National Scleroderma Foundation

Dear Friend,

Thank you for your recent inquiry about scleroderma. Our goal is to provide the most up-to-date information available. In addition to providing resources designed to give you a better understanding of scleroderma, we also strive to provide strategies for coping with challenges scleroderma causes. As you begin to learn more about scleroderma, it is important to know that its symptoms and the severity of the disease vary greatly from person to person.

**Important Programs & Services:**

- **HOPE Line (800) 722-4673:** Connects individuals and families impacted by scleroderma with support, peer counseling, physician referrals and educational information.
- **Scleroderma Resource Center:** Our fact sheets cover a wide range of topics on symptom management and more – https://scleroderma.org/resources-center
- **Support Groups:** The National Scleroderma Foundation offers more than 50 support groups around the country, both virtual and in-person. Support groups are led by trained volunteers who are committed to creating a safe, welcoming and inclusive environment- https://scleroderma.org/scleroderma-support-groups/
- **Education:** Programs are offered by the national office (virtually) and its chapters throughout the country. Recorded education sessions are available for 24/7 viewing on the You Tube page and our Virtual University Page- https://scleroderma.org/virtual-university/
- **Join Us for the Annual National Scleroderma Conference:** Held each year in July, the conference includes panel discussions , workshops and other activities to answer your questions about the disease – https://scleroderma.org/national-conference

**We are Here for You**

We encourage you to contact the national office or any of our chapters if we can be of assistance. Much more about the National Scleroderma Foundation and the disease can be found at www.scleroderma.org. We believe that you'll find it a valuable resource.

The Scleroderma Foundation is a national support system dedicated to helping each other— and working toward the day when a cure is found. Please join us!

Sincerely yours,

Mary J. Wheatley, IOM, CAE
Chief Executive Officer

National Scleroderma Foundation

**Scleroderma Facts**

- Scleroderma is a rare disease that affects connective tissue and the vascular system by producing excessive collagen.
- The disease causes fibrosis in the skin (localized scleroderma) or internal organs (systemic sclerosis). The result can be disfigurement or disability, and it can be life-threatening.
- No one knows what causes scleroderma and there is no cure.
- Symptoms may include sensitivity to cold in extremities, thickening of the skin, shortness of breath, difficulty swallowing, joint stiffness and pain, and damage to internal organs.
- Scleroderma is considered part of the family of autoimmune disease that affect more than 50 million Americans and are the third leading cause of death in the United States.
- It's estimated that there are 300,000 cases of scleroderma in the United States.
- Women make up 80 percent of scleroderma cases, but men, young children and teens also get scleroderma.
- Scleroderma typically strikes between the ages of 35 and 55.
- In 95 percent of cases, scleroderma begins with Raynaud Phenomenon (hands and feet abnormally sensitive to cold).
- Federal funding for scleroderma research lags behind funding for other diseases of similar prevalence.
- Misdiagnosis is common. It can take three years or more for an individual to be diagnosed and to receive appropriate treatment.
- Medical professionals often lack familiarity with scleroderma and might not recognize that symptoms are directly associated with the disease.

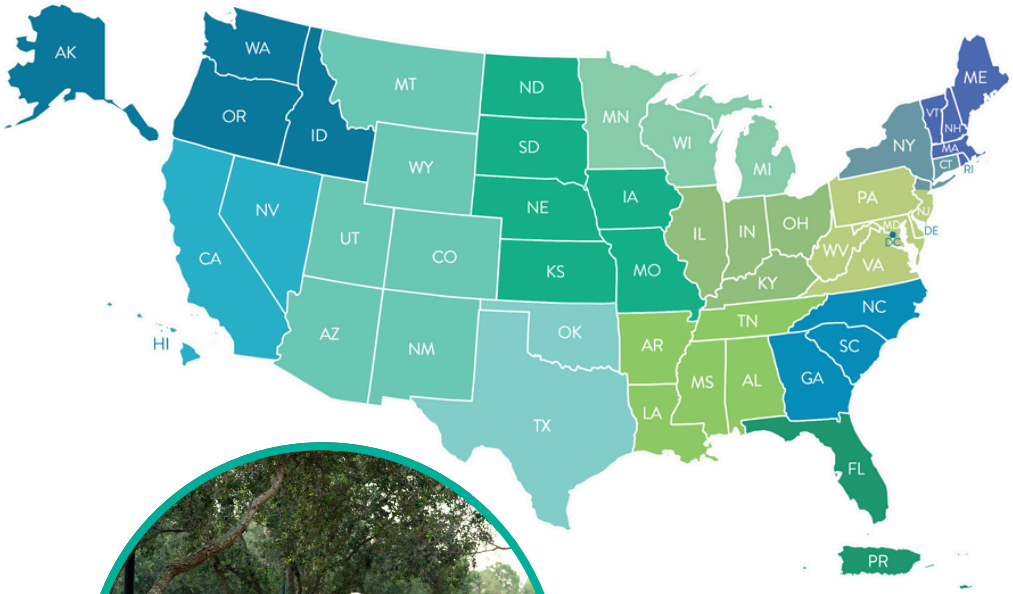
**What is Happening in Your Local Area?**

The National Scleroderma Foundation has a nationwide network of chapters and support groups that offers numerous opportunities that may be of interest to you. Throughout the country, our chapters and support groups provide educational programs to learn more about the disease; networking opportunities with others affected by scleroderma; events to raise awareness about scleroderma; and ways to raise money to fund some of the most promising scleroderma-related research. You'll find a list of chapters and support groups enclosed. If you live in an area served by a chapter or support group, we urge you to contact them to learn what's happening in your community.

National Scleroderma Foundation

# JOIN A LOCAL CHAPTER

The National Scleroderma Foundation has 13 chapters to serve you. To find your local chapter, visit **scleroderma.org/find-your-local-chapter/** or use the QR code below.




### Florida & Puerto Rico
Florida and Puerto Rico
**floridaprchapter@scleroderma.org**

### Heartland
Iowa, Kansas, Missouri Nebraska, North Dakota, South Dakota
**heartlandchapter@scleroderma.org**

### Lower Great Lakes
Illinois, Indiana, Kentucky, Ohio
**lglchapter@scleroderma.org**

### Mid-Atlantic
Delaware, District of Columbia, Maryland, New Jersey (Central & Southern), Pennsylvania, Virginia, West Virginia
**midatlanticchapter@scleroderma.org**

### New England
Maine, Massachusetts, New Hampshire, Rhode Island, Vermont
**nechapter@scleroderma.org**

### Pacific Northwest
Alaska, Idaho, Oregon, Washington
**pnwchapter@scleroderma.org**

### Rocky Mountain
Arizona, Colorado, Montana, New Mexico, Utah, Wyoming
**rmchapter@scleroderma.org**

### South
Alabama, Arkansas, Louisiana, Mississippi, Tennessee
**southchapter@scleroderma.org**

### Southeast
Georgia, North Carolina, South Carolina
**lglchapter@scleroderma.org**

### Texoma
Oklahoma, Texas
**texomachapter@scleroderma.org**

### Tri-State
Connecticut, New Jersey (Northern), New York
**lglchapter@scleroderma.org**

### Upper Great Lakes
Michigan, Minnesota, Wisconsin
**uglchapter@scleroderma.org**

### West Coast
California, Hawaii, Nevada
**heartlandchapter@scleroderma.org**

# Fact Sheet

National Scleroderma Foundation

## Scleroderma Overview and Causes

### Introduction

Scleroderma is an autoimmune disease which means that it is a condition in which the body's immune system attacks its own tissues. The normal role of the immune system is to provide protection from outside invaders such as bacteria and viruses. In autoimmune disorders, this ability to distinguish foreign from self is compromised. As immune cells attack the body's own tissue, inflammation and damage result. Scleroderma (the name means "hard skin") can vary a great deal in terms of severity. For some, it is a mild condition; for others it can be life-threatening. Although there are medications to slow down disease progression and help with symptoms, right now there is no cure for scleroderma.

### TYPES OF SCLERODERMA

There are two main forms of scleroderma: systemic (systemic sclerosis, SSc) that usually affects the internal organs or internal systems of the body as well as the skin, and localized that affects a local area of skin either in patches (morphea) or in a line down an arm or leg (linear scleroderma), or as a line down the forehead (scleroderma en coup de sabre). It is very unusual for localized scleroderma to develop into the systemic form.

### SYSTEMIC SCLEROSIS (SSc)

To make matters more confusing, there are two major types of systemic sclerosis or SSc: limited cutaneous SSc and diffuse cutaneous SSc. The difference between limited cutaneous and diffuse cutaneous SSc is the extent of skin involvement. In limited SSc, skin thickening only involves the hands and forearms, lower legs and feet. In diffuse cutaneous disease, the hands, forearms, upper arms, thighs, or trunk are affected. The face can be affected in both forms. The importance of making the distinction between limited and diffuse disease is that the extent of skin involvement tends to reflect the degree of internal organ involvement.

Systemic Sclerosis sine (without) skin thickening refers to the unusual occurrence (only about 5% of all cases) in which there is evidence of internal organ complications of SSc but no skin thickening.

Several clinical features occur in both limited and diffuse cutaneous SSc. Raynaud phenomenon, for example, occurs in both. Raynaud phenomenon is a condition in which the fingers turn pale or blue upon cold exposure, and then become ruddy or red upon warming up usually associated with a numb or tingling sensation in the fingers. These episodes are caused by a spasm of the small blood vessels in the fingers. As time goes on, these small blood vessels become damaged to the point that they may become totally blocked. This can lead to ulcerations of the fingertips. Raynaud phenomenon occurs in almost all (95%) SSc patients with either limited or diffuse disease, and painful finger ulcers can also be seen in both forms.

The esophagus is also affected in almost all SSc patients with loss of the usual movement. As a result, food can "hang up" in the esophagus, and stomach acid can reflux back up into the esophagus, causing heartburn.

Telangiectasias are small red spots that appear on the hands, arms, face, and/or trunk. These are tiny blood vessels in the skin that have widened. They are usually not dangerous in themselves, but are cosmetically unpleasing, particularly

if they occur on the face. Some people have telangiectasias in the esophagus, stomach, and bowel that can be a source of bleeding.

People with the diffuse form of SSc are at a greater risk of developing pulmonary fibrosis (scar tissue in the lungs that interferes with breathing, also called interstitial lung disease), kidney disease, and bowel disease.

All patients with SSc should have periodic pulmonary function tests to monitor for the development of pulmonary fibrosis. Symptoms of pulmonary disease include a dry cough and shortness of breath. However, in the early stages there may not be any symptoms at all.

Kidney involvement occurs more frequently in the diffuse than in the limited form of SSc, especially in the first five years after disease onset, and typically takes the form of a sudden increase in blood pressure. As is the case with usual high blood pressure, there are no symptoms at first. However, if undetected and untreated, this high blood pressure can damage the kidneys in a matter of weeks, which is why it is called scleroderma renal crisis. The key to management and prevention of permanent kidney damage is early detection and treatment of high blood pressure with a class of medications called ACE inhibitors.

The risk of extensive gut involvement, with slowing of the movement or motility of the stomach and bowel, is higher in those with diffuse rather than limited SSc. Symptoms include feeling bloated after eating, diarrhea, or alternating diarrhea and constipation.

Calcinosis refers to the presence of calcium deposits in, or just under, the skin. This takes the form of firm nodules or lumps that tend to occur on the fingers or forearms, but can occur anywhere on the body. These calcium deposits can sometimes break out to the skin surface and drain whitish material (described as having the consistency of toothpaste).

Pulmonary hypertension (PH) is high blood pressure in the blood vessels of the lungs. It is totally independent of the usual blood pressure that is taken in the arm. This tends to develop in patients with limited SSc after several years of disease. The most common symptom is shortness of breath on exertion. However, several tests need to be done to determine if PH is the real culprit. If the ultrasound of the heart, called an echocardiogram, is abnormal, then a right heart catheterization should be done to actually measure the pressure in the lung blood vessel (pulmonary artery) and to test for other abnormalities that can cause PH. Because there are now many medications to treat PH, the earlier it is detected and treated, the better the result will be.

## LOCALIZED SCLERODERMA

Localized scleroderma is almost always a purely skin condition, and is virtually never associated with the severe and potentially life threatening complications of SSc.

### Morphea

Morphea consists of patches of thickened skin that can vary from half an inch to six inches or more in diameter. Some people have only one or a few such patches, while others have multiple ones all over the body. The patches can be lighter or darker than the surrounding skin and thus tend to stand out. Also there is usually a loss of the fatty layer underneath the morphea spots. Morphea, as well as the other forms of localized scleroderma, does not affect internal organs.

### Linear scleroderma

Linear scleroderma consists of a line of thickened skin down an arm or leg on one side. The fatty layer under the skin can be lost, so the affected limb is thinner than the other one. In growing children, the affected arm or leg can be shorter than the other.

### Scleroderma en coup de sabre

Scleroderma en coup de sabre is a form of linear scleroderma in which the line of skin thickening occurs on the forehead or elsewhere on the face. In growing children, both linear scleroderma and en coup de sabre can result in distortion of the growing limb or lack of symmetry of both sides of the face.

## WHAT CAUSES SCLERODERMA?

The cause of scleroderma is unknown. However, we do understand a great deal about the biological processes involved. In localized

scleroderma, the underlying problem is the overproduction of collagen (scar tissue) in the involved areas of skin. In systemic sclerosis, there are three processes at work: blood vessel abnormalities, fibrosis (which is overproduction of collagen) and immune system dysfunction, or autoimmunity.

In systemic sclerosis, the small blood vessels are damaged and become narrowed. This is what is responsible for Raynaud phenomenon and the painful ulcers that can occur on the fingers. This vascular damage also occurs in the internal organs and is responsible for scleroderma renal crisis and PH.

The small arteries are normally capable of constricting (narrowing) or dilating (relaxing) to adjust blood flow to the needs of the body. For example, in very cold weather the blood vessels to the hands and feet narrow in order to maintain central body warmth. However, in SSc the blood vessel loses its normal method of relaxation, becoming prone to episodes of vasospasm (contraction of the muscle wall that closes the vessel). The vessels become overly sensitive to cold temperatures and other stimuli like emotional stress, which results in Raynaud attacks.

The thickened skin in scleroderma is caused by overproduction of collagen, which is the basic component of scar tissue. Abnormal accumulation of collagen is called fibrosis. Collagen is a normal part of skin and many organs. However, in scleroderma the balance of collagen formation and collagen breakdown is altered so that too much collagen builds up.

In localized scleroderma this process is confined to some areas of the skin. In SSc, excess collagen can cause fibrosis in the heart, lungs, and the muscles that line the GI tract.

Collagen is made by fibroblasts (a type of cell that is part of almost every tissue in the body) which can be provoked or activated to make more collagen. Under normal circumstances, the production of a scar is the last step in healing following an injury or an infection, for example, the production of a scar following a cut in the skin. Fibroblasts are activated by the immune system to produce collagen as part of the normal healing process. However, in SSc fibroblasts are activated for no apparent reason. The resulting scar causes tissue damage, decreased flexibility, and malfunction of the organ involved.

The third problem in SSc is the dysregulation of the immune system resulting in an immune attack on the body's own tissues. In patients with early disease, immune cells such as B cells, T cells and macrophages appear to be activated and poised to attack the patient's own tissues. This might be particularly prominent in the skin and the lungs. In addition, the body generates self-directed antibodies called autoantibodies. Some of these autoantibodies are found in several autoimmune diseases, while others are highly specific for scleroderma.

One way to detect activation of the immune system is to find antibodies (proteins made by immune cells, the bullets of our immune army) in the blood that targets the body's own tissue (autoantibodies). A very specific set of autoantibodies is found in scleroderma. These autoantibodies can be thought of as footprints of the scleroderma disease process because they are only made under very specific conditions. At this point, it is still not clear what role, if any, these autoantibodies play in damaging the blood vessels or stimulating collagen overproduction in SSc.

## WHO GETS SCLERODERMA?

There are many clues that define susceptibility to develop scleroderma. A genetic basis for the disease has been suggested by the fact that SSc is more common among patients whose family members have other autoimmune diseases (such as lupus). In rare cases, SSc runs in families, although for most patients there are no other family members affected. Scleroderma may affect some Native Americans and African Americans more severely than Caucasians.

Women are more likely to get SSc. Environmental factors may trigger the disease in the susceptible host. For example, silica exposure (as in coal mining or sand blasting) has been associated with systemic scleroderma and certain drugs can cause scleroderma-like reactions. Localized scleroderma is more common in children, whereas SSc is more common in adults. However, both can occur at any age.

## PUTTING IT ALL TOGETHER?

Research suggests that the susceptible host for scleroderma is someone with a genetic predisposition to injury from some external agent, such as a viral or bacterial infection or a substance in the environment. In localized scleroderma, the resulting damage is confined to the skin. In SSc, the process causes injury to blood vessels, or indirectly perturbs the blood vessels by activating the immune system. Fibroblasts are activated as part of the response to tissue injury. Interacting networks of immune inflammation and injury from inadequate blood supply drive the process, so it becomes chronic. Collagen made in excess interferes with normal organ function, sometimes leading to organ failure. In many cases, the process goes into remission after some years of activity. Research continues to assemble the pieces of the scleroderma puzzle to identify the susceptibility genes, to find the external triggers and cellular proteins driving fibrosis, and to interrupt the networks that perpetuate the disease.

Please note that this brochure is provided for educational purposes only. It is not intended to substitute for informed medical advice.

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The National Scleroderma Foundation thanks **Maureen Mayes, MD, MPH**, University of Texas/ Houston and **John Varga, MD**, Northwestern University, for their assistance in the preparation of this brochure.

# Fact Sheet

## Our Mission: Support, Education, and Research

National Scleroderma Foundation

### Lisa's Story

Lisa Hendricks was just seven years old when her parents noticed she was limping. Lisa couldn't lay her hands flat on a table. She did not complain of pain and learned to play the piano despite finger stiffness, but her parents knew something was wrong.

One day, Lisa suddenly could not stand up from a chair. Her parents rushed her to the doctor, who immediately recognized the symptoms of the linear and morphea forms of scleroderma. Two months later, Lisa's diagnosis was confirmed by specialists at the University of California, San Francisco. Her new life with scleroderma began.

Today, Lisa is a recent college graduate, elementary school teacher and church volunteer. She still plays the piano. She just does it all with scleroderma.

The National Scleroderma Foundation's resources, including research updates and support groups, have made a significant, positive impact on Lisa's life, she says.

"When you talk to other members of a National Scleroderma Foundation support group, you know they understand what you are talking about. It's very comforting," said Lisa, who belongs to the Foundation's Sacramento support group. "We get together once a month, but really, a lot of us are in constant contact. I finally found where I belong."

The National Scleroderma Foundation's mission is to advance medical research, promote disease awareness, and provide support and education to people with scleroderma, their families and support networks.

Awareness campaigns inform and educate individuals who have scleroderma, their families, medical professionals, and the public. The Foundation also funds innovative research to discover the cause, to understand the mechanism, and to overcome scleroderma forever.

### Support

Scleroderma is rare, affecting about 300,000 people in the U.S., mostly women. People newly diagnosed with scleroderma often feel alone. In the Foundation's local chapters and support groups, they find a safe and welcoming place to share, learn, cry and laugh. They can connect through online support groups through Inspire (www.inspire.com) and chat in a secure environment 24/7, or speak with each other on Facebook and Twitter.

### Education

Scleroderma can be difficult to diagnose. It mimics other diseases, has many forms, and may cause varied symptoms.

The Foundation's education programs help individuals affected by scleroderma, and their families, to better understand scleroderma. Education helps individuals manage and cope with their disease more effectively. Both chapters and support groups host regular scleroderma education events, including seminars with medical experts who discuss scleroderma treatments and research.

Here are other scleroderma education resources from the National Scleroderma Foundation:

- Our website, www.scleroderma.org, provides individuals and families with the latest health information, FAQs, events news, links to chapter and support groups, and opportunities to make a donation or serve as an advocate.
- The Scleroderma VOICE quarterly magazine, available to all members and supporters, includes inspiring personal stories, and news on research and advocacy.
- At the annual ***National Scleroderma Conference***, scleroderma clinical and research experts engage with individuals affected by the disease in informative workshops and panel discussions.
- The *eLetter*, a weekly online newsletter, shares current medical information and Foundation event updates.
- The Foundation's toll-free hotline, (800) 722-HOPE, has dedicated staff available to help individuals affected by scleroderma and their families to find resources and information near their home.

## Research

The National Scleroderma Foundation is a leading global funder of scleroderma-related research, allocating at least $1 million per year. New and established investigators annually apply for Foundation research grants that are evaluated by a Peer-Review Research Committee of scleroderma experts. Panelists use a model based on best practices established by the National Institutes of Health (NIH) to objectively critique and rank applications for funding. The goal is to foster new research and provide vital "seed" funding to allow new, younger investigators to advance their work, so they may go on to receive larger funding through the NIH and other sources.

Thanks to recent advances in research and treatment, people with scleroderma may now expect to live longer, more productive lives. The future offers more hope, yet research costs continue to climb. The Foundation's commitment to scleroderma research is unwavering. We are determined to achieve our ultimate goal of a cure.

## Advocacy

Advocacy blends each element of our mission. Volunteer advocates educate elected and appointed officials about scleroderma. They explain the critical need for public funding of scleroderma research, and the need to elevate the public profile of scleroderma and the needs of everyone whose life the disease affects. The Foundation's broad healthcare advocacy priorities include health insurance reform and expanding federal orphan drug research and development programs.

To support the Foundation's mission, volunteer with your local chapter, get involved in fundraising, or serve as an advocate, call (800) 722-HOPE (4673) or visit our website, www.scleroderma.org.

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