

Precipitins and the diagnosis of a hypersensitivity pneumonitis

Asthma, the hypersensitivity lung disease most familiar to the allergist, is frequently the result of an IgE-antigen-mediated immediate (type I) allergic reaction and is associated with an apparent autonomic nervous system alteration. Recently, however, chest physicians as well as allergists have become aware of patients with hypersensitivity lung diseases presenting with symptoms other than asthma and probably mediated by other immunologic mechanisms. A group of these lung diseases, known as hypersensitivity pneumonitis or extrinsic allergic alveolitis, is associated with the inhalation of a variety of organic dusts by sensitized individuals. The offending dusts, the number of which is steadily expanding, are usually present in the patient's environment. Theoretically, all foreign organic matter of proper size can serve as a potential antigen source, depending on the usual immunologic prerequisites such as molecular size, degree of "foreignness," number and configuration of determinant groups, and efficiency of macrophage processing, as well as intensity of exposure and the responsiveness of the individual. However, the most common sources of antigen are associated with thermophilic actinomycetes, various fungi, and a few foreign proteins. Exposure to them is often related to the patient's occupation (farmer's lung, bagassosis, malt worker's lung), his hobby (pigeon breeder's disease), or his home or office environment served by a "contaminated" forced-air heating or air conditioning system.¹⁻⁵

The clinical features of a hypersensitivity pneumonitis are usually determined by the manner in which a patient is exposed to the offending dust. Intermittent exposure results in acute episodes of chills, fever, cough, and dyspnea in 4 to 6 hours. These disorders are usually presumptively diagnosed on clinical grounds once the physician elicits the history and observes the patient during several episodes.¹⁻⁴

More constant exposure to organic dust antigens, such as found with individuals chronically exposed to contaminated home or working environments, may result in an insidious and less easily diagnosable hypersensitivity pneumonitis. Such patients may develop progressive dyspnea associated with pulmonary fibrosis but without acute episodic symptoms.³⁻⁵ In all types of hypersensitivity pneumonitis, however, identification of the offending material becomes most important since continued exposure may lead to irreversible

pulmonary damage, while avoidance of exposure can result in complete recovery.³⁻⁶

Serologic studies of patients with hypersensitivity pneumonitis have uniformly demonstrated precipitating antibodies against the offending antigen. These circulating antibodies, predominantly of the IgG type, have been characterized using such tests as radioisotope-labeled antigen binding and quantitative precipitin techniques, autoradiographic immunoelectrophoresis, and passive cutaneous anaphylaxis.⁷ In most studies, however, precipitins can be easily demonstrated in the laboratory by simple Ouchterlony gel double diffusion and by hemagglutination tests.^{8, 9} Thus, testing of sera patients against a number of suspected antigens using these simpler tests may provide an etiologic diagnosis when supported by the historical and clinical features of the illness.

Because of the ease of detection of precipitins, their importance in establishing the diagnosis, and the general interest of physicians in detecting cases of hypersensitivity pneumonitis, several commercial gel diffusion testing kits will shortly be available to help physicians arrive at a correct etiologic diagnosis. The demonstration of serum precipitins against an antigen present in a patient's environment, however, does not necessarily indicate the presence of hypersensitivity pneumonitis. It has been shown that up to 50 per cent of *asymptomatic* individuals inhaling organic dust antigens may develop serum precipitins to these materials without developing any features of a hypersensitivity pneumonitis.^{4-6, 10} Conversely, many antigens involved in production of hypersensitivity pneumonitis have likely not been identified. In addition, precipitins against known antigens tend to diminish or disappear with cessation of acute disease activity.⁴ Thus a negative precipitin test in no way excludes the diagnosis, while a positive test without interpretation of clinical findings does not establish the diagnosis.

Other limitations of the gel diffusion technique, such as the need for proper staining of the proteins, possible marked differences in antigen-antibody concentration ratios, and the presence of nonspecific lines due to cross-reacting antibody against teichoic acid cell wall constituents or to C substance-C-reactive protein interaction,^{4, 11} must also be considered in evaluating the results of the precipitin test.

In view of these facts, the clinician should realize that as tests for precipitating antibodies become widely available, a positive result, although quite helpful diagnostically, should be used only as confirmatory evidence, and a single negative result should not necessarily rule out the diagnosis. The history of the patient, which suggests that environmental exposure is related to his disease process or, in doubtful cases, observation of the patient after natural exposure to suspected antigenic material must be considered to have more significant diagnostic value.

Jordan N. Fink, M.D.

Abe J. Sosman, M.D.

John E. Salvaggio, M.D.

Joseph J. Barboriak, Ph.D.

Milwaukee, Wis., and New Orleans, La.

REFERENCES

- 1 Dickie, H. A., and Rankin, J.: Farmer's lung—an acute granulomatous interstitial pneumonitis occurring in agriculture workers, *J. A. M. A.* **167**: 1069, 1958.
- 2 Buechner, H. A., Prevatt, A. L., Thompson, J., and Blitz, O.: Bagassosis: A review with further historical data, studies of pulmonary function and results of adrenal steroid therapy, *Am. J. Med.* **25**: 234, 1958.
- 3 Reed, C. E., Sosman, A. J., and Barbee, R. A.: Pigeon breeder's lung: A newly observed interstitial pulmonary disease, *J. A. M. A.* **193**: 261, 1965.
- 4 Pepys, J.: Hypersensitivity diseases of the lungs due to fungi and organic dusts, Basel, 1969, S. Karger AG.
- 5 Banaszak, E. F., Thiede, W. H., and Fink, J. N.: Hypersensitivity pneumonitis due to contamination of an air conditioner, *N. Engl. J. Med.* **283**: 271, 1970.
- 6 Salvaggio, J. E., Buechner, H. A., Seabury, J. H., and Arquembourg, P.: Bagassosis. I. Precipitins against extracts of crude bagasse in the serum of patients, *Ann. Intern. Med.* **64**: 748, 1966.
- 7 Fink, J., Tebo, T., and Barboriak, J.: Characterization of human precipitating antibody to inhaled antigens, *J. Immunol.* **103**: 244, 1969.
- 8 Wenzel, F., Emanuel, D., and Gray, R.: A simplified hemagglutination test for farmer's lung, *Clin. Res.* **17**: 553, 1970.
- 9 Salvaggio, J. E., Arquembourg, P., Seabury, J., and Buechner, H.: Bagassosis. IV. Precipitins against extracts of thermophilic actinomycetes in patients with bagassosis, *Am. J. Med.* **46**: 538, 1969.
- 10 Fink, J. N., Barboriak, J. J., Sosman, A. J., Bukosky, R. J., and Arkins, J. A.: Antibodies against pigeon serum proteins in pigeon breeders, *J. Lab. Clin. Med.* **71**: 20, 1969.
- 11 Faux, J. A., Holford-Strevens, V., Wells, I. D., and Pepys, J.: False positive precipitation reactions to extracts of organic dusts due to a teichoic acid from *S. aureus*, *Clin. Exp. Immunol.* **7**: 897, 1970.