

Reactivity of cryptococcal lateral flow assay across multiple fungal infections.

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Introduction

Cryptococcal meningitis remains a life-threatening fungal infection, particularly among immunocompromised individuals such as those living with HIV/AIDS. Rapid and accurate diagnosis is essential for timely treatment and improved outcomes. The Cryptococcal Lateral Flow Assay (CrAg LFA) has emerged as a valuable point-of-care diagnostic tool due to its simplicity, speed, and high sensitivity. However, concerns about its specificity—especially in the presence of other fungal infections—have prompted investigations into its cross-reactivity. This article explores the reactivity of CrAg LFA across multiple fungal infections, its diagnostic performance, and implications for clinical practice [1].

The CrAg LFA is an immunochromatographic test designed to detect cryptococcal polysaccharide antigens in various body fluids, including serum, plasma, cerebrospinal fluid (CSF), and urine. It is particularly useful in resource-limited settings where conventional culture and microscopy are not feasible. The assay targets antigens from *Cryptococcus neoformans* and *Cryptococcus gattii*, the primary species responsible for cryptococcosis. Studies have demonstrated that CrAg LFA offers high sensitivity and specificity, especially in serum and CSF samples. A meta-analysis reported pooled sensitivity and specificity of 98–99% in these fluids, making it a reliable diagnostic tool for cryptococcal meningitis [2].

Despite its high accuracy, CrAg LFA may yield false-positive results in patients with other fungal infections. This is due to structural similarities between cryptococcal antigens and those produced

by other fungi. Cross-reactivity has been observed in vitro with mannans and polysaccharides secreted by *Histoplasma capsulatum*, *Paracoccidioides brasiliensis*, *Trichosporon spp.*, and *Aspergillus spp.*. A recent study evaluated the specificity of CrAg LFA in 217 serum specimens from patients with various fungal and bacterial infections. False-positive results were noted in 6.89% of *Aspergillus* cases, while no cross-reactivity was observed in *Histoplasma*, *Paracoccidioides*, or tuberculosis specimens. These findings suggest that while CrAg LFA is generally specific, clinicians should interpret results cautiously in patients with suspected non-cryptococcal fungal infections [3].

HIV-infected individuals are at high risk for cryptococcosis and other opportunistic infections. In a cohort of 149 HIV-positive patients, CrAg LFA demonstrated a sensitivity of 93.3% and specificity of 98%. However, three false-positive results were reported, two of which were associated with cytomegalovirus and toxoplasmosis co-infections. These cases highlight the importance of comprehensive clinical evaluation and confirmatory testing when interpreting CrAg LFA results in complex immunocompromised populations. Traditional diagnostic methods for cryptococcosis include India ink staining, culture, and latex agglutination tests (LAT). While culture remains the gold standard, it is time-consuming and requires specialized facilities. LAT offers good sensitivity but is prone to cross-reactivity and requires refrigeration [4].

In contrast, CrAg LFA is rapid, portable, and does not require laboratory infrastructure. A study comparing LFA with LAT and culture found that LFA had superior sensitivity and comparable specificity, making it suitable for point-of-care use.

The potential for cross-reactivity necessitates careful interpretation of CrAg LFA results, particularly in regions endemic for multiple fungal infections. Clinicians should consider the patient's clinical presentation, risk factors, and epidemiological context. Confirmatory testing using culture or molecular methods may be warranted in ambiguous cases. In HIV care settings, routine CrAg screening is recommended for patients with CD4 counts below 100 cells/ μ L. Early detection through LFA can prevent progression to meningitis and reduce mortality [5].

Conclusion

The Cryptococcal Lateral Flow Assay is a powerful diagnostic tool with high sensitivity and specificity for cryptococcal infections. While generally reliable, its reactivity across multiple fungal infections—particularly *Aspergillus*—warrants cautious interpretation. In high-risk populations and endemic regions, confirmatory testing and clinical correlation are essential. Continued innovation and validation will ensure that CrAg LFA remains a cornerstone of fungal diagnostics in global health.

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