Serologic classification can augment the clinical classification described previously. For example, 95% of patients with anticentromere antibody have lcSSc and are at increased risk for pulmonary hypertension during the follow-up period. Individuals with anti–topoisomerase I (i.e., anti-SCL70) or anti–RNA polymerase III antibody are more likely to have dcSSc. Those with anti–RNA polymerase III antibody have an increased risk of renal crisis, and those with anti-SCL70 have a higher frequency of interstitial lung disease.

The primary internal organ risks and cutaneous associations are depicted in Figure 80-2, which illustrates the combined clinical-serologic classification of SSc. It is uncommon for patients to have more than one SSc autoantibody.

Raynaud's Phenomenon and Peripheral Vascular Involvement

Most patients with SSc experience Raynaud's phenomenon during their disease course. Raynaud's phenomenon is a triphasic vasospastic response to cold consisting of pallor (i.e., blanching) with or without cyanosis (i.e., bluish discoloration followed by reactive hyperemia (i.e., erythema) with a characteristic distinct line of demarcation on the digits separating the affected from unaffected areas.

The onset of Raynaud's phenomenon can precede the development of skin changes by years in some patients. Severe involvement may result in ischemia with loss of digital tip tissue, including digital pitting scars, ulcers, and gangrene (rare). Digital tip ulcers are more frequent in patients who are anticentromere or anti–topoisomerase I autoantibody positive. Lower extremity ulcerations in SSc patients have been increasingly reported in recent years.

Interstitial Lung Disease

Interstitial lung disease (ILD) can be one of the most serious complications of SSc and should be monitored for routinely (see Chapter 17). The initial presentation is often a nonproductive cough and a gradual onset of dyspnea on exertion over several months to years. However, the onset can be abrupt.

High-resolution chest computed tomography (CT) typically shows bibasilar fibrotic changes, which can be progressive. Pulmonary function tests reveal reduced forced vital capacity (FVC). On pathologic examination, the most frequently seen pattern is nonspecific interstitial pneumonitis. Patients with anti-SCL70 autoantibody are at the highest risk for ILD.

Pulmonary Hypertension

SSc patients can develop pulmonary hypertension of three World Health Organization (WHO) classifications (see Chapter 18). Pulmonary arterial hypertension (PAH, group 1) is the most common, with an estimated 10% to 15% of patients in cohort studies developing PAH. It occurs most commonly in those with lcSSc. The clinical presentation includes rapidly progressive dyspnea occurring over several months. Pulmonary function tests reveal a reduced diffusion capacity for carbon monoxide (DLCO) out of proportion to any concomitant reduction in the FVC.

Less frequently, SSc patients develop pulmonary hypertension associated with ILD (group 3) or pulmonary hypertension associated with left ventricular diastolic dysfunction from myocardial fibrosis or non–SSc-associated left ventricular disorders (group 2). Screening for all types of pulmonary hypertension is performed by echocardiogram, and results should be confirmed by right heart cardiac catheterization.

Scleroderma Renal Crisis

Scleroderma renal crisis (SRC) manifests as the abrupt onset of accelerated arterial hypertension accompanied by a rise in serum creatinine levels and by microscopic hematuria and proteinuria on urinalysis. Microangiopathic hemolytic anemia and thrombocytopenia are common. Although once the major cause of mortality in SSc, SRC is now managed by aggressive blood pressure control with an angiotensin-converting enzyme (ACE) inhibitor.

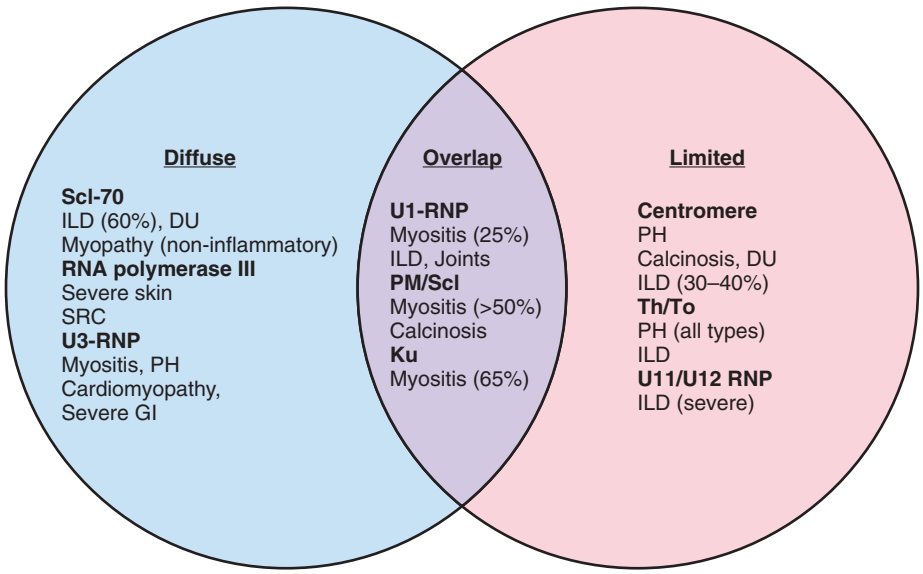

FIGURE 80-2 Clinical-serologic classification of systemic sclerosis and antibody-associated internal organ manifestations. *Bold text* indicates an antibody; clinical manifestations listed below are associated with that antibody. DU, Digital ulcers; ILD, interstitial lung disease; Ku, 70/80-kD protein (XRCC6/XRCC5); PH, pulmonary hypertension; PM, polymyositis; RNP, ribonucleoprotein; Scl, sclerosis; SRC, scleroderma renal crisis.