*Pathology of Pulmonary Disease*, edited by Mario J. Saldana.
J. B. Lippincott Company, Philadelphia © 1994.

# 67

# Pulmonary Involvement in Collagen-Vascular Disorders

J. T. Lie

The family of collagen-vascular diseases comprises a large, heterogeneous group of immune- or autoimmune-mediated inflammatory disorders, also known collectively as connective tissue diseases. The concept was first conceived by the German pathologist Fritz Klinge in the 1930s[1] and was promulgated by the American pathologist Paul Klemperer in the 1940s.[2,3] Although musculoskeletal manifestations are the most frequent clinical features of collagen-vascular disease, pulmonary involvement is not uncommon and may be a major cause of morbidity and mortality.[4–8] Interstitial pneumonitis, often accompanied by or terminating in fibrosis, is the most common pulmonary manifestation of collagen-vascular disease and accounts for an estimated 1600 deaths annually, or about 25% of all deaths from interstitial lung disease.[9] The incidence and type of pulmonary involvement in each individual collagen-vascular disease vary according to the criteria used to ascertain the involvement: clinical, roentgenographic, or pathologic. A definitive diagnosis usually requires histologic documentation of the disease, preferably with open lung biopsies.[10] The major types of collagen-vascular disease are presented in Display 67-1.

## *RHEUMATOID ARTHRITIS*

Rheumatoid arthritis (RA) is a systemic disease clinically characterized by symmetric, deforming, and nonsuppurative arthritis, predominantly affecting small peripheral joints. Pulmonary involvement in RA was first described by Ellman and Ball in 1948.[11] In the following 20 years, five major manifestations of rheumatoid lung disease became widely recognized:

1. Pleuritis
2. Pulmonary necrobiotic (*i.e.*, rheumatoid) nodules
3. Rheumatoid pneumoconiosis, or Caplan syndrome
4. Diffuse interstitial pneumonitis and fibrosis
5. Pulmonary vasculitis and pulmonary hypertension.[12–14]

Added to this classic pentad are lymphocytic interstitial pneumonitis and bronchiolitis obliterans organizing pneumonia.[15–17]

### *Pleuritis*

Pleuritis with effusion occurs usually in active RA with high titers of rheumatoid factor, and most rheumatoid effusions are exudates with low *p*H and glucose, high protein, and lactate dehydrogenase.[17–20] A needle biopsy of the pleura is seldom diagnostic, but it may be helpful in excluding tuberculous or malignant disease, both of which have biochemical constituents in pleural effusions similar to those of RA.[18–20] Open pleural biopsies usually reveal nonspecific chronic inflammation and fibrosis but may occasionally show the telltale necrobiotic or rheumatoid nodule (Fig. 67-1).

### *Rheumatoid Pneumoconiosis, or Caplan Syndrome*

This was initially described in 1953 as a typical chest roentgenographic appearance in coal miners with RA.[21] The concept of Caplan syndrome has since been expanded to include RA patients whose lungs have been exposed to inhaled silica.[22,23] It has been suggested that inhaled silica is a weak stimulus for the formation of rheumatoid factor. Independent immunologic studies showed that miners with the classic chest radiographic changes of Caplan syndrome who had no history or clinical evidence of RA had a high proportion of positive rheumatoid factor tests.[22,23] Histologically, the Caplan nodules in rheumatoid pneumoconiosis are similar to the simple rheumatoid necrobiotic nodules, with the addition of black coal dust or silica particles in the centers of the nodules (see Chaps. 34 and 35).

**DISPLAY 67-1. COLLAGEN-VASCULAR DISEASES WITH PULMONARY INVOLVEMENT**

Rheumatoid arthritis
Systemic lupus erythematosus
Systemic sclerosis (*i.e.*, scleroderma) and the CREST syndrome
Dermatomyositis-polymyositis
Ankylosing spondylitis

## *Diffuse Interstitial Pneumonitis and Fibrosis*

The prevalence of diffuse interstitial pneumonitis and fibrosis in RA ranges from 16% in a clinical survey of unselected patients[24] to 60% of open lung biopsies on unselected volunteers with RA.[25] In chest radiographic studies, the reported incidence of parenchymal rheumatoid lung disease varies from 1.5% to 4.5%,[26,27] whereas up to 40% of RA patients tested may exhibit abnormal pulmonary function tests.[28,29] Such discrepancies suggest that the chest roentgenogram is relatively insensitive in detecting early changes of interstitial lung disease and pulmonary fibrosis.[26–30] The histopathology of rheumatoid interstitial lung disease (Fig. 67-2) is indistinguishable from that of idiopathic usual interstitial pneumonia (UIP),[8,9,14–16,27] including the lymphocytic interstitial pneumonitis variant and end-stage fibrosis and honeycombing.

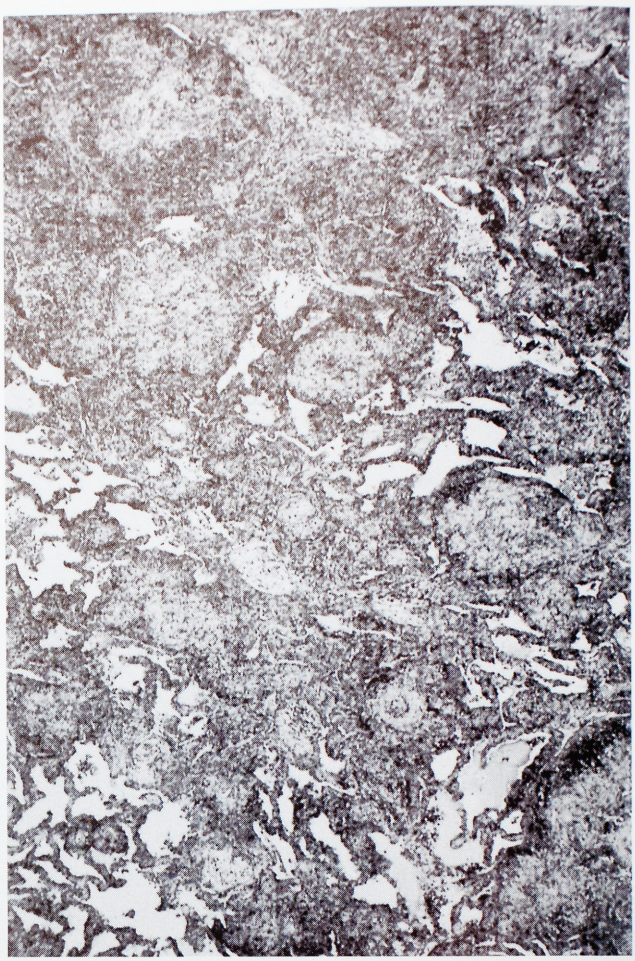

**FIGURE 67-2.** Usual interstitial pneumonia associated with bronchiolitis obliterans organizing pneumonia in rheumatoid arthritis. (H & E stain; low magnification.)

**FIGURE 67-1.** Pulmonary necrobiotic nodule in rheumatoid arthritis. (H & E stain; low magnification.)

Lymphocytic interstitial pneumonia (Fig. 67-3) occurs more commonly in juvenile RA.

Systemic vasculitis is a well-known clinical manifestation of seropositive RA and is a major cause of morbidity and mortality with this disease.[31,32] Pulmonary vasculitis occurs infrequently in RA, and it is an unfavorable prognostic predictor of the disease.[33] Pulmonary vasculitis in RA (Fig. 67-4) occurs in the absence of significant parenchymal lung disease and is usually unaccompanied by systemic rheumatoid vasculitis; it may be the cause of unexplained pulmonary hypertension in both adult-onset and juvenile RA.[34–40]

## *SYSTEMIC LUPUS ERYTHEMATOSUS*

Although Osler, at the turn of the century, had mentioned pulmonary consolidations and hemoptysis in a 24-year-old woman with systemic lupus erythematosus (SLE),[41] specific pulmonary lesions of SLE were first described by Rakov and Taylor in 1942.[42] The incidence of pulmonary involvement in SLE, according to subsequent reports, has varied from 9%[43] to 98%,[44] and it is probably in the 20% to 40% range.[45–50] Many of the pulmonary lesions previously attributed to SLE could be explained by alternative causes.[48]

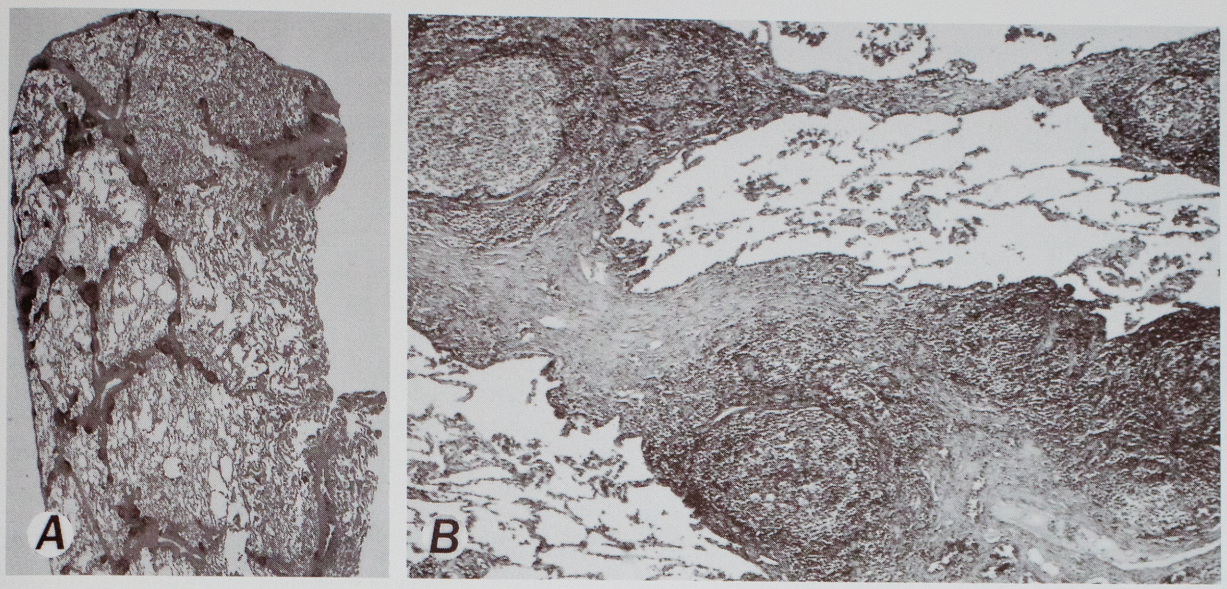


**FIGURE 67-3.** (**A**) Septal lymphoid hyperplasia and lymphocytic interstitial pneumonia in rheumatoid arthritis. (**B**) Reactive follicular hyperplasia and septal fibrosis. (H & E stains; low magnifications.)

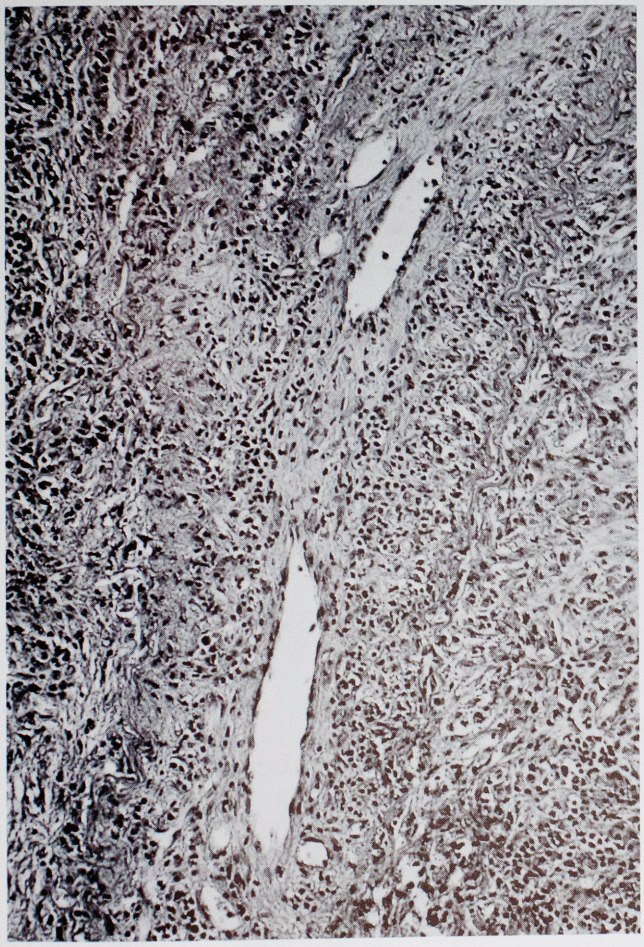

**FIGURE 67-4.** Vascular invasion by lymphocytes and plasma cells in a patient with rheumatoid arthritis. The adjacent lung tissue is also involved. (H & E stain; low magnification.)

### *Usual Interstitial Pneumonia*

UIP occurs in only 1% to 6% of SLE patients.[9] When diffuse pulmonary fibrosis is present in an SLE patient, the physician should question whether an overlap syndrome or other connective tissue disease might be involved. The possibility of pulmonary complications of antirheumatic drug therapy[51] must also be considered in the differential diagnosis. Among other less common pulmonary manifestations of SLE are bronchiolitis obliterans (Fig. 67-5) and lymphocytic interstitial pneumonitis with pseudolymphoma (Fig. 67-6), both probably immune-mediated diseases.[47,52–55]

### *Vascular Disease*

Vascular disease is a much more common and important pulmonary manifestation of SLE.[44,46,48,56–60] Pulmonary capillaritis with diffuse alveolar hemorrhage (Fig. 67-7), pulmonary vasculitis (Fig. 67-8), and pulmonary hypertension (Fig. 67-9) are a major cause of morbidity and mortality in SLE patients. Immune complexes are thought to have a key role in the pathogenesis of pulmonary vascular disease in SLE,[58] and immune deposits have been demonstrated mainly in the alveolar interstitium and vessel walls, primarily IgG1, IgM, IgA, and C3.[54,58,61–64]

## *SYSTEMIC SCLEROSIS AND THE CREST SYNDROME*

Clinical evidence of pulmonary disease in systemic sclerosis (*i.e.*, scleroderma) and the CREST (*i.e.*, calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, telangiectasia) syndrome variant is common and had been known since the time of

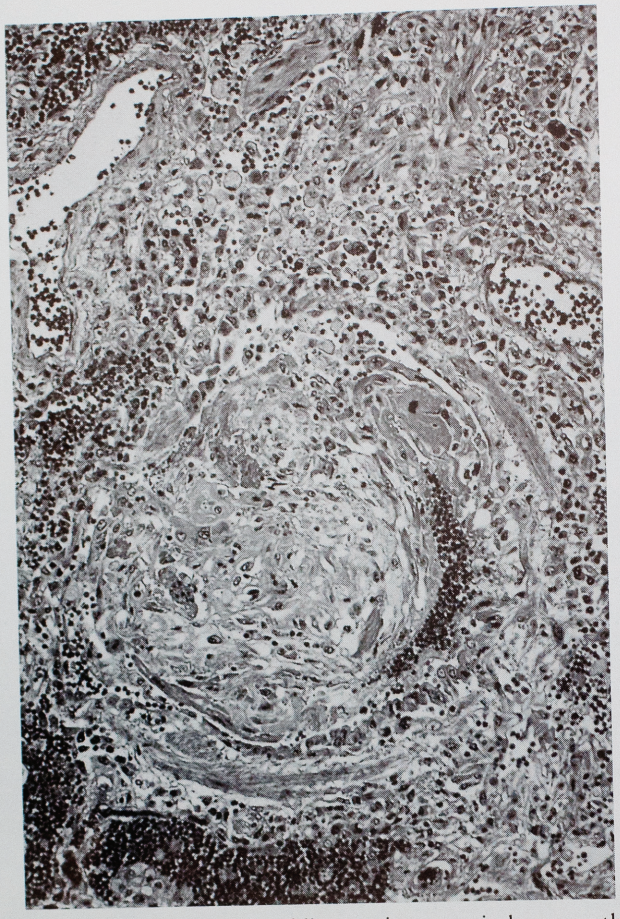

**FIGURE 67-5.** Bronchiolitis obliterans in systemic lupus erythematosus with total occlusion of lumen. (H & E stain; low magnification.)

Hippocrates.[65] Abnormal findings in the lungs of scleroderma and CREST patients at autopsy are almost universal.[66–75]

Systemic sclerosis patients with pulmonary involvement have significantly poorer survival prospects. The results of a multicenter cooperative follow-up study of 264 patients showed that patients with scleroderma lung disease survived a median of 28 ± 17 months, and 60 of 104 (58%) died before the last follow-up at an average of 5.2 years.[76] The major pulmonary complications of systemic sclerosis and the CREST syndrome are interstitial pulmonary fibrosis and pulmonary hypertension.[71–75]

Histologic evaluation of scleroderma lung disease has been based mainly on the results of autopsy studies,[66–70] which emphasize the end-stage fibrosis associated with bronchiectasis and subpleural honeycombing (Fig. 67-10). The earlier phase of interstitial lung disease in systemic sclerosis, as seen in open lung biopsies, is indistinguishable from idiopathic UIP. However, the interstitial fibrosis in scleroderma tends to be indolent and more slowly progressive than UIP, with the rare exception of a rapidly progressive diffuse alveolar damage and bronchiolitis obliterans type of lung injury (Fig. 67-11) also occurring (see Chap. 31).[77]

## *Pulmonary Hypertension*

Pulmonary hypertension occurs in 10% to 35% of patients with systemic sclerosis and in 40% to 65% of patients with the CREST syndrome variant.[69,71,73] In CREST patients, the pulmonary hypertension is often not associated with interstitial fibrosis.[72] The vascular changes in both scleroderma and CREST lungs show the same characteristic histologic features of marked, concentric intimal fibrosis and minimal medial hypertrophy (Fig. 67-12). Plexi-

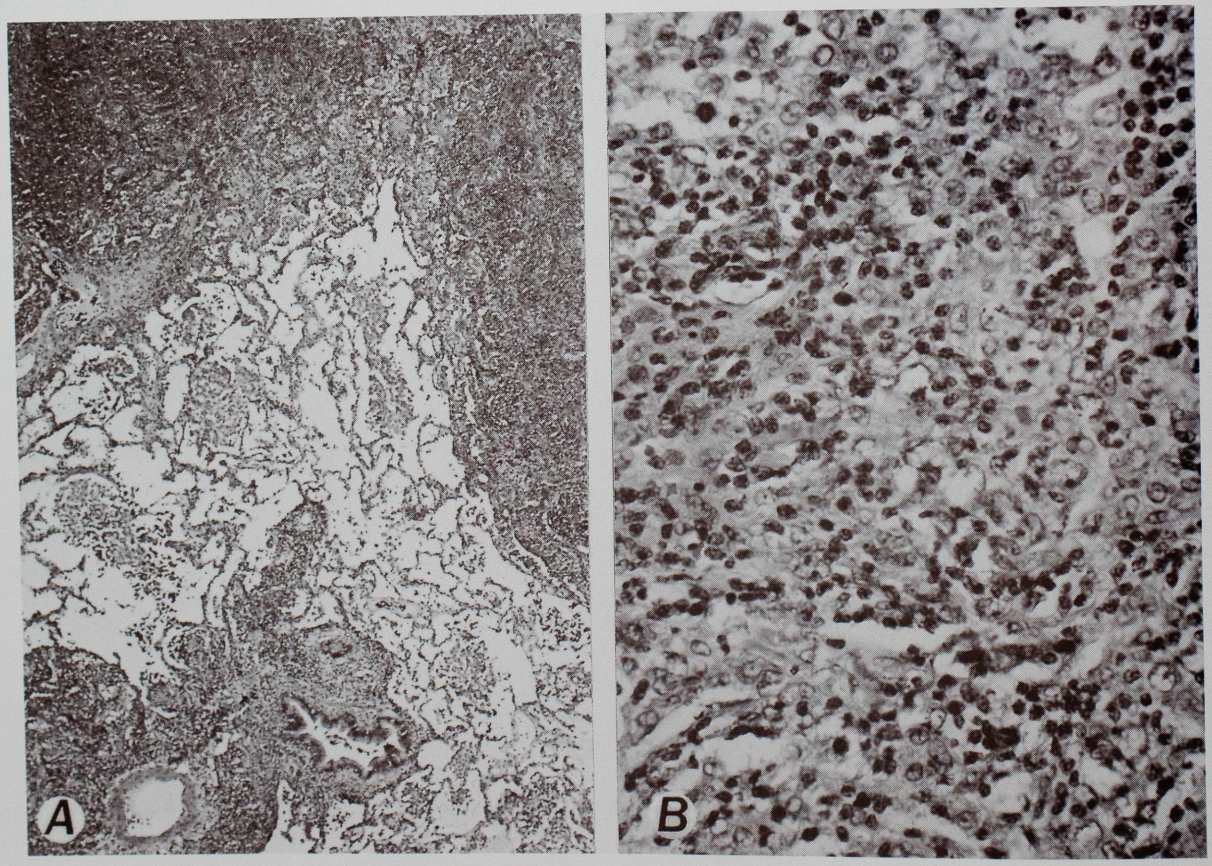


**FIGURE 67-6.** (**A**) Lymphocytic interstitial pneumonitis with pseudolymphoma in systemic lupus erythematosus. (H & E stain; low magnification.) (**B**) Close-up view of benign lymphoid cells admixed with larger macrophages in pseudolymphoma. (H & E stain; intermediate magnification.)

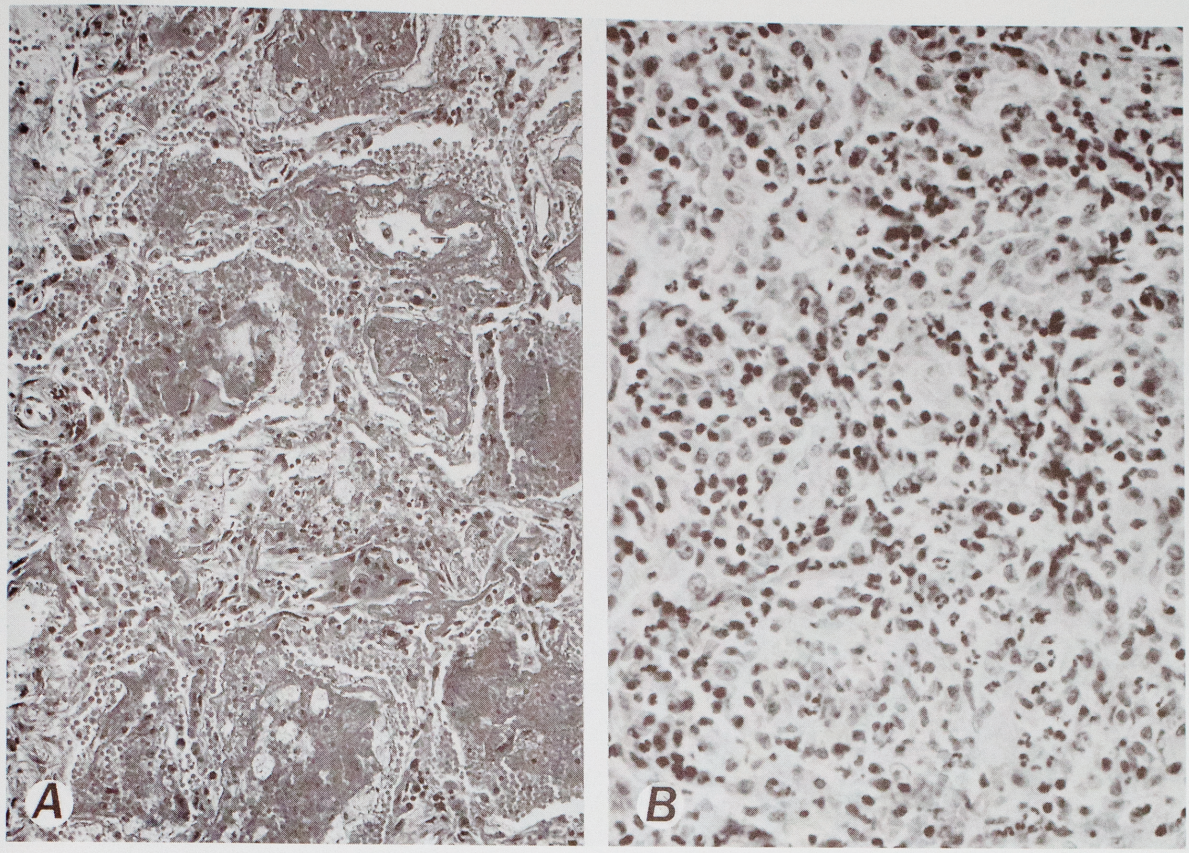


**FIGURE 67-7.** (**A**) Pulmonary capillaritis and diffuse alveolar hemorrhage in systemic lupus erythematosus. (H & E stain; low magnification.) (**B**) Close-up view of pulmonary capillaritis. (H & E stain; intermediate magnification.)

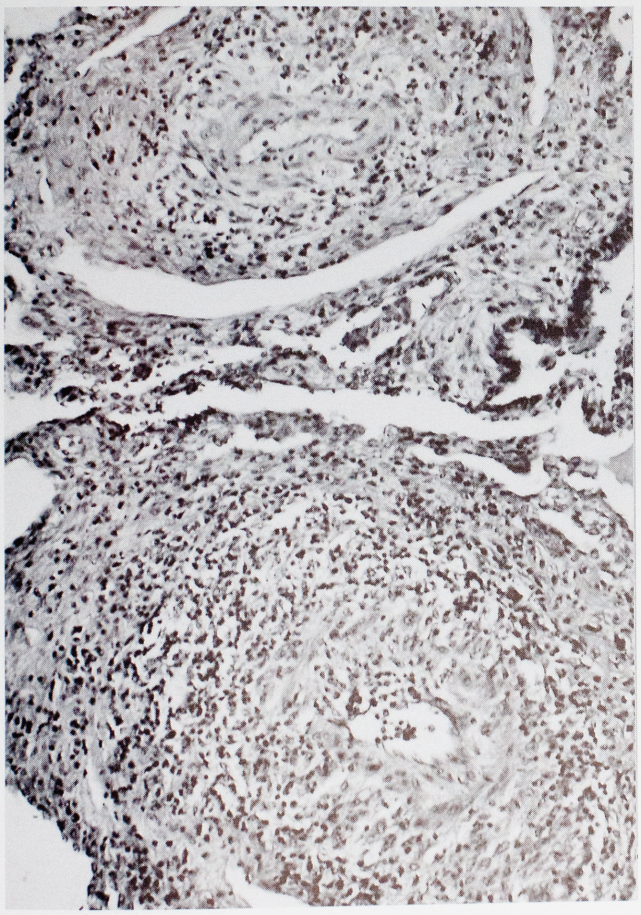

**FIGURE 67-8.** Pulmonary vasculitis in systemic lupus erythematosus. The lumens of these two arterial vessels are markedly reduced by a rich lymphoid infiltrate with fibrosis. (H & E stain; low magnification.)

form arteriopathy of pulmonary hypertension (Fig. 67-13) in systemic sclerosis and the CREST syndrome occurs only occasionally.[70–74]

## *DERMATOMYOSITIS AND POLYMYOSITIS*

Dermatomyositis and polymyositis (DPM) are usually regarded as clinical subgroups of the same inflammatory myopathy of unknown etiology.[78] DPM is a relatively uncommon disease with an incidence of 5 in 1,000,000 in the United States.[79,80] The disease affects principally the limb girdles, neck, and pharynx and is associated with a skin rash in about 40% of patients.[78] It occurs about twice as frequently in women of all age groups, with peaks in the first and fifth decades of life.[79]

Pulmonary involvement in DPM was first described by Mills and Matthews as recently as 1956,[81] and the reported prevalence rate varies from 0[82] to 64%[83] but is most probably in the 5% to 10% range.[84,85] Three types of pulmonary involvement in DPM were described by earlier investigators: UIP, ventilatory insufficiency due to respiratory muscle weakness, and aspiration pneumonia.[86,87] More recent studies[88–90] emphasize the occurrence of diffuse alveolar damage, fibrosis alveolitis, and bronchiolitis obliterans organizing pneumonia (Fig. 67-14), and, rarely, pulmonary vasculitis and pulmonary hypertension (Fig. 67-15).

The prognosis of DPM patients with pulmonary involvement is generally unfavorable; the case fatality rate for patients with histologically proven interstitial lung disease and inflammatory myopathy is 62% over a 2-year period.[91,92] Clinically, the appear-

(*text continues on page 788*)

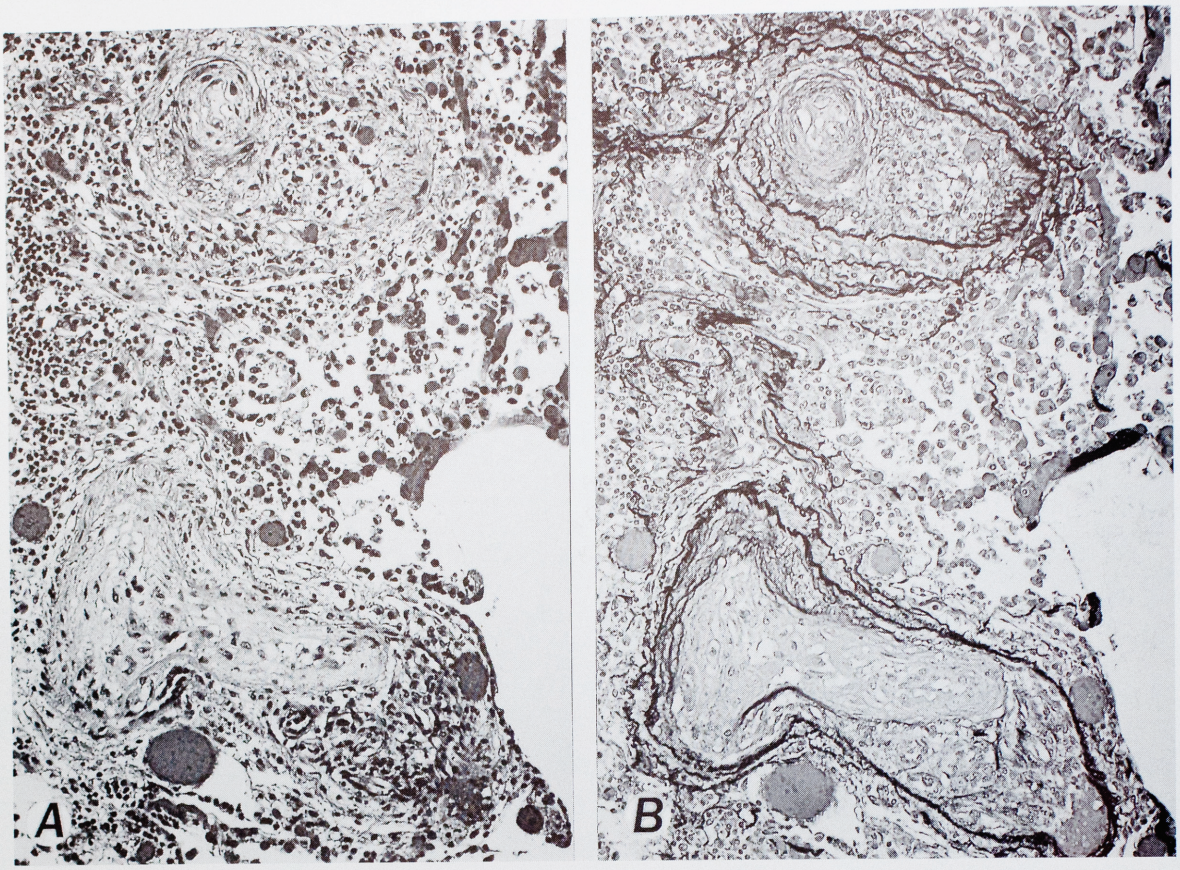


**FIGURE 67-9.** (**A** and **B**) Plexogenic pulmonary arteriopathy in systemic lupus erythematosus. (**A**: H & E stain; low magnification; **B**: elastic stain; low magnification.)

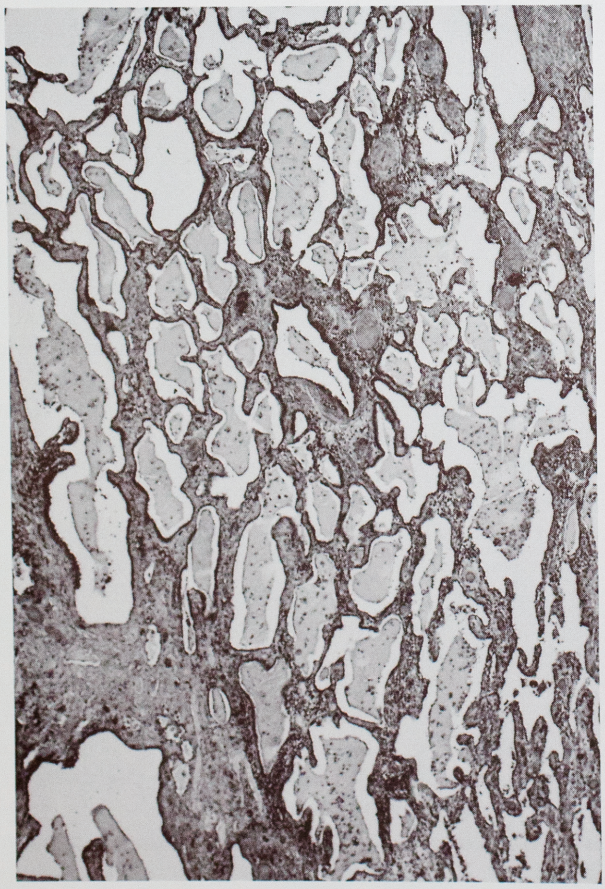

**FIGURE 67-10.** Usual interstitial fibrosis with honeycombing in the lung of a patient with systemic sclerosis. (H & E stain; low magnification.)

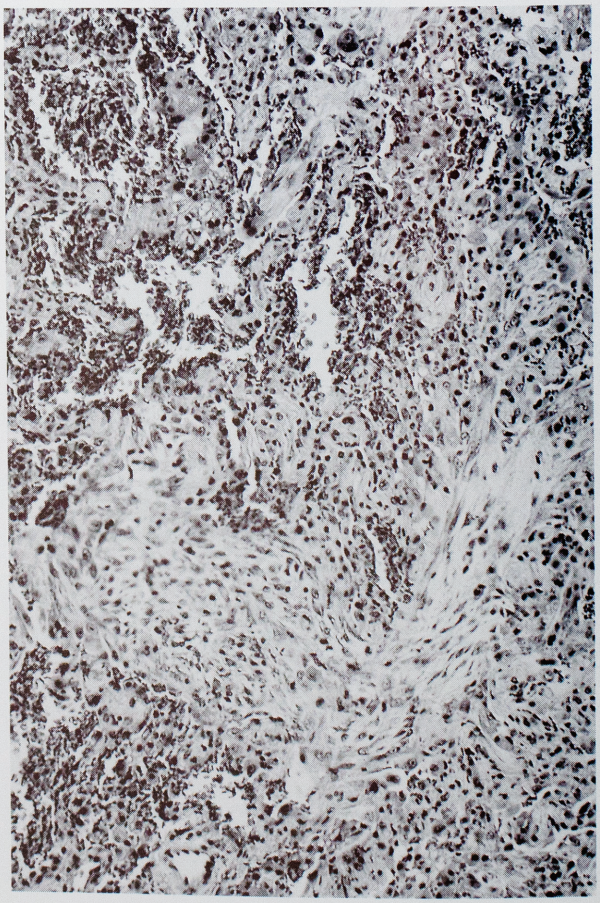

**FIGURE 67-11.** Bronchiolitis obliterans organizing pneumonia in a patient with systemic sclerosis. (H & E stain; low magnification.)

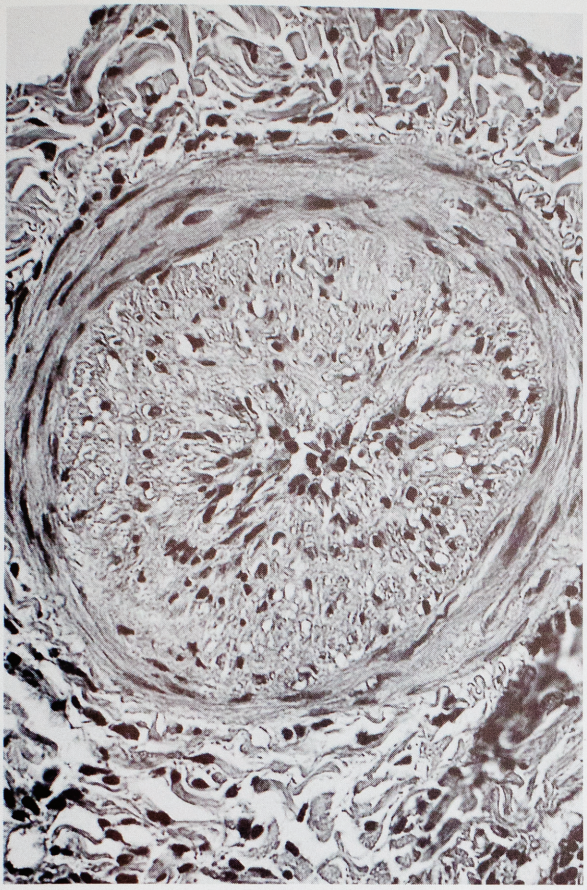

**FIGURE 67-12.** Proliferative intimal fibrosis with luminal occlusion and medial hypertrophy in the lung of a patient with systemic sclerosis. (H & E stain; intermediate magnification.)

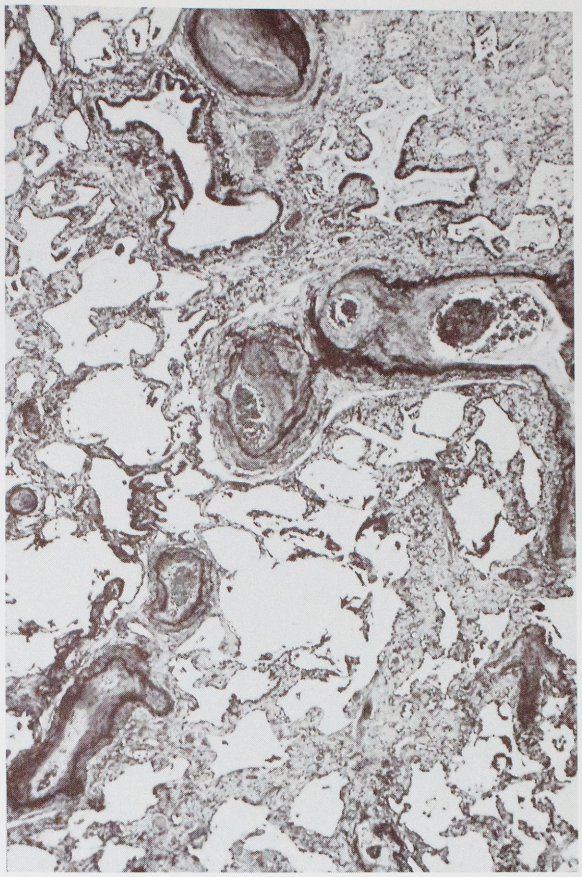

**FIGURE 67-13.** Hypertensive pulmonary vascular disease in a patient with systemic sclerosis. (Elastic tissue stain; low magnification.)

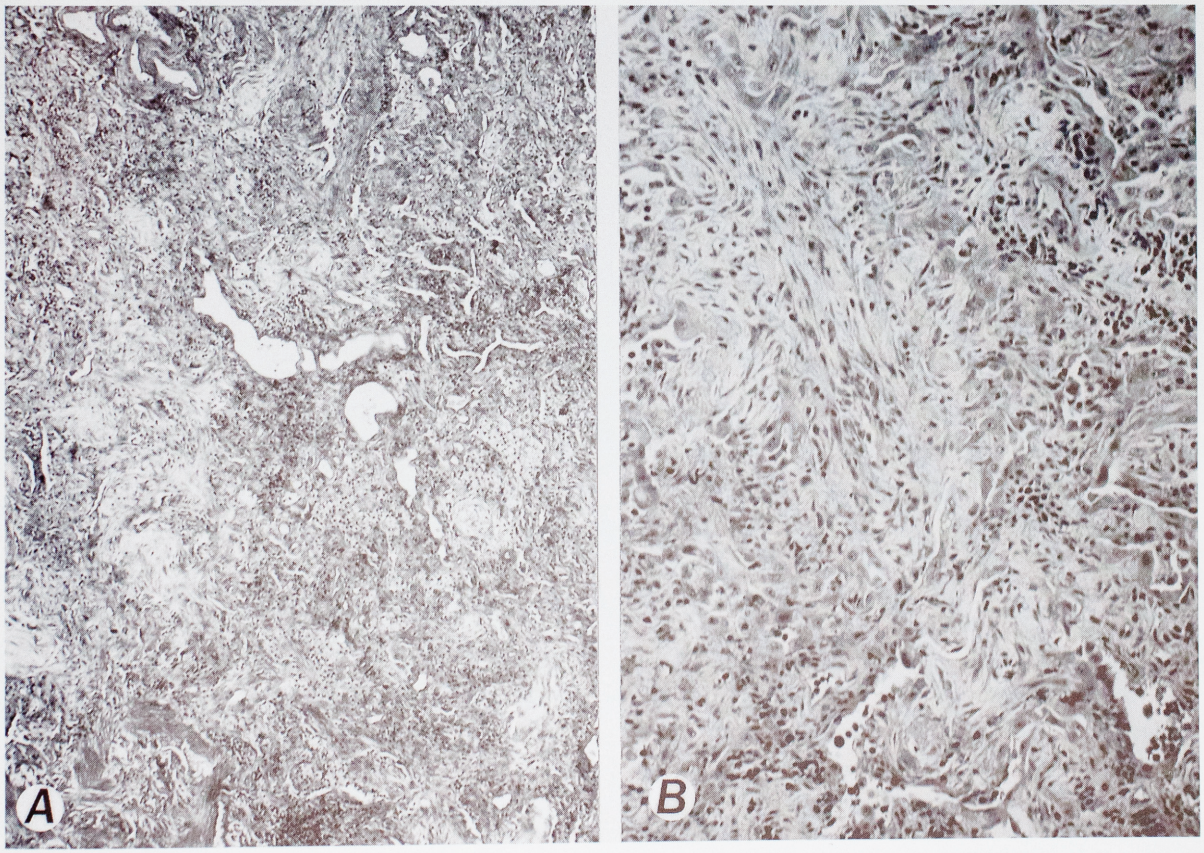


**FIGURE 67-14.** (**A**) Organizing diffuse alveolar damage and bronchiolitis obliterans in a patient with dermatopolymyositis lung disease. (H & E stain; low magnification.) (**B**) Close-up view of bronchiolitis obliterans. (H & E stain; low magnification.)

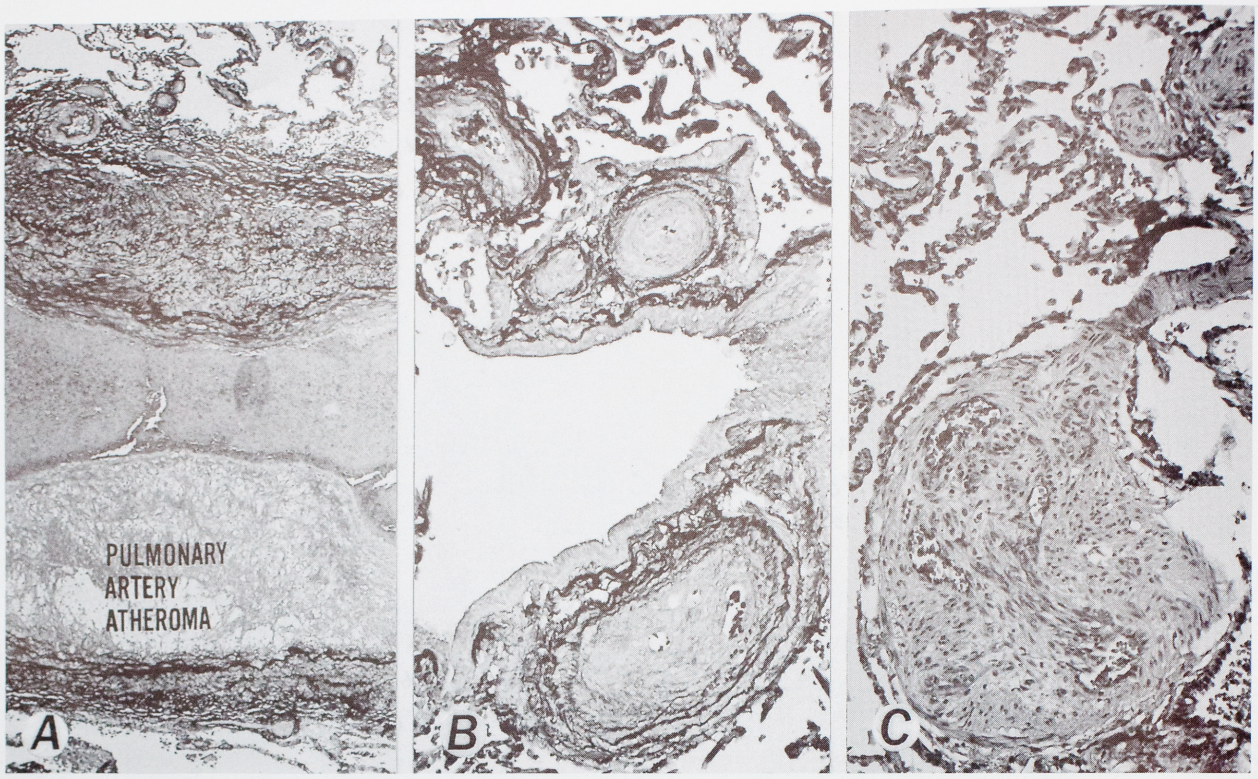


**FIGURE 67-15.** Pulmonary hypertension in a patient with dermatopolymyositis lung disease. (**A**) Atheroma of a lobar pulmonary artery. (Elastic tissue stain; low magnification.) (**B**) Occlusive intimal fibrosis of small pulmonary arteries. (Elastic tissue stain; low magnification.) (**C**) Plexogenic arteriopathy. (H & E stain; low magnification.)

ance of interstitial lung disease may precede evidence of inflammatory myopathy in about one third of DPM patients, and patients with diffuse alveolar damage or pulmonary vascular disease have a uniformly poor prognosis.[88–90]

## ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (AS) is an autoimmune disorder of the axial skeleton associated with the HLA-B27 antigen in about 90% of affected patients.[93] The first description of pulmonary involvement in AS was by Dunham and Kautz in 1941.[94] Pleuropulmonary manifestations of AS are uncommon and usually appear late in the disease; in a review of 2080 AS patients, Rosenow and colleagues identified only 28 (1.3%) who had evidence of lung disease.[95] The intrathoracic manifestations of AS are principally of two types: upper lobe fibrobullous disease with infection and chest wall restriction. Less frequently, organizing pneumonia, lymphocytic interstitial pneumonitis, and septal fibrosis have also been observed.[96]

## CONCLUSION

Pleuropulmonary involvement is often an important cause of morbidity and mortality in all major types of collagen-vascular disease. Histologic evidence of the disease in open lung biopsy specimens, or at autopsy, is required for the definitive diagnosis of pulmonary involvement. For each of the major collagen-vascular diseases, certain prognostically significant types of pathologic changes in the lungs tend to overshadow others. In RA, it is interstitial fibrosis; in SLE, it is pleuritis, pulmonary capillaritis, and alveolar hemorrhage; in systemic sclerosis and the CREST variant, it is pulmonary hypertension; in DPM, it is diffuse alveolar damage and bronchiolitis obliterans; and in AS, it is upper lobe fibrobullous disease with infection. Nevertheless, overlaps in the histopathologic features of pulmonary involvement among these major collagen-vascular diseases are common. Close consultations between the clinician, radiologist, and pathologist are essential for the correct interpretation and diagnosis of pulmonary involvement in collagen-vascular diseases.

## REFERENCES

1. Klinge F. Zur pathologischen Anatomie des Rheumatismus. Verh Dtsch Ges Orthop 1934;28:44.
2. Klemperer P, Pollack AD, Baehr G. Diffuse collagen disease: acute disseminated lupus erythematosus and diffuse scleroderma. JAMA 1942;119:331.
3. Klemperer P. The concept of collagen diseases. Am J Pathol 1950; 26:505.
4. Hunninghake GW, Fauci AS. Pulmonary involvement in the collagen vascular diseases. Am Rev Respir Dis 1979;119:471.
5. Boulware DW, Weissman DN, Doll NJ. Pulmonary manifestations of the rheumatic diseases. Clin Rev Allergy 1985;3:258.
6. Harmon KR, Leatherman JW. Respiratory manifestations of connective tissue disease. Semin Respir Infect 1988;3:258.
7. Wiedemann HP, Matthay RA. Pulmonary manifestations of collagen-vascular disease. Clin Chest Med 1989;10:677.
8. Wise RA. Pulmonary complications in collagen-vascular disease. In: Lynch JP III, DeRemee RA, eds. Immunologically mediated pulmonary diseases. Philadelphia: JB Lippincott, 1991:40.

9. Eisenberg H. The interstitial lung diseases associated with collagen-vascular disorders. Clin Chest Med 1982;3:565.
10. Gaensler EA, Carrington CB. Open biopsy for chronic diffuse infiltrative lung disease: clinical, roentgenographic and physiological correlation in 502 patients. Ann Thorac Surg 1980;30:411.
11. Ellman P, Ball RE. "Rheumatoid disease" with joint and pulmonary manifestations. Lancet 1948;1(2):816.
12. Petty TL, Wilkins M. The five manifestations of rheumatoid lung. Dis Chest 1966;49:75.
13. Walker WC, Wright V. Pulmonary lesions and rheumatoid arthritis. Medicine 1968;47:501.
14. Scadding JG. The lung in rheumatoid arthritis. Proc R Soc Med 1969;62:227.
15. Yousem SA, Colby TR, Carrington CB. Lung biopsy in rheumatoid arthritis. Am Rev Respir Dis 1985;131:770.
16. Hakala M, Paakko P, Huhi E, et al. Open lung biopsy of patients with rheumatoid arthritis. Clin Rheumatol 1990;9:452.
17. Shiel WC Jr, Prete PE. Pleuropulmonary manifestations of rheumatoid arthritis. Semin Arthritis Rheum 1984;13:235.
18. Patterson T, Klockars M, Hellstrom PE. Chemical and immunological features of pleural effusion: comparison between rheumatoid arthritis and other diseases. Thorax 1982;37:354.
19. Faurschou P. Decreased glucose in RA cell-positive pleural effusion, correlation of pleural glucose, lactic dehydrogenase and protein concentration to the presence of RA cells. Eur J Respir Dis 1984;65:272.
20. Faurschou P, Francis D, Faarup P. Thorocoscopic, histological and clinical findings in nine cases of rheumatoid pleural effusion. Thorax 1985;40:371.
21. Caplan A. Certain radiological appearances in the chest of coal miners suffering from rheumatoid arthritis. Thorax 1953;8:29.
22. Caplan A, Payne RB, Withey JL. A broader concept of Caplan's syndrome related to rheumatoid factors. Thorax 1962;17:205.
23. Benedik TG. Rheumatoid pneumoconiosis. Am J Med 1973;55:515.
24. Popper MS, Bogdonoff ML, Hughes RI. Interstitial rheumatoid lung disease. Chest 1972;62:243.
25. Cervantes-Perez P, Toro-Perez AH, Rodriguez-Jurado P. Pulmonary involvement in rheumatoid arthritis. JAMA 1980;243:1715.
26. Juirik AG, Davidsen D, Graudal H. Prevalence of pulmonary involvement in rheumatoid arthritis and its relationship to some characteristics of the patients: a radiological and clinical study. Scand J Rheumatol 1982;11:217.
27. Roschmann RA, Rothenberg RJ. Pulmonary fibrosis in rheumatoid arthritis: a review of clinical features and therapy. Semin Arthritis Rheum 1987;16:174.
28. Laitinen O, Nissila M, Salorinne Y, et al. Pulmonary involvement in patients with rheumatoid arthritis. Scand J Respir Dis 1975;56:297.
29. Geddes DM, Webley M, Emerson PA. Airway obstruction in rheumatoid arthritis. Ann Rheum Dis 1979;38:222.
30. Epler GR, McLoud TC, Gaensler EA, et al. Normal chest roentgenograms in chronic diffuse infiltrative lung disease. N Engl J Med 1978;298:934.
31. Scott DGI, Bacon PA, Tribe CR. Systemic rheumatoid vasculitis: a clinical and laboratory study of 50 cases. Medicine 1981;60:288.
32. Vollertsen RS, Conn RL, Ballard DJ, et al. Rheumatoid vasculitis: survival and associated risk factors. Medicine 1986;65:365.
33. Lakhanpal S, Conn DL, Lie JT. Clinical and prognostic significance of vasculitis as an early manifestation of connective tissue syndromes. Ann Intern Med 1984;101:743.
34. Kay JM, Banik S. Unexplained pulmonary hypertension with pulmonary arteritis in rheumatoid disease. Br J Dis Chest 1977;71:53.
35. Baydur A, Mongan DS, Slager UT. Acute respiratory failure and pulmonary arteritis without parenchymal involvement: demonstration in a patient with rheumatoid arthritis. Chest 1979;75:518.
36. Armstrong JG, Steel RH. Localized pulmonary arteritis in rheumatoid disease. Thorax 1982;37:313.
37. Morikawa J, Kitamura K, Habuchi Y, et al. Pulmonary hypertension in a patient with rheumatoid arthritis. Chest 1988;93:876.
38. Jordan JD, Snyder CH. Rheumatoid disease of the lung and cor pulmonale: observations in a child. Am J Dis Child 1964;108:174.
39. Sharma S, Vacharajani A, Mandke J. Severe pulmonary hypertension in rheumatoid arthritis. Int J Cardiol 1990;26:220.
40. Padeh S, Laxer RM, Silver MM, et al. Primary pulmonary hypertension in a patient with systemic-onset juvenile arthritis. Arthritis Rheum 1991;34:1575.
41. Osler W. On the visceral manifestations of the erythema group of skin diseases. Am J Med Sci 1904;127:1.
42. Rakov HL, Taylor JS. Acute disseminated lupus erythematosus without cutaneous manifestations and with heretofore undescribed pulmonary lesions. Arch Intern Med 1942;70:88.
43. Dubois EL, Tuffanelli DL. Clinical manifestations of systemic lupus erythematosus: computer analysis of 520 cases. JAMA 1964;190:104.
44. Gross M, Esterly JR, Earle RH. Pulmonary alterations in systemic lupus erythematosus. Am Rev Respir Dis 1972;105:572.
45. Eisenberg H, Dubois EL, Sherwin RP, et al. Diffuse interstitial lung disease in systemic lupus erythematosus. Ann Intern Med 1973;79:37.
46. Matthay RA, Schwartz MI, Petty TL, et al. Pulmonary manifestations of systemic lupus erythematosus: review of 12 cases of acute lupus pneumonitis. Medicine 1975;54:397.
47. Silberstein SL, Barland P, Grayzel AI, et al. Pulmonary dysfunction in systemic lupus erythematosus: prevalence, classification and correlation with other organ involvement. J Rheumatol 1980;7:187.
48. Haupt HM, Moore GW, Hutchins GM. The lung in systemic lupus erythematosus: analysis of the pathologic changes in 120 patients. Am J Med 1981;71:791.
49. Pines A, Kaplinsky N, Olchovsky D, et al. Pleuro-pulmonary manifestations of systemic lupus erythematosus: clinical features of its subgroups. Chest 1985;88:129.
50. Miller LR, Greenberg SK, McLarty JW. Lupus lung. Chest 1985; 88:265.
51. Cannon GW. Pulmonary complications of antirheumatic drug therapy. Semin Arthritis Rheum 1990;19:353.
52. Matthay RA, Schwartz MI, Petty TL, et al. Pulmonary manifestations of systemic lupus erythematosus: review of 12 cases of acute lupus pneumonitis. Medicine 1975;54:397.
53. Hum MN, Ziegler JR, Walker PD, et al. Pseudolymphoma of the lung in a patient with systemic lupus erythematosus. Am J Med 1979;66:172.
54. Churg A, Franklin W, Chan KW, et al. Pulmonary hemorrhage and immune-complex deposition in the lung. Arch Pathol Lab Med 1980; 104:388.
55. Kinney WW, Angellillo VA. Bronchiolitis in systemic lupus erythematosus. Chest 1982;82:646.
56. Eagen JW, Memoli VA, Roberts JL, et al. Pulmonary hemorrhage in systemic lupus erythematosus. Medicine 1978;57:545.
57. Nair SS, Askari AD, Pepilka CG, et al. Pulmonary hypertension and systemic lupus erythematosus. Arch Intern Med 1980;140:109.
58. Quismorio FP Jr, Sharma O, Koss M, et al. Immunopathologic and clinical studies in pulmonary hypertension associated with systemic lupus erythematosus. Semin Arthritis Rheum 1984;13:349.
59. Asherson RA, Hackett D, Gharavi AE, et al. Pulmonary hypertension in systemic lupus erythematosus. J Rheumatol 1986;13:416.
60. Kasukawa R, Nishimaki T, Takagi T, et al. Pulmonary hypertension in connective tissue disease: clinical analysis of sixty patients in multi-institutional study. Clin Rheumatol 1990;9:56.
61. Pertschuk LP, Moccia LF, Rosen Y, et al. Acute pulmonary complications in systemic lupus erythematosus. Immunofluorescence and light microscopic study. Am J Clin Pathol 1977;68:553.
62. Eagen JW, Roberts JL, Schwartz MM, et al. The composition of pulmonary immune deposits in systemic lupus erythematosus. Clin Immunol Immunopathol 1979;12:204.
63. Churg A, Franklin W, Chan KW, et al. Pulmonary hemorrhage and immune-complex deposition in the lung. Arch Pathol Lab Med 1980;104:388.
64. Segal AM, Calabrese LH, Ahmad M, et al. The pulmonary manifes-

tations of systemic lupus erythematosus. Semin Arthritis Rheum 1985;14:202.
65. Sackner MA. The visceral manifestations of scleroderma. Arthritis Rheum 1962;5:184.
66. Weaver AL, Divertie MB, Titus JL. Pulmonary scleroderma. Dis Chest 1968;54:4.
67. D'Angelo WEA, Fries JF, Masi AT, et al. Pathologic observations in systemic sclerosis (scleroderma): a study of fifty-eight autopsy cases and fifty-eight matched controls. Am J Med 1969;46:428.
68. Colp CR, Riker J, Williams MH. Serial changes in scleroderma and idiopathic interstitial lung disease. Arch Intern Med 1973;132:506.
69. Salerni R, Rodnan GP, Leon DF, et al. Pulmonary hypertension in the CREST syndrome variant of progressive systemic sclerosis (scleroderma). Ann Intern Med 1977;86:394.
70. Young RJ, Mark GJ. Pulmonary vascular changes in scleroderma. Am J Med 1978;64:998.
71. Ungerer RG, Tashkin DP, Furst D, et al. Prevalence and clinical correlates of pulmonary arterial hypertension in progressive systemic sclerosis. Am J Med 1983;75:65.
72. Steen VD, Owens GR, Fino GJ, et al. Pulmonary involvement in systemic sclerosis (scleroderma). Arthritis Rheum 1985;28:759.
73. Stupi AM, Steen VD, Owens GR, et al. Pulmonary hypertension in the CREST syndrome variant of systemic sclerosis. Arthritis Rheum 1986;29:515.
74. Lie JT. Pulmonary hypertension in the CREST syndrome variant of systemic sclerosis (scleroderma). Angiology 1989;40:764.
75. Silver RM, Miller KS. Lung involvement in systemic sclerosis. Rheum Dis Clin North Am 1990;16:199.
76. Altman RD, Medsger TA Jr, Bloch DA, et al. Predictors of survival in systemic sclerosis (scleroderma). Arthritis Rheum 1991;34:403.
77. Bettmann MA, Kantrowitz F. Rapid onset of lung involvement in progressive systemic sclerosis. Chest 1979;75:509.
78. Bohan A, Peters JB. Polymyositis and dermatomyositis. N Engl J Med 1975;292:344,403.
79. Medsger TA Jr, Dawson WN, Masi AT. The epidemiology of polymyositis. Am J Med 1970;48:715.
80. Oddis CV, Copnte CB, Steen VD, et al. Incidence of polymyositis-dermatomyositis: a 20-year study of hospital diagnosed cases in Allegheny County, PA, 1963–1982. J Rheumatol 1990;17:3129.
81. Mills ES, Matthews WH. Interstitial pneumonitis in dermatomyositis. JAMA 1956;160:1467.
82. Bohan A, Peter JB, Bowman RL, et al. A computer-assisted analysis of 153 patients with polymyositis and dermatomyositis. Medicine 1977;56:255.
83. Takizawa H, Shiga J, Moroi Y, et al. Interstitial lung disease in dermatomyositis: clinicopathological study. J Rheumatol 1987;14:102.
84. Frazier AR, Miller RD. Interstitial pneumonitis in association with polymyositis and dermatomyositis. Chest 1974;65:403.
85. Salmeron G, Greenberg SD, Lidsky MD. Polymyositis and diffuse interstitial lung disease: a review of the pulmonary histopathologic findings. Arch Intern Med 1981;141:1005.
86. Hepper NG, Ferguson RH, Howard FM Jr. Three types of pulmonary involvement in polymyositis. Med Clin North Am 1964;48:1031.
87. Schwarz MI, Matthay RA, Sahn SA, et al. Interstitial lung disease in polymyositis and dermatomyositis: analysis of six cases and review of the literature. Medicine 1976;55:89.
88. Tazelaar HD, Viggiano RW, Pickersgill J, et al. Interstitial lung disease in polymyositis and dermatomyositis: clinical features and prognosis as correlated with histologic findings. Am Rev Respir Dis 1990;141:727.
89. Lakhanpal S, Lie JT, Conn DL, et al. Pulmonary disease in polymyositis/dermatomyositis: a clinicopathological analysis of 65 autopsy cases. Ann Rheum Dis 1987;46:23.
90. Bunch TW, Tancredi RG, Lie JT. Pulmonary hypertension in polymyositis. Chest 1981;79:105.
91. Dickey BF, Myers AR. Pulmonary disease in polymyositis/ dermatomyositis. Semin Arthritis Rheum 1984;14:60.
92. Arsura EL, Greenberg AS. Adverse impact of interstitial pulmonary fibrosis on prognosis in polymyositis and dermatomyositis. Semin Arthritis Rheum 1988;18:29.
93. McGuigan LE, Geczy AF, Edmonds JP. The immunopathology of ankylosing spondylitis—a review. Semin Arthritis Rheum 1985;15:81.
94. Dunham CL, Kautz FG. Spondylarthritis ankylopoietica: a review and report of twenty cases. Am J Med Sci 1941;201:232.
95. Rosenow EC III, Strimian CV, Muhm JR, et al. Pleuropulmonary manifestations of ankylosing spondylitis. Mayo Clin Proc 1977;52:641.
96. Boushea DK, Sundstrom WR. The pleuropulmonary manifestations of ankylosing spondylitis. Semin Arthritis Rheum 1989;18:277.