

Why Test Urine and Serum for *Histoplasma* Antigen?

QUESTION: Is there a reason to test both urine and serum for *Histoplasma* antigen [1]?

CASE REPORT: A healthy 24-year-old man cleaned the gutters on his 16-year-old fishing cabin on a lake in Wisconsin. He presented for medical evaluation 12 days later for symptoms of fever, malaise and cough of 5 days' duration. Physical findings included a temperature of 100.5°F and the spleen tip that was palpable on examination. Chest radiograph showed right hilar and anterior mediastinal lymphadenopathy and miliary infiltrates. Histoplasmosis was suspected and urine was sent to MiraVista Diagnostics for *Histoplasma* antigen, which was negative.

QUESTION: Does a negative urine antigen exclude pulmonary histoplasmosis?

Most clinicians only order antigen on urine and do not recognize the value of testing serum. Analysis of the results obtained in 158 patients at one institution between 2014-2019 in whom both urine and serum were tested and at least one was positive are presented in the table below.

Analysis of Results: 158 Patients Between 2014-2019		
Result	Urine Positive	Urine Negative
Serum positive	57%	16%
Serum negative	8%	Not determined

DISCUSSION: 16% of cases may have been missed if only urine was tested: serum should also be tested for antigen. A study of patients with heavy exposure acute pulmonary histoplasmosis found that antigen was negative in urine but positive in serum in 46% of patients [2]. Testing for anti-*Histoplasma* IgG and IgM antibodies further increased the sensitivity for diagnosis. IgG antibodies were detected in 88%, IgM in 68%, and IgG and/or IgM in 89% of patients and combined antigen and antibody testing increased sensitivity to 96% [3].

RECOMMENDATION:

1. Send both urine and serum for antigen and test for both
2. Test the serum for anti-*Histoplasma* IgG and IgM antibodies and FID antibodies

Reference List

1. Libert D, Procop GW, Ansari MQ. *Histoplasma* Urinary Antigen Testing Obviates the Need for Coincident Serum Antigen Testing. *Am J Clin Pathol* 2018 Feb 15.
2. Swartzentruber S, Rhodes L, Kurkjian K, et al. Diagnosis of acute pulmonary histoplasmosis by antigen detection. *Clin Infect Dis* 2009 Dec 15; 49(12):1878-82.
3. Richer SM, Smedema ML, Durkin MM, et al. Improved Diagnosis of Acute Pulmonary Histoplasmosis by Combining Antigen and Antibody Detection. *Clin Infect Dis* 2016 Apr 1; 62(7):896-902.