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**Immediately report** any suspected or confirmed cases of plague to:

**SFDPH Communicable Disease Control  
(24/7 Tel: 415-554-2830)**

- By law, health care providers must report suspected or confirmed cases of plague to their local health department immediately [within 1 hr].
- SFDPH Communicable Disease Control can facilitate specialized testing and will initiate the public health response as needed.

**Also notify your:**

- Infection Control Professional
- Clinical Laboratory

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## INTRODUCTION

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Plague is an acute bacterial infection caused by *Yersinia pestis*, a member of the family *Enterobacteriaceae*. *Y. pestis* is a pleomorphic, nonmotile, nonsporulating, intracellular, Gram-negative bacillus that has a characteristic bipolar appearance on Wright, Giemsa, and Wayson's stains. There are three virulent biovars: *antiqua*, *medievalis*, and *orientalis* and a fourth avirulent biovar, *microtu*.<sup>1, 2</sup> The *orientalis* biovar is thought to have originated in southern China and caused the most recent pandemic.<sup>3</sup>

The Working Group for Civilian Biodefense considers plague to be a potential biological weapon because of the pathogen's availability "around the world, capacity for its mass production and aerosol dissemination, difficulty in preventing such activities, high fatality rate of pneumonic plague, and potential for secondary spread of cases during an epidemic." Of the potential ways that *Y. pestis* could be used as a biological weapon, aerosol release would be most likely. This method has been successfully demonstrated to cause disease in Rhesus macaques.<sup>4</sup>

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## EPIDEMIOLOGY

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### Plague as a Biological Weapon

In the 20<sup>th</sup> century, countries including the United States, the former Soviet Union, and Japan developed ways for using *Y. pestis* as a weapon.<sup>5-7</sup> Creating aerosolized plague is technically challenging; however, if an intentional release of aerosolized plague were to take place, an outbreak of pneumonic plague would be likely. This would be of serious concern because of the high case-fatality rate and the potential for person-to-person transmission.<sup>4, 7, 8</sup>

An outbreak of disease caused by an intentional release of *Y. pestis* would have the following characteristics:

- Clustering in time: multiple similarly presenting cases of severe, progressive multilobar pneumonia, generally 2-4 days after release (range of 1 to 6 days)
- Atypical host characteristics: unexpected, unexplained cases of acute illness in previously healthy persons who rapidly develop severe, progressive multilobar pneumonia with hemoptysis and gastrointestinal symptoms
- Unusual geographic clustering: multiple cases in an urban area where naturally occurring plague is not endemic
- Absence of risk factors: patients lack plague exposure risk factors (e.g., recent flea bite; exposure to rodents, especially rabbits, squirrels, wood rat, chipmunk, or prairie dogs; scratches or bites from infected domestic cats)

Intentionally-released *Y. pestis* strains may be altered to have enhanced virulence, antimicrobial resistance, or increased ability to evade vaccines and diagnostic tests.<sup>4, 7</sup>

## **Naturally Occurring Plague**

### **Reservoirs**

The natural reservoir for *Y. pestis* is primarily wild rodents. Around the world, the domestic rat has been associated with the most human cases; however in the western United States, burrowing rodents (e.g., ground squirrels, rock squirrels, and prairie dogs) are the most important reservoir.<sup>9</sup> A recent study has found soil to be a potential reservoir, with *Y. pestis* persisting from months to several years in association with wild rodents.<sup>10, 11</sup> Other mammals that act as hosts include cats, goats, sheep, camels, and humans.<sup>10, 12-17</sup> Human plague cases often follow epizootics in local rodent populations.<sup>10, 18, 19</sup>

### **Mode of Transmission**

Humans can become infected in a number of ways:<sup>4, 13, 14, 16, 17, 20</sup>

- Bite of infected rat flea
- Direct contact with infected draining buboes
- Direct contact (including bites or scratches) with infected animals
- Inhalation of respiratory droplets from pneumonic plague-infected humans or animals (within 2 meters)
- Ingestion of bacteria (e.g., eating infected meat)

Human plague cases in nature are most commonly acquired from animal reservoirs via bites of the Oriental rat flea.<sup>9, 21</sup>

### **Worldwide occurrence**

The first recorded plague pandemic was the Justinian plague (541-767 AD) which caused ~100 million deaths and is thought to have contributed to the demise of the Roman Empire. The second pandemic, also known as the Black Death, lasted from the 14<sup>th</sup> to the 19<sup>th</sup> centuries and was estimated to have killed between a third and a half of Europe's population. The third and most recent pandemic began in 1894 in China and caused an estimated 12 million deaths.<sup>14, 19, 22, 23</sup> Recent outbreaks in humans have included India (1994), Zambia (1996), Indonesia (1997), Algeria

(2003), Uganda (2004), and the Congo (2005).<sup>24-28</sup> Approximately 1,800 worldwide cases of plague are reported annually to the WHO, from all continents except Europe and Australia.<sup>10</sup>

### **Occurrence in the United States**

Ships carrying infected rats introduced plague to the Americas via the ports on the Pacific Ocean and Gulf of Mexico in the early 1900s. In San Francisco, urban rats passed along the disease to native rodent populations. Eventually, plague spread across the western half of the United States and has been found in the native rodent population, their fleas, and their predators. Naturally occurring human plague generally occurs during the summer months in persons exposed to the reservoir.<sup>27, 29</sup> The last urban plague outbreak in the US occurred in Los Angeles in 1925.<sup>25-27, 30</sup>

From 1990 to 2005, a median of 7 cases of plague per year were reported in the US.<sup>26</sup> Based on provisional data, in 2006, there were 17 cases, and in 2007, 7 cases.<sup>31</sup>

### **Occurrence in California and San Francisco**

From 1994 to 2007, 9 cases of plague were reported in California, and none of these occurred in San Francisco.<sup>32-35</sup>

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## **CLINICAL FEATURES**

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Human plague occurs in many forms, determined primarily by the route of infection. The most common forms of plague in humans are bubonic plague, septicemic plague, and pneumonic plague. These are presented in detail below.

Plague infection is a severe clinical illness that can be life-threatening. Case fatality rates vary based on the route of infection. Mortality was historically much higher with nearly 100% mortality for untreated septicemic and pneumonic plague and 50-60% mortality for untreated bubonic plague cases. Administration of appropriate antibiotic treatment within the first 18 to 24 hours has decreased mortality rates to 30-50% for septicemic plague, 5-15% for pneumonic plague, and less than 5% for bubonic plague.<sup>4</sup> Thus, early administration of appropriate antibiotic treatment is critical, as poor outcomes occur with delays in seeking care and/or instituting effective antimicrobial treatment.

### **Pneumonic Plague**

Primary pneumonic plague occurs when the organism is inhaled in respiratory droplets from infected humans or animals or in infectious aerosols accidentally or intentionally produced (e.g., spilled lab specimen or bioterrorism related release). Secondary pneumonic plague occurs when there is hematogenous spread of the organism to the lung. Primary pneumonic plague causes a more acute and fulminant disease. Pneumonic plague is not highly contagious but transmission can occur with prolonged close contact (within 2 meters) with a coughing patient in the end stage of illness. In a recent outbreak in Uganda, 1.3 pneumonic plague transmissions per pneumonic plague case were reported.<sup>24</sup> If untreated, pneumonic plague can spread and progress to septicemic plague.

<b>PNEUMONIC PLAGUE</b>	
<b>Incubation period</b>	<ul style="list-style-type: none"> <li>• 1-4 days, with a maximum of 6 days</li> </ul>
<b>Transmission</b>	<ul style="list-style-type: none"> <li>• Inhalation of contaminated aerosol</li> <li>• Inhalation of respiratory droplets from pneumonic plague-infected humans or animals (within 2 meters)</li> <li>• Secondary hematogenous spread to the lung</li> </ul>
<b>Signs and symptoms</b>	<ul style="list-style-type: none"> <li>• Acute fever, chills, malaise, myalgia, headache</li> <li>• Productive cough, with sputum becoming more and more bloody</li> <li>• Chest pain, dyspnea, cyanosis</li> <li>• Tachypnea in children</li> <li>• Gastrointestinal symptoms</li> </ul>
<b>Progression and complications</b>	<ul style="list-style-type: none"> <li>• Refractory pulmonary syndrome</li> <li>• Adult respiratory distress syndrome</li> <li>• Septicemia</li> </ul>
<b>Laboratory and Radiographic Findings</b>	<ul style="list-style-type: none"> <li>• Leukocytosis with left shift</li> <li>• Gram-negative bipolar bacilli on sputum smear</li> <li>• Elevated creatinine and abnormally high liver enzymes</li> <li>• CXR findings include alveolar infiltrates progressing to lobar consolidation, pleural effusion</li> <li>• Rarely, mediastinal widening on CXR due to adenopathy</li> </ul>

### **Bubonic Plague**

*Yersinia pestis* can cause bubonic plague in humans via the bite of an infected rodent flea. *Y. pestis* survives in the flea midgut after a blood meal from an infected host. The organism is transmitted to a new host when the flea regurgitates during its next feeding. *Y. pestis* migrates to regional lymph nodes where it causes hemorrhagic lymphadenitis, creating the swollen, painful buboes that are characteristic of bubonic plague. The organisms often enter the bloodstream, causing hemorrhagic lesions in distant lymph nodes and organs. If untreated, bubonic plague can spread and progress to pneumonic or septicemic plague. Approximately, 80% of cases develop bacteremia, 25% develop clinical septicemia and 10% develop pneumonia as a complication.

<b>BUBONIC PLAGUE</b>	
<b>Incubation period</b>	1-8 days
<b>Transmission</b>	<ul style="list-style-type: none"> <li>• Bite of infected rat flea</li> <li>• Direct contact with infected draining buboes</li> <li>• Direct contact (including bites or scratches) with infected animals</li> </ul>
<b>Signs and symptoms</b>	<p><u>Major</u></p> <ul style="list-style-type: none"> <li>• Sudden onset of chills, high fever, headache, lethargy</li> <li>• Buboes - Swollen, red, painful lymph nodes in areas proximal to the inoculation site (e.g., inguinal, axillary or cervical areas)</li> <li>• Rapid pulse</li> <li>• Hypotension</li> </ul> <p><u>Other</u></p> <ul style="list-style-type: none"> <li>• Gastrointestinal discomfort</li> <li>• Restlessness, confusion, lack of coordination</li> <li>• Skin lesion at the site of the flea bite occurs in &lt; 10% of cases</li> <li>• Buboes may rupture and suppurate in second week</li> </ul>

<b>Progression and complications</b>	<ul style="list-style-type: none"> <li>• Septicemia</li> <li>• Secondary pneumonic plague</li> <li>• Meningitis (rare)</li> </ul>
<b>Laboratory findings</b>	<ul style="list-style-type: none"> <li>• Leukocytosis with left shift</li> <li>• Gram-negative bipolar bacilli on bubo aspirate smear</li> <li>• Elevated creatinine and abnormally high liver enzymes</li> </ul>

### Septicemic Plague

In primary septicemic plague there is systemic sepsis caused by *Y. pestis*, but without noticeable, preceding lymph node or pulmonary involvement. Up to 25% of naturally-occurring plague cases may present with primary septicemic plague.<sup>19</sup> Secondary septicemic plague occurs commonly with either bubonic or pneumonic plague.

Septicemic plague causes a Gram-negative sepsis syndrome with multi-organ involvement, disseminated intravascular coagulation (DIC), and shock. In the late stages of infection, high-grade bacteremia often occurs, with identifiable organisms on peripheral blood smear.<sup>18</sup> Meningitis can occur and is characterized by cerebrospinal fluid (CSF) with many polymorphonuclear leukocytes.<sup>9</sup>

<b>SEPTICEMIC PLAGUE</b>	
<b>Incubation period</b>	1-4 days
<b>Transmission</b>	Site of primary infection may be unknown
<b>Signs and symptoms</b>	<ul style="list-style-type: none"> <li>• Acute fever, chills, weakness, malaise</li> <li>• Gastrointestinal symptoms</li> <li>• Purpuric skin lesions and gangrene of the distal digits</li> </ul>
<b>Progression and complications</b>	<ul style="list-style-type: none"> <li>• Disseminated intravascular coagulation (DIC)</li> <li>• Shock</li> <li>• Multi-organ failure</li> </ul>
<b>Laboratory findings</b>	<ul style="list-style-type: none"> <li>• Leukocytosis with left shift and toxic granulation</li> <li>• Gram-negative bipolar bacilli on blood smear</li> <li>• Disseminated intravascular coagulation (DIC)</li> <li>• Elevated creatinine and abnormally high liver enzymes</li> </ul>

Other syndromes caused by *Y. pestis* infection include:

- **Plague meningitis.** Although it is generally a complication of other forms of plague, it can be the presenting clinical syndrome. Plague meningitis results from hematogenous spread of *Y. pestis* organisms and is characterized by CSF with many polymorphonuclear leukocytes.<sup>9</sup>
- **Plague pharyngitis.** Plague pharyngitis generally results from direct inoculation of the pharynx. Eating raw infected meat is a risk factor. Clinically, plague pharyngitis presents as a severe pharyngitis or tonsillitis with cervical adenitis.
- **Pestis minor.** Pestis minor is a milder form of bubonic plague. Lymph nodes drain and patients convalesce without treatment.<sup>10</sup>

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## DIFFERENTIAL DIAGNOSIS

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The diagnosis of plague during the initial stages requires a high index of suspicion because of the nonspecific, flu-like picture early in the disease. Early diagnosis is critical because prompt administration of antibiotics can decrease mortality.

### **Differential: Pneumonic Plague**

Consider pneumonic plague in any case of severe Gram-negative pneumonia.

Key features that may help to distinguish plague pneumonia are:

Primary pneumonic plague:

- Rapid onset and rapid progression

Secondary pneumonic plague:

- Presence of painful adenitis (buboes)

Primary or secondary pneumonic plague:

- No response to typical antibiotic therapy for community-acquired pneumonia
- Hemoptysis in late stages of disease

Other conditions to consider are:

- bacterial pneumonia (*Mycoplasma*, *Legionella*, *Staphylococcus*, *Streptococcus*, *Haemophilus*, *Klebsiella*, *Moraxella*)
- viral pneumonia (influenza, respiratory syncytial virus [RSV], cytomegalovirus [CMV], hantavirus, severe acute respiratory syndrome [SARS])
- *Chlamydia* infection
- Q fever
- inhalation anthrax
- tularemia
- ricin
- rickettsial infections
- aerosolized exposure to staphylococcal enterotoxin B

### **Differential: Bubonic Plague**

A key feature that may help to distinguish bubonic plague is:

- Presence of painful adenitis (buboes) progressing to systemic disease

Other conditions to consider are:

- cat scratch disease (*Bartonella*)
- ulceroglandular tularemia
- adenitis due to staphylococcal, streptococcal, or filarial infection
- tuberculosis
- non-tuberculosis mycobacterial infection
- lymphogranuloma venereum
- *Capnocytophaga canimorsus* infection
- chancroid
- primary genital herpes
- primary or secondary syphilis
- appendicitis
- strangulated inguinal or femoral hernia
- lymphadenopathy (secondary lymphoma, Kikuchi's lymphadenitis, systemic lupus erythematosus, toxoplasmosis, infectious mononucleosis)

### **Differential: Septicemic Plague**

Key features that may help to distinguish septicemic plague are:

Primary septicemic plague:

- Absence of painful adenitis (buboes) or pulmonary involvement

Secondary septicemic plague:

- Presence of painful adenitis (buboes)

Other conditions to consider are:

- Gram-negative sepsis
- Gram-positive sepsis (*Staphylococcus*)
- meningococemia
- rickettsial infections
- malaria
- louse-borne relapsing fever
- appendicitis

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## LABORATORY DIAGNOSIS

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Routine laboratory and radiographic findings for specific clinical presentations of plague are listed in the clinical features tables.

Initial identification of the organism relies on microscopic evaluation of infected tissue (blood, sputum, CSF, or fluid aspirated from a bubo or skin lesion scraping). Staining of the infected tissue may reveal Gram-negative bacilli (Gram stain) and bipolar staining (Wright, Giemsa, or Wayson stain).<sup>4, 9</sup> Order a Gram stain, culture, and Giemsa, Wright or Wayson stain of the

material. Store and transport blood at room temperature. Transport other samples at room temperature, but store under refrigeration if transport time will be > 2 hours.

Although recommended, culture and isolation may be difficult. Blood and site-specific specimens should be collected prior to antibiotic administration as sterilization can occur rapidly. *Y. pestis* is slow-growing in culture and may not demonstrate growth until 48 hours after inoculation. Also, many commercial bacterial identification systems may misidentify *Y. pestis*.<sup>4</sup> To improve yield and ensure biosafety precautions, clinicians should notify laboratory personnel when plague is suspected.

Although rapid diagnostic tests are not widely available, the public health laboratory system may have access to rapid diagnostic testing on clinical specimens (e.g., polymerase chain reaction [PCR] or direct fluorescent antibody testing for *Y. pestis* F1 antigen).

**If you are testing or considering testing for plague, you should:**

- **IMMEDIATELY notify SFDPH Communicable Disease Control (24/7 Tel: 415-554-2830).** SFDPH can authorize and facilitate testing, and will initiate the public health response as needed.
- **Inform your lab that plague is under suspicion. Some commercial bacterial test systems cannot reliably identify *Y. pestis*.**

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## TREATMENT AND PROPHYLAXIS

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These recommendations are current as of this document date. SFDPH will provide periodic updates as needed and situational guidance in response to events ([www.sfdcp.org](http://www.sfdcp.org)).

### **Treatment**

Supportive care and timely administration of antibiotics are the keys to successful management of plague. Plague pneumonia is often fatal if antibiotics are not begun within 12-24 hours of symptoms. Many patients will require intensive care with respiratory support because of complications of Gram-negative sepsis.

Resistant strains may occur either naturally or be engineered. In 1995, 2 distinct strains of naturally-occurring antibiotic-resistant *Y. pestis* were isolated from human cases of bubonic plague in Madagascar. One strain was resistant to all drugs recommended for plague treatment and prophylaxis and the other had high-level resistance to streptomycin. Both patients recovered with oral trimethoprim-sulfamethoxazole and intramuscular injections of streptomycin.<sup>36, 37</sup> In addition, *in vitro* resistance to imipenem and rifampin has been seen.<sup>10</sup>

**Contained casualty setting:** The Working Group recommends parenteral antimicrobial therapy when individual medical management is available. Antibiotics should be administered to all patients for 10 days. Therapy may be switched to oral antimicrobials when clinically indicated.

**Mass casualty setting:** Replacement of parenteral antibiotics with oral antibiotics may be indicated if the number of patients exceeds the medical care system's capacity to administer parenteral antibiotics.



**PLAGUE - TREATMENT AND POST-EXPOSURE PROPHYLAXIS RECOMMENDATIONS<sup>A</sup>**

		Contained Casualty Setting	Mass Casualty Setting	Post-Exposure Prophylaxis
<b>Duration of Rx</b>		10 days	10 days	7 days
<b>Adult</b>	<b>Preferred</b>	<b>Streptomycin</b> , 1 gm IM q12 hrs <i>or</i> <b>Gentamicin</b> <sup>B</sup> , 5 mg/kg IM or IV q24 hrs, or 2 mg/kg loading dose followed by 1.7 mg/kg IM or IV q8 hrs	<b>Doxycycline</b> , 100 mg orally twice daily <i>or</i> <b>Ciprofloxacin</b> , 500 mg orally twice daily	
	<b>Alternative<sup>H</sup></b>	<b>Doxycycline</b> <sup>5,6</sup> , 100 mg IV q12 hrs or 200 mg IV q24 hrs <i>or</i> <b>Ciprofloxacin</b> , 400 mg IV q12 hrs <i>or</i> <b>Chloramphenicol</b> <sup>C</sup> , 25 mg/kg IV q6 hrs (max 4 g/day)	<b>Chloramphenicol</b> <sup>C</sup> , 25 mg/kg orally 4 times daily (max 4 g/day)	
<b>Children</b>	<b>Preferred</b>	<b>Streptomycin</b> , 15 mg/kg IM q12 hrs (max 2 g/day) <i>or</i> <b>Gentamicin</b> <sup>B</sup> , 2.5 mg/kg IM or IV q8 hrs	<b>Doxycycline</b> <sup>E,F</sup> : ≥45 kg, give adult dosage <45 kg, give 2.2 mg/kg orally twice daily (max 200 mg/day) <i>or</i> <b>Ciprofloxacin</b> <sup>E,G</sup> , 20 mg/kg orally twice daily (max 1 g/day)	
	<b>Alternative<sup>H</sup></b>	<b>Doxycycline</b> <sup>E,F</sup> : ≥45 kg, give adult dosage <45 kg, give 2.2 mg/kg IV q12 hrs (max 200 mg/day) <i>or</i> <b>Ciprofloxacin</b> <sup>E,G</sup> , 15 mg/kg IV q12 hrs (max 1 g/day) <i>or</i> <b>Chloramphenicol</b> <sup>C,D</sup> , 25 mg/kg IV q6 hrs (max 4 g/day)	<b>Chloramphenicol</b> <sup>C,D</sup> , 25 mg/kg orally 4 times daily (max 4 g/day)	
<b>Pregnant Women</b>	<b>Preferred</b>	<b>Gentamicin</b> <sup>B</sup> , 5 mg/kg IM or IV q24 hrs or 2 mg/kg loading dose followed by 1.7 mg/kg IM or IV q8 hrs	<b>Doxycycline</b> <sup>E,F</sup> , 100 mg orally twice daily <i>or</i> <b>Ciprofloxacin</b> <sup>E</sup> , 500 mg orally twice daily	
	<b>Alternative<sup>H</sup></b>	<b>Doxycycline</b> <sup>E,F</sup> , 100 mg IV q12 hrs or 200 mg IV q24 hrs <i>or</i> <b>Ciprofloxacin</b> <sup>E</sup> , 400 mg IV q12 hrs	<b>Chloramphenicol</b> <sup>C,D</sup> , 25 mg/kg orally 4 times daily	

For plague meningitis, pleuritis, or myocarditis: Chloramphenicol should be used for 21 days for conditions when tissue penetration is important<sup>I</sup>. Irreversible marrow aplasia is rare (1 in 40,000 patients).

<sup>A</sup> Treatment recommendations come from the Working Group of Civilian Biodefense and may not necessarily be approved by the US Food and Drug Administration. Table adapted from JAMA. 2000; 283: 2281-2290.

<sup>B</sup> Aminoglycoside doses must be further adjusted for newborns, and according to renal function.

<sup>C</sup> Therapeutic concentration is 5 - 20 mcg/mL; concentrations >25 mcg/mL can cause reversible bone marrow suppression.

<sup>D</sup> According to the Working Group on Civilian Biodefense, children younger than 2 years of age should not receive chloramphenicol due to risk of 'gray baby syndrome'; however, the American Academy of Pediatrics has recommended chloramphenicol as the drug of choice for plague meningitis in children.

<sup>E</sup> Tetracycline and quinolone antibiotics are generally not recommended during pregnancy or childhood; however their use may be indicated for life-threatening illness.

<sup>F</sup> Ciprofloxacin may be preferred in pregnant women and children up to 8 years of age because of the known adverse event profile of doxycycline (e.g., tooth discoloration).

<sup>G</sup> Doxycycline may be preferred in children 8 years and older because of the adverse event profile of ciprofloxacin (e.g., arthropathies).

<sup>H</sup> Trimethoprim-sulfamethoxazole has been successfully used to treat plague; however the Working Group considers this a second tier choice.

### **Post-Exposure Prophylaxis**

Post-exposure prophylaxis is the administration of antibiotics after suspected exposure to plague has occurred but before symptoms are present. If symptoms are present, see section above on treatment. Persons thought to have had an infective exposure should receive post-exposure prophylaxis. Infective exposures include household, hospital, or other close contact (less than 2 meters) with a person suspected or confirmed to have pneumonic plague who has received no treatment, less than 48 hours of antimicrobial therapy, or more than 48 hours of antimicrobial therapy without clinical improvement. Post-exposure prophylaxis may be recommended for persons exposed to intentional aerosol releases. In such an event, public health authorities will provide guidance. Regardless of whether post-exposure prophylaxis is recommended or taken, persons potentially exposed should be observed for fever or cough for 7 days after exposure. Any potentially-exposed person who develops a fever or cough should seek prompt medical attention and begin treatment. Quarantine is not currently recommended.<sup>4, 7, 9</sup>

### **Vaccination**

Current killed whole cell vaccines have been in use for military personnel and have been shown to generate cell-mediated responses lasting at least 15 years; however, they require repeat dosing with adjuvants, have questionable protection against respiratory infections, and are reactogenic. Vaccine production has been discontinued in the US. Microencapsulated subunit vaccines (of F1 and V proteins) requiring only single dose administration are under development and show the most promise against aerosol exposures.<sup>4, 38, 39</sup>

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## COMPLICATIONS AND ADMISSION CRITERIA

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Whereas primary pneumonic plague results from direct inhalation of plague bacilli, secondary pneumonic plague can manifest as a complication in patients with bubonic plague. Hematogenous dissemination of *Y. pestis* results in plague septicemia, which can be complicated by septic shock, disseminated intravascular coagulation, necrosis of small vessels, and purpuric skin lesions. Plague meningitis due to hematogenous seeding of the meninges occurs infrequently.

Patients with suspect or confirmed pneumonic or bubonic plague require hospitalization for intravenous antibiotics, supportive care, and close monitoring for decompensation and signs of toxemia.

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## INFECTION CONTROL

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These recommendations are current as of this document date. SFDPH will provide periodic updates as needed and situational guidance in response to events ([www.sfcddcp.org](http://www.sfcddcp.org)).

Clinicians should notify local public health authorities, their institution's infection control professional and their laboratory of any suspected plague cases. Public health authorities may conduct epidemiological investigations and implement disease control interventions to protect the public. Infection control professionals will guide and enforce implementation of infection control precautions within the healthcare setting. Laboratory personnel will take appropriate biosafety precautions.

Although not highly contagious, plague can be transmitted person-to person via respiratory droplets when the disease is end stage.<sup>30</sup> Both the Healthcare Infection Control Practices Advisory Committee of the CDC and the Working Group on Civilian Biodefense recommend **Droplet and Standard precautions** for patients with suspected or confirmed pneumonic plague. These precautions should be maintained until 48 hours of appropriate antibiotics have been administered AND the patient shows clinical improvement. Close contacts of pneumonic plague patients should be identified, assessed for prophylaxis and monitored for symptoms. For patients with suspected or confirmed bubonic plague or other non-pneumonic plague syndromes, **Standard precautions** are recommended. Aerosol-generating procedures should be avoided if possible. Routine laboratory procedures should be carried out under Biosafety level-2 conditions; however, manipulation of cultures or other activities that may produce aerosol or droplets (e.g., centrifuging, grinding, vigorous shaking, and animal studies) require Biosafety level -3 conditions.<sup>4, 40</sup>

### Decontamination

In general, environmental decontamination following an aerosol event has not been recommended, since experts have estimated that an aerosol of *Y. pestis* organism would be infectious for only about 1 hour.<sup>4, 40</sup> A recent study demonstrated that *Y. pestis* can survive on selected environmental surfaces for at least several days; however the potential for re-aerosolization of these organisms was not addressed.<sup>41</sup> Commercially available bleach or 0.5% hypochlorite solution (1:10 dilution of household bleach) is considered adequate for cleaning and decontamination. All persons exposed to an aerosol containing *Y. pestis* should be instructed to wash body surfaces and clothing with soap and water.

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## PEARLS AND PITFALLS

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- Bubonic plague is not transmitted directly from one human to another in the absence of lymph node suppuration and drainage. Persons with bubonic plague become more infectious as *Y. pestis* organisms reach the lungs via hematogenous spread. Once pneumonic plague develops, transmission occurs via direct contact with respiratory secretions or inhalation of respiratory droplets.

- Clinical clues pointing toward a diagnosis of primary pneumonic plague are sudden onset of headache, malaise, and fever, fulminant pneumonitis with rapid progression from dry cough to tachypnea, dyspnea, and productive cough, and in the late stage of disease, hemoptysis with copious amounts of bright red sputum.<sup>30</sup>

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