



FREQUENTLY ASKED QUESTIONS

General Fungal Testing

QUESTION: What are the endemic ranges of the various fungi?

ANSWER:

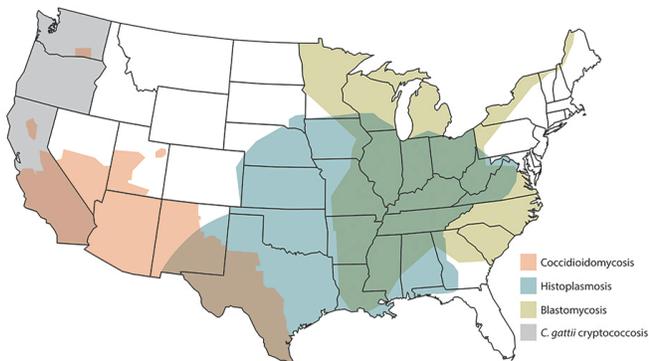


Figure 1: This map was taken from the CDC website.

Areas Endemic for Blastomycosis in the United States



Figure 2: This map was taken from the CDC website and it indicates the endemic blastomycosis area based on human screening. Vermont has also experienced an apparent increase in blastomycosis cases. Blastomycosis has recently been identified in patients exposed in the southwest US (not shown on map) [1]. Blastomycosis is also seen in Canada, especially in western Ontario and parts of Manitoba and Saskatchewan.

<https://www.cdc.gov/fungal/diseases/blastomycosis/causes.html>

- Blastomycosis and histoplasmosis are endemic in overlapping areas of the US and Canada (see figures 1-3). Blastomycosis caused by the new species, *Blastomyces helices*, occurs in areas of the southwest United States overlapping with the endemic region for coccidioidomycosis and in parts of Canada (Saskatchewan) [1]. They also occur in some areas that are endemic for coccidioidomycosis.

HEADQUARTERS

4705 Decatur Blvd. | Indianapolis, Indiana 46241, USA

888-841-8387



FREQUENTLY ASKED QUESTIONS CONTINUED...

Areas Endemic for Histoplasmosis in the United States

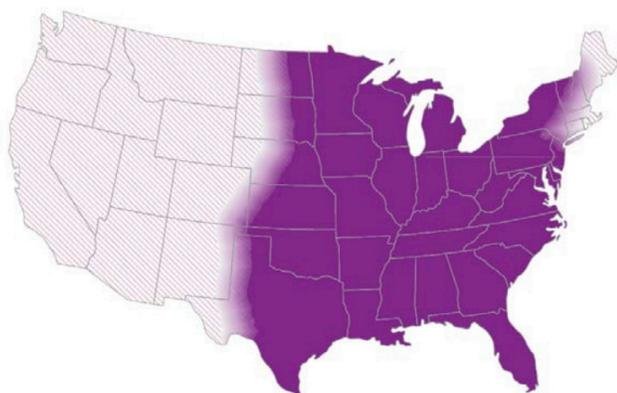


Figure 3: CDC map based on human screening for histoplasmosis. Histoplasmosis has also been identified in animals from California. High cross reactivity with coccidioidomycosis may explain the Suspected endemic region that extends into the southwestern United States [2].
<https://www.cdc.gov/fungal/diseases/histoplasmosis/maps.html>

- Blastomycosis and histoplasmosis are endemic in overlapping areas of the US and Canada (see figures 1-3). They also occur in some areas that are endemic for coccidioidomycosis.

Areas Endemic for Coccidioidomycosis in the United States

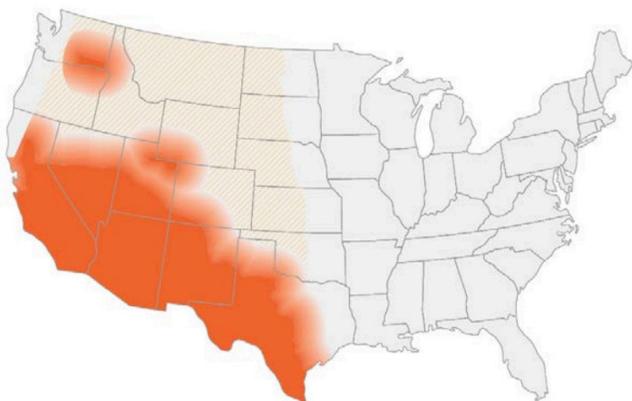


Figure 4: CDC map showing the endemic region for *Coccidioides*. Many residents of northern states choose to winter in AZ or CA with their pets; therefore, pet owners should be questioned regarding travel history. Also note that west Texas is endemic for coccidioidomycosis.
<https://www.cdc.gov/fungal/pdf/more-information-about-fungal-maps-508.pdf>

- Coccidioidomycosis is endemic to the desert southwest US and parts of Mexico, Central and South America. It may be seen outside the endemic area with dogs that have previously resided or visited that area. Histoplasmosis occurs in some areas where coccidioidomycosis is endemic including southwestern Texas and less often and other southwestern states.

Aspergillosis and cryptococcosis do not exhibit any endemic pattern of distribution except that *Cryptococcus gattii* is more common in British Columbia, Vancouver Island, Canada, Oregon and Washington state.

HEADQUARTERS

4705 Decatur Blvd. | Indianapolis, Indiana 46241, USA

888-841-8387



FREQUENTLY ASKED QUESTIONS CONTINUED...

QUESTION: What are the most common findings?

ANSWER: Non-specific signs seen in most cases include one or more of the following: lethargy, loss of interest, weakness, inappetence, weight loss, and fever. The more specific findings are listed below.

Blastomycosis in dogs:

- lower respiratory signs
- ocular involvement
- skin lesions
- bone lesions
- other sites (testes, prostate, kidneys, bladder, CNS, mammary gland, cardiac, oral lesions, nasal passages)

Histoplasmosis in dogs:

- gastrointestinal signs
- enlargement of spleen, liver, visceral lymph nodes
- lower respiratory signs
- other sites (bone or joint involvement, ocular lesions, skin lesions, rarely CNS)

Coccidioidomycosis in dogs:

- lower respiratory signs
- bone lesions
- skin lesions
- peripheral lymph node: enlargement, draining lesions
- CNS
- ocular involvement
- other sites (GI, cardiac, etc.)

Cryptococcosis in dogs:

- most dogs have severe disseminated disease at presentation
- CNS, ocular, nasal, and urinary involvement most common
- other sites (skin, GI, lymph nodes, kidneys)
- usually no lower respiratory signs detected antemortem

Aspergillosis (disseminated or pulmonary systemic) in dogs:

- general: usually involves multiple organ systems and is advanced by the time of diagnosis; at least 50% of cases in German shepherd breed
- diskospondylitis
- other bony involvement
- CNS involvement
- peripheral lymph node: enlargement, and drainage
- ocular involvement
- other sites (cardiac, GI, pulmonary, etc.)

Histoplasmosis in cats

- lower respiratory signs
- lymph node enlargement
- enlargement of spleen and/or liver
- ocular involvement
- other sites (skin lesions, bone lesions, oral ulcers, CNS; rarely nasal polyps, GI signs: less likely to occur in cats than dogs [3])

Cryptococcosis in cats

- upper respiratory signs
- subcutaneous swelling over nose
- CNS signs
- ocular involvement
- other sites (internal intra-abdominal lymph node enlargement, renal, spleen/liver/thyroid and/or salivary involvement, peripheral lymphadenopathy, bone/joint involvement)

HEADQUARTERS

4705 Decatur Blvd. | Indianapolis, Indiana 46241, USA

888-841-8387



FREQUENTLY ASKED QUESTIONS CONTINUED...

QUESTION: What tests should I order?

ANSWER:

Blastomycosis

- One study showed *Blastomyces* antigen is detected in the urine 94% and serum in 87% of pathology proven cases [4, 5], and another study showed sensitivity of 100% sensitivity in serum and urine samples from proven cases [5].
 - Suspected cases with negative antigen results in urine may be diagnosed by detecting IgG *Blastomyces* antibodies in serum. Histoplasmosis and blastomycosis antigens are entirely cross-reactive in the antigen detection assays but the antibody is specific. Test for IgG *Blastomyces* and IgG *Histoplasma* antibody and *Histoplasma* antibody by immunodiffusion.
 - MVista® *Blastomyces* Antigen Quantitative EIA (test code 316)
 - MVista® *Blastomyces* Canine IgG Antibody EIA (test code 330)
 - MVista® *Histoplasma* Canine IgG Antibody EIA (test code 327)
 - *Histoplasma* Antibody by Immunodiffusion (test code 321)
 - *Blastomyces* Antibody by Immunodiffusion (test code 322)

Histoplasmosis

- *Histoplasma* antigen is detected in the urine of 89.5% of cases in dogs and 94.4% in cats [6, 7].
 - Suspected cases with negative antigen results in urine may be diagnosed by detecting IgG *Histoplasma* antibodies in serum. Histoplasmosis and blastomycosis antigens are entirely cross-reactive in the antigen detection assays but the antibody is specific. Test for IgG *Blastomyces* and IgG *Histoplasma* antibody and *Histoplasma* antibody by immunodiffusion

- MVista® *Histoplasma* Antigen Quantitative EIA (test code 310)
- MVista® *Histoplasma* Canine IgG Antibody EIA (test code 327)
- MVista® *Blastomyces* Canine IgG Antibody EIA (test code 330)
- *Histoplasma* Antibody by Immunodiffusion (test code 321)
- *Blastomyces* Antibody by Immunodiffusion (test code 322)

Coccidioidomycosis

- Anti-*Coccidioides* antibodies are detected in 98.6% of cases if IgG *Coccidioides* antibody by enzyme immunoassay and immunodiffusion are performed compared to 91.9% if immunodiffusion alone is performed [8]. Both should be performed.
- *Coccidioides* antigen in dogs is detected in the urine in 12.1% and in the serum in 30% of cases.
- Testing the serum and urine for antigen may assist in diagnosis and the cases with negative antibody results [8, 9].
 - MVista® *Coccidioides* Antigen Quantitative EIA in urine and serum (test code 315)
 - MVista® IgG anti-*Coccidioides* Canine Antibody EIA (test code 329), and *Coccidioides* Antibody by Immunodiffusion (test code 320) [8-10]

Aspergillosis

- Systemic (pulmonary and disseminated)
 - *Aspergillus* galactomannan antigen is detected in the serum in 92% and urine in 88%. Serum is the preferred specimen [11].
 - *Aspergillus* galactomannan antigen EIA (test code 309)
 - Whether testing for *Aspergillus* antibodies would increase the sensitivity is unknown but should be considered if the antigen test is negative.
 - *Aspergillus* antibody by Immunodiffusion (test code 324)

HEADQUARTERS

4705 Decatur Blvd. | Indianapolis, Indiana 46241, USA

888-841-8387



FREQUENTLY ASKED QUESTIONS CONTINUED...

- Sinonasal
 - Aspergillus antibodies are detected in the serum by AGID in 67-77% of cases [12, 13], 88% by IgG ELISA [13].
 - Aspergillus antigens are detected in 24% by Platelia Aspergillus antigen EIA [13].
 - *Aspergillus* antibody by immunodiffusion (test code 324)
 - Whether testing for *Aspergillus* antigen would increase the sensitivity for diagnosis of sinonasal aspergillosis is unknown but should be considered if the antibody test is negative.

Cryptococcosis

- Cryptococcal antigen can be detected in the serum in 83% of dogs and 96% of cats [14].
 - Cryptococcal antigen latex agglutination (test code 319).

Pan-fungal (Fungitell beta-d-glucan)

- Positive in several fungal infections including yeast and mold[15]
 - *Candida*, (68%), human data [16]
 - *Cryptococcus* (79 - 89%, respectively, in serum and CSF for cryptococcal meningitis) human data [17]
 - *Histoplasma* (26/27, 96%) dogs and cats
 - *Blastomyces* (Per package insert: the yeast phase of *Blastomyces dermatitidis* produces little (1→3)-β-D-glucan and may not be detected by the assay).
 - *Coccidioides* (13/27, 46%), dogs and cats
 - *Aspergillus* (17/22, 77%), dogs and cats
 - Non-*Aspergillus* mold (4/4, 100%), dogs and cats

REFERENCES:

1. Schwartz, I.S., et al., *Blastomyces helicus, a New Dimorphic Fungus Causing Fatal Pulmonary and Systemic Disease in Humans and Animals in Western Canada and the United States*. Clin Infect Dis, 2019. **68**(2): p. 188-195.
2. Edwards, L.B., et al., *An atlas of sensitivity to tuberculin, PPD-B and histoplasmin in the United States*. Am. Rev. Respir. Dis, 1969. **99**: p. 1-18.
3. Sykes, J.E., *Canine and Feline Infectious Diseases*. 2014, St. Louis, MO: Elsevier. 915.
4. Spector, D., et al., *Antigen and antibody testing for the diagnosis of blastomycosis in dogs*. J Vet. Intern Med, 2008. **22**(4): p. 839-843.
5. Mourning, A.C., et al., *Evaluation of an enzyme immunoassay for antibodies to a recombinant Blastomyces adhesin-1 repeat antigen as an aid in the diagnosis of blastomycosis in dogs*. J. Am. Vet. Med. Assoc, 2015. **247**(10): p. 1133-1138.
6. Cunningham, L., et al., *Sensitivity and Specificity of Histoplasma Antigen Detection by Enzyme Immunoassay*. J. Am. Anim Hosp. Assoc, 2015. **51**(5): p. 306-310.
7. Cook, A.K., et al., *Clinical evaluation of urine Histoplasma capsulatum antigen measurement in cats with suspected disseminated histoplasmosis*. J. Feline. Med. Surg, 2012. **14**(8): p. 512-515.
8. Holbrook, E.D., et al., *Novel canine anti-Coccidioides immunoglobulin G enzyme immunoassay aids in diagnosis of coccidioidomycosis in dogs*. Med Mycol, 2019.
9. Kirsch, E.J., et al., *Evaluation of Coccidioides antigen detection in dogs with coccidioidomycosis*. Clin Vaccine Immunol, 2012. **19**(3): p. 343-5.
10. Chow, N.A., et al., *Development of an enzyme immunoassay for detection of antibodies against Coccidioides in dogs and other mammalian species*. PLoS One, 2017. **12**(4): p. e0175081.
11. Garcia, R.S., et al., *Sensitivity and specificity of a blood and urine galactomannan antigen assay for diagnosis of systemic aspergillosis in dogs*. J Vet Intern Med, 2012. **26**(4): p. 911-9.
12. Pomrantz, J.S., et al., *Comparison of serologic evaluation via agar gel immunodiffusion and fungal culture of tissue for diagnosis of nasal aspergillosis in dogs*. J. Am. Vet. Med. Assoc, 2007. **230**(9): p. 1319-1323.
13. Billen, F., et al., *Comparison of the value of measurement of serum galactomannan and Aspergillus-specific antibodies in the diagnosis of canine sino-nasal aspergillosis*. Vet Microbiol, 2009. **133**(4): p. 358-65.
14. Trivedi, S.R., et al., *Clinical features and epidemiology of cryptococcosis in cats and dogs in California: 93 cases (1988-2010)*. J Am Vet Med Assoc, 2011. **239**(3): p. 357-69.
15. Renschler, J.A. *Evaluation of (1,3)-B-D-Glucan as a Biomarker of Systemic Fungal Infections in Dogs and Cats*. in American College of Veterinary Pathologists. 2015. Minneapolis: IVIS.org.
16. Nguyen, M.H., et al., *Performance of Candida Real-time Polymerase Chain Reaction, beta-D-Glucan Assay, and Blood Cultures in the Diagnosis of Invasive Candidiasis*. Clin. Infect. Dis, 2012. **54**(9): p. 1240-1248.
17. Rhein, J., et al., *Detection of High Cerebrospinal Fluid Levels of (1→3)-beta-d-Glucan in Cryptococcal Meningitis*. Open Forum Infect Dis, 2014. **1**(3): p. ofu105.