Hypersensitivity Diseases of the Lung

Raymond G. Slavin, M.D.

Recently, great interest has been shown in the lung as an immunologic shock organ. Two conditions in man, hypersensitivity pneumonitis and allergic bronchopulmonary aspergillosis, exemplify the multiple immunologic processes that may interact to cause human disease. A better understanding of the basic mechanisms of these diseases has been gained in the laboratory from the study of animal models. Appreciation of the clinical presentation and the availability and application of appropriate laboratory tests have led to increasing recognition of these diseases. Keeping the diagnostic index of suspicion high and instituting proper environmental and therapeutic measures early will prevent the development of irreparable tissue damage.

The lung is being increasingly recognized as a superb immunologic shock organ. Certainly all of the ingredients for an immune response are present. There is ready access to a host of airborne antigens, and there are in the lung a battery of cells, including mast cells, antibody-producing plasma cells, macrophages, and lymphocytes, both of the T and B series, that are well equipped to respond to an antigenic onslaught.

During the past 15 years, there have been tremendous advances in the definition and characterization of an important group of disorders termed hypersensitivity diseases of the lung. These diseases offer a reminder to all clinicians to extend their scope of immunologically mediated pulmonary diseases beyond IgE-mediated bronchial asthma and cell-mediated diseases such as tuberculosis.

The present era of interest in hypersensitivity lung disease began in 1932 with the first description of farmer's lung, a disease caused by exposure to moldy hay. Recently, a renewal of interest based on more widely available immunologic techniques has stirred a great deal of study on a wide variety of similar diseases associated with different antigens and different exposure situations. Perhaps most significant is the finding that antigens responsible for these diseases need not be related to a special exposure associated with a person's avocation or occupation, but may be found in such common areas as air conditioners and home humidifiers. Thus, the physician must be aware of such exposures and his index of suspicion in dealing with this group of diseases must remain high for several reasons. First, these diseases are being recognized with increasing frequency. Second, the inexorable outcome of these disorders is irreparable tissue damage. It is therefore vital to recognize the disease early before these irreversible changes take place.

This discussion will deal with two widely different entities that have been generally lumped together under hypersensitivity diseases of the lung. The first is hypersensitivity pneumonitis and the second is allergic bronchopulmonary aspergillosis.

Hypersensitivity Pneumonitis

Synonyms for this entity include pulmonary hypersensitivity syndrome and extrinsic allergic alveolitis. This latter term is perhaps the best and most appropriate. "Extrinsic" refers to an exogenous antigen or allergen. "Allergic" refers to that part of the lung that is most affected. The different terms all refer to the same underlying pathogenesis, namely, a disease process that results from a hypersensitivity response to inhalation of a variety of organic dusts.

Several factors that determine the response to an organic dust inhalation have been described. First is the basic immunologic reactivity of the host, ie, is the host atopic or nonatopic? In general, inhalation of an organic dust by an atopic individual results in an immediate type I IgE-antibody response. A nonatopic person will tend to respond with a type III reaction characterized by precipitating antibody. Another important host factor may be the association of HL-A haplotypes with disease. In a study of pigeon-breeder's disease, a common form of hypersensitivity pneumonitis, HL-A 1, 8 was frequently found, suggesting the presence of an HL-associated immune response (Ir) gene. A second factor that determines the response to an organic dust is the nature and source of the

Table 1 • Causes of Hypersensitivity Pneumonitis

Antigen	Disease
Thermophilic Actinomycetes	
Micropolyspora faeni	Farmer's lung, mushroom-worker's disease, humidifier lung
Thermoactinomyces vulgaris	
Thermoactinomyces sacchari	Bagassosis
Mold	
Cryptostroma corticale	Maple bark disease
Aspergillus claatus	Malt-worker's lung
Alternaria	Wood pulp-worker's disease
Pullularia	Sequoiosis
Penicillium	Suberosis
Animal	
Ox or pig	Pituitary snuff-taker's lung
Pigeon	Pigeon-breeder's disease
Dove, parakeet, parrot	Bird-fancier's lung
Rat	Rat-handler's disease
Gerbil	Gerbil-keeper's lung

antigen. Can it grow in the respiratory tract? Is it small enough to reach the alveoli? Can it induce the proper immune response? A third factor is the nature and circumstances of the exposure. Is it an isolated but heavy exposure to the antigen, or is it a low-grade, chronic, insidious type of exposure?

Causative Antigens—Table 1 lists some common antigens that cause hypersensitivity pneumonitis. The list is by no means complete. Any organic dust of proper antigenicity and particle size can produce the identical syndrome. As physicians become increasingly aware of clinical features of hypersensitivity pneumonitis, other causes will undoubtedly be discovered.

One can divide the antigens that cause hypersensitivity pneumonitis into three general categories. The first is the thermophilic organisms. Diseases caused by these agents are associated with environmental exposure to materials that are subjected to high temperatures and high humidity. This is a fertile source for the growth of the thermophilic organisms, unicellular branching organisms that resemble true bacteria. An important recent finding is that an occupational exposure need not be incriminated. The disease has been described by a number of investigators in individuals who were exposed to the organism growing in home humidifiers or air conditioning systems.

The second general antigenic category is molds. Several examples are given in Table 1. A number of examples of hypersensitivity pneumonitis thought to be due to wood dust are, in fact, due to fungal contaminants of the wood including *Pullularia*, *Alternaria*, and *Penicillium* organisms.

The third category is animal protein. Pituitary snuff-taker's lung is no longer common because of the substitution of synthetic pituitary (Pituitrin) for the pituitary powder of ox or pig that was used to treat patients for hypopituitarism. Bird-fancier's lung is common and is due to sensitivity to avian antigen present in the droppings of a variety of birds including pigeons, parakeets, parrots, and doves. Two other animal sources recently described for hypersensitivity pneumonitis are rats and gerbils.

Clinical and Laboratory Characteristics—Extrinsic allergic alveolitis occurs mainly in nonatopic persons. The characteristic history is one of repeated episodes of fever, chills, chest pain, cough, and dyspnea that occur four to six hours after exposure to the organic dust. The acute symptoms often are mistaken for a bacterial or viral pneumonitis. Remission of symptoms on avoidance of the contaminated area is an important diagnostic feature. A common occurrence is the hospitalization of a patient with fever, cough, and pulmonary infiltrate. Antibiotics are administered and, in a few hours, the patient is considerably improved. This improvement may be attributed to the antibiotics when, in fact, the removal of the patient from his home or working environment accounts for his clinical improvement. In the more insidious form, progressively increasing malaise, dyspnea, and weight loss are the result of chronic exposure to smaller amounts of antigen.

The findings of physical examination are disproportionate to the patient's subjective complaints and the extent of parenchymal involvement observed roentgenographically. Examination of the chest usually reveals basilar, bilateral, crepitant rales. Wheezing may be heard in some instances of pigeon-breeder's disease.

Routine laboratory tests are of little value. Serum IgE levels are normal and, although leukocytosis is common, eosinophilia usually is not present. Findings on chest roentgenogram depend on the stage of disease. The acute form is most often associated with diffuse, finely granular infiltrations characteristic of alveolar or interstitial pneumonitis. Micronodular deposits are common. In the chronic stage, the infiltrates become confluent. Chest roentgenographic findings generally resolve after three to six months but may become permanent in more severe cases.

Pulmonary function testing demonstrates a restrictive type of ventilatory impairment. In classic cases, there is a decrease in forced vital capacity, decreased pulmonary compliance, and defects in alveolar gas exchange as demonstrated by a decrease in carbon monoxide diffusion capacity (DL_{co}). Arterial oxygen unsaturation is often seen with a further fall after exercise. Mild airway obstruction has been reported and, in chronic severe cases, there may be irreversible obstructive and restrictive changes.

Lung biopsy reveals the basic pathologic condition to be inflammation of the alveoli and interstitial pulmonary tissue with bronchiolar involvement. In the acute stage, there is alveolar septal thickening with infiltration of mononuclear cells, lymphocytes, and plasma cells. Occasionally, foamy histiocytes are found in the alveolar wall or within the alveoli. In the chronic stage, noncaseating granulomas are seen with Langerhans' giant cells, epithelioid cells, and varying degrees of fibrosis. Of great interest is the general absence of pulmonary vasculitis.

The immunologic hallmark in the clinical workup of extrinsic allergic alveolitis is the presence of serum precipitating antibody to the extrinsic antigen. This is generally an IgG immunoglobulin and can be detected by the Ouchterlony double-gel diffusion technique. The presence of precipitins is evidence of exposure and sensitiza-

tion and does not necessarily indicate that the clinical process is present. A substantial percentage of asymptomatic pigeon breeders and sugar cane workers have precipitating antibody to avian antigen and thermophilic organisms, respectively. The significance of precipitating antibody in the individual patient can only be determined by the associated clinical findings. Convenient gel diffusion kits are commercially available, but it has recently been noted that "home grown" extracts give substantially more positive precipitin reactions than do the commercial kits. A negative precipitin reaction in the face of convincing clinical evidence should not dissuade one from making the diagnosis of extrinsic allergic alveolitis.

Skin testing with the antigens responsible for extrinsic allergic alveolitis is of limited value. Extracts of thermophilic organisms are nonspecifically irritating and are therefore of no diagnostic use. When protein antigens such as pigeon serum are used, skin testing will generally result in a dual response, that is, an immediate wheal and erythema reaction followed by a late Arthus reaction occurring six to eight hours later.

In instances when the specific diagnosis is in doubt because of a question of the relevance of a particular exposure, bronchial provocation tests may be helpful. Under carefully controlled conditions, an aqueous extract of the particular antigen is delivered to the bronchial tree. A positive challenge consists of appropriate changes in pulmonary function and worsening of symptoms after four to six hours. The provocative tests should not be performed on a routine basis and must be used with great caution. Patients may become quite ill and may even require hospitalization after a positive challenge. One must be sure of the purity of the antigen preparation that is used, since impure preparations may contain substantial amounts of endotoxin which will nonspecifically cause fever, chills, and cough—in short, all of the symptoms and signs of extrinsic allergic alveolitis.

Pathogenesis—There seems little doubt that extrinsic allergic alveolitis or hypersensitivity pneumonitis represents a hypersensitivity reaction rather than an infectious process, but the precise mechanism is presently unclear. A type I IgE-mediated reaction would seem to be excluded by the nonatopic status of most of the patients, the normal IgE levels, and the absence of eosinophilia and significant bronchospasm. There are several features that strongly suggest a type III immune-complex mediated disease. These include the presence of precipitating antibodies in the sera of most patients against the offending organic antigen, an increase in antibody titers with the severity of the disease coupled with a decrease in titers on remission, the time interval of four to six hours between exposure and development of symptoms, and the presence of antigen, immunoglobulin, and components of serum complement in lung lesions. Arguing against a pure precipitating antibody-immune-complex mechanism is the relative absence of pulmonary vasculitis, the presence of precipitating antibody to organic dusts in a large percentage of asymptomatic exposed persons, and the failure to transfer the disease from man to monkey with serum.

There is a great deal of evidence that suggests that type IV delayed hypersensitivity plays an important role in the pathogenesis of hypersensitivity pneumonitis. Certainly, the pathologic changes, including granuloma formation, in this disease are consistent with delayed hypersensitivity. Studies have been carried out on symptomatic and asymptomatic pigeon breeders, both of whom had comparable titers of precipitating antibody. The results indicate that in vitro correlates of delayed hypersensitivity including antigen-induced migration-inhibition factor (MIF) production and lymphocyte transformation can be found in symptomatic breeders but not the asymptomatic breeders. As stated previously, skin testing with protein antigen such as pigeon serum results generally in a dual skin test response but not a delayed reaction. This may be due to interference with the expression of delayed hypersensitivity by the more immediate types I and III reactions.

Animal models of hypersensitivity pneumonitis have been created in the guinea pig, rat, mouse, rabbit, and monkey. These studies indicate that if immunization produces only precipitating antibody, hypersensitivity pneumonitis will not result after antigenic challenge. If, however, delayed hypersensitivity is also produced, then appropriate antigenic challenge will result in a disease process resembling hypersensitivity pneumonitis. Another bit of evidence favoring delayed hypersensitivity is the ability to transfer the disease from an affected animal to a normal animal with sensitized lymphoid cells.

The role of serum complement in production of disease is presently unclear. During inhalation challenge studies on symptomatic and asymptomatic pigeon breeders, it was observed that serum complement levels fell only in the asymptomatic breeders. The suggestion has been made that in the symptomatic breeder the inhaled antigen was trapped in the lung and did not gain access to the peripheral circulation. Persistence of antigen in the lung would be expected to favor disease production. In the asymptomatic pigeon breeder, the antigen was removed from the lung and cleared from the circulation by the formation of antigen-antibody and serum complement complexes. Rapid removal of antigen from the lung would be expected to result in less disease. Another finding implicating serum complement is the presence in pigeon breeders of a labile variant of C3 proactivator. This substance initiates C3 activation when activated by components of pigeon droppings. It has also been demonstrated that organic dust antigens can directly activate the alternate complement pathway.

Therefore, it would appear that at least three immunologic mechanisms as well as nonimmunologic factors are operative in the pathogenesis of hypersensitivity pneumonitis and that more information is needed to clarify the issue.

Treatment and Prognosis—The prognosis of hypersensitivity pneumonitis is excellent providing that the disease is recognized in the early stage and the antigen avoided before irreparable tissue damage has taken place. In the acute case, further avoidance of the offending antigen will result in a return of pulmonary function to normal. However, in the subacute or chronic case in which the individual is exposed to a lower antigen challenge over a long period of time, pulmonary fibrosis and far advanced ventilatory insufficiency may result. It must be emphasized, therefore, that an exhaustive environmental search for the offending antigen should be carried out in suspected cases. Preventive measures include the

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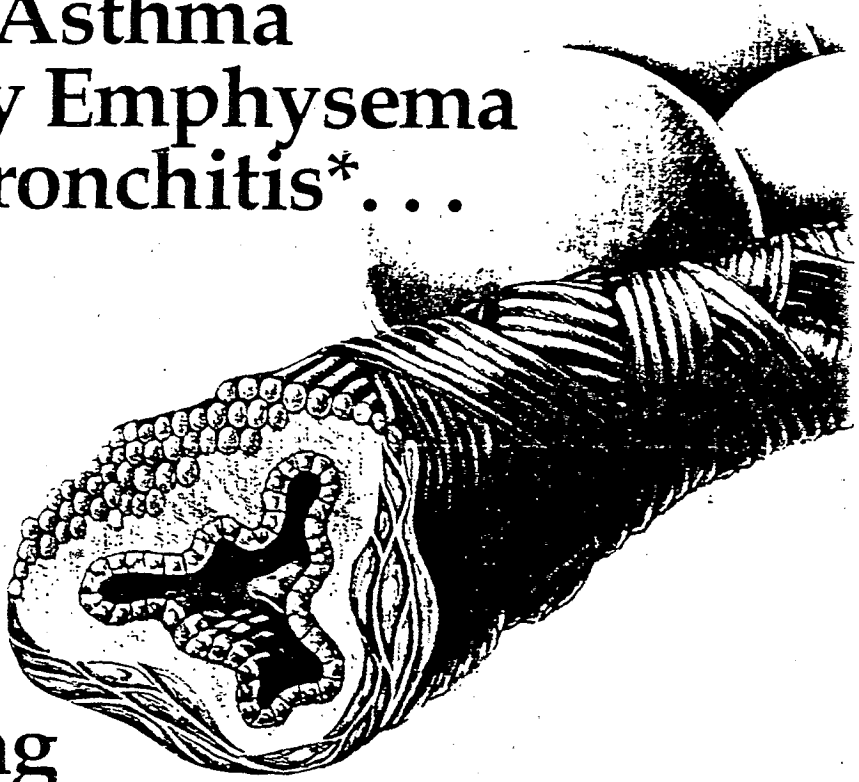

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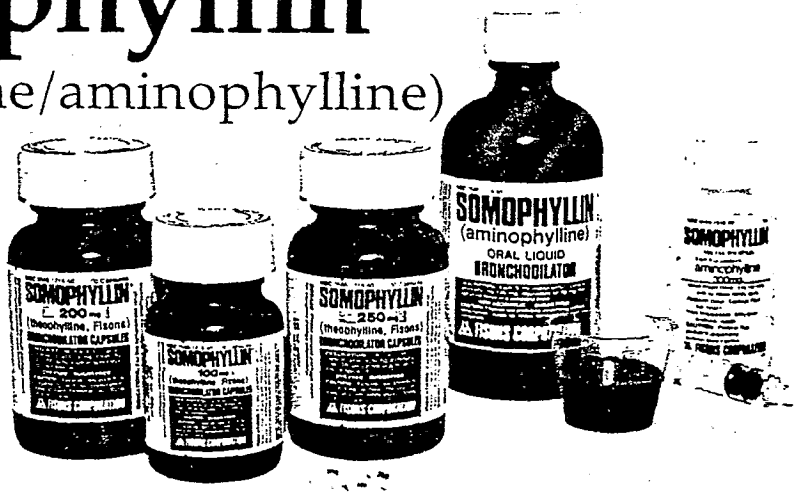

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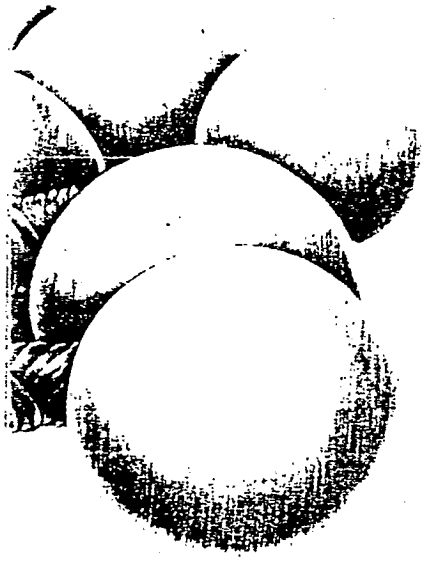

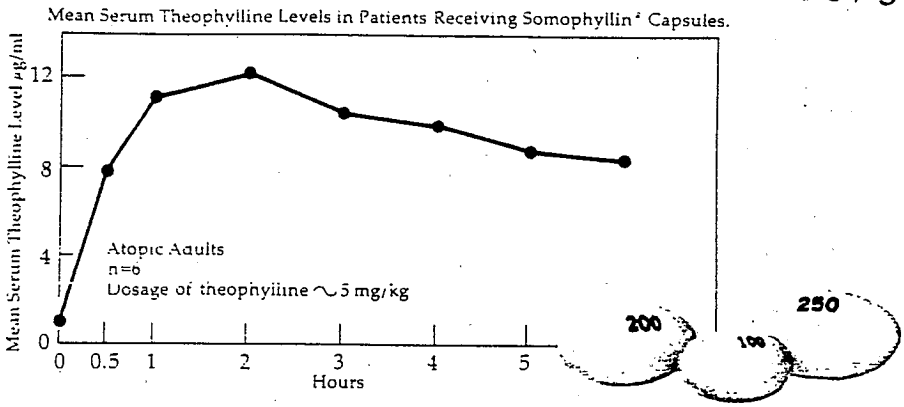

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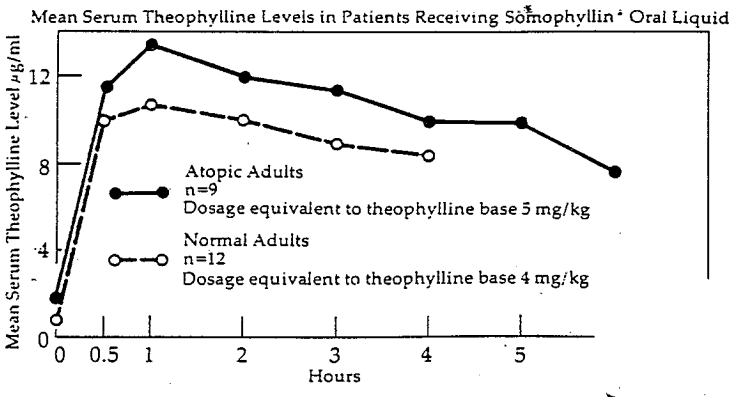

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wearing of masks by heavily exposed persons such as farmers and treatment of organic material with high pressure and high temperature to prevent organism growth.

Patients with acute hypersensitivity pneumonitis will usually respond to bedrest and supportive care. Corticosteroids are indicated in more severely affected patients and generally provide excellent results.

Allergic Bronchopulmonary Aspergillosis

A second group of diseases distinct from extrinsic allergic alveolitis is exemplified by allergic bronchopulmonary aspergillosis. *Aspergillus* is a hardy and ubiquitous organism. It thrives on a substrate with low moisture content and has been demonstrated in such diverse sources as fertile soil, air, decaying vegetation, and swimming pool water. It is commonly cultured from houses and is particularly frequent in basements, crawl spaces, bedding, and house dust. Several lung diseases in man can result from aspergillus. These include invasive or septicemic aspergillosis in which there is invasion of the bronchial wall that produces a definite bronchitis; aspergilloma in which there is superficial invasion of a bronchiectatic cavity or bronchogenic cyst; bronchial asthma; and hypersensitivity pneumonitis. In 1952, a condition caused by aspergillus was described and termed allergic bronchopulmonary aspergillosis; it is characterized by pulmonary eosinophilia, that is, pulmonary infiltrates and peripheral blood and sputum eosinophilia. Similar conditions can be caused by *Helminthosporium* and *Candida*.

Clinical and Laboratory Characteristics—Patients with allergic aspergillosis are almost always atopic and have a history of bronchial asthma. They complain of anorexia, headache, general aches and pain, loss of energy, temperature elevation, and acute attacks of wheezing dyspnea. Often, no clear relationship can be established between a history of exposure to moldy vegetable material and the onset of symptoms. Epidemiologic studies in Great Britain reveal that although the disease is frequently reported in urban dwellers, it is more common in certain agricultural areas where exposure to high atmospheric spore concentration may occur. Patients will also have more frequent episodes of illness during the winter months in Britain where aspergillus spores are found 100 times more commonly in the air from October to February.

On physical examination, general signs of airway obstruction are found in a high percentage of patients with allergic bronchopulmonary aspergillosis. Crepitant rales can sometimes be heard over areas where there is roentgenographic shadowing.

Production of solid sputum plugs is common. Direct examination often reveals fungal mycelium with large numbers of eosinophils. Good preservation of cytoplasm indicates active growth of the fungus in contrast to the dead mycelia devoid of cytoplasmic content seen in patients with aspergilloma. A sputum culture positive for aspergillus is not diagnostic of aspergillosis since aspergillus is commonly inhaled and expectorated by the population at large. Patients with allergic aspergillosis frequently give negative cultures during episodes of pulmonary infiltration and positive cultures at other times.

Peripheral blood eosinophils generally number more than 1,000/cu mm. There is significant elevation of total serum IgE in most patients. It has been suggested that serial determinations of IgE may be of value in monitoring the onset of the acute phase of allergic aspergillosis.

Most patients with allergic aspergillosis have general signs of airway obstruction on pulmonary function testing. FEV_1 is reduced and, in most instances, carbon monoxide diffusion is decreased. Therefore, although the obstructive component predominates, there is also a restrictive element.

The presence of a positive immediate wheal and erythema reaction to an aspergillus skin test is a necessary finding in the diagnosis of allergic aspergillosis. If the immediate skin test is negative, it is very unlikely that *A fumigatus* is the cause of pulmonary eosinophilia. The presence of immediate skin reactivity to *A fumigatus* is, of course, not diagnostic of allergic aspergillosis since skin sensitivity to this organism is common in atopic persons. In a high percentage of patients, the immediate wheal and erythema reaction subsides and, in three to four hours, erythema and poorly defined edema begin at the skin test site, reaching a peak at eight hours and

resolving by 24 hours. This "late" or Arthus skin reaction is indicative of a type III precipitating antibody response to aspergillus.

Serum precipitating antibody to *A fumigatus* is present in most patients with allergic aspergillosis. The antibody is generally of the IgG type and reflects recent or continued growth of the fungus in body tissues or within bronchi of patients with allergic aspergillosis. Again, the presence of precipitating antibody is not diagnostic of allergic aspergillosis for it can be found in significant numbers of patients with aspergilloma, farmer's lung, and allergic asthma.

The patient with allergic aspergillosis will respond to bronchial challenge of an aerosol of *A fumigatus* in the following way. There is an immediate fall in FEV_1 with associated wheezing. This clears shortly to be followed in four to six hours by another episode of asthma and a fall in FEV_1. This dual bronchial response is reminiscent of the dual skin test response and is more easily elicited with the protein fraction of *A fumigatus*.

A lung biopsy specimen of a patient with allergic aspergillosis shows the bronchial wall to be infiltrated with mononuclear cells and eosinophils. Some bronchi are dilated and filled with inspissated mucus and exudate. Fungal hyphae may be identified in the exudate, but there is generally no invasion of bronchial walls and lung parenchyma. In the parenchyma, one may see extensive consolidation with chronic inflammatory cells and a large number of granulomas.

A variety of radiographic shadows may be seen in patients with allergic aspergillosis. The most common abnormality is a massive homogeneous shadow without fissure displacement indicating a large area of consolidation. These opacities frequently shift rapidly from one site to another. A rather inconspicuous radiographic appearance can represent extensive tissue damage. Hairline shadows extending out from the hilum in the direction of the bronchi, called "tramlines," represent edema of a normal bronchial wall. Ring shadows indicate cavities. A common complication of allergic aspergillosis is atelectasis of a segment, a lobe, or total collapse of the whole lung. Permanent shrinkage, particularly of the upper lobes, may be seen in the later stages with hilar elevation.

Table 2 • Differential Characteristics of Extrinsic Allergic Alveolitis (Hypersensitivity Pneumonitis) and Allergic Bronchopulmonary Aspergillosis

	Extrinsic Allergic Alveolitis	Allergic Bronchopulmonary Aspergillosis
Basic nature of patient	Nonatopic	Atopic
Physical examination	±	Wheezing
Skin test	±*	Dual positivity
Roentgenographic examination	Pulmonary infiltrates—interstitial	Pulmonary infiltrates—lobar
Complications	Pulmonary fibrosis	Atelectasis, bronchiectasis
Blood	Normal	Eosinophilia
Sputum	Normal	Eosinophilia, mycelia
IgE	Normal	Elevated
Pulmonary function	Restrictive	Obstructive (restrictive, late)
Antibody	Precipitating (IgG)	Precipitating (IgG) and nonprecipitating (IgE)
Proposed immunologic basis	Immune complexes and delayed hypersensitivity (types III and IV)	Immediate hypersensitivity and immune complexes (types I and III)

*Positive reaction is immediate and late in some cases of pigeon breeder's lung

Table from Slavin RG: Allergic bronchopulmonary aspergillosis, in Middleton E Jr, Reed CE, Ellis EF (eds): *Allergy: Principles and Practice,* St. Louis, C.V. Mosby Co., 1978.

A distinctive type of bronchiectasis is seen in the patient with allergic aspergillosis. It is generally a saccular type with pronounced proximal involvement and peripheral or distal sparing. This suggests a localized toxic reaction in the bronchial wall which has resulted from the presence of the fungus rather than the usual sequence of events leading to bronchiectasis, that is, bronchial obstruction, atelectasis and infection.

Diagnosis—The presence of immediate or dual skin reactivity or serum precipitins to *A fumigatus* are not diagnostic of allergic aspergillosis. However, the presence of increasing bronchospasm in an asthmatic patient, with recurrent pulmonary infiltrates, immediate skin reactivity, and serum precipitins to *A fumigatus* and pronounced elevation of total serum IgE is good evidence for allergic aspergillosis. Bronchograms that show the typical proximal involvement with peripheral sparing are characteristic. Table 2 lists distinctive features of hypersensitivity pneumonitis and allergic bronchopulmonary aspergillosis.

Pathogenesis—The pathogenesis of allergic aspergillosis begins with inhalation of the short chain *A fumigatus* spores. The bronchospasm and viscid secretions characteristic of the asthmatic leads to trapping of the spores. The spores grow exceedingly well at body temperature and, in the larger subsegmental bronchi, they germinate and form mycelia. The major feature of allergic aspergillosis which distinguishes it from other forms of hypersensitivity to inhaled antigens is that the organism can grow in the bronchial lumen and continually shed antigens into the tissues. The high concentration of antigen locally provokes an inflammatory reaction that allows continued growth of the trapped fungus. Antigens released from the mycelia combine with IgE and IgG antibodies to set in motion a chain of immunologic reactions that culminates in bronchial wall damage and a surrounding pulmonary eosinophilic consolidation. If there is little structural damage to the lung, then the nidus of fungal infection will be expectorated as the asthma is relieved. If previous episodes have resulted in permanent

lung damage, then fungal colonization of the diseased air spaces will persist.

Both IgE skin-sensitizing antibody and IgG precipitating antibody are thought to play major pathogenetic roles in the production of this disease. The presence of IgE immunoglobulin has been shown to enhance the tissue-damaging effect of IgG precipitating antibody, perhaps by stimulating the uptake of immune complexes or their products by vascular endothelial cells. The importance of precipitating antibody in the pathogenesis of allergic aspergillosis is supported by passive transfer studies from man to monkey. Transfusion of serum from a patient with allergic aspergillosis to a monkey followed by aerosol challenge with aspergillus antigen resulted in the development of pulmonary lesions in the monkey consistent with the picture of human allergic aspergillosis. Transfusion of human serum containing only skin sensitizing antibody caused no pulmonary lesions. In another study, in monkeys immunized with *A fumigatus* to produce precipitating antibody to the organism pronounced pulmonary changes developed after inhalation challenge only if they also received human serum rich in IgE antibody against *A fumigatus*.

The paucity of pulmonary vasculitis, with little in the way of granulocytic infiltration, seen in lung biopsy specimens of patients with allergic aspergillosis argues against a precipitating antibody immune complex pathogenesis. The appearance of mononuclear cells and granulomas suggests a delayed hypersensitivity response and there is recent evidence through positive in vitro studies of lymphocyte transformation to indicate that cell-mediated immunity may play a role in the development of allergic aspergillosis.

The detection of circulating immune complexes and a fall in serum complement has recently been reported in the acute phase of allergic aspergillosis.

Prognosis—A long-term follow-up study of 50 patients with untreated allergic bronchopulmonary aspergillosis has been reported. All followed a chronic course with airway obstruction, recurrent pulmonary consolidation and, in many instances, severe lung destruction. A third of the patients with recurrent pulmonary consolidation were asymptomatic; that is, episodes could recur without gross functional deterioration. Therefore, the use of symptoms as a guide to therapy bears no relationship to the activity of the disease. Patients with allergic aspergillosis can continue to have clinically unrecognized pulmonary consolidations capable of progressing insidiously and causing severe lung damage. Total serum IgE levels, levels of specific IgE antibody to *A fumigatus*, measurements of pulmonary function, and regular chest roentgenograms may be helpful in monitoring the disease course.

Treatment—The most important drug in the treatment of allergic aspergillosis is corticosteroid. In terms of the interruption of the pathogenetic circle, corticosteroids decrease the allergic inflammatory response, decrease the viscid secretions, and relieve airway obstruction. All of these factors lead to more effective removal of the fungus. Corticosteroids must be given in large enough doses over a sufficient time to accomplish these aims. Two to three months of treatment are necessary but may have to be extended even longer. Even when the symptoms are minimal because of the localized nature of the disease, early and strenuous treatment is important to prevent the inexorable consequences of bronchiectasis, pulmonary fibrosis, and cor pulmonale. In resistive cases, efforts should be made to remove the viscid secretions with physiotherapy and bronchial lavage.

In terms of prophylaxis, it would be wise to discourage the exposure of patients with allergic aspergillosis or, indeed, all asthmatics to material containing high concentration of aspergillus spores such as compost heaps, decaying matter, and stored grain.

Conclusion

Perhaps the most important point to make in discussing hypersensitivity pneumonitis and allergic bronchopulmonary aspergillosis is to keep the index of suspicion high. In many patients, hypersensitivity pneumonitis may be diagnosed as idiopathic pulmonary fibrosis or Haman-Rich disease. Allergic bronchopulmonary aspergillosis may be diagnosed as Loeffler's pneumonia or the PIE syndrome. It is vital to recognize both diseases before irreparable tissue damage takes place. By removing the patient from a particular environmental exposure and thus eliminating the offending antigens or by beginning corticosteroids early in the course of the disease, the alert physician may well be able to spare his patient a life as a pulmonary cripple.

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