Plague (*Yersinia pestis*)

Manitoba
Public Health Branch

1. Case Definition

1.1 Confirmed Case:

Clinical evidence of illness* with laboratory confirmation of infection:

- Isolation of *Yersinia pestis* from body fluids (e.g., fluid from buboes, throat swab, sputum, blood)
  OR
- A significant (i.e., fourfold or greater) rise in serum antibody titre to *Y. pestis* fraction 1 (F1) antigen by enzyme immunoassay (EIA) or passive hemagglutination/inhibition titre (1).

1.2 Probable Case:

Clinical evidence of illness* with one or more of the following:

- Demonstration of elevated serum antibody titre(s) to *Y. pestis* F1 antigen (without documented significant [i.e., fourfold or greater] change) in a patient with no history of plague immunization
  OR
- Demonstration of *Y. pestis* F1 antigen by immunofluorescence
  OR
- Detection of *Y. pestis* nucleic acid
  OR
- > 1:10 passive hemagglutination/inhibition titre in a single serum sample in a patient with no history of vaccination or previous infection
  OR
- Detection of *Y. pestis* antibody by EIA (1).

*Plague is characterized by fever, chills, headache, malaise, prostration and leukocytosis, and is manifest in one or more of the following principal forms:

Bubonic plague: regional lymphadenitis

Septicemic plague: septicemia with or without an evident bubo

Primary pneumonic plague: resulting from inhalation of infectious droplets

Secondary pneumonic plague: pneumonia resulting from hematogenous spread in bubonic or septicemic cases

Pharyngeal plague: pharyngitis and cervical lymphadenitis resulting from exposure to larger infectious droplets or ingestion of infected tissues (1).

2. Reporting and Other Requirements

Laboratory:

- All positive laboratory results for *Yersinia pestis* are reportable to the Public Health Surveillance Unit by secure fax (204-948-3044). A phone report must be made to a Medical Officer of Health at 204-788-8666 on the **same day** the result is obtained, **in addition** to the standard surveillance reporting by fax.

- Manitoba clinical laboratories are required to submit residual specimens or isolate sub-cultures from individuals who tested positive for *Yersinia pestis* to Cadham Provincial Laboratory (CPL) (204-945-6123) within 48 hours of report. Submitting laboratories must notify CPL of the shipment PRIOR to submission.

Health Care Professional:

- Probable (clinical) cases of plague are reportable to the Public Health Surveillance Unit during regular hours (8:30 a.m. to 4:30 p.m.) by telephone (204-788-6736) AND by secure fax (204-948-3044) using the *Clinical Notification of Reportable Diseases and Conditions*

form MHSU-0013 http://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0013.pdf on the **same day** that they are identified. After hours telephone reporting is to the Medical Officer of Health on call at (204-788-8666) with a subsequent faxed report form MHSU-0013.

Regional Public Health or First Nations Inuit Health Branch (FNIHB):

- Once the case has been referred to Regional Public Health or FNIHB, the *Communicable Disease Control Investigation Form* MHSU-0002 http://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0002.pdf should be completed and returned to the Public Health Surveillance Unit by secure fax (204-948-3044).

3. Clinical Presentation/Natural History

Plague takes several different clinical forms, depending in part on the route of exposure (2). Initial signs and symptoms for all presentations may be nonspecific, with fever, chills, malaise, myalgia, nausea, prostration, sore throat, and headache (2). Naturally acquired plague usually takes the form of bubonic plague (3). The global distribution of *Y. pestis*, ease for its mass production, and aerosolized dissemination means it is considered to have a high potential for biological weapon use (2, 4).

Bubonic Plague: Bubonic plague results from cutaneous exposure (e.g., flea bite) and is characterized by the sudden onset of high fever, chills, weakness and headache (2). A bubo or swelling of regional lymph nodes becomes apparent in the groin, axilla, or neck within the first day (2). The size may vary from one cm to 10 cm in diameter (4). Bacteremia is common in patients with bubonic plague (5). High levels of bacteremia are often associated with gastrointestinal symptoms such as nausea, vomiting, abdominal pain and diarrhea (5). Untreated bubonic plague has a case fatality of 50-60% (3). Bubonic plague resulting from the bite of an infected flea, accounts for 80-85% of plague cases reported in the United States (6).

Septicemic Plague: The septicemic form of plague can occur subsequent to bubonic plague or without prior lymphadenopathy (primary septicemic plague) (3). The illness progresses rapidly, leading to overwhelming sepsis and organ failure within a few days (2). Septicemic plague may be complicated by bleeding and gangrene, especially of the fingers, toes and nose (7). Some patients have gastrointestinal symptoms as well (2). Untreated primary septicemic plague is almost invariably fatal (3). Septicemic plague accounts for approximately 10% of plague cases reported in the United States (6).

Pneumonic Plague: Pneumonic plague exists in two forms, primary and secondary (2). Primary pneumonic plague results from the direct inhalation of bacteria into the lungs (2). Patients experience sudden onset of fever, chills, headache, malaise, and rapidly advancing tachypnea, dyspnea, hypoxia, chest pain, cough, hemoptysis, and general signs of toxemia (2). Primary pneumonic plague accounts for approximately 2% of reported plague cases in the United States (8). Secondary pneumonic plague is the more common form of pneumonic plague and arises through hematogenous spread of bacteria to the lungs from a bubo or other source (2). Fatality rates are influenced by time to initiation of antibiotics, access to advanced supportive care and the dose of inhaled bacilli (9). Untreated pneumonic plague is almost always fatal, and mortality is very high in persons when treatment is delayed beyond 24 hours after symptom onset (2).

Other Forms of Plague: Pharyngeal plague is a rare presentation resembling acute tonsillitis (2). Plague meningitis is a rare complication of *Y. pestis* (2).

4. Etiology

Plague is caused by the gram-negative coccobacillus, *Yersinia pestis* (3).

5. Epidemiology

5.1 Reservoir and Source:

Humans are incidental hosts or "dead-end" hosts (2). The principal animal reservoir differs from region to region (10). Wild rodents are the natural vertebrate hosts of plague and maintain the natural plague cycle by serving as sources of infection and amplification for the flea vectors of the disease (3). Plague bacilli can survive in the soil for prolonged periods and might be a source of infection for rodents (2).

5.2 Transmission:

Plague is transmitted between animals and humans by the bite of infected fleas, direct contact with infectious body fluids or contaminated materials of infected animals or humans, and inhalation of infected respiratory droplets from a patient with pneumonic plague (11). Person-to-person transmission of pneumonic plague requires close contact, typically with a patient who is in the late stages of infection and coughing copious amounts of bloody sputum (2). Human cases have been linked to handling infected animals and domestic pets, particularly house cats and dogs, which can carry *Y. pestis*-infected wild rodent fleas into homes (3, 8). Domestic cats that eat infected rodents are particularly susceptible to plague (12) and pharyngeal infection in cats can be transmitted directly to humans through respiratory droplets, causing primary pneumonic plague (2). Dogs are less susceptible to the plague (so the dog could appear clinically normal) and transmission would mainly be via fleas that they carry (12). Cases of plague have been reported in people who have butchered or skinned an animal (13).

5.3 Occurrence:

General: Plague is a disease of poverty in Africa, South America, and India, where commensal rodents are the animal reservoir (10). In other endemic regions such as Peru and the western United States, plague is a sporadic disease associated with outdoor occupations and contact with infected domestic animals (cats and dogs) (10). Plague does occur in Asia, but is restricted to breeders and hunters since the reservoir consists mainly of gerbils in the steppe and marmots in the mountains (2). Madagascar is the most seriously affected country in the world (10). Most of the cases reported in a large 2017 Madagascar plague outbreak were pneumonic plague (14). Since the 1990s, most human cases have occurred in Africa (11).

Canada: Human cases of plague are very rare in Canada with the last case reported in 1939 (15).

Manitoba: No cases of human plague were reported in Manitoba since reporting became available in 1993.

5.4 Incubation:

The incubation period is usually two to seven days, but can be as short as one day for primary pneumonic plague (2).

5.5 Risk Factors for Infection:

Within endemic areas, elevated plague risk is associated with close contact with rodents and their feline and canine predators, harbouring food sources for wild rodents in the vicinity of homes and failure to control fleas on pet cats and dogs (2).

5.6 Host Susceptibility and Resistance:

Humans are universally susceptible (3). Immunity after recovery is relative; it may not protect against a future large inoculum (3).

5.7 Period of Communicability:

Person-to-person transmission of bubonic plague is rare (11). Pneumonic plague is communicable until 48 hours of appropriate antimicrobial therapy have been received (16). Fleas may remain infective for months (17).

6. Diagnosis

Confirmation of plague requires laboratory testing. Consult Cadham Provincial Laboratory (CPL) (204-945-6805) if plague is suspected. Label all specimens "SUSPECT PLAGUE" and notify the lab prior to transporting specimen(s). Serology is referred out.

7. Key Investigations for Public Health Response

- History of exposure to other potential cases.
- History of international travel.
- History of exposure to fleas, rodents (ground squirrels, chipmunks, wood rats, mice, black footed ferrets and prairie dogs are the most common in North America), wild felids or domestic cats and dogs (12).
- History of hunting or trapping.
- History of veterinary medicine as occupation.

8. Control

8.1 Management of Cases:

Plague is a medical and public health emergency.

- When plague is suspected, diagnostic specimens should be obtained promptly and effective antimicrobial therapy started immediately after obtaining diagnostic specimens (2).
- Supportive care.
- Drainage of abscessed buboes may be necessary; drainage material is infectious until effective antimicrobial therapy has been administered (18).

Infection Prevention and Control:

- Routine Practices are required for bubonic, septicemic and pharyngeal plague. Droplet precautions are required for pneumonic plague until 48 hours of appropriate antimicrobial therapy is received. Refer to the Manitoba Health, Seniors and Active Living document *Routine Practices and Additional Precautions: Preventing the Transmission of Infection in Health Care* available at: http://www.gov.mb.ca/health/publichealth/cdc/docs/ipc/rpap.pdf .

Treatment:

- Consultation with an infectious diseases specialist is recommended.
- Streptomycin is preferred (2). Gentamicin may also be used and is considered safer than streptomycin for use in pregnant women and children (2). Doxycycline is preferred for those with contraindications to aminoglycosides or tetracycline (2). Treatment duration should be 10-14 days (19). Fluoroquinolones may also be used (19) and have been proposed as alternatives for treatment of plague in mass casualty settings (2).

8.2 Management of Contacts and Other Exposed Individuals:

- Household contacts or persons who have had face-to-face contact with cases of pneumonic plague should be provided

chemoprophylaxis and placed on surveillance for 7 days (3). Persons refusing prophylaxis should be carefully watched for the development of fever or cough during the first 7 days after exposure and treated immediately should either occur (9). Chemoprophylaxis is also recommended for household members of bubonic plague cases (11).

- **Chemoprophylaxis:** Doxycycline, given in an adult dose of 100 mg twice daily for 7 days, or levofloxacin, 500 mg daily for 7 days, are appropriate choices for prophylaxis of adults (2). Consult a pediatric infectious diseases specialist for chemoprophylaxis of children.
- Contacts should also be advised about appropriate measures to protect themselves and their families from plague (3). Refer to section 8.5.

NOTE: Manitoba Health, Seniors and Active Living does not cover the cost of any prophylactic drug regimens prescribed for the management of contacts and other exposed individuals.

8.3 Management of Outbreaks:

- Refer to sections 8.1 and 8.2 above.

8.4 Bioterrorism-related Plague:

- Intentional aerosol release should be suspected in patients presenting with plague pneumonia in non-endemic areas or in patients without risk factors for acquisition (20). A plague outbreak among individuals without a common source of exposure should also raise the index of suspicion (4). *Y. pestis* is a relatively fragile organism that remains viable only an hour after aerosol release (20).
- For bioterrorist threats or suspected bioterrorist activity, the police should be contacted at 911 (24 hours) as well as the Office of Disaster Management Duty Officer at: 204-793-1632 (24 hours).

8.5 Preventive Measures:

- The World Health Organization does not recommend vaccination, except for high-risk groups (e.g., laboratory personnel working with samples infected with or potentially infected with plague bacilli) (11).
- Persons engaging in outdoor activities where plague is endemic or in areas experiencing outbreaks should wear long pants when possible and use insect repellent on clothing and skin (6, 7).
- Pet owners should regularly use veterinary approved flea control products on their pets and consult a veterinarian if their pet is ill (2, 6).
- Rodent proofing homes, workplaces and recreational areas. Prevent rodent access to food, and reduce brush, rock piles, junk and cluttered firewood close to housing to prevent rodent habitation.
- Avoid contact with rodent nests and burrows, sick or dead animals, and close contact with persons known or suspected to have plague (7).
- Frequent handwashing with soap and water for at least 20 seconds or alcohol-based hand sanitizer if soap and water are not available (7).

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