Case report. A healthy young woman from California presented with low-grade fever, cough, arthralgias and painful bumps on her legs of two weeks duration. Temperature was 100.6°F and examination showed tender erythematous nodules on both legs. Chest radiograph demonstrated right hilar lymphadenopathy and a patchy infiltrate in the right lower lobe. Pertinent laboratory findings included 12% eosinophilia. Coccidioidomycosis was suspected but the *Coccidioides* antigen and antibody tests (immunodiffusion [ID] and complement fixation [CF]) were negative.

**Question.** Do negative antigen and antibody test exclude coccidioidomycosis?

**Answer.** No. The diagnosis was acute pulmonary coccidioidomycosis (APC). Antigen is detected mostly in immunocompromised patients with disseminated coccidioidomycosis,[1, 2] ID and CF are negative in 40-60% of patients with APC.[3] The diagnosis in this case was based on positive IgG and IgM antibodies in a new EIA[4] (Journal of Clinical Microbiology Feb 2017, 55 (3) 893-901). The IgG level was > 80 units and the IgM level were 73 units six weeks after onset of symptoms and declined over the next 16 months (Figure 1).

The study evaluating the new EIA included 103 patients with pulmonary (70%) or disseminated (30%) coccidioidomycosis. Most had been ill for several months and 75% were receiving antifungal therapy.

Sensitivity of EIA was higher than ID or CF (Table 1) and not affected by disease manifestation (p=0.308), immune status (p=0.498) or antifungal therapy (p=.760).

IgG specificity was 91% and IgM was 97% in healthy persons from areas where 70% are skin test positive. Cross-reactivity occurred in 32% of patients with histoplasmosis and 8% with...

### Table 1

<table>
<thead>
<tr>
<th>Disease</th>
<th>EIA</th>
<th>ID</th>
<th>CF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disseminated-31</td>
<td>84%</td>
<td>71%</td>
<td>68%</td>
</tr>
<tr>
<td>Pulmonary-72</td>
<td>92%</td>
<td>54%</td>
<td>65%</td>
</tr>
<tr>
<td>Immunocompromise</td>
<td>83%</td>
<td>50%</td>
<td>65%</td>
</tr>
</tbody>
</table>

**Figure 1**

![Graph showing the relationship between MVD IgG and MVD IgM antibody levels over time.](image-url)
blastomycosis. In histoplasmosis cases, antibody levels are lower in the Coccidioides EIA compared to the Histoplasma antibody EIA.

Moreover, IgG and IgM levels are highly reproducible, which is essential for quantification (Figure 2). Quantification facilitates determination of seroconversion and antibody clearance during treatment. **Summary.** The new antibody EIA offers major advancement in diagnosis and management of coccidioidomycosis. Cross reactions can be resolved by comparison of antibody levels to the related fungi. Background IgG levels of 10-20 units occur in about 10% of healthy subjects from highly endemic areas, overlapping those in patients with recent coccidioidomycosis. Repeat testing may differentiate active from past infection. Some cases are negative by EIA but positive by ID, supporting testing by both methods.

**Reference List**


![Figure 2](image-url)