

What Tests Should I Order to Diagnose Fungal Infections?

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The most frequent question we are asked is "What tests should I order?". To answer that question, we need to know 3 things: clinical manifestations, location of residence and travel history. Most commonly we are asked about endemic mycoses, which have defined geographic distributions, with some overlap (figure). There also are endemic locations outside the endemic areas. For example, histoplasmosis occurs in California and coccidioidomycosis occurs in Washington state.



Travel history is important as pets often accompany their family on vacation to areas where other mycoses are endemic or participate in training activities or sports in other endemic areas. We also provide testing for diagnosis of *aspergillosis* and cryptococcosis, which are not endemic mycoses. Information regarding the clinical manifestations of the mycoses for which we offer testing is available on our website and in Sykes textbook of infectious diseases in dogs and cats ^[1].

The answer to the question "What tests should I order?" is addressed in table 1. Antigen testing is the

most sensitive method for diagnosis of histoplasmosis, blastomycosis, cryptococcosis and systemic *aspergillosis* while antibody testing is most sensitive for coccidioidomycosis and sinonasal *aspergillosis*. The antigen detected in histoplasmosis and blastomycosis is immunologically identical: No need to test both. Antibody detection is useful for diagnosing cases with negative antigen results, but these tests are relatively specific. Endemic regions for histoplasmosis and blastomycosis overlap. The *Blastomyces* ID antibody test has low sensitivity and has not detected antibody in cases with negative *Blastomyces* IgG antibody ^[2]. You must test for both *Blastomyces* IgG antibodies and *Histoplasma* IgG and ID antibodies to avoid missing the diagnosis. Antibody testing is more sensitive than the antigen detection in coccidioidomycosis and antibody should be tested by ID and IgG EIA to achieve the highest sensitivity ^[3].

Another common question is "What are the sensitivity and specificity of your tests?" This question is addressed in table 2. The study in the table reported sensitivity of 100% for *Blastomyces* antigen detection, but data from clinical testing indicates sensitivity is about 90%. Results below 1 ng/mL are falsely positive in some cases: correlation of clinical and imaging findings helps distinguish true and false positive results. Consultation is encouraged if the clinical and imaging findings are not entirely consistent with blastomycosis. Most of the studies had small numbers of cases and controls (25-50) reducing the accuracy of the data. There is no data for antibody testing in dogs or cats with histoplasmosis, and these are planned to obtain this information. *Cryptococcal* antigen at titers below 1:200, and especially below 1:16 may represent false positive results and should not consider definitive for diagnosis: Additional testing including cytology, histopathology or culture of lesions are recommended ^[4].

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Table 1. What Test Should I Order?

Mycosis	Primary tests	Secondary tests		
Blastomycosis	<i>Blastomyces</i> urine antigen (test code 316) ¹	<i>Blastomyces</i> IgG serum antibody (test code 330) ² <i>Histoplasma</i> IgG serum antibody (test code 327) ²		
Histoplasmosis	<i>Histoplasma</i> urine antigen (test code 310) ¹	<i>Histoplasma</i> IgG serum antibody (test code 327) ² <i>Histoplasma</i> ID antibody (test code 321) ² <i>Blastomyces</i> IgG serum antibody (test code 330) ²		
Coccidioidomycosis	<i>Coccidioides</i> IgG antibody (code 329) and <i>Coccidioides</i> ID antibody (code 320)	Coccidioides serum antigen (code 315)		
Cryptococcosis	<i>Cryptococcal</i> serum antigen (code 319)	None		
Aspergillosis-sinonasal	Aspergillus ID antibody (code 324)	Aspergillus serum or urine antigen (code 309)		
Aspergillosis-systemic ³	<i>Aspergillus</i> serum or urine galactomannan antigen (code 309)	Aspergillus ID antibody (code 324)		
Other	Cyto or histopathology and culture4	Fungitell beta-D-glucan5 (code 317)		

¹Histoplasma and Blastomyces antigen entirely cross-reactive, no need to order both

²*Histoplasma* IgG and *Blastomyces* IgG antibody are specific, need to order both

³Systemic *aspergillosis* includes pulmonary and/or disseminated

⁴Not offered at MiraVista

⁵May be used for diagnosis of rare mold infections for which antigen testing is not available but specificity is low (table 2)



Table 2. Summary of sensitivity and specificity

Test	Specimen	Sensitivity	Specificity	Specificity
Blastomyces antigen	Urine (canine) Serum (canine)	100% 100%	95% 100%	[5]
<i>Blastomyces</i> IgG antibody EIA <i>Blastomyces</i> ID antibody <i>Blastomyces</i> ID antibody	Serum (canine) Serum (canine) Serum (canine)	95% 65% 18%	95% 100% Not done	[5] [5] [2]
<i>Histoplasma</i> antigen <i>Histoplasma</i> antigen	Urine (canine) Urine (feline)	89% 94%	100% 100%	[6] [7]
Histoplasma IgG antibody EIA Histoplasma IgG antibody EIA Histoplasma ID antibody	Serum (canine) Serum (feline) Not done	78% 78% Not done	97% 84% Not done	MVD validation MVD validation
Coccidioides antigen Coccidioides antigen	Serum (canine) Urine (canine)	30% 12%	97% 97%	[3]
<i>Coccidioides</i> IgG antibody EIA <i>Coccidioides</i> ID antibody Combined IgG and ID antibodies	Serum (canine) Serum (canine) Serum (canine)	89% 92% 99%	94% 94% 92%	[3]
Cryptococcal CALAS	Serum (feline) Serum (canine)	96% 83%	False-positive <1:2003	[1, 4, 8]
Aspergillus galactomannan antigen-systemic aspergillosis	Serum (canine) Urine (canine)	92% 88%	86% 92%	[9]
Aspergillus galactomannan antigen-sinonasal aspergillosis	Serum (canine)	24%	76%	[10]
Aspergillus antibody ID- sinonasal aspergillosis	Serum (canine)	76%	76%	[10]
² Fungitell beta-D-glucan	Serum (canine)	100%4	100%4	MVD validation



¹Systemic *aspergillosis* includes pulmonary and/or disseminated ²Nonspecific (Pan fungal marker) useful for diagnosis of mycoses for which a specific antigen assay is not available ³especially titers <1:16

⁴systemic mold cases infections (N=4)

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