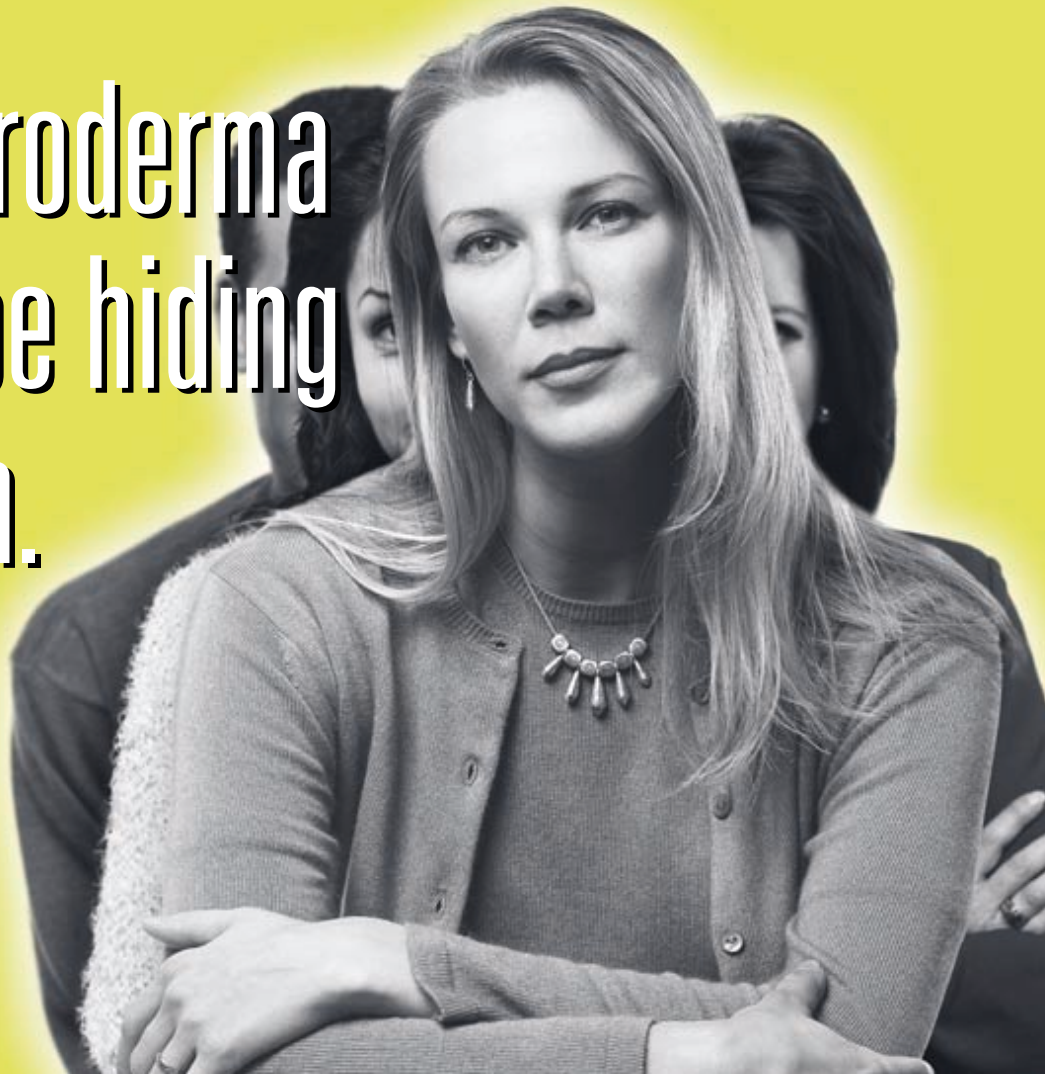
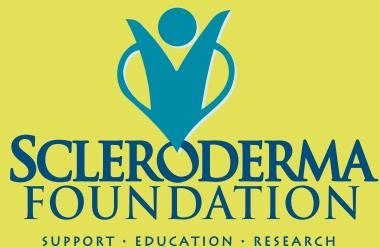


3 out of 4 scleroderma patients may be hiding out in the open.



Scleroderma = hard (*skleros*) + skin (*derma*)

Help starts with a prompt and proper diagnosis

Scleroderma is an autoimmune connective tissue disorder affecting the vasculature and collagen. In its most serious forms, scleroderma can threaten not only patients' physical and functional abilities but also their professional, social, and emotional lives. Because of its complexity and low prevalence, scleroderma can be a challenge to diagnose, especially in its initial stages. While it is estimated that approximately 100,000 persons have been diagnosed with systemic sclerosis in the United States, there is evidence that as many as three times that number remain unrecognized. Recent progress in understanding the cellular mechanisms and manifestations of scleroderma, and the potential for breakthroughs in therapeutics, emphasize the importance of increasing awareness

of this disorder. With prompt and proper diagnosis and treatment, the symptoms of scleroderma can be minimized and the chance of irreversible damage lessened.

Recognizing the subsets of scleroderma

Scleroderma may occur as a systemic disorder that affects the internal organs as well as the skin (systemic sclerosis) or as various localized forms that primarily affect the skin and the musculoskeletal system (localized scleroderma). Table 1 describes the subsets that fall under these two forms of scleroderma.

Table 1 The subsets of scleroderma

Localized Scleroderma	
Morphea	<ul style="list-style-type: none"> ▪ Skin plaques of fibrotic skin and subcutaneous tissue without systemic disease
Linear Scleroderma	<ul style="list-style-type: none"> ▪ Longitudinal fibrotic bands that occur predominantly on extremities and involve skin and deeper tissue
Systemic Sclerosis	
Diffuse	<ul style="list-style-type: none"> ▪ Skin thickening present on the trunk or proximal extremities in addition to the face and distal extremities ▪ Significant organ involvement: lung, heart, gastrointestinal, or kidney ▪ Associated with antinucleolar antibodies and Scl-70 antibodies and absence of anticentromere antibody
Limited	<ul style="list-style-type: none"> ▪ Also known as CREST syndrome (C, calcinosis; R, Raynaud's phenomenon; E, esophageal dysmotility; S, sclerodactyly; T, telangiectasia) ▪ Skin thickening limited to sites distal to the elbow and knee but also involving the face and neck ▪ Late organ involvement with prominent hypertension, digital ulceration, and possible digital amputation ▪ Association with anticentromere antibody
Other	<ul style="list-style-type: none"> ▪ Overlap syndrome ▪ Undifferentiated connective tissue disease

The diagnosis of this disease involves differentiating scleroderma from other connective tissue disorders as well as identifying the specific subset of scleroderma that is being exhibited. The process includes an in-depth medical history,

a thorough physical examination, and auto-antibody tests. In systemic sclerosis, a determination of the extent and severity of internal organ involvement is also essential.

Diagnosis of Scleroderma

Medical History

Physical Examination

Auto-Antibody Tests

Organ Involvement (systemic sclerosis)

Medical history

The diagnosis of scleroderma begins with an in-depth medical history, which is important because the initial complaints of scleroderma are typically nonspecific and may overlap with other diseases such as rheumatoid arthritis, polymyositis, and systemic lupus erythematosus (SLE). Some of the most common symptoms include lack of energy or fatigue, musculoskeletal complaints, gastroesophageal reflux symptoms, and Raynaud's phenomenon.

Physical examination

The findings of a physical examination can provide the clinician with specific clues that suggest a diagnosis of scleroderma and begin to define the subset of scleroderma that is present. The first such clue is often skin thickening that begins as swelling or puffiness of the fingers and hands. Skin tightness usually appears on both sides of the body and is symmetrical; the skin of the face and neck may also become involved. Other physical findings may include skin hypo- and hyperpigmentation, subcutaneous calcinosis, and telangiectasia.

Auto-antibody tests

Antinuclear antibody (ANA) tests are helpful and sometimes confirmatory, but rarely diagnostic. Many healthy individuals, especially family members of individuals with rheumatic diseases, can have positive ANAs. A high percentage (>90%) of patients with the diffuse and limited forms of scleroderma are antinuclear antibody-positive.

Certain auto-antibodies are more scleroderma-specific:

- Antitopoisomerase I or Anti-Scl-70
- Anticentromere
- Anti-RNA polymerase I, II, and III

Assays for these auto-antibodies can be helpful in assessing the subsets of scleroderma and can provide prognostic information.

Organ involvement

Finally, a diagnosis of systemic sclerosis requires a determination of the extent and severity of internal organ involvement. In addition to the involvement of the skin, the individual with systemic sclerosis can also experience a wide range of symptoms and difficulties involving such internal organs as the gastrointestinal tract, lungs, kidneys, and heart.

The Scleroderma Foundation

The Scleroderma Foundation is the national organization for people with scleroderma and their families and friends.

The Scleroderma Foundation's mission is threefold:

- To help patients and their families cope with scleroderma through mutual support programs, peer counseling, physician referrals, and educational information
- To promote public awareness and education through patient and health professional seminars, literature, and publicity campaigns
- To stimulate and support research to improve treatment and ultimately find the cause and cure for scleroderma and related diseases

The Scleroderma Foundation has funded millions of dollars in research. We also publish a quarterly magazine and an extensive line of brochures and pamphlets. We maintain chapters and support groups nationwide, and hold a national conference for patients every year featuring invited medical speakers.

For more information about the Scleroderma Foundation's research program, publications, chapters and support groups, and other activities, please visit our website: www.scleroderma.org

GI Tract

Kidneys

Systemic sclerosis

Lungs

Heart

Gastrointestinal involvement

The gastrointestinal (GI) tract is one of the most frequently involved organ systems in systemic sclerosis. GI involvement can be present in both diffuse and limited disease and may involve the esophagus, stomach, and small and large intestines. Esophageal reflux, dysphagia, and bloating with early satiety are common symptoms and are amenable to therapy. Proton pump inhibitors in particular have been an advance in treating severe reflux disease. Proton pump inhibitors in particular have been an advance in treating severe reflux disease. Promotility agents may be helpful.

Pulmonary involvement

Pulmonary disease is the leading cause of mortality and the principal source of morbidity in systemic sclerosis. The two most common pulmonary conditions in systemic sclerosis are

interstitial lung disease and pulmonary arterial hypertension (PAH). Patients with diffuse disease are at the highest risk for interstitial lung disease, although it can also occur in patients with limited disease. Studies suggest that cyclophosphamide may be effective for active alveolitis and an NIH-sponsored study of cyclophosphamide is underway.

In patients with systemic sclerosis, pulmonary arterial hypertension (PAH) may occur secondary to interstitial lung disease or as an isolated primary process. The highest risk for isolated PAH is associated with limited systemic sclerosis, although it is also found in diffuse disease.

Because of the seriousness of PAH, research into new treatments has been especially active. Severe advanced pulmonary hypertension is often treated with continuous central venous infusion of epoprostenol. Therapies in development, including subcutaneous, oral, and inhaled prostacyclin analogues and oral endothelin receptor antagonists, may provide important new treatment options for PAH.

Renal involvement

Renal involvement occurs in approximately 20% of systemic sclerosis patients, predominantly in diffuse disease. The most severe renal manifestation of systemic sclerosis is the scleroderma renal crisis, which is characterized by rapidly progressive renal failure with or without associated accelerated hypertension. The scleroderma renal crisis usually occurs within the first 5 years of disease. Early and aggressive treatment with angiotensin-converting enzyme inhibitors is critical, even in patients without hypertension.

Cardiac involvement

The clinical manifestations of heart disease secondary to systemic sclerosis are quite variable and often not seen until late in the

course of the disease. These manifestations commonly involve the myocardium, myocardial blood vessels, and pericardium, particularly in patients with diffuse disease. Overt clinical signs of any cardiac disease in systemic sclerosis are associated with a poor prognosis.

A multidisciplinary approach to management

The complex and diverse organ involvement associated with systemic sclerosis emphasizes the need for a multidisciplinary approach to the management of this disease. While rheumatologists and scleroderma specialists have the best training to handle the overall complexities of the disease, a team approach provides the flexibility to refer patients to pulmonologists, gastroenterologists, nephrologists, cardiologists, and neurologists for screening, diagnosis, and treatment of organ complications.

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