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Coccidioides

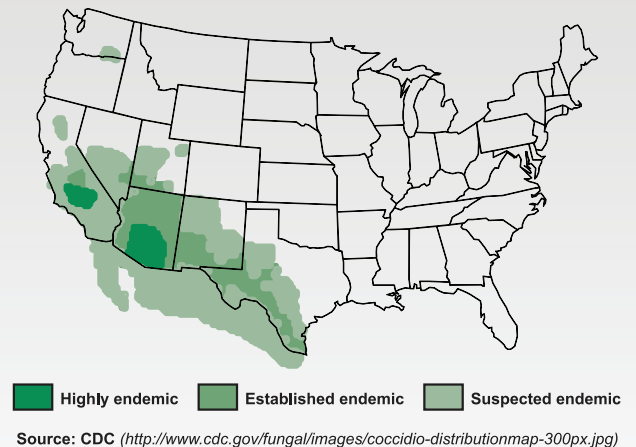
Improve Coccidioidomycosis Diagnosis with a New, More Sensitive, Anti-Coccidioides Antibody Enzyme Immunoassay

NEW: MVista® Coccidioides Antibody IgG and IgM EIA

CLINICAL BACKGROUND:

Coccidioidomycosis is endemic to the southwestern United States, northern Mexico and regions of Central and South America. Coccidioidomycosis often presents as community acquired pneumonia (CAP) and is estimated to be the cause of 15-30% of such infections in endemic areas. However, infections can range from asymptomatic to life-threatening, or acute pulmonary disease. Serology is the most common technique used for diagnosis, specifically the detection of IgG and IgM antibodies by immunodiffusion (ID) and enzyme immunoassay (EIA), followed by IgG quantification by complement fixation (CF). CF and ID are time consuming and laborious methods for laboratories, with turnaround times between 2 and 6 days. False negative results may occur in all of the antibody tests, especially in immunocompromised patients. The sensitivity of the two commercial antibody detection EIAs was estimated to be between 68% and 72% (Sunshine, R ICAAC 2014).

Areas Endemic for Coccidioidomycosis



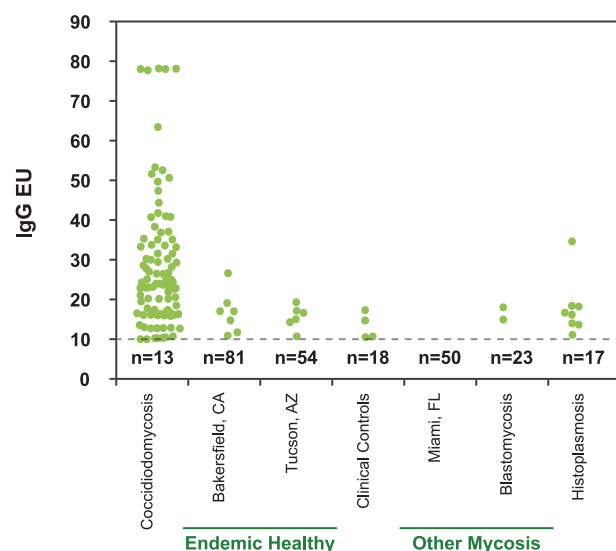
RESULTS

While MiraVista Diagnostics' MVista® Coccidioides Antigen EIA has demonstrated sensitivity between 70% and 87% in immunocompromised patients and those with severe disease, improved antibody detection could increase the sensitivity for diagnosis of the cases that are falsely-negative in the antigen assay and the currently available antibody assays, especially in patients with moderate to mild disease, allowing for earlier diagnosis and treatment. In 2016, MiraVista Diagnostics developed the MVista® Coccidioides Antibody IgG and IgM EIA to offer clinicians a more rapid and accurate testing method for coccidioidomycosis. The new assay has demonstrated a sensitivity of 88.3% in either IgG or IgM antibody, which is significantly higher than other commercially available tests, and specificity of 91.8%.

The EIA was positive in 31 of 41 (76%) cases in which the ID was negative. The EIA was positive in 60 of 61 cases in which the ID was positive, and was intermediate in that case. The EIA was positive in 18 of 20 (90%) cases in which the CF was negative. The EIA was positive in 39 of 41 cases in which the CF was positive, and was intermediate in the remaining 2 cases. The CF titer was less than 1:2 in one and 1:2 in the other EIA intermediate cases.

Cross-reactivity can be resolved by consideration of epidemiological factors and comparing results in the Coccidioides antibody EIA and the Histoplasma or Blastomyces antibody EIA: in the appropriate epidemiological setting, the higher antibody level is likely to indicate the correct diagnosis.

Anti-Coccidioides IgG Detection in Serum Specimens



The cut-off for antibody detection (10EU) is indicated by the dashed line and the number of negative samples is indicated underneath the line. The sensitivity was 87.4% and specificity was 92.3% for detection of IgG antibodies. IgM antibodies, which are thought to be more common in acute coccidioidomycosis, were detected in 61.2% of cases.

TEST	SENSITIVITY	SPECIFICITY
MVista® IgG	87.4%	90.0%
MVista® IgM	61.2%	95.3%
IDCF	53.4%	98.6%
IDTP	33.0%	100%
CF	66.1%	N/A
Commercial EIA 1 IgG	46.6%	94.6%
Commercial EIA 1 IgM	22.3%	98.2%
Commercial EIA 2 IgG	70.9%	96.4%
Commercial EIA 2 IgM	29.1%	99.1%

CONCLUSIONS

The new MVista® *Coccidioides* Antibody EIA offers significant improvements in the diagnosis of coccidioidomycosis. It is a reliable method for detecting anti-*Coccidioides* antibodies and it is more sensitive than ID and CF antibody detection as well as other commercially-available EIAs. Additionally, MVista® *Coccidioides* Antibody EIA complements the MVista® *Coccidioides* Antigen EIA by helping clinicians accurately identify and quickly diagnose patients with coccidioidomycosis, from moderate and mild cases to severe disease.

MVista® *Coccidioides* Antibody IgG and IgM EIA

TEST CODE: 325

CPT CODE: 86635 x2

SPECIMEN COLLECTION

- **Serum:** Collect serum specimens in serum separator or red top tube. Allow blood to clot for 30 minutes, then centrifuge. Pipette serum into a plastic screw cap vial.
- **CSF:** Sterile transport tube

MINIMUM SPECIMEN REQUIREMENTS

- **Serum/CSF:** 0.5 mL

SPECIMEN STABILITY

- **Refrigerated:** 14 Days
- **Frozen:** 14 Days

SPECIMEN REJECTION: Any specimen other than serum or cerebrospinal fluid

TRANSPORT TEMPERATURE: Refrigerated/Frozen

SHIPPING: Ship on dry ice or frozen packs for next day service. Monday - Friday delivery.

TURNAROUND: Testing performed Monday and Thursday

- **Serum or CSF:** Reported next day.

REFERENCE RANGE: Negative

INTERPRETATIVE INFORMATION

- **Negative:** <8.0 EU
- **Intermediate:** 8.0 EU - 9.9 EU
- **Positive:** 10.0 EU - ≥80.0 EU

METHODOLOGY: Semi-Quantitative Indirect Enzyme Immunoassay (EIA)

LIMITATIONS

- 8% cross reactivity with Blastomycosis
- 36% cross reactivity with Histoplasmosis

CLINICAL SIGNIFICANCE: IgM and IgG antibodies to *Coccidioides* antigen usually appear during the first month of infection, decline over the next 3-6 months but remain detectable for approximately 18-24 months in some cases with self-limited illnesses. Antibodies may persist in patients with chronic pulmonary complications or progressive extrapulmonary (disseminated) coccidioidomycosis. Antibodies may be falsely-negative in some progressive or chronic cases. Follow-up testing maybe considered at weeks 2 - 4 to determine if antibody levels are increasing especially in patients with low positive (10 EU – 20 EU) or intermediate results. Increase in antibody concentration would suggest recent infection. Antibodies may also be detected in healthy subjects who are asymptomatic as a result of sub-clinical infection within the last 18 - 36 months.