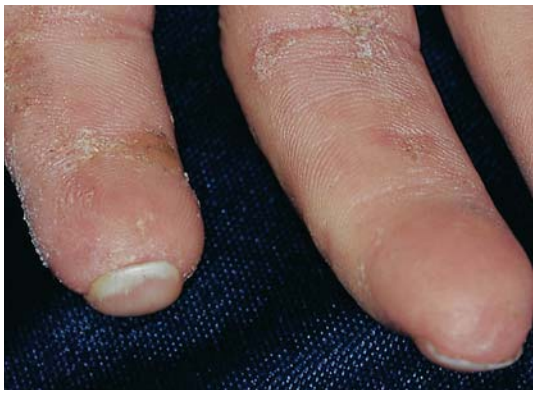
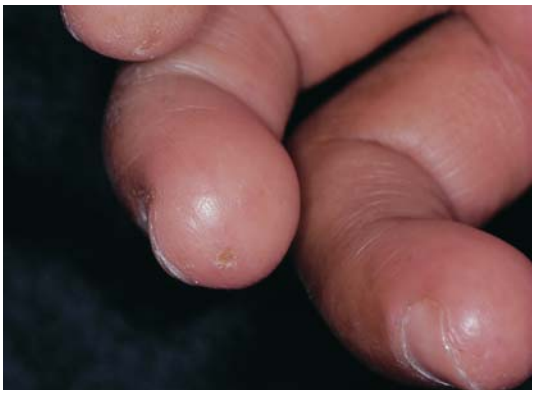
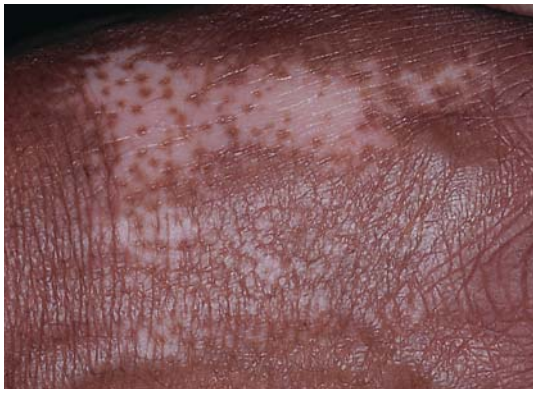
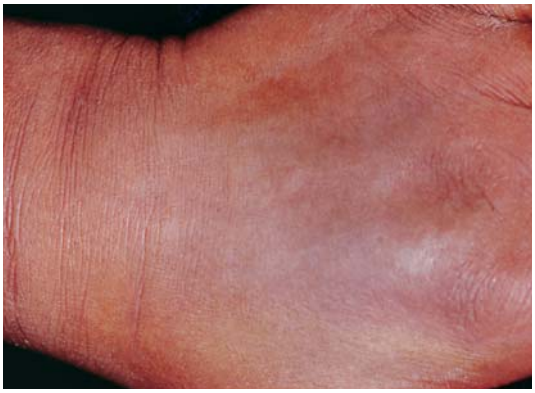
What Is Your Diagnosis?

All of the patients pictured have the same disorder.

PLEASE TURN TO PAGE 385 FOR DISCUSSION

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The author reports no conflict of interest.
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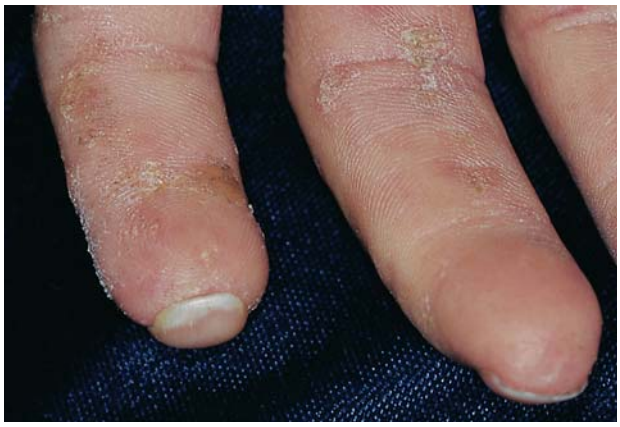
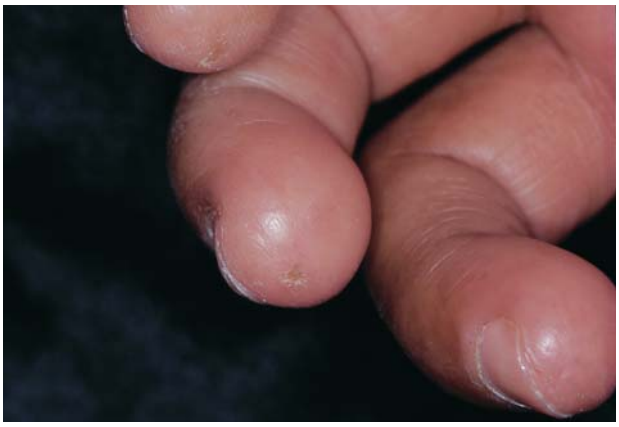
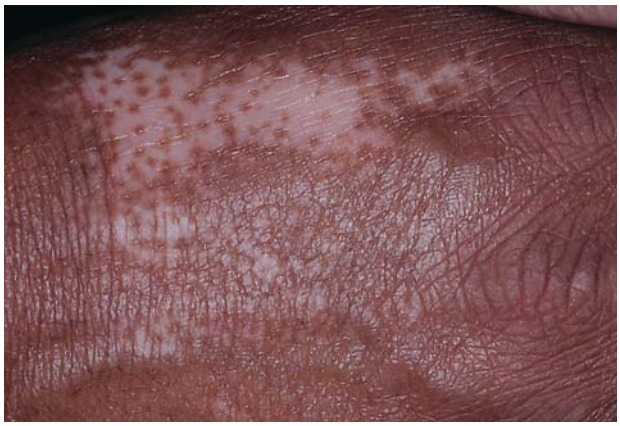
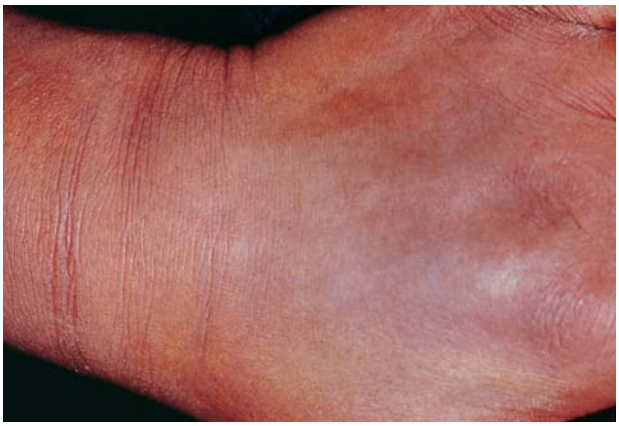
The Diagnosis: Progressive Systemic Sclerosis (Scleroderma)

Cutaneous features of progressive systemic sclerosis, a manifestation of scleroderma, include acral sclerosis and acral vasculopathy, which may produce erythema and edema of the hands, sclerodactyly, pulp atrophy, and/or digital pits. Proximal nail folds commonly demonstrate segmental avascularity (vessel drop out), ectasia, and hemorrhage.[1] The presentation of nail fold changes in patients with scleroderma is similar to patients with dermatomyositis but differs from the wandering capillary loops seen in patients with lupus erythematosus.[2] The presence of sclerodactyly and loss of digital pulp distinguish the distal finger changes of dermatomyositis and scleroderma. Nail fold changes are useful in predicting if undifferentiated connective tissue disease will progress to systemic sclerosis.[3] Raynaud phenomenon frequently is the presenting sign of progressive systemic sclerosis. CREST syndrome, associated with calcinosis cutis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, telangiectatic mats, and anticentromere antibodies, should be distinguished from progressive and diffuse cutaneous scleroderma/progressive systemic sclerosis.[4,5] Patients with systemic scleroderma exhibit early sclerosis of the proximal extremities and trunk and may have an antinucleolar antinuclear antibody pattern and autoantibodies to topoisomerase-1 (SCL-70). SCL-70 and antibodies to endothelial cells appear to be markers for lung disease in patients with scleroderma.[4,5] Affected areas of skin may demonstrate hyperpigmentation or hypopigmentation or a salt and pepper pattern resembling repigmenting vitiligo. All patterns of pigmentation are associated with marked induration of the skin. Progressive systemic sclerosis is the most aggressive form of scleroderma and carries a substantial risk for early death.

Substantial data suggest that immune mechanisms are important in the pathogenesis of scleroderma.

Although traditionally thought of as an autoimmune disorder, studies have detected microchimerism of maternal or fetal origin in patients with scleroderma, suggesting that at least some cases could represent an alloimmune phenomenon.[6-8] These studies must be interpreted cautiously because microchimerism also occurs in normal adults. A study of Japanese women with progressive systemic sclerosis failed to demonstrate significant incidence of fetal microchimerism.[9] Environmental and occupational triggering factors such as Parvovirus B 19,[10] vinyl chloride, trichloroethene, and epoxy resins may be important in the pathogenesis of some cases of scleroderma.[11] Occupational exposure to silica dust has been shown to be an environmental trigger in coal miners with scleroderma.[12] One animal model (University of California at Davis line 200 [UCD-200] chickens) for scleroderma expresses all features of the disease, including vascular injury. Sgonc[13] found that endothelial apoptosis, induced by antiendothelial cell antibody–dependent cellular cytotoxicity, is involved in the pathogenesis of systemic sclerosis.

Patients with Raynaud phenomenon should be advised to avoid cold exposure and wear warm gloves or mittens when exposed to cold temperatures. Smoking and vasoconstrictive medications should be avoided. Raynaud phenomenon commonly responds to treatment with long-acting calcium channel blockers. Prostaglandin E_1 and angiotensin receptor antagonists also may be beneficial.[14,15] Alternative agents such as peripheral α-adrenergic blockers, anticoagulant and antiplatelet therapy, prostaglandin analogs, and pentoxifylline have been used with anecdotal success.[16] Although many agents have been used in an attempt to treat widespread skin sclerosis, well-controlled studies are still needed. Anecdotal success has been reported with octreotide.[17] UV light therapy, photochemotherapy, and photophoresis have been used to treat scleroderma, but results are mixed and inconclusive.[18-20] Oral photochemotherapy has produced modest benefits in some patients with scleroderma.[21] Surgical management of disabling hand deformities in patients with scleroderma can help restore function.[22]

Systemic sclerosis may involve the musculoskeletal system, kidneys, gastrointestinal tract, lungs, and heart. Kidney disease and malignant hypertension can be rapidly progressive and require aggressive treatment. Early consultation with a rheumatologist and nephrologist is advised. Angiotensin-converting enzyme inhibitors, cyclophosphamide, and pulmonary vasodilators have been used to treat aggressive disease.[23-25] Severe systemic disease in children has been treated with chemotherapy followed by granulocyte colony stimulating factor to mobilize autologous peripheral blood progenitors. Marrow reconstitution is accomplished with lymphocyte-depleted progenitor cells,[26] which holds great promise for the treatment of any severe autoimmune disease.[27] As effective disease modifying therapy becomes available, it is important to determine when the course of disease therapy should be offered. Aggressive therapy may be most effective when disease manifestations are still mild. After sclerosis occurs, treatment may be less effective. More study is needed.

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