PATIENT INFORMATION LEAFLET

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Scleroderma

Understanding systemic sclerosis — an autoimmune disease of skin, vessels and organs

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Scleroderma — also known as systemic sclerosis — is a rare but serious autoimmune rheumatic disease that hardens the skin and may damage internal organs including the lungs, heart, kidneys and digestive tract. This leaflet has been prepared for patients attending our clinic to explain what scleroderma is, how and why it develops, how it is diagnosed, and how modern treatment — guided by the EULAR 2023 recommendations — can control the disease and protect organ function. It is intended to complement, not replace, your consultation with your rheumatologist.

4:1
Female : male ratio in systemic sclerosis

~19
Cases per 100,000 — global prevalence

30–50
Typical age of onset (years)

What this leaflet covers

1. What is scleroderma?
2. How common is it? — global and Pakistani data
3. Why does it happen? — pathogenesis explained
4. Recognising the symptoms
5. How the diagnosis is made
6. Treatment — organ-by-organ approach
7. Living well with scleroderma
8. When to seek urgent advice

1. What is scleroderma?

The word *scleroderma* comes from the Greek *skleros* ('hard') and *derma* ('skin'), and literally means 'hard skin'. Medically, the term is now used as shorthand for **systemic sclerosis (SSc)** — a chronic, multisystem autoimmune disease characterised by three core processes:

- **Vasculopathy** — abnormalities of small blood vessels (the earliest event), responsible for Raynaud's phenomenon and digital ulcers.
- **Immune dysregulation** — chronic activation of the innate and adaptive immune system, with disease-specific autoantibodies.
- **Tissue fibrosis** — excessive deposition of collagen leading to thickening of the skin and scarring of internal organs.

Scleroderma is not a single disease but a spectrum. At one end lies **localised scleroderma** (morphoea and linear scleroderma), in which only the skin is affected and internal organs are spared. At the other end lies **systemic sclerosis**, in which the same fibrotic and vascular process can affect any internal organ. This leaflet focuses on systemic sclerosis.

Subtypes of systemic sclerosis

Subtype	Skin involvement	Typical course
Limited cutaneous SSc (lcSSc)	Skin thickening restricted to fingers, hands, face and below the elbows and knees.	Slow onset; long history of Raynaud's; later risk of pulmonary hypertension. Includes the older 'CREST' pattern.
Diffuse cutaneous SSc (dcSSc)	Skin thickening also involving the trunk and proximal limbs (above elbows and knees).	More rapid onset; higher risk of interstitial lung disease, scleroderma renal crisis and cardiac involvement.
SSc sine scleroderma	No detectable skin thickening.	Typical autoantibodies and internal organ involvement without skin change. Uncommon but important to recognise.

What was 'CREST syndrome'?

An older term for the limited form, describing its five classical features: **C**alcinosis (calcium deposits in the skin), **R**aynaud's phenomenon, **E**sophageal dysmotility, **S**clerodactyly (tight skin of the fingers), and **T**elangiectasia (visible small blood vessels). The label is now used less often because not all patients show every feature, and the modern terminology of 'limited cutaneous systemic sclerosis' is more accurate.

2. How common is scleroderma?

Global figures

Systemic sclerosis is rare compared with rheumatoid arthritis or lupus, but it is consistently among the most lethal of the autoimmune rheumatic diseases. The best available evidence from recent systematic reviews and meta-analyses suggests:

- **Global prevalence** is estimated at approximately **17.6–18.9 cases per 100,000 adults** — meaning roughly 1.5 million people are affected worldwide.
- **Annual incidence** ranges from **1.4 to 8.6 new cases per 100,000 person-years**, with a global pooled estimate of about 8.6 per 100,000.
- Women are affected approximately **four times more often than men**, and the disease tends to be more severe in those of African and South Asian heritage.

- Peak age at diagnosis is **30 to 50 years**; juvenile and elderly-onset disease occur but are uncommon.
- **Prevalence is higher in North America, Australia and southern Europe**, and lower in northern Europe and Japan — likely reflecting both genetic and environmental factors.
- Around **50–60% of patients have limited cutaneous disease** and 35–45% have diffuse cutaneous disease, with the remainder having sine-scleroderma or overlap forms.

Data from Pakistan

Dedicated population-based studies on systemic sclerosis remain scarce in Pakistan, and the disease is widely believed to be underdiagnosed. However, an important single-centre prospective study (*Hashmi et al., Archives of Rheumatology, 2021*) provides valuable insight into the clinical pattern in our population:

- Among **38 Pakistani patients** with systemic sclerosis, **32 (84%) were women**, with a mean age of 34.5 years and a range of 16 to 60 years — confirming the female predominance and relatively young age at presentation.
- **Raynaud's phenomenon was the earliest symptom in 89.5%** of patients, with a mean delay of 3.8 years before other systemic features appeared — a vital window for early diagnosis and intervention.
- **Sclerodactyly was present in 89.5%**, digital ulcers in **65.8%**, and tendon friction rubs in **31.6%** of patients.
- **Interstitial lung disease (ILD) was strikingly common at 78.9%**, with universal involvement (100%) in those with diffuse disease and 70% in limited disease — considerably higher than figures reported from Western cohorts.
- **Pulmonary hypertension was present in 18 patients**, again with a much higher burden in diffuse (57.1%) than limited disease (11.8%).
- These figures suggest that, when patients do present in Pakistan, they tend to do so with more advanced disease and a higher prevalence of major organ involvement — underscoring the importance of early referral.

> **A note on local awareness**
>
> Many Pakistani patients are first seen for cold, colour-changing fingers (Raynaud's), for tight skin assumed to be eczema, or for unexplained breathlessness misattributed to asthma. Any patient — particularly a woman — with new Raynaud's phenomenon, puffy fingers, or progressive skin tightening deserves an urgent rheumatology referral.

3. Why does scleroderma happen?

The precise cause of systemic sclerosis remains unknown, but a great deal has been learned in the last two decades. It arises from a combination of **genetic susceptibility**, an **environmental trigger**, and a self-sustaining sequence of vascular, immune and fibrotic events. The 'pathogenic triad' of vasculopathy, autoimmunity and fibrosis is what defines the disease.

The key steps in pathogenesis

1 **Genetic susceptibility**
Specific HLA class II alleles (notably HLA-DRB1*11:04, HLA-DPB1*13:01 and HLA-DQB1*03) and non-HLA genes (IRF5, STAT4, BANK1) increase risk. Familial clustering is uncommon, and most cases are sporadic.

2 **Environmental trigger**
Occupational silica exposure is the strongest established trigger and is highly relevant in Pakistan; organic solvents, vinyl chloride and certain medications have also been implicated. Some viral infections (CMV, parvovirus B19) are under investigation.

3 Endothelial injury

The earliest detectable event is damage to the small blood vessels (capillaries and arterioles). The endothelium becomes activated and dysfunctional, vessels narrow and are eventually lost — producing Raynaud's phenomenon, digital ulcers and pulmonary hypertension.

4 Immune dysregulation

B cells, T cells, plasmacytoid dendritic cells and macrophages are abnormally activated. Type I interferon and IL-6 signalling are upregulated. Characteristic autoantibodies appear — anti-centromere, anti-topoisomerase I (Scl-70) and anti-RNA polymerase III — long before tissue damage becomes apparent.

5 Fibroblast activation

Inflammatory cytokines (especially TGF-β and IL-6) drive fibroblasts to differentiate into myofibroblasts, which produce excessive collagen and extracellular matrix.

6 Tissue fibrosis

Collagen accumulates in the skin (causing thickening and tethering) and in internal organs — particularly the lungs (interstitial fibrosis), gastrointestinal tract (dysmotility), heart (myocardial fibrosis) and kidneys.

7 Organ failure

If unchecked, fibrosis progressively destroys organ architecture. The leading causes of death in modern cohorts are interstitial lung disease and pulmonary arterial hypertension — making their early detection and treatment a priority.

> **Silica and scleroderma — the occupational link**
>
> Occupational silica exposure (sandblasting, foundry work, stone-cutting, construction, ceramics) is one of the few firmly established environmental causes of systemic sclerosis. Given how widespread these industries are in Pakistan, an occupational history should be sought in every male patient with a suspected diagnosis.

4. Recognising the symptoms

Scleroderma can affect almost every organ system. Symptoms develop gradually over months to years, and their pattern often determines the subtype.

Vascular features (often the earliest)

- **Raynaud's phenomenon** — the classic triphasic colour change of the fingers (white → blue → red) on exposure to cold or stress. Present in over 95% of patients and often precedes other features by months or years.
- **Digital ischaemia and ulcers** — painful, slow-healing sores at the fingertips or over the knuckles; in severe cases, gangrene and digital loss can occur.
- **Telangiectasia** — small dilated blood vessels on the face, lips, hands and tongue.
- **Calcinosis cutis** — chalky calcium deposits in the skin, particularly over pressure points; may extrude through the skin and become infected.

Skin and musculoskeletal features

- **Puffy hands** — the earliest skin sign, lasting weeks to months before tightening.
- **Sclerodactyly** — taut, shiny skin of the fingers, often with loss of fine wrinkles and reduced ability to flex or extend.

- **Facial changes** — a 'mauskopf' (mouse-face) appearance with thinned lips, reduced mouth opening (microstomia) and a pinched, expressionless face.
- **Skin pigmentation changes** — patchy darkening or 'salt-and-pepper' loss of pigment.
- **Arthralgia and arthritis** — joint pains in around 50% of patients; tendon friction rubs are characteristic of diffuse disease.
- **Muscle weakness and myositis** — particularly in overlap with inflammatory myopathy.

Internal organ involvement

Organ	Common manifestations
Lungs	**Interstitial lung disease (ILD)** — exertional breathlessness, a dry cough, fatigue. Most common cause of death. **Pulmonary arterial hypertension (PAH)** — late progressive breathlessness, often in limited disease.
Gastrointestinal tract	Acid reflux and heartburn (almost universal); difficulty swallowing solids; early satiety, bloating, alternating diarrhoea and constipation due to small-bowel bacterial overgrowth; rarely, faecal incontinence.
Heart	Myocardial fibrosis, conduction abnormalities, arrhythmia, pericardial effusion. Often clinically silent until advanced.
Kidneys	**Scleroderma renal crisis** — sudden, severe hypertension with acute kidney injury, typically in the first five years of diffuse disease; a medical emergency.
Other	Sexual dysfunction (erectile dysfunction in men; vaginal dryness and dyspareunia in women), depression, profound fatigue.

Why early diagnosis matters

Many of scleroderma's most serious complications — interstitial lung disease, pulmonary arterial hypertension and scleroderma renal crisis — can be detected before they cause symptoms. The first few years after the onset of Raynaud's and skin changes are the highest-risk window. Regular screening with pulmonary function tests, echocardiography and blood pressure monitoring is essential.

5. How the diagnosis is made

There is no single test that proves scleroderma. The diagnosis rests on the pattern of clinical features, supported by blood tests, nailfold capillary microscopy and screening for internal organ involvement. The internationally agreed **2013 ACR/EULAR classification criteria** are used to confirm the diagnosis and to standardise eligibility for research.

The diagnostic workup

- **History and examination** — duration of Raynaud's, pattern and extent of skin involvement, reflux symptoms, breathlessness, blood pressure trends, occupational exposures.
- **Nailfold capillaroscopy** — a simple bedside test using a dermatoscope or capillaroscope. Characteristic 'scleroderma pattern' changes (enlarged and giant capillaries, microhaemorrhages, capillary loss) confirm an autoimmune Raynaud's and support an early diagnosis.
- **Autoantibody profile** — antinuclear antibody (ANA), positive in over 90%, plus scleroderma-specific antibodies: **anti-centromere** (typically limited disease and pulmonary hypertension), **anti-topoisomerase I / Scl-70** (typically diffuse disease with ILD), and **anti-RNA polymerase III** (rapid skin progression and scleroderma renal crisis).

- **Modified Rodnan Skin Score (mRSS)** — a bedside clinical score that quantifies skin thickening across 17 body areas and tracks disease progression.
- **High-resolution CT of the chest (HRCT)** — to detect interstitial lung disease at baseline and then periodically.
- **Pulmonary function tests** — including FVC, FEV1 and DLCO; performed at diagnosis and at least annually thereafter.
- **Echocardiography** — to estimate pulmonary artery pressure and assess cardiac function; repeated annually as PAH screening.
- **Renal monitoring** — regular blood pressure checks (ideally home monitoring), renal function and urinalysis, particularly in the first five years of diffuse disease.
- **Gastrointestinal investigation** — when indicated, oesophageal manometry, gastric emptying studies and hydrogen breath tests for small-bowel bacterial overgrowth.

The 2013 ACR/EULAR classification criteria — at a glance

A patient can be classified as having systemic sclerosis when the sum of the weighted items reaches ≥ **9 points**. The single sufficient criterion is skin thickening of the fingers extending proximal to the metacarpophalangeal joints.

Item	Weight
Skin thickening of the fingers extending proximal to the MCP joints (sufficient alone)	**9**
Skin thickening of fingers (highest score only): puffy fingers (2), sclerodactyly distal to MCPs (4)	**2 or 4**
Fingertip lesions: digital tip ulcers (2), pitting scars (3)	**2 or 3**
Telangiectasia	**2**
Abnormal nailfold capillaries	**2**
Pulmonary arterial hypertension and/or interstitial lung disease	**2**
Raynaud's phenomenon	**3**
SSc-related autoantibodies (anti-centromere, anti-topoisomerase I, anti-RNA polymerase III) — maximum 3	**3**

Source: van den Hoogen F et al. Ann Rheum Dis 2013;72:1747–1755.

> **Very early diagnosis of systemic sclerosis (VEDOSS)**
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> The EUSTAR group has defined a 'very early' diagnostic approach that combines Raynaud's phenomenon, puffy fingers, a positive ANA, abnormal nailfold capillaries, and scleroderma-specific autoantibodies — even before classification criteria are met. Identifying patients in this window allows monitoring to begin before irreversible organ damage occurs.

6. Treatment

There is no cure for systemic sclerosis, but treatment has transformed in the past decade. Modern management — guided by the **EULAR 2023 recommendations** — is **organ-directed**: every major manifestation has its own evidence-based therapy. Most patients are looked after by a multidisciplinary team led by a rheumatologist.

Treatment by organ system

Problem	Recommended treatment
Raynaud's phenomenon	• Warm clothing, gloves and hand-warmers; smoking cessation • Dihydropyridine calcium channel blockers (nifedipine, amlodipine) first line • PDE-5 inhibitors (sildenafil, tadalafil) and topical nitrates as add-ons • Intravenous iloprost for severe attacks
Digital ulcers	• PDE-5 inhibitors and intravenous iloprost for healing of active ulcers • Bosentan to prevent new ulcers in patients with multiple lesions • Meticulous wound care; antibiotics for infection
Skin fibrosis	• **Methotrexate** for early diffuse skin disease • **Mycophenolate mofetil** increasingly used first line for progressive skin disease • **Tocilizumab** (anti-IL-6) or **rituximab** (anti-CD20) for refractory or rapidly progressive disease • Autologous haematopoietic stem cell transplantation in carefully selected early dcSSc patients with poor prognostic features
Interstitial lung disease (ILD)	• **Mycophenolate mofetil** or **cyclophosphamide** as first line • **Nintedanib** (an antifibrotic), alone or combined with mycophenolate, for progressive ILD • **Tocilizumab** and **rituximab** are additional options • Long-term oxygen, pulmonary rehabilitation and, in selected cases, lung transplantation
Pulmonary arterial hypertension	Combination therapy under specialist supervision: endothelin receptor antagonists (ambrisentan, macitentan), PDE-5 inhibitors (sildenafil, tadalafil), riociguat, and prostacyclin analogues (epoprostenol, treprostinil, selexipag).
Scleroderma renal crisis	• **Immediate ACE inhibition** (captopril, titrated rapidly) — life-saving • Avoid high-dose corticosteroids in early diffuse disease, as these can precipitate renal crisis • Renal replacement therapy where required
Gastrointestinal disease	• Proton pump inhibitors (PPIs) for reflux • Prokinetics (domperidone, prucalopride) for dysmotility • Cyclical antibiotics for small-bowel bacterial overgrowth • Nutritional support; dietitian input
Joint and muscle involvement	Methotrexate for inflammatory arthritis; short courses of low-dose corticosteroid with caution; physiotherapy and occupational therapy.

Corticosteroids — a word of caution

Unlike many other rheumatic diseases, high-dose corticosteroids (prednisolone above 15 mg/day) should be **avoided** in early diffuse systemic sclerosis, as they can trigger scleroderma renal crisis. When steroids are unavoidable, the dose should be kept low and blood pressure monitored daily.

7. Living well with scleroderma

Scleroderma is a long-term condition, and outcomes have improved markedly with modern screening and treatment. A few practical principles make a real day-to-day difference.

- **Keep warm** — protect the whole body, not just the hands. Layered clothing, thermal undergarments, gloves, woollen socks and warm headwear reduce Raynaud's attacks. Avoid sudden temperature changes; use warm water when washing.
- **Stop smoking** — smoking constricts blood vessels and accelerates digital ulcer and lung disease. This is the single most important lifestyle change.
- **Look after your skin** — daily emollients, gentle handwashing, sun protection, and prompt treatment of any small skin break to prevent ulcers.
- **Look after your mouth and teeth** — reduced mouth opening makes dental care harder. Six-monthly dental review, fluoride toothpaste and mouth-stretching exercises help.
- **Eat little and often** — small frequent meals, sitting upright for 30 minutes after eating, raising the head of the bed, and avoiding late evening meals reduce reflux.
- **Stay active** — graded aerobic exercise, hand and facial stretches, and physiotherapy preserve joint mobility, lung function and mood. Pulmonary rehabilitation is particularly valuable in ILD.
- **Attend your screening appointments** — annual pulmonary function tests, echocardiogram and review of skin score and autoantibodies are essential — they detect organ involvement before symptoms develop.
- **Vaccinations** — influenza and pneumococcal vaccines are recommended, particularly if you are on immunosuppression. Live vaccines should be discussed with your rheumatologist.
- **Pregnancy** — pregnancy is possible but requires careful planning with a high-risk obstetric and rheumatology team. It should ideally be deferred until disease is stable and avoided in the first 3–4 years of diffuse disease.
- **Mental wellbeing** — depression and anxiety are common in scleroderma and very treatable. Please raise any concerns; support groups and counselling help significantly.

8. When to seek urgent advice

Please contact the clinic, or attend a hospital, promptly if you experience any of the following:

- **A new severe headache, blurred vision or unusually high blood pressure** — possible scleroderma renal crisis (a medical emergency)
- **Sudden or worsening breathlessness**, chest pain or palpitations
- A **fingertip ulcer that is increasingly painful, red or discharging pus** — possible infection
- **Blackening of a finger or toe** — possible critical ischaemia
- **Severe vomiting, difficulty swallowing or unintended weight loss**
- **Reduced urine output** or marked leg swelling
- **A high temperature** while on immunosuppressive treatment
- **Sudden weakness, numbness or change in speech**

A word from your rheumatologist

Scleroderma is a complex disease, but it is one in which careful, long-term care makes a real difference. The earlier we identify and treat organ involvement, the better the outlook. Please bring this leaflet to your next appointment, mark anything that resonates with your own experience, and we will go through it together. You are not alone — millions of people around the world live with scleroderma, and modern treatment continues to improve their lives.

— Dr Saira Khan, Consultant Rheumatologist

Selected references

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***Important note:** This leaflet is for general information only and does not replace personal medical advice. Every patient is different; please discuss any questions or concerns directly with Dr Saira Khan or another qualified rheumatologist. Version 1.0 — May 2026.*