



FEATURED ARTICLE

MiraVista (MVD) Fungal Diagnostic Tests

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I'm often contacted for advice on diagnosis of the endemic mycoses. Many physicians are unaware of these tests and publications describing their use for diagnosis.

For example, some believe the *Histoplasma* antigen test is performed only on urine. Others believe that antigen testing on serum is unnecessary. In fact, nearly half of the cases of acute pulmonary histoplasmosis would have been missed if only urine were tested (sensitivity 83% for combined serum and urine testing; 45% with urine alone) ⁽¹⁾. At least 5% of disseminated cases would be missed if only urine were tested (unpublished). **Both urine and serum** should be tested for maximum sensitivity. Antigen testing of CSF is the most sensitive method for diagnosis of *Histoplasma* meningitis ^(2,3). Detection of antigen in the bronchoalveolar lavage fluid (BAL) is useful for diagnosing pulmonary histoplasmosis ⁽⁴⁾.

Some also believe that *Histoplasma* antibody detection is not useful for diagnosis because most individuals from endemic areas have had histoplasmosis, and antibody tests would not differentiate active infection from previous exposure. Studies in Indianapolis, where 50% of residents are histoplasmin skin test positive, reported positive antibody results by immunodiffusion (ID) in 0.5% and by complement fixation (CF) in 5% ⁽⁵⁾. Skin test reactivity persists for life in most individuals while antibodies clear over a few years.

The newly described MVD IgG and IgM enzyme immunoassay (EIA), combined with antigen detection, improves the sensitivity for diagnosis of acute pulmonary histoplasmosis over antigen and antibody detection by ID or CF ⁽⁶⁾. The assay is quantitative and was useful for detecting seroconversion in these cases. Similarly, sensitivity for diagnosing *Histoplasma* meningitis by testing CSF increased from 78% to 98% by combining antigen and IgG/IgM antibody testing ⁽²⁾. **Both antigen and MVD antibody EIA** should be tested for maximum sensitivity.

Many are unaware of the MVD *Coccidioides* antigen detection assay or believe that its sensitivity is low. The limit of detection is the same in our *Coccidioides* and *Histoplasma* antigen assays, <0.2ng/mL. The clinical sensitivity in disseminated cases is somewhat lower, about 70% in coccidioidomycosis ^(7,8) and 90% in histoplasmosis ⁽⁹⁾. The reason for the lower clinical sensitivity in coccidioidomycosis is the lower fungal burden. For example, the lungs, liver, spleen, bone marrow, other tissues are often involved in disseminated histoplasmosis and fungemia is common. Isolated sites of dissemination to skin, bone, or CNS are more common in coccidioidomycosis and fungemia is rare. Larger unpublished studies indicate the sensitivity was 80% in disseminated cases, most of whom were immunocompromised, if **both urine and serum** were tested. Antigen detection in CSF is the most sensitive method (91%) for diagnosing *Coccidioides* meningitis ⁽¹⁰⁾.

The MVD *Coccidioides* IgG and IgM antibody EIA was introduced in 2017 ⁽¹¹⁾. MVD EIA is more sensitive than ID or CF and is not impacted by immunocompromise ⁽¹¹⁾. The assay is quantitative and useful for monitoring changes in antibody concentrations (unpublished). Sensitivity in CSF in *Coccidioides* meningitis is 73% (unpublished).

The MVD *Blastomyces* antigen EIA is the most sensitive method for diagnosing disseminated and pulmonary blastomycosis ⁽¹²⁾. Antigen also may be detected in CSF ⁽¹³⁾ in patients with meningitis and BAL fluid in patients with pneumonia ⁽⁴⁾. We have developed an IgG *Blastomyces* antibody EIA that is more sensitive than immunodiffusion ⁽¹⁴⁾. **Combined antigen and MVD EIA antibody** testing increased the sensitivity from 88% to 98%. This IgG test is available as "research use only (RUO)" pending completion of validation and requires preapproval by the laboratory director. The MVD *Blastomyces* antibody EIA is projected to be validated and offered routinely in mid-2019.



MVD Test	Specimen	Sensitivity	Specificity	Ref
<i>Histoplasma</i> antigen¹	Urine-disseminated, AIDS	97%	99%	(15)
	Serum-disseminated, AIDS	100%	100%	
	CSF-meningitis	78%	93%	
	BAL-pulmonary	94%	98%	
<i>Histoplasma</i> IgG and IgM antibody	Serum-pulmonary, acute	89%	95%	(2;6)
	CSF-meningitis	82%	93%	
<i>Coccidioides</i> antigen¹	Urine-disseminated ³	51%	98%	(10)
	Serum-disseminated ³	72%	100%	
	Urine or serum, disseminated ³	80%	ND	
	CSF-meningitis	91%	100%	
	BAL-pulmonary	ND2	ND	
<i>Coccidioides</i> IgG and IgM antibody	Serum-pulmonary, disseminated	88%	90%	(11)
	CSF-meningitis ³	73%	88%	
<i>Blastomyces</i> antigen	Urine-pulmonary or disseminated	90%	99%	(4;12)
	Serum-pulmonary or disseminated	57%	ND ²	
	CSF-meningitis ³	86%	ND	
	BAL	80%	98%	
<i>Blastomyces</i> IgG antibody (RUO)⁴	Serum, pulmonary or disseminated	88%	99%	(14)

¹ Disseminated only, ² ND-not determined, ³ unpublished; ⁴ RUO, research use only

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