Necrotizing granulomas have rarely been reported in sarcoidosis, but this finding should prompt an intense search for infection. In contrast to most ILDs, in which tissue diagnosis requires open lung biopsy, the granulomas in sarcoidosis can be identified in skin nodules or in lymph nodes. Due to frequent lung and lymph node involvement, bronchoscopy is commonly used to diagnose sarcoidosis. Results of bronchoscopy with transbronchial lung biopsy are positive for 50% to 60% of patients, but the procedure poses the risks of hemorrhage and pneumothorax. Because airway involvement is common, endobronchial biopsies may also demonstrate granulomas. However, there is increasing evidence that transbronchial needle aspiration of mediastinal and hilar lymph nodes using endobronchial ultrasound guidance may have a higher diagnostic yield for granulomas than conventional bronchoscopic techniques (level 1 evidence).

After the diagnosis is made, all patients should have an ophthalmologic evaluation and a 24-hour collection of urine to assess for hypercalciuria. Electrocardiographic examination and sometimes Holter monitoring should be performed to assess for conduction system abnormalities or arrhythmias resulting from involvement of the heart by sarcoidosis. If cardiac sarcoidosis is suspected, magnetic resonance imaging (MRI) or PET scanning may be helpful.

Treatment

Corticosteroids are the standard therapy, but they should not be used indiscriminately in all patients with the diagnosis of sarcoidosis because sarcoidosis may not cause symptoms or complications and the disease may undergo spontaneous remission. Whether corticosteroids alter the disease course is uncertain. However, corticosteroid therapy should be considered in patients with extrapulmonary organ involvement or progressive pulmonary symptoms. In patients with pulmonary involvement, oral prednisone at a dosage of 20 to 40 mg per day may be initiated (level 2 evidence). Because the duration of treatment may be prolonged, steroid-sparing agents, particularly methotrexate, have been used (level 2). Infliximab, an anti-TNF agent, has resulted in a small improvement in vital capacity compared with placebo in patients with pulmonary sarcoidosis (level 1).

Patients with erythema nodosum in the setting of Löfgren syndrome may be treated with nonsteroidal anti-inflammatory medications alone. Other skin involvement may respond to hydroxychloroquine or topical corticosteroids. The treatment of lupus pernio is challenging, but it may respond to infliximab (level 3 evidence). Given the role of TNF in T_H1-type immunity, anti-TNF agents may also have roles in treating other forms of extrapulmonary disease not responding to conventional therapy (level 3).

Anterior uveitis may be treated with topical steroids, but other eye involvement may require systemic corticosteroids. Systemic corticosteroids are also used for the treatment of cardiac sarcoidosis (level 3 evidence). Conduction system disease and arrhythmias may necessitate placement of pacemakers or automatic implantable cardioverter-defibrillators (level 3). Neurosarcoidosis and hypercalcemia are among the other indications for systemic steroid treatment (level 3 for both).

Prognosis

The course of sarcoidosis varies. Spontaneous remission is common, and death and disability occur rarely, making decisions regarding treatment initiation difficult. The acute sarcoidosis syndromes tend to remit and not recur. However, about one third of patients with sarcoidosis have chronic, progressive disease, and some patients develop pulmonary fibrosis or other end-organ damage.

For a deeper discussion on this topic, please see Chapter 95, "Sarcoidosis," in Goldman-Cecil Medicine, *25th Edition.*

INTERSTITIAL LUNG DISEASES RELATED TO CONNECTIVE TISSUE DISORDERS

In patients with ILD, a thorough history and physical examination may reveal abnormalities such as arthritis and hand deformities, rashes, esophageal dysmotility, Raynaud's syndrome, and skin changes suggesting an underlying connective tissue disease. Connective tissue disorders, such as systemic lupus erythematosus, rheumatoid arthritis, mixed connective tissue disorder, systemic sclerosis (i.e., scleroderma), polymyositis or dermatomyositis, and Sjögren syndrome, can cause ILD and a wide variety of other pulmonary manifestations (Table 17-3). Lung disease is a major cause of morbidity and mortality in some of these conditions, especially systemic sclerosis. Although not typical, a connective tissue disorder–related ILD (CTD-ILD)

TABLE 17-3 PULMONARY INVOLVEMENT IN CONNECTIVE TISSUE DISORDERS

DISORDER	RA	LUPUS	SS	PM/DM	SJÖGREN SYNDROME
Pleural effusion	+ (5-40%)	+ (30-40%)			
Necrobiotic nodules	+				
Fibrosis	+ (20-60%)	+ (3%)	+ (15-90%)	+ (10-40%)	+ (33%)
Bronchiolitis	+	+			+
Pulmonary arteriopathy	+	+	+	+	
Atelectasis		+			
Pulmonary edema		+			
Pneumonitis, hemorrhage		+			
Diaphragm dysfunction		+			
Aspiration			+	+ (14%)	
Secondary carcinoma			+		

DM, Dermatomyositis; PM, polymyositis; RA, rheumatoid arthritis; SS, systemic sclerosis.