University of Nebraska Medical Center
Nebraska Medicine

Histoplasmosis Diagnostic Guidance

Table 1: Tests Available for Ordering

Test (Designation in EPIC)	Indication	Sensitivity Specificity	Cost	Turn Around
Histoplasma Antigen Serum (LAB909) Urine (LAB 3667)	Immunocompromised or immunocompetent Pulmonary or disseminated	Sens 79-82% Spec 97-99%	\$88 Serum \$88 Urine	1-3 days
Histoplasma Antibodies (CF and ID) LAB795	Immunocompetent pulmonary or disseminated	Sens 70-95% Spec 100%	\$25	4-6 days
Histoplasma Antibodies by CF (LAB4376)	Immunocompetent pulmonary Use to follow up low initial titer to confirm infection	Sens 72-95% Spec 70-80%	\$16	3-7 days
Histoplasma Antigen BAL (LAB4718)	Immunocompromised or immunocompetent Pulmonary only	Sens 93.5% Spec 97.8%	\$88	1-3 days

CF=Complement Fixation, sensitivity and specificity vary depending on immune status and site of infection

Use of Diagnostic Testing:

Based on Presentation:

- Pulmonary – consider testing with solitary pulmonary nodule, cavitary lung lesion, nodular lung infiltrate, or CAP that fails to improve despite appropriate antibiotic treatment in patient from endemic area
- Disseminated – consider testing with for patients with unexplained cytopenia, LAD, hepatosplenomegaly, skin lesions, meningitis, elevated LFTs
- Sensitivity of antigen testing is highest in disseminated disease (91.8%) followed by chronic pulmonary histoplasmosis (87.5%) then acute pulmonary histoplasmosis (83%), very low sensitivity in pulmonary nodules
- Serology does not differentiate current from previous infection

Test Utility:

Immunocompetent patients, especially those with lung disease only:

- EIA urine and serum antigen – sensitivity low but recommended first tier
- Consider concurrent ID and CF antibody to increase sensitivity
    - Takes 4-8 weeks to develop histoplasma antibodies
    - In endemic areas less than 5% of individuals have positive serology on CF or ID
    - Can have positive results from previous infection
- If negative and histoplasma still suspected, consider repeating serology as it can be negative in early infection
- If diagnosis still in question, obtain biopsy and culture although these have low sensitivity

Suspected disseminated disease or immunocompromised patients (SOT, HIV/AIDS, chemotherapy, TNF inhibitor, high dose steroid, etc.):

- First line: EIA urine and serum antigen have high sensitivity
  - Patients with SOT may have persistent but low-level urinary antigen despite having completed an effective course of treatment
- Serologic testing is not recommended due to poor sensitivity
- If antigens are negative, and still suspicious obtain biopsy and culture

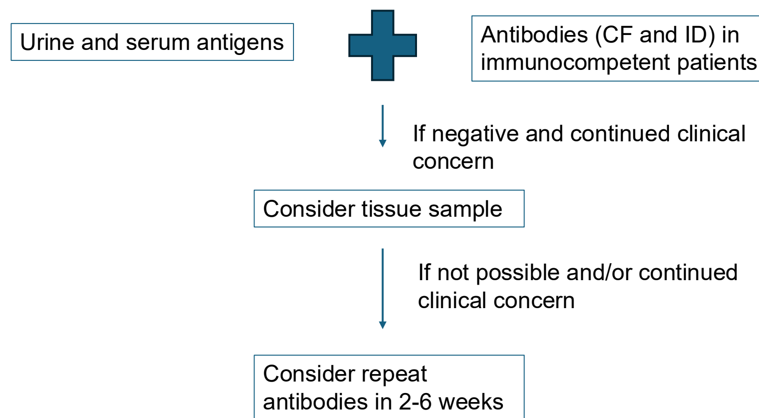

Figure 1: Diagnostic Testing in Suspected Pulmonary Histoplasmosis

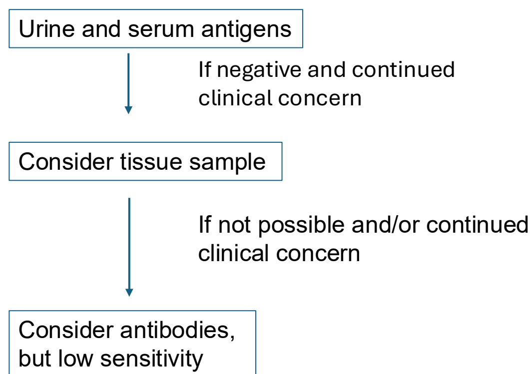

Figure 2: Possible Disseminated Histoplasmosis or Any Form in Immunocompromised Patients

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