Clinical Chemistry

# Disseminated Coccidioidomycosis in Immunocompetent Hosts: Opportunities for Increased Recognition and Timely Diagnosis

**Article:**
Anna C H Hoge, Thomas E Grys, Erin H Graf.
*Disseminated Coccidioidomycosis in Immunocompetent Hosts: Opportunities for Increased Recognition and Timely Diagnosis.*
Clin Chem 2026; 72(5): 575–82. https://doi.org/10.1093/clinchem/hvaf187

**Guests:** Dr. Anna Hoge is a resident physician in internal medicine at the University of Washington, conducting microbiome and genomics research. Dr. Erin Graf is an Associate Professor and Co-Director of Microbiology at the Mayo Clinic in Phoenix, Arizona.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett.

Pulmonary coccidioidomycosis, also known as Valley Fever, is caused by soil-dwelling fungi commonly found in the southwestern United States and other desert regions. When the soil is disturbed, the fungal spores become airborne and can enter the lungs through inhalation. In most individuals, infection is asymptomatic. Others experience flu-like symptoms but clear the infection without medical intervention. In a very small subset of patients, the infection leaves the lungs and lodges in other tissues, including skin, bones, and the central nervous system.

This is where it gets scary, as approximately one-third of patients with disseminated disease die of the infection. Which patients are at greater risk of progressive infection? And what tools can medical providers use to rapidly identify and resolve infection at an early stage? A new research article in the May 2026 issue of *Clinical Chemistry* performs a retrospective review of infections in immunocompetent individuals to gain insight into these questions.

Today, we are joined by two of the article's authors. Dr. Anna Hoge is a resident physician in internal medicine at the University of Washington, conducting microbiome and genomics research. Dr. Erin Graf is an Associate Professor and Co-Director of Microbiology at the Mayo Clinic in Phoenix, Arizona and Dr. Hoge, let's start with you. Could you please provide some background on coccidioidomycosis and explain why disseminated disease remains such an important clinical concern?

Anna Hoge: Yeah, of course. Coccidioidomycosis, or cocci, is an infection caused by fungi of the genus *Coccidioides* and as these fungi are endemic to semi-arid regions of the western hemisphere, and these regions are expanding, the geographic range of *Coccidioides* is expanding, putting more people at risk of infection. And pulmonary coccidioidomycosis is a common

cause of community-acquired pneumonia in endemic areas, up to about 25% of cases, and these infections are often self-limiting, so antifungal treatment is only recommended for patients with severe disease or risk factors for severe disease but cocci can be complicated by extrapulmonary dissemination weeks to years after the initial pulmonary infection. And disseminated coccidioidomycosis remains such an important clinical concern because morbidity and mortality are high.

So, disseminated disease requires long-term, if not lifelong, antifungal treatment to try to prevent further progression, for example, to the central nervous system. And disseminated cocci is, unfortunately, fatal in roughly one-third of cases.

Bob Barrett: Okay, Dr. Graf, let's turn to you. Many clinicians associate disseminated coccidioidomycosis with immunocompromised patients. What prompted your team to specifically focus on immunocompetent hosts?

Erin Graf: Thanks so much, Bob. We were really interested in this question because as Dr. Hoge was rotating as a medical student in our lab, we noticed an uptick in disseminated cases in this particular population, in immunocompetent hosts, that appeared to have some significant delays in recognition. So often, the micro lab is the first to find evidence of cocci. So, when she was rotating, we were seeing it grow in routine bacterial cultures in cases in which a fungal culture wasn't even ordered and it wasn't really on the differential. And then it was kind of a surprise to the care team that we had this mold growing in the laboratory. And some of these delays were really devastating to read about in terms of the morbidity associated with the worsening of disease.

In the immunocompromised population, obviously, those folks are at risk for a much broader array of potentially life-threatening infections and as a result, appropriately, they're followed more closely and worked up more broadly. But that's different with immunocompetent patients, who may have more subacute signs and symptoms or not really apparently life-threatening infections with something like cocci. And so we really wanted to focus on this population and highlight some of these issues with delays and under-recognition, really with the hopes of broadening awareness.

Bob Barrett: Dr. Hoge, one of your striking findings was that many patients initially presented for care within endemic regions. What does this tell us about current awareness of the disease among frontline healthcare providers?

Anna Hoge: I think most clinicians in endemic areas have a general awareness of cocci, but as Dr. Graf mentioned, diagnostic delays are really common, leading to further healthcare visits,

unnecessary use of antibiotics, and disease progression. There are multiple reasons for these diagnostic delays.

Firstly, the symptoms of disseminated cocci are nonspecific. The patients in our study presented with back pain, joint pain, subcutaneous masses, severe headaches, skin lesions, abdominal pain, and flu-like illnesses, and clinicians might consider more common causes of these conditions before pursuing testing for cocci, especially in immunocompetent patients. And we know that rates of testing for cocci are quite low, even when suspicion should remain high.

So, only a small percentage of patients presenting with community-acquired pneumonia in endemic areas are tested for pulmonary cocci and the reasons for these low testing rates are likely multifactorial. So, for example, prior studies have noted that uninsured patients are tested less frequently and that ER doctors cite difficulty arranging proper follow-up for patients as a barrier to ordering testing. And finally, diagnostic delays may be due in part to limitations with the currently available testing. So, there are multiple serologic tests, which can require careful interpretation, and clinicians may be confused about which ones to order. And then, getting specimens required for culture or histopathology might be difficult.

Bob Barrett: Okay. Dr. Graf, could you discuss the role of serologic testing and explain why the immunoglobulin G enzyme immunoassay emerged as a particularly useful screening tool?

Erin Graf: Sure. Dr. Hoge did a great job of just describing some of the complexities around the different testing modalities for cocci and this is really often cited as a reason for not testing or not being sure how to manage the follow-up related to the delays associated with serologic testing. So, in our study, we were fortunate that at our institution, folks tend to order the big three available assays for serologic testing, which is the enzyme immunoassay, or the EIA, along with complement fixation and immunodiffusion. Now, those two latter methodologies, they're older, and they're far more manual and complex to run in terms of testing and so they're limited to specialized laboratories -- specialized reference laboratories, a few centers across the United States.

The EIA, however, there are now a few FDA-cleared options and so that is helpful in that it can be more broadly used. FDA-cleared assays, particularly EIAs, which can be adapted to a number of different serologic testing platforms, kind of open up the window for more laboratories to take this testing on and so we were just interested in the findings overall of how those three different antibody assays performed with this particular question in mind of disseminated infection in immunocompetent hosts.

Bob Barrett: So Dr. Hoge, what are the most important points laboratorians and clinicians should understand when selecting and interpreting coccidioides antibody assays?

Anna Hoge: I think the most important point is to start with the IgG EIA test, which is available at most of the major reference laboratories that serve U.S. practices. In our study, the IgG EIA test was 100% sensitive for disseminated coccidioidomycosis in immunocompetent patients. So if a patient tests negative, odds are low that the patient has disseminated cocci. If a patient tests positive, more testing could be pursued, like the complement fixation titer or immunodiffusion that Dr. Graf mentioned, and/or sampling of the infected site for culture and pathology, and interestingly, unlike many other infections, IgG antibodies against antigens of *Coccidioides* species decline and become undetectable as pulmonary and disseminated symptoms resolve. So in an endemic population, a positive IgG in a symptomatic patient has a high predictive value for active coccidioidomycosis.

Bob Barrett: Well, finally, Dr. Graf, based on your findings, should diagnostic algorithms in endemic areas be modified to encourage earlier testing in immunocompetent patients with compatible symptoms?

Erin Graf: Well, hopefully after listening to this and reading our story, the answer is a clear-cut 'yes.' I like to use the example of my dogs. I'm a huge dog lover and we moved to Arizona about seven years ago. I cannot tell you the number of times that my dogs have been tested for cocci when it's something as simple as a little bit of arthritis. The veterinarian wants to immediately rule out cocci and then consider other etiologies. So it's a little puzzling that we don't do the same thing in humans here when it's so well embedded in the veterinary world and some of that relates to testing and the issues that we already discussed and so, hopefully with the findings of this study and the performance of the EIA in immunocompetent patients, that gives folks a little more comfort or a little more reliance in using this assay in particular to potentially rule in or rule out cocci.

Bob Barrett: That was Dr. Erin Graf from the Mayo Clinic in Phoenix, Arizona and Dr. Anna Hoge from the University of Washington. They wrote a research article in the May 2026 issue of *Clinical Chemistry,* highlighting the need for improved recognition of coccidioidomycosis, and they've been our guests in this podcast on that topic. I'm Bob Barrett. Thanks for listening.