



13-ID-15

**Submission Date:** May 23, 2013

**Committee:** Infectious Diseases

**Title:** Revision of the pertussis surveillance case definition to more accurately capture the burden of disease among infants <1 year of age

## I. Statement of the Problem

The pertussis case definition approved in the 2009 CSTE Position Statement 09-ID-51 entitled, “National Surveillance for Pertussis” does not accurately capture the burden of disease among infants (defined as children aged <1 year). Additionally, the laboratory criteria portion of the 2009 case definition does not adequately reflect the state of pertussis diagnostics in the U.S. The significant challenges for surveillance with the application of the 2009 pertussis case definition include, 1) clinical criteria that do not accurately represent the range of clinical presentations of pertussis among infants, 2) a requirement of cough duration of  $\geq 14$  days (in the absence of a *B. pertussis* positive culture) for all age groups, and 3) the exclusion of serology as a confirmatory laboratory test for pertussis case reporting.

The current pertussis case definition is used to classify cases across all age groups and sensitivity is reduced when applied to infants. In general, there are two main reasons pertussis occurring in infants may not meet the case definition and is not reported to CDC. First, presenting signs and symptoms of pertussis in infants may differ from those of pertussis occurring among other age groups and the current clinical case definition does not accommodate these differences. Apnea, a common clinical symptom among infants with pertussis, is currently not included and can be an important case-defining symptom in this age group. Second, infants may die or have interruption of cough as a result of pertussis (e.g., mechanical ventilation) before reaching cough duration of 14 days. As nationwide reductions in the use of culture for pertussis diagnosis continue, an increasing number of infants are being diagnosed by positive PCR, but still requiring a cough of  $\geq 14$  days and at least one pertussis clinical symptom for reporting purposes. With a growing burden of pertussis in the U.S., it is estimated that 10-20% of infant cases are not currently being captured. Additionally, it is common for CDC to be notified of infant pertussis deaths that do not meet the reporting case definition, an issue of great concern. Of the infant deaths communicated to CDC during 2012, illnesses in approximately 50% did not meet the current case definition.

PCR has become the primary diagnostic test used in most clinical settings in part because of its speed and high sensitivity. While PCR is included in the current case definition, a cough of  $\geq 14$  days and at least one pertussis clinical symptom is required for reporting PCR positive cases, as noted above. The quality of PCR in the U.S. has improved during the last decade; PCR now has acceptable specificity, especially among persons with clinically-compatible disease. Although serologic testing is a standard method of diagnosis in some countries, additional work is needed to better understand the clinical accuracy of commercially available serologic assays in the U.S. and the impact of these assays on pertussis case finding before proposing the inclusion of serology as a confirmatory test for pertussis reporting purposes. To maintain consistency in reporting, the cough duration requirement for persons aged  $\geq 1$  year who are PCR positive for pertussis and addition of serology across all age groups will be addressed simultaneously in a future CSTE position statement.

## II. Background and Justification

### Background

*Bordetella pertussis* is the most poorly controlled bacterial vaccine-preventable disease in the U.S., with peaks in disease occurring every 3-5 years. Although routine childhood vaccination has resulted in



substantial reductions in disease, the number of reported pertussis cases has been steadily increasing since the 1980s. Notable peaks in disease occurred in 2004 (25,827 cases, 27 deaths), 2010 (27,550 cases, 27 deaths), and most recently in 2012 when more than 41,000 cases and 18 deaths were reported, the largest number of cases in the U.S. since 1959. Furthermore, the epidemiologic features of pertussis have changed in recent years with an increasing burden of disease among fully-vaccinated children and adolescents.

Infants are at highest risk for severe morbidity and mortality from pertussis, particularly those too young to be vaccinated. Since 2000, approximately 80% of pertussis hospitalizations and 90% of pertussis-related deaths occurred among infants <1 year of age. Infants with pertussis may present differently than older patients and may not exhibit the “classic” pertussis signs and symptoms that include paroxysmal cough, whoop, or post-tussive vomiting. Apnea is a common clinical symptom among young infants and was reported in more than half of infant pertussis cases captured through NNDSS between 2000 and 2012. Additionally, numerous studies have suggested the importance of including apnea as a case-defining symptom for infants which is reflected in pertussis surveillance case definitions around the world. Because current pertussis prevention and control strategies are focused on protecting high risk infants from severe disease and death, having a clinical case definition that accurately captures the true burden of infant pertussis is critical for monitoring the impact of these strategies.

In the clinical setting the diagnosis of pertussis is based on clinical presentation, as well as a variety of laboratory tests (culture, PCR, and serology). Culture remains the gold standard laboratory test with virtually 100% specificity. However, fastidious growth requirements make *B. pertussis* difficult to culture and the sensitivity of culture depends heavily on timing of specimen collection. Culture has poor sensitivity when performed later in the course of illness or on specimens from persons who have received antibiotics or have been vaccinated.

PCR is a rapid test and has high sensitivity. Although the specificity can vary, considerable improvements have been made in the quality of PCR testing performed in many public health, clinical and commercial laboratories during the last decade as a result of ongoing communication and training efforts from CDC. PCR provides excellent sensitivity when specimens are obtained 0-3 weeks after cough onset, but may also provide accurate results for up to 4 weeks of cough in infants (<6 months) or unvaccinated persons. The adoption of PCR assay protocols that include multiple targets allowing for speciation of *Bordetella* species has further improved specificity at many public health and clinical laboratories. Although the high sensitivity of PCR can increase the risk of false-positivity, CDC has developed simple best practices to reduce the risk of obtaining inaccurate results (<http://www.cdc.gov/pertussis/clinical/diagnostic-testing/diagnosis-pcr-bestpractices.html>).

Serologic testing has proven useful for those individuals presenting late during the course of illness, when both culture and PCR are likely to be negative. CDC and FDA have collaboratively developed a serologic assay that has been extremely useful for confirming diagnosis. As of December 2012, staff at 20 state public health laboratories have been trained on this assay, but to date only two state laboratories have included the assay as part of their pertussis testing regimen. Additionally, this test currently is not commercially available. Commercial labs in the U.S. use a number of different serologic tests with unproven or unknown clinical accuracy. CDC is actively engaged in better understanding the usefulness and clinical accuracy of commercial assays, and results from a number of evaluations should be available during the next 12 months.

### Justification

To address the problems with the existing case definition outlined above, the following actions are being proposed:

1. Revise the pertussis surveillance case definition to more accurately capture the burden of disease among infants. Specifically,
  - a. Add apnea to the list of case-defining clinical signs and symptoms for infants.



- b. Classify PCR positive *or* epi-linked cases occurring among infants with cough of any duration *and* one other clinical symptom as “probable”.
2. Continue to assess pertussis laboratory diagnostics and lay the groundwork for further revisions to the pertussis case definition, including addressing the requirement of 14 days cough duration for PCR positive cases occurring among persons aged ≥1 year and adding serology as a confirmatory test among all age groups.

Because the true burden of infant pertussis is currently being underestimated, there is a public health urgency to address pertussis case reporting for infants. Including apnea as a case-defining clinical symptom for infants will increase the sensitivity and specificity of the current clinical case definition. Additionally, the classification and addition of PCR positive or epi-linked cases that have at least one pertussis clinical sign or symptom but have cough duration <14 days as “probable” cases will more accurately capture the burden of infant disease and maintain the specificity of the “confirmed” category, allowing CDC to monitor important changes in the epidemiology of infant pertussis during this critical time. This probable classification can easily be reassessed when modifications are considered for the classification of PCR positive cases in the absence of ≥14 days cough among other age groups. These proposed modifications to the clinical and classification criteria for infants will substantially enhance public health surveillance for pertussis.

Although the current case definition does not fully reflect the state of pertussis diagnostics in the U.S., modifications to the laboratory criteria within the case definition are best implemented in a unified way, to maintain consistency and understanding of surveillance data. Because information is not yet available to fully inform the application of serology within the case definition among all age groups, the requirement of ≥14 days cough for PCR positive cases among persons aged ≥1 year will be considered when both issues can be addressed simultaneously.

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

1. Revise the pertussis surveillance case definition to more accurately capture the burden of disease among infants. Specifically,
  - a. Add apnea to the list of case-defining clinical signs and symptoms for infants.
  - b. Classify PCR positive *or* epi-linked cases occurring among infants with cough of any duration *and* one other clinical symptom as “probable”.
2. Continue to assess pertussis laboratory diagnostics and lay the groundwork for further revisions to the pertussis case definition, including addressing the requirement of 14 days cough duration for PCR positive cases occurring among persons aged ≥1 year and adding serology as a confirmatory test among all age groups.

X 1. Use standard sources (e.g. reporting\*) for case ascertainment for pertussis. Surveillance for pertussis should use the following recommended sources of data to the extent of coverage presented in Table III.

**Table III. Recommended sources of data and extent of coverage for ascertainment of cases of pertussis.**

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers)	X	



Death certificates	X	
Hospital discharge or outpatient records	X	
Extracts from electronic medical records	X	
Telephone survey		
School-based survey		
Other _____		

2. Use standardized criteria for case identification and classification (Sections VI and VII) for **pertussis** but do not add the condition to the *Nationally Notifiable Condition List*. If requested by CDC, jurisdictions (e.g. States and Territories) conducting surveillance according to these methods may submit case information to CDC.

X 3. Use standardized criteria for case identification and classification (Sections VI and VII) for **pertussis** and add this condition to the *Nationally Notifiable Condition List*.

- 3a. Immediately notifiable, extremely urgent (within 4 hours)
- 3b. Immediately notifiable, urgent (within 24 hours)
- 3c. Routinely notifiable

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.

X 4. CDC should publish data on **pertussis** as appropriate in *MMWR* and other venues (see Section IX).

CSTE recommends that all jurisdictions (e.g. States or Territories) with legal authority to conduct public health surveillance follow the recommended methods as outlined above.

Terminology:

\* Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance TO local or state public health

\*\*Notification: process of a local or state public health authority submitting a report (case information) of a condition on the Nationally Notifiable Condition List TO CDC.

**IV. Goals of Surveillance**

To provide information regarding the epidemiology of pertussis to facilitate prevention and control efforts

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

**VI. Criteria for case identification**

**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:

1. An acute cough illness of any duration with an inspiratory whoop
2. Any person with isolation of *B. pertussis* from a clinical specimen or a positive PCR test for pertussis.
3. An acute cough illness of any duration in a person who is a contact of a laboratory-confirmed pertussis case.
4. An acute cough illness of any duration in a person who is a member of a defined risk group during an outbreak.
5. A person whose healthcare record contains a diagnosis of pertussis.



6. A person whose death certificate lists pertussis as a cause of death or a significant condition contributing to death.

**B. Table of criteria to determine whether a case should be reported to public health authorities**

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

Criterion	Reporting			
<i>Clinical Evidence</i>				
Cough (any duration)	N		N	
Cough ≥2 weeks duration				
Inspiratory whoop	N			
Healthcare record contains diagnosis of pertussis				S
Death certificate lists pertussis as a cause of death or a significant condition contributing to death				S
<i>Laboratory Evidence</i>				
Isolation of <i>B. pertussis</i> from a clinical specimen		S		
Positive PCR for pertussis		S		
<i>Epidemiological Evidence</i>				
Contact with a lab-confirmed pertussis case			O	
Member of a defined risk group during an outbreak			O	

Notes:

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

N = All “N” criteria in the same column are Necessary to report a case.

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

\* A requisition or order for any of the “S” laboratory tests is sufficient to meet the reporting criteria.

**C. Disease-specific data elements**

Disease-specific data elements to be included in the initial report are listed below.

*Clinical Findings*

Duration of cough

*Epidemiologic risk factors*

Immunization history

Number of doses of DTaP received

Date of last DTaP vaccination

Whether a dose of Tdap vaccine was given to a patient ≥10 years of age

Date of Tdap vaccination

Contact with a known or suspected pertussis case

Contact with a high-risk individual (e.g., infant or pregnant woman)

**VII. Case Definition for Case Classification**

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

**Clinical Criteria**



In the absence of a more likely diagnosis, a cough illness lasting  $\geq 2$  weeks, with at least one of the following signs or symptoms:

- Paroxysms of coughing; *or*
- Inspiratory whoop; *or*
- Post-tussive vomiting; *or*
- Apnea (with or without cyanosis) (FOR INFANTS AGED  $< 1$  YEAR ONLY)

#### Laboratory Criteria

- Isolation of *B. pertussis* from a clinical specimen
- Positive PCR for pertussis

#### Epidemiologic Linkage

- Contact with a laboratory-confirmed case of pertussis\*

#### Case Classification

**\*Note:** An illness meeting the clinical case definition should be classified as “probable” rather than “confirmed” if it occurs in a patient who has contact with an infant aged  $< 1$  year who is PCR positive for pertussis and has  $\geq 1$  sign or symptom and cough duration  $< 14$  days (classified as “probable” case).

#### Confirmed:

- Acute cough illness of any duration, with isolation of *B. pertussis* from a clinical specimen.

OR

- Cough illness lasting  $\geq 2$  weeks, with
  - At least one of the following signs or symptoms:
    - Paroxysms of coughing; or
    - Inspiratory “whoop”; or
    - Post-tussive vomiting; or
    - Apnea (with or without cyanosis)(FOR INFANTS AGED  $< 1$  YEAR ONLY)

*and*

- Polymerase chain reaction (PCR) positive for pertussis.

OR

- Cough illness lasting  $\geq 2$  weeks, with
  - At least one of the following signs or symptoms:
    - Paroxysms of coughing; or
    - Inspiratory “whoop”; or
    - Post-tussive vomiting; or
    - Apnea (with or without cyanosis)(FOR INFANTS AGED  $< 1$  YEAR ONLY)

*and*

- Contact with a laboratory-confirmed case of pertussis\*.

#### Probable

- In the absence of a more likely diagnosis, a cough illness lasting  $\geq 2$  weeks, with



- At least one of the following signs or symptoms:
  - Paroxysms of coughing; or inspiratory "whoop"; or
  - Post-tussive vomiting; or
  - Apnea (with or without cyanosis)(FOR INFANTS AGED<1 YEAR ONLY)

*and*

- Absence of laboratory confirmation;

*and*

- No epidemiologic linkage to a laboratory-confirmed case of pertussis.

OR, FOR INFANTS AGED<1 YEAR ONLY

- Acute cough illness of any duration, with
  - At least one of the following signs or symptoms:
    - Paroxysms of coughing; or
    - Inspiratory "whoop"; or
    - Post-tussive vomiting; or
    - Apnea (with or without cyanosis)

*and*

- Polymerase chain reaction (PCR) positive for pertussis.

OR, FOR INFANTS AGED <1 YEAR ONLY

- Acute cough illness of any duration, with
  - At least one of the following signs or symptoms:
    - Paroxysms of coughing; or
    - Inspiratory "whoop"; or
    - Post-tussive vomiting; or
    - Apnea (with or without cyanosis)

*and*

- Contact with a laboratory-confirmed case of pertussis.

**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**

Not applicable.



**B. Classification Tables**

Criterion	Confirmed			Probable			
	1	2	3	1	2 (FOR INFANTS <1 YEAR ONLY)	3 (FOR INFANTS <1 YEAR ONLY)	4
<i>Clinical Evidence</i>							
Acute cough illness (any duration)	N				N	N	
Cough ≥2 weeks duration		N	N	N			N
Inspiratory whoop		O	O	O	O	O	O
Paroxysms of coughing		O	O	O	O	O	O
Post-tussive vomiting		O	O	O	O	O	O
Apnea (with or without cyanosis), (FOR INFANTS <1 YEAR OF AGE ONLY)		O	O	O	O	O	O
<i>Laboratory Evidence</i>							
Isolation of B. pertussis from a clinical specimen	N						
Positive PCR for pertussis		N			N		
<i>Epidemiological Evidence</i>							
Contact with a laboratory-confirmed case (classified as “confirmed”)			N			O	
Contact with a laboratory-confirmed infant case (classified as “probable”)						O	N

Notes:

S = This criterion alone is Sufficient to classify a case.

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).

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

O = At least one of these “O” (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all “N” criteria in the same column—is required to classify a case. (These optional criteria are alternatives, which means that a single column will have either no O criteria or multiple O criteria; no column should have only one O.) A number following an “O” indicates that this criterion is only required for a specific disease/condition subtype.

**VIII. Period of Surveillance**

Surveillance should be on-going.

**IX. Data sharing/release and print criteria**

Notification to CDC for confirmed and probable cases is recommended.

- Pertussis cases reported electronically through NNDSS are summarized weekly in the MMWR Notifiable Diseases tables and yearly in the MMWR Surveillance Summaries. Additional epidemiologic summaries may be published in the MMWR or peer-reviewed journals.
- State-specific compiled data will continue to be published in the weekly and annual MMWR. Twice annually, reports of state-level case counts, incidence, and fatalities are sent to state and territory partners from the NCIRD program to ensure case reports received at CDC are accurate.



- State-specific compiled data will continue to be published in the weekly reports and annual MMWR Surveillance Summaries. Aggregate data are included in PAHO and WHO annual reports. The frequency of additional publication of this data, in the MMWR and peer-reviewed journals, will be dependent on current epidemiology of disease at the national level.
- We currently report aggregate data on cases of pertussis reported through NNDSS to PAHO on a yearly basis. No personal identifying or state specific information is re-released to PAHO, WHO, or other parties

## X. References

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## XI. Coordination

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