

Application and Interpretation of Serologic Tests

A. Our usual serologic tests for coccidioidomycosis are the following:

1. **Qualitative:** Immunodiffusion (ID) to determine presence of coccidioidal IgM ("precipitin") (test may be termed "IDTP"), or IgG (CF) (test may be termed "IDCF") antibody in body fluids. This is appropriate if no diagnosis of coccidioidomycosis has previously been established. [Non-specific reactions resembling that given by the coccidioidal precipitin (IgM) are encountered infrequently with some sera, e.g. from patients who do not have coccidioidomycosis.]
2. **Quantitative:** Determination of level (titer) of the IgG by complement fixation (CF). [Under some circumstances - very small volume, or unsatisfactory specimen for CF test - a quantitative immunodiffusion will be done, and this provides an approximation of the CF titer.] Determination of titer is appropriate after a diagnosis has been established, e.g. by positive immunodiffusion or recovery of *C. immitis* from the patient.

B. Results and interpretation:

1. Detection of coccidioidal antibody in a single specimen can be diagnostically significant; testing sequential samples can be helpful in following the course of the disease.
2. **Immunodiffusion (ID)** - presence or not of precipitin (IgM) or CF (IgG) antibody. The IgM is important in the diagnosis of acute primary coccidioidomycosis, and is detectable in most patients in 1 to 2 weeks after onset of symptoms, may persist several months, occasionally longer in association with a pulmonary cavity or disseminated disease. Presence of IgM in the CSF is associated with coccidioidal meningitis.

The CF(IgG) can be associated with a recent infection but can be detected in the serum months or years after the initial infection. Once positive, the qualitative immunodiffusion test may not need to be repeated*.

3. **Complement fixation (CF)** - reactivity given as 4+, 3+, 2+, 1+ or no ("0") fixation of complement at a given serial dilution of specimen. 4+ is significant CF (or 3+ provided immunodiffusion is also positive). 2+ and 1+ are not significant. A rising titer is unfavorable - titer greater than 1:16 in the serum is often associated with metapulmonary dissemination, but a lower titer can be associated with limited dissemination e.g., single osseous, or cutaneous lesion, or meningeal involvement. CF by the CSF is usually indicative of coccidioidal meningitis but the IgG can be detected in the CSF in the absence of meningitis. Approximately 5% of patients with coccidioidal meningitis may initially have CSF negative by CF.

When available, a prior positive serum, CSF, etc. is frozen for later simultaneous testing with a new specimen to control for variability in the CF test. This is rarely carried out in other laboratories.

4. Negative serologic tests do not rule out coccidioidal disease. By our methods, approximately 5% of patients with AIDS and coccidioidomycosis are seronegative as are some other immunocompromised patients.
5. The enzyme linked immunoassay (EIA) and latex particle agglutination (LPA) are qualitative tests carried out in other laboratories. The EIA is very sensitive and quite specific for the detection of coccidioidal IgG, though some specimens that are EIA positive for IgG yield only a reaction for coccidioidal IgM by immunodiffusion. The EIA yields some false positive reactions for the IgM. At present the EIA is not useful in determining titer. The LPA was intended to detect IgM but yields false positive reactions (perhaps 10 to 15%), and is sometimes reactive when only coccidioidal IgG is detected by ID test.

* Under some circumstances, it may be appropriate to repeat the qualitative immunodiffusion test, both to confirm presence of coccidioidal antibody and to determine whether the IgG or IgM is present.