

07-ID-13

Committee: Infectious Disease

Title: Revision of the Surveillance Case Definition for Coccidioidomycosis

The purpose of this recommended revision to the surveillance case definition for coccidioidomycosis is to more accurately reflect current laboratory diagnosis of coccidioidomycosis (Appendix A). Recommended revisions to the coccidioidomycosis surveillance case definition primarily involve the following:

The proposed changes would allow a positive serologic test (any of several clinically accepted methods) for IgG without a confirmation of a rising IgG titer to be sufficient for case confirmation (Appendix A). If this change to the laboratory criteria is adopted, it is also recommended that health departments performing surveillance for coccidioidomycosis check for and remove duplicate cases during the previous five years, at minimum.

Statement of problem:

A single positive IgG by any one of several serologic tests for coccidioidomycosis (Appendix A) is sufficient for clinical diagnosis of coccidioidomycosis in a patient living in or having recently traveled to *Coccidioides* endemic areas, with a clinically compatible syndrome [1]. However, under the current surveillance case definition, a single positive IgG for coccidioidomycosis is not sufficient for case confirmation (Appendix B).

Unlike serologic tests for other infections, the majority of positive serologic tests for IgG among patients with coccidioidomycosis revert to negative within one year [1]. In a minority of patients with coccidioidomycosis, such as patients who develop chronic disease (<1%), disseminated disease (<1%), or asymptomatic pulmonary residua (about 5%), IgG may persist [1, 2]. It is therefore possible that a small number of cases with persistently positive serology would be reported by laboratories in more than one year. However, it is common surveillance practice to remove duplicate cases reported in previous years, such as with HIV. This practice would likely address problems surrounding multiple reporting of case-patients with persistently positive IgG, especially if the de-duplication procedure involves several previous years (e.g. five years).

In 1997, Arizona Department of Health Services (ADHS) adopted a case definition for their *Coccidioides* surveillance involving one positive IgG serology. ADHS has procedures for removal of duplicates to avoid double reporting and have had success with this modified case definition.

In light of the current understanding of *Coccidioides* serology and clinical diagnosis of coccidioidomycosis, and an inability of the current surveillance case definition to classify many clinically relevant cases of coccidioidomycosis as confirmed cases, we conducted a consultation with experts from state and local health departments, CDC and the academic community. The goals of this consultation were to:

- 1) Review the current case definition for coccidioidomycosis and the proposals for revision
- 2) Review evidence for changes that would simplify and improve the case definition for coccidioidomycosis based on current scientific evidence, and ultimately
- 3) Recommend revisions to the surveillance case definition for coccidioidomycosis.

Consultation participants included experts in coccidioidomycosis surveillance and epidemiology, and in clinical infectious diseases with particular expertise in the diagnosis of coccidioidomycosis. Consultants represented CDC, state and local health departments from all six states in the U.S. endemic area (AZ, CA, NM, NV, TX, UT), and the academic community. Upon conclusion of the consultation, a plan was composed for revision of the case definition (see Statement of Desired Action below). If implemented, the revised definition (Appendix A) will supersede the 1996 case definition for coccidioidomycosis (Appendix B)

Statement of desired action to be taken:

CSTE recommends adoption of the new surveillance case definition for coccidioidomycosis, as presented in Appendix A. In conjunction with this new case definition, CSTE also recommends that state and/or local health departments performing surveillance for coccidioidomycosis have procedures for removing duplicate case-patients, reported within the previous five years.

Public health impact:

All proposed changes to the coccidioidomycosis surveillance case definition are shown in Appendix A. There are several benefits of this new definition.

- 1) **Increased Representativeness.** The acceptance of serologic evidence involving a single positive IgG (with or without a confirmation of a rising IgG titer) as sufficient for case confirmation, will allow surveillance data to better reflect the true disease burden. Since the adoption of this change will also increase simplicity and acceptability and decrease cost (see below, Public Health Impact #2), laboratory-based reporting is more likely to be adopted by state and local health departments, thereby also increasing representativeness.
- 2) **Increased Simplicity and Acceptability and Decreased Cost.** Since the current case definition requires confirmation of a rising IgG titer, extensive resources are required to perform follow up of laboratory reports of a positive IgG serology to assess whether a second IgG serology has been performed and whether these results represent a rising titer. State and local health departments currently requiring laboratory-based reporting differ in their methods for handling a single positive IgG serology, in large part due to differences in health department resources to perform follow up. For example, some health departments requiring laboratory reporting are able to perform follow up on all positive IgG serologic tests to attempt to confirm a rising titer, while others are unable to perform follow up. The proposed changes will obviate the need for such follow up and improve uniformity among state and local health departments. In summary, surveillance for coccidioidomycosis will be simpler, more acceptable to stakeholders, and require fewer resources from health departments.

Other minor modifications are proposed:

- 1) Primary pulmonary coccidioidomycosis, the most important clinical syndrome, encompasses a syndrome accurately described as both “influenza-like” and “pneumonia-like” [3]. Therefore, it is proposed that the clinical description include disease which “resembles influenza-like or pneumonia-like febrile illness” (Appendix A).
- 2) It is proposed that “*Coccidioides immitis*” be changed to “*Coccidioides* species” since it is now recognized that more than one *Coccidioides* species may cause coccidioidomycosis [4].
- 3) Although positive serologic tests for coccidioidal antibodies from other body fluids (e.g. pleural fluid, peritoneal fluid), are much less common than tests from serum and cerebrospinal fluid, they are also clinically diagnostic of coccidioidomycosis [1]. It is therefore proposed that “other body fluids” be added as an acceptable specimen type in the case definition (Appendix A).

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2. Chiller TM, Galgiani JN, Stevens DA. Coccidioidomycosis. *Infect Dis Clin North Am* **2003** Mar;17(1):41-57, viii.

3. Valdivia L, Nix D, Wright M, et al. Coccidioidomycosis as a common cause of community-acquired pneumonia. *Emerg Infect Dis* **2006** Jun;12(6):958-62.
4. Saubolle MA. Laboratory Aspects in the Diagnosis of Coccidioidomycosis. *Ann N Y Acad Sci* **2007** Mar 15.

**APPENDIX A:
2007 CSTE Case Definition for Coccidioidomycosis**

CLINICAL DESCRIPTION

Infection may be asymptomatic or may produce an acute or chronic disease. Although the disease initially resembles an influenza-like or pneumonia-like febrile illness primarily involving the bronchopulmonary system, dissemination can occur to multiple organ systems.

CLINICAL CASE DEFINITION

An illness characterized by one or more of the following:

- Influenza-like signs and symptoms (e.g., fever, chest pain, cough, myalgia, arthralgia, and headache)
- Pneumonia or other pulmonary lesion, diagnosed by chest radiograph
- Erythema nodosum or erythema multiforme rash
- Involvement of bones, joints, or skin by dissemination
- Meningitis
- Involvement of viscera and lymph nodes

LABORATORY CRITERIA FOR DIAGNOSIS

A confirmed case must meet at least one of the following laboratory criteria for diagnosis:

- Cultural, histopathologic, or molecular evidence of presence of *Coccidioides* species, or
- Positive serologic test for coccidioidal antibodies in serum, cerebrospinal fluid, or other body fluids by:
 - Detection of coccidioidal immunoglobulin M (IgM) by immunodiffusion, enzyme immunoassay (EIA), latex agglutination, or tube precipitin, or
 - Detection of coccidioidal immunoglobulin G (IgG) by immunodiffusion, EIA, or complement fixation, or
- Coccidioidal skin-test conversion from negative to positive after onset of clinical signs and symptoms

CASE CLASSIFICATION

Confirmed: A case that meets the clinical case definition and is laboratory confirmed.

**APPENDIX B:
1996 CSTE Case Definition for Coccidioidomycosis (Revised 1996)**

CLINICAL DESCRIPTION

Infection may be asymptomatic or may produce an acute or chronic disease. Although the disease initially resembles an influenza-like febrile illness primarily involving the bronchopulmonary system, dissemination can occur to multiple organ systems.

CLINICAL CASE DEFINITION

An illness characterized by one or more of the following:

- Influenza-like signs and symptoms (e.g., fever, chest pain, cough, myalgia, arthralgia, and headache)
- Pneumonia or other pulmonary lesion, diagnosed by chest radiograph
- Erythema nodosum or erythema multiforme rash
- Involvement of bones, joints, or skin by dissemination
- Meningitis
- Involvement of viscera and lymph nodes

LABORATORY CRITERIA FOR DIAGNOSIS

- Cultural, histopathologic, or molecular evidence of presence of *Coccidioides immitis*, or
- Positive serologic test for coccidioidal antibodies in serum or cerebrospinal fluid by:
 - Detection of coccidioidal immunoglobulin M (IgM) by immunodiffusion, enzyme immunoassay (EIA), latex agglutination, or tube precipitin, or
 - Detection of rising titer of coccidioidal immunoglobulin G (IgG) by immunodiffusion, EIA, or complement fixation, or
- Coccidioidal skin-test conversion from negative to positive after onset of clinical signs and symptoms

CASE CLASSIFICATION

Confirmed: A case that meets the clinical case definition and is laboratory confirmed.