



Plague

Disease Plan

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Last updated: March 15, 2016 by Dallin Peterson

Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.

✓ WHY IS PLAGUE IMPORTANT TO PUBLIC HEALTH?

Plague is a disease that affects humans and other mammals. Humans usually get plague after being bitten by rodent fleas that are carrying the bacteria, or by handling an animal infected with plague. Although plague is treatable with antibiotics, without treatment, the disease can cause serious illness or death. Utah has endemic plague each year in rodent burrows, thus making it more important to be diligent in finding potential cases and exposures.

The Centers for Disease Control and Prevention (CDC) considers the plague organism, *Yersinia pestis*, as a critical biological agent with the potential to be modified to be used by terrorists and others as a bioterrorism (BT) agent. Therefore, early awareness and investigation of plague cases is critical to ensure protection of the public's health.

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description

Initial signs and symptoms may be nonspecific with fever (which is usually present), chills, malaise (tiredness), myalgias (muscle aches), nausea, prostration, sore throat, and headache.

- If the presentation is “bubonic”, then lymph nodes in the inguinal (groin), axillary (armpit), and cervical (neck) areas may become swollen, inflamed, and tender, and may suppurate (discharge pus). These are called buboes. If not treated with appropriate antibiotics, the bacteria could spread to other parts of the body.
- The presentation may become “septicemic,” where the organism becomes disseminated throughout the body including the meninges. Skin and other tissue may turn black and die, especially on fingers, toes, and the nose. Septicemic plague can occur as the first symptom of plague, or may develop from untreated bubonic plague. This form results from bites of infected fleas or from handling infected animals.
- If the presentation is “pneumonic”, pneumonia may be present. Pneumonic plague is especially concerning from an infection control and public health standpoint. This form may develop from inhaling infectious droplets, or may develop from untreated bubonic or septicemic plague after the bacteria has spread to the lungs. The pneumonia may cause respiratory failure and shock. This form is the most serious form of the disease and is the only form of plague that can be spread from person to person (through infectious droplets). Contacts must be identified and given prophylaxis or isolated if they refuse prophylaxis.



Plague can also present as “pharyngeal”, with an inflamed pharynx, or “meningitis”, with nuchal rigidity, or “cutaneous”— but, these forms are rare.

Causative Agent

Plague is caused by a bacterium known as *Yersinia pestis*. *Yersinia* species are Gram-negative rods that can exhibit a bipolar or “safety pin” staining pattern.

Differential Diagnosis

Plague can be mistaken for influenza or other acute febrile illnesses, especially in initial stages.

Laboratory Identification

If plague is suspected, pre-treatment specimens should be taken if possible, but treatment should not be delayed. The laboratory should be notified if plague is suspected. Plague should be identified as a presumptive isolate at a clinical lab, and then forwarded to a reference lab and to the Utah Public Health Laboratory (UPHL) for final identification. All hospitals should be encouraged to report even SUSPECT cases of plague, as final identification can be a lengthy process. 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 patient 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.

Treatment

Plague is a very serious illness, but is treatable with commonly available antibiotics. The earlier a patient seeks medical care and receives appropriate treatment, the better the chances for a full recovery.

Begin appropriate IV therapy as soon as plague is suspected. Gentamicin and fluoroquinolones are typically first-line treatments in the United States (U.S.). Duration of treatment is 10-14 days, or until two 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 appropriate clinical judgment. Additional information can be found at:

<http://www.cdc.gov/plague/healthcare/clinicians.html>.

	Antibiotic	Dose	Route of administration	Notes
Adults	Streptomycin	1 g twice daily	IM	Not widely available in the U.S.
	Gentamicin	5 mg/kg once daily, or 2 mg/kg loading dose followed by 1.7 mg/kg every 8 hours	IM or IV	Not FDA approved but considered an effective alternative to streptomycin. ¹ Due to poor abscess penetration, consider alternative or dual therapy for patients with bubonic disease.
	Levofloxacin	500 mg once daily	IV or po	Bactericidal. FDA approved based on animal studies but limited clinical experience treating human plague. A higher dose (750 mg) may be used if clinically indicated.
	Ciprofloxacin	400 mg every 8-12 hours	IV	Bactericidal. FDA approved based on animal studies but limited clinical experience treating human plague.
		500-750 mg twice daily	po	
	Doxycycline	100 mg twice daily or 200 mg once daily	IV or po	Bacteriostatic, but effective in a randomized trial when compared to gentamicin. ²
	Moxifloxacin	400 mg once daily	IV or po	
	Chloramphenicol	25 mg/kg every 6 hours	IV	Not widely available in the U.S.

Children³	Streptomycin	15 mg/kg twice daily (maximum 2 g/day)	IM	Not widely available in the U.S.
	Gentamicin	2.5 mg/kg/dose every 8 hours	IM or IV	Not FDA approved but considered an effective alternative to streptomycin. ¹ Due to poor abscess penetration, consider alternative or dual therapy for patients with bubonic disease.
	Levofloxacin	10 mg/kg/dose (maximum 500mg/dose)	IM or po	Bactericidal. FDA approved based on animal studies but limited clinical experience treating human plague.
	Ciprofloxacin	15 mg/kg/dose every 12 hours (maximum 400 mg/dose)	IV	Bactericidal. FDA approved based on animal studies but limited clinical experience treating human plague.
		20 mg/kg/dose every 12 hours (maximum 500 mg/dose)	po	
	Doxycycline	Weight < 45 kg: 2.2 mg/kg twice daily (maximum 100 mg/dose) Weight ≥ 45 kg: same as adult dose	IV or po	Bacteriostatic, but FDA approved and effective in a randomized trial when compared to gentamicin. ² No tooth staining after multiple short courses. ⁴
Chloramphenicol (for children >2 years)	25 mg/kg every 6 h (maximum daily dose, 4 g)	IV	Not widely available in the U.S.	
Pregnant women³	Gentamicin	Same as adult dose	IM or IV	See notes above
	Doxycycline	Same as adult dose	IV	See notes above
	Ciprofloxacin	Same as adult dose	IV	See notes above

Notes:

¹Boulanger LL, Ettestad P, Fogarty JD, Dennis DT, Romig D, Mertz G. [Gentamicin and tetracyclines for the treatment of human plague: Review of 75 cases in New Mexico, 1985–1999.](#) *Clin Infect Dis.* 2004 38(5):663-669.

²Mwengee W, Butler T, Mgema S, Mhina G, Almasi Y, Bradley C, Formanik JB, Rochester CG. [Treatment of plague with gentamicin or doxycycline in a randomized clinical trial in Tanzania.](#) *Clin Infect Dis.* 2006 42(5):614-21.

³All recommended antibiotics for plague have relative contraindications for use in children and pregnant women; however, use is justified in life-threatening situations.

⁴Todd SR, Dahlgren FS, Traeger MS, Beltrán-Aguilar ED, Marianos DW, Hamilton C, McQuiston JH, Regan JJ. [No visible dental staining in children treated with doxycycline for suspected Rocky Mountain spotted fever.](#) *J Pediatr.* 2015 May;166(5):1246-51.

Case Fatality

The case fatality for untreated bubonic plague is 50-60%. Cases of untreated pneumonic or primary septicemic plague are invariably fatal. Appropriate therapy (if initiated early) will reduce the case fatality rate. Overall, about 14% of plague cases in the U.S. are fatal.

Reservoir

Plague is usually a zoonosis involving wild rodents as the natural hosts and their fleas as vectors for the disease. Plague is endemic in rodents throughout the southwestern U.S. Ground squirrels are the natural vertebrate host, but it can also be found in rats, prairie dogs, rabbits, hares, wild carnivores, chipmunks, mice and domestic cats, as well as their fleas.

Transmission

Typically plague occurs in humans when they come into contact with infected fleas or animals. During plague epizootics, many rodents die, causing hungry fleas to seek other sources of blood. When people or animals visit the places where rodents recently died from plague, they are at risk of contracting it from flea bites. Humans can also become infected when handling tissue or body fluids from an infected animal. A hunter skinning an animal without using proper precautions can become infected.



When a person has plague pneumonia, they may cough droplets containing the bacteria into the air. When they are inhaled by another person, the bacteria can cause pneumonic plague. Typically, this requires direct and close contact with the infected person.

Cats are particularly susceptible to plague and can be infected by eating infected rodents. Sick cats can transmit infectious plague to owners or veterinarians.

Susceptibility

All people are susceptible to this organism.

Incubation Period

The typical incubation period for septicemic plague is 1-7 days. Bubonic plague usually occurs between 2-6 days, and pneumonic plague occurs 1-3 days, following exposure.

Period of Communicability

Patients with pneumonic plague are considered infectious throughout their symptomatic illness, and for 72 hours following initiation of effective antibiotic treatment. Discharge from lesions in patients with bubonic plague is considered infectious.

Epidemiology

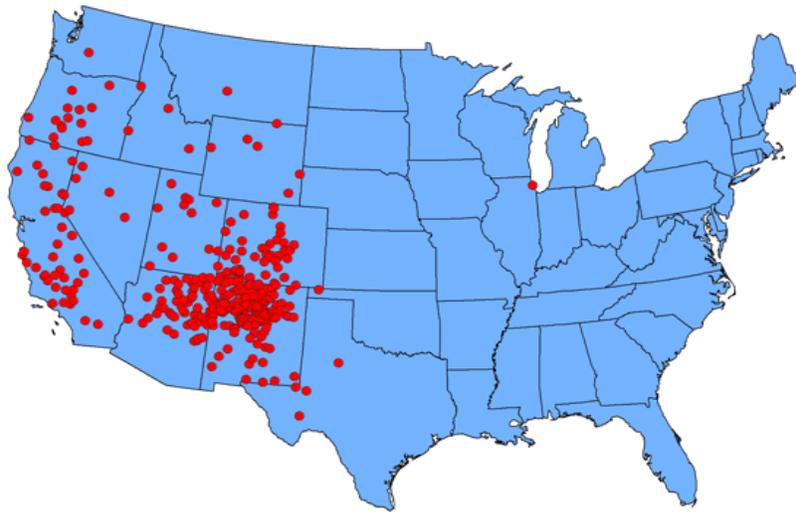
Cases of plague have occurred sporadically in rural areas of the western U.S. since the early 1900s. Plague is considered an endemic zoonotic disease in Utah. Each year, rodent burrows in

rural parts of the state are found to carry plague. In Utah, cats are frequently transmission vehicles. They acquire plague through hunting rodents, develop the disease, and then can transmit the disease.

The bubonic form of plague accounts for over 80% of plague cases in the U.S. The septicemic form occurs in about 10%. About 12% of plague patients in the U.S. develop pneumonic plague, of which 50% die.

An average of seven (7) human cases of plague are reported to the CDC each year in the U.S. Two cases of plague have been reported in Utah since 2009.

Reported cases of human plague--United States, 1970-2012



1 dot placed in county of exposure for each plague case

✓ PUBLIC HEALTH CONTROL MEASURES

Public Health Responsibility

- **Notify the UDOH BOE and UPHL and the LHD by phone immediately.**
- Thoroughly investigate all suspect cases of disease.
- Determine the probable source (location) of the infection (including ruling out the possibility of a Bioterrorism event).
- Determine if and where transmission is occurring in Utah.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Ensure proper treatment of cases.
- Initiate active surveillance immediately upon notification of suspect cases.
- Identify contacts if pneumonic plague is suspected.
- Identify environmental risks that need to be remediated that could include (pets, handling infected animals, or around infected persons).

Prevention

As this disease is a vectorborne illness, public health needs to assure that evidence of endemic activity (either through rodent or flea trapping) is swiftly remediated. Working through sister agencies (such as the Division of Wildlife Resources and the National Park Service), affected rodent burrows should be dusted with pesticides, and warning signs posted for campers/visitors. Information should reinforce not interacting with rodents, etc.

Personal protective measures should be used while in a rural area where plague is endemic:

1. Reduce rodent habitat around your home, work place, and recreational areas. Remove brush, rock piles, junk, cluttered firewood, and possible rodent food supplies, such as pet and wild animal food. Make your home and outbuildings rodent-proof.
2. Wear gloves if you are handling or skinning potentially infected animals to prevent contact between your skin and the plague bacteria. Contact your local health department if you have questions about disposal of dead animals.
3. Use repellent if you think you could be exposed to rodent fleas during activities such as camping, hiking, or working outdoors. Products containing DEET can be applied to the skin as well as clothing, and products containing permethrin can be applied to clothing (always follow instructions on the label).
4. Keep fleas off of your pets by applying flea control products. Animals that roam freely are more likely to come in contact with plague infected animals or fleas and could bring them into homes. If your pet becomes sick, seek care from a veterinarian as soon as possible.
5. Do not allow dogs or cats that roam free in endemic areas to sleep on your bed.

Large numbers of dead or sick rodents should be reported to the local or state health department or Utah Division of Wildlife Resources.

Prevention in Healthcare Settings:

Contact and droplet precautions are advised for healthcare settings; in addition, if the patient has evidence of pneumonic plague, respiratory isolation precautions should be put in place. Patients should be isolated until after 72 hours of appropriate antibiotic therapy.

Chemoprophylaxis

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. Duration of post-exposure prophylaxis to prevent plague is seven days. 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
Pregnant women	Doxycycline ¹	100 mg twice daily	PO
	Ciprofloxacin ¹	500 mg twice daily	PO

Notes:

Adapted from: Inglesby TV, Dennis DT, Henderson DA, et al. [Plague as a biological weapon: medical and public health management](#) Working Group on Civilian Biodefense. JAMA. 2000 May 3;283(17):2281-90.

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

Vaccine

A plague vaccine is no longer available in the U.S. New plague vaccines are in development, but are not expected to be commercially available in the immediate future.

Isolation and Quarantine Requirements

- Bubonic and septicemic plagues are not typically transmitted from person to person, **isolation** and **quarantine** are generally not appropriate.
- Precautions toward pneumonic plague should be taken due to the transmission of disease by droplets. Droplet precautions should be maintained for 72 hours after starting treatment. Persons in household or have had face to face contact with a case with pneumonic plague should be education on signs and symptoms and antibiotic prophylaxis is recommended through their healthcare provider. If contacts of pneumonic plague are unable to receive prophylaxis, quarantine for a 7-day period is required.
- While the plague bacillus is labile, it should not be considered an ongoing threat in an environmental setting. Therefore, no environmental **quarantine** is necessary.

✓ CASE INVESTIGATION

Reporting

Plague is an immediately reportable disease in Utah.

Criterion	Reporting
<i>Clinical Presentation</i>	
Fever	C
Chills	C
Headache	C

Prostration		C
Malaise		C
Regional lymphadenitis (bubo)		O
Septicemia		O
Pneumonia		O
Pharyngeal lymphadenitis		O
Healthcare record contains a diagnosis of plague	S	
Death certificate lists plague as a cause of death or a significant condition contributing to death	S	
<i>Laboratory Findings</i>		
Leukocytosis		
Elevated serum antibody titer(s) to <i>Y. pestis</i> fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination	S*	
Detection of <i>Y. pestis</i> F1 antigen in a clinical specimen by fluorescent	S*	
Isolation of <i>Y. pestis</i> from a clinical specimen	S*	
Fourfold or greater change in serum antibody titer to <i>Y. pestis</i> F1 antigen	S*	
<i>Epidemiological Risk Factors</i>		
History of exposure to rodents, rodent fleas, wild rabbits, or sick or dead carnivores		N
History of being in areas with endemic plague (e.g., NM, AZ, CO, CA, TX)		N
Work in a microbiology laboratory that handles <i>Y. pestis</i> or is in a plague endemic area		
Vaccination for plague		

Notes:

S = This criterion alone is sufficient to report a case.

N = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to report a case.

O = At least one of these “O” criteria in each category (e.g., clinical presentation and laboratory findings) is required to report a case.

C = This finding corroborates (e.g., supports) the diagnosis of—or is associated with—plague, but is not required for reporting.

* A requisition or order for any of the “S” or “N” laboratory tests is sufficient to meet the reporting criteria. A requisition or order for any of the “O*” laboratory tests—in conjunction with all other “N” criteria in the same column AND at least one of any “O” criteria in the other non-laboratory categories in the same column—is sufficient to meet the reporting criteria.

Case Definition

Plague (2010)

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)
-

Laboratory Criteria for Diagnosis

Presumptive

- Elevated serum antibody titer(s) to *Yersinia 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

Case Classification

Suspected

A clinically compatible case without presumptive or confirmatory laboratory results

Probable

A clinically compatible case with presumptive laboratory results

Confirmed

A clinically compatible case with confirmatory laboratory results

Classification Tables

Criterion	Case Definition		
	Confirmed	Probable	Suspected
<i>Clinical Presentation</i>			
Fever	C	C	C
Chills	C	C	C
Headache	C	C	C
Prostration	C	C	C
Malaise	C	C	C

Regional lymphadenitis (bubo)	O	O	O
Septicemia	O	O	O
Pneumonia	O	O	O
Pharyngeal lymphadenitis	O	O	O
Healthcare record contains a diagnosis of plague			
Death certificate lists plague as a cause of death or a significant condition contributing to death			
<i>Laboratory Findings</i>			
Leukocytosis	C	C	C
Elevated serum antibody titer(s) to <i>Y. pestis</i> fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination		O	
Detection of <i>Y. pestis</i> F1 antigen in a clinical specimen by fluorescent assay		O	
Isolation of <i>Y. pestis</i> from a clinical specimen	O		
Fourfold or greater change in serum antibody titer to <i>Y. pestis</i> F1 antigen	O		
<i>Epidemiological Risk Factors</i>			
History of exposure to rodents, rodent fleas, wild rabbits, or sick or dead carnivores			
History of being in areas with endemic plague (e.g., NM, AZ, CO, CA, TX)			
Work in a microbiology laboratory that handles <i>Y. pestis</i> or is in a plague endemic area			
Vaccination for plague		A	

Notes:

O = At least one of these “O” criteria in each category (e.g., clinical presentation and laboratory findings)—in conjunction with all other “N” criteria in the same column—is required to classify a case.

A = This criterion must be absent (e.g., NOT present) for the case to meet the reporting criteria or case classification.

C = This finding corroborates (e.g., supports) the diagnosis of—or is associated with—plague, but is not included in the case definition.

Case Investigation Process

Suspect cases of plague should be investigated immediately, even if the cases haven’t been confirmed. There are several immediate goals to the investigation process:

- **Notify the UDOH Bureau of Epidemiology (BOE) or Local Health Department by phone immediately.**

- Do not leave a message on an answering machine; you must have a direct, in-person contact with an employee to ensure appropriate notification is made.
- UDOH BOE staff will ensure immediate notification to UPHL and the Local Health Department (1-888-EPI-UTAH).
- **Actions taken with the case patient**
 - It is important to identify the source of each case. To do this, fill out both the disease investigation form as well as the BT investigation form. The possibility of bioterrorism needs to be ruled out as soon as possible.
 - Identify the type of disease. Is it septicemic, bubonic, or pneumonic?
 - Assure that infection control precautions are appropriate for the type of disease.
 - Assess if the case has pets. If so, educate on prevention techniques intended for pets that can include not allowing pets to roam on your bed, using flea control products, and if pet becomes sick, seek care from a veterinarian.
- Complete CMR in UT-NEDSS. Some of the information on this form must be provided by a clinician or other medical personnel.
- Verify case status.
- Complete disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and assist with eliminating it.

Outbreaks

Due to the serious nature of this disease, single cases should be investigated as soon as possible. Public health will assume that a single case could be leading to an outbreak and will respond accordingly. Public health will have a critical mission of providing public, clinician, and first responder education in the event of a significant outbreak.

Identifying Case Contacts

- Identify persons having household, hospital, or other close contact with persons with pneumonic plague and educate them of symptoms of illness to facilitate diagnosis.
- Identify laboratory workers and healthcare providers exposed to specimens or laboratory isolates, and educate them of symptoms of illness to facilitate diagnosis.

Case Contact Management

Plague is only transmissible from person to person if it is pneumonic.

- IF the case is pneumonic, then rapid identification of close contacts to the patient from the date of symptom onset until after 72 hours of antibiotic treatment AND post exposure prophylaxis of those contacts is essential.
- Pneumonic plague is transmissible via droplets; therefore, appropriate contacts should be identified and notified of the potential exposure.
- Assure that contacts receive appropriate prophylaxis.
- Monitor contacts daily. If any report development of a fever or cough for 7 days after exposure, they should be seen immediately by a clinician.

✓ REFERENCES

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✓ VERSION CONTROL

Update Mar 2016. Changes per LHD suggestions.

Update Aug 2015. Changes to document format.

Update Nov 2015. Updated most sections and added minimum data set.

✓ UT-NEDSS Minimum/Required Fields by Tab

Demographic

- County
- State
- Street
- City
- Zip Code
- Date of Birth
- Birth Gender
- Ethnicity
- Race
- First Name
- Last Name
- Phone Number

Clinical

- Date Diagnosed
- Died
- Date of Death
- Disease
- Onset Date
- Hospitalized
- Syndrome
- Lymphadenitis, regional (buboe)
- Lymphadenitis, pharyngeal
- Pneumonia
- Septicemia

Laboratory

- Organism
- Specimen Sent to State Lab
- Specimen Source
- Test Result
- Test Type
- Collection Date

Epidemiological

- Occupation

- Imported From
- Date of Exposure

Investigation

- Did this patient have an appropriate exposure history for this disease?
- Is this patient an appropriate age for this disease?
- Is this an appropriate time of year for this disease?
- Are the symptoms appropriate for the disease?
- Does the patient work in a clinical or microbiological lab, processing samples that could potentially contain the organism?
- Does patient have any animal exposure in the 10 days prior to illness onset? If so, when and where was the contact, and what was the animal?
- Does the patient have history of flea bites?
- Within 2 weeks of the onset of illness, did the patient travel or stay overnight somewhere other than main residence? If yes, list dates and locations.
- History of vaccination for the indicated disease?

Reporting

- Date First Reported to Public Health

Administrative

- Outbreak Name
- Outbreak Associated
- State Case Status