratory work
 - Contact with suspicious substance (respiratory inhalation) or associated with possible bioterrorism (BT) event
 - If suspected BT event, identify other possible exposed or symptomatic contacts
 - Determine whether exposed or symptomatic contact(s) have had laboratory evaluation
 - Determine need for prophylaxis for exposed contact(s)
 - Provide education on transmission and prevention
 - Reduce the likelihood of people bitten by infectious fleas, having direct contact with infective tissues or exudates, or of being exposed to disease bearing animals and their fleas:
 - Watch for plague activity in rodent populations where plague is known to occur and report any dead or disease animals to the health department
 - Eliminate sources of food and nesting places
 - If anticipating exposure to rodent fleas, apply insect repellent and wear gloves if handling potentially infected animals.
 - If you live in an area where rodent plague occurs, treat pet cats and dogs for flea control regularly and do not allow them to roam freely
 - Address patient's questions or concerns
- Follow-up on special situations such as need for environmental control
- Enter additional data obtained from interview into Merlin

Plague

1. DISEASE REPORTING

A. Purpose of reporting and surveillance

1. To rapidly detect plague and promptly treat those who are ill.
2. To promptly identify the source of *Yersinia pestis* infection, especially in pneumonic plague, including identification of intentional release in context of a bioterrorist attack.
3. To support rapid implementation of control measures.

B. Legal reporting requirements

1. Laboratories and physicians are required to immediately report persons suspected of being infected with *Yersinia pestis* by phone to the county health department (CHD) upon initial suspicion or laboratory test order.
2. CHDs should immediately notify (24/7) the DCBE at 850-245-4401.
3. Of particular concern is pneumonic plague due to the high case mortality and the potential for secondary infection transmission. Any isolates from infected persons or those suspected of infection must be sent to the BPHL. Detection of a suspected outbreak of pneumonic plague is characterized by fever, cough, fulminant course, high case fatality rate (50% to 60% if untreated) and hemoptysis is a **MEDICAL AND PUBLIC HEALTH EMERGENCY**.
4. All suspected plague infections must be reported to CHDs and DCBE. In turn, the DCBE will notify the CDC for disease confirmation. In the event that this is determined to be a public health event of international significance, the CDC will notify the World Health Organization.

C. County health department investigation responsibilities

1. Work with the DCBE to facilitate the transport of confirmatory laboratory, environmental and animal specimens to the BPHL if needed.
2. Work with the DCBE to determine the source of infection.
3. If applicable, identify other persons exposed and recommend chemoprophylaxis as indicated.
4. Report all confirmed cases to DCBE via Merlin (**PLAGUE CODE = 02000, Bubonic or 02050 Pneumonic**). Complete CDC case report form "Plague Case Investigation Report" available at: <http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/index.html#P>

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic agent

An acute bacterial zoonotic disease, caused by *Yersinia pestis*, which is carried by rodents. Transmission is through fleabites or direct contact with an infected animal. Human disease is rarely acquired through inhalation of infectious respiratory droplets or materials.

B. Description of illness

The disease is characterized by fever, chills, malaise, headache, sore throat, myalgia and prostration. It may take on a number of clinical presentations.

1. **Bubonic plague** – Naturally occurring plague usually presents as bubonic plague. It is characterized by development of lymphadenitis in the lymph nodes that drain the site of inoculation. Regional lymphadenitis develops in different locations based on exposure. For example, fleabites on the leg are associated with inguinal buboes. Axillary buboes may develop after fleabites or with handling an infected animal. Cervical buboes are rare in the U.S., but are more common in developing countries where people may sleep on the floor. The infected nodes become inflamed, tender, “hot-to-the-touch” and may suppurate.
2. **Septicemic plague** – May develop secondary to bubonic plague or occur without lymphadenitis. This type is characterized by bloodstream infection that can disseminate throughout the body, including the meninges. Infected persons can also develop endotoxic shock and disseminated intravascular coagulation (DIC).
3. **Pneumonic plague** – May occur as a result of hematogenous spread to lungs from buboes, or as a primary infection due to infected droplets, resulting in pneumonia and possible mediastinitis and pleural effusion. Pneumonic plague is of particular significance since respiratory droplets may serve as the source of person-to-person transmission of secondary infection, which can lead to localized outbreaks or epidemics under favorable circumstances. **Persons exposed to intentional aerosol disseminate would present primarily as pneumonic plague.**

While crowding, poor sanitary and hygiene conditions increase the likelihood of spread, the risk of infection for contacts is quite low under normal circumstances and reduced even further with simple protective measures such as distancing, turning away from a cough, etc. This has been demonstrated repeatedly in past outbreaks.

4. **Pharyngeal plague** – Pharyngitis and cervical lymphadenitis may result from exposure to larger infectious droplets or ingestion of infected tissues.

Worldwide, untreated bubonic plague has a case-fatality rate of 50% to 60%. Untreated primary septicemic plague and pneumonic plague are almost uniformly fatal. Fatalities are greatly reduced by early recognition and appropriate medical intervention, including antibiotic therapy with streptomycin, gentamycin, or other drugs. In the United States, about 14% (1 in 7) of all plague infections are fatal.

C. Plague in the United States

There have been no infections with plague reported in Florida since the 1920s when there were ten cases of bubonic plague in Pensacola, including six deaths. In September 1994, in response to a reported epidemic of plague in India, the CDC enhanced surveillance in the U.S. for imported pneumonic plague. No confirmed cases were found at that time.

Worldwide, there are 1,000 to 2,000 cases each year. In the U.S., 10 to 15 sporadic human cases are acquired from wild rodents, their fleas or direct contact with an infected animal. Of these reported sporadic human cases, one to two are reported as pneumonic plague each year. While most U.S. cases are in New Mexico or adjacent states, the influx of visitors to Florida each year presents an opportunity for imported disease.

D. Reservoir

Wild rodents are the natural vertebrate hosts of plague and are the source of infection for flea vectors. Some species may survive for weeks to months in the burrows of their hosts. In North America, the most important rodents include ground squirrels, prairie dogs, chipmunks, wood rats, deer mice and voles. Other mammals such as rabbits and domestic cats also can become infected.

E. Modes of transmission

Transmission of naturally acquired human plague occurs in two primary ways. 1) The first is through human intrusion into the zoonotic cycle through activities such as hunting, trapping and farming. Human cases may also be acquired through plague-infected wild rodent fleas that are carried by domestic pets such as cats and dogs. Cats can transmit infection through bites or respiratory droplets, and may develop abscesses that are infective. 2) Infection can also occur through rodents and their fleas via an entry into human habits due to poverty and inadequate hygiene. Worldwide, the most frequent source of infection for human cases is infected rat fleas. In North America, the ground squirrel flea is the primary vector.

Transmission may also occur through handling infected animals, infectious airborne droplets or careless manipulation of laboratory cultures.

F. Incubation period

The incubation period is from one to seven days, with a few days longer in immunized persons. For primary plague pneumonia, the incubation period is typically short, from one day or less to four days.

G. Period of communicability

Fleas may remain infective for months under suitable conditions of temperature and humidity. Bubonic plague is usually not transmitted to others unless there is direct contact with pus from the bubo(es). Pneumonic plague is highly communicable under conditions of overcrowding and cool temperatures.

H. Susceptibility

Susceptibility among humans is general, and immunity is relative after recovery. Future infection may occur with a large inoculum.

I. Isolation and laboratory confirmation

As soon as a diagnosis of suspected plague is made, the patient should be placed in isolation as appropriate. Hospitalized patients with bubonic plague should be cared for using standard contact precautions if uncontrolled drainage is occurring from a wound. Strict contact and respiratory precautions should be used in the event of a patient with pneumonic plague. County and state health departments should be notified immediately. Confirmatory laboratory work should be initiated, including blood cultures and examination of lymph node specimens if possible.

J. Treatment *

Streptomycin (preferred) and gentamycin are the drugs of choice, but other antibiotics such as chloramphenicol, tetracyclines, sulfonamides and fluoroquinolones are also effective. For septicemia or pneumonic plague, aggressive management of possible septic shock, multiple organ failure, adult respiratory distress syndrome (ARDS), and disseminated intravascular coagulopathy should be instituted.

* Sources: World Health Organization's Plague Manual, Chapter 3
http://www.who.int/csr/resources/publications/plague/WHO_CDS_CSR_EDC_99_2_EN/en/

CDC website Plague: <http://www.cdc.gov/plague/>

3. CASE DEFINITIONS

A. Clinical description

Plague is transmitted to humans by fleas or by direct exposure to infected tissues or respiratory droplets; the disease is characterized by fever, chills, headache, malaise, prostration and leukocytosis that manifests in one or more of the following principal clinical forms:

- Regional lymphadenitis (bubonic plague)
- Septicemia without an evident bubo (septicemic plague)
- Plague pneumonia, resulting from hematogenous spread in bubonic or septicemic cases (secondary pneumonic plague) or inhalation of infectious droplets (primary pneumonic plague)
- Pharyngitis and cervical lymphadenitis resulting from exposure to larger infectious droplets or ingestion of infected tissues (pharyngeal plague)

B. Laboratory criteria for diagnosis

Presumptive:

- Elevated serum antibody titer(s) to *Y. pestis* fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination,
OR
- Detection of F1 antigen in a clinical specimen by fluorescent assay.

Confirmatory:

- Isolation of *Y. pestis* from a clinical specimen,
OR
- Fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen.

C. Case classification

Confirmed: a clinically compatible case with confirmatory laboratory results

Probable: a clinically compatible case with presumptive laboratory results

Suspect: a clinically compatible case without presumptive or confirmatory laboratory results

Comment: Specimens from any case or suspect case must be sent to the Bureau of Public Health Laboratories for confirmation. This condition has been identified as a potential bioterrorism agent by the CDC.

4. DIAGNOSIS AND LABORATORY SERVICES**A. Laboratory diagnosis**

Laboratory testing will vary depending on the clinical presentation, but at a minimum includes a complete blood count (WBC count with differential, hemoglobin, hematocrit, platelet count) and renal function tests (BUN, creatinine) for initial screening. In addition, blood cultures, aspirates of buboes (if applicable), sputum sample or aspirate (if indicated) from bronchial and tracheal washings is preferred, cerebral spinal fluid specimen (if indicated) and involved tissues (liver, spleen, bone marrow, lymph node, and/or lung). As listed above, sputum may be examined but is not advised for culture due to contamination by normal throat flora. Serology for increased antibody titers to *Y. pestis* F1 antigen or antigen detection by fluorescent assay is presumptive evidence. Isolation of *Y. pestis* from a clinical specimen or a fourfold increase in serum antibody titer to *Y. pestis* F1 antigen.

B. Tests available at the Bureau of Public Health Laboratories

Confirmatory testing for *Y. pestis* is available at laboratories participating in the Laboratory Response Network of which the BPHL is a participant. The laboratory has the capability to conduct rapid real-time polymerase chain reaction (PCR) testing in addition to conventional microbiological methods. Appropriate specimens for the testing of *Y. pestis* infection by real-time PCR include bronchial wash, transtracheal aspirate, sputum, nasopharyngeal swabs or suspect cultures isolated from specimen types listed above (see Section 4A).

C. Specimen collection

As detailed above, specimens should be obtained from appropriate sites for isolating the bacteria. Bacteria may be intermittently released from affected lymph nodes into the bloodstream; therefore, a series of blood culture specimens taken 10-30 minutes apart may be productive in the isolation of *Y. pestis*. Specimens intended for culture should be taken **before** initiation of antibiotic treatment. Serum specimens should be taken as early in the

illness as possible with a second sample one to four months after the conclusion of antibiotic therapy.

In cases where live organisms are unculturable (e.g., in specimens taken postmortem, lymphoid tissues, lung and bone marrow) samples may yield evidence of plague infection by FA test or by detection of *Y. pestis* DNA.

All submissions should be accompanied by a Clinical Lab Submission Form:

Clinical Lab Submission Form 1



Adobe Acrobat
Document

5. ROUTINE CASE INVESTIGATION

Immediately interview the case, suspect or confirmed, and others who may be able to provide pertinent information.

A. Evaluate the diagnosis

Review the clinical presentation and laboratory findings. Facilitate the transport of specimens (obtained before antibiotic therapy) to BPHL for confirmatory testing.

B. Identify potential sources of infection

Treat any case of pneumonic plague as a potential bioterrorism incident until it can be ruled out; travel to endemic areas suggests unintentional sporadic exposure. Any resulting investigation is potentially both a public health and a criminal investigation. Local law enforcement or the Federal Bureau of Investigation (FBI) may be involved.

Ask about potential sources of transmission during the exposure period, including:

- Travel to endemic areas, **AND**
- Has been bitten by fleas, **AND**
- Presents with symptoms of plague.
- Known contact with others who have developed similar symptoms and who had an airborne exposure(s) in common, indicating a potential outbreak

C. In the event of possible intentional exposure/outbreak, identify potentially exposed persons

Once the route and likely venue of exposure have been established:

1. Determine the time and spatial extent of the exposure.
2. Develop a list of persons with suspected exposure based on interviews with ill persons as well as other evidence such as attendee lists or credit card receipts of any functions where exposure is suspected to have occurred.

3. Contact all potentially exposed persons to assess for illness and to discuss possible prophylaxis (see Section 6).

D. Environmental measures

Consider directed environmental sampling of a suspect venue to localize the exposure.

6. CONTROLLING FURTHER SPREAD

A. Infection control/case management

As soon as a diagnosis of suspected plague is made, the patient should be placed in isolation. Hospitalized patients with bubonic plague should be cared for using standard contact precautions if uncontrolled drainage is occurring from a wound. Strict contact and respiratory precautions should be used in the event of a patient with pneumonic plague.

B. Contact management

Contacts should be evaluated for prophylaxis, which may be indicated to prevent development of infecting additional persons. Educate persons potentially exposed to the same source as the patient about the incubation period and symptoms of plague including specific symptoms that should prompt immediate medical evaluation such as fever, chills, malaise, headache, sore throat, myalgia, prostration and development of pneumonia.

C. Prophylaxis

Persons in close contact with pneumonic plague patients, persons likely exposed to *Y. pestis*-infected fleas, persons that had direct contact with body fluids or tissues of a *Y. pestis*-infected mammal, and persons exposed during a laboratory accident to known infectious materials should receive antibiotic preventive therapy for two to three weeks, if the exposure was in the previous six days. The preferred antimicrobials for preventive or abortive therapy are the tetracyclines or one of the effective sulfonamides.

D. Environment measures

Controlling rodents and their fleas around places where people live, work, and play is very important in preventing human disease. Therefore, preventive measures are directed to home, work, and recreational settings where the risk of acquiring plague is high. This includes removing food sources, applying chemicals to kill fleas and rodents, and controlling rats that inhabit ships and docks by trained professionals who can inspect and fumigate if necessary.

7. MANAGING SPECIAL SITUATIONS

A. Response following a suspicious mass exposure event

1. Evaluation by local law enforcement:

Immediately call 911 if a suspicious mass exposure event is suspected. The initial key

step for law enforcement is to assess whether or not a credible threat exists. They may call in a hazardous materials (haz-mat) team to assess the situation.

2. Public health response:

If law enforcement concludes that there is a credible threat, additional laboratory tests may be performed at state or federal laboratories. Public health agencies may be involved with the ongoing investigation or prophylaxis of those exposed.

8. ROUTINE PREVENTION

A. Vaccine recommendations

The plague vaccine is no longer commercially available in the United States.

B. Prevention recommendations

Reduce the likelihood of people bitten by infectious fleas, having direct contact with infective tissues or exudates, and exposure to disease-bearing animals and their fleas.

- Watch for plague activity in rodent populations where plague is known to occur and report any dead or diseased animals to the health department.
- Eliminate sources of food and nesting places.
- If anticipating exposure to rodent fleas, apply insect repellent and wear gloves if handling potentially infected animals.
- If you live in an area where rodent plague occurs, treat pet cats and dogs for flea control regularly and do not allow them to roam freely.

9. REFERENCES

- A. Heymann, D.L. (Ed.). (2008). *Control of communicable diseases manual* (19th Ed.). Washington: American Public Health Association.
- B. Centers for Disease Control and Prevention, Plague Home Page <http://www.cdc.gov/plague/>
- C. Kool, J. *Risk of Person-to-Person Transmission of Pneumonic Plague, Clinical Infectious Disease*, 2005, (40), April, pg 1166-1172.
- D. Plague, Bureau of Environmental Public Health Medicine, Division of Environmental Health: <http://www.floridahealth.gov/diseases-and-conditions/diseases-from-animals/plague.html>