Committee: Infectious Disease

Title: Update to Rubella Case Definition

I. Statement of the Problem
The current case definition for Rubella does not provide for consistent classification of cases with only laboratory evidence of current or recent infection (IgM positive), but lack of clinical symptoms. Additional detail is needed to accurately classify positive serologic tests for rubella IgM antibody without further testing.

II. Background and Justification

Background
Endemic rubella transmission was declared eliminated in the United States in 2004. Despite progress in the United States, there is still risk of rubella importations and rubella outbreaks, especially if transmission of imported disease occurs in unvaccinated communities. In addition to sustained high vaccine coverage, sensitive rubella surveillance with thorough public health response to every rubella case is required to prevent re-establishment of endemic disease transmission. Accurate case definition criteria prevent delays in reporting of rubella cases to the Nationally Notifiable Disease Surveillance System (NNDSS) resulting in timely reporting of current rubella cases to state, national, and international partners.

Justification
Rubella meets the following criteria for a nationally and immediately notifiable condition as specified in CSTE position statement 08-EC-02:

- The condition has been declared eliminated (absence of endemic disease transmission) in the United States.
- A majority of state and territorial jurisdictions—or jurisdictions comprising a majority of the US population—have laws or regulations requiring immediate reporting of rubella to public health authorities;
- The Centers for Disease Control and Prevention (CDC) requests immediate notification of rubella; and
- the CDC has condition-specific policies and practices concerning its response to, and use of, notifications.

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

CSTE recommends that States and Territories conducting surveillance according to these methods report case information to CDC.

We propose to update the case definition for rubella to better align clinical and laboratory evidence of infection with case classification criteria.

IV. Goals of Surveillance
To rapidly identify and contain any rubella importations into the United States

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

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Table V. Recommended sources of data and extent of coverage for ascertaining cases of Rubella.
### VI. Criteria for case identification

Reporting refers to the process of healthcare providers or institutions (e.g., clinicians, clinical laboratories, hospitals) submitting basic information to governmental public health agencies about cases of illness that meet certain reporting requirements or criteria. The purpose of this section is to provide those criteria to determine whether a specific illness should be reported.

#### A. Narrative: A description of suggested criteria that may be for case ascertainment of a specific condition.

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

1. **Acute illness with fever and rash in a person with any epidemiological linkage as listed below and without a more compelling diagnosis:**
   - Contact of a confirmed rubella case
   - Belonging to a defined risk group during an outbreak
   - Residence in a geographic area of the US where an outbreak of rubella is occurring
   - Travel during the 21 days before illness onset to a geographic area where an outbreak of rubella is occurring

2. **Acute illness with fever and rash in a person for whom any of the diagnostic tests listed below has been ordered:**
   - Culture rubella virus
   - PCR, rubella-specific nucleic acid
   - Rubella IgM antibody
   - Acute and convalescent rubella IgG antibodies

3. **Acute illness with fever, generalized, maculopapular rash and at least one of the 3 symptoms listed below, without a more compelling diagnosis:**
   - Lymphadenopathy (cervical)
   - Arthralgia or arthritis
   - Conjunctivitis

### Other recommended reporting procedures

- All cases of rubella should be reported.
- Reporting should be on-going and routine.
- Reporting should be immediate.
B. Table of criteria to determine whether a case should be reported to public health authorities

Requirements for reporting are established under State and Territorial laws and/or regulations and may differ from jurisdiction to jurisdiction. These criteria are suggested as a standard approach to identifying cases of this condition for purposes of reporting, but reporting should follow State and Territorial law/regulation if any conflicts occur between these criteria and those laws/regulations.

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

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Reporting*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Fever &gt; 99.0° F (37.2° C)</td>
<td>N N N</td>
</tr>
<tr>
<td>Rash: generalized maculopapular</td>
<td>N N N</td>
</tr>
<tr>
<td>Lymphadenopathy (cervical)</td>
<td>O</td>
</tr>
<tr>
<td>Arthralgia or arthritis</td>
<td>O</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>O</td>
</tr>
<tr>
<td>Absence of a more compelling diagnosis</td>
<td>N N</td>
</tr>
<tr>
<td><strong>Laboratory Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Culture rubella virus</td>
<td>O*</td>
</tr>
<tr>
<td>PCR, rubella-specific nucleic acid</td>
<td>O*</td>
</tr>
<tr>
<td>Rubella IgM antibody</td>
<td>O*</td>
</tr>
<tr>
<td>Acute and convalescent rubella IgG antibodies</td>
<td>O*</td>
</tr>
<tr>
<td><strong>Epidemiological Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Contact of a confirmed rubella case</td>
<td>O</td>
</tr>
<tr>
<td>Belonging to a defined risk group during an outbreak</td>
<td>O</td>
</tr>
<tr>
<td>Residence in a geographic area of the US where an outbreak of rubella is occurring</td>
<td>O</td>
</tr>
<tr>
<td>Travel during the 21 days before illness onset to a geographic area where an outbreak of rubella is occurring</td>
<td>O</td>
</tr>
</tbody>
</table>

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 “O” laboratory tests—in conjunction with all “N” criteria in the same column—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 information
- Date of onset, fever
- Date of onset, rash

Epidemiological Risk Factors
- Contact with rubella case
- Destination(s) of recent travel (if any)
- Date of return from travel
- Total doses rubella-containing vaccine
VII. Case Definition for Case Classification

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

Suspected: Any generalized rash illness of acute onset that does not meet the criteria for probable or confirmed rubella or any other illness.

Probable: In the absence of a more likely diagnosis, an illness characterized by all of the following:
- acute onset of generalized maculopapular rash; and
- temperature greater than 99.0° F or 37.2° C, if measured; and
- arthralgia, arthritis, lymphadenopathy, or conjunctivitis; and
- lack of epidemiologic linkage to a laboratory-confirmed case of rubella; and
- noncontributory or no serologic or virologic testing.

Confirmed:
- A case with or without symptoms who has laboratory evidence of rubella infection confirmed by one or more of the following laboratory tests:
  - isolation of rubella virus; or
  - detection of rubella-virus specific nucleic acid by polymerase chain reaction; or
  - IgG seroconversion or a significant rise between acute- and convalescent-phase titers in serum rubella IgG antibody level by any standard serologic assay; or
  - positive serologic test for rubella IgM antibody†

OR

- An illness characterized by all of the following:
  - acute onset of generalized maculopapular rash; and
  - temperature greater than 99.0°F or 37.2°C; and
  - arthralgia, arthritis, lymphadenopathy, or conjunctivitis; and
  - epidemiologic linkage to a laboratory-confirmed case of rubella.

†Not explained by MMR vaccination during the previous 6-45 days.
*Not otherwise ruled out by more specific testing in a public health laboratory.

Epidemiologic Classification of Internationally-Imported and U.S.-Acquired

Internationally imported case: An internationally imported case is defined as a case in which rubella results from exposure to rubella virus outside the United States as evidenced by at least some of the exposure period (12–23 days before rash onset) occurring outside the United States and the onset of rash within 23 days of entering the United States and no known exposure to rubella in the United States during that time. All other cases are considered U.S.-acquired cases.

U.S.-acquired case: A U.S.-acquired case is defined as a case in which the patient had not been outside the United States during the 23 days before rash onset or was known to have been exposed to rubella within the United States. These cases are subclassified into four mutually exclusive groups:

Import-linked case: Any case in a chain of transmission that is epidemiologically linked to an internationally imported case.
Imported-virus case: a case for which an epidemiologic link to an internationally imported case was not identified but for which viral genetic evidence indicates an imported rubella genotype, i.e., a genotype that is not occurring within the United States in a pattern indicative of endemic transmission. An endemic genotype is the genotype of any rubella virus that occurs in an endemic chain of transmission (i.e., lasting \( \geq 12 \) months). Any genotype that is found repeatedly in U.S.-acquired cases should be thoroughly investigated as a potential endemic genotype, especially if the cases are closely related in time or location.

Endemic case: a case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of rubella virus transmission continuous for \( \geq 12 \) months within the United States.

Unknown source case: a case for which an epidemiological or virological link to importation or to endemic transmission within the U.S. cannot be established after a thorough investigation. These cases must be carefully assessed epidemiologically to assure that they do not represent a sustained U.S.-acquired chain of transmission or an endemic chain of transmission within the U.S.

Note: Internationally imported, import-linked, and imported-virus cases are considered collectively to be import-associated cases. States may also choose to classify cases as “out-of-state-imported” when imported from another state in the United States. For national reporting, however, cases will be classified as either internationally imported or U.S.-acquired.

Comments: Serum rubella IgM test results that are false positives have been reported in persons with other viral infections (e.g., acute infection with Epstein-Barr virus [infectious mononucleosis], recent cytomegalovirus infection, and parvovirus infection) or in the presence of rheumatoid factor. Patients who have laboratory evidence of recent measles infection are excluded.

B. Classification Tables

Table VII-B lists the criteria that must be met for a case to be classified as confirmed, probable (presumptive), or suspected (possible).

Table VII-B. Proposed table of criteria to determine whether a case is classified.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Case Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Rash: generalized maculopapular</td>
<td>N</td>
</tr>
<tr>
<td>Fever &gt; 99.0° F (37.2° C)</td>
<td>N</td>
</tr>
<tr>
<td>Lymphadenopathy (cervical)</td>
<td>O</td>
</tr>
<tr>
<td>Arthralgia or arthritis</td>
<td>O</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>O</td>
</tr>
<tr>
<td>Absence of a more likely diagnosis</td>
<td></td>
</tr>
<tr>
<td><strong>Laboratory Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Culture rubella virus</td>
<td>S</td>
</tr>
<tr>
<td>PCR, rubella-specific nucleic acid</td>
<td>S</td>
</tr>
<tr>
<td>IgG seroconversion*</td>
<td>S</td>
</tr>
<tr>
<td>Significant rise in serum anti-rubella IgG antibodies</td>
<td>S</td>
</tr>
<tr>
<td>Positive serologic test for rubella IgM antibody†*</td>
<td>S</td>
</tr>
<tr>
<td>Noncontributory or no serologic or virologic testing</td>
<td>N</td>
</tr>
<tr>
<td><strong>Epidemiological Evidence</strong></td>
<td></td>
</tr>
</tbody>
</table>

Epidemiologic linkage to a laboratory-confirmed case

<table>
<thead>
<tr>
<th>Notes:</th>
<th>N</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>S = This criterion alone is Sufficient to classify a case.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A = This criterion must be absent (i.e., NOT present) for the case to meet the reporting criteria.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Not explained by MMR vaccination during the previous 6-45 days.

*Not otherwise ruled out by more specific testing in a public health laboratory.

VIII. Period of Surveillance

Surveillance should be ongoing.

IX. Data sharing/release and print criteria

- Notification to CDC for confirmed cases of rubella is recommended.
- Data reported to NCIRD staff is summarized weekly internally via an NCIRD weekly surveillance report for vaccine preventable diseases. Electronic reports of rubella cases in NNDSS are also summarized weekly in the MMWR Tables. However, because of delays in data entry and data transmission via NNDSS, these two data sources may not correspond. Annual case data on rubella is used in the yearly Summary of Notifiable Diseases. Cumulative data is used for Healthy People 2010 reviews.
- State-specific compiled data will continue to be published in the weekly NCIRD reports as well as annual MMWR Summaries of Notifiable Diseases. In addition to those reports, the frequency of reports/feedback to the states and territories will be dependent on the current epidemiologic situation surrounding the case patient. Frequency of cases, epidemiologic distribution, importation status, transmission risk to non-immune pregnant females will guide frequency and method of communication and information feedback.
- State-specific compiled data will continue to be published in the weekly reports and annual MMWR Surveillance Summaries. All cases are verified with the state(s) before publication. Data are also included in PAHO and WHO annual reports. The frequency of release of additional publication of this data will be dependent on the current epidemiologic situation in the country. These publications might include annual epidemiologic summaries in the MMWR or manuscripts in peer-reviewed journals.
- As part of an effort to document rubella elimination in the Americas, we will share data on rubella cases known to NCIRD with PAHO. Rubella is endemic outside the Western Hemisphere, also in Argentina and Brazil. Although no longer endemic in the U.S., rubella continues to be identified due to importation. NCIRD shares rubella case information with the Division of Global Migration & Quarantine, CDC, when potential for air travel transmission exists. State Health Departments are notified when cases are identified communicable in their jurisdiction. Rubella information will be shared with PAHO upon request such as sex, age, rash onset, vaccination status, genotype and source (import, import-associated etc.). No personal identifying or state specific information is re-released to PAHO or WHO.
X. References


XI. Coordination

Agencies for Response

(1) Centers for Disease Control and Prevention
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