Centers for Disease Control and Prevention
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Resources for Clinicians

Diagnosis

Plague should be considered in any patient with clinical signs of plague and a recent history of travel to the western United States or any other plague endemic area (/plague/maps/index.html) . Bubonic plague is the most common primary manifestation, with a bubo usually occurring in the groin, axilla or cervical nodes. Buboes are often so painful that patients are generally guarded and have restricted movement in the affected region. The incubation period for bubonic plague is usually 2 to 6 days.

If bubonic plague is untreated, plague bacteria invade the bloodstream and spread rapidly, causing septicemic plague, and if the lungs are seeded, secondary pneumonic plague. Septicemic and pneumonic plague may also be primary manifestations. A person with pneumonic plague may experience high fever, chills, cough, and breathing difficulty and may expel bloody sputum. If pneumonic plague patients are not given specific antibiotic therapy, the disease can progress rapidly to death.

Although the majority of patients with plague present with a bubo, some may have nonspecific symptoms. For example, septicemic plague can present with prominent gastrointestinal symptoms such as nausea, vomiting, diarrhea, and abdominal pain (MMWR, 2006 (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5534a4.htm)). Additional rare forms of plague include pharyngeal, meningeal, and cutaneous.

Appropriate diagnostic samples include blood cultures, lymph node aspirates if possible, and/or sputum, if indicated. Drug therapy should begin as soon as possible after the laboratory specimens are taken. If plague is suspected, local and state health departments should be notified immediately. If the patient has pneumonic signs, he/she should also be isolated and placed on droplet precautions.

Diagnostic Testing

If plague is suspected, pre-treatment specimens should be taken if possible, but treatment should not be delayed. Specimens should be obtained from appropriate sites for isolating the bacteria, and depend on the clinical presentation:

- Lymph node aspirate: An affected bubo should contain numerous organisms that can be evaluated microscopically and by culture.
- Blood cultures: Organisms may be seen in blood smears if the patient is septicemic. Blood smears taken from suspected bubonic plague patients early in the course of illness are usually negative for bacteria by microscopic examination but may be positive by culture.
- Sputum: Culture is possible from sputum of very ill pneumonic patients; however, blood is usually culture-positive at this time as well.
- Bronchial/tracheal washing may be taken from suspected pneumonic plague patients; throat specimens are not ideal for isolation of plague since they often contain many other bacteria that can mask the presence of plague.
- In cases where live organisms are unculturable (such as postmortem), lymphoid, spleen, lung, and liver tissue or bone marrow samples may yield evidence of plague infection by direct detection methods such as direct fluorescent antibody (DFA) or PCR.

Y. pestis may be identified microscopically by examination of Gram, Wright, Giemsa, or Wayson's stained smears of peripheral blood, sputum, or lymph node specimen. Visualization of bipolar-staining, ovoid, Gram-negative organisms with a "safety pin" appearance permits a rapid presumptive diagnosis of plague.

If cultures yield negative results, and plague is still suspected, serologic testing is possible to confirm the diagnosis. One serum specimen should be taken as early in the illness as possible, followed by a convalescent sample 4-6 weeks or more after disease onset.

More information about specimen submission.
(http://www.cdc.gov/ncezid/dvbd/specimensub/bacterial-zoonotic-shipping.html)

Recommended antibiotic treatment for plague

Begin appropriate therapy as soon as plague is suspected. The drugs of choice are streptomycin or gentamicin, but tetracyclines, fluoroquinolones and chloramphenicol are also effective.

Select one antibiotic from the table below. Duration of treatment is 10 days, or until 2 days after fever subsides. Oral therapy may be substituted once the patient improves.

The regimens listed below are guidelines only and may need to be adjusted depending on a patient's age, medical history, underlying health conditions, or allergies. Please use clinical judgment.

Adults	**Preferred agents**	**Dose**	**Route of administration**
	Streptomycin[1]	1 g twice daily	IM
	Gentamicin[1]	5 mg/kg once daily, or 2 mg/kg loading dose followed by 1.7 mg/kg every 8 hours	IM or IV
	Alternative agents	**Dose**	**Route of administration**
	Doxycycline	100 mg twice daily or 200 mg once daily	IV
	Ciprofloxacin	400 mg twice daily	IV
	Chloramphenicol[2]	25 mg/kg every 6 hours	IV
Children	**Preferred agents**	**Dose**	**Route of administration**
	Streptomycin[1]	15 mg/kg twice daily (maximum daily dose, 2 g)	IM
	Gentamicin[1]	2.5 mg/kg every 8 hours	IM or IV
	Alternative agents	**Dose**	**Route of administration**
	Doxycycline (for children ≥ 8 years)	Weight < 45 kg: 2.2 mg/kg twice daily (maximum daily dose, 200 mg) Weight ≥ 45 kg: same as adult dose	IV
	Ciprofloxacin	15 mg/kg twice daily (maximum daily dose, 1 g)	IV
	Chloramphenicol[2] (for children > 2 years)	25 mg/kg every 6 h (maximum daily dose, 4 g)	IV
Pregnant women	**Preferred agent**	**Dose**	**Route of administration**

Gentamicin[1, 3]	Same as adult dose	IM or IV
Alternative agents	**Dose**	**Route of administration**
Doxycycline[4]	Same as adult dose	IV
Ciprofloxacin[4]	Same as adult dose	IV

Adapted from: Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological weapon: medical and public health management (http://jama.jamanetwork.com/article.aspx?articleid=192665) (http://www.cdc.gov/Other/disclaimer.html). Working Group on Civilian Biodefense. JAMA. 2000 May 3;283(17):2281-90.

[1]Aminoglycoside dose should be adjusted in patients with impaired renal function.

[2]Chloramphenicol serum concentration should be 5-20 µg/mL to avoid bone marrow suppression.

[3]Gentamicin is pregnancy category C but has been used safely and effectively for treatment of plague in pregnant women.

[4]Doxycycline and ciprofloxacin are pregnancy categories D and C, respectively. These agents should be administered only if gentamicin is not available.

For additional information, see: Koirala J. Plague: disease, management, and recognition of act of terrorism. (http://www.sciencedirect.com/science/article/pii/S089155200600016X) (http://www.cdc.gov/Other/disclaimer.html) Infect Dis Clin North Am. 2006 Jun;20(2):273-87, viii.

Recently levofloxacin has been FDA approved for treatment and prophylaxis of plague: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm302220.htm (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm302220.htm) (http://www.cdc.gov/Other/disclaimer.html).

Post-exposure prophylaxis (PEP)

Post-exposure prophylaxis is indicated in persons with known exposure to plague, such as close contact with a pneumonic plague patient or direct contact with infected body fluids or tissues. The recommended antibiotic regimens for PEP are as follows:

	Preferred agents	**Dose**	**Route of administration**
Adults	Doxycycline	100 mg twice daily	PO
	Ciprofloxacin	500 mg twice daily	PO
Children	Doxycycline (for children ≥ 8 years)	Weight < 45 kg: 2.2 mg/kg twice daily (maximum daily dose, 200 mg) Weight ≥ 45 kg: same as adult dose	PO
	Ciprofloxacin	20 mg/kg twice daily (maximum daily dose, 1 g)	PO

Adapted from: Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological weapon: medical and public health management (http://jama.jamanetwork.com/article.aspx?articleid=192665) (http://www.cdc.gov/Other/disclaimer.html) Working Group on Civilian Biodefense. JAMA. 2000 May 3;283(17):2281-90.

[1]Doxycycline and ciprofloxacin are pregnancy categories D and C, respectively. PEP should be given only when the benefits outweigh the risks.

Pregnant women	Doxycycline[1]	100 mg twice daily	PO
	Ciprofloxacin[1]	500 mg twice daily	PO

Adapted from: Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological weapon: medical and public health management (http://jama.jamanetwork.com/article.aspx?articleid=192665) (http://www.cdc.gov/Other/disclaimer.html) Working Group on Civilian Biodefense. JAMA. 2000 May 3;283(17):2281-90.

[1]Doxycycline and ciprofloxacin are pregnancy categories D and C, respectively. PEP should be given only when the benefits outweigh the risks.

Case Definition and Report Forms

- Plague Surveillance Case Definition (http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/plague_current.htm) (1996)
- Plague Case Report Form [PDF - 3 pages] (/plague/resources/PlagueCaseReportForm.pdf) (for public health officials' use)

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