MiraVista
VETERINARY DIAGNOSTICS

FREQUENTLY ASKED QUESTIONS
Histoplasma Testing

J.S. Renschler, DVM, PhD, Dipl ACVP

If I suspect histoplasmosis, should I order the antigen or the antibody test?

The MVista *Histoplasma* antigen test (Test Code 310) is the preferred screening test to aid in the initial diagnosis of histoplasmosis. We also offer canine and feline *Histoplasma* IgG by EIA (Test Codes 327 and 328) which may be useful as a follow-up test in cases with suspected false negative or equivocal low positive antigen results. In cases with localized disease presentation (e.g., suspected ocular or GI histoplasmosis), testing both antigen and antibody will likely improve sensitivity as we have observed more false negative antigen results in such cases. The antigen test may be used as a marker of therapeutic efficacy; therefore, obtaining a baseline urine antigen concentration is useful for any case.

What is the preferred specimen for the antigen test?

Urine has shown the highest sensitivity in the antigen assay. Serum is also an acceptable specimen, although the sensitivity is slightly lower resulting in more false negative results. Typically the urine antigen concentration will be higher than serum antigen concentration; however, occasionally, the reverse is true. For this reason, some clinicians prefer to screen both urine and serum. CSF, BAL fluid and other body fluids may also be tested.

What is the sensitivity and specificity of the antigen tests?

- The *Histoplasma* urine antigen test has consistently shown around 90-95% sensitivity in studies with dogs, cats and humans with acute disseminated histoplasmosis. The sensitivity when testing serum is slightly lower; therefore, urine is typically the preferred specimen. False negative results are uncommon but do occur, and this would be more likely in cases with very early infection, mild disease, chronic disease or localized clinical signs. We are currently studying the sensitivity of the antigen test in ocular histoplasmosis. Antibody testing by EIA may be useful in cases with suspected false negative results (if the organism cannot be identified by cytology or histopathology). The specificity of the antigen test has been around 98% in studies. Usually false positive results are low positives (less than 1-2 ng/mL). False positives in the moderate-high positive range are very rare (excepting cross reactivity due to blastomycosis or other fungal infections).
- Yes, nearly complete (99%) cross-reactivity occurs in histoplasmosis and blastomycosis, and the discrepancies are in the low positive range. Thus, **there is no need to order both tests**. Less cross reactivity may be seen in other mycoses: *Histoplasma* antigen is positive in about 20% of cases of coccidioidomycois, 5% with aspergillosis and perhaps in sporotrichosis. Antibody testing may assist in resolving cross-reactivity.

If my practice is located in an area that is considered to be endemic for both *Blasto* and *Histo*, which antigen test should I submit?

- Due to cross reactivity, it is typically not necessary or recommended to submit both antigen tests from the same patient. In states such as IN, IL, KY, TN and OH, the incidence of both blastomycosis and histoplasmosis is high; however, clinical blastomycosis seems to be more commonly observed in dogs. Blastomycosis is also more likely if bone lesions and/or skin lesions are observed in dogs. In these instances, submitting the Blasto antigen test would be recommended. For canine patients with GI signs, histoplasmosis would be more likely. Additionally, cats in the overlapping endemic areas are much more likely to have clinical histoplasmosis. Histo antigen testing would be recommended in those cases.
- If a baseline antigen result is obtained in either the Histo or Blasto antigen assays, the same assay should be utilized during therapeutic monitoring. The scale of reporting is different for the two assays (0.4 – 19.0 ng/mL for Histo; 0.2 – 14.7 ng/mL for Blasto).
- Differentiation of the two infections is often not necessary, as treatment and monitoring are very similar. If it is necessary to differentiate, antibody testing and/or definitive diagnosis by cytology/histopathology/culture should be undertaken.

I received an antigen result that says "Positive, Below the Limit of Quantification (BLQ)". What does this mean?

- A BLQ result is a very low positive (<0.4 ng/mL). For further description of BLQ, see the BLQ information page.
- If this is a screening test for use in diagnosing histoplasmosis, this result is somewhat equivocal and may represent a false positive. The antigen concentration is expected to generally correlate with severity of signs; therefore, it would be more likely that a BLQ result is a true positive for a case with localized disease (GI or ocular signs only), very early infection, chronic long-standing infection or mild disease. Conversely, a case with severe disseminated disease is less likely to have a BLQ result. For equivocal low positive results, further efforts should be made to identify the organism. Additional testing in the antibody EIA and/or repeat antigen testing are also recommended.
- If this result is obtained during treatment for histoplasmosis, it indicates that the urine antigen concentration has decreased to *almost* negative. The most conservative approach to treatment indicates that antifungal therapy should be continued, and antigen reassessed every 1-2 months until a "negative, none detected" result is obtained.

I have previously tested for histoplasmosis through serology at the state diagnostic lab. What is the difference between that and the MiraVista testing?

Most state diagnostic labs perform only agar gel immunodiffusion (AGID) antibody testing. This is a time consuming (at least 3 days turnaround time) and insensitive method. The MVista antigen test has much higher sensitivity, faster turnaround time, and provides quantitative results for use in monitoring therapy. The MVista IgG EIA is also preferable to AGID antibody testing, as semi-quantitative results are available in a single day and sensitivity is higher than AGID. For these reasons, we recently removed AGID from our test menu.

4705 DECATUR BLVD. INDIANAPOLIS, INDIANA 46241 MAIN 888.841.VETS (8387) FAX 317.856.3685 MiraVistaVets.com