19-ID-01

Committee: Infectious Disease

Title: Public Health Reporting and National Notification of Plague

☒Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: 09-ID-52.

Synopsis:

This position statement updates the case definition for plague by adding new laboratory criteria and creating more flexibility in clinical syndrome and epidemiologic linkage.

I. Statement of the Problem

Plague is a life-threatening condition caused by *Yersinia pestis* that is endemic in the western United States (1-3). Technical formatting changes to the surveillance case definition for plague went into effect in 2009 and 2011; however, the last substantive change to the clinical criteria, laboratory evidence of infection, and case classifications was made in 1996 (4-7). Since that time, additional laboratory assays, including polymerase chain reaction (PCR) and immunohistochemical (IHC) assays have been validated for use in plague diagnostics (8-12).

PCR is currently performed at Laboratory Response Network (LRN) laboratories, has improved ability to rapidly identify the causative agent and allowed for increased diagnostic sensitivity early in illness or in circumstances where culture recovery may be limited, such as subsequent to initiation of antimicrobial therapy. IHC is performed at specialized laboratories but has proven useful at identification of the etiology in post-mortem tissues at times when other diagnostic modalities have limited utility.

The current case definition does not explicitly allow for clinically-compatible illness that might not align with a discrete clinical syndrome, such as a non-specific febrile illness that can be present early in the disease course. Additionally, the current definition does not allow for epidemiologic linkage to provide supportive evidence for case classification.

II. Background and Justification

The plague bacterium (*Yersinia pestis)* exists in enzootic cycles of rodents and their fleas in the western United States (1-3). People are infected with the plague bacterium through flea bites and direct contact with infected animal tissues or fluids. People are also infected by inhalation of droplets coughed by an infected human or animal. Plague is a febrile illness that typically manifests into one or more clinical syndromes, often reflecting the route of exposure to the bacterium. These clinical syndromes include bubonic, septicemic, and pneumonic plague. Several classes of antibiotics are effective against plague. Plague can be rapidly fatal if appropriate antimicrobial therapy is not initiated early in illness (1,2).

Yersinia pestis is classified as a Tier 1 bioweapon due to its potential for high mortality, aerosol exposure, and ability to be weaponized (13). Public health surveillance provides information on the temporal, geographic, and demographic patterns of *Yersinia pestis*. This information facilitates prevention and control activities and fosters awareness of current epidemiologic patterns of a potential bioweapon.

Laboratory diagnostic methods for plague include culture, microscopy, direct fluorescent antibody (DFA) assays, immunohistochemical (IHC) assays, PCR assays, and serological assays (1). A highly sensitive and specific multi-target real-time PCR assay is routinely used in Laboratory Response Network (LRN)

facilities as a rapid presumptive test for plague but is not currently included as laboratory evidence in the plague surveillance case definition. IHC assays are only available at certain specialized testing laboratories and can facilitate accurate diagnosis and case classification particularly in unusual and post-mortem situations.

This position statement incorporates newer laboratory diagnostics (PCR and IHC) which currently are not reflected in the approved case definition. This inclusion will minimize the potential for under-reporting of cases diagnosed using only those techniques, and therefore, prompt public health investigation and intervention. The proposed position statement also allows for clinically-compatible illness that may not align with a discrete clinical syndrome, such as a non-specific febrile illness that may be present early in the disease course as well as allowing for epidemiologic linkage to provide supportive evidence to case classification.

III. Statement of the desired action(s) to be taken

CSTE recommends the following actions:

1. Implement a standardized surveillance case definition for plague.

    A. Utilize standard sources (e.g. reporting*) for case ascertainment for plague. Surveillance for plague should use the recommended sources of data to the extent of coverage presented in Section V.

    B. Utilize standardized criteria for case ascertainment for plague presented in Section VI and Table VI in Technical Supplement.

    C. Utilize standardized criteria for case classification for plague presented in Sections VII and Table VII in Technical Supplement.

2. Utilize standardized criteria for case ascertainment and classification (based on Sections VI and VII and Technical Supplement) for plague and retain plague on the *Nationally Notifiable Condition List.*

    ☒ Immediately notifiable, extremely urgent (within 4 hours) - suspected intentional act
    ☐ Immediately notifiable, urgent (within 24 hours)
    ☒ Routinely notifiable
    ☐ No longer notifiable

3. CSTE recommends that all States and Territories enact laws (statue or rule/regulation as appropriate) to make this disease or condition reportable in their jurisdiction. Jurisdictions (e.g. States and Territories) conducting surveillance (according to these methods) should submit case notifications** to CDC.

4. Expectations for Message Mapping Guide (MMG) development for a newly notifiable condition: the National Notifiable Diseases Surveillance System (NNDSS) is transitioning to HL7-based messages for case notifications; the specifications for these messages are presented in MMGs. When CSTE recommends a new condition be made nationally notifiable, CDC must obtain Office of Management and Budget Paperwork Reduction Act (OMB PRA) approval prior to accepting case notifications for the new condition. Under anticipated timelines, notification using the Generic V2 MMG would support transmission of the basic demographic and epidemiologic information common to all cases and could begin with the new *MMWR* year following the CSTE annual conference. Input from CDC programs and CSTE would prioritize development of a disease-specific MMG for the new condition among other conditions waiting for MMGs.

5. CDC should publish data on plague as appropriate (see Section IX for additional information).

NNC data sharing/release and print criteria

CSTE recommends the following case statuses be included in the CDC Print Criteria:

☒Confirmed
☒Probable
☐Suspect
☐Unknown

- State/territorial health agency will share core data on confirmed and probable cases.
- CDC will re-release only fully de-identified case data to the general public, other releases by CDC require signed data sharing agreements using a format pre-approved by the state/territorial health agency).

6. CSTE recommends that all jurisdictions (e.g. States, Localities, or Territories) with legal authority to conduct public health surveillance follow the recommended methods outlined in this standardized surveillance position statement.

*Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance TO local, state, or territorial public health. Note: notification is addressed in a Nationally Notifiable Conditions Recommendation Statement and is the process of a local, state, or territorial public health authority submitting a report (case information) of a condition on the *Nationally Notifiable Conditions List* TO CDC.
**Notification: process of a local or state public health authority submitting a report (case information) of a condition on the *Nationally Notifiable Conditions List* to CDC.

IV. Goals of Surveillance

1. To provide information on the temporal, geographic, and demographic occurrence of *Yersinia pestis* to facilitate the prevention and control of plague.
2. To ensure rapid detection of pathogens on the Tier I bioterrorism agent list.
3. To ensure rapid intervention early in the course of illness to minimize morbidity and to prevent human-to-human spread of infection.

V. Methods for Surveillance: Surveillance for plague should use the recommended sources of data and the extent of coverage listed in Table V.

Table V. Recommended sources of data and extent of coverage for ascertainment of cases of plague.

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities, specify: hospitals, veterinarians, medical examiners	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Data from electronic medical records	X	
2019 Template		

VI. Criteria for case ascertainment

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.

Report any illness to public health authorities that meets any of the following criteria:

- A person with an acute illness consistent with plague AND clinical suspicion of plague.
- A laboratory order for plague, including but not limited to results positive for plague.
- A person whose healthcare record contains a diagnosis of plague.
- A person whose death certificate lists plague as a cause of death or a contributing factor to death.

Other recommended reporting procedures:

- All cases of plague should be reported.
- Reporting should be ongoing and routine.
- Reporting should be immediate*.

**Immediate per the definition provided by individual state reporting guidance.*

A1. Clinical Criteria for Reporting

Plague is an acute febrile illness often accompanied by chills, headache, malaise, prostration, and leukocytosis. It may ultimately manifest in one or more of the following clinical forms:

- Regional lymphadenitis (bubonic plague)
- Septicemia without evident lymphadenitis (septicemic plague)
- Pneumonia (pneumonic plague)
- Pharyngitis with cervical lymphadenitis (pharyngeal plague)

A2. Laboratory Criteria for Reporting

- Any laboratory order for *Y. pestis* testing, including for culture, direct fluorescent antibody assay, or PCR, with or without results, OR
- Any identification of *Y. pestis* in a clinical laboratory (isolation, elevated serum antibody titer(s) to *Y. pestis* F1 antigen in a patient with no history of plague vaccination, or detection of *Y. pestis* specific antigens by fluorescent antibody assay, immunohistochemical assay, or PCR).

A3. Epidemiologic Linkage Criteria for Reporting

- A suspected infection in a person that is epidemiologically linked to a person or animals with confirmatory plague laboratory evidence[+] within the prior two weeks;
- A suspected infection in a person with close contact with a confirmed pneumonic plague case, including but not limited to presence within two meters of a person with active cough due to pneumonic plague;
- A suspected infection in a person that lives in or has traveled within two weeks of illness onset to an area with confirmed plague epizootic activity.

[+]*confirmatory laboratory evidence as indicated below applies for humans and animals*

A4. Vital Records Criteria for Reporting

- Plague listed anywhere on a death certificate.

A5. Other Criteria for Reporting

- A person whose healthcare record contains a diagnosis of plague

B. Disease-specific data elements to be included in the initial report

Epidemiological evidence

- Works, or recently worked, in a laboratory that handles *Y. pestis* isolates or clinical specimens from plague patients.
- Works, lives in, or recently traveled to a western state or region of the world with enzootic plague activity;
- History or evidence of a flea bite;
- Exposure to carcasses, tissues, or body fluids of potentially infected animals, such as wild rodents;
- Exposure to infectious respiratory droplets of a suspected human or animal pneumonic plague case;
- Sustained bites or scratches from a suspected infected animal;
- Has a companion animal with a suspected or confirmed *Y. pestis* infection;
- Has a household contact with plague infection or is otherwise epidemiologically linked to a person with a confirmed or presumptive plague infection.

VII. Case Definition for Case Classification

A. Narrative: Description of criteria to determine how a case should be classified.

A1. Clinical Criteria

An illness characterized by acute onset of fever as reported by the patient or healthcare provider with or without one or more of the following specific clinical manifestations:

- Regional lymphadenitis (bubonic plague)
- Septicemia (septicemic plague)
- Pneumonia (pneumonic plague)
- Pharyngitis with cervical lymphadenitis (pharyngeal plague)

A2. Laboratory Criteria

Confirmatory laboratory evidence:

- Isolation of *Y. pestis* from a clinical specimen with culture identification validated by a secondary assay (e.g., bacteriophage lysis assay, direct fluorescent antibody assay) as performed by a CDC or Laboratory Response Network (LRN) laboratory, OR
- Fourfold or greater change in paired serum antibody titer to *Y. pestis* F1 antigen

*Presumptive laboratory evidence**:

- 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 *Yersinia pestis* specific DNA or antigens, including F1 antigen, in a clinical specimen by direct fluorescent antibody assay (DFA), immunohistochemical assay (IHC), or PCR

**Other laboratory tests, including rapid bedside tests, are in use in some low resourced international settings but are not recommended as laboratory evidence of plague infection in the United States.*

A3. Epidemiologic Linkage

- Person that is epidemiologically linked to a person or animals with confirmatory laboratory evidence within the prior two weeks;
- Close contact with a confirmed pneumonic plague case, including but not limited to presence within two meters of a person with active cough due to pneumonic plague; or

- A person that lives in, or has traveled within two weeks of illness onset to a geographically-localized area with confirmed plague epizootic activity in fleas or animals as determined by the relevant local authorities

A4. Case Classifications

Confirmed:

- a clinically-compatible case with confirmatory laboratory evidence, OR
- a clinically-compatible case with presumptive laboratory evidence AND epidemiologic linkage.

Probable:

- a clinically-compatible case with presumptive laboratory evidence without epidemiologic linkage in absence of an alternative diagnosis

Suspect:

- a clinically-compatible case with epidemiologic linkage without laboratory evidence, OR
- confirmed or presumptive laboratory evidence without any associated clinical information.

B. Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance

Serial or subsequent plague infections in one individual should only be counted if there is a new epidemiologically-compatible exposure and new onset of symptoms.

VIII. Period of Surveillance

Surveillance is expected to be ongoing.

IX. Data sharing/release and print criteria

- Immediate (extremely urgent) notification to CDC by phone call should occur for all possible plague cases, regardless of case classification, if illness is suspected to be the result of an intentional act.
- All other cases will use standard (routine) notification.

1. CSTE recommends the following case statuses* be included in the 'case' count released outside of the public health agency:
   ☒Confirmed
   ☒Probable
   ☐Suspect
   ☐Unknown

   * Which case statuses are included in the case counts constitute the "print criteria."

2. Jurisdictions (e.g., States and Territories) conducting surveillance under this case definition can voluntarily submit de-identified case information to CDC, if requested and in a mutually agreed upon format.
   Production of national data summaries and national data re-release for non-NNCs:

- CDC programs have a responsibility, in collaboration with states, localities, and territories, to ensure that CDC program-specific data re-release procedures meet the needs of those responsible for protecting data in the states and territories.

X. Revision History

This position statement updates 09-ID-52 and reflects

- newer diagnostic modalities as laboratory evidence of infection
- allows for febrile illness alone to be clinically-compatible illness, and
- allows for epidemiologic linkage to increase confidence in case classification status.

This position statement revision **does not** update methods for surveillance, criteria for reporting to public health authorities, period of surveillance (which is ongoing), OR timeliness of report to CDC, or print criteria. This position statement clarifies past discrepancy in print criteria.

Position Statement ID	Section of Document	Revision Description
09-ID-52	VI. Criteria for case ascertainment • A1. Clinical Criteria VII. Case Definition for Case Classification • A1. Clinical Criteria	Expanded clinical criteria
09-ID-52	VI. Criteria for case ascertainment • A2. Laboratory Criteria for reporting VII. Case Definition for Case Classification • A2. Laboratory Criteria	Added presumptive laboratory evidence criteria
09-ID-52	VI. Criteria for case ascertainment • A3. Epidemiologic Linkage Criteria for reporting VII. Case Definition for Case Classification • A3. Epidemiologic	Added Epidemiologic Linkage criteria
09-ID-52	VII. Case Definition for Case Classification • A4. Case Classification	Added new criteria for a confirmed case Added new criteria for a suspect case

XI. References

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Technical Supplement

Table VI. Table of criteria to determine whether a case of plague should be reported to public health authorities.

Criterion	Plague
Clinical Criteria for Reporting	
Clinical suspicion of plague	N
Acute onset of fever as reported by the patient or healthcare provider	O
Regional lymphadenitis	O
Septicemia	O
Pneumonia	O
Pharyngitis with cervical lymphadenitis	O
Laboratory Criteria for Reporting	
A laboratory order for plague testing, with or without results	S
Isolation of *Y. pestis* from a clinical specimen	S
Elevated serum antibody titer(s) to *Y. pestis* F1 antigen in a patient with no history of plague vaccination	S
Detection of *Y. pestis* specific antigens, including F1 antigen, in a clinical specimen by fluorescent antibody assay, immunohistochemical assay, or PCR	S
Epidemiological Linkage Criteria for Reporting	
Any suspect plague infection in a person with epidemiologic linkage to a person or animal with confirmed or suspected plague.	S
A suspect plague infection in a person that lives in or has traveled within two weeks of illness onset to an area with confirmed plague epizootic activity.	S
Vital Records Criteria for Reporting	
Death certificate lists plague as a cause of death or a contributing factor	S
Other Criteria for Reporting	
Healthcare record contains a diagnosis of plague	S

Notes:
S = This criterion alone is SUFFICIENT to report a case.

Table VII. Classification Table: Criteria for defining a case of plague

Criterion	Suspect				Probable		Confirmed			
Clinical Evidence										
Acute onset of fever as reported by the patient or healthcare provider	N				N	N	N	N	N	N
Regional lymphadenitis	O				O	O	O	O	O	O
Septicemia	O				O	O	O	O	O	O
Pneumonia	O				O	O	O	O	O	O
Pharyngitis	O				O	O	O	O	O	O
No history of plague vaccination				N		N			N	
No clinical information available		N	N	N						
Laboratory Evidence										
Isolation of *Y. pestis* from a clinical specimen		N					N			
Culture identification validated by a secondary assay (e.g., bacteriophage lysis assay, direct fluorescent antibody assay)		N					N			
Fourfold or greater change in paired serum antibody titer to *Y. pestis* F1 antigen			O					N		
Elevated serum antibody titer to *Y. pestis* F1 antigen in at least one specimen				N		N			N	
Detection of *Y. pestis* specific DNA in a clinical specimen by PCR			O		O					O
Detection of *Y. pestis* specific antigens in a clinical specimen by direct fluorescent antibody assay			O		O					O
Detection of *Y. pestis* specific antigens in a clinical specimen by immunohistochemical assay			O		O					O
No laboratory evidence available	N									
Epidemiologic Linkage Evidence										
Person that is epidemiologically linked to a person or animals with confirmatory laboratory evidence within the prior two weeks	O								O	O
Close contact with a confirmed pneumonic plague case (e.g., within two meters of a person with active cough due to pneumonic plague)	O								O	O
Recently in a geographically-localized area with confirmed plague epizootic activity in fleas or animals as determined by the relevant local authorities	O								O	O
Criteria to distinguish a new case:										
Not counted as a case within the previous 12 months	N	N	N	N	N	N	N	N	N	N

Notes:

N = All “N” criteria in the same column are NECESSARY to classify a case. A number following an “N” indicates that this criterion is only required for a specific disease/condition subtype (see below). If the absence of a criterion (i.e., criterion NOT present) is required for the case to meet the classification criteria, list the absence of criterion as a necessary component.

O = At least one of these “O” (ONE OR MORE) criteria in **each category** (categories=clinical evidence, laboratory evidence, and epidemiologic evidence) **in the same column**—in conjunction with all “N” criteria in the same column—is required to classify a case. A number following an “O” indicates that this criterion is only required for a specific disease/condition subtype.