

Coccidioides Diagnostic Guidance

Table 1: Tests Available for Ordering

Test (Designation in EPIC)	Tests included	Indication	Cost	Turn around
Coccidioides Reflex Panel (LAB4524)	IgG and IgM by Enzyme Immunoassay with reflex to immunodiffusion and complement fixation if positive	Immunocompetent (preferred)	\$35-59	4-7 days
Coccidioides Antibody Panel (LAB4523)	Complement fixation, immunodiffusion, IgG and IgM by Enzyme Immunoassay	Immunocompromised (preferred)	\$41	4-7 days
Coccidioides Antibodies (LAB791)	Complement fixation only	Follow up previously positive complement fixation titers only	\$9	4-6 days
Coccidioides antigen (Special Procedure ARUP)	Enzyme Immunoassay antigen	Immunocompromised	\$121	3-4 days

Table 2: Reported Test Performance

Test	Reported Value	Sensitivity	Specificity
Enzyme Immunoassay IgG and IgM	Positive vs. negative	Mira vista: IgM 61%, IgG 87% Immy: IgM 11%, IgG 64% Meridian: IgM 36%, IgG 65%	Mira vista: IgM 95%, IgG 90% Immy: IgM 100%, IgG 99% Meridian: IgM 92%, IgG 99%
Immunodiffusion	Positive vs. Negative	60%-84%	>98.8%
Complement Fixation	Ratio	56%-66%	could not be determined
Enzyme Immunoassay Antigen, urine and serum	Number value	57%	99%

Use of Diagnostic Testing:

Based on Presentation:

- Pulmonary – Consider testing in patients who reside or have recently traveled to/through an at-risk area who present with findings suggestive of typical CAP (cough, fever, chest pain, etc.) but do not respond to antibiotic therapy. Differentiating coccidiomycosis from other causes of CAP is difficult, although procalcitonin and WBC count are often normal. Other findings which could prompt testing include hilar or mediastinal lymphadenopathy, development of *E. nodosum* or *E. multiforme*, or unexplained night sweats, weight loss, or eosinophilia.
- Disseminated – Consider testing in those who reside or have recently traveled to/through an at risk who are increased risk of severe or disseminated infection including older patients, pregnant women, immunocompromised patients (DM, defects in cellular immunity such as HIV, SOT, etc.), and those with certain ancestral backgrounds including African Americans and Filipinos. Additional findings that might prompt testing include unexplained granulomatous skin lesions, bone and joint disease, vertebral infection, or chronic meningitis (sometimes with eosinophils).

Test Utility:

Immunocompetent patients:

- Multiple antibodies available including enzyme immunoassay (EIA, IgG and IgM), complement fixation (CF) and immunodiffusion (ID)
 - Initial testing with EIA (IgG and IgM) is faster, lower cost and more sensitive than ID/CF
 - Positive EIA will reflex to ID and CF
 - CF antibodies should not be used for diagnosis but can be ordered as a stand-alone test for disease staging, prognosis, and antifungal response monitoring
 - Complicated (i.e., disseminated and chronic pulmonary) usually have titer $\geq 1:32$, while uncomplicated (i.e., acute/non-disseminated) usually have titer of $< 1:32$
- If antibody negative and strong suspicion, consider repeating serology after 2-6 weeks as it can be negative early
- Fungal culture and microscopy of sputum or BAL can be helpful as can biopsy although these have low sensitivity

Immunocompromised:

- Antibody development takes several weeks in immunocompetent hosts and likely longer in immunocompromised hosts.
 - Negative serology cannot be used to rule out disease
- Tissue biopsy may be necessary in immunocompromised.
- Urine and serum antigens may be helpful, particularly when combined with serology
 - When combined with ID serology sensitivity can increase to 93%
 - According to one study, antigen testing detected an additional 16% of immunocompetent cases and in 24% of immunocompromised

Coccidiomycosis

Pulmonary: pulmonary nodule, cavitary lung lesion, non-resolving CAP with recent travel or residence in endemic region

OR

Disseminated: bony lesions, skin lesions, meningitis

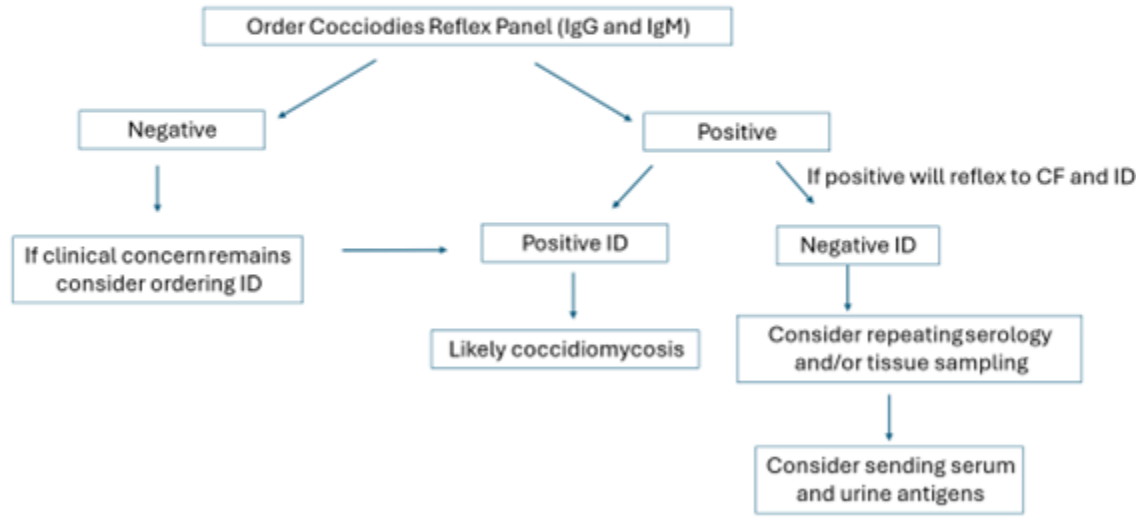


Figure 1: A diagnostic algorithm for coccidiomycosis

References:

1. Malo J, Holbrook E, Zangeneh T, et al. Enhanced Antibody Detection and Diagnosis of Coccidioidomycosis with the MiraVista IgG and IgM Detection Enzyme Immunoassay. *J Clin Microbiol.* 2017;55(3):893-901. doi:10.1128/JCM.01880-16
2. McHardy IH, Barker B, Thompson GR 3rd. Review of Clinical and Laboratory Diagnostics for Coccidioidomycosis. *J Clin Microbiol.* 2023;61(5):e0158122. doi:10.1128/jcm.01581-22
3. Kassis C, Durkin M, Holbrook E, Myers R, Wheat L. Advances in Diagnosis of Progressive Pulmonary and Disseminated Coccidioidomycosis. *Clin Infect Dis.* 2021;72(6):968-975. doi:10.1093/cid/ciaa188