



CLINICAL DIAGNOSIS

When is testing SERUM for *Histoplasma* antigen indicated?

At a Glance – Key Points

1. The MVista® *Histoplasma* Antigen EIA is highly sensitive
2. Samples that can be tested include urine and serum
3. If only urine is tested, 5-10% of diagnoses will be missed
4. Approximately ½ of these cases will have a positive serum antigen test
5. Serum should be tested for *Histoplasma* antigen if urine antigen is negative and clinical suspicion remains
6. GI histoplasmosis should be considered when interpreting an IBD panel

Case Example

Lacey, a 3-year-old, spayed female Chihuahua was presented for chronic large-bowel diarrhea and intermittent anorexia of 2 years duration. Clinical signs had not improved with tylosin and hypoallergenic diet. Routine lab work showed mild hypoalbuminemia (2.4 g/dL; RI 2.7-4.4), mature neutrophilia (23,306 / mL; RI 2060-10600), monocytosis (3252 / mL; RI 0-840), and lymphopenia (542 / mL; RI 690-4500). Serum cobalamin, folate, cPLI, and TLI concentrations were normal. Fecal flotation for intestinal parasites and fecal PCR for *Herterobilharzia* were negative. Serum IBD panel showed elevated anti-porin IgA, anti-calprotectin IgA, and

anti-giladin IgA, suggestive of inflammatory bowel disease. Abdominal ultrasound showed a thickened colonic wall with segmental loss of layering and mesenteric lymphadenopathy (Figure 1). Urine was negative for antigen with the MVista® *Histoplasma* Antigen Quantitative EIA.



Figure 1: Abdominal ultrasound showing thickened colonic wall with loss of normal layering (arrow).

Based on the presumptive diagnosis of inflammatory bowel disease, prednisone was prescribed. Short term clinical improvement was minimal. Due to the continued suspicion for GI histoplasmosis, serum was tested for antigen by the MVista® *Histoplasma* Antigen Quantitative EIA (test code 310) and for antibodies by the MVista® Canine *Histoplasma* IgG Antibody EIA (test code 327). *Histoplasma* antigen was detected in serum (1.2 ng/mL; RI=none) as were anti-*Histoplasma* IgG antibodies (>80 EU; RI <8). Considering Lacey's clinical findings, either test result is sufficient to make the diagnosis of GI histoplasmosis.

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Discussion

Lacey's case is a good example of when to test serum for *Histoplasma* antigen. When urine is tested for antigen with the MVista® *Histo* Antigen EIA it is highly sensitive (89% dog and 94% cat) for histoplasmosis [1-4]. While uncommon, most false negative results occur in animals with localized disease [2,3,5,6]. In dogs, localized histoplasmosis most commonly affects the GI tract found in about 1/4 of cases.

Serum *Histoplasma* antigen testing should be done when urine is negative, and suspicion remains high

In cats, localized histoplasmosis most often affects the eyes and bone/joints and less commonly the skin and GI tract. In a review of 183 samples submitted to MiraVista Diagnostics, approximately 3% of urine samples were negative when tested for *Histoplasma* antigen while serum, submitted at the same time, was positive. This data suggests that if only urine is tested, the diagnosis will be missed in at least 3% of samples. This number does not include cases where both urine and serum antigen tests are negative, which is estimated to occur in about 5% of cases. In that case, testing for anti-*Histoplasma* antibodies with the MVista® *Histoplasma*

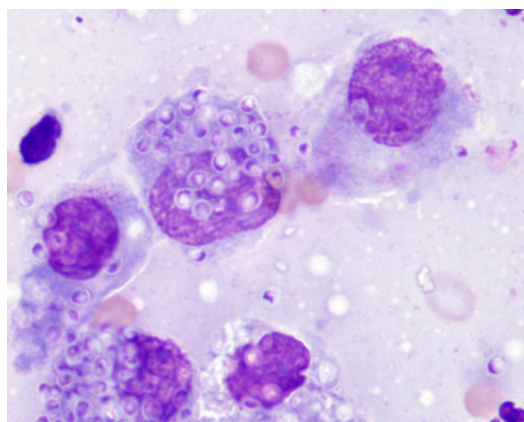


Figure 2: *Histoplasma* yeasts seen mostly within macrophages. Photo courtesy of Dr. Jim Meinkoth.

IgG Antibody EIA is indicated. In Lacey's case, the *Histoplasma* IgG antibody concentration was very high (>80 EU).

Histoplasmosis is the most common fungal infection to affect the GI tract in dogs

Lacey is a classic example of GI histoplasmosis. Large bowel involvement is almost always present and often diarrhea contains frank blood or mucous or both. Straining and urgency might also be present. Affecting the most distal GI tract, proctitis is also relatively common. Routine lab work can be normal or have changes consistent with chronic inflammation. Abdominal ultrasound generally reveals a thickened colonic wall with a loss of normal layering. Local mesenteric lymph nodes can be enlarged. Cytology of FNA of mesenteric lymph nodes will often show evidence of antigenic stimulation, but not *Histoplasma* yeasts. A rectal scrape, where rectal mucosal cells are digitally scraped off and rolled onto a slide, might reveal *Histoplasma* yeast (Figure 2). As with Lacey's case, many dogs have clinical signs for months or even years before a definitive diagnosis is made. During that time, there is usually short term and incomplete response to multiple empiric treatments.

Histoplasmosis must be considered with a positive serum IBD panel

Other common diagnostic rule-outs for a case similar to Lacey's include intestinal neoplasia, such as lymphoma, and inflammatory bowel disease. Other endemic mycoses such as blastomycosis, coccidioidomycosis and cryptococcosis much less commonly affect the GI tract. Pythiosis more commonly affects the stomach or small bowel. One additional important aspect of Lacey's case includes the positive results on the serum IBD panel. In enzootic areas, GI histoplasmosis must be ruled-out before an IBD panel can be used to make a presumptive diagnosis of inflammatory bowel disease.

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