

# Systemic Scleroderma

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Systemic scleroderma is an autoimmune disorder that affects the skin and internal organs. Autoimmune disorders occur when the immune system malfunctions and attacks the body's own tissues and organs. The word "scleroderma" means hard skin in Greek, and the condition is characterized by the buildup of scar tissue (fibrosis) in the skin and other organs. The condition is also called systemic sclerosis because the fibrosis can affect organs other than the skin. Fibrosis is due to the excess production of a tough protein called collagen, which normally strengthens and supports connective tissues throughout the body.

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## 1. Introduction

The signs and symptoms of systemic scleroderma usually begin with episodes of Raynaud phenomenon, which can occur weeks to years before fibrosis. In Raynaud phenomenon, the fingers and toes of affected individuals turn white or blue in response to cold temperature or other stresses. This effect occurs because of problems with the small vessels that carry blood to the extremities. Another early sign of systemic scleroderma is puffy or swollen hands before thickening and hardening of the skin due to fibrosis. Skin thickening usually occurs first in the fingers (called sclerodactyly) and may also involve the hands and face. In addition, people with systemic scleroderma often have open sores (ulcers) on their fingers, painful bumps under the skin (calcinosis), or small clusters of enlarged blood vessels just under the skin (telangiectasia).

Fibrosis can also affect internal organs and can lead to impairment or failure of the affected organs. The most commonly affected organs are the esophagus, heart, lungs, and kidneys. Internal organ involvement may be signaled by heartburn, difficulty swallowing (dysphagia), high blood pressure (hypertension), kidney problems, shortness of breath, diarrhea, or impairment of the muscle contractions that move food through the digestive tract (intestinal pseudo-obstruction).

There are three types of systemic scleroderma, defined by the tissues affected in the disorder. In one type of systemic scleroderma, known as limited cutaneous systemic scleroderma, fibrosis usually affects only the hands, arms, and face. Limited cutaneous systemic scleroderma used to be known as CREST syndrome, which is named for the common features of the condition: calcinosis, Raynaud phenomenon, esophageal motility dysfunction, sclerodactyly, and telangiectasia. In another type of systemic scleroderma, known as diffuse cutaneous systemic scleroderma, the fibrosis affects large areas of skin, including the torso and the upper arms and legs, and often involves internal organs. In diffuse cutaneous systemic scleroderma, the condition worsens quickly and organ damage occurs earlier than in other types of the condition. In the third type of systemic scleroderma, called systemic sclerosis sine scleroderma ("sine" means without in Latin), fibrosis affects one or more internal organs but not the skin.

Approximately 15 percent to 25 percent of people with features of systemic scleroderma also have signs and symptoms of another condition that affects connective tissue, such as polymyositis, dermatomyositis, rheumatoid arthritis, Sjögren syndrome, or systemic lupus erythematosus. The combination of systemic scleroderma with other connective tissue abnormalities is known as scleroderma overlap syndrome.

## 2. Frequency

The prevalence of systemic scleroderma is estimated to range from 50 to 300 cases per 1 million people. For reasons that are unknown, women are four times more likely to develop the condition than men.

## 3. Causes

Researchers have identified variations in several genes that may influence the risk of developing systemic sclerosis. The most commonly associated genes belong to a family of genes called the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders (such as viruses and bacteria). Each HLA gene has many different normal variations, allowing each person's immune system to react to a wide range of foreign proteins. Specific normal variations of several HLA genes seem to affect the risk of developing systemic sclerosis.

Normal variations in other genes related to the body's immune function, such as *IRF5* and *STAT4*, are also associated with an increased risk of developing systemic sclerosis. Variations in the *IRF5* gene are specifically associated with diffuse cutaneous systemic sclerosis, and a variation in the *STAT4* gene is associated with limited cutaneous systemic sclerosis. The *IRF5* and *STAT4* genes both play a role in initiating an immune response when the body detects a foreign invader (pathogen) such as a virus.

It is not known how variations in the associated genes contribute to the increased risk of systemic sclerosis. Variations in multiple genes may work together to increase the risk of developing the condition, and researchers are working to identify and confirm other genes associated with increased risk. In addition, a combination of genetic and environmental factors seems to play a role in developing systemic sclerosis.

### 3.1 Learn more about the genes associated with Systemic sclerosis

- *IRF5*
- *PTPN22*
- *STAT4*

## 4. Inheritance

Most cases of systemic sclerosis are sporadic, which means they occur in people with no history of the condition in their family. However, some people with systemic sclerosis have close relatives with other autoimmune disorders.

A small percentage of all cases of systemic sclerosis have been reported to run in families; however, the condition does not have a clear pattern of inheritance. Multiple genetic and environmental factors likely play a part in determining the risk of developing this condition. As a result, inheriting a genetic variation linked with systemic sclerosis does not mean that a person will develop the condition.

## 5. Other Names for This Condition

- familial progressive sclerosis
- progressive sclerosis
- systemic sclerosis

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