eMedicine Specialties > Dermatology > Connective Tissue Diseases

Systemic Sclerosis

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Updated: May 5, 2009

Introduction

Background

Systemic sclerosis (SSc) is a systemic connective tissue disease. Characteristics of systemic sclerosis include essential vasomotor disturbances; fibrosis; subsequent atrophy of the skin, subcutaneous tissue, muscles, and internal organs (eg, alimentary tract, lungs, heart, kidney, CNS); and immunologic disturbances accompany these findings.

Also see Systemic Sclerosis for a pediatric focus.

Pathophysiology

Excessive collagen deposition causes skin and internal organ changes. Many factors, including environmental factors, can lead to immunologic system disturbances and vascular changes. Endothelial alterations may lead to a cascade of stimulatory changes that involve many cells, including fibroblasts, T lymphocytes, macrophages, and mast cells. In turn, the activated cells secrete a variety of substances, including cytokines and their soluble receptors and enzymes and their inhibitors. These substances lead to changes in the extracellular matrix compounds, including fibronectin; proteoglycans; and collagen types I, III, V, and VII. Increased collagen deposition in tissues is a characteristic feature of systemic sclerosis. Increased collagen production or disturbances in its degradation can cause excessive collagen deposition in tissues.

Fibrosis can be caused by profibrotic cytokines, including transforming growth factor-beta (TGF-beta), interleukin-4 (IL-4), platelet-derived growth factor (PDGF), and connective-tissue growth factor.[1] The vasculopathy may be linked to TGF-beta and PDGF, while the diminution of lesional cutaneous blood vessels can be attributed to antiendothelial cell autoantibodies. The activation of the immune system is of paramount importance in the pathogenesis of systemic sclerosis. Antigen-activated T cells, activated infiltrate early, infiltrate the skin, and produce the profibrotic cytokine IL-4. B cells may contribute to fibrosis, as deficiency of CD19, a B-cell transduction molecule, results in decreased fibrosis in animal models.

Different factors, including genetic, environmental, vascular, autoimmunologic, and microchimeric factors are involved in systemic sclerosis pathogenesis. One theory states that antigens from the human leukocyte antigen (HLA) histocompatability complex, including HLA-B8, HLA-DR5, HLA-DR3, HLA-DR52, and HLA-DQB2, are involved in systemic sclerosis. Some data suggest that apoptosis and the generation of free radicals may be involved in the pathogenesis of systemic sclerosis.

In systemic sclerosis, affected organs and systems include the skin, lungs, heart, digestive system, kidneys, muscles, joints, and nervous system.

Frequency

United States

Systemic sclerosis is a rare disease. Systemic sclerosis is diagnosed in approximately 67 male patients and 265 female patients per 100,000 people each year.

International

Systemic sclerosis is estimated to occur in 2.3-10 people per 1 million. Systemic sclerosis is rare in the resident population of Japan and China.

Mortality/Morbidity

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International

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Mortality/Morbidity

The mortality rate is increasing in the United States and Europe; as many as 3.08 persons are affected per 1 million.

- Generally, renal and lung changes are responsible for death in patients with systemic sclerosis.
- Pulmonary hypertension leads to 12% of systemic sclerosis–related deaths.
- Lung fibrosis and heart changes are responsible for 9% of systemic sclerosis – related deaths.

Race

No apparent racial predominance exists. However, systemic sclerosis is rare in the resident population of Japan and China. Diffuse systemic sclerosis (dSSc) occurs more often in black women than in white women.

Sex

Overall, a substantial female predominance exists, with a female-to-male ratio of 3-6:1. However, dSSc occurs equally in males and females. The limited form of systemic sclerosis (lSSc) has a strong female predominance, with a female-to-male ratio of 10:1.

Age

Systemic sclerosis usually appears in women aged 30-40 years, and it occurs in slightly older men. In approximately 85% of cases, systemic sclerosis develops in individuals aged 20-60 years. Cases also are observed in children and in the elderly population.

Clinical

History

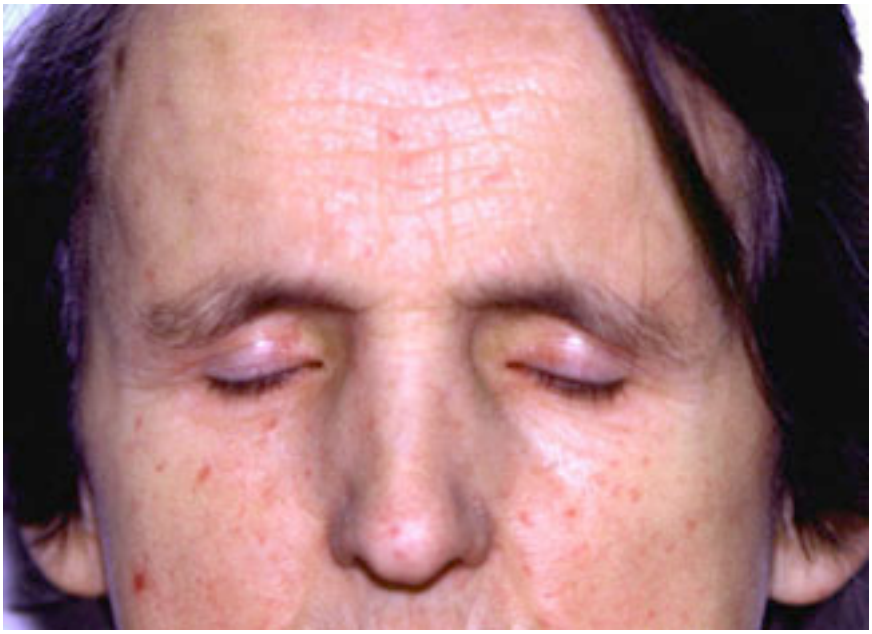
Systemic sclerosis can have many different presentations. It involves the skin and many internal organs. Therefore, the presenting symptoms may differ among patients.

- Cutaneous pruritus is common.
- Raynaud phenomenon, or whitening of the hands on exposure to cold, is a common finding. Pain in the affected digits, blanching, cyanosis, and hyperemia can follow.
- Difficulty in swallowing solid foods can be followed by difficulty with swallowing liquids and subsequent nausea, vomiting, weight loss, abdominal cramps, blotting diarrhea, and fecal incontinence.
- The patient can have shortness of breath on exertion and, subsequently, at rest.
- Palpitations may occur without characteristic pain in thoracic cavity.
- The patient may have a nonproductive cough.
- Atypical chest pain, fatigue, dyspnea, and hypertension may be present.
- Joint pain, limitation of movement, joint swelling, and muscle pain may be present. Systemic sclerosis begins as joint pain in 15% of patients. It begins as inflammatory myopathy in 10% of patients.
- Weakness is present in 80% of patients.
- Medical signs and symptoms associated with disability, pain, and psychosocial adjustment in systemic sclerosis were assessed.[2] In one study, 114 patients underwent examination, including a determination of skin thickening. Signs and symptoms were a significant correlate of all outcomes. Patient-reported dependent edema significantly correlated with all outcomes. For disability, significant correlates were (1) physician-determined joint tenderness and number of tender points and (2) patient-reported joint pain with motion, joint contracture, extremity ulcers other than digital, and dyspnea.

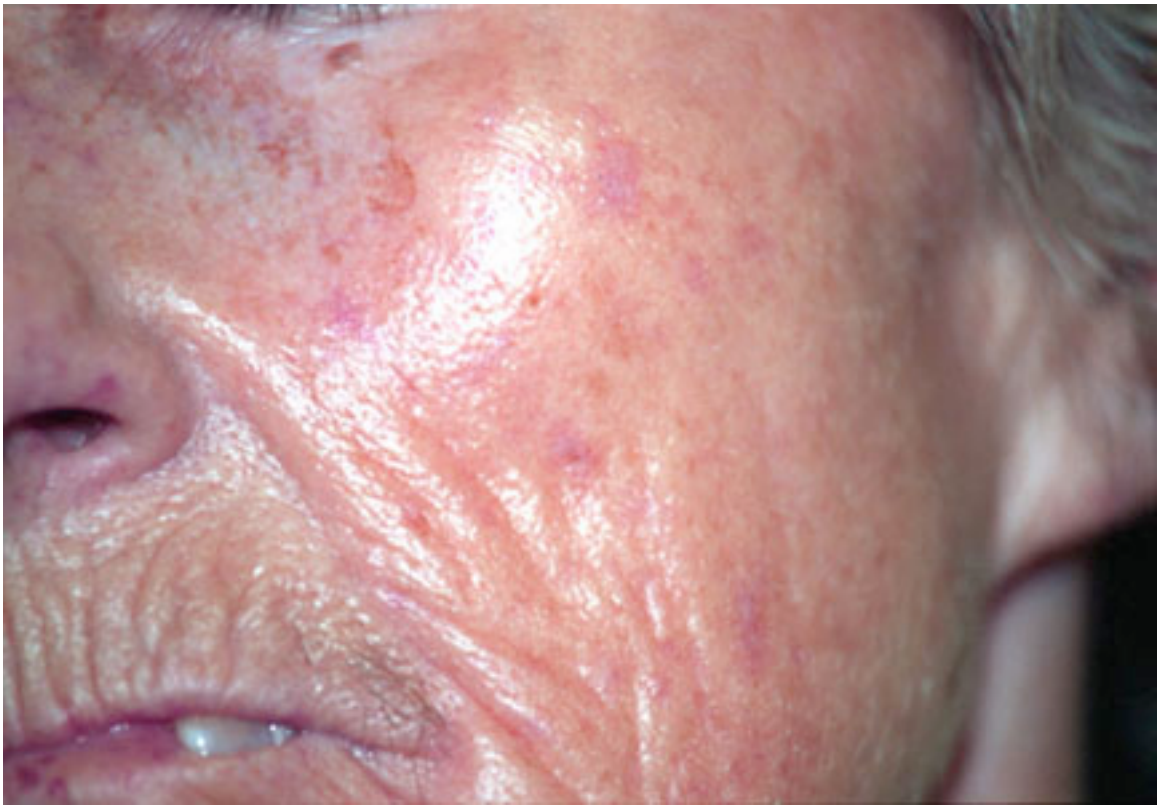
Physical

- According to the American College of Rheumatology (ACR), features characteristic for scleroderma are divided into 2 groups:
    - Major features include centrally located skin sclerosis that affects the arms, face, and/or neck.
    - Minor features include sclerodactyly, erosions, atrophia of the fingertips, and bilateral lung fibrosis.

- Systemic sclerosis is diagnosed when a patient has 1 major and 2 minor criteria.

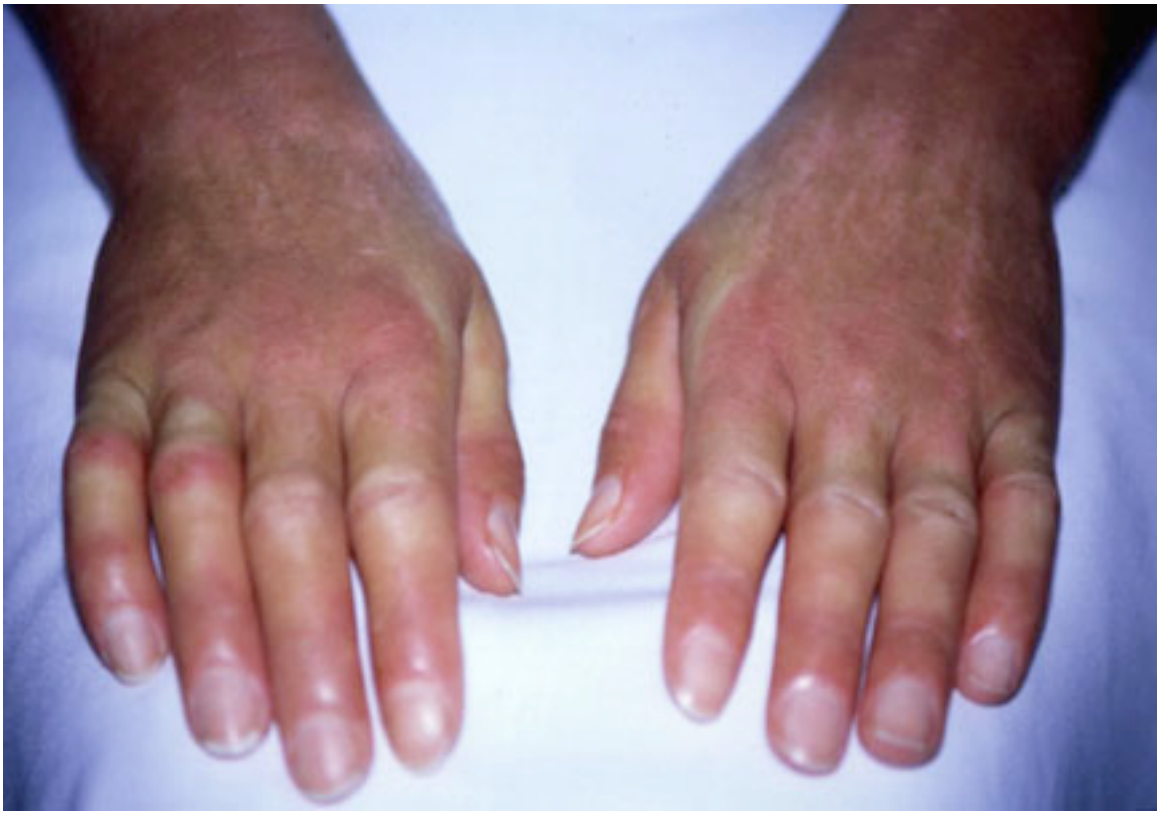


Face of 65-year old woman with systemic sclerosis and skin thickening of 20 years' duration: Note the pinched nose, taut skin with numerous telangiectasias, and retraction of the lips.



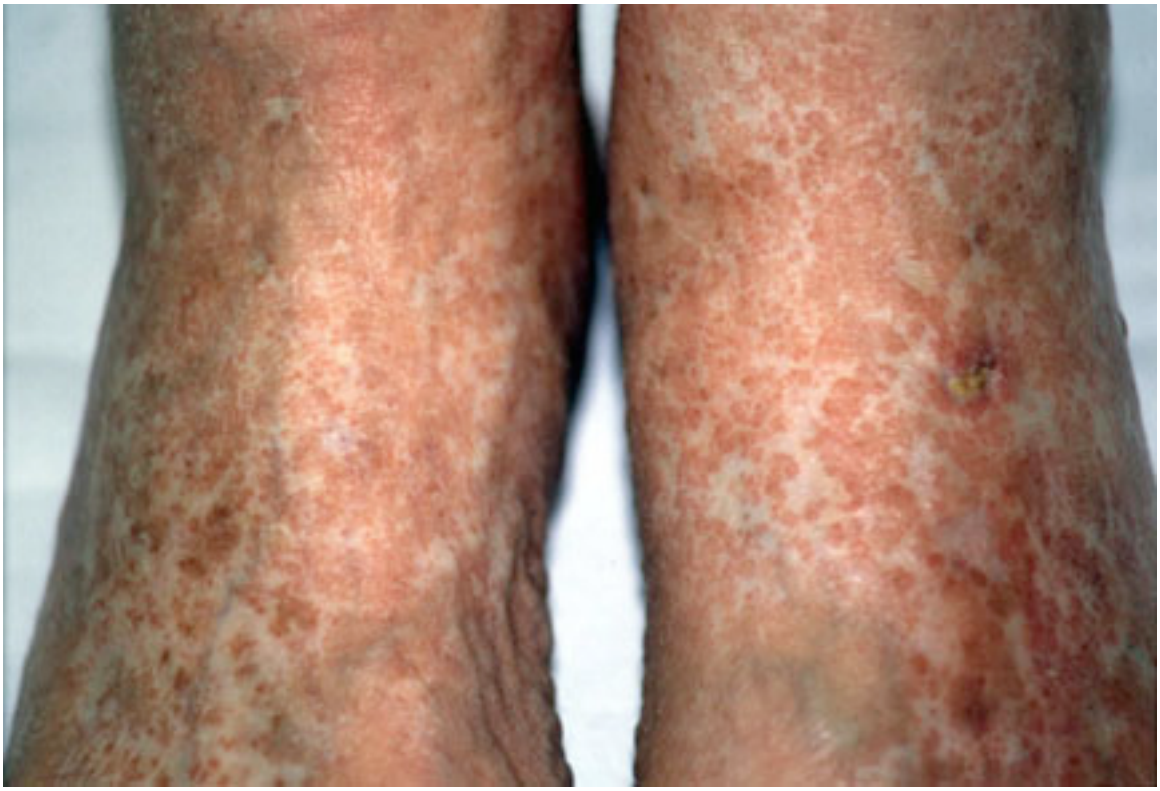
Telangiectasias affecting the face: They are pronounced and numerous, especially in the atrophic phase of the disease. Radical furrowing around the mouth is also characteristic in the later stage of the disease.

- Cutaneous involvement has 3 phases: (1) edematous, (2) indurative, and (3) atrophic. Skin becomes thickened and tight.



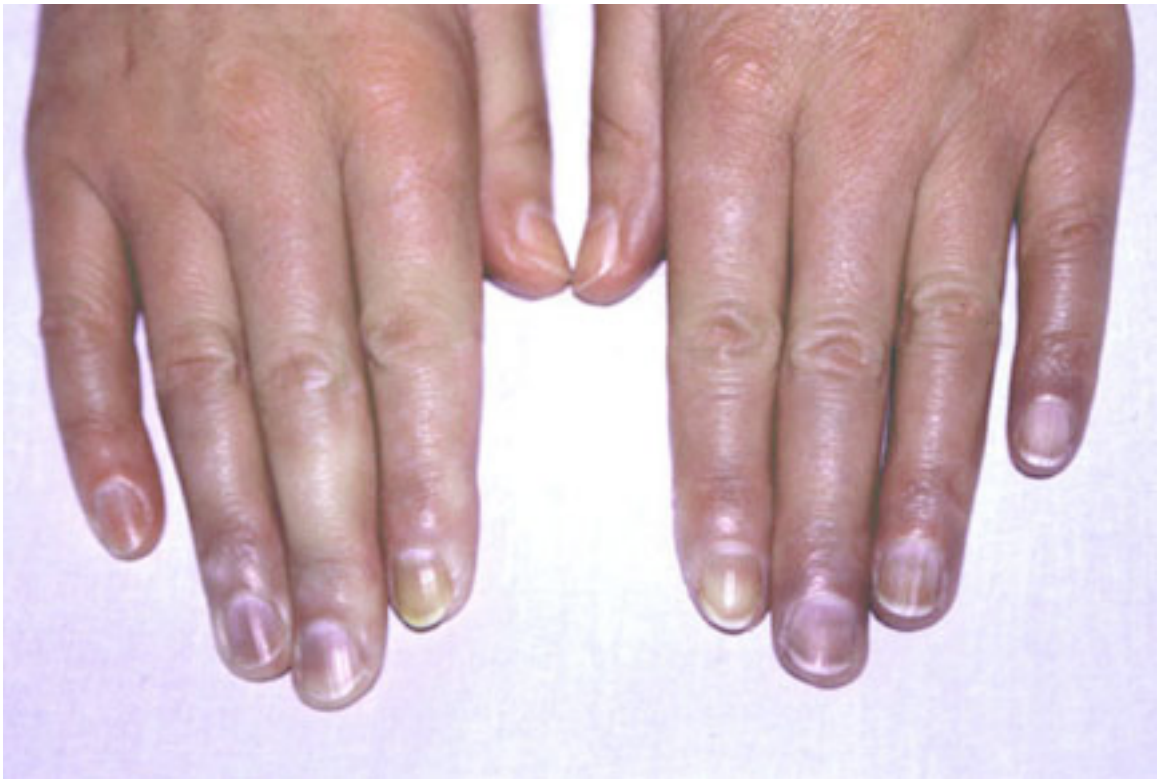
Puffy appearance of the woman's hand in the edematous phase of early scleroderma.

- Systemic sclerosis is divided into 5 forms: (1) dSSc, (2) lSSc, (3) transitory form (dSSc/lSSc), (4) systemic scleroderma sine scleroderma, and (5) malignant scleroderma. The principal forms are dSSc and lSSc.
- In addition to the following features, dSSc is characterized by Raynaud phenomenon that precedes the development of skin changes by approximately 1 year:
    - Generalized skin fibrosis of the chest and limbs
    - Areas of skin hyperpigmentation and hypopigmentation



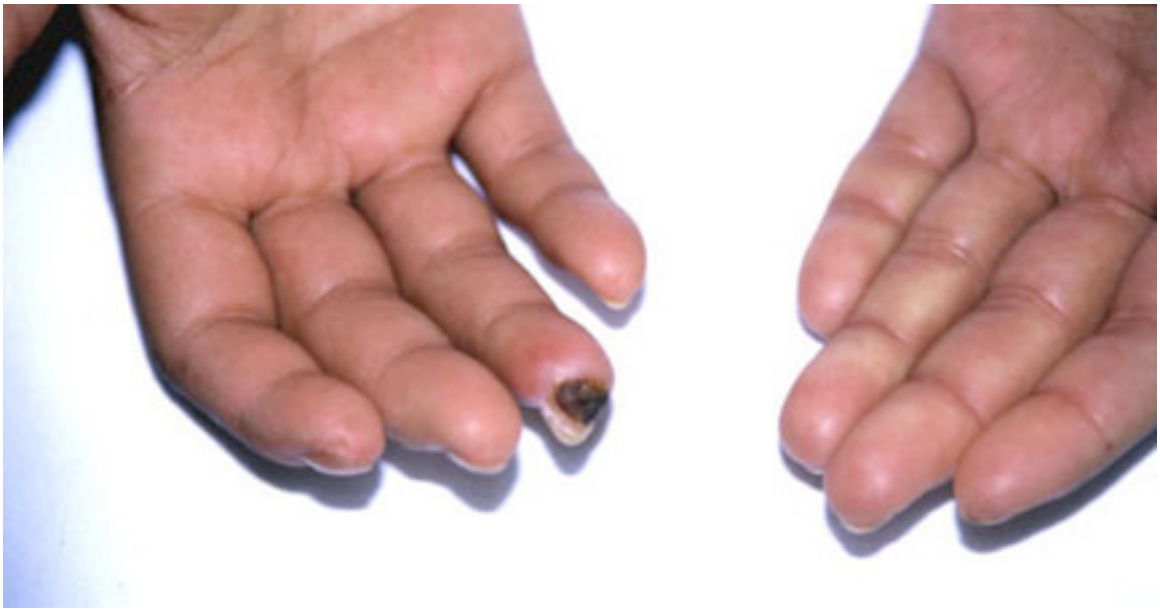
In systemic sclerosis, skin hyperpigmentation of the lower legs is surrounded by areas of hypopigmentation. The result is a salt-and-pepper appearance.

- Tendon friction rubs
- Early involvement of the lungs, kidneys, digestive system, and heart
- Antibodies against topoisomerase I DNA (Scl 70) in approximately 30% of patients[3,4]
- Nail-fold capillary dilatation and capillary destruction

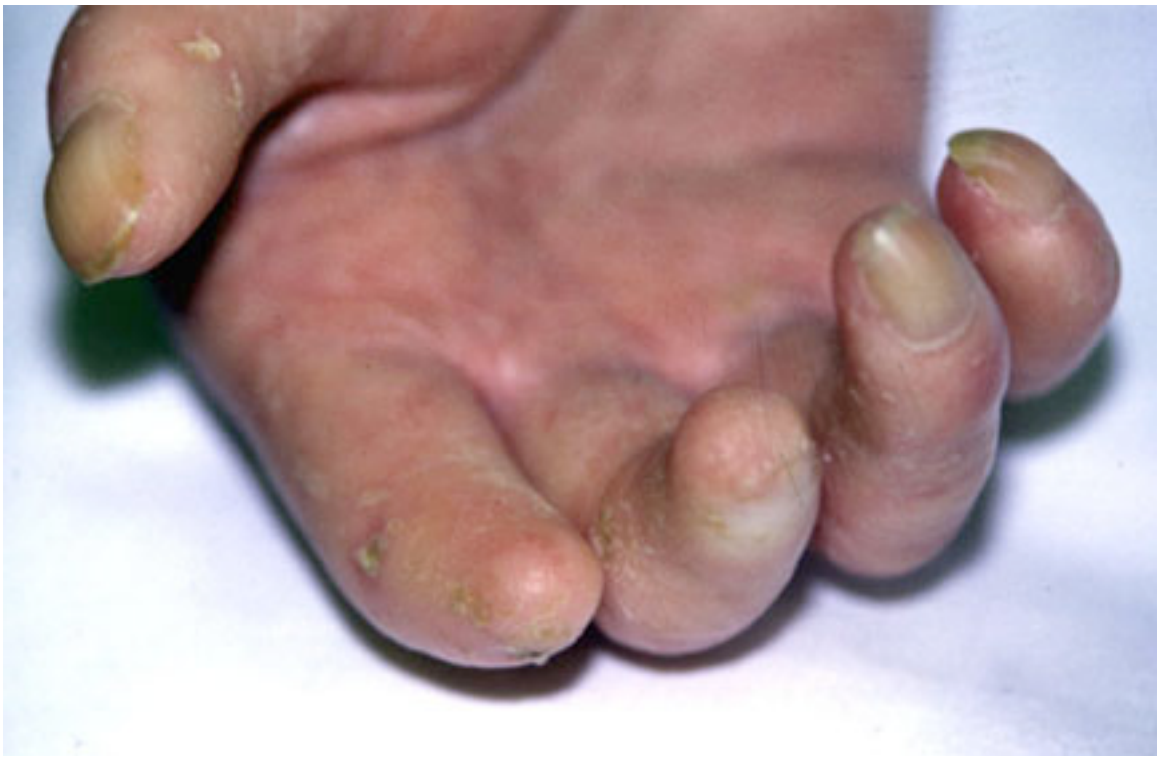


Raynaud phenomenon of the hands: Symmetrical acral vasospasm is present, with characteristic pallor, cyanosis, suffusion, and a sense of fullness and tautness.

- lSSc is characterized by sclerotic changes of the hands, face, feet, and forearms in addition to the following features:
    - Atrophic changes of the ala nasi and lips, facial amimia
    - Telangiectasia of the skin
    - Late involvement of the lungs and late development of pulmonary hypertension
    - Anticentromere antibodies in approximately 70-80% of patients
    - Dilated capillary loops in nail folds
    - Cutaneous calcification



In systemic sclerosis, ulceration at the tip of the finger is regarded to be secondary to ischemia.



Hand of a woman with scleroderma of several years' duration: The thickened, tight, thin skin over the fingers is the result of self-

amputation of the distal phalanx due to ischemia. Moderately severe flexion contractures of the fingers are present.

- dSSc and/or lSSc are described in a few cases in which internal organ changes preceded or simultaneously occurred with cutaneous changes.
- Systemic scleroderma sine scleroderma is difficult to diagnose because only internal organs are involved. Systemic scleroderma sine scleroderma usually is diagnosed after the patient's death.
- Malignant scleroderma most often occurs in men, usually in elderly men. An accelerated course of malignant scleroderma leads to death.

Causes

Systemic sclerosis is an autoimmunologic disease, but the pathogenesis is only partially understood. Certain factors are well known to trigger occurrence of the disease or create a similar clinical appearance. Environmental factors include exposure to the following:

- Vibration injury (similar vascular changes)
- Silica
- Organic solvents (eg, toluene, benzene, xylene)
- Aliphatic hydrocarbons (eg, hexane, vinyl chloride, trichloroethylene)
- Epoxy resin
- Amino acid compound L-5-hydroxytryptophan
- Pesticides
- Drugs (eg, bleomycin, carbidopa, pentazocine, cocaine, penicillamine, vitamin K): A limited form of cutaneous systemic sclerosis has been described with paclitaxel in with the setting of breast cancer.[5]
- Appetite suppressants (eg, phenylethylamine derivatives)
- Substances used in cosmetic procedures (eg, silicone or paraffin implants)

Differential Diagnoses

CREST Syndrome
Eosinophilia-Myalgia Syndrome
Eosinophilic Fasciitis
Graft Versus Host Disease
Lichen Myxedematosus
Lichen Sclerosus et Atrophicus
Scleredema

Other Problems to Be Considered

- Spider angiomas in person with alcoholism
- Hereditary hemorrhagic telangiectasia
- Taxane-induced scleroderma: Scleroderma due to taxanes may mimic systemic sclerosis. Taxane chemotherapy for metastatic breast cancer may show marked edema first, followed by skin sclerosis occurring mainly at the distal ends of the extremities 6-12 months after the administration of taxane, in all patients. Although skin biopsy samples may show (1) full-layer dermal fibrosis with thickened collagen bundles and (2) perivascular monocytic cell infiltration, resembling systemic sclerosis in clinical course and histological findings, Raynaud phenomenon, pulmonary fibrosis, and immunological abnormalities associated with systemic sclerosis may not be detected.[6]

Workup

Laboratory Studies

- Increased erythrocyte sedimentation rate
- Thrombocytopenia
- Hypergammaglobulinemia
- Microangiopathic hemolytic anemia
- Increased creatine phosphokinase levels in patients with muscle involvement
- Increased urea and creatinine levels in patients with kidney involvement

Imaging Studies

- Chest radiographs may show normal findings in 5-10% of the patients, even when the patients have respiratory tract symptoms.
    - In approximately 30-60% of patients, fibrosis of the basal parts of the lungs is observed.
    - Occasionally, pictures of diffuse ground-glass and honeycomb lung patterns are observed. In patients with honeycomb lung patterns, changes are irreversible. These changes can be an important feature of patient's response to treatment.
- Bone radiography reveals generalized osteopenia, which most commonly affects the hands. Intra-articular calcifications often are observed.
- High-resolution computed tomography (HRCT) and scintigraphy reveal thickening of the alveolar walls and intestinal tissue and honeycomb-appearing lungs.
- Gastrointestinal tract changes may be depicted.
    - Scintigraphy of the esophagus may reveal a disturbance of the esophageal passage.[7]
    - Manometric esophageal changes may be observed during invasive examination.
- Cardiac and pulmonary vascular involvement in systemic sclerosis should be evaluated. Cardiac abnormalities may be assessed by Doppler echocardiography.[8] Left- and right-sided heart diseases were found to be common in persons with systemic sclerosis. A few patients had a restrictive mitral flow pattern, possibly due to primary cardiac involvement of systemic sclerosis.
- Because cardiac involvement is one of the major problems in systemic sclerosis, evaluation of ventricular function using echocardiographic strain imaging should be considered, because it appears to be useful to detect subclinical cardiac involvement in systemic sclerosis patients with normal standard echocardiographic and tissue Doppler velocity findings.[9]

Other Tests

- With bronchoalveolar lavage (BAL), abnormal numbers of granulocytes, particularly neutrophils and eosinophils are present.
- Lung function tests reveal ventilation-perfusion changes, including the following:
    - Reduced carbon monoxide diffusion capacity
    - A reduced partial pressure of oxygen, with a normal or low partial pressure of carbon dioxide
    - Restrictive ventilatory defect, with reductions in pulmonary compliance, vital capacity, and total lung capacity
    - Decreased diffusion capacity of carbon monoxide transfer factor (DLCO) levels, which is a measure of diffusion capacity
- The gas transfer measurement (KCO), adjusted for alveolar volume, is also reduced.
- Heart changes, including myocardial disease, pericardial problems, conduction system disease, and arrhythmias, can be observed with the following tests:
    - Electrocardiography (ECG)
    - Holter 24-hour monitoring
    - Doppler ultrasonography (US)
- Exophthalmos, macroglossia, and/or gigantism may be present, with increased polyphasic potentials of normal or decreased amplitude.
- Antihistone antibodies can be observed in the course of systemic sclerosis, but they are not characteristic. The following antinuclear antibodies (ANAs) are characteristic of scleroderma:
    - Antibodies against topoisomerase I DNA (Scl 70) are detected in the serum of patients with systemic sclerosis. The antibodies are detected in two thirds of patients with dSSc and interstitial lung fibrosis.
    - Anticentromere antibodies (ACAs) are most commonly detected in patients with lSSc; in these patients, changes in the heart, kidneys, and lungs (without fibrosis) are observed less frequently than in other patients.

- ANAs can be detected in the course of systemic sclerosis. ANAs include antibodies against fibrillarin, a 34-kd protein of ribonucleoprotein U3 RNP; antibodies against the ribonucleoprotein nucleolar 7-2 RNA protein particle Th RNP; and antibodies to 20-110-kd proteins related to preribosomes (PM-Scl). Anti-PM/Scl antibodies are seen in roughly 24% of patients with polymyositis/systemic sclerosis overlap syndrome. They are also found in 3-10% of systemic sclerosis patients.[10,11]
- Elevated high-sensitivity C-reactive protein appears related to the occurrence of antimitochondria antibody in these patients.[12]
- With capillary microscopy, enlarged capillaries are observed in all 3 portions of the capillary nail fold–arterial, apical, and venous–and especially at the edge of the nail fold. Adjacent areas are avascular.
- Spirometry demonstrates functional lung disturbances. In approximately 70% of patients, the DLCO is decreased.

Histologic Findings

In the active indurative phase, a loss of rete ridges occurs, epidermal skin appendages atrophy, and collagen fibers in the reticular dermis appear broad and hyalinized. A loss of space between collagen bundles is noted. Mononuclear cells, mostly T cells, form a variable perivascular infiltrate in the deep dermis and subcutis. Later, sclerotic changes predominate. The number of adnexal structures is reduced, and a loss of periadnexal fat is noted.

Treatment

Medical Care

Different treatment regimens for systemic sclerosis exist. The therapeutic approach depends on the presentation of the disease and complexity of symptoms.

- In pruritus, the following agents are sometimes helpful:
    - Camphor and menthol
    - Topical emollients
    - Psoralen UV-A (PUVA) treatment
    - UVA-1 phototherapy
- In patients with calcinosis, surgery may be of some benefit, but healing time is often prolonged.
- When Raynaud phenomenon is present, the most effective nonpharmacologic method of preventing Raynaud episodes is avoiding exposure to cold temperature and wearing layers of warm, loose-fitting clothing, including socks and gloves. Also, smoking cessation is advised. In the pharmacologic regimen, consider the use of agents such as calcium-channel blockers, vasodilating drugs, intravenous prostaglandins, prostacyclin analogs, or aspirin.[13]
- In patients with kidney involvement, ACE inhibitor therapy is indicated.
- In patients with GI tract involvement, proton pump inhibitors (eg, omeprazole) and H2 blockers can help to control reflux symptoms.
- In patients with lung involvement, calcium-channel blockers (eg, nifedipine), prostaglandins (eg, prostacyclin), and cyclophosphamide have been used with variable success. When inflammatory myositis is present, the use of high doses of corticosteroids (eg, prednisolone with a starting dose of 1 mg/kg/d) is suggested.
- The following antifibrotic agents have been investigated, although results have varied and none is clearly shown to be of consistent benefit:
    - D-penicillamine
    - Interferon alfa and interferon gamma
    - Immunomodulatory agents
        - Photopheresis[14]
        - Corticosteroids (in inflammatory myositis, pericarditis, refractory arthritis, or alveolitis)
        - Methotrexate (15 mg/wk)[15]
        - Chlorambucil
        - Cyclosporine[16]
        - FK506 (tacrolimus)
        - Thalidomide

        - Low-dose intravenous cyclophosphamide[17,18]
        - Statins[19,20]
        - Immunosuppressive drugs with autologous peripheral hematopoietic stem cell transplantation[21]
- With its antifibrotic properties, imatinib mesylate may be a potential therapy.[22,23]

Consultations

The symptoms of systemic sclerosis are diverse; therefore, consider consultations with the following specialists, if applicable:

- Dermatologist
- Pulmonologist
- Nephrologist
- Radiologist
- Cardiologist
- Orthopedic surgeon

Medication

Treatment regimens have enormous diversity. Currently, no standard therapy is available for skin sclerosis. Raynaud phenomenon often responds to calcium channel blockers, and scleroderma kidney disease often responds to angiotensin-converting enzyme and angiotensin II inhibitors. The treatment depends on the presentation of systemic sclerosis.

Immunomodulatory agents

These agents are used to stop disease progression. They act on the host's immune system; they suppress the immune system to prevent fibrosis.

Prednisone (Deltasone, Meticorten, Orasone, Sterapred)

Immunosuppressant used for the treatment of autoimmune disorders; may decrease inflammation by reversing increased capillary permeability and suppressing PMN activity. Stabilizes lysosomal membranes. Suppresses lymphocytes and antibody production.

Dosing

Adult

5-60 mg/d PO qd or divided bid/qid; taper over 2 wk as symptoms resolve

Pediatric

4-5 mg/m^2/d PO or 0.05-2 mg/kg PO divided bid/qid; taper over 2 wk as symptoms resolve

Interactions

Coadministration with estrogens may decrease clearance; concurrent use with digoxin may cause digitalis toxicity secondary to hypokalemia; phenobarbital, phenytoin, and rifampin may increase metabolism of glucocorticoids (consider increasing maintenance dose); monitor for hypokalemia with coadministration of diuretics

Contraindications

Documented hypersensitivity; viral infection; peptic ulcer disease; hepatic dysfunction; connective tissue infections; fungal or tubercular skin infections; GI disease

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Abrupt discontinuation of glucocorticoids may cause adrenal crisis; hyperglycemia, edema, osteonecrosis, myopathy, peptic ulcer disease, hypokalemia, osteoporosis, euphoria, psychosis, myasthenia gravis, and growth suppression may occur

Methotrexate (Rheumatrex)

Antimetabolite that inhibits dihydrofolate reductase, thereby hindering DNA synthesis and cell reproduction. Satisfactory response is observed in 3-6 wk after administration. Adjust dose gradually to achieve satisfactory response.

Dosing

Adult

10-25 mg/wk PO/IM or 2.5-7.5 mg PO q12h with 3 doses/wk

Pediatric

Not established

Interactions

Oral aminoglycosides may decrease absorption and blood levels of concurrent oral MTX; charcoal lowers levels; coadministration with etretinate may increase hepatotoxicity; folic acid or its derivatives contained in some vitamins may decrease response; coadministration with NSAIDs may be fatal; indomethacin and phenylbutazone can increase plasma levels; may decrease phenytoin serum levels probenecid, salicylates, procarbazine, and sulfonamides (including TMP-SMZ) may increase effects and toxicity; may increase plasma levels of thiopurines

Contraindications

Documented hypersensitivity; alcoholism; hepatic insufficiency; documented immunodeficiency syndromes; preexisting blood dyscrasias (eg, bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anemia); renal insufficiency

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Monitor CBC counts monthly; monitor liver and renal function every 1-3 mo during therapy (more frequently during initial dosing, dose adjustments, or when elevated levels possible [eg, dehydration]); has toxic hematologic, renal, GI, pulmonary, and neurologic effects; discontinue if blood counts significantly decrease; aspirin, NSAIDs, or low-dose steroids can be administered concomitantly (increased toxicity with NSAIDs, including salicylates, has not been tested)

Chlorambucil (Leukeran, Leukeran)

Alkylates and cross-links strands of DNA, inhibiting DNA replication and RNA transcription.

Dosing

Adult

0.1-0.2 mg/kg/d PO or 3-6 mg/m^2/d PO for 3-6 wk; adjust dose depending on blood counts

Pediatric

Administer as in adults

Interactions

None reported

Contraindications

Documented hypersensitivity; previous resistance to medication

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Caution in history of seizure disorders and in bone marrow suppression

Cyclosporine (Neoral, Sandimmune)

Helpful in a variety of skin disorders.

Dosing

Adult

2.5-5 mg/kg/d PO in divided doses

Pediatric

Administer as in adults

Interactions

Carbamazepine, phenytoin, isoniazid, rifampin, and phenobarbital may decrease concentrations; azithromycin, itraconazole, nicardipine, ketoconazole, fluconazole, erythromycin, verapamil, grapefruit juice, diltiazem, aminoglycosides, acyclovir, amphotericin B, and clarithromycin may increase toxicity; risk of acute renal failure, rhabdomyolysis, myositis, and myalgias increases with concurrent lovastatin

Contraindications

Documented hypersensitivity; uncontrolled hypertension or malignancies; do not administer concomitantly with PUVA or UV-B radiation in psoriasis (may increase risk of cancer)

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Evaluate renal and liver functions (measure BUN, serum creatinine, serum bilirubin, and liver enzyme levels); may increase risk of infection and lymphoma

Tacrolimus (Prograf)

Suppresses humoral (T-lymphocyte) immunity.

Dosing

Adult

0.05 mg/kg/d IV or 0.15-0.3 mg/kg/d PO divided bid

Pediatric

0.1 mg/kg/d IV or 0.3 mg/kg/d PO

Interactions

Diltiazem, nicardipine, clotrimazole, verapamil, erythromycin, ketoconazole, itraconazole, fluconazole, bromocriptine, grapefruit juice, metoclopramide, methylprednisolone, danazol, cyclosporine, cimetidine, and clarithromycin may increase levels; rifabutin, rifampin, phenobarbital, phenytoin, and carbamazepine may reduce levels

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Do not administer simultaneously with cyclosporine (tonic-clonic seizures may occur)

Cyclophosphamide (Neosar, Cytoxan)

Chemically related to nitrogen mustards.
As an alkylating agent, the mechanism of action of the active metabolites may involve DNA cross-linking, which may interfere with growth of healthy and neoplastic cells.

Dosing

Adult

Nonmalignant disease: 2.5-3 mg/kg/d PO qid
Lupus: 500-750 mg/m^2 IV every mo

Pediatric

Administer as in adults

Interactions

Allopurinol may increase risk of bleeding or infection and enhance myelosuppressive effects; may potentiate doxorubicin-induced cardiotoxicity; may reduce digoxin serum levels and antimicrobial effects of quinolones; chloramphenicol may increase half-life while decreasing metabolite concentrations; may increase effect of anticoagulants; coadministration with high doses of phenobarbital may increase rate of metabolism and leukopenic activity; thiazide diuretics may prolong cyclophosphamide-induced leukopenia and neuromuscular blockade by inhibiting cholinesterase activity

Contraindications

Documented hypersensitivity; severely depressed bone marrow function

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Regularly examine hematologic profile (particularly neutrophil and platelet counts) to monitor for hematopoietic suppression; regularly examine urine for RBCs, which may precede hemorrhagic cystitis

Antifibrotic agents

These agents are used to decrease fibrosis by interference with collagen metabolism.

Penicillamine (Cuprimine, Cuprimine, Depen)

Metal chelation agent used to treat arsenic poisoning. Forms soluble complexes with metals excreted in urine.

Dosing

Adult

100 mg/kg PO qd; not to exceed 2 g/d divided qid for 5 d

Pediatric

Administer as in adults

Interactions

Increases effects of immunosuppressants, phenylbutazone, and antimalarials; decreases digoxin effects; coadministration of zinc salts, antacids, and iron may decrease effects

Contraindications

Documented hypersensitivity; renal insufficiency; previous penicillamine-related aplastic anemia

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Thrombocytopenia; agranulocytosis; aplastic anemia

Colchicine

Decreases leukocyte motility and phagocytosis in inflammatory responses.

Dosing

Adult

0.6 mg/d PO

Pediatric

Not established

Interactions

Significantly increases sympathomimetic agent toxicity and effect of CNS depressants

Contraindications

Documented hypersensitivity; severe renal, hepatic, GI, or cardiac disorders; blood dyscrasias

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Renal failure; hepatic failure; permanent hair loss; bone marrow suppression; numbness or tingling in hands and feet; disseminated intravascular coagulopathy; decreased sperm count; dose-dependent GI upset common

Vasoactive agents

These agents are used to modify disease with its vasoactive actions.

Nifedipine (Adalat, Procardia)

Relaxes coronary smooth muscle and causes coronary vasodilation, which, in turn, improves myocardial oxygen delivery. Sublingual administration generally is safe, despite theoretic concerns.

Dosing

Adult

10-30 mg IR cap PO tid; not to exceed 120-180 mg/d; 30-60 mg SR tab PO qd; not to exceed 90-120 mg/d

Pediatric

0.25-0.5 mg/kg/dose PO tid/qid prn

Interactions

Caution with coadministration of any agent that can lower BP, including beta-blockers and opioids; H2 blockers (eg, cimetidine) may increase toxicity

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Lower extremity edema; allergic hepatitis rare

Antiplatelet agents

These agents inhibit the cyclo-oxygenase system, decreasing the level of thromboxane A_2, which is a potent platelet activator.

Aspirin (Bayer Buffered Aspirin, Bayer Aspirin, Anacin)

Inhibits prostaglandin synthesis, preventing the formation of platelet-aggregating thromboxane A_2. May be used in low doses to inhibit platelet aggregation and improve complications of venous stases and thrombosis.

Dosing

Adult

1-2 mg/kg/d PO for antiplatelet effect

Pediatric

Not established

Interactions

Antacids and urinary alkalinizers may decrease effects; corticosteroids decrease salicylate serum levels; additive hypoprothrombinemic effects and increased bleeding time may with coadministration of coagulants; may antagonize uricosuric effects of probenecid and increase toxicity of phenytoin and valproic acid; doses >2 g/d may potentiate glucose-lowering effect of sulfonylurea drugs

Contraindications

Documented hypersensitivity; liver damage; hypoprothrombinemia; vitamin K deficiency; bleeding disorders; asthma; do not use in children <16 y with flu (association with Reye syndrome)

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

May cause transient decrease in renal function and aggravate chronic kidney disease; avoid in severe anemia, history of blood coagulation defects, or anticoagulant use

Antihypertensive agents

These agents are used to reduce blood pressure.

Reserpine

Depletes norepinephrine and epinephrine. This effect, in turn, depresses sympathetic nerve functions, decreasing the heart rate and lowering the arterial blood pressure.

Dosing

Adult

Initial: 0.5 mg/d PO for 1-2 wk
Maintenance: 0.1-0.25 mg/d PO qd or divided bid

Pediatric

0.01-0.02 mg/kg divided q12h; not to exceed 0.25 mg/d

Interactions

Concurrent TCAs may decrease antihypertensive effects; cardiac arrhythmias may occur with concurrent digitalis or quinidine

Contraindications

Documented hypersensitivity; mental depression

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in renal impairment and peptic ulcer disease

Methyldopa (Aldomet)

Stimulates central alpha-adrenergic receptors, resulting in decreased sympathetic outflow. Results in inhibition of vasoconstriction.

Dosing

Adult

250 mg PO bid/tid; increase q2d prn; not to exceed 3 g/d

Pediatric

10 mg/kg/d PO divided bid/qid; increase q2d prn to maximum 65 mg/kg/d; not to exceed 3 g/d

Interactions

Concurrent barbiturates and TCAs may decrease effects; coadministration of iron supplements, MAOIs, sympathomimetics, phenothiazines, or beta-blockers may increase blood pressure

Contraindications

Documented hypersensitivity; acute liver disease

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in previous history of liver disease; hemolytic anemia and liver disease may occur; reduce dose in renal disease

Follow-up

Further Inpatient Care

Female patients should be evaluated for breast cancer. Epidemiologic studies have suggested that patients with scleroderma have an increased risk of cancer. However, large-scale case-control studies are needed to substantiate a possible association between scleroderma — both cutaneous and systemic — and breast cancer.[24]

Complications

- Neoplastic diseases may complicate the disease course.
- Examples include breast carcinoma; multiple myeloma; lymphoma; and cancer of the ovary, esophagus, colon, or rectum.

Prognosis

- The prognosis depends on the type of systemic sclerosis (SSc).
- In lSSc, a patient's condition can be stable for years.
- However, in dSSc, the disease can rapidly lead to death, if it is not treated promptly.
- Pulmonary hypertension may be an important cause of mortality in these patients. Survival complicated by pulmonary hypertension remains poor despite currently available treatment options.[25]

Patient Education

- The most effective method for preventing a Raynaud episode is to avoid exposure to cold temperatures.
- Smoking cessation should be discussed with patients and their families, as applicable.

Miscellaneous

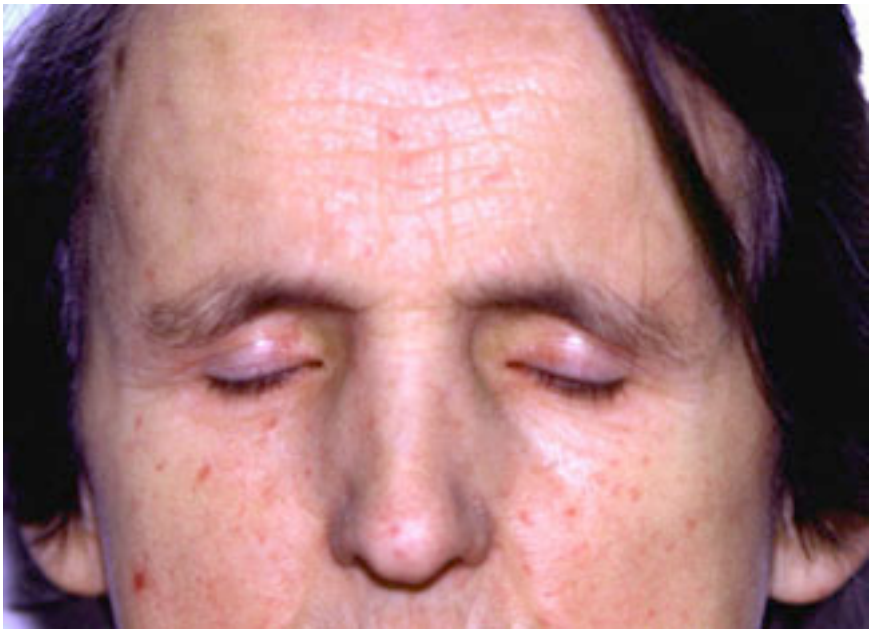
Medicolegal Pitfalls

- Capillary nail fold changes are one of the earliest signs of SSc.

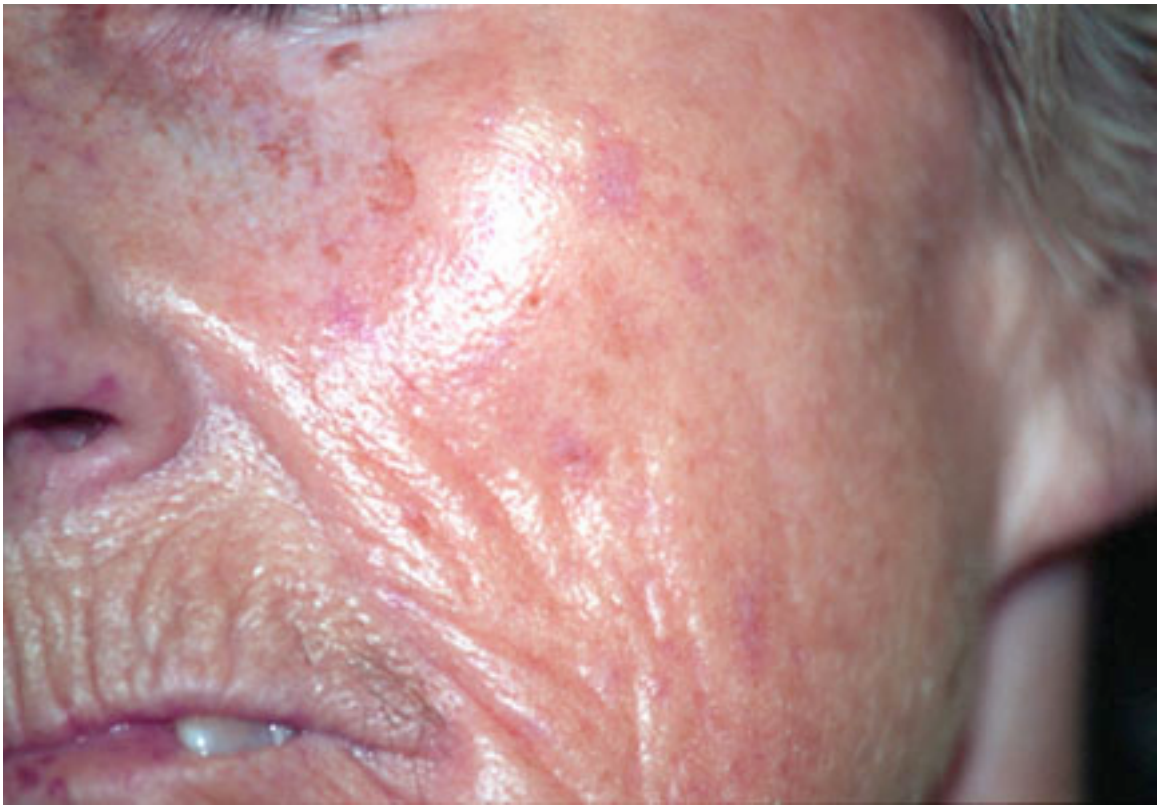
Special Concerns

- ANA serum levels in patients with systemic sclerosis are not correlated with disease activity.
- The undeniable impact of systemic sclerosis on quality of life underscores the need for a biopsychosocial approach to the clinical management. Timely detection of psychosocial difficulties and appropriate psychological or psychiatric intervention are also important steps toward better adherence to medical treatment.[26]

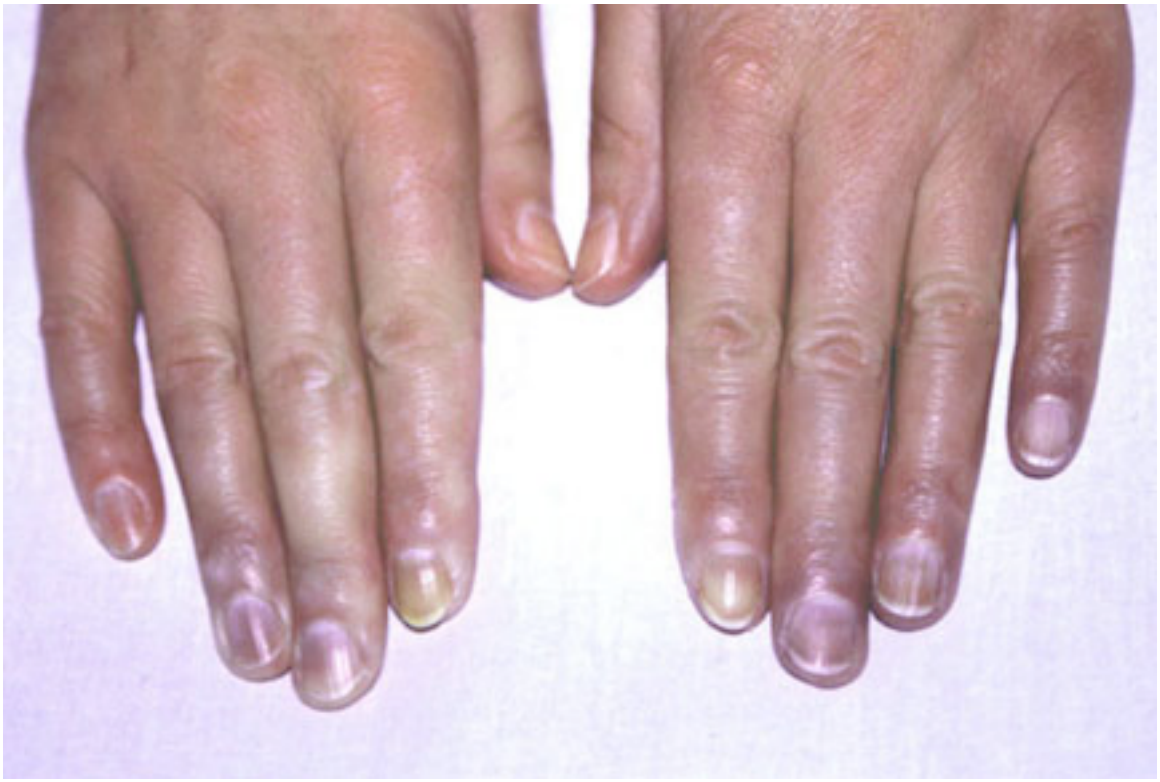
Multimedia



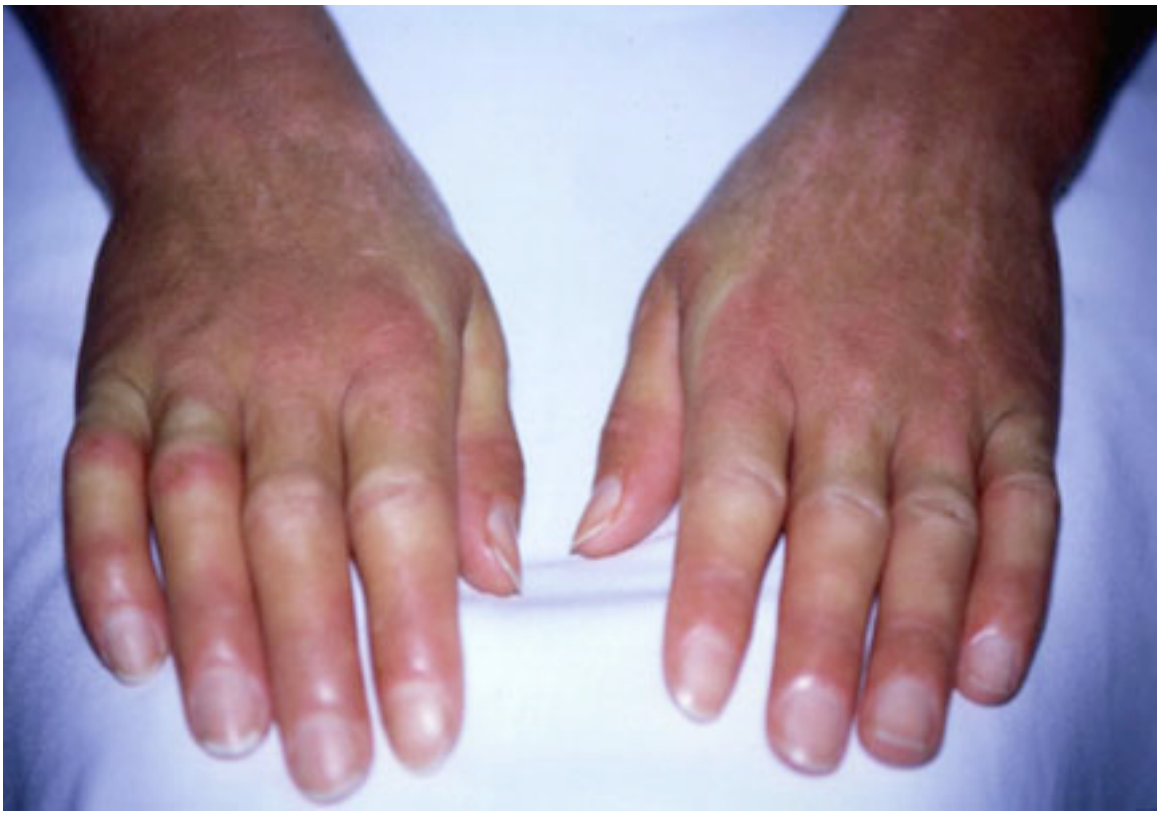
Media file 1: Face of 65-year old woman with systemic sclerosis and skin thickening of 20 years' duration: Note the pinched nose, taut skin with numerous telangiectasias, and retraction of the lips.



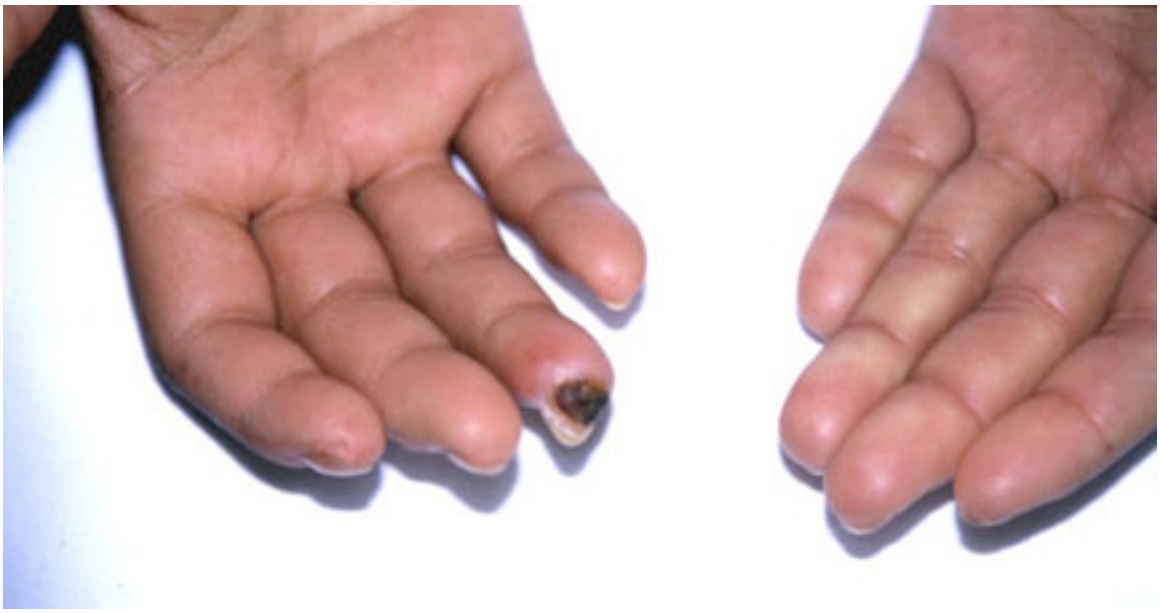
Media file 2: Telangiectasias affecting the face: They are pronounced and numerous, especially in the atrophic phase of the disease. Radical furrowing around the mouth is also characteristic in the later stage of the disease.



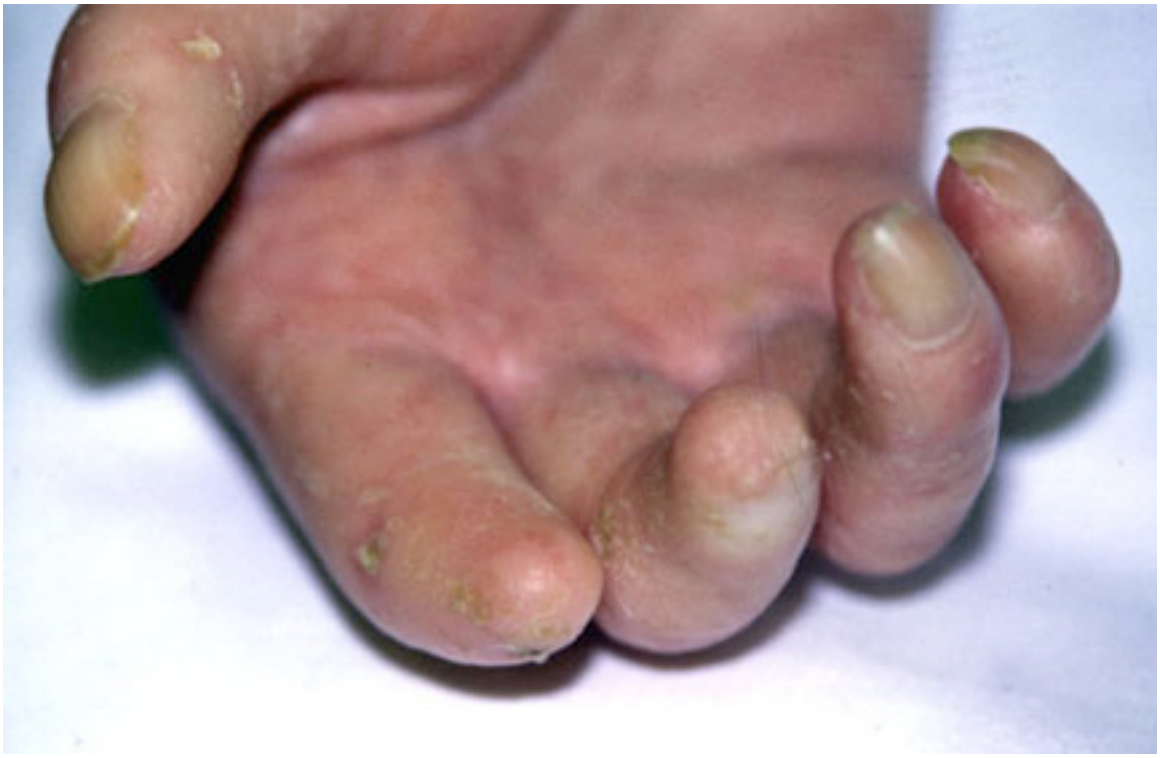
Media file 3: Raynaud phenomenon of the hands: Symmetrical acral vasospasm is present, with characteristic pallor, cyanosis, suffusion, and a sense of fullness and tautness.



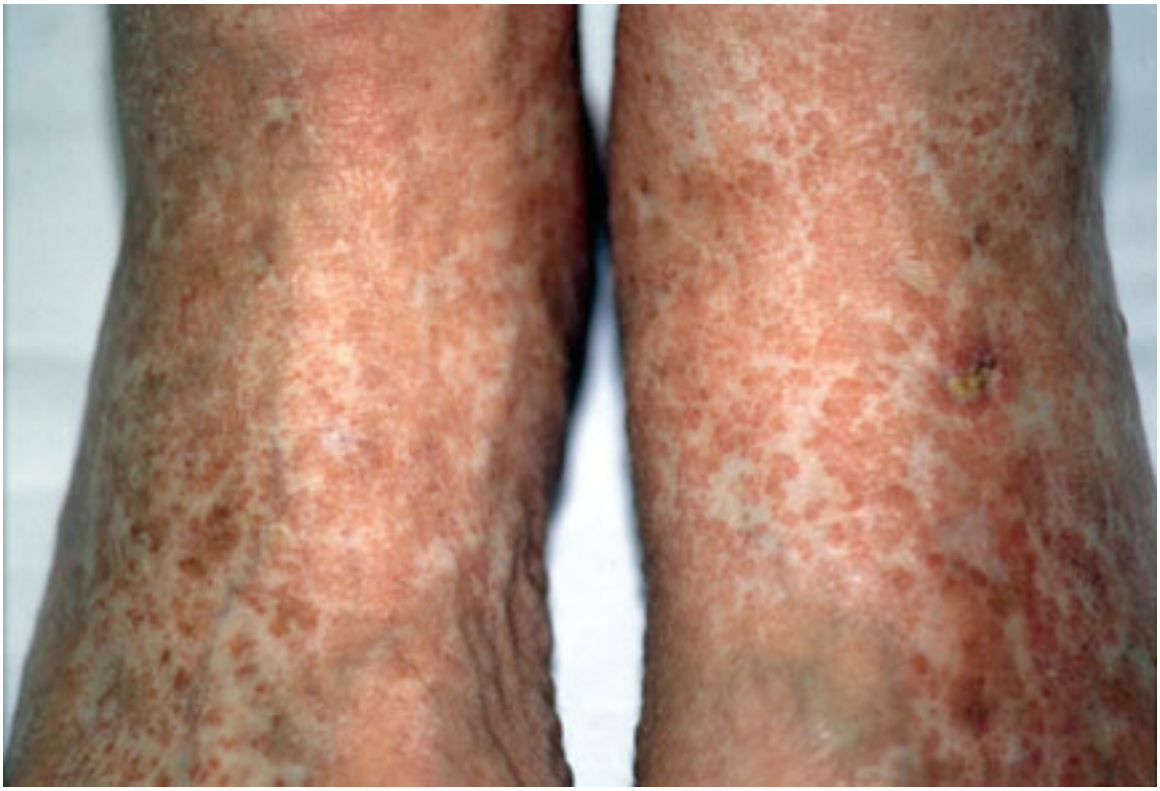
Media file 4: Puffy appearance of the woman's hand in the edematous phase of early scleroderma.



Media file 5: In systemic sclerosis, ulceration at the tip of the finger is regarded to be secondary to ischemia.



Media file 6: Hand of a woman with scleroderma of several years' duration: The thickened, tight, thin skin over the fingers is the result of self-amputation of the distal phalanx due to ischemia. Moderately severe flexion contractures of the fingers are present.



Media file 7: In systemic sclerosis, skin hyperpigmentation of the lower legs is surrounded by areas of hypopigmentation. The result is a salt-and-pepper appearance.

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