

## Scleroderma

Scleroderma is a progressive autoimmune disorder that can disable its victims. In people with scleroderma, the body's immune system is activated, which results in inflammation and overproduction of thick layers of collagen. This resulting scar tissue can form anywhere in the body, especially in the skin. Other organ systems affected by scleroderma include the kidneys, lungs, heart, and eyes.

The cause of scleroderma is unknown. It affects women four times more frequently than men, and its symptoms usually occur in people between the ages of 35 and 65. While scleroderma is usually encountered in adults, it does occur (although rarely) in children (Mayes MD 2000, 2003; Mayes MD et al 2003).

Managing scleroderma presents a challenge for physicians, and a multidisciplinary approach is usually best. Because it can affect such a variety of organ systems, patients with systemic scleroderma often need to rely on the guidance of physicians from several specialties. It is very important that people with scleroderma work with physicians who are familiar with their disease, including dermatologists and rheumatologists, among others.

Because of the challenges associated with conventional treatment of scleroderma, many people with scleroderma turn to nutrient therapy to reduce inflammation, interfere with the creation of scar tissue, and reduce symptoms. It is imperative that your physician know all the therapies you are using and that you be an active self-advocate, asking for specific information, educating yourself about your disease, and seeking support.

### WHAT IS SCLERODERMA?

Scleroderma is a chronic disease characterized by three main features:

1. Formation of scar tissue in the tissue (fibrosis)
2. Changes in small blood vessels
3. An autoimmune response

Although scleroderma primarily affects the skin, in more involved cases it also affects internal organ systems, including the lungs, kidneys, and heart. Scleroderma-like symptoms may also be part of a phenomenon called "mixed connective tissue disease." This diagnosis is reserved for patients who exhibit symptoms from several connective tissue diseases. These patients may have symptoms common in systemic lupus erythematosus, polymyositis, and rheumatoid arthritis.

Scleroderma is often broken down into two subtypes:

**Localized scleroderma.** Localized scleroderma is considered a mild form of scleroderma that affects the skin. Although it may affect muscles and joints, it does not affect organs. It is very rare for localized disease to become systemic; if it does become systemic, the initial diagnosis was likely mistaken. In a limited number of patients, localized scleroderma may contribute to pulmonary hypertension after a decade or more, along with biliary cirrhosis. There are two common forms of localized scleroderma:

- *Linear scleroderma.* Linear scleroderma is characterized by hardened skin affecting the underlying tissues (muscles, bones). It usually occurs on the arms, legs, and forehead on one side of the body and is more common in children.
- *Morphea.* Morphea is characterized by patches of yellowish or ivory-colored rigid, dry skin that become hard, slightly depressed oval plaques. Morphea usually occurs on the trunk, although it may be widespread (generalized morphea).

**Systemic scleroderma.** Systemic scleroderma occurs throughout the body, affecting internal organs. Treatment for these individual complications is usually specific to each organ system. Systemic scleroderma can affect the connective tissue of the lung, kidney, heart, and other organs, as well as blood vessels, muscles, and joints. The skin thickening is symmetrical on both sides of the body, usually beginning on the fingertips and moving up the arms. Legs and thighs also are affected. Systemic scleroderma has several complications:

- About 90 percent of patients experience problems in the esophagus and digestive tract. The lower two thirds of the esophagus sometimes develops a tough inflexibility. The associated dysfunction of the lower esophageal sphincter may lead to gastroesophageal reflux (Cotran RS 1999).
- About 66 percent of patients experience kidney abnormalities. The kidneys may thicken as a result of fibrous collagen

deposits forming in them (Cotran RS 1999).

- More than half of patients experience lung problems, including pulmonary hypertension and scarring within the lungs (interstitial fibrosis) (Cotran RS 1999).
- About one third of patients experience pericarditis (inflammation of the covering of the heart) or the deposition of scar tissue in the heart muscle (myocardial fibrosis), as well as thickening of the intramyocardial arterioles (small arteries within the middle portion of the heart (Cotran RS 1999).

In addition, a lesser form of scleroderma known by the acronym CREST may exist. CREST may occur alone or in combination with any autoimmune disease. There is no way to predict whether or when it will progress to diffuse scleroderma (Cotran RS 1999).

CREST stands for the following conditions, occurring together:

- **Calcinosis**, the buildup of calcium deposits in the tissues (It may occur under the skin of the fingers, arms, feet, and knees, causing pain and infection if the calcium deposits pierce the surface of the skin.)
- **Raynaud's phenomenon**, characterized by localized episodes of vasoconstriction in the fingers and extremities
- **Esophageal dysmotility**, a malfunction in the ability to move the esophagus spontaneously
- **Sclerodactyly**, hardening of skin on the fingers
- **Telangiectasia**, an abnormal dilatation of capillaries and small arteries that often forms an angioma (a swelling or tumor)

## **SYMPTOMS AND DIAGNOSIS OF SCLERODERMA**

Scleroderma is characterized by the overproduction and accumulation of collagen, the most abundant form of protein in the skin. The disease process involves activation of the immune system, along with vascular endothelial cell activation. Because of the vascular injury, scleroderma is often preceded by Raynaud's phenomenon (in about 95 percent of cases). During Raynaud's, the small arteries in the fingers constrict, causing abnormal blood flow. As a result, the fingers turn white and become numb and cold. The majority of patients who are eventually diagnosed with scleroderma will report first suffering from Raynaud's. In most cases, the presence of Raynaud's and skin changes are enough to diagnose scleroderma.

There is no single test that can diagnose scleroderma. Rather, the diagnosis is based on symptoms and trademark characteristics of the disease. The following symptoms (with approximate percentages, when available, of patients in whom those organ systems are affected) may constitute scleroderma:

- Thickening of the skin (90 percent)
- Swelling of the hands and feet
- Pain and stiffness of the joints (30 to 50 percent)
- Joint contractures (fingers curling up, difficulty of movement)
- Raynaud's phenomenon (70 to 90 percent)
- Gastrointestinal tract problems (90 percent)
- Sjögren's syndrome (dry mucus membranes)
- Facial problems (tightening of skin, limiting mobility of mouth and eyelids; temporomandibular joint syndrome, or pain in the joint of the jaw)
- Dental problems (change in bite; loosening of teeth because of collagen deposition, increasing the size of the ligaments around the teeth; tooth sensitivity)
- Fatigue attributable to fibrosis in the heart muscle
- Generalized aching and weakness caused by fibrosis in the muscles (20 percent)
- Kidney, heart, and lung involvement

In addition, a variety of laboratory studies may help physicians pinpoint their diagnosis. People with scleroderma may have an elevated erythrocyte sedimentation rate and suffer from anemia. Additional blood tests may reveal abnormalities in the gastrointestinal tract or kidneys. In addition, certain antibodies (e.g., antitopoisomerase 1, antinuclear, and anticentromere) may be present in the blood. Testing for these antibodies often helps physicians differentiate between localized scleroderma and systemic scleroderma and helps diagnose CREST.

Many patients describe their path toward diagnosis as one of the most difficult periods of the illness, in part because the difficulty of the diagnosis can lead both physicians and patients to label the symptoms as psychosomatic, that is, caused by the mind.

## **CONVENTIONAL TREATMENT OF SCLERODERMA**

Scleroderma therapy is guided by the specific needs of the patient; not all patients have the same symptoms. In general, conditions that may have been caused by scleroderma, such as heart or kidney failure, will be managed in much the same way as in any other patient. Conventional treatments, organized according to symptoms, may be summarized briefly as follows:

**Treatments for general symptoms.** D-penicillamine has been the treatment of choice for many years because it was thought to interfere with the deposition of collagen. However, recent studies found it ineffective in softening skin or preventing organ involvement (Clements PJ et al 2004; Furst DE 2000, 2001). High-dose D-penicillamine, up to 1000 mg/day, is associated with significant side effects.

Gamma-interferon may inhibit the proliferation of fibroblasts, the cells that produce collagen. Steroids such as prednisone are frequently used for their anti-inflammatory action, which includes alteration of white blood cell function. However, steroids have significant side effects, including loss of bone density and weight gain. Steroids also suppress the body's natural ability to handle stress and are typically used for a short term.

Other treatments, including some with significant side effects, are being investigated for more serious forms of the disease. Immunosuppressive drugs that have been used for cancer chemotherapy and organ transplants may reduce the autoimmune response. These drugs kill cells that rapidly proliferate, which includes immune cells. High-dose cyclophosphamide is the drug of choice; azathioprine has fewer side effects but is less potent. Bone marrow transplants can be used in conjunction with these drugs. Some physicians, however, argue that this is unnecessary since the stem cells that will produce new white blood cells will not be affected by the cytotoxic drugs.

Cyclosporin, which blocks the activation and stimulation of immune T-cells, may also limit damage to skin. However, cyclosporin causes kidney toxicity and does not affect pulmonary or cardiac complications. Thus it has a limited place in the treatment of systemic scleroderma.

Photopheresis is a procedure similar to dialysis and may help relieve some symptoms. During photopheresis, the patient's blood is removed, the white blood cells are treated to quell the autoimmune activity, and then the blood is returned to the body. Research has been done using this treatment method for a variety of diseases, with encouraging results for scleroderma patients (Zic JA et al 1999). It is also believed that photopheresis, if used as a long-term treatment, is efficacious if started within the first two years following the onset of the disease, as long as there is no visceral involvement (Krasagakis K et al 1998).

Biomechanical stimulation has been shown in one small study to improve joint mobility and reduce edema (Klyszcz T et al 1999).

A new, experimental drug, halofuginone, is a collagen synthesis inhibitor that has shown promise in animal models of scleroderma. It was granted orphan drug status by the Food and Drug Administration (FDA) in 2000. Orphan drug status is designed to encourage clinical research into a particular drug even though it has not been formally approved by the FDA. Halofuginone is produced by Collgard Biopharmaceuticals, Ltd.

**Treatments for skin disease and musculoskeletal and joint pain.** Swelling during the early stage of skin thickening may be controlled with steroids, but the side effects must be considered. Some physicians feel that colchicine can reduce skin thickening if used early. Calcinosis can be treated with low-dose warfarin, colchicine, or probenecid, but may not be treated at all because it causes no clinical problems. Musculoskeletal and joint pain are commonly treated with nonsteroidal anti-inflammatory drugs or with steroids. Topical pain relievers such as salicylate or capsaicin creams may be used.

Some centers specializing in dermatology offer PUVA therapy, in which repeated sessions of exposure to ultraviolet light are coupled with psoralen, a drug that makes the skin more sensitive to light. This technique has been found to soften skin and reduce the diameter of plaques or even cure them. It is considered effective for localized disease.

A "wellness lifestyle" involves the use of thoughts and activities that will benefit the mind and body. In addition to conventional treatments, physical therapy and regular, gentle stretching and exercise are critical to maintain range of motion. Exercise also keeps the heart, lungs, and bones strong and helps many people relieve stress (a trigger for autoimmune diseases), cope with pain, and achieve a feeling of well-being. Other pain-relief and stress-relief strategies include getting enough sleep and using heat treatments (heating pads, electric blankets, or a 20-minute warm bath every night before bed).

Xerosis, or severe dry skin, is a common problem and can be treated with creams such as Eucerin and Vanicream or with bag balm, which has antiseptic properties. Skin should be kept moist and protected from cold, injury, or infection by clothing, especially gloves. Avoid strong detergents and soaps and use a humidifier.

**Treatments for gastrointestinal symptoms.** Metoclopramide and cisapride can aid esophageal contraction and stomach emptying. Acid reflux (heartburn) can be managed by diet; sleeping on the left side; antacids; and proton pump inhibitors, including Prilosec® (omeprazole), Prevacid® (lansoprazole), Nexium® (esomeprazole), and others.

A balanced diet that includes nutritional supplements is considered vital to maintain body weight and health. Some literature advises avoiding caffeine, refined sugars, and food additives that have been implicated as carcinogens (e.g., sodium nitrite) or have

side effects (e.g., caffeine, olestra, and MSG).

**Treatments for pulmonary symptoms.** Fibrosis, or interstitial disease, of the lungs can be treated with steroids or immunosuppressants such as cyclophosphamide. Pulmonary hypertension will be treated with drugs that dilate the vessels, such as calcium channel blockers or epoprostenol.

Treatments for renal symptoms. Kidney problems are thought to result not only from fibrosis but also from overall hypertension or high blood pressure. It is critical, then, to control blood pressure carefully using angiotensin-converting enzyme inhibitors.

### ***For More Information***

The following chapters may also be of interest:

- GERD
- Kidney Health
- Inflammation
- Chronic Pain
- Raynaud's Phenomenon

## **NUTRITIONAL THERAPY**

**Dimethylsulfoxide.** Dimethylsulfoxide (DMSO) is a solvent that readily penetrates the skin and is typically used to "carry" another substance. In scleroderma, it is used to soften the skin. Clinical studies with DMSO have yielded cautiously optimistic results. In several studies, it has been shown to relieve skin symptoms when applied directly to hand ulcers (Engel MF 1972). However, a significant number of patients (up to 25 percent) cannot withstand the skin toxicity that is sometimes associated with high-concentration DMSO and must discontinue treatment (Williams HJ et al 1985). Because of this risk, DMSO treatment should be highly individualized for maximum benefits (Scherbel AL 1983).

**Gamma-linolenic acid (GLA).** GLA is an essential fatty acid that is converted to the precursor for prostaglandin E1, a potent anti-inflammatory hormone-like fatty acid. Raising prostaglandin formation in scleroderma patients could be useful (Horrobin DF 1984, 1986). GLA has also been shown to reduce autoimmune dysfunction in rheumatoid arthritis patients. GLA can be obtained from evening primrose oil, borage oil, or black currant seed oil.

**Docosahexaenoic acid and eicosapentaenoic acid.** Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are essential long-chain fatty acids with anti-inflammatory effects and are found in flaxseed oil and fish oil. Fish oils have been shown to help relieve Raynaud's, which is closely related to scleroderma (DiGiacomo RA et al 1989). Together, EPA and DHA suppress arachidonic acid, reducing inflammation and supporting healthy cell membranes.

**Antioxidants.** Free-radical damage (oxidation) has long been suspected as a major mechanism of autoimmune disease. Low-density lipoproteins (LDLs) from patients with scleroderma are more susceptible to oxidation than those from healthy people (Bruckdorfer KR et al 1995) and patients with primary Raynaud's. Micronutrient antioxidant status in patients with primary Raynaud's and scleroderma revealed reduced vitamin C and selenium, especially in those patients with diffuse scleroderma (Herrick AL et al 1996).

One study argued that autoimmune diseases are caused by a relative deficiency of vitamin E. This deficiency damages the membranes of lysosomes (cellular organelles that digest waste), allowing the escape of hydrolytic enzymes that denature (destroy) proteins to the point that they are no longer recognizable by the immune system and are attacked as if they were foreign particles. This process resembles the enhanced lipid peroxidation seen in patients with scleroderma, which is four times higher than a normal person's. In one study, after supplementation with vitamin E, there was a decrease in the indicator of lipid peroxidation by two-thirds (Sommerburg O et al 1996). In a case study, vitamin E was administered to a 33-year-old woman with scleroderma who had suffered from several miscarriages. After five months of tocopherol nicotinate treatment, she conceived and later delivered a healthy baby (Harada M et al 2005).

The antioxidant N-acetylcysteine (NAC) has recently shown promise in reducing the frequency of Raynaud's phenomenon in people with scleroderma. In one study, patients received NAC for two years through intravenous infusion. Imaging studies revealed that patients who underwent treatment with NAC had increased blood flow to their hands. The therapy also found negligible side effects, leading researchers to suggest that NAC was a successful vasodilator (Salsano F et al 2005). Another study examined the role of NAC in reducing pulmonary complications of scleroderma. In this study, macrophages taken from the lungs of patients with scleroderma were studied for their expression of inducible nitric oxide synthase, which causes vasoconstriction, and peroxynitrite, a pro-oxidant by-product of nitric oxide. Researchers found that concentrations of both chemicals were higher in the lungs of people

with scleroderma and that NAC therapy reduced the expression of peroxynitrite, which may help reduce oxidant damage and thus fibrosis in the lungs (Failli P et al 2002).

**Melatonin.** Melatonin is a pineal hormone that is usually associated with sleep. Recent studies have revealed, however, that melatonin plays a varied role in the body. A recent study looked at the effect of concurrent melatonin and vitamin E treatment to reduce vascular damage among people with scleroderma. Researchers found that none of their test participants with stable or responding disease (all of them) experienced disease progression after five months of treatment (Todisco M 2006).

**Centella asiatica.** Centella asiatica is an herb found in Madagascar and East Africa. An extract of Centella asiatica has been used for wound healing and venous insufficiency. Various studies have shown active components in Centella to be effective in scar management by aiding in the production of collagen Type I (Bonte F et al 1994; Maquart FX et al 1999; Widgerow AD et al 2000). Centella, under the name Madecassol, has been used on localized and systemic scleroderma with positive results. A six-month trial was carried out with 54 patients ranging from 15 to 70 years of age. A tablet, powder, or ointment combination was used on the patients. In 31 of the systemic scleroderma patients using 30 mg daily, indurative lesions, hyperpigmentation, or vascular trophic disorder decreased, and their general condition improved. Lack of disease progression corresponded with a subjective improvement in 10 patients. The researchers concluded that Madecassol works for oral and topical use in combined treatment of systemic scleroderma (Guseva NG et al 1998). Centella, under the name Gotu Kola, is available in capsule or liquid form from several manufacturers.

## LIFE EXTENSION FOUNDATION RECOMMENDATIONS

Scleroderma can be a debilitating disease that dramatically affects quality of life and can be life threatening. It is essential that people with scleroderma seek out specialists who have experience dealing with the disease. They may include dermatologists, gastroenterologists, and rheumatologists, among others. For additional information on specific complications, such as cardiac or kidney complications, please see the relevant chapter in this book.

The following steps may help relieve the symptoms of scleroderma:

1. Incorporate physical or occupational therapy and regular exercise into your daily routine.
2. Manage stress and pain and practice relaxation techniques. Consult a counselor if you feel it would be helpful or if you feel overwhelmed, helpless, or depressed.
3. If Raynaud's is present, aggressively control it (see the Raynaud's Syndrome chapter).
4. Protect your skin by keeping it moist and covered, and use your hands wisely.

In addition, the following nutrients may help reduce the severity of symptoms:

- **DMSO**—concentrations as tolerated, applied to affected areas for 30 minutes daily, or 50 percent DMSO bath for hand immersion, with gradually increased duration and frequency, depending on tolerance
- **GLA**—900 to 1800 milligrams (mg) daily
- **DHA/EPA**—1400 mg EPA and 1000 mg DHA daily
- **NAC**—600 mg daily
- **Melatonin**—300 micrograms (mcg) – 3 mg at bedtime (discontinue if symptoms or signs worsen)
- **Centella asiatica** (Gotu Kola)—300 mg daily, or topical Centella ointment twice daily
- **Vitamin E**—400 international units (IU) daily (with at least 200 mg gamma tocopherol)
- **Vitamin C**—2500 mg daily
- **Beta-carotene**—5000 IU daily
- **Selenium**—200 mcg daily

## PRODUCT AVAILABILITY

All the nutrients and supplements discussed in this section are available through the Life Extension Foundation Buyers Club, Inc. For ordering information, call anytime toll-free 1-800-544-4440, or visit us online at [www.LifeExtension.com](http://www.LifeExtension.com).

The blood tests discussed in this section are available through Life Extension National Diagnostics, Inc. For ordering information, call anytime toll-free 1-800-208-3444, or visit us online at [www.LifeExtension.com](http://www.LifeExtension.com).

## SCLERODERMA SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of

the nutrients suggested in this protocol may have adverse effects. These include:

### **Beta-Carotene**

- Do not take beta-carotene if you smoke. Daily intake of 20 milligrams or more has been associated with a higher incidence of lung cancer in smokers.
- Taking 30 milligrams or more daily for prolonged periods can cause carotenoderma, a yellowish skin discoloration (carotenoderma can be distinguished from jaundice because the whites of the eyes are not discolored in carotenoderma).

### **EPA/DHA**

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

### **GLA**

- Consult your doctor before taking GLA if you take warfarin (Coumadin). Taking GLA with warfarin may increase the risk of bleeding.
- Discontinue using GLA 2 weeks before any surgical procedure.
- GLA can cause gastrointestinal symptoms such as nausea and diarrhea.

### **Melatonin**

- Do not take melatonin if you are depressed.
- Do not take high doses of melatonin if you are trying to conceive. High doses of melatonin have been shown to inhibit ovulation.
- Melatonin can cause morning grogginess, a feeling of having a hangover or a “heavy head,” or gastrointestinal symptoms such as nausea and diarrhea.

### **NAC**

- NAC clearance is reduced in people who have chronic liver disease.
- Do not take NAC if you have a history of kidney stones (particularly cystine stones).
- NAC can produce a false-positive result in the nitroprusside test for ketone bodies used to detect diabetes.
- Consult your doctor before taking NAC if you have a history of peptic ulcer disease. Mucolytic agents may disrupt the gastric mucosal barrier.
- NAC can cause headache (especially when used along with nitrates) and gastrointestinal symptoms such as nausea and diarrhea.

### **Selenium**

- High doses of selenium (1000 micrograms or more daily) for prolonged periods may cause adverse reactions.
- High doses of selenium taken for prolonged periods may cause chronic selenium poisoning. Symptoms include loss of hair and nails or brittle hair and nails.
- Selenium can cause rash, breath that smells like garlic, fatigue, irritability, and nausea and vomiting.

### **Vitamin C**

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute).
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

### **Vitamin E**

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).

- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.
- Discontinue using vitamin E 1 month before any surgical procedure.

For more information see the Safety Appendix

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