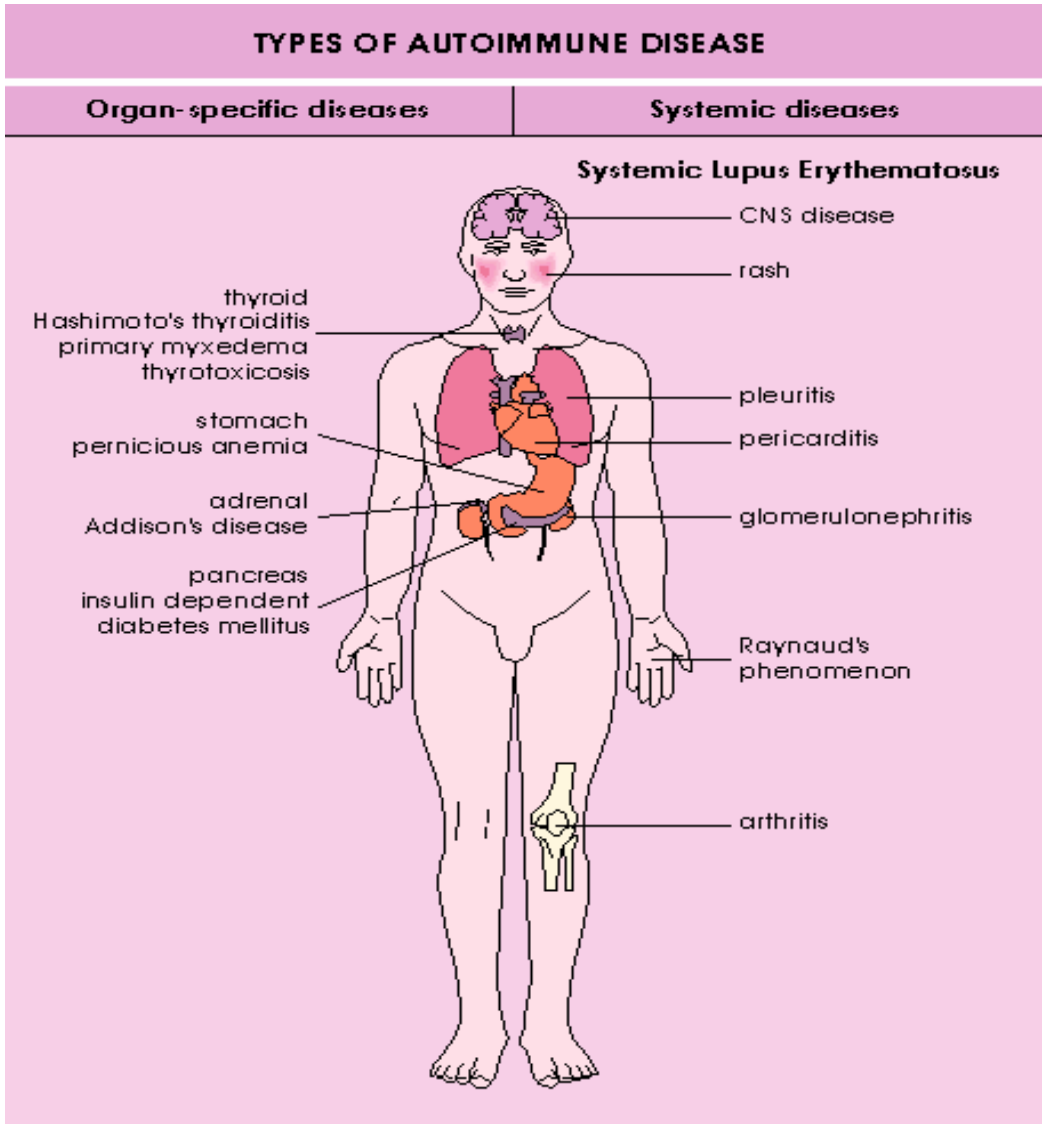
Connective Tissue Diseases

Dr. C. C. Visser



Two types of autoimmune diseases – organ-specific and systemic. Although the systemic autoimmune diseases produce symptoms in multiple organs, each disease may be marked by characteristic patterns of organ involvement.

Systemic lupus erythematosis

THE 1982 REVISED ACR CRITERIA

Criterion	Definition
1. Malar rash	Fixed erythema, flat or raised, over the malar eminences, sparing the nasolabial folds
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging: atrophic scarring may occur in older lesions
3. Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
5. Arthritis	Nonerosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion
6. Serositis	a) Pleuritis – convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion; or b) pericarditis – documented by ECG or rub or evidence of pericardial effusion
7. Renal disorder	a) Persistent proteinuria greater than 0.5 g per day or greater than 3+ if quantitation not performed b) Cellular casts – may be red cell, hemoglobin, granular, tubular, or mixed
8. Neurologic disorder	a) Seizures – in the absence of offending drugs or known metabolic derangement: e.g. uremia, ketoacidosis, or electrolyte imbalance; or b) psychosis – in the absence of offending drugs or known metabolic derangement: e.g. uremia, ketoacidosis, or electrolyte imbalance
9. Hematologic disorder	a) Hemolytic anemia with reticulocytosis; or b) leukopenia – less than 4000/mm^3 on more than two occasions; or c) lymphopenia – less than 1500/mm^3 on more than two occasions; or d) thrombocytopenia – less than 100,000/mm^3 in the absence of offending drugs
10. Immunologic disorder	a) Positive LE cell preparation; or b) anti-DNA: antibody to native DNA in abnormal titer; or c) anti-Sm: presence of antibody to Sm nuclear antigen; or d) false positive serologic test for syphilis known to be positive for at least 6 months and confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody test.
11. Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time in the absence of drug

CLASSIFICATION OF CUTANEOUS LESIONS

LE-specific lesions

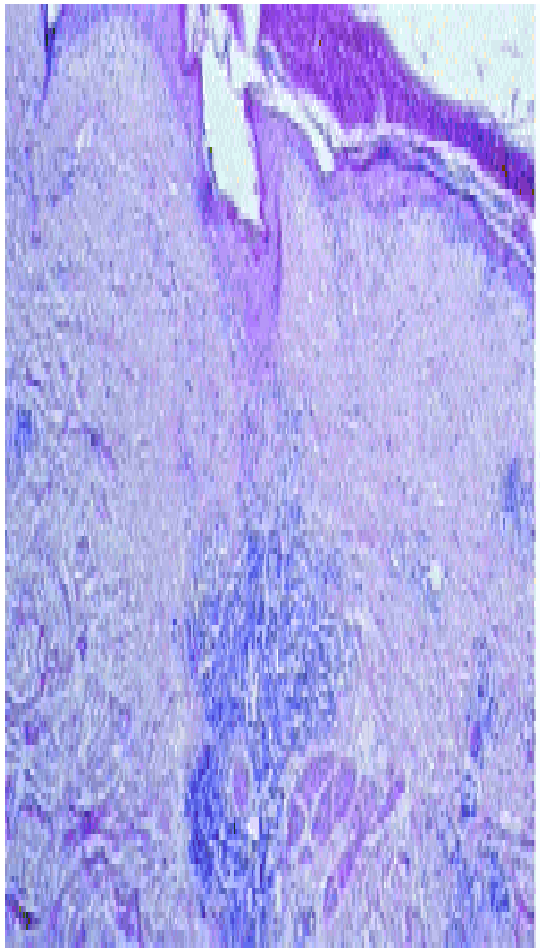
Acute
- Malar `butterfly' rash
- Generalized erythema
- Bullous LE

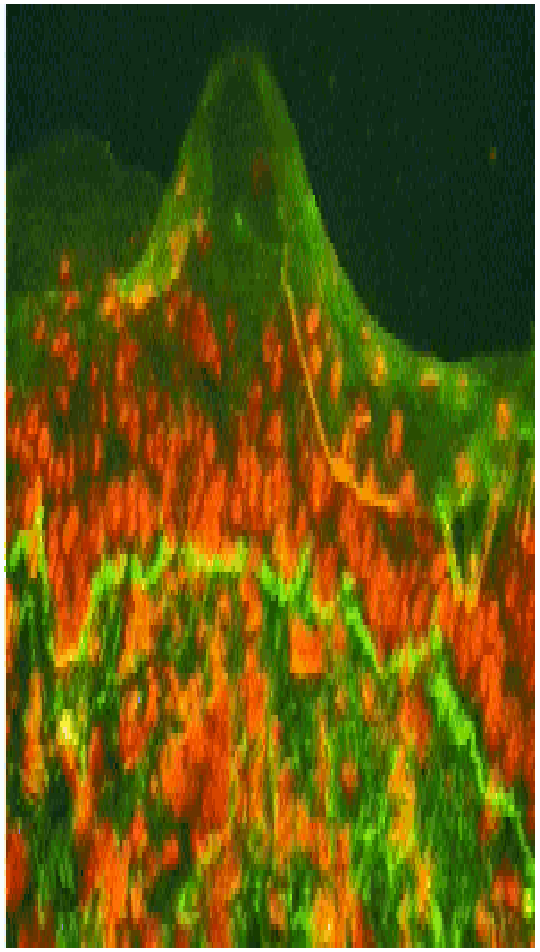
Subacute cutaneous lupus
- Annular – polycyclic
- Papulosquamous (psoriasiform)

Chronic lupus
- Localized discoid
- Generalized discoid
- Lupus profundus

LE-nonspecific lesions

- Panniculitis
- Urticarial lesions
- Vasculitis
- Livedo reticularis
- Oral lesions
- Nonscarring alopecia
- Associated skin conditions (psoriasis, lichen planus, porphyria)

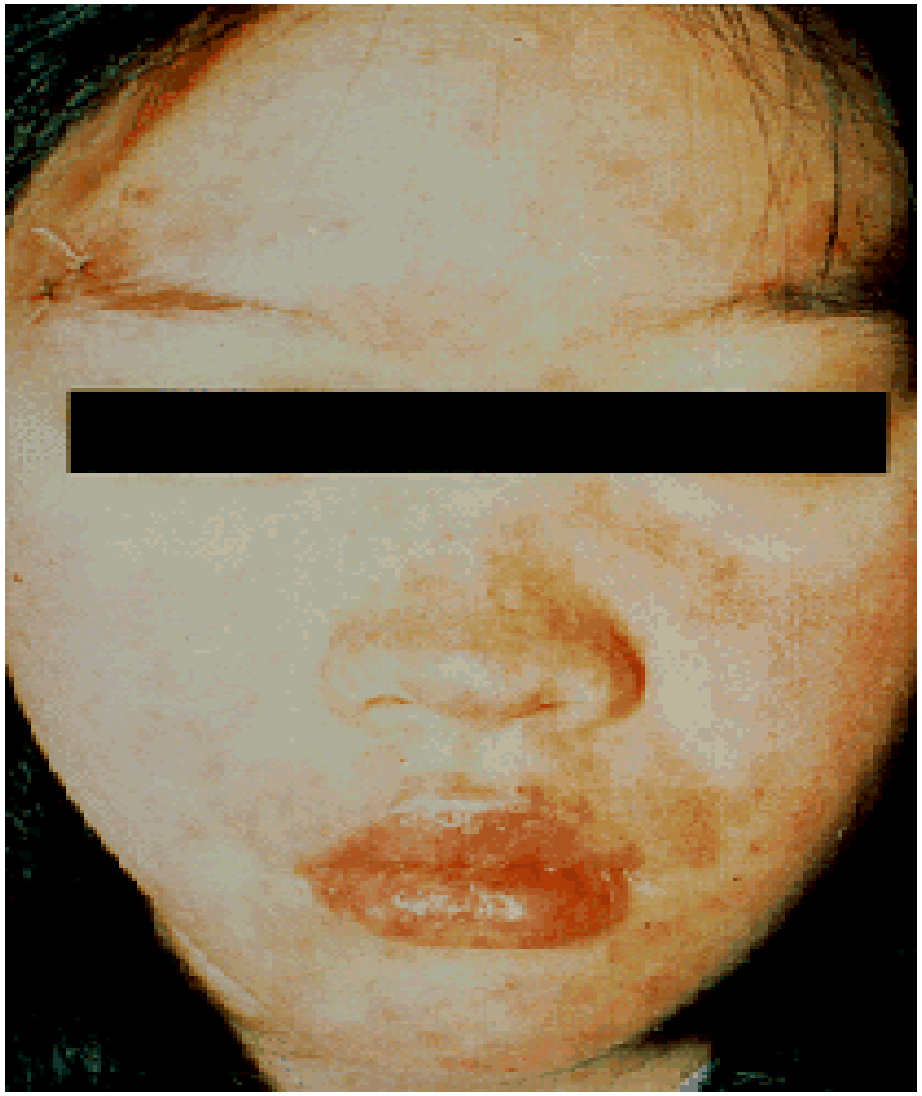




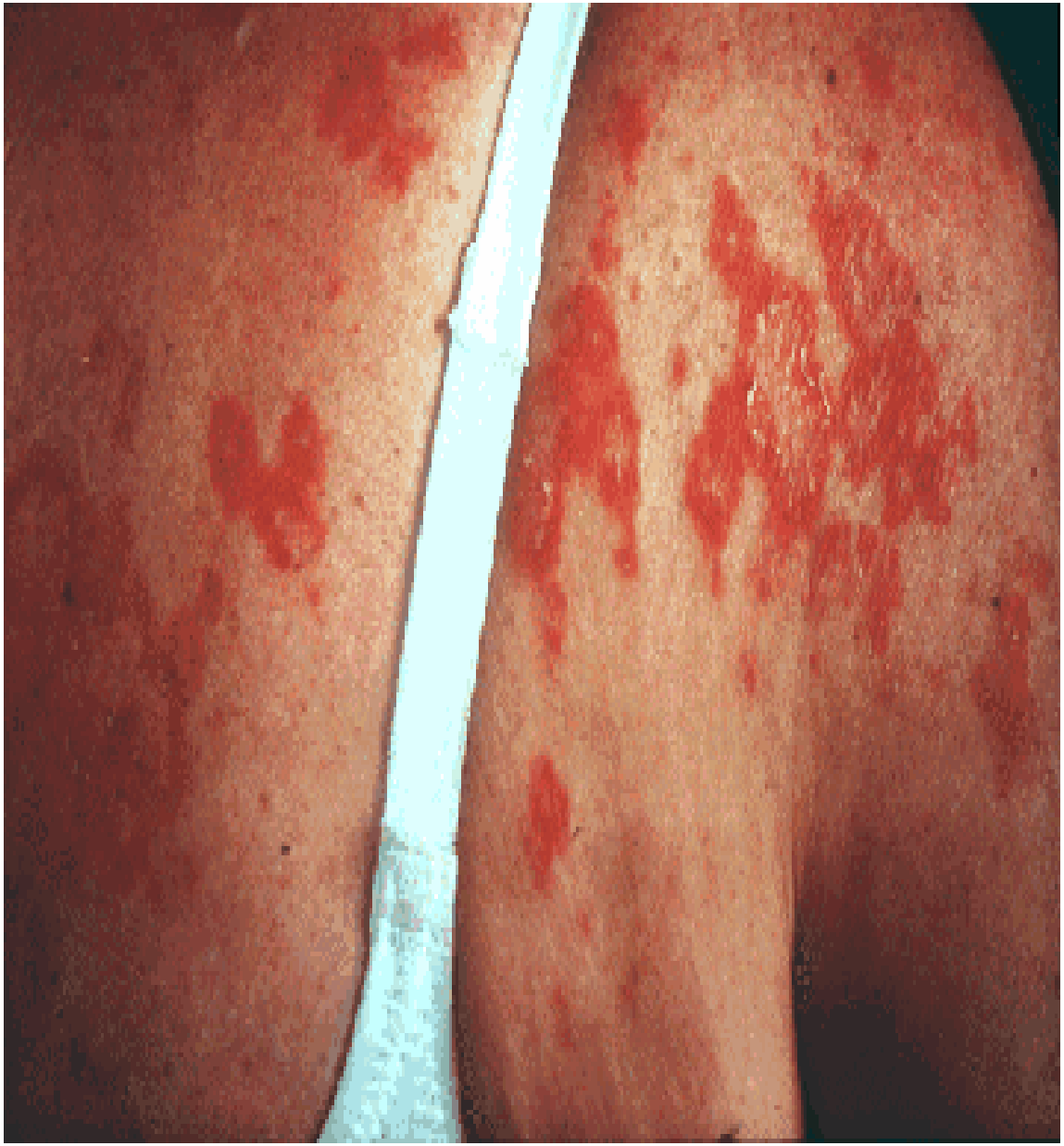
The lupus band test demonstrating immuno-globulin and complement deposition on non-sun exposed skin.

Light microscopy: thickening of the dermal–epidermal junction, inflammatory cells associated with a dermal appendage.

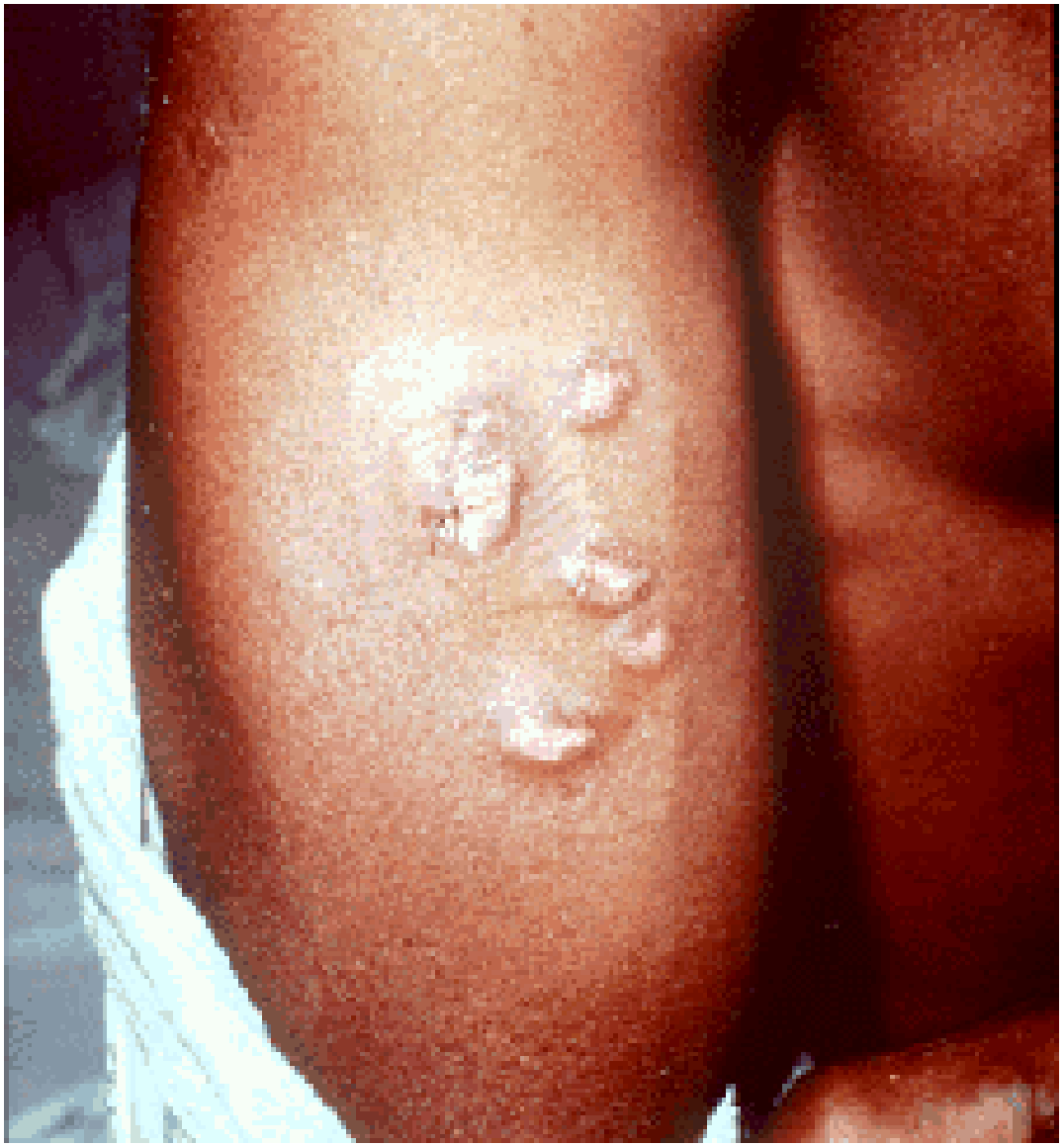
Immunofluorescence: IgM and C3b at the dermal–epidermal junction (bright green horizontal band)



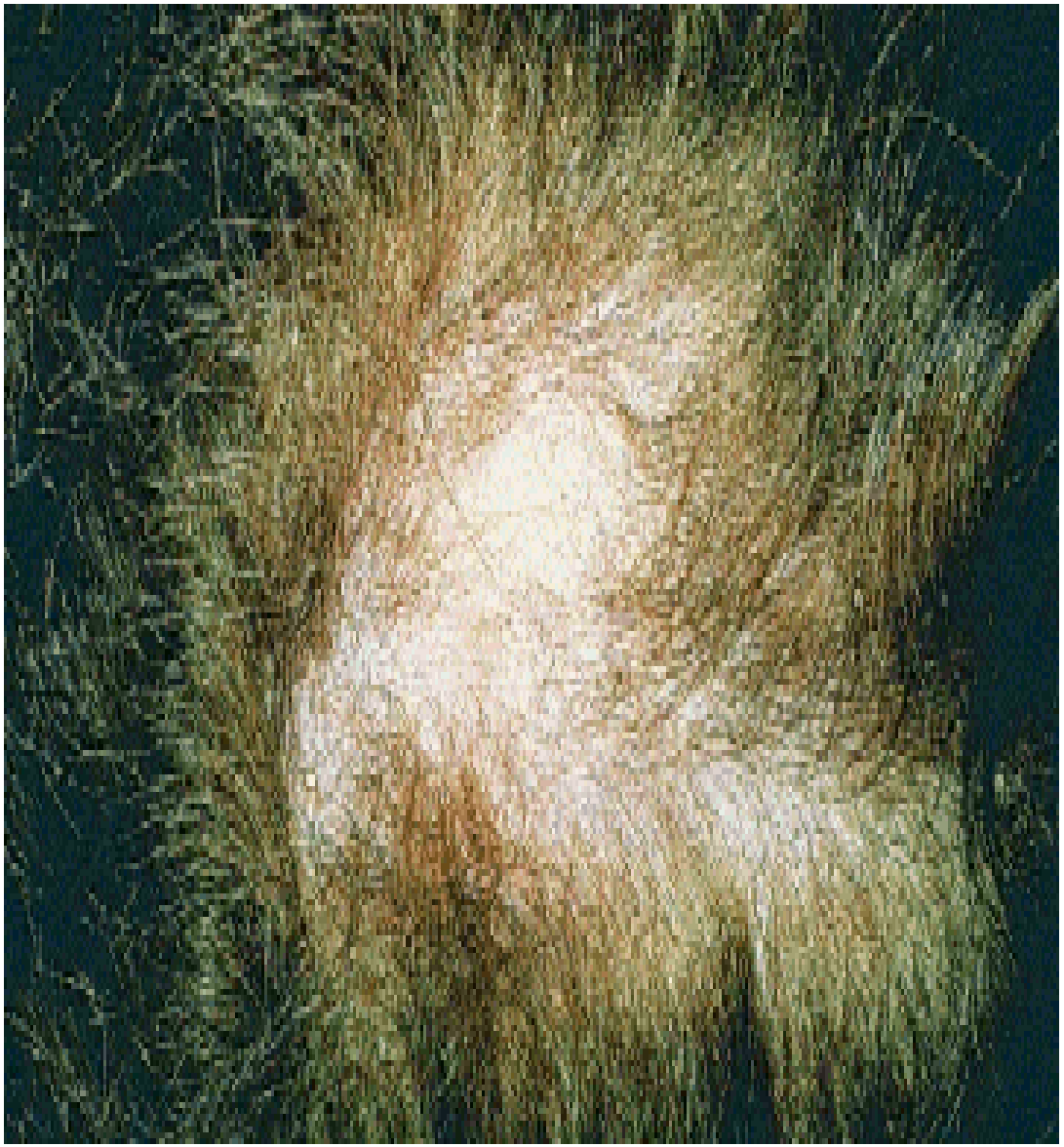
Malar rash in a patient with SLE.



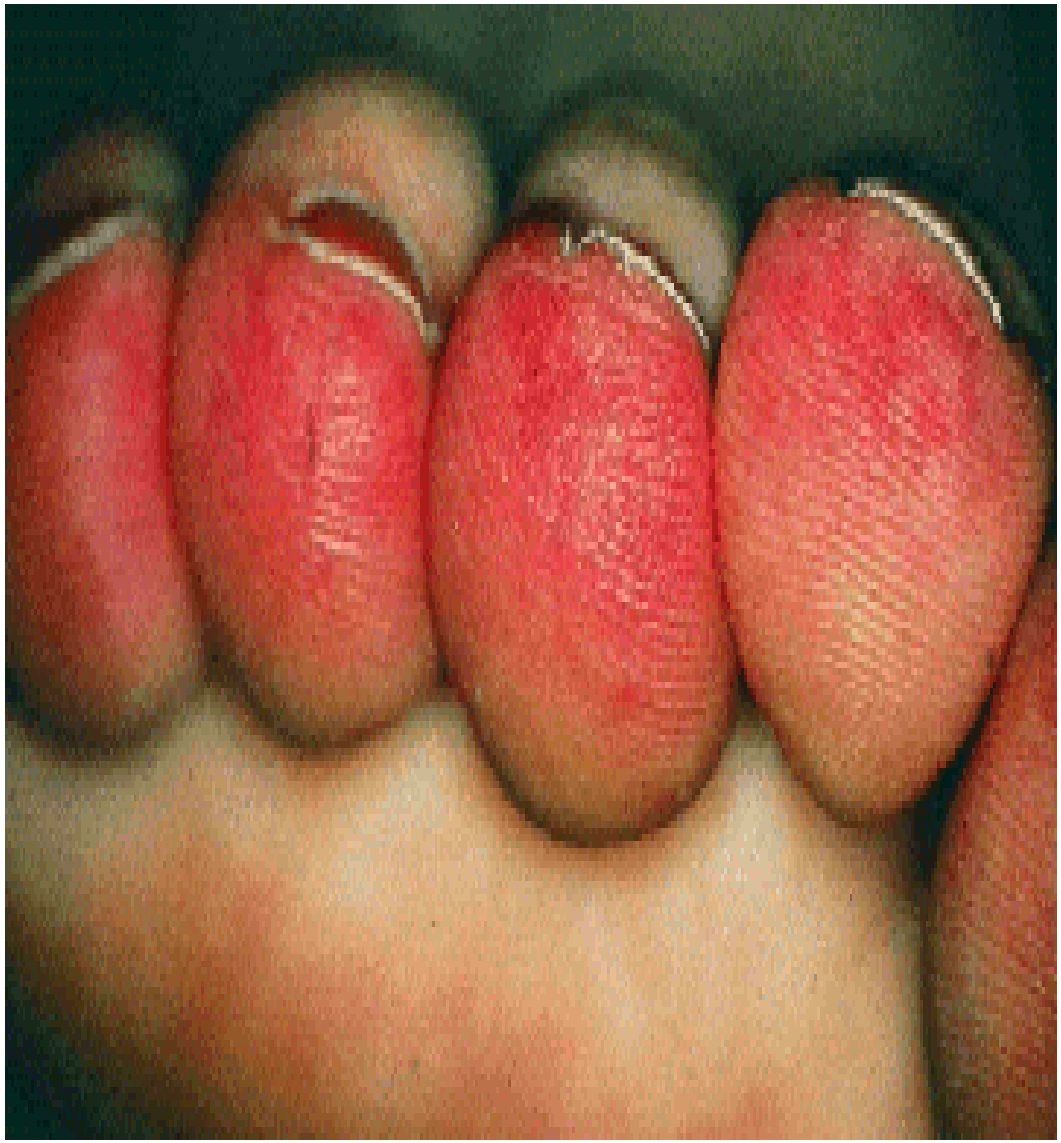
Subacute cutaneous lupus lesions.



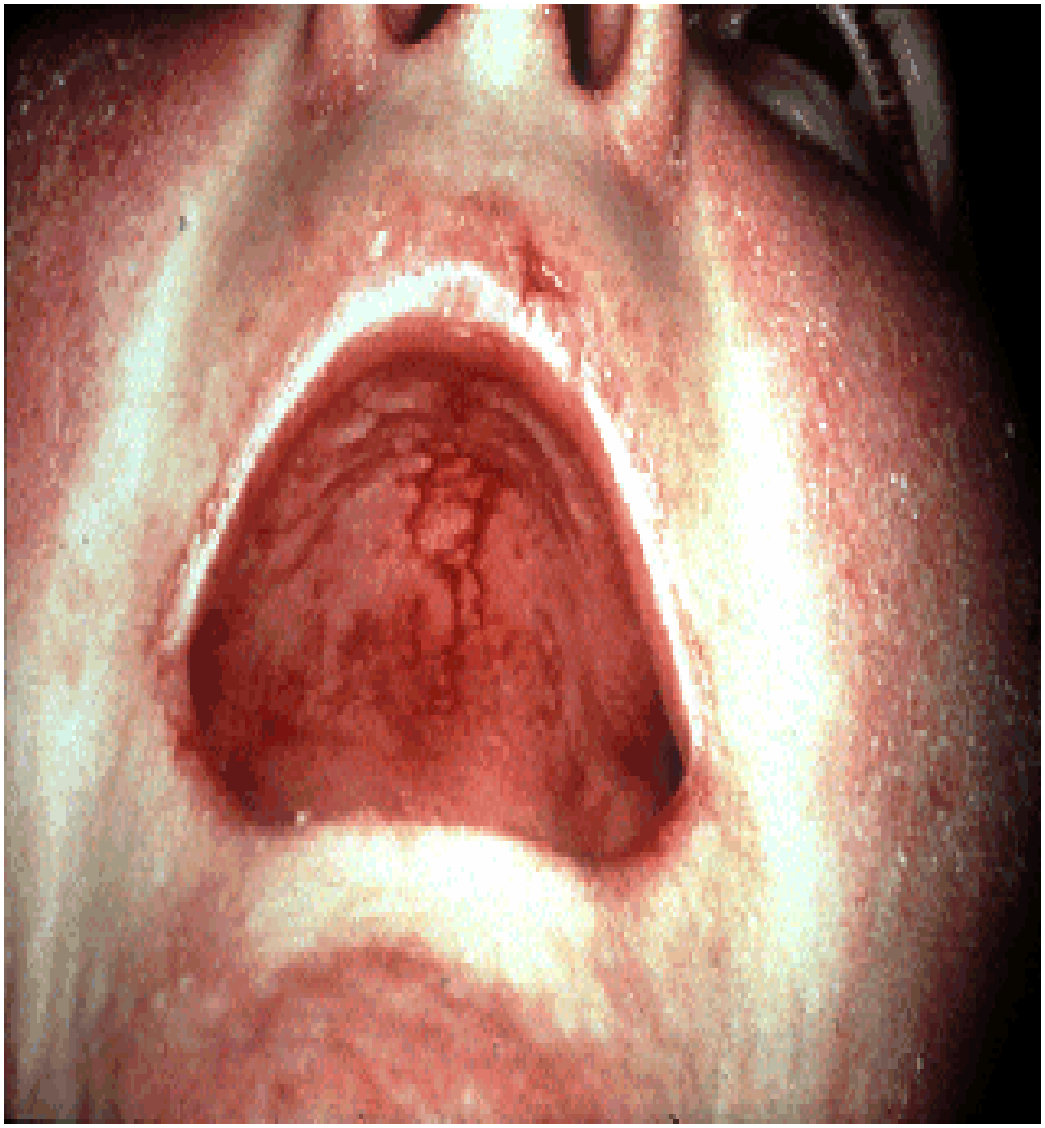
Discoid lupus lesions.



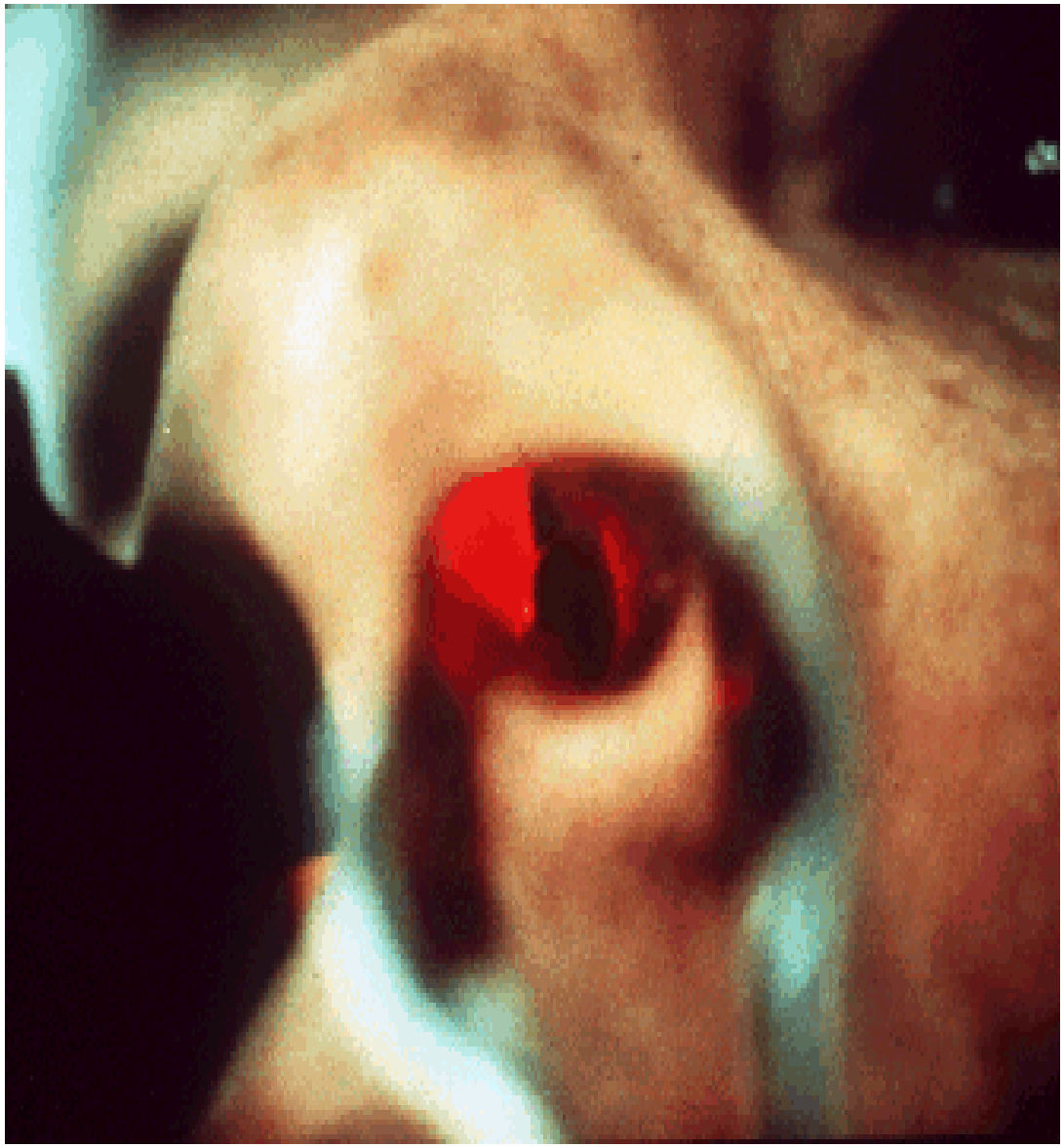
Alopecia in a patient with SLE.



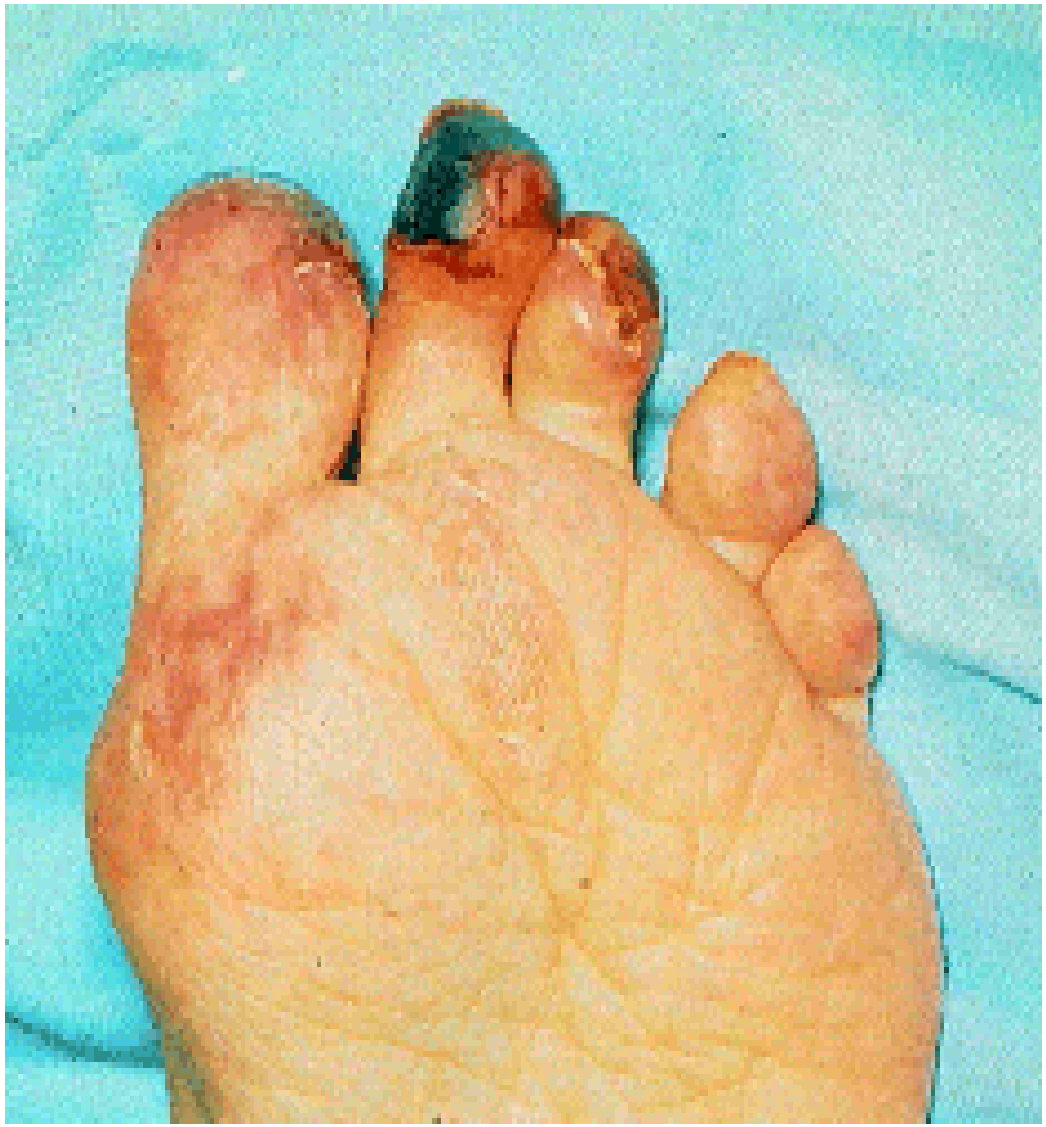
Early vasculitic lesions over the tips of the toes in a patient with active SLE.



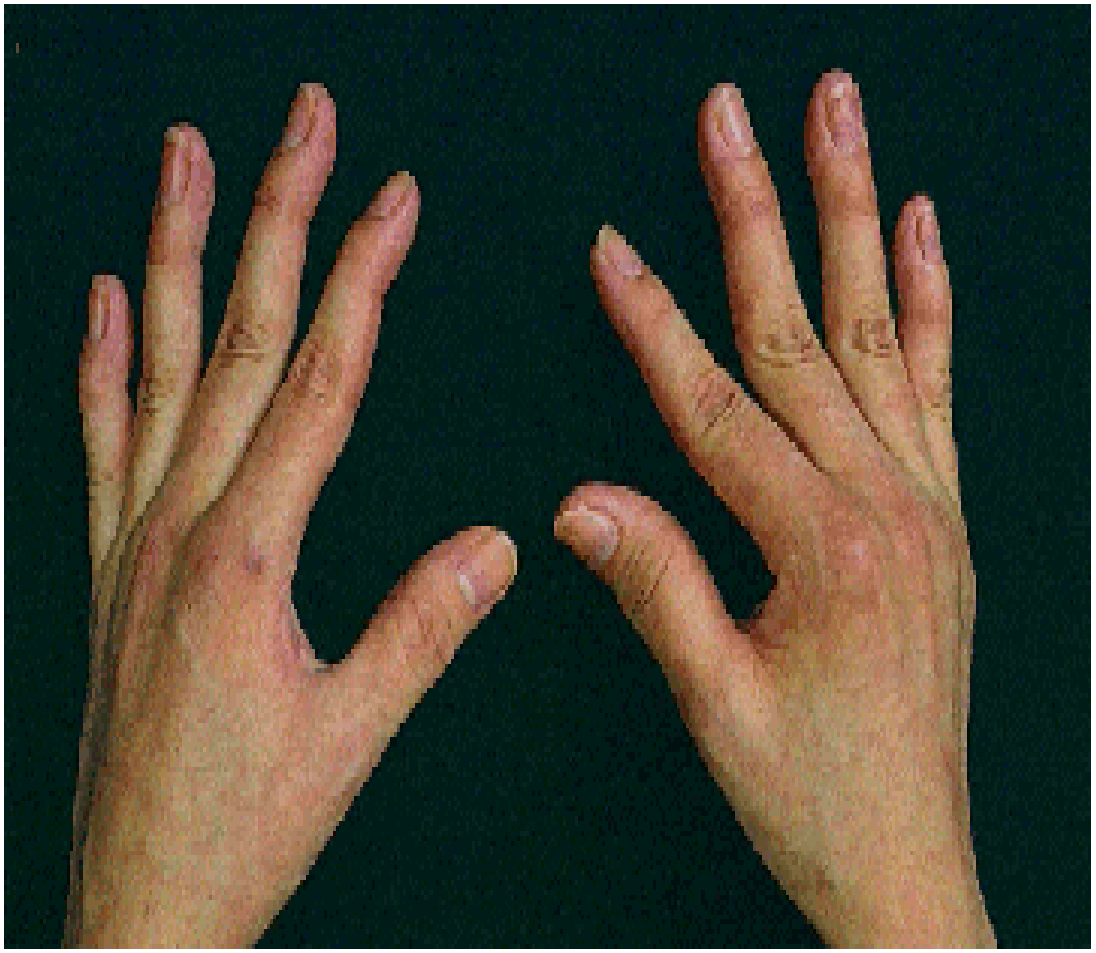
Mouth ulcers in a patient with SLE.



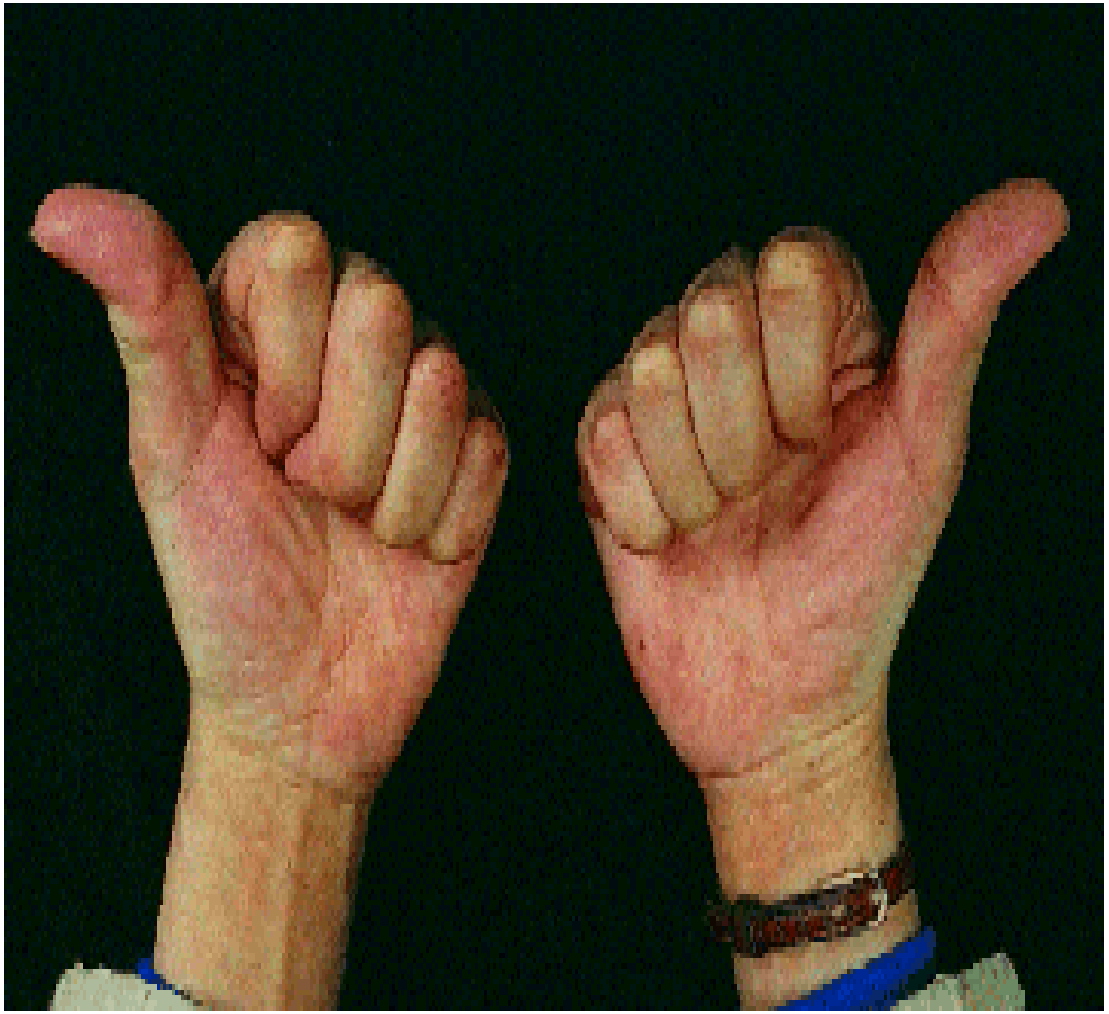
Nasal septal perforation in a patient with SLE.



Gangrene of the toe in a patient with SLE and vasculitis.

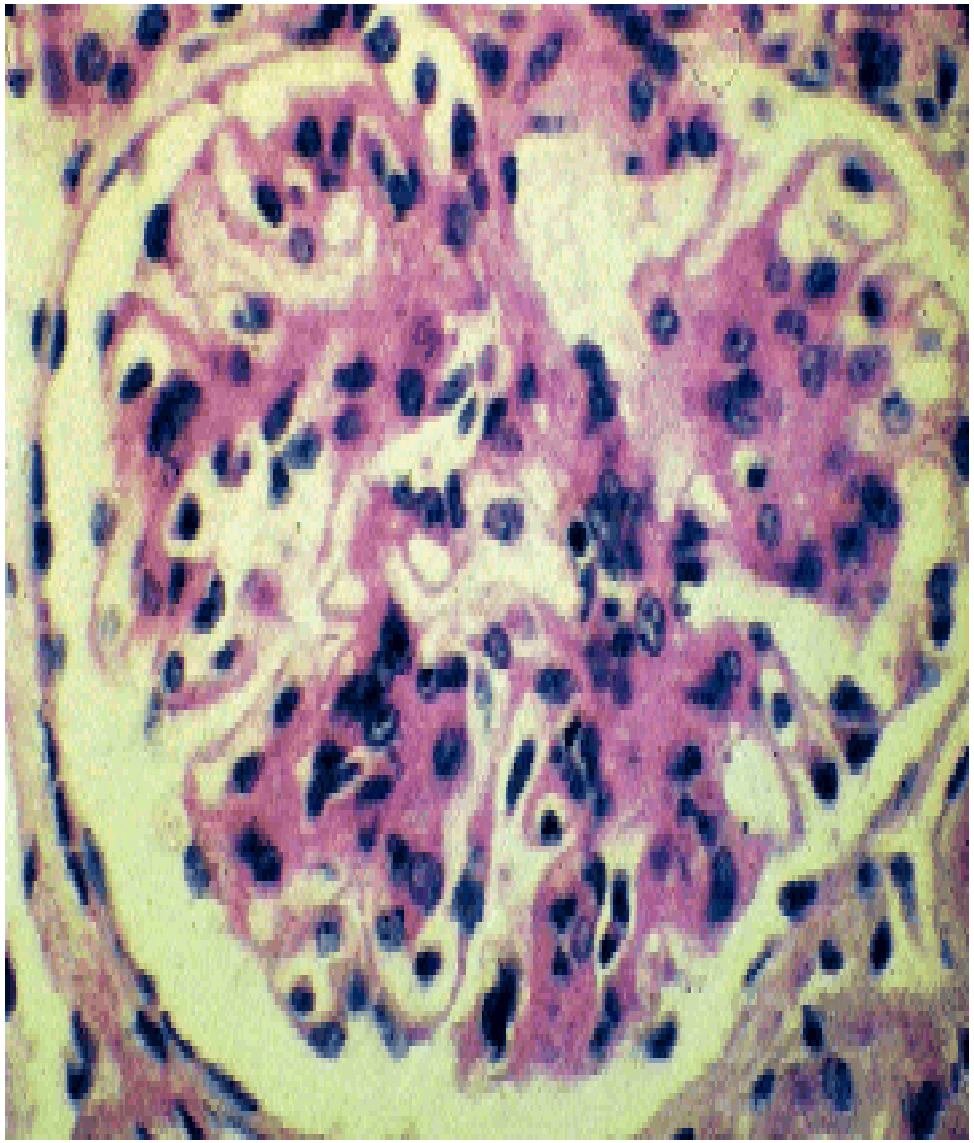


Swan neck deformities in a patient with SLE.

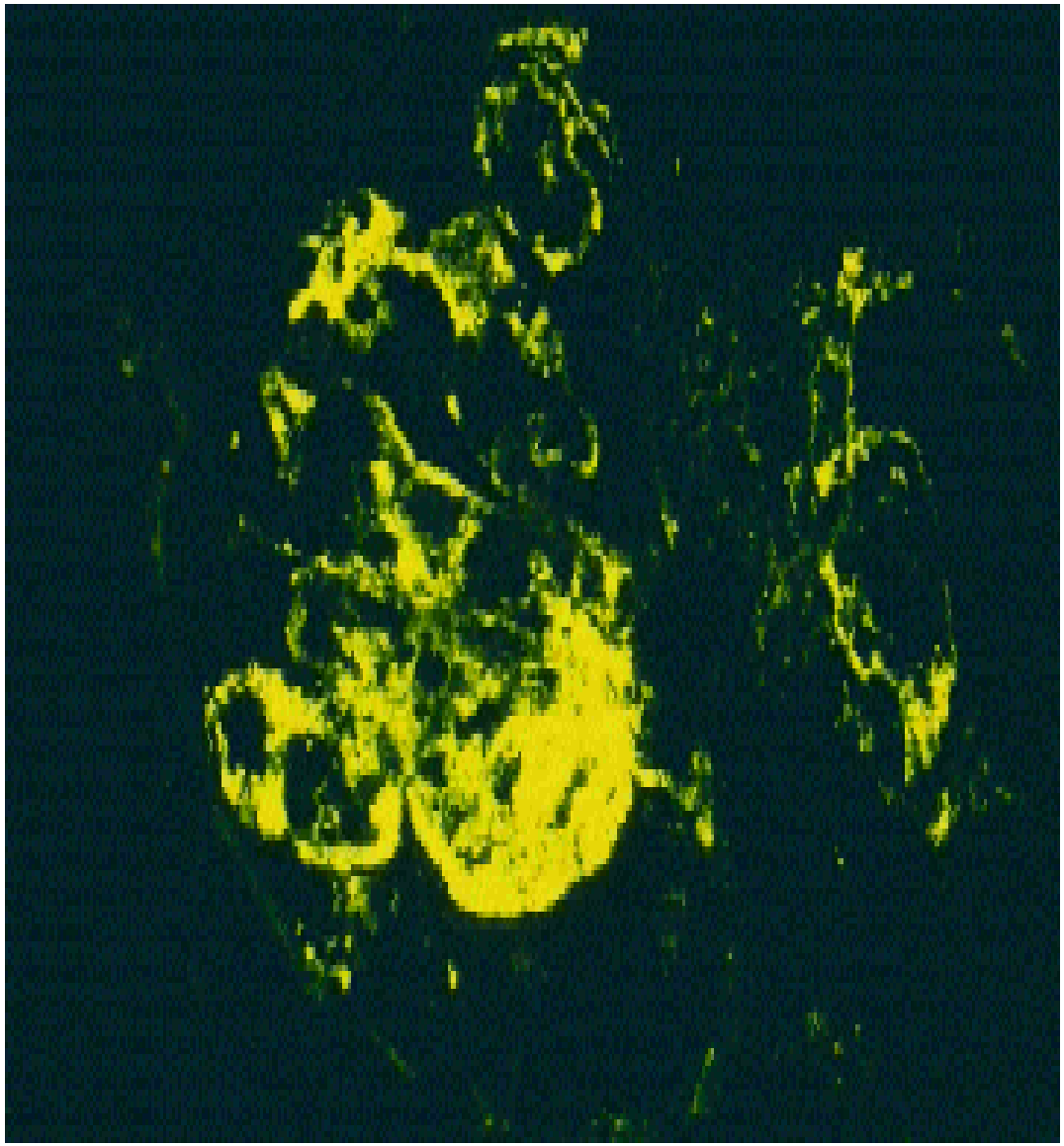


Fists of the previous patient showing the deformities reduced.

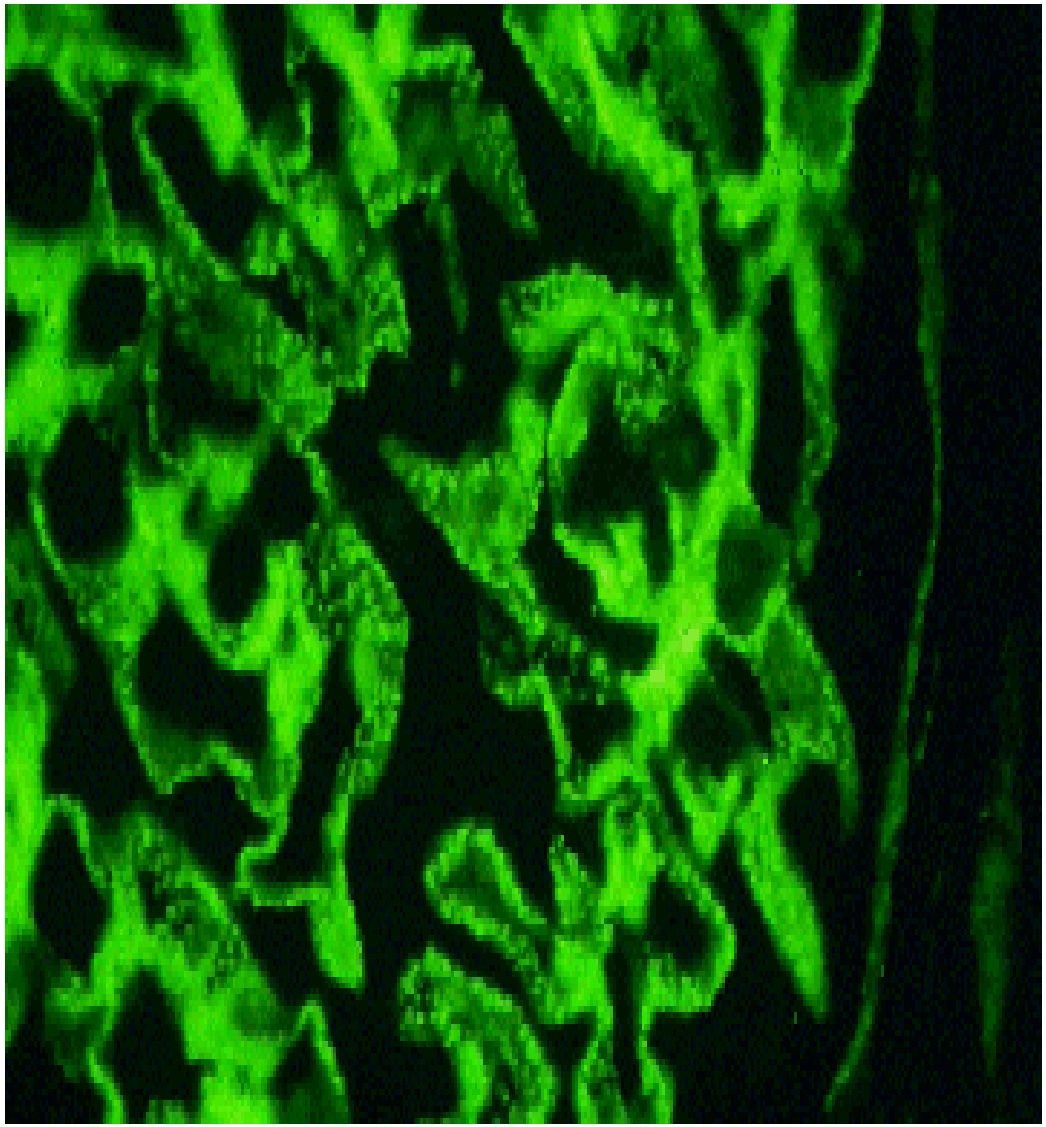
WHO CLASSIFICATION OF LUPUS NEPHRITIS IN 148 BIOPSIES		
I	Normal glomeruli	12
	a) Nil (by all techniques) b) Normal by light but deposits on electron microscopy or immunofluorescence	3 9
II	Pure mesangial alterations (mesangiopathy)	62
	a) Mesangial widening and/or mild hypercellularity (+) b) Moderate hypercellularity (11)	51 11
IIIA	Focal segmental glomerulonephritis	19
	a) 'Active' necrotizing lesions b) 'Active' and sclerosing lesions c) Sclerosing lesions	14 5
IIIB	Focal proliferative glomerulonephritis	3
	a) 'Active' necrotizing lesions b) 'Active' and sclerosing lesions c) Sclerosing lesions	1 2
IV	Diffuse glomerulonephritis	37
	a) Without segmental lesions b) With `active' necrotizing lesions c) With `active' and sclerosing lesions d) With sclerosing lesions	9 13 14 1
V	Diffuse membranous glomerulonephritis	11
	a) Pure membranous glomerulonephritis b) Associated with lesions of category II c) Associated with lesions of category III d) Associated with lesions of category IV	2 7 0 2
VI	Advanced sclerosing glomerulonephritis	4



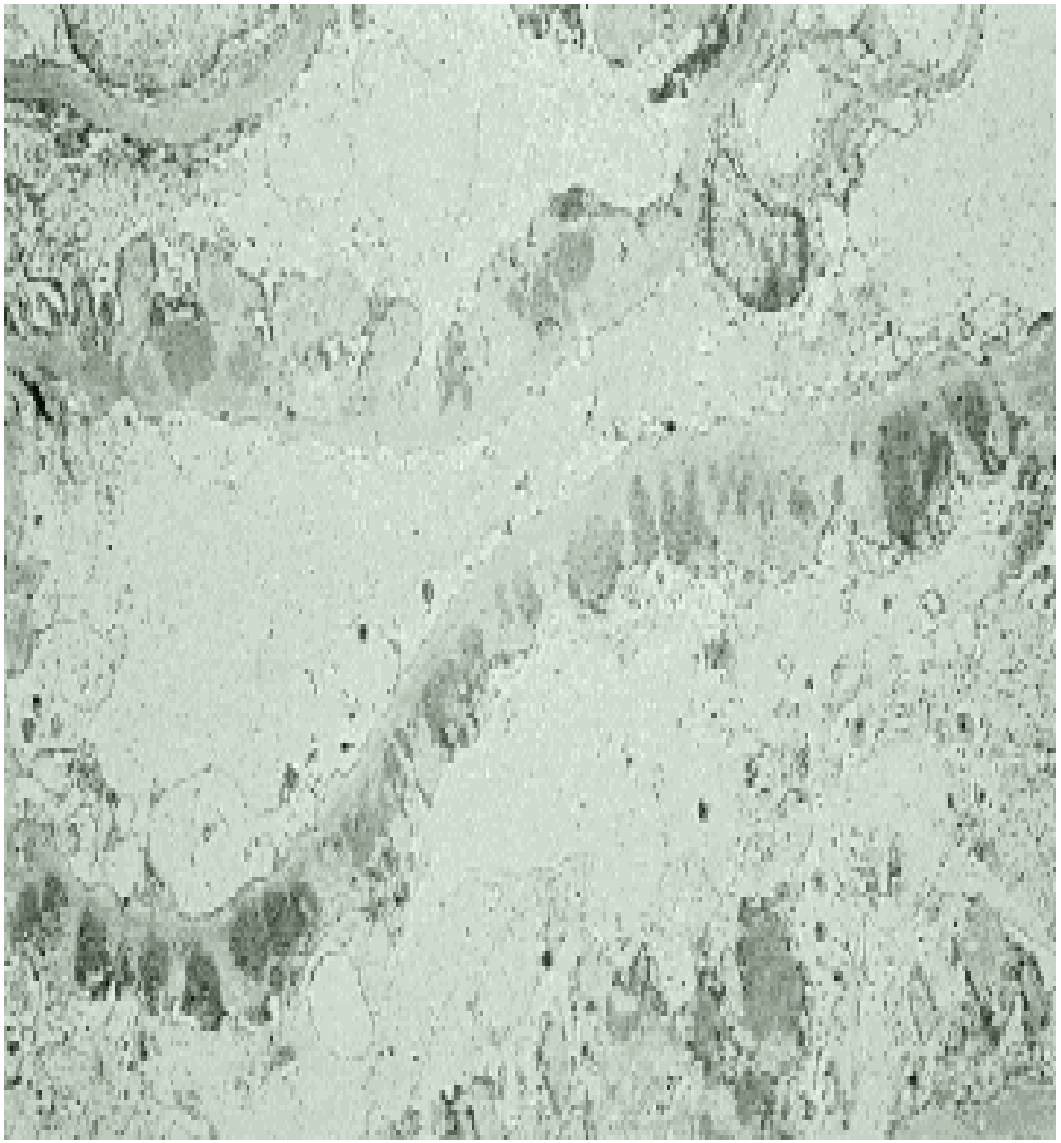
Kidney biopsy specimen showing mesangial lesions.



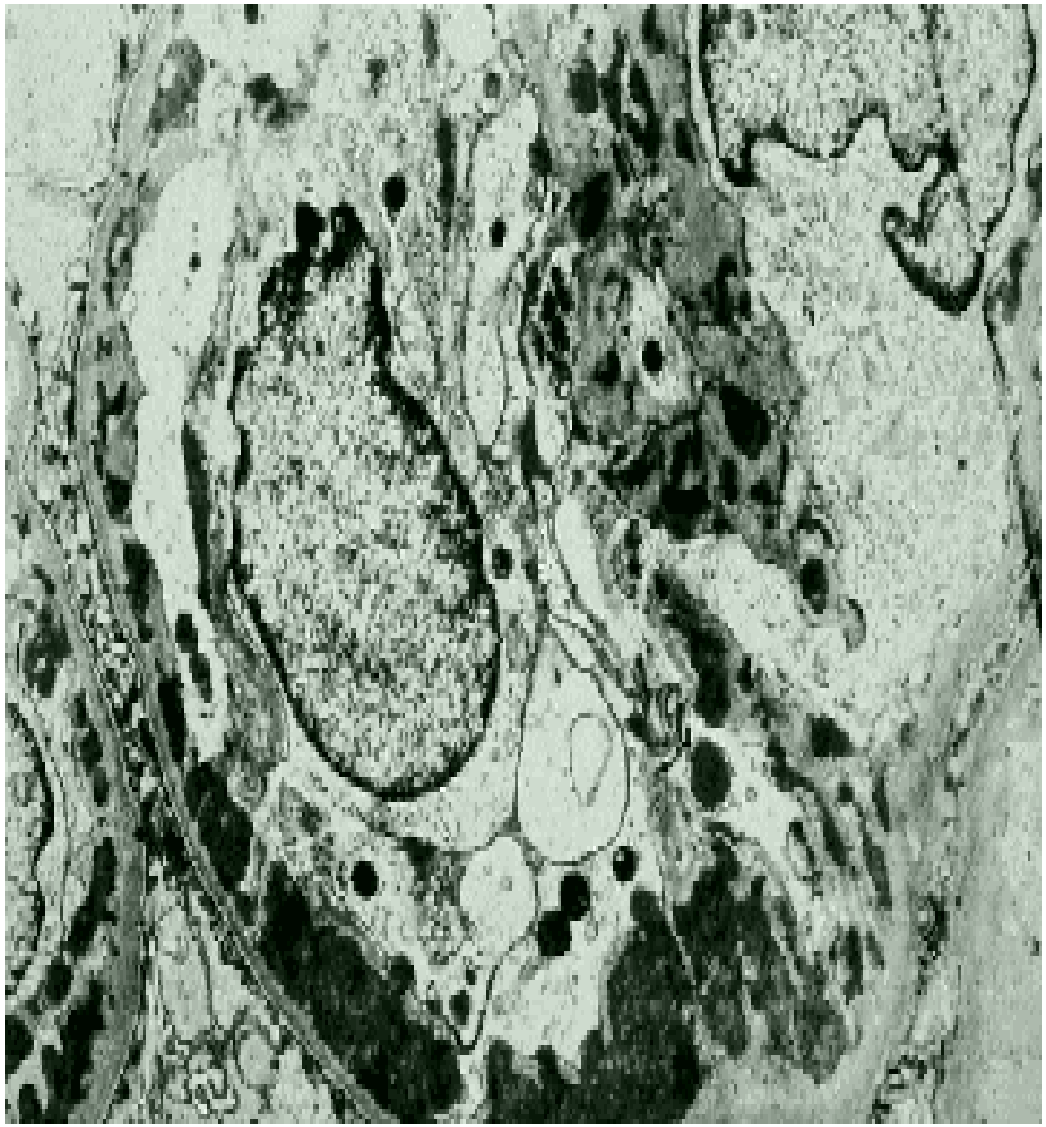
Immunofluorescence showing IgG deposits in a mesangial distribution.



Immunofluorescence showing C3 deposits in a capillary distribution.



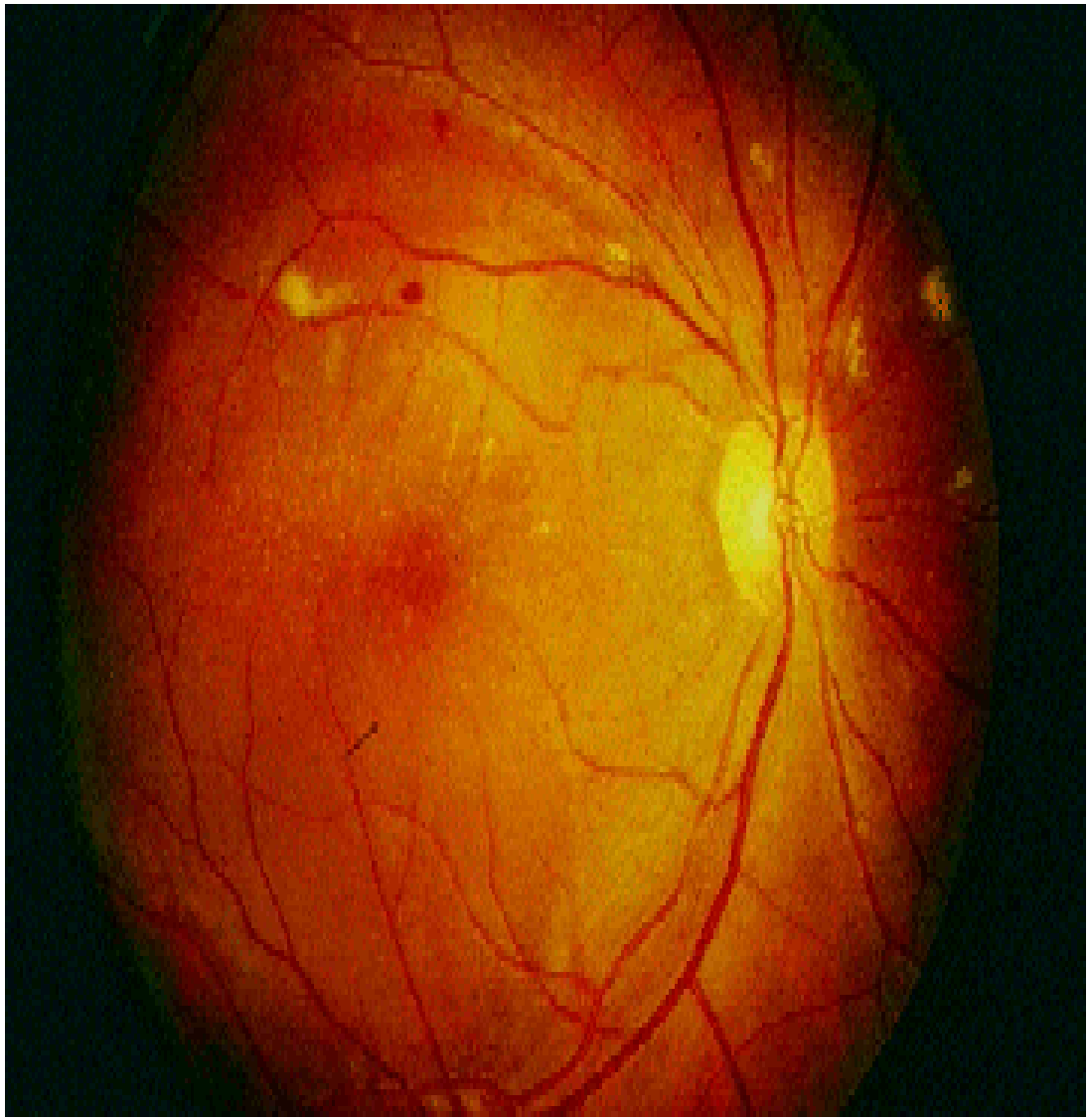
Electron micrograph of a glomerulus showing intra-membranous immune deposits.



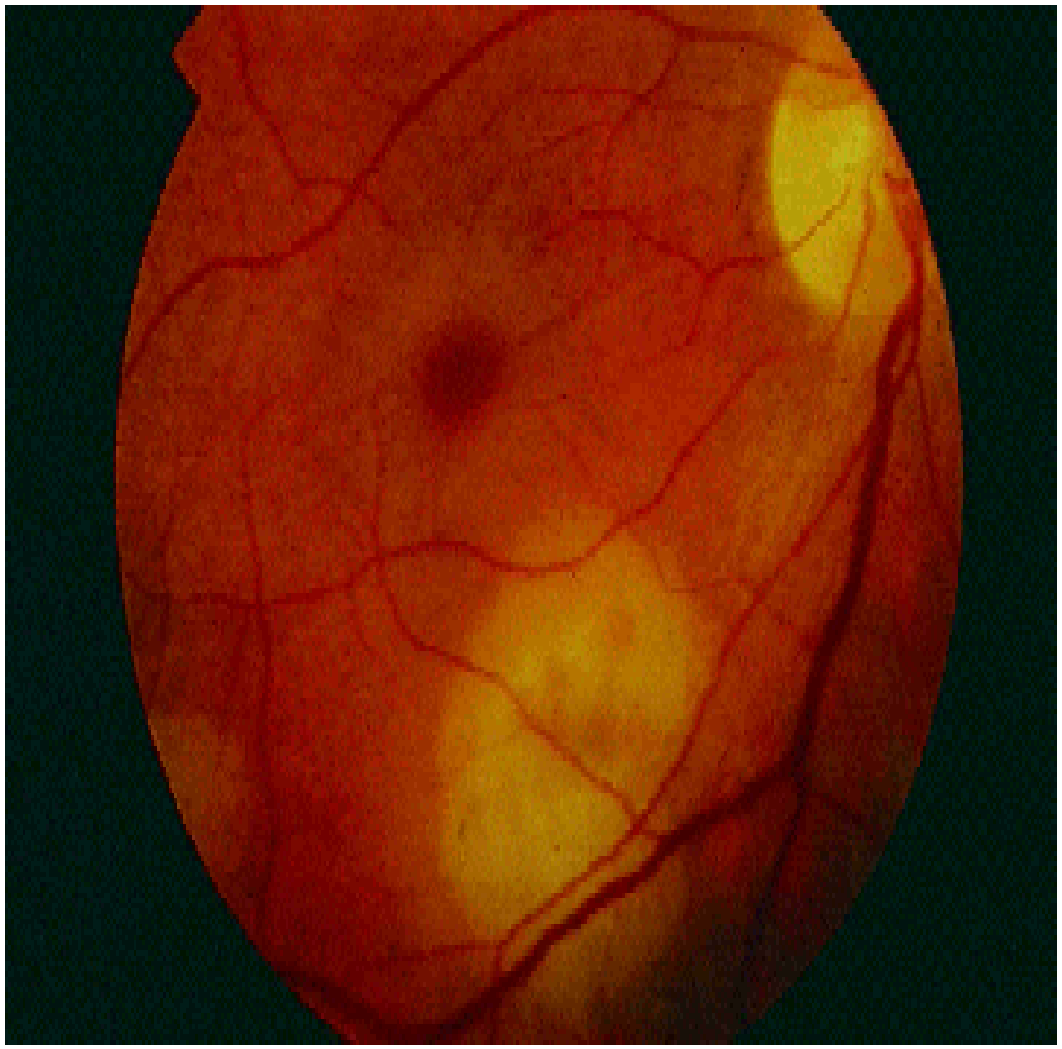
Electron micrograph of a glomerulus showing subendothelial immune deposits.

NEUROPSYCHIATRIC MANIFESTATIONS OF SLE

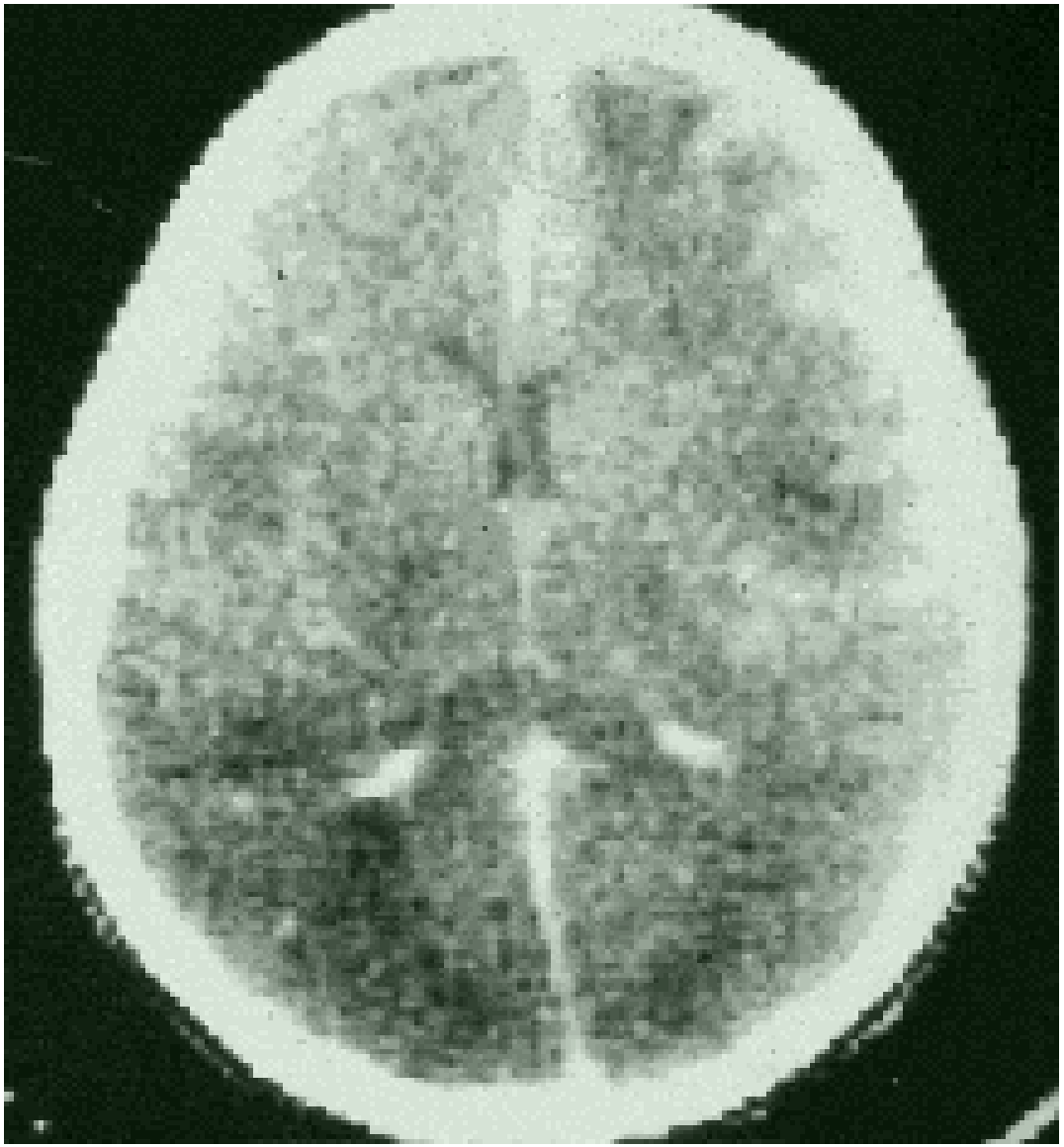
Neurolgic
Seizures - grand mal, petit mal, focal, temporal lobe Stroke syndrome Movement disorder Headache Transverse myelitis Cranial neuropathy Peripheral neuropathy
Psychiatric
Organic brain syndrome Psychosis Psychoneurosis Neurocognitive dysfunction



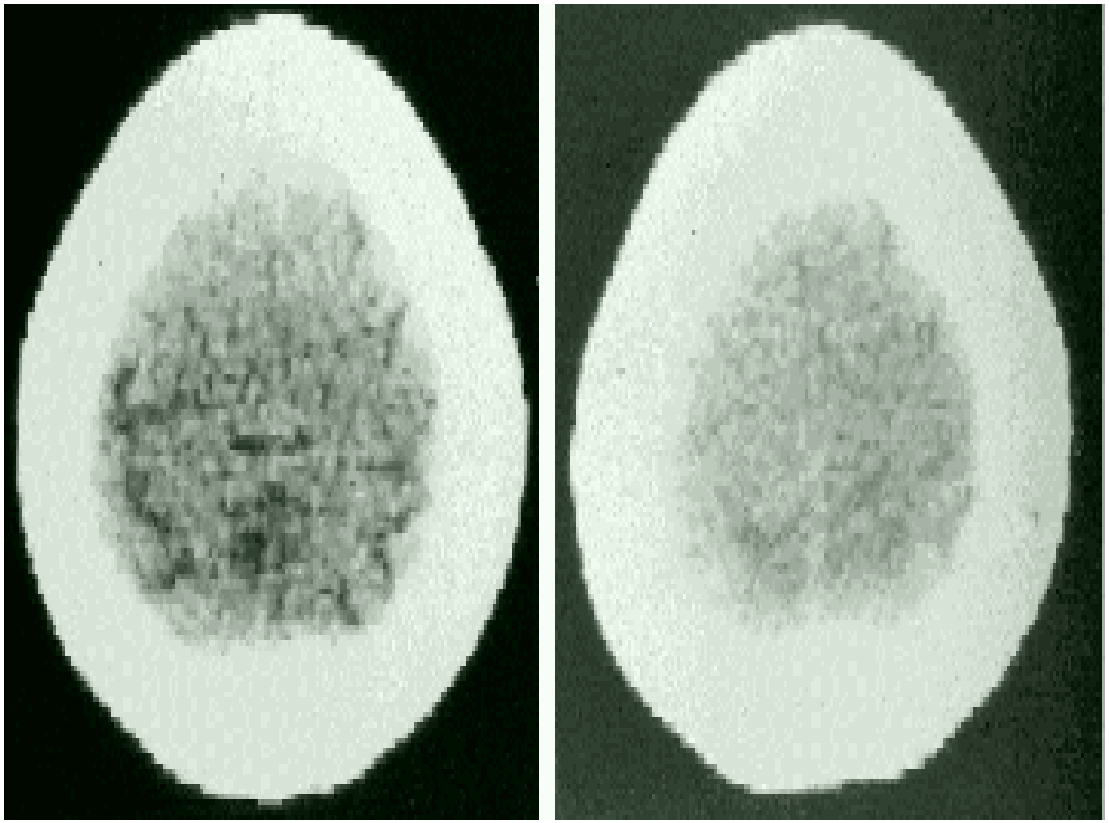
Funduscopic examination in a patient with SLE demonstrating cytoid bodies.



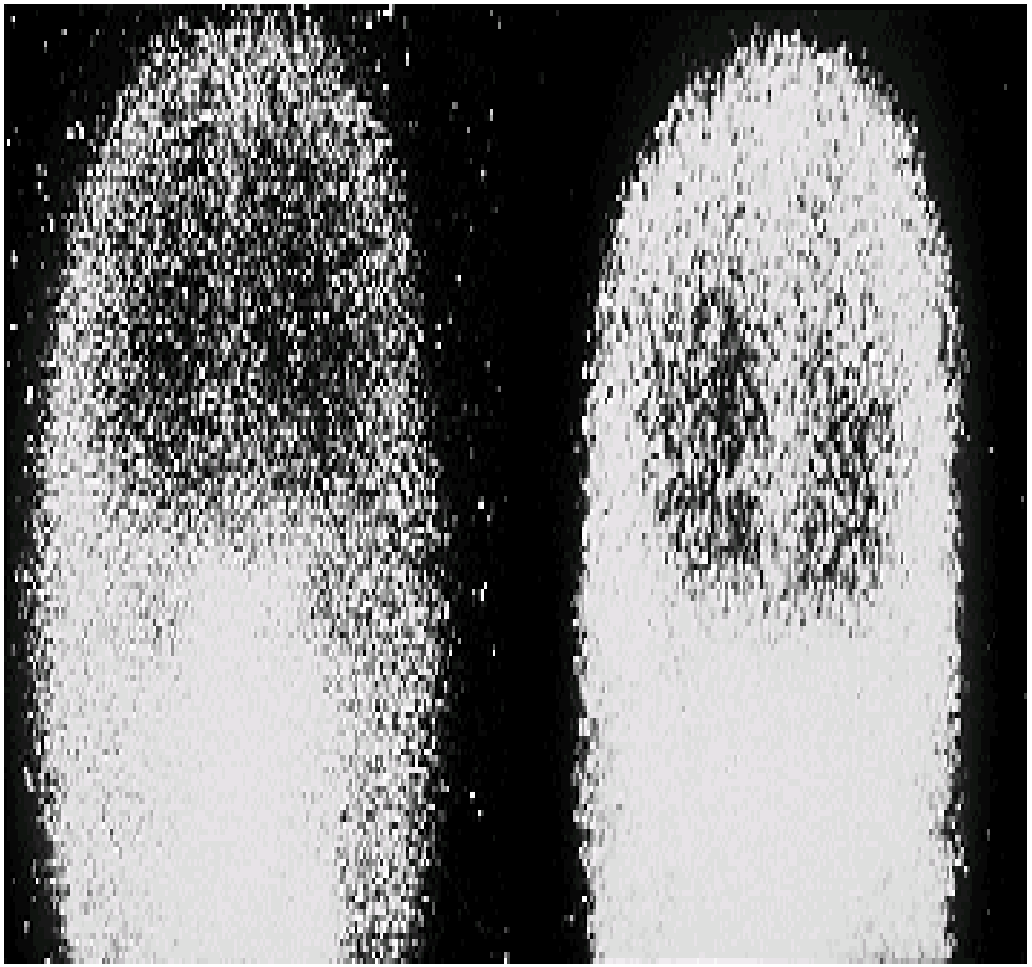
Funduscopic examination in a patient with SLE demonstrating choroidal vasculitis.



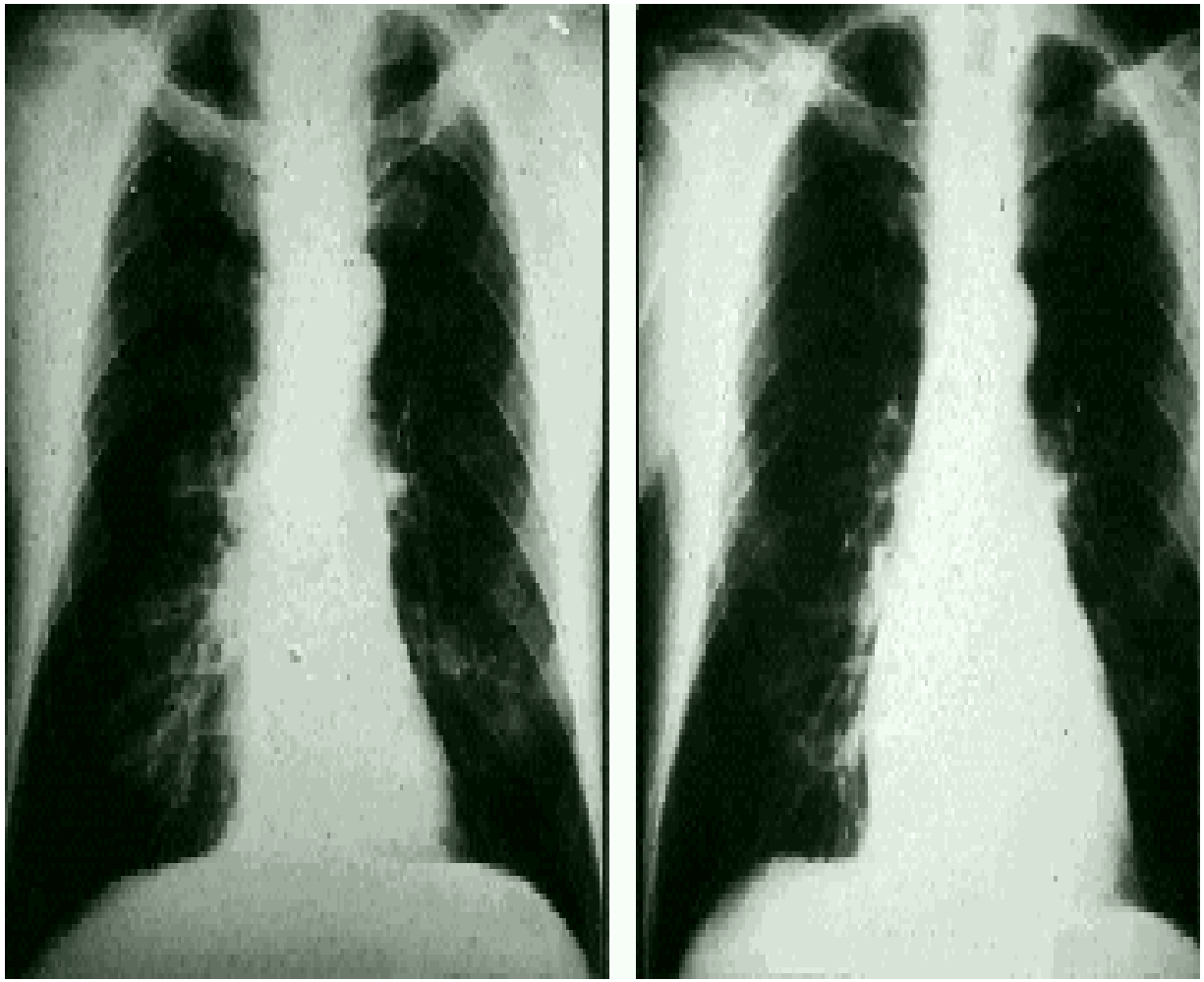
CT scan of the brain demonstrating microinfarcts.



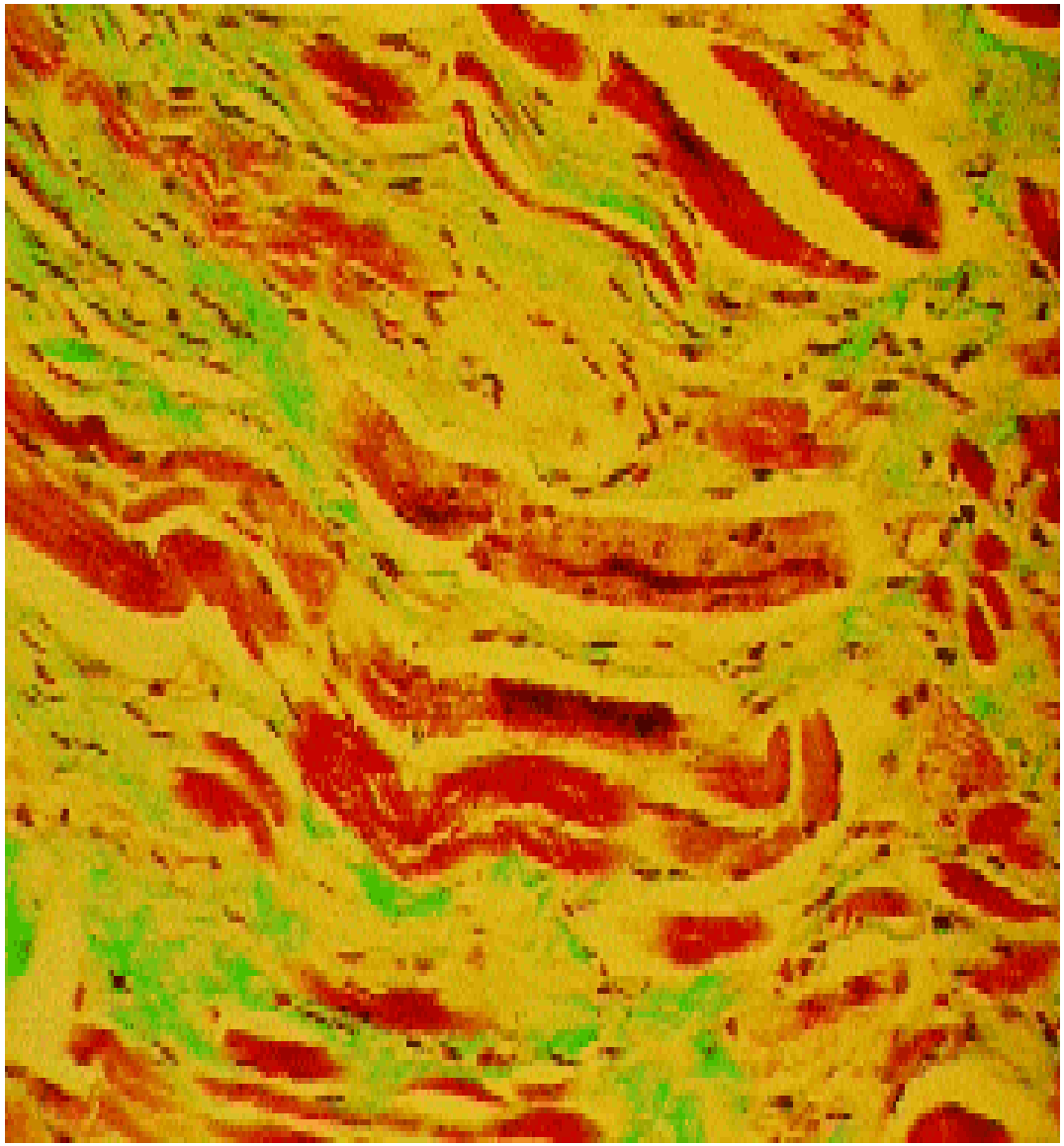
CT scan of the brain demonstrating diffuse cerebral atrophy.



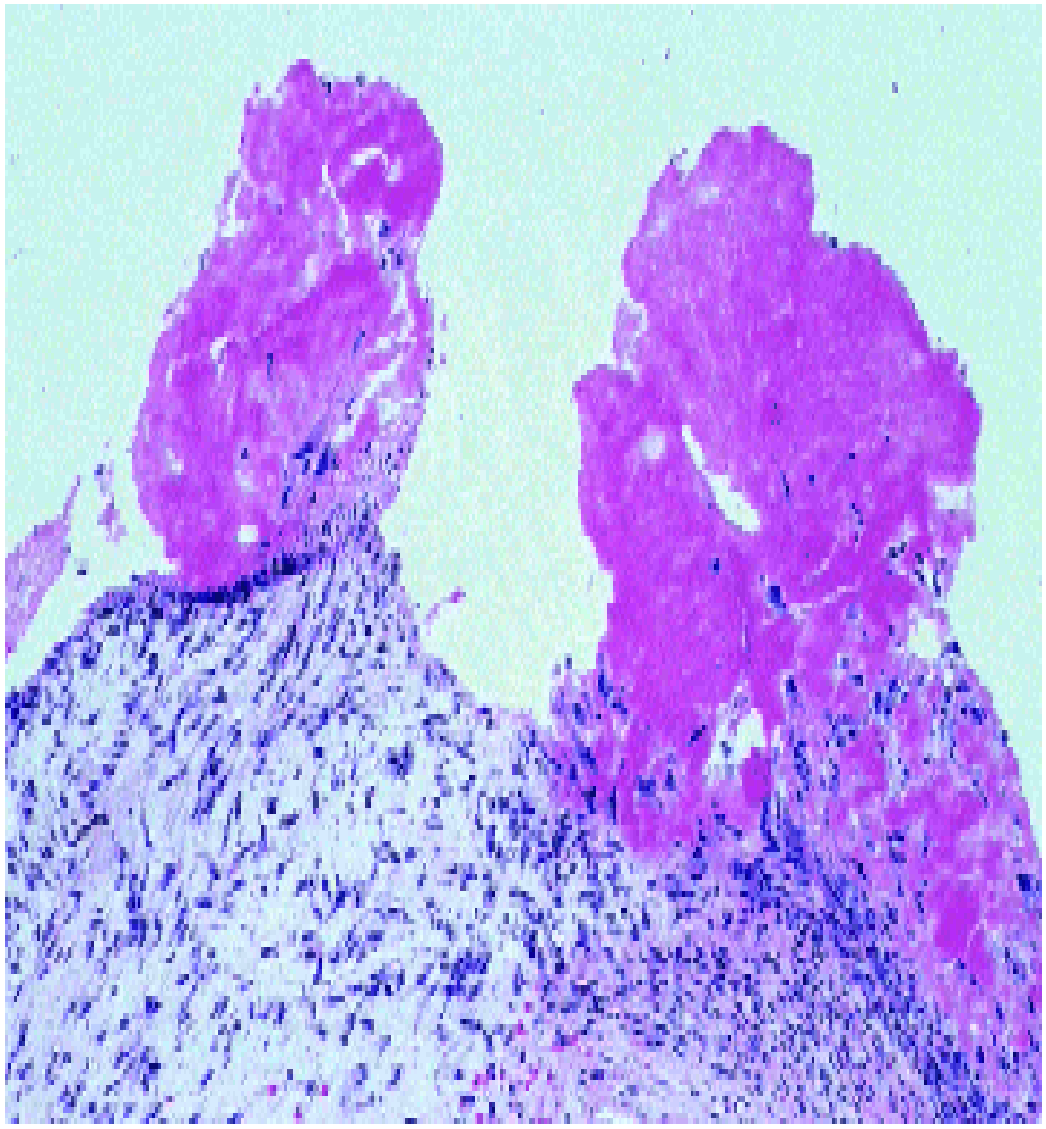
Technetium brain scan demonstrating increased uptake in a ‘draped curtain’ pattern on the anterior view. A normal anterior view is shown on the left for comparison.



Chest radiographs demonstrating the development of a pericardial effusion in a patient with SLE.



Micrograph of the diaphragm in a patient with a shrinking lung syndrome demonstrating fibrosis.



Libman-Sacks endocarditis. Two verrucae on the surface of this valve contain fibrin and necrotic cell debris. Inflammatory cells are localized primarily at the endocardial surface (hematoxylin and eosin).

Diagnosis

CLINICAL ASSOCIATIONS OF AUTOANTIBODIES IN SLE

Antibody	Frequency (%)*	Specificity† for SLE	Clinical subset
dsDNA	60–90	1	Nephritis
ssDNA	90	2	
Histones	50–70	1	
H2A, H2B		1	Drug-induced lupus
ao(SS-A)	20–60	1	Subacute cutaneous lupus,
La(SS-B)	15–40	1	congenital heart block
Sm	10–30	1	? Nephritis, ? CNS
RNP	10–30	1	Mixed connective tissue disease§
U1 RNP	10	1	
P	10–15	1	Lupus psychosis
28S RNA	8–12	1	
Ku/Ki	10	1	
Cardiolipin	10–30	2	Thrombosis, fetal loss, thrombocytopenia

* The frequency depends upon the sensitivity of the test used to detect the antibodies. The higher frequencies are usually observed in ELISAs or radioimmunoassays. In the case of anti-Sm antibodies, higher frequencies are observed in Blacks

† 1 1 5 highly specific; 1 5 antibody present in other autoimmune disorders; 2 5 antibody present in other inflammatory diseases

§ An overlap syndrome of SLE, polymyositis, and scleroderma occuring in higher frequency in patients with anti-RNP and anti-Sm antibodies [56]

Management

PREVENTIVE MEASURES IN LUPUS MANAGEMENT

Regular evaluation	Assess lupus activity. Routine chemistries, blood counts, urinalysis. Control of blood pressure, edema, and hyperlipidemia.
Photoprotection	Avoid intense sun exposure. Sun screens.
Infection control	Suspect infection in all febrile lupus patients. Antibiotic prophylaxis for dental and genitourinary procedures. Influenza and pneumococcal immunizations.
Pregnancy issues	Birth control with very active lupus (especially nephritis) and with cytotoxic or antimetabolite drugs. High-risk obstetrical care required.

DRUGS USED IN LUPUS MANAGEMENT

	Manifestations of SLE				
Approved	**Constitutional**	**Musculoskeletal**	**Serositis**	**Cutaneous**	**Major Organ**
Nonsteroidal drugs	+	+	+		
Corticosteroids Topical				+	
Low dose (i.e. prednisone ≤ 0.5mg/kg/day)	+	+	+	+	
High dose (i.e. prednisone 1.0mg/kg/day) or 1 g i.v. methylprednisolone					+ +
Antimalarials	+	+	+	+	
Investigational					
Azathioprine		+	+	+	+
Cyclophosphamide/chlorambucil					+
Methotrexate		+?	+?		
Dapsone	+?			+	
Immune globulin					+ (thrombocytopenia)
Danazol					+ (thrombocytopenia)
Cyclosporin A					??

Systemic sclerosis

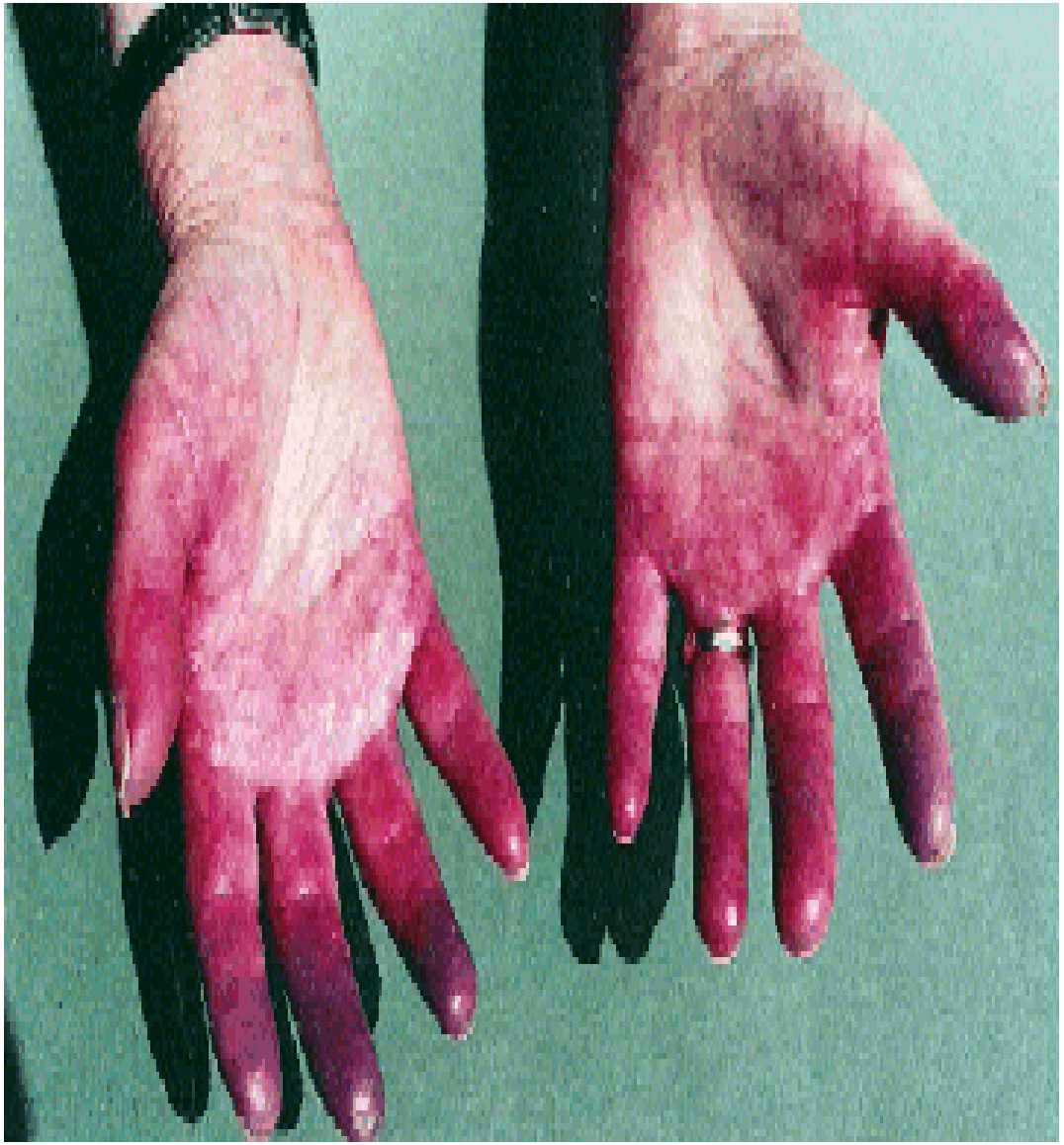
EPIDEMIOLOGY OF SYSTEMIC SCLEROSIS

Peak age (years)	30–50
Sex distribution (F:M)	4:1
Prevalence rate (/100,000)	10–20
Annual incidence (/100,000)	1–2
Geography	Unrestricted
Genetic associations	?? DR5, DRw52, DR4
Relative risk	Unknown

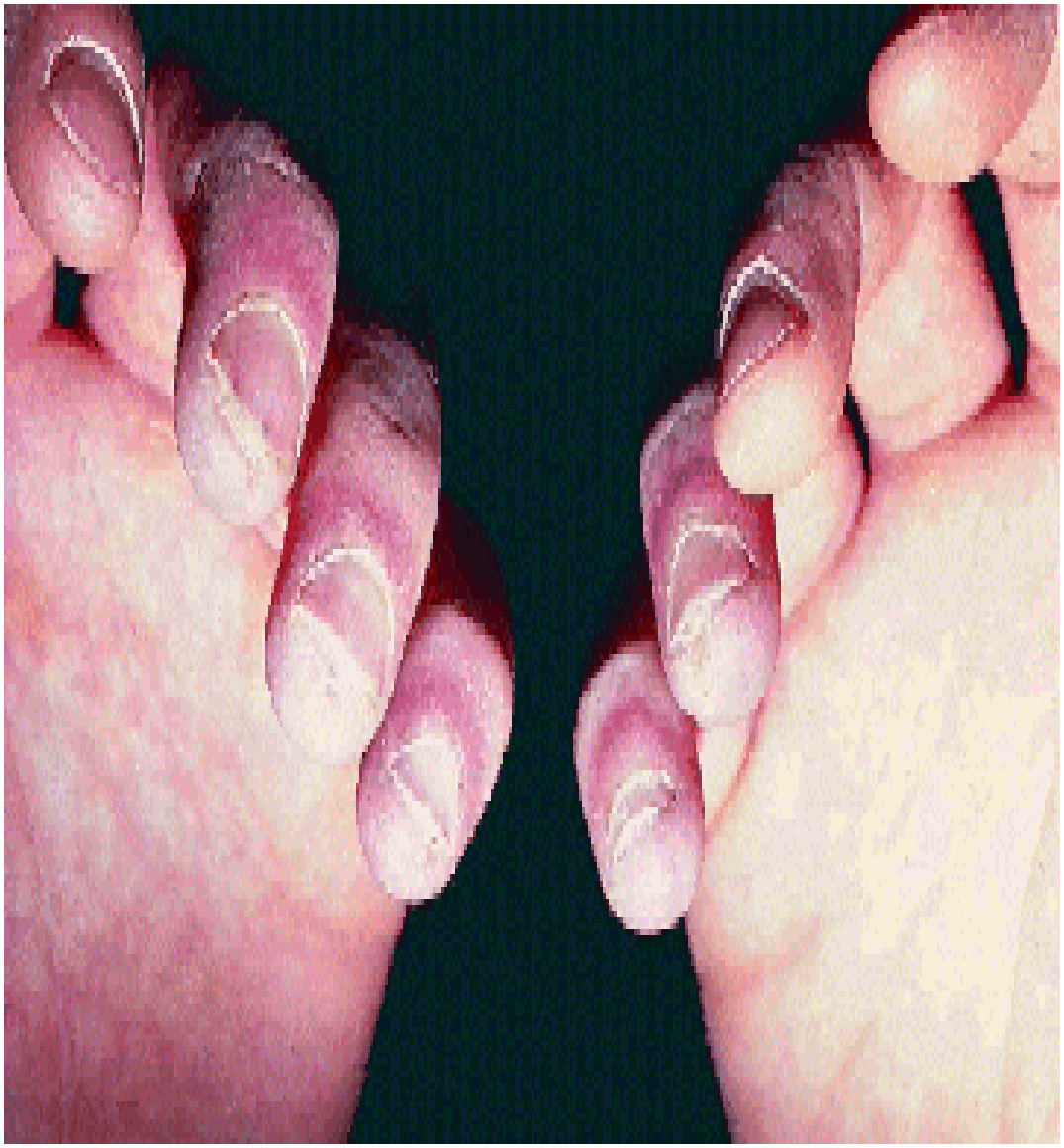
ENVIRONMENTAL FACTORS ASSOCIATED WITH SYSTEMIC SCLEROSIS
Chemicals
Vinyl chloride Benzene Toluene Trichloroethylene Spanish toxic oil
Drugs
Bleomycin Pentazocine L-Tryptophan

CLASSIFICATION OF SYSTEMIC SCLEROSIS

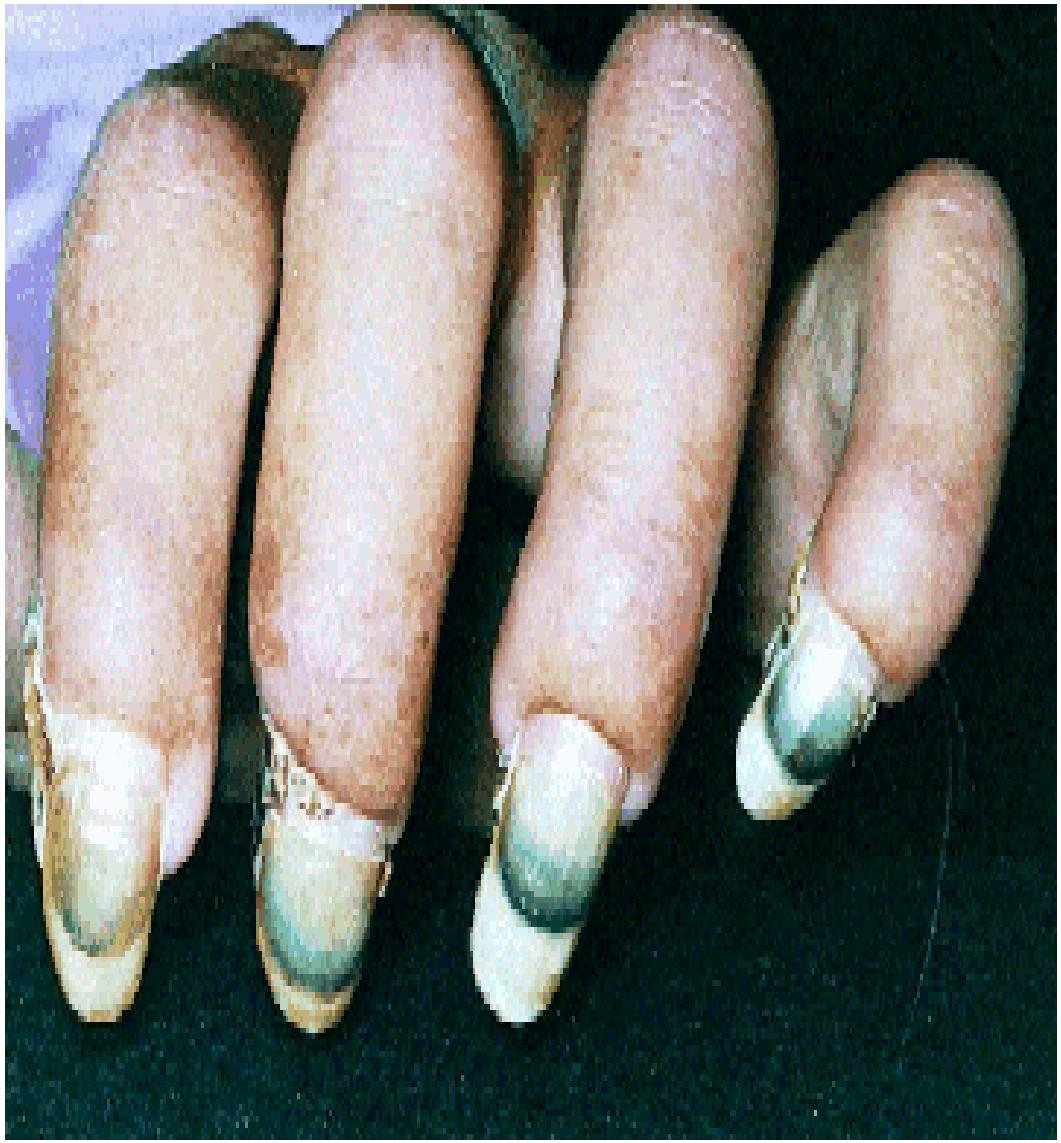
I	Diffuse scleroderma – skin thickening present on the trunk in addition to the face, proximal and distal extremities.
II	Limited scleroderma – skin thickening restricted to sites distal to the elbow and knee but also involving the face and neck. Synonym – CREST syndrome (C – subcutaneous Calcinosis, R – Raynaud's phenomenon, E – Esophageal dysmotility, S – Sclerodactyly, T – Telangiectasias).
III	Sine scleroderma – no clinically apparent skin thickening but with characteristic internal organ changes, vascular and serologic features.
IV	In overlap – criteria fulfilling systemic sclerosis occurring concomitantly with criteria fulfilling diagnoses of SLE, RA or inflammatory muscle disease.
V	Undifferentiated connective tissue disease – Raynaud's phenomenon with clinical and/or laboratory features of systemic sclerosis. These features include serum anticentromere antibody, abnormal nailfold capillaroscopy, finger edema and ischemic injury.



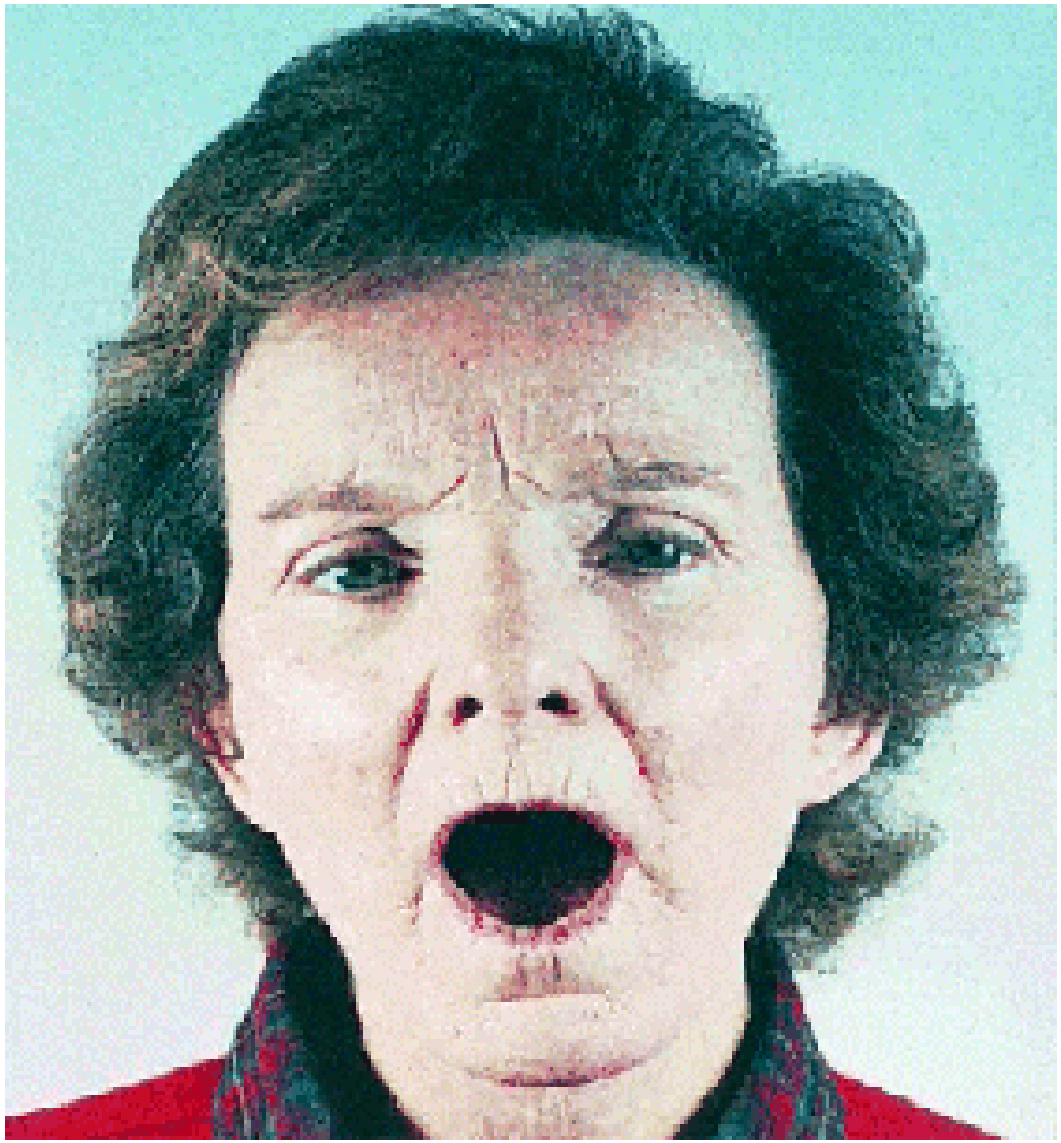
The hands of a young woman with Raynaud’s phenomenon. There is sharply demarcated cyanosis of the fingers with more proximal livedoid venular congestion.



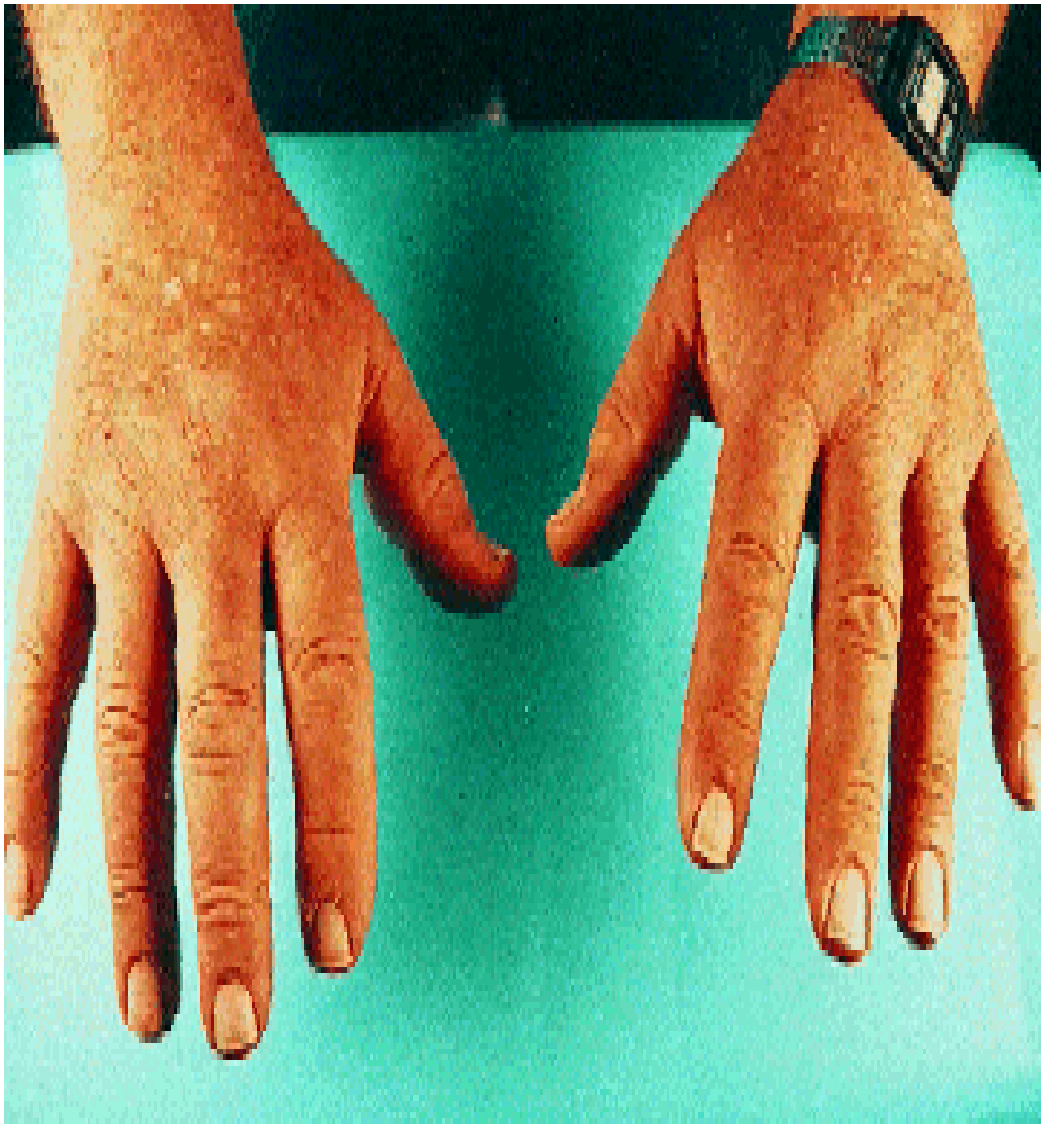
Multiple digital ischemic ulcerations. Small areas of infarction at different stages of development and of variable severity of the fingertips of a young woman with several months of rapidly progressive scleroderma.



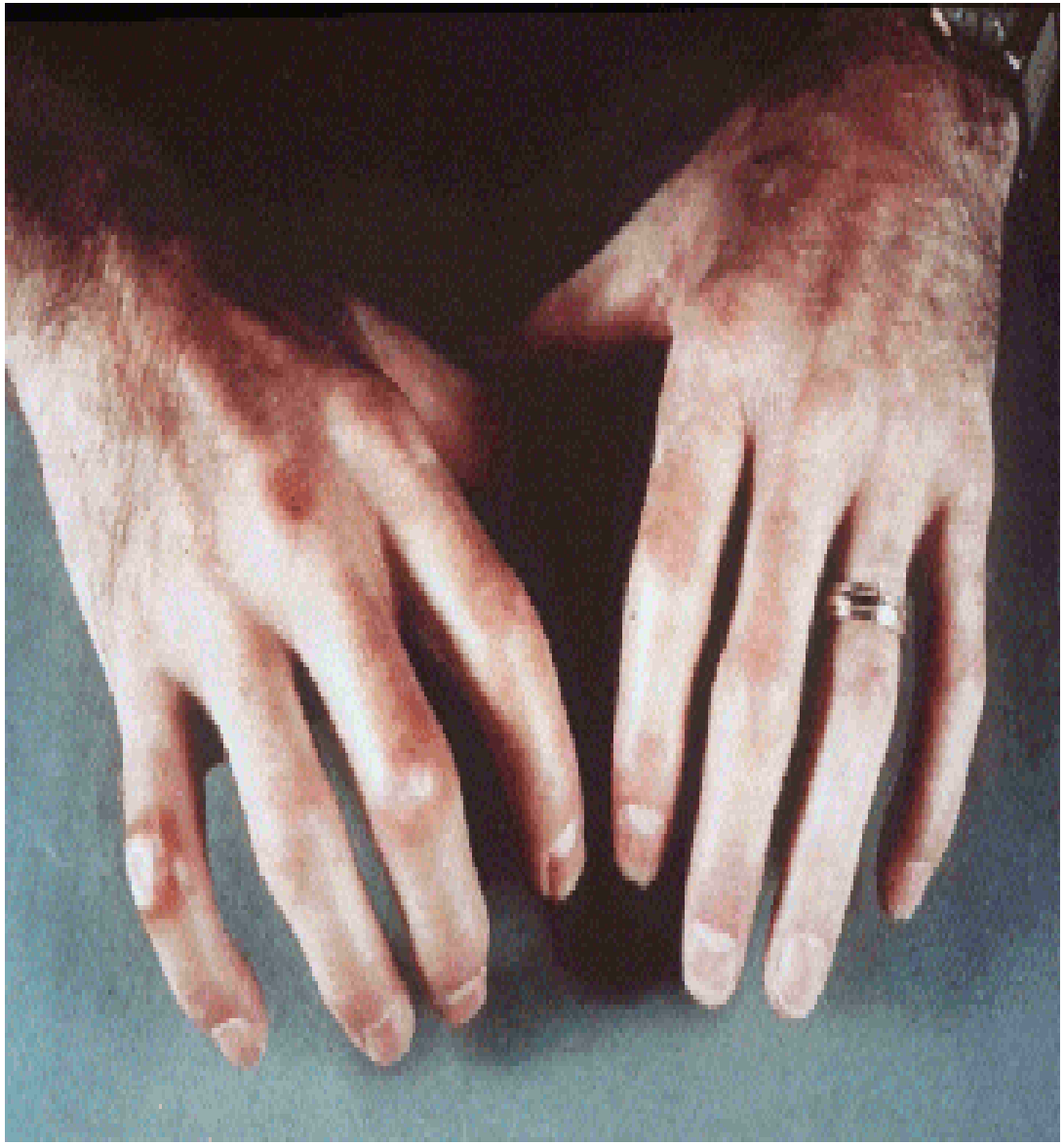
Digital gangrene. Sharply demarcated gangrene of several weeks duration of multiple fingertips of a woman with recent onset of systemic sclerosis. Ultimately, these were managed with surgical debridement.



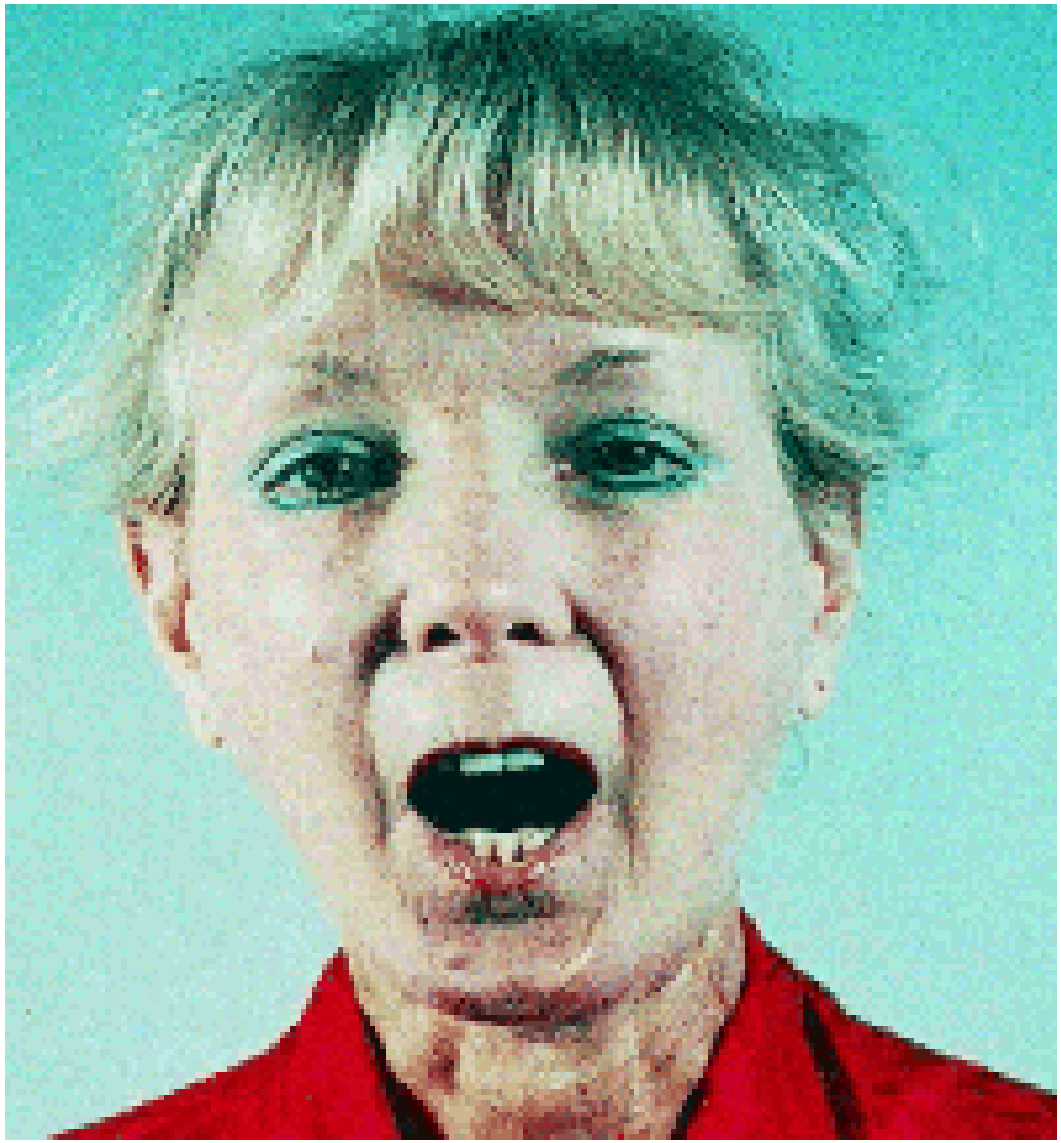
Facial telangiectasias. Punctate telangiectasias are present on the lips and cheeks of this woman with long-standing limited scleroderma.



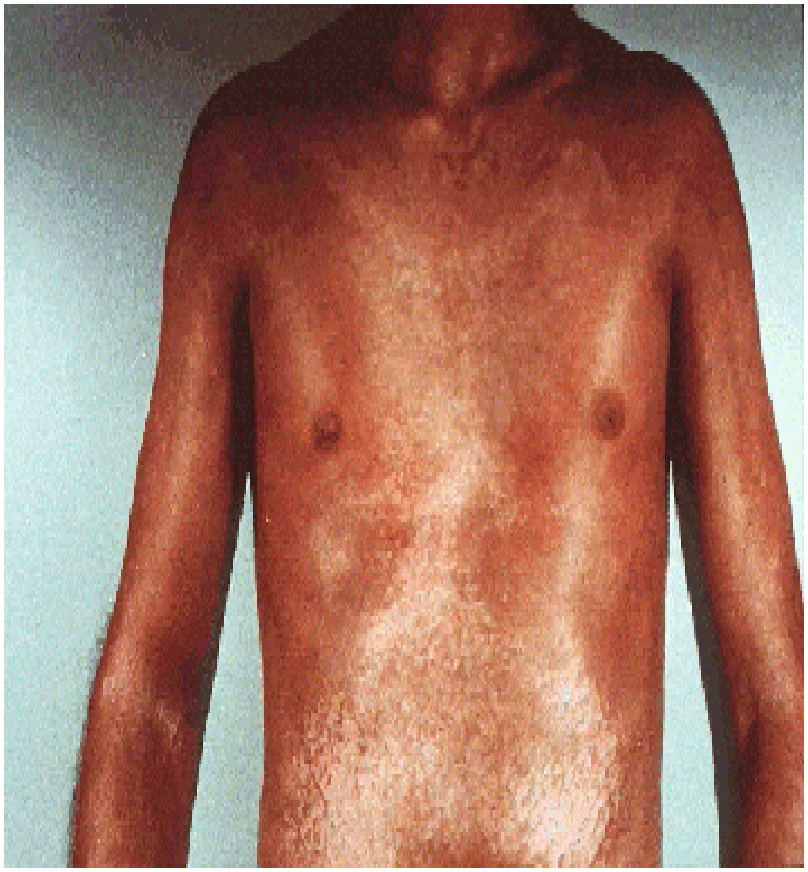
Early, puffy scleroderma. Extensive edema of the fingers and hands in a man with several months of preceding Raynaud's phenomenon. Skin was not clinically thickened but became so on follow up.



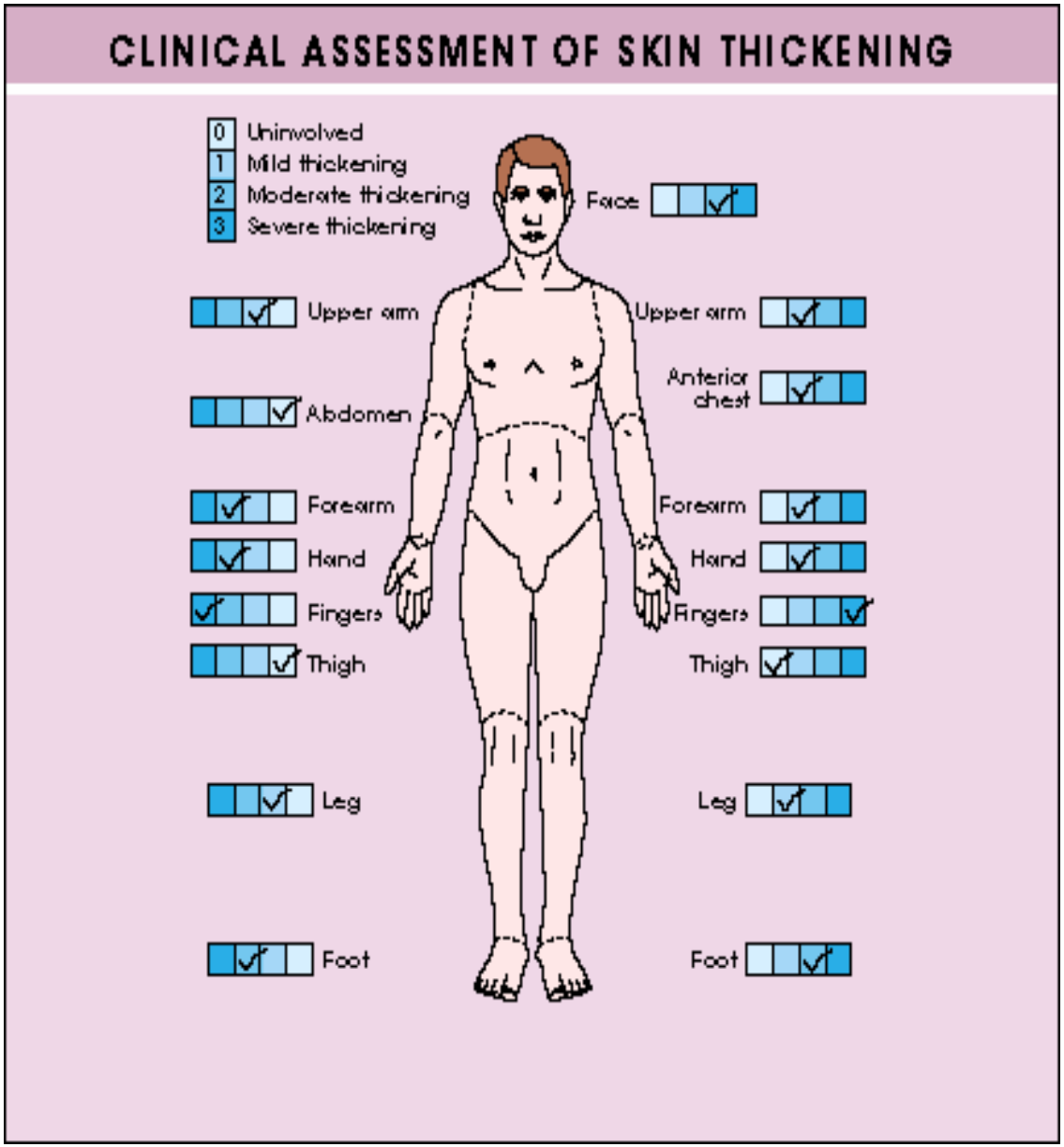
Digital scleroderma. Advanced changes of scleroderma in the hand of a man with diffuse disease of several months duration. Fingers are held at maximum active extension.



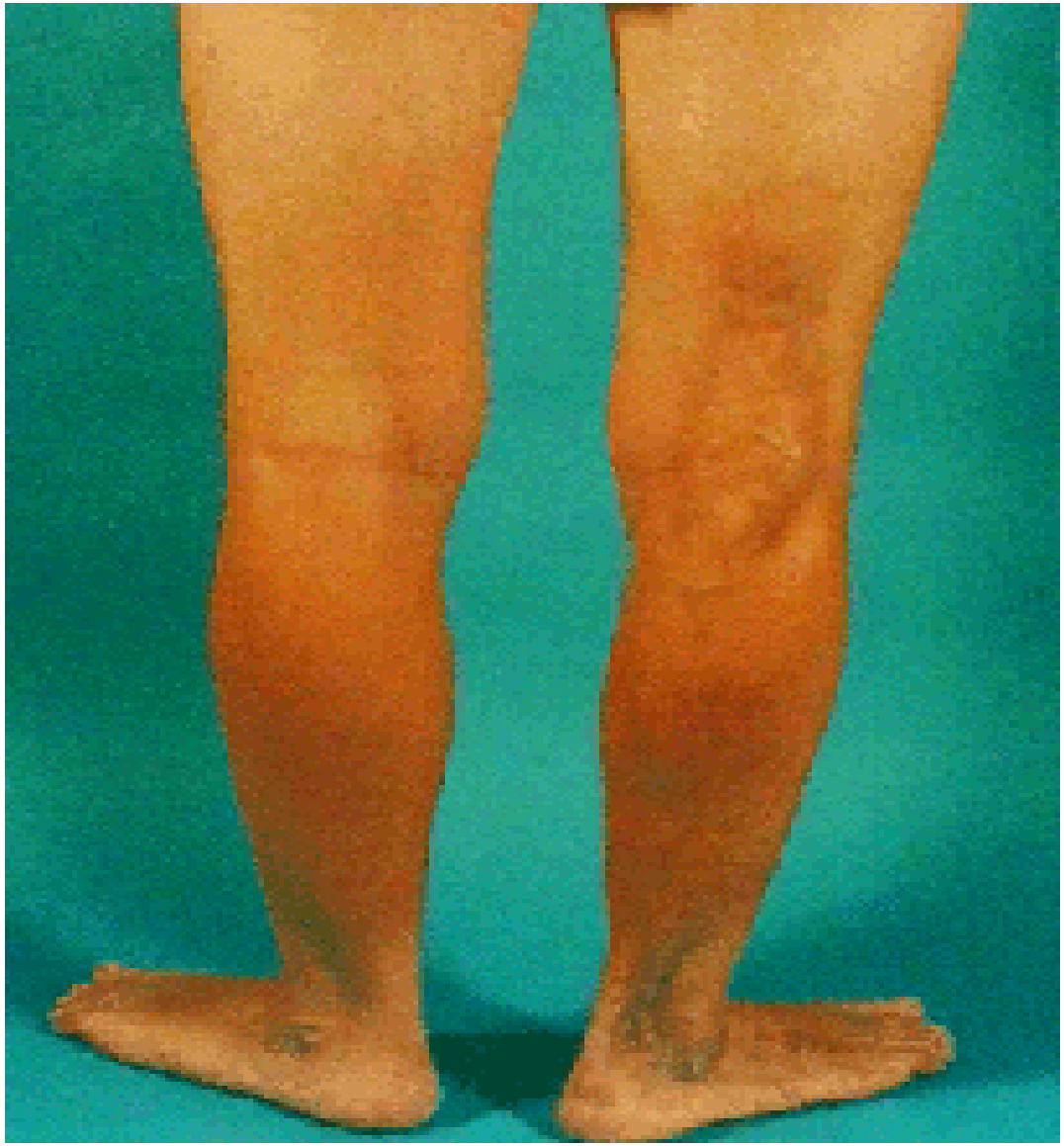
Facial scleroderma. Taut smooth skin over the face of a woman with long-standing disease. Oral aperture is reduced and radial furrowing is present about the lips.



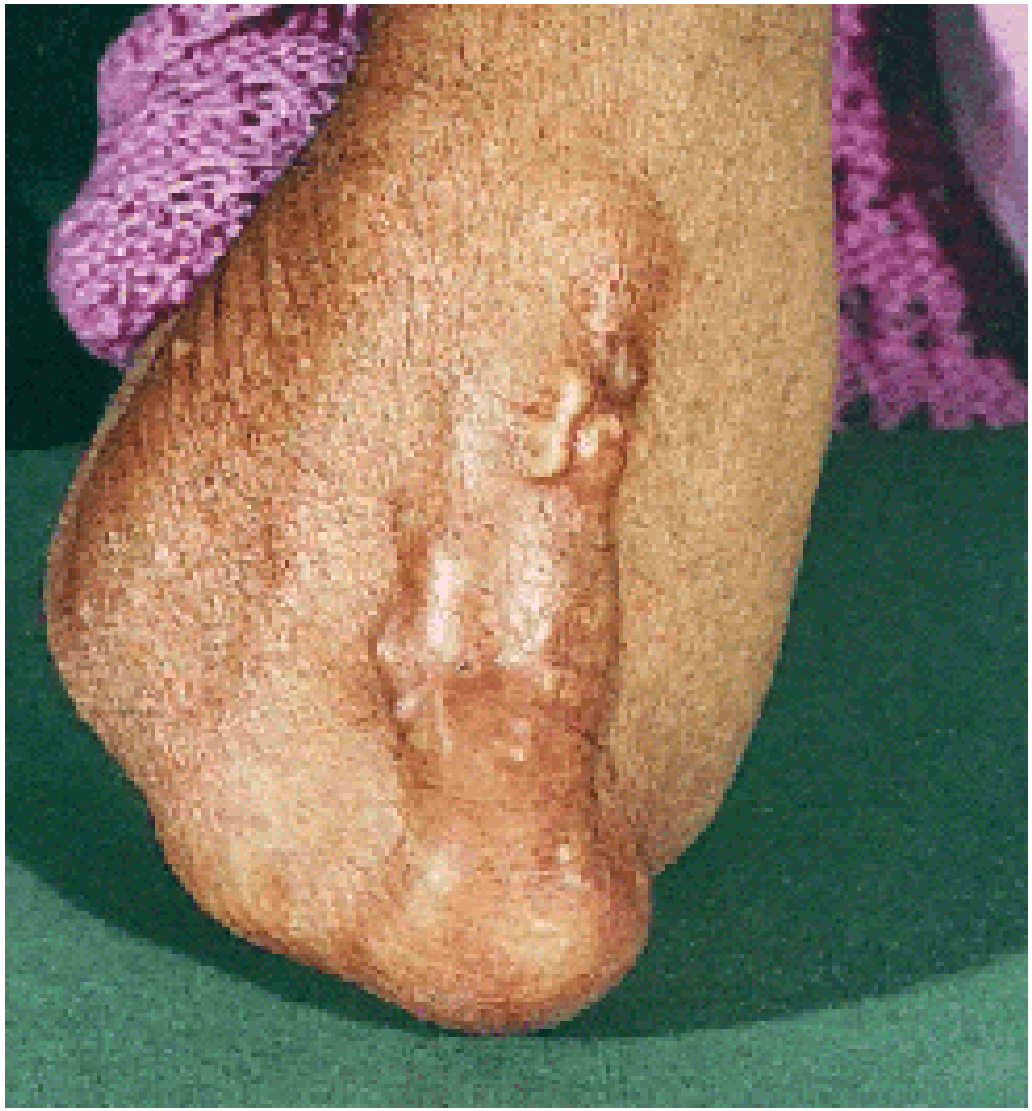
Truncal scleroderma. Skin thickening of the chest and abdomen permit classification as diffuse scleroderma. There is both hyperpigmentation of the chest and hypopigmentation of the upper abdomen.



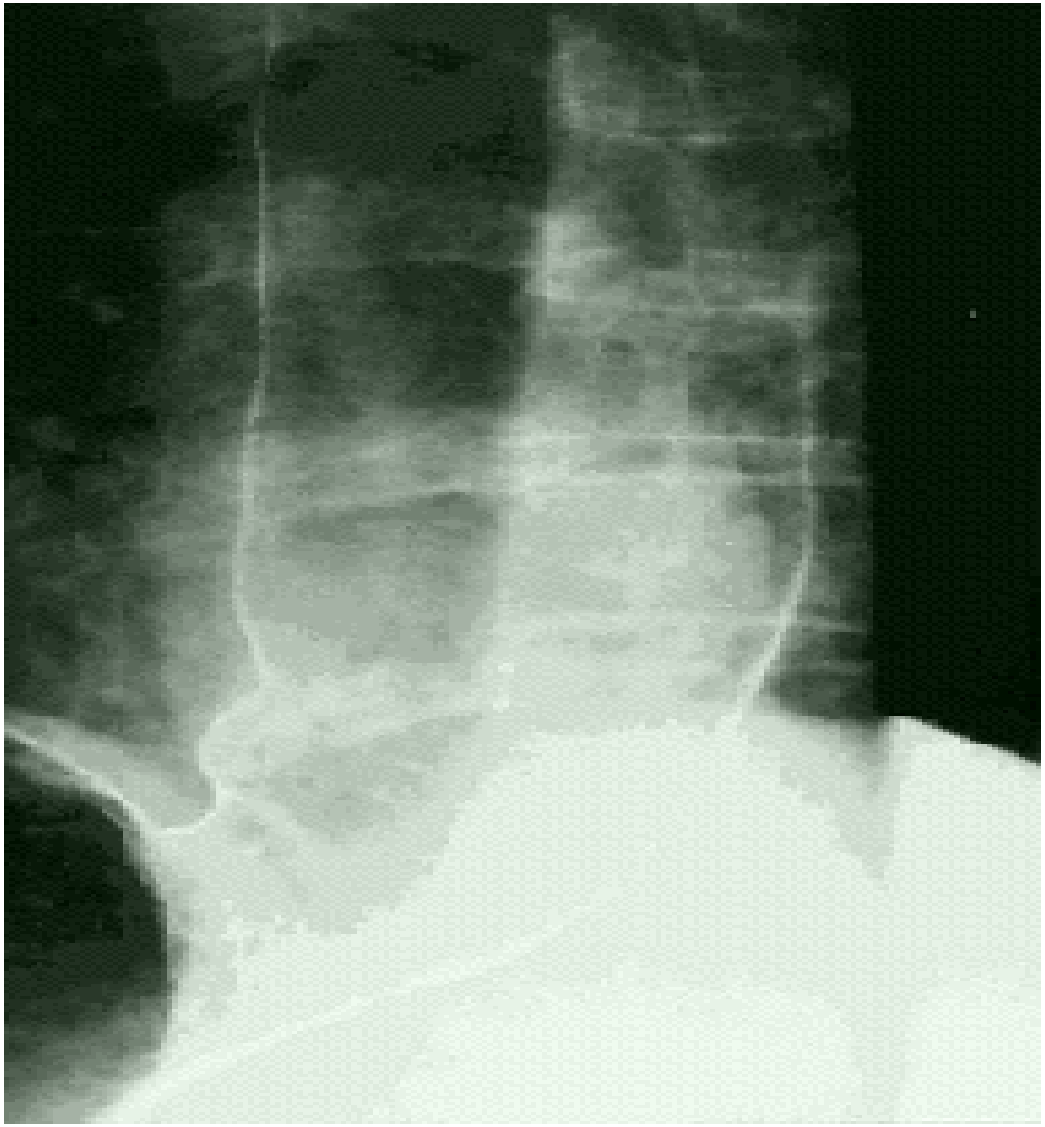
Total skin score. Semiquantitative estimates by clinical palpation of the extent and severity of scleroderma skin change. In all cases, the initial areas involved are peripheral and are the most severely affected. The mild skin change on the chest permits classification of this subject as diffuse scleroderma.



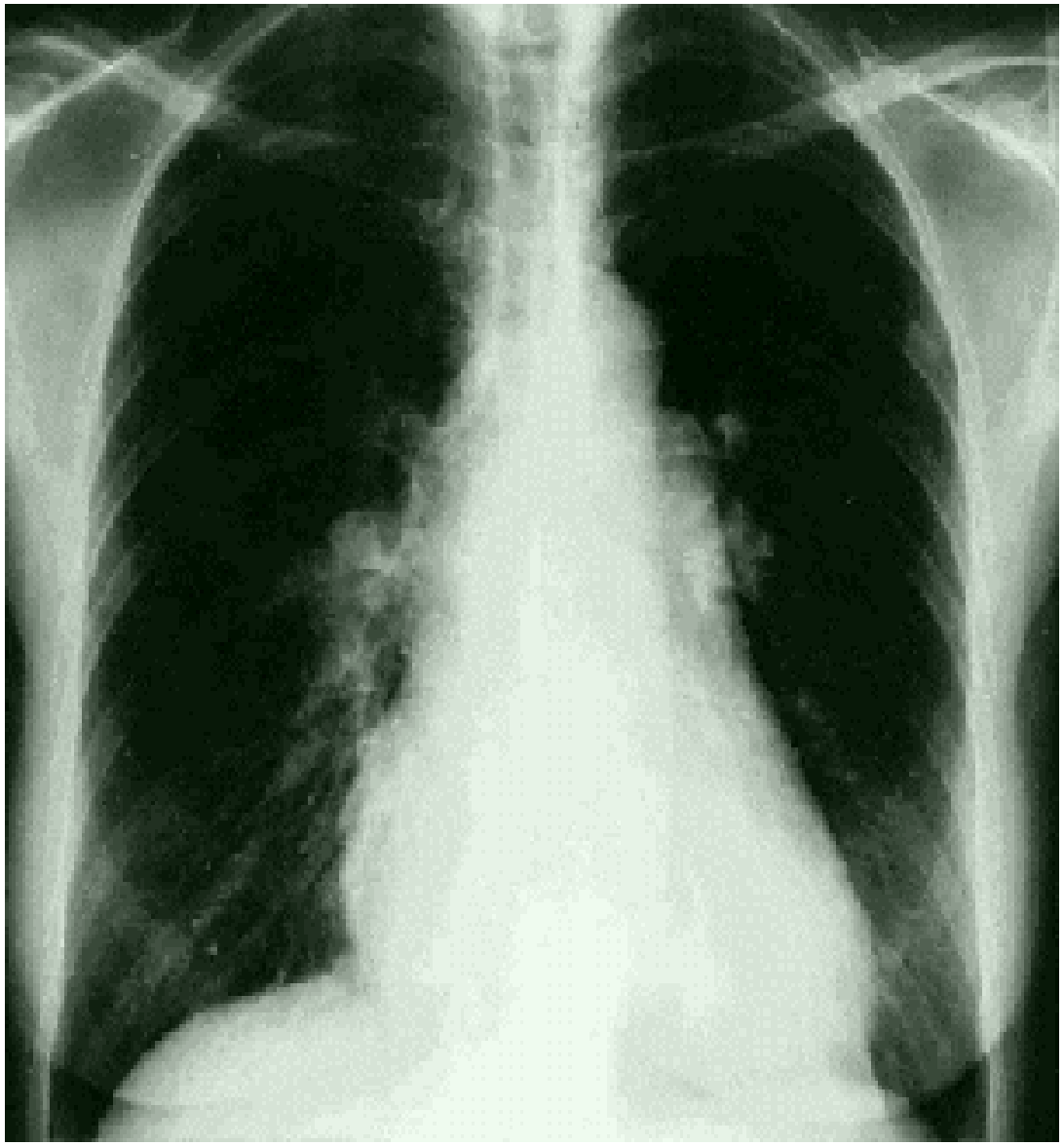
Linear scleroderma. Present since age 5 in this 12-year-old girl, atrophy of the thigh and calf are apparent. As growth continues, leg length discrepancy would be anticipated.



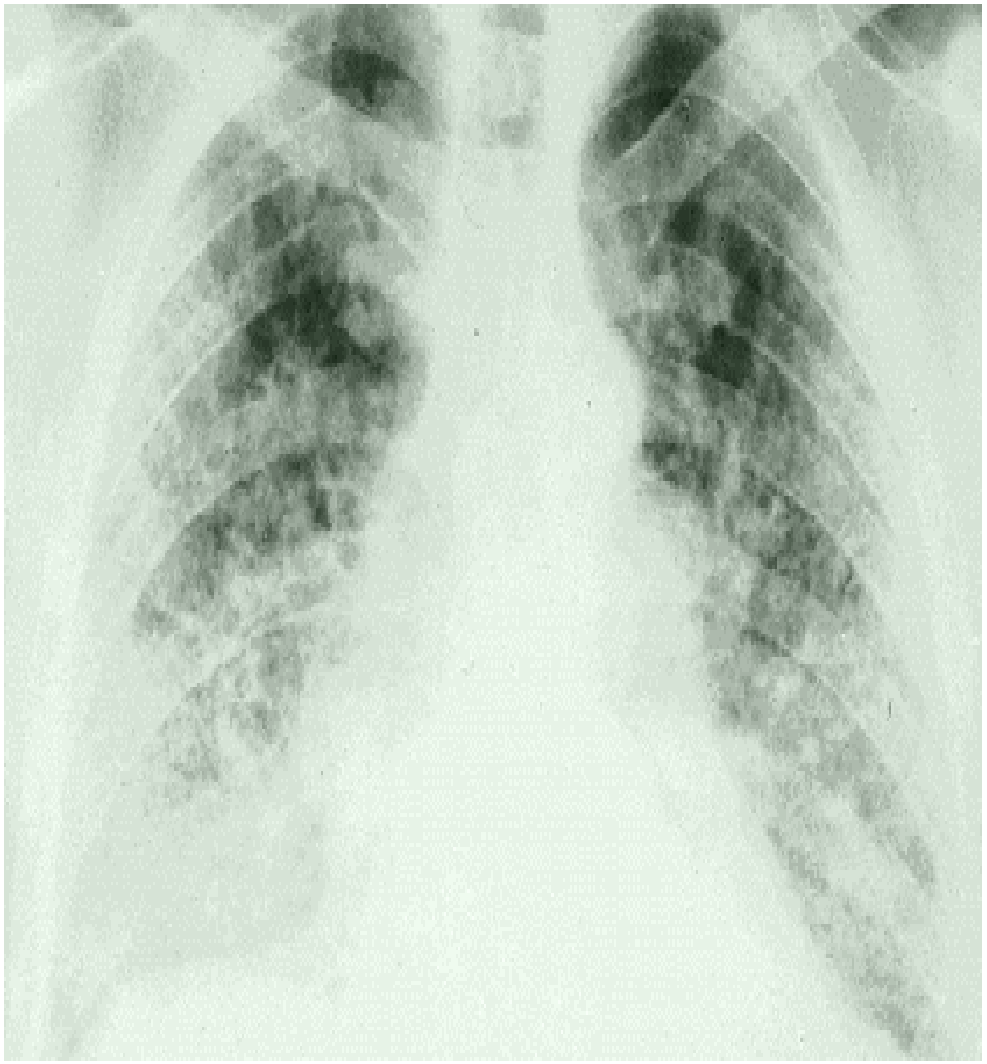
Subcutaneous calcinosis. Extensive calcinosis is present in the preolecranon area of this woman with long-standing limited scleroderma.



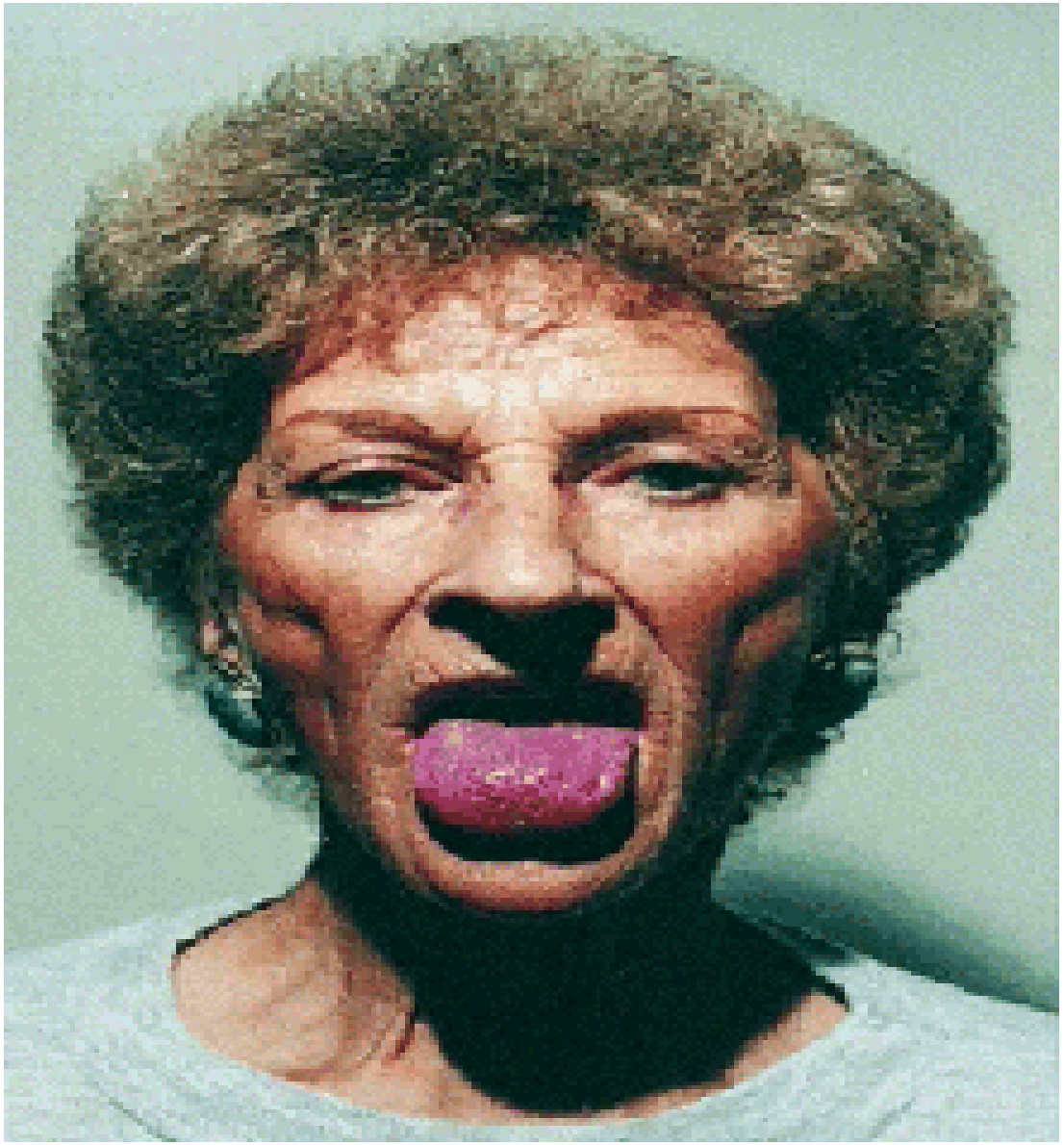
Esophageal involvement. This barium contrast study reveals the characteristic findings of a hypomotile lower esophagus and an incompetent lower esophageal sphincter.



Pulmonary hypertension. This patient had severe pulmonary hypertension documented on right heart catheterization. The lung fields are clear but the left heart border is straightened from elevation of the pulmonary conus and there is enlargement of the pulmonary arteries. This syndrome is most typical of later years of limited scleroderma.



Pulmonary interstitial fibrosis. Extensive parenchymal disease is apparent on this chest radiograph. Pulmonary functions confirmed severe restriction in this syndrome which occurs in both diffuse and limited scleroderma.

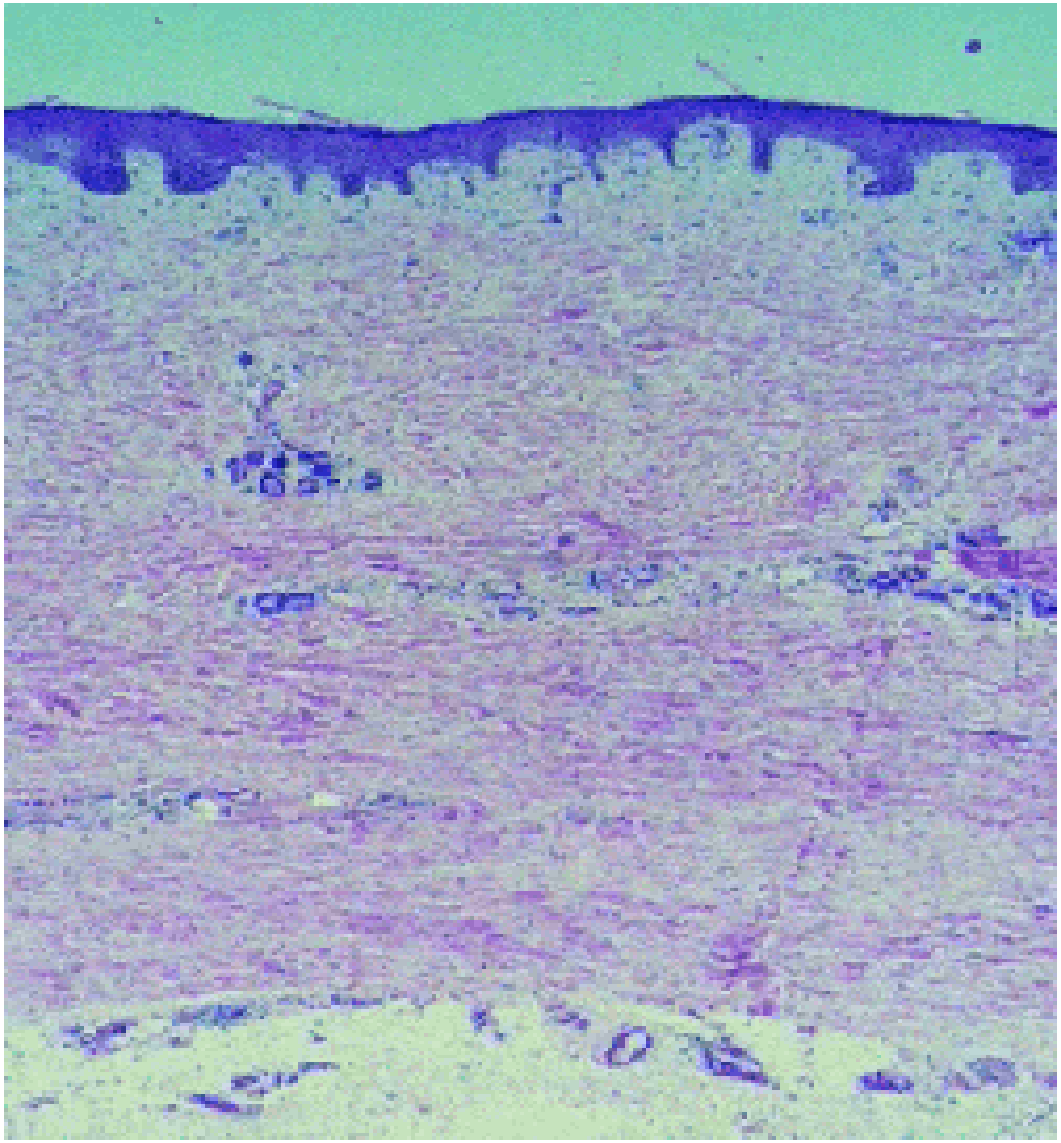


Sicca syndrome in scleroderma. The tongue is parched and hypopapillated in this woman with sicca syndrome complicating long-standing diffuse scleroderma.

CLINICAL DIFFERENCES BETWEEN LIMITED AND DIFFUSE DISEASE	
Limited scleroderma	Diffuse scleroderma
Long duration of Raynaud's phenomenon	Short duration of Raynaud's with skin changes often occurring before Raynaud's
Puffy fingers intermittently for long time	Swollen hands and legs
Slow pace of progression	Rapid pace of progression
Mild constitutional symptoms, mild arthralgias, rare tendon rubs	Many constitutional symptoms, arthralgias/arthritis, carpal tunnel and tendon rubs
Most common problems – digital ulcers, esophageal, small bowel, pulmonary fibrosis	All organ systems involved – pulmonary fibrosis, cardiac and renal crisis most common causes of death
Pulmonary hypertension (10%) fatal	Rare pulmonary hypertension
Anticentromere antibody (50–90%)	Anticentromere antibody (5%)
Anti-Scl-70 antibody (10–15%)	Anti-Scl-70 antibody (20–30%)

AUTOANTIBODIES IN SYSTEMIC SCLEROSIS

Autoantigen recognized	Percentage of systemic sclerosis patients
Nuclei	90%
Centromere	5% (50–90% of limited)
Scl-70 (topoisomerase I)	20–30% (10–15% of limited)
Nucleoli	30–80%



Excess collagen deposition in the dermis of a patient with systemic sclerosis. There is marked thickening of the dermis with collagen and some inflammatory infiltrate surrounding vasculature. There is entrapment of cutaneous glands. Although atrophy of the epidermal rete pegs is a frequent finding, it is not evident in this example. (Hematoxylin and eosin).

TREATMENT OF JOINT AND TENDON INVOLVEMENT

Pharmacologic measures:

- Nonsteroidal anti-inflammatory drugs
- Adequate analgesia
- Rarely, low dose steroids

Physical measures:

- Aggressive active and passive physical therapy
- Extension and flexion exercise to preserve and prevent loss of joint motion
- Dynamic splinting not well tolerated

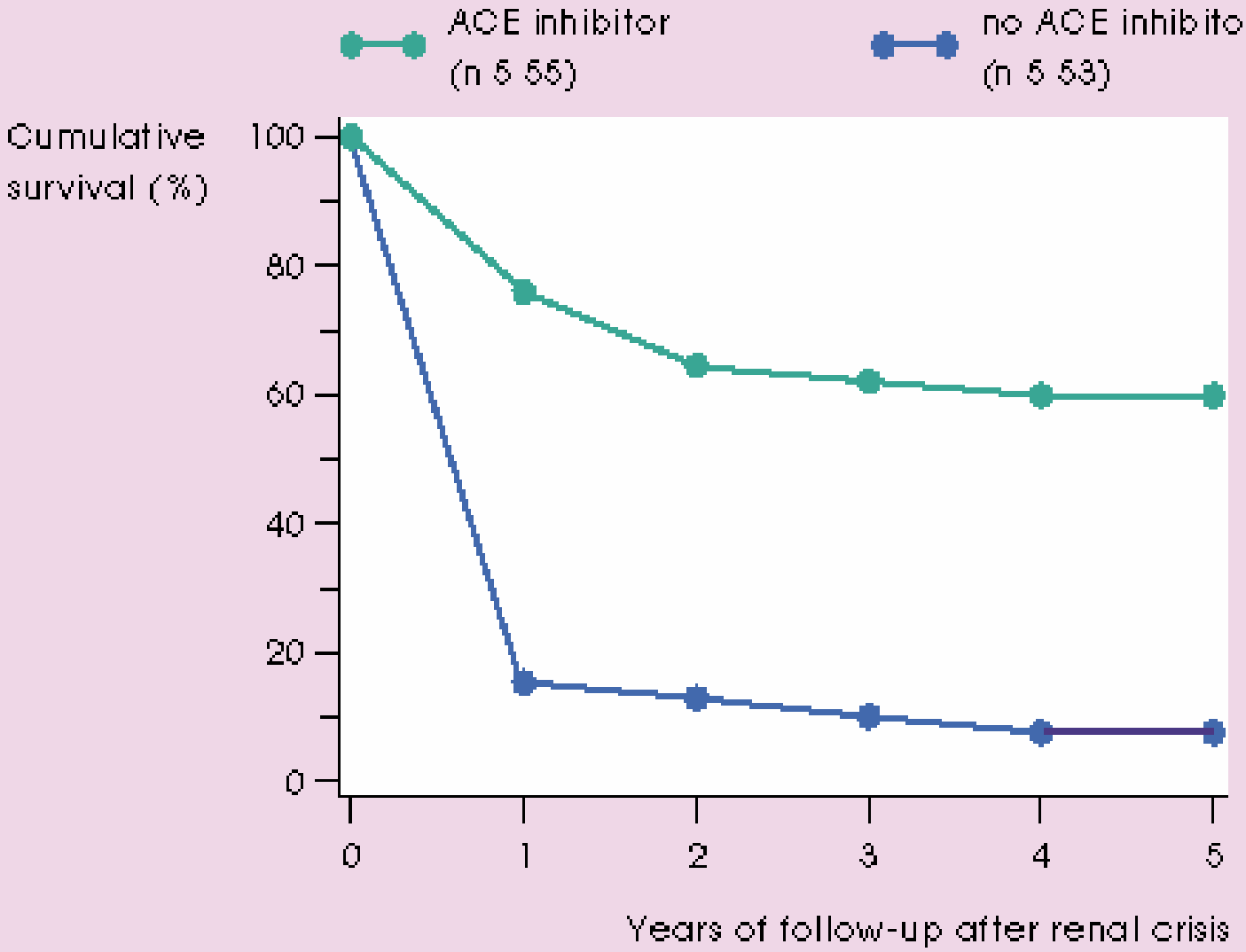
TREATMENT OF GASTROINTESTINAL INVOLVEMENT

Symptom	Gastrointestinal abnormality	Treatment
Heartburn	Esophageal reflux from decreased lower esophageal pressure	Mild – simple eating adjustments, antacids Moderate – H2 receptor blocking agents, cytoprotective agent (sucralfate), avoid calcium channel blockers and nonsteroidal anti-inflammatory drugs Severe – omeprazole
Dysphagia, vomiting	Esophageal dysmotility	Eat upright with liquids Prokinetic drugs (metaclopromide, cisapride)
	Esophageal stricture from chronic esophagitis	Esophageal dilatation Reflux treatment (above)
Nausea, vomiting, bloating	Gastric atony (infrequent)	Prokinetic drugs, ? erythromycin
Bloating, diarrhea	Small bowel hypomotility Bacterial growth	Prokinetic drugs Broad spectrum antibiotics Nutritional or parenteral supplement as needed
Bloating, pseudo-obstruction	Small and large intestinal hypomotility and dilatation	Conservative decompression with nasogastric suction and bowel rest Avoid surgery Prokinetic drugs Antibiotic trial
Constipation	Large intestinal hypomotility	Stool softeners Bulk to stimulate muscles

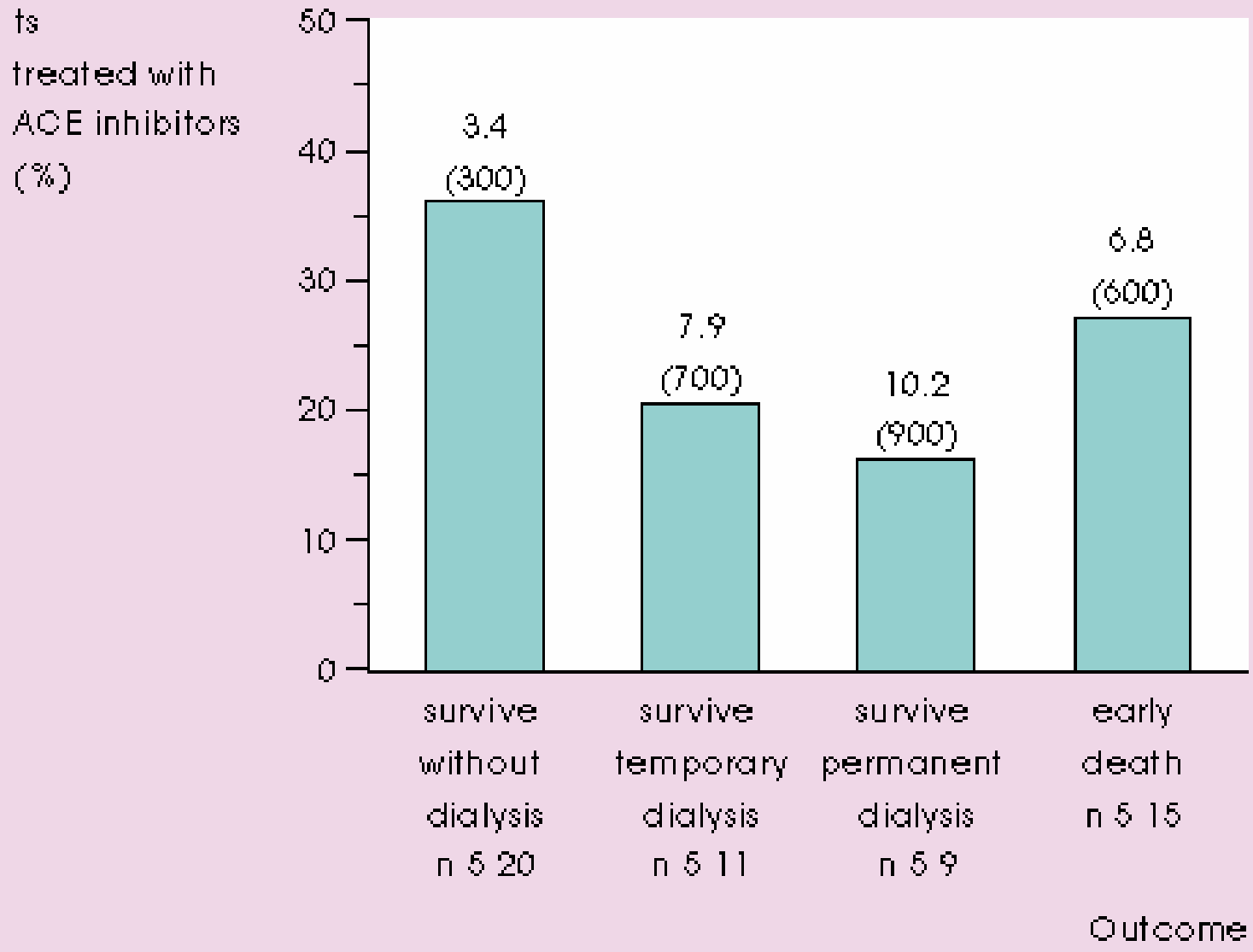
TREATMENT OF PULMONARY INTERSTITIAL ALVEOLITIS WITH CYCLOPHOSPHAMIDE WITH OR WITHOUT CORTICOSTEROIDS

	Medical University of South Carolina (n 5 7)	University of Pittsburgh (n 5 15)	University of Pittsburgh untreated patients (n 5 27)
Baseline FVC% of predicted	51.4%	53.5%	59.1%
Change in FVC	400ml/year	389ml/year	214ml/year

SURVIVAL WITH RENAL CRISIS WITH AND WITHOUT ACE INHIBITORS



OUTCOME IN RENAL CRISIS TREATED WITH ACE INHIBITORS



Dermatomyositis/Polymyositis

Diagnosis

- Muscle pain and weakness proximally
- Raised creatine kinase
- Abnormalities on EMG
- Muscle biopsy

- Dermatomyositis
  - Grotton papules
  - Heliotrope rash

FREQUENCIES OF PRESENTING CLINICAL SYNDROMES IN POLYMYOSITIS/DERMATOMYOSITIS

Syndrome	Estimated freqeuncy
1. Painless proximal weakness (over 3–6 months)	55%
2. Acute or subacute proximal pain and weakness (over weeks–2 months)	30%
3. Insidious proximal and distal weakness (over 1–10 years)	10%
4. Proximal myalgia alone	5%
5. Dermatomyositis rash alone	<1%

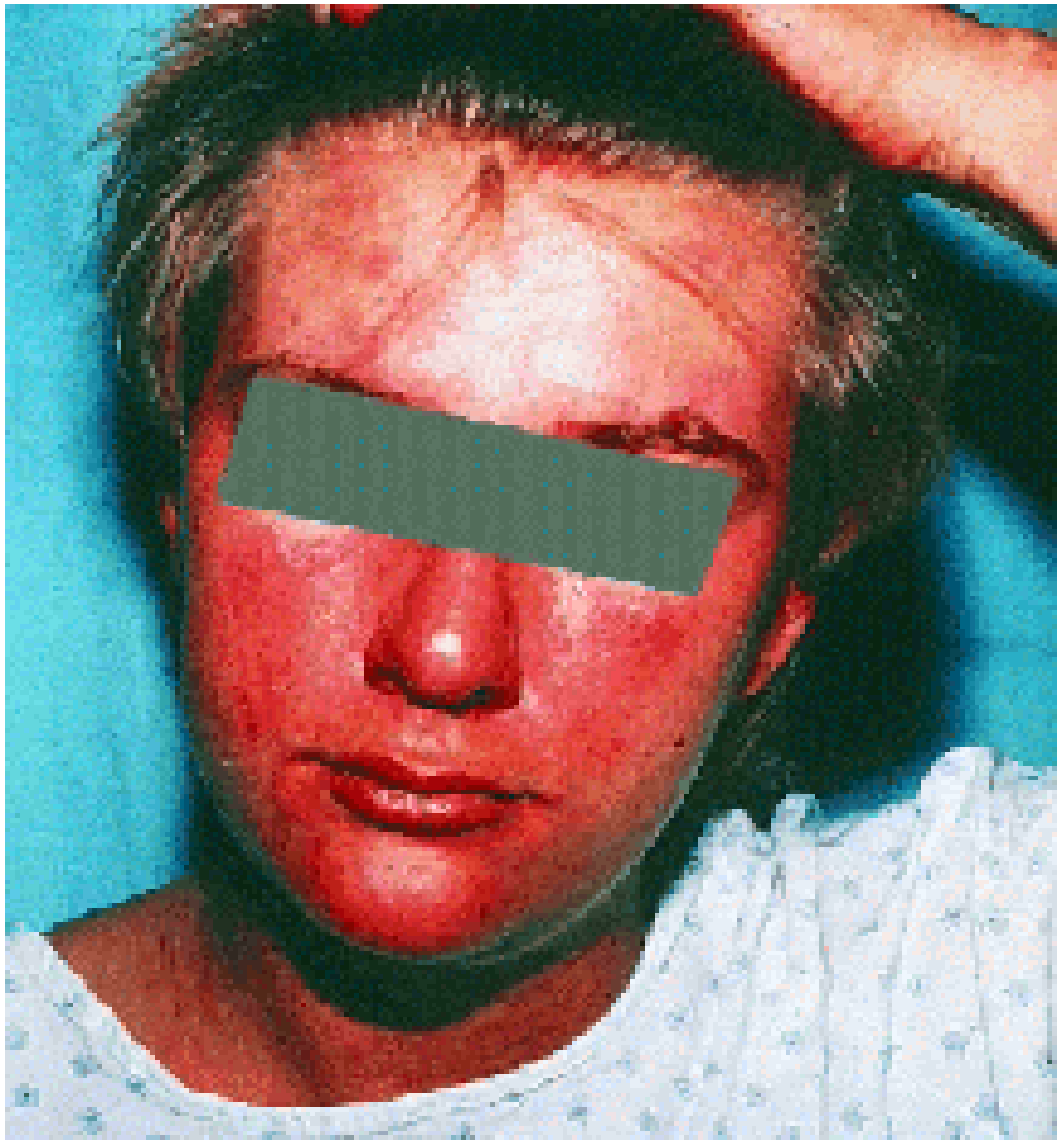
NON-NEUROMUSCULAR CAUSES OF WEAKNESS
Episodic weakness (acute attacks with recurrence)
Hypotension, cardiac arrhythmias
Hypoxia, hypercapnia
Hyperventilation
Hypoglycemia
Cerebrovascular insufficiency
Emotional states; anxiety attacks
Persistent weakness
Anemia
Chronic and acute infection
Malignancy
Malnutrition
Advanced organ system failure (lung, heart, liver, kidney)
Metabolic (hyperthyroidism, hyperparathyroidism, hypophosphatemia)

DRUGS ASSOCIATED WITH MYOPATHY

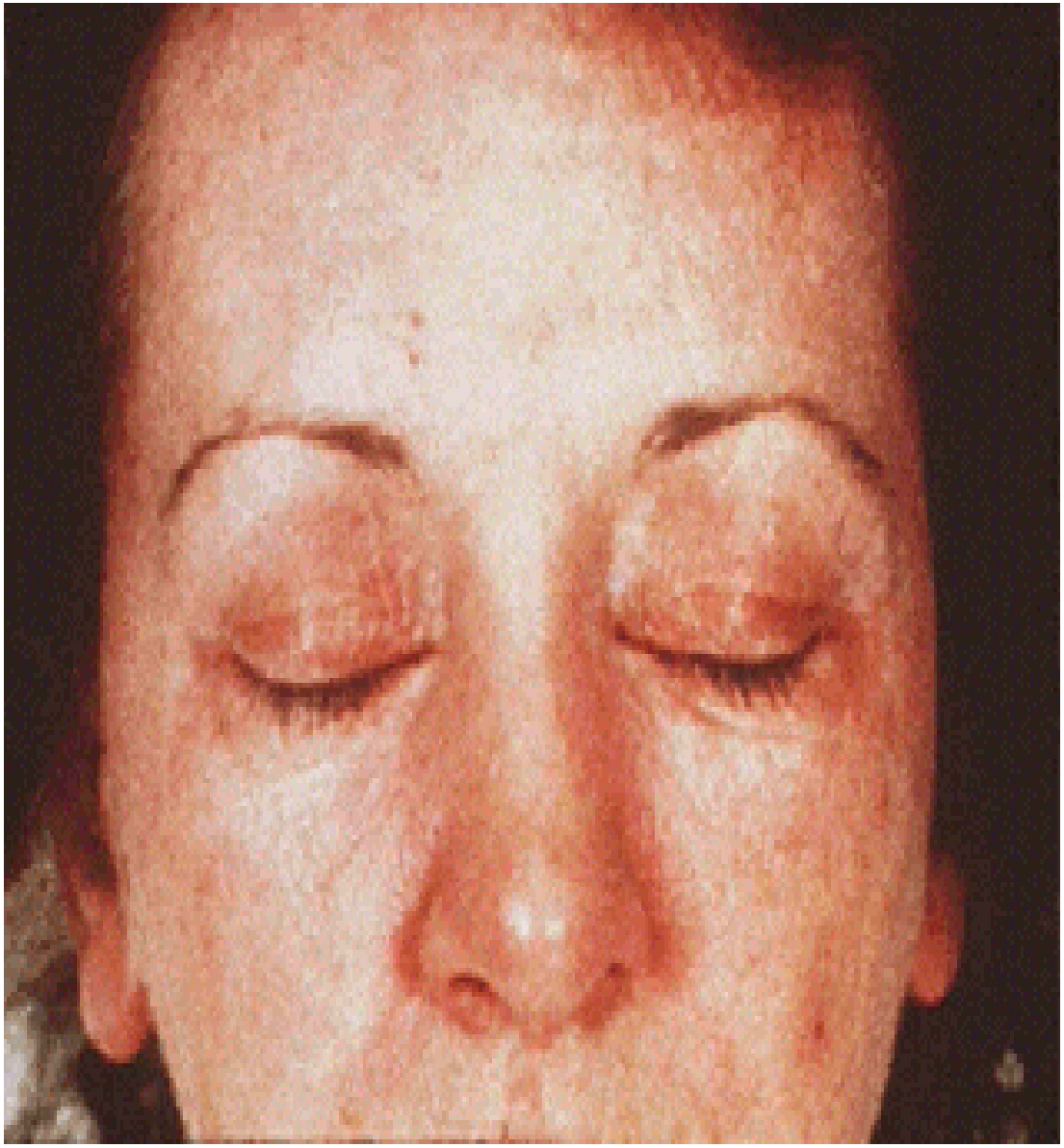
- Chloroquine
- Cimetidine
- Clofibrate
- Colchicine
- Corticosteroids
- Cyclosporin
- Danazol
- Emetine
- Epsilon amino-caproic acid
- Ethanol
- Gemfibrozil
- Heroin
- Hydralazine
- Ipecac
- Levadopa
- Lovastatin
- Penicillamine
- Penicillin
- Phenylbutazone
- Phenytoin
- Procainamide
- Nicotinic acid
- Rifampicin
- Sulfonamides
- Vincristine
- Zidovudine (AZT)

AFFECTED ORGANS AND THEIR EVALUATION IN INFLAMMATORY MUSCLE DISEASE

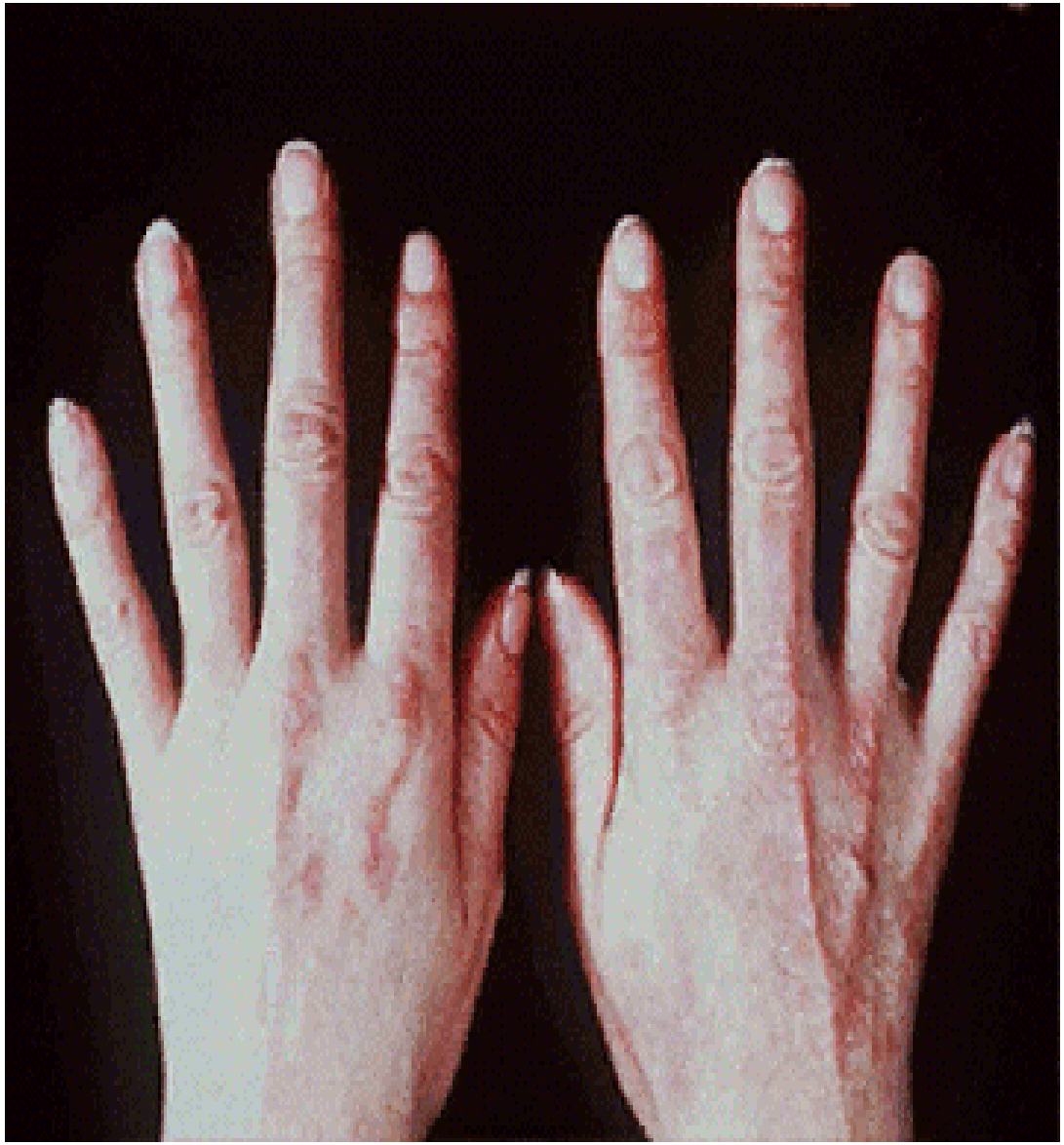
Organ system	Modalities of evaluation	Pathologic processes	Findings
Muscle	Biopsy	Myofiber degeneration–regeneration Inflammation Fibrosis	Myofiber size variation Mononuclear cell infiltration Increased interstitium and fatty replacement of muscle
	EMG	Myofiber destruction	Low amplitude, short, polyphasic potentials; spontaneous fibrillations; irritability
	Gallium scan MRI T1 image STIR image	Inflammation Fibrosis Inflammation	Increased uptake in affected muscle Atrophy of muscle, scarring Bright signal in inflamed muscle
Heart	EKG, CXR	Myocarditis, fibrosis	Arrhythmias, left ventricular hypertrophy
	Biopsy	Myocarditis, fibrosis	Myofiber size variation, mononuclear cell infiltrates, fibrosis
Lungs	CXR	Inflammation, fibrosis	Interstitial markings
	PFTs	Inflammation, fibrosis	Decreased TLV and D_LCO
	Radionuclide scan	Inflammation, fibrosis	Ventilation/perfusion mismatches
	BAL (bronchial lavage)	Inflammation, fibrosis	Abnormal leukocyte numbers and differentials
	Biopsy	Inflammation, fibrosis	Mononuclear cell infiltration, destruction of alveolar space and fibrosis
Skin	Biopsy	Inflammation	Vacuolization of the basal layer, mononuclear cell infiltration
Gastrointestinal	X-ray studies	Inflammation, fibrosis	Reflux and uncoordinated peristalsis



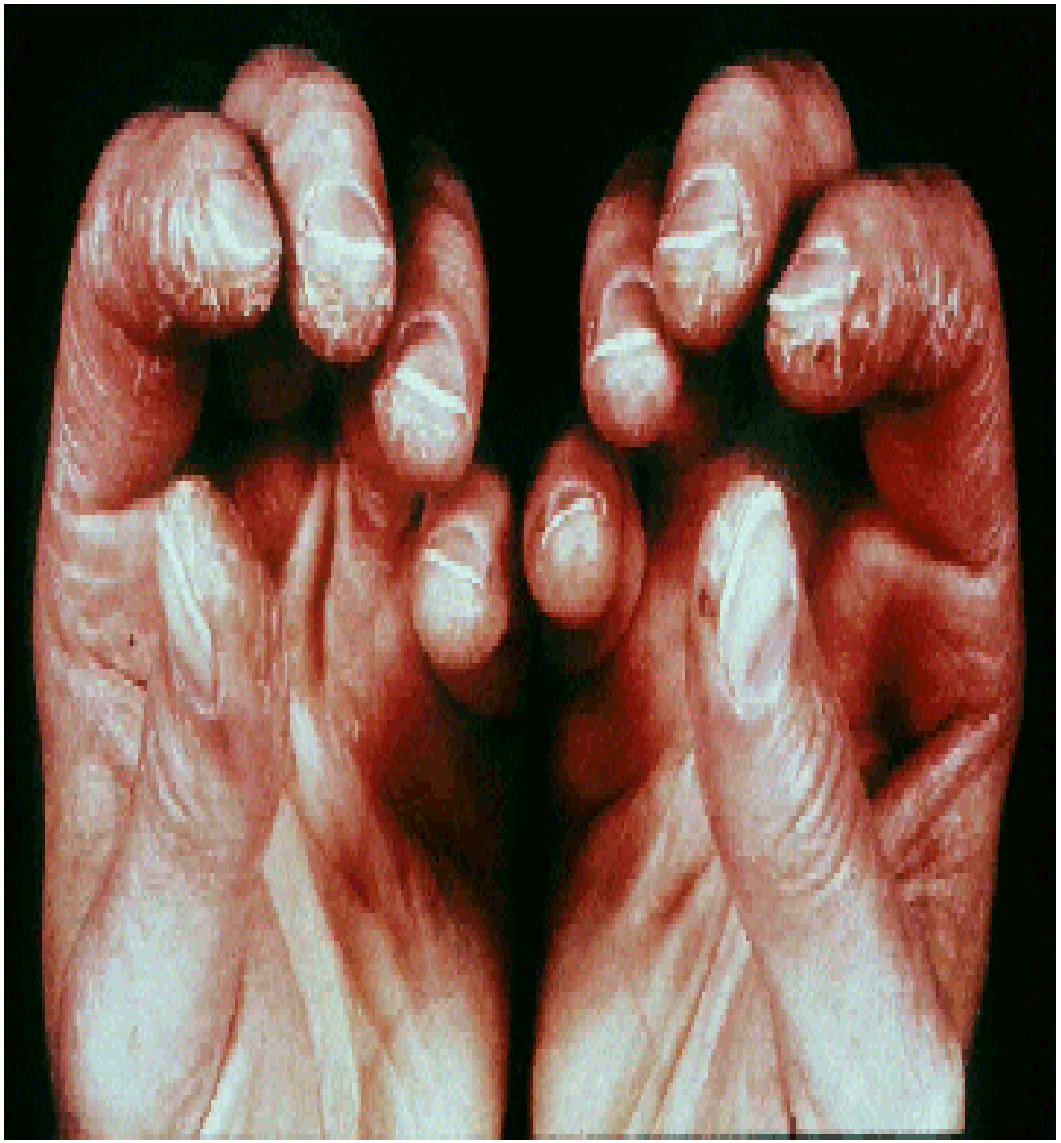
The facial rash of dermatomyositis. Note the malar-like rash of dermatomyositis which involves the nasolabial area (an area often spared in SLE). Patchy involvement of the forehead and chin is also present in this patient.



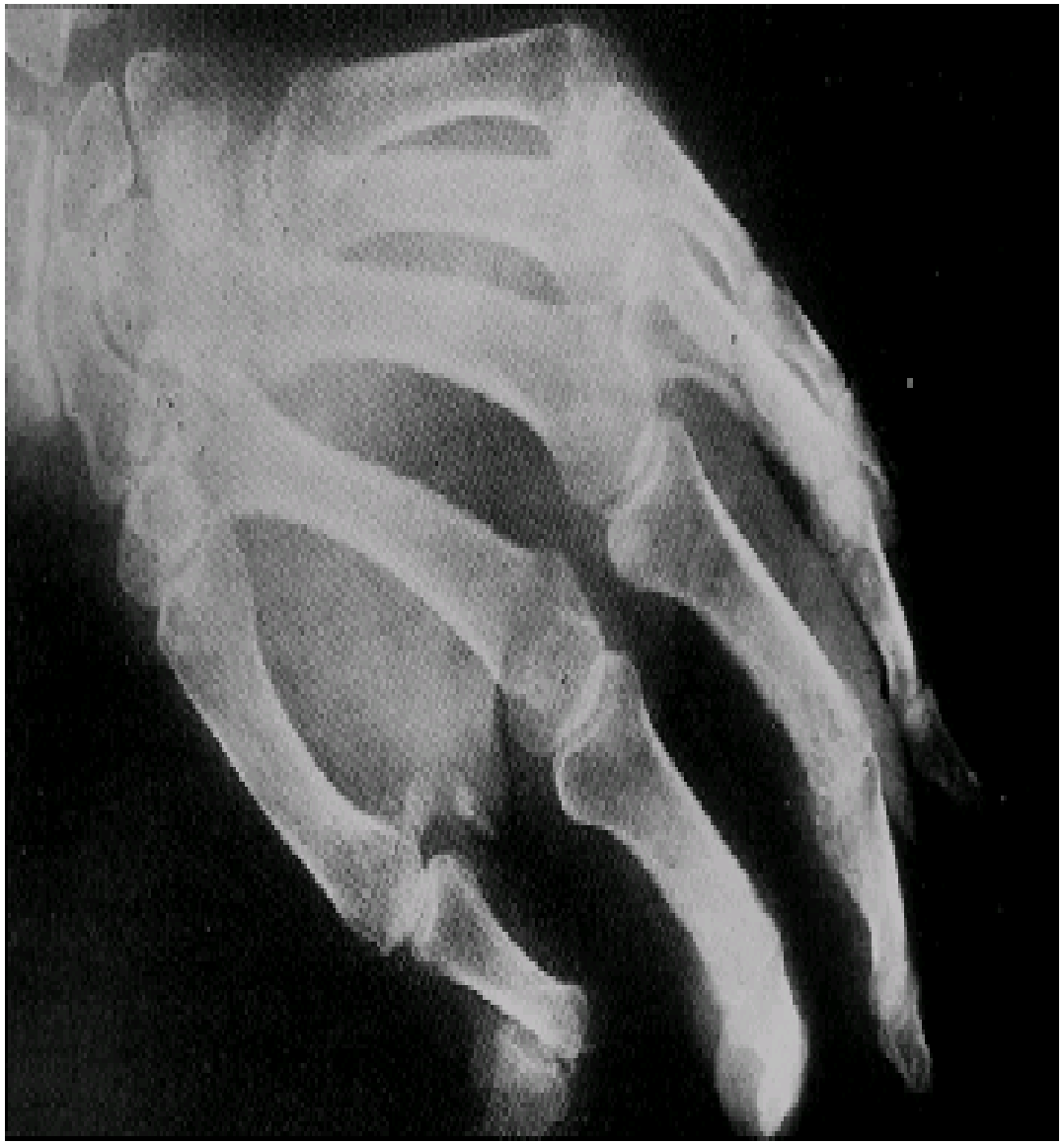
Heliotrope rash of dermatomyositis. The erythematous/violaceous rash over the eyelids of this patient with dermatomyositis and breast cancer is a characteristic cutaneous feature.



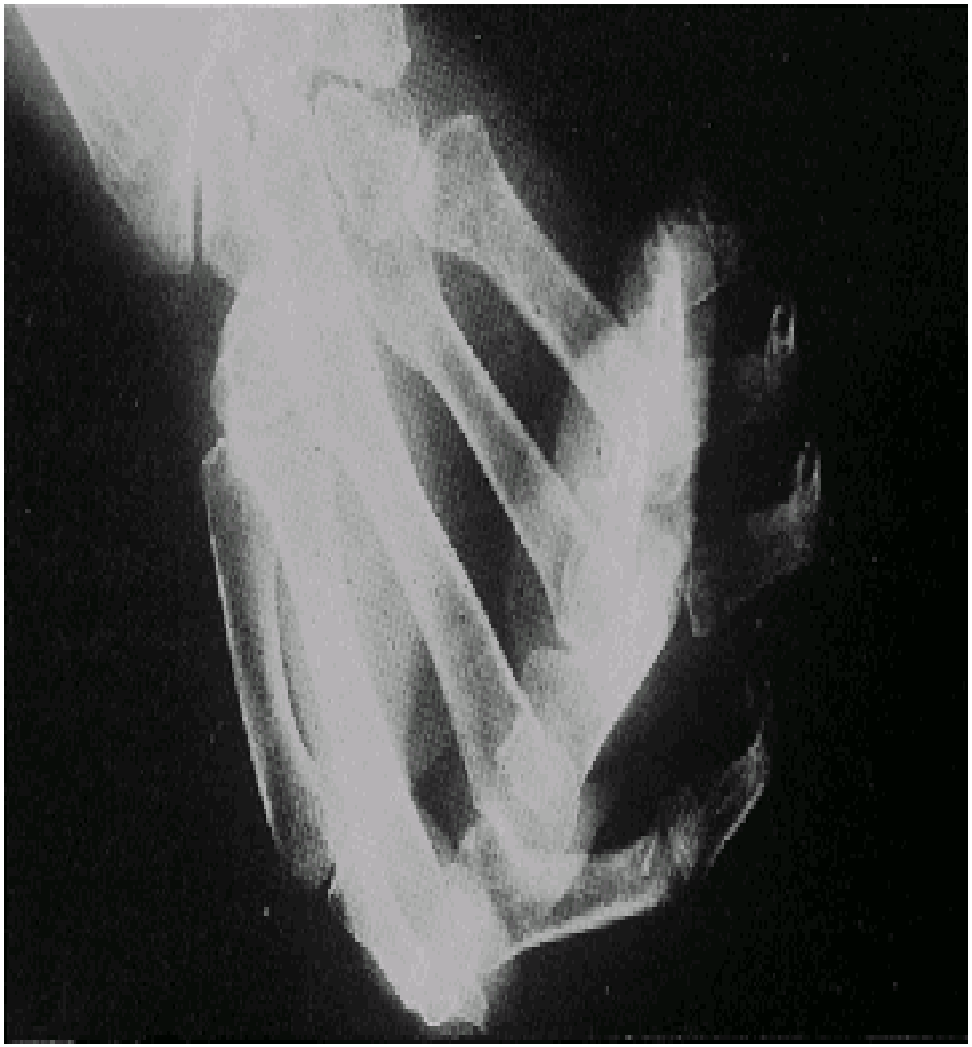
Gottron sign. This erythematous, scaling rash over the knuckles and dorsum of the hand is a common early sign in dermatomyositis. It can be distinguished from the rash of SLE which usually affects the phalanges and spares the knuckles.



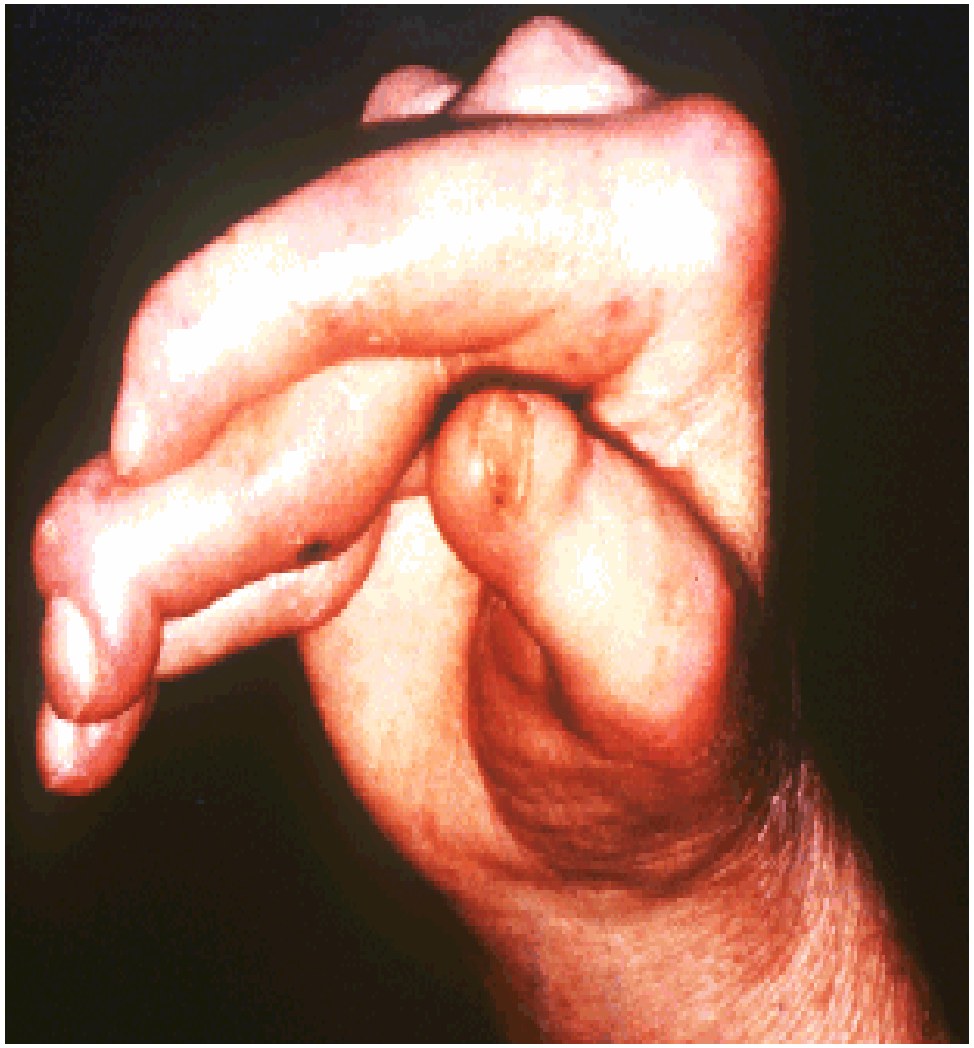
’Machinist’s hands’. Note the cracking and fissuring of the distal digital skin of the fingerpads in this patient with dermatomyositis.



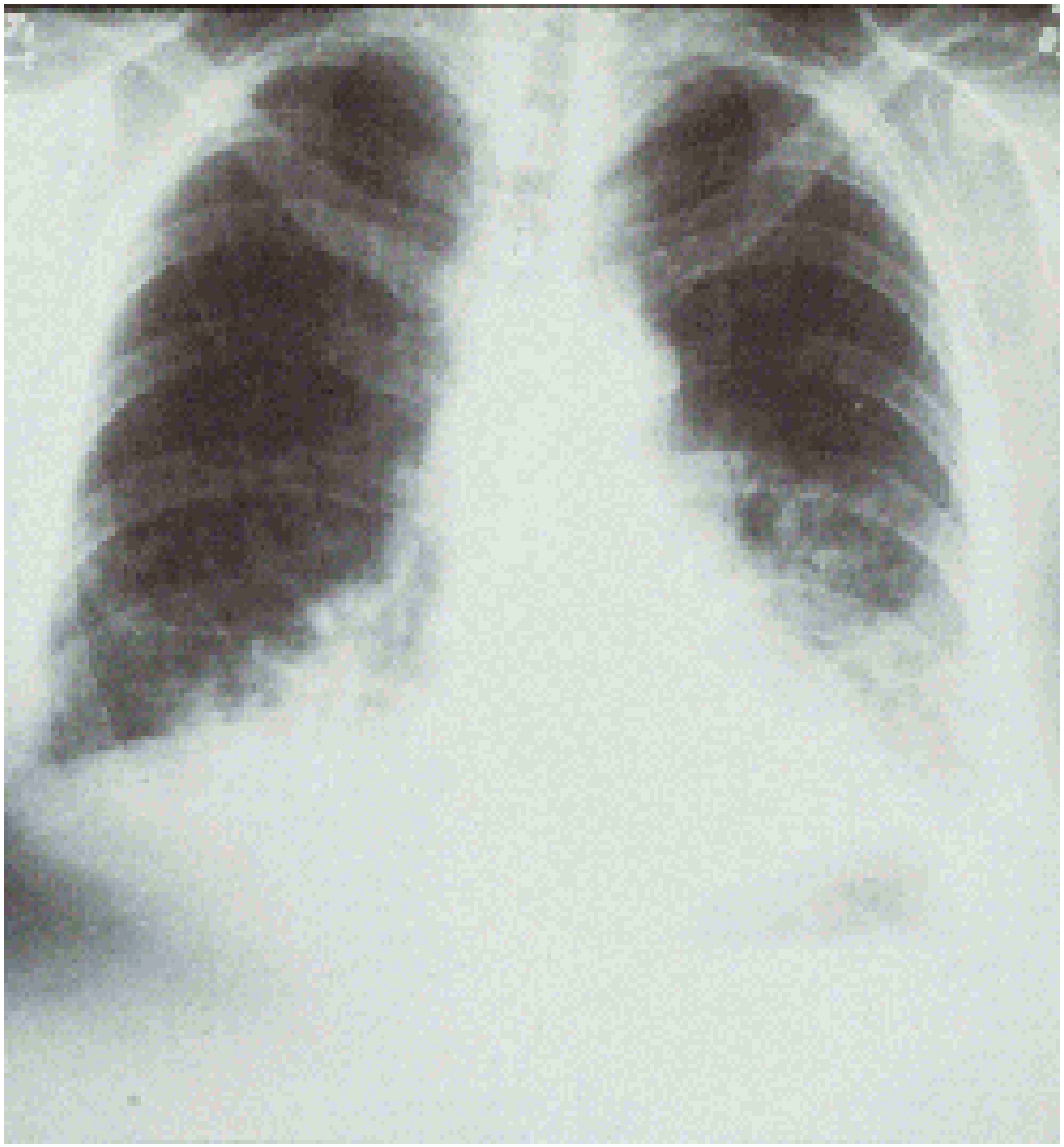
Deforming arthropathy of polymyositis. Radiograph of the right hand of a patient with the anti-Jo-1 antibody showing subluxation of the interphalangeal joint of the thumb (i.e. floppy thumb). No erosive changes were seen.



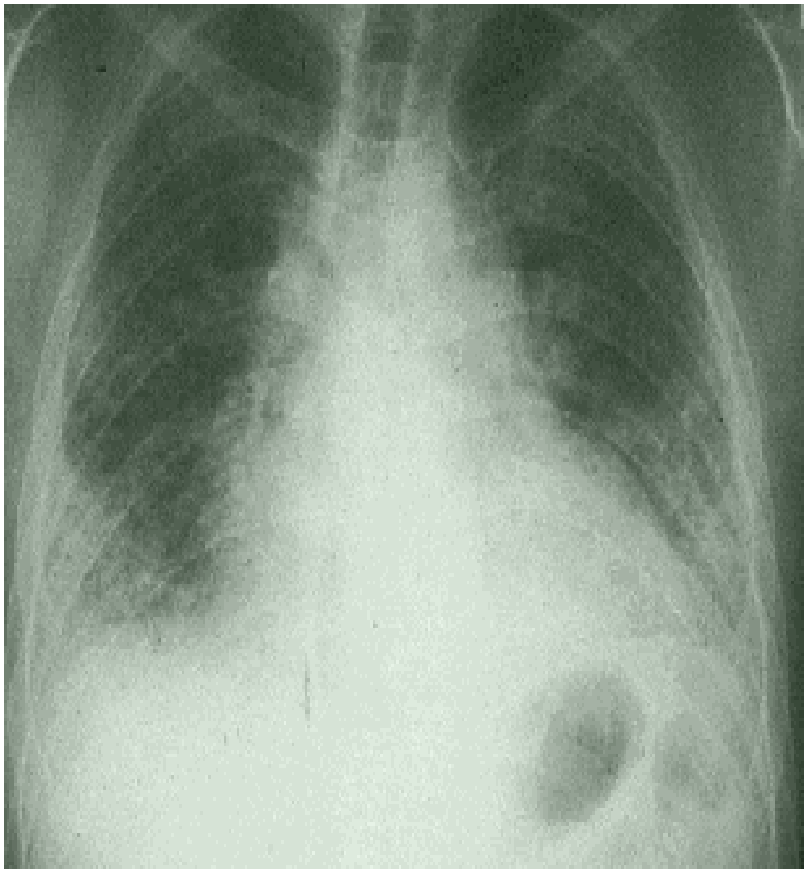
Deforming arthropathy of polymyositis: Radiograph taken 4 years later, showing progressive deformity with numerous metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joint subluxations, but no bony erosive changes.



Deforming arthropathy of polymyositis. Photograph of the same patient’s right hand showing significant deformity of multiple joints.



Interstitial lung disease of polymyositis/dermatomyositis. Chest radiograph of a patient with interstitial lung disease and dermatomyositis demonstrating severe basilar fibrosis and mid-lung interstitial changes as well.



The lung in a patient with myositis. Standard chest radiograph showing typical findings of interstitial lung disease.

Gross autopsy specimen from the heart of a patient with myositis who died from myocarditis showing dilated left ventricle and fibrosis

Diagnosis

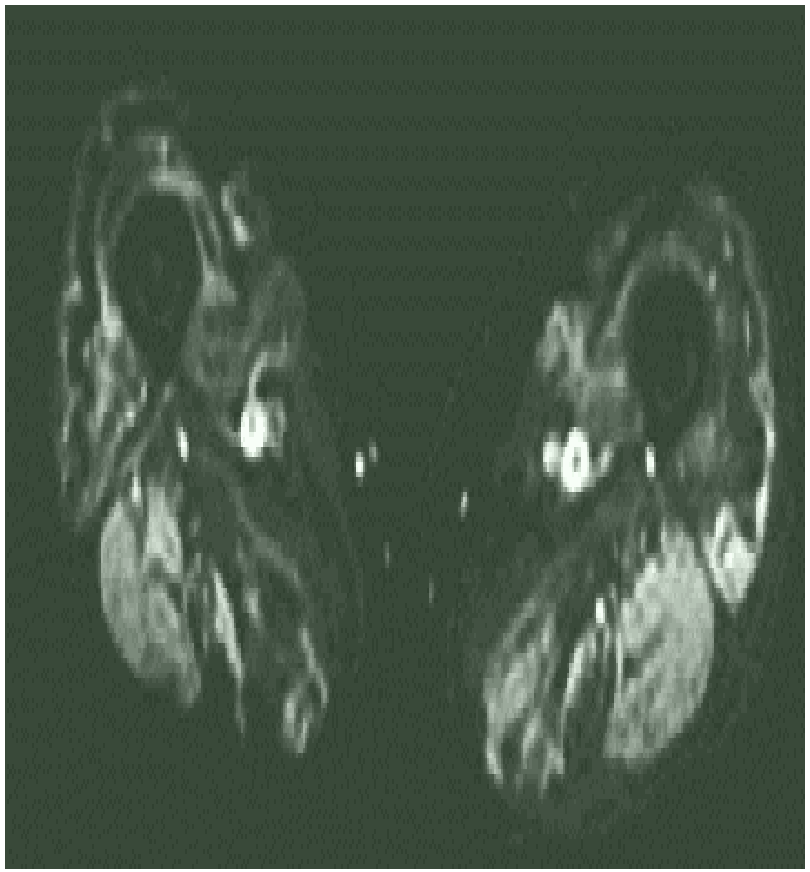
SERUM AUTOANTIBODIES IN POLYMYOSITIS AND DERMATOMYOSITIS PATIENT SUBSETS

Autoantibody	Polymyositis	Dermatomyositis	Childhood	Overlap	Malignancy
Jo-1	30% *	5%	0	15%	0
PM-Scl **	10%	<5%		10%	0
nRNP	10%	5%	<5%	30–40% ***	0
Others					
Ku				5%	
Mi-2		10%			
PL-7, PL-12, OJ, EJ	–<5%–				
SRP	<5%				

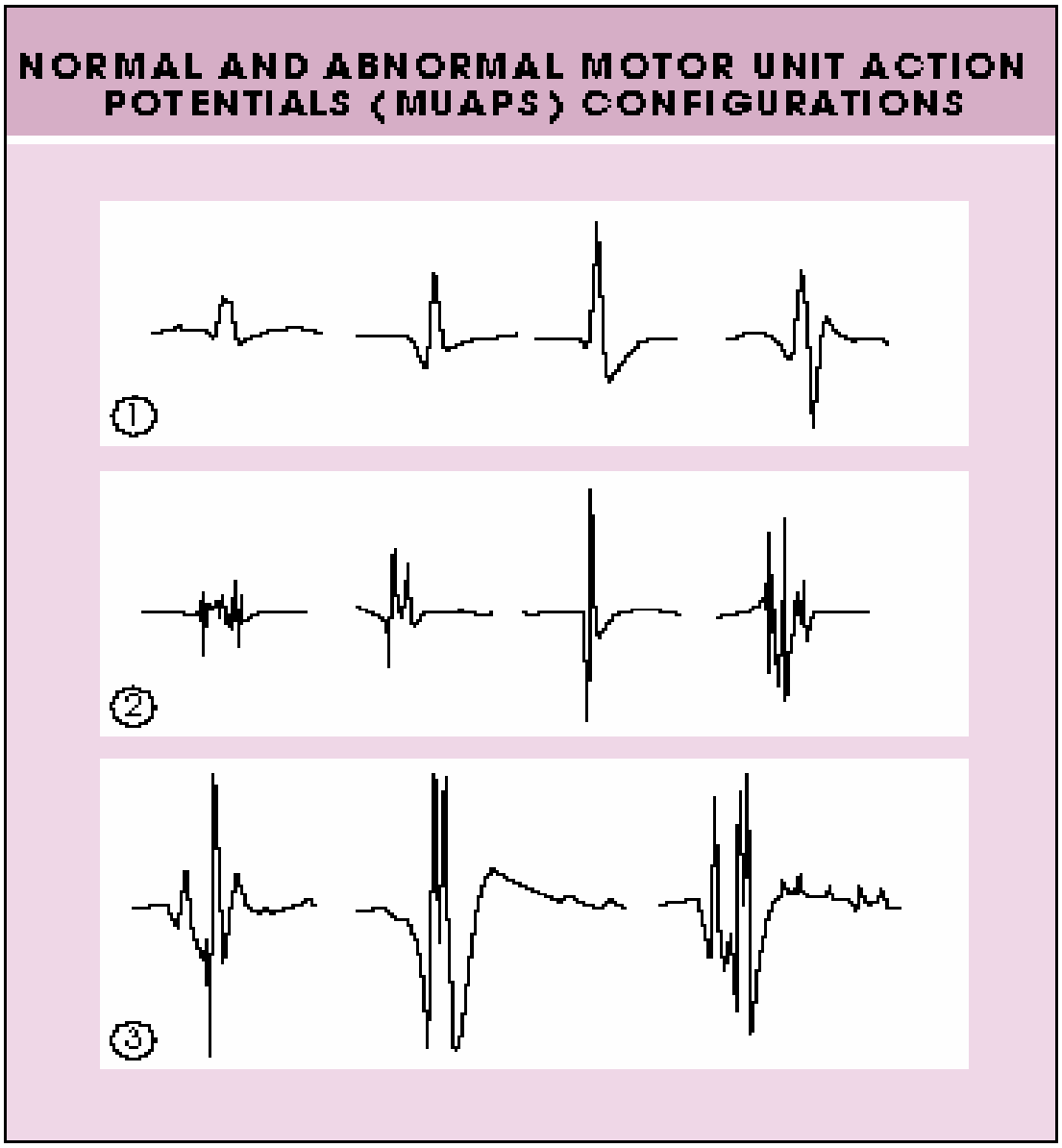
* Associated with interstitial lung disease

** Predominantly overlap with systemic sclerosis

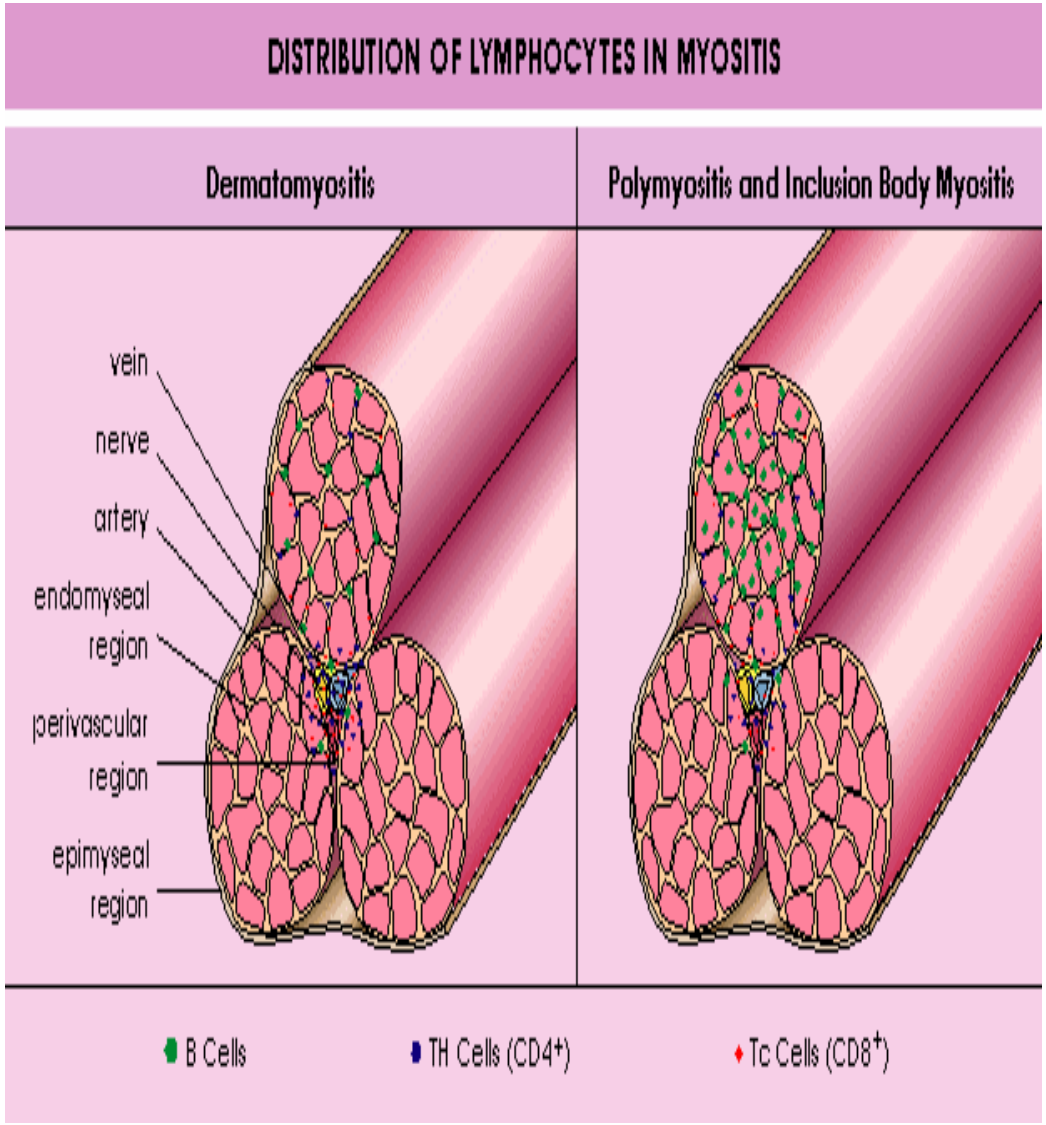
*** Predominantly overlap with systemic lupus erythematosus



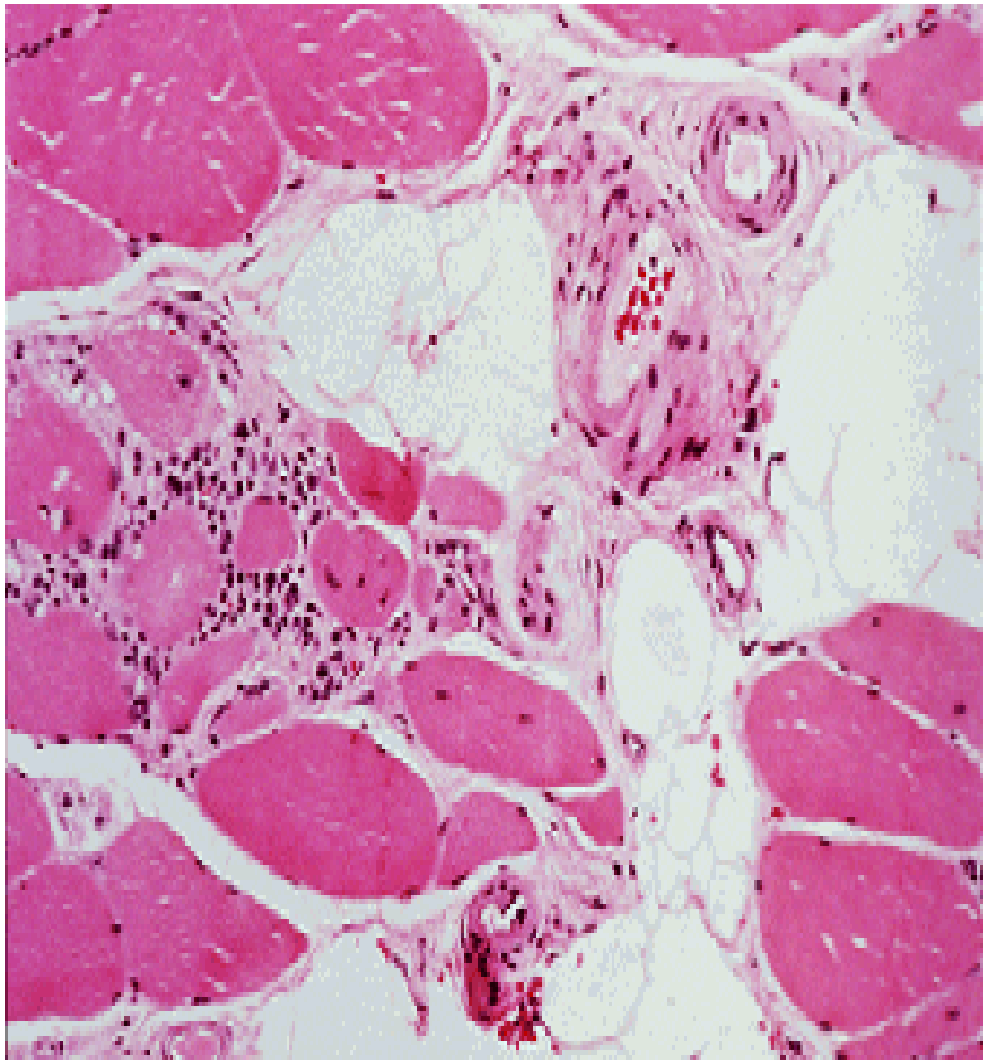
Magnetic resonance images of the thigh. In cross-section using the short Tau inversion recovery (STIR) technique, atrophy of the anterior muscles is evident. Inflammation shows up as bright areas in the posterior muscles



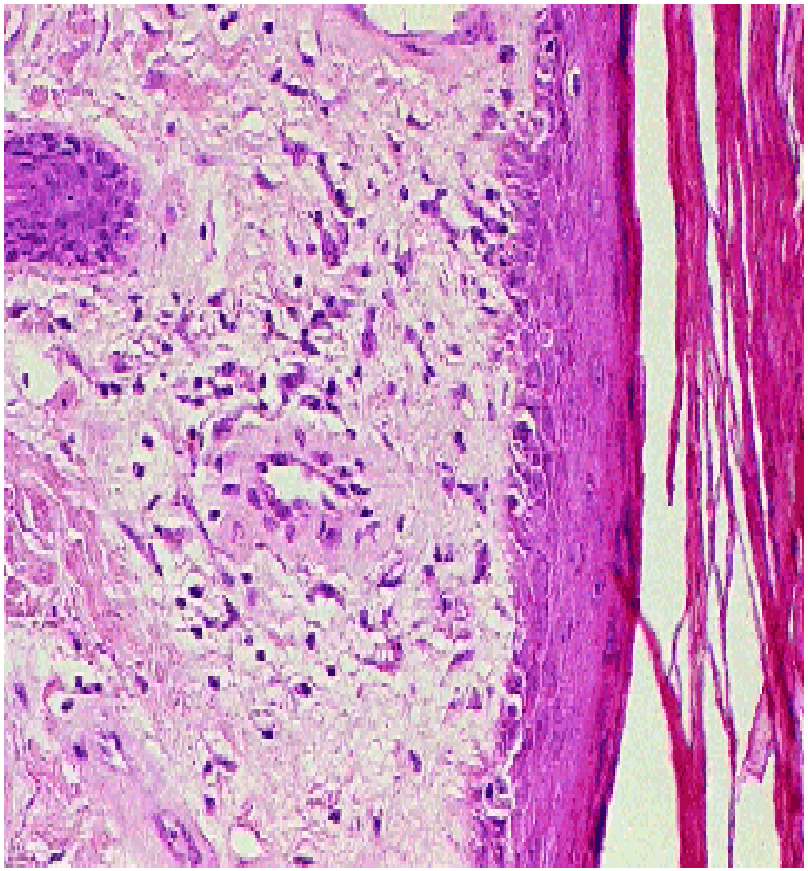
Normal and abnormal motor unit action potentials (MUAPs) configurations. Normal MUAPs (1). Short duration, low amplitude, polyphasic MUAPs seen with myositis (2). Large amplitude, long duration polyphasic MUAPs as seen in neuropathic disorders (3).



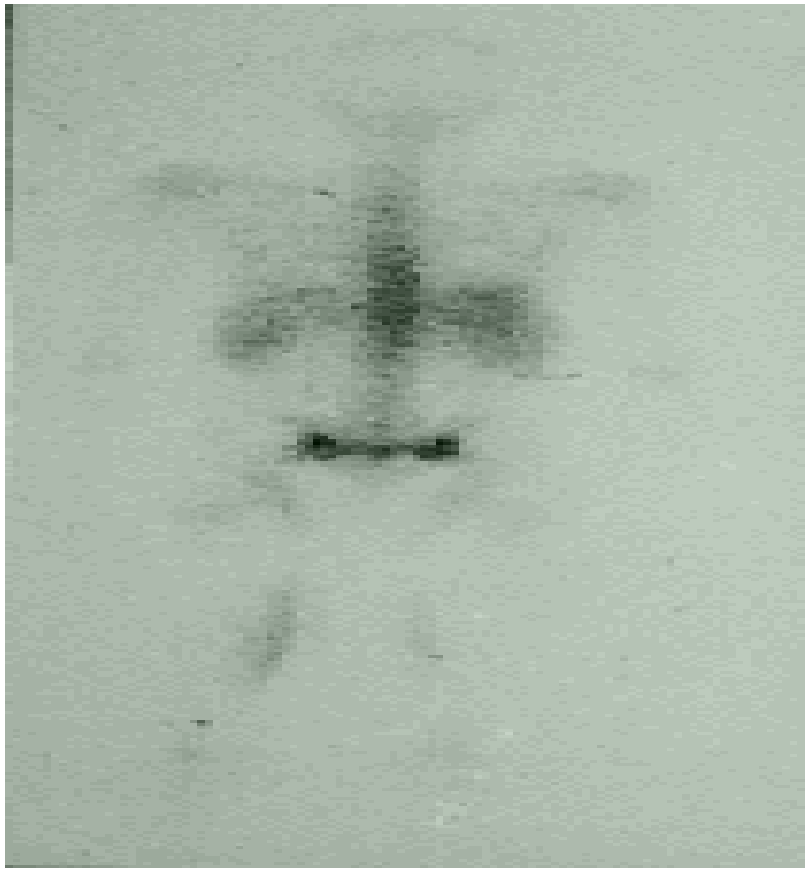
Distribution of lymphocytes in muscle biopsies from patients with myositis.



Pathologic changes in myositis by light microscopy. Longitudinal and cross-sectional views of inflammatory myopathy showing variation in cell size, necrosis, regeneration, and inflammation (hematoxylin and eosin)



Skin biopsy of a Gottron's lesion in a patient with dermatomyositis. The biopsy demonstrates hyperkeratosis, epidermal thinning, vacuolar degeneration of the basal layer, dilated superficial capillaries with perivascular lymphohistiocytic infiltrates, and mild mucin deposition in the dermis.



Myositis is focal both macroscopically and microscopically. Gallium scan in a patient with active myositis showing abnormal uptake limited to the medial thigh muscles

REQUIREMENTS FOR SUCCESSFUL THERAPY

Accuracy of diagnosis

Compatible criteria
- History and physical findings
- Laboratory studies
- Histological findings
- Electrophysiological (EMG) findings

Rule out disorders of the nervous system
- Neuropathic disorders
- Lower motor neuron disease
- Myasthenia gravis

Rule out other causes of myopathies
- Metabolic
- Inherited
- Endocrine
- Electrolyte disorders
- Drug and toxin
- Infectious
- Traumatic
- Ischemic

Accuracy of assessment of course of illness

Muscle function

Muscle strength

Laboratory studies

Treatment

- Symptomatic
- Steroids
- Immunosuppressants (methotrexate)