MiraVista DIAGNOSTICS
Rapid Fungal Testing. Accurate Results.

CLINICAL DIAGNOSIS

Advances in Diagnosis of Histoplasmosis by Urine Antigen Detection in Resource Limited Countries

Introduction.

Histoplasmosis is a common cause of death in people living with HIV/AIDS (PLHIV) in resource limited countries (RLC). The most cases occur in Mexico, Central and South America, and the Caribbean, where access to diagnostic tests for histoplasmosis is severely limited or unavailable [1]. Cases also occur in southeast Asia, Asia, India, Africa, and less frequently in a few other RLC. The Guideline Development Group for Diagnosing and Managing Disseminated Histoplasmosis Among PLHIV emphasized the importance of rapid diagnostic tests such as lateral flow assays (LFA) [2]. The Pan American Health Organization (PAHO) also emphasize the importance of rapid diagnostic tests for histoplasmosis in RLC.

Access to diagnostic tests is limited in RLC. The MiraVista (MVD) *Histoplasma* antigen enzyme immunoassay (EIA) is the most sensitive test for diagnosing progressive histoplasmosis [3, 4] but is unavailable outside the United States. MVD has developed a *Histoplasma* urine antigen LFA. Two large studies, one in Mexico and another in the US established its accuracy. Distribution networks have been established in many RLC in the Americas and are being developed in Asia, Africa, and the United Kingdom.

Mexico Study.

Martinez-Gamboa and colleagues reported results of a prospective study evaluating the MVD LFA and the IMMY Clarus EIA in proven cases in PLHIV in Mexico [5]. The study included 108 patients with culture or pathology proven progressive disseminated histoplasmosis and 266 controls without histoplasmosis. Comparison of results in the LFA and EIA are presented in table 1, demonstrating sensitivities and specificities of the MVD LFA and IMMY Clarus EIA were similar.

They concluded "the MiraVista LFA is a promising tool for point of care testing of people suspected to have histoplasmosis."

Colombia Study.

Caceres evaluated the MVD LFA and MVD EIA in 26 Colombian PLHIV with culture proven histoplasmosis and 74 controls without histoplasmosis. The LFA was performed in Colombia and the EIA at MVD. The sensitivities of the MVD LFA and the MVD EIA were similar, table 2. Specificities differed however, 96% for the LFA and 77% for the EIA.

However, specificity of 77% for the MVD EIA is inconsistent with other studies: specificity was 99% in two studies [3, 4]. A possible explanation for the low specificity in the Colombian study is that 38% of patients had mycobacterial disease or pneumocystis pneumonia, frequent coinfections with histoplasmosis [6, 7] or paracoccidioidomycosis which shares a cross-reactive galactomannan with *Histoplasma* galactomannan [8]. Cross-reactivity with mycobacterial disease and histoplasmosis is unknown; however, MiraVista is conducting a study to assess this possibility.

The authors concluded "urine *Histoplasma* antigen detection tests showed excellent performance for the diagnosis of PDH in PLHIV" and that "integration of these test in clinical laboratories will certainly impact early diagnosis and treatment, and consequently the outcome of patients."

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United States Study.

Abdullah and Hage compared the MVD LFA and MVD EIA in a multicenter US study in highly endemic areas for histoplasmosis [4]. The limit of detection was 1.8 ng/mL in the LFA compared to 0.2 ng/mL in the EIA. About 10% of cases may be falsely negative in the LFA. Results are shown in table 3. Cross reactivity occurred in other endemic mycoses sharing a similar galactomannan [8], table 4.

In RLC, the MVD LFA provides high performance, rapid turn-around time, and reduced cost per test since the sample doesn't have to be shipped to a reference laboratory. MVD has identified distributors for its LFA in Mexico, Argentina, Brazil, and Singapore and is actively exploring distribution opportunities in other RLC.

1. Validated and CE marked
2. Registered in many RLC and others pending
3. Rapid accurate results/Near to patient care
4. Can be performed in low-complexity settings

Table 1. Comparison of antigen results in urine in the MVD LFA and IMMY Clarus EIA in PLHIV with proven progressive disseminated histoplasmosis and controls with other conditions in Mexico

Parameter	MVD LFA	IMMY Clarus EIA
Sensitivity (N = 108)	90.4%	91.3%
Specificity (N = 266)	92.3%	90.9%
Diagnostic accuracy	91.8%	91.0%

Table 2. Comparison of antigen results in urine in the MVD LFA and MVD EIA in PLHIV with proven progressive disseminated histoplasmosis and controls with other conditions in Colombia

Parameter	MVD LFA[1]	MVD EIA[2]
Sensitivity (N = 26)	96%	96%
Specificity (N = 74)	96%	77%
Diagnostic accuracy	91.8%	91.0%

[1] Performed in Colombia, [2] Performed at MVD

Table 3. Evaluation of MVD LFA in proven histoplasmosis in the US

Parameter	LFA	EIA
Sensitivity (N = 44)	93.2%	95.46%
Specificity (N = 286)	99.3%	99.6%
Accuracy	98.9%	Not determined

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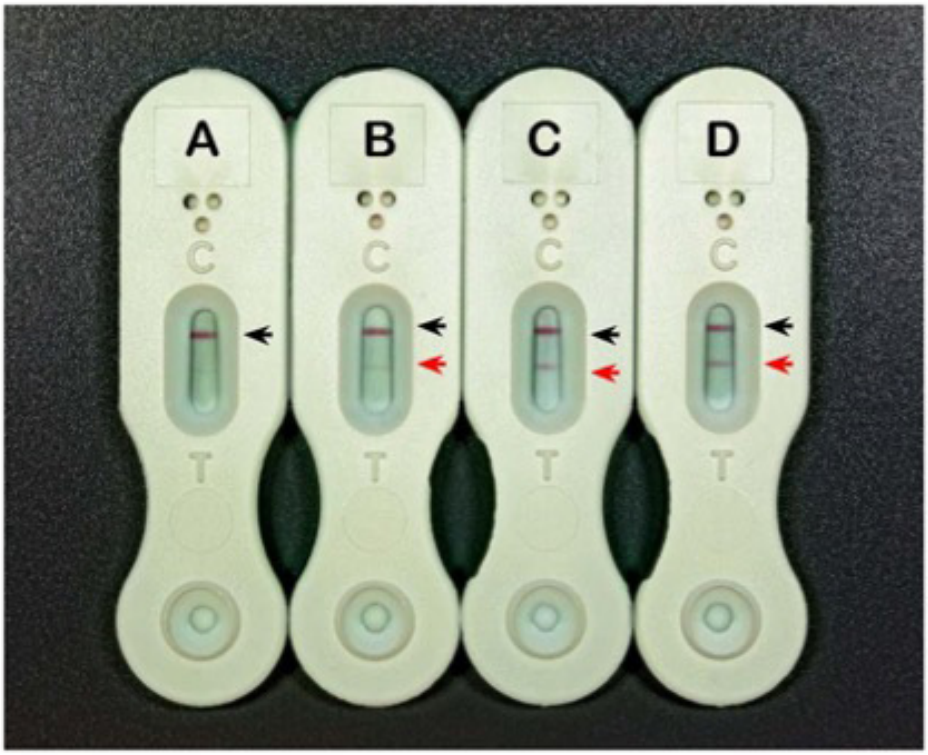
Table 4. Cross-reactivity in other endemic fungal infections

Mycosis	Cross reactivity
Blastomycosis (n=27)	81.5%
Paracoccidioidomycosis (n=7)	85.7%
Talaromycosis (n=52)	75%
Coccidioidomycosis (n=20)	30%

Figure 1. Lateral flow cassettes for positive and negative controls.



The red line with black arrow is positive control line and red line with red arrow are urine standards showing absence of antigen in cassette A and progressively higher concentrations in cassettes A-D.

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VETERINARY DIAGNOSTICS

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