



Update

FOR IMMEDIATE RELEASE

Elaine Baldwin (301) 496-5717
Colleen Henrichsen (301) 496-2563

A rapid, sensitive, and non-invasive test for diagnosing the most common and deadly AIDS-associated infection, *Pneumocystis carinii* pneumonia (PCP), has been developed by scientists at the National Institutes of Health (NIH) in Bethesda, Maryland, and used successfully in patients treated at NIH and at San Francisco General Hospital. The technique uses a new, highly accurate method of identifying *P. carinii* organisms in the sputum of patients.

Results of a collaborative study involving scientists at the NIH Clinical Center, the National Institute of Allergy and Infectious Diseases (NIAID), the University of California at San Francisco (UCSF), and San Francisco General Hospital were reported by Joseph A. Kovacs, M.D., NIH Clinical Center, in the March 10, 1988 issue of *The New England Journal of Medicine*.

PCP, the leading cause of death in persons with AIDS, affects 70 percent of AIDS patients at some point in their illness. By 1991, 10 years into the AIDS epidemic in the United States, an estimated 100,000 Americans will have been diagnosed with AIDS-related PCP.

"The earlier we can detect PCP, the better the prognosis for effective treatment," Dr. Kovacs said. "Presenting symptoms of PCP often resemble less serious respiratory conditions, and it is important to establish the diagnosis and begin therapy promptly."

Currently, PCP is most frequently diagnosed by inserting a bronchoscope into the lungs and either irrigating the lungs to obtain fluid samples (lavage) or using the bronchoscope to obtain a tissue sample (biopsy). Although these techniques are generally safe and sensitive, many physicians are reluctant to use them because of potential complications, cost, and discomfort to patients. Occasionally it is necessary to perform a biopsy through open lung surgery, a more risky and costly procedure.

As an alternative to these invasive diagnostic techniques, Dr. Kovacs and his colleagues induced patients to cough up sputum by having them inhale a saline mist generated by an ultrasonic nebulizer. This technique had previously been shown to be useful in diagnosing PCP by investigators at UCSF and at the University of Miami, but in only 55 percent of cases.

In the NIH study, the sputum specimens were stained with three different preparations--using two conventional techniques and a newly developed method--to compare their sensitivity and specificity in the detection of *P. carinii*. Results of the induced sputum tests were compared against results of tests of fluid samples obtained by bronchoscopy. The studies were blinded to avoid any bias in the interpretation of results with the various stains.

The investigators found that the most sensitive test employed monoclonal antibodies, developed in the NIH Clinical Center's Critical Care Medicine Department, that react specifically with *P. carinii* organisms. The monoclonal antibodies were used in an indirect immunofluorescence assay; i.e., when tagged with fluorescent dye they could be viewed under a fluorescent microscope.

Of 63 patients at San Francisco General Hospital from whom sputum specimens were obtained, PCP was ultimately diagnosed in 49 patients, 46 by staining of sputum. Compared to two traditionally used stains, which identified 76 percent and 80 percent of the patients, respectively, the indirect immunofluorescence assay identified 92 percent of the patients with PCP. In a study of similar techniques at the NIH Clinical Center, 23 of 25 patients with PCP were diagnosed by staining of induced sputum.

All of the patients with sputum specimens that were positive by immunofluorescence were documented to have PCP by a second sputum staining technique or by follow-up bronchoscopy. Dr. Kovacs said, "Indirect immunofluorescence is the most sensitive stain we have tested. It is a practical, economical diagnostic technique that can be easily adapted by most microbiology laboratories." Dr. Kovacs said that the Federal government has applied for permission to license the monoclonal antibodies against PCP. Diagnostic kits utilizing the monoclonal antibodies are currently being developed and should be commercially available to laboratories in the near future, he added.

"Staining of induced sputum is clearly a safe, non-invasive method for rapidly diagnosing PCP in patients with AIDS," Dr. Kovacs said, "and is a significant advance in our efforts to respond quickly with appropriate therapy for this major killer."

In addition to Dr. Kovacs, the authors of the report included Vee J. Gill, M.D., Henry Masur, M.D., Frederick P. Ognibene, M.D., Joseph E. Parillo, M.D., James H. Shelhamer, M.D., and Gloria Evans, B.S., NIH Clinical Center; H. Clifford Lane, M.D., NIAID; and W. Keith Hadley, M.D., Ph.D., Valerie Ng, M.D., Ph.D., and Gifford Leung, M.D., UCSF and SFGH.

#

Prepared by
Office of Communications
National Institute of Allergy
and Infectious Diseases

March 1988