Cutaneous Manifestations of Systemic Disease

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ABOIM Board Review

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Cutaneous Multisystem

Cutaneous Connective Tissue Conditions

Connective Tissue Diease

- Discoid Lupus Erythematosus
- Subacute Cutaneous LE
- Systemic Lupus Erythematosus
- Scleroderma
- CREST Syndrome
- Dermatomyositis

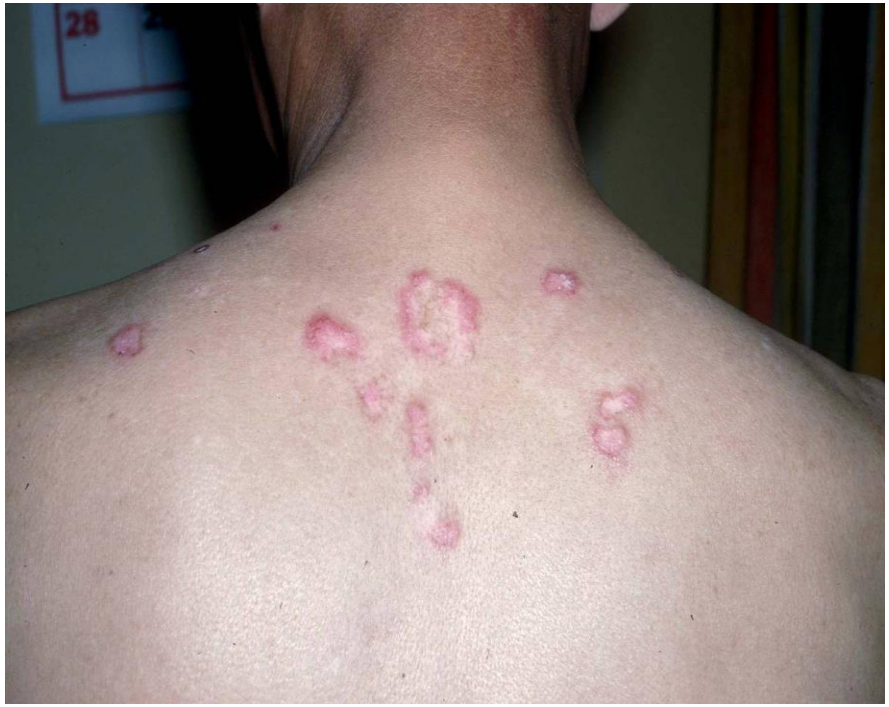
Lupus Erythematosus

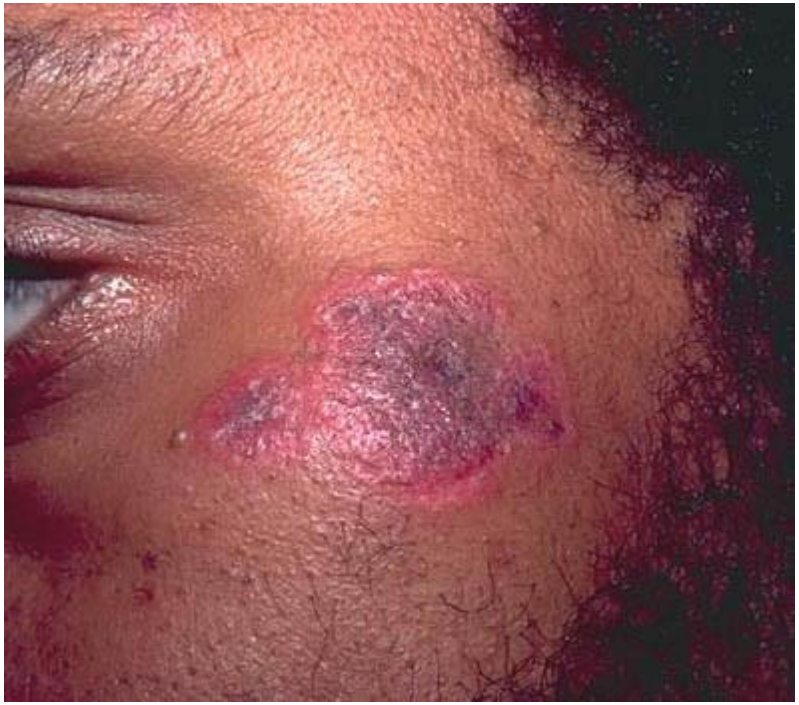
- Spectrum from cutaneous to severe systemic involvement
  - Discoid LE (DLE) / Chronic Cutaneous
  - Subacute Cutaneous LE (SCLE)
  - Systemic LE (SLE)
- Cutaneous findings common in all forms
- Related to autoimmunity

Discoid LE (Chronic Cutaneous LE)

- Primarily cutaneous
- Scaly, erythematous, atrophic plaques with sharp margins, telangiectasias and follicular plugging
- Possible elevated ESR, anemia or leukopenia
- Progression to SLE only 1-2%
- Heals with scarring, atrophy and dyspigmentation
- 5% ANA positive

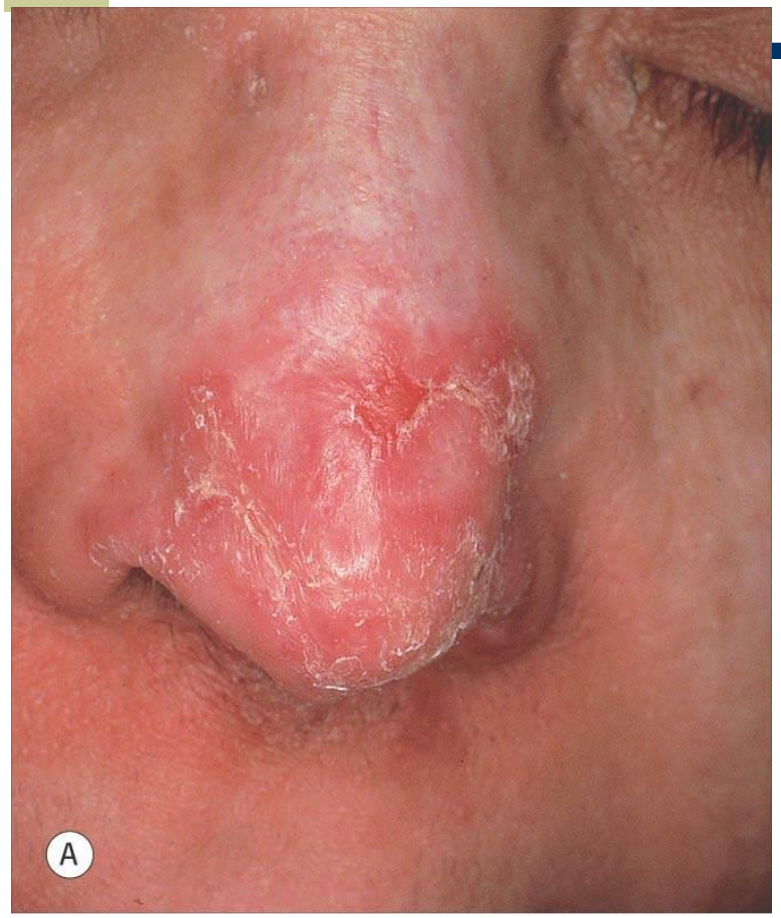
Discoid LE (Chronic Cutaneous LE)

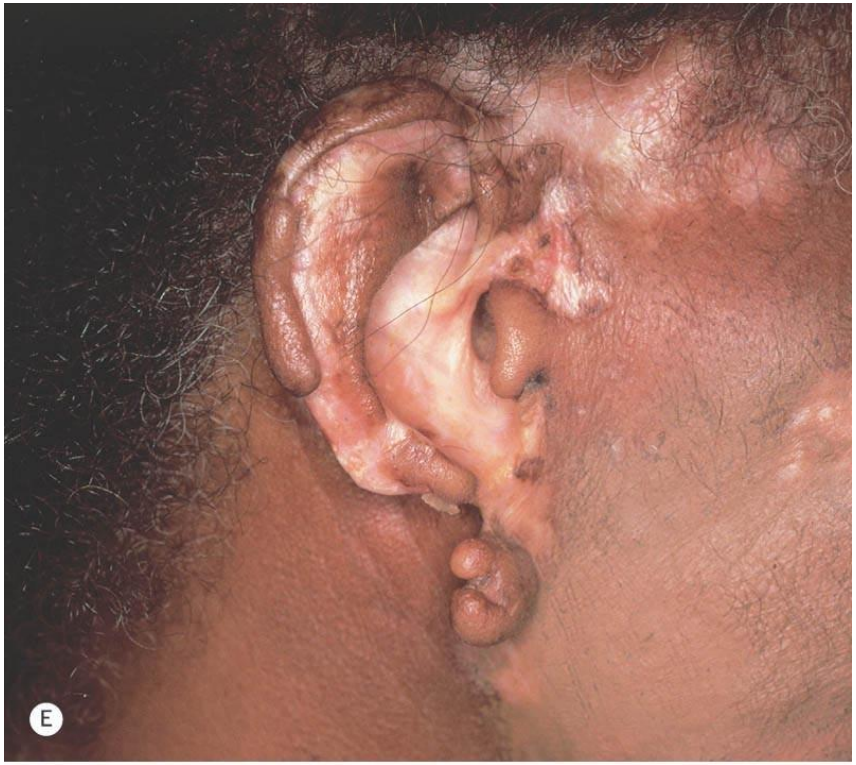




Scaly, atrophic plaques with defined margins

Discoid LE (Chronic Cutaneous LE)



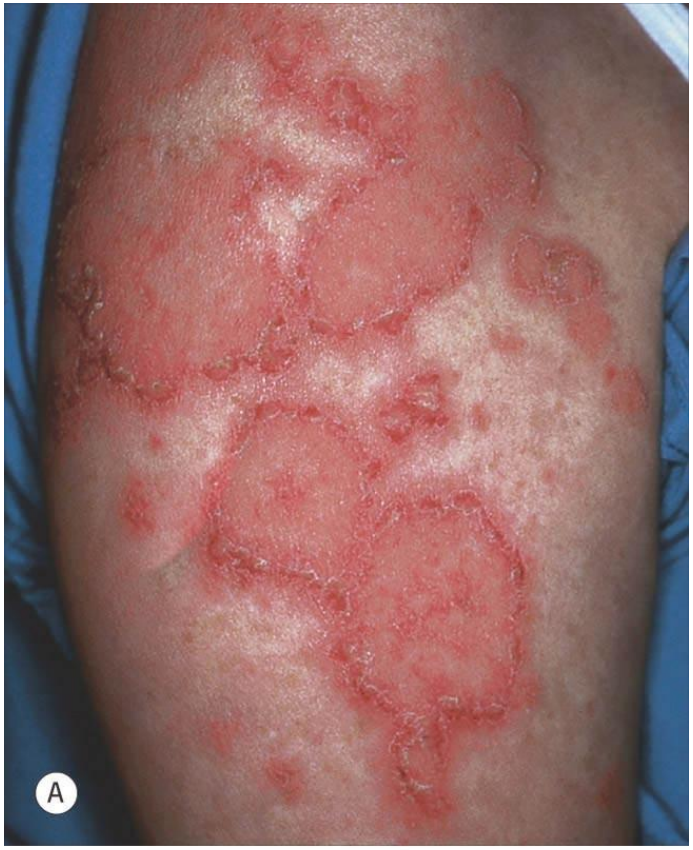


Scaly, erythematous plaques with scarring, atrophy, dyspigmentation

Subacute Cutaneous LE (SLCE)

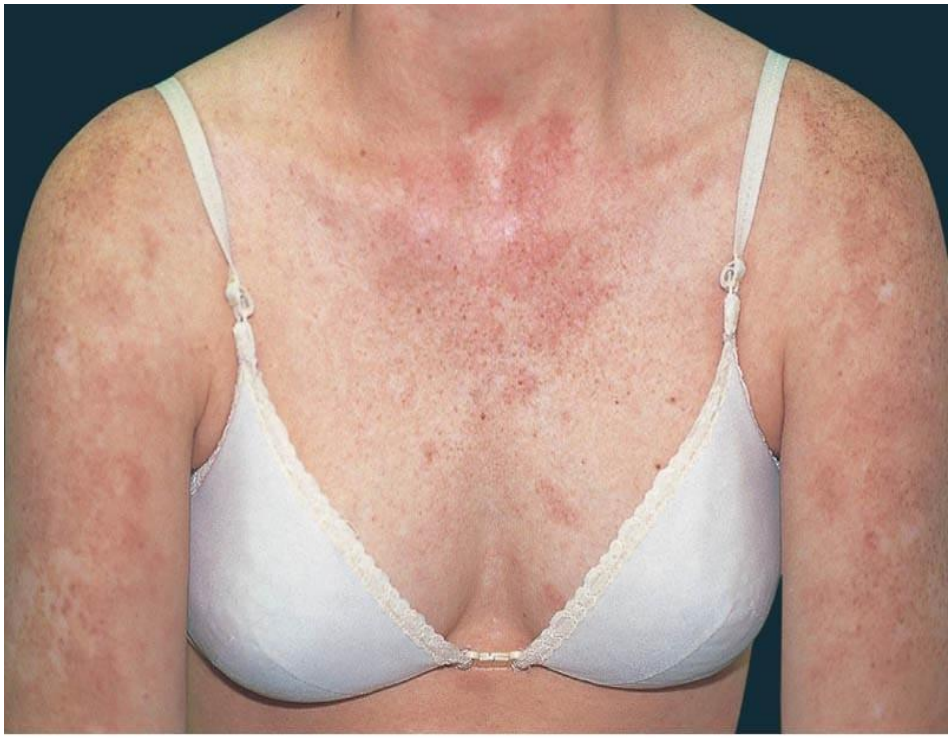
- Cutaneous disease with internal involvement
  - 20% Leukopenia, 75% arthralgias
- Psoriasiform, polycyclic, annular lesions
- Sun exposed sites commonly
  - Shawl distribution: V neck, upper outer and inner arms
- 80% ANA positive
  - Anti-Ro

Subacute Cutaneous LE (SLCE)



(Courtesy of Jean L Bolognia MD.)

Psoriasiform, scaly plaques



"Shawl" distribution

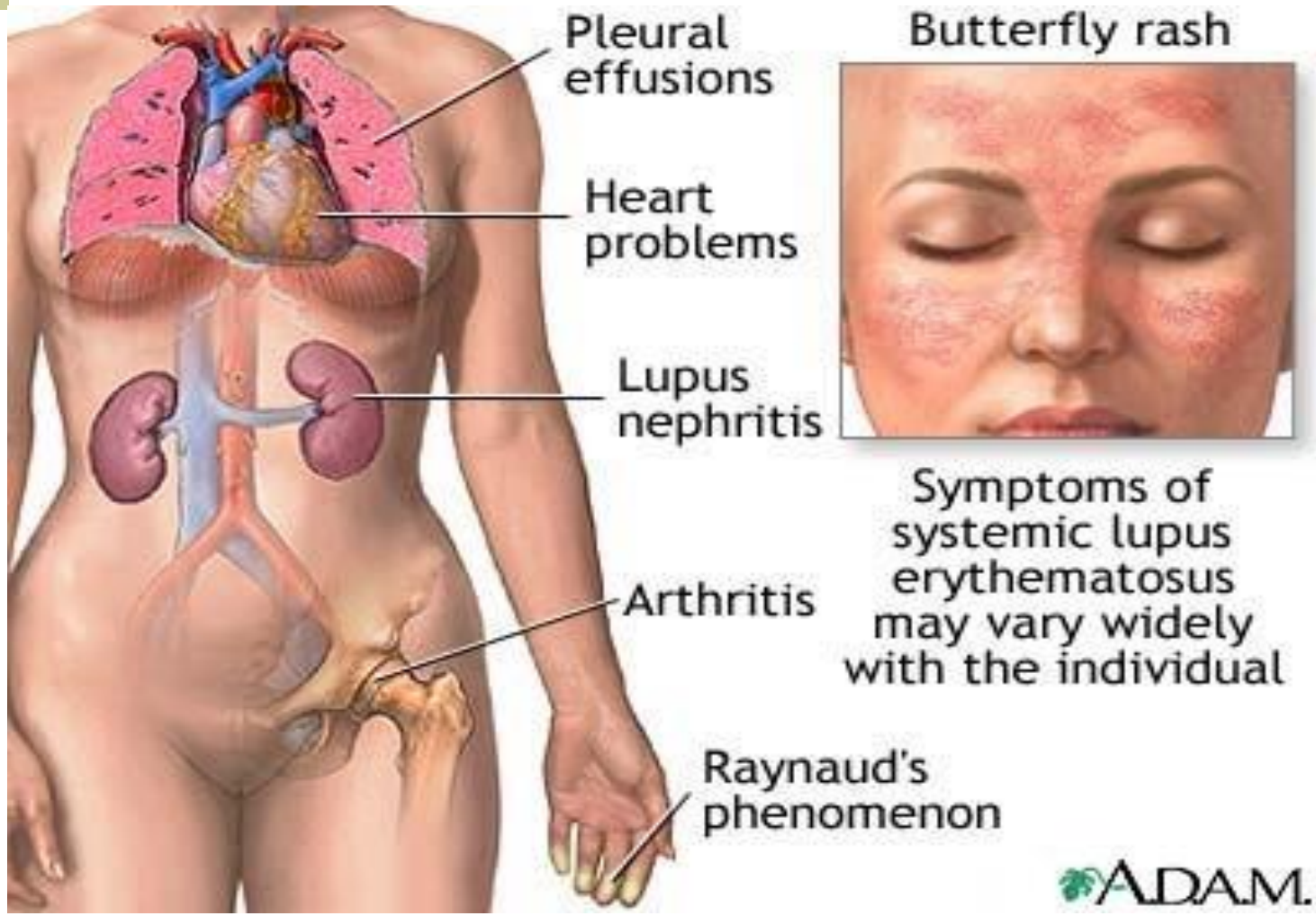
Systemic Lupus Erythematosus (SLE)

- Young to middle age women
- Skin involvement in 80% of the cases (often malar rash)
- American College of Rheumatology has
  11 criteria for SLE diagnosis
- If 4 or more of the criteria are satisfied, then the patient is said to have SLE
  - ANA + 99%

- Possible drug induced
  - Procainamide, Hydralazine, Isoniazid, etc

THE AMERICAN COLLEGE OF RHEUMATOLOGY 1982 REVISED CRITERIA FOR CLASSIFICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS	
Criterion	**Definition**
1. Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare 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 physician
5. Arthritis	Non-erosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling or effusion
6. Serositis	**a)** **Pleuritis** – convincing history of pleuritic pain, rubbing heard by a physician, or evidence of pleural effusion *OR* **b)** **Pericarditis** – documented by ECG, rub or evidence of pericardial effusion
7. Renal disorder	**a)** Persistent **proteinuria** greater than 0.5 g/day or greater than 3+ if quantitation not performed *OR* **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 derangements, e.g. uremia, ketoacidosis or electrolyte imbalance *OR* **b)** **Psychosis** – in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance
9. Hematologic disorder	**a)** **Hemolytic anemia** with reticulocytosis *OR* **b)** **Leukopenia** – less than 4000/mm3 total WBC on two or more occasions OR **c)** **Lymphopenia** – less than 1500/mm3 on two or more occasions OR **d)** **Thrombocytopenia** – less than 100 000/mm3 in the absence of offending drugs
10. Immunologic disorder	**a)** **Anti-DNA antibody to native DNA** in abnormal titer *OR* b)**Anti-Sm:** presence of antibody to Sm nuclear antigen *OR* **c)** Positive finding of **antiphospholipid antibodies** based on: (1) an abnormal serum level of IgG or IgM anticardiolipin antibodies; (2) a positive test result for lupus anticoagulant using a standard methods; or (3) a 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 absorption test (FTA-ABS)
11. Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence (or an equivalent assay) at any point in time and in the absence of drugs known to be associated with 'drug-induced lupus' syndrome

Systemic Lupus Erythematosus (SLE)



Systemic Lupus Erythematosus (SLE) ACR Criteria*

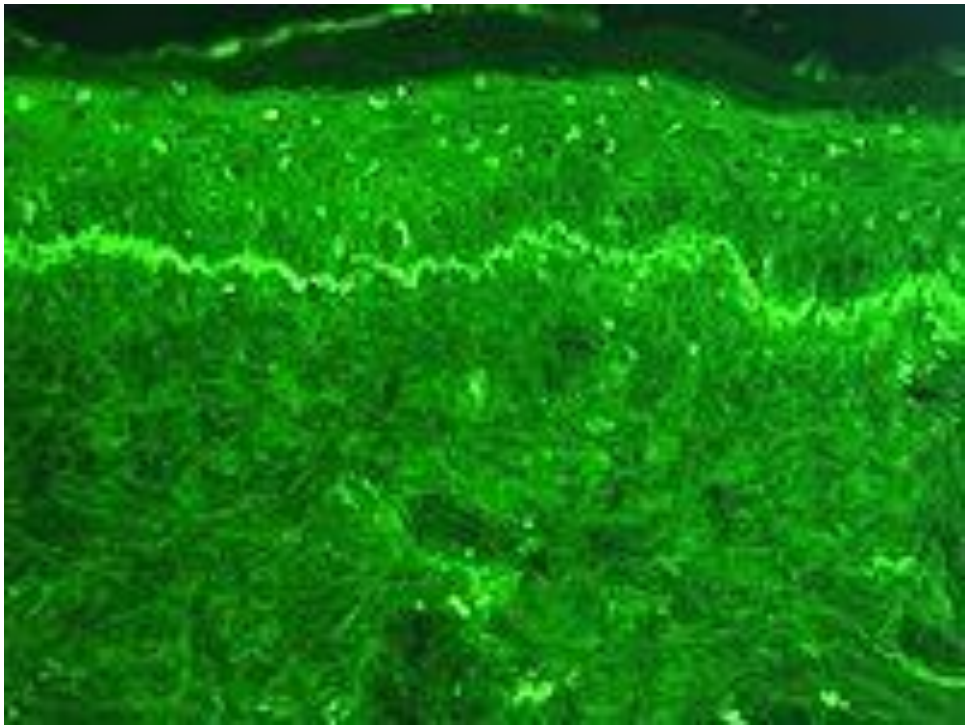
1) D – Discoid Rash
2) O – Oral Ulcers
3) P – Photosensitivity
4) A – ANA + (99%)
5) M – Malar Rash
6) I – Immunologic DO
7) N – Neurologic DO
8) R – Renal Disorder
9) A – Arthritis
10) S – Serositis
11) H – Hematologic DO

Lupus Erythematosus Laboratory Findings

- Antinuclear Antibodies (ANA)
  - 5% DLE
  - 80% SCLE
  - 99% SLE
- Anti-dsDNA + in SLE
  - Correlates with renal disease and SLE activity
  - (anti-histone + in drug-induced)
- False + VDRL
- Anemia, leukopenia, thrombocytopenia, low complement, urinary findings

Lupus Erythematosus Laboratory Findings

- Lupus Band Test
  - direct immunofluorescence of skin biopsy
  - Linear IgG deposition at dermal-epidermal junction



Lupus Erythematosus Differential Diagnosis*

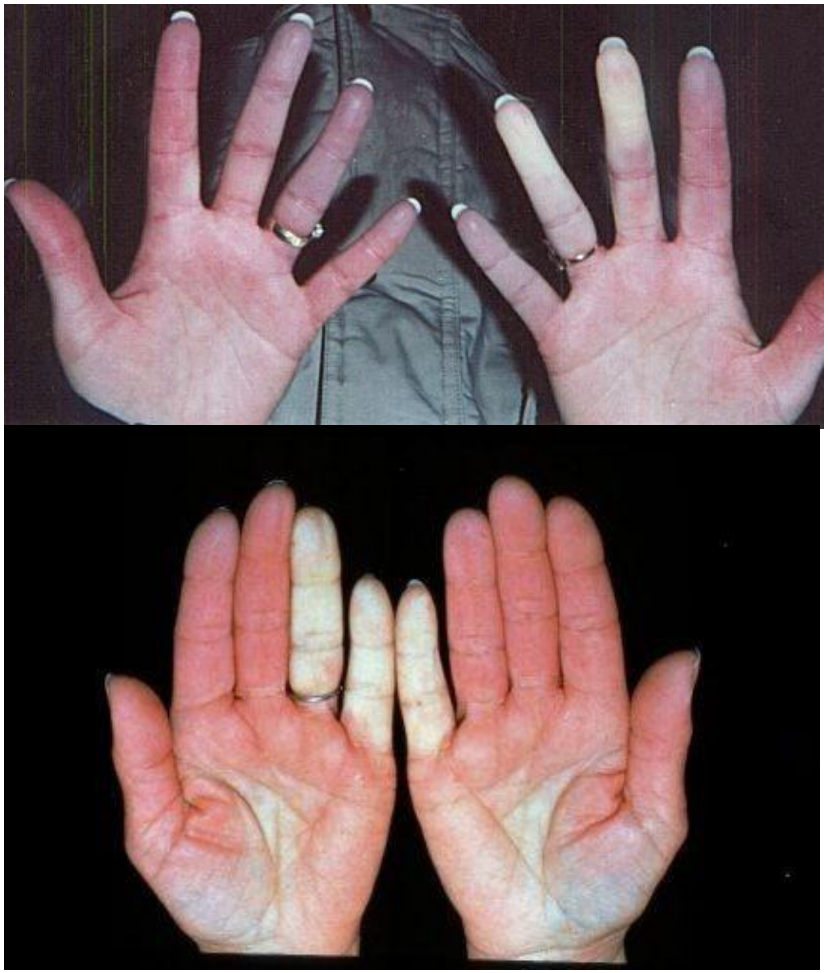
- If DLE
  - Sarcoid – lacks atrophy & follicular plugging
  - Lymphocytic infiltrating dz – lack of atrophy
- If erythematous lesions
  - Rosacea – central face, pustules, no atrophy, "triggers"
  - Photosensitivities – history, clinical, labs

Lupus Erythematosus Treatment

- DLE
  - Sunscreen
  - Antimalarials - gold standard (hydroxychloroquine)
  - Topical/intralesional/ systemic steroids
  - Most common morbidities – scarring, rare SCC
- SLE
  - PLUS:
  - Systemic steroids for renal, CNS, hematologic, rheumatologic findings
  - Treat secondary infections
  - Most common cause of death – renal & CNS

Raynaud's Phenomenon

- Clinical
  - Episodic vascular insufficiency of digital arterioles
  - Related to cold and emotions
  - Pallor, cyanosis, hyperemia
  - Often painful



Raynaud's Phenomenon Etiology

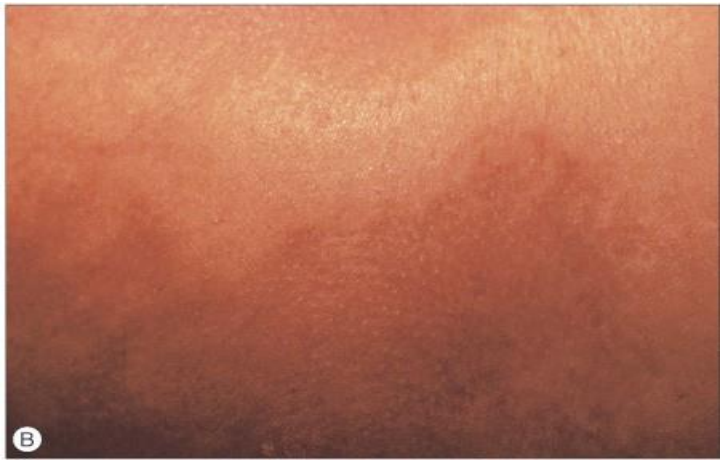
- Less than half have connective tissue disease
  - Idiopathic (Raynaud's *Disease*)
- Scleroderma (>50%), SLE, Dermatomyositis
- Pneumatic hammer operators
- Ergotism
- Vinyl chloride (industrial)
- Cryoglobulins/macroglobulins

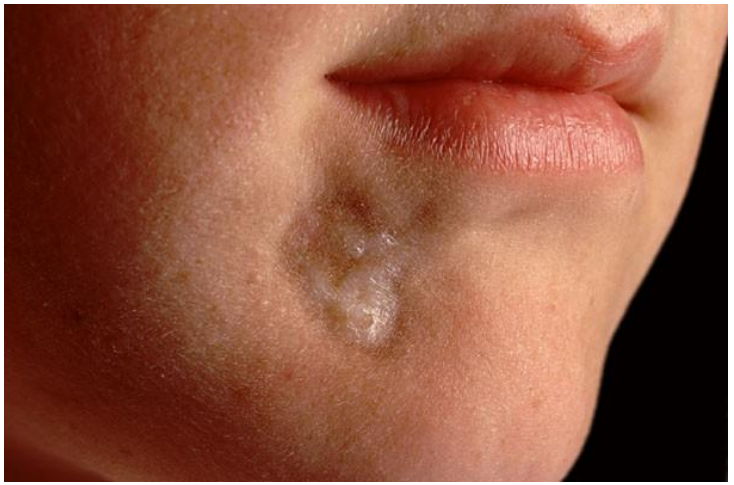
Raynaud's Phenomenon Treatment

- Avoidance of cold
- Vasodilators
  - Nifedipine (Ca+ channel blockers)
  - Prazosin (alpha blockers)
  - Nitroglycerin 2% topical
  - Sympathectomy in severe cases

Scleroderma

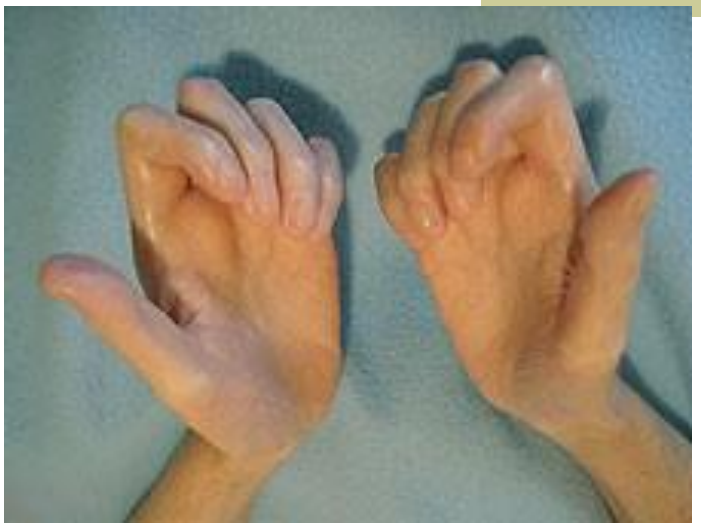
- Cutaneous to severe systemic
- Morphea
  - Localized scleroderma - atrophic scar with dyspigmentation
  - Smooth, hard, somewhat depressed, yellowish white, or ivory-colored lesions
  - Common on the trunk



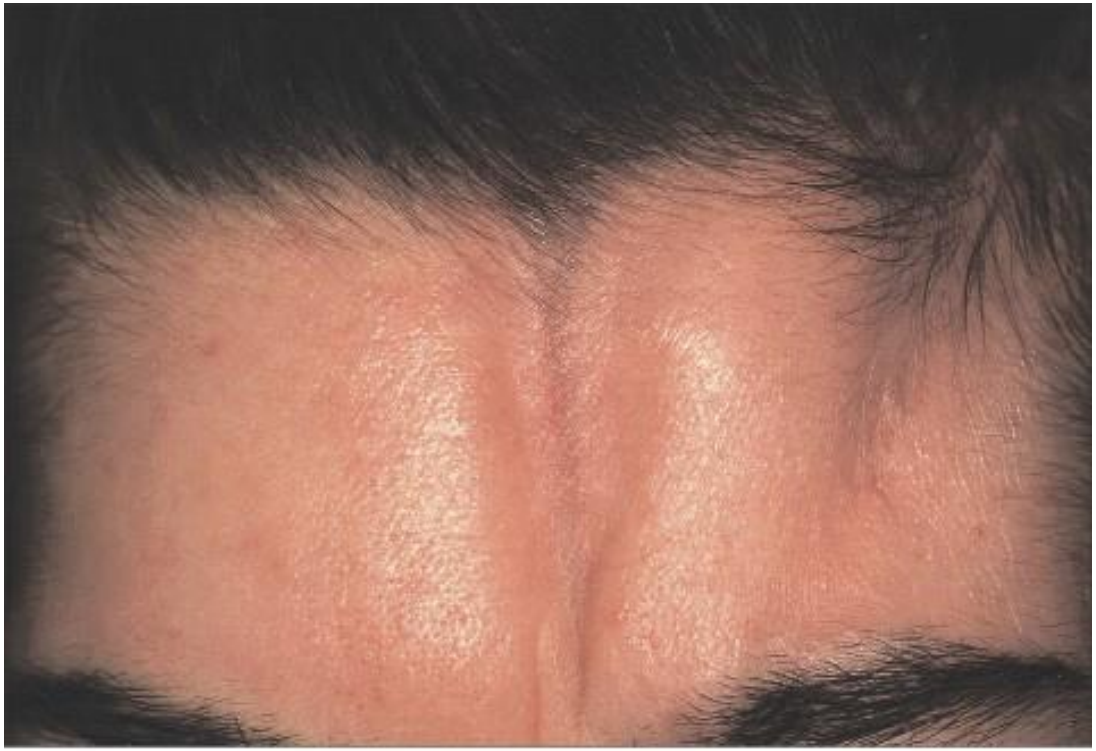


Scleroderma

- Acrosclerosis
  - Sclerodactyly – tight skin over hands, digits
  - Sclerosis of skin
  - Poikiloderma (slight atrophy, telangiectasia, dyspigmentation)
  - Telangiectatic mats
  - Calcinosis cutis



Scleroderma



En coupe de sabre (linear morphea)

Scleroderma Systemic Findings

- Abnormal esophageal/intestinal motility
- Pulmonary fibrosis
- Renal disease
  - Possibly rapid, fatal
- Most often anti Scl-70

Scleroderma: CREST Syndrome*

- Calcinosis
- Raynaud's
- Esophageal dysmotility
- Sclerodactyly
- Telangiectasias

- Mild form of progressive systemic sclerosis
- Most often anti-centromere

Scleroderma Etiology

- Unknown
- Autoimmune
  - Anti-centromere (limited/CREST)
  - Anti Scl-70 (systemic sclerosis)
- Overproduction of collagen

Scleroderma Differential

- If Morphea
  - Lichen sclerosus (often genital, can coexist)
- If Telangiectasias
  - Osler-Weber-Rendu (nasal bleeds, no sclerosis)
- If Sclerodactyly
  - Porphyria cutanea tarda (bulla, photosensitive, hypertrichosis)

Scleroderma Treatment

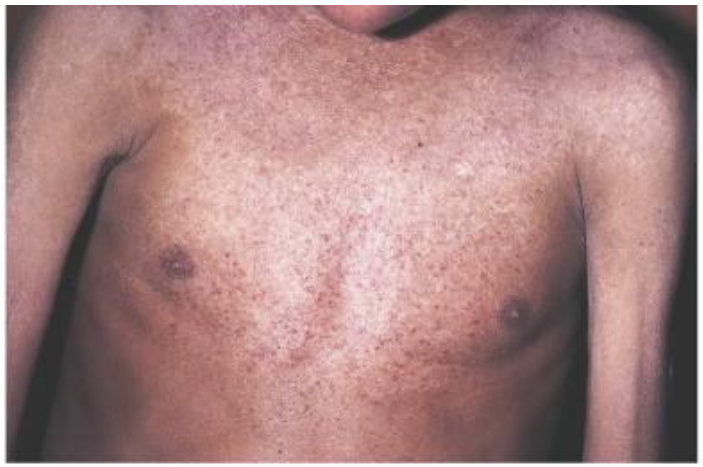
- Morphea – intralesional steroids
- Raynaud's –
  - Primarily calcium channel blockers (nifedipine, verapamil)
- Progressive systemic sclerosis
  - No approved therapies
  - Symptomatic
  - Some uncontrolled studies with D-penicillamine

Dermatomyositis*

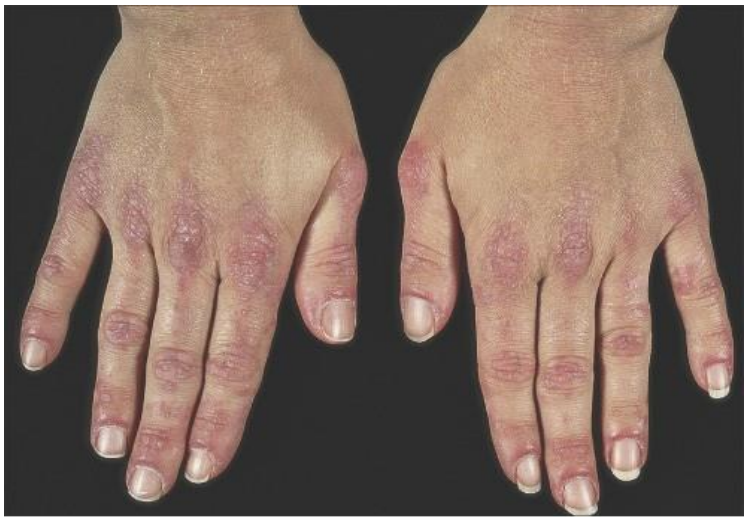
- Heliotrope – violaceous discoloration around eyes
- Gottron's papules – erythematous, papules over interphalangeal joints
- Telangiectasias/poikiloderma
- Raynaud's phenomenon
- Symmetrical proximal muscle weakness

- Children – calcinosis common, possible ulceration

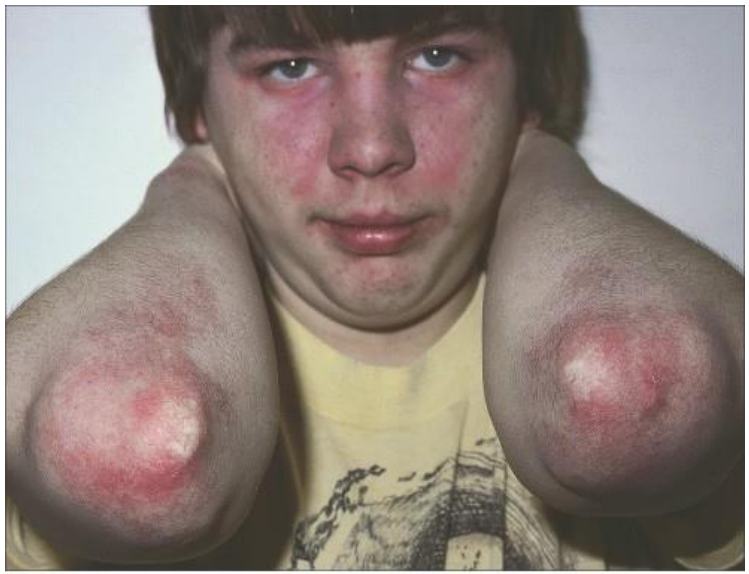
Dermatomyositis



Poikiloderma



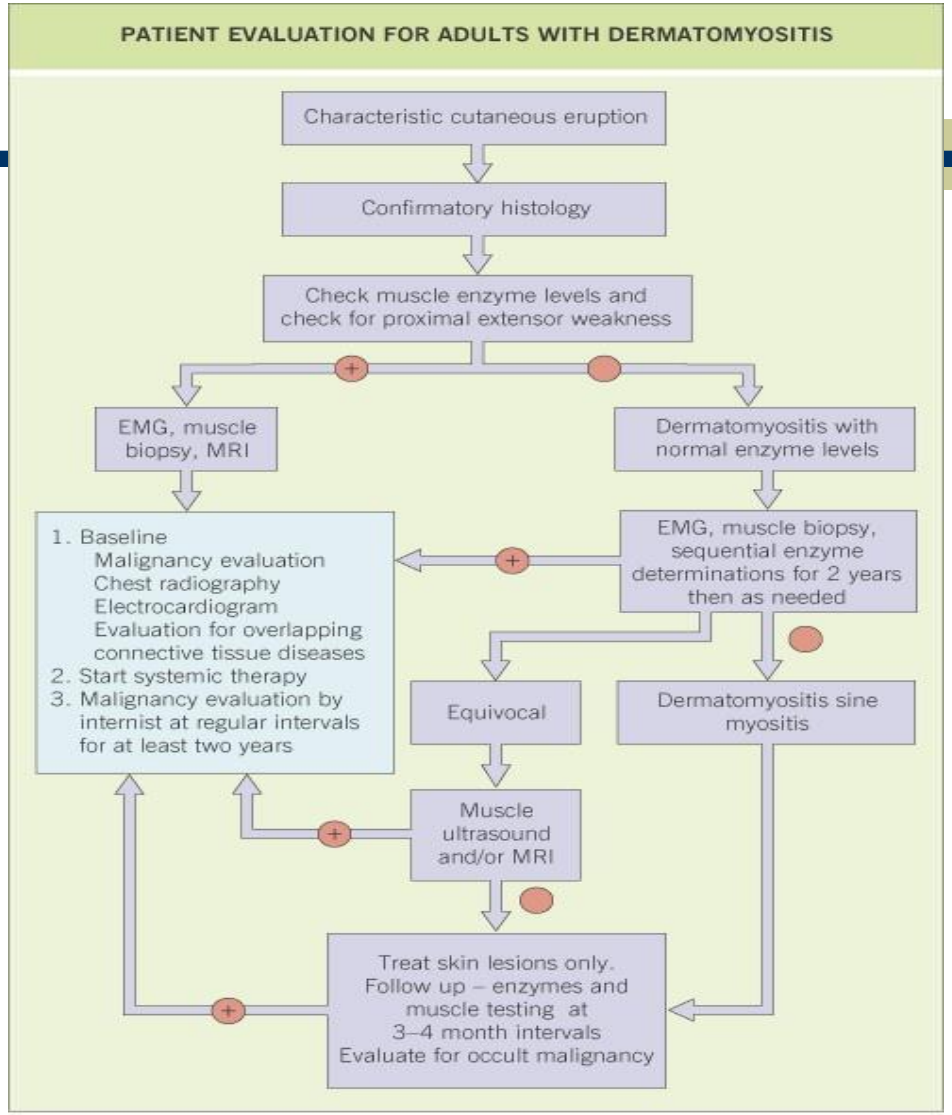
Gottron's



Heliotrope rash

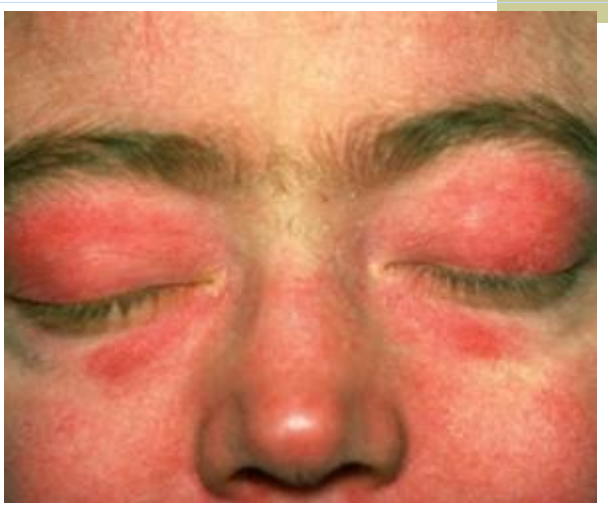
Dermatomyositis Labwork

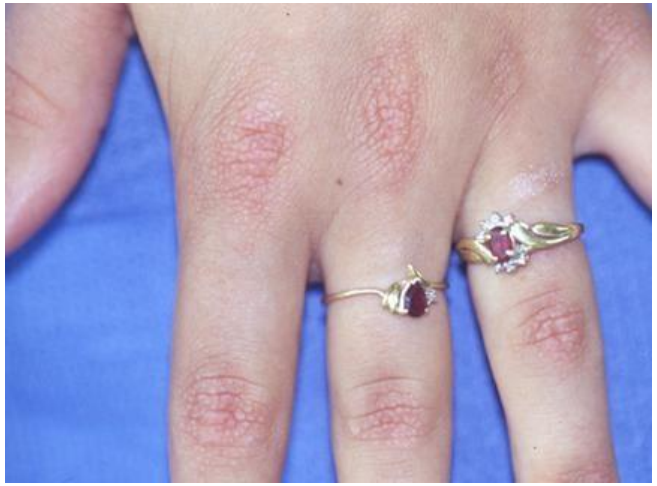
- Elevated muscle enzymes
- EMG
- Muscle biopsy
- Ultrasound/MRI



Dermatomyositis Differential

- Almost always pathognomonic
  - Heliotrope rash
  - Gottron's papules
- Exclude other causes of muscle disease





Dermatomyositis

- Associated with malignancy in 10-50% of adults (often lymphoma)
- Increased malignancy rate over general population

Dermatomyositis Treatment

- Physical Therapy
- Symptomatic Treatment
- Systemic Steroids
- Immunosuppressives
  - Ex. methotrexate

THERAPEUTIC LADDER FOR DERMATOMYOSITIS

Systemic therapy

Oral prednisone:	1 mg/kg tapered to 50% over 6 months and to zero over 2–3 years ①
	option to use pulse, split dose, or alternate day ①
Low-dose weekly methotrexate ②	
Azathioprine:	2–3 mg/kg/day ③
Others:	high dose intravenous γ-globulin ①
	pulse cyclophosphamide ③
	chlorambucil ③
	cyclosporin ②
	not plasmapheresis ③

Cutaneous lesions

Sunscreens (high solar protection factor with some protection against UVA) ③
Topical corticosteroids ③
Hydroxychloroquine (increased frequency of drug eruptions in patients with dermatomyositis)②
Hydroxychloroquine plus quinacrine ③
Low-dose weekly methotrexate ②
Retinoids ③

Others:	dapsone ③
	thalidomide ③
	mycophenolate mofetil ③

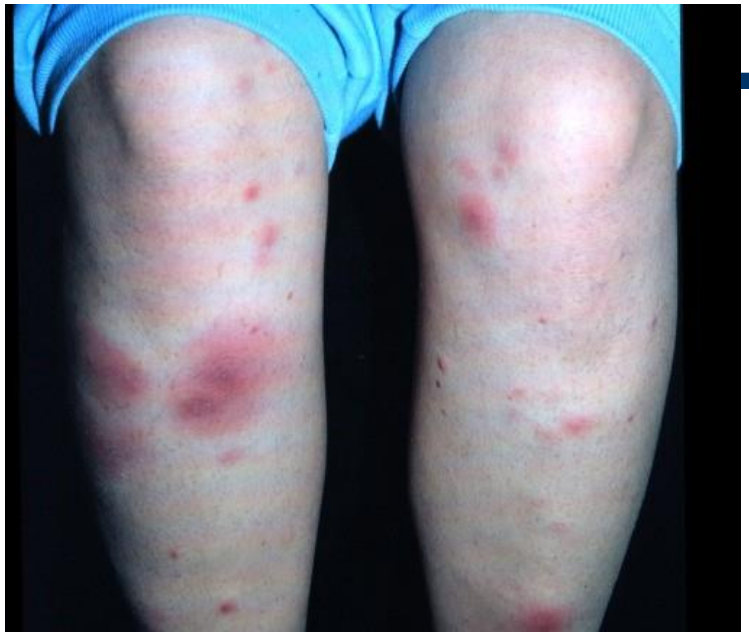
Dermatomyositis Prognosis

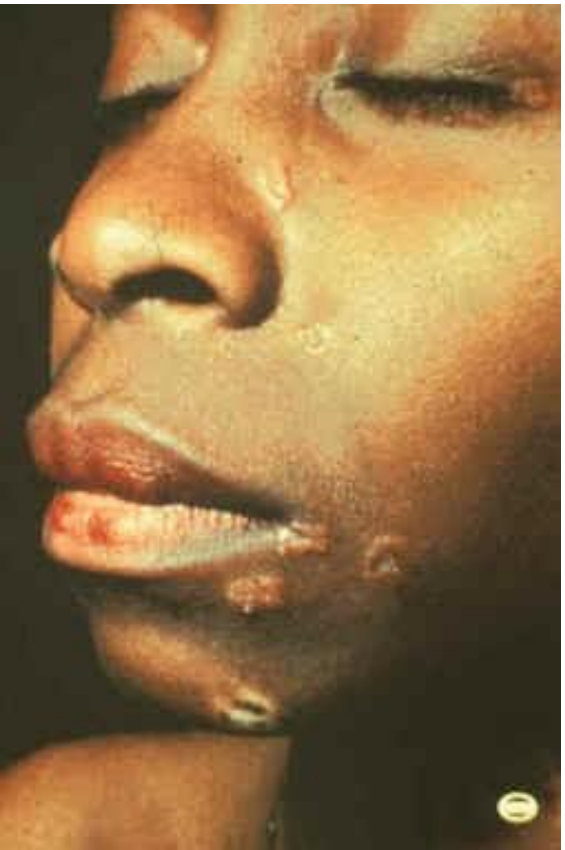
- Children
  - Generally good
  - Possible residual from calcinosis or contractures
- Adults
  - Often progressive and fatal
  - Aspiration common
  - Cardiac involvement with failure
  - Possible malignancy

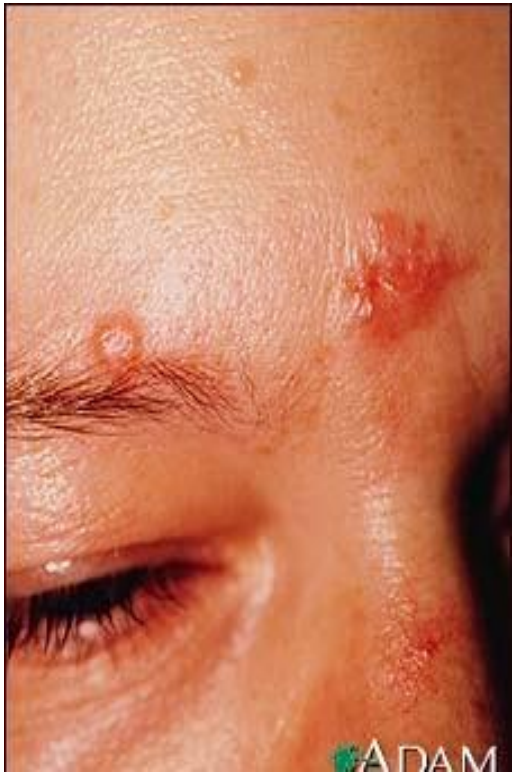
Sarcoidosis Clinical

- Systemic disorder
- Persistent with remissions and recurrences
- Common in blacks (10x higher)
- Cutaneous variation
  - Plaques, annular lesions, nodules, papules
  - Lupus pernio: violaceous, atrophic plaque on nose, cheeks or ears
- Erythema nodosum common early
- Diagnosis of exclusion

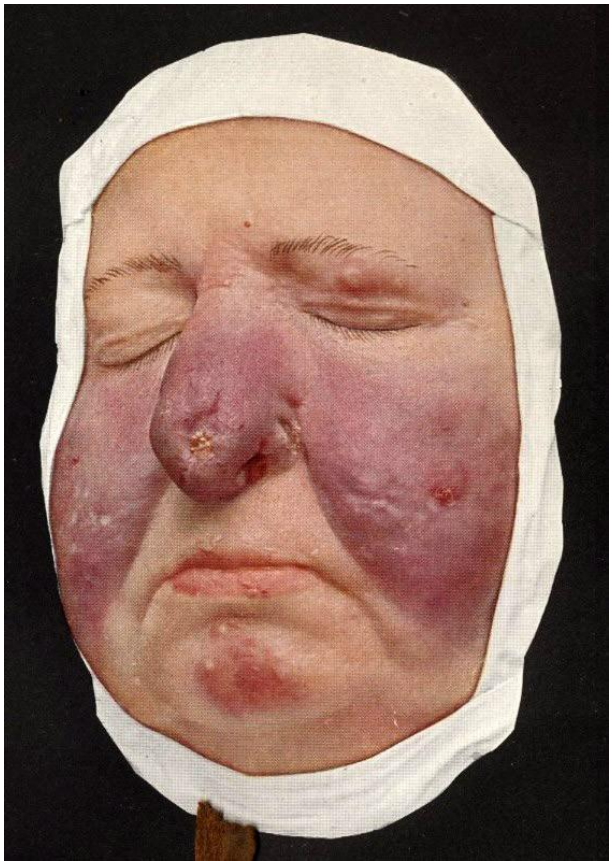
Sarcoidosis

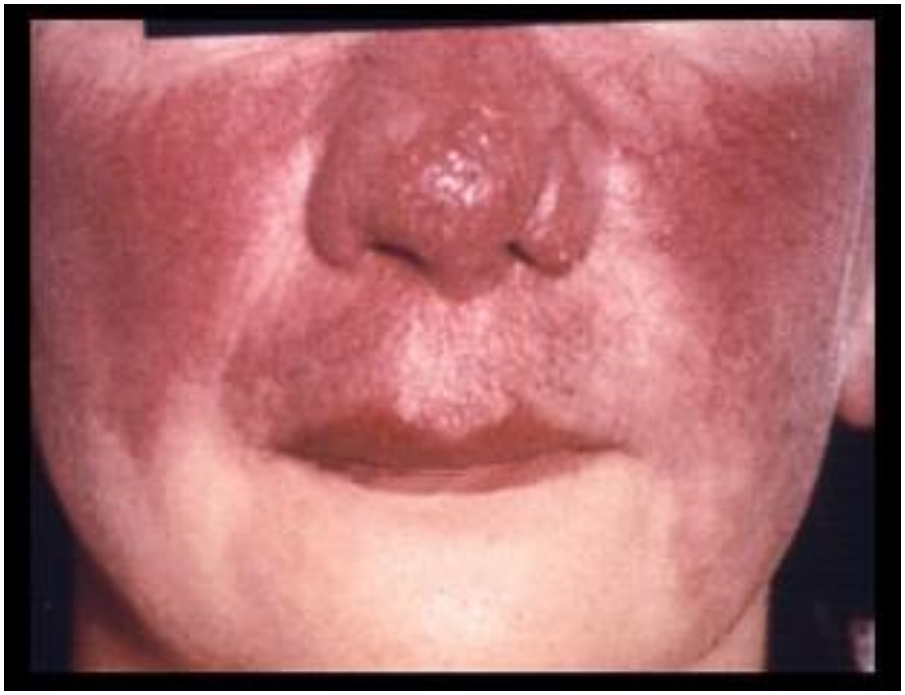






Sarcoidosis – Lupus Pernio

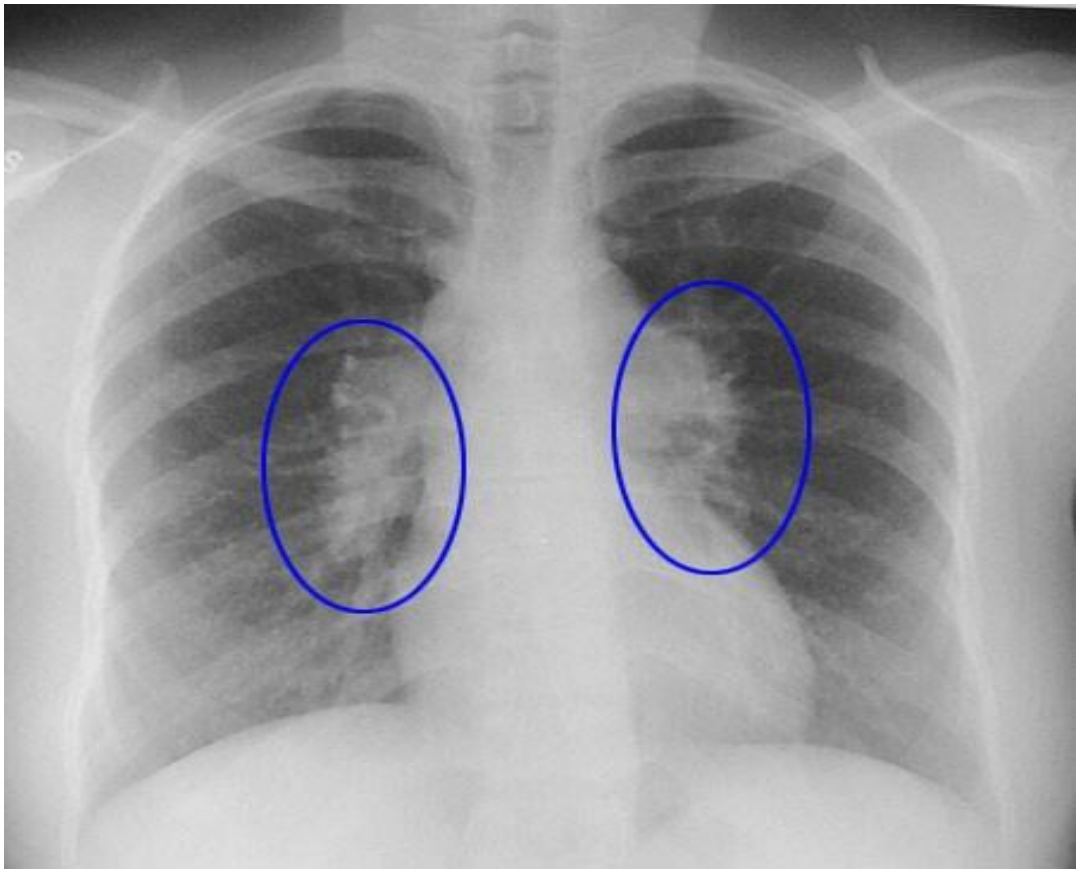




Violaceous, mildly atrophic plaques

Sarcoidosis Pulmonary Involvement

- Three stages
  - I – hilar adenopathy
  - II – hilar adenopathy with parenchymal disease
  - III – diffuse parenchymal disease

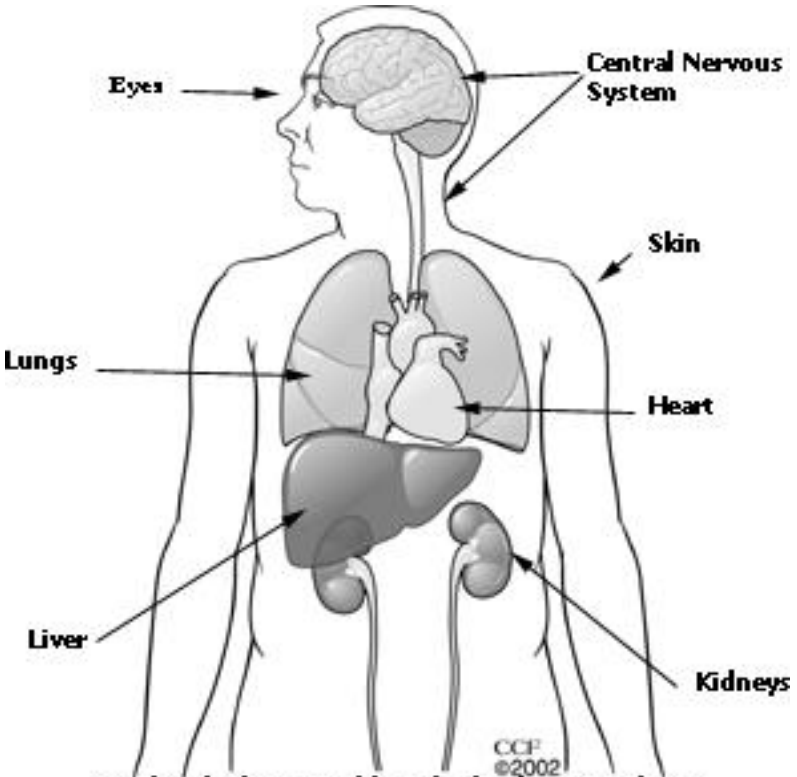


Sarcoidosis

- Lofgren's syndrome
  - Early sarcoid
  - Erythema nodosum, hilar adenopathy, arthritis
    - uveitis, fever, fatigue
  - Prognosis – 80-90% resolution 6 months to 2 years

Sarcoidosis Systemic Involvement

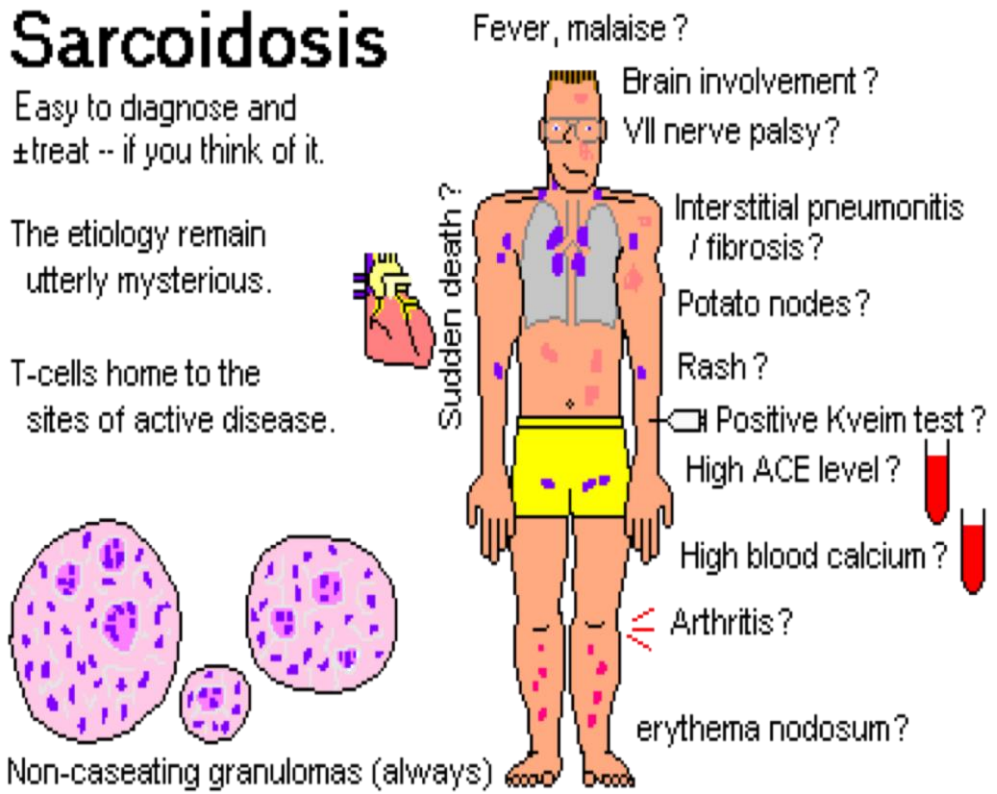
- Hepatic granulomas
- Bone cysts
- Lymphadenopathy
- Muscle granulomas
- Cardiac granulomas
- CNS granulomas
- Hypercalcemia
- Hyperglobulinemia



Besides the lungs and lymph glands, sarcoidosis can affect skin, eyes, joints, liver, heart and other organs and body systems.

Sarcoidosis Etiology*

- Unknown
- Abnormalities in immune response
- ACE (angiotensin converting enzyme) elevation 35-80%



Sarcoidosis Treatment*

- 30-70% need no treatment
- 10-20% severe
- 5-10% life-threatening
- Variable responses to treatment

- Cutaneous lesions
  - Corticosteroid injection
  - Antimalarials
  - Systemic corticosteroids
  - Immunosuppressants

- Pulmonary involvement
  - Controversial benefit of systemic steroids

- Hypercalcemia
  - ? Medications
  - Dietary modification

RENAL

- Renal Pruritis
- Perforating Dermatoses
- Nephrogenic Sclerosing Dermopathy
- Nail findings

Pruritus

- Generalized pruritus without a rash requires further workup
- Rule out ectoparasitic and cutaneous diease
- May demonstrate prurigo nodules, excoriations or no findings at all

- Differential?

Pruritus Differential

- Xerosis
- Medication
- Iron deficiency anemia
- Polycythemia
- Leukemia
- Lymphoma
- Multiple myeloma
- Uremia (most common cutaneous of ESRD)
- Cholestasis
- Hyperthyroidism
- Hypothyroidism
- Other

Pruritus workup

- Based on History and Physical findings

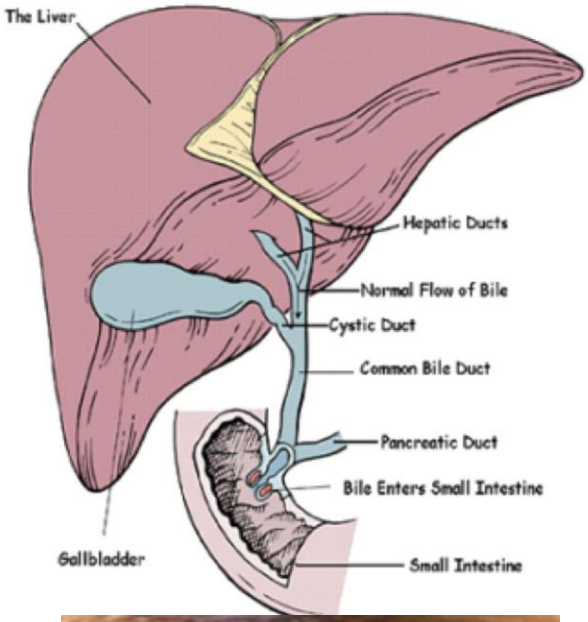
  Exclude primary disorder (eczema, scabies, xerosis)
- Conservative treatment depending on history and physical: mild soaps & detergents, moisturize, antihistamines, +/- topical anti-itch or steroids
- CBC +/- iron studies
- CMP
- TSH
- CXR
- HIV, Hepatitis Serology
- +/- SPEP

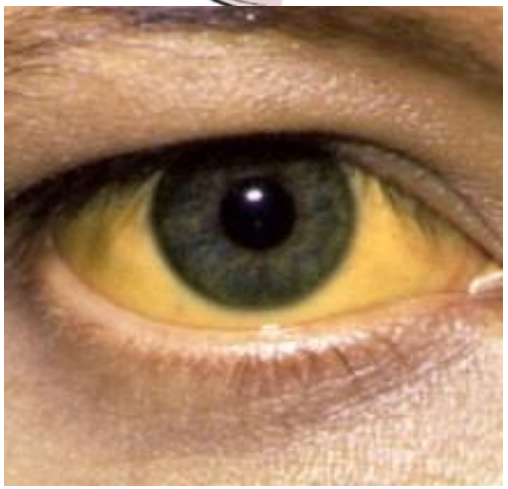
Internal Causes of Pruritus

- CRF/Uremic Pruritus
- Liver Disease
  - Obstructive disease
  - Hep C infection
  - Biliary Pruritus
  - Primary Biliary Cirrhosis
- Infections
  - AIDS
  - Parasites
- Hematopoietic diseases:
  - Polycythemia Vera
  - Iron-Deficiency Anemia
- Malignancy
  - Lymphoma (Hodgkin's)
    - Incidence of 10-25%
    - Presenting feature in 7%
  - Leukemia
  - Myeloma
  - Internal malignancies
  - Carcinoid
- Hyper or hypothyroidism
  - Diabetes +/-
- Neuropsychiatric
  - Anorexia nervosa
  - Multiple sclerosis

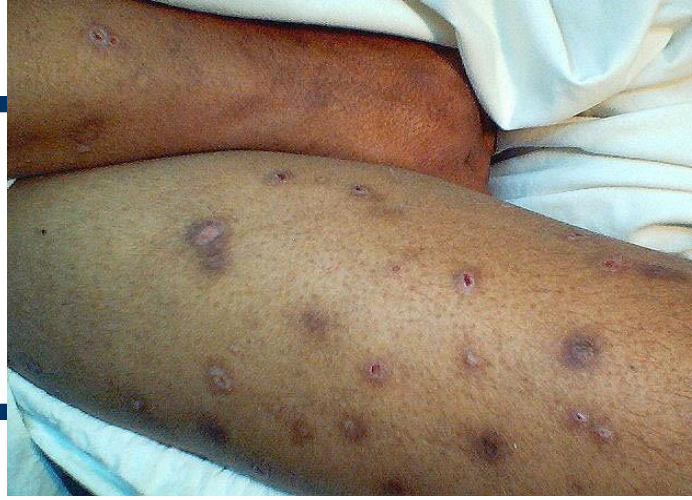
Biliary Pruritis

- **20-50% of pts w/ jaundice have pruritus**
- Chronic liver disease
  - Primary biliary cirrhosis, primary sclerosing cholangitis, obstructive choledocholithiasis, carcinoma of the bile duct, cholestasis, HCV
- Generalized, migratory, & not relieved w/ scratching
- Serum level of conjugated bile acid does ***not*** correlate to degree of pruritus
  - *Likely a central mechanism*
    - *Have elevated opioid peptide levels*
- Treat underlying condition
  - Naloxone, naltrexone, or nalmefene
  - cholestyramine





RENAL DISEASE

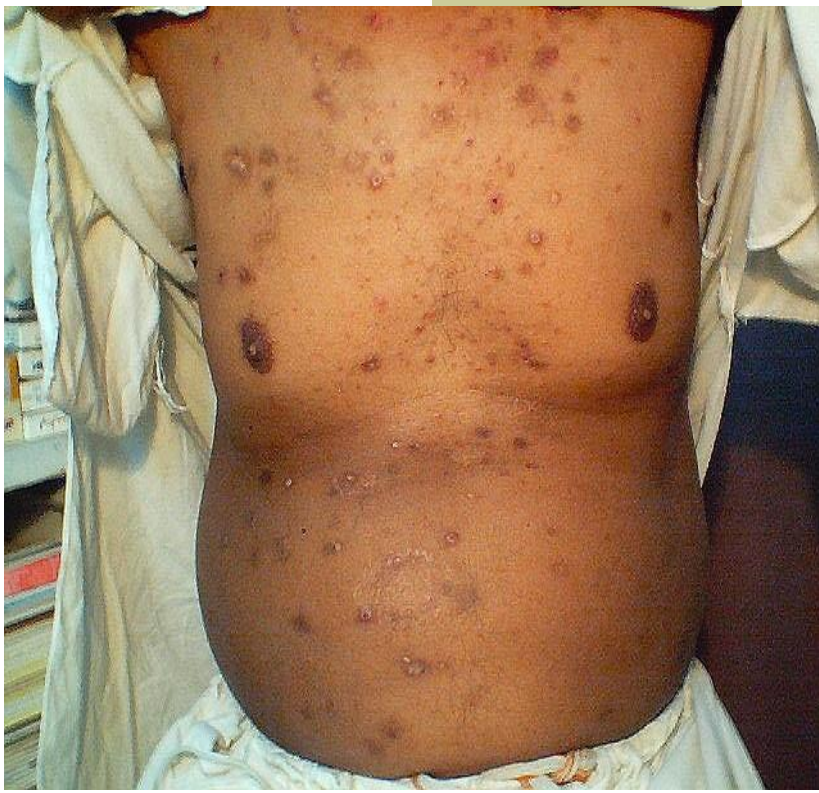


RENAL PRURITIS

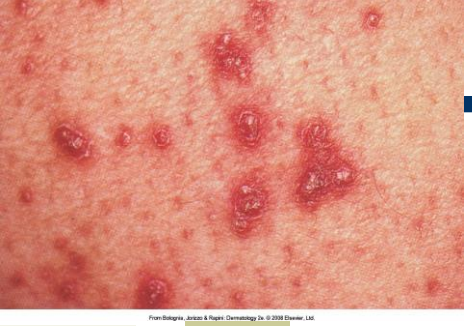
- *"Uremic pruritus"* = used synonomously
  - However not secondary to elevated levels of serum urea
- ***Chronic renal failure is the MC internal cause of systemic pruritus***
  - 20-80% of patients with CRF
- Typically **generalized, severe, and intractable**
- Multifactorial mechanism:
  - **Xerosis**, secondary hyperparathyroidism, inc. serum histamine, hypervitaminosis A, iron-deficiency anemia, neuropathy, **inc. levels of poorly dialyzed compounds**
  - Complications = Lichen simplex chronicus, prurigo nodularis may result

Treatment Renal Pruritis

- **Responds well to NB/UVB**
  - Recurs after discontinuation
- Aggressive emollients for xerosis
- *Gabapentin*
  - 3x weekly w/ hemodialysis
- Nalfurafine (TRK-820)
  - IV 3x weekly
  - k-opioid agonist
- Thalidomide

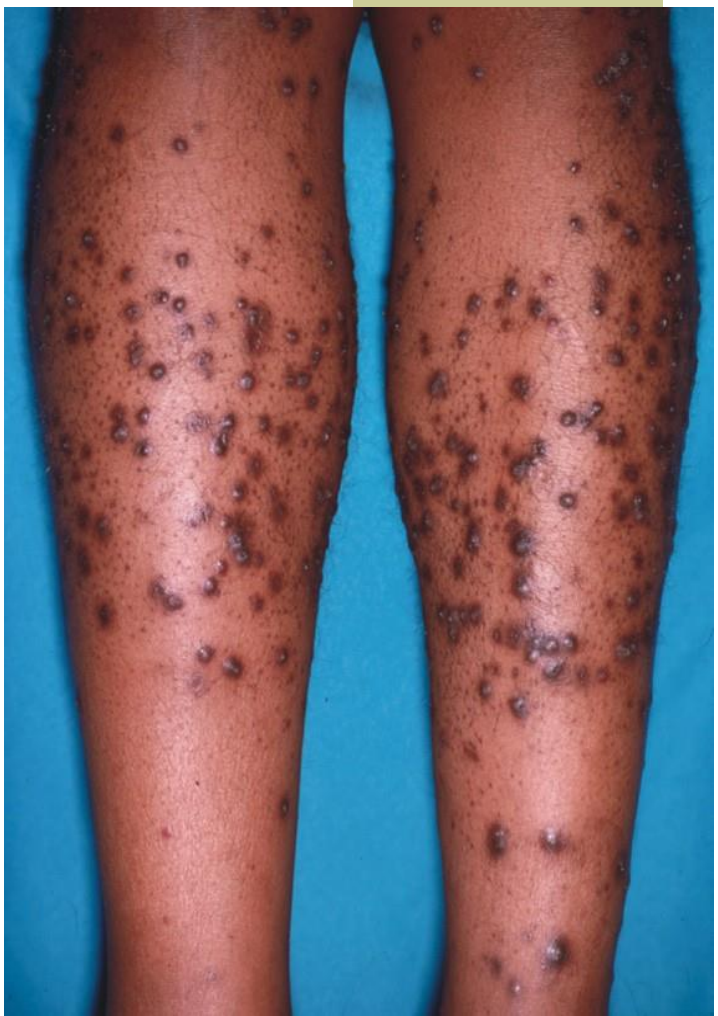


- ❖ Pruritus lowest during day after HD
- ❖ Pruritus peaks 2nd night after HD
- ❖ Pruritus is HIGH during HD



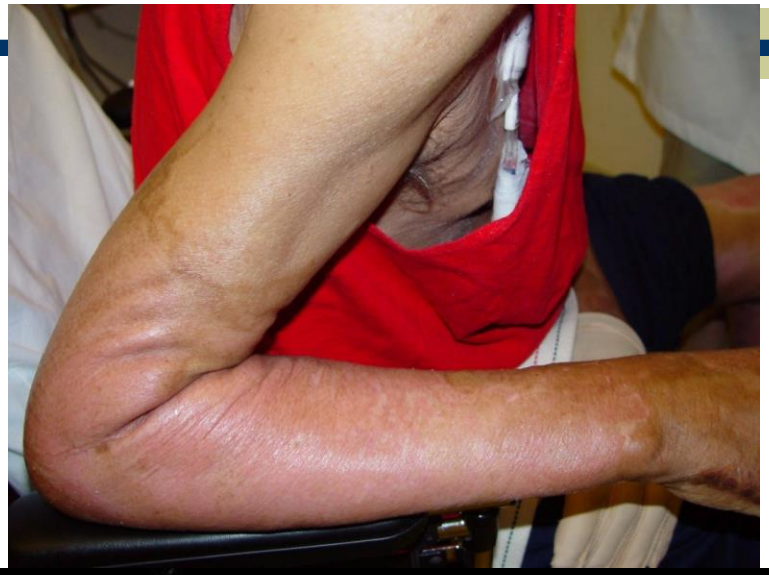
Acquired Perforating Dermatoses

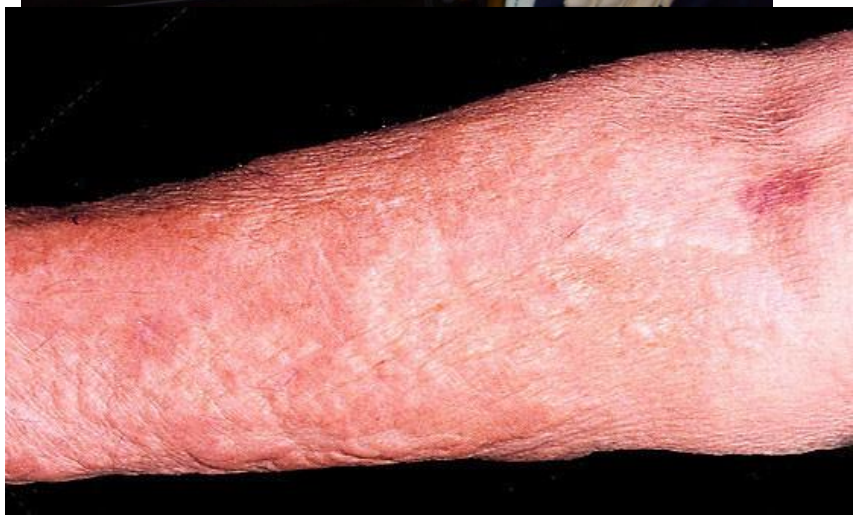
- Perforating disease
  - Arising in adults
  - "Kyrle's disease"
- Associated with **renal failure**, DM, and rarely liver disease and internal malignancy
- Clinical:
  - **Pruritic keratotic papules**
    - *Result of collagen extrusion from dermis to epidermis*
    - *Likely secondary to trauma*
  - ***Legs are MC location***
- Treatment:
  - UV light, emollients



Nephrogenic Fibrosing Dermopathy

- Patient with renal insufficiency & hemodialysis
  - **Exposure to gadolinium based contrast medium**
- Clinical:
  - Thickened, sclerotic, edematous, hyperpigmented papules or plaques
    - **"Woody induration"**
  - *MC on the Extremities*
    - **face is spared** (unlike scleroderma)
- Treatment:
  - *Ineffective- optimize renal function via transplantation*
  - Phototherapy, rapamycin





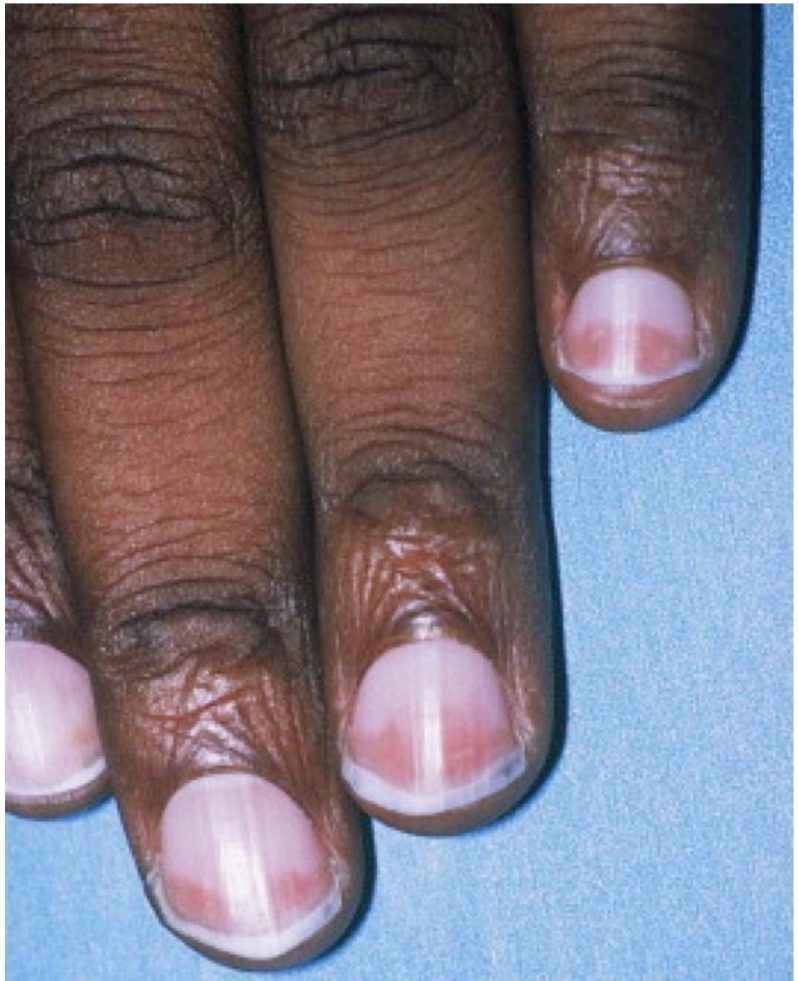
Half and Half Nails

Nail changes are common in renal patients:

- Hemodialysis: 76%
  - **Half & half (MC)**
  - Splinter hemorrhages
  - Absent lunula
- Renal transplant: 56%
  - Leukonychia (MC)

Half & half nails

- Proximal nail is white
- Distal ½ is red/pink/brown
- *Sharp demarcation line*



Cutaneous and Gastrointestinal

These patients have an increased risk of:

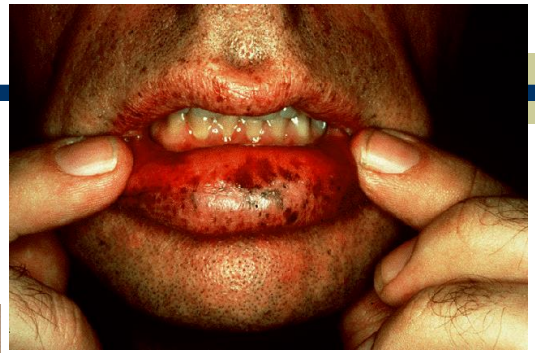
A. Melena and intussusception.

B. Adenomatous polyps.

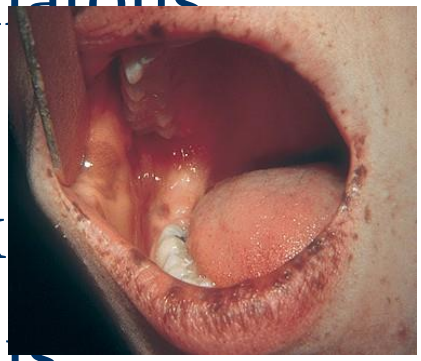
C. Epistaxis.

D. Halitosis.

E. Oral ulcers.



Melanin deposits



Medicine Net.com

STK gene mutation (autosomal dominant) - Hamartomatous polyps. Increased chance of cancer of colon, pancreatic cancer in men; and ovary, breast and endometrial in women.

LIVER DISEASE

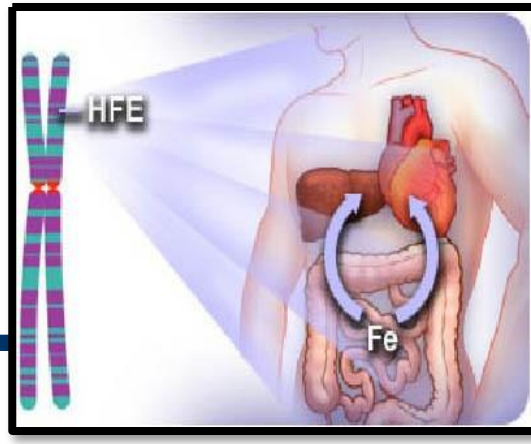
- Gardner syndrome
- Hemochromatosis
- Porphyria Cutanea Tarda
- Associated nail findings

Cutaneous and Gastrointestinal (Intestine)

- Gardner's Syndrome
  - Epidermal cysts, osteomas, lipomas, fibromas
  - Colon or rectal polyps (adenomas)
  - High malignant potential by age 40
    - Half with carcinoma by age 30, most die before age 50
  - Autosomal dominant
  - Tx: total colectomy

Hemochromatosis

Bronze Diabetes

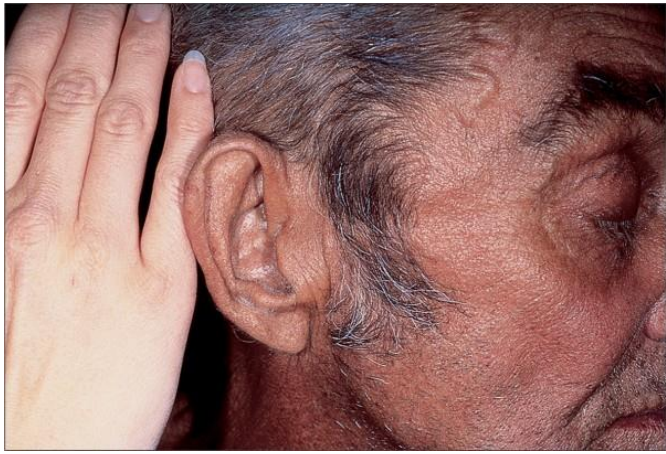


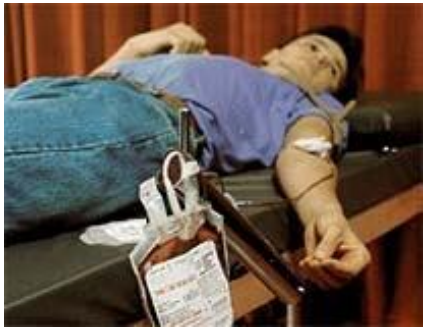
- AR → HFE-gene
- MC white European population; 5th decade
- M>F (2° female iron loss w/ menses)
- Inc. intestinal Iron absorption → iron overload → organ deposition
- Clinical Features:
  - Skin = metallic-grey hyperpigmentation
    - Sun-exposed areas w/ mm involvement in 20%
    - Nails = koilonychia (50%)
    - Hair = sparse to absent
  - GI = **hepatomegaly, hepatocellular CA,** abd. pain, wt. loss
  - CVS = arrhythmias, **heart failure**
  - Endocrine = **IDDM**; hypogonadism; loss of libido
  - MSK = **polyarthritis (20-70%)**

Hemochromatosis

Bronze Diabetes

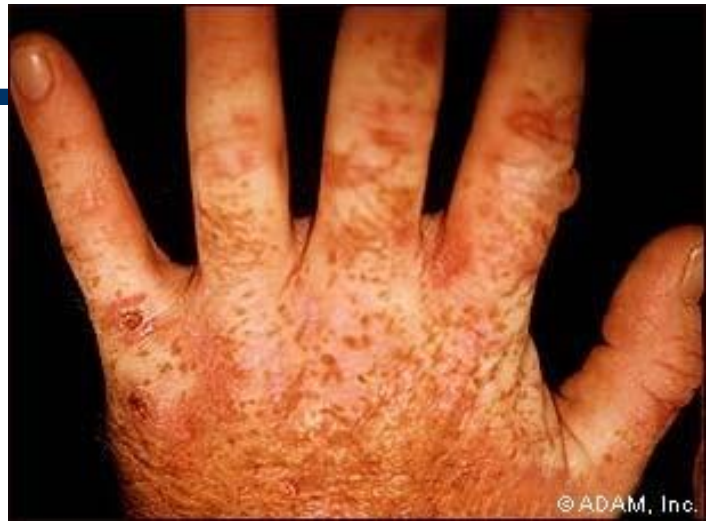
- Many with genetic mutations do **not** develop disease
  - **Increased risk: alcohol, smoking** and **Hep C**
- Dx:
  - Elevated plasma iron & serum ferritin
  - Transferrin saturation (TS) >45
  - Liver bx: if ferritin >1000, Inc. LFTs or >40yrs
  - Gene studies
- Once cirrhosis is present → HCC risk is 30%
- Tx:
  - **Phlebotomy (can prevent cirrhosis)**
  - Deferoxamine (chelator)
  - Supportive care (insulin, testosterone, anti-arrhythmics)
  - ***Restrict Vit. C***

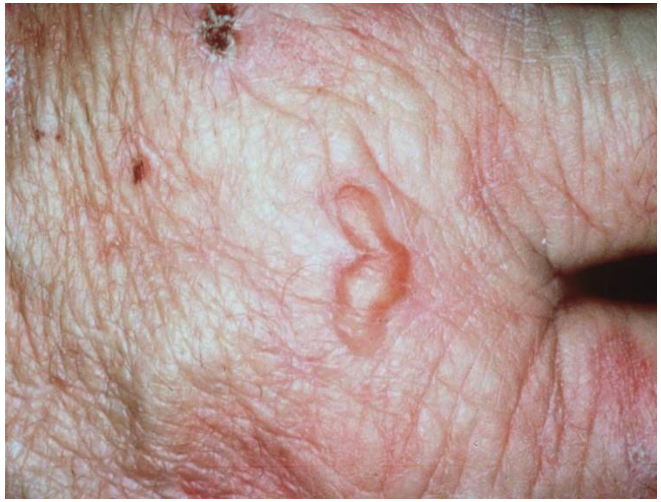




Porphyria Cutanea Tarda

- ***Uroporphyrinogen decarboxylase deficiency***
- *Most common type of porphyria*
- Clinical Manifestations:
  - Bullae, erosions on **sun-exposed skin**
    - heal with scars, milia and dyspigmentation
  - Hypertrichosis on face
  - Sclerodermoid changes of skin
  - Wine/tea colored urine





- DRUGS & CHEMICALS
- **Ethanol**
- **Estrogens**
- Iron
- Hexachlorobenzene (fungicide)
- Chloroquine (high dose)

- PREDISPOSITIONS
- Diabetes mellitis (25%)
- **Hepatitis**
  - **HCV (94% in US)**
  - HAV, HBV
- HIV infection
- **Hemochromatosis** genes

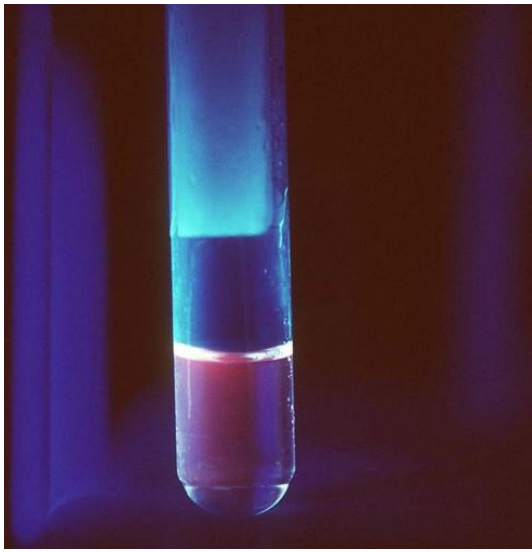
PCT Diagnosis & Treatment

Diagnosis

- Plasma porphyrin level
- 24 hour URINE PORPHYRINS
- WOOD'S LIGHT on urine specimen in office
  - Orange-red fluorescence *(high false negative rate)*

Treatment

- **Sunlight Avoidance**
- *Avoid drugs/chemicals/ETOH that precipitate attacks*
- Decrease consumption of iron-rich foods
- **Therapeutic phlebotomy (TOC)**
- Low dose Chloroquine

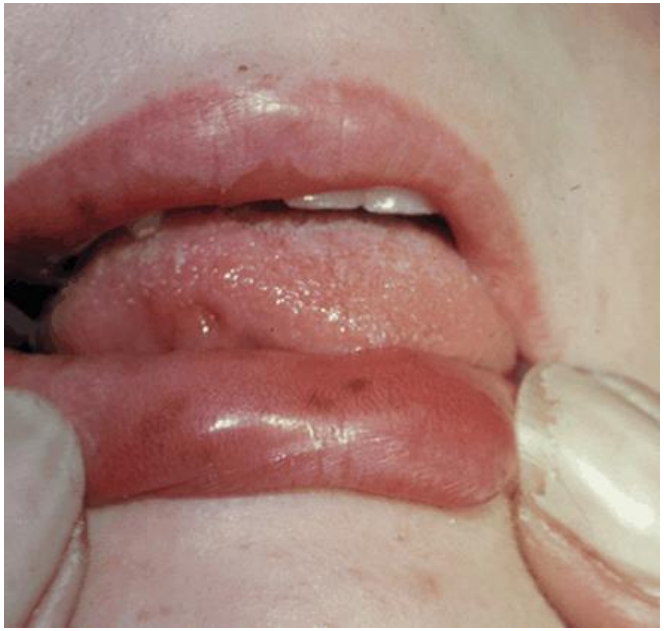


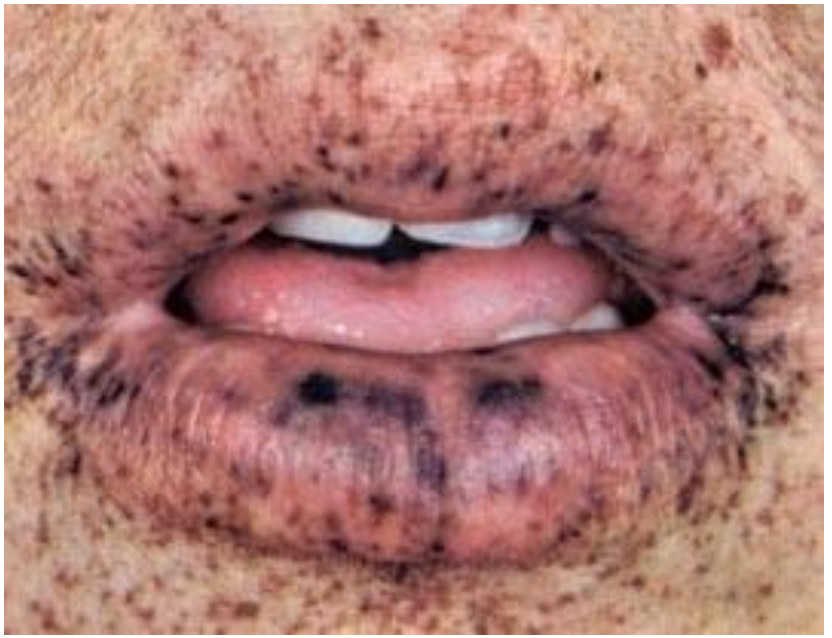
Cutaneous and Gastrointestinal* (Intestine)

- Peutz-Jeghers Syndrome
  - Perioral melanotic freckles (often infancy)
    - Also gingiva, buccal and genital mucosa
  - GI polyps
  - 10-18x cancer risk (1/2 develop by age 40)
    - Colon, duodenum, pancreas, breast, thyroid, lung
  - Abdominal: pain, bleeding, intussusception
  - Autosomal dominant
  - Regular, frequent gastrointestinal screening

Cutaneous and Gastrointestinal

Peutz-Jeghers Syndrome





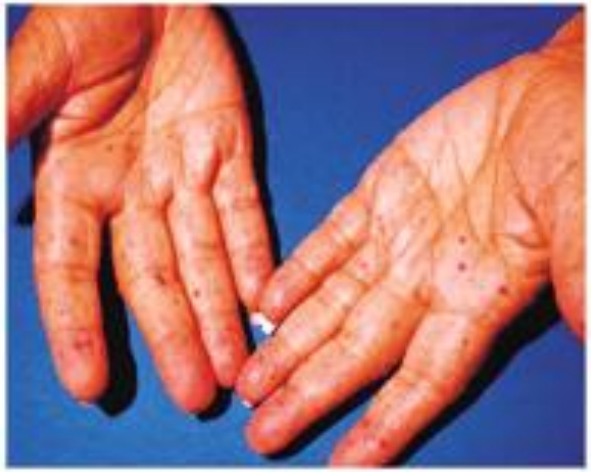
Melanotic macules

Cutaneous and Gastrointestinal* (Intestine)

- Osler-Weber-Rendu (hereditary hemorrhagic telangiectasias)
  - Autosomal dominant
  - Mat-like telangiectasias on any body area
    - Mucous membranes, acral common
    - Earliest location under tongue
  - GI bleeding, epistaxis (first symptom), ulcers, A-V fistulas, hematuria
  - Treatment: blood replacement, address vessels

Cutaneous and Gastrointestinal

- Osler-Weber-Rendu (hereditary hemorrhagic telangiectasias)



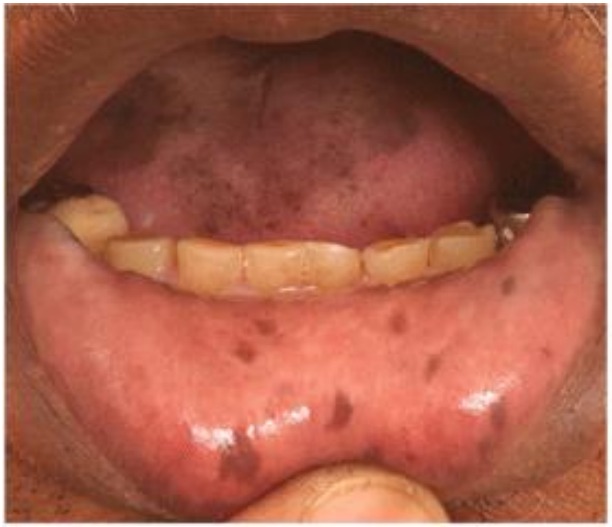


Figure 1—Multiple small telangiectases of the tongue and buccal mucosa.

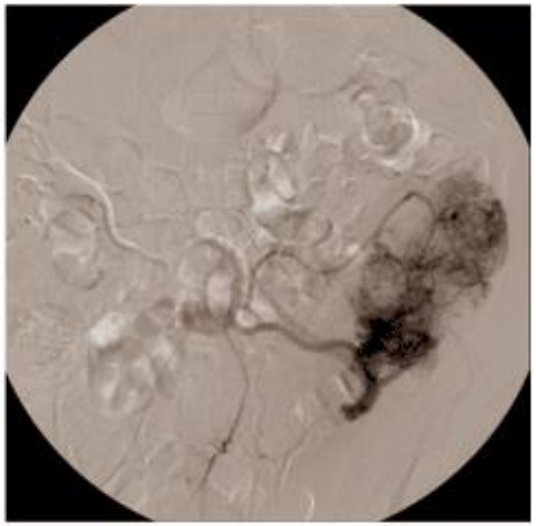


Figure 2—Arteriovenous malformation along the descending colon.

telangiectasias

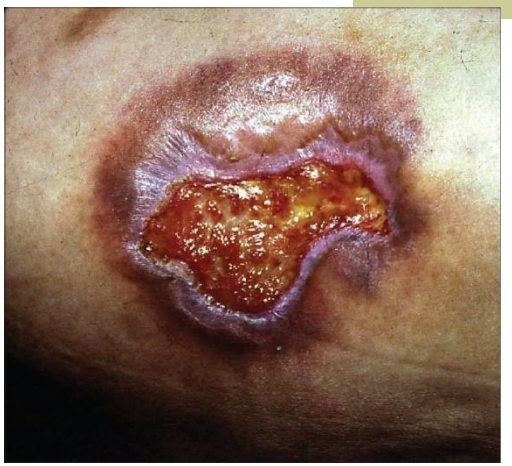
A-V malformation

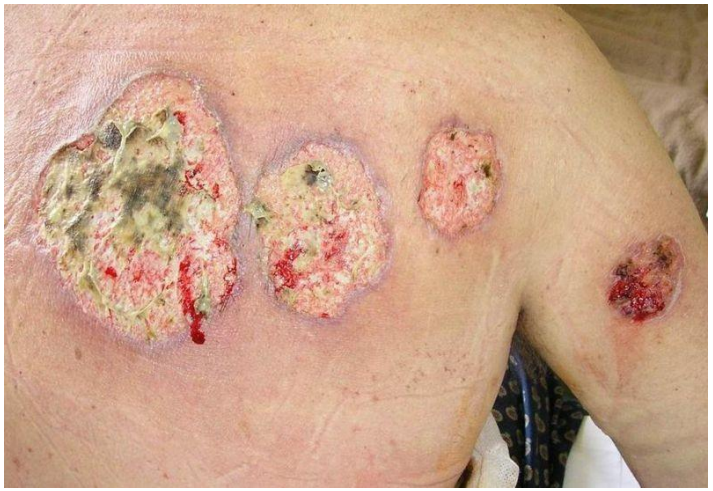
Cutaneous and Gastrointestinal (Intestine)

- Inflammatory Bowel Disease
  - Manifestations of ulcerative colitis and regional enteritis (Crohn's) identical
  - Apthous ulcerations during exacerbations
  - Erythema nodosum in 5% of exacerbations
  - Treatment
    - Therapy for bowel disease

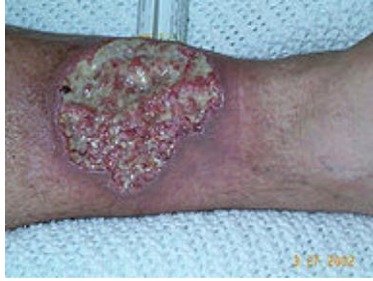
Cutaneous and Gastrointestinal (Intestine)

- Inflammatory Bowel Disease
  - Pyoderma Gangrenosum
    - 1-10% of IBD
    - Undermined necrotic violaceous ulcer
    - Pustular onset
    - More common in UC
    - Frequent precipitation by trauma
    - Treatment: steroids and immunosuppressives

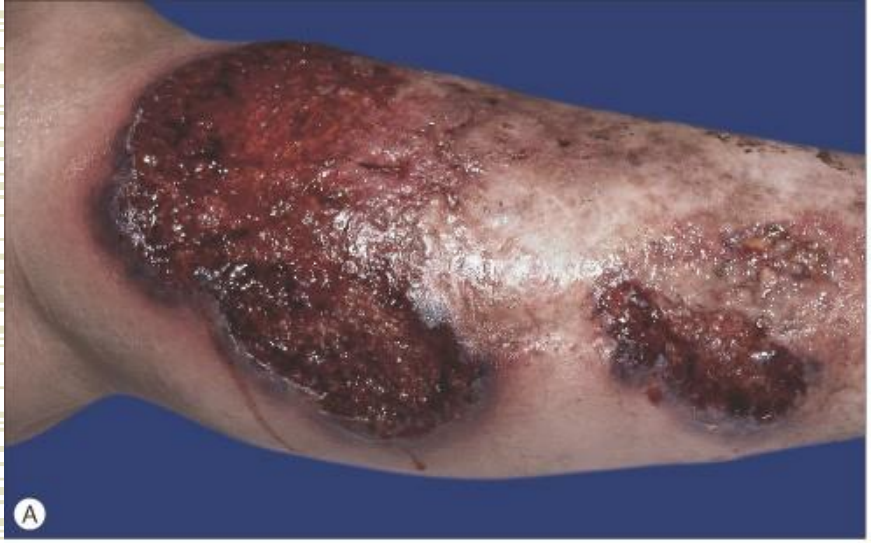


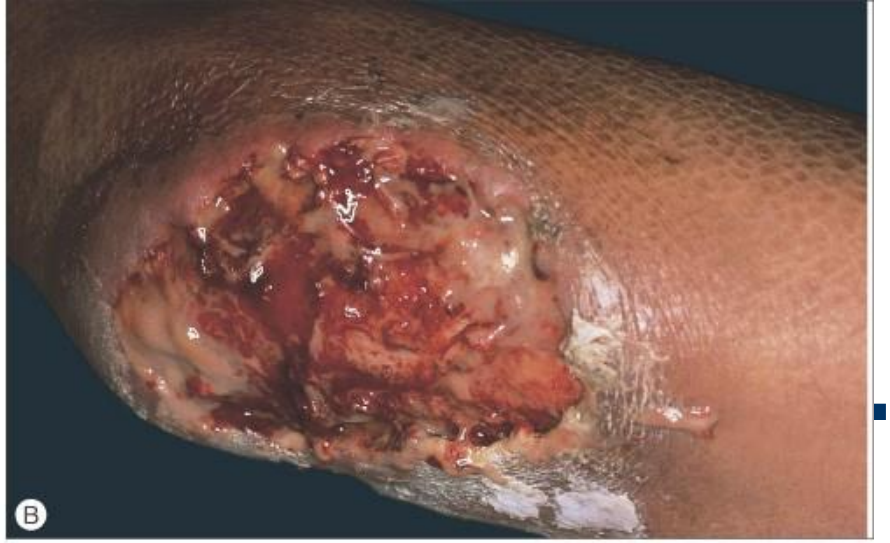


Pyoderma Gangrenosum

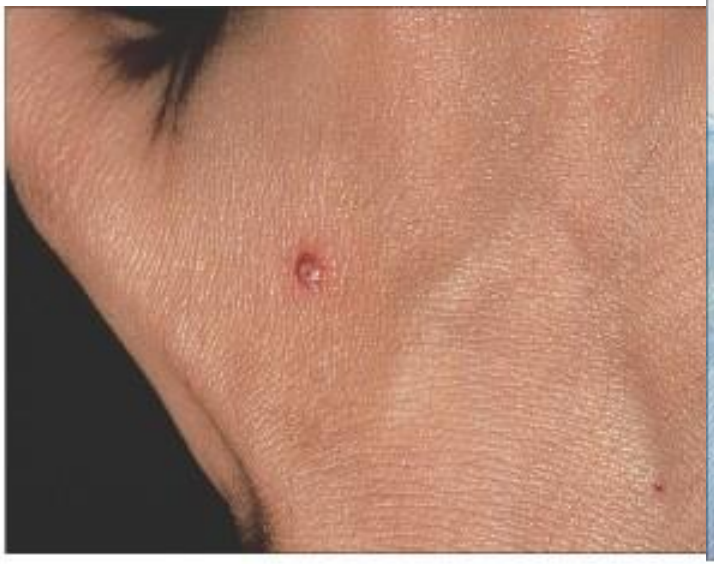


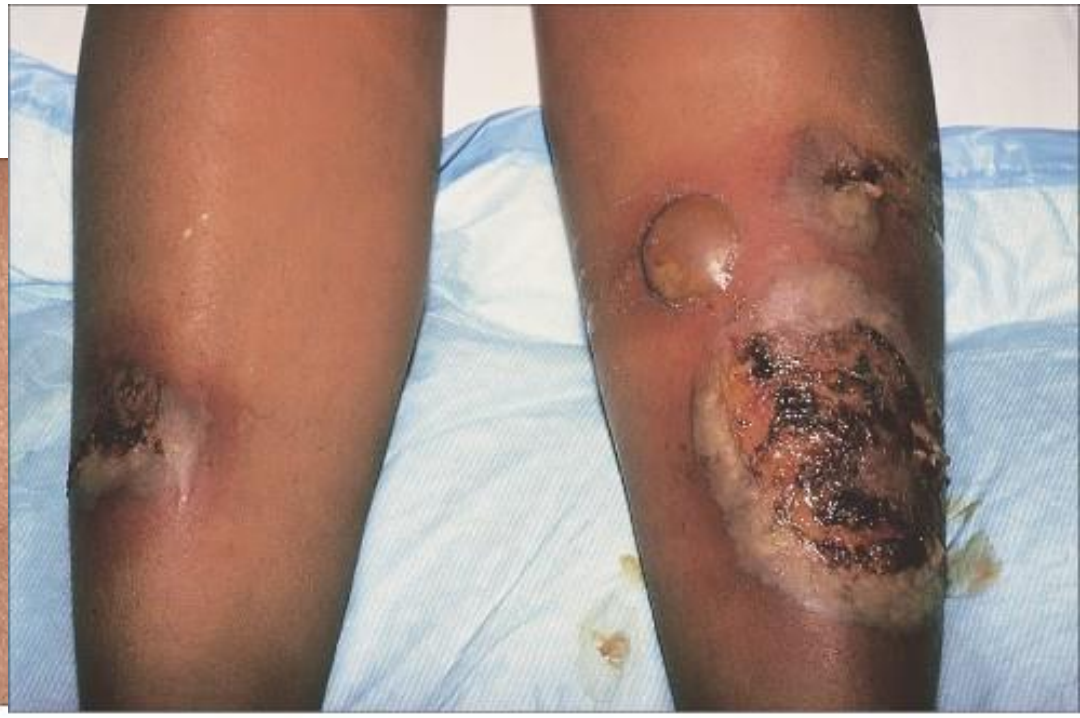
- Uncommon, recurrent, **ulcerative neutrophilic disease**
- Tender papulopustule → undergoes necrosis and ulceration with an **irregular, undermined border**
  - Heals with atrophic, cribiform, pigmented scars
- **50-70% have associated disease**
  - MC **Ulcerative colitis, Crohn's** (20-30%)
    - *1.5-5% of pts. with IBD develop PG*
  - Arthritis (20%)
    - Seronegative arthritis, RA, spondylitis of inflammatory bowel dz
  - **Hematologic disease (15-25%)**
    - Leukemia (AML, CML), IgA gammopathy, myeloma,
  - 25-50% of cases are idiopathic





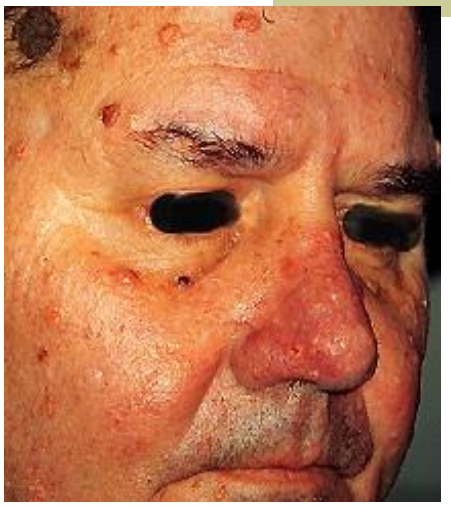
Early lesion: papule with erythematous base

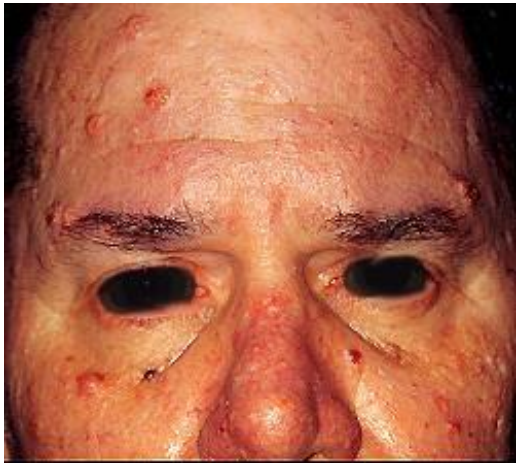




Cutaneous and Gastrointestinal (Intestine)

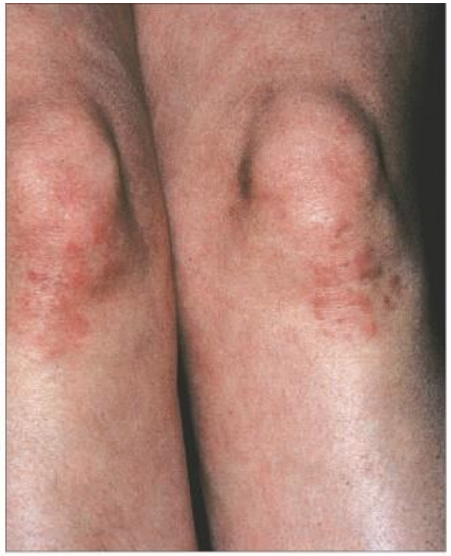
- Muir-Torre Syndrome
  - Autosomal dominant
    - Sebaceous neoplasms
    - Multiple keratoacanthomas
    - Internal malignancy
  - Cutaneous 10-20 years prior (preventative medicine!)
  - Colon cancer most common

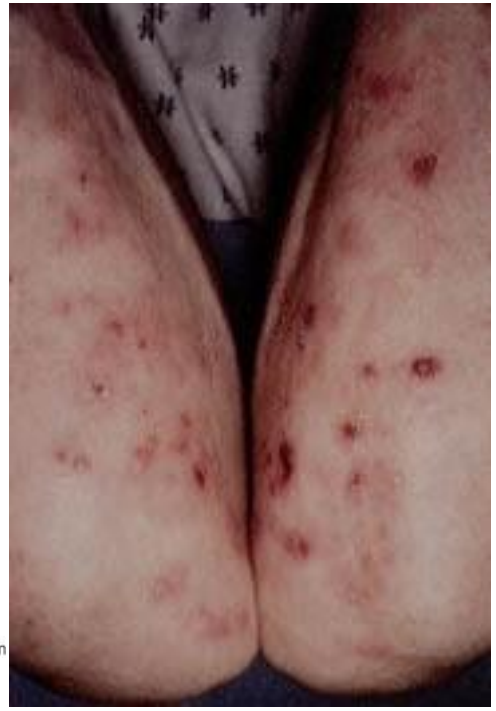




Cutaneous and Gastrointestinal (Intestine)

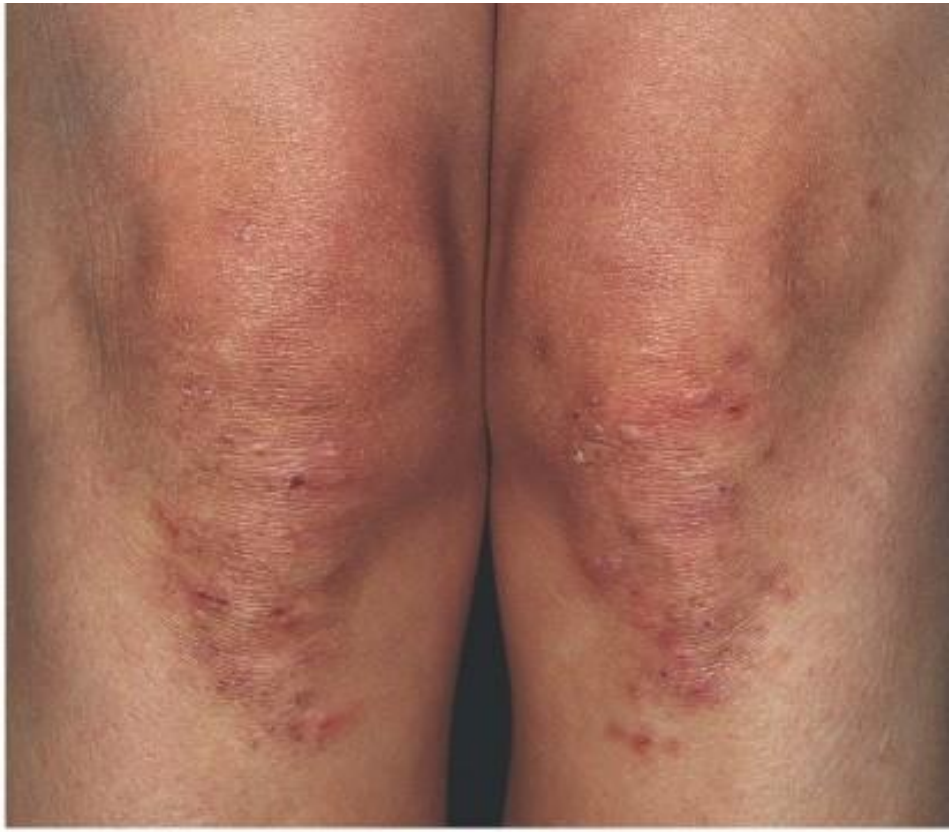
- Dermatitis Herpetiformis
  - Chronic, relapsing/remitting, severely pruritic dz
  - Symmetrical, polymorphous (often extensor)
  - Itching and burning are intense (often only excoriations)
  - Associated with gluten-sensitive-enteropathy
  - Treatment: medication plus gluten-free diet





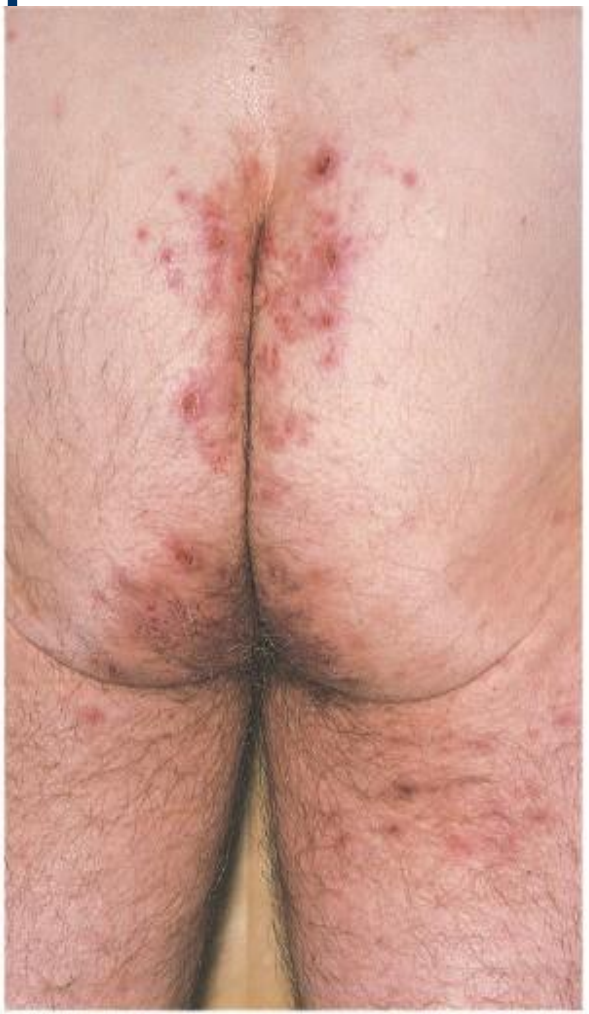
Dermatitis Herpetiformis

- Cutaneous manifestation of gluten sensitivity (Celiac Dz)
- Relapsing, severely **pruritic grouped vesicles**
  - May also be papules, urticaria, tense bullae
  - ***May only see crusts → scratching!!***
  - Intense itching and burning
- Symmetrically on **extensor surfaces, scalp, nuchal area, buttocks**



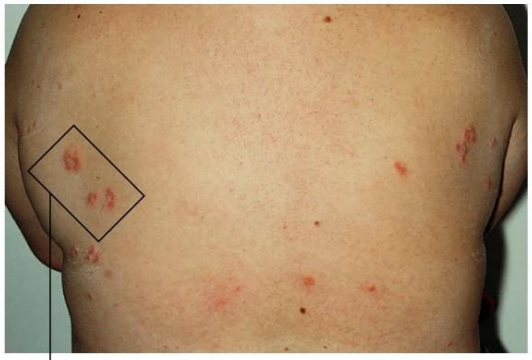
Dermatitis Herpetiformis

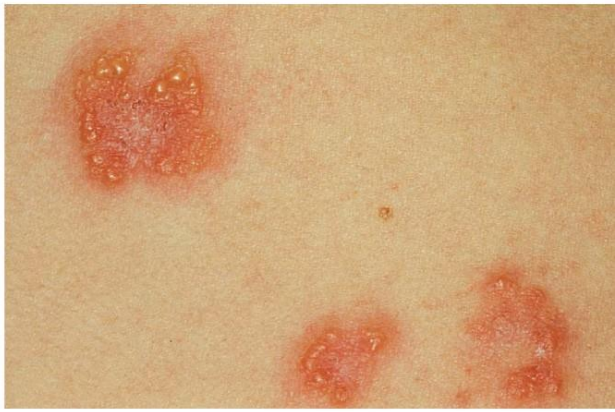
- Male=female
- 2nd-5th decade (20-40)
- **Related to celiac disease**
  - 70-100% of DH pts. have abnormalities of jejunal mucosa (often asymptomatic)
  - 25% of celiac pts. have DH



Dermatitis Herpetiformis

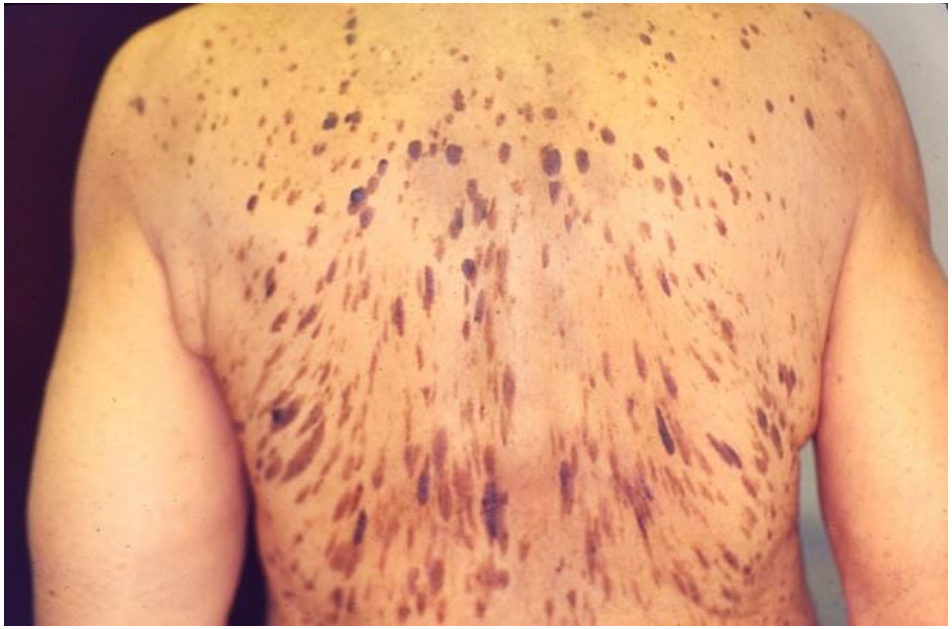
- Diagnosis
  - Skin biopsy → characteristic histology!
  - **Antiendomysial antibodies** (endomysial Ag is TTG)
    - Sensitive and specific (>80%)
    - Reflect severity of enteropathy and compliance of diet
  - **Antigliadin antibodies** (>66%)
  - Endoscopy: blunting and flattening of villi (80-90%)
- Treatment
  - **Gluten free diet**
  - Dapsone





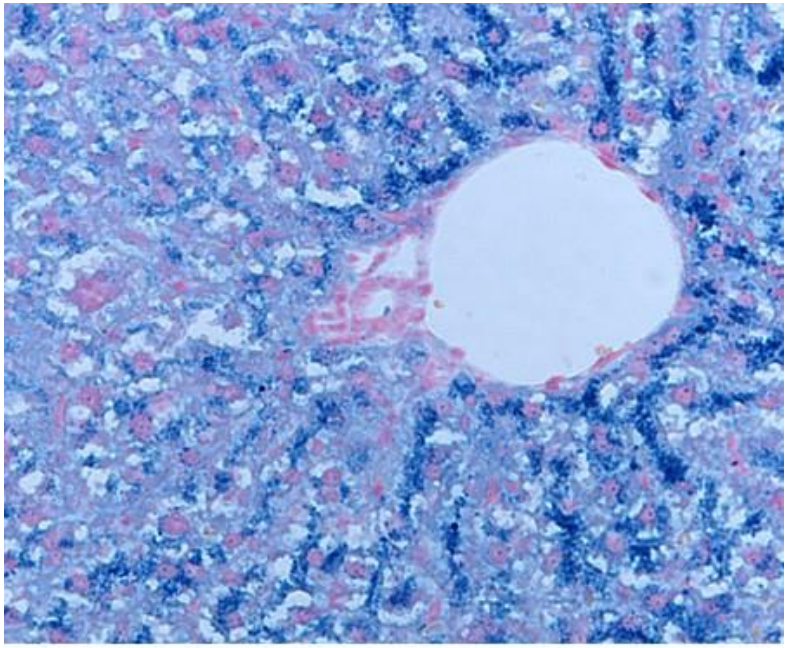
Cutaneous and Gastrointestinal (Intestine)

- Sign of Lesser-Trelat
  - Rapid increase in size/number of seborrheic keratoses
  - Occ also AN
  - Assoc Colon (or gastric) carcinoma



Cutaneous and Gastrointestinal (Liver)

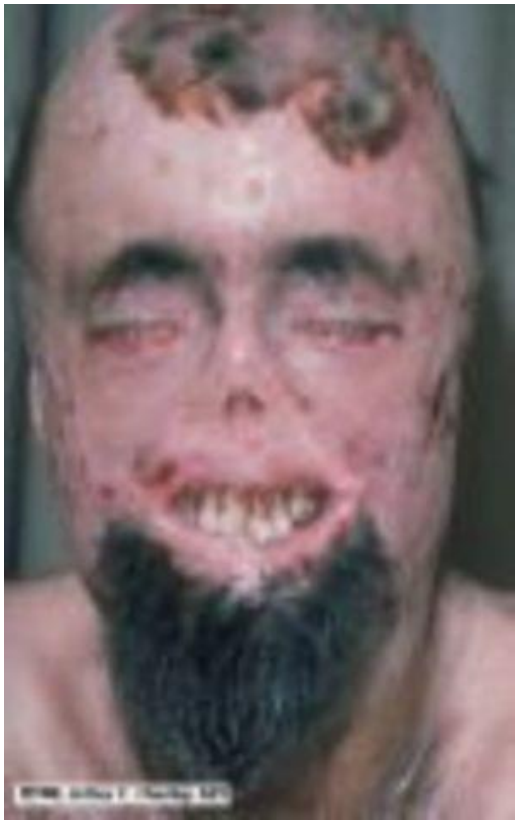
- Hemochromotosis
  - Hyperpigmentation
  - Cirrhosis
  - Diabetes
  - Koilonychia
  - Elevated iron



Iron stain of liver

Cutaneous and Gastrointestinal (Liver)

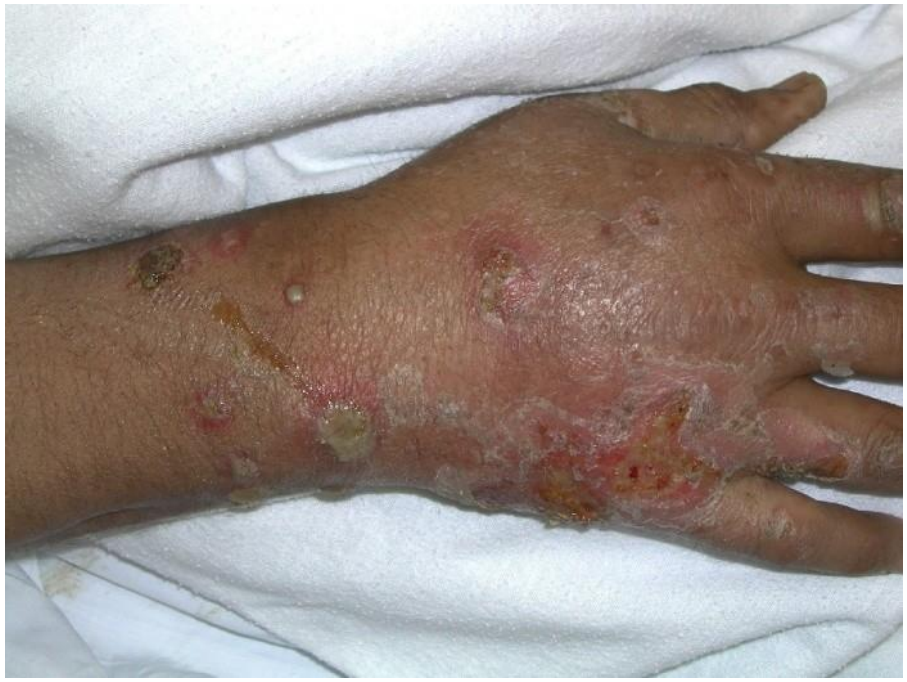
- Porphyrias
  - Each associated with deficiency of enzyme in heme synthesis
  - Hepatic or Erythropoietic
  - Some forms with photosensitivity
  - Frequent alcoholism and Hep C



Vampire legend

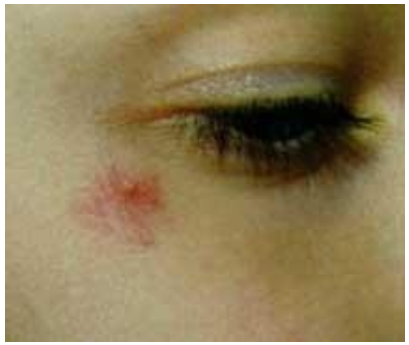
Cutaneous and Gastrointestinal (Liver)

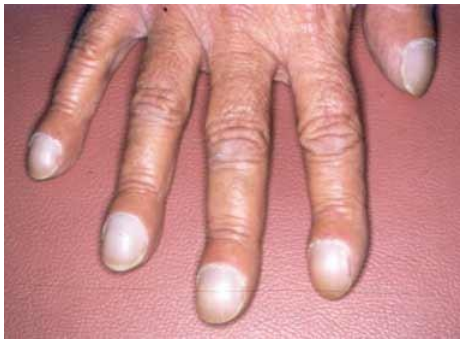
- Porphyrias
  - Vesicles and bullae (subepidermal) on sun-exposed areas
  - Atropic scarring
  - Milia
  - Facial hypertrichosis

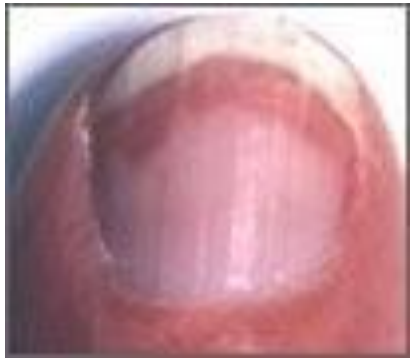


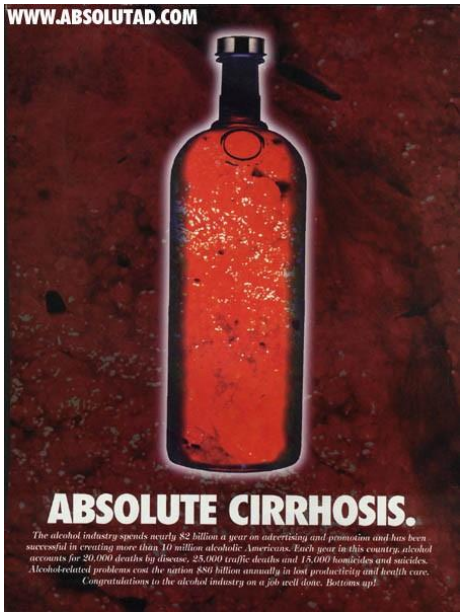
Cutaneous and Gastrointestinal* (Liver)

- Cirrhosis
- Spider angiomas
  - Palmar erythema
  - Clubbing
  - Terry's nails (white)
  - Jaundice
  - Gynecomastia









Cutaneous and Gastrointestinal (Renal)

- Birt-Hogg-Dube
  - Autosomal dominant
  - Trichodiscomas, fibrofolliculomas, acrochordons
  - Numerous firm, flesh-color papules of head, neck, trunk
  - Assoc bilateral renal tumors (pulmonary cysts, pneumothorax)

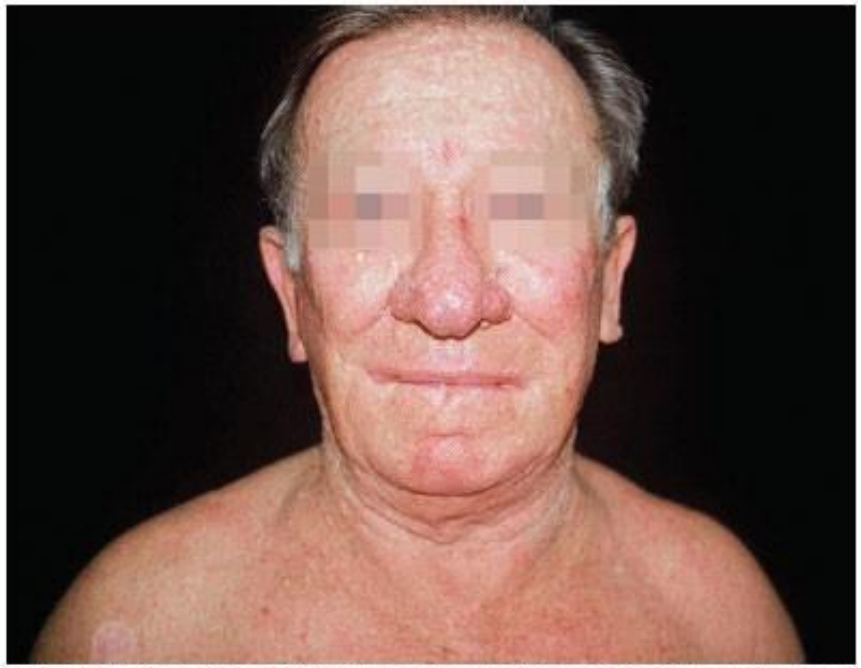
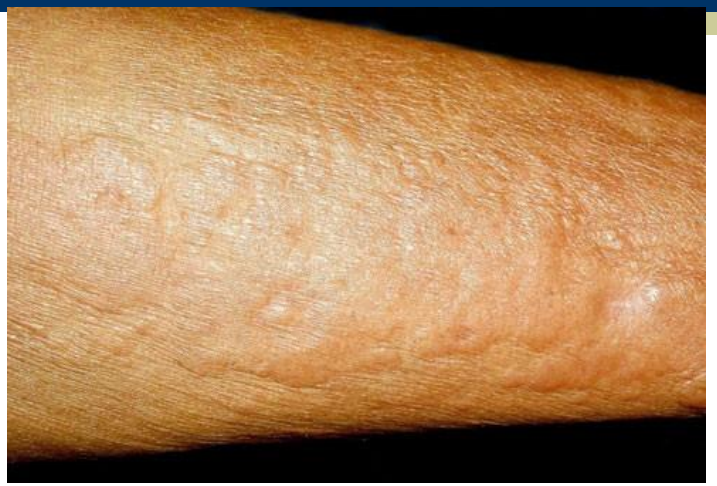
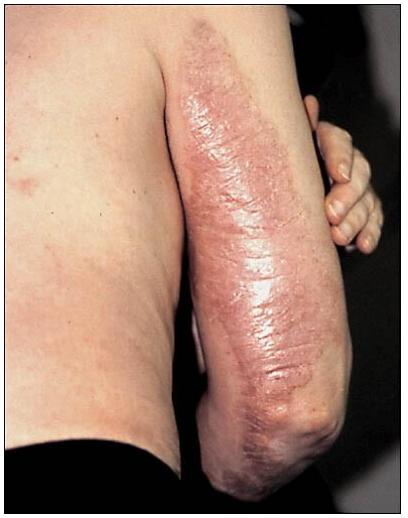


FIGURE 1: Multiple whitish or skin-colored papular lesions in the upper third of the body: head, neck and upper trunk.

Cutaneous and Gastrointestinal (Renal)

- Nephrogenic Systemic Fibrosis
  - Gadolinium MRI contrast associated
  - Renal failure patients
  - Woody nodules/plaques, usually extremities
  - Variable course
  - <5% fatal (respiratory muscle fibrosis)

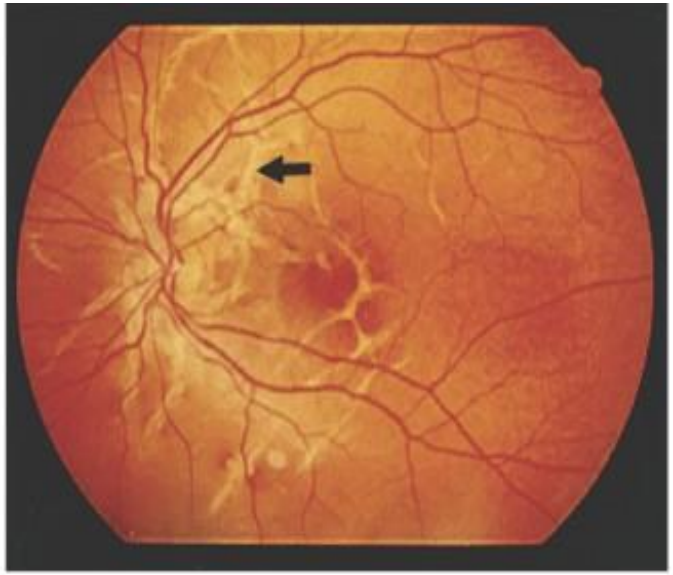




Cutaneous and Gastrointestinal (Renal)

Pseudoxanthoma Elasticum

- Clinical
  - Autosomal recessive more commc
  - Yellow-tan papules (“plucked chicken skin”) in flexural areas
  - Lax skin
- Internal
  - HTN frequent (renal vasculature)
  - Claudication
  - Angina
  - Recurrent GI bleed, epistaxis, rare GU
  - Angioid streaks (blindness possible)

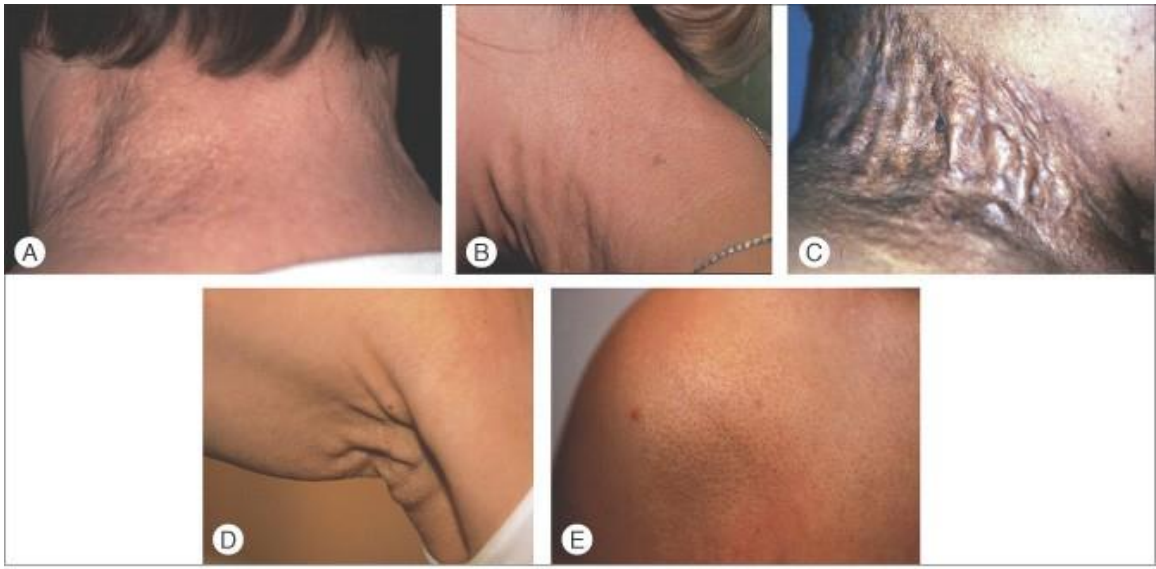


Angioid streaks

Cutaneous and Gastrointestinal (Renal)

Pseudoxanthoma Elasticum

- Treatment
  - None distinctive
  - Possibly limit calcium and phosphorus intake



Cutaneous and Endocrine

ENDOCRINE DISORDERS

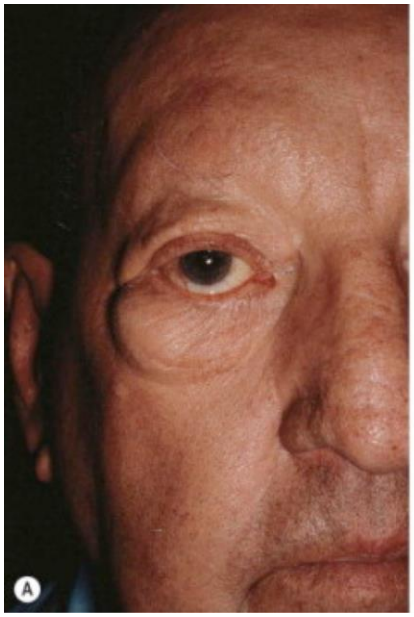
- Hypo- and hyperthyroidism
- Addison's Disease
- Acanthosis Nigricans
- Necrobiosis Lipoidica Diabeticorum
- Diabetic Dermopathy
- Diabetic Bullae
- Xanthomatoses

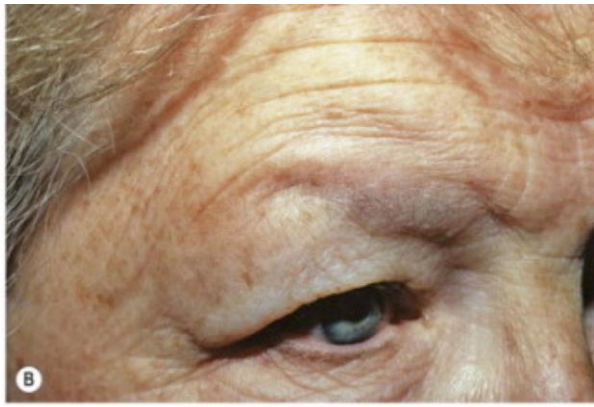
Hypothyroidism

Skin changes	Dry, rough, or coarse; cold and pale, boggy and edematous (myxedema) Yellow discoloration as a result of carotenemia Easy bruising (capillary fragility)
Cutaneous diseases	Ichthyosis and palmoplantar keratoderma Eruptive and/or tuberous xanthomas
Hair changes	Dull, coarse, and brittle Slow growth (increase in telogen hair phase) Alopecia of the lateral third of the eyebrows
Nail changes	Thin, brittle, striated Slow growth Onycholysis (rare)

Hypothyroidism
Myxedema

- *Systemic mucinosis*
- Severe lack of thyroid hormone
- Clinical:
  - Skin becomes rough & dry
  - **Facial skin is puffy**
    - **dull, flat expression**
  - Macroglossia, broad nose
  - **Chronic periorbital infiltration**
  - Carotenemia → palms & soles
  - Diffuse hair loss
    - lateral 3rd eyebrow hair
  - Onycholysis

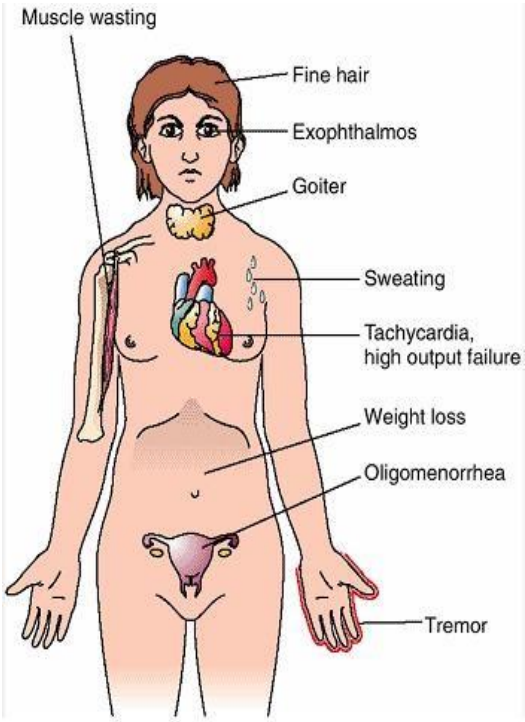




Hyperthyroidism

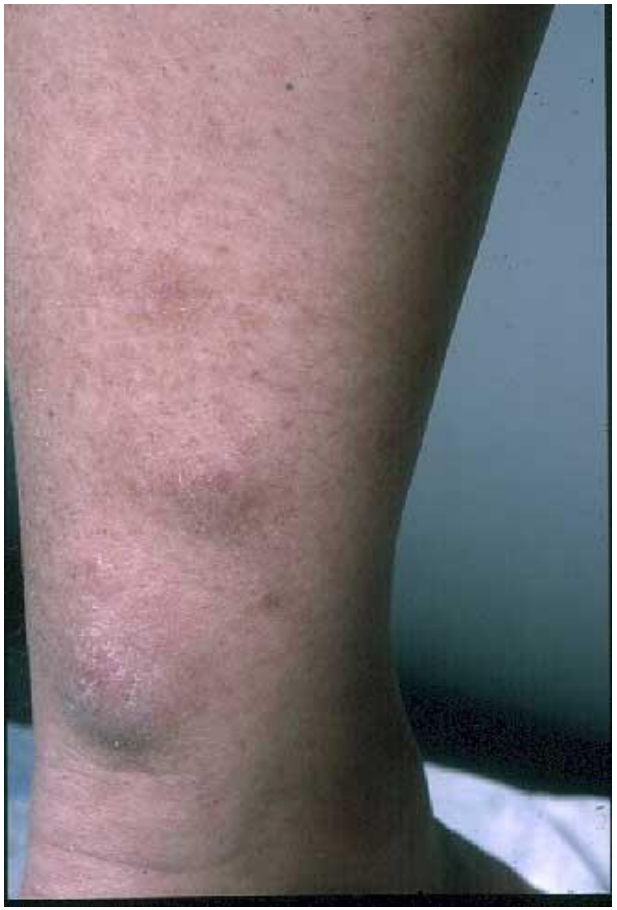
Table 53.5 Dermatologic manifestations of hyperthyroidism.

DERMATOLOGIC MANIFESTATIONS OF HYPERTHYROIDISM	
Cutaneous changes	Fine, velvety, or smooth skin Warm, moist skin due to increased sweating Hyperpigmentation – localized or generalized
Cutaneous diseases	Vitiligo Urticaria, dermatographism Pretibial myxedema and thyroid acropachy
Hair changes	Fine, thin Mild, diffuse alopecia
Hair disease	Alopecia areata
Nail changes	Onycholysis Koilonychia Clubbing from thyroid acropachy



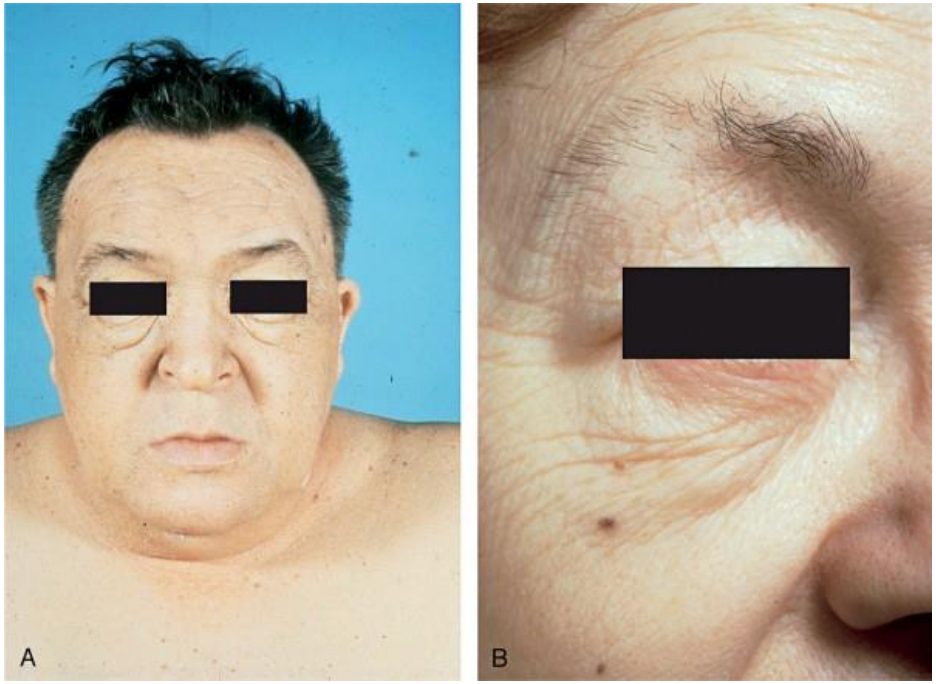
Endocrine Disorders

- Pretibial myxedema
  - Pretibial plaque with dry scaly epidermis
  - Often hyperthyroidism
  - Possible euthyroid
  - Frequent exopthalmos
  - Accumulation of glycosaminoglycans assoc with thyroid stimulating antibodies
  - Tx: intralesional or topical steroids



Endocrine Disorders*

- Hypothyroidism
  - Cold, thick, dry skin
  - Coarse hair
  - Loss of lateral eyebrows
  - Brittle nails
  - Xanthomas
  - Purpura



Endocrine Disorders*

- Hyperthyroidism
  - Fine, moist skin
  - Diffuse hair loss
  - Possible association with
    - Alopecia areata
    - Vitiligo

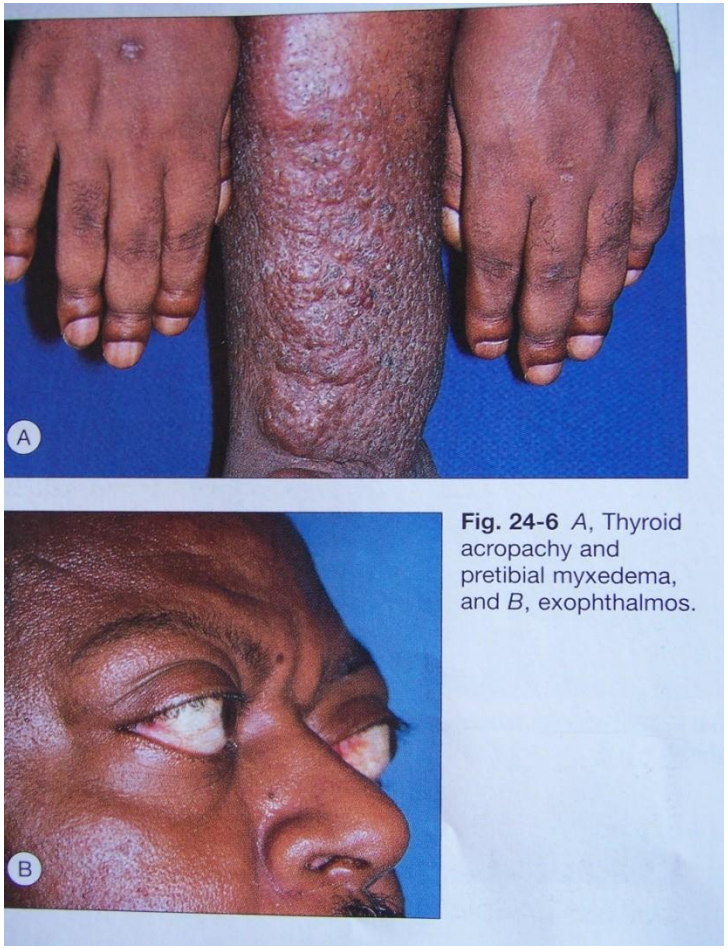
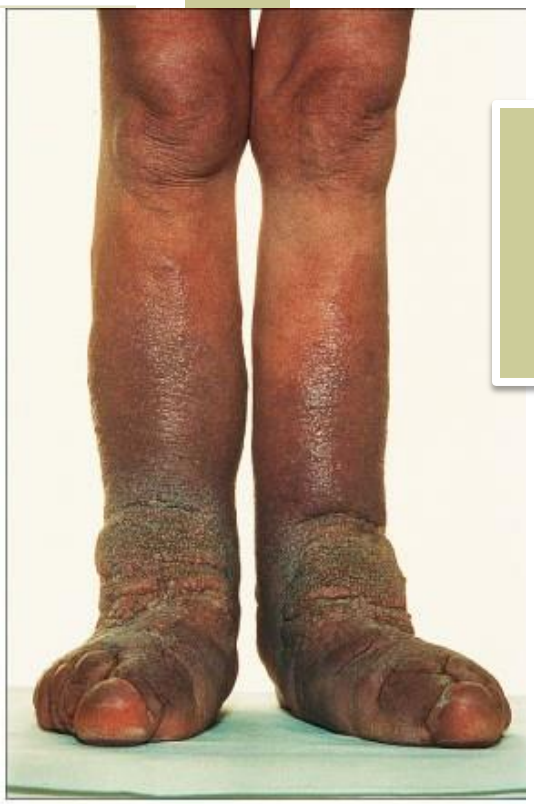


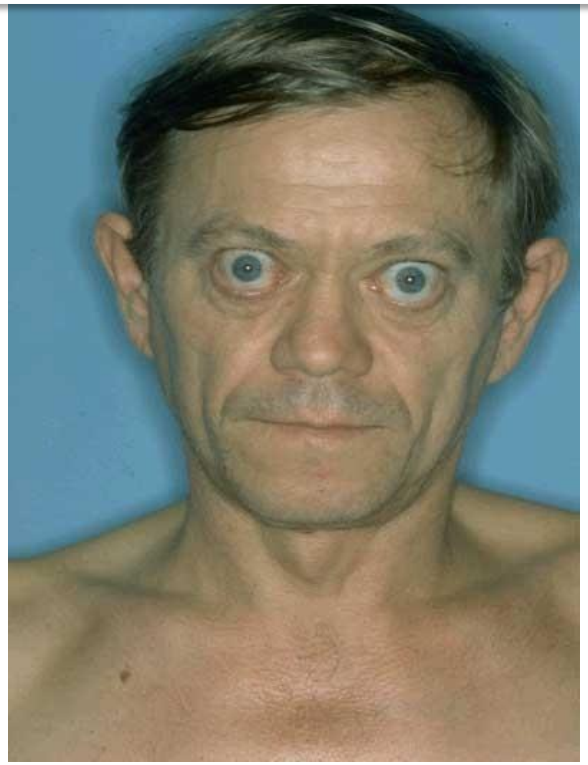
Fig. 24-6 *A*, Thyroid acropachy and pretibial myxedema, and *B*, exophthalmos.

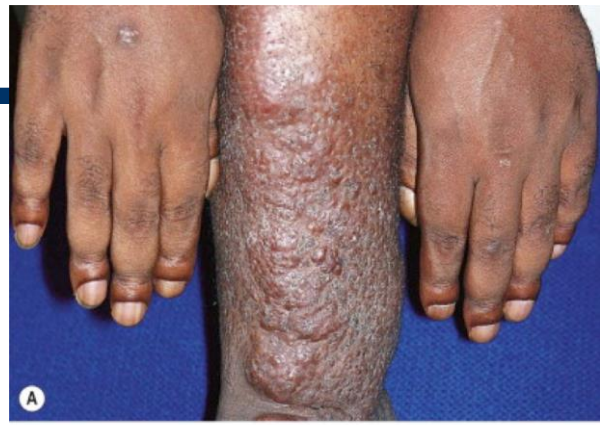
Hyperthyroidism

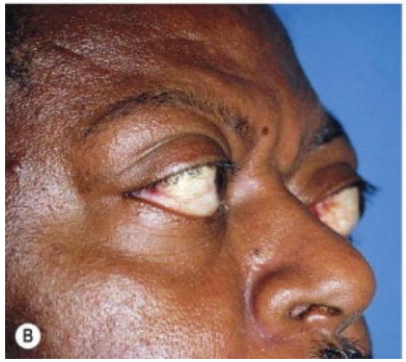


2005. McKee et al.: Pathology of the Skin with Clinic

Grave's Disease
Pretibial Myxedema
Exophthalmos

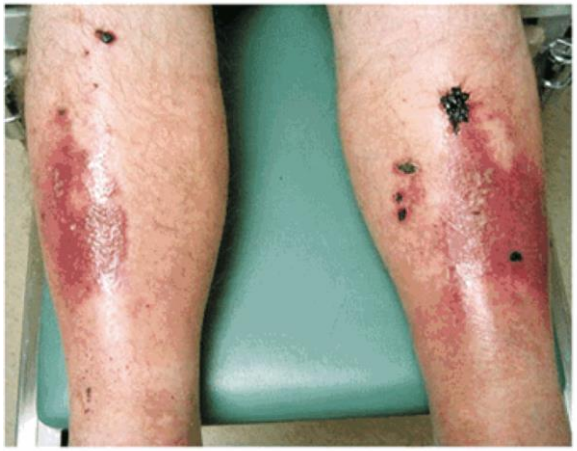


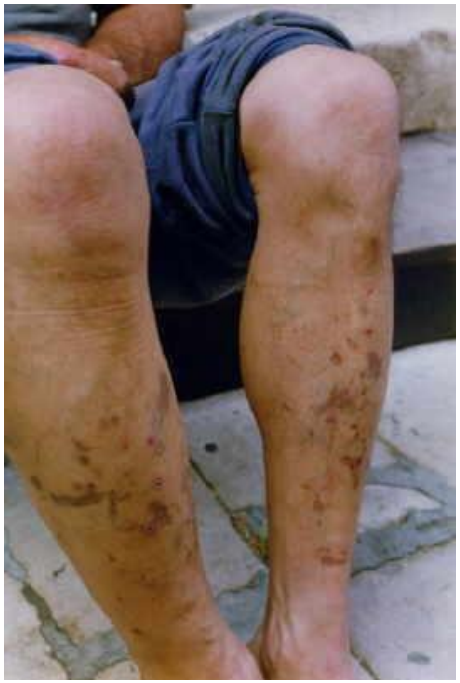




Endocrine Disorders

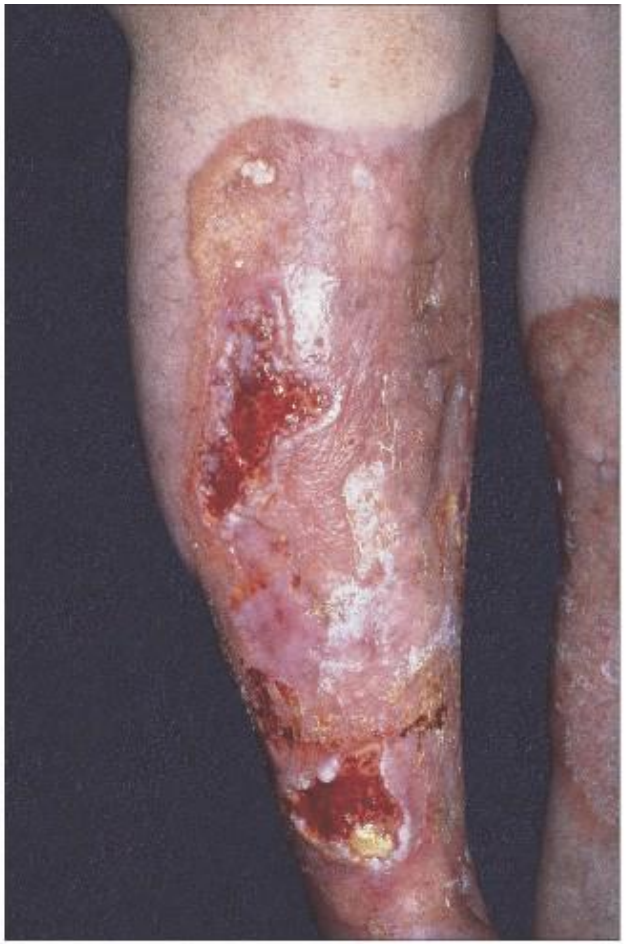
- Diabetes
  - Necrobiosis lipoidica (dibeticorum) (NLD)
    - Red-yellow atrophic plaques
    - Usually lower legs
    - Control of diabetes does not influence
    - Treatment not satisfactory





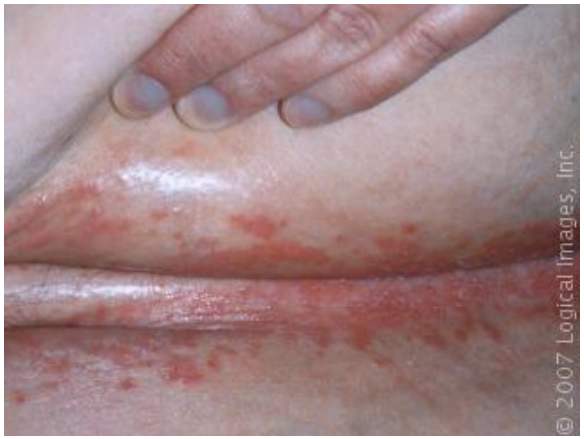
Necrobiosis Lipoidica Diabeticorum

- 20% of patients have **diabetes or glucose intolerance**
  - 0.3-3% of diabetics have NLD
- F>M
- Clinical:
  - Red-brown papules that progress to yellow-brown atrophic, telangiectatic plaques with violaceous, irregular border
- Common sites include shins, ankles, calves, thighs and feet
- Ulceration occurs in 35% lesions

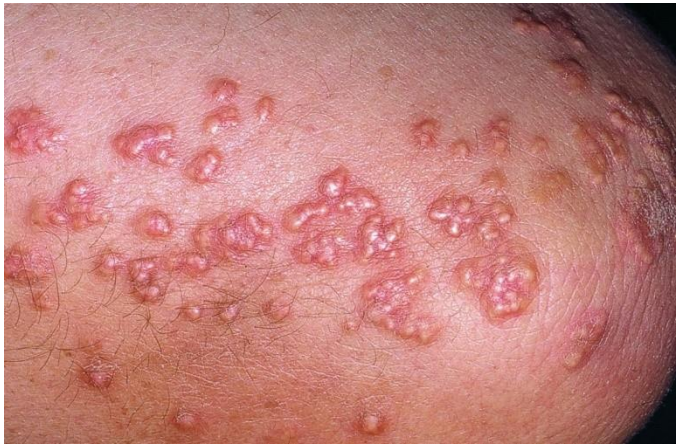


Endocrine Disorders

- Diabetes
  - Recurrent candidiasis



  - Eruptive xanthomas (also manifestations of lipid abnormalities)



Endocrine Disorders

- Diabetes
  - Ulcers secondary to vascular impairment or neuropathy
  - Fat necrosis secondary to insulin injections