80

Systemic Sclerosis

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INTRODUCTION

Systemic sclerosis (SSc) is a connective tissue disease that is characterized by cutaneous and visceral fibrosis. The more common term for the disease, *scleroderma*, reflects its derivation from the Greek *scleros,* which means thick, and *derma*, which means skin.

The disorder can range from a relatively benign condition to a rapidly progressive disease leading to significant morbidity or death. Although cutaneous manifestations are the most obvious features, visceral involvement can be severe and disabling. Monitoring for potential organ complications is essential in caring for SSc patients, because early detection and treatment may minimize morbidity and mortality.

EPIDEMIOLOGY

The annual U.S. incidence of SSc is approximately 20 cases per million persons. Because patients with SSc often live for many years, the prevalence is 240 cases per million persons. Incidence and prevalence vary somewhat throughout the world, and they typically are lower in Europe and Asia. SSc more commonly affects women, with a 3 : 1 female-to-male ratio. It occurs in individuals of all ages, from childhood to the elderly, but it most frequently affects those between the ages of 40 and 60 years.

A familial pattern of inheritance is not as evident in SSc as in other connective tissue diseases. Twin studies have demonstrated only a 5% rate of concordance in monozygotic and dizygotic twins, implying that there are significant environmental contributions to its occurrence. Many patients with SSc, however, have family histories of other autoimmune diseases (e.g., thyroid disease, rheumatoid arthritis, systemic lupus erythematosus [SLE]). Genome-wide association studies have revealed a handful of genes associated with SSc that are shared with other diseases such as rheumatoid arthritis and SLE (e.g., major histocompatibility complex class I and II genes *STAT4* and *IRF5*). These findings suggest a shared genetic predisposition to autoimmune conditions.

PATHOLOGY

The pathogenesis of SSc has not been fully elucidated. There are three clearly identified components: endothelial and vascular injury with associated vasculopathy, immune system activation, and fibrosis with overproduction of collagen and other connective tissue matrix proteins (Fig. 80-1). Involvement of these systems initially became evident from autopsy studies. Vascular changes include endothelial cell injury and subintimal thickening leading to luminal narrowing with occasional vascular occlusion

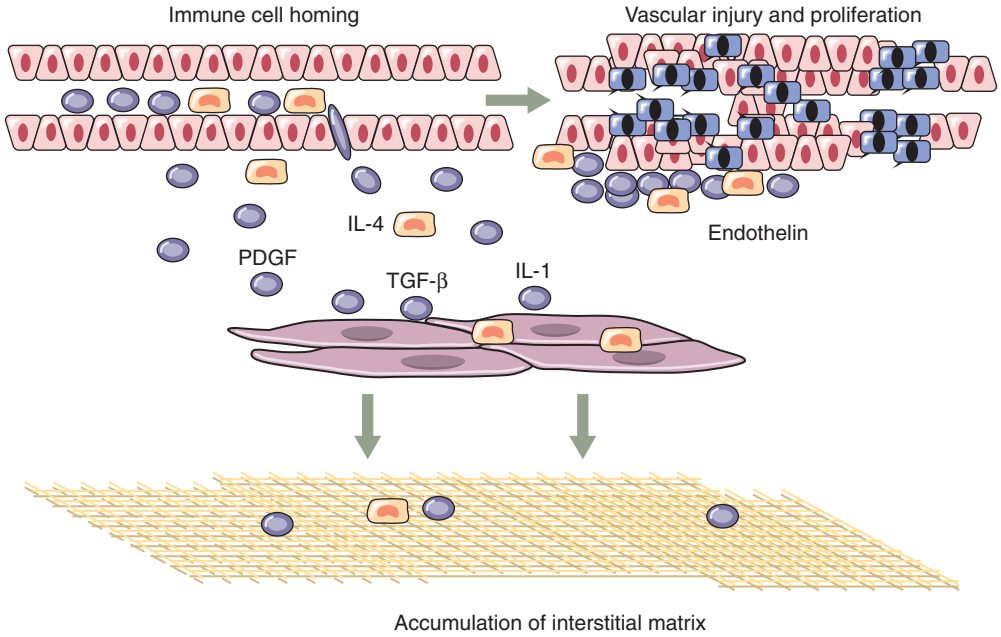

FIGURE 80-1 Pathogenetic processes in systemic sclerosis. Vascular injury leads to intimal proliferation of endothelial cells *(red)* and smooth muscle cells *(blue)*. Fibroblasts are activated to deposit increased amounts of interstitial matrix. IL, Interleukin; PDGF, platelet-derived growth factor; TGF-β, transforming growth factor-β.