Pathology of Pulmonary Disease, edited by Mario J. Saldana.
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65

Hypersensitivity Pneumonitis

Roberto Barrios

Hypersensitivity pneumonitis (HP) or extrinsic allergic alveolitis is a generic term used to describe an immunologic reaction of the lung in which diffuse inflammation of the parenchyma including distal airways and alveoli develops from recurrent exposure and sensitization to a variety of inhaled antigens. Antigenic particles generally consist of organic proteins of birds and mammals, fungi, and thermophylic bacteria (Table 65-1).[1–3]

For centuries, the association between inhalation of various agents and respiratory disease has been recognized. According to Parkes, there is "an old country tradition that moldy hay has a baneful effect on the lungs," and Icelandic farmers already referred to this as *Heymaedi* (*i.e.*, hay-induced shortness of breath).[4] In 1831, Kay described a series of patients with byssinosis, and in 1932, Campbell described the clinical manifestations of what is now known as farmer's lung in five farmers exposed to hay dust.[5,6] Since then, the literature on the subject has grown profusely.

Fawcitt in 1938 and Dickie and Rankin in 1958 suggested that farmer's lung might arise from hypersensitivity to molds or their products.[4] Several investigators demonstrated the presence of precipitins against extracts of hay and molds in the serum of farmers with the disease, implicating the formation of immune complexes with moderate antigen excess as the principal pathogenetic mechanism of farmer's lungs.[7–10] Pepys coined the term "extrinsic allergic alveolitis," which included all cases of inflammatory diseases of the lungs resulting from antigen inhalation.[7] Alternative terms for HP include those alluding to specific occupations, such as farmer's lung, pigeon breeder's disease, coffee worker's lung, and bagassosis, or those that reflect the circumstances of exposure, such as air conditioner lung and summer pneumonitis (see Table 65-1).

Regardless of the antigen responsible for the disease, the clinical features are common in all forms of HP. The presentation may be acute, subacute, or chronic, depending on frequency, intensity, and duration of inhalational exposure and perhaps depending on host or other factors.[11] Systemic and respiratory symptoms may occur.

In the acute form, influenzalike symptoms may predominate, consisting of chills, fever, sweating, myalgias, lassitude, headache, and nausea beginning 2 to 9 hours after exposure, peaking between 6 and 24 hours, and lasting from hours to days. Cough is common. The subacute form may appear gradually over several days to weeks. The patient usually complains of cough and dyspnea that may become severe, and dyspnea with cyanosis. The chronic form has an insidious onset over many months or years with increasing cough and exertional dyspnea. Fatigue and weight loss may be prominent. Physical examination may be within normal limits or may disclose bibasilar or more generalized crackles. Cyanosis may be seen in severe disease and right heart failure may complicate cases with extensive fibrosis.[12] Clubbing has been proposed as a poor prognostic indicator.[13] The clinical manifestations of HP disappear within days, weeks, or months in most patients if no longer exposed to the antigen. A careful occupational and environmental history is mandatory if HP is suspected; the importance of indirect exposure has been demonstrated in some cases.[14]

The chest x-ray film usually shows evidence of interstitial disease, but it may vary from normal in some persons to a pattern associated with small, diffuse, bilateral nodulations. In the chronic fibrotic stage, the interstitial pattern becomes prominent, and there is loss of volume. Other abnormalities, such as pleural effusion or thickening, calcification, cavitation, and atelectasis, have been described as rare events.[12]

LABORATORY FINDINGS

There is no single laboratory test to reach a specific diagnosis. In many patients, there is leukocytosis, with leukocyte counts in the range of 20,000 to 30,000 cells/mm^3. Eosinophilia is uncommon, but an excess of polymorphonuclear leukocytes is frequently seen. Immunoglobulins are increased.

Precipitating antibodies against the casual antigen are present in the serum of most patients.[15] However, the prevalence of serum antibodies in antigen exposed population is much higher than the prevalence of HP. Antibodies have been reported in as many as 10% of farmers and as many as 40% of pigeon breeders.[16,17] In

TABLE 65-1
Forms of Hypersensitivity Pneumonitis

Disease	Antigen	Source of Antigen
FUNGAL AND BACTERIAL ANTIGENS		
Farmer's lung	*Micropolyspora faeni*	Moldy hay, grain, silage
Ventilation pneumonitis	*Thermoactinomyces vulgaris, Thermoactinomyces sacchari, Thermoactinomyces candidus*	Contaminated forced-air systems and contaminated water in humidification
Bagassosis	*Thermoactinomyces vulgaris*	Moldy sugarcane (*i.e.*, bagasse)
Mushroom worker's lung	*Thermoactinomyces sacchari*	Moldy mushroom compost
Suberosis	*Thermoactinomyces viridis*	Moldy cork
Detergent lung	*Bacillus subtilis* enzymes	Detergents (during processing or use)
Malt worker's lung	*Aspergillus fumigatus, Aspergillus clavus*	Moldy barley
Sequoiosis	Graphium, Bullularia, *Aureobasidium* sp	Moldy wood dust
Maple bark disease	*Cryptostroma corticale*	Moldy maple bark
Cheese washer's lung	*Penicillium casei, Aspergillus clavatus*	Moldy cheese
Woodworker's lung	*Alternaria* sp, wood dust	Oak, cedar, and mahogany dust; pine and spruce pulp
Cheese worker's lung	*Penicillium casei*	Cheese mold
Paprika slicer's lung	*Mucor stolonifer*	Moldy paprika pods
Sauna taker's lung	*Aureobasidium* sp, other sources	Contaminated sauna water
Familial HP	*Bacillus subtilis*	Contaminated wood dust in walls
Streptomyces albus HP	*Streptomyces albus*	Contaminated fertilizer
Wood trimmer's lung	*Rhizopus* sp, *Mucor* sp	Contaminated wood trimmings
Compost lung	*Aspergillus*	Compost
Cephalosporium HP	*Cephalosporium* sp	Sewage-contaminated basement
Hot-tub lung	*Cladosporium* sp	Mold on ceiling
Wine maker's lung	*Botrytis cinerea*	Mold on grapes
Woodsman's disease	*Penicillium* sp	Oak and maple trees
Thatched-roof lung	*Sacchoromonospora viridis*	Dead grasses and leaves
Tobacco grower's lung	*Aspergillus* sp	Tobacco plants
Potato riddler's lung	*Thermophilic actinomycetes, M. faeni, T. vulgaris, Aspergillus* sp	Moldy hay around potatoes
Summer pneumonitis	*Trichosporon cutaneum*	Contaminated old houses
ANIMAL PROTEINS		
Laboratory worker's HP	Male rat urine	Laboratory rat
Bird fancier's, breeder's, or handler's lung	Avian droppings, feathers, serum	Parakeets, budgerigars, pigeons, chickens, turkeys
Pituitary snuff taker's lung	Pituitary snuff	Bovine and porcine pituitary proteins
Fish meal worker's lung	Fish meal	Fish meal dust
Bat lung	Bat serum protein	Bat droppings
Furrier's lung	Animal-fur dust	Animal pelts
Rat handler's lung	Rat serum	Rat serum proteins
INSECT PROTEINS		
Miller's lung	*Sitophilus granarius* (*i.e.*, wheat weevil)	Dust-contaminated grain
Lycoperdonosis	Puffball spores	Lycoperdon puffballs

(*continued*)

TABLE 65-1
(Continued)

Disease	Antigen	Source of Antigen
UNKNOWN		
Bible printer's lung		Moldy typesetting water
Coptic lung (mummy handler's lung)		Cloth wrappings of mummies
Grain measurer's lung		Cereal grain
Coffee worker's lung		Coffee-bean dust
Tap water lung		Contaminated tap water
Tea grower's lung		Tea plants
OTHERS		
Pauli HP	Pauli reagent	Laboratory reagent
Chemical worker's lung	Isocyanates	Polyurathane foam, varnishes, lacquer, foundry casting

HP, hypersensitivity pneumonitis.

other studies, precipitating antibodies against avian antigens were detected in all patients and in 50% of exposed but asymptomatic persons.[18]

The presence of serum antibodies to suspected antigens must be considered evidence of antigen exposure rather than disease. Similarly, the titer of serum antibodies does not necessarily correlate with the disease. An interesting finding is the presence of IgM and IgG rheumatoid factors in a high proportion of patients with chronic pigeon breeder's lung, but these same antibodies are absent in persons exposed to avian antigens but without evidence of disease.[19] No clinical feature or laboratory test is diagnostic of HP; diagnosis should be made from a combination of history, x-ray abnormalities, pulmonary function test results, and immunologic features.[20] In some patients, a lung biopsy is needed to clarify the diagnosis.

ETIOLOGY AND PATHOGENESIS

Many organic proteins have been implicated as causes of HP, and a summary of the more common causative agents is shown in Table 65-1. The pathogenesis of HP is controversial.[21–23] For many years, a role for immune complexes has been proposed because of the presence of precipitating antibodies against the specific antigen, circulating and local, and a positive Arthus-type reaction.[7,8,24,25] However, even healthy persons who have been exposed to an antigen may demonstrate immune complexes.[18,26] Complement levels in the bronchoalveolar lavage (BAL) of these patients are normal.[27] In a series of biopsies of pigeon breeder's disease, electron-dense deposits suggestive of immune complex were not found by electron microscopy.[28,29]

A cell-mediated immunopathogenesis has also been proposed, and several findings seem to support this mechanism.[24,30–35] Specific lymphocyte reactivity to various causative antigens has been shown, and there is an increase of T cells in BAL. There is lymphokine production by avian antigen–stimulated lymphocytes, and it is possible to reproduce the lesions with the transfer of sensitized T cells that does not occur with the passive transfer of immunoglobulin. However, the acute form of the disease and the infrequent evidence of delayed skin tests cannot be explained through a cell-mediated mechanism. Humoral and cell-mediated immune mechanisms probably play a role in the pathogenesis of HP.

Many questions still remain unanswered. Why do only a few persons develop disease in antigen-exposed populations? Why is there such a variable time between exposure and full-blown picture? What are the factors that at a given moment trigger the disease in an person exposed to an antigen? Why is the prognosis so variable? I have seen patients who progress to interstitial fibrosis despite avoidance of antigen exposure.

We proposed a hypothesis for the progression or regression of the disease (Fig. 65-1).[27] For inflammation to occur, the presence of an inductor factor (*i.e.*, inhaled antigen) and a promoter factor are necessary. If regression factors are dominant, the tissue damage can be controlled, but in the presence of progression factors, inflammation persists and results in the development of fibrosis. For inductor factors, the physical characteristics of the antigen are important. The inhaled material should be between 1 to 3 μm in diameter to reach the alveolar space and must be in particulate form.[36] Studies show that soluble antigens do not produce histologic lesions characteristic of HP.[37] Lysosomal enzymes act on antigens, and resistance to degradation may allow the antigen to persist long enough to sensitize the host.[38] Promoter factors include genetic predisposition, immunoregulatory abnormalities, and environmental exposure to other offending agents.[39,40] Pregnancy and delivery, for instance, have been associated with worsening of the condition.[27]

There is evidence that the exposure to a second aggressor may be associated with the development of HP. One group has seen several patients who were exposed without problems to pigeons over the years but became ill after exposure to a second agent such as weed-killers, pesticides, and other inorganic particles. These

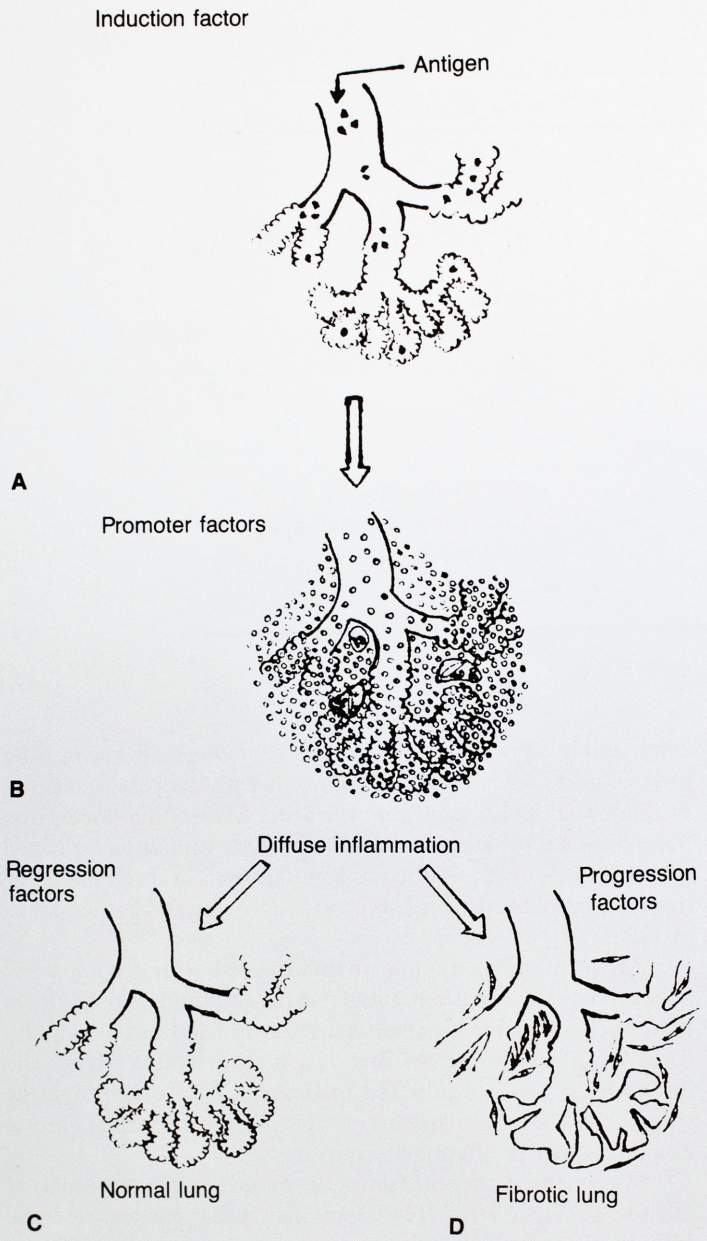

FIGURE 65-1. Hypothesis that explains the pathogenesis of hypersensitivity pneumonitis. (**A**) Antigen is the inductor factor. (**B**) Promoter factors include genetic susceptibility, immunoregulatory abnormalities, pregnancy, and environmental factors. (**C**) Regression factors include avoiding antigen exposure, steroid treatment, or adequate antiinflammatory response. (**D**) Progression factors include a lack of immunosuppressive and antiinflammatory host response and collagen metabolism abnormalities.

patients developed classic HP with a clear association to pigeon's antigens.[27] For regulatory factors, the most important regression factors are avoidance to antigen exposure and treatment with steroids. Anothter factor is adequate host response, in which I think suppressor T lymphocytes, pulmonary macrophages, and antiidiotype antibodies play an important role.[41] Any inflammatory reaction induces antiinflammatory responses to prevent a deleterious reaction. The release of oxygen free radicals, which has been proposed as an important factor in the pathogenesis of HP, is followed by the production of some specific antioxidant enzymes; the secretion of proteases induces the production of antiproteases.[42] If these regression factors are appropriately elicited, there is regression of the disease.

One progression factor is an abnormal collagen metabolism, which would explain why a particular group of patients develop fibrosis despite treatment and antigen suppression. Selman and colleagues have shown the production of platelet-derived growth factor, a well-known potent inducer of fibroblast duplication, by alveolar macrophages in 30% of patients with pigeon breeder's disease.[27] The same investigators have shown that the patients who progress to fibrosis have a low local collagenolytic activity similar to that found in patients with idiopathic pulmonary fibrosis.[43] These findings suggest that at least in some cases of HP a disequilibrium in the control of fibroblast proliferation and collagen metabolism plays an important role and transforms a potentially reversible disease into a progressive and irreversible fibrotic lung.

PATHOLOGIC FEATURES

The pathologic changes seen in HP are uniform, regardless of the causative antigen and depend on the stage of the disease, and perhaps, host factors. The gross pathologic changes in the lung vary. In acute cases, the lungs may be normal or reddish gray and consolidated. In patients with chronic disease, the lung is firm and similar to that seen in pulmonary fibrosis due to other causes (see Chaps. 31 and 32).[44]

Microscopically, HP is characterized as a chronic noncaseating granulomatous bronchioloalveolitis. The most constant feature is a diffuse interstitial lymphoplasmacytic infiltrate. The intensity of the infiltrate varies and causes irregular thickening of the alveolar septa (Figs. 65-2 through 65-4). The inflammatory infiltrate is composed of plasma cells and lymphocytes. The pneumonitis is usually patchy and more pronounced around respiratory bronchioli. Areas of uninvolved parenchyma are usually seen.

Coleman and Colby observed as a constant feature a triad consisting of interstitial inflammation, nonnecrotizing granulomas, and cellular bronchiolitis.[45] Clusters of epithelioid histiocytes in association with multinucleated Langhans-type giant cells occur in most cases. This cell population forms the small nonnecrotizing granulomas; the giant cells may contain cholesterol clefts, Schaumann bodies, calcium oxalate, and asteroid bodies. These poorly formed granulomas appear around bronchioli, within the interstitium, or even in alveolar spaces (Fig. 65-5).[46]

Striking aggregates of foam cells in interstitial and in intraalveolar locations in the background of interstitial pneumonia have been proposed as a distinctive morphologic feature of pigeon breeder's disease, but they are also found in other forms of HP and may represent nonspecific foci of obstructive pneumonitis (Figs. 65-6 and 65-7).[47]

By electron microscopy, I have seen intraalveolar clusters of loose connective tissue attached to alveolar walls by a stalk. These structures have been called buds and contain small numbers of mononuclear phagocytes, fibroblasts, and myofibroblasts. Eventually they are covered by epithelium, representing organization of exudates, and they become incorporated into the alveolar walls (Figs. 65-8 and 65-9).[29] The changes observed by electron microscopy favor the view that in most patients with HP the fibrotic changes represent the reparative stage of an exudative process associated with a limited amount of epithelial cell necrosis and connective tissue destruction.

Endothelial damage, thrombosis of capillaries, and perivascular edema are also seen and may contribute to the fibrotic

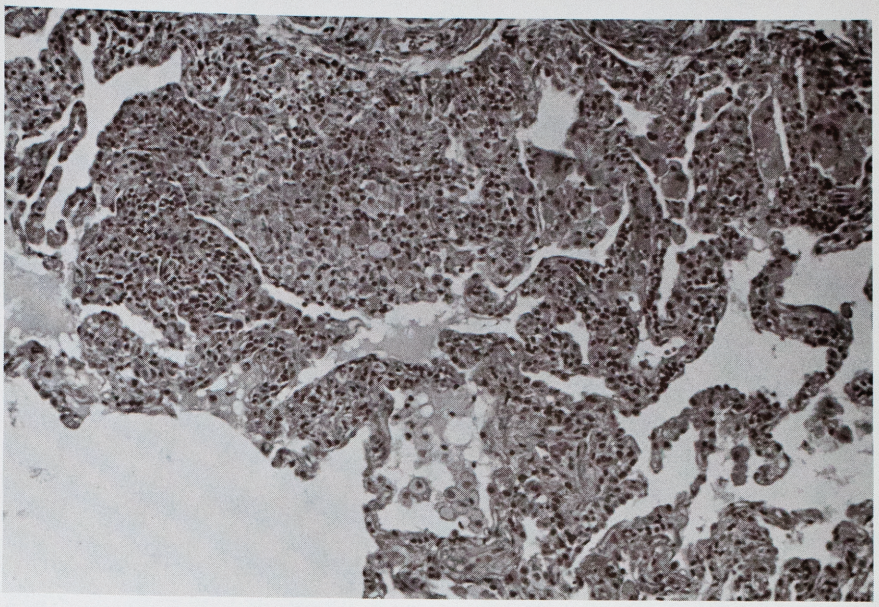

FIGURE 65-2. A prominent intraalveolar and interstitial inflammatory cellular infiltrate occurs in pigeon breeder's disease. (H & E stain; low magnification.)

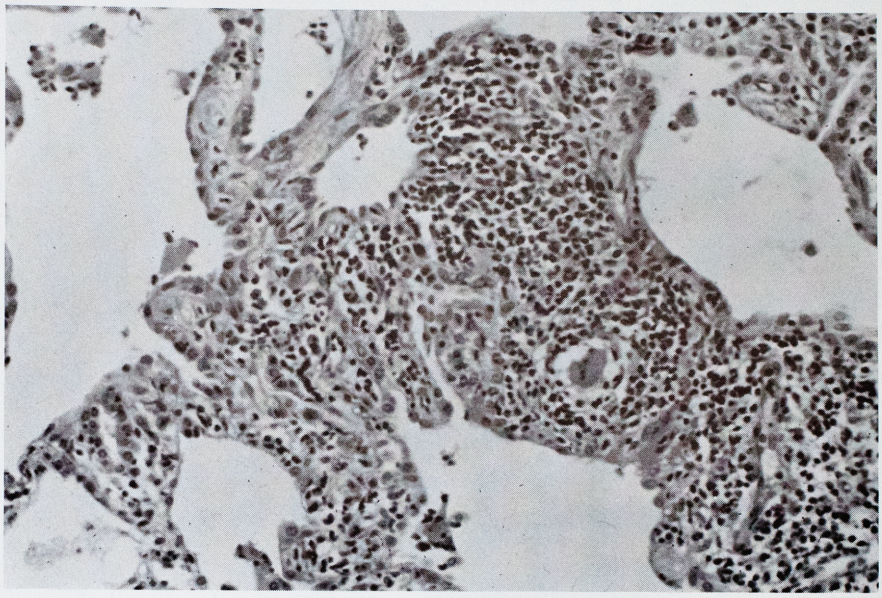

FIGURE 65-3. The lung tissue from a patient with farmer's lung shows a prominent interstitial lymphocytic infiltrate with giant cells. (H & E stain; low magnification; contributed by the editor.)

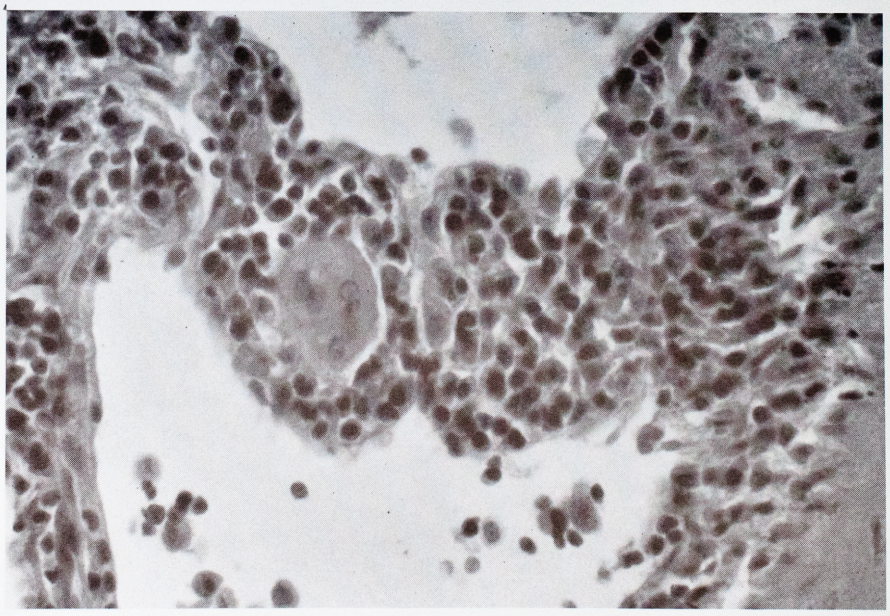

FIGURE 65-4. A closer magnification of the tissue in Figure 65-3 shows an intense lymphoplasmacytic cellular infiltrate and giant cells. (H & E stain; intermediate magnification; contributed by the editor.)

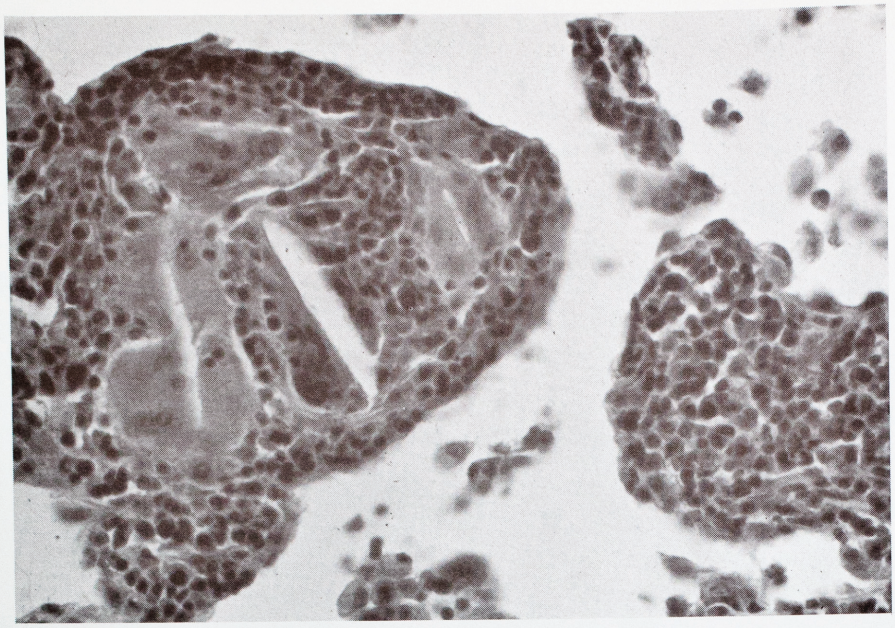

FIGURE 65-5. A biopsy specimen from a patient with pigeon breeder's lung shows granuloma composed of multinucleated giant cells containing cholesterol clefts, numerous lymphocytes, and plasma cells. (H & E stain; intermediate magnification; contributed by the editor.)

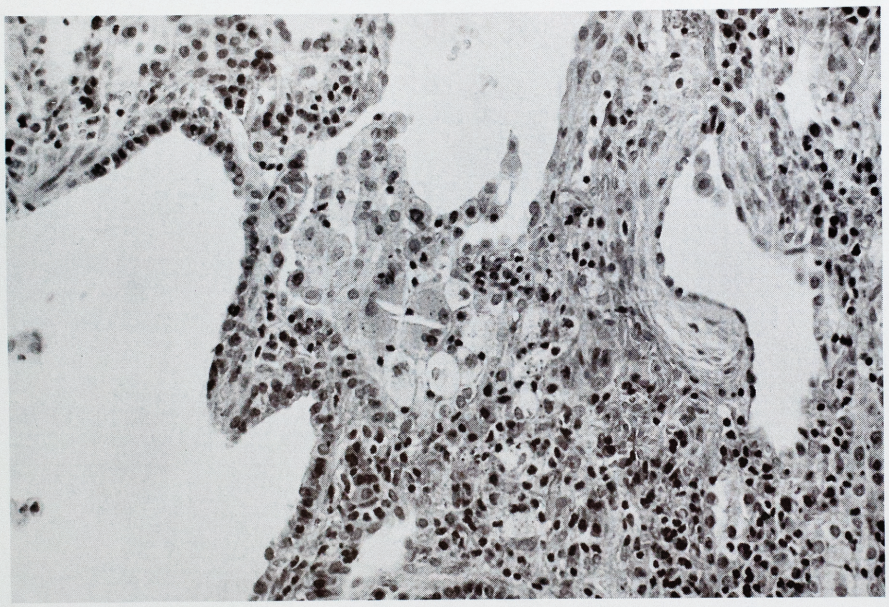

FIGURE 65-6. In this example of endogenous lipid pneumonia in a pigeon breeder's lung, there are intra-alveolar collections of foamy histiocytes with cholesterol clefts and a dense lymphoplasmacytic cellular infiltrate. (H & E stain; intermediate magnification.)

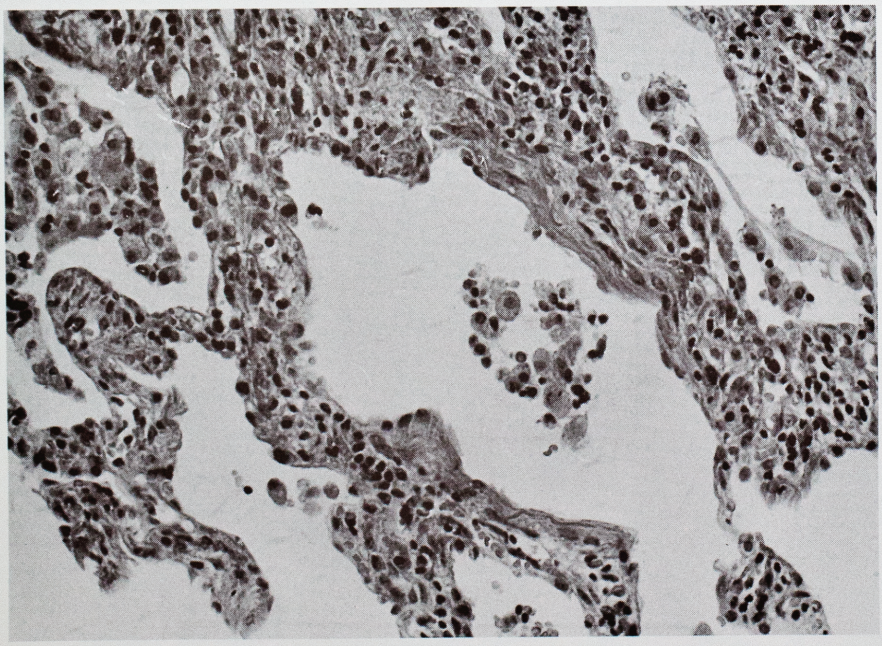

FIGURE 65-7. Another view of the tissue specimen in Figure 65-6 shows a lymphoplasmacytic infiltrate and early fibrosis. Collections of foamy histiocytes are seen in the left upper quadrant of the picture. (H & E stain; intermediate magnification.)

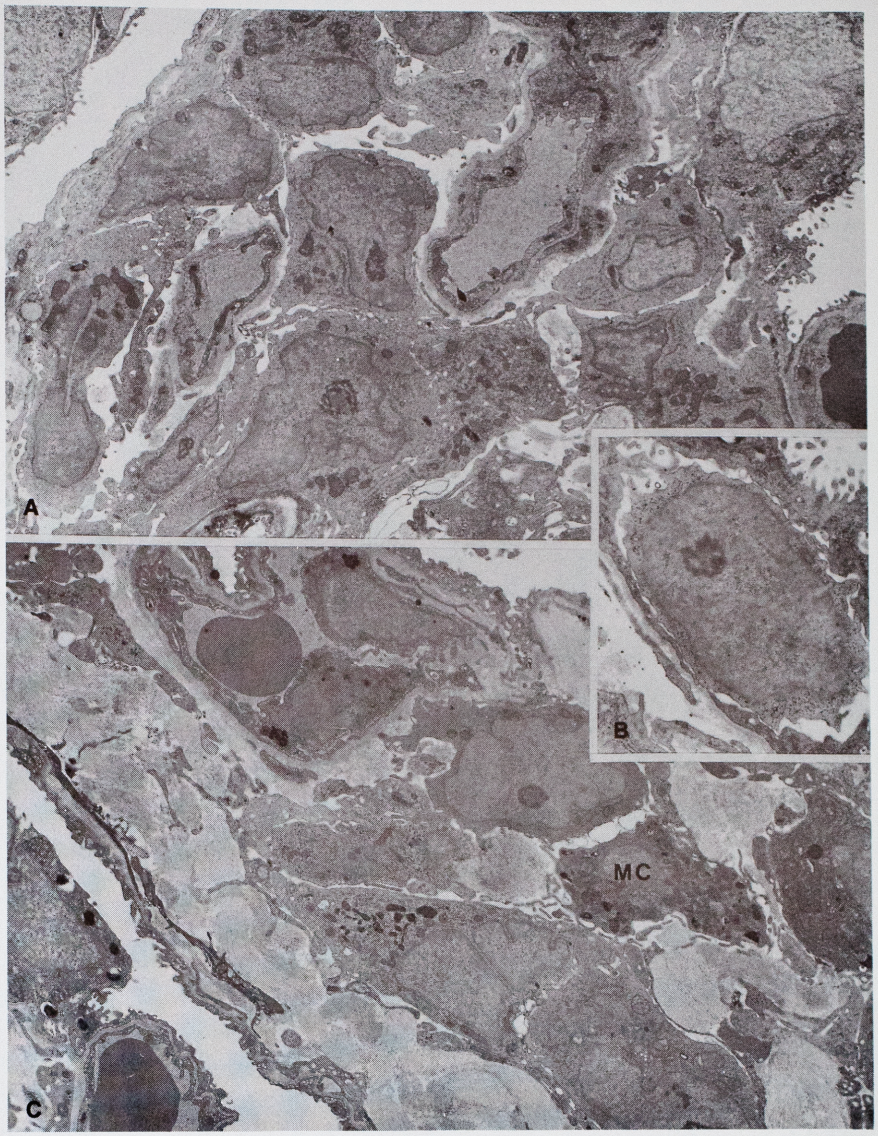

FIGURE 65-8. (**A**) Electron micrograph of an alveolar wall infiltrated by lymphocytes and macrophages. (Original magnification × 6400.) (**B**) Electron micrograph showing a mononuclear cell migrating through the alveolar epithelial lining. Notice the epithelial cell microvilli (*upper right*). (**C**) Cellular infiltrate, composed of lymphocytes, macrophages, and a mast cell, is in an alveolar wall that contains increased amounts of collagen. (Original magnification × 6300.) (From Kawanami O, Basset F, Barrios R, Ferrans VJ, Crystal R. Hypersensitivity pneumonitis in man. Light and electron microscopy studies of 18 lung biopsies. Am J Pathol 1983;110:2.)

alterations in vascular walls.[29] I have used monoclonal antibodies to study the T-cell subsets in tissue sections obtained in nine patients from open lung biopsies.[27,48] In all cases, the percentage of lymphocytes identified as suppressor or cytotoxic subpopulations ($CD8^+$) was greater than those recognized as helper cells ($CD4^+$), and similar results were obtained using BAL. Neutrophils were found in the alveolar spaces in some patients with chronic HP.

Several pathologic changes can be observed in the small airways in patients with HP; the most common were bronchiolitis obliterans, peribronchiolar and intrabronchiolar inflammation, and occasionally lymphoid follicles associated with bronchioli (Figs. 65-10 and 65-11). My observations suggest that the incidence of bronchiolitis obliterans is associated with several factors, such as type of antigen and host response. Inflammation even without obliteration of the airway is a constant finding. Immunoglobulins have been found by immunofluorescence and by immunoperoxidase techniques but their precise role in the pathogenesis remains to be elucidated (Color Fig. 65-1; Fig. 62-12).[28,49,50] In many patients, fractions of complement are absent and the presence of different immunoglobulins may represent nonimmunologic trapping.

The severity and extension of the fibrotic changes vary from patient to patient, and they are more prominent in the chronic form of the disease. When fibrosis is a conspicuous finding in the biopsy specimen, the histologic and ultrastructural findings do not differ from those found in other chronic interstitial fibrotic lung diseases. Nevertheless, a slight or moderate infiltration with lymphocytes and some giant cells and the observation of a few remaining poorly formed granulomas or bronchiolitis may suggest the diagnosis of HP.[51]

We have never observed the presence of vasculitis, but in one acute fatal case of farmer's lung, reported by Barrowcliff and Arblaster, there was acute vasculitis.[52] In a series of 100 consecutive biopsies performed on patients with subacute and chronic pigeon breeder's disease, vasculitis was not found in any case, but this is to be expected, because most biopsies are performed in subacute forms of the disease.[27] Despite the absence of acute

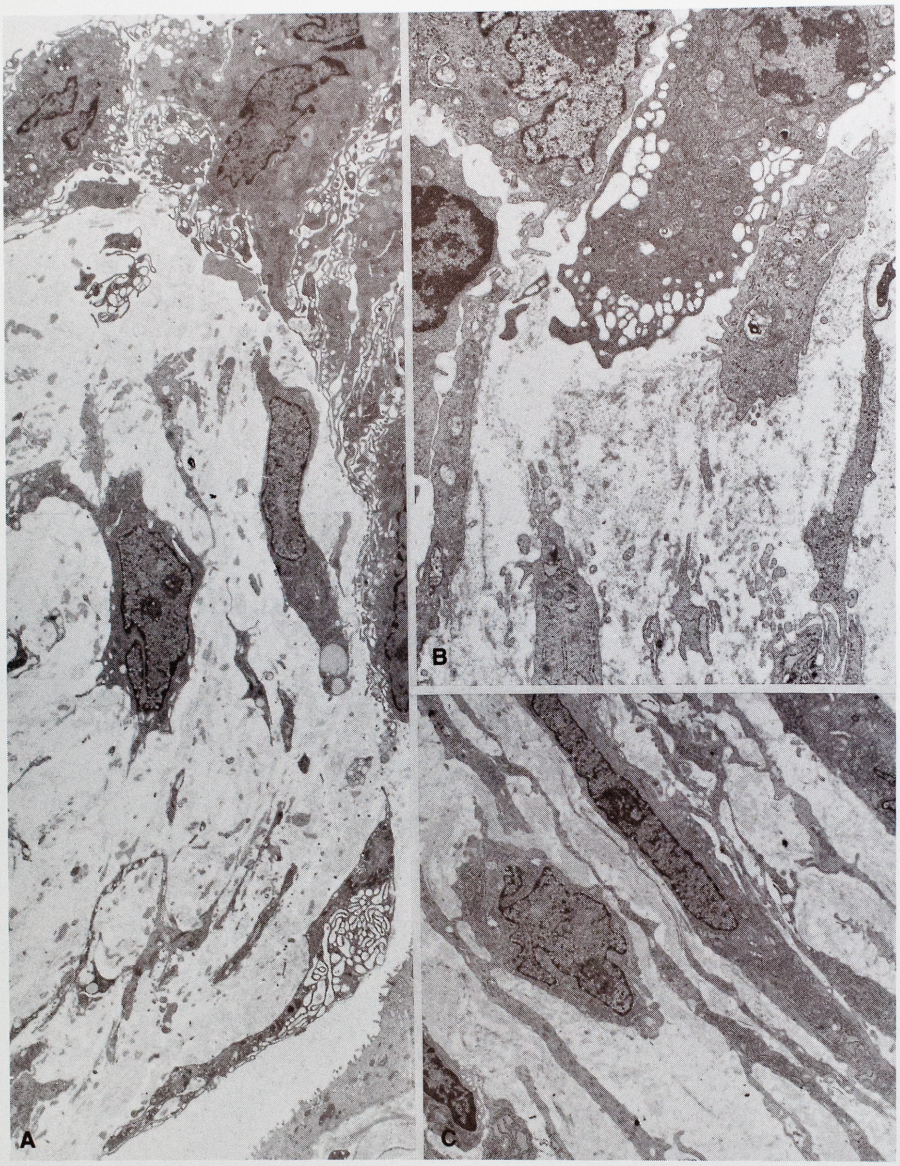

FIGURE 65-9. (**A**) The surface of an organizing intraalveolar bud is covered by alveolar macrophages. The bud contains fibroblastlike cells and connective tissue in a very loose stoma. (Original magnification × 3500.) (**B**) The detail of a bud shows alveolar macrophages, fibroblastlike cells, and loose connective tissue composed of finely fibrillar material. (Original magnification × 5500.) (**C**) A parallel arrangement of fibroblasts within an alveolar bud. (Original magnification × 7500.) (From Kawanami O, Basset F, Barrios R, Ferrans VJ, Crystal R. Hypersensitivity pneumonitis in man. Light and electron microscopy studies of 18 lung biopsies. Am J Pathol 1983;110:2.)

vasculitis, almost all patients displayed vascular lesions of the type seen in pulmonary hypertension, such as medial hypertrophy of arteries and arterioles and cellular intimal proliferation in the smallest muscular arteries and arterioles. Occasionally, more severe hypertensive changes were observed; these vascular changes were present even in early inflammatory stages of the disease and correlated with the pulmonary arterial pressure.[53]

Specific etiologic diagnosis through histologic examination is impossible in most cases. In some patients with pigeon breeder's disease, the presence of abundant foci of foamy macrophages in the interstitium and alveoli may be suggestive, but bronchiolar obstruction may produce similar findings.[47] Specific antibodies to pigeon fecal extract have been detected in lung tissue by indirect immunofluorescent methods. Other sporadic situations in which the cause may be suggested are staining for thermophilic actinomycetes in lung biopsies of patients with farmer's lung. In biopsies from patients with maple bark stripper's disease, sometimes it is possible to find spores of *Cryptostroma corticale* within the granulomas.

DIFFERENTIAL DIAGNOSIS

In the case of chronic interstitial granulomatous inflammation, cultures and special stains to rule out an infectious cause should be performed. The differential diagnosis includes all chronic interstitial lung diseases that show some histologic features of HP. The histologic triad of bronchiolitis, interstitial inflammation, and granulomas is highly characteristic but by no means specific.[45]

Sarcoidosis may begin as a lymphocytic interstitial pneumonitis with nonnecrotizing granulomas. The granulomas seen in HP are usually smaller and less numerous than those seen in sarcoidosis. The two entities can be separated histologically by the type and distribution of granulomas—sarcoid granulomas are more numerous, more well developed, better demarcated, and follow the distribution of the lymphatics. HP usually presents with poorly formed granulomas around bronchioli with extension of the inflammatory infiltrate to alveolar septa (Table 65-2).

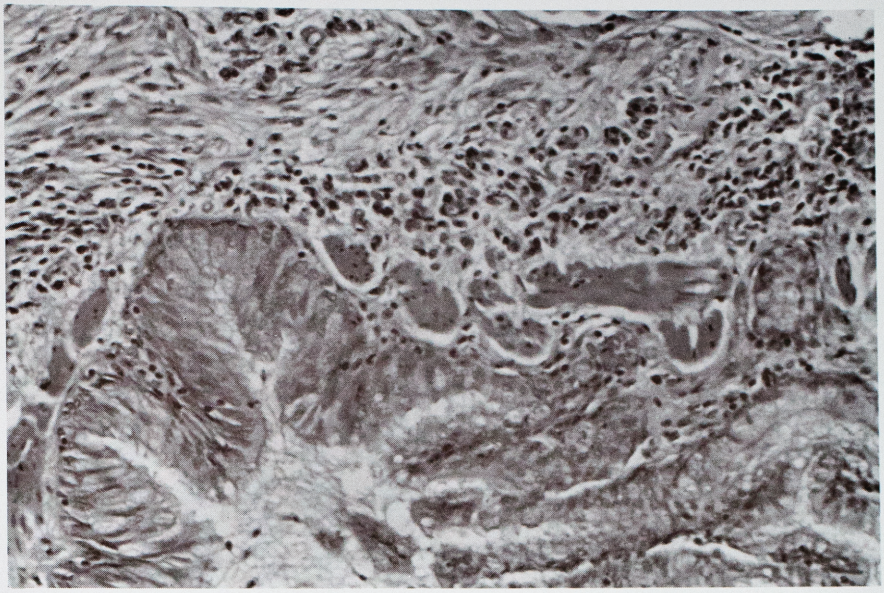

FIGURE 65-10. Marked lymphoplasmacytic peribronchiolar inflammatory infiltrate and fibrosis were found in a patient with pigeon breeder's lung. Bronchoconstriction is suggested by the thick bands of contracted bronchiolar smooth muscle and the mucosa thrown into folds within the lumen. This probably explains the wheezing of some patients. (H & E stain; low magnification; contributed by the editor.)

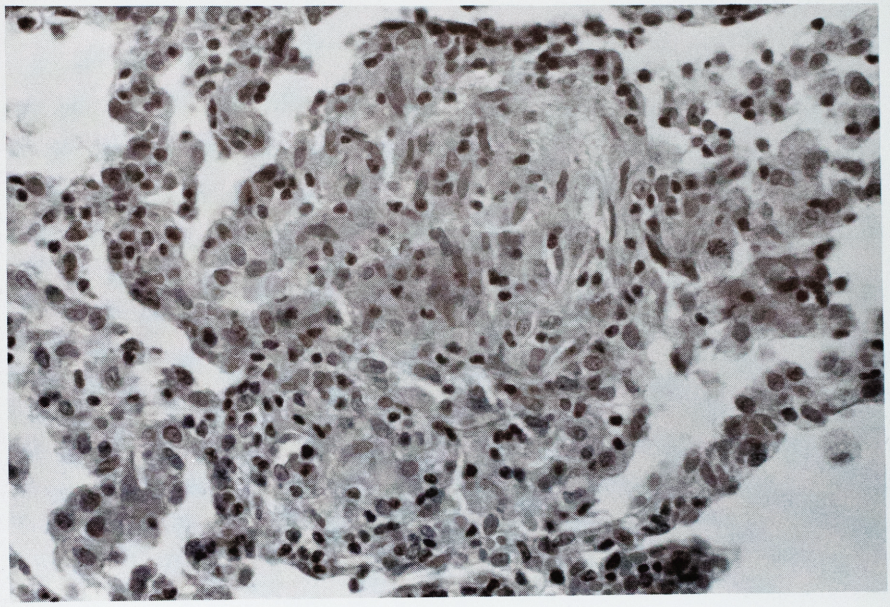

FIGURE 65-11. A granulomatous and fibrotic mass developed within an alveolar duct in a patient with hypersensitivity pneumonitis with prominent bronchiolitis obliterans (not shown). (H & E stain; intermediate magnification; contributed by the editor.)

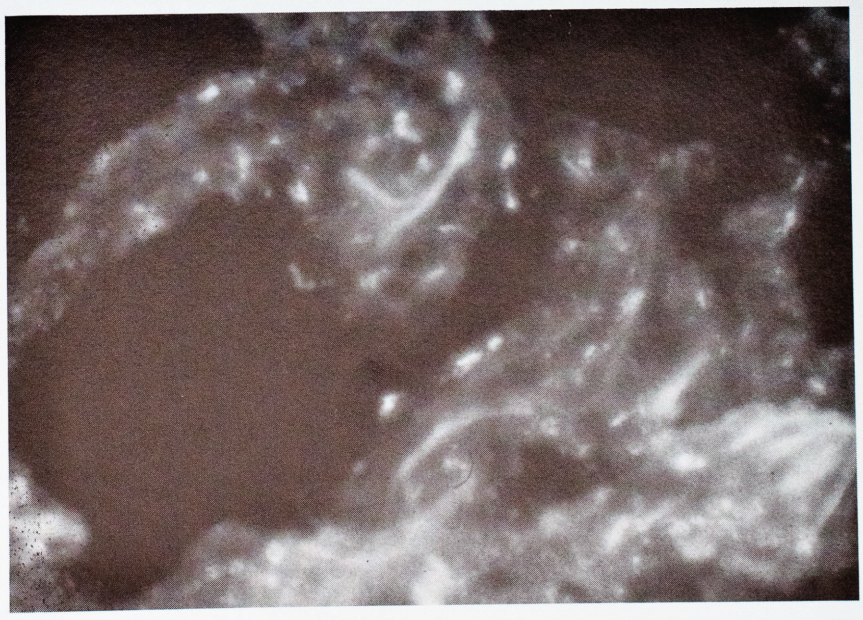

FIGURE 65-12. Immunofluorescence stains were applied to specimens from a patient with pigeon breeder's disease. In addition to the autofluorescence of elastic fibers, there are irregular deposits of plasma proteins. However, no electron-dense deposits could be identified in the pulmonary interstitium by electron microscopy. (Intermediate magnification.)

TABLE 65-2
Histopathologic Differential Diagnosis Between Sarcoidosis and Hypersensitivity Pneumonitis

Findings	Sarcoidosis	Hypersensitivity Pneumonitis
Alveolitis	Uncommon	All cases
Cellular bronchiolitis	Rare	All cases
Bronchiolitis obliterans	Rare	50% of cases
Granulomas	Well defined in 100% of cases located along lymphatics	Poorly formed, centriolobular in position in the airway wall
Foreign particles	Uncommon	60% of cases

Adapted from Reyes CN, Wenzel FJ, Lawton BR, Emanuel DA. The pulmonary pathology of farmer's lung disease. Chest 1982;81:142.

At the time the biopsy specimen is obtained, the alveolitis in sarcoidosis usually is not as prominent as that seen in HP.[54] Hilar adenopathy is frequently present in sarcoidosis, but is not seen in HP. Well-defined noncaseating granulomas are found in the lamina propria of large bronchi in over 65% of the cases of sarcoidosis, a feature not seen in HP (see Chap. 66). The T-cell population between sarcoidosis and HP is also different. Suppressor or cytotoxic lymphocytes are dominant in HP, and helper or inducer T lymphocytes are predominant in sarcoidosis.[44] This cell population can be identified by immunocytochemistry on sections or in BAL specimens.[48]

Another chronic interstitial disease that may be confused with HP is lymphoid interstitial pneumonia (LIP). Both HP and LIP are characterized by dense diffuse lymphoplasmacytic infiltrate. LIP is more cellular and distorts alveolar septa; giant cells are rarely seen.[51] Foamy macrophages are found in both entities but are nonspecific. The differential diagnosis between HP and LIP can be difficult and may require clinical and serologic information.

Usual interstitial pneumonia (UIP) should also be included in the differential diagnosis. Although occasional giant cells may be seen in some cases of UIP, they are sporadic. There is more heterogeneity in the population of inflammatory cells in UIP and the granulomatous interstitial inflammation in HP is not usually seen in UIP. Desquamative interstitial pneumonia is characterized by a more homogeneous cell population and does not show the features previously mentioned in HP (see Chaps. 31 and 32).

BRONCHOALVEOLAR LAVAGE

Fiberoptic bronchoscopy and BAL are used in many medical centers for evaluating interstitial lung diseases. Initial cell counts and their identification guide the differential diagnosis. However, BAL findings are not pathognomonic. An increased percentage of lymphocytes is seen in sarcoidosis and HP; only in a few cases of idiopathic pulmonary fibrosis is lymphocytosis found.[35] In HP, over 60% of the cells in BAL are usually lymphocytes, but a differential count with 10% to 20% of neutrophils and some eosinophils and basophils is more consistent with idiopathic pulmonary fibrosis. Subtyping of lymphocytes gives useful information for the differential diagnosis. In normal persons, about 10% of cells are lymphocytes, most are T cells, and the proportions of T_h/T_s cells is about 60/40, which gives a ratio of about 1.5. In some interstitial lung diseases, these T-cell proportions can be distinctive. In sarcoidosis, helper T cells are in excess of the suppressor subtype, and the T_h/T_s ratio may be 3 to 4. In patients with HP, T cells show a reversed ratio, which reflects a relative increase in suppressor T lymphocytes.[35] Mast cells have been related to disease activity.[55] Although most authorities agree that BAL may be a diagnostic guide and aid in monitoring disease activity, the available information is still insufficient to use the procedure in the routine diagnostic workup of patients with suspected HP.[12,56–62]

Acknowledgements

I am grateful for the helpful suggestions of Drs. Patricia Chévez and S. Donald Greenberg.

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