07-ID-05

Committee: Infectious Diseases

Title: Revision of the Surveillance Case Definition for Rocky Mountain spotted fever

Statement of the Problem:

The purpose of the recommended revisions to the surveillance case definition of Rocky Mountain spotted fever (RMSF), a tick-borne rickettsial disease under public health surveillance, is to clarify misleading or poorly defined laboratory statements, and to improve case classification for reporting.

Statement of the desired action to be taken:

Revise the national surveillance case definition for Rocky Mountain spotted fever (RMSF).

Goals of surveillance:

The improved case definition will provide the tools to help establish the burden of disease due to this pathogen. This will provide a greater understanding of this disease among physicians, nurses, and public health professionals and allow for appropriate prevention messages to the public.

Methods for surveillance:

Case finding is conducted through clinician and laboratory reporting. Core surveillance data will be reported to the National Notifiable Disease Surveillance System (NNDSS) through the National Electronic Telecommunications System for Surveillance (NETSS) or the National Electronic Disease Surveillance System (NEDSS), as per state protocol.

Case Definition:

Clinical presentation

Rocky Mountain spotted fever (RMSF) is an illness caused by *Rickettsia rickettsii*, a bacterial pathogen transmitted to humans through contact with ticks. *Dermacentor* species of ticks are most commonly associated with infection, including *Dermacentor variabilis* (the American dog tick), *Dermacentor andersoni* (the Rocky Mountain wood tick), and more recently *Rhiphicephalus sanguineus* (the brown dog tick). Disease onset averages one week following a tick bite. Age-specific illness is highest for children and older adults. Illness is characterized by acute onset of fever, and may be accompanied by headache, malaise, myalgia, nausea/vomiting, or neurologic signs; a macular or maculopapular rash appears 4-7 days following onset in many (~80%) patients, often present on the palms and soles. RMSF may be fatal in as many as 20% of untreated cases, and severe, fulminant disease can occur. Acute illness is best detected by polymerase chain reaction (PCR) and immunohistochemical methods (IHC) in skin biopsy specimens, and occasionally by PCR in appropriate whole blood specimens taken during the 1st week of illness, prior to antibiotic treatment. Serology can also be employed for detection, however an antibody response may not be detectable in initial samples, and paired acute and convalescent samples are essential for confirmation.

Clinical evidence:

Any reported fever and one or more of the following: rash, headache, myalgia, anemia, thromobocytopenia, or any hepatic transaminase elevation.

Laboratory evidence:

For the purposes of surveillance,

Laboratory confirmed:

- Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer reactive with *Rickettsia rickettsii* antigen by indirect immunofluorescence assay (IFA) between paired serum specimens (one taken in the first week of illness and a second 2-4 weeks later), **or**
- Detection of *R. rickettsii* DNA in a clinical specimen via amplification of a specific target by PCR assay, **or**
- Demonstration of spotted fever group antigen in a biopsy/autopsy specimen by IHC, **or**
- Isolation of *R. rickettsii* from a clinical specimen in cell culture.

Laboratory supportive:

- Has serologic evidence of elevated IgG or IgM antibody reactive with *R. rickettsii* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination.

Note: Current commercially available ELISA tests are not quantitative, cannot be used to evaluate changes in antibody titer, and hence are not useful for serological confirmation. IgM tests are not strongly supported for use in serodiagnosis of acute disease, as the response may not be specific for the agent (resulting in false positives) and the IgM response may be persistent. Complement fixation (CF) tests and other older test methods are neither readily available nor commonly used.

CDC uses in-house IFA IgG testing (cutoff of $\geq$1:64), preferring simultaneous testing of paired specimens, and does not use IgM results for routine diagnostic testing.

Exposure:

Exposure is defined as having been in potential tick habitats within the past 14 days before onset of symptoms. A history of a tick bite is not required.

Case definition tables:

Suggested codes for case ascertainment

To be developed.

Detailed definitions for case classification

Confirmed: A clinically compatible case (meets clinical evidence criteria) that is laboratory confirmed.

Probable: A clinically compatible case (meets clinical evidence criteria) that has supportive laboratory results.

Suspect: A case with laboratory evidence of past or present infection but no clinical information available (e.g. a laboratory report).

Period of surveillance:

Ongoing. This revision of the surveillance case definition will be effective January 1, 2008.

Data sharing/release and print criteria:

States and territories will send CDC case data for all confirmed and probable cases. Final printed counts published in MMWR by CDC will distinguish between confirmed and probable cases. Provisional case report data will not be used until verification procedures are completed. Suspect cases will be excluded from final printed counts published by CDC.

Background and Justification:
The case definition for RMSF was last modified in 2004. CDC has noted an increase in calls from state epidemiologists regarding case classification. For many years, the case definition of RMSF relied upon testing conducted at either the CDC or at the state public health laboratories. Recently, a growing number of case reports have included commercial laboratory results as supportive evidence. The proposed revised case definition attempts to clarify the details of the testing as it has been traditionally conducted. For example, the previous case definitions have used the word “antibody”. A review of testing protocols and reagents distributed to the state laboratories reveal that these existing tests were specific for IgG-class immunoglobulins. With the increased availability of IgM testing at commercial laboratories, it becomes necessary to clarify the traditional meaning of the word “antibody” as used in all previous definitions and routinely used by rickettsial laboratories. The use of IgM is less supported by scientific evidence, and actually is complicated by false negatives when IgG is present and false positives when rheumatoid factor or cross-reactive, non-rickettsial, antibodies are present. Thus, IgM testing cannot be recommended for confirmation of cases at this time.

References:

- 2004 Case Definition
- 1996 Case Definition
- 1990 Case Definition

Coordination:

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