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CLINICAL DIAGNOSIS

MiraVista *Blastomyces* Antigen EIA Advantage

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Background

Blastomycosis is endemic in the United States around the Great Lakes, St. Lawrence seaway, southeastern states, and less frequently elsewhere. Clinical findings include pulmonary disease alone or accompanied by disseminated disease. Antigen detection is a rapid method for diagnosis with recognition that cross reactions occur in histoplasmosis. From MiraVista's review of data, urine antigen is positive in 4.2% and serum antigen 3.2% of large customers from Wisconsin, Minnesota, Arkansas, Tennessee, and Iowa, which are endemic for blastomycosis. Reviews by Drs. Smith and Kauffman on blastomycosis are recommended resources [1, 2].

Performance

The MiraVista *Blastomyces* antigen enzyme immunoassay (EIA) was introduced in 2003 [3] and modified for quantification in 2011 [4], table 1. The sensitivity for detection of antigen in urine is 90% and 57% in serum [4], table 1. Specificity is 99% in controls with non-fungal diseases and healthy subjects and cross reactions occurred in 96% of patients with histoplasmosis. Day-to-day reproducibility (figures 1 and 2) and precision are excellent (table 2).

The EIA also is used for detection of antigen in bronchoalveolar lavage (BAL). The galactomannan antigen detected in histoplasmosis and blastomycosis is identical and cross reactions in the *Histoplasma* antigen EIA occurred in 80% (8/10) of BAL specimens from patients with blastomycosis [5]. *Blastomyces* antigen also may be detected in CSF in patients with *Blastomyces* meningitis, table 3 [6].

Monitoring Treatment

Serial testing is used as an aid in judging success of treatment. Results of testing on different days exhibit reliable reproducibility, figure 1. Change in antigen concentration between current and prior specimens also show strong agreement, (R2 0.9338, slopes 0.8454, Y intercept 0.0401), figure 2. Testing at 3 months intervals during and at least one year after stopping treatment is recommended.

Gotham *Blastomyces* Antigen EIA

The Gotham EIA was introduced in 2021 [7]. Results from testing are compared to those in the Gotham EIA. Positive agreement was 97.4% and negative agreement was 100%, but agreement of antigen concentration was low (y= 0.6067x + 2.4889, R2 0.2031). Urine from 4 patients with blastomycosis were positive in the MiraVista and Gotham EIA. Urine was tested from 9 patients with histoplasmosis, and antigen was detected in 5 (55.5%) in the Gotham EIA and 7 (77.7%) in the MiraVista EIA.

Advantages of MiraVista EIA

MiraVista has been offering its *Blastomyces* EIA for over 17 years. It has been validated for testing serum, urine, and BAL and is also offered for testing CSF as a rare specimen type pending validation, Table 4. These improvements have increased the sensitivity for diagnosis of different forms of blastomycosis.

Turn-around time is 1 day in 92%, 2 days in 98% and 3 days in 99%, providing rapid results permitting accurate diagnosis earlier, table 5.

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Recommendations for Diagnosis

1. Testing urine and serum provides the most sensitive method for diagnosis, table 6
2. BAL should be tested if bronchoalveolar lavage is performed, table 4
3. CSF should be tested if meningitis is suspected, table 4
4. Send directly to MiraVista for results in 1-3 days in 99% of cases, table 5

Table 1. Sensitivity and specificity

Specimen type	Sensitivity	Specificity [1]	Reference
Urine	85%	100%	[8]
Serum	82%	100%	[8]
Urine	93%	100%	[3]
Serum	Not done	Not done	[3]
Urine	90%	99%	[4]
Serum	57%	Not done	[4]
Urine	87%	Not done	[9]
Serum	67%	Not done	[9]
BAL	80%	100%	[5]

[1] Excludes cross-reactive galactomannan (histoplasmosis, paracoccidioidomycosis, talaromycosis)

Table 2. Precision MiraVista *Blastomyces* antigen EIA

Calibrator	Mean (ng/mL)	Standard deviation (ng/mL)	Coefficient variation percent
High	11.92	0.71	5.91
Moderate/high	8.42	0.48	5.66
Moderate	2.87	0.21	7.16
Moderate/low	0.77	0.07	9.19
Low	0.19	0.03	14.00

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Table 3. Detection of antigen in the CSF from patients with *Blastomyces* meningitis

Immunity	CSF Culture	Antigen n/mL	References
Competent	Negative	1.82	Walkty [10]
Compromised	Positive	Positive	Bariola [6]
Competent	Negative	Positive	Bariola [6]
Competent	Positive	Positive	Bariola [6]

Table 4. Antigen results from a single institution January 2020-June 2021

Specimen	Positive	Negative	Total	Positive %
BAL	5	98	103	4.9
CSF	2	51	53	3.8
Serum	35	1061	1096	3.2
Urine	99	2245	2344	4.2
Total	141	3455	3596	3.9

Table 5. MiraVista *Blastomyces* Antigen EIA

Parameter	Finding
Years offered	17
Years' personnel experience	108
Number of EIAs weekly	8
Cross-reactivity	Histoplasmosis, 96% Coccidioidomycosis, ~10% Aspergillosis, <5%
TAT	1-day 92%, 2-day 98%, 3-days, 99%

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Table 6. Importance of testing urine and serum: Results single institution

Results		Percentage	Advantage
Urine	Serum	Number (%)	
Positive	Positive	37 (61.7%)	Highest sensitivity testing serum and urine
Positive	Negative	10 (16.7%)	Urine sensitive single test
Negative	Positive	6 (10%)	Urine alone misses 10%
Serum >urine		4 (6.7%)	Serum better for serial testing 6.7%
Serum positive Urine BLQ (< 0.2 ng/mL)		3 (5%)	Positive serum true positive BLQ

Figure 1. Reproducibility of *Blastomyces* antigen EIA for diagnosis

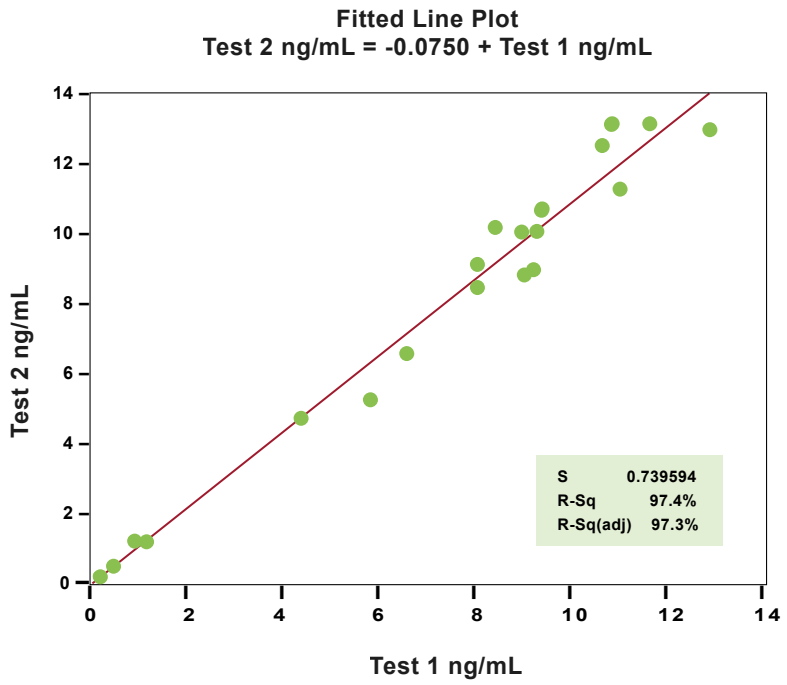

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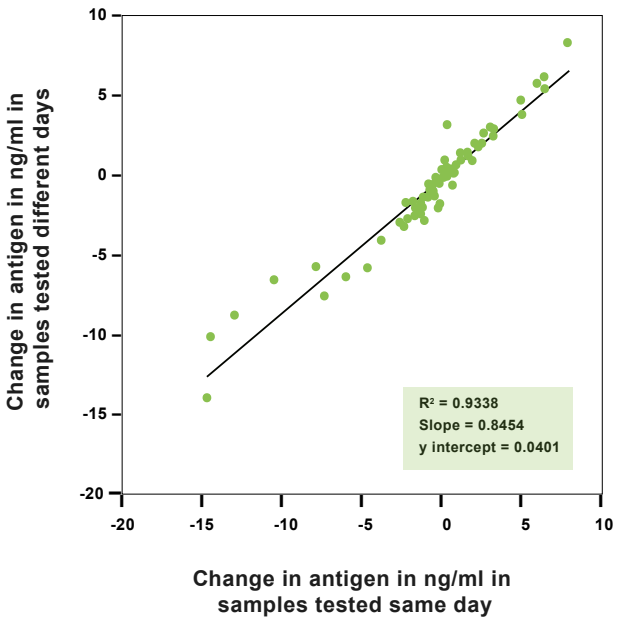
Figure 2. Reproducibility of *Blastomyces* antigen EIA for monitoring antigen clearance during treatment [4]



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