

SYSTEMIC SCLEROSIS (SCLERODERMA)

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1. [LeRoy EC](#). Connective tissue synthesis by scleroderma skin fibroblasts in cell culture. J Exp Med 135: 1351-1352, 1972.

Landmark study demonstrating increased production of collagen in monolayer cell cultures of fibroblasts taken from scleroderma skin biopsies.

2. [LeRoy EC](#), [Black C](#), [Fleischmajer R](#), [Jablonska S](#), [Krieg T](#), [Medsker TA](#), [Rowell N](#), [Wollheim F](#). Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. J Rheumatol 15(2): 202-205, 1988.

Consensus classification system for systemic sclerosis patients, with division into limited cutaneous systemic sclerosis and diffuse cutaneous systemic sclerosis.

3. [Varga J](#). Scleroderma and Smads: dysfunctional Smad family dynamics culminating in fibrosis. Arthritis Rheum 46:1703-1713, 2002.

A good review highlighting TGF- signaling and the fundamental role of the Smad family of transcription factor proteins.

4. [Ghosh AK](#). Factors involved in the regulation of type I collagen gene expression: implication in fibrosis. Exp Biol Med 227(5):301-314, 2002.

This very thorough review describes the different transcription factors involved in the regulation of type I collagen gene expression.

5. [DeMarco PJ](#), [Weisman MH](#), [Seibold JR](#), [Furst DA](#), [Wong WK et al](#). Predictors and outcomes of scleroderma renal crisis: The high-dose versus low-dose D-penicillamine in early diffuse systemic sclerosis trial. Arthritis Rheum 46(11): 2983-2989, 2002.

A spin-off from a previous study in patients with diffuse systemic sclerosis reconfirming the poor survival related with scleroderma renal crisis even with the increased use of ACE inhibitors and dialysis in these patients. Of note is that low dose prednisone was not associated with an increased incidence of scleroderma renal crisis.

6. [Artlett CM](#), [Smith JB](#), [Jimenez SA](#). Identification of fetal DNA and cells in skin lesions from women with systemic sclerosis. N Engl J Med 338: 1186-1191, 1998.

One of several reports supporting the hypothesis that fetal anti-maternal graft-versus-host reaction may be involved in the pathogenesis of systemic sclerosis in some women, though this may just be an epiphenomenon related to a fundamental defect in immune surveillance.

7. [Rubin LJ, Badesch DB, Barst RJ, et al.](#) Bosentan therapy for pulmonary arterial hypertension. *N Engl J Med* 346: 896-903, 2002.

Randomized placebo controlled intervention in patients with pulmonary arterial hypertension, demonstrating that bosentan, an endothelin-1 receptor, prevented clinical deterioration of the 6 minute walk, significantly improved symptoms, and reduced the risk of clinical worsening at 24 weeks.

8. [Dong C, Zhu S, Wang T et al.](#) Deficient Smad 7 expression: a putative molecular defect in scleroderma. *Proc Natl Acad Sci USA* 99: 3908-3913, 2002.

A marked Smad 7 deficiency and Smad 3 upregulation is suggested by this study to be responsible for TGF- hyperresponsiveness observed in systemic sclerosis.

9. [Lunardi C, Bason C, Navone R, et al.](#) Systemic sclerosis immunoglobulin G autoantibodies bind the human cytomegalovirus late protein UL94 and induce apoptosis in human endothelial cells. *Nat Med* 6: 1183-1186, 2000.

Direct evidence linking CMV and systemic sclerosis through molecular mimicry and endothelial cell apoptosis.

10. [Athreya BH.](#) Juvenile scleroderma. *Curr Opin Rheumatol* 14: 553-561, 2002.

Concise review of this relatively rare disorder in children.

11. [Jimenez SA, Derk CT.](#) Pathogenesis of systemic sclerosis: formulation of testable hypothesis. *Ann Intern Med* 2003, in press. CANNOT FIND!

A review of the different hypothesis behind the pathogenesis of systemic sclerosis.

12. [Rose S, Young MA, Reynolds JC.](#) Gastrointestinal manifestations of scleroderma. *Gastroenterol Clin North Am* 27: 563-94, 1998.

13. [Cheema GS, Quismorio FP Jr.](#) Interstitial lung disease in systemic sclerosis. *Curr Opin Pulm Med* 7:283-90, 2001.

14. [Coghlan JG](#), [Mukerjee D](#). The heart and pulmonary vasculature in scleroderma: clinical features and pathobiology. *Curr Opin Rheumatol* 13: 495-9, 2001.
15. [Steen VD](#). Scleroderma renal crisis. *Rheum Dis Clin North Am* 22: 861-78, 1996.
16. [Gordon MB](#), [Klein I](#), [Dekker A](#), [Rodnan GP](#), [Medsger TA Jr](#). Thyroid disease in progressive systemic sclerosis: increased frequency of glandular fibrosis and hypothyroidism. *Ann Intern Med* 95: 431-5, 1981.
17. [Lally EV](#), [Jimenez SA](#). Impotence in progressive systemic sclerosis. *Ann Intern Med* 95: 150-3, 1981.
18. [Nietert PJ](#), [Silver RM](#). Systemic sclerosis: environmental and occupational risk factors. *Curr Opin Rheumatol* 12:520-526, 2000.

A concise review of the environmental agents possibly involved in the pathogenesis of systemic sclerosis.

19. [Clark DA](#), [Coker R](#). Transforming growth factor- beta (TGF- β). *Int J Biochem Cell Biol* 30: 293-298, 1998.

The mechanisms involved in the synthesis and activation of TGF- β .

20. [Ihn H](#), [Yamane K](#), [Kubo M](#), et al. Blockade of endogenous transforming growth factor β signaling prevents up-regulated collagen synthesis in scleroderma fibroblasts: association with increased expression of transforming growth factor β receptors. *Arthritis Rheum* 44:474-480, 2001.

Promising therapeutic option using monoclonal antibodies or an antisense oligonucleotide blocking TGF β 1 function and reducing excess collagen production by SSc fibroblasts to normal levels.

21. [Shi-Wen X](#), [Denton CP](#), [Dashwood MR](#), et al. Fibroblast matrix gene expression and connective tissue remodeling: role of endothelin-1. *J Invest Dermatol* 116: 417-425, 2001.

In normal fibroblasts, endothelin-1 (a potent vasoconstrictor seen in elevated levels in the circulation of SSc patients) raises matrix gene expression and can induce a fibrogenic process similar to SSc. Potential use of endothelin-1 inhibitors as antifibrotics for SSc.

22. [Clements PJ](#), [Wong WK](#), [Hurwitz EL](#), et al. The disability index of the health assessment questionnaire is a predictor and correlate of outcome in the high-

dose versus low-dose penicillamine in systemic sclerosis trial. *Arthritis Rheum* 44:653-661, 2001.

Part of prior negative therapeutic trial, it shows that the relative risk of dying in 4 years is greater than 3 if the HAQ score is 1 or more. May be used as a prognostic tool in the day to day evaluation of scleroderma patients.

23. [Fritzler MJ](#). Autoantibodies in scleroderma. *J Dermatol* 20(5): 257-268, 1993.

A detailed review of the autoantibodies seen in systemic sclerosis and their diagnostic and prognostic utility.

24. [Ferri C](#), [Valentini G](#), [Cozzi F](#), et al. Systemic sclerosis: Demographic, clinical and serologic features and survival in 1,012 Italian patients. *Medicine* 81: 139-153, 2002.

25. [MacGregor AJ](#), [Canavan R](#), [Knight C](#) et al. Pulmonary hypertension in systemic sclerosis: risk factors for progression and consequences for survival. *Rheumatol* 40(4): 453-459, 2001.

An increased mortality is seen in those patients with high initial pressures on echocardiography. Value of echocardiography as a screening tool for pulmonary hypertension in all systemic sclerosis patients.

26. [Arnett FC](#), [Cho M](#), [Chatterjee S](#), et al. Familial occurrence frequencies and relative risks for systemic sclerosis (scleroderma) in three United States cohorts. *Arthritis Rheum* 44(6): 1359-1362, 2001.

A positive family history is the strongest risk factor to develop systemic sclerosis.

27. [Steen VD](#), [Medsger TA Jr](#). Severe organ involvement in systemic sclerosis with diffuse scleroderma. *Arthritis Rheum* 43(11): 2437-2444, 2000.

Severe organ involvement in patients with diffuse scleroderma occurs early in the course of the disease and close monitoring is suggested for the first three years of the disease.

28. [Johnson RW](#), [Tew MB](#), [Arnett FC](#). The genetics of systemic sclerosis. *Curr Rheumatol Rep* 4(2): 99-107, 2002.

Up-to-date review of the genetics involved in the pathogenesis of systemic sclerosis.

29. [Pope JE](#). Scleroderma overlap syndromes. *Curr Opin Rheumatol* 14: 704-710, 2002.

30. Subcommittee for scleroderma criteria of the American Rheumatism Association diagnostic and therapeutic criteria committee: Preliminary criteria for the classification of systemic sclerosis (scleroderma). *Arthritis Rheum* 23: 581-590, 1980.

American College of Rheumatology criteria for the classification of systemic sclerosis.