To the Editor: I appreciate the opportunity to respond to Dr. Pifer’s comments about my statements regarding serologic tests for *P. carinii* pneumonitis. I concluded that further studies are required before the antigenemia test can be used as an alternative to an invasive diagnostic procedure.

The original study in 1978, describing the use of rabbit antiserum to *P. carinii* for the detection of circulating antigen by counterimmunoelectrophoresis (CIE), led me to believe that this approach might become a useful diagnostic test for this disease. However, two subsequent studies and experience in my laboratory have convinced me that this is not a dependable diagnostic test for *P. carinii* pneumonitis. In my review I referred to one of these reports, the controlled study by Meyers et al., in which coded sera from the Seattle patients were tested as unknowns by Dr. Pifer. The results are summarized in Dr. Pifer’s table under category No. 6, the bone marrow allophage study. This was a well-designed study and the cases were well-documented by lung biopsy. The fact that the *P. carinii* antigen test result was “positive” in 69 percent of viral pneumonias, 65 percent of idiopathic pneumonias and 44 percent of individuals with no pneumonia clearly showed the test was of no diagnostic aid in this study.

The second study of significance was done at the Centers of Disease Control in 1982. The antiserum was used by the method of Dr. Pifer, was tested in her laboratory and found to detect *P. carinii* antigen. However, when tested at the CDC using the CIE method, it detected *P. carinii* antigen in only 8 (11 percent) of 70 proved cases of *P. carinii* pneumonitis and in one of 99 healthy serum bank donors.

Recently, another study from the CDC found the antigen test positive in 41 percent of 32 AIDS patients with *P. carinii* pneumonitis, 18 percent of 123 homosexual and 33 percent of 12 heterosexual control subjects without AIDS.

In my laboratory we have prepared two separate batches of rabbit antiserum to *P. carinii* with high antibody titers, but when tested by CIE with stored sera from human cases and rat sera from experimental *P. carinii* pneumonitis, the yield was no greater than 30 percent positive. These results failed to confirm the high sensitivity of the earlier report.

As a physician at the bedside of an immunosuppressed patient with pneumonitis, I must ponder which data base I should use to interpret the CIE test. If the patient’s test is positive, should I consider the data in the study by Meyers and Pifer where 69 percent of the cases of viral pneumonias and 44 percent of cases with no pneumonia were positive (Table)? If the patient’s test is negative, should I rely on the CDC data wherein 89 percent of the proven cases of *P. carinii* pneumonitis were negative? Dr. Pifer states that the antigen test results are useful when considered in perspective with other clinical data. However, clinicians will realize that identification of the etiology of diffuse pneumonitis, in the immunosuppressed host is not aided by the clinical assessments mentioned. For example, the clinical features of cytomegalovirus, adenovirus, E-B virus and *P. carinii* pneumonitis may be identical.

What accounts for the disagreement of dedicated and sincere investigators? Several possibilities come to mind. One consideration is the concepts of disease and infection by the clinical physician and the laboratory physician. Clinicians are seeking a test that will identify the cause of a diffuse, life-threatening pneumonitis (the disease), more so than a test that will include the latent, inactive, dormant or subclinical infection from *P. carinii*. To explain the "false positives" in the laboratory as representing subclinical infection could be valid, though not proven. This is the problem with the diagnosis of other opportunistic infectious diseases such as those caused by *Candida* sp and cytomegalovirus. A secondary problem is thorough characterization of "documented" cases of *P. carinii* pneumonitis and the temporal relationship to the serologic test. Properly done the serum specimen should be collected prior to the diagnostic biopsy and only that (not subsequent serial samples) should be tested, since this is the critical time for its use. For such a test to be accepted for general use it must be accurately standardized with a system for quality control. The *P. carinii* antigen preparation used for antibody production is not purified, contains components of the host cell culture, and has not been characterized or quantitated. Another problem stems from the need for several laboratories working independently to evaluate this test.

I believe the CIE test for *P. carinii* antigen as performed in Dr. Pifer’s laboratory may indeed detect some antigenic component of *P. carinii*, or a closely related antigen. Further efforts in the laboratory to characterize the antigen and antibody components, evaluate newer systems more sensitive than CIE (ELISA and radioimmunossay), quantitate the circulating antigen and establish methods for quality control seem warranted. However, at the present time I must contend that it cannot be recommended as a dependable test for the critically ill patient with *P. carinii* pneumonitis. Probably no one is more hopeful than I for such a test. Despite the fact that numerous reports of antigen detection systems for *Candida albicans*, *Aspergillus* sp, *cytomegalovirus*, *herpes simplex*, etc have appeared in recent years, and such tests are marketed, I still stand at the bedside of the immunosuppressed febrile patient disappointed, confused and diagnostically incompetent. I hope the pace of development of precise and dependable diagnostic tests for disease will exceed the pace of development of safe empirical therapy.

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