



CLINICAL TREATMENT & MONITORING

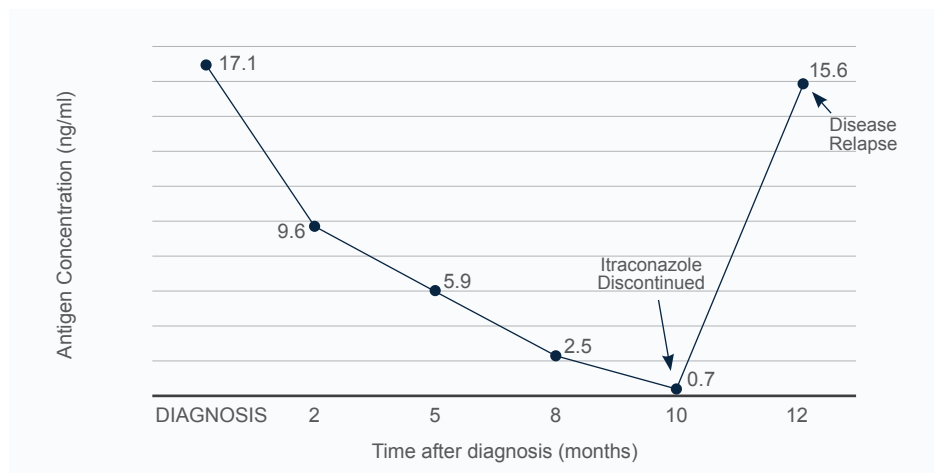
Antigen Testing Guides Individualized Medical Care — Treatment Monitoring for Histoplasmosis and Blastomycosis

Case Example

Boone is a 3-year-old, male, mixed breed dog that was diagnosed with disseminated histoplasmosis. *Histoplasma* yeasts were found on a blood smear (fungemia). Boone's presenting signs included mixed bowel diarrhea, weight loss, lethargy, and anorexia. Physical examination revealed a fever (103.8F), poor body condition (2/9), abdominal organomegaly, and peripheral lymphadenopathy. Boone was started on FDA generic itraconazole capsules (6 mg/kg/day PO). MVista® *Histoplasma* Antigen Quantitative EIA on urine was positive (17.1 ng/mL).

Boone responded well to treatment and over the following 2 months his clinical signs significantly improved. For treatment monitoring, urine antigen concentrations were measured by the MVista® *Histoplasma* Antigen Quantitative EIA, every 2-3 months. Antigen concentrations decreased over time (Figure 1). After 8 months of treatment, Boone was reportedly back to normal. Against the attending veterinarian's advice, after 10 months of treatment, the pet-owners discontinued Boone's itraconazole. Urine antigen concentration at that time was 0.7 ng/mL. Approximately 2 months later, Boone was represented for fever, anorexia, and lethargy. Urine *Histoplasma* Antigen concentration at that time had significantly increased from previous visit (15.6 ng/mL). Itraconazole was again prescribed and Boone again responded positively.

Figure 1. Boone's urine *Histoplasma* antigen concentrations over time



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Discussion

Boone's case is an example of how urine antigen concentrations can be used to help guide individualized antifungal treatment. It is common for clinical signs to resolve before the fungus is completely eliminated. Studies have shown, that for histoplasmosis and blastomycosis, antigen concentrations decrease with successful treatment [1, 2]. Likewise, antigen concentration fails to decrease, or rises, with unsuccessful treatment. In fact, in one study, all cats with increasing antigen concentrations during treatment, had a poor outcome [1]. In Boone's case, itraconazole was discontinued too soon (urine antigen = 0.7 ng/mL), making disease relapse inevitable.

Antigen concentrations decrease with successful treatment and should be monitored during treatment.

A negative urine antigen test is 1 of 4 criteria for stopping antifungal treatment.

Recommendations include treating until the urine antigen concentration is negative. Ideally all of the following criteria are met before discontinuing antifungal treatment for histoplasmosis or blastomycosis. Less commonly, when all other criteria are met, antifungal therapy can be successfully discontinued when urine antigen concentrations are very low (positive but below the limit of quantification, BLQ. Early

on, if *Histoplasma* urine antigen concentrations are extremely high, and not quantifiable (above the limit of quantification, ALQ), serum antigen concentrations can be used instead for monitoring.

1. Minimum of 6 months of antifungal treatment
2. Resolution of clinical signs
3. Resolution of diagnostic imaging abnormalities (or minimal static disease)
4. Negative urine antigen test

Disease relapse can be demoralizing for the pet-owner and places the pet at risk for euthanasia. Ideally disease relapse is avoided, but when it does occur, early detection is essential. Studies have shown that urine antigen concentrations increase with disease relapse [1, 2]. It is recommended to test for urine antigen at 6 and 12 months after stopping antifungal therapy and then annually thereafter. Moreover, antigen testing should be done anytime there is clinical concern for disease relapse.

Antigen concentrations increase with disease relapse and should be monitored after antifungal treatment.

Itraconazole blood levels should be monitored after steady-state, 2 weeks in dogs and 3 weeks in cats.

In addition to antigen concentration monitoring, itraconazole blood levels should be monitored. The absorption of itraconazole in dogs and cats is highly variable and a starting dose is only a starting point [3]. Monitoring itraconazole blood levels can help ensure a positive treatment outcome while facilitating treatment cost efficiency.



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REFERENCES:

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2. Foy DS, Trepanier LA, Kirsch EJ, et al. *Serum and urine Blastomyces antigen concentrations as markers of clinical remission in dogs treated for systemic blastomycosis*. J VET INTERN MED 2014;28:305-310.
3. Renschler J, Albers A, Sinclair-Mackling H, Wheat LJ. *Comparison of compounded, generic, and innovator-formulated itraconazole in dogs and cats*. J AM ANIM HOSP ASSOC 2018;54:195-200.

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