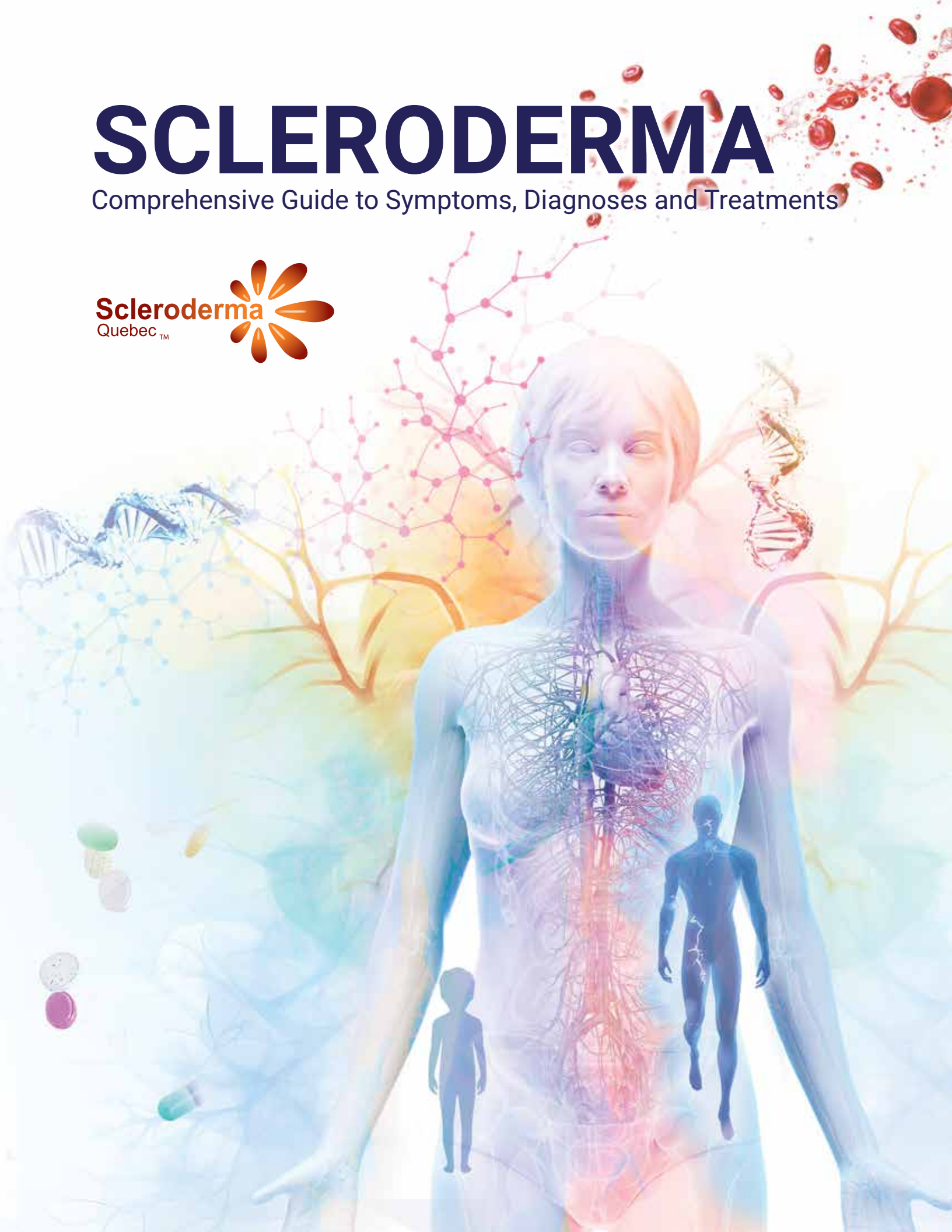
SCLERODERMA

Comprehensive Guide to Symptoms, Diagnoses and Treatments

Scleroderma Quebec™



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The SOCIÉTÉ DE LA SCLÉROSE SYSTÉMIQUE (SCLÉRODERMIE) DU QUÉBEC INC., also called SCLERODERMA QUEBEC was founded in 1989 by Mr. Gilles Houlé and his wife, Suzanne Houlé. It was registered as a charity (no. 89808 9693 RR 0001) with the federal Government in 1992.

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Scleroderma Quebec's Mission

The ultimate objective: defeat the disease. Working on several fronts, the organization has made its mission to:

- Help scleroderma patients by providing medical or moral support;
- Raise funds for scleroderma research;
- Develop information tools for the general public and stakeholders in the medical community.

Scleroderma Quebec™

Message from the President and the Outgoing President

Armand Des Rosiers
President
Scleroderma Quebec

Gaétan Baril
Outgoing President
Scleroderma Quebec

Dear Readers,

It is with immense pride that we present to you "***Scleroderma: A Comprehensive Guide to Symptoms, Diagnoses, and Treatments.***" This book is intended to be an essential resource for people living with scleroderma, their families, and healthcare professionals.

This book was designed to achieve a dual objective. Firstly, it aims to fill a gap in the information available about scleroderma, a still too little-known and very complex disease. Each person is affected differently, which makes understanding and treating this condition particularly challenging. Each chapter provides detailed and up-to-date knowledge on symptoms, diagnosis, and available treatments, allowing patients and their loved ones to better understand the disease and make informed decisions in collaboration with their healthcare providers.

Secondly, this book is intended to be a valuable tool to support patients in their medical and personal journeys. It gathers contributions from numerous experts and healthcare professionals, highlighting different therapeutic approaches and best practices to improve patients' quality of life. By providing clear and precise information, we hope to strengthen the partnership between patients and their caregivers, thereby promoting optimal disease management.

We wish to express our profound gratitude to all those who contributed to the creation of this book. Their dedication and expertise have made it possible to create an invaluable resource for the scleroderma community. This book is the result of a collective effort and stands as a testament to Scleroderma Quebec's ongoing commitment to supporting and informing all those affected by this disease.

We hope that this book will become an indispensable reference and that it will help many people navigate the challenges posed by scleroderma with greater confidence and serenity.

Sincerely,

Gaétan Baril, Armand Des Rosiers

SCLERODERMA

Preface

Jean-Luc Senécal
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Professor of Medicine, Faculty of Medicine, University of Montreal

When someone is diagnosed with scleroderma, he/she is often overwhelmed and deeply concerned by the diagnosis of "the disease that mummifies." What are the symptoms? What form of scleroderma do I have? What are the treatments? What can I do? Where can I find more information and answers?

This book aims to answer these questions, to enrich the understanding of scleroderma, and thereby facilitate a more productive and informed relationship between those affected and their treating physicians.

It is a remarkable collective work, an exhaustive synthesis of great interest, while remaining accessible due to its readability.

The book promises to be a goldmine, an inexhaustible source of information that those affected by scleroderma, their family members, healthcare professionals, and anyone in the media or the general public who is interested can read and consult to get the facts straight on one or another of the many aspects of the disease.

This book is, therefore, a remarkable source of information and hope for patients and all those touched by scleroderma, either directly or indirectly.

As one reads this book, it becomes clear that an exceptional, sustained, and enduring medical and public interest in scleroderma has developed in Quebec.

This book embodies that interest. It attests to the multitude of healthcare professionals, including not only doctors but also nurses, pharmacists, psychoeducators, psychologists, and other volunteer authors who are often personally involved in the care of scleroderma patients. The testimony of this public and collective interest in scleroderma in Quebec deserves to resonate beyond our borders.

Finally, it is important to highlight the leadership of Scleroderma Quebec and its board of directors and to thank its general management and successive presidents who have patiently gathered the information foundational to this work and made its realization possible.

THANK YOU!

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SCLERODERMA

Comprehensive Guide to Symptoms, Diagnoses, and Treatments

Notice to readers

This book, ***Scleroderma: A Comprehensive Guide to Symptoms, Diagnoses, and Treatments***, was designed to provide general information about scleroderma. All educational materials in this book have been written by doctors specializing in scleroderma or by professionals from various fields, including pharmacists, a nutritionist, a psychoeducator, and other experts. Although this book is an excellent source of information, it in no way replaces the advice, diagnosis, or treatment of a qualified healthcare professional.

The information contained in this book is intended for educational and informational purposes only. It should not be used to diagnose or treat a disease without consulting a qualified healthcare professional.

We strongly recommend that you consult your doctor or another healthcare professional before undertaking any action based on the information contained in this book. Your doctor is best positioned to provide advice tailored to your personal situation and to guide you towards appropriate treatments.

Scleroderma Quebec disclaims any responsibility for actions taken based on the information provided in this book without prior consultation with a healthcare professional.

HOW SCLERODERMA CAN AFFECT THE HUMAN BODY

The symptoms of scleroderma vary greatly from person to person, so that patients will not necessarily develop all the complications of the disease.

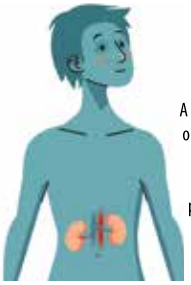
The symptoms of the disease may be visible, as is the case when the skin is affected, or the symptoms may be invisible, as when internal organs are affected.

SYMPTOMS AND MANIFESTATIONS OF SCLERODERMA

SKIN HARDENING
Thickening and loss of elasticity of the skin on different parts of the body. Hence the name «scleroderma», which means hard skin.

PULMONARY FIBROSIS
A potentially serious complication where normal lung tissue is gradually replaced by scarred fibrotic tissue, making it difficult to breathe and deliver needed oxygen to the body.

Pulmonary fibrosis causes shortness of breath and also sometimes a dry cough.



RENAL CRISIS
A renal crisis, which is due to an acute obstruction of arterioles and capillaries in the kidneys, leads to a sudden and sharp increase in arterial blood pressure. The symptoms are those of a hypertensive crisis: new and severe headaches, marked shortness of breath (left heart failure), and even epileptic seizures (convulsions). This is a very serious complication which requires urgent medical attention. Often during a scleroderma renal crisis, the kidneys stop functioning and dialysis (filtering the blood to avoid uremia) is then needed.

BLOOD VESSELS
The narrowing of the arteries, small blood vessels, and capillaries, can lead to many complications, including the development of pulmonary arterial hypertension (PAH), digital ulcers, and other conditions.

PULMONARY ARTERIAL HYPERTENSION (PAH)
Increased pressure in the pulmonary arteries due to the narrowing of small arteries in the lungs. Blood flow to the lungs is significantly restricted, making the heart work harder to pump blood through the lungs.

As arterial blood pressure rises in the pulmonary arteries, small pulmonary vessels slowly become clogged (a process which may take several years). This occurs through fibrosis of the small vessels, eventually leading to thrombosis, and the blood can no longer reach all parts of the lungs. Thus, it becomes more difficult for the lungs to supply enough oxygen to the body.

Sustained high blood pressure in the arteries of the lungs puts a strain on the heart, making it more difficult to circulate the blood through the lungs. Over time, this can eventually lead to congestive heart failure, particularly the right side, what is referred to as right heart failure (RHF). Right heart failure is indicative of significant PAH and is a serious complication of scleroderma.

PAH results in one or more of the following symptoms:

- Shortness of breath on exertion and at rest
- Palpitations (heart rhythm disorder)
- Fatigue
- Chest pain
- Dizziness
- Temporary loss of consciousness (syncope)
- Swelling of the ankles and legs

SCLERODERMA FACES
Hollow eyes, pinched nose, thin pursed lips, mask-like face, small puckered mouth (microstomia), and peri-oral folds.

Thinning lips and facial muscle atrophy can make the teeth appear more prominent.

EYES
Dry eyes caused by a decrease in tear production.

TELANGIECTASIA
Small dilated capillaries visible on the face and hands, sometimes referred to as «spider veins».

RAYNAUD'S PHENOMENON
Raynaud's is present in up to 95% of people with scleroderma. Whitening of fingers and/or toes triggered by cold or severe stress. The whiteness phase can be followed by a blue phase and then a red phase.

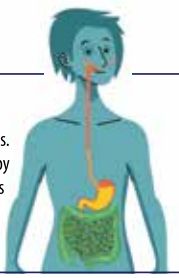
SCLERODACTYLY
The skin of the fingers, which have become infiltrated with collagen (fibrosis), may look full and sausage-like. Functional loss or decreased range of motion.

CALCINOSIS
Calcium deposits under the skin that may require antibiotics to cure occasional infections and sometimes surgery to drain calcium deposits and relieve pain.

DIGITAL ULCERS
Ulcers occur on the fingertips or on the top of the fingers. They are painful and difficult to heal.

In the most severe cases, it can lead to necrosis and amputation may be needed.

SKIN PIGMENTATION
Dark or pale spots occurring in one-third of patients.



DIGESTIVE SYSTEM
Gastrointestinal disorders affect the vast majority of patients. Gastric reflux is a common symptom that manifests itself by a burning sensation radiating up to the throat after meals and may cause inflammation of the lining of the esophagus (esophagitis reflux) if left untreated.

MUSCLE AND JOINT PAINS
Joint pain is common. It is caused by inflammation of the joints and tendons, which quite often leads to joint swelling and stiffness that can become quite debilitating.

Muscular pain (myalgia) can be intermittent or continuous. It can also be associated with muscle weakness (myositis). Symptoms include difficulty in climbing stairs, lifting objects and getting up, and also difficulty swallowing.

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I UNDERSTANDING SCLERODERMA

What Is Scleroderma?

Dr. Alena Ikic, MD, FRCPC
Rheumatologist, CHU
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Scleroderma, or systemic sclerosis, is a relatively misunderstood chronic disease affecting about one in 5,000 people. In Quebec, it is estimated that several thousand people suffer from scleroderma.

Disease onset usually occurs in the fourth decade of life and is five time more prevalent in women than men. Scleroderma is one of the so-called "autoimmune" diseases in which the body's antibodies attack its own cells.

Scleroderma is not a contagious disease. The disease is characterized by the overproduction of collagen and damage to small blood vessels that causes excessive scarring in multiple internal organs. The overproduction of collagen causes a hardening (fibrosis) of the skin and, sometimes, internal organs, such as the lungs, heart, kidneys and the gastrointestinal tract.

There are two types of scleroderma:

- Limited scleroderma (or CREST syndrome, which includes Calcinosis, Raynaud's phenomenon, Esophageal dysmotility, Sclerodactyly and Telangiectasia);
- Diffuse scleroderma.

The distinction between these two types of scleroderma is based on the pattern and severity of skin and internal organs involvement, which is more extensive and have a more rapid progression in the diffuse type. The skin, digestive system, heart, lungs and kidneys are the most commonly affected organs that can be negatively impacted by the potentially serious complications of scleroderma. At first, these complications may go unnoticed.

There is still no cure for scleroderma. However, medical treatments currently exist for most of the complications associated with scleroderma, hence the clinical importance of screening for patients, even in the absence of symptoms.

To learn more about the most common complications of scleroderma, we encourage you to familiarize yourself with the warning signs that you and your loved ones should regularly be watching for.

The Skin

An abnormal and temporary decrease in the size (calibre) of blood vessels In fingers and/or toes triggered by exposure to cold or emotional stress is referred to as Raynaud's phenomenon. The narrowing of blood vessels can cause a decrease in blood flow that manifests itself as a blanching of fingers and/or toes which may be associated with numbness. Raynaud's phenomenon is present in over 95% of patients with scleroderma, but can also be seen outside of this disease. Treatments and medications are currently available for Raynaud, when indicated.

It is to be noted that the prolonged narrowing (constriction) of blood vessels can cause painful ulcers that may be very slow or difficult to heal because of poor circulation, and in rare cases might even require amputation.

Thus, it is recommended to inform your doctor if you notice :

* An increase in the severity or frequency of Raynaud's symptoms.
* The presence of a wound at the extremity (pulp) of a finger and/or toe which is slow to heal or is accompanied by a discharge.

To limit this complication, we suggest that you examine your hands and feet regularly (especially the pulp), in addition to:

- Avoid trauma to the fingers and toes;
- Wear two pairs of mittens, socks, and warm boots when it is cold;
- Always cover your head outside during the cold season;
- Use lukewarm water in your daily tasks;
- Stop smoking;
- Apply moisturizing cream on dry skin.

Calcinosis is characterized by calcium deposits in the skin, which occur just below the skin surface in the form of hard lumps or nodules. It is found mainly around the pulp of the fingers or the joints.

It is recommended to inform your doctor if you notice:

* An ulcer or discharge of pus at the site of the calcinosis.

The Digestive System

Involvement of the digestive system, particularly the esophagus (swallowing tube), occur in nearly all SSc patients.

Gastroesophageal reflux is acid regurgitation in the esophagus that manifests itself by a burning sensation radiating up to the throat after meals. If left untreated, it may be further complicated by an inflammation of the esophagus and lead to a narrowing (stricture) which might then require esophageal dilatation. In rare cases, it may develop into cancer of the esophagus.

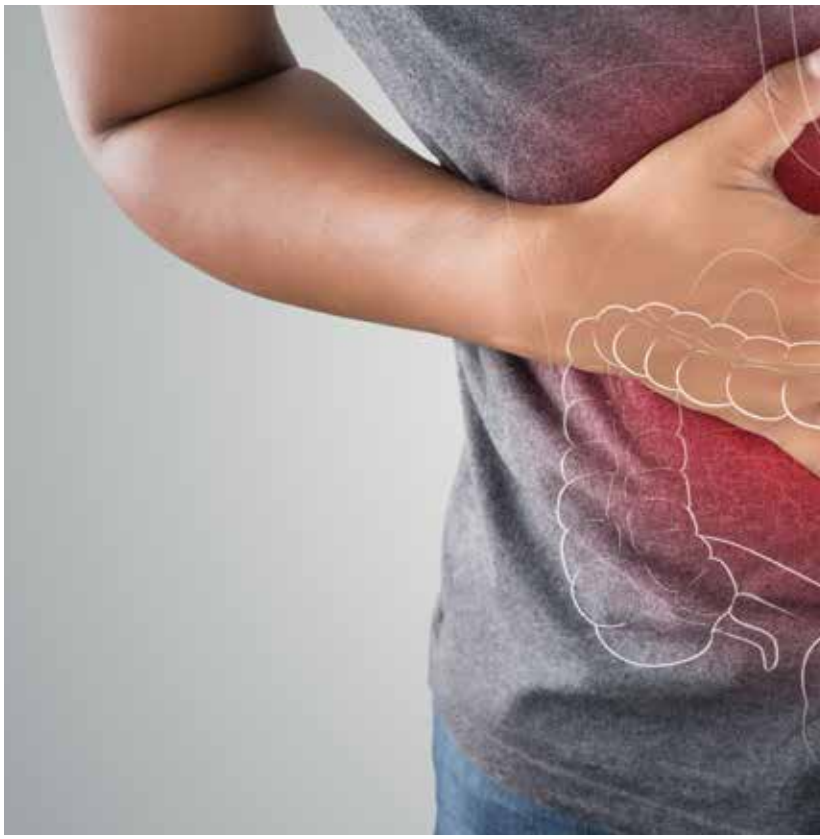
It is recommended to inform your doctor if:

* You have a persistent sensation of blockage in the esophagus when you swallow. He/she will determine if you need a gastroscopy and if your digestive condition requires treatment.

The Lungs and its Blood Vessels

An abnormal elevation of blood pressure in the pulmonary arteries, also known as pulmonary arterial hypertension (PAH), develops in 10% of SSc patients. This is a serious complication that can quickly lead to death if left untreated. Although patients with pulmonary arterial hypertension are usually short of breath on exertion, screening for this condition is critical and should be done regularly even in absence of symptoms. This screening helps your doctor determine if your pulmonary condition requires treatment. Regular echocardiogram is recommended — in most cases, yearly.

The lungs can also suffer from a condition called pulmonary fibrosis (PF) which can manifest itself as shortness of breath or dry cough. To check for early signs of PF, your physician might prescribe chest X-rays and pulmonary function tests.



Inform your doctor immediately if you notice any of the following symptoms:

* An increased shortness of breath while carrying out activities of daily living.
* Episodes of dizziness (lightheadedness) and/or loss of consciousness.
* Chest pain on exertion.
* Persistent swelling of the legs.

The most severe complication affecting the kidneys, called scleroderma renal crisis (SRC), which occurs in 5% of SSc patients, manifests itself as an increase in blood pressure. This may be accompanied by shortness of breath, headaches, visual changes or an altered state of consciousness. Patients experiencing this complication usually require temporary, or even sometimes, permanent dialysis. It should be noted that people taking cortisone (Prednisone) or have diffuse skin involvement are at greater risk of developing SRC.

We recommend that you take and record your blood pressure at least once a month, or more often according to your doctor's recommendations. We also recommend that you show your blood pressure readings (numbers) to your doctor's so that he/she can determine whether medical treatment is required in your case.

It is recommended to inform your doctor:

* If your blood pressure is consistently higher than usual (Normal blood pressure is less than 140/90 mmHg).
* Be sure to inform any physician who is considering prescribing you cortisone that you suffer from scleroderma.

Checklist

Medical treatments currently exist for most of the complications of scleroderma mentioned in this document. Therefore, it is important to screen all patients for these problems, even in the absence of clinical symptoms, so that appropriate treatment can start as soon as possible.

I immediately inform my doctor if:

* I notice an increase in the severity and/or frequency of Raynaud's symptoms.
* I notice a sore that does not heal or presents a discharge flow.
* I notice a recurring blockage in the esophagus when I swallow.
* I feel more short of breath or dizzy while carrying my usual everyday activities (e.g. being unable to do activities with friends, difficulty keeping up with a task, such as answering the phone, doing housework, etc.).
* My legs are swollen.
* My blood pressure is consistently higher than usual.

The Different Forms of Scleroderma

Dr. Sabrina Anh-Tu Hoa, MD, MSc, FRCPC
Rheumatologist at the Centre hospitalier de l'Université de Montréal, Associate Professor, Department of Medicine, Université de Montréal, researcher at the CHUM Research Centre, holder of the Université de Montréal Scleroderma Chair

The name "scleroderma" is derived from the Greek words "sclero", meaning hard and "derma", meaning skin. Thus, the characteristic feature of scleroderma is the hardening of the skin. Scleroderma is generally divided into two main forms: localized scleroderma and systemic scleroderma (or systemic sclerosis). Systemic sclerosis can, in turn, be classified according to the extent of skin hardening (limited or diffuse systemic sclerosis) or according to the presence of specific autoantibodies in the blood.

Localized Scleroderma (or Morphea)

Localized scleroderma is a fibrotic disease of the skin and sometimes of the underlying tissues, but does not affect internal organs. It affects mostly children, but can also occur in adulthood. There are several forms of localized scleroderma, including circumscribed or plaque morphea (involving one or multiple well-defined, oval to round areas of skin thickening), generalized morphea (when at least 4 plaques involving at least two anatomical sites are present), linear scleroderma (characterized by tight, thick bands, frequently affecting extremities) and scleroderma en coup de sabre (a type of linear scleroderma that affects the forehead and scalp area on one side of the head, with resemblance to the cut of a saber). Raynaud's phenomenon is usually absent in localized scleroderma.

Systemic Sclerosis: Limited or Diffuse

In contrast, systemic sclerosis (or systemic scleroderma) is a fibrotic skin disease that can also affect internal organs (hence the term "systemic"). When fibrotic skin involvement is limited to the hands, forearms, feet, legs below the knees, face and/or neck, it is referred to as limited systemic sclerosis. When the skin involvement goes up above the elbows and knees, affecting the skin of the upper arms, thighs, trunk and/or abdomen, it is then referred to as diffuse systemic sclerosis. Involvement of the skin and internal organs is generally more common and extensive in the diffuse form of systemic sclerosis. There is also a rarer form of scleroderma called sine scleroderma, in which the skin is not affected, although there is fibrotic damage to the internal organs.

Systemic Sclerosis: by Autoantibodies

Systemic sclerosis is an autoimmune disease in which the immune system becomes dysfunctional and turns against oneself. Evidence of this autoimmunity can be found by the presence of autoantibodies in the blood, i.e., antibodies directed against one's own cells. Several systemic sclerosis-related autoantibodies have been identified in recent decades and are useful in predicting potential complications of systemic sclerosis. For example, anti-centromere (or anti-CENP-B) autoantibodies are usually associated with the limited form of systemic sclerosis, a slower disease course at the onset of disease and less severe involvement of internal organs, but with more pulmonary arterial hypertension later in the course of the disease. Anti-topoisomerase I (or anti-Scl-70) autoantibodies are usually associated with the diffuse form of systemic sclerosis, a more rapidly progressive disease course at the onset of disease, and an increased frequency of pulmonary fibrosis. Anti-RNA polymerase III autoantibodies are usually associated with the diffuse form of systemic sclerosis, a more severe disease course and a higher risk of developing scleroderma renal crisis. In these patients, blood pressure should be closely monitored and corticosteroids should be avoided. These three autoantibodies are the most common autoantibodies found in systemic sclerosis, with approximately 75% of patients being positive for one of these three autoantibodies.

Scleroderma in Children

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What is Scleroderma?

Scleroderma is a rare condition in children. It often affects the skin. It can cause the skin to become hard and tight. In some children, it can affect other organs (e.g., lungs, kidneys, joints, stomach, and intestines).

Scleroderma is an autoimmune disease. It happens when the body attacks its own skin, and sometimes organs, by mistake. In autoimmune diseases, our immune system (the chemicals and blood cells that are supposed to fight off germs) is overactive. Extra chemicals and blood cells get trapped in the blood vessels of the skin (and sometimes organs). This causes inflammation and damage there. It is a chronic (ongoing) condition. It may get worse over time.

There are two types of scleroderma in children.

The first is called 'localized scleroderma'. This is the most common in children. It affects the skin in one area of the body only.

The other type is called 'systemic scleroderma'. This can affect many areas of the skin, as well as the organs of the body. It is rare in children.

What are the symptoms?

It is important to remember that scleroderma can affect every child differently. The most common things that happen are:

- Tightness and swelling of the skin; sometimes the skin changes colour.
- Pain or swelling in the joints.
- Pale, tingling or numb fingers, often in cold weather or when stressed. (This is called Raynaud's Phenomenon).
- Hard bumps (calcium) under the skin.
- Sores on the fingertips or knuckles.
- Spider veins.
- Heartburn and trouble swallowing.
- Shortness of breath.

How is it diagnosed?

If you or your doctor think your child has scleroderma, the first step is to be seen by a specialist doctor (called a 'pediatric rheumatologist'). The specialist will ask about your child's illness and give your child a check-up. They may ask for extra blood tests or X-rays. Depending on how your child is feeling, this may include:

- Blood and urine (pee) tests to look at blood counts, antibodies (chemicals found in the blood that may contribute to causing scleroderma), how well the liver is working, and how well the kidney is working.
- Imaging tests (such as X-rays, CTs, and MRIs). These look for any changes in the body's organs.
- Breathing tests (called Pulmonary Function Tests) to look at how well the lungs are working.
- Ultrasound of the heart (called an echocardio-gram) to look at how well the heart and blood vessels are working.
- Biopsy of the skin to look at the skin more closely under a microscope.

How is it managed?

Scleroderma cannot be cured. The goal is to improve the skin and stop the organs from becoming damaged. Every child's treatment will be different.

It may include:

- Medicines (such as ibuprofen) to help with pain and reduce inflammation.
- Skin creams to work directly on softening the skin.
- Medicines to reduce the strength of the overactive immune system and stop inflammation. These are called 'immunosuppressive'. They can be given by mouth, by needle under the skin or through the vein.
- Treating symptoms such as heartburn or Raynaud's Phenomenon.
- Physical therapy and exercise to keep muscles strong, and the joints from tightening up.
- Regular visits with your child's rheumatology specialist.

Localized scleroderma treatment often must last for several years. It is very rare for localized scleroderma to change and become systemic scleroderma.

Children with systemic scleroderma are at a higher risk of getting damage to the skin and organs. With the proper treatment, patients may have few or no symptoms (i.e., remission) for years at a time.

How to Diagnose Systemic Sclerosis

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Rheumatologist at the Centre hospitalier de l'Université de Montréal, Associate Professor, Department of Medicine, Université de Montréal, researcher at the CHUM Research Center, holder of the Université de Montréal Scleroderma Chair

The diagnosis of systemic sclerosis (SSc, systemic scleroderma) is usually based on the presence of a combination of symptoms and signs typical of systemic sclerosis:

- Raynaud's phenomenon;
- Skin thickening or puffy "sausage-like" swelling of the fingers;
- Autoantibodies associated with systemic sclerosis in a blood sample;
- Abnormalities in small blood vessels at the base of the nails;
- Other skin and internal organ involvement associated with systemic sclerosis.

Raynaud's Phenomenon

The most common and earliest problem observed in systemic sclerosis is Raynaud's phenomenon. This phenomenon is characterized by a change in colour of the fingers (typically from a white discoloration to a blue then red colour) and is most commonly provoked by exposure to cold. Raynaud's phenomenon can be "primary", meaning that it is isolated and not associated with a systemic autoimmune disease such as systemic sclerosis. However, when Raynaud's phenomenon occurs after the age of 40-50 years or is associated with ulcerations of the fingers (open lesions of the skin that heal very slowly) or other symptoms and signs of systemic sclerosis, a diagnosis of systemic sclerosis should be suspected and sought.

Thickening of the skin of the fingers

Thickening of the skin of the fingers, especially when it extends to the back of the hand, or puffy swelling of the fingers with a sausage-like appearance in the earlier stages, are characteristic signs of systemic sclerosis.

Autoantibodies

Systemic sclerosis is an autoimmune disease in which the immune system becomes dysfunctional and turns against its own cells. Evidence of this autoimmunity can be found by the presence of autoantibodies in the blood, i.e., antibodies directed against oneself. Several autoantibodies specific to systemic sclerosis have been identified, including anti-centromere, anti-topoisomerase I (Scl 70) and anti-RNA polymerase III. Their presence, detected by a blood test, supports the diagnosis of systemic sclerosis when it is associated with Raynaud's phenomenon and other symptoms and signs of systemic sclerosis.

Nailfold capillary abnormalities

Systemic sclerosis is also a disease of the small blood vessels. Abnormalities of these small vessels, or "capillaries", can be seen at the base of the nails. Specialized examination by high magnification microscopy of the capillaries in the nail bed, or "capillaroscopy", is often useful to support a diagnosis of systemic sclerosis.

Other skin and internal organ involvement

Systemic sclerosis can also present with skin ulcerations on the fingertips, telangiectasias (dilations of small blood vessels that form red or sometimes purple spots on the surface of the skin) and calcinosis (small, white bumps of calcium deposits under the skin). Systemic sclerosis can also affect the digestive, pulmonary, cardiac and renal systems. In the presence of other symptoms and signs suggestive of systemic sclerosis, these additional manifestations support the diagnosis of systemic sclerosis.

Classification criteria

In scientific research, classification criteria are used to standardize the definition of systemic sclerosis (see Table below for the classification criteria issued jointly in 2013 by the American College of Rheumatology and the European League Against Rheumatism). Patients with a score of at least 9 points are classified as having systemic sclerosis. However, a diagnosis of systemic sclerosis (often at an early stage) can be made in a patient who does not meet the classification criteria.

Summary

In summary, the diagnosis of systemic sclerosis is based on a constellation of symptoms and signs typical of systemic sclerosis, particularly Raynaud's phenomenon and thickening of the skin of the fingers, as well as the presence of specific autoantibodies in blood samples and characteristic abnormalities on examination of the small blood vessels (capillaries) at the base of the nail.

TABLE

Classification criteria for systemic sclerosis, issued in 2013 by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR).

Criteria	Points
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints	9
Puffy fingers or	2
Sclerodactyly (skin thickening of the fingers)	4
Digital tip ulcers or	2
Fingertip pitting scars	3
Telangiectasia	2
Abnormal nailfold capillaries	2
Pulmonary arterial hypertension or	2
Interstitial lung disease	2
Raynaud’s phenomenon	3
Systemic sclerosis-related autoantibodies (anti-centromere, anti-topoisomerase I, anti-RNA polymerase III)	3

How Does Systemic Sclerosis Evolve

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The evolution of systemic sclerosis is variable, depending on the extent of skin thickening (limited or diffuse systemic sclerosis), the presence of specific autoantibodies in the blood and the presence of internal organ involvement.

Limited or diffuse skin involvement

When skin thickening is limited to the hands, forearms, feet, legs below the knees, face and/or neck, this is referred to as ***limited systemic sclerosis***. This form of systemic sclerosis is usually associated with a lower risk of developing severe internal organ involvement, except for pulmonary arterial hypertension, the risk of which increases after 5 to 10 years of disease.

When skin involvement extends above the elbows and knees, affecting the skin of the upper arms, thighs, trunk and/or abdomen, this is referred to as diffuse systemic sclerosis. In this form of systemic sclerosis, internal organ involvement is generally more common and extensive.

Limited or diffuse skin involvement does not usually change in the same patient. Thus, a patient with the limited form does not progress to the diffuse form of the disease. However, at disease onset, it may be difficult to be certain of the limited nature of the disease. A patient may initially have limited involvement of the hands (and be classified as having limited disease), but the involvement may rapidly progress to diffuse involvement over the next few months. The presence of swelling of the fingers and hands, and the presence of autoantibodies associated with the diffuse form of systemic sclerosis (e.g., anti-topoisomerase I/Scl-70 or anti-RNA polymerase III) usually point to a possible evolution towards the diffuse form of the disease.

In the diffuse form, skin thickening generally progresses in the first 2 to 5 years of the disease, then progression halts with a tendency towards spontaneous "softening" of the skin. The skin then becomes thinner and more fragile, but less "hard" than in the initial phase. In the limited form, skin involvement is restricted to the areas defining the limited form and does not progress further.

Systemic sclerosis-specific autoantibodies

Anti-centromere (or anti-CENP-B) autoantibodies are usually associated with the limited form of systemic sclerosis, a slower disease course at the onset of disease and less severe involvement of internal organs, but with more pulmonary arterial hypertension later in the course of the disease.

Anti-topoisomerase I (or anti-Scl-70) autoantibodies are usually associated with the diffuse form of systemic sclerosis, a more rapidly progressive disease course at the onset of disease, and an increased frequency of pulmonary fibrosis.

Anti-RNA polymerase III autoantibodies are usually associated with the diffuse form of systemic sclerosis, a more severe disease course and a higher risk of developing scleroderma renal crisis. In these patients, blood pressure should be closely monitored and corticosteroids should be avoided.

Anti-Th/To autoantibodies are associated with the limited form of systemic sclerosis, as well as an increased risk of pulmonary fibrosis and pulmonary hypertension. Anti-fibrillarin (or anti-U3-RNP) autoantibodies are associated with diffuse systemic sclerosis and an increased risk of pulmonary fibrosis. These autoantibodies are not available in all centres, but give a "nucleolar" pattern on the antinuclear antibody (ANA) test by immunofluorescence.

Internal organ involvement

Unlike skin involvement which tends to improve over the years, internal organ involvement usually does not regress. In the case of pulmonary fibrosis, disease progression is highly variable: some patients will have a mild and relatively stable disease, some will have a disease that progresses slowly over the years, and some will progress rapidly. Patients whose thoracic CT scan shows involvement that extends beyond the lung bases are usually at higher risk of developing more progressive pulmonary fibrosis.

It is commonly said that organ involvement (skin, lungs, heart, kidneys, and others) occurs in the first 3 to 5 years of the disease, with the exception of pulmonary arterial hypertension, which occurs after 5 to 10 years of disease progression. However, more recent studies have questioned this notion. Pulmonary fibrosis frequently occurs early in the course of the disease, but can also appear later on. Inflammatory damage to the heart (myocarditis) usually occurs early in the disease, but fibrotic damage gradually progresses throughout the disease course. Digestive involvement also becomes progressively more important as the disease moves from the vascular and inflammatory phase to the more fibrotic phase of disease. The tissues of the digestive system then become weaker and unable to contract, leading to greater motility disorders and malabsorption over the course of the disease.

In summary

The course of systemic sclerosis is highly variable. An initial assessment of skin and internal organ involvement and the search for systemic sclerosis-specific autoantibodies in the blood can help predict the course of systemic sclerosis in an individual and inform the approach to screening for internal organ involvement.

II SYMPTOMS AND COMPLICATIONS

Dermatological Interventions for Facial Manifestations in Scleroderma

As a result of scleroderma, many patients experience functional and cosmetic impairment of the face. This may affect the quality of life and psychological health of patients. Unfortunately, despite the increasing use of cosmetic procedures in the general population, there is a lack of evidence evaluating the safety and effectiveness of these procedures in scleroderma patients. In this article, we explore some dermatological interventions used to address common facial manifestations of scleroderma.

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Telangiectasias

Telangiectasias are dilations of small blood vessels that can appear as red spots on the skin in patients with scleroderma. They commonly occur on the face, and less commonly on other sun-exposed areas. Although not dangerous, telangiectasias can be a source of psychological distress and body image dissatisfaction. There are few studies on the treatment of telangiectasias in scleroderma, which are described as more resistant to treatment than non-scleroderma-related telangiectasias. Although evidence is lacking, there are two promising treatments: pulsed dye laser (PDL) and intense pulse light (IPL), both of which are non-invasive treatments with good safety profiles.

PDL (a type of laser) converts a narrow range of light waves into heat to destroy the damaged blood vessels causing telangiectasias while keeping healthy tissues and vessels safe. A retrospective study of 23 scleroderma patients with facial telangiectasias treated monthly with PDL for an average of 3 months showed improvement in all patients, and clearance of telangiectasias in 44% of patients [(1)]. However, 26% of patients had a recurrence of facial telangiectasias after 6-36 months. Common side effects include purple spots (which represent bruising) that appear for 5-10 days after the procedure. Other less common side effects include swelling, self-healing blistering in treated areas, changes in skin pigment colour, and very rarely scarring. All patients in this study stated they would repeat the treatment.

IPL (a type of flashlamp emitting visible light) works similarly to PDL. The main difference between IPL and PDL, however, is the type of light being used: IPL uses a broadband pulsed light source, whereas PDL uses a monochromatic coherent light source. A few studies in scleroderma patients have shown that IPL can be effective for facial telangiectasias as well and is well tolerated. One study comparing PDL and IPL in scleroderma patients with facial telangiectasias confirmed that they were both effective treatments, but that PDL was perhaps more effective and that IPL had fewer side effects [(2)]. As IPL emits a broader range of light waves, it may also help to improve skin pigmentary changes (sun or scleroderma-induced) and signs of skin aging through its effect on pigmentary cells and collagen [(3)].

While there are no studies that assessed the effect of sun and smoking on the number and severity of scleroderma-associated telangiectasias, telangiectasias in general (including scleroderma-associated) are typically more prominent in skin chronically exposed to ultraviolet light and in patients who are smokers [(4,5)]. As such, it is a common practice for dermatologists and other healthcare providers to recommend daily sun protection to limit ultraviolet-induced skin damage and prevent skin cancer. Recommendations regarding sun safety can be found on the Canadian Dermatology Association website (https://dermatology.ca/public-patients/sun-protection/sun-safety-every-day/). Tobacco cessation is prudent to limit scleroderma-associated complications, skin cancer and skin aging.

Microstomia

Microstomia is defined as a mouth opening of less than 50 mm, when measured between the top and bottom front teeth (called inter-incisor distance). It is a common feature in scleroderma, affecting up to 80% of patients. Because of the decreased mouth opening, microstomia also impairs eating, dental hygiene, and speaking, and alters facial appearance. Although further research is needed to determine the most effective treatments for microstomia, there are some promising treatment options available for patients who suffer from these negative consequences on their oral and digestive health, as well as body image.

Hyaluronidase is a protein enzyme that breaks down hyaluronic acid, which contributes to skin tightening in scleroderma. Thus, its use is proposed to soften the tight skin in scleroderma. It has only been studied in a few case reports and case series, but the results of these studies and the proposed mechanism of action are promising. It is injected into several regions around the mouth and can be injected monthly for multiple doses, with reported improvements in interincisor distance of up to 15 mm [(6)]. There are several ongoing studies aiming to determine dosing, frequency and number of injections needed to improve the mouth opening. Outside of scleroderma, hyaluronidase has been used routinely for many years in the cosmetic industry and thereby its safety is well established. The main potential side effects of hyaluronidase injection include pain during injection (which can be minimized by using topical analgesia or nerve blocks), bruising and very rarely an allergic reaction.

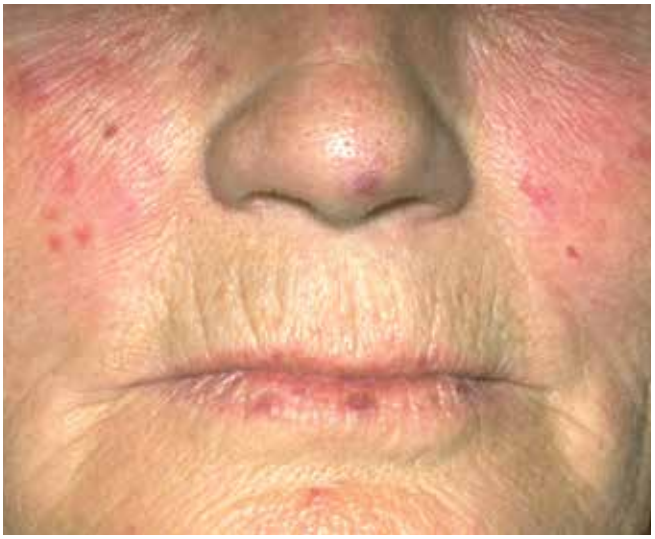
Other more invasive treatments such as autologous fat grafting have shown promising results as well. Autologous fat grafting involves taking fat from a patient (such as around the hips, knees, or abdomen), and re-injecting it (sometimes mixed with another substance, platelet-rich plasma) around the mouth. There have been clinical trials, as well as case series and case reports showing varying levels of improvement in the inter-incisor distance following this procedure. However, this procedure is invasive, costly and requires general anesthesia in an operating room setting.

As mentioned above, because IPL emits a broader spectrum of light wavelength and is used to reverse signs of skin aging, it has been explored as a treatment for microstomia. In a small study of 4 patients who received 3-5 monthly IPL treatments in the perioral region, all 4 noted softening of the perioral skin and 3 patients described an improved mouth opening [(7)]. However, the data regarding its efficacy remains very scarce. Other light sources (such as phototherapy or other lasers) and botulinum toxin have either shown limited improvement or have only been studied in a few studies.

Perioral wrinkles and lip thinning

Cosmetic procedures such as fillers and botulinum toxin injections to reduce wrinkles and increase lip thickness have become more popular in recent years, with many more providers offering these services – sometimes without sufficient training, which can result in harmful complications. Scleroderma patients who suffer from perioral wrinkles (around the mouth) and lip thinning due to their disease may wonder if these procedures are appropriate for them.

Several types of fillers can be injected including hyaluronic acid, calcium hydroxylapatite and poly-L-lactic acid. There is a theoretical risk that hyaluronic acid fillers could worsen or reactivate autoimmune diseases such as scleroderma by increasing local tissue inflammation. Because of this, specialized doctors often refuse to perform this procedure in patients with autoimmune diseases such as scleroderma. However, there are some case reports and series (mostly involving patients with stable scleroderma disease on no immune modifying medication [3]) that have shown positive results following the use of hyaluronic acid filler injections and there have been no published reports of scleroderma relapse following filler injection to our knowledge [8]. Although it remains controversial, hyaluronic acid filler injections can be considered in scleroderma patients with stable disease and on no immune modifying medication, but their safety needs to be verified in larger and higher quality studies. On the other hand, hyaluronic acid fillers of the Vycross family are not recommended, given case reports of late-onset immune-mediated nodules that appear after these types of injections and that are difficult to treat [8].



Few studies have involved calcium hydroxylapatite and poly-L-lactic acid, thus more studies would be needed to confirm their safety in scleroderma. On a cautionary note, although silicone and paraffin fillers have been banned by the *Food and Drug Administration* and other regulatory agencies for many years due to their high risk of adverse events (local and systemic complications), they are still available on the black market. For these reasons, and because of case reports of scleroderma development following these procedures, we advise against silicone and paraffin filler injections [9].

There have been case reports describing the use of botulinum toxin to treat various facial sequelae of scleroderma or skin aging without any adverse effects. To our knowledge, there are no described cases of adverse events following facial botulinum toxin use in scleroderma.

Conclusion

Although more research is required, there are some promising methods of addressing facial telangiectasias and microstomia. The use of botulinum toxin and certain fillers in stable scleroderma on no immunosuppressants may be safe.

II SYMPTOMS AND COMPLICATIONS

Oral Health and Scleroderma

Christine Brunet, D.M.D
Retired Dentist

Everyone should have oral health that enables them to eat, drink, and speak comfortably throughout their life. However, scleroderma often interferes with these vital actions, either directly by disrupting the physiological function of the oral space, or indirectly by significantly hindering hygiene methods. Fortunately, most people living with scleroderma will not experience the full range of these problems, and the severity of symptoms will vary from person to person.

This text is not intended to be scientific or exhaustive. Its goal is to address the main known concepts to better understand how a disease like scleroderma can affect the function of this unique part of the body: the mouth.

Let us explore how scleroderma influences oral health and the various approaches that can help improve quality of life for many people who may face these challenges.

It is equally important to highlight the need to consult a dental professional regularly as soon as the first signs of scleroderma appear, to help prevent or limit the progression of the oral complications outlined below.

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Microstomia

Reduced mouth opening and loss of facial elasticity

The skin of the face loses elasticity, and mouth opening can become significantly restricted. This leads to difficulties with speaking and eating, especially as the tongue may lose mobility and the lingual frenulum, a thin membrane connecting the tongue to the floor of the mouth, may become fibrotic and limit movement. Basic hygiene routines become harder to carry out, and dental visits may be uncomfortable or even impossible to perform properly, particularly in the back areas of the mouth.

Facial skin thickening may also cause the teeth to shift due to compression. It can also worsen dryness in the mouth because of an inability to close the lips and achieve a proper seal, leaving the mouth slightly open at all times.

Clearly informing your dentist about your scleroderma diagnosis allows care to be properly adapted to your needs, whether it involves the duration of the procedures, a more comfortable position, the choice of instruments, or the type of restoration if needed, to make treatment easier and more comfortable.

Strategies for improvement

Numerous studies show that positive results can be achieved through daily stretching exercises of the mouth using fingers or tongue depressors. These exercises need to be performed several times a day to yield meaningful improvements. Physical therapy, kinesiology and occupational therapy can also suggest relevant exercises and techniques. In more severe cases, hyaluronidase injections may be used to soften the skin, along with autologous fat grafts taken from the patient, or IPL treatment, a technique using intense pulsed light.

For more information, refer to the *"Dermatological Interventions for Facial Manifestationsin Scleroderma"* section.

Toothbrushes with small heads or designed for children, or electric toothbrushes with rotating heads and larger handles, can help improve access to back teeth. Interdental brushes and oral irrigators, such as Waterpik, may also be considered. If subtle dental shifting causes discomfort when chewing or muscle pain, the dentist can perform minor adjustments by carefully grinding the teeth that no longer fit together properly.

More frequent dental visits, ideally every three months, are highly recommended to detect and prevent issues before they arise and require longer or more demanding treatments. In addition, when cleanings are done more often, they are much quicker.

Xerostomia

Dry mouth caused by reduced saliva flow

Xerostomia is common among people with scleroderma. While salivary gland fibrosis may be the cause, in some cases it is due to Sjögren's syndrome, a chronic, systemic autoimmune disorder. Both conditions lead to a similar outcome: a permanent reduction in saliva production, causing dry mouth.

Saliva lubricates the mouth, helping with speech and swallowing. It cleans food debris and contains substances that neutralize the acid produced by oral bacteria and that help remineralize tooth enamel. It also contains components that help control the number of microbes and viruses in the mouth.

A decrease in saliva flow significantly raises the risk of tooth decay and enamel erosion, primarily because of increased acidity in the mouth. Dryness also affects the comfort and fit of removable prostheses. Xerostomia can also disturb the oral microbial balance, leading to candidiasis, fungal infections caused by microscopic yeast, especially under prostheses or in the corners of the lips, where they trigger painful inflammation known as angular cheilitis.

Strategies for Improvement

To help compensate for reduced saliva flow, it is recommended to:

- Drink small amounts of water frequently.
- Keep indoor humidity between 40% and 50%.
- Avoid smoking, alcohol, salty or spicy foods.
- Use sugar-free candies or chewing gum to stimulate saliva production.

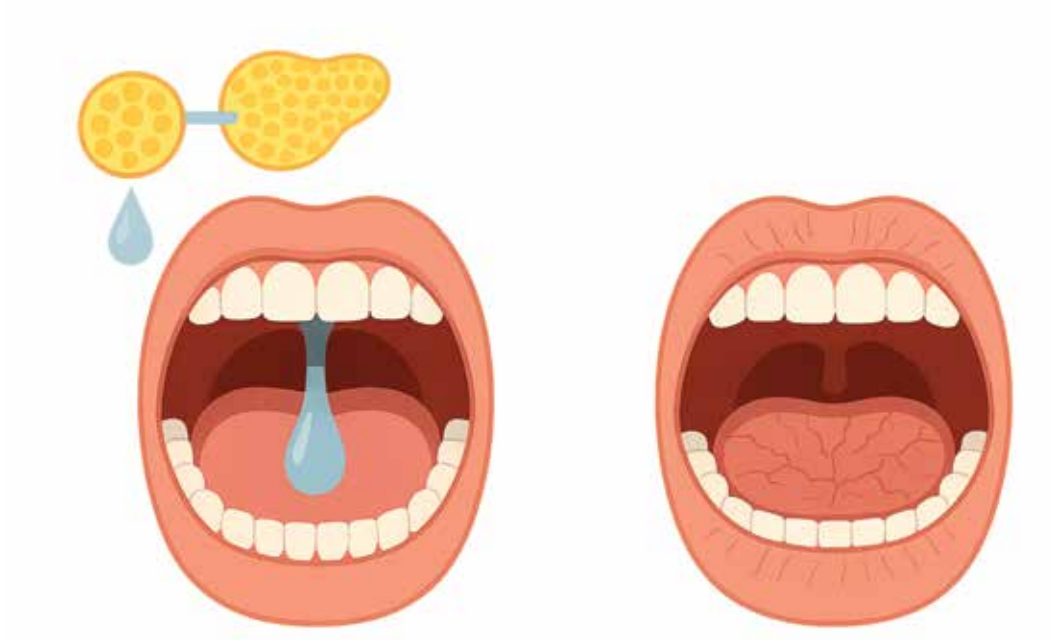
Saliva substitutes, oral lubricants, and stimulants are available either over the counter, such as lozenges, or by prescription, like pilocarpine.

For more information, refer to the "*Sjögren's Syndrome Associated With Systemic Scleroderma*" section.

To reduce the risk of cavities, it is advised to:

- Avoid sticky or sugary foods, soda, fruit juices, wine, coffee and tea.
- Maintain good dental hygiene, including brushing and flossing.
- Remove dental prostheses before bedtime and brush the sides of the teeth that serve as anchors.

In case of candidiasis, dentists can prescribe antifungal creams, which are usually effective. For more persistent cases, oral medication may be used.



Tooth decay

Tooth decay is the most widespread infectious disease in the world. According to the World Health Organization, nearly all adults have had cavities. It is rare to find someone who has never had one. People living with scleroderma who also experience microstomia, xerostomia, gastroesophageal reflux, or reduced manual dexterity are especially at risk.

When the mouth opening is limited and hand movements are difficult, brushing and flossing become extremely challenging.

Xerostomia is an aggravating factor for the development of new tooth decay because it reduces the beneficial effects of saliva. Saliva normally helps clear food particles from teeth, neutralizes acid, and strengthens enamel.

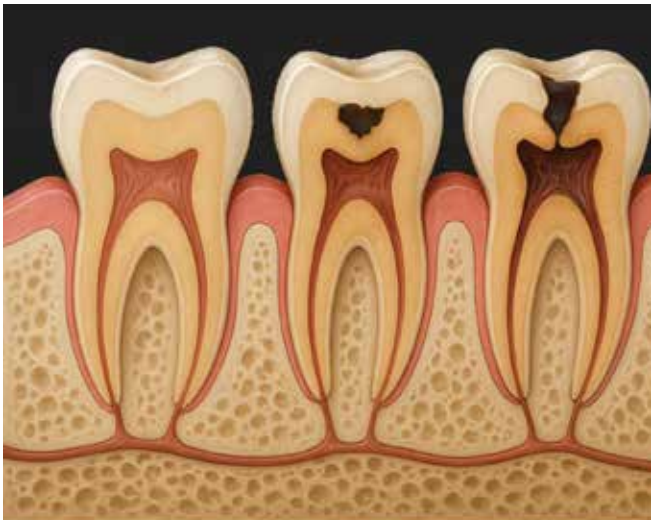
Gastroesophageal reflux, or GERD, increases the presence of acid in the mouth. This further raises the risk of cavities and contributes to enamel erosion.

Strategies for improvement

Dental plaque must be removed regularly. It contains salivary proteins, food debris, and many bacteria that turn sugars into acid. This includes natural sugars such as those found in honey, maple syrup, or fruit. The acid then attacks the enamel, eventually creating a cavity, and can also irritate the gums. Reducing sugar intake, whether from foods or drinks, helps protect teeth. Bacteria make no distinction. They use all forms of sugar to produce acid.

People who are at higher risk of cavities or who experience frequent tooth decay would certainly benefit from fluoride. This natural element strengthens enamel and helps reduce the number of bacteria that produce acid. Its antimicrobial and protective action makes the enamel more resistant to acid attacks.

Fluoride comes in various forms, and discussing with your dental team can help determine the most suitable option for your needs.



There are high-fluoride toothpastes available, such as Colgate PreviDent Booster Plus, which contains 5000 ppm fluoride and is safe for regular use. Fluoride gels applied at night using trays may also be recommended. Topical creams containing calcium, phosphate, and fluoride, such as MI Paste Plus, can be useful for people with low saliva flow. Fluoride varnish applied professionally at the dental office, as is done with children, is also well suited for adults at high risk of cavities. In addition, the occlusal or chewing surface of molars can be sealed to block bacteria from settling in grooves and to make cleaning easier.

Daily exercises to maintain or increase mouth opening and hand mobility are valuable. They make oral hygiene easier to perform at home.

These exercises are described in the educational sheet "*The Scleroderma Patient-centered Intervention Network (SPIN) and the SPIN-HAND Program*."

Toothbrushes with adapted handles or electric toothbrushes can improve grip for those with limited dexterity. Floss holders and interdental brushes are also practical tools to replace regular flossing when needed.

Periodontal disease

Gingivitis and periodontitis worsened by scleroderma

The periodontium refers to the set of tissues that support the teeth, namely the bone, the periodontal ligament, and the gum. The root is firmly anchored in the jawbone, covered with a protective layer called cementum, and held in place by small fibers that form the periodontal ligament. The gum acts as a protective tissue over the bone. Many adults suffer from periodontal disease, which often leads to tooth loss due to the gradual destruction of these supporting tissues by bacteria. A tooth may appear completely normal, with no decay or visible wear, but without a solid anchor in the bone, its stability and long-term survival are compromised.

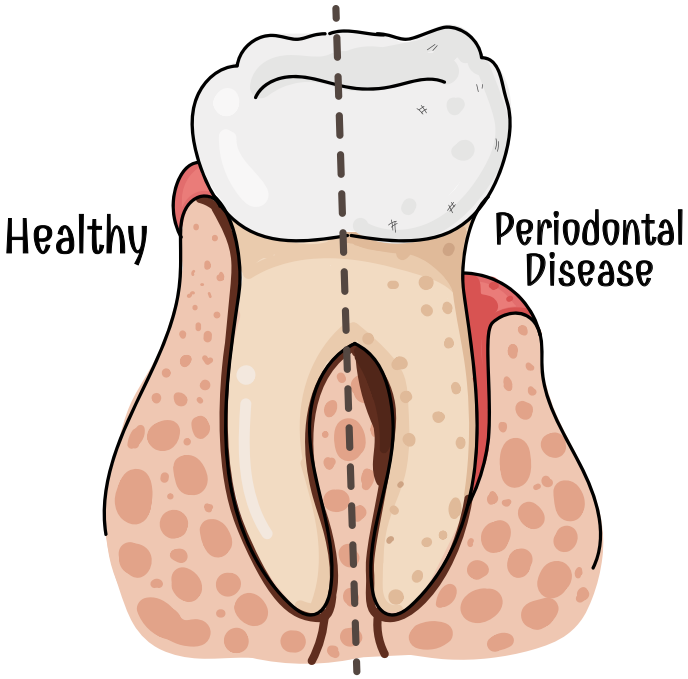
Scleroderma can increase the severity of periodontal disease through fibrosis of the oral mucosa and frena, creating tension on the gums and thereby increasing gingival recession, that is, receding gums. In addition, microstomia and reduced manual dexterity greatly complicate the hygiene techniques essential for eliminating the bacteria responsible for gum inflammation, known as gingivitis, as well as the possible damage to the supporting structures of the teeth, known as periodontitis. Furthermore, reduced saliva flow worsens the situation, since its cleansing and bacterial-regulating roles are compromised.

Strategies for improvement

The simplest and most effective way to prevent periodontal disease is to remove dental plaque loaded with bacteria before they produce enough toxins and acid to first damage the gums, then reach deeper areas and cause bone resorption, meaning a progressive loss of the bone that supports the teeth.

Therefore, with each brushing, it is important to pay close attention to the gumline by gently massaging this area using a soft-bristled toothbrush. The same applies to dental floss, which should be adapted to the curved surface of the tooth to dislodge bacteria hidden beneath the gum. Floss can be gently inserted under the gum without risk.

Your dental hygienist is without a doubt the best person to teach you these techniques. Your hygienist or your dentist is also the one who can effectively remove tartar deposits, which are made up of hardened or calcified dental plaque, using specialized instruments, as this cannot be done with a toothbrush. Tartar also harbours a large number of bacteria that can cause irreversible damage to the periodontium. It is therefore essential to remove these deposits regularly to avoid progressive deterioration that could lead to tooth loss.



Gastroesophageal reflux disease (GERD)

Oral acidity and tooth enamel erosion

GERD, which is common among adults, is even more frequent in people living with scleroderma. The esophagus, the tube that connects the mouth to the stomach, may have weak or ineffective contractions, and the lower esophageal sphincter, which is the valve that separates the esophagus from the stomach, may become deficient and fail to close properly. This results in the backflow of stomach acid and bile into the esophagus, sometimes reaching the mouth.

The acid produced by the stomach has a very low pH, between 1 and 3, whereas a neutral pH, like that of most drinking water, is 7. This extreme level of acidity makes it particularly aggressive or damaging to tooth enamel. When saliva production is also reduced, a condition known as hyposialia, this acidity becomes even more harmful.

Unfortunately, lost enamel does not regenerate naturally. Once it is damaged, it can only be restored through dental treatments.

Strategies for improvement

THERE ARE SEVERAL PROVEN TECHNIQUES TO HELP REDUCE GERD:

- Keep the head of the bed raised to prevent acid from rising during sleep.
- Avoid eating for three hours before going to bed.
- Limit or avoid caffeine, alcohol, fatty foods, chocolate, and acidic drinks.
- Drink water regularly or rinse the mouth frequently.
- Avoid sugary foods and drinks, since oral bacteria turn them into acid.

For more information, refer to the "*Gastrointestinal Involvement in Systemic Sclerosis*" section.

In more serious cases, antacids or medications such as proton pump inhibitors may be prescribed to reduce stomach acid production.

It is also recommended to use fluoride in all its forms. This includes toothpaste, fluoride varnish, gels, and topical creams. Fluoride helps protect enamel by making it more resistant to acid and supporting remineralization.

The amount of enamel already lost cannot be naturally restored. Severely eroded areas may eventually require dental restorations, such as fillings, crowns, or inlays. However, if the remaining enamel becomes stronger and more resistant to acid, further damage can be significantly reduced.

TMJ and facial pain

Temporomandibular joint and muscle or nerve pain

The temporomandibular joint (TMJ) connects the lower jaw to the skull and is located on both sides of the face, just in front of the ears. Due to its complex structure and wide range of motion, it is often susceptible to discomfort.

Scleroderma can affect this joint just as it affects other joints in the body. Muscle fibrosis, reduced blood flow, and shifting of the teeth caused by tightening of the facial skin can all contribute to joint pain. Bruxism, which refers to involuntary grinding as well as clenching of the teeth, is a common cause of TMJ discomfort. In addition, when the teeth no longer fit together properly, this can increase the strain on the joint. Pain in the jaw and facial muscles can be especially bothersome, since this area is constantly engaged in eating, speaking, swallowing, and even smiling.

In some cases, people report sharp, intense, and brief nerve pain. This usually involves the trigeminal nerve, which has several branches across the face, and generally affects only one side of the face. These neuralgic pains can be triggered by chewing or even by a light touch on certain areas of the face.

Bone resorption, referring to damage affecting the bone, has been observed at the attachment points of the jaw muscles, particularly at the posterior angle of the lower jaw and in the region of the condyles, located near the ears. These bone changes are usually asymptomatic and are often discovered incidentally during X-rays.

Strategies for improvement

The dentist may carry out selective grinding of misaligned teeth to restore balanced contact and reduce tension or sensitivity. Night guards, also known as occlusal splints, are often worn at night to relieve TMJ pain and protect the teeth from wear. In some cases, anti-inflammatory medication or muscle relaxants may be recommended.

It is advisable to avoid chewing gum and to limit hard or sticky foods to reduce strain on this already sensitive joint. Taking small bites and avoiding always chewing on the same side are also good habits to adopt.

Applying warm, moist compresses to painful areas may also help relieve discomfort, especially during more intense episodes.

In cases of trigeminal neuralgia or bone resorption, which are more complex and less common situations, the dentist may recommend a consultation in oral medicine.

II SYMPTOMS AND COMPLICATIONS

Calcinosis in Systemic Sclerosis

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Systemic sclerosis (or scleroderma) is characterized by many skin changes, including calcinosis. In this article, we will discuss what is calcinosis, how it is diagnosed and available treatments.

What is calcinosis?

Calcinosis is an accumulation of calcium in the skin and surrounding tissues. It can affect up to 20-40% of people with scleroderma, with a similar rate between limited and diffuse scleroderma. It often occurs on the hands, forearms, elbows, and knees, despite normal calcium levels in the blood. Small lesions may go unnoticed, but may also cause pain, interfere with joint function, or be complicated by ulcers, infections, or nerve compression. Unfortunately, few cases of calcinosis improve spontaneously with time, with most lesions remaining stable or worsening after 1 year.

Why does calcinosis develop, and which scleroderma patients are most at risk?

We still do not completely understand why calcinosis develops. Studies have found that people with scleroderma who are men, who have ulcers on their fingers, who have osteoporosis, or internal organ involvement of scleroderma (especially lung fibrosis) are at higher risk for calcinosis. Some autoantibodies have also been associated with calcinosis, including anti-centromere, anti-PM-Scl and anti-RNA-polymerase-3 autoantibodies. Other potential factors include longer disease duration, poor blood circulation, and trauma.

How is calcinosis diagnosed?

It is often detected by the physician on physical exam and can be confirmed by plain radiographs. Other ways to identify calcinosis include ultrasound, computed tomography and magnetic resonance imaging.

How do we treat calcinosis?

Calcinosis remains a challenging aspect of scleroderma to manage, as there is no cure or highly effective treatment. We generally do not treat calcinosis that does not bother a patient. At present, no medical therapies have proven to be efficacious in large randomized controlled trials.

General measures

Generally, it is recommended to avoid injuries and ensure good blood flow to prevent new calcinosis, as these are thought to play a role in calcinosis development. This includes smoking cessation, avoiding exposure to cold and stress, and managing Raynaud and ulcers on the fingers. If a wound develops, proper wound care is important, and antibiotics should be given for nonhealing and infected ulcers. If there is an open wound, warm soaks can help squeeze out calcinosis and may help prevent infections.

Medical therapies

Sodium thiosulfate is thought to improve calcinosis because it binds to calcium. A systematic review that looked at 40 studies (including 1 small randomized controlled trial) found that the topical form of this medication improved calcinosis in over 80% of patients over an average of 5 months. Topical sodium thiosulfate needs to be prepared by a pharmacist in a mixture with either Vaseline or zinc oxide. Possible side effects include skin irritation, allergy to zinc and pain with application. Sodium thiosulfate can also be injected directly into calcinosis lesions, usually by a dermatologist. A case series of 5 scleroderma patients showed improvement or complete resolution of calcinosis with weekly injections for 4 weeks. A common side effect is a burning sensation in the area of the injection site.

Several medications have also been shown to improve calcinosis in small studies. Two pill form medications, colchicine and minocycline, may decrease the inflammatory aspect of calcinosis, when there is associated pain, redness, warmth and swelling, as shown in small studies involving fewer than 10 patients each. One of the side effects of colchicine is diarrhea, while the side effects of minocycline include nausea, dizziness, and a blue-black discoloration of calcinotic lesions. Other medications, such as diltiazem, bisphosphonates, rituximab, and intravenous immunoglobulins, have been reported to help calcinosis in small studies, but with no larger or higher quality studies to support these observations.

Finally, neem oil with Hypericum plant extract is an herbal therapy that is often used in wound care. A pilot study of 21 scleroderma patients with open calcinotic wounds followed over 40 days found that neem oil helped complete healing in 45% of patients, perhaps by softening and facilitating excision of calcium deposits. This would need to be further supported in larger studies.

Interventions

Surgery to remove calcinosis can be an effective treatment and is considered for lesions that are affecting hand or joint function, compressing a nerve, or causing severe discomfort. Complications include recurrence in 15%, delayed wound healing in 13%, and wound infection in 10% of cases.

Extracorporeal shockwave therapy uses acoustic shock waves to break apart and destroy calcinosis. It is performed by physiotherapists who have received the appropriate training. It can help relieve pain associated with calcinotic lesions that are not amenable to surgery. Several prospective studies have found improvements in pain and size of calcinotic lesions. It often involves 3 to 5 sessions done every 7 to 10 days.

In summary

Calcinosis is a feature of scleroderma that is common but unfortunately difficult to treat. Important preventative measures include avoiding trauma and ensuring good blood circulation such as through smoking cessation, cold avoidance, proper management of Raynaud, and treating ulcers. For calcinotic lesions that are symptomatic, topical or injected sodium thiosulfate may be helpful. Surgery may be considered for lesions that significantly affect function and quality of life. More research is needed to understand the cause and optimal treatment of calcinosis.

II SYMPTOMS AND COMPLICATIONS

Sjögren's Syndrome Associated With Systemic Scleroderma

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Systemic scleroderma is an autoimmune disease that affects the functioning of small blood vessels and leads to excessive scarring. Individuals with scleroderma are at a higher risk of developing other autoimmune diseases, such as Sjögren's syndrome. In this article, we will discuss what Sjögren's syndrome is, and how it is diagnosed, treated, and monitored.

What is Sjögren's syndrome?

Sjögren's syndrome is a chronic autoimmune disease that causes the immune system to attack the glands responsible for producing saliva (salivary glands) and tears (lacrimal glands). This results in reduced saliva production, leading to a dry mouth and dental problems such as tooth decay. Damage to the lacrimal glands causes excessive dryness in the eyes, with a sensation of having sand in the eyes, which requires the regular use of artificial tears. Although Sjögren's syndrome is commonly known as "dry eyes and dry mouth syndrome," it can also affect other organs such as the lungs, kidneys, lymphatic system, and neurological system.

I have scleroderma. How likely is it that I also have Sjögren's syndrome?

It is estimated that about 20% of patients with systemic scleroderma also have Sjögren's syndrome. This is the autoimmune disease that is the most commonly associated with scleroderma. Patients with limited scleroderma or with anti-centromere autoantibodies are more likely to develop Sjögren's syndrome. However, patients may experience dry eyes or mouth due to other causes like medication side effects.

How can we diagnose Sjögren's syndrome?

The diagnosis of Sjögren's syndrome is based on a combination of clinical symptoms, blood markers, and disease-specific tests. Blood markers such as anti-SSA, anti-SSB, and anti-Ro52 can be markers of Sjögren's syndrome. An oral medicine specialist can measure the amount of saliva produced to confirm a dysfunction of the salivary glands, and an ophthalmologist can assess dry eyes using the Schirmer test (which measures the amount of tears produced over a five-minute period) and tests to detect any damage to the surface of the eye caused by a lack of tears. A biopsy of the salivary glands in the lip may also be performed to confirm the diagnosis; however, this procedure is rarely required in the context of scleroderma, as the results usually do not change the treatment being administered for Sjögren's syndrome.

How do we treat Sjögren's syndrome?

Treatment for Sjögren's syndrome primarily aims to relieve the symptoms of dry eyes and dry mouth. Some environmental and lifestyle changes are recommended to prevent worsening of these symptoms (see Tables 1 and 2).

For dry eyes, over-the-counter artificial tears in the form of eye drops can be used throughout the day. If eye drops are not effective enough, artificial tears in the form of gels can be tried. Ointments are best used at bedtime to avoid blurred vision. Preservative-free products are preferred and can be applied every 2 to 4 hours, whereas products with preservatives may increase inflammation if used more than 4 times a day. If symptoms persist, your ophthalmologist may recommend more intensive treatments. Omega-3 supplements (2000 to 3000 mg per day) may also help with symptoms.

For dry mouth, sugar-free products such as chewing gum and candy can help stimulate salivation. It's important to use sugar-free products to prevent tooth decay. Long-lasting lozenges can also be inserted inside the mouth. Saliva substitutes (artificial saliva) are available over the counter in mouthwash, spray, or gel form.

Oral medications to stimulate saliva and tear production (pilocarpine - Salagen®; anethole trithione - Sialor®) may be prescribed if the above treatments are not effective. These medications are effective in improving dryness in 60-70% of patients and may also improve dryness of the skin, nose and vagina. These drugs can cause side effects such as hot flashes, sweating, nausea, headaches and increased urination, but can be well tolerated when dosages are adapted and when taken with food. They are not recommended for people with angle-closure glaucoma, severe asthma, or liver dysfunction.

It is strongly recommended that people with Sjögren's syndrome have regular dental checkups every 3 to 6 months because of the increased risk of tooth decay. High fluoride toothpastes, mouthwashes, gels, and varnishes may be prescribed to prevent cavities.

Are there any other complications to watch for in Sjögren's syndrome?

People with Sjögren's syndrome should also be monitored for complications involving internal organs, such as the lungs, kidneys, lymphatic system, and neurological system. This includes a medical questionnaire, physical examination, and annual blood tests. It is important to report symptoms such as involuntary weight loss, persistent swelling of the salivary glands (in front of the ears or under the jaw), or swollen lymph nodes to your doctor, as these symptoms can be indicative of lymphoma, a complication that can affect around 5% of people with Sjögren's syndrome.

Conclusion

Sjögren's syndrome is an autoimmune disease that can affect people with scleroderma and cause dry mouth and dry eyes. The main focus of treating this syndrome is to relieve the symptoms by optimizing the environment and lifestyle, using local treatments, and prescribing medications when needed. Regular check-ups with specialists in rheumatology, ophthalmology and dentistry are recommended to ensure proper treatment and to detect possible complications.

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Table 1
Tips to improve dry eyes by making environmental and lifestyle changes

- Avoid being in low-humidity environments.
- Use a humidifier in your bedroom to increase moisture in the air.
- Avoid being in areas with cold air currents, such as those created by air conditioners or fans.
- Stay away from smoke and dust.
- Avoid using eye makeup.
- Take short breaks with eyes closed when reading or using a computer to reduce strain.
- Apply warm compresses to the eyelids for 5 to 10 minutes at a time, 2 to 4 times a day to increase glandular secretion.
- Avoid wearing contact lenses. If you must wear contact lenses, use disposable lenses and replace them daily.
- Wear safety glasses with side shields or moisture chamber glasses that slow the evaporation of tears (such as Ziena® or 7eye® glasses).
- Consult your doctor about medications that may cause dry eyes and that can be avoided.

* Table adapted from the **Guide de traitement de la xérophtalmie et de la kératoconjonctive sèche chez les patients atteints du syndrome de Sjögren** (A Treatment Guide for Xerophthalmia and Kerato-conjunctiva Sicca in Patients with Sjögren's Syndrome), with kind permission from Dr. Alexandra Albert and Dr. Marie-May Collin-Castonguay.

Table 2
Tips to improve dry mouth by making environmental and lifestyle changes

- Stop smoking, as it can dry and irritate the mouth and increase the risk of developing candidiasis (fungal infection) and periodontitis (gum disease).
- Stay hydrated by drinking small amounts of water frequently to keep your mouth moist.
- Gargle with olive oil or coconut oil to soothe your mouth.
- Avoid acidic or sweet drinks such as carbonated soft drinks, caffeinated drinks (coffee, tea, energy drinks) and alcohol.
- Avoid acidic foods such as citrus fruits, kiwi, pineapple, strawberries, etc.
- Avoid very hot drinks or foods.
- Avoid very dry or hard foods.
- Avoid very spicy foods.
- Accompany foods with sauces to make them easier to swallow.
- Prefer meats that have been simmered or cooked in foil.
- Prefer fatty meats.
- Avoid sweet, sticky foods to reduce the risk of tooth decay.
- Brush your teeth after each meal. If you cannot, rinse with water.
- Floss daily.
- Consult your doctor about medications that may cause dry mouth and that can be avoided.

* Table adapted from the **Guide de traitement de la xérostomie chez les patients atteints du syndrome de Sjögren** (A Treatment Guide for Xerostomia in Patients with Sjögren's Syndrome) with kind permission from Dr. Alexandra Albert and Dr. Marie-May Collin-Castonguay.

II SYMPTOMS AND COMPLICATIONS

Raynaud's Phenomenon and Scleroderma-related Digital Ulcers

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With the collaboration of
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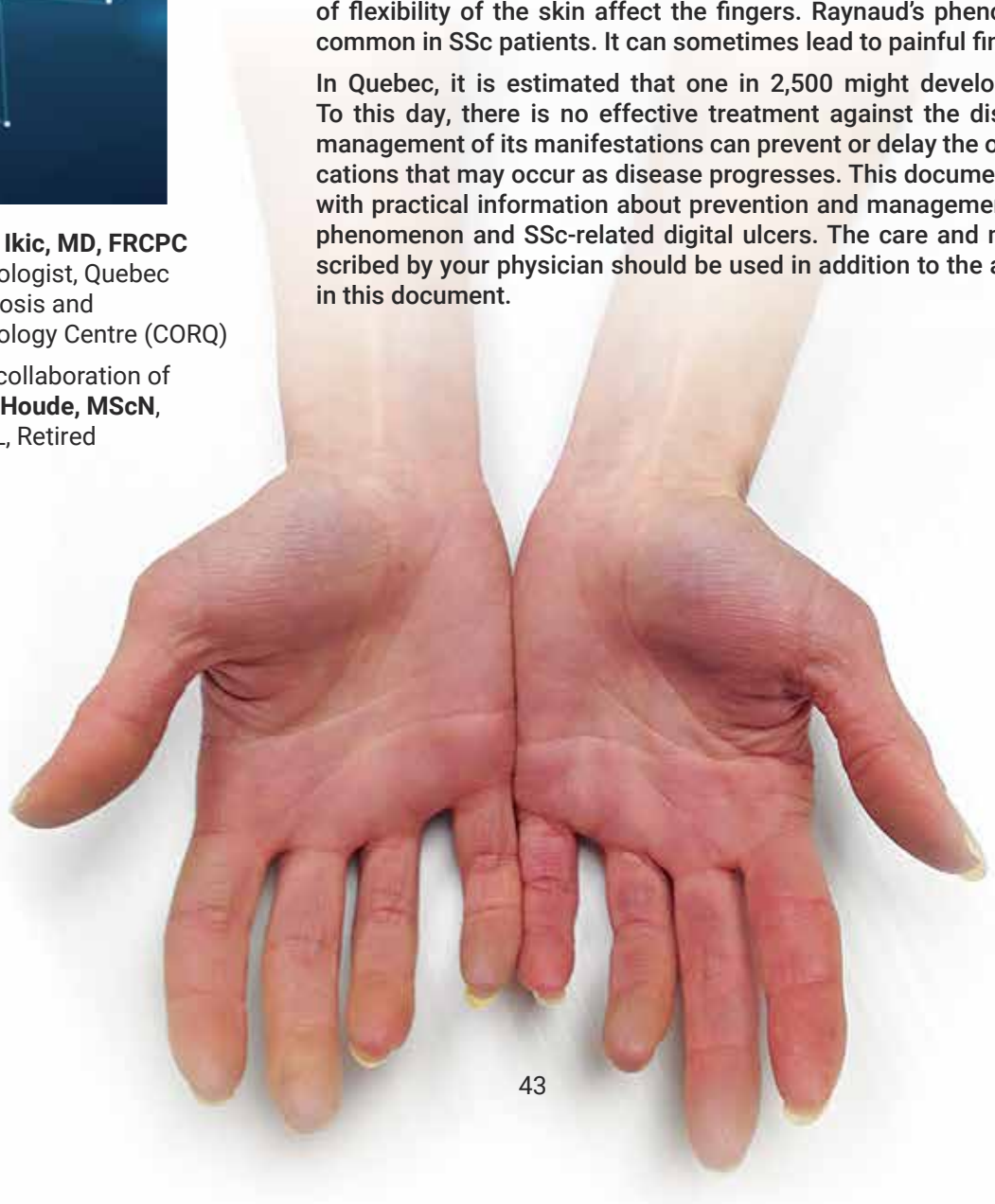
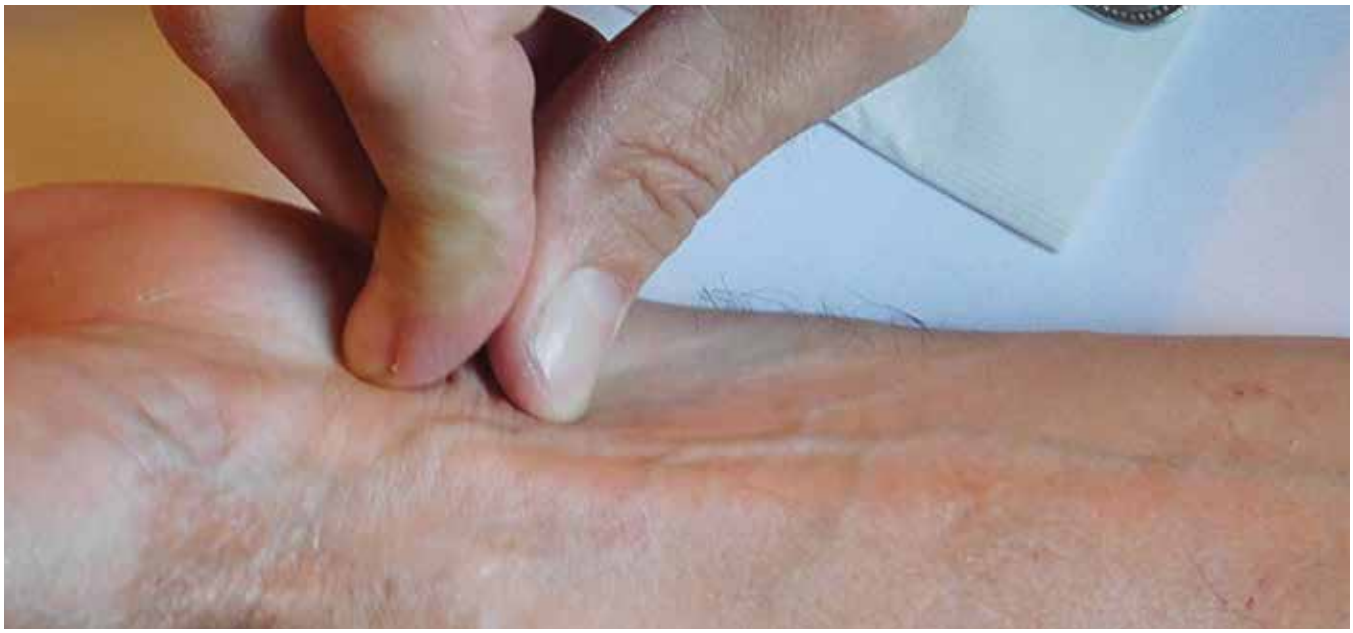
Systemic Sclerosis (SSc) is an autoimmune disease that can affect various organs, in addition to the skin. In almost all cases, the thickening and loss of flexibility of the skin affect the fingers. Raynaud's phenomenon is very common in SSc patients. It can sometimes lead to painful fingertip ulcers.

In Quebec, it is estimated that one in 2,500 might develop scleroderma. To this day, there is no effective treatment against the disease. Efficient management of its manifestations can prevent or delay the onset of complications that may occur as disease progresses. This document provides you with practical information about prevention and management of Raynaud's phenomenon and SSc-related digital ulcers. The care and medication prescribed by your physician should be used in addition to the advice provided in this document.





REMINDERS ABOUT THE DISEASE

What "Systemic Sclerosis (SSc)" stands for

The term "Scleroderma" means

Hardening (sclero) of the skin (derma). This disease is characterized by the thickening and reduced flexibility of the skin of the fingers and other body parts.

The term "Scleroderma" means hardening (sclero) of the skin (derma).

This disease is characterized by the thickening and reduced flexibility of the skin of the fingers and other body parts:

- The heart
- The lungs
- The kidneys
- The digestive system
- Muscles
- Joints

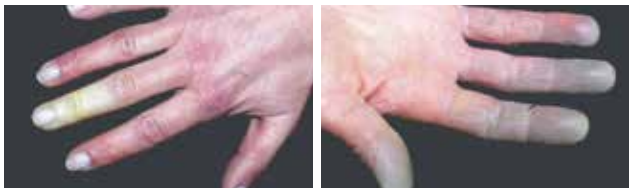
What is the cause of Scleroderma?

The cause of Scleroderma is unknown. It is an autoimmune disease in which the body produces antibodies against itself. The overproduction of collagen in the skin and in some organs of the body causes their hardening, a process called "fibrosis".

Common manifestations of vascular involvement in SSc patients

1. Raynaud's phenomenon:

It is a disorder resulting in the reduction of blood circulation in the fingers and toes, which is typically characterized by colour changes. The body's extremities can vary in colour from white through blue, and sometimes red. This is usually triggered by cold, sudden temperature changes or stress.



About 10% of the population is affected by Raynaud's phenomenon, whereas 95% of SSc patients have Raynaud's.

2. Digital ulceration:

It is a wound which develops mostly on the fingers. Ulcers are painful and difficult to heal. In the most severe cases, necrosis (death of tissue) and amputation may occur.

Types Of SSC-Related Digital Ulcers

Digital ulcers occur in 50% of scleroderma patients. They should be taken seriously, as they are painful, interfere with daily activities and tend to recur.

It is essential to conduct regular self-examinations of the hands to detect the presence of ulcers and to notify your specialist physician as soon as one is suspected.

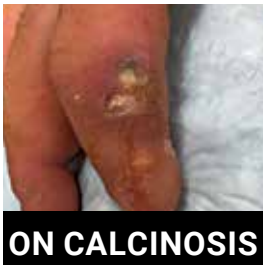
There are 3 types of ulcers

Reduction of the blood flow

Traumas

Dryness of the skin

Hand deformations



Calcinosis refers to a calcium deposit under the skin

Preventing Raynaud's Phenomenon and ulcer care

- Stop smoking.
- Always tell your pharmacist when you start a new medication, either prescription or over-the-counter, because some may cause or worsen.
- Raynaud's phenomenon.
- Protect your entire body against the cold and wind. It is easier to keep your body heat than to warm it once it's already cold:
  - Cover your head and neck;
  - Protect your hands with gloves (e.g. silk gloves in summer, mittens in winter);
  - Use gloves with hand-warmer packs or heated mittens in winter;
  - Wear footwear with thick soles and waterproof seams in cold weather;
  - Dress in layers, according to planned activities, for optimal moisture transfer and body heat retention.
- Avoid sudden temperature changes (e.g. air conditioning, cold water, food in the refrigerator or freezer, cold metal objects) by protecting your hands with gloves.
- Identify and avoid potential traumas for they may contribute to the development of ulcers:
  - Typing on the computer keyboard, sewing, gardening...;
  - Cooking, tinkering, cutting nails.
- Learn to manage stress because it can trigger Raynaud's phenomenon.
- The goal of treating digital ulcers is to prevent loss of the tissue that forms the skin layer of the fingertips, to prevent infection, and to relieve pain.

Despite these precautions, if Raynaud's occurs, quickly put your hands in a warm place (e.g. warm water or under your armpits) to improve blood circulation.

Skin care

It is essential to provide special care for your skin. Ulcers on the fingers can be a source of pain, stress or frustration as they can affect all activities of daily living. Here are some ways to help you take care of your skin.

Products recommended by my healthcare team:

Do's

- Use mild soaps or soap-free cleansers.
- Moisturize the skin every day during daily cleansing.
- Massage the skin to soften it with fragrance and allergen-free sensitive skin creams.
- Remember to moisturize the skin after each hand washing
- Do regular exercises to fight against joint deformations, according to the recommendations of your specialist physician and occupational therapist.
- Wear an orthosis if prescribed by your specialist physician.

Dont's

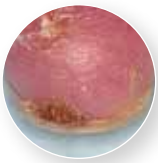
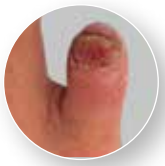
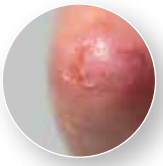
- Use foaming scented soaps because they may dry out the skin and cause irritation.
- Take hot baths because by macerating the skin it could further compromise the skin integrity.
- Dry your hands by rubbing them together vigorously: blot them up gently instead.
- Use antiseptic gels because they can dry out the skin.

Patient involvement in ulcer care

Describing wound's appearance

Skin acts as a natural barrier against the external environment. When an ulcer occurs, a natural repair process begins: wound healing (i.e. scarring). Your role in caring for digital ulcers is to:

- **NOTIFY** your specialist physician as soon as an ulcer occurs so that he/she can assess it and start or adjust treatment if needed.
- Learn how **TO DESCRIBE THE APPEARANCE** of your wounds.

APPEARANCE AND DESCRIPTION OF WOUNDS	MEANING	PURPOSE OF TREATMENT
	**YELLOW** Presence of yellow or grayish debris, sometimes moist.	Cleaning the wound to eliminate the debris
	**RED** Healthy, bright red, shiny tissue. This indicates that wound healing is well under way.	Stimulating the healing process.
	**PINK** Pinkish or lavender, shiny tissue, pearlescent and fragile in appearance. The wound is now closed.	Protecting the healing wound site.
	The appearance of ulcers shown below is a warning sign indicating that you should be quickly assessed by a physician.	
	**BLACK** The wound is covered by a black or brownish crust with a leather-like texture. There is a risk of losing part of the finger.	Cleaning the wound to eliminate this type of tissue.
	**GREEN** The wound is infected. There is redness, a sensation of heat, discharge and increased pain. A bad smell can also emanate from the wound.	Cleaning the wound and treating the infection.

Ulcer care

- If the pain is too strong, take the prescribed pain medication 30 to 60 minutes before beginning care.
- Wash your hands with a mild soap under tap water.
- Dry your hands with a disposable towel (e.g. "paper towel") or a clean cloth towel and blot them up gently without rubbing.
- Clean the ulcers to remove debris with physiological saline solution and dry them with a clean gauze pad cover with the recommended dressing.

The choice of dressing is very important to promote wound healing. The idea is to keep ulcers moist (but not too much!) and protect them from traumas. The dressings prescribed by your doctor or nurse are chosen according to the appearance of your ulcers.

Recipe to prepare physiological saline solution at home:

1/2 teaspoon of salt in 250 ml of water boiled for at least one minute. This solution can be stored for 24 hours at room temperature.

TIP:

Avoid applying antiseptics, disinfectants and creams or antibiotic ointments directly on the wounds unless advised by your doctor.

Regular ulcer self-monitoring

- Number each ulcer.
- Enter assessment date for each ulcer.
- Describe the appearance of each ulcer.
- Note the type of dressing being used.

TIP:

If you can, take pictures of your ulcers once a week in order to facilitate follow-up assessments by your healthcare team.

Checklist

Remember that it is essential to:

- Protect your hands from the cold and traumas.
- Moisturize your skin with fragrance-free, sensitive skin products.
- Consult your specialist physician promptly when an ulcer occurs.
- Take time to record the appearance of each of your ulcers and initiate proper treatment.

II SYMPTOMS AND COMPLICATIONS

Pulmonary Fibrosis in Systemic Sclerosis

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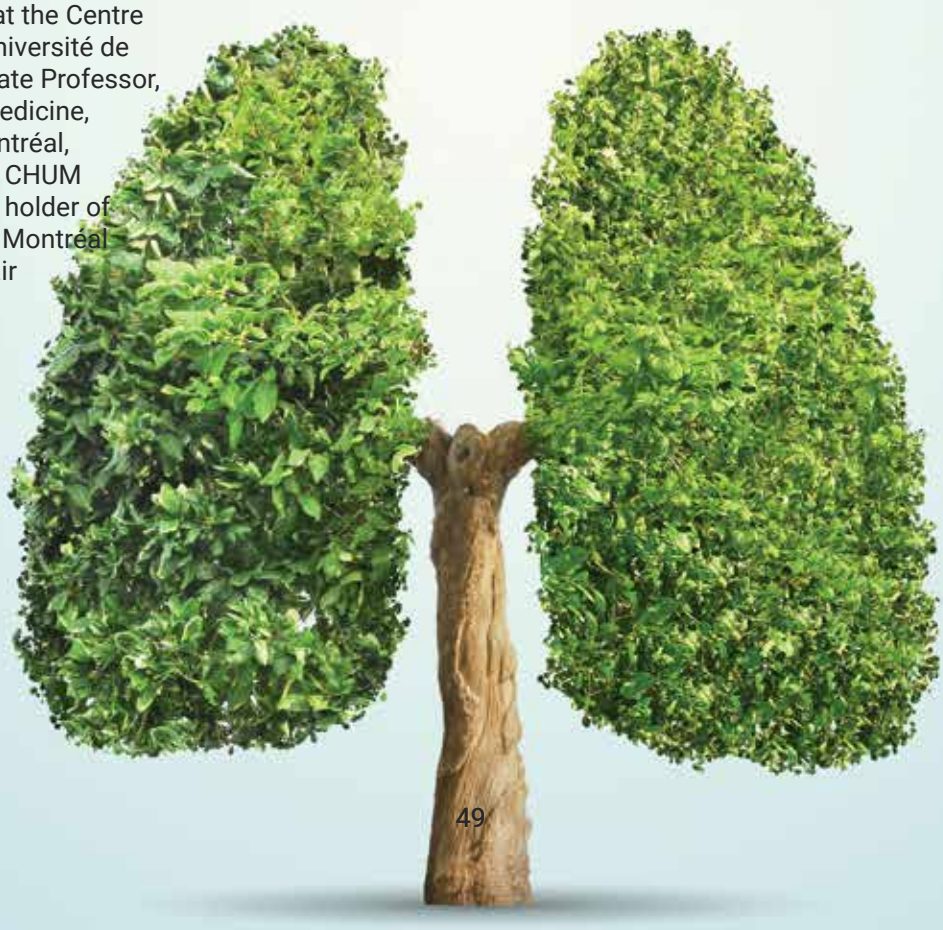
Systemic sclerosis (SSc, systemic scleroderma) is a disease characterized by abnormalities in the functioning of small blood vessels and of the immune system, ultimately leading to inflammation and excessive fibrosis (hardening) of the skin and various organs. When the inflammation and fibrosis reach the lungs, it is called "interstitial lung disease" (ILD) or "pulmonary fibrosis".



Who is at risk of developing pulmonary fibrosis in systemic sclerosis?

Pulmonary fibrosis is a common manifestation of systemic sclerosis, being present in about half of the patients. However, pulmonary fibrosis is severe in only about 15% of patients. Patients who are men, of Black race, with the diffuse form of systemic sclerosis, with anti-topoisomerase I (Scl-70) autoantibodies or who have cardiac, muscular or upper gastrointestinal disease may be at higher risk of developing severe pulmonary fibrosis.

What are the symptoms of pulmonary fibrosis?

Pulmonary fibrosis often presents itself silently in the early stages of the disease. With more severe involvement, patients may have symptoms of fatigue, decreased exercise capacity, shortness of breath and a persistent dry cough. However, in a sedentary patient, pulmonary fibrosis may remain asymptomatic even in more advanced stages of the disease.

How is pulmonary fibrosis diagnosed?

Physical examination may reveal abnormalities during the auscultation of the lungs with the stethoscope. A chest X-ray may reveal more advanced changes in pulmonary fibrosis, but a high-resolution chest CT scan is a better test to detect pulmonary fibrosis in its earliest stages. Pulmonary function tests (PFTs) are useful to measure the severity of lung function impairment. The six-minute walk test, during which blood oxygenation and walking distance reached after 6 minutes are measured, can also be useful in assessing the severity of the disease.

Given that pulmonary fibrosis in systemic sclerosis is often silent, periodic screening is recommended in all patients, knowing that appropriate treatment started early will result in better outcomes.

What are the treatments for pulmonary fibrosis?

According to current guidelines, indications for initiating treatment for pulmonary fibrosis are:

- the presence of respiratory symptoms attributable to pulmonary fibrosis;
- moderate to severe involvement as evidenced by thoracic CT scan and pulmonary function tests;
- worsening of pulmonary fibrosis as evidenced by thoracic CT scan or lung function tests.

There are now two classes of medications used in the treatment of pulmonary fibrosis associated with systemic sclerosis. First, immunosuppressive medications, such as mycophenolate mofetil (Cellcept®), cyclophosphamide and rituximab, work by decreasing the activity of the immune cells responsible for inflammation. These medications can slow the progression of pulmonary fibrosis associated with systemic sclerosis. Mycophenolate is commonly used as a first-line treatment because a randomized trial showed that it is as effective as cyclophosphamide and has a better safety profile.

Recently, a randomized trial also showed that an anti-fibrotic medication, nintedanib (Ofev®), is effective in slowing the progression of systemic sclerosis-associated pulmonary fibrosis compared to placebo. Nintedanib is now approved by Health Canada. Although this medication is new in its use in systemic sclerosis, it has already been used for several years in the treatment of idiopathic pulmonary fibrosis (IPF).

When a medication is started for the treatment of pulmonary fibrosis, the patient is assessed monthly with blood tests to detect side effects of the medication. Pulmonary function tests are repeated every 3 to 6 months to determine the effectiveness of the treatment. Success is currently defined as stabilization of the disease.

Research studies are underway to determine whether earlier treatment in the mild stage of pulmonary fibrosis could be effective in preventing more severe involvement over the years. Considering that immunosuppressive and anti-fibrotic treatments may cause side effects, the decision to begin treatment should be made after assessing the risk of toxicity of the treatment compared to the expected benefits.

To reduce the risk of complications associated with certain infections when taking immunosuppressive medications, it is recommended to get the flu shot once a year and to get vaccinated against the pneumococcal bacteria (a cause of severe pneumonia) every five years. If the patient is a smoker, it is recommended to quit smoking to avoid further damage to the lungs. In patients with gastroesophageal reflux disease (GERD), it is recommended that this condition be treated aggressively in order to prevent further damage to the lungs due to reflux and aspiration of gastric contents into the lungs.

Home oxygen administration can be used for patients with very severe pulmonary fibrosis. Finally, in very advanced cases not responding to treatment, an autologous stem cell transplant or a lung or heart-lung transplant may be considered after a detailed medical and multidisciplinary assessment.

In summary

Pulmonary fibrosis is a common and potentially serious complication of systemic sclerosis. Careful monitoring by treating physicians and appropriate early treatment can improve the quality of life and life expectancy of patients with systemic sclerosis.

II SYMPTOMS AND COMPLICATIONS

Pulmonary Arterial Hypertension in Systemic Sclerosis

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Dr. Tamara Grodzicky, MD, FRCPC
Rheumatologist, clinical researcher at the CHUM Research Centre

Pulmonary arterial hypertension (PAH) means "high pressure in the arteries of the lungs". PAH is different from systemic arterial hypertension, which is usually referred to as "high blood pressure" and measured at the upper arm with a blood pressure monitor.

Understanding PAH in Systemic Sclerosis

PAH in systemic sclerosis is due to an exaggerated and progressive narrowing of the small blood vessels in the lungs. This is caused, on the one hand, by the increased presence of molecules (chemical signals) that promote the contraction and obliteration of the pulmonary arteries, and on the other hand, by a relatively insufficient quantity of molecules that promote their dilation. The factor that triggers this imbalance is unknown.

When the blood vessels in the lungs are narrowed, it is harder for the blood to circulate and get oxygenated. As a result, the level of oxygen in the blood becomes reduced, leading to suboptimal oxygenation of the body's organs and tissues.

The danger of having persistently very high pressure in the arteries of the lungs is also due to the fact that it makes it harder for the right side of the heart to pump blood through the lungs. Over time (several years), this eventually causes the right side of the heart to fail (right-side heart failure).

Who is at risk of developing PAH?

PAH occurs in 10 to 15% of patients with systemic sclerosis. PAH is most often associated with the limited form of systemic sclerosis and with more than 5 years of disease. The presence of certain autoantibodies, including anti-centromere, anti-U1-RNP, anti-Th-To and anti-U3-RNP (fibrillarin), are also risk factors for PAH.

What are the symptoms of PAH?

PAH is often silent at first, but over time it can cause a variety of symptoms: shortness of breath and fatigue during physical exertion, chest pain, impending loss of consciousness or even unconsciousness (syncope) in more advanced cases.

Physical examination by the doctor is often not very revealing in the early stages, but it will show signs of heart dysfunction in more severely affected people. In these latter cases, the examination will show, for example, abnormal auscultation of the heart with the stethoscope and, in the event of heart failure, abnormal distension of the neck veins and swelling (edema) of the feet and legs.

How to screen for PAH?

Given the absence of specific symptoms at the onset of PAH, rheumatologists routinely screen all systemic sclerosis patients using pulmonary function tests (PFTs) and echocardiograms. A blood test for NT-proBNP, a specific marker for the heart, can also be used for screening. These tests are done annually in patients at higher risk of developing PAH, such as patients with the limited form of systemic sclerosis and long disease duration, or those with autoantibodies specified earlier.

When PAH is suspected, a more invasive type of investigation, i.e., catheterization of the right side of the heart, is necessary to confirm the diagnosis. This is performed by a cardiologist. The pressure in the pulmonary arteries is then measured directly using a catheter inserted through a vein in the crease of the elbow or the groin.

Other tests may also be performed at this time to rule out other potential causes of pulmonary hypertension, such as heart disease, small clots in the lungs, lung fibrosis or emphysema, or sleep apnea.

Treatment for PAH in systemic sclerosis

Given the complexity of the diagnosis, initial assessment, administration of certain medications and follow-up, patients suspected of having PAH are referred to specialized centres for management, with concomitant follow-up by the treating rheumatologist.

Indications for starting treatment for PAH include confirmation of the diagnosis by cardiac catheterization and the presence of symptoms (shortness of breath on physical exertion) with moderate to severe functional impairment. Treatments for PAH act by dilating vessels that are too narrowed, thus reducing the high pressure in the pulmonary arteries. Medications for PAH work through different mechanisms:

- Endothelin-1 receptor antagonists: bosentan (Tracleer®), ambrisentan (Volibris®) and macitentan (Opsumit®);
- Phosphodiesterase-5 inhibitors: sildenafil (Revatio®) and tadalafil (Adcirca®); Soluble guanylate cyclase stimulator: riociguat (Adempas®);
- Prostacyclins: epoprostenol (Flolan®), treprostinil (Remodulin®) and selexipag (Uptravi®).
- Activin signaling inhibitor: sotatercept (Winrevair®)

In patients with moderate functional impairment, medications from the first two categories above are used alone or in combination. These medications are often prescribed in combination and selected based on the severity, progression, and the patient's specific medical condition. If the disease is progressive or severe with symptoms at the slightest exertion, then inhaled, subcutaneous or intravenous prostacyclins may be added.

Concomitant treatment with medications such as diuretics (e.g., furosemide/Lasix®) and inotropic agents (improve the contractility of the heart muscle) are also useful for treating heart failure. Home oxygen therapy is reserved for patients with very severe disease. As a last resort, there is the option of lung or heart-lung transplantation, after a detailed medical and multidisciplinary assessment.

The follow-up of patients with PAH is done through a medical questionnaire, physical examination, and periodic investigations: blood samples, echocardiogram, pulmonary function test and in some cases, a repeat cardiac catheterization. The 6-minute walking distance can also be used to evaluate the effectiveness of treatment, typically associated with decreased shortness of breath and improved tolerance to physical exertion, which translates to the ability to walk farther in 6 minutes.

In summary

PAH is a serious complication of systemic sclerosis. However, over the past two decades, several new medications have been studied and approved for the treatment of PAH and can improve the quality of life and life expectancy of systemic sclerosis patients with PAH. Given that PAH is often a silent disease in its early stages, it is essential to screen at-risk patients in order to make an early diagnosis and begin treatment if indicated.

II SYMPTOMS AND COMPLICATIONS

Cardiac Involvement in Systemic Sclerosis

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Systemic sclerosis (or systemic scleroderma) is a disease characterized by abnormalities in the functioning of small blood vessels and of the immune system, ultimately leading to inflammation and excessive fibrosis of the skin and various organs, including the heart.

Who is at risk of developing cardiac involvement?

Cardiac involvement occurs in 10 to 30% of patients with systemic sclerosis. Cardiac involvement occurs in both the limited and diffuse forms of the disease, but is generally more frequent and severe in patients with diffuse disease with rapidly progressing skin involvement and in those with associated myositis (inflammation of the muscles).

What are the symptoms of cardiac involvement?

Symptoms indicative of cardiac involvement include:

- Unusual shortness of breath or fatigue (tiredness) during physical exertion;
- Shortness of breath at rest;
- Shortness of breath when lying down;
- Awakening during the night due to shortness of breath;
- Painless swelling of the feet and legs (edema);
- Chest pain that increases with physical exertion (angina);
- Chest pain aggravated by inspiration (breathing in) and when lying down;
- Palpitations or feeling that the heartbeat is irregular or abnormal;
- Dizziness or fainting;
- Generalized fatigue (tiredness).

It should be pointed out that a number of very different heart problems can cause identical symptoms. Therefore, the doctor will proceed to a more in-depth evaluation in order to determine the underlying cause of these symptoms and decide on the most appropriate course of treatment.

What are the cardiac manifestations of systemic sclerosis?

Patients with systemic sclerosis can have cardiac problems that are directly caused by systemic sclerosis (small vessel abnormalities, inflammation, fibrosis), but can also have heart diseases commonly found in the general population around the age of 50, which is also the typical age at onset of systemic sclerosis (e.g., atherosclerotic coronary artery disease, valve problems, heart problems related to high blood pressure or "hypertension", etc.).

Cardiac involvement associated with systemic sclerosis can be classified according to the affected component of the heart (see Table for details):

Diseases of the pericardium (envelope of the heart):

- **Acute pericarditis:** inflammation of the pericardium;
- **Pericardial effusion:** accumulation of fluid around the heart; may be related to kidney damage or pulmonary arterial hypertension (high pressure in the arteries of the lungs);
- **Constrictive pericarditis:** compression of the heart due to prolonged inflammation and excessive fibrosis of the pericardium (rare).

Diseases of the myocardium (heart muscle):

- **Myocardial fibrosis:** hardening of the heart muscle caused by excessive collagen deposition;
- **Myocarditis (acute or chronic):** inflammation of the heart muscle; may be associated with inflammatory muscle disease (myositis);
- **Heart failure:** reduced ability of the heart to function; may be caused by myocardial fibrosis, acute or chronic myocarditis, high blood pressure (measured at the upper arm with a blood pressure monitor), pulmonary arterial hypertension, vascular disease or other causes.

Vascular diseases (vessels in the heart)

- **Microvascular ischemia:** abnormalities of small blood vessels that constrict (narrow) spasmodically (as in Raynaud's phenomenon), leading to a decrease in oxygen supply to the tissues of the heart, which over time may lead to myocardial fibrosis.

Heart rhythm disorders (electrical system in the heart)

- Arrhythmias and heart blocks: abnormal heart rhythm that is too fast or too slow, due to a disruption in the flow of electrical current through the different parts of the heart; can be caused by myocardial fibrosis, myocarditis, pulmonary arterial hypertension or other causes;
- Dysfunction of the autonomic system: abnormal control of blood pressure and heart rate; may be an early sign of myocardial fibrosis.

How to screen for cardiac involvement in systemic sclerosis

Given the sometimes silent progression of the various cardiac abnormalities, it is important to perform a targeted cardiac assessment approximately once a year. This involves a questionnaire and physical examination, as well as certain screening tests such as an electro-cardiogram (or EKG, measures the passage of electrical current through the heart) and an echocardiogram. Further tests are sometimes necessary depending on the symptoms reported (stress tests, cardiac magnetic resonance, Holter, cardiac catheterization). Once detected, cardiac problems associated with systemic sclerosis usually require a consultation and concomitant follow-up with a cardiologist.

CARDIAC MANIFESTATION	DESCRIPTION	SYMPTOMS/SIGNS	INVESTIGATIONS	TREATMENT
Acute pericarditis	Inflammation of the envelope of the heart	Constant chest pain, aggravated by deep breathing and when lying on the back	• Electrocardiography • Echocardiography +/- Cardiac MRI	• Anti-inflammatory drugs • Colchicine • Prednisone
Pericardial effusion	Accumulation of fluid around the heart	Accumulation of fluid around the heart		• Observation (if asymptomatic) +/- Drainage
Constrictive pericarditis	Compression of the heart due to inflammation/ fibrosis of the pericardium	Shortness of breath, fatigue, swelling of the stomach and legs		• Pericardiectomy (surgery to decompress the heart)
Myocardial fibrosis	Hardening of the heart muscle caused by excessive deposition of collagen	Often asymptomatic; symptoms of heart failure and/or heart rhythm disorders (see below)	• Echocardiography • Cardiac MRI	• Monitoring +/- treatments for heart failure and rhythm disorders
Myocarditis	Inflammation of the heart muscle	Symptoms of heart failure and/or heart rhythm disorders (see below)	• CK, troponin (blood) • Echocardiography • Cardiac MRI • Catheterization, biopsy	• Prednisone • Immuno-suppressants • Treatments for heart failure
Heart Failure	Reduced ability of the heart to contract and/or relax	Shortness of breath on exertion or at rest, aggravated when lying on the back; swelling of feet, fatigue, weight gain	• Echocardiography • Investigations for underlying causes	• Treatment according to underlying cause • Diuretics
Microvascular ischemia	Abnormalities in the small blood vessels of the heart	Chest pain aggravated on exertion or by cold weather (angina), shortness of breath	• Scintigraphy or echocardiography with exercise or stress test • Coronarography	• Aspirin, statins, nitrates, calcium channel blockers
Arrhythmias and heart blocks	Abnormal heart rhythm that is too fast or too slow	Palpitations (abnormal heartbeat), shortness of breath, chest pain, dizziness, fainting	• Electrocardiography • «Holter» monitor for 24-48 hours	• +/- Anti-arrhythmic drugs • +/- Catheter ablation • +/- Pacemaker
Dysfunction of the autonomic system	Abnormalities in the control of blood pressure and heart rate	Symptoms of low blood pressure (dizziness) when making the transition from lying down to standing up, exercise intolerance, abnormal sweating	• Blood pressure and heart rate in lying and upright positions • Tilt-table test	• Staying hydrated • Salt intake • Compression stockings • Standing up slowly

MRI: Magnetic resonance imaging

II SYMPTOMS AND COMPLICATIONS

Systemic Scleroderma and Cancer

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Cancer affects about two in five Canadians over the course of their lives [1]. Some individuals diagnosed with systemic scleroderma may also face a concomitant cancer diagnosis. This article discusses the association between scleroderma and cancer, as well as issues and precautions related to the treatment of scleroderma and cancer.

Is there an association between scleroderma and cancer?

Individuals with systemic scleroderma have a higher risk of cancer than the general population, particularly within the three to five years surrounding the scleroderma diagnosis. Research studies suggest that scleroderma may be a cross-reactive immune response that arises in the context of an anti-cancer response in certain individuals [2]. In other words, the immune system detects cancer cells, tries to fight them by producing antibodies, but also develops antibodies that recognize the body's normal cells (autoantibodies), leading to the development of scleroderma. When scleroderma develops simultaneously with cancer, it is referred to as "paraneoplastic scleroderma."

Who is at risk of cancer around the time of a scleroderma diagnosis?

The identified risk factors for paraneoplastic scleroderma are the presence of anti-RNA polymerase III and anti-U11/U12-RNP autoantibodies in the blood, as well as older age at the time of diagnosis. Anti-topoisomerase I (or anti-Scl70) autoantibodies may also be associated with a higher risk of paraneoplastic scleroderma, especially in older individuals. Traditional risk factors for cancer development, such as smoking, a strong family history of cancer, or significant unexplained weight loss, are additional elements that should raise suspicion of cancer [2].

Is there also a risk of cancer later in the course of scleroderma?

Certain manifestations of scleroderma and some medications used to treat scleroderma may also increase the risk of cancer later in the disease. For example, lung fibrosis can increase the risk of developing lung cancer after several years. Chronic irritation of the esophagus due to uncontrolled reflux may also increase the risk of esophageal cancer. Individuals with a concomitant autoimmune liver or thyroid disease may also be at higher risk for cancer affecting these organs. Finally, cyclophosphamide, an immunosuppressive drug used in severe forms of scleroderma, may increase the risk of bladder cancer and hematological cancers, particularly in smokers [2].

What types of cancer are most associated with scleroderma?

Individuals with scleroderma have a higher risk of lung, liver, esophageal, and blood cancers (multiple myeloma, leukemia, and lymphoma). Breast cancer is also associated with scleroderma, particularly in the year preceding or following the onset of scleroderma [2, 3].

Should I undergo tests for cancer screening?

All individuals with scleroderma should undergo cancer screening tests recommended for the general population based on age, sex, and other risk factors (see Table 1) [4], along with a thorough physical examination by their doctor. It is important to note that screening programs vary by province and evolve over time based on available scientific evidence.

For individuals with a recent diagnosis of scleroderma and the risk factors for paraneoplastic scleroderma mentioned above, additional investigations may be considered. Some experts suggest, for instance, annual mammograms, an abdominal-pelvic ultrasound or CT scan, or even a positron emission tomography (PET) scan. However, the optimal screening approach remains to be determined, as few studies currently guide screening practice in patients at higher risk for paraneoplastic scleroderma [2].

Finally, for individuals who have been treated with cyclophosphamide as an immunosuppressive therapy for severe manifestations of scleroderma, annual tests for blood and cancer cells in the urine are recommended to screen for bladder cancer [2].

TABLE 1

TYPE OF CANCER	TARGET POPULATION	RECOMMENDED SCREENING
Breast Cancer	Women aged 50 to 74 years	Mammogram every 2 to 3 years
Cervical Cancer	Women aged 21 to 69 years who are or have been sexually active	Pap test every 3 years; screening may cease at age 70 if 3 consecutive tests have been negative in the past 10 years
Colorectal Cancer	Adults aged 50 to 74 years	Fecal occult blood test every 2 years or sigmoidoscopy every 10 years
	Family history of colorectal cancer in a first-degree relative	Colonoscopy every 5 to 10 years, starting at age 40 to 50 or 10 years before the relative's age at diagnosis
Lung Cancer	Adults aged 55 to 74 with a significant smoking history, who are currently smoking or quit within the last 15 years	Low-dose CT scan

Can radiation therapy be used in the context of scleroderma?

One of the possible side effects of radiation therapy is an exaggerated fibrotic reaction at the site of radiation, including the skin (leading to localized scleroderma or morphea) or the lungs (leading to localized pulmonary fibrosis). For this reason, there is concern that radiation therapy could also worsen skin and lung fibrosis in individuals with systemic scleroderma. Systemic scleroderma is therefore generally considered a relative contraindication to radiation therapy. In fact, a few cases have been reported in the literature of the onset or worsening of skin or lung fibrosis in individuals with scleroderma who received radiation therapy, particularly in the context of breast cancer.

However, in a large recent study reporting the experience of nearly 70 women with systemic scleroderma who received radiation therapy for breast cancer, exaggerated local skin fibrosis in the irradiated breast area was observed in half of the patients, and localized lung fibrosis at the irradiation site was observed in only 10% of patients [(5)]. Moreover, no worsening of systemic scleroderma skin or lung involvement was observed.

Thus, radiation therapy is a therapeutic option that may be considered in individuals with systemic scleroderma but should be discussed, weighing the expected benefits on cancer against the potential associated risks.

Is chemotherapy safe in the context of scleroderma?

Chemotherapy is often the basis of cancer treatments, and the vast majority of these treatments are safe in the context of scleroderma. However, certain chemotherapies, notably taxanes (docetaxel, paclitaxel) and gemcitabine, are known to have the rare (<1%) side effect of inducing skin hardening similar to limited or diffuse scleroderma, and sometimes even severe Raynaud's phenomenon. Bleomycin can also induce pulmonary fibrosis and, more rarely, skin fibrosis [6, 7].

However, the safety of these drugs has not been specifically studied in individuals with systemic scleroderma. Nevertheless, given the rare but well-documented risks of drug-induced scleroderma, it is important that oncologists and rheumatologists discuss the risks, benefits, and treatment alternatives with the patient when such chemotherapy is being considered.

Can immune checkpoint inhibitors be used in the context of scleroderma?

Immune checkpoint inhibitors (such as nivolumab, pembrolizumab, and durvalumab) are drugs that help the patient's own immune system to fight their cancer. These drugs have revolutionized the treatment of certain otherwise incurable cancers. However, in some patients, these drugs can overstimulate the immune system, leading to the onset of new autoimmune diseases, including scleroderma (<1%).

The safety of these drugs in individuals with systemic scleroderma was studied in 17 patients: 4 (24%) of them experienced a severe flare of their disease. The risk may be higher in patients with diffuse scleroderma (flare in 3/9) than in those with limited scleroderma (flare in 1/9), and particularly in those with the anti-RNA polymerase III autoantibody (flare in 2/2) [8].

Ultimately, the risks and benefits of treatment with an immune checkpoint inhibitor must be discussed with the patient in close collaboration with their oncologist and rheumatologist.

Conclusion

In summary, individuals living with scleroderma are at a higher risk of developing cancer compared to the general population. Cancer screening is recommended and should be personalized based on age, sex, and risk factors. Radiation therapy, chemotherapy, and immune checkpoint inhibitors are therapeutic options that can be considered. Close collaboration between the rheumatologist, oncologist, and patient is necessary to discuss the risks, benefits, and treatment alternatives, in order to minimize the risks of exacerbating the autoimmune disease while maximizing the chances of curing the cancer.

II SYMPTOMS AND COMPLICATIONS

Gastrointestinal Involvement in Systemic Sclerosis

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Who is at risk of developing gastrointestinal disease in systemic sclerosis?

The digestive tract is involved in nearly all systemic sclerosis patients and can be present even in the absence of symptoms in half of patients.

The frequency is similar in diffuse and limited forms of systemic sclerosis. However, severe manifestations are uncommon, occurring in less than 10% of patients.

What causes digestive tract abnormalities in systemic sclerosis?

Abnormalities of the digestive tract are caused by the same pathophysiological mechanisms that affect all other organs in systemic sclerosis: there are early abnormalities in the small blood vessels, in the nervous system that controls the propulsive movements of the gut after a meal (peristalsis), and in the immune system (white blood cells and autoantibodies), eventually leading to weakening of the muscles of the digestive tract and fibrosis. The latter stage is often associated with more pronounced symptoms.

What are the gastrointestinal manifestations in systemic sclerosis?

The earliest and most common gastrointestinal manifestation is the malfunction (dysfunction) of the esophagus (the digestive tube that connects the mouth to the stomach). However, a dysfunction can affect the digestive tract at any level, from the mouth to the anus.

Oropharyngeal involvement (mouth and throat)

Fibrosis of the tissues of the mouth, including the tongue, soft palate (back of the palate) and larynx, as well as of the surrounding skin often leads to a narrowing of the mouth opening and can cause several problems due to stiffness and thinning of these structures. This leads to difficulties in chewing and swallowing food, especially when accompanied by a lack of saliva production due to salivary gland disease (sicca syndrome or Sjögren's syndrome). These problems may occur in up to 25% of patients.

Patients may be inconvenienced during meals, with a variety of symptoms: pain in the mouth, feeling that food sticks in the throat, retention of food in the mouth or throat, coughing after swallowing, small leakage of saliva and/or food at the corners of the mouth, and, rarely, aspiration of food into the lungs. Some patients may also have some difficulty speaking. Teething problems may also occur, such as malalignment of the teeth or abnormal wear (resorption) of the jaw bone and gums due to excessive pressure caused by tight facial skin.

The treatment of oropharyngeal problems remains mainly focused on prevention and support. It is important to maintain the flexibility of the facial skin through regular exercise. A physiotherapy consultation can be helpful for learning the most appropriate exercises and, in some cases, how to use stretching devices. Good dental hygiene and regular visits (at least twice a year) to the dentist can go a long way in preventing tooth decay. There are several models of toothbrushes and floss applicators that are suitable for patients with reduced hand mobility, and the advice of a dentist or occupational therapist may be helpful. The dentist can also suggest specialized mouthwashes and toothpastes that offer increased protection against cavities. It is important to contact the dentist when there is persistent abnormal pain or ulceration in the mouth, or when teeth become too loose.

To improve dryness of the mouth, one should drink water at regular intervals, eat soft foods, and use ice cubes, sugar-free gum or sugar-free candy. Also avoid tobacco, alcohol and dry foods. Severe rigidity of the mouth can make it difficult to drink from a regular glass. In this case, the use of a straw or specialized glass can be useful. If these measures are insufficient, the use of artificial saliva or certain medications that stimulate saliva production (Salagen®) may be considered, if indicated according to the treating physician. In more severe and advanced cases, local injections to increase the volume of the lips, as well as certain highly specialized surgical procedures, may be used to improve mouth closure and chewing.

Esophageal involvement (tube between the mouth and stomach)

Involvement of the esophagus is the earliest and most common gastrointestinal involvement in systemic sclerosis. It may occur in 90% of patients. It is characterized by a dysfunction in the motility of the esophagus (reduced or absent contraction movements) and by a reduction in the tightness of the closure between the esophagus and the stomach (lower esophageal sphincter). These abnormalities can be demonstrated by a barium meal, an esophageal transit scintigraphy and/or by esophageal manometry.

The symptoms most frequently associated with esophageal involvement are due to the following problems:

Gastroesophageal reflux disease

Gastroesophageal reflux disease (GERD) is caused by incompetence of the lower esophageal sphincter, which normally closes after food passes from the esophagus to the stomach. As mentioned above, this incompetence is one of the first abnormalities of systemic sclerosis and may be the reason that prompts someone to consult their doctor for the first time. The resulting loss of tightness allows the very acidic contents of the stomach to rise up into the esophagus and can lead to several symptoms: sensations of burning or pain (spasms) in the chest or stomach cavity after eating, which can also occur during the night.

Treatment for GERD is primarily based on lifestyle changes:

- Establishing and maintaining a normal weight because excess weight promotes GERD;
- Raising the head of the bed with blocks under the legs (pillows are ineffective);
- Eating several small meals at regular intervals, instead of 3 meals a day;
- Avoiding acidic, spicy, high-fat foods and some foods that are more difficult to digest (e.g., cabbage, onions, broccoli);
- Avoiding going to bed less than three hours after a meal;
- Quitting smoking or other tobacco products;
- Minimizing alcohol and caffeine intake.

It is worth noting that some medications used to treat other manifestations of systemic sclerosis, such as calcium channel blockers, (e.g., Adalat®) for Raynaud's phenomenon, can sometimes make GERD worse. If lifestyle modification is not enough, the most effective medications to treat GERD are proton pump inhibitors, or PPIs, e.g., pantoprazole (Pantoloc®), dexlansoprazole (Dexilant®), omeprazole (Losec®), esomeprazole (Nexium®), lansoprazole (Prevacid®) or rabeprazole (Pariet®). These medications are taken once a day and can be increased up to twice a day.

If GERD symptoms persist despite the treatments listed above, a gastroscopy (direct visualization of the esophagus and stomach through the passage of a tube by a gastroenterologist) is then indicated to rule out alternative causes of pain.

Surgery to correct GERD is reserved for patients with severe reflux that is refractory to any treatment, as it can sometimes worsen some digestive symptoms, and the benefits may not always be long-lasting.

Hypomotility

Decreased normal movement of the esophagus (hypomotility) may result in difficulty swallowing or a feeling that food sticks in the throat.

Unlike GERD, the treatment of hypomotility is mostly pharmaceutical, with agents that increase esophageal motility (contractions occurring in the esophagus), thus facilitating the propulsion of food through the tract (prokinetic drugs). The most commonly used medications are domperidone and metoclopramide (Metonia®) in the order of 10 mg four times a day, taken thirty minutes before meals. Erythromycin (250 mg three times a day, thirty minutes before meals) can sometimes be useful if the other medications have failed. However, because of the possibility of side effects and undesirable interactions with some other medications, these treatments should be prescribed and monitored with caution.

It is also important to avoid, if possible, or use with caution, certain medications that may increase the risk of esophageal ulceration in systemic sclerosis patients, such as tablet bisphosphonates used in the treatment of osteoporosis, such as alendronate (Fosamax®) or risedronate (Actonel®).

Stenosis

Narrowing of the esophagus (stenosis) may occur if GERD is prolonged and left untreated. This can lead to significant difficulty swallowing food (a feeling of food blockage in the chest or stomach) and regurgitation of fluid through the mouth. The treatment of stenosis involves the dilation of the stricture after a tube is passed through the esophagus (gastroscopy) by a gastroenterologist.

Infection

Some esophageal symptoms refractory to conventional treatments may be caused by a fungal infection (Candida). The diagnosis is made by gastroscopy and treatment is very effective: the drug nystatin in the form of a liquid suspension 400,000 to 600,000 units four times a day for two weeks, or fluconazole 100 mg once a day for seven days.

Gastric involvement (stomach)

Fibrosis of the stomach is often less pronounced than that of other parts of the digestive tract, which is why significant symptoms are uncommon. The main symptoms in more severe cases are slower emptying of gastric contents (gastroparesis) and, more rarely, bleeding from the stomach.

Gastroparesis

Slower emptying of gastric contents leads to a feeling of fullness soon after starting a meal, with more or less severe bloating and vomiting beginning a few hours after meals. Symptoms are often intermittent, with quiet periods that can last several months. However, this problem can lead to significant weight loss and nutritional deficiencies over time. Some tests may give indirect clues to the presence of gastroparesis (barium meal or gastroscopy), but the most reliable test is the gastric emptying scintigraphy in nuclear medicine. The treatment is similar to that for hypomotility of the esophagus (see above), but the drugs are less effective. During periods of vomiting, it is preferable to use certain medications that reduce nausea (such as Gravol® 50-100 mg or Stemetil® 10 mg three times daily) and to avoid solid foods.

Bleeding

Abnormal dilations of small blood vessels (telangiectasia) or veins (venous ectasia) are sometimes present in the stomach. These abnormalities can lead to more or less severe bleeding, resulting in anemia and new fatigue. If the bleeding is heavy, black stools or vomiting of blood may occur. But most often the bleeding occurs slowly and the only symptoms will be the progressive development of new fatigue and sometimes shortness of breath. Diagnosis and treatment (coagulation of the abnormal vessels by laser beam) require direct visualization by gastroscopy. These treatments are generally very effective, but usually need to be repeated periodically (e.g., several months apart). Surgical resection of part of the stomach is very rarely performed nowadays.

Involvement of the small intestine (small bowel)

Abnormalities in the function of the small bowel are reported in 20 to 60% of patients with systemic sclerosis. The symptoms most frequently associated with these abnormalities are due to the following problems:

Malabsorption

About 10-30% of systemic sclerosis patients suffer from malabsorption. Normally, the absorption of nutrients from ingested food is carried out specifically from the small intestine into the bloodstream. It should be pointed out that ordinarily bacteria residing in the small intestine, called the normal bacterial flora, play an important role in the digestion and absorption of food. However, in systemic sclerosis patients, the ability of the small intestine to contract effectively and, therefore, to propel food through the digestive tract may be reduced. This slowed intestinal transit promotes excessive development of the normal bacterial flora of the small intestine (bacterial overgrowth), leading to nutrient absorption problems.

Malabsorption is manifested by several symptoms that are usually intermittent: abdominal bloating, abdominal pain and constipation (stoppage of stool). When the problem becomes more serious and prolonged, diarrhea and weight loss may occur, eventually leading to more or less severe malnutrition. Malabsorption is often suspected by the doctor because of the typical symptoms reported by the patient. An examination in radiology ("small bowel study" or "small bowel transit") may then show abnormalities suggestive of small bowel involvement (dilated intestinal loops, slowed transit time and other abnormalities). This test may be falsely negative in the earlier stages. The best test to detect malabsorption is the "breath test". This test is done in nuclear medicine and consists of administering a predetermined load of sugar contained in a drink with subsequent measurement of the sugar degradation products in the air exhaled by the patient. An endoscopic investigation (introduction of a small tube through the mouth to the small intestine) by a gastroenterologist may sometimes be necessary for patients not responding to treatment, or when an alternative diagnosis is sought.

Treatment of malabsorption involves taking antibiotics by mouth to restore normal intestinal flora. This antibiotic therapy is typically administered cyclically, i.e., the antibiotic is taken intermittently (e.g., for 3 weeks at a time) with antibiotic-free intervals (e.g., for one week) since continued use of the same antibiotic is associated with poorer results. Also, there is usually a rotation in the antibiotics used. Thus, for example, the patient takes a first antibiotic during the first week, a second during the second week and a third during the third week, and then takes a break (no antibiotic) during the fourth week. The antibiotics most often used in this cyclic manner are amoxicillin with clavulanate, trimethoprim, cephalosporin, ciprofloxacin, metronidazole, and tetracycline. The previous examples are provided for general information purposes only, as the selection of antibiotics, their duration of administration, and the sequence of rotation necessary to achieve good symptom control must be tailored to each patient.

It is encouraging to know that, in our experience, cyclic antibiotic therapy is usually effective in stopping malabsorption and its symptoms. Some patients may even have a prolonged remission (several months) of malabsorption after a certain period of cyclic treatment.

Dysmotility

The abnormal movements of contraction and propulsion of food (dysmotility) that are so often present in the esophagus can also occur in the small intestine. Symptoms of small bowel dysmotility include abdominal pain, bloating, constipation, and in more severe cases, malabsorption as discussed in the previous section. The treatment of small bowel dysmotility is the same as for hypomotility of the esophagus, including agents that stimulate contractions of the gastrointestinal tract and thus the propulsion of food (prokinetic drugs, see above). Unfortunately, dysmotility of the small intestine sometimes responds less well to treatment than dysmotility of the esophagus.

Some patients with malabsorption may have extremely bothersome chronic diarrhea. In these cases, in addition to cyclic antibiotic therapy, administering octreotide (Sandostatin®) as a subcutaneous injection at bedtime can often greatly improve the diarrhea.

Pseudo-occlusions

Intestinal pseudo-occlusions are prolonged episodes of significant decrease in the contraction of the small intestine (severe dysmotility), with complete cessation of the progression of food through the gastrointestinal tract. These episodes are associated with severe abdominal pain, significant bloating, and even vomiting. The treatment of pseudo-occlusions in the acute phase involves stopping the intake of food or liquids through the mouth until the crisis is resolved, as improvement may occur spontaneously in several cases. When episodes of pseudo-occlusion are frequent and/or severe, prokinetic drugs may be tried with caution.

In more severe cases of pseudo-occlusion, a short hospital stay may be necessary to ensure proper hydration (administration of fluid through a vein). Abdominal surgery should generally be avoided in pseudo-occlusions related to systemic sclerosis.

Malnutrition

Malnutrition can occur in the context of multiple types of gastrointestinal involvement in systemic sclerosis. Between episodes of pseudo-occlusion, the patient should adhere to a lactose-free, low-fibre diet, and fats should be replaced by medium-chain triglycerides. Some patients require vitamin B12 injections, as well as calcium, iron and vitamin supplements. A consultation with a clinical nutrition specialist is often helpful.

If the various treatments available fail, including cyclic antibiotic therapy, a state of malnutrition may set in, gradually causing loss of muscle mass and weight loss. This condition is life-threatening. In a patient with partially preserved bowel function, a percutaneous gastrostomy tube (creation of an opening from the stomach to the skin) or jejunostomy tube (creation of an opening from the small intestine to the skin) may be placed to deliver nutrients directly into the digestive tract.

However, if the gastrointestinal tract is barely functioning, total parenteral nutrition (administration of essential nutrients through a permanent intravenous catheter) may be required. Total parenteral nutrition is an extreme measure of last resort for systemic sclerosis patients whose small intestine is so severely affected that nutrients are no longer absorbed. This requires a great deal of discipline on the part of patients as they must self-administer nutrients intravenously. On the other hand, total parenteral nutrition can be done at home and is a very effective measure to maintain a normal state of nutrition.

Involvement of the large intestine (colon)

Involvement of the large intestine or colon occurs in 10-50% of systemic sclerosis patients and can also occur early. The most common manifestation is dysmotility of the last part of the colon, particularly the rectum and anus. These abnormalities often come with very uncomfortable symptoms, such as constipation (fewer than two bowel movements per week) and fecal incontinence (involuntary loss of stool).

Diarrhea and fecal incontinence

When incontinence is accompanied by diarrhea, the treatment is that of malabsorption (the cyclic regimen of oral antibiotics discussed above), a low-residue diet, medications for diarrhea (e.g., loperamide), and resins to conjugate bile acids (e.g., cholestyramine). Patients who do not respond to these treatments may sometimes benefit from specialized techniques, such as bio-feedback or the use of an electro-stimulator for the anal sphincter.

Constipation

Prokinetic drugs could be tried to treat constipation, but unfortunately they are not very effective. Medications to soften stools (e.g., docusate) or to stimulate intestinal contraction (e.g., lactulose or polyethylene glycol) may also be used.

Much rarer problems are prolapse of the rectum and perforation of the colon, both of which require prompt surgical consultation.

Involvement of the liver, bile ducts, and pancreas

Problems affecting the liver and bile ducts are uncommon in systemic sclerosis. The most common liver involvement is primary biliary cholangitis (an autoimmune chronic inflammatory disease of the liver), which occurs mainly in patients with the limited form of systemic sclerosis and those with the presence of anti-centromere (CENP-B) autoantibodies in the blood. This disease typically causes few symptoms initially and it is prudent to screen for it with blood tests when systemic sclerosis is diagnosed. Treatment of primary biliary cirrhosis associated with systemic sclerosis is usually effective but requires regular follow-up with a hepatologist (doctor who specializes in liver disease) or gastroenterologist.

Exocrine pancreatic insufficiency (a condition in which the pancreas is unable to produce enough digestive enzymes to break down food in the intestine) due to fibrosis is rarely reported in systemic sclerosis. However, it should be sought when symptoms of malabsorption persist despite adequate treatment. If pancreatic insufficiency is confirmed by specific tests, treatment with pancreatic enzyme supplements may be beneficial.

Conclusion

Systemic sclerosis affects the gastrointestinal tract in the majority of patients, although severe manifestations are uncommon. The earliest and most common involvement is esophageal dysfunction. However, a dysfunction can affect the digestive tract at any level from the mouth to the anus. Despite the complexity of the various symptoms related to gastrointestinal involvement in systemic sclerosis patients, it should be noted that the majority of patients lead a relatively normal life by following the treatments recommended by their doctors and having appropriate medical follow-up.

Digestive tract involvement	Description	Symptoms/signs	Possible investigations	Usual treatments
OROPHARYNX	• Reduced mouth opening • Dry mouth • Difficulty chewing and swallowing • Teething problems	• Mouth pain • Retention of food in the mouth or throat • Coughing after swallowing • Leakage of saliva and/or food from the corner of the mouth	• Regular visit to the dentist • Physiotherapy • Ergotherapy	• Exercises to preserve the flexibility of the face • Dental hygiene • Avoid tobacco, alcohol, dry food • Sugarless gum/ candy • Artificial saliva
ESOPHAGUS	• Reduced or absent contraction movements • Acid reflux from the stomach • Irritation, ulcer, infection • Narrowing	• Bruising or pain in the chest or pit of the stomach after a meal or during the night • Acid reflux	• Gastroscopy • Barium meal • Esophageal transit scintigraphy	• Raising the head of the bed • Small regular meals • Anti-reflux medications • Prokinetic drugs • Avoid irritating medications • +/- Antifungal agents • +/- Dilation (gastroscopy)
STOMACH	• Slow emptying of stomach contents • Bleeding from dilated small vessels or veins in the stomach • Excessive bacterial flora overgrowth • Malabsorption of nutrients • Episodes of stoppage in intestinal transit	• Feeling full soon after starting a meal • Bloating • Vomiting • Fatigue, anemia	• Gastric emptying scintigraphy • Gastroscopy	• Prokinetic drugs • Drugs for nausea
SMALL INTESTINE	• Slowing of intestinal transit • Excessive bacterial flora overgrowth • Malabsorption of nutrients • Episodes of stoppage in intestinal transit	• Bloating • Abdominal pain • Constipation • Diarrhea • Weight loss • Vomiting	• Breath test • Endoscopy	• Cyclic antibiotics • Prokinetic drugs • Nutritional supplements
LARGE INTESTINE (OR COLON)	• Slowing of colonic transit time (through the colon to the rectum and anus) • Rectal prolapse	• Constipation • Fecal incontinence • Diarrhea	• Barium enema • Anorectal manometry	• Low-residue diet • Medications for diarrhea or constipation • Biofeedback, anal stimulator
LIVER AND BILE DUCTS	• Primary biliary cholangitis	• Fatigue • Pruritus (itchy skin) • Jaundice (yellow skin)	• Blood test	• Ursodiol • Drugs for pruritus
PANCREAS	• Insufficient production of pancreatic enzymes needed for digestion	• Diarrhea, flatulence • Bloating, cramps	• Pancreatic function tests	• Pancreatic enzyme supplements

II SYMPTOMS AND COMPLICATIONS

The Kidney in Systemic Sclerosis

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The kidneys play a critical role in removing chemical waste products from the body, maintaining body fluid volume and controlling blood pressure. Kidney abnormalities encountered in systemic sclerosis are relatively common and, fortunately, most often with few consequences (e.g., small amount of protein in the urine, slight decrease in kidney function, slight increase in blood pressure). These problems are most often associated with a good prognosis and do not progress. However, there is a rarer but more urgent complication to identify: scleroderma renal crisis.

Who is at risk of developing scleroderma renal crisis?

Renal crisis occurs in 10-20% of patients with the diffuse form of systemic sclerosis. In the limited form of systemic sclerosis, its occurrence is less frequent. The risk is higher in patients with rapidly progressive skin involvement and in those with anti-RNA polymerase III autoantibodies. The use of high-dose corticosteroids (> 20 mg daily in the last 6 months) is also associated with an increased risk of developing a renal crisis. Renal crisis most commonly occurs during the first five years of disease progression. Joint contractures, new anemia and new heart problems (e.g., fluid in the envelope surrounding the heart or heart failure) may also be associated with a higher risk.

What causes scleroderma renal crisis?

Scleroderma renal crisis is caused by a sudden narrowing of the small blood vessels of the kidneys, causing an acute decrease in blood flow to the kidneys and rapidly leading to their loss of function. The clinical consequences of the sudden narrowing of the small blood vessels of the kidneys are a very abrupt increase in blood pressure (hypertension), kidney failure (the kidneys stop working normally), anemia and a decrease in the number of platelets in the blood.

What are the clinical features of scleroderma renal crisis?

Scleroderma renal crisis is most commonly associated with one or more of the following signs and symptoms:

- Sudden and new increase in blood pressure to >150/85 mm Hg, measured at least twice in the last 24 hours; or persistent increase of 20 mm Hg in the systolic pressure (the first or upper digit) or of 10 mm Hg in the diastolic pressure (the second or lower digit);
- Unusual headaches;
- Blurred vision;
- Difficulty breathing (a sign of the presence of fluid in the lungs, referred to as pulmonary edema);
- Palpitations, or sensation of a rapid heartbeat;
- Nausea and vomiting;
- Decrease in the amount of urine excreted;
- Drowsiness or confusion (or seizure in more severe cases).

If any of the above symptoms arise in a patient with systemic sclerosis, the blood pressure should be taken immediately. If the blood pressure is >150/85 mm Hg, measured at least twice in the last 24 hours, the patient should go to the emergency room immediately for a medical evaluation and treatment.

How to diagnose scleroderma renal crisis?

The presence of new and sudden hypertension, in conjunction with new and progressive kidney failure detected by blood and urine analysis in a patient with systemic sclerosis, strongly suggests the diagnosis of scleroderma renal crisis. The presence of anemia, fragmented red blood cells and a low platelet count in the blood test also supports the diagnosis. In contrast, kidney problems in systemic sclerosis may be due to other causes (see below). In cases where the diagnosis is less clear, additional tests including a kidney biopsy may be performed to help rule out alternative causes of kidney failure. Collaboration between the rheumatologist, nephrologist, hematologist and ophthalmologist is very helpful in making the diagnosis.

How is scleroderma renal crisis treated?

One of the great success stories against systemic sclerosis was the discovery of a new treatment for scleroderma renal crisis. This new treatment has significantly reduced the mortality associated with renal crisis. If left untreated, scleroderma renal crisis can lead to a severe loss of kidney function in as little as 4 to 8 weeks, and even death in less than a year.

The main objective when treating scleroderma renal crisis is to control the rise in blood pressure as quickly as possible. The drug of choice according to several studies is captopril (Capoten®), which belongs to the class of medication called angiotensin-converting enzyme inhibitor (ACE-I). The dose of captopril should be increased rapidly to bring blood pressure levels back to the patient's baseline within 72 hours. The required dose of captopril may vary from patient to patient. Treatment is started at a dose of 6.25 to 12.5 mg, and increased by 12.5 to 25 mg every four to eight hours as needed, up to 300 to 450 mg daily.

The addition of other medications to control pressure is sometimes necessary, such as calcium channel blockers (e.g., amlodipine or Norvasc®). Beta-blocker medications should be avoided given that they could theoretically worsen the narrowing of blood vessels. The treating physician should also monitor blood samples regularly to ensure that the kidney function is improving with treatment.

Some patients, especially those who were diagnosed and treated late in the course of the renal crisis, may require dialysis for varying lengths of time. In this case, there is still reason to be hopeful because we know that improvement in kidney function can be slow (up to 18-24 months), and that some patients will recover and eventually stop dialysis despite this delay. In very severe cases, some patients may need to have a kidney transplant, but with poorer short- and long-term outcomes compared to transplant patients who do not have scleroderma.

Once scleroderma renal crisis is resolved, medications in the longer-acting ACE inhibitor class should be continued indefinitely (e.g., enalapril (Vasotec®) or ramipril (Altace®)), even if the blood pressure returns to normal levels. It is also prudent to avoid medications that could be toxic to the kidneys, such as non-steroidal anti-inflammatory drugs (e.g., Advil®, Naprosyn®, Celebrex®) and contrast agents used in certain X-rays (e.g., CT scan with iodine injection).

Can scleroderma renal crisis be prevented?

No medication has been shown to be effective in protecting the kidneys and preventing scleroderma renal crisis. However, early detection of a renal crisis can help to start treatment as soon as possible and thus avoid serious complications of renal crisis. We therefore suggest to:

- Check blood pressure twice a week, or daily in very high-risk patients (with a device at home);
- Assess kidney function by taking blood samples and testing the urine for the presence of protein every three to six months; a deterioration in the kidney function or the persistent presence of protein in the urine could be a warning sign to the treating physician of an early scleroderma renal crisis;
- Prednisone should be used with great caution. If required, prednisone should be given at a dose of 20 mg daily or less, if possible, and for the shortest time possible. However, some potentially serious conditions associated with systemic sclerosis may require higher doses of prednisone, such as inflammatory involvement of the lungs (alveolitis) or inflammatory involvement of the muscles (myositis). The dose and duration of treatment with prednisone is then at the discretion of the treating physician who prescribes and monitors the treatment.

What are other possible renal manifestations in systemic sclerosis?

In addition to scleroderma renal crisis, kidneys can also be affected by:

- Glomerulonephritis associated with ANCA or anti-GBM autoantibodies (inflammation in the wall of the small vessels of the kidneys; rare);
- Thrombotic thrombocytopenic purpura (a disease in which platelets are too large and block the vessels in the kidneys; rare);
- Oxalate nephropathy (in patients with severe digestive involvement and malabsorption associated with systemic sclerosis);
- Other causes of kidney failure that are not directly related to systemic sclerosis, e.g., in the context of chronic high blood pressure, diabetes, medications toxic to the kidneys, dehydration, infection or blockage of the urinary system.

Therefore, depending on the patient's clinical presentation, the physician may perform additional blood, urine and imaging tests to rule out alternative causes of kidney failure. This is important because treatment depends on the diagnosis.

In summary

Renal crisis is a relatively rare but potentially serious complication of systemic sclerosis. It is important to follow recommendations to prevent renal crisis and to recognize the early signs and symptoms of renal crisis, especially in high-risk patients. When scleroderma renal crisis is suspected, the patient should go to the nearest hospital emergency department without delay for medical evaluation and to start treatment as soon as possible, thereby minimizing the risk of serious long-term consequences.

II SYMPTOMS AND COMPLICATIONS

Scleromyositis: A Specific Muscle Manifestation of Scleroderma

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Scleroderma is a disease characterized by abnormalities in the functioning of small blood vessels and the immune system, ultimately leading to inflammation and excessive fibrosis (hardening) of the skin and various organs. When the inflammation reaches the muscles of scleroderma patients, it is called "scleromyositis". Scleroderma patients frequently report weakness, which may be due to a variety of causes (e.g., skin thickening, joint contractures, heart or lung involvement, and deconditioning). Weakness due to muscle inflammation (myositis) can therefore easily be missed.

What are the symptoms of scleromyositis?

Muscle weakness:

The main symptom of myositis is usually muscle weakness, mainly in the shoulders and hips. People with myositis may have difficulty lifting their arms above their shoulders, lifting heavy objects, climbing stairs or getting up from a seat. Neck and back muscles may also be involved with difficulty lifting the head from a pillow or holding the head upright (dropped head). In some cases, the swallowing muscles are involved resulting in difficulty swallowing food.

Raynaud's phenomenon:

Scleromyositis is often associated with a discoloration (successively white, blue and/or red) of the fingertips caused, in particular, by cold exposure. Raynaud's phenomenon is often the first clinical manifestation of scleroderma and may precede the onset of myositis by several years.

Other scleroderma manifestations:

All the usual organ involvement of scleroderma can be found in scleromyositis. It should be noted, however, that the classic skin thickening of scleroderma is not always present at the time of onset of myositis, which may result in a delay in diagnosis.

Cardiopulmonary symptoms:

Myositis can weaken the muscles needed to breathe and cause shortness of breath. Some people may also develop inflammation and/or fibrosis of the lungs, which can contribute to shortness of breath and coughing. More rarely, myositis can cause inflammation of the heart muscle (myocarditis) and eventually lead to heart rhythm problems (arrhythmia) or heart weakness (heart failure) which can cause shortness of breath or swelling of the legs.

Joint pain/swelling:

Occasionally, inflammation of the small joints of the hands may precede or accompany muscle weakness.

How is scleromyositis diagnosed?

Detailed questionnaire and physical examination:

- Assessment of muscle strength.
- Evaluation for cutaneous signs of scleroderma (e.g., skin thickening, vessel abnormalities visible at the nailfold).
- Cardiopulmonary examination.
- Evaluation for joint pain and/or swelling.

Laboratory tests:

- **Muscle enzymes:** Measurement of creatine kinase (CK) or other muscle enzymes (AST, ALT, LD, aldolase) that may be increased following muscle injury. These markers are however not specific for myositis and may be increased in the blood for other reasons.
- **Autoantibody assay:** The presence of autoimmune markers in the blood may be useful in supporting a diagnosis of myositis, predicting associated organ involvement, and predicting a patient's response to certain treatments. However, it should be noted that autoantibodies in scleroderma are not found in all patients.

Electromyogram (EMG):

EMG measures electrical activity in the muscles using electrodes applied to the skin and may be abnormal in scleromyositis.

Magnetic resonance imaging (MRI):

MRI is an imaging technique that uses magnetic fields rather than radiation to produce an image of the muscles. It can detect inflammation and muscle damage that may result from myositis.

Muscle biopsy:

The muscle biopsy consists of taking a small piece of muscle tissue (usually from the shoulder or thigh) under local anesthesia, which is then examined under a microscope.

Recent research has identified abnormalities of small blood vessels (capillaries) in muscle biopsies from patients with scleromyositis. The presence of multiple layers (reduplication) in the wall (basement membrane) of the majority of capillaries assessed in muscle biopsies is specifically found in scleromyositis. Identification of these vascular abnormalities, in addition to other autoimmune markers, on muscle biopsy is useful to support a diagnosis of scleromyositis, even when the patient does not have other scleroderma manifestations, including the classic skin thickening of scleroderma.

Capillaroscopy:

Capillaroscopy is a simple and painless examination performed on the hands to look for abnormalities in the small blood vessels called capillaries, located at the nailfold.

Cardiac investigations:

Additional tests such as an electrocardiogram (EKG), cardiac ultrasound or cardiac MRI will help to assess the presence and severity of cardiac involvement.

Pulmonary investigations:

Additional tests such as a pulmonary function test or a chest CT scan will help to assess the presence and severity of pulmonary involvement.

Gastrointestinal investigations:

Additional tests to evaluate the esophagus, stomach, small intestine and large intestine will help to assess the presence of various digestive system disorders associated with scleroderma.

All or some of these different diagnostic tools can be implemented by your treating physician depending on your situation.

Are there treatments for scleromyotis?

Myositis can be treated with immunosuppressive drugs and muscle rehabilitation.

Immunosuppressive drugs will help regulate the immune system and block muscle inflammation. Current data suggest that these treatments are most effective in inflammatory muscle disease and less effective in fibrosing forms. Muscle biopsy is therefore very important for diagnosis but also to help guide treatment and anticipate the clinical response of patients. Immunosuppressive drugs are usually administered in combination with corticosteroids (cortisone), initially at a high dose and then gradually reduced.

High doses of corticosteroids are associated with an increased risk of developing a scleroderma renal crisis, a rare but urgent complication of scleroderma, which is caused by an acute decrease in blood flow to the kidneys and rapidly leading to their loss of function. Clinical factors such as the disease duration, the form of scleroderma (diffuse vs. limited) and the autoantibody profile will allow the physician to assess which patients are most at risk of developing this complication. Monitoring of certain symptoms and blood pressure at home will be recommended while taking corticosteroids. If the risk of a scleroderma renal crisis is considered too high, the doctor may suggest a blood product called intravenous immunoglobulin for a few months to allow the dose of corticosteroids to be lowered.

Muscle rehabilitation with physical therapy is an important aspect of the treatment of scleromyositis patients and is aimed at reducing inflammation and rebuilding muscle strength.

When muscle disease is very active, a light exercise program is usually recommended. Once inflammation is under control, muscle training should be intensified to prevent loss of strength and endurance. With the guidance of a physician and a physiotherapist, patients can be directed to an exercise program that is appropriate for their cardiorespiratory capacities.

In summary

Scleromyositis is a muscular manifestation of systemic scleroderma and may be the earliest feature of the disease. Weakness may be multifactorial and careful evaluation must be performed to make the diagnosis of scleromyositis and provide optimal patient management.

The identification of specific vascular abnormalities on muscle biopsy is useful to support an early diagnosis of scleromyositis especially when the patient does not have other scleroderma manifestations, including scleroderma skin thickening, or scleroderma autoantibodies.

II SYMPTOMS AND COMPLICATIONS

Bone Health and Scleroderma

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Osteoporosis is a disease in which the bones become more fragile. People with osteoporosis are at risk of breaking their bones more easily. In fact, a fracture could occur following a fall to the ground or a minor trauma, or even spontaneously. Fractures, particularly of the hip, can have a significant impact on mobility and autonomy. This is why it is important to treat osteoporosis to prevent fractures before they occur.

Who is at risk of developing osteoporosis?

The risk factors for developing osteoporosis are the following:

- **Your age:** the risk increases with age, especially after menopause in women and after the age of 65 in men;
- **Your gender:** women are more at risk of developing osteoporosis because of the decrease in estrogen levels after menopause. However, men are also affected by osteoporosis. In fact, at least one in three women and one in five men will experience a fracture caused by osteoporosis in their lifetime;
- A history of fracture of the hip, spine, or other sites occurring spontaneously or following minor trauma;
- A history of hip fracture in one of your parents;
- **Your calcium intake:** if your body does not get enough calcium from food to perform its vital functions, it will draw calcium from your bones. Calcium is a mineral that is essential for the architecture of the bone, and a deficiency will lead to weaker bones.
- **Your vitamin D intake:** vitamin D helps the body to absorb calcium. A vitamin D deficiency can therefore contribute to a calcium deficiency;
- Physical inactivity;
- Smoking;
- Alcohol consumption (three or more drinks per day);
- Low body weight (less than 60 kg or 132 lbs) or significant weight loss;
- Use of glucocorticoid medications for three months or more;

- Other health problems or medications that contribute to bone loss, such as premature menopause (before age 45), chronic inflammatory diseases such as rheumatoid arthritis, bowel diseases causing malabsorption (Crohn's, ulcerative colitis, celiac disease, weight loss surgery), malnutrition, type 1 diabetes, untreated hyperthyroidism, primary hyperparathyroidism, hypogonadism, Cushing's disease, chronic obstructive pulmonary disease, chronic liver and kidney disease, and certain drugs used in the treatment of breast and prostate cancer, among others.

The risk of fracture is increased in people with osteoporosis because fracture can occur after a minor trauma such as a simple fall to the ground. If you have had a fall in the past, this is the best predictor of another fall in the future. In fact, a history of falls triples your risk of falling again. Certain medical conditions (joint, muscle or neurological problems) or medications can also increase your risk of falling and therefore of breaking a bone.

How common is osteoporosis in scleroderma?

The prevalence of osteoporosis is increased in people with scleroderma, affecting approximately 30% of individuals. This increased risk may be related to the presence of risk factors for osteoporosis, such as advanced age, early menopause, use of glucocorticoid drugs, malabsorption related to bowel involvement, vitamin D deficiency and chronic inflammation. It is therefore important to screen for osteoporosis in people with scleroderma, especially if risk factors are present.

How do I know if I have osteoporosis?

Osteoporosis is also known as the "silent thief" because the disease can build up gradually over the years without any apparent symptoms, until a fracture occurs. The most common fracture sites associated with osteoporosis are the hips (pelvis), vertebrae (in the spine) and wrists. A decrease in height can be a warning sign that a vertebral fracture has occurred.

Since osteoporosis is most often asymptomatic before a fracture occurs, a test is necessary to detect this condition: the evaluation of bone mineral density (BMD). This density is measured by osteodensitometry, a test done in radiology that measures the density of bones at the vertebrae, hip and wrist. The "T-score" is then generated and reflects the deviation of your bone density from that of a young adult. A T-score below -2.5 is classified as "osteoporosis" and a T-score between -1 and -2.5 means low bone density ("osteopenia").

Screening by BMD assessment is recommended for everyone over the age of 65. In addition, screening is also recommended for post-menopausal women and men over the age of 50 with risk factors for fracture, or adults younger than 50 with a medical condition associated with bone loss.

What can I do to keep my bones healthy?

- Optimize your calcium intake by eating calcium-rich foods such as dairy products (milk, yogurt, cheese), calcium-fortified beverages (soy milk, orange juice), leafy green vegetables (kale, broccoli), tofu and vegetables. The daily target intake is 1,200 mg. If your dietary intake is insufficient, you can supplement with calcium tablets.
- Optimize your vitamin D intake to ensure proper calcium absorption by eating vitamin D-rich foods, such as vitamin D-fortified dairy products and orange juice, fatty fish, fish liver oils and egg yolks. A vitamin D supplement is often necessary and can be taken on a daily or weekly basis. Vitamin D levels are measured in the blood and can be used to determine the amount of supplementation needed.
- Regular weight-bearing exercise (to improve bone health) and balance and strength training (to prevent falls).
- Avoid or quit smoking.

- Limit alcohol consumption (no more than two drinks per day).
- Secure your environment to prevent falls. For example, make sure no electrical wires are lying around. Anchor rugs to the floor with non-slip rug pads to prevent slipping. Keep hallways well lit. Watch out for slippery floors. Wear comfortable shoes with rubber soles. Have your eyes checked. Minimize the use of medications that can increase your risk of falling (discuss this with your physician).

Are there treatments for osteoporosis?

Yes. Depending on the results of your BMD test and whether you have risk factors for osteoporosis, your doctor can assess your risk of having a fracture. If your risk is high, several medications can be used to reduce that risk.

There are two main categories of treatments for osteoporosis: anti-resorptive therapies, which slow down bone loss; and anabolic agents, which stimulate bone formation.

- **Bisphosphonates,** such as alendronate (**Fosamax®**) and risedronate (**Actonel®**), are first-line anti-resorptive therapies. These medications are usually taken by mouth once a week. They must be taken on an empty stomach (no food or drink except water), otherwise they will not be absorbed. They can irritate the esophagus (the part of the digestive tract between the mouth and the stomach), so they must be taken with a large glass of water and you must remain upright (not lying down) for at least half an hour afterwards. Some bisphosphonates can also be given intravenously, such as zoledronate (Aclasta®). It is important to tell your dentist that you are taking these medications, as they may increase the risk of complications with certain dental procedures.
- **Denosumab (Prolia®)** is an anti-resorptive drug administered by subcutaneous injection every six months. This drug is generally reserved for patients who have an intolerance or contraindication to bisphosphonates. Since people with scleroderma often have esophageal motility problems that may put them at risk for digestive intolerance to bisphosphonates, denosumab represents an alternative option in this population.
- **Hormone replacement therapy** (or estrogen/progesterone) is an alternative for women with menopausal symptoms such as hot flashes and night sweats.
- **Raloxifene (Evista®)** is another anti-resorptive drug that reduces the risk of vertebral fractures.
- **Anabolic agents**, such as teriparatide, abaloparatide and romosozumab, are used in severe or refractory cases.

The duration of treatment varies depending on the type of medication, the patient's risk of fracture and the response to treatment. BMD testing is repeated every one to two years to ensure that bone density has stabilized. Blood markers may also be done to monitor the effect of treatment on bone metabolism. The success of the treatment is measured by a stabilization or an increase in BMD, as well as by the absence of new fractures.

In summary

Osteoporosis is a disease that makes bones more fragile and increases the risk of fracture. Osteoporosis is common in people with scleroderma, affecting about one-third of indviduals presenting scleroderma. Risk factors include advanced age, menopause, nutritional deficits, digestive malabsorption and use of glucocorticoid medication. Bone density testing is useful for detecting osteoporosis and initiating treatment early on in order to prevent fractures.

III DIAGNOSIS AND MEDICAL FOLLOW-UP

Capillaroscopy and complementary observations

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DEFINITION

Nailfold capillaroscopy is a simple, non-invasive, painless examination mainly performed on the hands that allows the study of small blood vessels, called capillaries, located around the nail beds. After depositing a drop of oil to make the skin more transparent, the periungual capillaries are observed under a microscope.

The observation of animal and human cells began more than 300 years ago, and the addition of a magnifying glass 200 years later allowed the observation of capillaries at the surface of the skin. Over 100 years ago, significant changes in capillary morphology have been observed during scleroderma; and, in the last 40 years, studies have been carried out showing the morphological evolution of capillaries in relation to scleroderma-specific antibodies.

The functions of the capillaries

The capillaries, so named for their resemblance to hair, although they are ten times smaller, are the smallest visible vascular structure on the skin. They form a loop that connects the smallest end of the arteries to that of the veins. They act as a barrier that filters certain structures, bringing essential nutrients to the surrounding cells and capturing waste products that are then eliminated by other organs.

With today's high-magnification microscopes (from 50 to 200 times) their shapes can be accurately revealed thanks to the red blood cells that circulate in them and which define their contours since their walls, made up of just a few cells, are too thin to be visible.

Why perform a capillaroscopy?

Diagnostic criteria for scleroderma have gradually evolved, as these were initially based on the degree of skin and lung involvement (1980). Later, the growing interest of clinicians and researchers in this disease, the introduction of capillaroscopy, the notion of Raynaud's phenomenon and the discovery of scleroderma-specific antibodies have led to the development of new diagnostic criteria (1988, 2001).

Since 2013, following a consensus between American and European physicians on what are the key features for diagnosing scleroderma, new diagnostic criteria are being used. These criteria are based on a points-scoring system that relies on the presence of certain physical aspects (cutaneous and pulmonary), Raynaud's phenomenon, capillary abnormalities and specific antibodies found in 85% of cases (anticentromere (ACA), anti-topoisomerase, anti-Th, anti-RNA Polymerase 3).

Capillary changes in scleroderma

The presence of specific abnormalities of the nailfold capillaries provides further evidence for supporting the diagnosis of scleroderma especially in the absence of specific antibodies (15% of cases). An examination is required when a patient develops symptoms in the hands, whether or not these are related to Raynaud's phenomenon. Capillary abnormalities are not necessarily related to the number of fingers affected or the frequency of episodes of capillary discolouration.

In scleroderma, the walls of the capillaries and the surrounding tissue appear to change more or less rapidly depending on the antibodies detected and disease duration: normal pattern appears as a row of hairpin-like capillary loops (**image No 1**) become disorganized. The capillary loops enlarge, at more than 50 µm (**image No 2**), they thrombosed (self-destruct) and disappear with or without a trace of bleeding. They may cluster together and are often visible as small red dots on the skin surface (capillary telangiectasias) with little evidence of replacement of the missing vessels (angiogenesis). Changes in capillaries have been observed up to 15 years before the onset of involvement of skin or other internal organs during scleroderma. However, some patients with long-standing scleroderma may have normal capillaries.

Nailfold capillaroscopy alone does not allow for the diagnosis of scleroderma in all cases because the capillaries may also be enlarged in patients with other autoimmune diseases such as lupus erythematosus and dermatomyositis. Capillaroscopy findings should thus be interpreted according to some specific questions, the clinical examination and the antibodies detected.

Capillaroscopy remains an important tool for the early diagnosis of scleroderma. The pathophysiological mechanisms leading to changes in the number of capillaries, their shape and arrangement during the course of the disease are still poorly understood, as is the relationship with the antibodies detected. Fortunately, research continues to provide a better understanding of this disease and to identify treatments that are not only curative but also preventive.

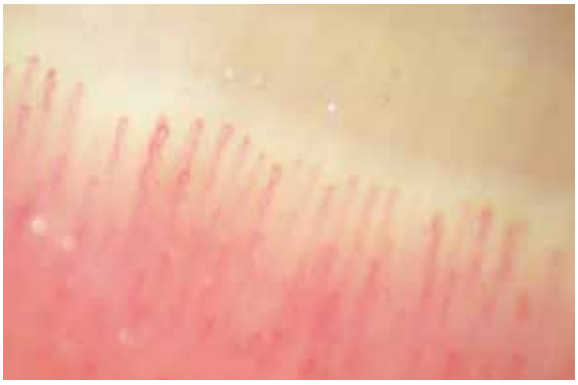

Image No. 1
Normal pattern: row of hairpin-like capillary loops

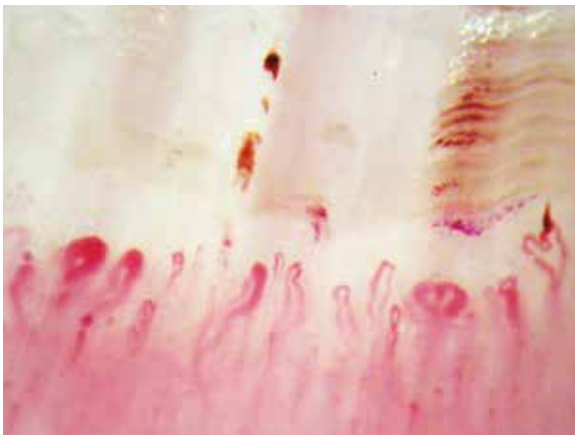

Image No. 2
Scleroderma pattern with positive ACA antibodies: successive hemorrhages, enlarged and disorganized capillaries

III DIAGNOSIS AND MEDICAL FOLLOW-UP

Autoantibodies in Scleroderma

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Scleroderma, also known as systemic sclerosis (abbreviated hereafter as SSc), remains to this day a disease of unknown cause. However, research has made considerable progress in understanding the mechanisms involved in the lesions caused by the disease, both in the skin and in the internal organs. The study of the mechanisms of a disease is called "pathophysiology". The mechanisms that contribute to pathophysiology are referred to as "pathogenic".

Four major mechanisms of scleroderma

Four major pathogenic mechanisms are recognized in the pathophysiology of SSc.

1. First, there is a dysfunction of the immune system that causes it to attack the individual's own body. This explains why SSc is considered an "autoimmune" disease.
2. There is also microvascular damage, meaning that it targets the small blood vessels. Raynaud's phenomenon (fingers changing colour when exposed to cold temperatures) is present in almost all SSc patients, and is so often both the first symptom and the first sign of the disease, and is the typical manifestation of this vascular damage.
3. There is also inflammation. Although it is often underestimated in SSc, research has shown its crucial importance, to the point that "without inflammation, there is no fibrosis".
4. Finally, fibrosis (or sclerosis, which gives its name to SSc) is the ultimate result of the previous intertwined mechanisms, both in the skin and in the internal organs.

As we can see, the pathophysiology of SSc is complicated. These pathogenic mechanisms have been the subject of intensive research in order to understand their interrelationships and to find "weak points" in the pathophysiological cascades that may become new therapeutic targets. In this article, we will focus on the dysregulation of the immune system and, in particular, on the specific antibodies that are typically found in the blood of SSc patients. Other important and complex aspects of immune system dysfunction in SSc (such as cellular immunity, innate immunity and signalling) will not be discussed here.

Immune system dysfunction in scleroderma

One of the primary functions of the immune system is to protect the individual from infection. Normally, the immune system does this job extraordinarily well, even though every day each individual is exposed to countless potentially dangerous microbes both in the human body itself and in the environment.

However, there are times when the immune system goes haywire and produces antibodies that attack the individual instead of protecting them. This is what happens in several autoimmune diseases, and the antibodies produced are called "autoantibodies".

Indeed, SSc is characterized by highly specific autoantibodies in the blood of affected individuals. By "specific" we mean that these autoantibodies are not seen in other diseases.

Autoantibodies contribute to the diagnosis of scleroderma

There are four main autoantibodies, referred to as "classic", which are named as follows:

- anti-centromere
- anti-topoisomerase I
- anti-RNA polymerase III
- anti-Th/To

These autoantibodies, their synonyms, and the molecules against which they are directed (antigens) are listed in Table 1. In general, the SSc autoantibodies are mutually exclusive: in a given individual, only one of the four autoantibodies will be present. Several other less common autoantibodies have been described in recent years that are also associated with SSc, but because of their rarity and the fact that their significance still needs to be better defined, they will not be discussed here.

In fact, the four classic autoantibodies are so specific to SSc that there are now laboratory tests for their detection. In an individual with certain signs of SSc, such as Raynaud's phenomenon and skin thickening, the presence of a high titer (a significant amount) of any of these autoantibodies in the blood helps to support the diagnosis of the disease.

Thus, after a detailed questionnaire and physical examination, the rheumatologist or other medical specialist will request a blood test for these autoantibodies if they suspect a diagnosis of SSc. The diagnostic workup is usually completed by a capillaroscopy (microscopic examination of the small blood vessels around the nails) and also by tests to evaluate the internal organs, such as a CT scan of the lungs and lung function tests to look for pulmonary fibrosis.

It should be noted that the mere presence of one of the four autoantibodies in the blood does not definitively establish a diagnosis of SSc: there must be other clinical manifestations to support this diagnosis.

TABLE 1

Classic scleroderma (systemic sclerosis) autoantibodies

Name of the autoantibody	Synonym	Targeted antigen	Scleroderma subset	Associated phenotypes
Anti-centromere	Anti-CENP-B	Centromere protein B (CENP-B)	limited	- digital ulcers - pulmonary arterial hypertension - primary biliary cirrhosis - decreased risk of renal crisis and pulmonary fibrosis
Anti-topoisomerase I	Anti-topo I Anti-Scl70	DNA topoisomerase I	limited, diffuse	- pulmonary fibrosis - cardiac involvement - increased mortality
Anti-RNA polymerase III	Anti-RNApol III	RNA polymerases	diffuse	- renal crisis - cancer
Anti-Th/To		Macromolecular complex	limited	- pulmonary arterial hypertension - pulmonary fibrosis

Each autoantibody is associated with specific clinical manifestations.

A striking feature of the four autoantibodies is that each is associated with particular clinical manifestations, called "phenotypes," as shown in **Table 1**.

For instance, anti-centromere autoantibodies are associated with the limited cutaneous form of SSc, in which skin thickening is typically limited to the fingers and forearms and life expectancy is longer. Patients with these autoantibodies appear to be at lower risk of some potentially serious manifestations of SSc, such as renal crisis (sudden cessation of kidney function accompanied by extremely high blood pressure that can lead to death) or lung fibrosis (pulmonary fibrosis).

On the other hand, anti-centromere autoantibodies are associated with the eventual occurrence (often after a long evolution) of increased pressure in the arteries of the lungs (pulmonary hypertension) which can be become life-threatening over time.

Anti-centromere autoantibodies are common in the Quebec scleroderma population of French-Canadian origin. In fact, in our study of SSc in French Canada involving 309 affected individuals, more than 40% of the patients were anti-centromere carriers [(1)].

In comparison, anti-topoisomerase I autoantibodies are less common, occurring in about 15% of our population with SSc. However, their detection is important because they are associated with a higher risk of potentially severe pulmonary fibrosis and also heart (myocardial) damage.

In a study comparing the life expectancy of our patients separated according to the four autoantibodies, the survival ten years after diagnosis was worse in patients with anti-topoisomerase I (67% survival rate) or anti-RNA polymerase III (85%) autoantibodies, and better in those with anti-centromere (90%) or anti-Th/To (100% autoantibodies).

Thus, testing for SSc autoantibodies is not only useful for diagnosing SSc but also provides important clinical information for predicting the associated phenotype and potential disease course. The physician can then individually tailor the follow-up and intensity of treatments according to the risks identified by the autoantibody present.

Presence of autoantibodies from the onset of scleroderma - prescleroderma

Another characteristic of the four autoantibodies is that they are present in the blood early in SSc, at the onset of the first signs of the disease. This concept was derived from a small number of observations made in the 20th century involving individuals with Raynaud's phenomenon only and carrying anti-centromere or anti-topoisomerase I autoantibodies who subsequently developed SSc. However, this concept had never been validated in a large number of subjects with long-term follow-up. Our research team, therefore, undertook a 20-year prospective study of 586 adult individuals with isolated Raynaud's phenomenon (without any other manifestation of SSc or other autoimmune diseases) to see who would develop SSc over time[2]. These individuals all had capillaroscopy at baseline and also had blood drawn for the four SSc autoantibodies.

Of course, given that isolated Raynaud's phenomenon is common in the adult female population in Quebec, most of these individuals did not develop SSc. However, 74 individuals, or 12.6% of the 586 participants, developed SSc at follow-up.

At follow-up, 80% of individuals who had one of the four SSc autoantibodies at baseline and an abnormal capillaroscopy developed SSc[2]. These individuals were 60 times more likely to develop SSc than those who tested negative. The time interval for developing SSc ranged from a few months to a few years.

This study, therefore, identified factors that predict a high risk of progression to SSc in individuals with isolated Raynaud's phenomenon[2]. In addition, the study demonstrated the existence of an early phase of SSc, now referred to as **prescleroderma**, during which the disease appears to be incubating but cannot be formally diagnosed by physicians.

This novel concept opens the door to research projects aimed at better understanding the pathophysiology of this incubation period and the mechanisms leading to the progression to definitive SSc, with the hope of identifying new preventive therapeutic targets.

Do autoantibodies contribute to scleroderma lesions?

As we have seen, the presence of highly specific autoantibodies is compelling evidence of immune system involvement in SSc. Moreover, each autoantibody is associated with a specific SSc phenotype **(Table 1)**. Finally, SSc autoantibodies are present as far back as possible, presumably from the onset of Raynaud's phenomenon[2].

These data inevitably raise the question: is there evidence that these autoantibodies themselves contribute to the pathophysiology of SSc lesions? In other words, are SSc autoantibodies pathogenic?

In 2019, our research team was approached by the editors of the *Journal of Scleroderma and Related Disorders*, the only medical journal dedicated to scientific research in SSc. Drs. M. Matucci-Cerinic (University of Florence) and M. Kuwana (Nippon Medical School, Tokyo) asked us to prepare an article aimed at answering this very thorny question. The question is not theoretical: if evidence were to show a pathogenic role of SSc autoantibodies, would it not be of great interest to develop new treatments targeting these autoantibodies to block their deleterious effects?

Our team at the Centre hospitalier de l'Université de Montréal, composed of Sabrina Hoa, MD, Roger Yang, MD, Martial Koenig, MD, and the undersigned, set out to review all the data accumulated over the past 40 years. The result was a 27-page article, with 182 references, published in 2020[3]. Here are the two main conclusions.

The first conclusion is that in order to assert the pathogenic role of an autoantibody in SSc (or in any systemic autoimmune disease), one must first establish rigorous scientific criteria for pathogenicity. We have therefore proposed 7 rigorous criteria that should ideally be present to state without any doubt that an autoantibody is pathogenic. These criteria are presented in **Table 2**.

TABLE 2

Pathogenicity criteria for the definition of pathogenic autoantibodies in scleroderma (systemic sclerosis) and other systemic autoimmune diseases

Clinical pathogenicity criteria	
CRITERION 1	The autoantibody should be specific to the disease. An even greater pathogenic value is suggested when the autoantibody is phenotype-specific, that is, within the disease spectrum, it associates with a particular set of clinical and laboratory manifestations.
CRITERION 2	The autoantibody is serologically present before the onset of clinical manifestations.
CRITERION 3	Autoantibody levels and disease activity/severity should, in general, correlate
CRITERION 4	Removal of the autoantibody, or blocking its functional effects, should ameliorate the disease process (e.g. by immunosuppression, plasma exchange, biological agent, immunotherapy, or other means).
Experimental pathogenicity criteria	
CRITERION 5	The autoantibody should be capable of causing in experimental systems the lesions attributed to it (e.g. in living cells or in an experimental animal model).
CRITERION 6	A suitable immunization that leads to the production of similar autoantibodies should lead to a similar disease process.
CRITERION 7	The autoantibody should be found along with a plausible target antigen at the site of tissue damage.

As we can see in TABLE 2, the scientific bar has been set high!

In a second phase, the team screened all published articles on the pathogenic role of autoantibodies in SSc and classified them for each of the 7 criteria according to the following grading scale:

- **—** No evidence;
- **?** Contradictory, inconclusive data;
- **+** Weak evidence;
- **++** Some evidence;
- **+++** Strong, definitive evidence..

Finally, using these assessments, a verdict was reached as to whether the pathogenic role of autoantibodies was definitive, probable, possible, or whether the data were insufficient. **Table 3** shows the results.

Of the four classic SSc autoantibodies, only anti-centromere and anti-topoisomerase I autoantibodies have been extensively studied for their pathogenic role. The second conclusion was that there is indeed some evidence of pathogenicity for these two autoantibodies and therefore their pathogenic role is possible[3]. As shown in Table 3, the evidence for a pathogenic role is strongest for anti-topoisomerase I.

Thus, further research is needed to better understand how these autoantibodies contribute to SSc lesions.

TABLE 3

Scientific evidence of a pathogenic role for autoantibodies in scleroderma (systemic sclerosis)

Classic autoantibodies	Strength of scientific evidence according to seven pathogenicity criteria*							Pathogenic role**
	1	2	3	4	5	6	7	
ANTI-TOPOISOMERASE I	+++	+++	+++	++	++	++	—	Possible
ANTI-CENP-B (ANTICENTROMERES)	+++	+++	++	—	++	—	—	Possible

Legend

* Criteria as described in Table 2.
Grading: —, no evidence; ?, contradictory, inconclusive evidence;
+ , Weak evidence; ++, Some evidence; +++, Strong definitive evidence;

** Grading: definitive, probable, possible, and insufficient data.

Conclusion

As we have seen, the four classic SSc autoantibodies are essential for the diagnosis of the disease and are useful in predicting its manifestations, course and associated life expectancy. The high specificity of these autoantibodies for SSc, their association with a particular phenotype and their presence from the onset of the disease suggest that they play a pathogenic role, the demonstration of which according to rigorous scientific criteria is well underway and needs to be completed.

Moreover, the remarkable association of these autoantibodies with SSc suggests that they are directly and intimately linked to the cause of the disease, the identity of which remains a mystery to this day.

III DIAGNOSIS AND MEDICAL FOLLOW-UP

Patient-reported outcomes in scleroderma: why it matters

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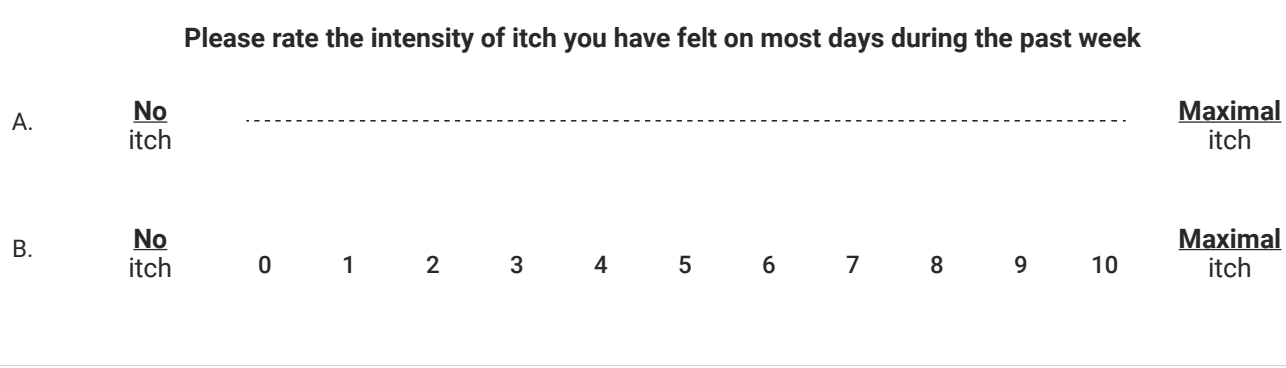
Scleroderma patients are the experts in how they feel and function. They are the only ones capable of describing first-hand the long list of symptoms associated with scleroderma, including Raynaud's, skin changes, gastro-intestinal problems and breathlessness to name a few, and how these impact their day-to-day life. They also have lived experience with the disfigurement and the complex psychosocial impacts of this disease.

The growing recognition that patients have unique experiences and values has resulted in a paradigm shift in the 21st century from a traditional paternalistic model of medicine with the physician deciding what is in the best interest of the patient to one of patient-centred care where patients are at the centre of the healthcare continuum and their specific needs and goals are the driving force behind all healthcare decisions. Patient-centred care paved the way for patient-centred research.

FIGURE 1

Examples of (a) visual analogue and (b) numerical rating scales



PROs and PROMs

Patient-reported outcomes (PROs) are defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else" [1]. PROs is an umbrella term that covers not only symptoms but also function, health-related quality of life (HRQL), satisfaction and so on. They capture patient experiences of disease that clinical assessments, blood tests, imaging (eg. CT scans and cardiac echocardiograms) and biopsies cannot. PROs have in fact become a central part of drug approvals as regulatory agencies including Health Canada, the US Food and Drugs Administration and the European Medicines Agency now require data not only on survival (and other measures of biological effectiveness) but on how patients "feel and function" when considering applications for new drug approvals.

Patient-reported outcomes measures (PROMs) are the questionnaires that measure PROs in a standardized way. PROMs are either generic, in that they can be used across various health conditions, or specific, in that they aim to capture aspects of disease that are particular to a certain condition.

Generic PROMs

The three most commonly used generic PROMs in scleroderma are patient global assessments, the Health Assessment Questionnaire (HAQ) and the Medical Trust Short-Form 36 (SF-36). The Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) is emerging as a novel generic PROM for scleroderma.

Patient Global Assessments of disease generally ask patients to rate their overall health over a given period of time (e.g. past week, past month), for example using a 10 cm visual analogue scale or numerical rating scale ranging from 0 to 10 **(Figure 1)**. Studies have shown that scleroderma patients often rate disease severity as worse compared to physician ratings, suggesting that patient ratings capture different, possibly more complex psychosocial factors that physicians do not take into account [2]. On the other hand, in a disease as heterogeneous as scleroderma, with some patients having predominantly skin, others gastrointestinal and others still respiratory symptoms, Patient Global Assessments lack granularity.

The HAQ is one of the earliest PROs used in rheumatic diseases. It is a questionnaire developed in 1980 to assess functional ability in patients with rheumatoid arthritis. It includes 20 questions in 8 categories (dressing and grooming, arising, eating, walking, hygiene, reach, grip, and performing activities). The patient rates his/her difficulty over the past week in performing the specific tasks in each category as none, mild, moderate or severe difficulty. The final score ranges from 0 (no disability) to 3 (severe disability). Although the HAQ is widely used, including in scleroderma, it has some limitations. It focuses mainly on musculoskeletal function and does not take into account the panoply of other functional limitations encountered in scleroderma, for example from breathlessness, gastrointestinal symptoms or body image distress. Also, there are concerns that even as a measure of musculoskeletal function, it may be outdated. For example, it does not include hand function such as keyboarding or using a cell phone, which is often compromised in scleroderma.

The SF-36 is possibly the most widely used generic measure of health-related quality of life. It is composed of 36 questions that can be grouped into 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. The scores of the domains and summary scores are standardized with means of 50 and standard deviations of 10. Lower scores represent worse health-related quality of life. A systematic review of the literature reported that the physical component summary score of the SF-36 was more than 1 standard deviation below the general population (38.3; 95% credible interval 35.2, 41.5)[3]. This translates into saying that, on average, scleroderma patients are among the 15% of the population with the worst physical health-related quality of life. The SF-36 has the advantage that it has been used in many diseases and allows for cross-disease comparisons. The impairments in SF-36 in scleroderma are worse than the general population and as high if not higher than other more common chronic diseases namely heart disease, lung disease, hypertension, diabetes, and depression[4]. This provides valuable information to advocate for healthcare resources for scleroderma, which remains relatively unknown among the public and healthcare decision-makers.

PROMIS-29 is a more recent generic measure of health-related quality of life developed by the National Institutes of Health (https://www.healthmeasures.net). It has the advantage of including a domain for sleep, which is often impaired in scleroderma. A study from the Scleroderma Patient-centered Intervention Network (SPIN) cohort showed that joint contractures and gastrointestinal symptoms were the strongest predictors of worse PROMIS-29 scores [5], providing valuable priorities for further scleroderma research with the potential to improve health-related quality of life.

FIGURE 2
Symptom scales of the S-HAQ
(Health assessment questionnaire adapted for scleroderma)

1. In the past week, how was your overall health?

No disease	0	1	2	3	4	5	6	7	8	9	10	**Very severe** disease

2. In the past week, how much has Raynaud's interfered with your daily activities?

Raynaud's does **not** limit activities	0	1	2	3	4	5	6	7	8	9	10	**Very severe** limitation

3. In the past week, how much have your finger ulcer(s) interfered with your daily activities?

Finger ulcers do **not** limit activities	0	1	2	3	4	5	6	7	8	9	10	**Very severe** limitation

4. In the past week, how much have your intestinal problems interfered with your daily activities?

Intestinal problems do **not** limit activities	0	1	2	3	4	5	6	7	8	9	10	**Very severe** limitation

5. In the past week, how much have your breathing problems interfered with your daily activities?

Breathing problems do **not** limit activities	0	1	2	3	4	5	6	7	8	9	10	**Very severe** limitation

PROMs specific for scleroderma

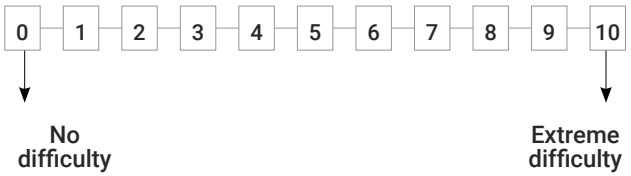
As mentioned above, the HAQ is a generic measure of musculoskeletal function. To supplement the HAQ with scleroderma-specific content, Steen and Medsger proposed in 1997 to add 5 symptom scales asking patients to rate how much overall disease, Raynaud's phenomenon, finger ulcers, breathing and gastrointestinal problems interfere with daily activities (**Figure 2** [6]). Higher scores represent worse symptoms. The addition of these symptom scales to the HAQ, which is commonly referred to as the ***Scleroderma-HAQ*** or S-HAQ, was an important first step towards developing scleroderma-specific PROs and capturing important information from the patient's perspective.

The extent of skin disease has traditionally been measured by the modified Rodnan skin score (mRSS), which is an assessment of skin thickness ranging from 0-3 in 17 areas of the body ***performed by a physician*** (range 0-51, with higher scores representing worse skin thickening). The mRSS is commonly used as a primary endpoint in clinical trials as it has been shown to predict internal organ involvement and mortality in scleroderma. However, it does not capture the subjective experience of skin changes in scleroderma. The ***Scleroderma skin patient-reported outcome*** (SSPRO) was recently developed with the input of patients to capture the patients' experiences of skin-related health changes in scleroderma[7]. It is an 18-item patient questionnaire

FIGURE 3
Raynaud Score

The Raynaud's Condition score is your rating of how much difficulty you had with your Raynaud's **TODAY**. Consider how many attacks you had and how long they lasted. Consider how much pain, numbness, or other symptoms the Raynaud's caused in your fingers (including painful sores) and how much the Raynaud's ALONE affected the use of your hands today.

SELECT the number that best indicates the difficulty you had today with your Raynaud's condition by marking an "X" in the appropriate box:



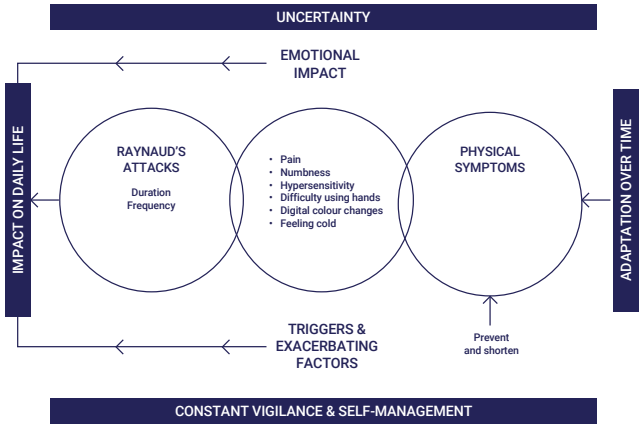
that assesses 4 domains: physical effects, physical limitations imposed by skin tightness, emotional effects and social effects, with each item being graded from 0 to 6 (range 0-108, with higher scores representing worse assessments). The SSPRO has been shown to capture how a patient feels and functions (by correlating it with traditional PROMs). Interestingly, in one clinical trial, the SSPRO correlated only moderately with the mRSS[8], indicating that there are likely additional factors beyond assessments of skin severity by physicians that shape the experience of SSc patients regarding their skin condition.

Raynaud's phenomenon is highly variable and episodic. By its nature, it is one of the symptoms of scleroderma that is best measured by patient reports. In the past, many studies of treatments for Raynaud's phenomenon used Raynaud's Condition Score **(Figure 3)**. Patients are asked to rate their Raynaud's phenomenon from 0–10, taking into account the frequency, duration, pain, numbness, and impact of RP attacks on that day. An average can be taken when the questionnaire is rated on multiple days using a diary. However, several clinical trials of potent vasodilators such as tadalafil, selexipag and bosentan have not shown the expected beneficial results when using Raynaud's Condition Score, while other PROs such as the HAQ showed improvement. This suggests that the single-item Raynaud's Condition Score does not capture the multifaceted experience of Raynaud's phenomenon.

In recent years, there has been remarkable progress in better measuring Raynaud's phenomenon. Extensive patient input was collected to develop a conceptual framework for capturing the lived experience of how scleroderma patients "feel and function" concerning their Raynaud's **(Figure 4)**[9]. From this, a novel scleroderma-specific measure of ***Raynaud's phenomenon, the Assessment of Systemic sclerosis-associated RAynaud's Phenomenon (ASRAP)*** questionnaire, was developed and recently published[10]. It consists of 10 items covering not only frequency and duration of attacks but also facets such as 'emotional distress', 'exacerbating factors', 'self-management' and 'adaptation'. The ASRAP should provide a more nuanced measure of Raynaud's phenomenon in scleroderma and provide a useful tool to test new treatments for this often debilitating problem.

Visible disfigurement especially of the face and hands is common in scleroderma and has been associated with body image dissatisfaction and social discomfort. Body image is inherently personal and PROs have been developed and tested in scleroderma. In particular, the Body Concealment Scale for Scleroderma (BCSS) was developed to capture the unique body image concerns of scleroderma patients (**Table 1**)[11].

FIGURE 4
CONCEPTUAL MAP OF THE PATIENT EXPERIENCE OF SCLERODERMA-ASSOCIATED RAYNAUD'S PHENOMENON



Source : Adapted from Pauling et al. Arthritis Care & Research Sep 2018; 70(9) : 1373-1384

TABLE 1

The questions in the body concealment scale for scleroderma (BCSS)

I wear clothes I do not like.
I wear long sleeves to hide skin changes.
I avoid wearing revealing clothes (e.g. bathing suits, tank tops, or shorts).
I wear clothes that hide the changes to my skin.
I wear clothes that will divert attention from my appearance.
I wear gloves to hide my hands.
I avoid shaking hands with people.
I hide my hands so that people do not see them.
I avoid directly giving change or other items to people.

TABLE 2

Selected PROMs commonly used in scleroderma research

	PROMS	Scleroderma specific
RESPIRATORY SYMPTOMS	Mahler Dyspnea Index	NO
	St George's Respiratory Questionnaire	NO
	Borg Dyspnea Scale	NO
	Leicester Cough Questionnaire	NO
GASTROINTESTINAL SYMPTOMS	UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract 2.0 questionnaire	YES
	Patient-Reported Outcomes Measurement Information System (PROMIS) Gastrointestinal symptom scales	YES
HAND FUNCTION	Cochin Hand Function Scale (CHFS)	NO

FIGURE 5
The EULAR systemic sclerosis impact of disease (ScleroID) questionnaire

How much have the different aspects of systemic sclerosis affected you during the last week?
Please make your responses on the scale by choosing the appropriate no for each of the following dimensions during the last week:

Raynaud's phenomenon:											
None	0	1	2	3	4	5	6	7	8	9	10	**Extreme**
Hand function:											
No limitation	0	1	2	3	4	5	6	7	8	9	10	**Extreme limitation**
Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):											
None	0	1	2	3	4	5	6	7	8	9	10	**Extreme**
Pain:											
None	0	1	2	3	4	5	6	7	8	9	10	**Extreme**
Fatigue:											
None	0	1	2	3	4	5	6	7	8	9	10	**Extreme**
Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation and incontinence):											
None	0	1	2	3	4	5	6	7	8	9	10	**Extreme**
Limitation of life choices and activities (e.g. social life, personal care, work):											
None	0	1	2	3	4	5	6	7	8	9	10	**Extreme**
Body mobility:											
Not affected	0	1	2	3	4	5	6	7	8	9	10	**Extremely affected**
Breathlessness:											
None	0	1	2	3	4	5	6	7	8	9	10	**Extreme**
Digital Ulcers:											
None	0	1	2	3	4	5	6	7	8	9	10	**Extreme**

Reproduced from: Becker MO, Dobrota R, Garaiman A, et al. Development and validation of a patient-reported outcome measure for systemic sclerosis.
Ann Rheum Dis 2022;81(4):507-15.

Visible disfigurement especially of the face and hands is common in scleroderma and has been associated with body image dissatisfaction and social discomfort. Body image is inherently personal and PROs have been developed and tested in scleroderma. In particular, the Body Concealment Scale for Scleroderma (BCSS) was developed to capture the unique body image concerns of scleroderma patients **(Table 1)** [11] .

Many other PROMs cover a broad range of scleroderma patient experiences including breathlessness, gastrointestinal symptoms and hand function (**Table 2**). Most of the measures are limited to a single organ and are not specific to scleroderma. The EULAR ScleroID is a novel, disease-specific, composite PROM that was designed to capture the global burden of disease (**Figure 5**) [12]. It consists of 10 items including pain and fatigue. Each of the items is weighted and the final score ranges from 0 to 10, with higher scores indicating worse disease. It is a promising new tool to capture patient experience in future studies of scleroderma.

Although there has been tremendous progress in measuring PROs in scleroderma in the last 2 decades, the disease-specific instruments developed with extensive patient input, in particular the ASRAP and EUSTAR ScleroID, have yet to be used in clinical trials. Those studies are highly anticipated.

Importance of measuring PROs

PROs provide a unique opportunity to capture the personal experiences of scleroderma patients and add tremendous depth to our understanding of how they “feel and function”, above and beyond standard biomedical measures of disease. PROs are used to identify research priorities of relevance to patients, to advocate for healthcare resources and for regulatory drug approvals. Although more work on PROs in scleroderma remains, the advances of the last two decades have given a voice to scleroderma patients that can only get stronger with time.

IV TREATMENTS AND THERAPY

Scleroderma Medications Guide (Canada)

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Symptoms and treatments

- Raynaud's Phenomenon
- Gastrointestinal Symptoms
- Arthritis and Myositis
- Pulmonary Fibrosis/Interstitial Lung Disease
- Pulmonary Arterial Hypertension
- Renal Crisis/New Onset Hypertension
- Skin Fibrosis
- Sjögren's Syndrome
- Localized Scleroderma
- Skin Itching (Pruritus)/Dryness

For full consultation of the Scleroderma Medications Guide, visit Scleroderma Quebec's website at **www.en.sclerodermie.ca.**

Although there isn't a cure for scleroderma, there are effective treatment options that can help alleviate symptoms and slow down disease progression. Current prescription and over-the-counter medication are designed to treat scleroderma by targeting:

- **Inflammation**
- **Autoimmunity**
- **Vascular disease**
- **Tissue fibrosis**

As a medical doctor or healthcare professional caring for persons with scleroderma, it is important to ensure patients understand the nature of the medications they may be prescribed and how they work to help control disease symptoms from progressing. Patient knowledge is powerful, as it reduces fear and increases compliance, resulting in a higher percentage of successful treatment.

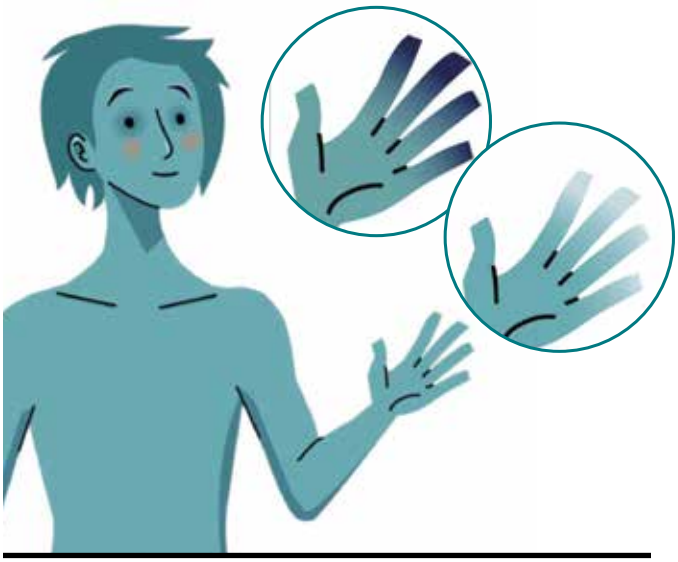
The following guide includes a list of drugs commonly prescribed by doctors in Canada to treat patients with scleroderma. The list is provided for informational purposes only, and is not to be taken as an endorsement of any drug by Scleroderma Quebec. This list presents the most frequent side effects and those that may require monitoring and is not exhaustive. The list describes the medications used as of the date of publication of this guide, but could change over time as new studies are published.

The efficacy of many of these physician prescribed drugs has not been demonstrated in scleroderma-specific clinical trials.

It is important to consider, that not every medication is appropriate for every patient. The treating physician, who is familiar with the patient's medical history, health status and disease progression, will be able to determine the most appropriate treatment options.

RAYNAUD'S PHENOMENON

Raynaud's is present in up to 95% of people with scleroderma. Whitening of fingers and/or toes triggered by cold or severe stress. The whiteness phase can be followed by a blue phase and then a red phase.



CALCIUM CHANNEL BLOCKERS

- NIFEDIPINE (ADALAT®)
- AMLODIPINE (NORVASC®)
- DILTIAZEM (CARDIZEM®)
- FELODIPINE (PLENDIL®)

Action - Relax blood vessels

Side Effects
Flushing, headache, dizziness, constipation, low blood pressure, peripheral edema, palpitations.

PHOSPHODIESTERASE TYPE 5 INHIBITORS

- SILDENAFIL (REVATIO®)

Action - Relax blood vessels

Side Effects
Headache, flushing, dyspesia, nose bleed, vision abnormalities, nasal congestion, diarrhea, insomnia, dizziness.

- TADALAFIL (ADCIRCA®)

Action - Relax blood vessels

Side Effects
Headache, myalgia, flushing, dyspepsia, nausea, nasopharyngitis, nasal congestion, dizziness.

ANGIOTENSIN II RECEPTOR ANTAGONIST

- LOSARTAN (COZAAR®)

Action - Block constriction of blood vessels

Side Effects
Headache, respiratory tract infection, dizziness, tiredness, dry cough, hyperkalemia.

TOPICAL NITRATE

- NITROGLYCERIN OINTMENT

Action - Relax blood vessels

Side Effects
Flushing, headache, dizziness, low blood pressure, heart rhythm disorders.

PROSTACYCLIN AND ANALOGUE

- EPOPROSTENOL (FLOLAN®, CARIPUL®)
- TREPROSTINIL (REMODULIN®)

Actions - Relax blood vessels. Used for severe, refractory or complicated Raynaud's

Side Effects
See section of Pulmonary Arterial Hypertension page 108.

ALPHA-ADRENERGIC BLOCKER

- PRAZOSIN (MINIPRESS®)

Action - Relax blood vessels

Side Effects
Dizziness, headache, drowsiness, tiredness, weakness, palpitations, nausea.

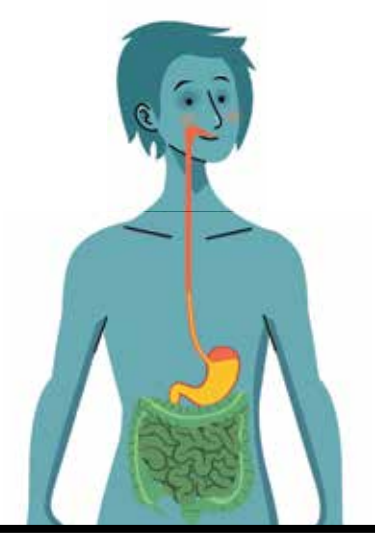
SELECTIVE ENDOTHELIN RECEPTOR ANTAGONIST

- BOSENTAN (TRACLEER®)

Action - Acts on blood vessels. For the prevention of digital ulcers

Side Effects
Headache, flushing, liver function abnormalities, pulmonary edema, low blood pressure, palpitations, dyspepsia, nasopharyngitis, tiredness, fertility disorders.

GASTROINTESTINAL SYMPTOMS



Gastrointestinal disorders affect the vast majority of patients. Gastric reflux is a common symptom that manifests itself by a burning sensation radiating up to the throat after meals and may cause inflammation of the lining of the esophagus (esophagitis reflux) if left untreated.

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

ANTACIDS

- DIOVOL®, GAVISCON®,
- ROLAIDS®, TUMS®

Action - Neutralize stomach acidity

Side Effects
Abdominal cramping, chalky taste, nausea, vomiting, diarrhea or constipation, pale stool.

HISTAMINE H2-RECEPTOR BLOCKERS

- CIMETIDINE
- RANITIDINE (ZANTAC®)
- FAMOTIDINE (PEPCID®)
- NIZATIDINE (AXID®)

Action - Inhibit stomach acid secretion

Side Effects
Drowsiness or insomnia, dizziness, headache, nausea, vomiting, diarrhea or constipation, malabsorption of vitamin B12 with long term use.

PROTON PUMP INHIBITORS

- OMEPRAZOLE (LOSEC®)
- LANSOPRAZOLE (PREVACID®)
- DEXLANSOPRAZOLE (DEXILANT®)
- ESOMEPRAZOLE (NEXIUM®)
- RABEPRAZOLE (PARIET®)
- PANTOPRAZOLE (PANTOLOC®)

Action - Inhibit stomach acid secretion

Side Effects
Headache, diarrhea, abdominal cramping, flatulence, nausea, vomiting, dizziness, malabsorption of vitamin B12 with long term use.

OTHER

- SUCRALFATE (SULCRATE®)

Action - Coat esophagus & stomach; forms protective barrier

Side Effects
Headache, diarrhea or constipation, abdominal cramping, nausea.

SWALLOWING DIFFICULTIES

GI STIMULANTS

- METOCLOPRAMIDE (METONIA®)

Action - Stimulate intestinal muscle contractions, may improve heartburn

Side Effects
Drowsiness, tiredness, dizziness, headache, diarrhea, heart rhythm disorders.

- DOMPERIDONE

Action - Stimulate intestinal muscle contractions, may improve heartburn

Side Effects
Headache, dry mouth, diarrhea, dizziness, arrhythmias.

- ERYTHROMYCIN

Action - Stimulate intestinal muscle contractions

Side Effects
Nausea, abdominal pain, diarrhea, headache, rash, vomiting, arrhythmias.

- OCTREOTIDE ACETATE (SANDOSTATIN®)

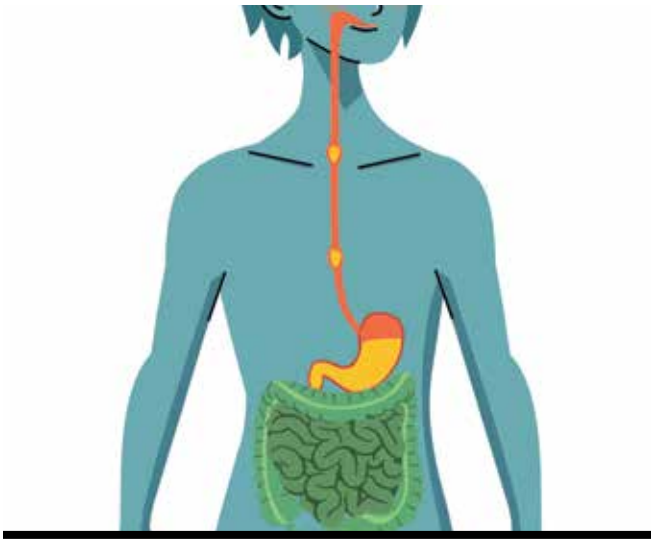
Action - An injectable medication. Can be helpful in very severe cases for improving bowel motility

Side Effects
Diarrhea or constipation, abdominal pain, flatulence, flu-like symptoms, anemia, headache.

- PRUCALOPRIDE (RESOTRAN®)

Action - Stimulate intestinal muscle contractions

Side Effects
Headaches, nausea, diarrhea, abdominal pain, vomiting, flatulence, unusual fatigue, flu-like symptoms, anemia, heart rhythm disorders.



CONSTIPATION

BULKING AGENTS

- CALCIUM POLYCARBOPHIL
- PSYLLIUM HYDROPHYLIC MUCILLOID (METAMUCIL®)

Action - Improve stool consistency, shorten colon transit time and increase frequency of bowel movements

Side Effects
Abdominal bloating, flatulence, abdominal cramps and pain, constipation.

SOFTENING AGENTS

- DOCUSATE CALCIUM
- DOCUSATE SODIUM (COLACE®)

Action - Soften stool

Side Effects
Abdominal cramp and pain, diarrhea, nausea, vomiting.

OSMOTIC AGENTS

- LACTULOSE

Action - Keep liquids inside bowels to soften stools

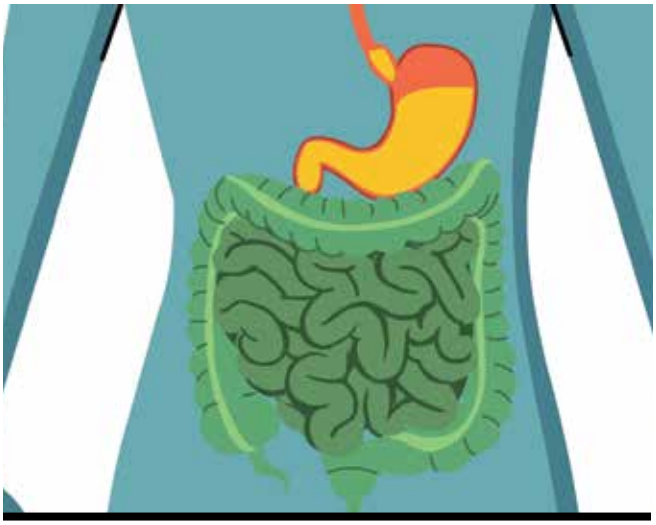
Side Effects
Abdominal cramps , diarrhea, flatulence, nausea, vomiting.

- POLYETHYLENE GLYCOL (LAX-A-DAY®, PEGALAX®, RELAXA®, RESTORALAX®)

Action - Keep liquids inside bowels to soften stools

Side Effects
Cramping, diarrhea, abdominal pain, flatulence, nausea.

SMALL INTESTINE DYSFUNCTION: BACTERIAL OVERGROWTH/ DIARRHEA



Broad Spectrum Antibiotic use is the mainstay of treatment for this complication. There are many potential approaches to this therapy. For example: Antibiotics are given in 2–3 week courses followed by a 1–2 week drug holiday. Generally a few cycles of this treatment can allow for quiet periods of a few months to a few years. However, some persons may require almost continuous antibiotics.

Alternating antibiotics and increasing the antibiotic-free period will decrease the development of resistant strains of bacteria.

Note: Prolonged use of Broad Spectrum Antibiotics may lead to superinfections such as C. difficile colitis and infections with resistant bacteria.

BROAD SPECTRUM ANTIBIOTICS

Action - Prevent bacterial growth

EXAMPLES INCLUDE:

- TETRACYCLIN

  Side Effects
  Altered taste, nausea, vomiting, diarrhea, abdominal pain, skin photosensitivity, skin rash.

- METRONIDAZOLE (FLAGYL®)

  Side Effects
  Metallic taste, headache, nausea, vomiting, diarrhea, reduced appetite, dizziness, vaginitis.

- CIPROFLOXACIN (CIPRO®)

  Side Effects
  Drowsiness, dizziness, abdominal discomfort, nausea, diarrhea, vomiting, skin photosensitivity.

- AMOXICILLIN/CLAVULANATE (CLAVULIN®)

  Side Effects
  Nausea, abdominal discomfort, vomiting, diarrhea, skin rash, vaginitis.

- CLARITHROMYCIN (BIAXIN®)

- AZITHROMYCIN (ZITHROMAX®)

  Side Effects
  Altered taste , diarrhea, nausea, vomiting, heartburn, abdominal pain, metallic taste (clarithromycin), photosensitivity (azithromycin).

- CEPHALEXIN

  Side Effects
  Diarrhea, nausea, vomiting, dyspepsia, abdominal cramps and pain, skin rash, genital candidiasis, vaginitis.

- TRIMETHOPRIM/SULFAMETHOXAZOLE

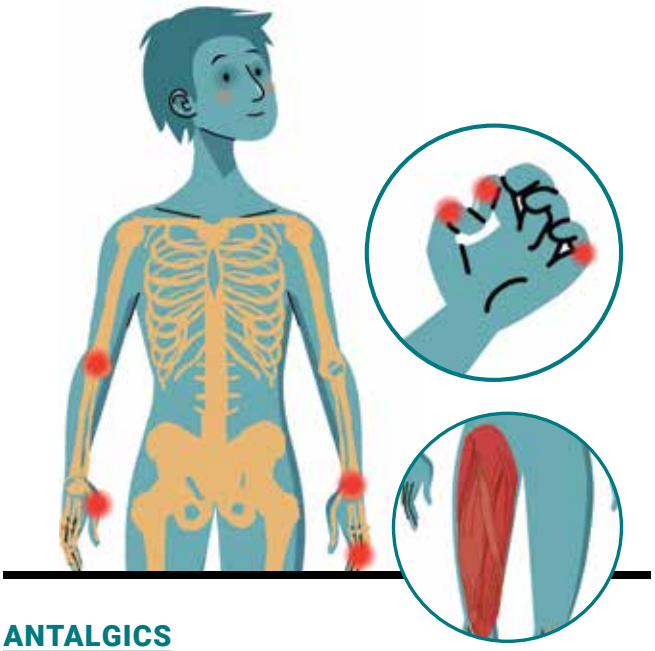
  Side Effects
  Nausea, vomiting, diarrhea or constipation, dyspepsia, headaches, loss of appetite, skin rash, dizziness, vaginitis, photosensitivity.

- RIFAXIMIN (ZAXINE®)

  Side Effects
  Peripheral edema, nausea, dizziness, fatigue, headache, abdominal pain, muscle cramps, skin rash, C. difficile colitis superinfection.

ARTHRITIS

When joint pain is caused by arthritis (joint inflammation with significant morning stiffness and possibly swelling), anti-inflammatories, analgesics, immunosuppressants, and immunomodulators may be used to reduce the inflammation and pain.



NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

- DICLOFENAC (VOLTAREN®)
- DICLOFENAC & MISOPROSTOL (ARTHROTEC®)
- DICLOFENAC SODIUM (VOLTAREN®)
- FLURBIPROFEN
- IBUPROFEN (MOTRIN®, ADVIL®)
- KETOPROFEN
- KETOROLAC (TORADOL®)
- MELOXICAM
- CELECOXIB (CELEBREX®)
- NABUMETONE
- NAPROXEN (NAPROSYN®, ANAPROX®, ALEVE®)
- PIROXICAM
- SULINDAC

Action - Suppress inflammation

Side Effects
Abdominal pain and cramping, dyspepsia, nausea, diarrhea or constipation, headache, dizziness, high blood pressure, bleeding, skin photosensitivity.

COX-2 INHIBITORS

- CELECOXIB (CELEBREX®)
- MELOXICAM

Action - Suppress inflammation

Side Effects
Abdominal pain and cramping, dyspepsia, nausea, diarrhea, headache, dizziness, high blood pressure, increased liver enzymes, skin photosensitivity.

ANTALGICS

- ACETAMINOPHEN (TYLENOL®)

Action - Relieve pain

Side Effects
Skin rash, nausea, increased liver enzymes, Overdosage manifestations include: metabolic acidosis, decreased appetite, fatigue extreme, hepatic impairment, jaundice, pallor, vomiting.

- TRAMADOL (ULTRAM®)

Action - Relieve pain

Side Effects
Nausea, constipation, vomiting, fatigue, drowsiness, dizziness, headache, dependence.

IMMUNOSUPPRESSANTS/ IMMUNOMODULATORS

- HYDROXYCHLOROQUINE (PLAQUENIL®)

Action - Modulate the immune response

Side Effects
Decreased appetite, diarrhea, nausea, vomiting, headaches, skin rash, itching, visual disturbances, low blood sugar, weakness, photosensitivity, arrhythmias.

- METHOTREXATE

Action - Decrease the immune response

Side Effects
Fatigue, nausea, vomiting, diarrhea, decreased appetite, liver and kidney disorders, mouth ulcers, skin rashes, bone marrow suppression, increased susceptibility to infections, skin photosensitivity, fertility disorders.

- SULFASALAZINE

Action - Modulate the immune response

Side Effects
Nausea, vomiting, diarrhea, stomach pain, skin reaction, headaches, anemia, decreased white blood cells and platelets, yellow urine.

- LEFLUNOMIDE (ARAVA®)

Action - Decrease the immune response

Side Effects
High blood pressure, diarrhea or constipation, vomiting, loss of appetite, weight loss, headaches, dizziness, mouth ulcers, skin rash, visual disturbances, urinary tract issues, liver problems.

- RITUXIMAB (RITUXAN®, RIXIMYO®, RUXIENCE®, TRUXIMA®, RIABNI®)

Action - Decrease the immune response

Side Effects
Nausea, vomiting, diarrhea, infusion reaction, headaches, pain, weakness, skin reactions, increased susceptibility to infections.

- TOCILIZUMAB (ACTEMRA®)

Action - Decrease the immune response

Side Effects
Reaction at the injection or infusion site, headaches, respiratory tract infections, nasopharyngitis, increased blood pressure, elevated liver enzymes.

- ABATACEPT (ORENCIA®)

Action - Decrease the immune response

Side Effects
Infections, headaches, nausea, vomiting, diarrhea, respiratory tract infection, dizziness, fatigue, arrhythmias.

Myositis

Myositis occurs when there is inflammation in the muscles, causing weakness. This condition can be confirmed through blood tests and muscle testing. In some cases, it may also be accompanied by inflammation of the heart muscle. Myositis should be treated with corticosteroids and immunosuppressants to reduce inflammation.

SYSTEMIC TREATMENTS

- PREDNISONE, METHYLPREDNISOLONE

Action – Suppress inflammation.

Side Effects
Indigestion, insomnia, nervousness, increased appetite, elevated blood sugar levels, headaches, dizziness, glaucoma, cataracts, skin photosensitivity.

Warning about the risk of renal crisis related to corticosteroid use.

Corticosteroids, such as prednisone and methylprednisolone, are sometimes used to treat certain complications of systemic scleroderma, such as inflammation of the muscles, heart, lungs, joints, and pruritus (itching).

However, the use of corticosteroids at daily doses higher than 15 mg (for prednisone) has been associated with an increased risk of developing scleroderma renal crisis.

Therefore, corticosteroids are used with great caution and only in a carefully selected group of patients.

If you are taking corticosteroids, monitor your blood pressure frequently and notify your doctor immediately if there are any changes (refer to the article “The Kidney in Systemic Sclerosis” in this book).

IMMUNOSUPPRESSANTS

- METHOTREXATE

Action - Decrease the immune response

Side Effects
Tiredness, nausea, vomiting, diarrhea, decreased appetite, liver and kidney disorders, mouth ulcers, skin rash, bone marrow suppression, increased risk of infections, skin photosensitivity, fertility disorders.

- MYCOPHENOLATE MOFETIL (CELLCEPT®)

Action - Decrease the immune response; anti-fibrotic effect

Side Effects
Abdominal pain, diarrhea or constipation, nausea, vomiting, headaches, increased susceptibility to infections,anemia, insomnia, high blood pressure, pain, skin photosensitivity and increased risk of skin cancer.

- RITUXIMAB (RITUXAN®, RIXIMYO®, RUXIENCE®, TRUXIMA®, RIABNI®)

Action - Decrease the immune response

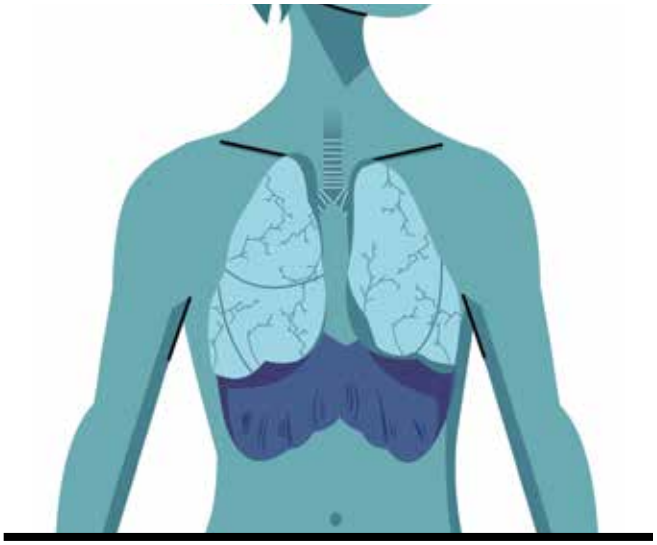
Side Effects
Nausea, vomiting, diarrhea, infusion reaction, headaches, pain, weakness, skin rash, increased susceptibility to infections.

OTHERS:

- INTRAVENOUS IMMUNOGLOBULINS (IVIG):

Action - Modulate the activity of the immune system.

Side Effects
Fatigue, headaches, chills, fever, nausea, vomiting, unusual pain, post-infusion high or low blood pressure, flu-like symptoms, hives.



PULMONARY FIBROSIS/ Interstitial lung disease

A potentially serious complication where normal lung tissue is gradually replaced by scarred fibrotic tissue, making it difficult to breathe and deliver needed oxygen to the body. Pulmonary fibrosis causes shortness of breath and also sometimes a dry cough.

IMMUNOSUPPRESSANTS

- MYCOPHENOLATE MOFETIL (CELLCEPT®)
- MYCOPHENOLATE SODIUM (MYFORTIC®)

Action - Decrease the immune response; anti-fibrotic effect

Side Effects
Abdominal pain, diarrhea or constipation, nausea, vomiting, headache, increased susceptibility to infections, anemia, insomnia, high blood pressure, pain, skin photosensitivity and increased risk of skin cancer.

- CYCLOPHOSPHAMIDE (PROCYTOX®)

Action - Suppress immune response

Side Effects
Hair loss, decreased appetite, bladder inflammation, bone marrow suppression, nausea, diarrhea, vomiting, mouth ulcers, increased susceptibility to infections, increased cancer risk, fertility disorders.

- **RITUXIMAB (RITUXAN®, RIXIMYO®, RUXIENCE®, TRUXIMA®, RIABNI®)**

Action - Decrease the immune response

Side Effects
Nausea, vomiting, diarrhea, Infusion reaction, headache, pain, weakness, skin rash, increased susceptibility to infections.

- **TOCILIZUMAB (ACTEMRA®)**

Action - Decrease the immune response

Side Effects
Infusion or injection site reaction, headache, respiratory tract infection, nasopharyngitis, high blood pressure, elevated liver enzymes.

- **AZATHIOPRINE (IMURAN®)**

Action - Decrease the immune response

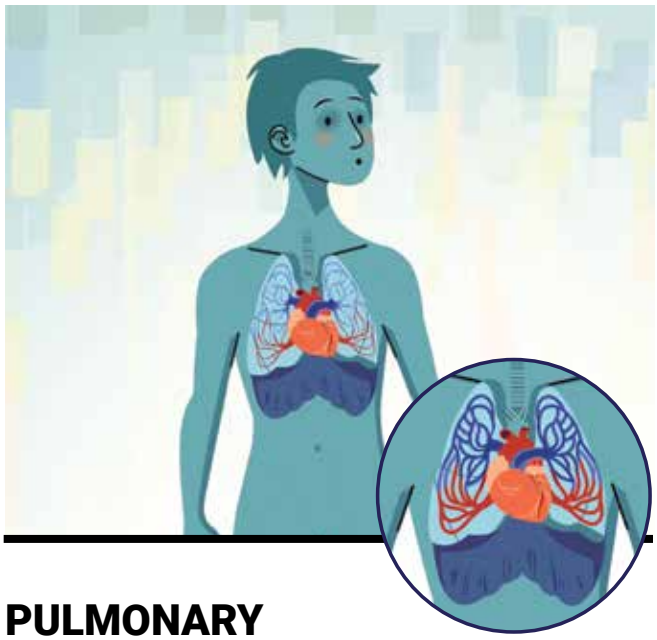
Side Effects
Nausea, vomiting, diarrhea, decreased appetite, bone marrow suppression, increased cancer risk, increased risk of infections, anemia, skin photosensitivity.

ANTI-FIBROTIC DRUG

- **NINTEDANIB (OFEV®)**

Action - Blocks the activity of fibroblasts which contribute to tissue fibrosis

Side Effects
Diarrhea, nausea, vomiting, abdominal pain, decreased appetite, weight loss, elevated liver enzymes, headache, bleeding, liver toxicity.



PULMONARY ARTERIAL HYPERTENSION

Increased pressure in the pulmonary arteries due to the narrowing of small arteries in the lungs. Blood flow to the lungs is significantly restricted, making the heart work harder to pump blood through the lungs.

Patients diagnosed with pulmonary arterial hypertension should be referred to a pulmonary hypertension center for experienced evaluation and management of this serious scleroderma complication.

ENDOTHELIN RECEPTOR ANTAGONISTS

- **AMBRISENTAN (VOLIBRIS®)**

Action - Act on blood vessels

Side Effects
Peripheral edema, headache, decreased hemoglobin, nasal stuffiness, palpitations, hot flushes, constipation.

- **BOSENTAN (TRACLEER®)**

Action - Act on blood vessels

Side Effects
Headache, hot flushes, liver function abnormality, pulmonary edema, low blood pressure, palpitations, dyspepsia, nasopharyngitis, fatigue.

- MACITENTAN (OPSUMIT®)

Action - Act on blood vessels

Side Effects
Edema, nasopharyngitis, headache, anemia, bronchitis, urinary tract infection, hypotension, pharyngitis, flu infection, fertility disorders.

ACTIVIN SIGNALING INHIBITOR

- SOTATERCEPT (WINREVAIR®)

Action - Improve the balance between pro-proliferative and anti-proliferative signaling to modulate vascular proliferation.

Side Effects
Headache, upper respiratory tract infection, diarrhea, injection site reaction, tiredness, dizziness, bleeding, increased hemoglobin, fertility disorders.

PROSTACYCLIN AND ANALOGUE

- EPOPROSTENOL (FLOLAN®, CARIPUL®)

Action - Act on blood vessels, inhibit platelet aggregation

Side Effects
Headache, dizziness, muscle weakness, hot flushes, jaw pain, nausea, diarrhea, bone and joint pain, decreased appetite, weight loss, heart rhythm disorders, bleeding, potential serious infection associated with central line catheter in the chest wall.

- TREPROSTINIL (REMODULIN®)

Action - Act on blood vessels, inhibit platelet aggregation

Side Effects
Pain and reaction at infusion site, headache, jaw pain, diarrhea, nausea, vomiting, hot flushes, edema, skin rash.

PROSTACYCLIN RECEPTORS AGONIST

- SELEXIPAG (UPTRAVI®)

Action - Act on blood vessels

Side Effects
Headache, diarrhea, nausea, vomiting, jaw pain, muscle and joint pain, hot flushes, skin rash, anemia, decreased appetite.

SOLUBLE GUANYLATE CYCLASE STIMULATOR

- RIOCIGUAT (ADEMPAS®)

Action - Act on blood vessels

Side Effects
Headache, dizziness, dyspepsia, diarrhea, nausea, vomiting, peripheral edema, low blood pressure, anemia, bleeding.

PHOSPHODIESTERASE TYPE 5 (PDE5) INHIBITOR

- SILDENAFIL (REVATIO®)

Action - Act on blood vessels

Side Effects
Headache, hot flushes, dyspepsia, nosebleeds, vision disturbances, nose congestion, diarrhea, insomnia, dizziness.

- TADALAFIL (ADCIRCA®)

Action - Act on blood vessels

Side Effects
Headache, hot flushes, muscle pain, dyspepsia, nausea, nasopharyngitis, nose congestion, dizziness.

COMBINATION OF TREATMENTS

- MACITENTAN AND TADALAFIL (OPSYNVI®)

Actions and side effects - See sections on individual drugs above.

RENAL CRISIS/NEW ONSET HYPERTENSION

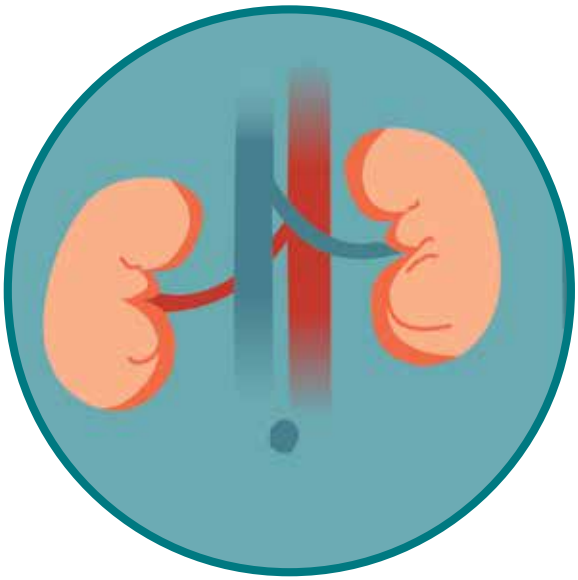
A renal crisis, which is due to an acute obstruction of arterioles and capillaries in the kidneys, leads to a sudden and sharp increase in arterial blood pressure. The symptoms are those of a hypertensive crisis: new and severe headaches, marked shortness of breath (left heart failure), and even epileptic seizures (convulsions). This is a very serious complication which requires urgent medical attention. Often during a scleroderma renal crisis, the kidneys stop functioning and dialysis (filtering the blood to avoid uremia) is then needed.

ANGIOTENSIN CONVERTING ENZYME INHIBITORS

- CAPTOPRIL
- ENALAPRIL (VASOTEC®)
- LISINOPRIL (ZESTRIL®)
- QUINAPRIL
- RAMIPRIL (ALTACE®)
- FOSINOPRIL
- BENAZEPRIL
- TRANDOLAPRIL (MAVIK®)

Action - Inhibit blood vessel constriction constriction of blood vessels

Side Effects
Low blood pressure, dizziness, increased blood-potassium level, headache, dry cough, tiredness, skin photosensitivity.



SKIN FIBROSIS

Thickening and loss of elasticity of the skin on different parts of the body. Hence the name «scleroderma», which means hard skin.

IMMUNOSUPPRESSANTS/ IMMUNOMODULATORS

- METHOTREXATE

Action - Decrease the immune response immune response

Side Effects
Tiredness, nausea, vomiting, diarrhea, decreased appetite, liver and kidney disorder, mouth ulcers, skin rash, bone marrow suppression, increased risk of infections, skin photosensitivity, fertility disorders.

- MYCOPHENOLATE MOFETIL (CELLCEPT®)
- MYCOPHENOLATE SODIUM (MYFORTIC®)

Action - Decrease the immune response immune response and anti-fibrotic effect

Side Effects
Abdominal pain, diarrhea or constipation, nausea, vomiting, headache, increased susceptibility to infections, anemia, insomnia, increase of blood pressure, pain, skin photosensitivity and increased risk of skin cancer.

- CYCLOPHOSPHAMIDE (PROCYTOX®)

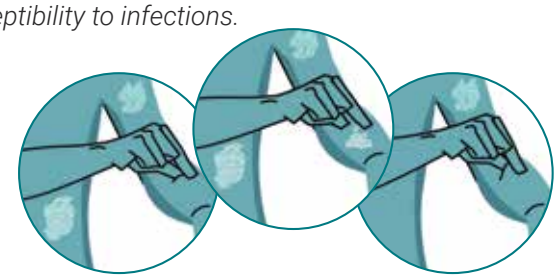
Action - Decrease the immune response immune response

Side Effects
Hair loss, decreased appetite, bladder inflammation, bone marrow suppression, nausea, diarrhea, vomiting, mouth ulcers, increased susceptibility to infections, increased cancer risk, fertility disorders.

- RITUXIMAB (RITUXAN®, RIXIMYO®, RUXIENCE®, TRUXIMA®, RIABNI®)

Action - Decrease the immune response

Side Effects
Nausea, vomiting, diarrhea, infusion reaction, headaches, pain, weakness, skin rash, increased susceptibility to infections.



SJÖGREN'S SYNDROME

Sjögren's syndrome is an autoimmune disease affecting mainly lacrimal glands (which produce tears) and salivary glands. This syndrome is caracterized by symptoms of dry mouth and dry eyes. Sjögren's syndrome can coexist with scleroderma.

PRESCRIPTION DRUGS

- PILOCARPINE HYDROCHLORIDE (SALAGEN®)

Action - Increase the secretion of exocrine glands including the salivary and lacrimal glands

Side Effects
Increased sweating, nausea, shiver, dizziness, headache, hot flushes, frequent urination, tiredness, rhinitis, skin photosensitivity.

- ANETHOLTRITHIONE (SIALOR®)

Action - Stimulate saliva secretion

Side Effects
Soft feces, yellow urine.

OVER-THE-COUNTER PRODUCTS

DRY MOUTH

- MOUTH KOTE ORAL MOISTURIZER®
- BIOTÈNE ORAL BALANCE® – MOISTURIZING GEL®
- BIOTÈNE DRY MOUTH – GUM®
- BIOTÈNE DRY MOUTH – TOOTHPASTE®
- BIOTÈNE DRY MOUTH – MOUTHWASH®
- XYLIMELTS – TIME-RELEASE ADHERING PASTILLES

Action - Moisturize and lubricate the mouth or stimulate saliva production

Side Effects
No significant side effect observed.

DRY EYES

- ARTIFICIAL TEARS
  Available in the form of solutions, gels or ointments. Products without preservatives are preferable.

Action - Lubricate the eyes

Side Effects
Slight stinging of the eyes, temporary blurred vision.

LOCALIZED SCLERODERMA

Localized scleroderma is a fibrotic disease of the skin and sometimes of the underlying tissues, but does not affect internal organs. It affects mostly children, but can also occur in adulthood. There are several forms of localized scleroderma, including circumscribed or plaque morphea (involving one or multiple well-defined, oval to round areas of skin thickening), generalized morphea (when at least 4 plaques involving at least 2 anatomical sites are present), linear scleroderma (characterized by tight, thick bands, frequently affecting extremities) and scleroderma en coup de sabre (a type of linear scleroderma that affects the forehead and scalp area on one side of the head, with resemblance to the cut of a saber). Raynaud's phenomenon is usually absent in localized scleroderma.

LOCAL TREATMENTS

- TOPICAL STEROIDS

Action - Anti-inflammatory and anti-fibrotic effects

Side Effects
Skin atrophy, hypopigmentation at application site, erythema, rash, acne rash, local irritation, skin dryness, skin infection, skin photosensitivity with some agents.

- INTRALESIONAL STEROIDS

Action - Anti-inflammatory and anti-fibrotic effects

Side Effects
Pain and irritation at the injection site, delayed wound healing, allergic reaction, a kind of meshwork on the skin due to the dilation of the capillaries (definition of telangiectasia), changes in skin pigmentation.

- TOPICAL TACROLIMUS (PROTOPIC®)

Side Effects
Burning sensation, itching, erythema, headache, skin infection, acne, folliculitis, hypersensitivity reaction, skin photosensitivity.

- TOPICAL VITAMIN D ANALOGUE (CALCIPOTRIOL = DOVONEX®)

Side Effects
Skin irritation, itching, local erythema, dermatitis, skin dryness, skin photosensitivity.

PHOTOTHERAPY

Action - Decrease skin thickening

Side Effects
Burning, itching, nausea, skin aging.

SYSTEMIC TREATMENTS

- METHOTREXATE

Action - Decrease the immune response

Side Effects
Tiredness, nausea, vomiting, diarrhea, decreased appetite, liver and kidney disorder, mouth ulcers, skin rash, bone marrow suppression, increased susceptibility to infections, skin photosensitivity, fertility disorders.

- MYCOPHENOLATE MOFETIL (CELLCEPT®)
- MYCOPHENOLATE SODIUM (MYFORTIC®)

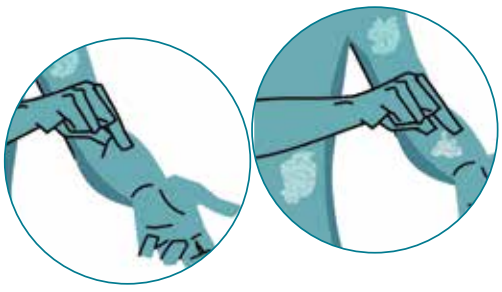
Action - Decrease immune response and anti-fibrotic effect

Side Effects
Abdominal pain, diarrhea or constipation, nausea, vomiting, headache, increased susceptibility to infections, anemia, insomnia, increase of blood pressure, pain, skin photosensitivity and increased risk of skin cancer.

- PREDNISONE, METHYLPREDNISOLONE

Action - Suppress inflammation

Side Effects
Indigestion, insomnia, nervousness, increased appetite, hyperglycemia, headache, dizziness, glaucoma, cataracts, skin photosensitivity.



SKIN ITCHING (PRURITUS)/ DRYNESS

Itch (pruritus) and skin dryness are frequent symptoms in systemic sclerosis. They are usually caused by skin irritation due to inflammation and fibrosis. Pruritus can also sometimes be a sign of liver disease associated with systemic sclerosis (primary biliary cholangitis).

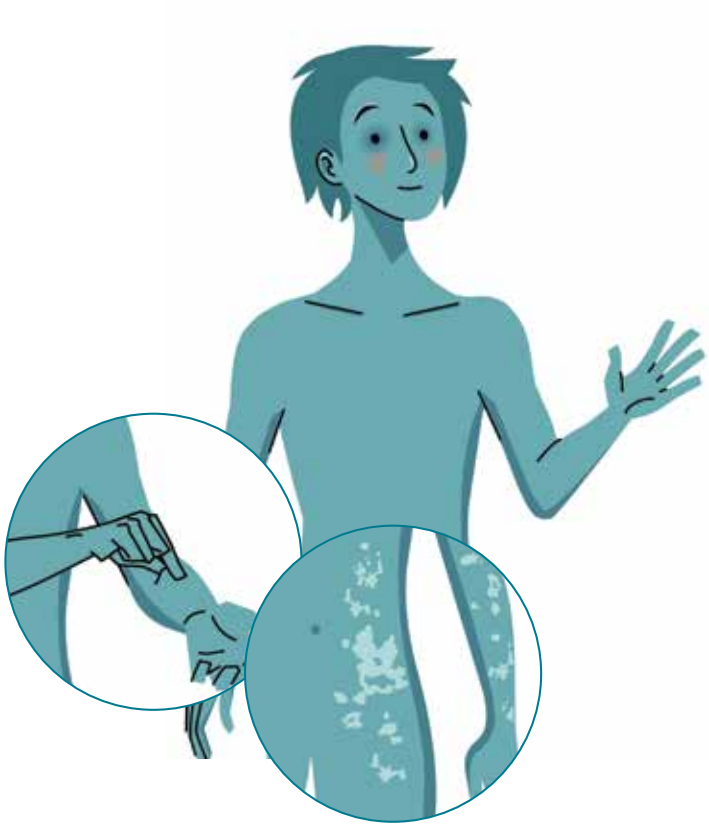
To relieve dry itchy skin, it is necessary to moisturize often. Also, the skin must be protected from harsh detergents, hot water, and the cold winter air, all of which will rob moisture from the skin. Using a humidifier in the home during the cold winter heating months to replace much-needed moisture into the air may be helpful. Not everyone will have the same response to every product. A few products may need to be tried until one is found to work for the patient.

OVER-THE-COUNTER SKIN LOTIONS

- CETAPHIL® CREAMS AND LOTIONS
- GLAXAL BASE® CREAMS AND LOTIONS
- EUCERIN® CREAMS AND LOTIONS
- CERAVE® CREAMS AND LOTIONS
- CUTIBASE® CREAMS AND LOTIONS
- KERI® BATH OIL
- AVEENO® BATH OIL, CREAMS AND LOTIONS

Action - Moisturize skin

Side Effect
No significant side effect observed.



ANTIHISTAMINES (PRESCRIPTION)

- CETIRIZINE (REACTINE®)
- DIPHENHYDRAMINE (BENADRYL®)
- HYDROXYZINE (ATARAX®)
- LORATADINE (CLARITIN®)
- DESLORATADINE (AERIUS®)

Action - Inhibit histamine response, thereby decreasing itching

Side Effect
Dry mouth, nausea, fatigue, drowsiness, dizziness, headaches, increased appetite (hydroxyzine and diphenhydramine), weight gain, ocular dryness.

IV TREATMENTS AND THERAPY

Cellular therapies for scleroderma

Dr. Marie Hudson
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Rheumatologist, Epidemiologist,
Associate Professor, Department of
Medicine, McGill University

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Introduction

Systemic sclerosis (SSc) is a chronic, systemic autoimmune disease characterized by a pathogenic triad of vasculopathy, immune dysregulation and fibrosis that results in multi-organ dysfunction affecting primarily the skin, gastrointestinal tract, lungs, heart and kidneys. Mortality rates for SSc compared to the general population have remained high (standardized mortality ratios above 3.5) in the past 50 years, in sharp contrast to the significant reductions in mortality in numerous other diseases, including cancer and cardiorespiratory diseases.

In addition to reduced survival, SSc is also notable for significant morbidity that results from Raynaud's phenomenon, finger ulcers, joint contractures, gastro-esophageal reflux disease, malabsorption, diarrhea, constipation, fecal incontinence, and exertional dyspnea, among others. These translate into limitations in physical mobility and function, disfigurement, pain, fatigue, sleep disturbance, and depression. SSc is associated with significant impairment in health-related quality of life on average 1½ standard deviations below the general population, comparable to or worse than that of patients with other chronic conditions, including heart disease, lung disease, hypertension, diabetes and depression.

SSc remains an orphan disease with high unmet needs in the field of therapeutics. The recommended treatments are mostly symptomatic, with drugs alleviating the symptoms mentioned above rather than targeting the disease as a whole. Also, immunosuppressive drugs such as cyclophosphamide and mycophenolate mofetil have at best modest effects aimed at stabilizing disease, without improving survival.

Similar to lung or kidney transplant where a whole organ is harvested from a healthy donor and transferred to someone with lung or kidney failure, cell therapies involve the harvesting of healthy human cells (whether from a donor or even the patients themselves) which are then transfused into a patient to restore or repair a diseased cell or organ. The best-known type of cell therapy is blood transfusions. Some cells used as cell therapies have long-lasting effects and are therefore valued for their regenerative properties.

The purpose of this chapter is to provide an overview of the cellular therapies presently available or currently under investigation for the treatment of SSc.

Hematopoietic stem cell (HSC) transplantation

Overview

Hematopoietic stem cells (HSCs) are special undifferentiated cells that reside in our bone marrow and give rise to mature cells that circulate in the blood, including red blood cells (which carry oxygen), platelets (which prevent excessive bleeding) and white blood cells (which protect us from infections). In certain blood cancers (e.g., leukemias), treatment is given to eradicate diseased HSCs and 'new - healthy' HSCs are transplanted. In scleroderma, some abnormal white blood cells are involved in the development of the disease by causing excessive inflammation and fibrosis. So as in leukemia, those diseased cells are removed and replaced with healthy HSC that regenerate a 'new – healthy' immune system. Many good studies have shown that HSC transplant can improve outcomes in scleroderma, including survival. However, HSC transplant is associated with considerable risks (e.g., acute infections, heart toxicity) and transplant-related mortality (5-10%).

Who is and is not a candidate for HSC transplant for scleroderma?

Given the toxicity associated with the transplant itself, **HSC transplant is not for everyone**. Patients are carefully selected. The main selection criteria are the following:

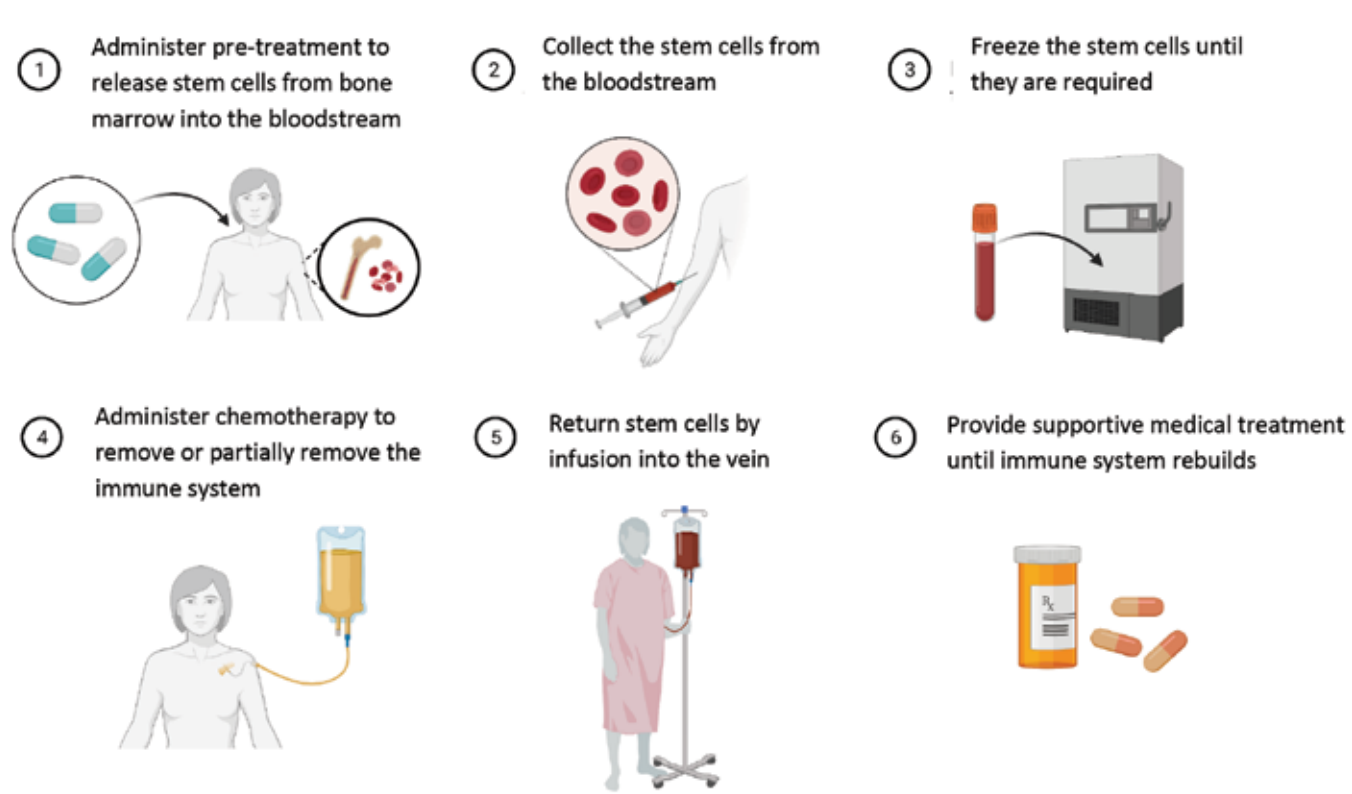
Main indications for HSC transplant

- Early disease (< 5 years)
- Rapidly progressive disease refractory to standard treatments
- Mild to moderate organ damage.

Main contraindications for HSC transplant

- Longstanding disease
- Mild, slowly progressive disease
- Irreversible organ damage, including pulmonary arterial hypertension.

What are the steps for a HSC transplant?



Step 1: Mobilization (a few days)
First, you receive injections of a medication that allows your hematopoietic stem cells to be released from your bone marrow into your circulation.

Step 2: Stem cell collection (1 day)
The stem cells are then collected using an IV. The collection is sometimes manipulated to remove any remaining diseased cells and purify the stem cells.

Step 3: Storage
The stem cells are stored in a cell therapy laboratory until they are needed.

Step 4: Pre-transplant treatment (i.e., conditioning, 5-10 days
High dose chemotherapy, and sometimes radiotherapy, is given to eliminate your unhealthy immune cells.

Step 5: Getting your stem cells back (i.e. HSC transplant, around 30 minutes)
Your own stem cells that were previously collected and stored are infused back into you through an IV.

Step 6: Recovery
Close monitoring is required for weeks in the hospital and then months as an outpatient until your stem cells recover their normal function and regenerate a healthy immune system.

What to consider before a transplant?

Studies have shown that the most common questions from scleroderma patients considering HSC transplant were the following:

1. **Will I be supported by a multidisciplinary team?**
2. **What are the financial risks?**
3. **Where can I get reliable information about HSC transplant?**
4. **Are there physical risks associated with HSC transplant?**
5. **What are the benefits of HSC transplant for someone in my condition?**

Here are some resources to help with answering some of these important questions:

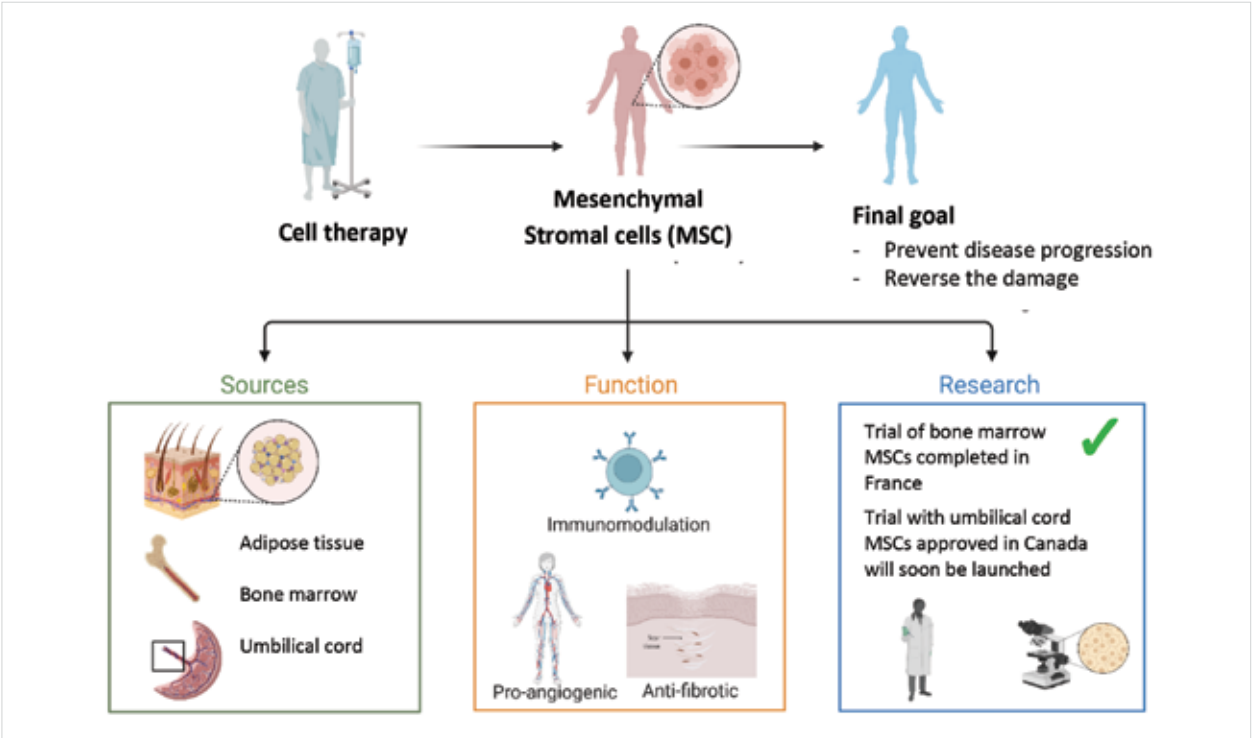
www.astemcelljourney.com

https://mathec.com

What to expect after transplant?

HSC transplant is not a cure for scleroderma and the damage that has occurred prior to transplant is generally not reversible. However, HSC transplant is currently the best treatment to prevent disease progression and the only one shown to increase survival in scleroderma. Also, people with scleroderma have much better function and quality of life after HSC transplant compared to those treated with standard treatments.

Mesenchymal stromal cells (MSCs)



Given that HSC transplant can be toxic and is not for everyone, different types of cellular therapies are being investigated. Mesenchymal stromal cells (MSCs) have immunomodulatory, pro-angiogenic, and anti-fibrotic properties and therefore have the potential to target all three axes of the SSc pathogenic triad. MSCs are present in nearly every tissue. They are responsible for keeping those tissues healthy. For therapeutic uses, they are usually harvested from bone marrow, adipose tissue, and umbilical cord. Injections of MSCs have been studied in a wide range of diseases, including other autoimmune diseases, and have been shown, first, to be safe (in large part because they do not need to be administered with chemotherapy) and second, to help in tissue repair and regeneration.

In scleroderma, MSCs are thought to work by resetting the diseased immune system. This in turn can lead to less fibrosis and better circulation. To date, an early trial of bone marrow derived MSCs has been completed in France and results are promising. However, harvesting MSCs from the bone marrow is fairly invasive. Umbilical cords represent a promising alternative. A study of umbilical cord derived MSCs in scleroderma has been approved in Canada and should begin soon.

Many questions remain around the benefits of MSCs for scleroderma. What is the best source of MSCs? How can the function of MSCs from different donors be standardized? Will the benefits be sustained or will repeated infusions be required? If so, can MSCs from different sources and donors be used? In addition to infusions through the veins, can MSCs be injected locally, for example in the fingers, face or muscles? Can MSCs be produced in sufficient quantities to meet the demands? Instead of whole cells, are there specific components of MSCs or alternative cell products that could be more effective and more easily manufactured? And the list goes on!

Conclusion

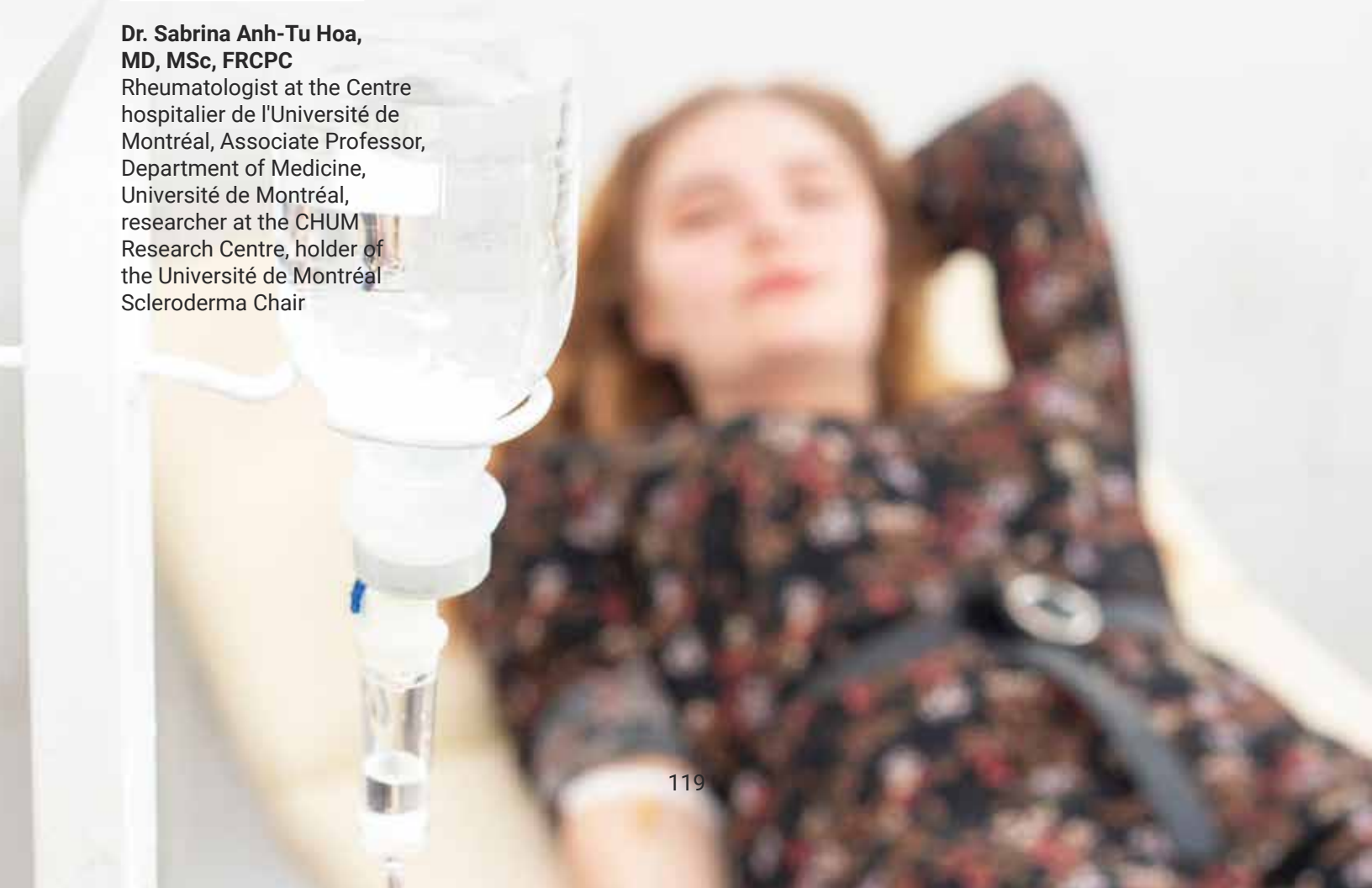
Research is key to answering these and other questions. Identifying new, safe and accessible therapies that not only prevent disease progression but ideally reverse the damage that has already accumulated should remain the top priority for scleroderma research.

IV TREATMENTS AND THERAPY

Intravenous Immunoglobulin and Scleroderma

Dr. Sabrina Anh-Tu Hoa, MD, MSc, FRCPC
Rheumatologist at the Centre hospitalier de l'Université de Montréal, Associate Professor, Department of Medicine, Université de Montréal, researcher at the CHUM Research Centre, holder of the Université de Montréal Scleroderma Chair

Systemic sclerosis (or scleroderma) is an autoimmune disease in which the immune system is dysfunctional and attacks its own cells, leading to excessive scarring (fibrosis) of the skin and internal organs. Intravenous immunoglobulin (IVIg) is a blood product used to treat certain autoimmune diseases. In this article, we will discuss the role of this treatment in scleroderma.



What is intravenous immunoglobulin?

IVIg is a blood product made from a mixture of antibodies that can be given intravenously (through a vein). Antibodies are proteins produced by the body to fight infections. IVIg is prepared from the blood of thousands of human blood donors and, therefore, contains a wide variety of antibodies.

What is the mechanism of action of intravenous immunoglobulin?

IVIg is used primarily in two types of diseases: immunodeficiencies and autoimmune diseases.

In immunodeficiencies, the body does not produce enough antibodies, making it vulnerable to infections. In this situation, immunoglobulin treatments are used to replace the missing antibodies to help the body protect itself from infections.

In autoimmune diseases, the immune system is dysfunctional and produces antibodies that attack its own cells (autoantibodies). In this situation, the antibodies and other substances contained in IVIg could act by neutralizing the abnormal autoantibodies and interfering with the development and function of immune cells, including B-cells, which are responsible for producing the abnormal autoantibodies. IVIg might also act on fibrosis, by interfering with small proteins in the blood (cytokines) that are involved in fibrosis formation. The mechanism of action of IVIg in autoimmune diseases is complex and only partially understood, but overall, IVIg appears to interfere with various components of the immune system and may be beneficial in the treatment of some autoimmune diseases.

How is intravenous immunoglobulin administered?

Immunoglobulins are administered intravenously, that is, through a vein. The total dose of IVIg required depends on the individual's weight and is usually divided over two to five days, with each infusion lasting several hours. This allows for a more gradual infusion, which reduces the risk of side effects. Each infusion cycle (over two to five days) may be repeated every 2 to 4 weeks and the total duration of treatment is determined by the specific disease under consideration and response to treatment. IVIg infusions are usually administered in a hospital medical day unit or infusion clinic.

Are immunoglobulins effective in the treatment of systemic sclerosis?

A systematic review of the literature was published in 2021 summarizing clinical studies performed on IVIg treatments in systemic sclerosis from the years 2000 to 2020 (Agostini et al.)

A total of 17 studies, including 182 patients, were identified.

Most of these studies reported the experience of patients with scleroderma who received IVIg treatments, but without a control group. These patients were treated with IVIg because of severe and refractory disease (unresponsive to conventional therapies), coexisting muscle inflammation (IVIg is used to treat myositis) and/or concomitant infections (thus precluding the use of conventional immunosuppressive therapies). IVIg has been used primarily to treat diffuse skin and muscle involvement, but also for severe joint (arthritis), cardiac (myocarditis/inflammation of the heart), pulmonary (inflammation of the lungs) and/or gastrointestinal manifestations. Improvements have been noted in many of these patients after one or more cycles of treatment, with rapid and sometimes sustained benefits.

Only one study was a randomized, placebo-controlled, double-blind clinical trial. This type of study is the best way to determine the efficacy of a treatment, because it allows the treatment to be compared to a control group (and thus compared to the natural course of the disease), eliminates the placebo effect (improvement in the disease related to the psychological benefit of receiving the treatment), and reduces the effect of confounding factors (by randomly separating the groups). In this study published in 2013 by Takahera et al., 63 participants with the diffuse form of systemic sclerosis from 17 medical institutions in Japan received an IVIg treatment or placebo. The results: the mean decrease in skin fibrosis score was not significantly different between the two study groups at 3 months after a single cycle of treatment. However, when a second cycle of treatment was given at 6 months to all participants who had not improved, a significantly greater reduction in skin fibrosis score was observed in the group that received 2 doses of IVIg compared to the group that initially received a placebo.

In summary, IVIg may be effective in the treatment of systemic sclerosis, given its potential effect on autoimmunity and fibrosis, and based on mostly uncontrolled studies reporting benefits in patients with severe and refractory disease. However, randomized controlled trials with a longer duration of treatment and larger numbers of participants would be required before a more definitive conclusion can be reached regarding the efficacy and role of IVIg in the treatment of systemic sclerosis.

Could I benefit from treatment with immunoglobulins?

As previously discussed, the efficacy of IVIg has not yet been definitively established and, therefore, this treatment is not commonly used in the treatment of systemic sclerosis. However, IVIg may be considered in certain specific situations, such as for severe skin, muscle, joint, heart, lung or gastrointestinal involvements that are refractory to conventional treatments. IVIg may also be considered when there is a contraindication or intolerance to conventional immunosuppressive treatments. For instance, IVIg is considered safer than immunosuppressive drugs for the risk of infectious complications. It should be noted, however, that current access to IVIg is limited due to a worldwide shortage of this blood product and its very high cost, and may require special authorization.

What are the possible risks of intravenous immunoglobulin treatment?

Most patients who receive IVIg tolerate the infusion very well. However, some patients may experience side effects, such as headache, chills, fever, muscle aches, fatigue or nausea. These symptoms are usually mild and occur most often after the first dose. More serious side effects, such as an allergic reaction, heart or kidney failure, non-infectious meningitis or anemia, may occur but are very rare. Myocardial infarction (heart attack), stroke and thrombosis (blood clots) have been reported, but are very rare when the infusion is administered slowly over several days. Although IVIg is a blood product, the risk of infection is extremely low because the methods used to purify the immunoglobulins destroy bacteria, hepatitis viruses and other infectious organisms.

In summary

IVIg is a blood product composed of a mixture of antibodies and have beneficial effects on autoimmunity and fibrosis. Studies have reported a beneficial effect of IVIg in some patients with severe scleroderma refractory to conventional treatments, but more clinical studies are needed before a more definitive conclusion can be made about their efficacy. Nevertheless, IVIg may be tried in certain specific situations, such as when other therapeutic options have failed or are contraindicated.

IV TREATMENTS AND THERAPY

Natural Health Products

Amélie Granger-Pouliot,
Pharm. D

What is a Natural Health product?

It is a natural substance used to restore or maintain good health. Natural products are often derived from plants, but can also be derived from micro-organisms or animal and marine sources.

What indicates that it is a Natural Health product?

Natural health products evaluated by Health Canada all have an NPN (i.e., Natural Product Number), or in the case of homeopathic remedies, a DIN-HM. The NPN is an eight-digit number which means that it has been licensed by Health Canada. By having an NPN or a DIN-HM, Health Canada is indicating that the product is authorized for sale in Canada and that it is safe and effective when used according to label directions. If there is no NPN or DIN-HM, it means that there is no control over the product and no evidence of effectiveness and/or safety has been demonstrated. Similarly, for prescription drugs a DIN is assigned to each drug, which is a Drug Identification Number. This DIN is an eight-digit number assigned by Health Canada before it is marketed in Canada. Thus the NPN and the DIN-HM are subject to regulations similar to the DIN, but they are specific to natural health products and homeopathic medicines.

What does an NPN or a DIN-HM look like?

Is a Natural Health product always safe?

Although it is generally safe to use, it is not without risk. Just because a product is called "natural" does not mean it is "harmless"! Natural health products, like prescription drugs, can have side effects and may even be toxic if not taken at the recommended dose. In fact, 12% of Canadians who use natural health products have reported experiencing adverse reactions to these products!

In addition, natural health and homeopathic products may not be suitable for some people with health problems, or they may interact with prescription drugs. These interactions may result in a decrease, cancellation or increase in the therapeutic effects of prescription drugs.

For example, echinacea is a natural product that is not recommended for scleroderma patients. Indeed, echinacea has, among other properties, that of stimulating the immune system. As a result, all diseases considered "autoimmune", including scleroderma, may potentially interact with echinacea. Thus, this product can exacerbate the symptoms of autoimmune disease by stimulating the immune system.

Another example of a product to be used with caution in people living with scleroderma is melatonin. Although melatonin can lower nighttime blood pressure in people with essential hypertension, it may paradoxically interact with the antihypertensive drug nifedipine. This pharmacodynamic interaction may lead to an increase in blood pressure. Therefore, melatonin may interact with several medications that scleroderma patients may be taking, including anti-inflammatory drugs and immunosuppressants. In addition, its drowsy effect may compound the sedative effects of narcotic pain medications. For all these reasons, scleroderma patients should be very careful before taking melatonin.

A final example is probiotics. Immunosuppressants such as cyclophosphamide or azathioprine may often be necessary to help control the symptoms of the disease in scleroderma patients. However, probiotics are not recommended for this immunosuppressed population because although probiotics are considered "good" bacteria, they can be harmful or even dangerous to someone who is immunosuppressed.

Therefore, even with natural health products, one must be very vigilant and only a pharmacist can check for these numerous potentially harmful interactions.

How to reduce the risks?

ALWAYS consult a doctor or pharmacist before choosing a product, even if it is a natural or homeopathic product, just as you would consult a healthcare professional for a prescription drug. This precaution is even more important for people who are taking multiple medications, to ensure that there are no interactions with them.

Furthermore, it is preferable to use natural health products for a short period of time (less than 3 months), as the effects of long-term use are often unknown because there are very few long-term studies on the subject.

In summary

In short, there is still a lack of clinical studies and research on natural health products and homeopathic remedies. Therefore, great caution must be exercised. It is difficult to say with certainty whether a natural health product will interact with prescription drugs, and one should be aware of this risk. Always talk to your doctor and pharmacist when taking a natural or homeopathic product to make sure it is safe and effective.

The Scleroderma Patient-centered Intervention Network and the SPIN-HAND Program

Dr. Brett Thombs
Ph.D. Director, Scleroderma Patient-centered Intervention Network (SPIN); Professor, Faculty of Medicine, McGill University; Senior Investigator, Lady Davis Institute of Medical Research, Jewish General Hospital; Canada Research Chair (Tier 1)

The Scleroderma Patient-centered Intervention Network (SPIN) is a patient-oriented research organization that provides evidence and creates tools to better inform patients and scleroderma clinicians. SPIN consists of researchers, healthcare providers and people living with scleroderma worldwide. SPIN's mission is to work with people living with scleroderma to identify their needs and prioritize research in the areas most important to them. SPIN aims to develop, test, and disseminate accessible patient programs that improve quality of life and empower people with scleroderma and their loved ones.

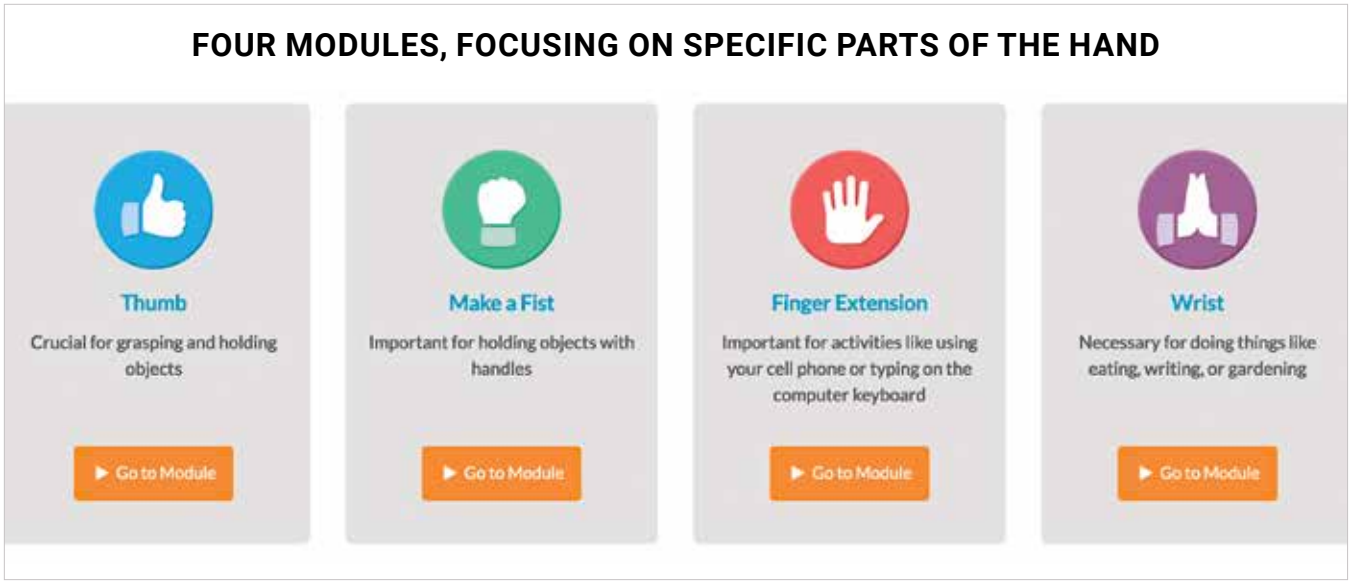
The areas of research covered by the programs developed by SPIN include, but are not limited to, managing symptoms, emotions and appearance changes related to illness, as well as balancing activity and rest.

SPIN employs an innovative research model that uses the SPIN Cohort (approx. 1,400 patients) as a framework to conduct trials of its online patient programs. Once patients are enrolled in the SPIN Cohort via SPIN healthcare sites, trials are conducted with patients from around the world. SPIN programs are jointly designed by health experts, clinicians, and people with scleroderma to ensure that patient needs and concerns are met.

The SPIN-HAND Program

We use our hands in just about everything we do. When you have scleroderma, this can be a real challenge. There are many different changes to your body caused by scleroderma that can make it difficult to use your hands effectively. These include damage to the blood vessels, swelling, muscle pain and weakness, and damage or ulceration to the skin. Reduced hand mobility due to scleroderma can have serious consequences for daily activities, such as dressing, eating and drinking, driving, getting change from your pocket or purse, or using a computer or another electronic device. In fact, impaired hand function has the potential to impact almost every aspect of your life.

The SPIN-HAND program provides you with gentle hand exercises explicitly designed for people with scleroderma, with sections to help you develop a personalized program, set goals, and track your progress. Instructional videos demonstrate how to perform each exercise properly with pictures to illustrate common mistakes. Doing hand exercises regularly can help you to maintain - and even potentially improve - your ability to use your hands effectively, so that you can do more of the things that you need to do to work, take care of yourself and your home, or just to enjoy life.



There are four modules in this program. Each module includes different types of exercises, along with a short video with instructions on how to perform the exercises properly. There are exercises to help you increase your thumb mobility, increase the mobility of your other fingers and your ability to make a fist, extend your fingers more fully, and use your wrists.

These exercises correspond to movements that are important for many different daily activities. For example, thumb mobility is crucial for grasping and holding objects. Finger mobility is also important for this, particularly for objects with handles, such as a spoon, a pencil, or the steering wheel of your car. Finger extension allows you to do things like using your cellphone or typing on your computer keyboard. Finally, wrist mobility is necessary to place your hand in the correct position for doing things like eating, writing, gardening, and wringing out a towel or a rag.

THUMB EXERCISES

Thumb Stretching

Thumb Bending

Thumb Grip

EXERCISES FORMING A FIST

Knucle Bending

Finger-by-Finger Bending

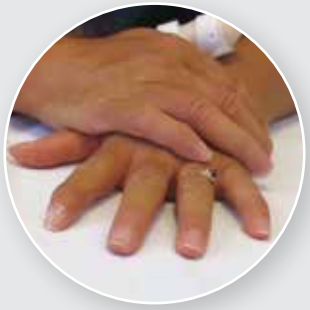
Grip Strength

FINGER EXTENSION EXERCISES

Finger Spreading

Finger-by-Finger Straightening

Flat Hand



WRIST EXERCISES

Wrist Rotation

Wrist Extension

There are separate versions of each exercise in the four modules for people with mild to moderate hand involvement and for people with more severe hand involvement.

Example of Thumb Exercise

Start with the palm of your left hand flat on the table. Use your right hand to take hold of your thumb, down at the base of your thumb. Move the thumb away from your index finger as far as possible without pain and hold for 10 seconds. Let go and relax for 5 seconds. Now, switch hands and do the same thing with your other hand. Put the palm of your right hand flat on the table. Use your left hand to take a hold of your thumb at the base of your thumb. Move the thumb away from your index finger as far as possible without pain and hold for 10 seconds. Let go and relax for 5 seconds. Don't forget to keep breathing calmly while you are doing the exercise. Do this exercise 5 times with each hand.

For this program to be helpful, it is important that you do the exercises regularly. So, once you have learned the basics, please also take the time to set up an exercise schedule. There are examples of weekly routines in the toolkit that involve doing 3 to 4 sessions a week, doing a few selected exercises every day, or doing all of the exercises 7 days a week. You can pick a plan that works best for you or modify the plans to fit your needs.

You can access SPIN-HAND for free at:
tools.spinsclero.com

To reap the benefits of this program, start out at a slow and comfortable pace and keep it going!

WEEKS 1 TO 4

Here is an example of a routine for weeks 1 to 4. This table shows an example in which you practice one module per week and steadily increase the amount of time spent exercising each week. The order in which you select the modules is up to you.

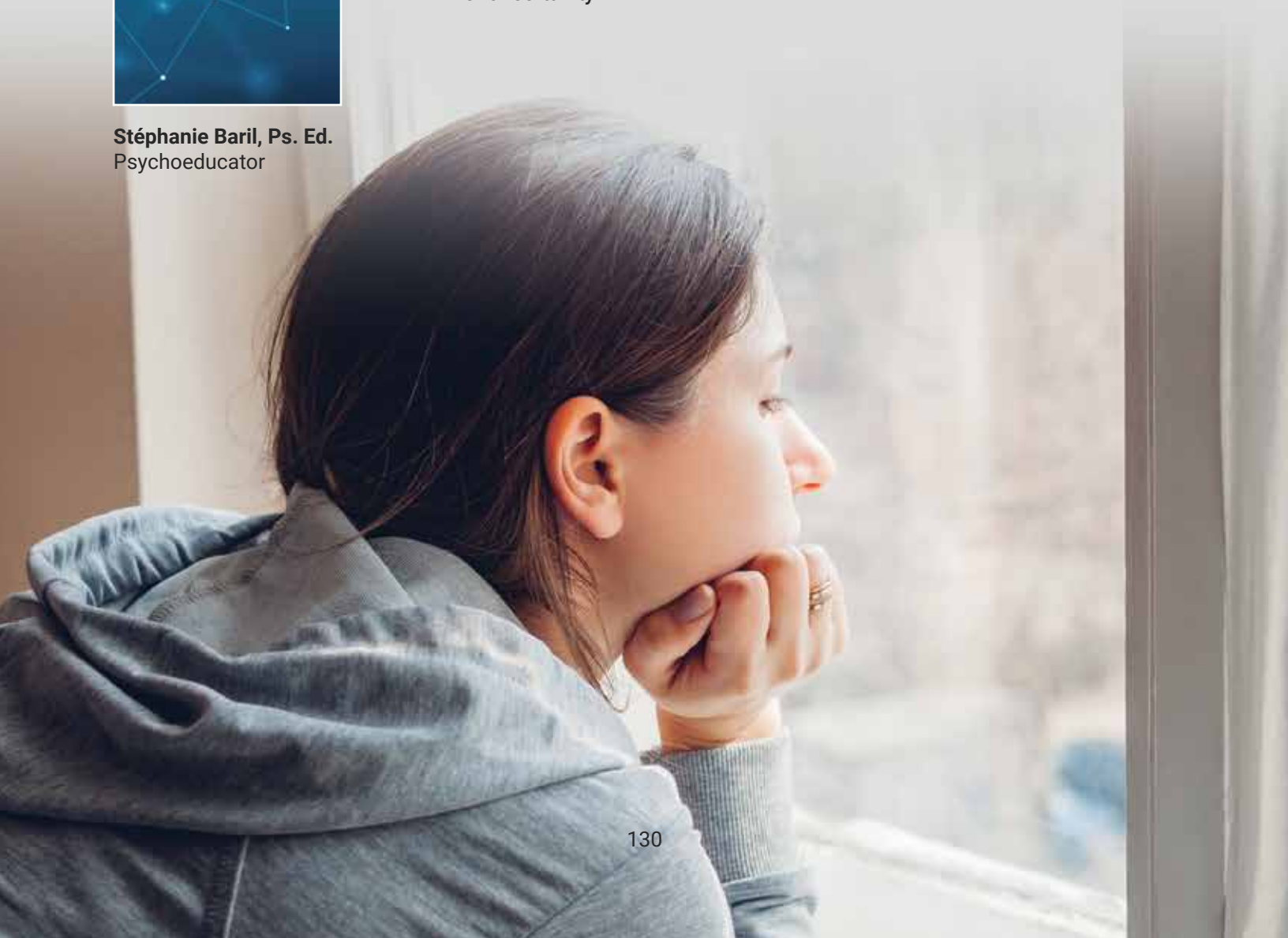
WEEK 1 **Wrist**	**WEEK 2** **Make Fist**	**WEEK 3** **Finger Extension**	**WEEK 4** **Thumb**
Wrist rotation *(1 to 2 minutes per day)*	Knuckle bending *(1 to 2 minutes per day)*	Finger spreading *(1 to 2 minutes per day)*	Thumb stretching *(2 to 3 minutes per day)*
Wrist extension *(1 to 2 minutes per day)*	Finger-by-finger bending *(1 to 2 minutes per day)*	Finger-by-finger straightening *(6 to 7 minutes per day)*	Thumb bending *(2 to 3 minutes per day)*
	Grip strength *(1 to 2 minutes per day)*	Flat hand *(1 to 2 minutes per day)*	Thumb grip *(10 to 11 minutes per day)*
Total routine time: (2 to 4 minutes per day)	**Total routine time:** (3 to 6 minutes per day)	**Total routine time:** (8 to 11 minutes per day)	**Total routine time:** (14 to 17 minutes per day)

V LIVING WITH SCLERODERMA

Accepting the Diagnosis of Scleroderma

Stéphanie Baril, Ps. Ed.
Psychoeducator

Accepting the diagnosis of scleroderma is a unique experience for each person. Some adapt quickly, while others require more time to assimilate the information. Certain people are upset by the news while others can feel a sense of relief, putting a name on their symptoms and reducing their feeling of uncertainty [(1)].



TOWARDS ACCEPTANCE

Someone who has difficulty accepting their diagnosis may need to grieve for their previous life before being able to adapt and accept their new reality. This process may include progressions and regressions. It is not necessarily linear [2] and it varies from one person to the other, depending on their interpretation of their situation and their ability to bounce back [1]. Regardless of the path taken, it is important to respect the person's pace.

State of Shock

Upon the confirmation of the diagnosis of scleroderma, the person may feel shocked [2]. Various physiological reactions may occur, such as an apparent insensitivity to the news, a ringing in the ears, blurred eyes, a cold sensation, a feeling of heaviness, uncontrollable laughter, a feeling of paralysis, etc.

Denial

The person may experience denial towards the news, refusing the diagnosis, and adopting behaviours to protect themselves [2] [3]. For example, they may seek a second medical opinion, distract themselves with other activities, or suppress their emotions.

A Whirlwind of Emotions

The person may feel various emotions, which can change in nature or intensity, and may leave and resurface at times [2]. They may feel helpless towards the situation, not knowing how to proceed with the confirmation of scleroderma [3]. They may tend to have more negative interpretations of certain situations and may seek to isolate themselves.

By gradually accepting the situation, the person can experience their emotions with less intensity, better understand their situation, and continue their path towards acceptance.

Acceptance And Adaptation

Finally, acceptance occurs when the person accepts their current situation [3], including the reality of scleroderma. They let go of elements beyond their control (like the presence of the illness) and focus on the things within their control (like decisions and actions).

SUGGESTIONS

Here are concrete actions that a person can take during their process of acceptance of scleroderma.

Information

Because scleroderma is a little-known disease, a person is likely to have many questions and concerns when the diagnosis is confirmed. They can therefore develop their knowledge on this subject [1]. They can learn about scleroderma, its forms, symptoms, and causes. They can also learn more about the different treatments available. They can obtain information from their doctor, specialized professionals on this subject, or the Scleroderma Quebec website.

Healthy Lifestyle

Responding to basic physiological needs (e.g., eating, sleeping, etc.) is essential for the body to function optimally [4]. Therefore, a person should try to ensure that these primary needs are met. In doing so, they can facilitate their acceptance process by avoiding additional challenges, such as difficulty regulating stress [5], fatigue, difficulty concentrating, etc.

In practical terms, a person could:

- Eat at regular hours and have balanced meals. However, they must follow their doctor's medical recommendations.
- Sleep at regular hours and maintain a sleeping routine.
- Practice physical activity according to their interests and capabilities (e.g., walking, sitting outside, taking in the fresh air, etc.).
- Try to maintain a daily routine by continuing their regular activities [2].

Enjoyable Activities

To clear their mind, a person can focus on activities they enjoy [2][5]. These may include current or new activities, which can be done individually or with others. The choice of activities varies from one person to another depending on their interests, abilities, schedule, etc. Examples include music, art, social activities, cooking, exercising, etc.

Socialization

When a person receives confirmation of the diagnosis, they may feel isolated. To help them get through this period, they can talk about it with others and seek support. For example, they can speak with their family and friends, contact helplines, speak with a professional, and/or participate in a support group. These suggestions could help break their isolation, help them feel more supported, and lower their level of stress [6][7].

Emotional Recognition and Acceptance

Each person follows a unique path to accepting their diagnosis and may experience various emotions. By acknowledging and accepting these emotions they can then allow themselves to express rather than repress them and this can help to regulate emotions [2]. For example, a person becomes anxious while learning about their diagnosis. They allow themselves to express this emotion, which helps them to reduce its intensity. They are then more open to address it by seeking help, and trying treatments recommended by professionals, etc.

In conclusion

In summary, confirmation of the diagnosis of scleroderma may require a process of acceptance. We encourage the person to progress at their own pace, practice self-care, and seek support.

If a person has concerns during their acceptance process, they can seek professional help by contacting the CLSC in their region, calling ***Info-Social*** (811, option 2), requesting a professional follow-up, or participating in a support group.

Managing Anxiety and Stress

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Everyone experiences anxiety and stress, this includes people with scleroderma. This article aims to demystify these two terms, to understand them, and to learn coping strategies.

STRESS OR ANXIETY?

The terms anxiety and stress are often mixed up and used interchangeably. Even though they have similarities, they also have differences.

Anxiety is a healthy, normal, and universal emotion. It protects us, it is essential for survival and it allows us to adapt to situations [1] [2]. It is present when we anticipate a potential threat and varies depending on our interpretation of the situation.

Stress is the body's physiological reaction to an actual or potential threat. Like anxiety, it is healthy, normal, universal, and has a protective function. When our brain detects a threat, several mechanisms are triggered, and we present various physiological reactions (increased heart rate, sweating, etc.). These reactions allow us to react to the threat, by fighting, fleeing or freezing [2].

In short, anxiety is the emotion we feel in the face of potential danger and stress is our body's reaction to it. For example, we feel anxious in our doctor's waiting room, anticipating the start of the appointment. Our stress response activates to prepare us to react to the situation; our heartbeat increases, our breathing accelerates, and our pupils dilate.

ADVANTAGES AND DISADVANTAGES

Anxiety and stress often carry negative labels, but they also have benefits. In the short term and in small doses, they can stimulate us to perform better, motivate us, increase our creativity, improve our concentration [3] [4], help us plan, and project us into the future to analyze a situation [1]. They become problematic when they are long-lasting and in large doses, which can tire us, decrease our concentration, change our mood, etc.

STRESS TRIGGERS

Regardless of age, life experiences or characteristics, we all share the same stress triggers. However, the way our response is expressed may vary depending on our interpretation of a situation.

There are four universal stress triggers [5]. A single trigger is enough to activate stress, but there is an additive effect. The more triggers there are, the more stressed we can feel.

The Triggers

- **Low Control:** When we feel like we have little or no control over a situation (e.g., feeling like we have no control over the progression of the disease / feeling that we are losing control over our body).
- **Unpredictability**: When something completely unexpected happens or we can't predict something (e.g., learning that we have scleroderma / being unsure if the treatments will alleviate our symptoms).
- **Novelty**: When we face something that we have never experienced before (e.g., knowing little information about the disease, its causes, its symptoms / not knowing how to navigate the medical world).
- **Threatened Ego**: When we feel that our skills or ego are being tested or that someone doubts our abilities (e.g., thinking that we will have difficulty living with the disease / having difficulty performing some daily tasks).

SOME COPING STRATEGIES

Having a better understanding of anxiety and stress, we can now focus on concrete ways to regulate them.

Meeting Basic Needs

Properly meeting our physiological needs, such as sleeping or eating, can be a helpful tool for regulating emotions. In fact, a person can experience various side effects if they are hungry or tired, such as they may have aches, mood changes, etc. [6]. Thus, if their basic physiological needs are met, a person may be more available to regulate their anxiety and may experience fewer side effects related to an unmet physiological need.

Routines and Activities

To concentrate on the positives and lower their stress [3], a person can maintain their regular routine and complete their daily tasks. They can also participate in enjoyable projects, alone or with others [7]. These activities can vary from one person to another, depending on their interests, capabilities, etc.

In addition, spending time outdoors and observing nature can decrease stress [8]. So, getting fresh air can be part of a healthy routine.

Getting to Know Oneself

A person with scleroderma may experience anxiety and stress about their situation. Therefore, they can start by having a better understanding of their stress triggers. Here are some examples:

- **Low Control:** "I feel like I have no control over the disease."
- **Unpredictability:** "I just learned that the change in the colour of my skin's fingertips is related to Raynaud's phenomenon."
- **Novelty:** "I don't know how to navigate the medical world. What do I do?
- **Threatened Ego:** "I feel discouraged because I need help with certain tasks that I could do independently beforehand."

Once they have a better understanding of their triggers, a person can then find ways to address them and reduce their impact. Here are some examples:

- **Low Control:** The person can talk to their doctor to explore ways to manage their symptoms.
- **Unpredictability:** They can learn more about the various symptoms of scleroderma and become more familiar with warning signs.
- **Novelty:** With their doctor or Scleroderma Quebec, they can discuss which steps to take to receive a medical follow-up adapted to their needs.
- **Threatened Ego:** They can share their challenges with their loved ones to clarify their needs. They can maintain or perform tasks that they can complete.

In summary, several options exist and vary from one person to another. Nevertheless, a good starting point to reduce stress is to inform ourselves [3]. In fact, by developing our knowledge, the stressful effect of novelty and unpredictability decreases, which increases our sense of control over the situation.

Socialization

Socialization can help to decrease feelings of isolation and anxiety. Creating social connections, especially in the presence of stress triggers, can help a person feel more empathy, connect with others, and increase their sense of security [4]. Simply being in the presence of others can help reduce feelings of isolation [4] [8].

It is also possible to seek specialized help related to scleroderma in a support group. Although people may hesitate to participate, it can have several benefits. In fact, a person can develop a better understanding of the illness and ask questions. By discussing with others and learning about their experiences, they can normalize their suffering and learn that they are not alone in overcoming challenges [4]. They can even support others by talking about their experiences and sharing their knowledge. Helping others and practicing empathy can help reduce anxiety and stress.

Breathing

Breathing exercises can be a useful strategy because they can help curb a stress response, decrease anxiety and improve mood [3] [9]. Several breathing techniques exist, including singing. Most people recommend deep breathing to counteract a stress response.

Some studies show that listening to classical music helps reduce stress [3]. A person tends to synchronize their breathing with a musical rhythm. A gentle rhythm, like classical music, can help reduce stress hormones.

Mindfulness

Several studies demonstrate the benefits of meditation and mindfulness on general health and on the reduction of anxiety [10] [11] [12]. In short, these techniques consist of focusing one's attention to regain mental calm and positive emotions [10]. To accomplish this, a person concentrates on the present moment by focusing on their breathing. They can then observe their emotions, physical sensations, and thoughts, identify them and let them pass on their own. The person tries to accept them by adopting a non-judgmental attitude rather than trying to modify or react to them.

Planning and Time Management

Planning and time management can be effective in decreasing anxiety and stress [5]. They can be applied in various moments of everyday life. For example, a person with scleroderma may have several medical appointments, which may require some planning (e.g., planning transportation, knowing their route to the appointment, bringing documents, etc.). Therefore, they can plan their schedule and get ready ahead of time to reduce their anxiety for the meeting. Also, if they feel overwhelmed, they can ask for help or delegate tasks to others.

Personal Limits

A person may have varying levels of energy, depending on their condition or symptoms, and may experience changes in their abilities, depending on their treatments or the progression of the disease. They can learn to prioritize and refuse certain activities if they require rest. Therefore, listening to the body and enforcing limits can be good ways to regulate anxiety and stress [5].

IN CONCLUSION

It is important to specify that the tools presented in this article are suggestions to regulate anxiety and stress. These do not replace, in any way, a consultation with a professional. Moreover, some people may have certain physical or medical restrictions; they are strongly encouraged to follow their doctor's recommendations.

Although anxiety and stress have a protective function and ensure our survival, it is always possible to seek professional help if concerns arise or persist. A person can contact the CLSC in their region, call *Info-Social* (811 option 2), request professional follow-up, or participate in support groups.

V LIVING WITH SCLERODERMA

Scleroderma and Pain Management:

Don't underestimate your power to act

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What is pain?

Pain is: "*An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage*." [1] According to this definition by the International Association for the Study of Pain (IASP), this complex experience is not solely dependent on physical factors. Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors. Depending on its duration, pain can be described as acute or chronic. The IASP defines chronic pain as "pain that persists or recurs for more than 3 months". [2]

We distinguish three types of pain, which may coexist:

- Nociceptive pain arises from damage to body tissues and is the typical pain experienced following injury or caused by inflammation. It is usually described as a sharp, stabbing, or throbbing pain.

- Neuropathic pain results from direct damage to the nervous system itself. It is usually described as a burning or shooting pain and may cause numbness or tingling of the skin or extreme sensitivity to even the lightest touch.

- Nociplastic pain arises from a change in the functioning of pain-sensitive nerves rather than from direct damage to the nervous system. The sensitive nerves become more reactive (sensitized). It is similar in nature to neuropathic pain [3].

This definition of nociplastic pain is recent and much work remains to be done to better understand its mechanisms [4]. However, this type of pain is a good example of neural plasticity, a concept according to which neurons have the capacity to change in response to stimulation or learning. This plasticity may lead to the chronification of pain because your brain has somehow become accustomed to sending you danger signals whenever you move or are touched, for example. Conversely, it can also be used to reverse these changes and reduce chronic pain.

What about pain in people with scleroderma?

Authors have pointed out that pain in scleroderma patients has long been underestimated and understudied [5, 6]. Fortunately, several teams have recently contributed to a better understanding of the pain experience of people with scleroderma to guide assessment and management. Their findings show that more than 80% of people with systemic scleroderma experience various types of pain related to their condition [7, 8]. Approximately 45% experience pain on a daily basis [8, 9], and 38% report moderate to severe pain, defined as ≥ 5 on a scale of 0 to 10 [9]. Hand pain, associated with typical scleroderma manifestations such as ulcers, joint contractures, and impaired hand function, increases in importance with disease progression. These are common pains, present in approximately 80% of patients with systemic scleroderma [5, 8]. A large number of people also report low back pain as their main pain, especially in the early stages of the disease [5]. Pain associated with Raynaud's phenomenon, headache, chest pain, gastrointestinal pain, and pain on swallowing are also reported [8]. Contrary to what might be expected, the intensity and chronicity of pain would not be associated with an increase in the disease severity [5]. The pain would change minimally over time, and the change that does occur in the long term suggests that overall pain tends to improve slightly, not worsen [6]. For localized scleroderma, 46% of participants in a European study reported experiencing mild (32%), moderate (9%) or severe (4%) pain or itching [10].

Consistent with the definition of pain, emotional health, perceived physical health and social support are associated with the initial experience of pain in people with scleroderma [6]. Social support would be of great interest in understanding the pain experience, especially since some people with scleroderma may avoid socializing because of changes in their appearance. It is important to note that it is not the number of relationships that matters, but the availability and quality of perceived social support [11].

How do these findings guide pain management?

Regardless of the severity of scleroderma and the exact nature of the disorder, it is important to address pain, pain management and psychosocial functioning with healthcare professionals [6]. Strategies that address psychosocial factors (e.g. depression, sleep, coping skills, social network) should be considered. As previously mentioned, these factors influence perceived pain.

One approach that should be considered is to follow an adapted program of physical activity [12]. Regular physical activity is associated with reduced pain intensity and interference in people with scleroderma [13]. People with scleroderma who are physically active report lower levels of fatigue than those who are inactive. Participants in one study reported that following a combined exercise program that included aerobics and resistance training, for example, improved their physical fitness and social life, and helped them feel more energetic and stronger [14].

Other authors suggest taking part in psychosocial follow-up [15]. Some also recommend developing skills in various areas [6, 9, 11], such as:

- Mindfulness, a meditation technique that involves focusing on the present moment and being aware of one's thoughts, emotions, and bodily sensations without judging them;
- Relaxation, a technique that aims to reduce stress and anxiety through methods such as deep breathing, visualization, and muscle relaxation;
- Adaptation, the ability to adapt to life changes and face challenges in a positive way;
- Modification of maladaptive beliefs, reframing ideas or beliefs by challenging them and replacing them with more positive and realistic thoughts. In this sense, beliefs that may be false, exaggerated, irrational, or limiting can contribute to mental and emotional health problems.

It should be noted that these strategies are not specifically designed to reduce perceived pain, but rather to better manage and minimize its impact on function and quality of life.

Medication is also an option, but given its limited improvement in pain, it is a complementary option to the non-pharmacological strategies listed above.

How to self-manage pain?

Pain education is the first step to better managing chronic pain. The web portal My pain management offers a wide range of expert-validated resources on the topic, as well as the pain self-management program "***Agir pour moi***" (Taking action) [in French only].

As the name suggests, self-management is an approach that emphasizes the active role we can play in managing our health condition by adopting positive behaviours. The idea is to be a key player in your own care. Self-management means developing the ability to manage symptoms, treatments, physical and psychosocial consequences, as well as the lifestyle changes associated with having a chronic disease. Compared with usual care, participation in a self-management skills program improves several measures of physical and emotional functioning in the short-to-medium term. In this sense, it is beneficial to consider both the application of certain self-management strategies in daily life and consultation with health professionals. These are two approaches that should be combined to manage pain appropriately.

The self-management strategies promoted for chronic pain are essentially the same regardless of the pain condition. Self-management programs typically include some or all of the strategies related to managing stress, energy, physical activity, thoughts and emotions, sleep, diet, and maintaining change. The program ***Agir pour moi***, available at gerermadouleur.ca/agir-pour-moi/, addresses all of these strategies. We developed it using patient-centred research principles through a close partnership between a Ph.D. candidate, people living with chronic pain, healthcare professionals, and a graphic designer. Agir pour moi is completely online, free, and can be follow without the assistance of a healthcare professional. We are pleased to announce that Agir pour moi will be available in English in the coming months. Short videos of inspirational stories are interspersed throughout each lesson to support the theoretical content. The development team wanted learners to feel understood and supported in making lifestyle changes. Input from patient partners has helped add details that normalize the experience of those in the program.

Scleroderma poses certain obstacles to the practice of physical activity, including dexterity or impaired hand function, which may or may not be related to Raynaud's phenomenon, fatigue, gastrointestinal problems, and possibly lower motivation [12]. Different adaptations may be considered when applying the proposed strategies. Keep in mind that you are the expert on your situation.

Although scleroderma requires you to rethink your daily life, eating habits, social relationships, work life, and plans, rethinking the way you care for yourself can slowly transform your quality of life. There are no shortcuts, but your power to take action is probably greater than you think.

V LIVING WITH SCLERODERMA

Energy Management

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Scleroderma is an autoimmune disease that consumes a portion of your energy. Among other factors, the fatigue you may experience can be linked to the inflammatory process, organ dysfunction, sleep disturbances, side effects of medication, nutritional deficiencies, mental and emotional stress, or reduced physical activity. It is therefore normal for fatigue to be one of the common symptoms of this condition. However, there are strategies to manage your energy levels.

The Battery Analogy

First, it is essential to understand energy use, which can be compared to a smartphone battery.

Often, we start the day with our phone charged at 100%. Naturally, the battery drains with use. Some activities, like watching videos, consume more battery. Regardless of the type of activity, the battery inevitably drains and needs recharging.

However, we often wait until the battery is at 5% or even 0% before plugging it in. In this digital age, we may also be impatient for it to fully recharge. This can lead to the need for frequent recharging, operating with a low battery, and a disruption in productivity, particularly when the phone is needed for urgent tasks.

This analogy applies to you. If you only take breaks when you are completely exhausted, it takes time to recover. Additionally, if you don't allow enough time for recharging, you will constantly feel tired, as your energy level will remain low. It is, therefore, important to recharge your battery before it runs empty.

The Basics of Energy Management: The 5Ps

For effective energy management, it is beneficial to explore the application of the 5Ps:

1. Pacing
2. Prioritizing tasks and activities
3. Planning your time
4. Positioning and posture
5. Problem-solving

1. Pacing

- Get to know and respect your capacities and limits.
- Break an activity into several steps and include rest periods (relaxation, meaningful activities, etc.) between them.
- Alternate between light and heavy tasks.
- Take breaks in the morning, noon, and evening; or, if possible, about 10 minutes every hour to prevent excessive fatigue (which facilitates recovery).
- In your activities, adopt a calm rhythm, with a steady, moderate pace rather than a fast one.
- Work in a pleasant, temperate, and relaxing environment.

2. Prioritizing tasks and activities

- Analyze your daily activities and rank them by importance in your schedule.
- Is this task essential?
- Does this task need to be done TODAY?
- Do I need to do this task myself? (ask for help or delegate)
- How can I simplify this activity?
- Evaluate the possibility of eliminating or delegating some tasks to allow you to accomplish more meaningful tasks.

3. Planning your time

- Organization is key to planning. Creating a typical weekly schedule is a good way to start.
- Have a flexible and realistic schedule with regards to the time allocated for each activity (i.e., considering your capacities and limits).
- Spread your activities and heavy tasks over an entire week.
- Plan your essential activities for when you have the most energy.
- Plan your outings.

  Example: If you go shopping, make a list, prioritized by the places you need to visit and items to buy.

  Example: Prepare everything you need before starting an activity (recipe, study materials, gardening tools, etc.)
- Schedule personal time and leisure activities.
- Use what is available to conserve energy, such as elevators, food processors, frozen vegetables, etc.

4. Positioning and posture

- Adopt a good posture to prevent fatigue and physical stress. Frequently change your posture to keep your joints moving.
- Sit down for certain activities, such as meal preparation, ironing, folding laundry, or talking on the phone (saving about 25% of your energy compared to standing).
- Organize your workspace according to ergonomic principles.
- Adjust the height and organization of work surfaces (surface should be level with your elbows).
- Arrange storage areas in a functional way (place items you frequently use between shoulder and hip height).
- Use postural aids and technical aids as needed.
- Use tools to facilitate each task, such as longer handles or larger, cushioned grips.

5. Problem-solving

- Be creative, resilient, and patient in finding solutions.
- Be open to changing your habits and doing things differently.
- Try new activities.
- Consider restructuring your schedule.

Other Strategies to Remember:

Negative attitudes can affect your quality of life. Learn to communicate your needs. Here are some attitudes to adopt:

- Remind yourself that it's normal not to be able to do everything.
- Remember that results are not always visible while you are taking action.
- Focus on the positives.

Allow yourself to say "no" to some requests from others and to some of your own demands. Understand that stress can stem from how you interpret events, situations, etc. Remind yourself that any new situation/condition can lead to somewhat exaggerated reactions. Allow yourself to step back when faced with new challenges.

When you need to communicate your needs effectively to better manage your energy, ask yourself the following questions: ***To whom should I speak? When? Where? How?***

Change certain habits: reduce those that drain you and increase those that give you energy.

For example:

- Engage in physical exercise appropriate for your condition.
- Improve your sleep quality.
- Manage your stress, practice relaxation, and identify sources of anxiety and stress.
- Adopt a balanced diet (follow the food guide).

V LIVING WITH SCLERODERMA

How to Prepare for an Appointment with Your Healthcare Team

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HERE ARE A FEW TIPS TO PREPARE FOR YOUR APPOINTMENT WITH YOUR MEDICAL TEAM.

Medications

Have your medication list up to date and note if there are any side effects to the medications. If you are not taking some of the medications as prescribed, it is important to report this to your doctor so that a fair assessment can be made of the effectiveness of the treatments. Also, tell your doctor if you take over-the-counter medications or natural products.

Blood pressure

Blood pressure should ideally be taken at home twice a week, or daily in patients at higher risk of developing scleroderma renal crisis. Bring your blood pressure log to help your doctor determine if further investigation is needed to detect a kidney complication.

Blood tests

If blood tests were prescribed at the last appointment, do them early enough (1 to 2 weeks) before the appointment so that the results can be available at the time of the appointment.

Symptoms of scleroderma

Take note of any change in symptoms associated with the disease. For example, have there been any new symptoms? Have the symptoms worsened, or have they improved following a change in treatment? More specifically for each symptom, the following details are particularly relevant:

- **Raynaud's phenomenon**: frequency and duration of attacks;
- **digital ulcers**: pain, discharge, redness, fever;
- **skin**: progression of thickening, itchy skin;
- **cardiopulmonary**: chest pain, palpitations, shortness of breath (after what level of effort), cough, loss of consciousness, leg swelling;
- **digestive**: reflux, heartburn, early satiety, nausea and vomiting, abdominal pain, bloating, diarrhea, constipation, fecal incontinence, weight loss;
- **renal**: high blood pressure at home, decreased urine output, headaches, blurred vision, confusion;
- **arthritis**: joint pain (where and when), morning stiffness (duration);
- **myositis**: difficulty climbing stairs or getting up from a chair without using your arms due to muscular fatigue.

Vaccines

Vaccination against certain infections, such as influenza and pneumococcus, is recommended to prevent serious infection-related complications in the context of a chronic disease such as systemic sclerosis, particularly in patients with pulmonary involvement and in patients taking immunosuppressive medications. Make sure to bring your immunization record to your appointment so your doctor can determine if you need an update.

Investigations

Consultations and hospitalizations: if you have undergone additional examinations or consulted other doctors, or if you have been hospitalized since your last appointment, make a note of the details: dates, clinic or hospital centre, reason for consultation, change in medication, etc. It is important that your doctor taking care of your systemic sclerosis is familiar with the general state of your health. If necessary, the doctor may ask for a copy of the investigation or hospitalization reports.

V LIVING WITH SCLERODERMA

Sexuality and Scleroderma

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When it comes to sexuality, there is no single ideal model. In the general population, at least one third of men and women experience sexual difficulties. Scleroderma can affect a patient's sexuality. This chapter explains the main difficulties and how to solve them.

Fatigue and pain

Fatigue

Sexual intercourse requires a significant energy expenditure, approximately 200 to 300 calories. That's why it's important to choose the right moment to have sex, preferably when your energy reserves are high, for example in the morning, during the day or after a nap. Before intercourse, you should avoid any strenuous activity that requires a high energy expenditure. Save your energy for moments of pleasure. Talk to your partner about your energy level. Truthful communication allows partners to understand each other, help each other and respect each other's needs.

Pain

Pain during sex is reported by 62% of scleroderma patients. It can be difficult to awaken sexual desire when you suffer from back, joint and muscle pain, contractures and vaginal dryness or erectile difficulties.

VAGINAL DRYNESS

Vaginal dryness is a common symptom in women with scleroderma. It can worsen with menopause because of declining estrogen levels. This disorder can have a significant psychological impact and lead to a decreased libido (sex drive), which in turn can affect the couple's relationship. However, there are solutions that can help address this problem.

Vaginal moisturizers and lubricants are first-line treatments. Hormonal treatments should only be used if recommended by your doctor.

Vaginal moisturizers

Applying a hormone-free moisturizer can help restore vaginal moisture and improve the elasticity of the vaginal walls, thus improving comfort. You can buy these products at a pharmacy without a prescription. Typically, these moisturizers can be easily applied in the vagina either as a gel, or in liquid form. Regular application every three days can increase their effectiveness. However, used regularly, these products can cause vaginal discharge. Applying the product at bedtime and using panty liners can help reduce discharge. Your pharmacist can tell you more about these products.

Vaginal lubricants

Unlike vaginal moisturizers, which can be applied every three days, lubricants are only used, if needed, during sexual intercourse. Lubricants facilitate intercourse and also increase comfort. They also enhance sexual pleasure. They are usually applied on genital organs and at the entrance of the vagina before or during sexual activity. Some women use both vaginal moisturizer and lubricant to improve comfort during sexual intercourse.

There are two types of lubricants: water-based and silicone-based.

There are several water-based lubricants available on the market. They contain mainly water and most are harmless to your health. K-Y™ and LIQUID SILK™ are two of them.

Silicone-based lubricants have a thinner texture and a longer lasting lubricating effect than water-based ones. They are usually hypoallergenic. YES™ is one of them.

Read the list of ingredients to know the product's contents, to make the right choice. Your pharmacist can help you with this.

Other solutions

In addition to using lubricants or moisturizers during sexual intercourse, give yourself more time to achieve natural vaginal lubrication and reach sexual arousal. Do Kegel exercises regularly. These exercises aimed at strengthening the perineal region can be beneficial to your health and overall comfort, but also allow you to experience more pleasure during sexual activity. They are suitable for women and men of any age. Better muscle tone and increased blood flow in the genital organs enhance sensitivity, improve vaginal lubrication and erections, and promote sexual pleasure in both man and woman. Contracting the muscles that prevent urination and bowel movement will help you identify your pelvic floor muscles. Tighten these muscles and hold the contraction for 3 to 5 seconds. Do this 10 times. Repeat these exercises 5 times in the course of the day. You can do these exercises discreetly, at anytime and anywhere. If you want to learn more, there are a number of excellent websites that explain how to do Kegel exercises.

SEXUAL DYSFUNCTION IN MEN

Erectile dysfunction (ED) is the repeated inability to achieve or maintain an erection long enough to perform sexual intercourse.

This condition is found in 80% of men with scleroderma. It is due to vascular problems and fibrosis of the cavernous tissues in the penis (corpora cavernosa) which reduce or obstruct the blood flow needed to achieve an erection. Today it is widely recognized that erectile dysfunction often has multifactorial causes, and in many instances physiological causes are compounded by psychological ones. Commonly held stereotypes of virility according to which the male asserts his masculinity by his capacity to have an erection, may further exacerbate this difficulty and contribute to a loss of sexual desire.

Treatments for erectile dysfunction are very effective. Several drugs are available in tablet form, to be taken as needed before sexual intercourse. They work by increasing blood flow to the penis, helping the man achieve and maintain an erection. These treatments require a medical prescription. Sildenafil (Viagra™), vardenafil (Levitra™), tadalafil (Cialis™) and avanafil (Spedra™) fall in this category. These drugs are sometimes used to treat other symptoms of scleroderma such as pulmonary hypertension and complications associated with Raynaud's phenomenon.

There are alternatives to these medications if they are ineffective or their use is contraindicated.

- **UA urethral suppository** (MUSE™) or cream (Vitaros™) containing a vasoactive agent called alprostadil relaxes certain muscles in the erectile tissue and increases blood flow to the penis. The drug is introduced into the urethra 5 to 30 minutes before sexual activity.
- **A penile injection** is the process whereby a vasoactive substance (e.g. alprostadil) is injected directly into the corpus cavernosum of the penis. Self-injection is carried out on the side of the penis for an erection that lasts 30 minutes to one hour.
- **Penile constriction rings** are devices placed at the base of the penis to maintain an erection. Essentially, they trap blood in the penis, making for a stronger and longer erection. When the penile ring is not sufficient, a vacuum erection device (VED) or vacuum pump can be used in conjunction with a penile ring. It involves a cylindrical device placed over the penis to create a vacuum that triggers an erection, which is maintained by a penile ring.

  When all other treatment options have failed, a penile implant may be considered.
- **A penile implant** is an inflatable device with flexible stems which is inserted in the penis. A pump is used to produce an erection. This permanent solution requires surgery.
- In addition to conventional medical treatment addressing physical health problems, psychotherapy and behavioural therapy can be beneficial to sexual well-being.

LOSS OF SEXUAL DESIRE

Sexual desire will fluctuate through a person's life. Its intensity highly depends on the state of the person's relationship, physical health and state of mind, as well as life's many ups and downs. Lack of desire can affect both men and women. Scleroderma greatly affects one's energy, physical and psychological health, and lifestyle habits. All these changes can impact a person's sex drive. In addition, some drugs have adverse side effects on sexual health. If you think your medication is affecting your libido and your sex life, talk it over with your physician, who might be able to recommend some adjustments.

WAYS TO BEAUTIFY YOUR SEX LIFE

Body Image

If your physical appearance has changed during the course of the disease, you may suffer from low self-esteem, which in turn can affect your sex life. Here are some tips to improve your self-confidence. Share your fears and feelings with your partner or someone you trust and who will reassure you. Beauty is subjective and you might be pleasantly surprised by how others see you. Focus on what you believe are your best features. Take care of yourself. Pamper yourself and get a new hairstyle, clothing or a massage. Whatever it is that makes you feel good. Dim the lights during sex or turn them off completely if this reassures you.

To help you get through this period of adjustment in your life, use your sense of humour, give yourself time to find what works for you and engage your partner in the process. Overall, this will greatly improve your sex life!

Communication

Here is some advice to promote sexual desire and increase pleasure:

- Maintain effective communication with your partner. Effective communication allows for the expression of feelings, inclinations, preferences and desires. A mutual understanding of each other's needs and desires will do a great deal towards promoting a satisfactory relationship.
- Tell your partner how you feel and listen to him or her.
- Clearly communicate how and where you like to be touched.
- Remember that the way you communicate affects your relationship with your partner.
- Choose the right time to talk and listen to each other.
- Communicate your preferences and be open to those of your partner.
- Tell your partner what you like, not just what you don't like.
- Deal with only one issue at a time instead of venting your spleen all at once. This will allow your partner to make adjustments.
- Write down your expectations to help start the discussion and facilitate communication.

Indulge your desire for fantasy, romance and inventiveness.

- The brain is a sex organ. Ultimately, all signals stem from our head and play a fundamental role in facilitating sexual arousal. Spark your imagination and allow yourself to fantasize. You don't have to carry out all of your sexual fantasies. What gives us pleasure in our imagination will not necessarily have the same effect in real life. That being said, carrying out some fantasies can bring novelty in one's sex life, provided the fantasy is shared and you know to what extent your partner is ready to go along for the ride.

Awaken your sexuality

Make use of all your senses to be in touch with the world around you so that you may experience things more intensely, building a connection with your partner through sensuality, developing a new sense of closeness and intimacy.

Your goal should not be to achieve arousal or an orgasm. The objective is to become fully aware and enjoy the sensations perceived through your senses. Be creative and use whatever works for you: movies, an erotic or romantic ambiance, music, flowers, pleasing smells, caresses, a massage with soothing cream or essential oils, light touches, sex toys, food, candles, wine, soft bedding, sex shops, etc. In the absence of desire, gentle touches, hugs, cuddles and kisses can help foster intimacy. Take advantage of these opportunities to experience closeness and pleasure with your partner. Maintaining sexual health throughout the course of the disease might require adjusting your expectations.

Physical intimacy is not limited to sexual intercourse. It can take many forms; hugging, kissing, masturbating, taking long walks, talking, and using stimulation and massage can all contribute to the expression of sexual intimacy. Follow those recommendations which you believe will have a positive effect on your physical and sexual health. Save your energy to be able to enjoy fulfilling moments with your partner. ***Despite the changes brought upon by the disease, remember that you remain in control of your renewed sexual life and intimacy.***

Pregnancy and Systemic Scleroderma

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Will I be able to have children?

Yes. Fertility in women with systemic scleroderma is generally comparable to that of women without the disease. Overall, the risk of miscarriage is also not increased compared to the general population.

On the other hand, pregnancy is not recommended in patients with the following conditions due to the high risk of complications:

- Pulmonary arterial hypertension;
- Progressive pulmonary fibrosis;
- Kidney failure or severe high blood pressure;
- Heart failure;
- A recent diagnosis of diffuse systemic scleroderma.

Pregnancy is also to be avoided in patients using medications that pose a risk to the babies (e.g., certain immunosuppressants). It is therefore important to use effective contraception and to discuss the desire for pregnancy with your doctor before becoming pregnant.

What are the risks associated with pregnancy in the context of systemic scleroderma?

If systemic scleroderma is well controlled and there is no cardiac, pulmonary, or renal involvement, there is a good chance of an uncomplicated pregnancy. Approximately 70-80% of women will have a successful pregnancy.

The risks associated with pregnancy in the context of scleroderma are:

- Premature birth (2-3 times more common);
- Intrauterine growth retardation and/or low birth weight (3-4 times more common);
- Renal failure, especially in patients with baseline renal failure;
- A difficulty in case of general anesthesia due to the limited opening of the mouth; local or epidural anesthesia is to be preferred.

A consultation with a gynecologist specializing in high-risk pregnancies is essential to ensure adequate follow-up in the context of scleroderma.

What are the possible effects of pregnancy on systemic scleroderma?

In general, pregnancy does not appear to have any effect on the overall course of systemic scleroderma. However, pregnancy may worsen gastroesophageal reflux disease (GERD), with more heartburn and shortness of breath, especially if these problems were present before pregnancy. On the other hand, Raynaud's phenomenon may improve in about 30% of patients, due to increased body temperature and blood supply to the extremities in the context of pregnancy.

Rare cases of scleroderma renal crisis occurring in late pregnancy or after delivery have been reported in patients with a recent diagnosis of diffuse scleroderma (within the first 4 years). Pregnancy is therefore not recommended at this time in these patients but could be planned at a less progressive stage of the disease.

Will scleroderma affect my baby?

The majority of babies are not affected by their mother's diagnosis of scleroderma. However, if the mother has anti-Ro or anti-La autoantibodies, these antibodies can cross the placenta and occasionally cause inflammation in the baby's heart, leading to heart block (heart rhythm disorder) in 1-2% of pregnancies. Serial fetal echocardiograms are then necessary during pregnancy to quickly detect a heart problem in the fetus. Also, the presence of anti-phospholipid autoantibodies in the mother is associated with an increased risk of miscarriage and preeclampsia. Ongoing monitoring of high-risk pregnancies is essential to ensure adequate assessment according to the level of risk.

Will I be able to breastfeed?

Yes, breastfeeding is possible and encouraged even in women with scleroderma. Some medications that can be passed into breast milk should be avoided. Scleroderma patients with active Raynaud's phenomenon in the post-pregnancy period may experience Raynaud's disease in the nipples, especially after breastfeeding or with any exposure to cold, which causes pain and discomfort. The use of heating pads to improve blood circulation before breastfeeding may be beneficial. A breast pump can also be used when Raynaud's is most active.

What about men?

Few studies have looked at the fertility of men with Systemic Scleroderma. However, scleroderma can cause erectile dysfunction, possibly due to reduced blood flow to the penis. Some immunosuppressive drugs can also decrease fertility in men, most often reversibly.

In summary

The majority of women with systemic scleroderma can become pregnant and have healthy children. Close collaboration between the patient, the rheumatologist and the gynecologist specializing in high-risk pregnancies is essential to minimize the risk of complications.

V LIVING WITH SCLERODERMA

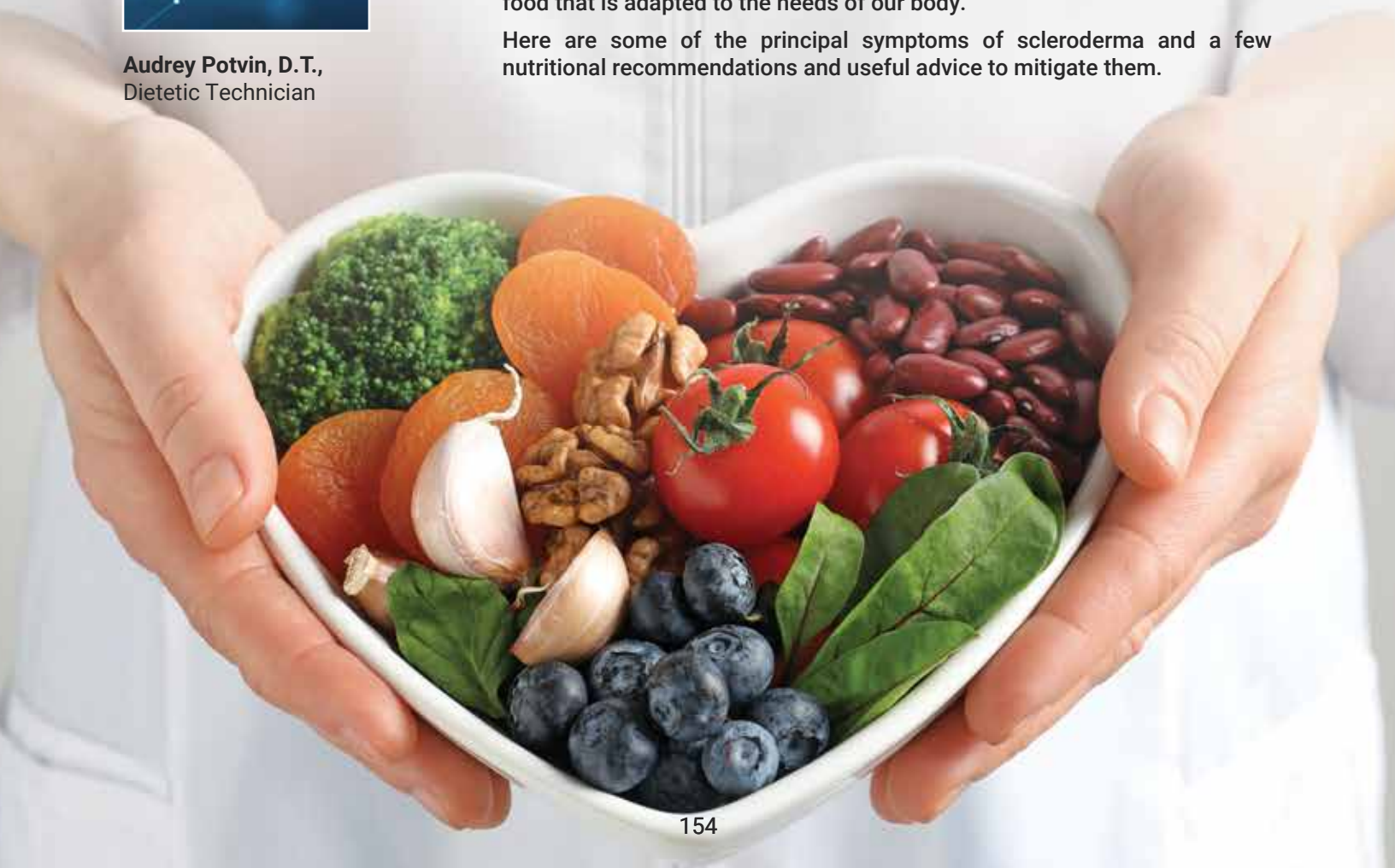
Nutrition and Scleroderma

Audrey Potvin, D.T.,
Dietetic Technician

Knowing that scleroderma can manifest itself in several parts of the affected person's body (visible symptoms when the skin is affected and/or invisible symptoms when internal organs are affected), it is important to have the best nutritional intake to help in better coping with the symptoms of the disease.

Whether or not we are perfectly healthy, the food we eat is an integral part of a global approach to our health and can greatly influence our general well-being. It is in our best interest, especially when ill, to consume quality food that is adapted to the needs of our body.

Here are some of the principal symptoms of scleroderma and a few nutritional recommendations and useful advice to mitigate them.



Acid reflux and scleroderma

For several people affected by scleroderma, acid reflux (or gastroesophageal) is a particularly bothersome, sometimes painful symptom of the disease.

First, what is gastroesophageal reflux?

It is acid reflux from the stomach to the esophagus, due to a malfunctioning lower esophagus sphincter (a valve that serves as a protective barrier) which, having lost its tone, can no longer close. This dysfunction of the esophagus sphincter can cause complications, such as inflammation, ulcers in the esophagus, dental cavities due to loss of enamel caused by acid regurgitations.

Gastric reflux

Here are some tips that can help if you suffer from this symptom:

- Maintain a healthy weight;
- Considerably diminish, or even eliminate, certain foods such as: chocolate, coffee (caffeinated or decaf), alcohol, soft drinks, tomatoes, citrus, sugar, fried fatty foods, strong spices, white vinegar, mustard and mint;
- Eat lots of vegetables, preferably raw or lightly steamed. At least half of our plate should consist of vegetables, one quarter of starchy foods, and one quarter of lean proteins;
- Avoid eating two to three hours before lying down;
- Have several small meals and snacks;
- Eat slowly and chew properly;
- Drink liquids at least a half-hour before or after the meal;
- Avoid swallowing air (for example talking while eating, eating with your mouth open, drinking with a straw, drinking carbonated drinks, etc.);
- Avoid chewing gum;
- If, on a special occasion, you are offered alcohol, don't drink on an empty stomach, as alcohol increases stomach acid and irritates the digestive system;
- Svoid constipation by drinking a lot of water and by eating enough fibres (consult a nutritionist if needed).

Here is more advice that may help neutralize gastric acid:

- At the onset of the reflux, drink a tall glass of water to dilute the stomach acid;
- Try raw potato juice if you have a juicer. Thoroughly wash the unpeeled potato before putting it in the juicer and mix with equal parts of water. Drink three times a day;
- In case of acid reflux between meals, eating half a ripe banana as a snack can bring some relief;
- Drinking fennel or ginger tea stimulates digestion and helps neutralize acid. Aloe juice or gel is effective in alleviating the burning sensation of the digestive tract and stomach acidity. Avoid as much as possible baking soda and milk. Even though they are effective at temporarily reducing the burning sensation and digestive discomfort caused by gastric reflux, in the long run they will cause the stomach to produce even more acid and make the problem worse!

Gastrointestinal discomfort

If you have scleroderma, you may have intestinal transit problems, causing symptoms such as constipation and/or diarrhea, bloating, pain, abdominal distention, etc.

In 2005, a new approach to nutrition was developed by Sue Shepherd, an Australian nutritionist. She discovered that the range of foods that cause gastrointestinal disorders extends much further than consumption of wheat and dairy products. What is this new approach? It is called the FODMAP diet, which consists in reducing consumption of certain foods that contain carbohydrates. These, when fermenting in the colon, produce bloating, gas, and abdominal pain. They are called "fermentable".

What does the acronym FODMAP mean?

F	=	Fermentable (rapidly fermented by bacteria in the colon)
O	=	Oligosaccharides
D	=	Disaccharides (lactose)
M	=	Monosaccharides (fructose)
A	=	And
P	=	Polyols (sorbitol, mannitol, xylitol and maltitol)

Here are some examples of foods rich in FODMAP to watch for and, eventually, to limit or eliminate in order to improve intestinal comfort:

Fructose:
Apple, watermelon, mango, corn syrup

Lactose:
Milk, yogurt, cottage cheese, ricotta

Frutane:
Asparagus, cabbage, onion, wheat and rye (in large quantity), apple

Galacto-oligosaccharides:
Legumes (chickpeas, lentils, soybeans)

Polyols:
Apple, pear, watermelon, cauliflower, mushrooms, peppers, sugar "alcohol" (sorbitol, xylitol, maltiltol), gum and unsweetened candy, etc.

Here are a few of my personal tricks to prevent or soothe discomfort following consumption of fermentable foods:

- Add a piece of kombu seaweed when you cook legumes, to improve digestion. Some canned legumes already contain kombu;
- Germinate legumes before cooking;
- Add ginger to your meals;
- Eat more gluten-free cereal (quinoa, buckwheat, etc.)
- Replace milk with lactose-free milk or plant-based milks (almond, coconut, etc.)
- Season with tamari sauce and miso. These condiments contain probiotics and/or enzymes that aid digestion (on top of adding flavour to dishes!);
- Avoid eating dessert after a meal containing fermentable components;
- Mint, fennel, ginger and cinnamon teas are excellent to promote digestion and eliminate gas after a heavy meal;
- Puree vegetables to break the fibres that could cause irritation. Some people suffering from scleroderma sometimes have difficulty chewing raw vegetables, which can prevent adequate digestion. For example, cabbage-type vegetables, grated in a salad, will cause much less symptoms than if they are cut in large pieces;
- Avoiding chewing gum (especially on an empty stomach, between meals), soft drinks or talking less while eating, can reduce bloating;
- Eat slowly, chew your food well, and watch for repletion signals.

Arterial hypertension and scleroderma

Arterial hypertension (AHT) is a frequent health problem for a lot of people. It happens when arterial blood pressure is abnormally high.

When arterial tension is caused by a disease, for example in case of renal involvement in a person suffering from scleroderma, or by frequent use of certain medications, it is called secondary arterial hypertension.

Even though we can't eliminate every risk factor, here are some recommendations that, mainly for primary AHT, but also for secondary AHT, can clearly contribute to a better control of arterial tension:

- Minimize the consumption of salty foods, especially ultra-processed items (such as chips, crackers, canned soups and sauces, prepared meals, deli meats, etc.), as well as added salt. If needed, opt for reduced-sodium versions, consumed in moderation;
- Eat fresh fruits and vegetables that are rich in potassium, such as green vegetables (asparagus, spinach and peas), cruciferous vegetables (cabbage and broccoli), squash, sweet potato, apples, bananas, plums, grapes, cantaloupe, eggplant and melon;
- Eat whole grain products;
- Eat foods rich in omega-3, such as linseed, chia or hemp (vegetal sources) or oily fish such as salmon and trout (animal sources);
- Avoid caffeine, alcohol and tobacco;
- Maintain a healthy weight;
- The following foods can, by promoting better blood circulation, help to lower arterial tension: Cayenne pepper, garlic, saffron, ginger, non-pasteurized apple-cider vinegar, olive oil and dark chocolate.

The above recommendations are for information only and do not replace medication prescribed by your doctor. Scleroderma is a serious condition but I firmly believe in a global health approach that aims at adopting healthy life habits, starting with the food we eat.
References: Nutrition and Recipe Book for people with Scleroderma and articles from Scleroderma Quebec's Bulletin.

VI SUPPORT AND COMMUNITY

Scleroderma Quebec's Support Groups

Violet Konrad
Support group leader for the Eastern Townships and trainer of support group leaders

Edouard Lebeau
Support group leader for the Eastern Townships

Louise Vidricaire
Support group leader for the Three Regions Group

Scleroderma Quebec's Support Groups meet in person or on Zoom for mutual support with the challenges of living with scleroderma. These groups are composed of people living with scleroderma and may also include spouses or other natural caregivers. They are led by one or more trained leaders who have taken a course specifically designed to equip them to facilitate the groups and to share pertinent information about living with scleroderma. The leaders are volunteers within the Scleroderma Quebec organization and most are themselves living with scleroderma. The well-prepared, warm, and welcoming meetings include pertinent information for coping with scleroderma. Members feel free to share their experience of living with scleroderma with others who understand from within. Many members feel that belonging to a support group has changed their lives for the better.

Why join a scleroderma support group?

For Community

Many people living with scleroderma feel alone because their condition is not well known or understood. Joining a group of people who have this disease and are willing to share the tricks of the trade for living better with symptoms can give a real sense of well-being and community. Madone Coulombe has been a part of a support group for close to ten years. She writes:

"***I believe that medical appointments are not sufficient for really understanding the complexity of this disease. Through sharing with people living with scleroderma I recognize myself, and it makes me realize that I am not alone in living with these sometimes difficult symptoms that are so hard to explain to people who do not have this disease.***"

Support group members are good listeners for each other. They have personal knowledge of the disease, and they are very supportive of one another.

For Information

Although one of the important rules in support groups is to not give medical advice but rather to refer one another to medical professionals, members can and do share their experiences. Often another person's experience can be a valuable source of information, hope, and inspiration.

Various themes are discussed and information is shared from reputable sources including among other topics:

nutrition with scleroderma, bone health, mindfulness, pain management, dental health, digestive issues, skin health, managing anxiety, getting the most from your medical appointments, communicating about your disease with family members and others, becoming an expert on your own health and keeping a personal health record, coping with changes in appearance, accepting your limits and learning to live the best you can with them, living with Raynaud's syndrome, managing energy, how to promote better sleep habits, travelling with scleroderma, and many many more subjects.

Members can suggest subjects that are important to them and bring their questions and concerns to meetings. They can also contact Scleroderma Quebec or leaders directly, with topics that they would like to see addressed.

For Confidentiality

Support groups are safe, caring, and confidential places to share about life with scleroderma. Confidentiality is an important value in these support groups. Anything said in a group remains confidential. Meetings are not recorded. The commitment to confidentiality is explained and reviewed at the first meeting of a new year and new members are introduced to this and other important rules that help the groups maintain a positive, caring, and confidential space.

For Fun

The goal of each support leader is that the meetings will bring a smile and maybe a laugh to the members. Meetings may include Christmas parties, humour, costumes, and silliness. As we know, "Laughter is the best medicine." Some groups have picnics or other activities just for the fun of it. In the groups, you may be asked to talk about and share your enthusiasm about your hobbies, travel, pets, favourite memories, etc.

What support groups are not?

Support groups are not led by medical professionals. They do not diagnose or treat individuals. They do not provide therapy.

Who are support groups for?

For the recently diagnosed

Support groups can be very valuable for people who have been diagnosed recently. They will be reassured that members have full and active lives even after many years of living with the disease. They will find compassionate listeners who understand the distress of a scleroderma diagnosis, and they will gain more understanding of their disease and learn where to look for pertinent information.

For anyone with scleroderma

No matter how long a person has lived with scleroderma there may be new challenges or symptoms. Anyone living with scleroderma, no matter the length of time, will find a community to support them. Being able to give support and share experiences with the more recently diagnosed can be a very positive experience. You may benefit from a support group but the support group will also benefit from your presence and your experiences.

For anyone supporting someone with scleroderma

Spouses and family members can also feel alone and overwhelmed by their role in supporting a person with scleroderma. Joining a support group can give them valuable information and support.

For men with scleroderma

There are more women than men living with scleroderma. Groups are open to both men and women but tend to have many more women members. To offer men with scleroderma their own space, we have a men's group. Please see the list of groups and meetings on the Scleroderma Quebec website for contact information, dates, and times.

For young people with scleroderma

Scleroderma affects people of all ages, from children to seniors. Young people with scleroderma feel doubly alone. Not only do they have a rare disease, but they are also a minority of the people living with the disease. As well, fewer young people have chronic conditions. To give young people living with scleroderma a place to share their experiences and form a community with their peer group, we propose meetings specifically for young people between the ages of about 14 to 35. Again, please see the list of groups and meetings on the Scleroderma Quebec website for contact information, dates, and times. Young people are also cordially invited to all other Scleroderma Quebec support groups.

For English-speaking people

Up until recently, all our support groups have been in the French language. We are very happy to now have a Zoom support group in English that meets once a month. It is open to anglophones and to bilingual members who prefer the afternoon time slot. Scleroderma Quebec is very attentive to the needs of English-speaking members. The website is bilingual, the various publications are translated and available in English, and our magazine, Le Bulletin, has an English version available online, by request. You can contact the association in English for any enquiries or support.

What are meetings like?

In-person meetings

In-person meetings can be occasional or regular. They could be held in a restaurant, a community hall or at a member's home. They usually last about two hours. They could have a guest speaker or be a time of discussion around a theme, or a freer, less structured discussion. Usually, there would be a snack time. All in-person meetings are announced on the Scleroderma Quebec website with contact information, dates and times and details about the location. You are welcome to visit in-person meetings in different regions of Quebec. If you would like to attend an in-person meeting and there is not one announced for your region, you could contact the support group leader in your area and express your interest. That could be the spark that helps get one organized.

Zoom meetings

Like in-person meetings, Zoom meetings can be occasional or regular. Many groups hold meetings once a month or every six weeks, for example. They can have special guests and free or structured discussions. Zoom meetings usually last a maximum of ninety minutes. Because they are online, you are not limited to your geographical region. You can attend a Zoom meeting organized by a leader who lives anywhere in the province. You will want to choose a Zoom group that meets at a time and on a day that suits your schedule. Again, please see the list of groups and meetings on the Scleroderma Quebec website for contact information, dates, and times. You can try out more than one group to find the group that suits your needs best.

What do I need to join a Zoom meeting?

To join a Zoom meeting, you will need a computer, tablet or cell phone with a camera and microphone. After you contact the leader of the support group, they will send you a link to the meeting by email. To attend the meeting, you will need to click on the link in the email. ***If you are unfamiliar with this technology, please tell the leader that you would appreciate some help in becoming proficient***. They will be more than happy to do a practice Zoom with you in preparation for your meeting. For those who do not have Internet, it is still possible to join a Zoom meeting by telephone but that would incur long-distance charges if you do not have a long-distance phone plan.

When do support groups meet?

Most support groups meet from September through May or June. Some meet once a month, others every six weeks and some meet occasionally. Generally, there are no meetings in the summer. Before the pandemic, most groups stopped for the winter months because of road conditions and concerns about Raynaud's syndrome. Now, with the possibility of Zoom meetings, many groups meet throughout the winter via Zoom. Some groups meet in the morning, and others in the afternoon or evening. Most groups meet on weekdays but there are occasional meetings on weekends. For more details, check the Scleroderma Quebec website.

How do I join a support group?

The first step for joining a support group is to contact Scleroderma Quebec at 514-990-6789 or by email at info@sclerodermie.ca. They will refer you to a leader who will help you find the right group for you. Alternatively, you can go to the list of meetings posted on the first page of the Scleroderma Quebec website, and find the contact information for the group you are interested in. Then you can contact the leader of the group directly by phone or email. Usually, they will set up a time for a phone call or Zoom to get to know you better and answer your questions about their group.

If you are planning on attending an in-person meeting and the place and time are available on the website, it is still a good idea to contact the leader to let them know you are planning to attend. If there is a last-minute change in plans, they will be able to contact you and let you know about any changes.

How can I become a leader of a support group?

Scleroderma Quebec is always recruiting support group leaders for both in-person and Zoom groups. Many leaders find that this volunteer commitment contributes to their own well-being as they find valorization in supporting others and using their talents of organization and compassionate caring. Scleroderma Quebec provides a training course for leaders developed by SPIN, a detailed guidebook, and a support committee. It is very important to the association that leaders feel affirmed and supported in their volunteer work.

If becoming a leader interests you, first contact Scleroderma Quebec to communicate your interest. Second, join an existing support group to learn how groups function by being a part of a group. Finally, apply formally to Scleroderma Quebec to go through the selection process. Many groups have co-leaders so even when you become a leader you will be supported by your co-leader.

Thank you

Many thanks to all the volunteer leaders who have pioneered the Scleroderma Quebec support groups over the last thirty or so years. Sincere thanks to Scleroderma Quebec and the professionals and volunteers working for the association who make these groups possible by providing the structure within which the groups can thrive. Special thanks to SPIN and Brett Thombs for developing the SPIN-SSLED program that equips leaders to develop healthy support groups.

In Conclusion

Joining a support group can be a real help to many people living with scleroderma. Sharing with others with the same condition reduces the feeling of isolation. Groups offer a safe, positive, and confidential space to share concerns and learn more about coping with the disease. Often members experience increased hope and resilience. Leaders are well-trained and supported under the supervision of Scleroderma Quebec. There are well-defined guidelines for group members which help maintain the quality of the interactions. If you are interested do not hesitate to contact Scleroderma Quebec by phone at 514-990-6789 or by email at **info@sclerodermie.ca** or contact a support group leader for more information. We are looking forward to hearing from you.

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HOW SCLERODERMA CAN AFFECT THE HUMAN BODY

The symptoms of scleroderma vary greatly from person to person, so that patients will not necessarily develop all the complications of the disease.

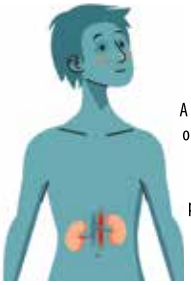
The symptoms of the disease may be visible, as is the case when the skin is affected, or the symptoms may be invisible, as when internal organs are affected.

SYMPTOMS AND MANIFESTATIONS OF SCLERODERMA

SKIN HARDENING
Thickening and loss of elasticity of the skin on different parts of the body. Hence the name «scleroderma», which means hard skin.

PULMONARY FIBROSIS
A potentially serious complication where normal lung tissue is gradually replaced by scarred fibrotic tissue, making it difficult to breathe and deliver needed oxygen to the body.

Pulmonary fibrosis causes shortness of breath and also sometimes a dry cough.



RENAL CRISIS
A renal crisis, which is due to an acute obstruction of arterioles and capillaries in the kidneys, leads to a sudden and sharp increase in arterial blood pressure. The symptoms are those of a hypertensive crisis: new and severe headaches, marked shortness of breath (left heart failure), and even epileptic seizures (convulsions). This is a very serious complication which requires urgent medical attention. Often during a scleroderma renal crisis, the kidneys stop functioning and dialysis (filtering the blood to avoid uremia) is then needed.

BLOOD VESSELS
The narrowing of the arteries, small blood vessels, and capillaries, can lead to many complications, including the development of pulmonary arterial hypertension (PAH), digital ulcers, and other conditions.

PULMONARY ARTERIAL HYPERTENSION (PAH)
Increased pressure in the pulmonary arteries due to the narrowing of small arteries in the lungs. Blood flow to the lungs is significantly restricted, making the heart work harder to pump blood through the lungs.

As arterial blood pressure rises in the pulmonary arteries, small pulmonary vessels slowly become clogged (a process which may take several years). This occurs through fibrosis of the small vessels, eventually leading to thrombosis, and the blood can no longer reach all parts of the lungs. Thus, it becomes more difficult for the lungs to supply enough oxygen to the body.

Sustained high blood pressure in the arteries of the lungs puts a strain on the heart, making it more difficult to circulate the blood through the lungs. Over time, this can eventually lead to congestive heart failure, particularly the right side, what is referred to as right heart failure (RHF). Right heart failure is indicative of significant PAH and is a serious complication of scleroderma.

PAH results in one or more of the following symptoms:

- Shortness of breath on exertion and at rest
- Palpitations (heart rhythm disorder)
- Fatigue
- Chest pain
- Dizziness
- Temporary loss of consciousness (syncope)
- Swelling of the ankles and legs

SCLERODERMA FACES
Hollow eyes, pinched nose, thin pursed lips, mask-like face, small puckered mouth (microstomia), and peri-oral folds.

Thinning lips and facial muscle atrophy can make the teeth appear more prominent.

EYES
Dry eyes caused by a decrease in tear production.

TELANGIECTASIA
Small dilated capillaries visible on the face and hands, sometimes referred to as «spider veins».

RAYNAUD'S PHENOMENON
Raynaud's is present in up to 95% of people with scleroderma. Whitening of fingers and/or toes triggered by cold or severe stress. The whiteness phase can be followed by a blue phase and then a red phase.

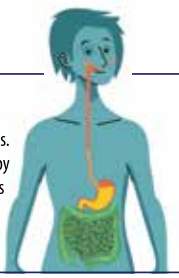
SCLERODACTYLY
The skin of the fingers, which have become infiltrated with collagen (fibrosis), may look full and sausage-like. Functional loss or decreased range of motion.

CALCINOSIS
Calcium deposits under the skin that may require antibiotics to cure occasional infections and sometimes surgery to drain calcium deposits and relieve pain.

DIGITAL ULCERS
Ulcers occur on the fingertips or on the top of the fingers. They are painful and difficult to heal.

In the most severe cases, it can lead to necrosis and amputation may be needed.

SKIN PIGMENTATION
Dark or pale spots occurring in one-third of patients.



DIGESTIVE SYSTEM
Gastrointestinal disorders affect the vast majority of patients. Gastric reflux is a common symptom that manifests itself by a burning sensation radiating up to the throat after meals and may cause inflammation of the lining of the esophagus (esophagitis reflux) if left untreated.

MUSCLE AND JOINT PAINS
Joint pain is common. It is caused by inflammation of the joints and tendons, which quite often leads to joint swelling and stiffness that can become quite debilitating.

Muscular pain (myalgia) can be intermittent or continuous. It can also be associated with muscle weakness (myositis). Symptoms include difficulty in climbing stairs, lifting objects and getting up, and also difficulty swallowing.

About the book

Scleroderma: A Comprehensive Guide to Symptoms, Diagnoses, and Treatments
is an essential resource for patients, their families, and healthcare professionals.
This guide, written by renowned experts, offers an in-depth understanding of this complex disease, facilitating informed collaboration between patients and their doctors. It aims to empower scleroderma patients to better understand their symptoms and treatment options, helping them to actively participate in their care journey.

Shirley Dorismond,
Member of the National Assembly for Marie-Victorin and Parliamentary Assistant for Social Services

"As a Member of the National Assembly, Parliamentary Assistant to the Minister Responsible for Social Services, and Nurse Clinician, I applaud the release of this essential book on scleroderma. This comprehensive guide to symptoms, diagnosis, and treatment is an invaluable resource for patients, healthcare professionals, and families affected by this complex disease.

I express my deep gratitude for the dedication and expertise of everyone who contributed to the completion of this valuable tool. Your hard work and compassion for those suffering from this chronic illness are reflected in the pages of this informative guide.

I also want to extend my words of encouragement to all those battling scleroderma. May the information contained in this book bring light, hope, and support on your journey.

Together, let us continue to raise awareness, provide support, and fight against scleroderma. Congratulations on this source of knowledge and inspiration."

"I am happy to endorse this important work. Providing accurate and up-to-date information to patients and their caregivers remains an important priority for me as a physician. It also allows me to take stock as a researcher and realize how many more questions remain unanswered. I look forward to answering many of those questions in the years to come."

Dr. Marie Hudson, MD, MPH, FRCPC
Rheumatologist, epidemiologist,
Associate Professor Department
of Medicine at McGill University

"It is essential that individuals living with scleroderma and their caregivers be well informed about the symptoms of the disease, potential complications and available treatments. Well-informed patients are the best allies of health professionals. I am honored to have been able to contribute to this work and to share what I know with patients beyond my clinical practice."

Dr. Sabrina Anh-Tu Hoa, MD, MSc, FRCPC
Rheumatologist, Epidemiologist,
Associate Clinical Professor, Department
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Scleroderma Quebec™

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