gene signatures have been associated with more severe disease, such as cardiac, neurologic, and fibrotic pulmonary disease.

At diagnosis the natural history of the disease may be difficult to predict. One form of the disease, *Löfgren's syndrome*, consists of erythema nodosum and hilar adenopathy on chest roentgenogram. In some cases, periarticular arthritis may be identified without erythema nodosum. Löfgren's syndrome is associated with a good prognosis, with >90% of patients experiencing disease resolution within 2 years. Recent studies have demonstrated that the HLA-DRB1*03 was found in two-thirds of Scandinavian patients with Löfgren's syndrome. More than 95% of those patients who were HLA-DRB1*03 positive had resolution of their disease within 2 years, whereas nearly one-half of the remaining patients had disease for more than 2 years. It remains to be determined whether these observations can be applied to a non-Scandinavian population.

CLINICAL MANIFESTATIONS

The presentation of sarcoidosis ranges from patients who are asymptomatic to those with organ failure. It is unclear how often sarcoidosis is asymptomatic. In countries where routine chest roentgenogram screening is performed, 20–30% of pulmonary cases are detected in asymptomatic individuals. The inability to screen for other asymptomatic forms of the disease would suggest that as many as one-third of sarcoidosis patients are asymptomatic.

Respiratory complaints including cough and dyspnea are the most common presenting symptoms. In many cases, the patient presents with a 2- to 4-week history of these symptoms. Unfortunately, due to the nonspecific nature of pulmonary symptoms, the patient may see physicians for up to a year before a diagnosis is confirmed. For these patients, the diagnosis of sarcoidosis is usually only suggested when a chest roentgenogram is performed.

Symptoms related to cutaneous and ocular disease are the next two most common complaints. Skin lesions are often nonspecific. However, because these lesions are readily observed, the patient and treating physician are often led to a diagnosis. In contrast to patients with pulmonary disease, patients with cutaneous lesions are more likely to be diagnosed within 6 months of symptoms.

Nonspecific constitutional symptoms include fatigue, fever, night sweats, and weight loss. Fatigue is perhaps the most common constitutional symptom that affects these patients. Given its insidious nature, patients are usually not aware of the association with their sarcoidosis until their disease resolves.

The overall incidence of sarcoidosis at the time of diagnosis and eventual common organ involvement are summarized in Table 390-1. Over time, skin, eye, and neurologic involvement seem more apparent. In the United States, the frequency of specific organ involvement appears to be affected by age, race, and gender. For example, eye disease is more common among African Americans. Under the age of 40, it occurs more frequently in women. However, in those diagnosed over the age of 40, eye disease is more common in men.

TABLE 390-1 FREQUENCY OF COMMON ORGAN INVOLVEMENT AND LIFETIME RISK[a]

	Presentation, %[b]	Follow-Up, %[c]
Lung	95	94
Skin	24	43
Eye	12	29
Extrathoracic lymph node	15	16
Liver	12	14
Spleen	7	8
Neurologic	5	16
Cardiac	2	3

[a]Patients could have more than one organ involved. [b]From ACCESS study of 736 patients evaluated within 6 months of diagnosis. [c]From follow-up of 1024 sarcoidosis patients seen at the University of Cincinnati Interstitial Lung Disease and Sarcoidosis Clinic from 2002–2006.

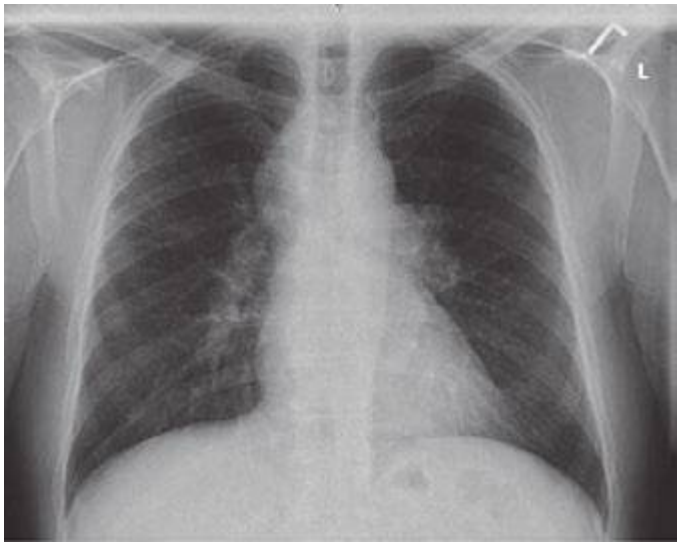

FIGURE 390-2 Posterior-anterior chest roentgenogram demonstrating bilateral hilar adenopathy, stage 1 disease.

LUNG

Lung involvement occurs in >90% of sarcoidosis patients. The most commonly used method for detecting lung disease is still the chest roentgenogram. Figure 390-2 illustrates the chest roentgenogram from a sarcoidosis patient with bilateral hilar adenopathy. Although the computed tomography (CT) scan has changed the diagnostic approach to interstitial lung disease, the CT scan is not usually considered a monitoring tool for patients with sarcoidosis. Figure 390-3 demonstrates some of the characteristic CT features, including peribronchial thickening and reticular nodular changes, which are predominantly subpleural. The peribronchial thickening seen on CT scan seems to explain the high yield of granulomas from bronchial biopsies performed for diagnosis.

Although the CT scan is more sensitive, the standard scoring system described by Scadding in 1961 for chest roentgenograms remains the preferred method of characterizing the chest involvement. Stage 1 is hilar adenopathy alone (Fig. 390-2), often with right paratracheal involvement. Stage 2 is a combination of adenopathy plus infiltrates, whereas stage 3 reveals infiltrates alone. Stage 4 consists of fibrosis. Usually the infiltrates in sarcoidosis are predominantly an upper lobe process. Only in a few noninfectious diseases is an upper lobe

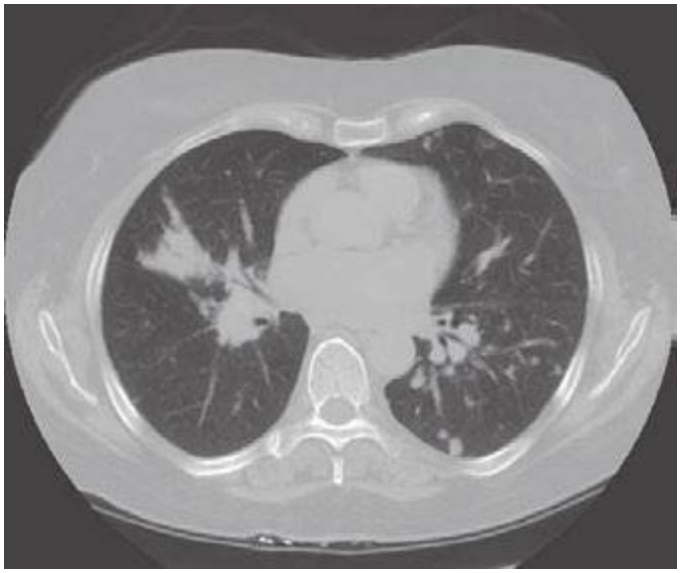

FIGURE 390-3 High-resolution computed tomography scan of chest demonstrating patchy reticular nodularity, including areas of confluence.