

Yersinia pestis as a Bioterrorist Agent

Agent: *Yersinia pestis*, a Gram-negative bacillus, may be delivered by aerosol to cause pneumonic plague, or by infected fleas to cause bubonic plague. The organism may remain alive from months to years at freezing temperatures. It may also remain viable in dry sputum and flea feces.

Disease: Pneumonic or bubonic plague

Incubation Period: 2-3 days (pneumonic) and 2-10 days (bubonic)

Signs/Symptoms: In the pneumonic form, the onset of symptoms is acute and fulminant with high fever, chills, headache, malaise, myalgia, and cough. The patients may have lymphadenopathy and blood-tinged sputum. The pneumonia progresses rapidly, resulting in dyspnea, stridor and cyanosis. The terminal events are respiratory failure, circulatory collapse, and hemorrhage; mortality is 100% in untreated patients. In the bubonic form, initial symptoms include malaise, high fever, and one or more painful swollen lymph nodes. The vast majority of buboes occur in the groin, as the legs are the most commonly “flea-bitten” parts of the body. However, cervical and axillary lymph nodes may also be involved. Up to 80% of patients with bubonic plague also become septic; 5 to 15% develop pneumonia. Circulatory collapse, hemorrhage and peripheral thrombosis are the terminal events. About half of untreated bubonic cases die.

Diagnosis:

Differential Diagnosis: For the bubonic form the differential diagnosis includes, tularemia adenitis, staphylococcal or streptococcal adenitis, meningococemia, enteric gram-negative sepsis, cat-scratch disease, and rickettsioses. In tularemia or cat-scratch disease, the inoculation site is usually more evident than in bubonic plague, and the patient will not usually be septic. The differential for pneumonic plague includes tularemia, anthrax and staphylococcal enterotoxin B (SEB) inhalation. Continued deterioration without stabilization effectively rules out SEB. The presence of a widened mediastinum on chest X-ray should alert the physician to the probability of anthrax. Patients with plague have a cough productive of bloody sputum, while those with tularemia generally have a nonproductive cough. Secondary spread may occur with pneumonic plague, but is highly unlikely with anthrax or tularemia.

Laboratory: *Yersinia. pestis* may be readily cultured from blood, sputum, and bubo aspirates. *Y. pestis* typically produces a small, pinpoint grey-white and

translucent colony on agar media at 24 hours. At 48 hours the colonies grow to about 1 –1.5 mm in diameter and are whitish gray to slightly yellow and opaque. A Gram stain of the organism will sometimes show the characteristic fat, Gram-negative “safety-pin” shape, or bipolar-staining. Presumptive diagnosis can be made by identification of Gram-negative coccobacilli with safety-pin bipolar staining organisms when stained directly from a lymph node needle aspirate, sputum, cerebrospinal fluid (CSF) or buffy coat smears. This bipolar staining is not very noticeable when using the Gram stain and is much easier to see when using the Wayson stain. However, other enteric organisms may also exhibit bipolar staining so this test is not very specific. In tissue the organism may appear in ring forms. *Y. pestis* is oxidase and motility negative and produces a flocculent growth at 24-48 hours in BHI broth. These clumps of cells are visible at the side and bottom of the tube while the rest of the medium remains clear. The optimum growth temperature of *Y. pestis* is 25-28°C. If you suspect *Y. pestis*, all additional culture manipulation should be within a biological safety cabinet. Isolates should be sent to **the Oregon State Public Health Laboratory (OSPHL)** immediately. Confirmation of isolates may take up to 2- 3 days.

A specimen suspected of containing *Y. pestis* or isolates thought to be *Y. pestis* are considered to be “infectious agents” by the Department of Transportation (29 CFR Parts 171-189, <http://hazmat.dot.gov/rules.htm>) and must be shipped accordingly. Contact the OSPHL for further information on the shipping of infectious agents and the Select Agent Rule for transferring cultures of *Y. pestis*. Prior to shipment call the OSPHL at 503-229-5882 and Acute and Communicable Disease Prevention at (503) 731-4024. The address is 1717 SW Tenth Avenue, Portland, OR 97201. Prior notification is requested if you suspect *Yersinia pestis*.

Early postexposure (0-24 hours) nasal swabs, sputum, and induced respiratory secretions may be collected for culture, and for fluorescent antibody (FA) assay. During the clinical phase (24 - 72 hours) blood may be collected in a tiger-top (SST) or red-top tube for F1 antigen assay. Blood may be collected in a 3-ml EDTA tube, 3-ml citrate tube, or heparin tube for PCR, in a 3-ml EDTA tube for Gram stain of the buffy coat, and in a blood culture bottle or 3-ml citrate tube for culture. Blood for convalescent sera may be collected in tiger-top (SST) or red-top tubes for serology.

Supportive Tests: Chest X-ray reveals a patchy or consolidated bronchopneumonia. Thrombocytopenia, leukocytosis, and elevated liver function tests (LFT's) are common; fibrinogen-fibrin degradation products (DIC) may be noted.

Treatment: Streptomycin 30 mg/kg/day IM in 2 divided doses for 10 days or gentamicin 2.0 mg/kg IV loading dose, then 1.7 mg/kg q8h IV. Alternate treatments are doxycycline 200 mg IV initially, then 100 mg q12h IV for 10-14 days; or chloramphenicol 1000 mg qid IV for 10-14 days (preferred for plague meningitis). Supportive therapy should be provided as required.

Prophylaxis: Tetracycline 500 mg qid po or Doxycycline 100 mg bid po for 7 days or duration of exposure, whichever is longer. Ciprofloxacin 500 mg bid po for seven days may also be used. Other alternatives include ofloxacin, levofloxacin, chloramphenicol, and trimethoprim-sulfamethoxazole.

Infection Control: Although buboes may be aspirated for diagnostic purposes, incision and drainage (I&D) may pose a hazard to medical personnel. Droplet precautions in addition to standard precautions should be strictly enforced for at least 72 hours after the initiation of effective therapy. Surface decontamination may be accomplished by using 0.5% sodium hypochlorite solution (1 part household bleach added to nine parts water).

Report: Immediately report any suspect cases to your local health department or the Oregon Health Division at (503) 731-4024 during working hours (8:00 am to 5:00 pm Monday through Friday) or (503) 731-4030 nights, weekends and holidays.

Adapted with permission from the Texas Department of Health