Systemic Sclerosis *(SSc)*

A Rare, Life-Threatening Autoimmune Disease

What is SSc?[1,2]

SSc, also known as scleroderma, is a rare, life-threatening autoimmune disease characterized by progressive thickening and scarring (fibrosis) of the skin and internal organs. It often affects the skin but can also involve the lungs, gastrointestinal tract, kidney, and heart.

While SSc is rare, it carries significant disease burden due to frequent and severe comorbidities, and has the highest mortality rate of any rheumatic disease.

Who is impacted by SSc?

~300,000 people in the U.S., E.U., and Japan[3]

5x more common in females[4]

Disease onset typically occurs **between the ages of 30 and 50**[5]

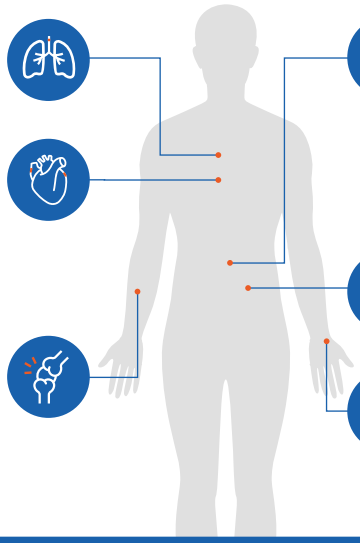
What symptoms and complications are associated with SSc?

SSc affects multiple systems in the body and can be difficult to diagnose early due to its wide range of symptoms. Initial symptoms are nonspecific and include fatigue, musculoskeletal discomfort, hand swelling, and Raynaud's phenomenon, a condition that causes blood vessels in the fingers and toes to go into spasm and restrict blood flow.[6] Organ damage can also occur due to fibrosis or blood vessel abnormalities called vasculopathy.

Severe complications of SSc include:[7]

- Hypertension
- Kidney failure
- Interstitial lung disease *(ILD)*
- Cardiac failure
- Pulmonary hypertension
- Digital ischemia

Additional symptoms and complications related to the different organs involved may include:[8]



Lungs

Coughing and shortness of breath

Heart

Abnormal heartbeat

Fluid buildup around the heart

Fibrosis

Nerves, muscles, and joints

Numbness

Loss of mobility

Joint and muscle pain

Gastrointestinal tract

Difficulty swallowing

Heartburn

Bloating

Constipation

Diarrhea

Kidneys

Kidney failure

Skin

Thickening of the skin

Difficulty with hand grip

How is SSc diagnosed and assessed for disease progression?[9,10]

There is no single test for diagnosing SSc. Diagnosis requires a thorough review of a person's medical history, a physical examination to determine the presence and extent of skin involvement, blood tests, and imaging, which may include:

- Pulmonary function tests
- Skin biopsies
- Gastrointestinal endoscopies
- X-rays
- CT scans
- Ultrasounds

How does SSc impact quality of life?[11,12]

As a chronic disease, SSc has a **profoundly negative impact on the health-related quality of life** of affected individuals, specifically associated with:

- Fatigue
- Difficulty performing daily activities
- Emotional distress
- Sleep disorders
- Low-self esteem
- Depression

What are the subtypes of SSc?[13]

SSc is traditionally classified by the extent of skin involvement, accompanying internal organ disease, and the presence of other autoimmune disease. The two main subtypes are:

→ Limited cutaneous SSc (lcSSc)

Involves the face and the extremities, often presenting with vascular and dermatologic symptoms, including Raynaud's phenomenon and skin thickening. Internal organ involvement is less common, though there is risk of pulmonary hypertension.

→ Diffuse cutaneous SSc (dcSSc)

Causes extensive skin changes which can progress rapidly and early visceral organ involvement. Systemic manifestations include gastrointestinal disruption and life-threatening pulmonary and renal complications.

How is SSc currently managed?

Due to the wide spectrum of disease manifestations and organ involvement, current recommended treatment includes a combination of immunosuppressants, particularly mycophenolate mofetil or cyclophosphamide, alongside organ-specific therapies, which are used off-label in the U.S.[14] These agents can cause side effects, including gastrointestinal issues like diarrhea, nausea, and vomiting.[15] In the U.S., there are two drugs indicated for slowing the rate of decline in pulmonary function in patients with SSc-associated ILD; but there are no approved therapies for treating the totality of the disease.[6]

Treatment goals and outcomes should focus on slowing progression of fibrosis in the skin and visceral organs, slowing the decline in lung disease, and decreasing mortality.

What is the prognosis?

Prognosis in SSc varies based on disease subtype, antibody profile, and organ involvement.[16]

Overall, prognosis is worse in men, people who develop the disease at an older age, people with dcSSc, and those with internal organ involvement, such as the lungs, heart, or kidneys.[17] The overall five-year survival rate is approximately 75% with the primary cause of death often being pulmonary involvement, including ILD or pulmonary arterial hypertension (PAH).[18]

References 1. Allanore. Systemic sclerosis. Nature (2019). 2. Nature Primers. Systemic Sclerosis (2019). 3. Clarivate/DRG. Projected Prevalence 2032. 4. Bairkdar, M. et al. (2021). Incidence and prevalence of systemic sclerosis globally: A comprehensive systematic review and meta-analysis. Rheumatology. https://doi.org/10.1093/rheumatology/keab190 5. Scleroderma. Mayo Clinic. (2024, June 15). https://www.mayoclinic.org/diseases-conditions/scleroderma/symptoms-causes/syc-20351952 6. Systemic sclerosis (scleroderma) - Symptoms, diagnosis and treatment. BMJ Best Practice US. (n.d.). https://bestpractice.bmj.com/topics/en-us/295?q=Systemic+sclerosis+%28scleroderma%29&c=suggested 7. National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Board on Health Care Services, & Committee on Selected Immune Disorders and Disability. (2023). Selected immune disorders and disability. National Academies Press. 8. Systemic Scleroderma. National Organization for Rare Disorders (NORD). (2024, December 19). https://rarediseases.org/rare-diseases/systemic-scleroderma/#symptoms 9. Scleroderma Diagnosis. Johns Hopkins Medicine. (2019, November 19). https://www.hopkinsmedicine.org/health/conditions-and-diseases/scleroderma/scleroderma-diagnosis 10. Scleroderma. Cleveland Clinic. (2025, February 7). https://my.clevelandclinic.org/health/diseases/scleroderma 11. Sierakowska, M. et al. (2019). Factors associated with quality of life in systemic sclerosis: A cross-sectional study. Quality of Life Research. https://doi.org/10.1007/s11136-019-02284-9 12. Mura, G. et al. (2012). Psychiatric symptoms and quality of life in systemic sclerosis. Clinical Practice & Epidemiology in Mental Health. https://doi.org/10.2174/1745017901208010030 13. Adigun, R. et al. (2024, April 5). Systemic Sclerosis (Scleroderma). StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK430875/ 14. Pope, J. E. et al. (2023). State-of-the-art evidence in the treatment of systemic sclerosis. Nature Reviews Rheumatology. https://doi.org/10.1038/s41584-023-00909-5 15. Omair, M. A. et al. (2015). Safety and effectiveness of mycophenolate in systemic sclerosis. A systematic review. PLOS ONE. https://doi.org/10.1371/journal.pone.0124205 16. Hu, S., Hou, Y., Wang, Q. et al. Prognostic profile of systemic sclerosis: analysis of the clinical EUSTAR cohort in China. Arthritis Res Ther 20, 235 (2018). https://doi.org/10.1186/s13075-018-1735-4 17. Sampaio-Barros, P. D. et al. (2012). Survival, causes of death, and prognostic factors in systemic sclerosis: Analysis of 947 Brazilian patients. The Journal of Rheumatology. https://doi.org/10.3899/jrheum.111582 18. De Almeida Chaves, S. et al. (2021). Sine scleroderma, limited cutaneous, and diffused cutaneous systemic sclerosis survival and predictors of mortality. Arthritis Research & Therapy. https://doi.org/10.1186/s13075-021-02672-y