SEROLOGY OF COCCIDIOIDOMYCOSIS

by

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For more than thirty years, coccidioidomycosis has been recognized as a primary respiratory infection resulting in symptoms which may simulate those of any other known respiratory disease. This infection is caused by the fungus, *Coccidioides immitis*, which appears to have a distribution restricted to the desert-like areas of the New World. Definitive diagnosis is accomplished best by isolation of the fungus or by demonstrating characteristic endosporulating spherules in diseased tissues. Frequently, this cannot be accomplished and one must rely on immunological tests as an aid for establishing a diagnosis. The work of Dr. C. E. SMITH and his colleagues (4) has established that several of these tests yield results useful not only for diagnosis but also for prognosis in this disease.

Recent evidence, however, has indicated that it is time to re-investigate the question of the limited distribution of this fungus. We have reported that as many as 20 % of proven cultures of *C. immitis* have cultural characteristics which differ markedly from earlier descriptions (3). This raises the question, “How many times have we failed to recognize cultures like these as *C. immitis*?” In addition to this, we must note that Dr. GONZALEZ-OCHOA (1) has reported that coccidioidomycosis exists in at least two areas in Mexico where the climate and ecology is tropical rather than arid. Furthermore, persistent reports of coccidioidal-like disease in the Soviet Union have been related to me by Professor KASHKIN. These observations indicate that coccidioidomycosis may be present but not generally recognized in areas which have a climate other than desert-like and in countries outside of the New World. We now propose that these possibilities be investigated by immunological methods.

The clinical interpretations which can be derived from the established immunological tests are important to consider (Fig. 1.) Infection by *C. immitis* results in development of the delayed type of dermal hypersensitivity to coccidioidin. A positive skin test is

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apparent usually during the first week of clinical disease and remains positive for long periods. This is a useful and practical test but a single positive result indicates only a past exposure to the fungus and not necessarily current active infection. For detection of recent disease, serological procedures are more valuable. The tube precipitin test usually becomes positive by the first week of clinical illness, but the frequency of positive results declines to less than 10% by the fourth month. Therefore a positive tube precipitin test indicates early active disease. The complement fixation, or CF, test also becomes positive early but it tends to remain positive for longer periods than the tube precipitin test. Therefore, a single positive complement fixation test may indicate either early active disease or a residual positive from previous infection. It is important, however, that both serological tests be done, because the tube precipitin result may have reverted to negative by the time a specimen has been obtained or the complement fixation reaction may not yet be positive. Unfortunately, these two serological tests are not practical for studies in population groups. The complement fixation test requires too much time and special laboratory equipment, and the tube precipitin test presents some difficulty in obtaining reproducible readings and high sensitivity. For these reasons we have evaluated an agar-gel immunodiffusion method as a substitute for complement fixation, and latex particle agglutination as a substitute for the tube precipitin test (2). The immunodiffusion (ID) and latex particle agglutination tests were chosen because earlier studies had shown that they have a high level of sensitivity, that they require only minor equipment that is adaptable to use in the field, that many specimens can be tested in a few minutes, and that results are obtained in four minutes with the latex particle agglu-