Cutaneous Manifestations of Systemic Disease

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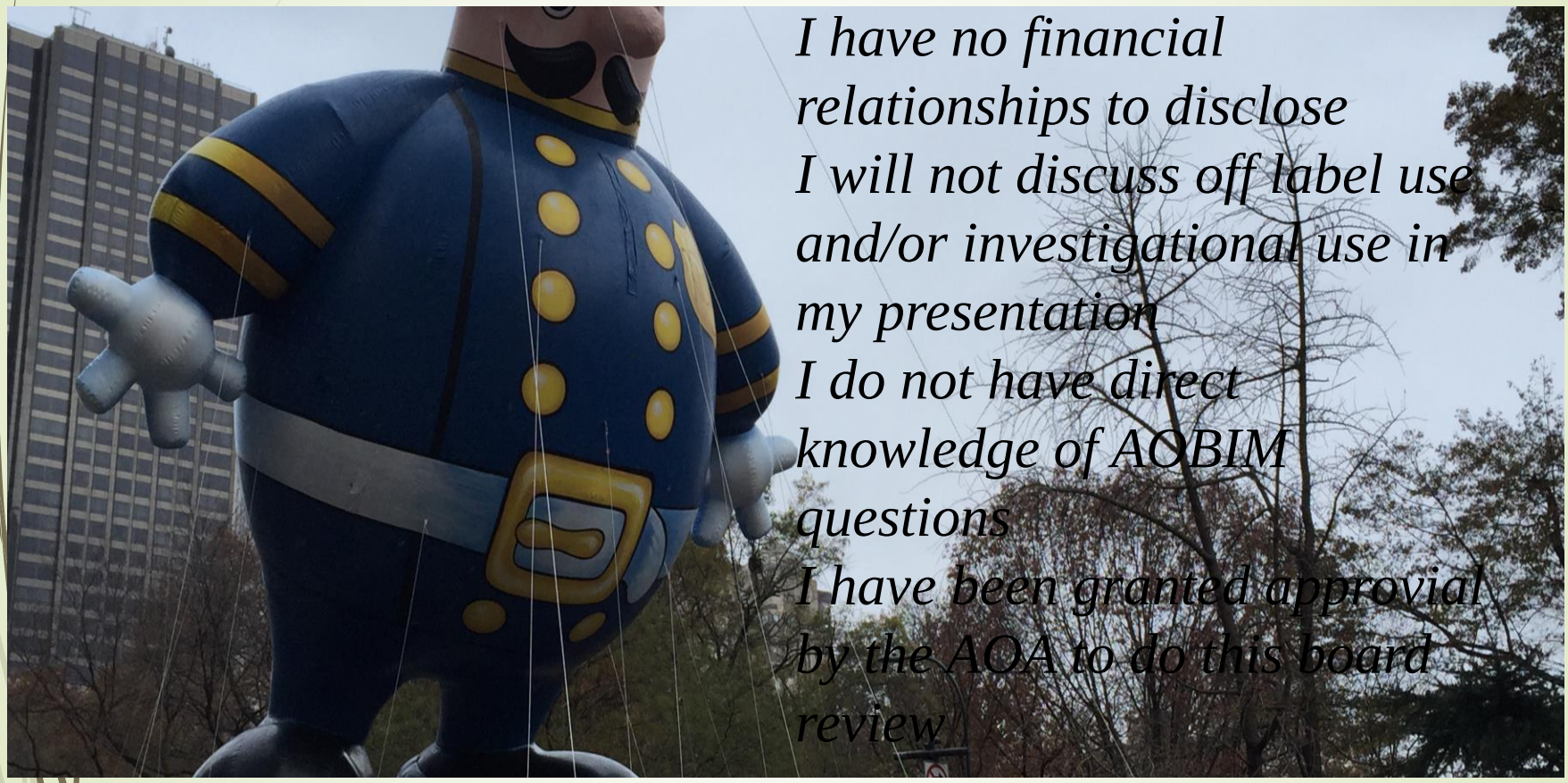
ACOI Board Review

Disclosure



I have no financial relationships to disclose
I will not discuss off label use and/or investigational use in my presentation
I do not have direct knowledge of AOBIM questions
I have been granted approvial by the AOA to do this board review

Dermatology on the AOBIM

- "1-4%" of exam is Dermatology
- Table of Test Specifications is unavailable
- Review Syllabus for Internal Medicine
- Large amount of information

Cutaneous Multisystem

Cutaneous Connective Tissue Conditions

Connective Tissue Diease

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

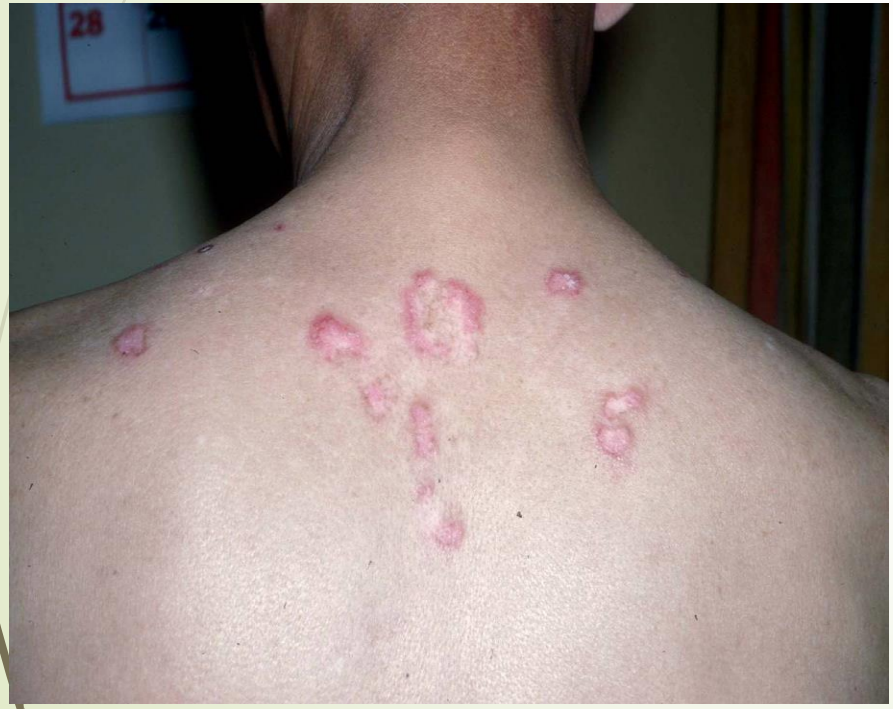
Lupus Erythematosus

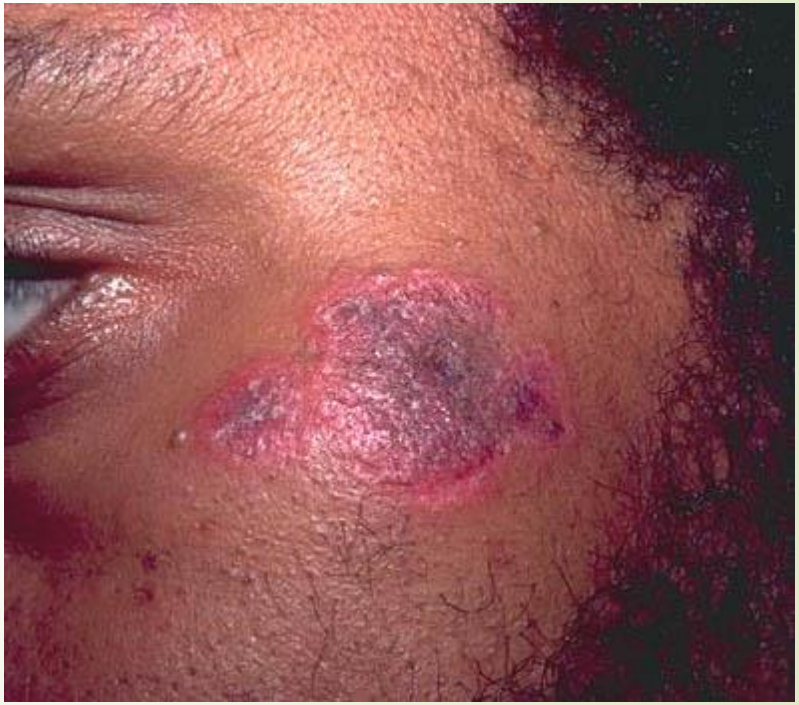
- Spectrum from cutaneous to severe systemic involvement
  - Discoid LE (DLE) / Chronic Cutaneous
  - Subacute Cutaneous LE (SCLE)
  - Systemic LE (SLE)
- Cutaneous findings common in all forms
- Related to autoimmunity

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

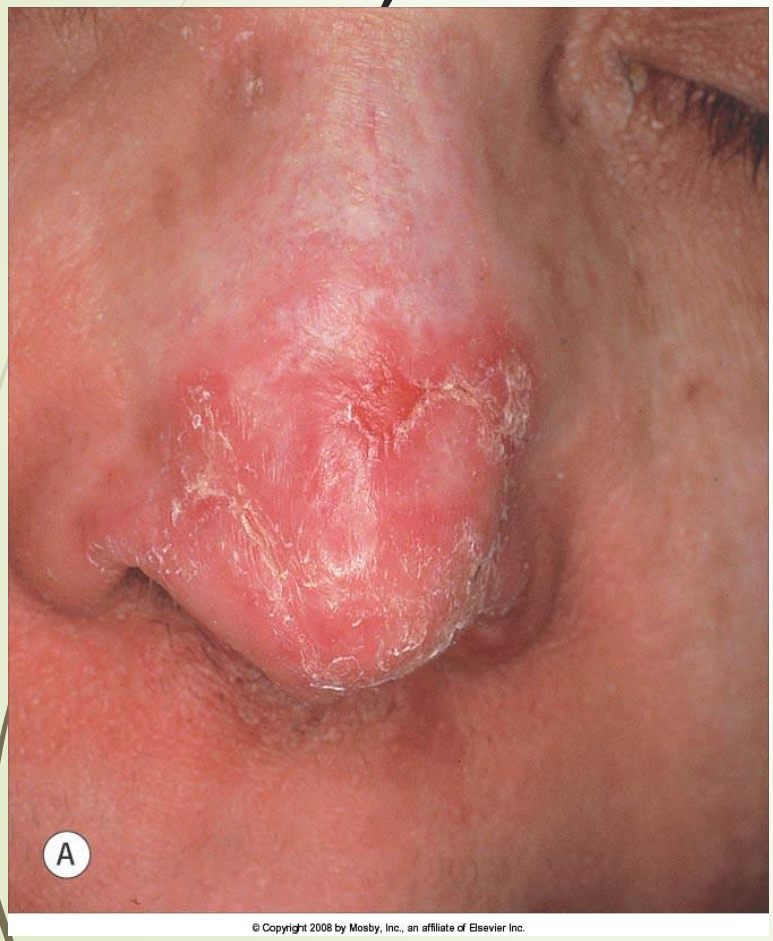
Discoid LE (Chronic Cutaneous LE)

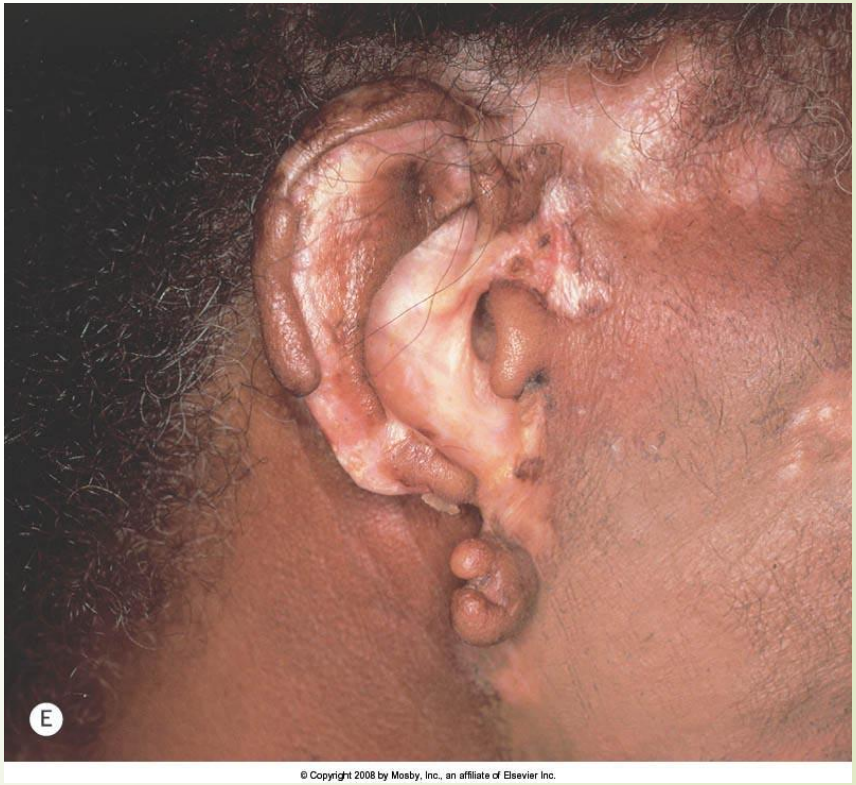




Scaly, atrophic plaques with defined margins

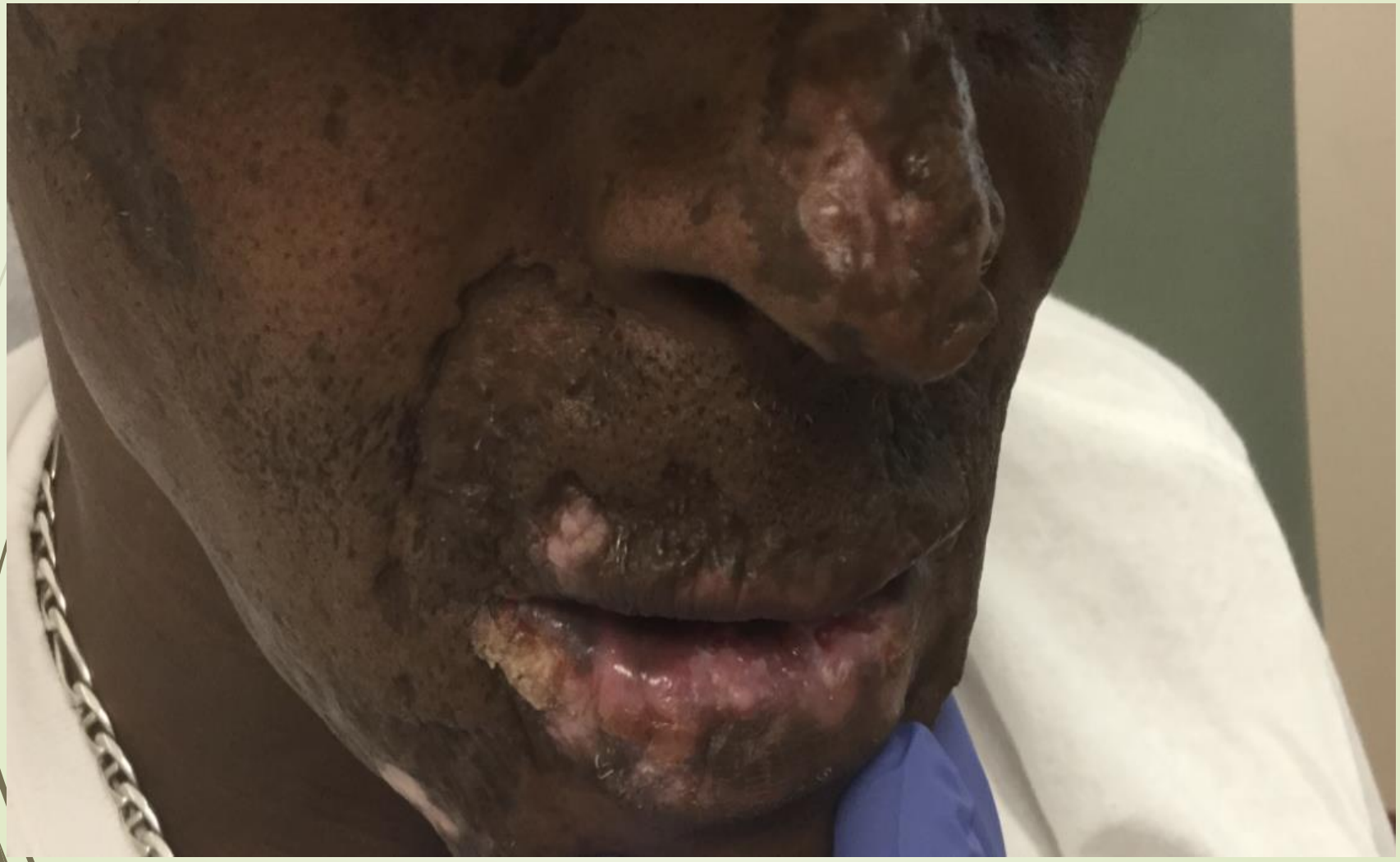
Discoid LE (Chronic Cutaneous LE)





Scaly, erythematous plaques with scarring, atrophy, dyspigmentation

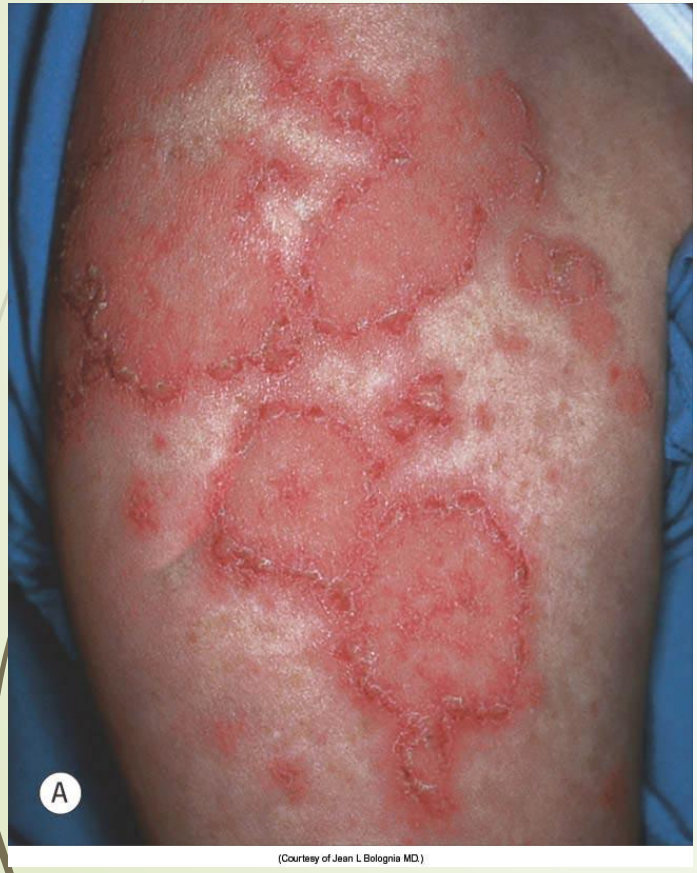
DISCOID LUPUS



Subacute Cutaneous LE (SLCE)

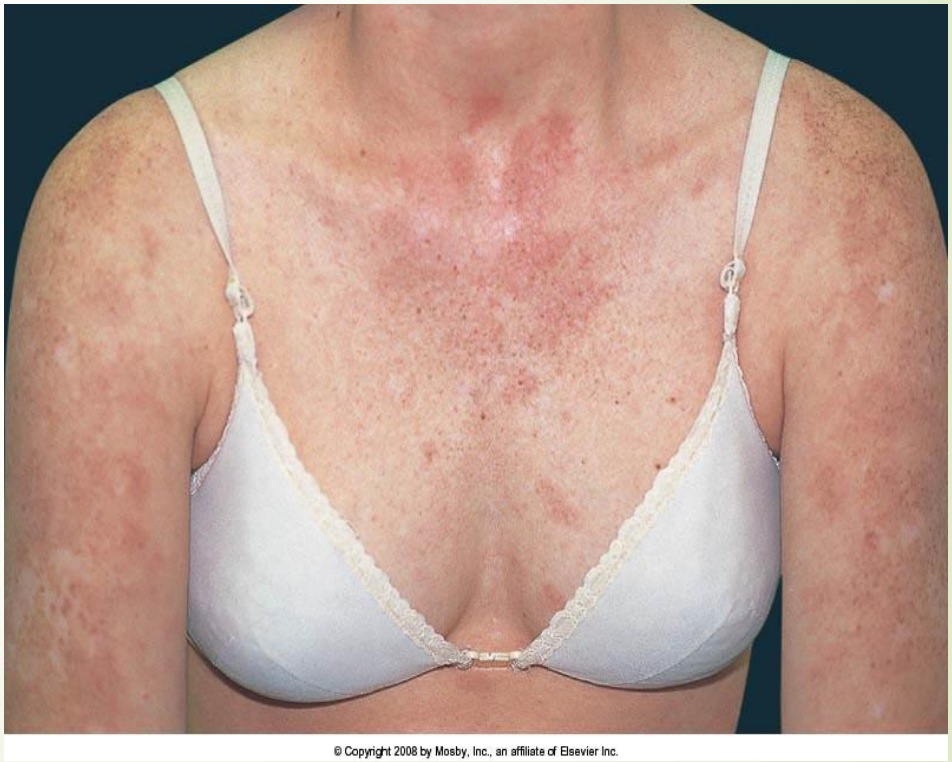
- Cutaneous disease with internal involvement
  - 20% Leukopenia, 75% arthralgias
- Psoriasiform, polycyclic, annular lesions
- Sun exposed sites commonly
  - Shawl distribution: V neck, upper outer and inner arms
- 80% ANA positive
  - Anti-Ro

Subacute Cutaneous LE (SLCE)



(Courtesy of Jean L Bolognia MD.)

Psoriasiform, scaly plaques



"Shawl" distribution

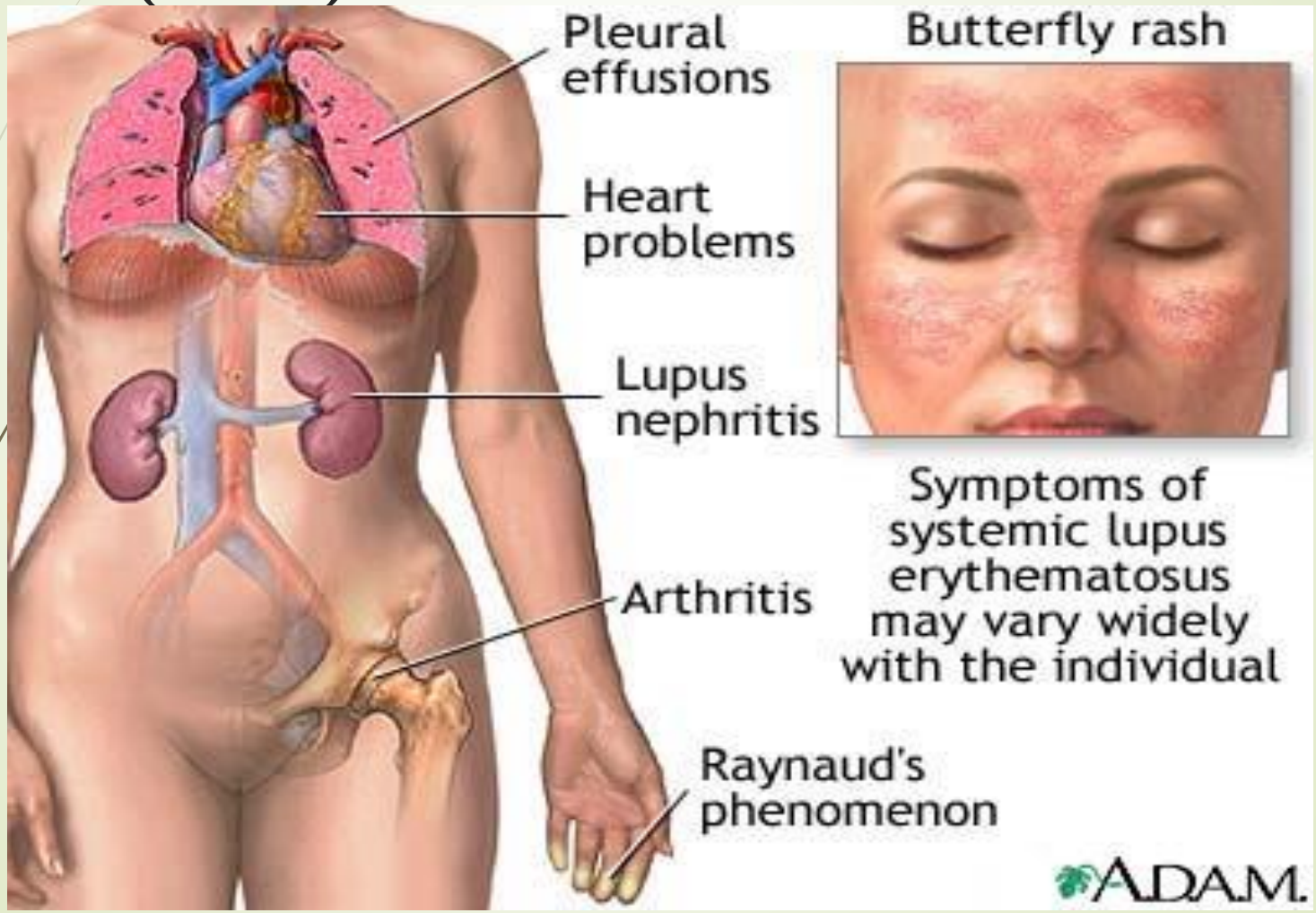
Systemic Lupus Erythematosus (SLE)

- 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

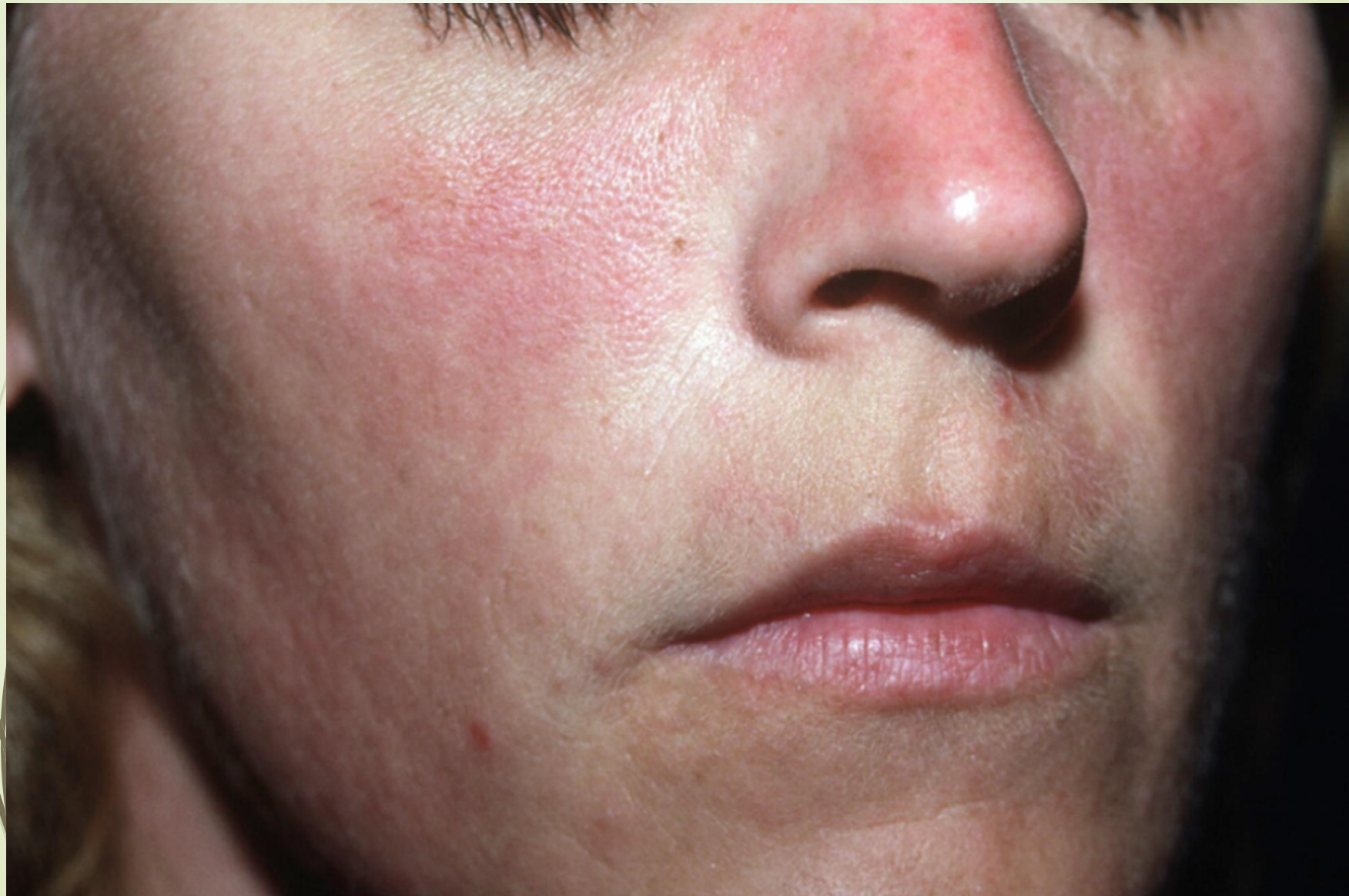
Systemic Lupus Erythematosus (SLE)
ACR Criteria*

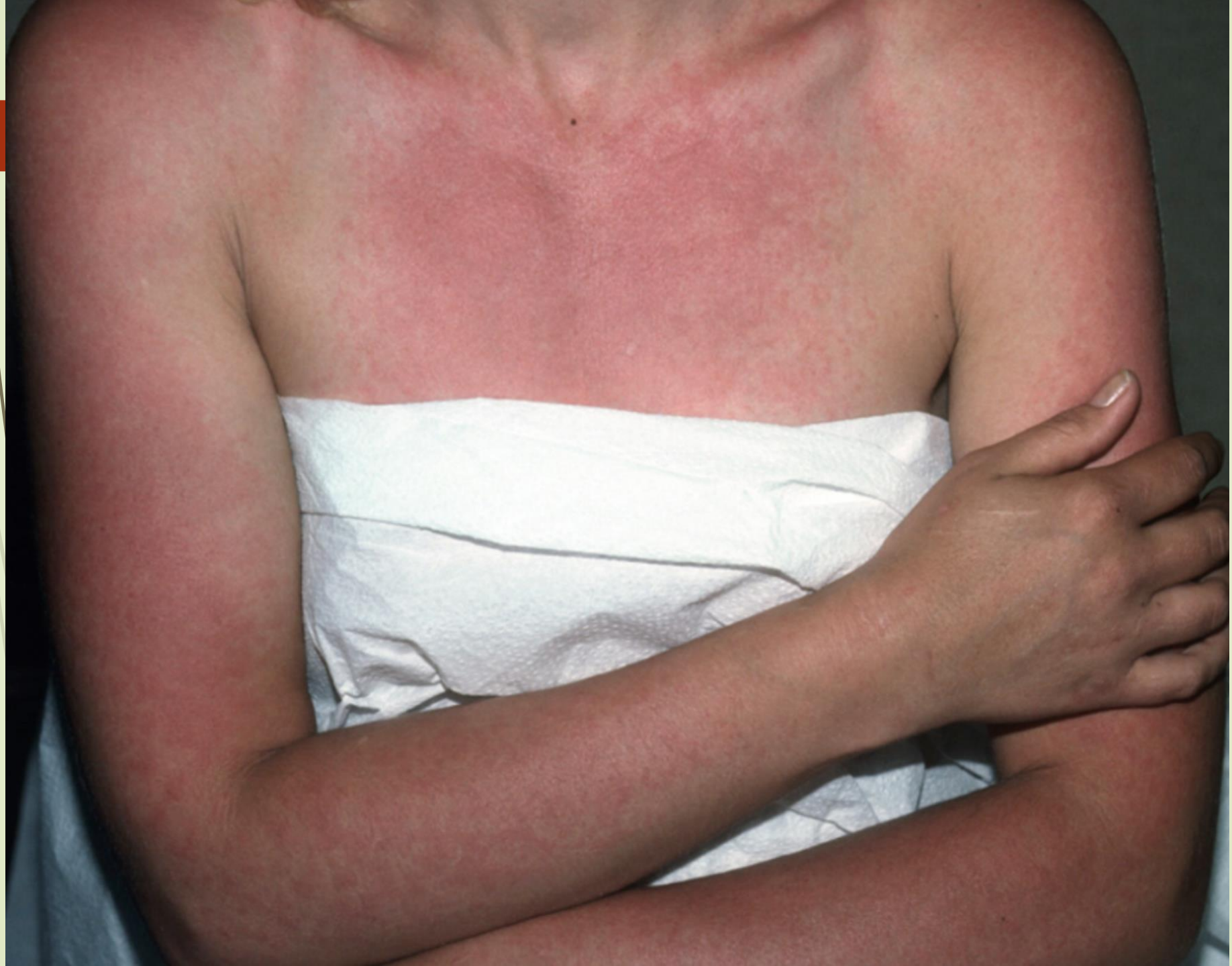
1) D – Discoid Rash
2) O – Oral Ulcers
3) P – Photosensitivity
4) A – ANA + (99%)
5) M – Malar Rash
6) I – Immunologic DO
7) N – Neurologic DO
8) R – Renal Disorder
9) A – Arthritis
10) S – Serositis
11) H – Hematologic Dx

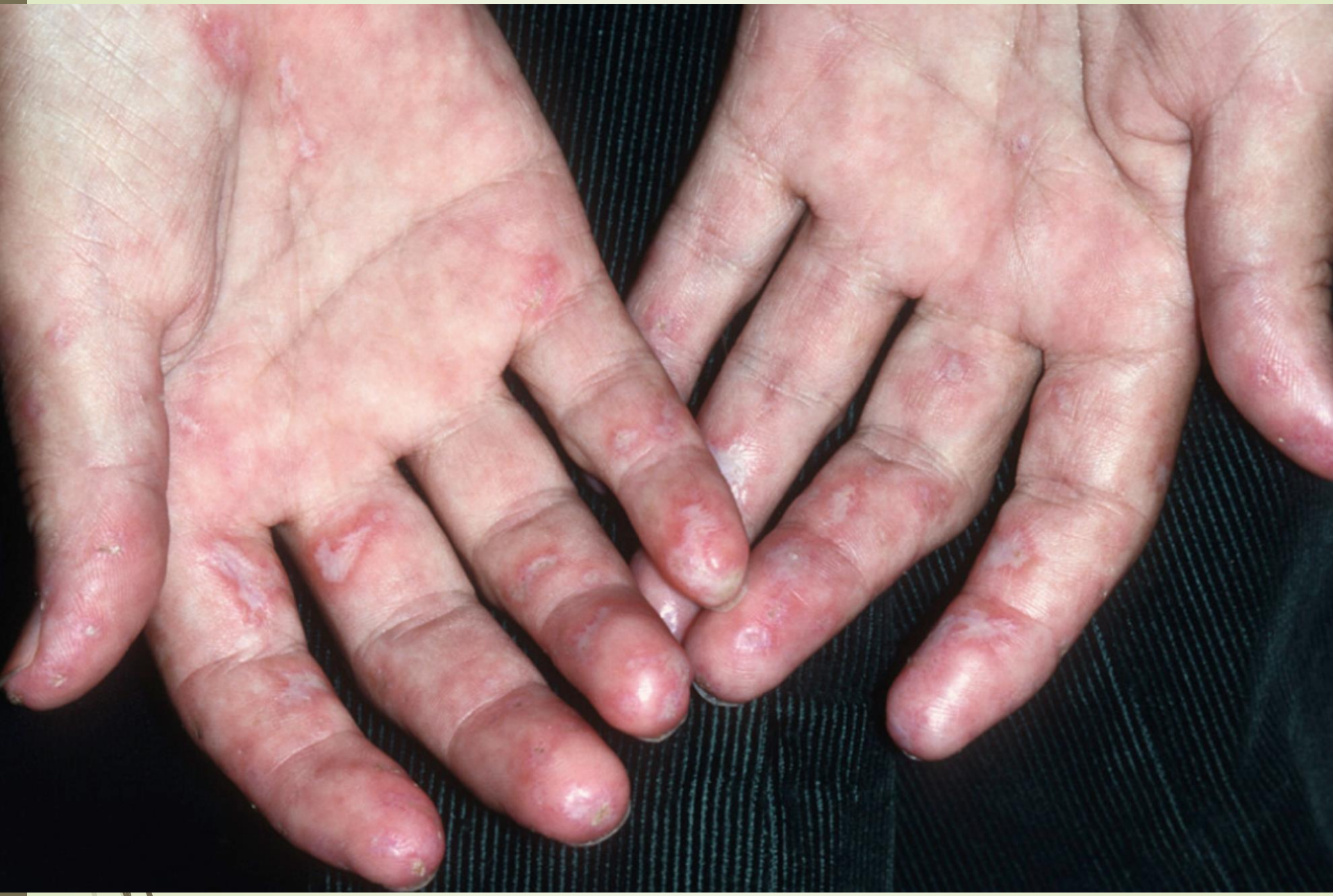
Systemic Lupus Erythematosus (SLE)

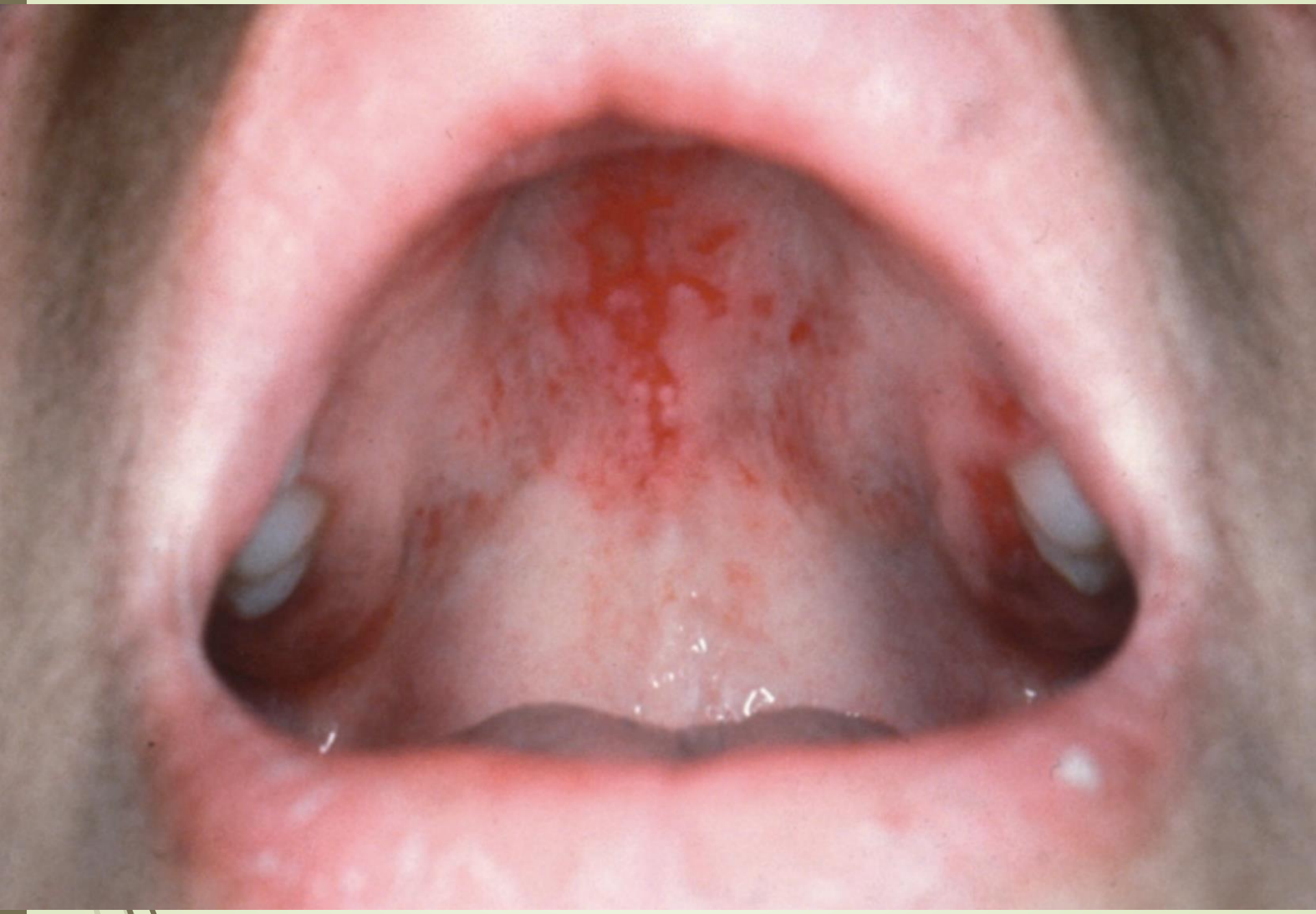


SLE







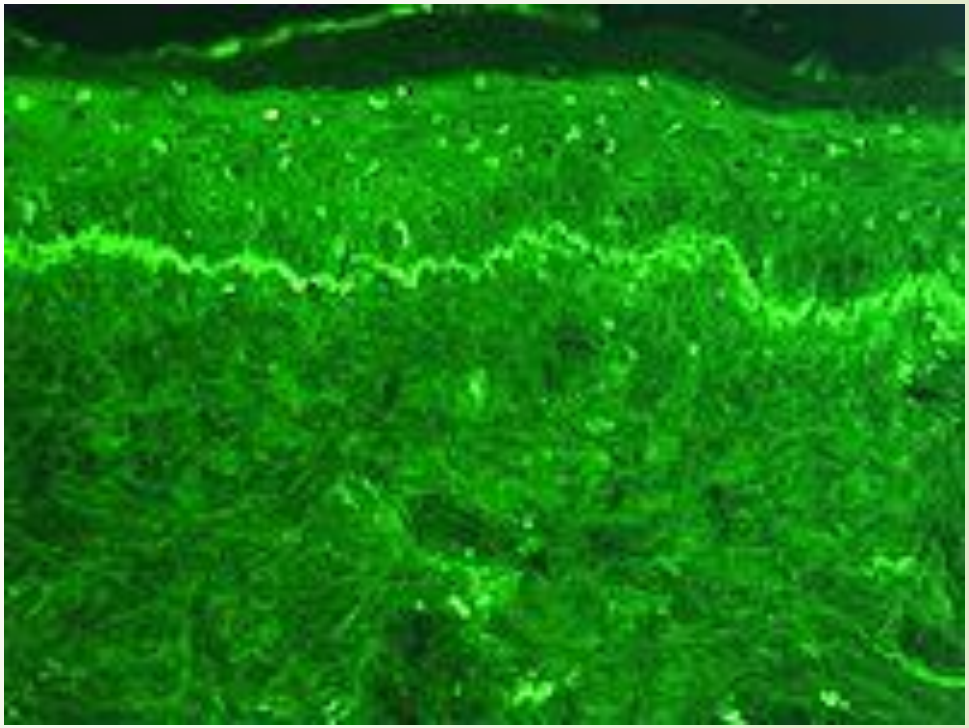


Lupus Erythematosus Laboratory Findings

- 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

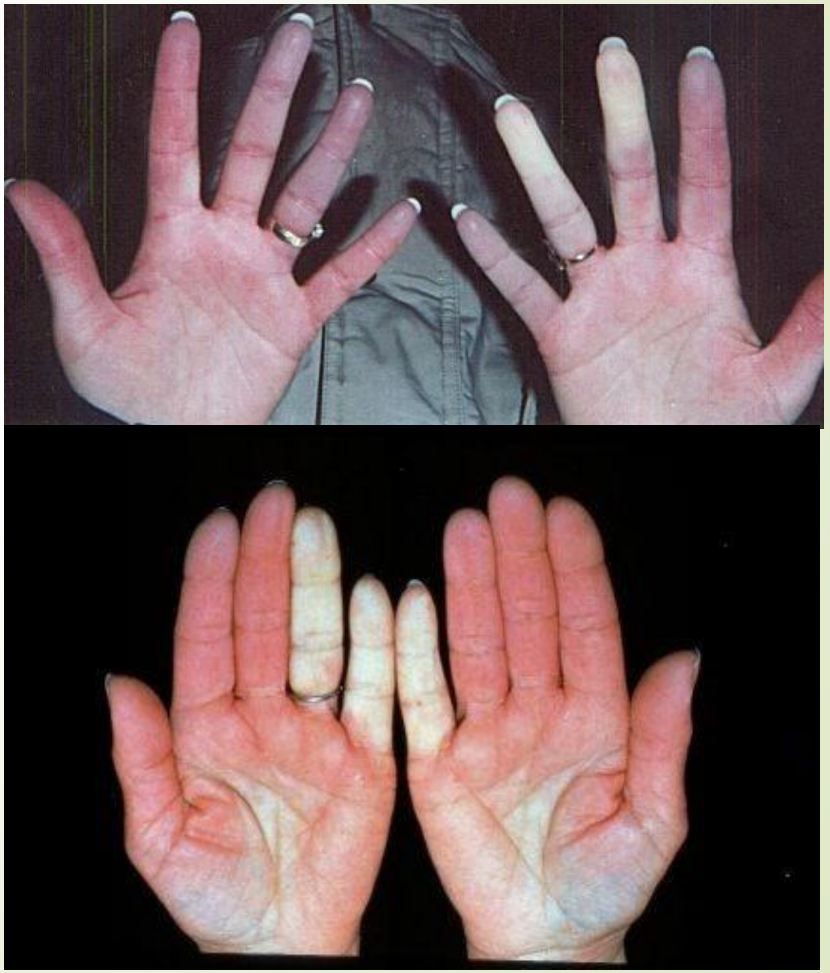


Lupus Erythematosus Treatment

- 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

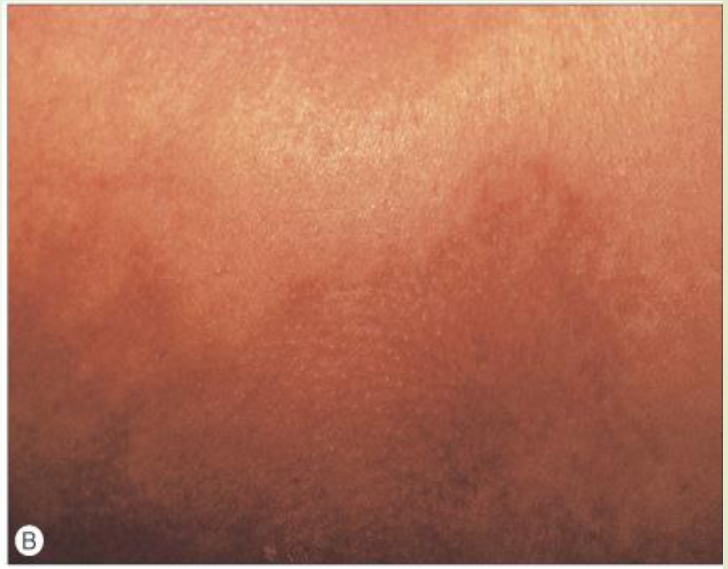
- Less than half have connective tissue disease
  - Idiopathic (Raynaud's *Disease*)
- Scleroderma (>50%), SLE, Dermatomyositis
- Pneumatic hammer operators
- Ergotism
- Vinyl chloride (industrial)
- Cryoglobulins/macroglobulins

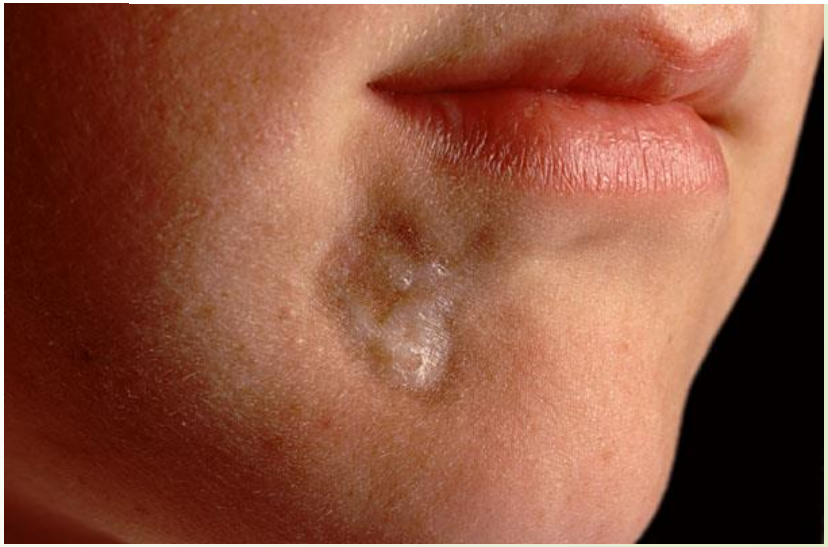
Raynaud's Phenomenon Treatment

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

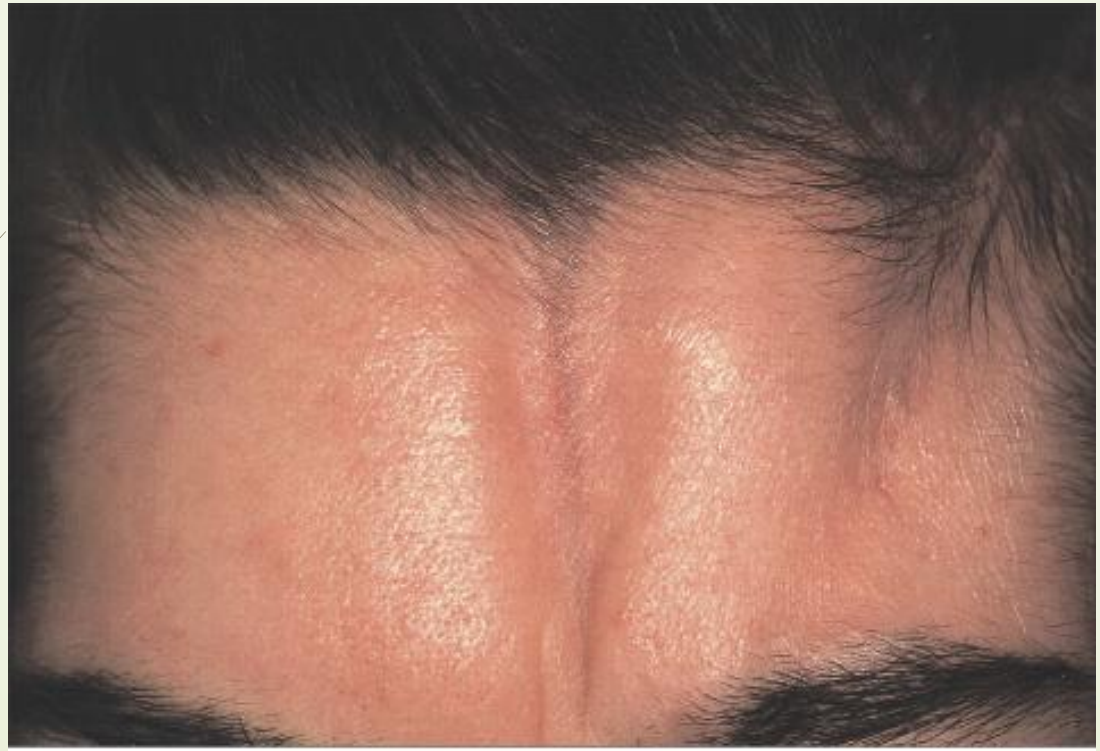
Scleroderma

- 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





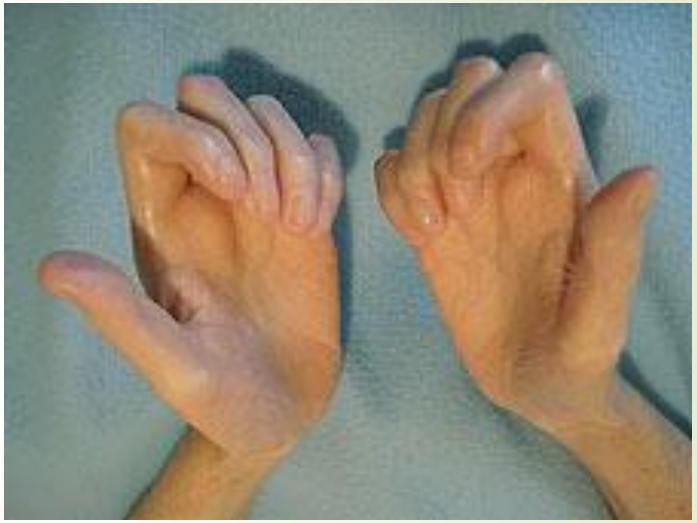
Scleroderma



En coupe de sabre (linear morphea)

Scleroderma

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



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

MAJOR CLINICAL AND LABORATORY MANIFESTATIONS OF SYSTEMIC SCLEROSIS AND OTHER SELECTED CONDITIONS CHARACTERIZED BY CUTANEOUS INDURATION							
	Systemic sclerosis	**Morphea**	**Eosinophilic fasciitis**	**Scleredema**	**Scleromyxedema**	**NSF**	**Chronic GVHD**
Major clinical variants	• Limited • Diffuse	• Plaque-type (circumscribed) morphea • Linear morphea • Generalized morphea		• Post-infectious (type I) • Monoclonal gammopathy-associated (type II) • Diabetes mellitus-associated (type III)			• Lichen sclerosis-like • Morphea-like • Scleroderma like • Fasciitis
Raynaud phenomenon	++	–	–	–	–	–	–
Symmetric induration	++*	– plaque-type and linear ± generalized	++*	++	++	+	+
Sclerodactyly	++	–	–	–	–	–	–
Facial involvement	+	– plaque-type and generalized + linear (en coup de sabre)	–	± types I and II – type III	+	–	±
Systemic involvement	++	– for plaque-type but ± for linear involving head (ocular, CNS)	+	–	++	+	+
Antinuclear antibodies	++	± generalized and linear – plaque-type	–	–	–	–	±
Anti-centromere antibodies	+ limited	–	–	–	–	–	–
Anti-topoisomerase I (Scl-70)	+ diffuse	–	–	–	–	–	–

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

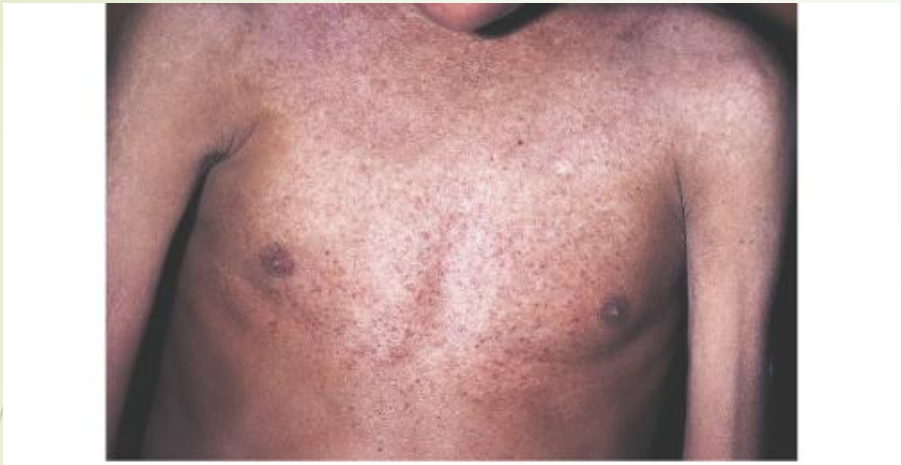
- Immunosuppressive drugs
  - Azathioprine
  - Cyclophosphamide
  - Cyclosporine
  - Tacrolimus
  - Mycophenolate mofetil
- Anti-inflammatory agents
  - Methotrexate
  - Nonsteroidal anti-inflammatory drugs
- Collagen modulators
  - #1-Penicillamine
  - Interferons
  - Colchicine
- Vasoactive agents
  - Captopril
  - Nifedipine
  - Pentoxifylline
- Others
  - Endothelin-1 antagonist
  - Photopheresis
  - Aminobenzoate potassium
  - Autologous bone marrow transplantation following high-dose ablative

Dermatomyositis

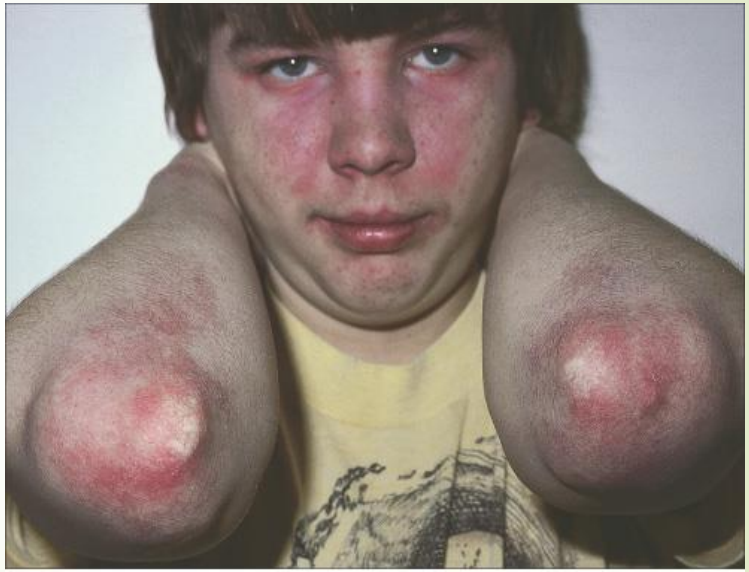
- Heliotrope –
  - violaceous discoloration around eyes
- Gottron's papules –
  - erythematous, papules over interphalangeal joints
- Telangiectasias/poikiloderma
- Raynaud's phenomenon
- Symmetrical proximal muscle weakness

- Children –
  - calcinosis common, possible ulceration

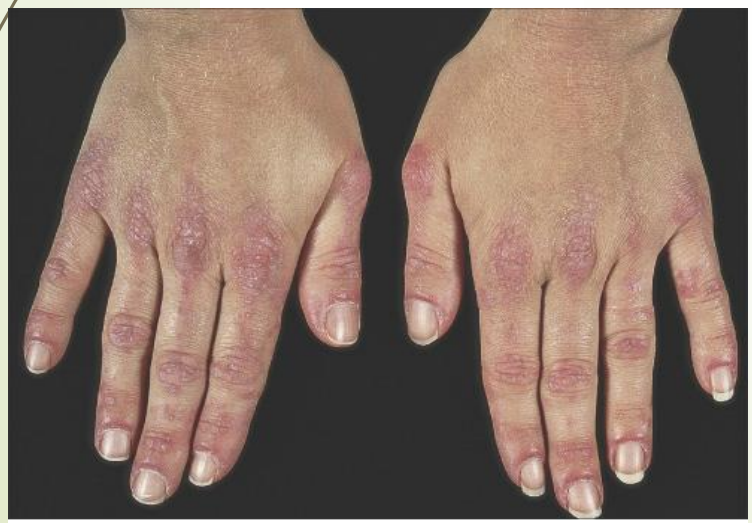
Dermatomyositis



Poikiloderma



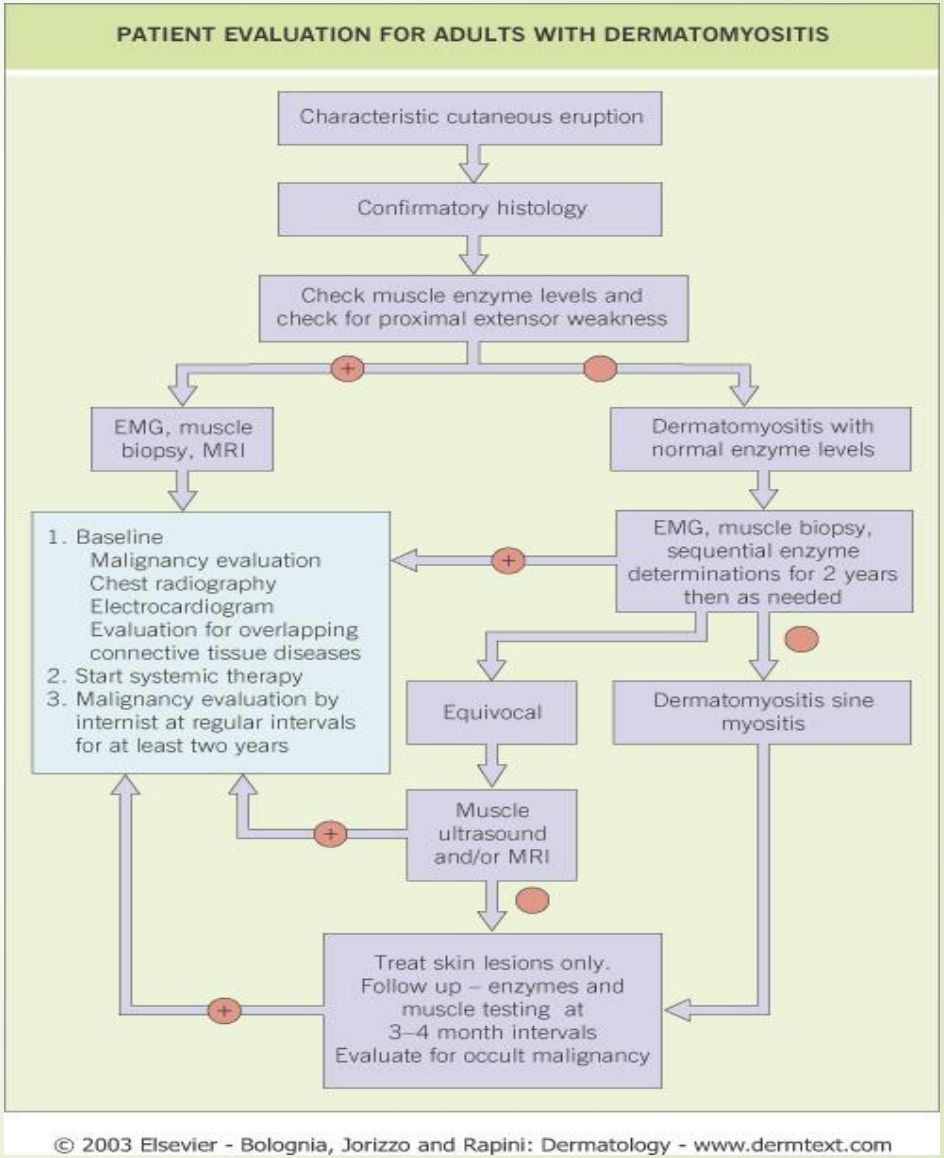
Heliotrope rash



Gottron’s

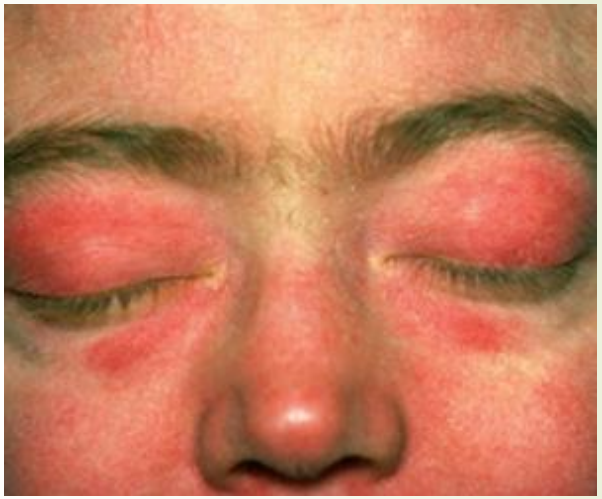
Dermatomyositis Labwork

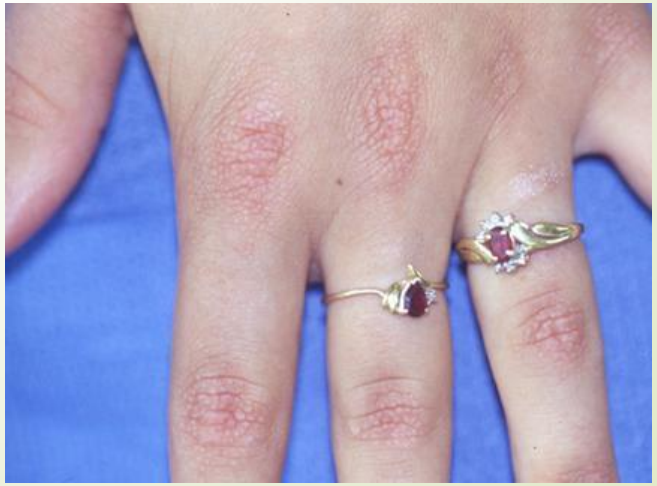
- Elevated muscle enzymes
- EMG
- Muscle biopsy
- Ultrasound/MRI



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

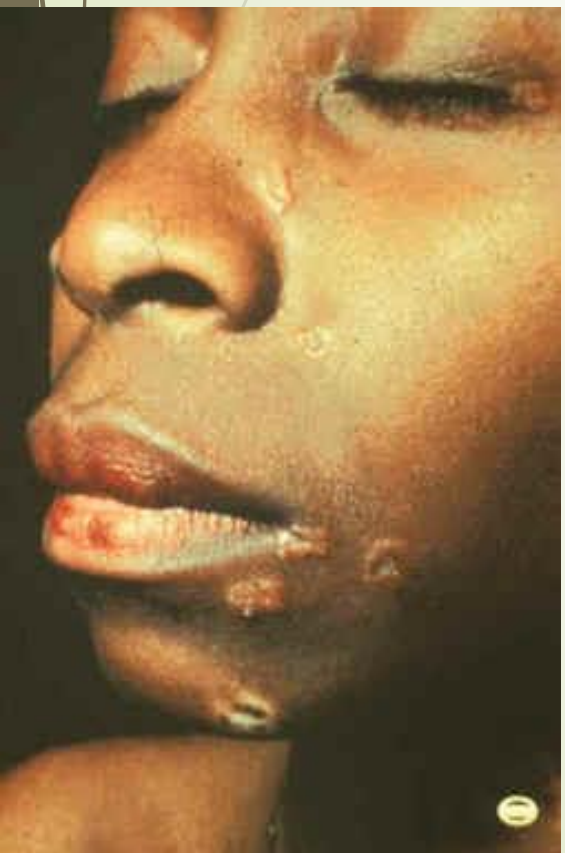
- Physical Therapy
- Symptomatic Treatment
- Systemic Steroids
- Immunosuppressives
  - Ex. methotrexate

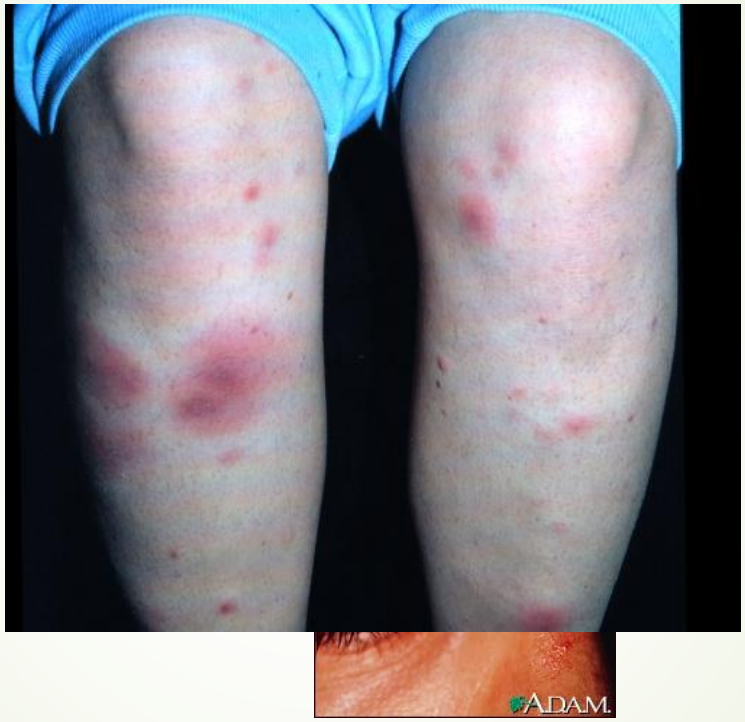
THERAPEUTIC LADDER FOR DERMATOMYOSITIS	
Systemic therapy	
Oral prednisone:	1 mg/kg tapered to 50% over 6 months and to zero over 2–3 years ①
	option to use pulse, split dose, or alternate day ①
Low-dose weekly methotrexate ②	
Azathioprine:	2–3 mg/kg/day ③
Others:	high dose intravenous γ-globulin ①
	pulse 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

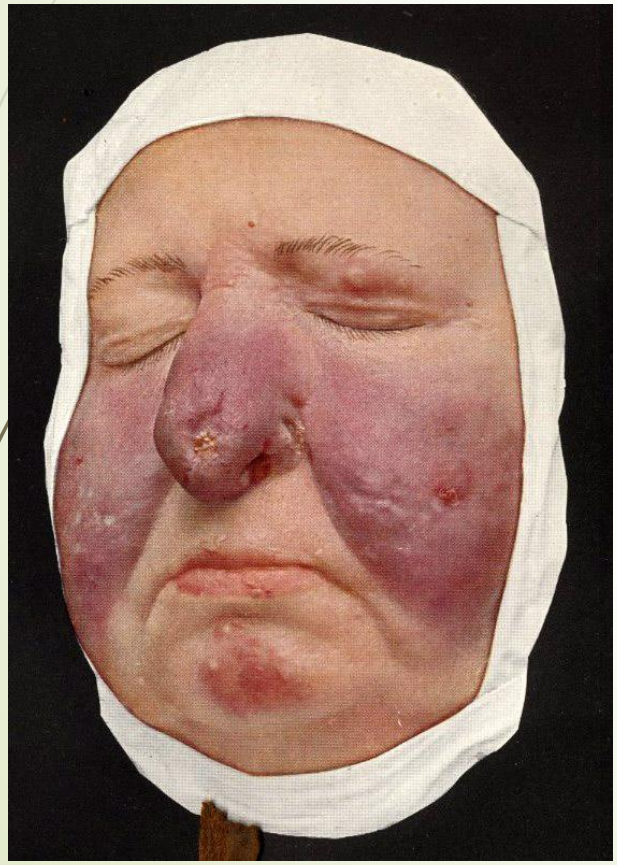


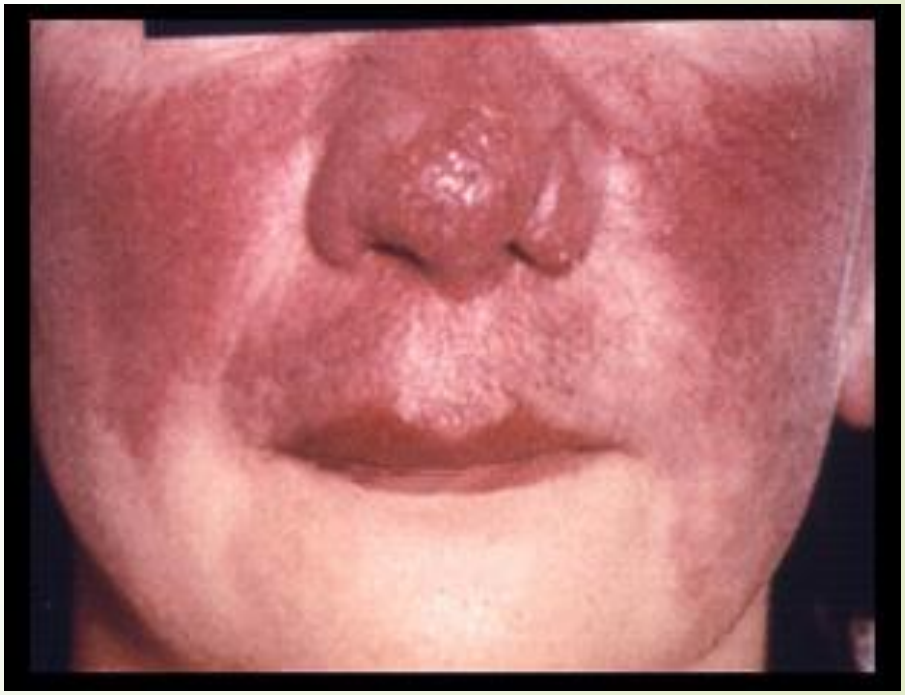


Sarcoidosis Clinical

- 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 – Lupus Pernio

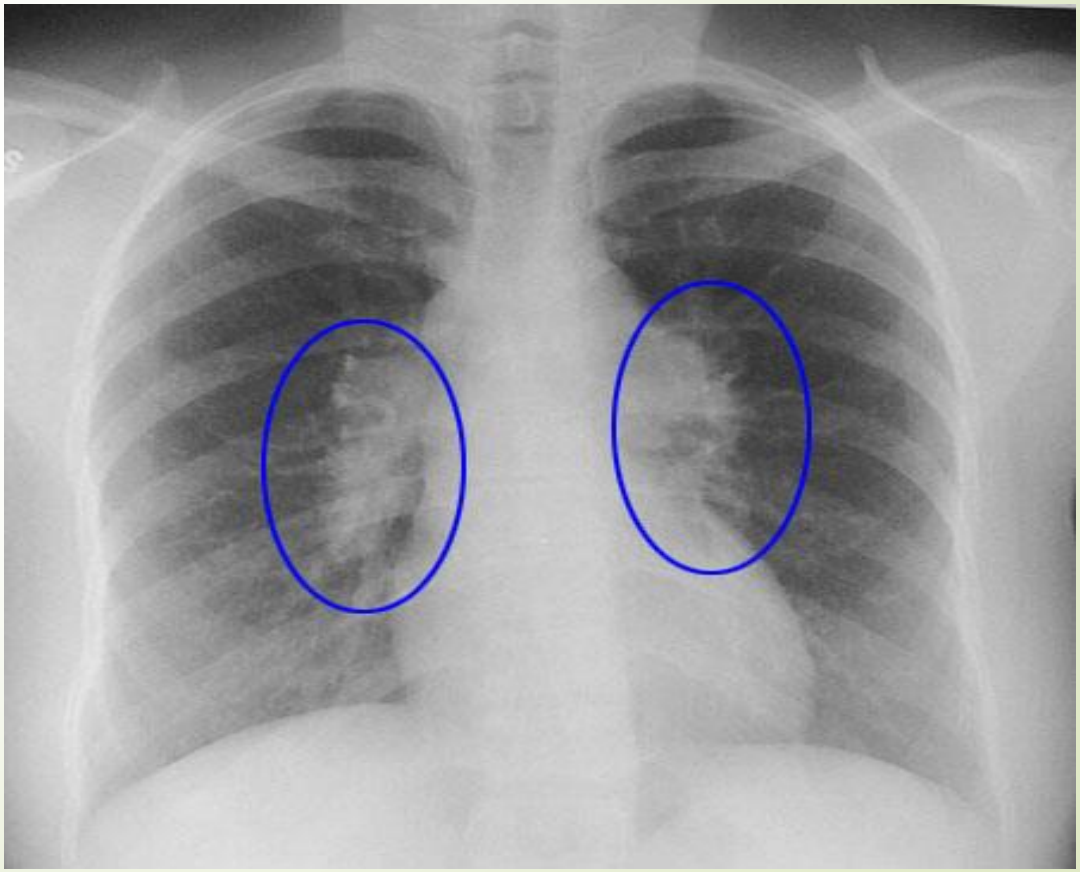




Violaceous, mildly atrophic plaques

Sarcoidosis Pulmonary Involvement

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

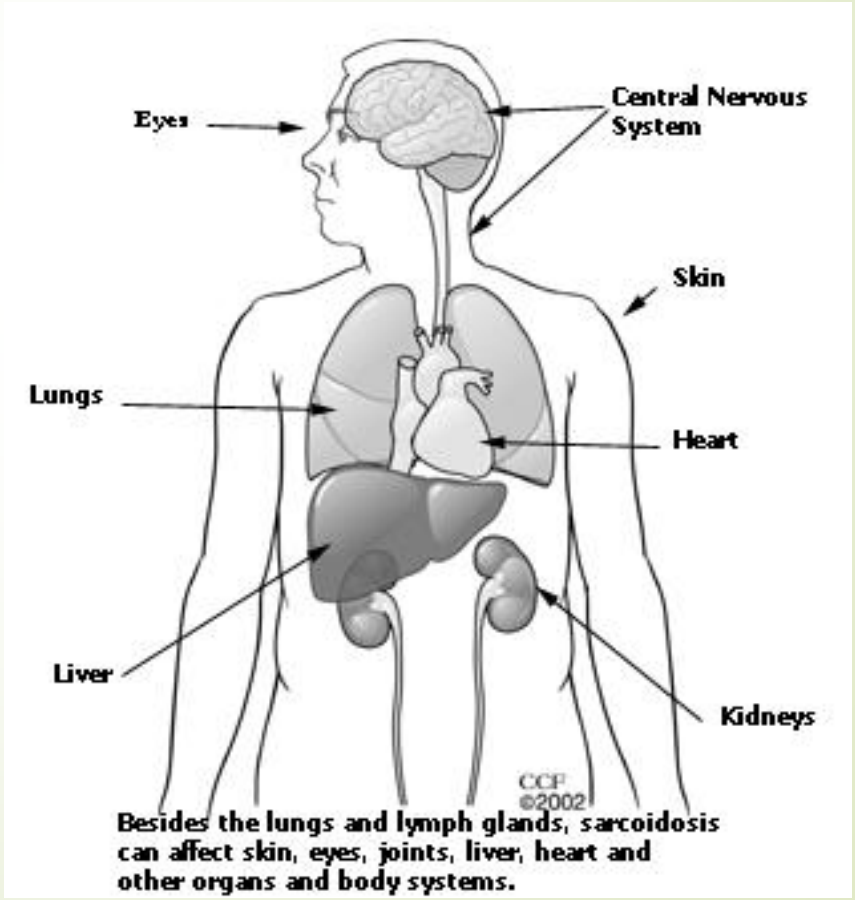


Sarcoidosis

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

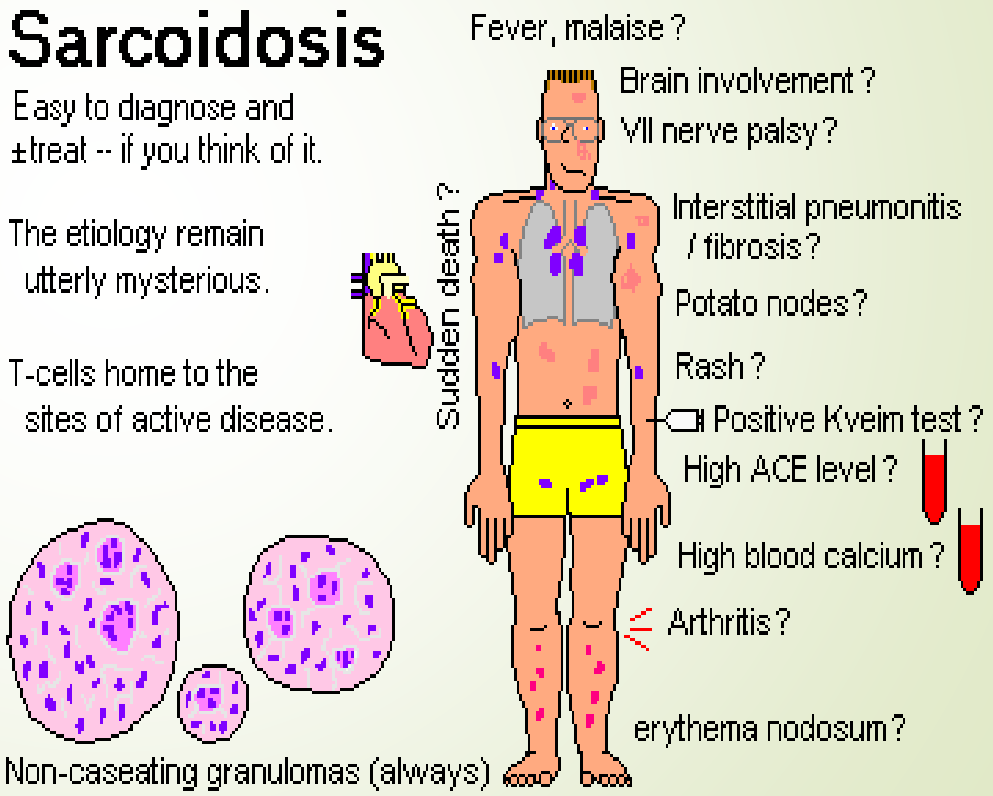
Sarcoidosis Systemic Involvement

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



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

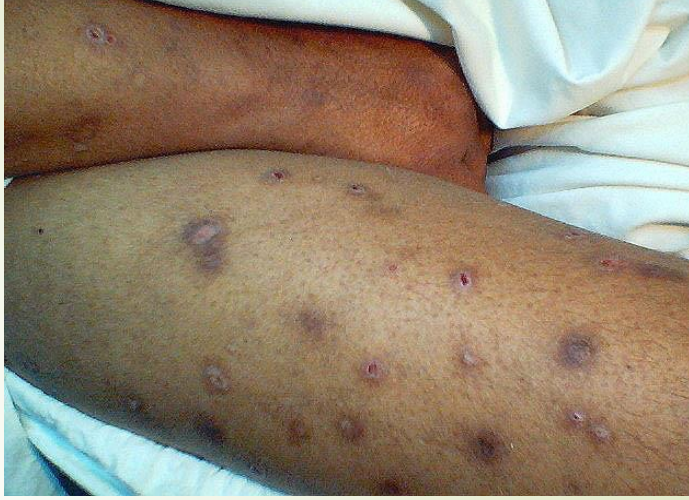
Pruritus workup

- 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
- Labs
  - 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

RENAL DISEASE

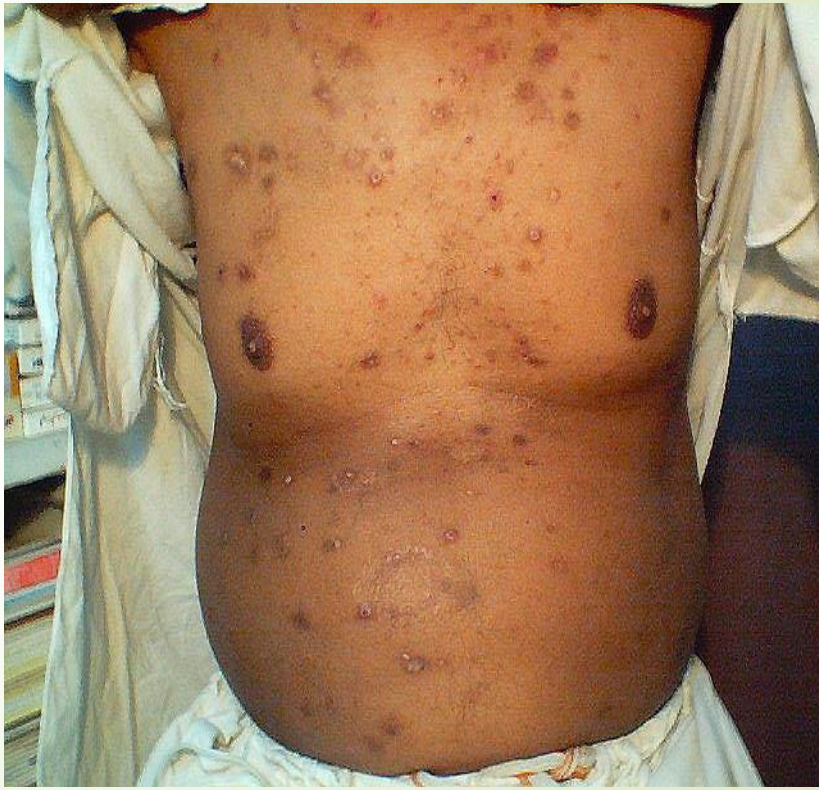


RENAL PRURITIS

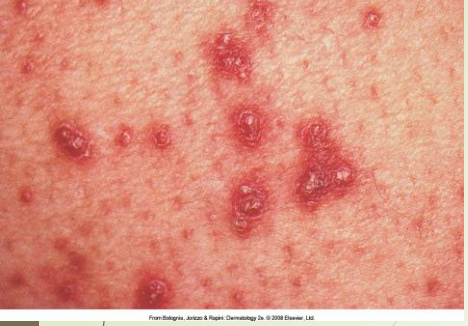
- *"Uremic pruritus"* = used synonomously
  - However not secondary to elevated levels of serum urea
- ***Chronic* renal failure is the MC internal cause of systemic pruritus**
  - 20-80% of patients with CRF
- Typically **generalized, severe, and intractable**
- Multifactorial mechanism:
  - **Xerosis**, 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

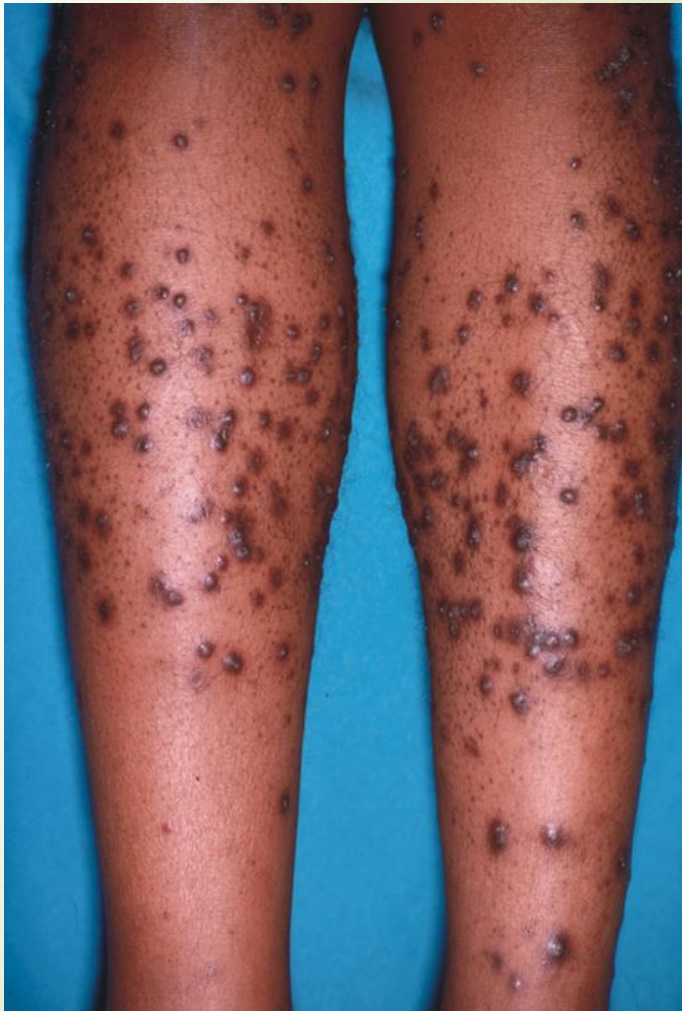


- Pruritus lowest during day after HD
- Pruritus peaks 2nd night after HD
- Pruritus is HIGH during HD



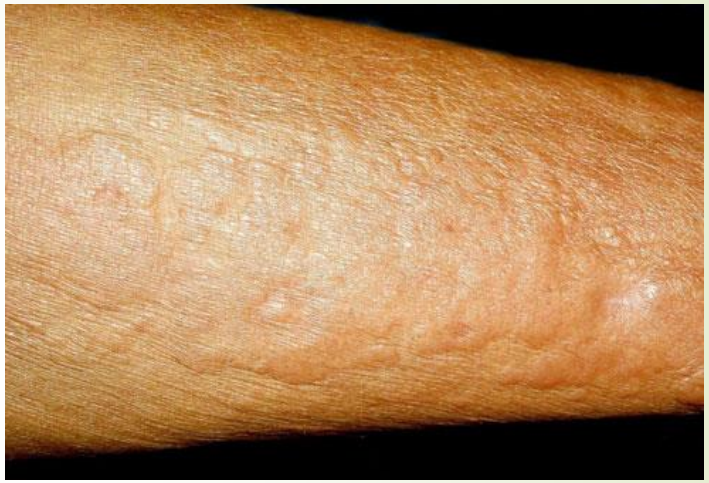
Acquired Perforating Dermatoses

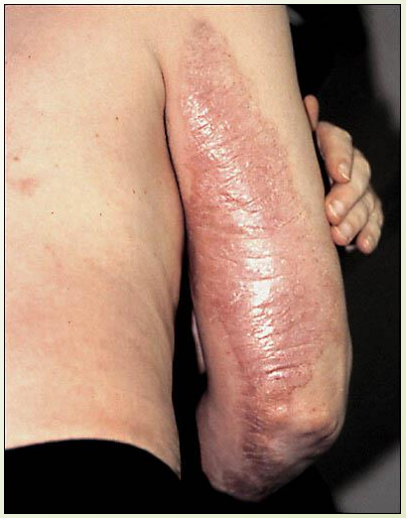
- Perforating disease
  - Arising in adults
  - "Kyrle's disease"
- Associated with **renal failure**, DM, and rarely liver disease and internal malignancy
- Clinical:
  - **Pruritic keratotic papules**
    - *Result of collagen extrusion from dermis to epidermis*
    - *Likely secondary to trauma*
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



Cutaneous and Gastrointestinal (Renal)

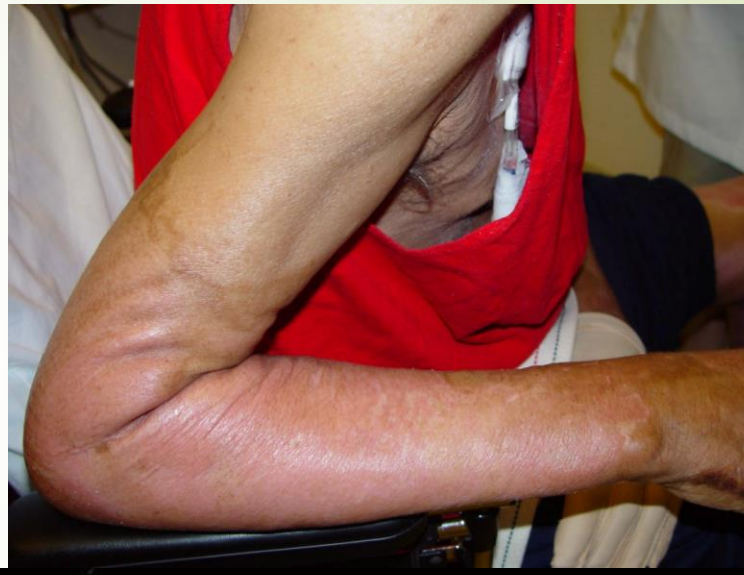
- Nephrogenic Systemic Fibrosis
  - Gadolinium MRI contrast associated
  - Renal failure patients
  - Woody nodules/plaques, usually extremities
  - Variable course
  - <5% fatal (respiratory muscle fibrosis)

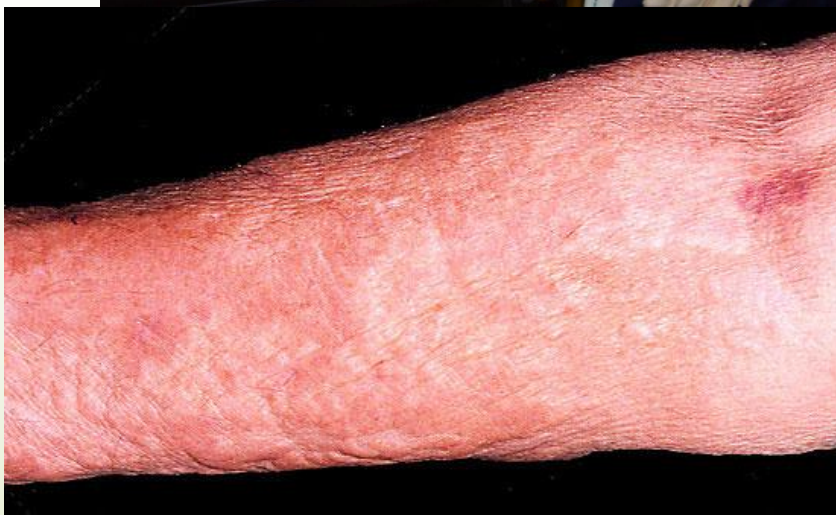




Nephrogenic Fibrosing Dermopathy

- 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

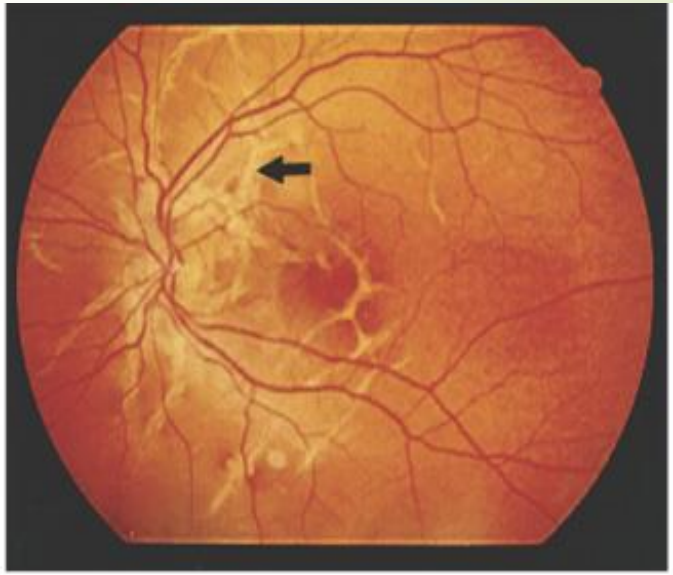




Cutaneous and Gastrointestinal (Renal)

Pseudoxanthoma Elasticum

- Clinical
  - Autosomal recessive more comm
  - 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)

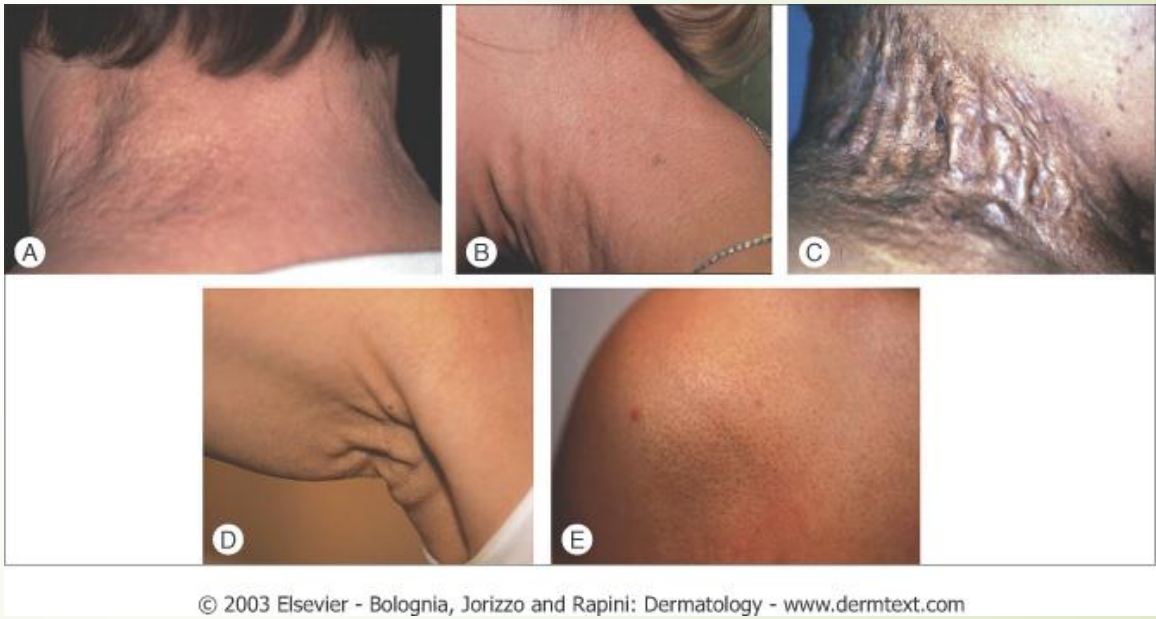


Angioid streaks

Cutaneous and Gastrointestinal (Renal)

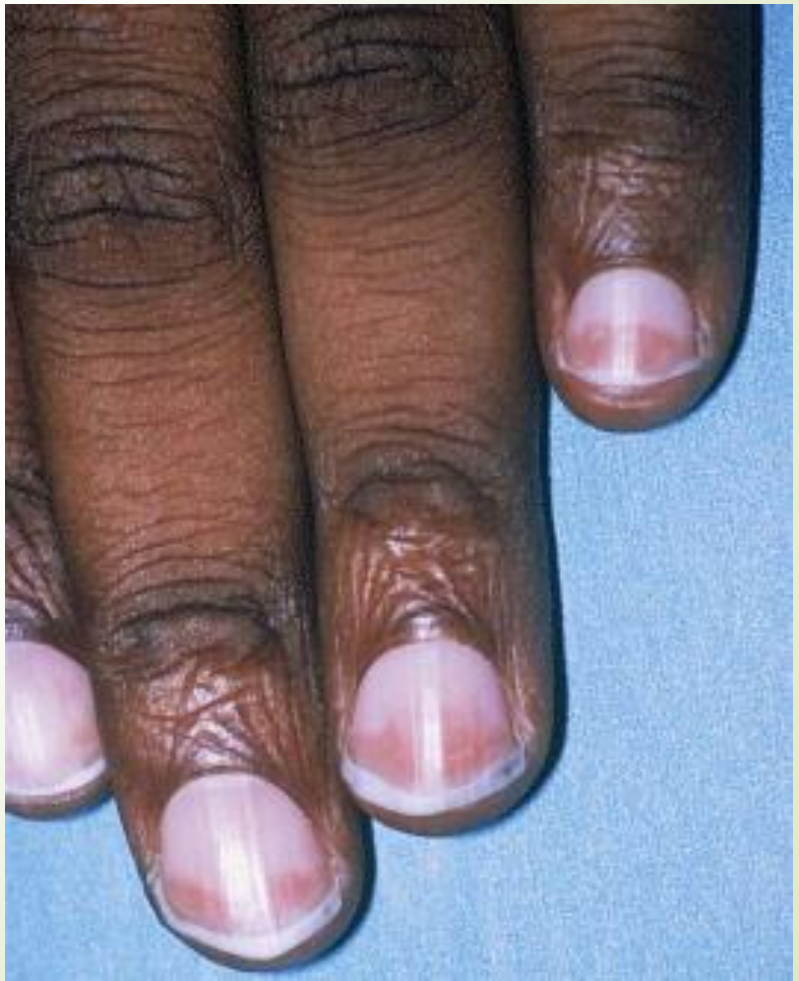
Pseudoxanthoma Elasticum

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



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*



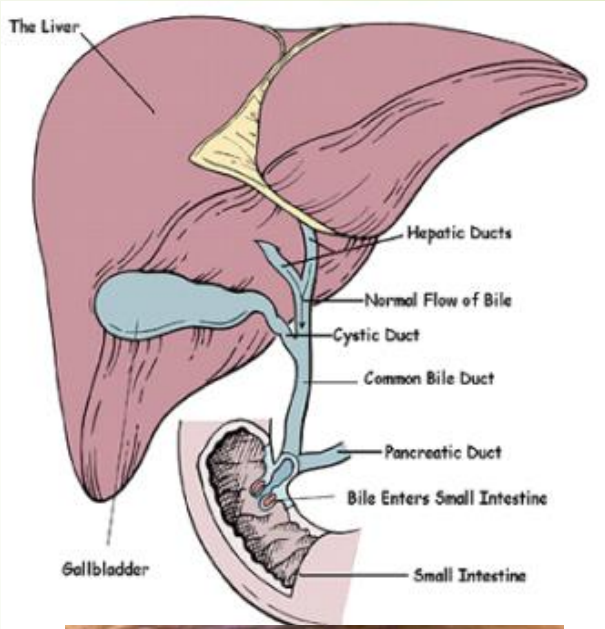
Cutaneous Signs and Gastrointestinal

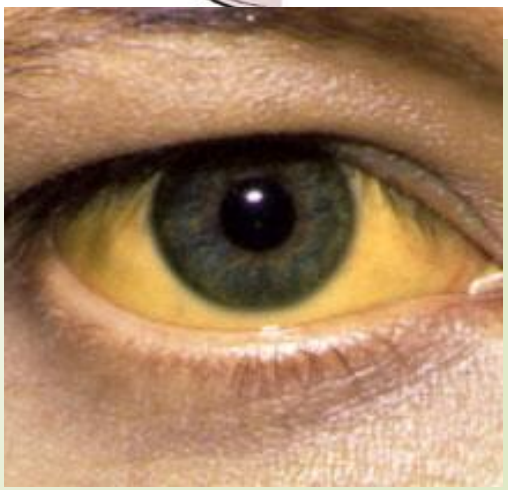
LIVER DISEASE

- Biliary Pruritis
- Hemochromatosis
- Porphyria Cutanea Tarda

Biliary Pruritis

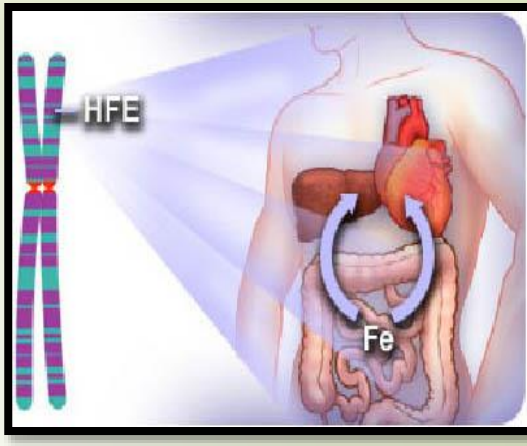
- **20-50% of pts w/ jaundice have pruritus**
- Chronic liver disease
  - Primary biliary cirrhosis, primary sclerosing cholangitis, obstructive choledocholithiasis, carcinoma of the bile duct, cholestasis, HCV
- Generalized, migratory, & not relieved w/ scratching
- Serum level of conjugated bile acid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





Hemochromatosis

Bronze Diabetes

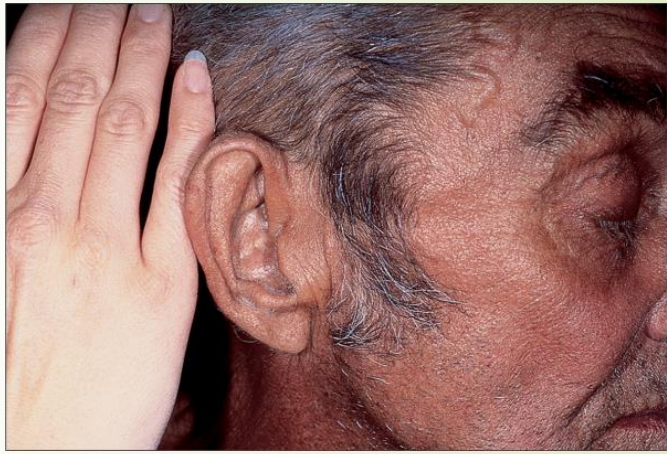


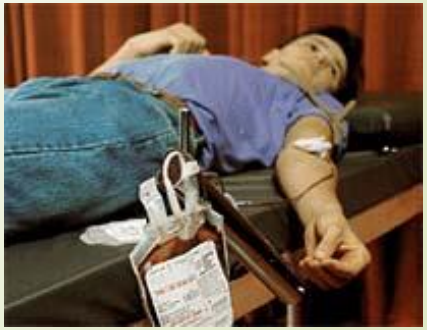
- AR → HFE-gene
- MC white European population; 5th decade
- M>F (2° female iron loss w/ menses)
- Inc. intestinal Iron absorption → iron overload → organ deposition
- <u>Clinical Features:</u>
  - Skin = metallic-grey hyperpigmentation
    - Sun-exposed areas w/ mm involvement in 20%
    - Nails = koilonychia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

Hemochromatosis

Bronze Diabetes

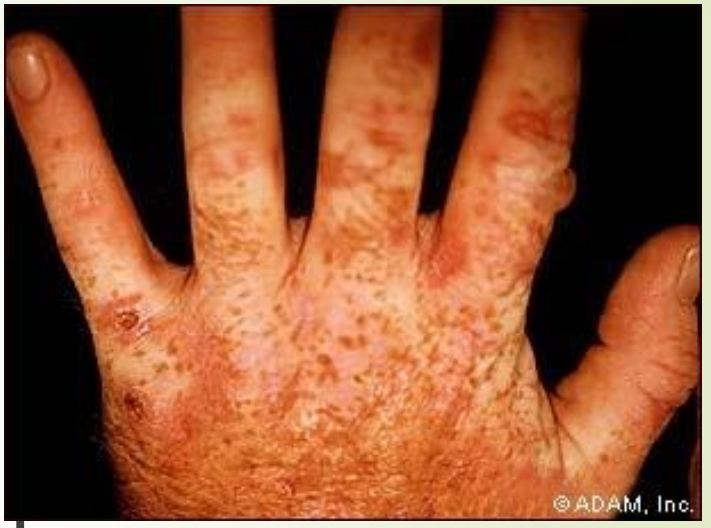
- Many with genetic mutations do **not** develop disease
  - **Increased risk: alcohol, smoking** and **Hep C**
- Dx:
  - Elevated plasma iron & serum ferritin
  - Transferrin saturation (TS) >45
  - Liver bx: if ferritin >1000, Inc. LFTs or >40yrs
  - Gene studies
- Once cirrhosis is present → HCC risk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

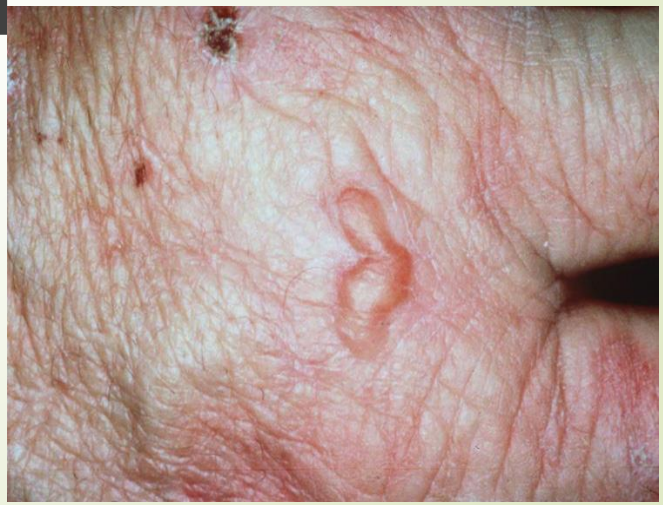




Porphyria Cutanea Tarda

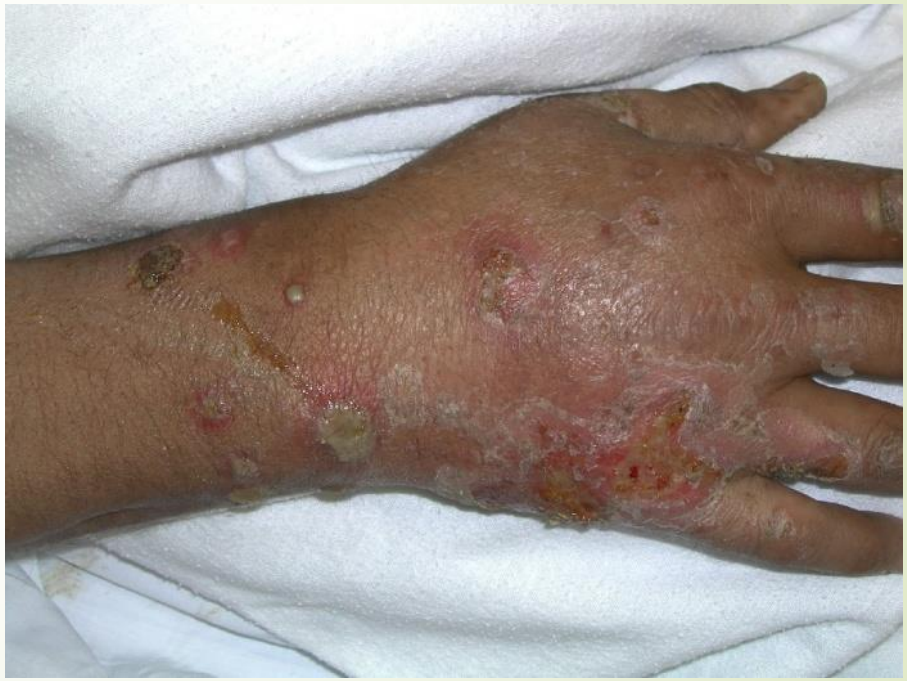
- ***Uroporphyrinogen decarboxylase deficiency***
- *Most common type of porphyria*
- Clinical Manifestations:
  - Bullae, erosions on **sun-exposed skin**
    - heal with scars, milia and dyspigmentation
  - Hypertrichosis on face
  - Sclerodermoid changes of skin
  - Wine/tea colored urine





Cutaneous and Gastrointestinal (Liver)

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



PrecipiPCPPPPPPCTTtat/PredisPP pppposi Factors

- 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

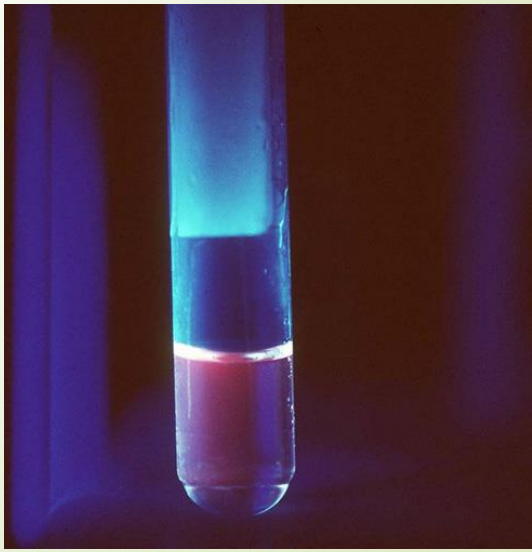
PCT Diagnosis & Treatment

Diagnosis

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

Treatment

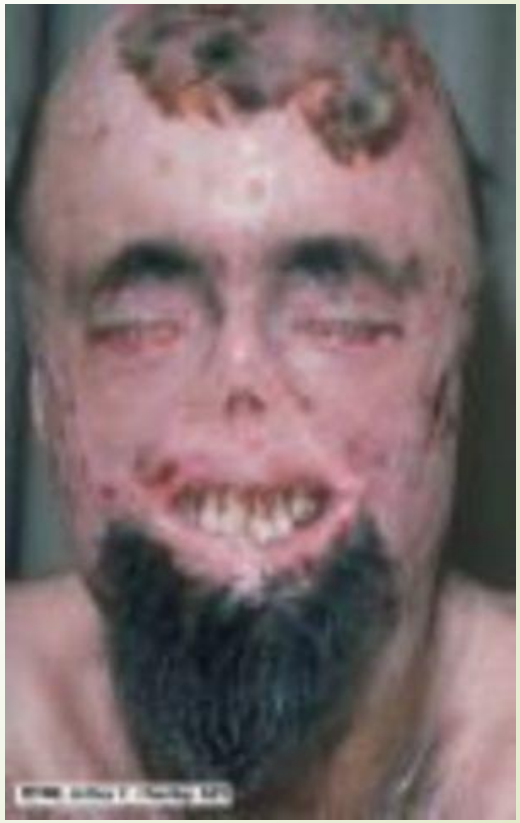
- **Sunlight Avoidance**
- *Avoid drugs/chemicals/ETOH that precipitate attacks*
- Decrease consumption of iron-rich foods
- **Therapeutic phlebotomy (TOC)**
- Low dose Chloroquine



Coproporphyrinogen is elevated more than uroporphyrinogen in 24 hour urine samples in porphyria cutanea tarda

Cutaneous and Gastrointestinal (Liver)

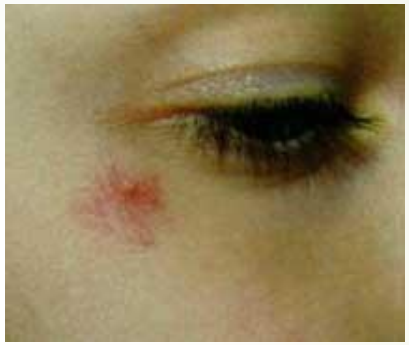
- Porphyrias
  - Each associated with deficiency of enzyme in heme synthesis
  - Hepatic or Erythropoietic
  - Some forms with photosensitivity
  - Frequent alcoholism and Hep C

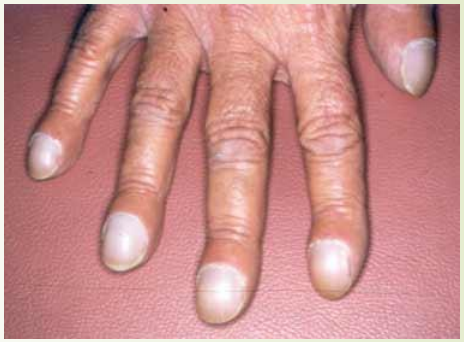


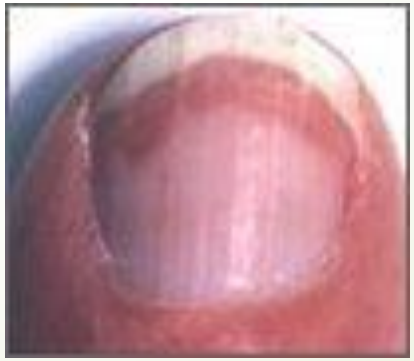
Vampire legend

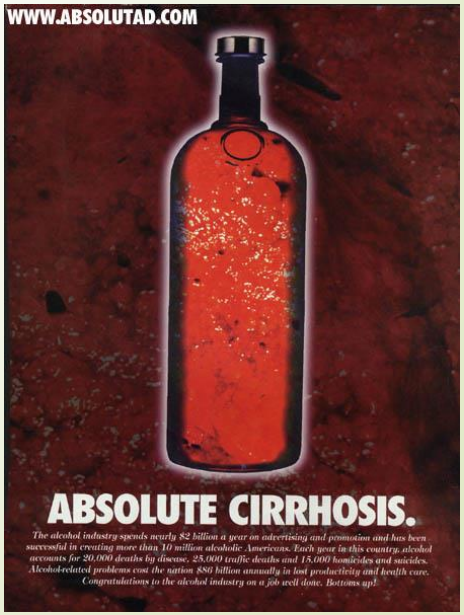
Cutaneous and Gastrointestinal* (Liver)

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



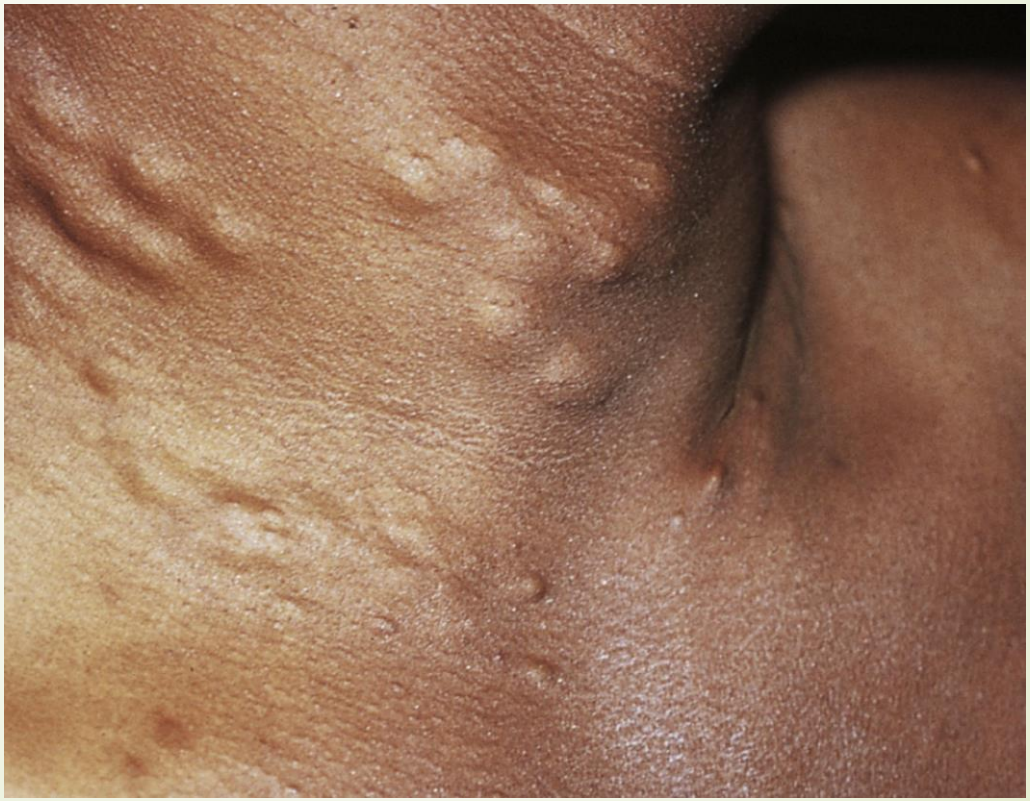






Cutaneous and Gastrointestinal (Intestine)

- 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

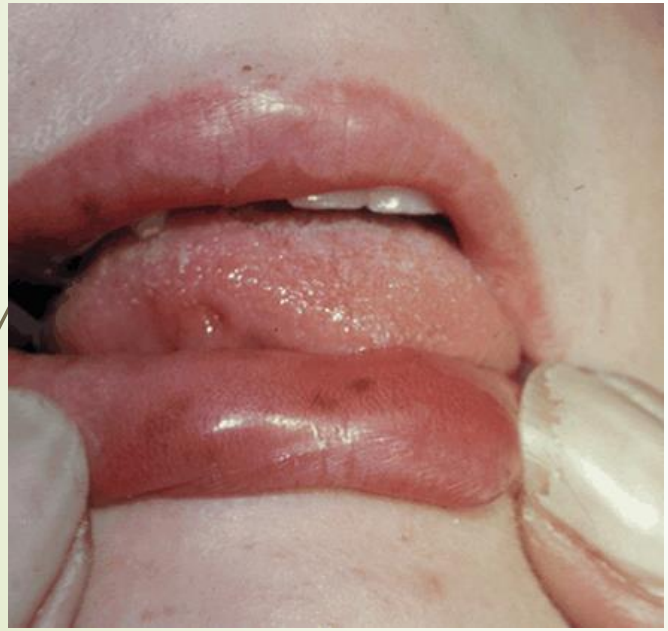


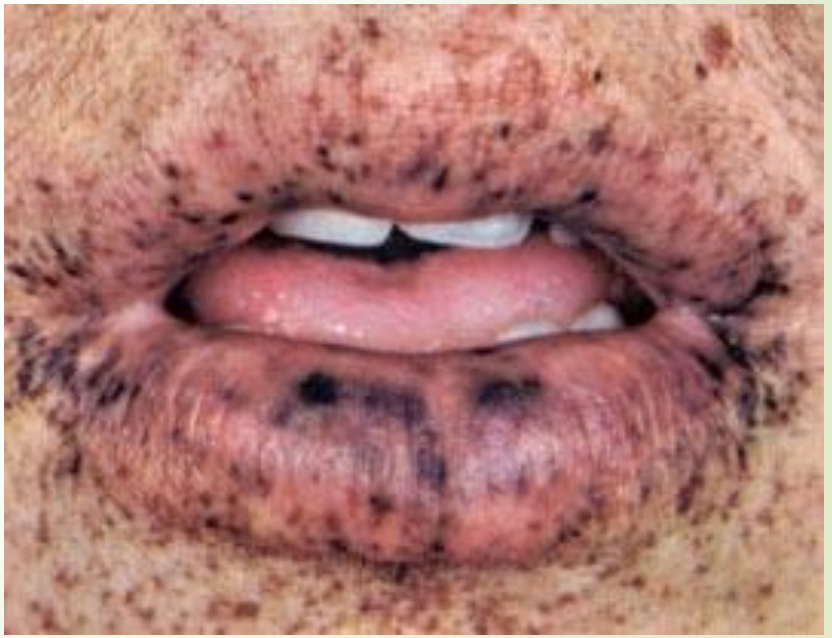
Cutaneous and Gastrointestinal* (Intestine)

- 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)

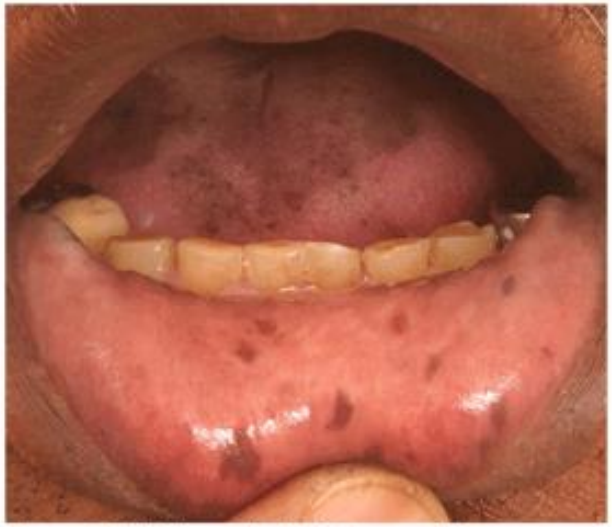


Figure 1—Multiple small telangiectases of the tongue and buccal mucosa.

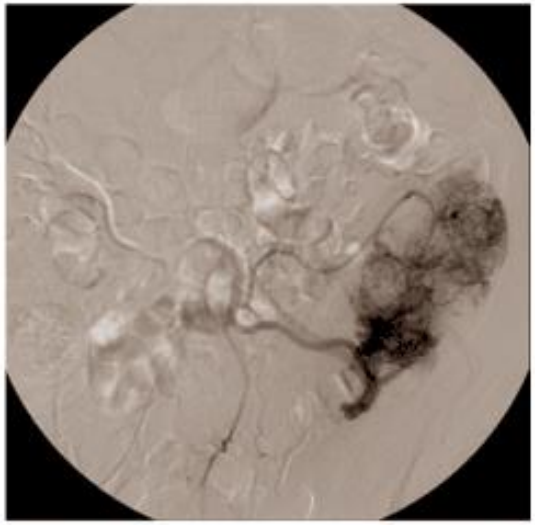


Figure 2—Arteriovenous malformation along the descending colon.

telangiectasias

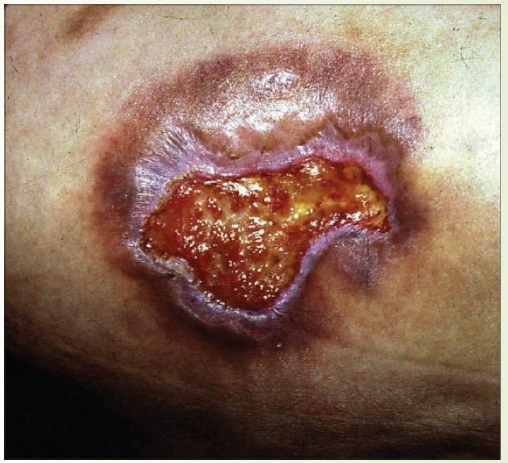
A-V malformation

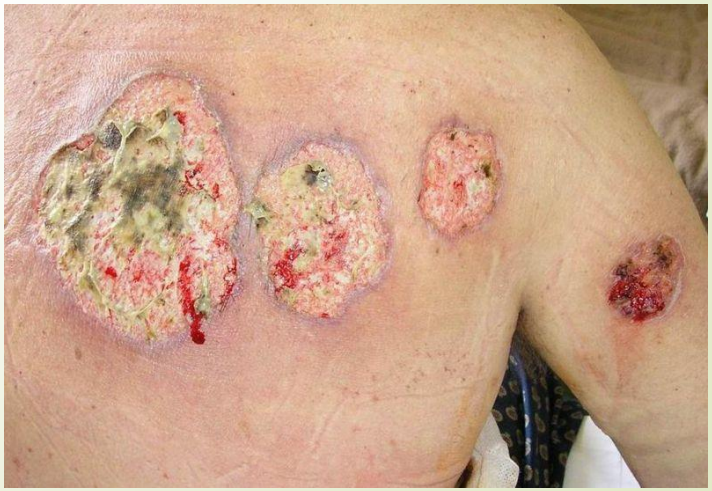
Cutaneous and Gastrointestinal (Intestine)

- 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)

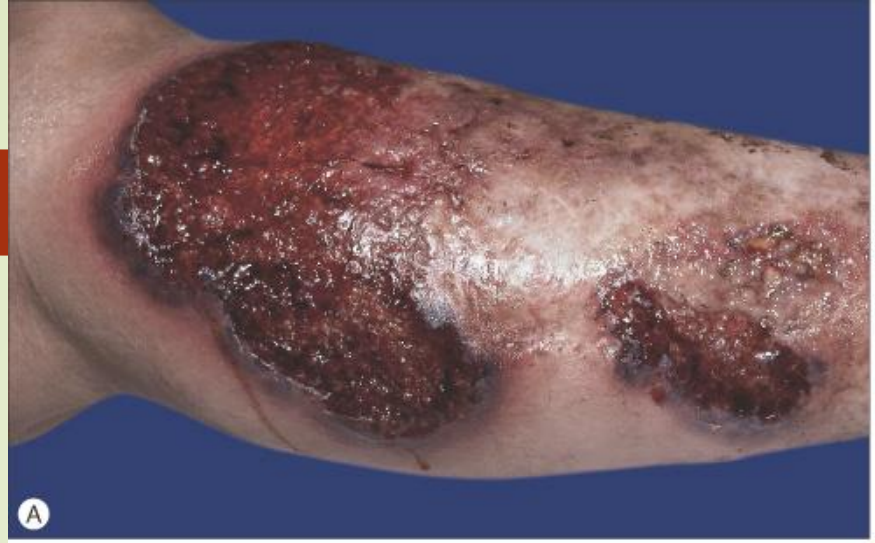
- Inflammatory Bowel Disease
  - Pyoderma Gangrenosum
    - 1-10% of IBD
    - Undermined necrotic violaceous ulcer
    - Pustular onset
    - More common in UC
    - Frequent precipitation by trauma
    - Treatment: steroids and immunosuppressives

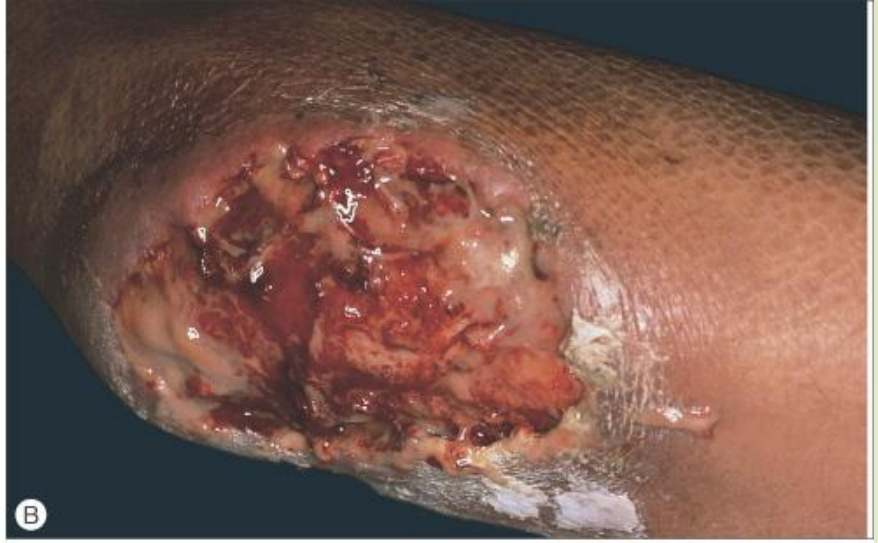




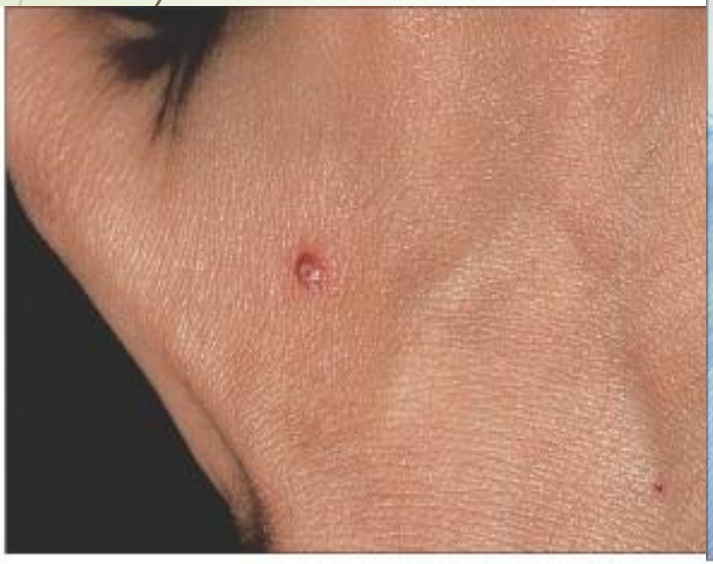
Pyoderma Gangrenosum

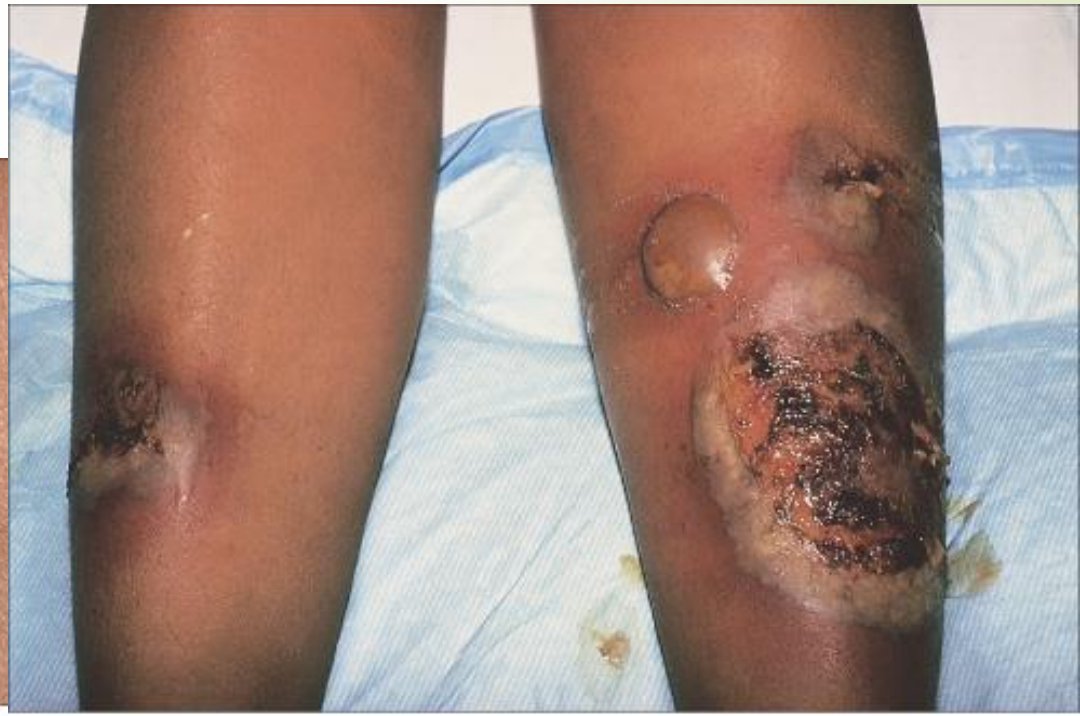
- Uncommon, recurrent, **ulcerative neutrophilic disease**
- Tender papulopustule → undergoes necrosis and ulceration with an **irregular, undermined border**
  - Heals with atrophic, cribiform, pigmented scars
- **50-70% have associated disease**
  - MC **Ulcerative colitis**, **Crohn's** (20-30%)
    - *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





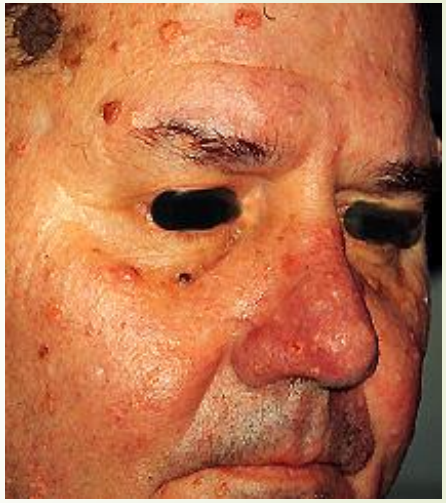
Early lesion: papule with erythematous base

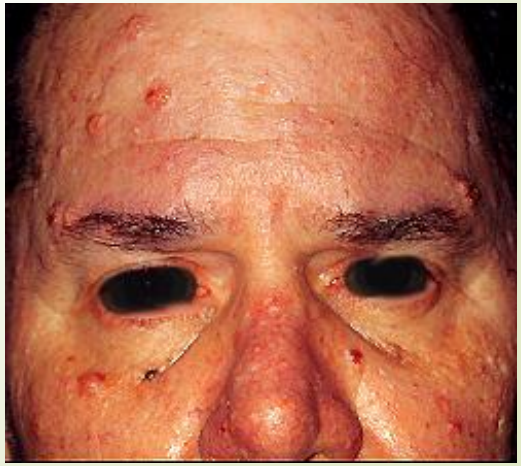




Cutaneous and Gastrointestinal (Intestine)

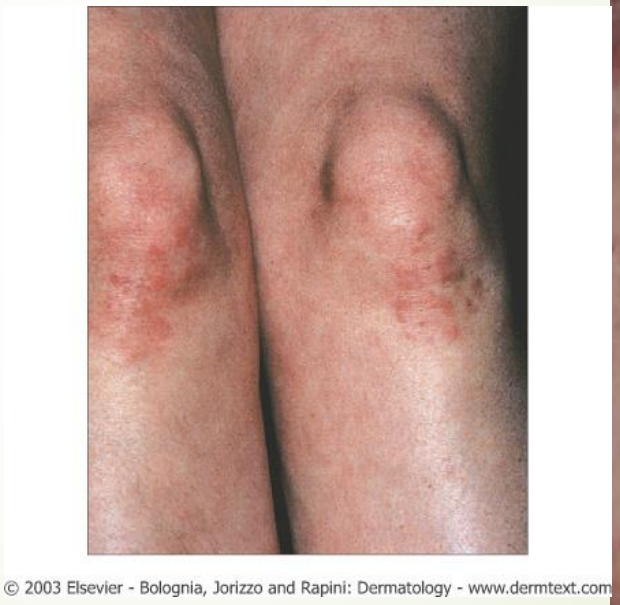
- Muir-Torre Syndrome
  - Autosomal dominant
    - Sebaceous neoplasms
    - Multiple keratoacanthomas
    - Internal malignancy
  - Cutaneous 10-20 years prior (preventative medicine!)
  - Colon cancer most common

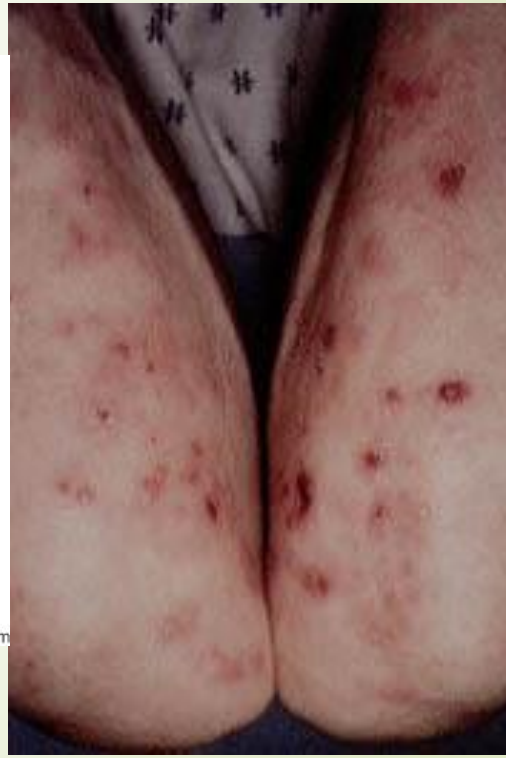




Cutaneous and Gastrointestinal (Intestine)

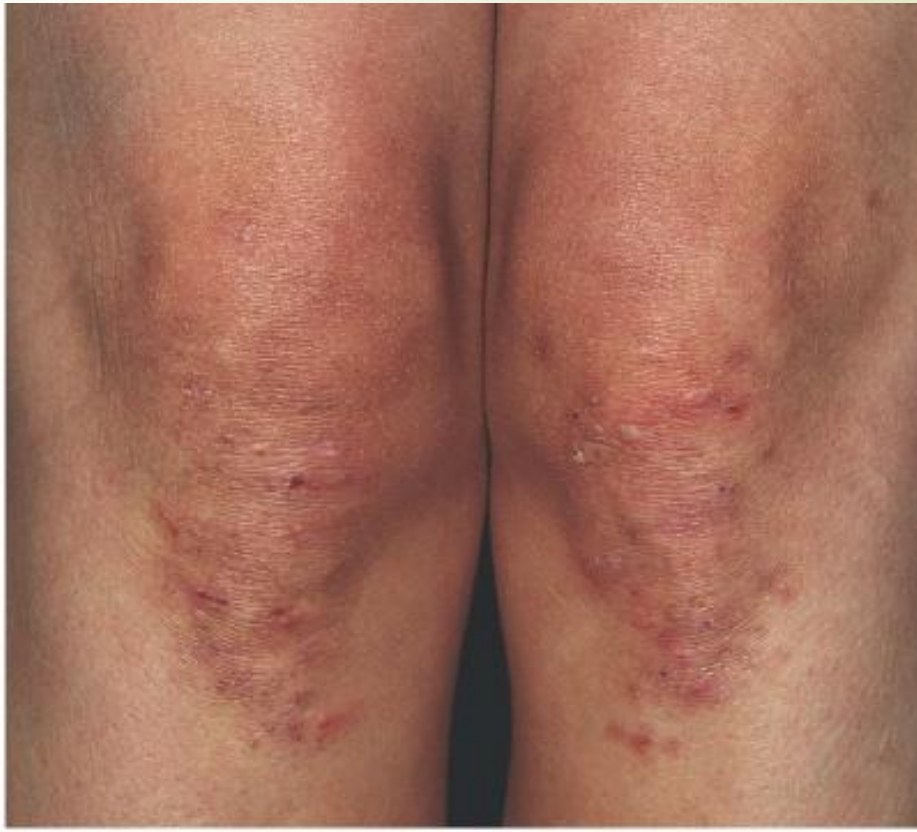
- Dermatitis Herpetiformis
  - Chronic, relapsing/remitting, severely pruritic dz
  - Symmetrical, polymorphous (often extensor)
  - Itching and burning are intense (often only excoriations)
  - Associated with gluten-sensitive-enteropathy
  - Treatment: medication plus gluten-free diet





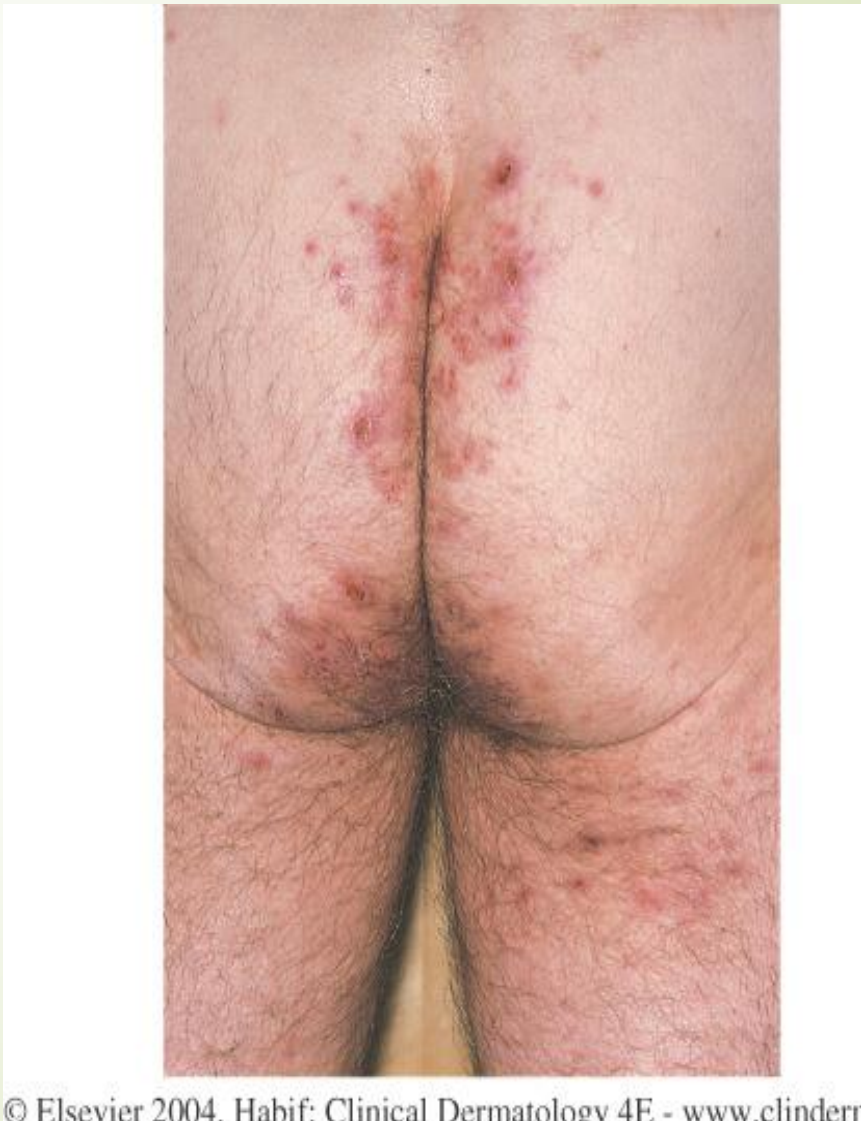
Dermatitis Herpetiformis

- 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**



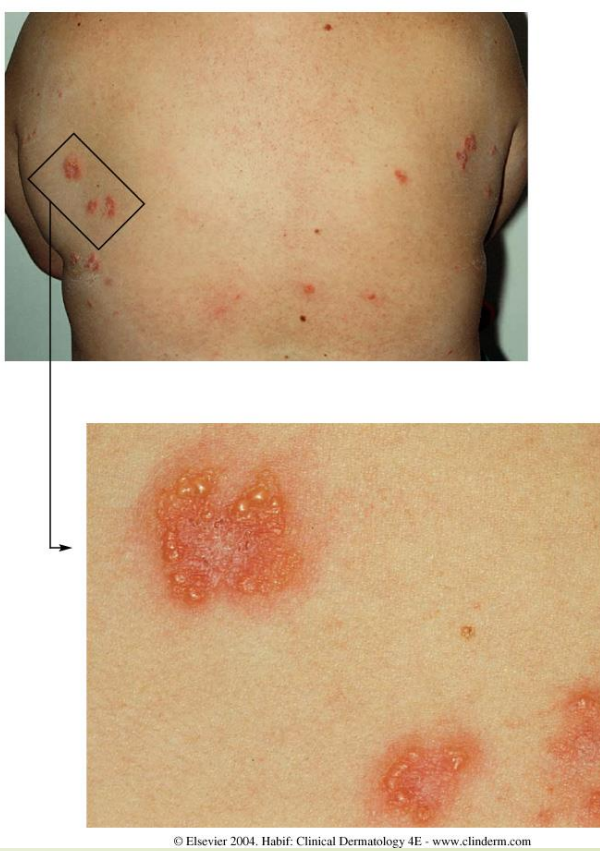
Dermatitis Herpetiformis

- 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 die
  - **Antigliadin antibodies** (>66%)
  - Endoscopy: blunting and flattening of villi (80-90%)
- Treatment
  - **Gluten free diet**
  - Dapsone



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 (pulmonar cysts, pneumothorax)

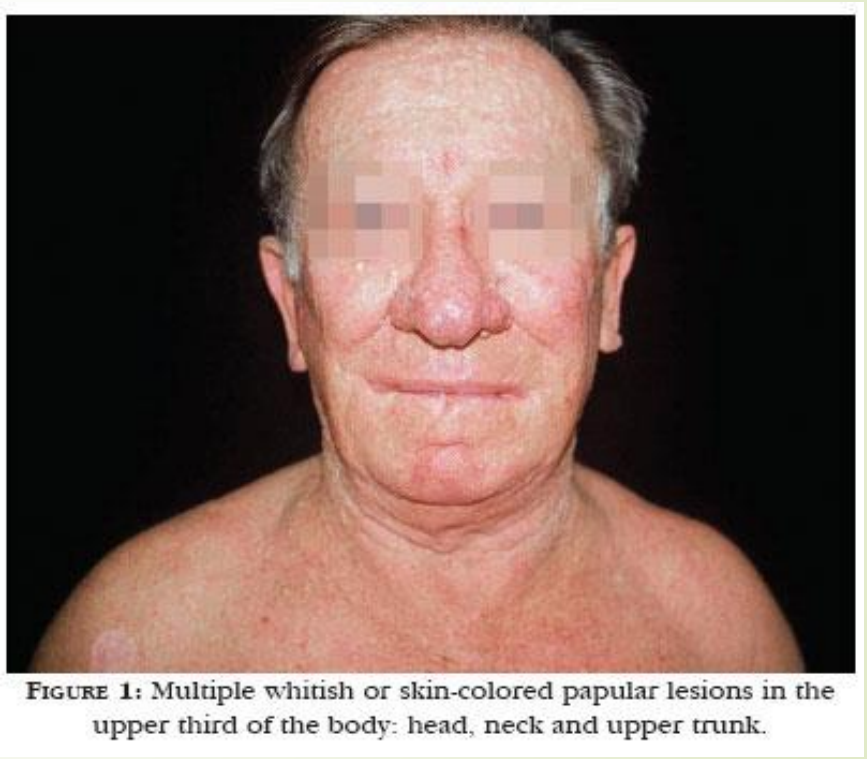


FIGURE 1: Multiple whitish or skin-colored papular lesions in the upper third of the body: head, neck and upper trunk.

Cutaneous and Endocrine

ENDOCRINE DISORDERS

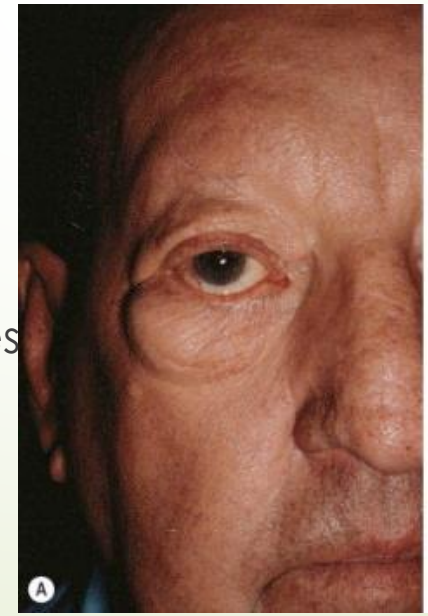
- Hypo- and hyperthyroidism
- Addison's Disease
- Acanthosis Nigricans
- Necrobiosis Lipoidica Diabeticorum
- Diabetic Dermopathy
- Diabetic Bullae
- Xanthomatoses

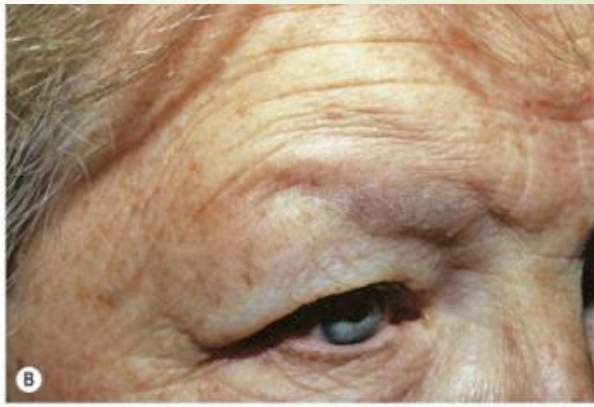
Hypothyroidism

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

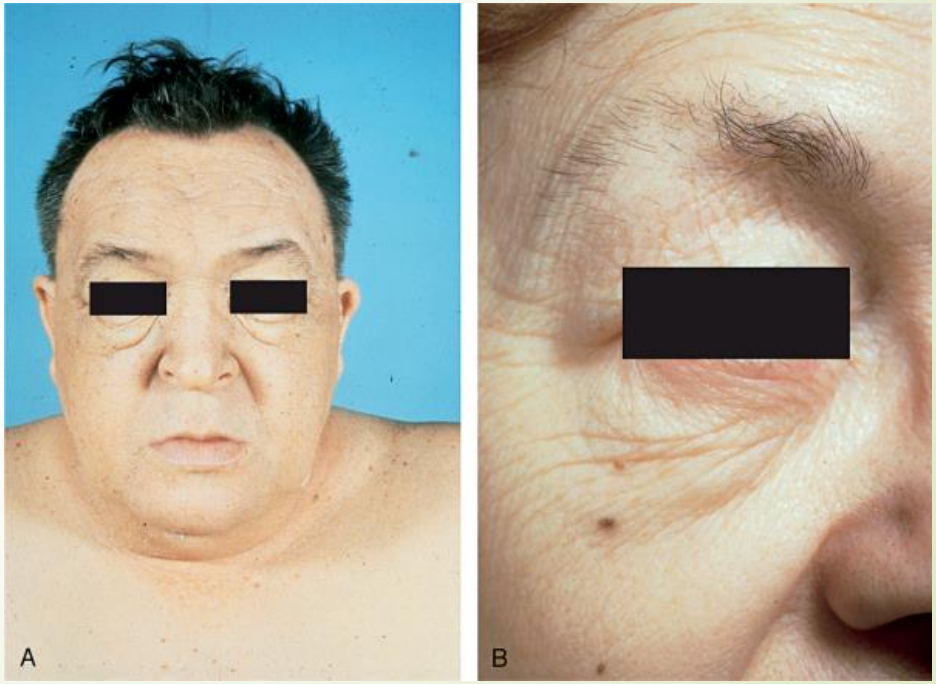
- *Systemic mucinosis*
- Severe lack of thyroid hormone
- Clinical:
  - Skin becomes rough & dry
  - **Facial skin is puffy**
    - **dull, flat expression**
  - Macroglossia, broad nose
  - **Chronic periorbital infiltration**
  - Carotenemia → palms & soles
  - Diffuse hair loss
    - lateral 3rd eyebrow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





Endocrine Disorders*

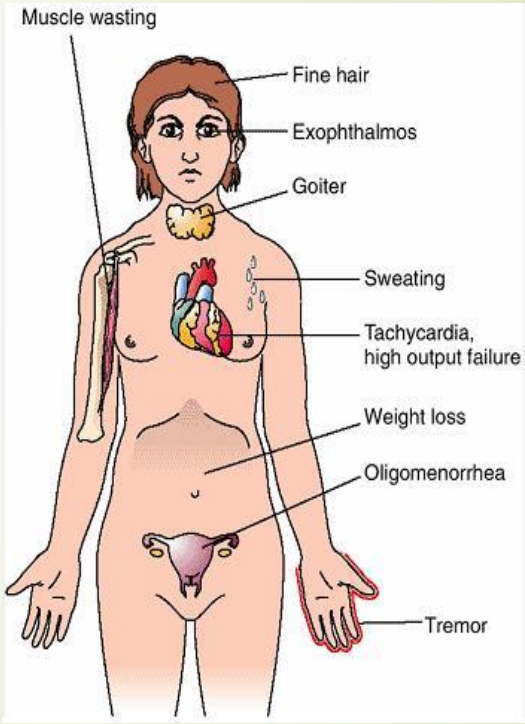
- Hypothyroidism
  - Cold, thick, dry skin
  - Coarse hair
  - Loss of lateral eyebrows
  - Brittle nails
  - Xanthomas
  - Purpura



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*

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

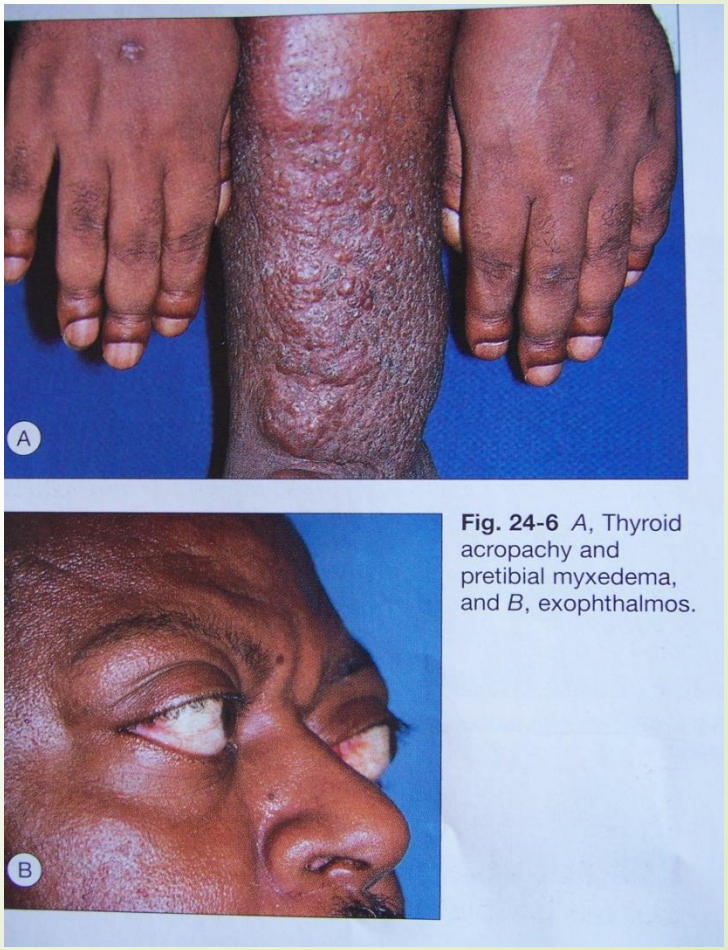
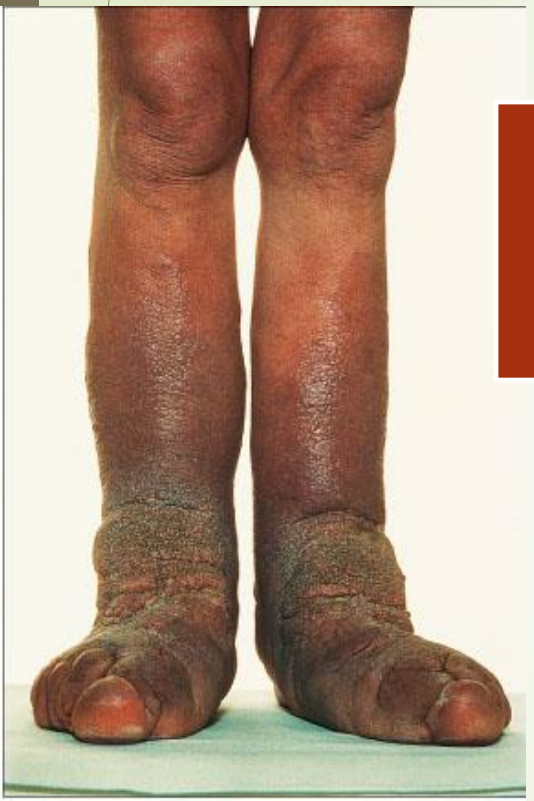


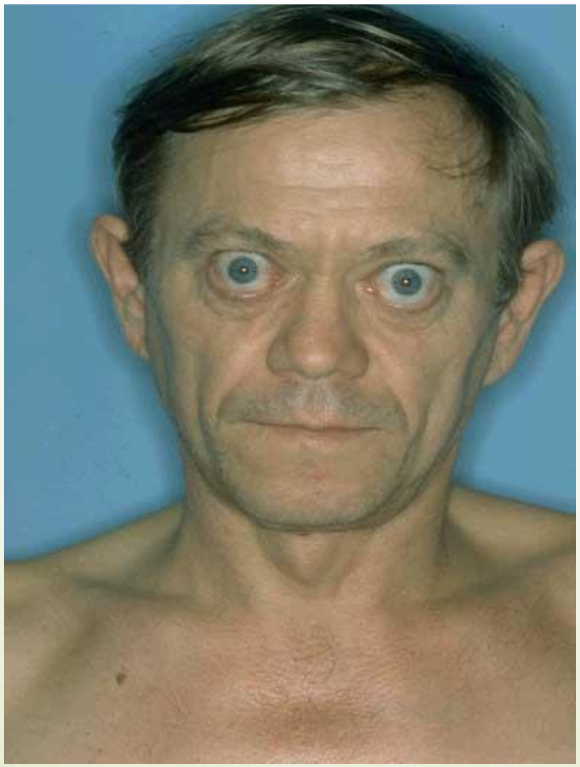
Fig. 24-6 *A*, Thyroid acropachy and pretibial myxedema, and *B*, exophthalmos.

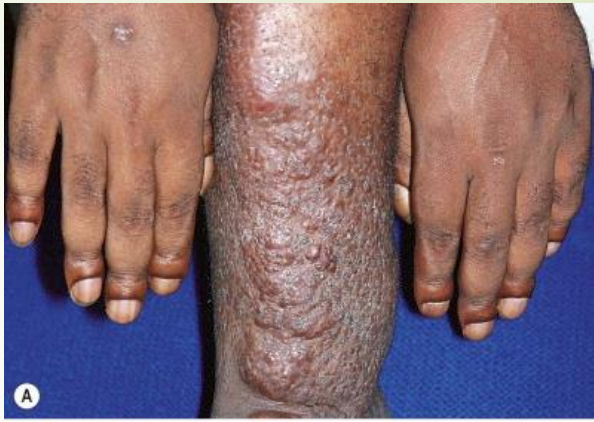
Hyperthyroidism

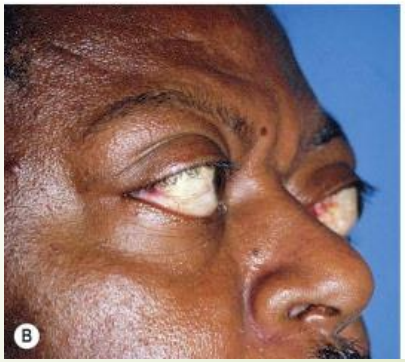


2005. McKee et al.: Pathology of the Skin with Clinic

Grave's Disease
Pretibial Myxedema
Exophthalmos

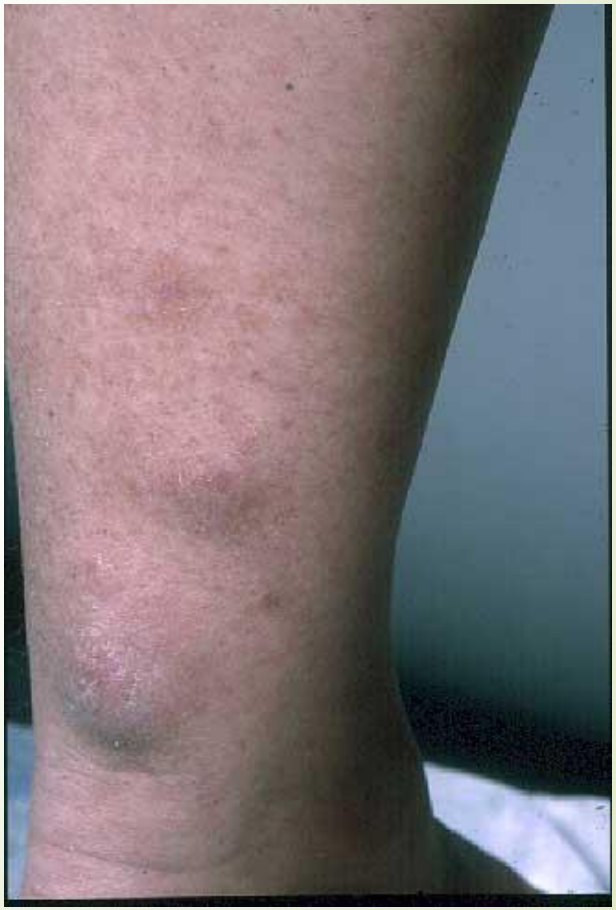






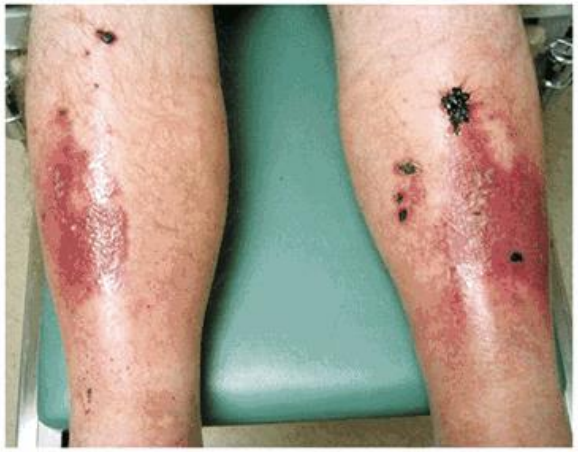
Endocrine Disorders

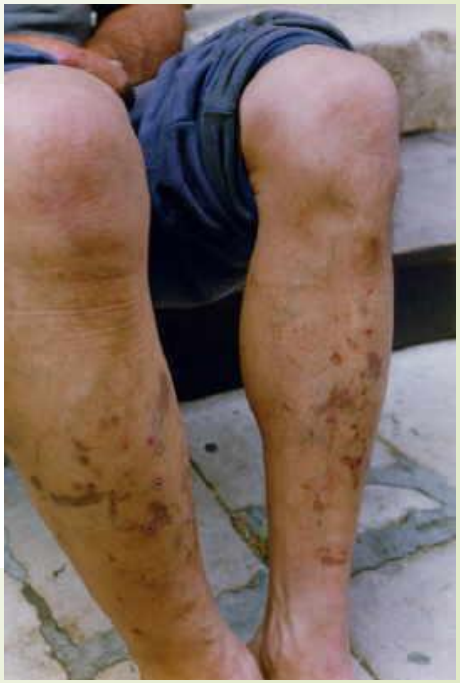
- Pretibial myxedema
  - Pretibial plaque with dry scaly epidermis
  - Often hyperthyroidism
  - Possible euthyroid
  - Frequent exopthalmos
  - Accumulation of glycosaminoglycans assoc with thyroid stimulating antibodies
  - Tx: intralesional or topical steroids



Endocrine Disorders

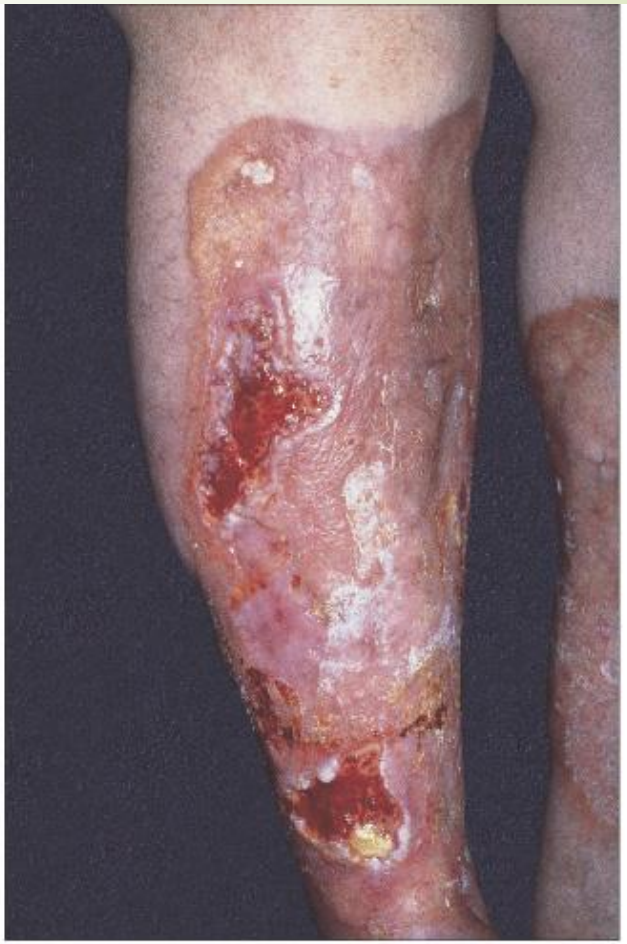
- Diabetes
  - Necrobiosis lipoidica (dibeticorum) (NLD)
    - Red-yellow atrophic plaques
    - Usually lower legs
    - Control of diabetes does not influence
    - Treatment not satisfactory





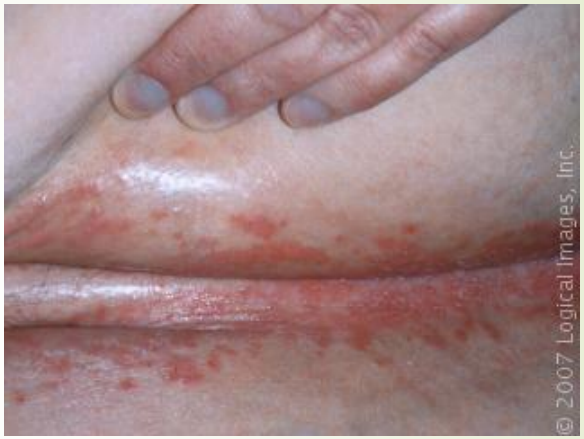
Necrobiosis Lipoidica (Diabeticorum)

- 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, telangiecta plaques with violaceous, irregular b
- Common sites include shins, ankle calves, thighs and feet
- Ulceration occurs in 35% lesions

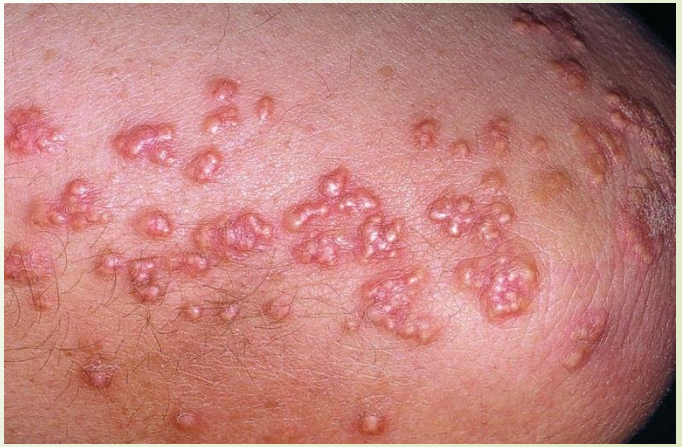


Endocrine Disorders

- Diabetes
  - Recurrent candidiasis

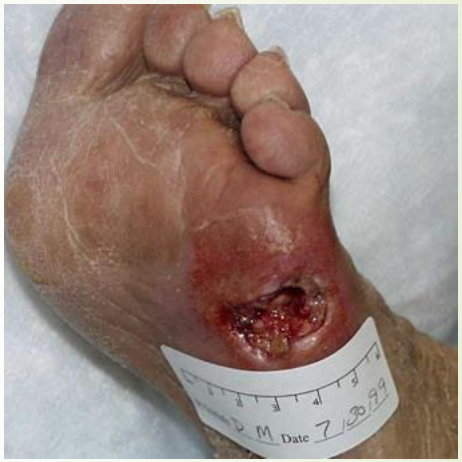


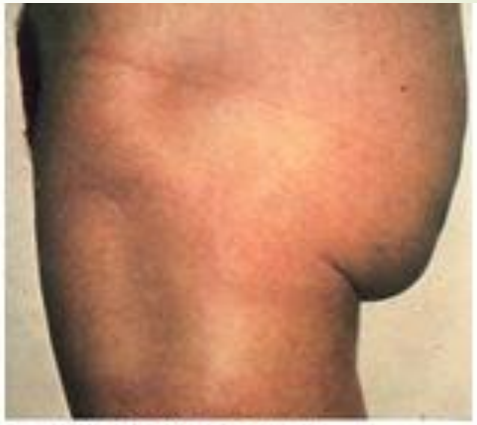
  - Eruptive xanthomas (also manifestations of lipid abnormalities)



Endocrine Disorders

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



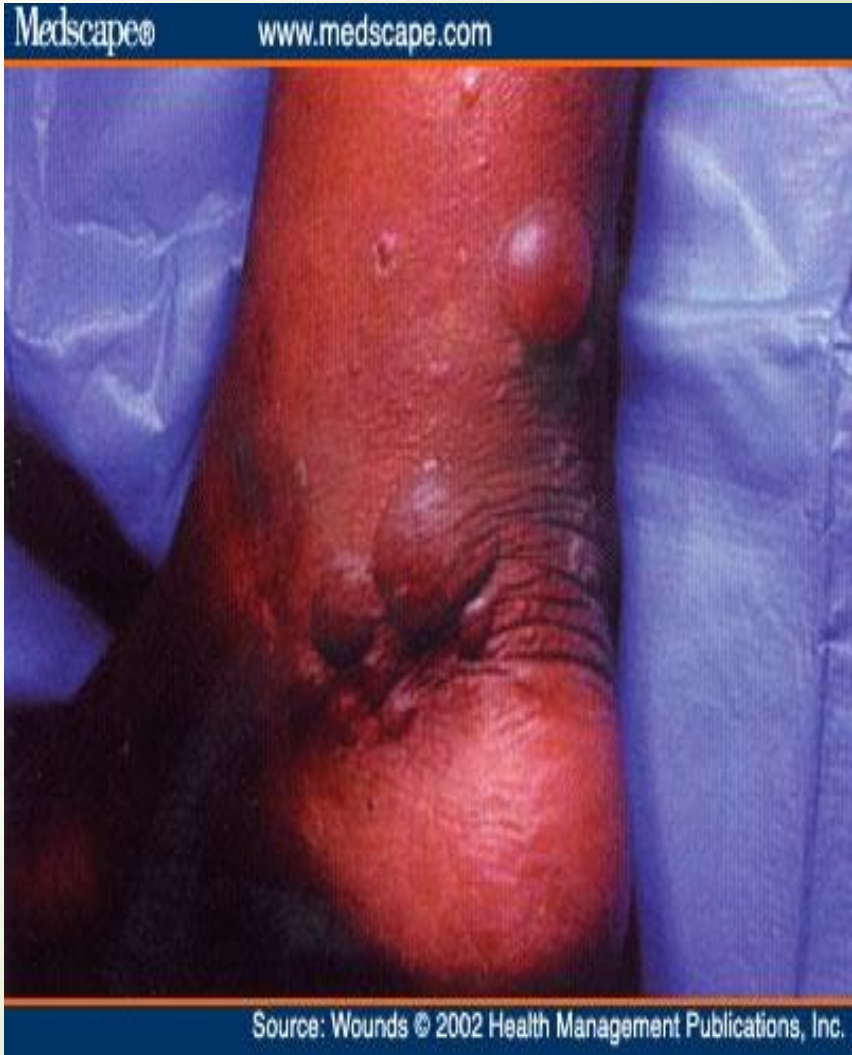


Diabetic Dermopathy: *Shin Spots*

- **MC cutaneous lesion in diabetics (50% of pts)**
- Dull-red papules → well-circumscribed, small, round, atrophic, hyperpigmented plaques
  - SHINS mc site!
  - > 4+: *High specificity for microvascular disease*

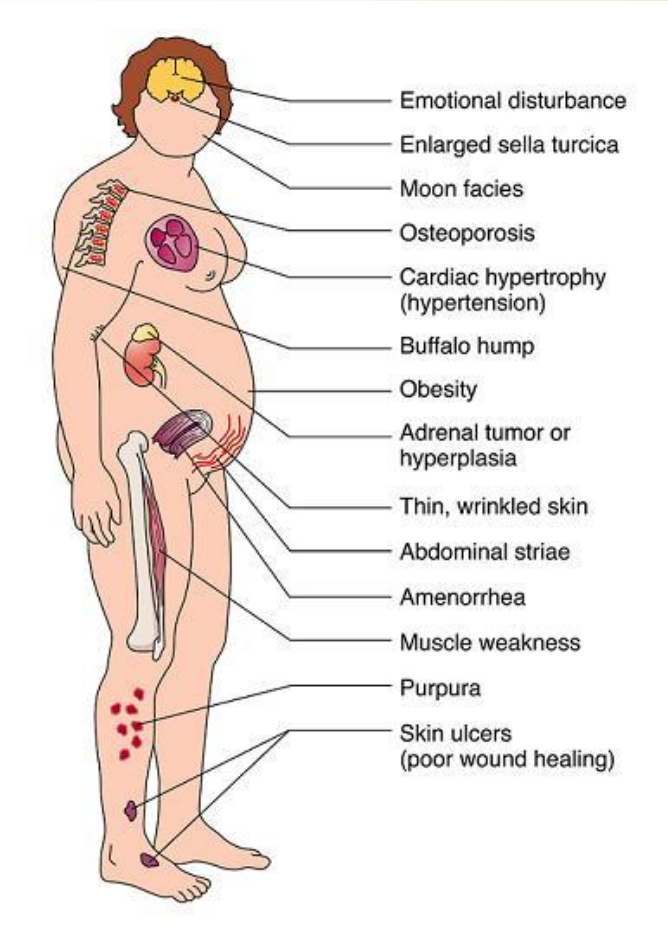
Diabetic Bullae

- *Rare complication*
- M>F
- Painless tense bullae
  - Rapid onset
  - Acral site
- Pathogenesis:
  - Trauma
  - Neuropathy
  - UV light
- Tx: spontaneously heal
  - 2-5 wks



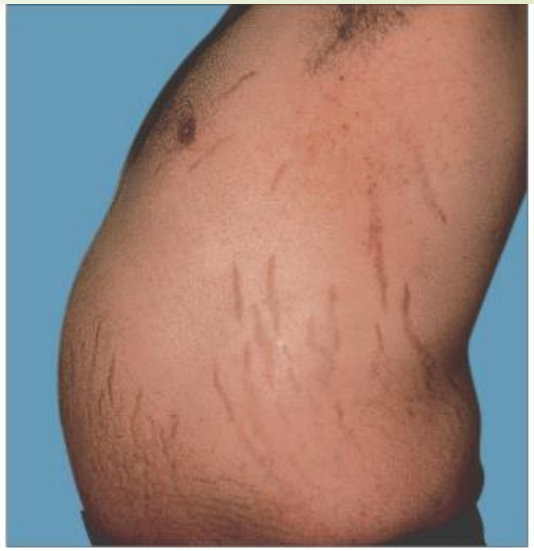
Endocrine Disorders*

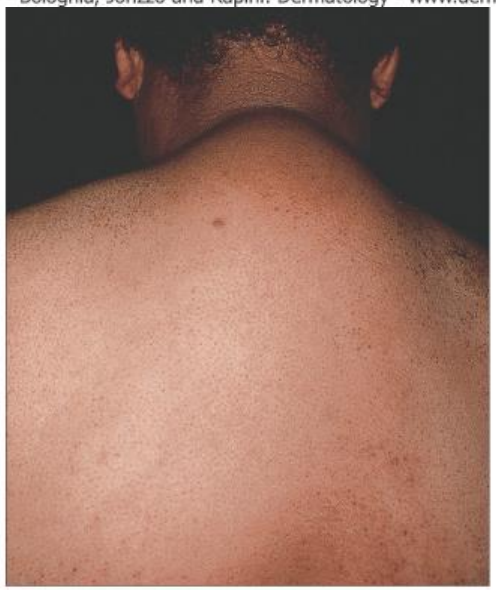
- Cushing's Syndrome
  - Chronic excess of glucocorticoids
  - Central obesity (face, neck, upper back and abdomen)
  - Striae
  - Hypertrichosis –face/body
    - Thin hair - scalp
  - Dryness
  - Skin fragility
  - Plethora
  - Facial acne
  - ↑dermatophyte infections



Cushing's Disease

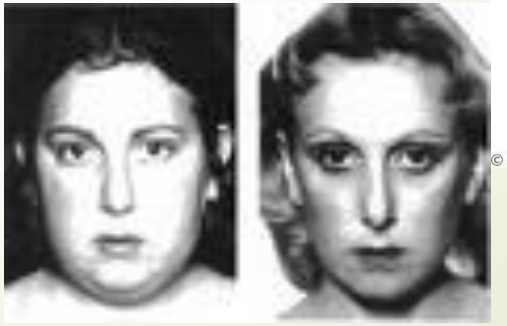
- **Chronic excess of glucocorticoids**
  - Microadenomas of pituitary (10%)
  - **Iatrogenic**
    - **systemic corticosteroids**
    - topical steroids in children
- Clinical:
  - *skin fragility; poor wound healing*
  - ***Purple atrophic striae***
  - *central adiposity (moon face, buffalo hump)*
  - *peripheral muscle wasting*
- Dx
  - Dexamethasone suppression test
  - Urinary free cortisol
  - Serum ACTH

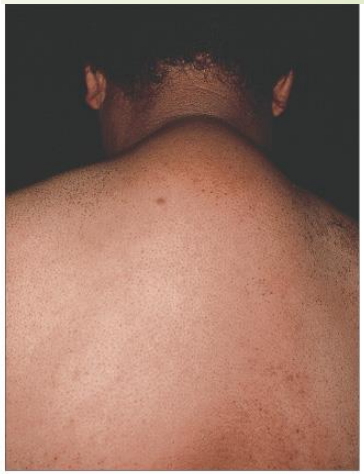




Endocrine Disorders*

- Cushing's Syndrome
  - Non – Iatrogenic: Women affected 4 x more than men
  - Peak age 20-30s
  - Named Features
    - Moon facies
    - Buffalo hump
  - Systemic: HTN, weakness, decreased bone density, DM, atherosclerosis, osteoporosis, decreased libido

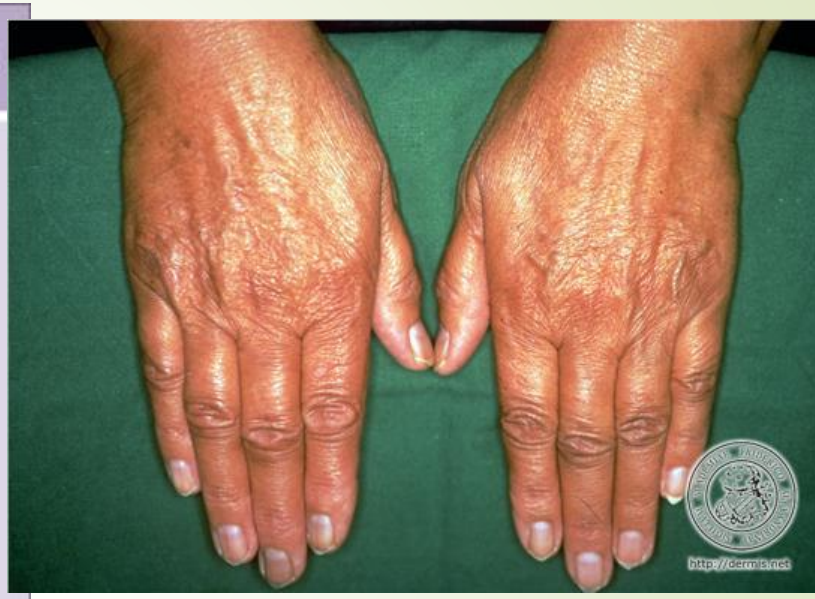


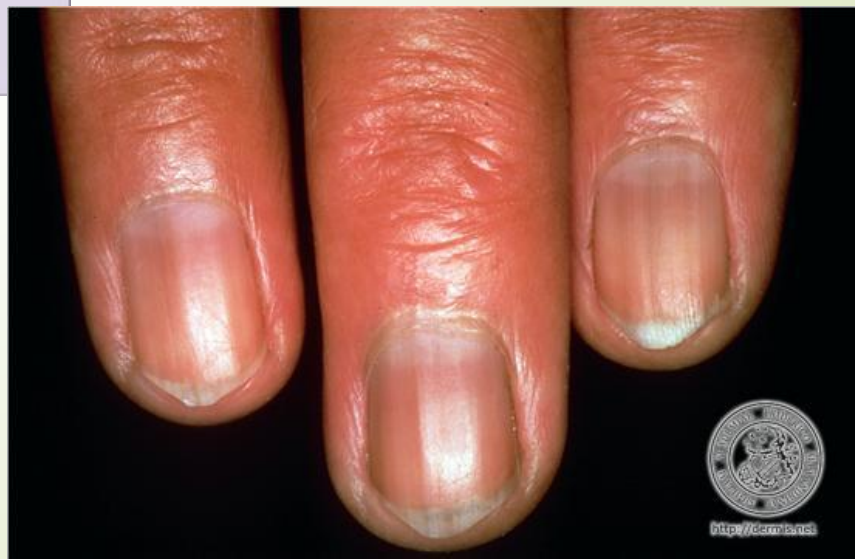


Addison's Disease

SELECTED DERMATOLOGIC MANIFESTATIONS OF ADDISON'S DISEASE

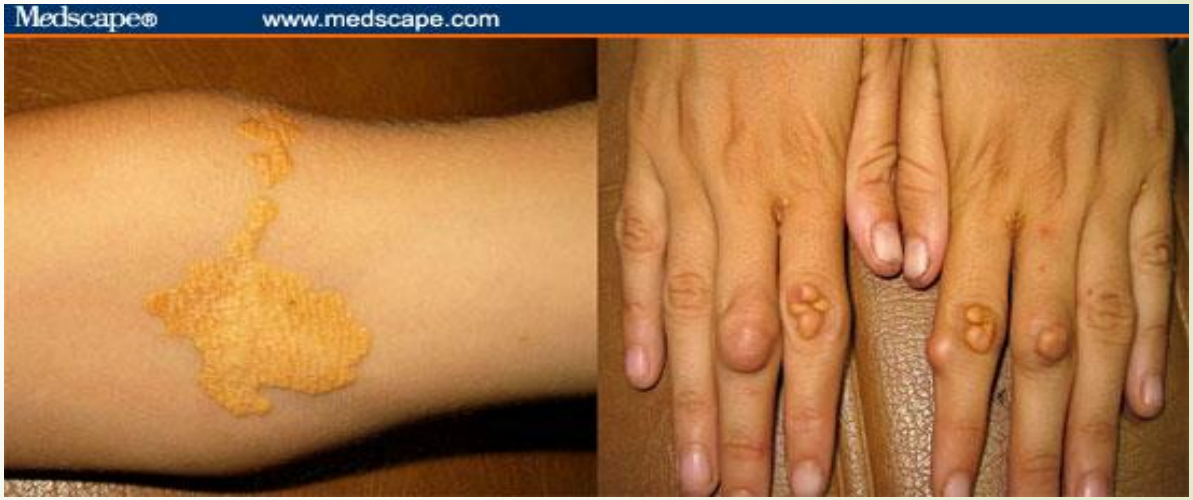
- Hyperpigmentation (MSH-like effect due to secretion of ACTH)
  - Diffuse with sun-exposed accentuation
  - Sites of trauma
  - Axillary, perineum, and nipples
  - Palmar creases
  - Nevi
  - Mucous membranes
  - Hair
  - Nails
- Loss of ambisexual hair in postpubertal women
- Fibrosis and calcification of cartilage including the ear (rare)
- Vitiligo
- Chronic mucocutaneous candidiasis





Endocrine Disorders

- Xanthomas
  - Tumors of lipid containing cells
  - Rare spontaneous regression



Endocrine Disorders
Xanthoma classification (location/appearance)

- Tendinous xanthomas
  - Tendons or fascia
  - Hands, feet, knees
  - Often with elevated cholesterol
- Planar xanthomas
  - Yellow-tan macules/ plaques on head, trunk, extremities
  - Assoc with myeloma or biliary cirrhosis
- Tuberous xanthomas
  - Yellow-orange papules on extensor surfaces
  - Elevated cholesterol
- Eruptive xanthomas
  - Sudden appearance
  - High triglycerides
- Xanthelasma
  - Plane xanthomas of eyelids
  - Most common
  - Elevated or normal cholesterol

Endocrine Disorders

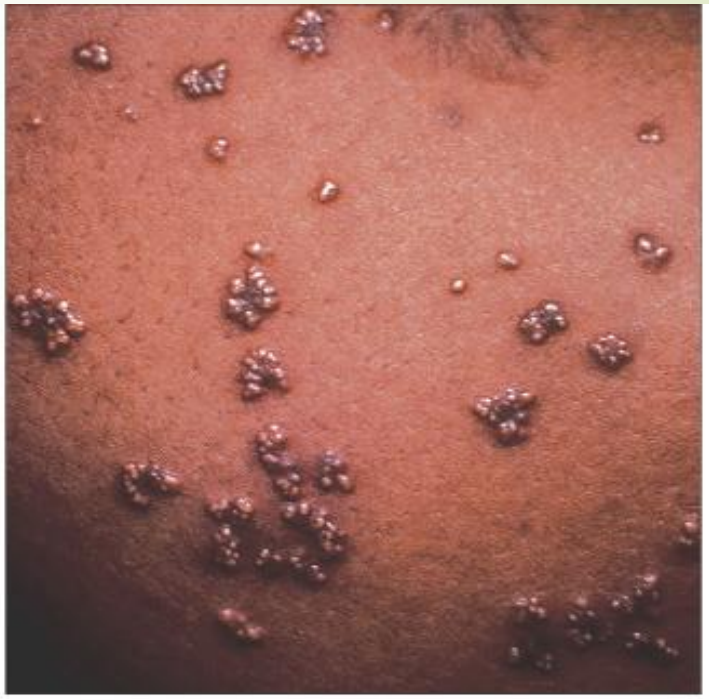
- Xanthoma Differential
  - Tuberous – dermatofibroma, granuloma annulare, gout, rheumatoid nodule, calcinosis cutis
  - Plane – easily recognized
  - Tendinous – gout, ganglion cysts, tendon sheath tumors
  - Xanthelasma – syringomas, basal cell
  - Eruptive – disseminated granuloma annulare, sarcoidosis, leiomyomas

Endocrine Disorders

- Xanthoma treatment
  - Treatment of underlying disorder if present
  - Dietary changes
  - Lipid-lowering medications when indicated
  - Surgical removal if necessary

Lipid Abnormalities- Xanthomatosis

- Cutaneous lipidosis
  - Accumulation of lipid in histiocytes in the tissues
  - Cholesterol or TGs
- MOST ASSOCIATED W/ HIGH CHOLESTEROL
  - Eruptive *w TGs*
- <u>Work-up:</u>
  - **Fasting lipid profile**
  - **Skin biopsy**



<u>Eruptive Xanthomas</u>

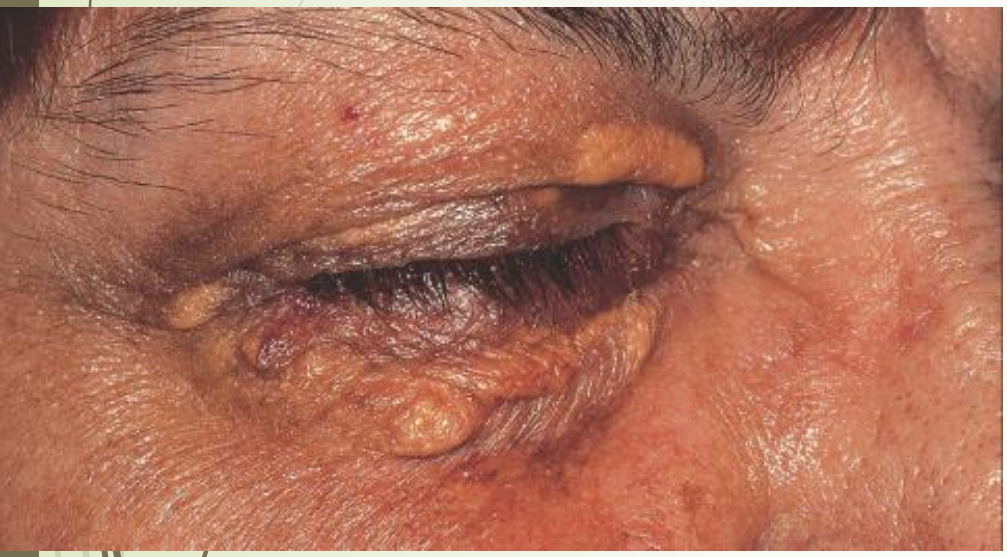
Hypertriglyceridemia

Entire body

Lipoprotein lipase deficiency

DM, obesity, pancreatitis

Lipid Abnormalities- Xanthomatosis



Xanthelasma

MCC

XANTHOMA!

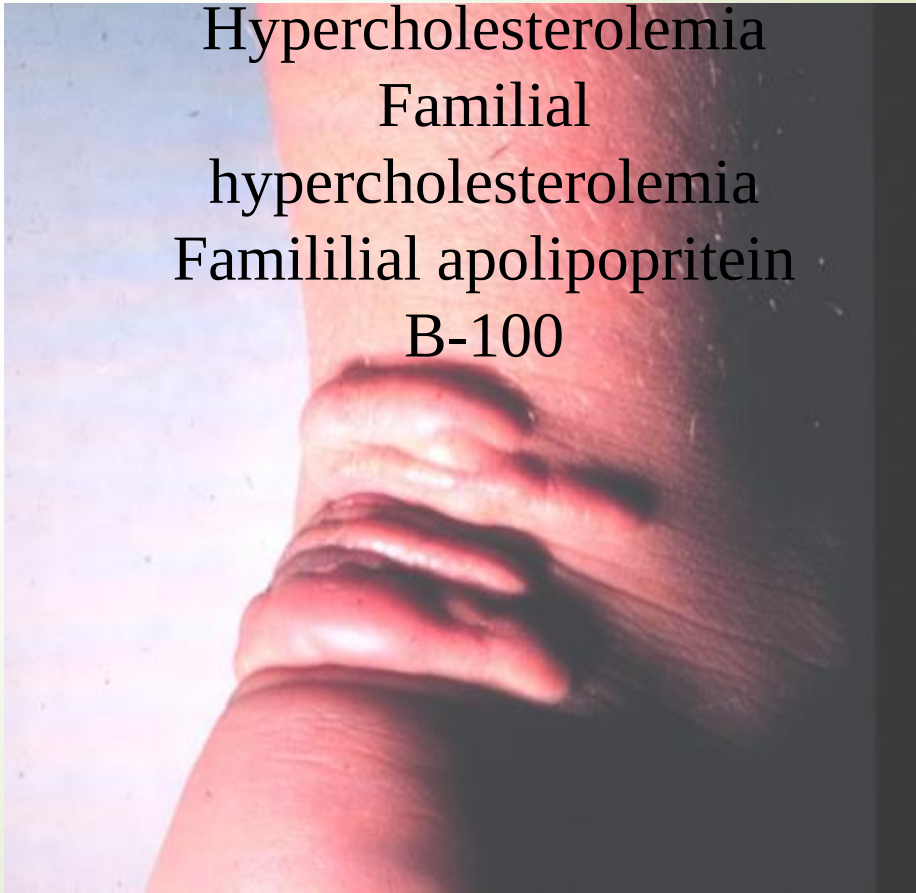
50% of pts have normal lipids

Tendinous Xanthoma

Hypercholesterolemia

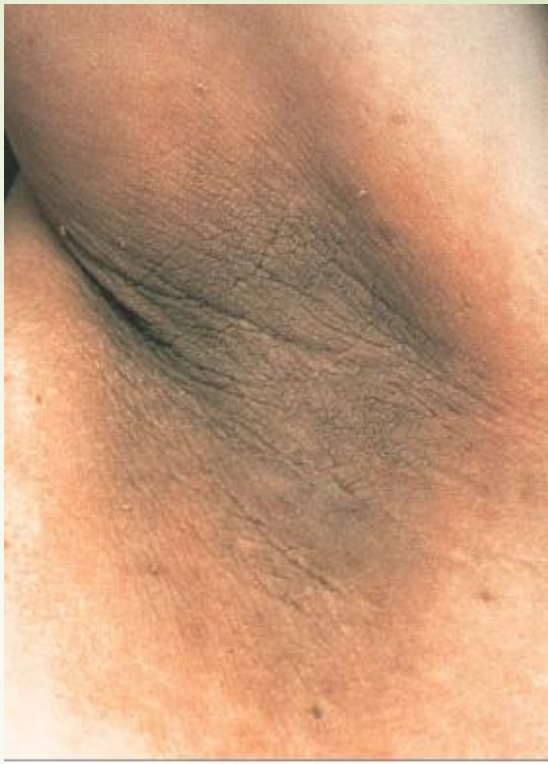
Familial hypercholesterolemia

Famililial apolipopritein B-100



Acanthosis Nigricans

- Symmetric, velvety hyperpigmented plaques
  - Face (conjunctiva, lips)
  - Neck, axillae, areola
  - Groin, inner thighs, anus
  - Dorsal joints, umbilicus
- Palm



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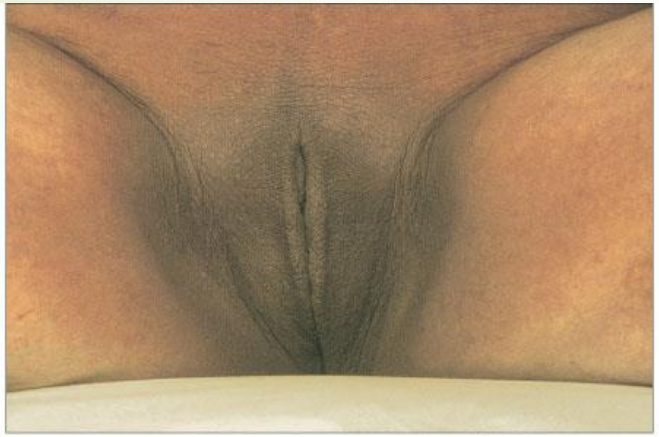

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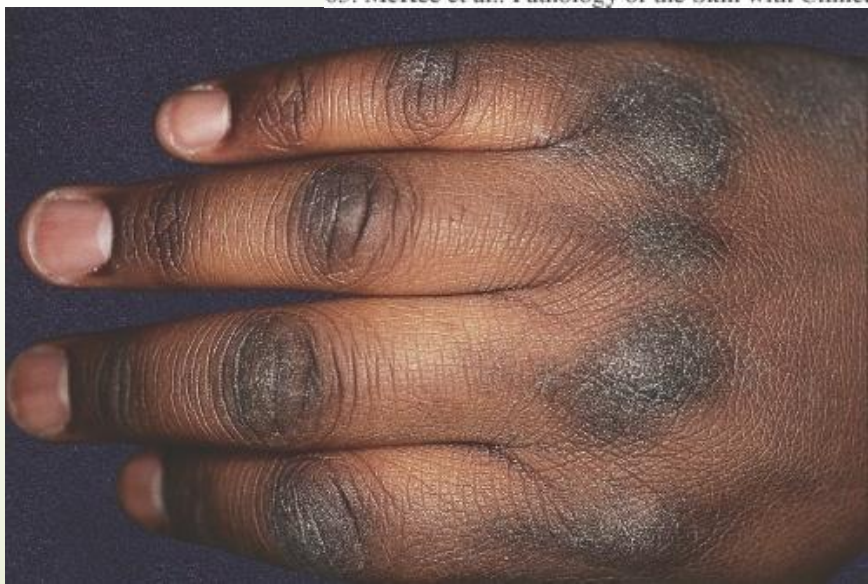


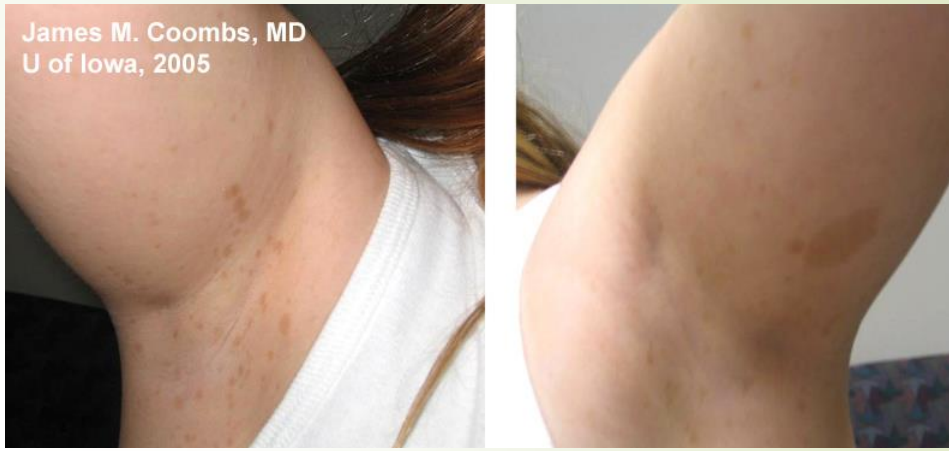
Acanthosis Nigricans

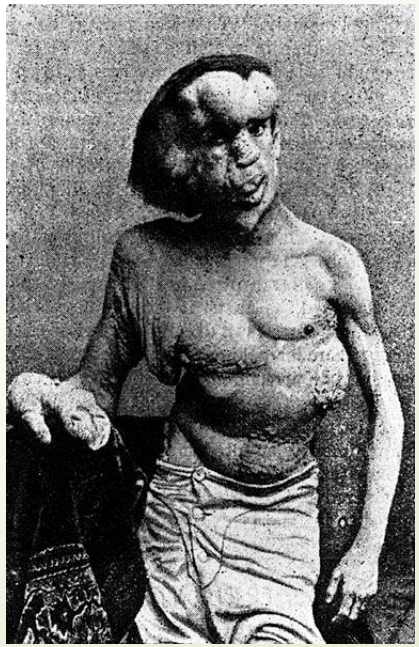
- **<u>Type 1</u>: associated with malignancy**
  - Adenocarcinomas
    - ***GI most common (60%)***; followed by lung and breast
- **<u>Type 3</u>: associated with obesity, insulin-resistance, endocrinopathy**
  - ***Most common type***
    - Obese pts, hyperandrogenic states
    - DM, Addison's, PCOS, Cushing syndrome
- Dx = Measure gludcose and insulin
  - Ratio <4.5 is abnormal
- Tx: Treat underlying malignancy, weight loss, CO2 laser, urea, tretinoin

Cutaneous and Neurologic

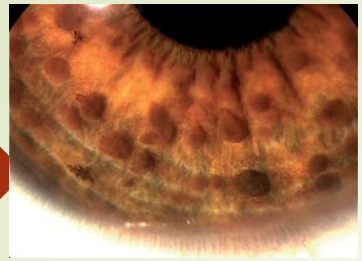
Cutaneous and Neurologic

- Neurofibromatosis 1 (NF1)
  - Autosomal dominant
  - Café-au-lait macule (CALM)
  - Axillary/inguinal freckles (Crowe's sign) pathognomonic
  - Neurofibromas
  - CNS
    - learning disability, seizures
  - Malignancy
    - 20-30x juvenile chronic myelogenous leukemia (if JXG also)
    - Plexiform NF can transform



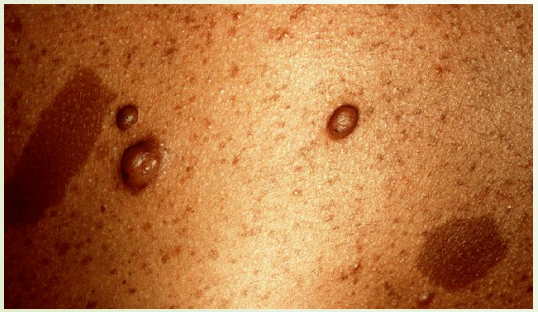


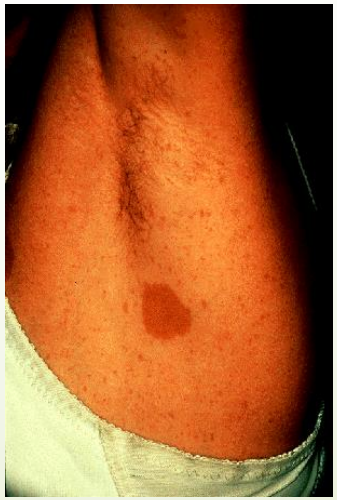
"Elephant man"
Joseph Merrick



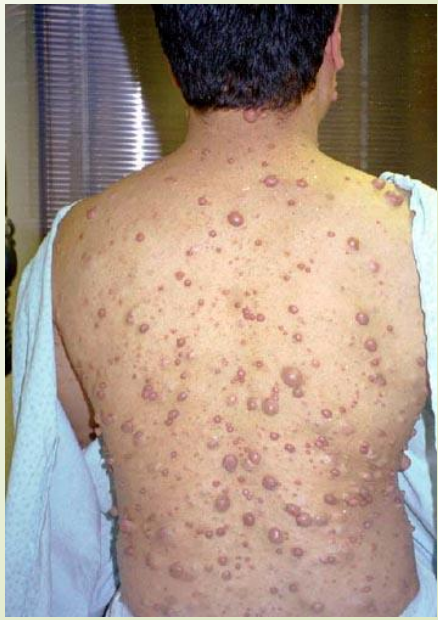
Neurofibroman gene (NF1 – von Recklinghausen disease) inhibits the RAS
oncogene associated with cutaneous, neurologic and orthopedic problems. Type 1 has
skin findings with café au lait spots, axillary freckling, skeletal dysplasia, and neurofibromas. Also have optic gliomas and Lisch nodules. complications of NF1 can include visual loss secondary to optic nerve gliomas, spinal cord tumors, scoliosis, vascular lesions, and long-bone abnormalities.

Iris with Lisch nodules





Crowe's sign.



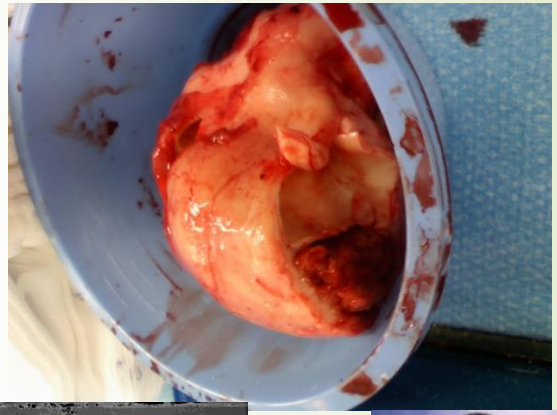
Cutaneous and Cardiac

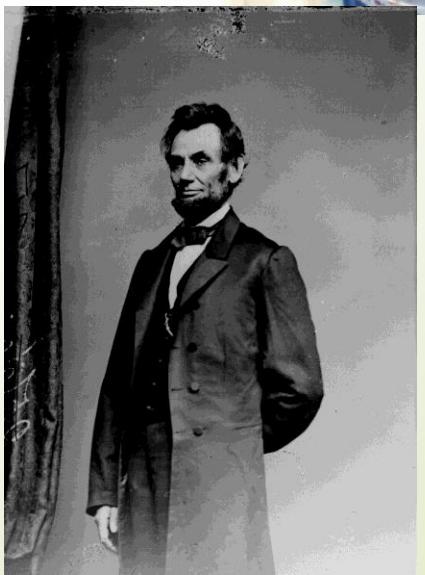
Cutaneous and Cardiac

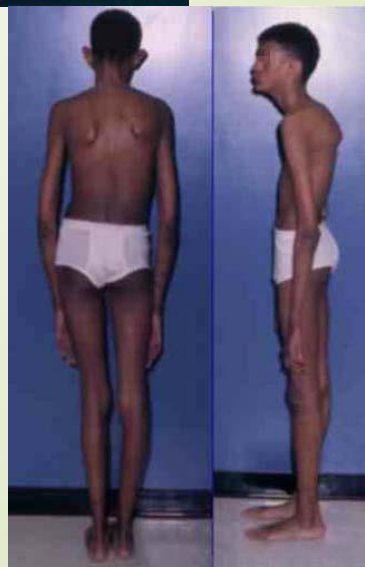
- Ehlers-Danlos (type IV, vascular)
  - Autosomal dominant
  - Collagen disorder
  - Arterial rupture
  - Thin skin
  - Easy bruisability
  - Atlantoaxial subluxation (OMT?)

Cutaneous and Cardiac

- Marfan's Syndrome
  - Autosomal dominant
  - Striae
  - Herniations
  - Tall, long head, long ears, pectus excavatum, arachnodactyly, flat feet
  - Aortic aneurysms, rupture, dissection (possible mitral valve prolapse, pneumothorax)





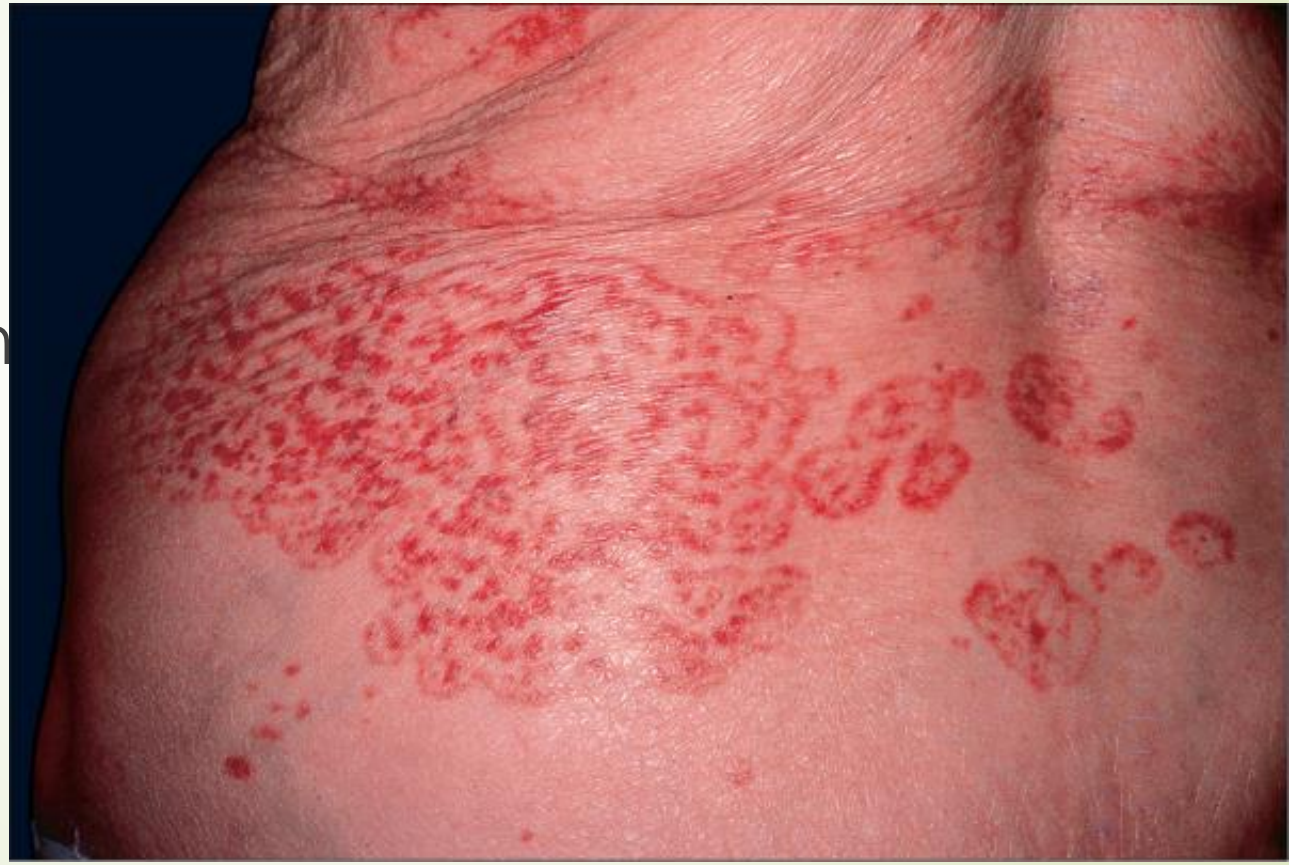


INTERNAL MALIGNANCY

- Erythema Gyratum Repens
- Sign of Lesar Trelat
- Glucagonoma Syndrome
- Dermatomyositis
- Paraneoplastic Pemphigus
- Paget's Disease
- Extramammary Paget's

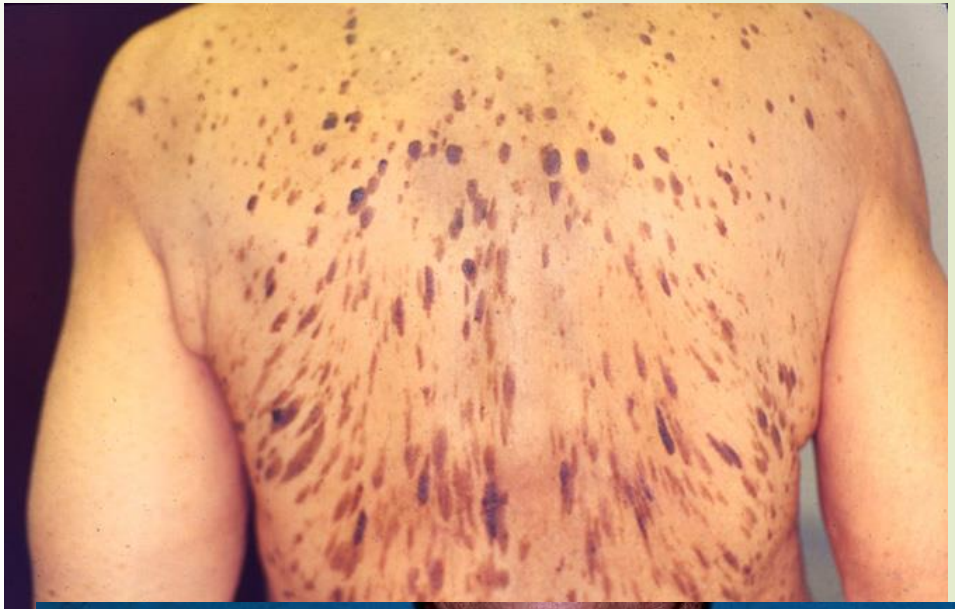
Erythema Gyratum Repens

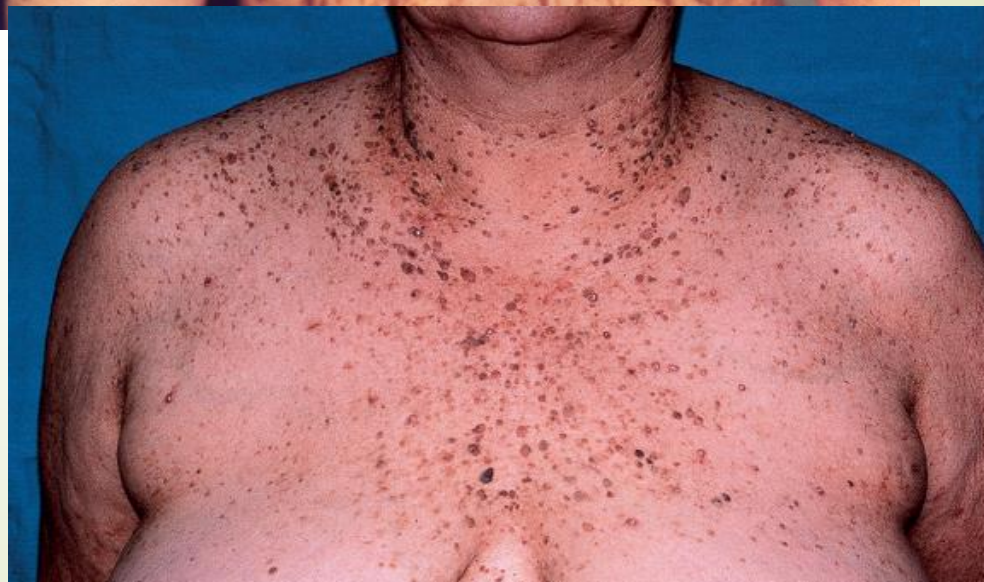
- Gyrate serpiginous erythema with wood grain pattern scale
- Cancer associations:
  - **Lung**
  - Breast
  - Stomach
  - Bladder
  - Prostate
  - Cervix

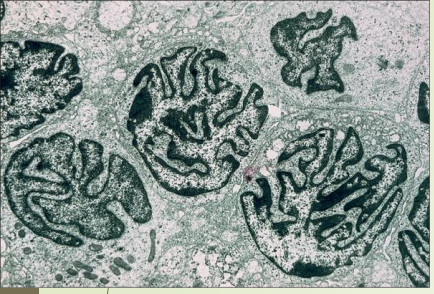


Cutaneous and Gastrointestinal (Intestine)

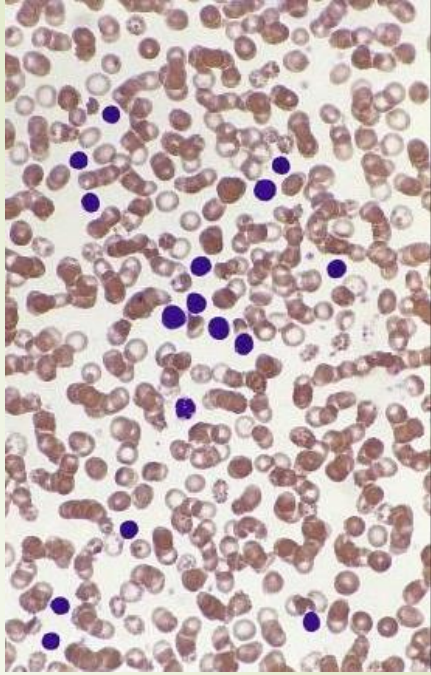
- Sign of Lesser-Trelat
  - Rapid increase in size/number of seborrheic keratoses
  - Occ also AN
  - **Gastrointestinal adenocarcinoma**
  - **Colon or gastric**



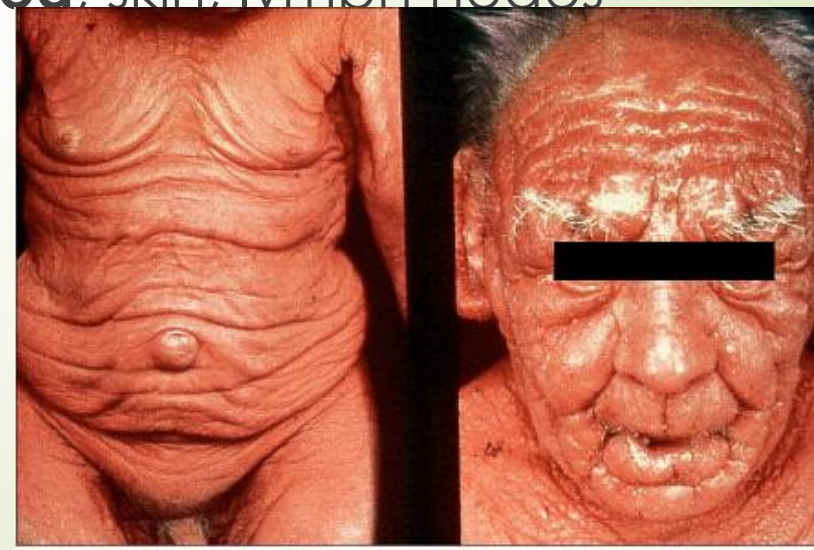




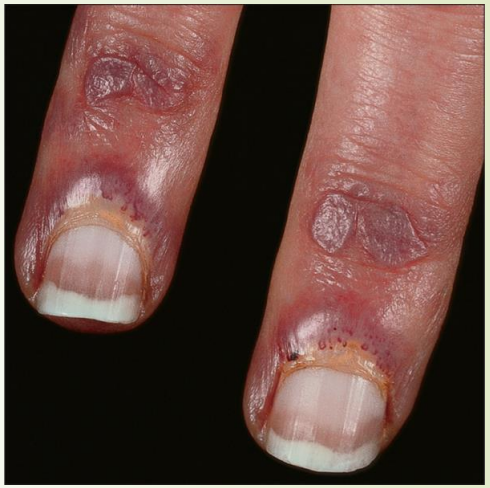
Sezary Syndrome



- Leukemic variant of Mycosis Fungoides
  - Exclusively in **adults**
- Characterized triad:
  - Pruritic **erythroderma** (fiery red)
  - Generalized **lymphadenopathy**
  - **Sézary cells** (abnormal, large hyperconvoluted lymphocytes) **in peripheral blood**, skin, lymph nodes
- Intense pruritus
- Diagnosis:
  - Sezary cells in the blood
  - more than **1,000 cell/mm^3**

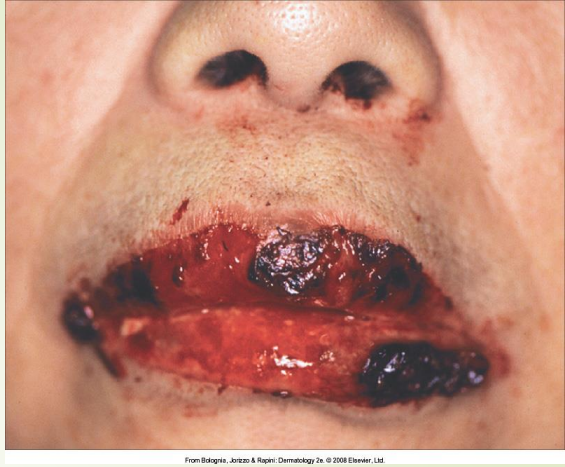


Dermatomyositis



- Malignancy Association
  - ***Up to 10-50% in adult type***
  - Usually presents in first 3 years
  - **Ovarian cancer MC in white women**
  - **Nasopharyngeal cancer MC in Asian men**
- Clinical Manifestations:
  - *Skin findings usually precede muscle symptoms by 2-3 months*
  - **Heliotrope rash**– periorbital, symmetric, violaceous patches
  - **Gottron's sign**– violaceous, atrophic discoloration of knuckles, knees or elbows
  - **Gottron's papules** – flat topped, papules on knuckles
  - **Shawl sign** – erythema & scale over shoulder region
  - **Mechanic's hands -** scaling, fissuring & pigmentation of fingers
  - Nailfold telangiectasias

Paraneoplastic Pemphigus



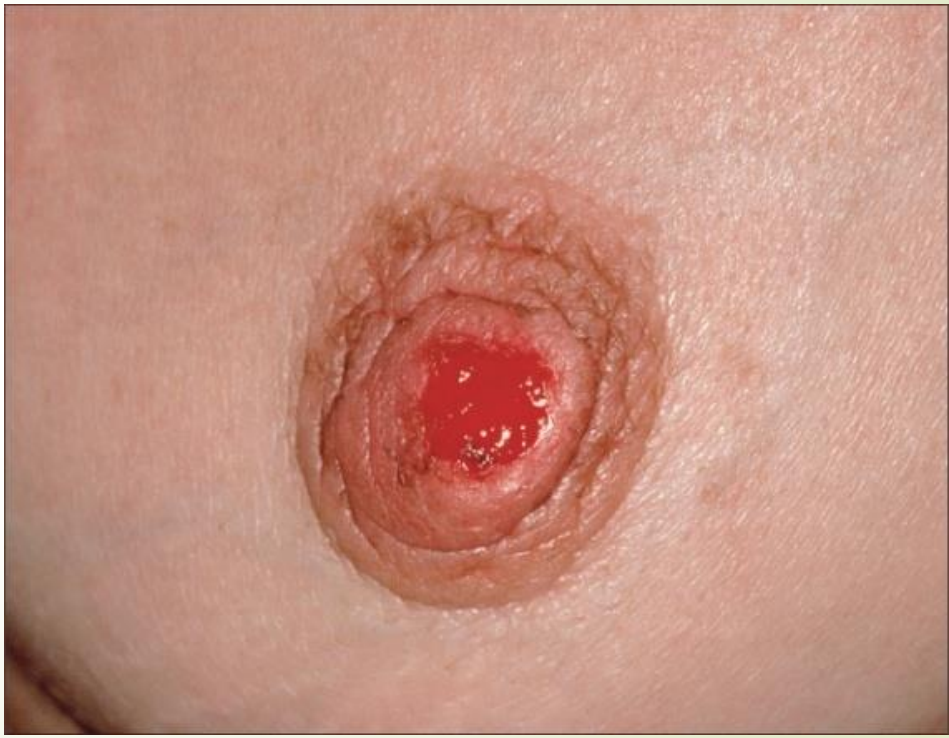
- Cutaneous lesions
  - Polymorphous
    - erythematous macules, lichenoid lesions, **targetoid lesions/EM-like**, flaccid bullae, and erosions, or more tense bullae
- Mucosal lesions
  - **100% have mucosal involvement**
  - **Painful oral ulcerations**, **crusting of lips**, **intractable stomatitis involving vermilion border**, severe pseudomembranous conjunctivitis
  - May also include vaginal, labial, and penile lesions

Paraneoplastic Pemphigus

- Related malignancies
  - **Non-Hodgkin's lymphoma** (40%)
  - **Chronic lymphocytic leukemia** (**CLL**) (30%)
  - **Castleman's disease** (10%)
  - Sarcoma (6%)
  - Thymoma (6%)
  - Waldenstrom's macroglobulinemia (6%)
- Treatment
  - Lesions usually resolve with treatment of malignancy

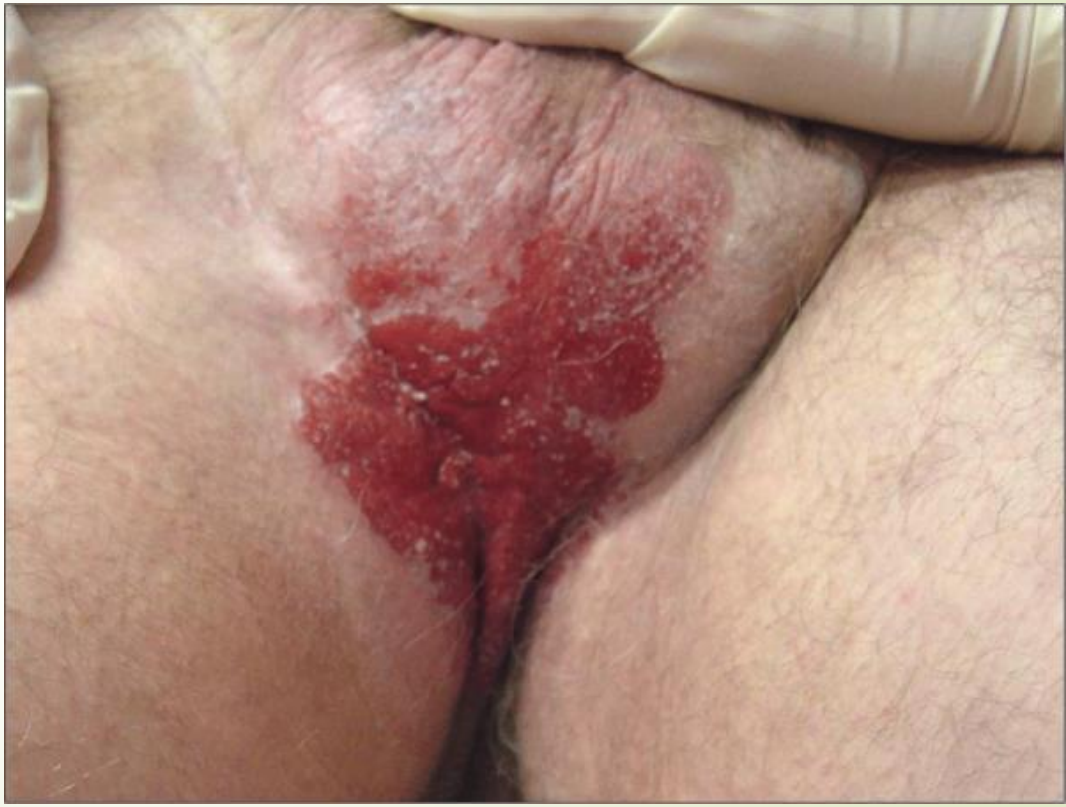
Paget's Disease

- Eczematous to psoriasiform plaque surrounding the nipple
  - *Nipple retraction*
- Extension of underlying **ductal adenocarcinoma of the breast**



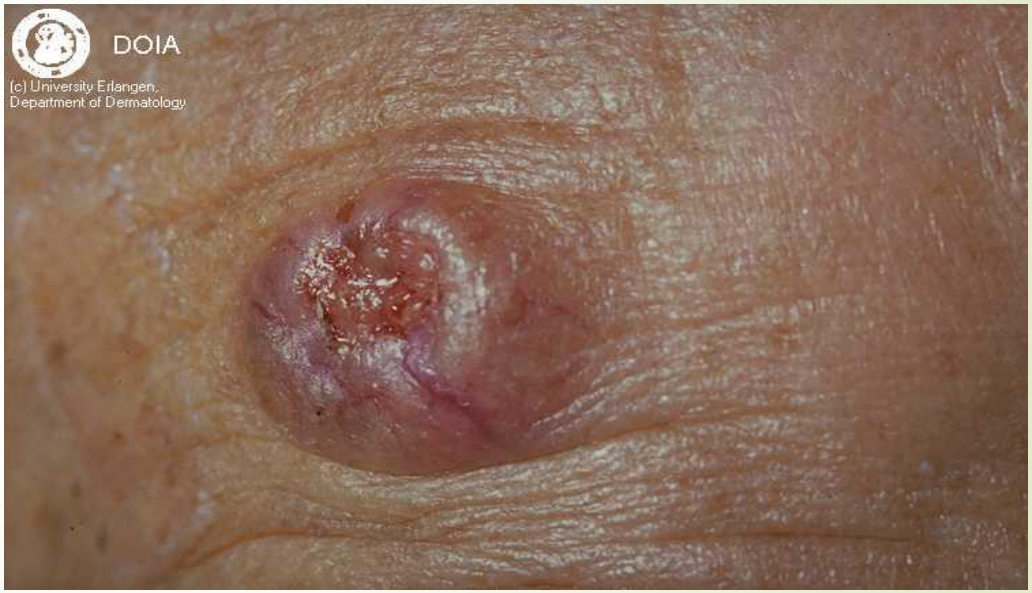
Extramammary Paget's

- Erythematous, scaly patch or plaque of the ***anogenital region***
- Extension of an underlying **GI or GU carcinoma**

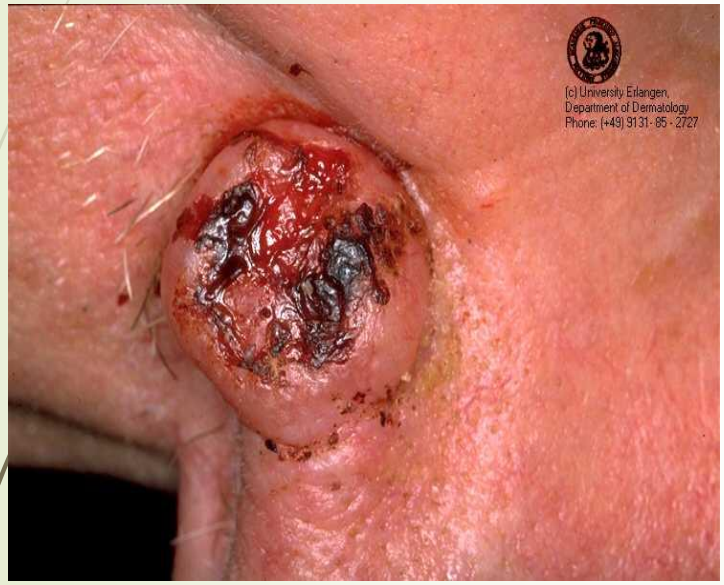


Basal Cell Carcinoma

- Basal Cell Epithelioma
- Basalioma
- Rodent ulcer
- Jacobi's ulcer
- Rodent carcinoma



BCC: What are they?

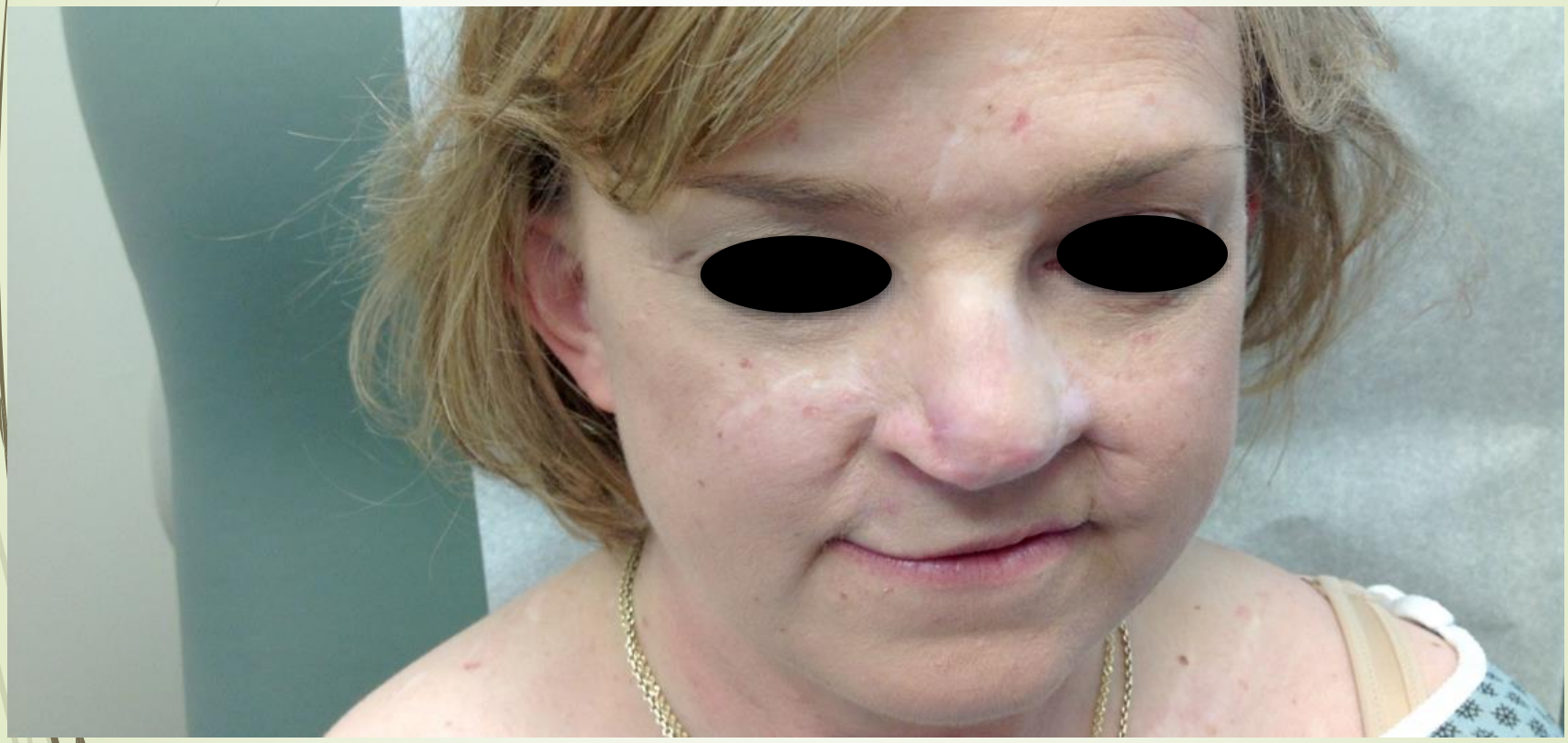


- PEARLY PAPULES OR NODULES
- ROLLED BORDER
- TELANGIECTASES
- CENTRAL ULCER
- CRUSTING
- BLEED EASILY

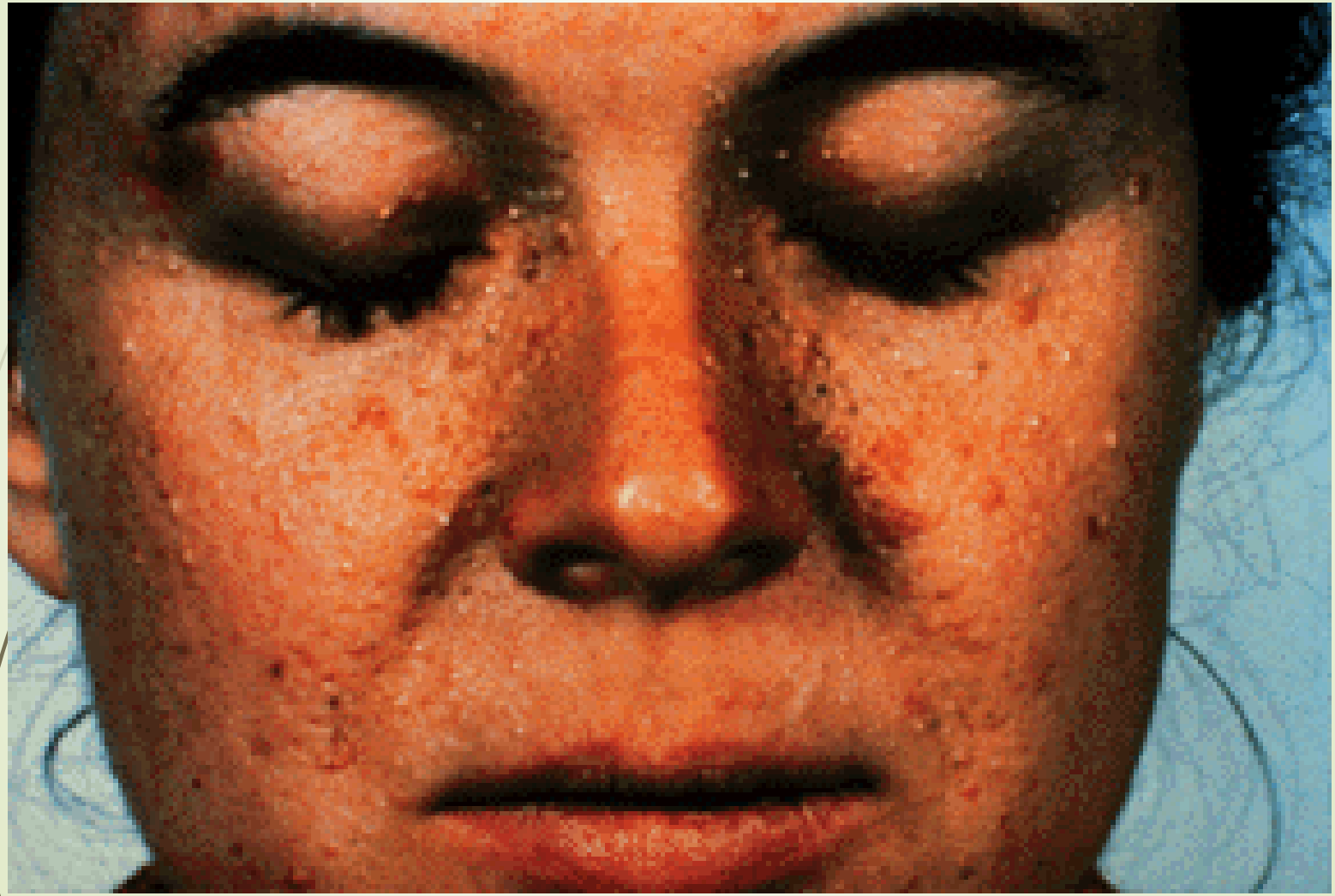
BCC: Variants

- SUPERFICIAL BCC
- MORPHEAFORM BCC
- PIGMENTED BCC
- CYSTIC BCC
- BASAL CELL NEVUS SYNDROME (GORLIN'S SYNDROME)

Basal Cell Nevus Syndrome



Basal Cell Nevus Syndrome



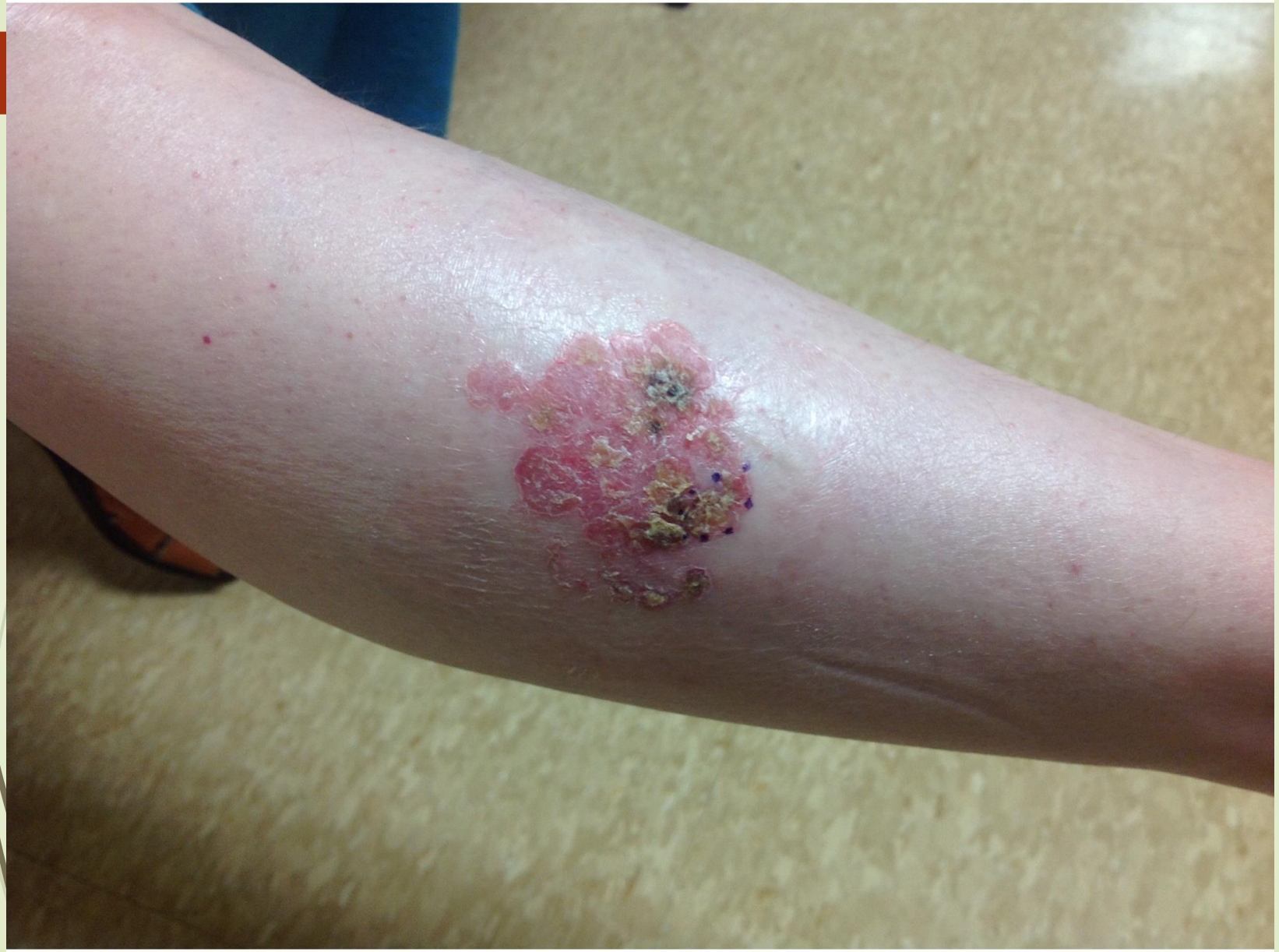
Gorlin's Syndrome

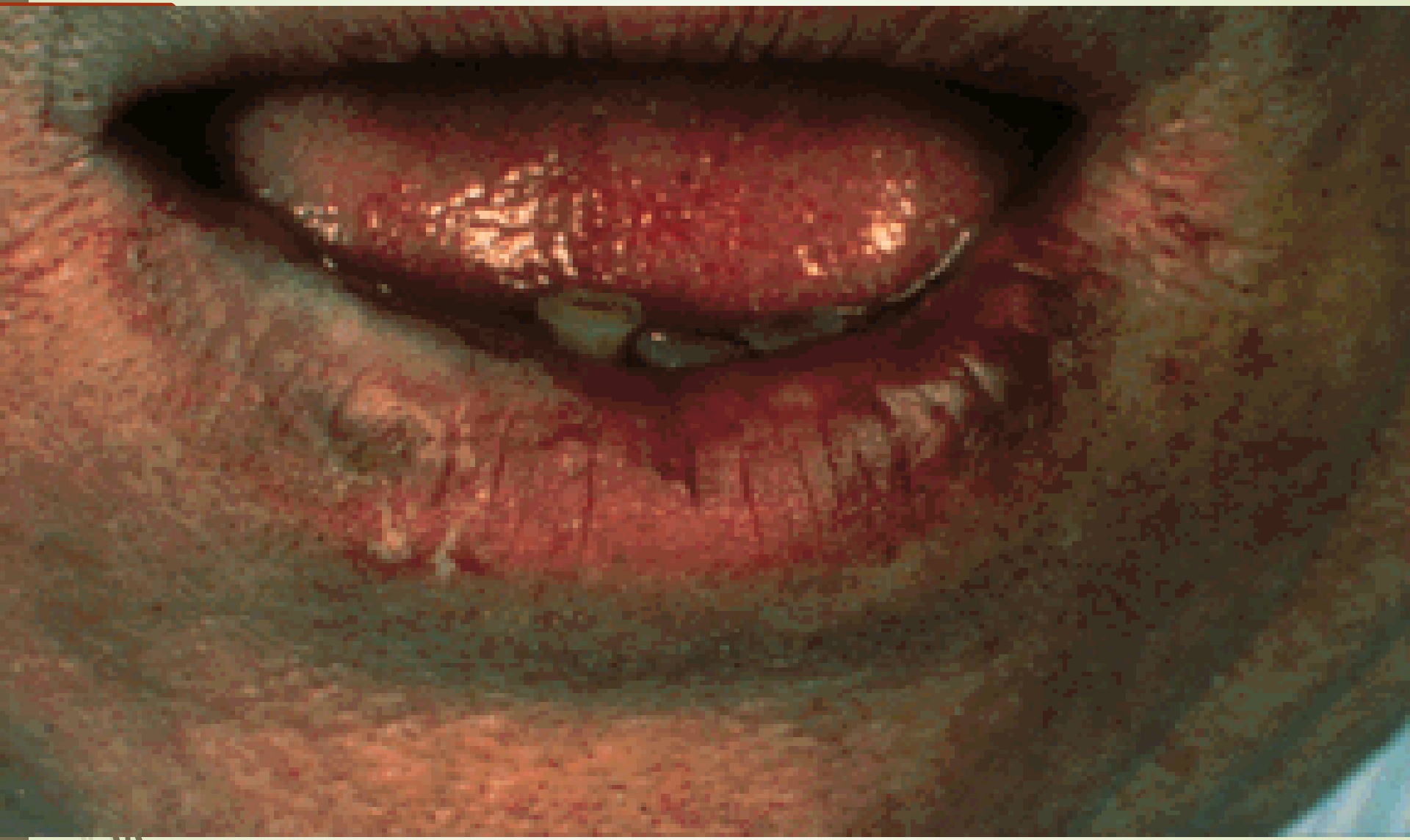
- Basal Cell Nevus Syndrome
- AD
- Normal tissue: PTCH (patched) gene inhibits sonic hedge hog signaling → unbound PTCH inhibits smoothened SMO signaling
  - When inactivating mutation occurs in PTCH→ repression of SMO removed → constitutive activation of GLI and downstream targets = tumors
- Gene Defect: PTCH

Gorlin's Syndrome- Presentation

- Numerous basal cell carcinomas
- Palmoplantar pits
- Odontogenic keratocysts of jaw
- Frontal bossing/hyper telorism
- Cataracts
- Glaucoma
- Bifid Ribs
- Calcification of Falx cerebrum
- Ovarian fibromas
- Medulloblastoma
- Meningioma

Squamous Cell Carcinoma





VERRUCOUS CARCINOMA (CARCINOMA CUNICULATUM)

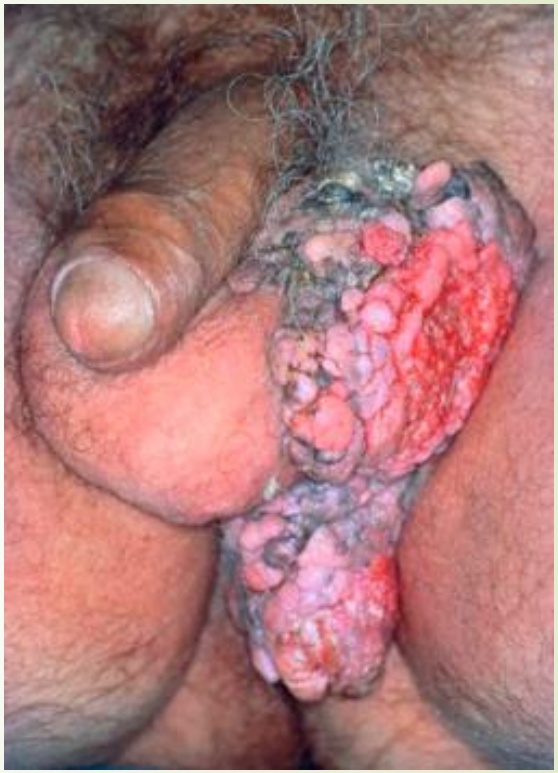
Distinct, well-differentiated, low-grade SCC

Exophytic tumors with a papillomatous or verrucous surface

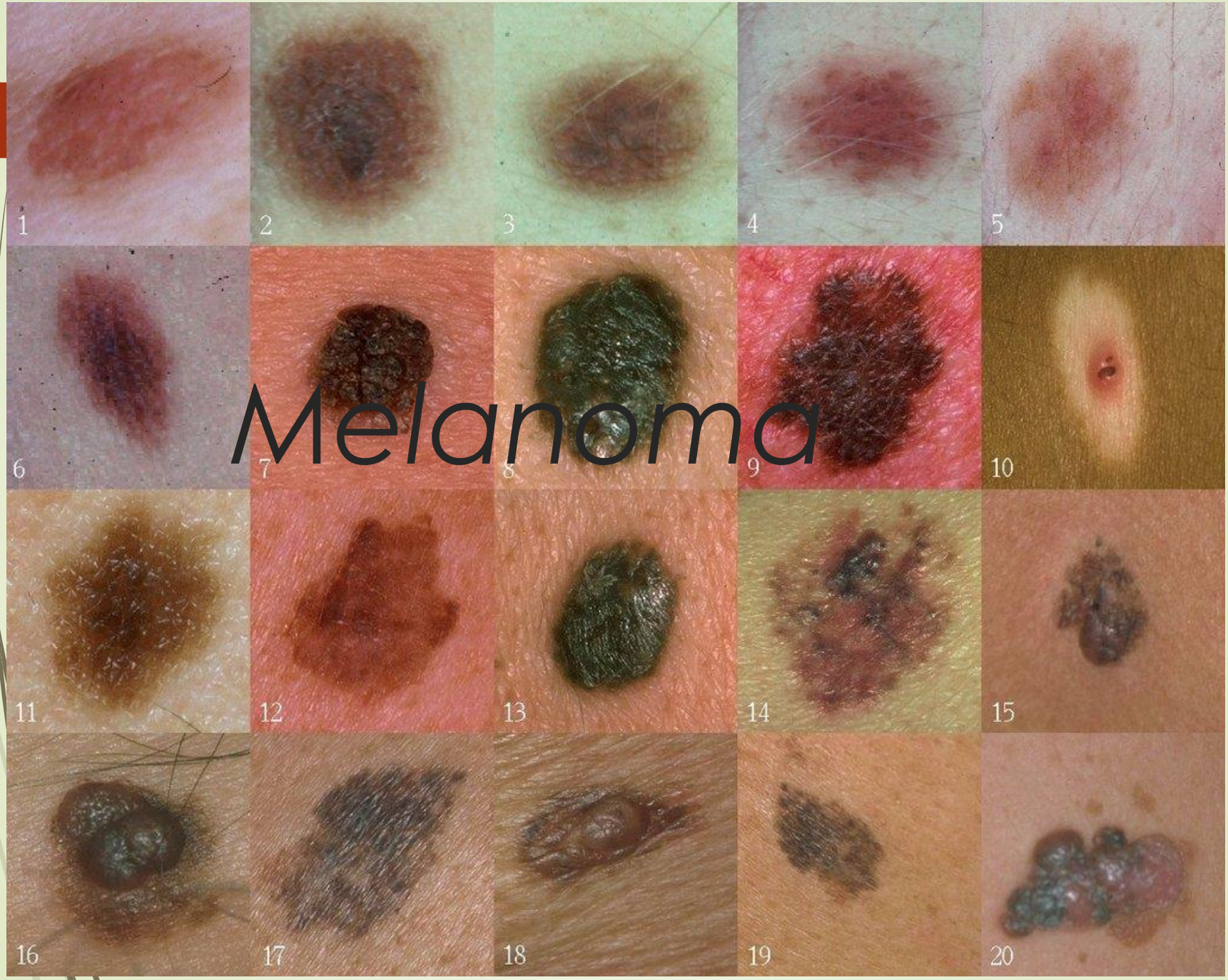
MC –sole in middle age to older men

Types:

- Epithelioma cuniculatum (plantar foot)
- Giant condyloma acuminatum of the genitalia- Giant condyloma of Buschke and Lowenstein
  - Induced by low-risk HPV 6, 11 or high risk 16,18
  - Minimal cytologic atypia
- Oral florid papillomatosis



Melanoma



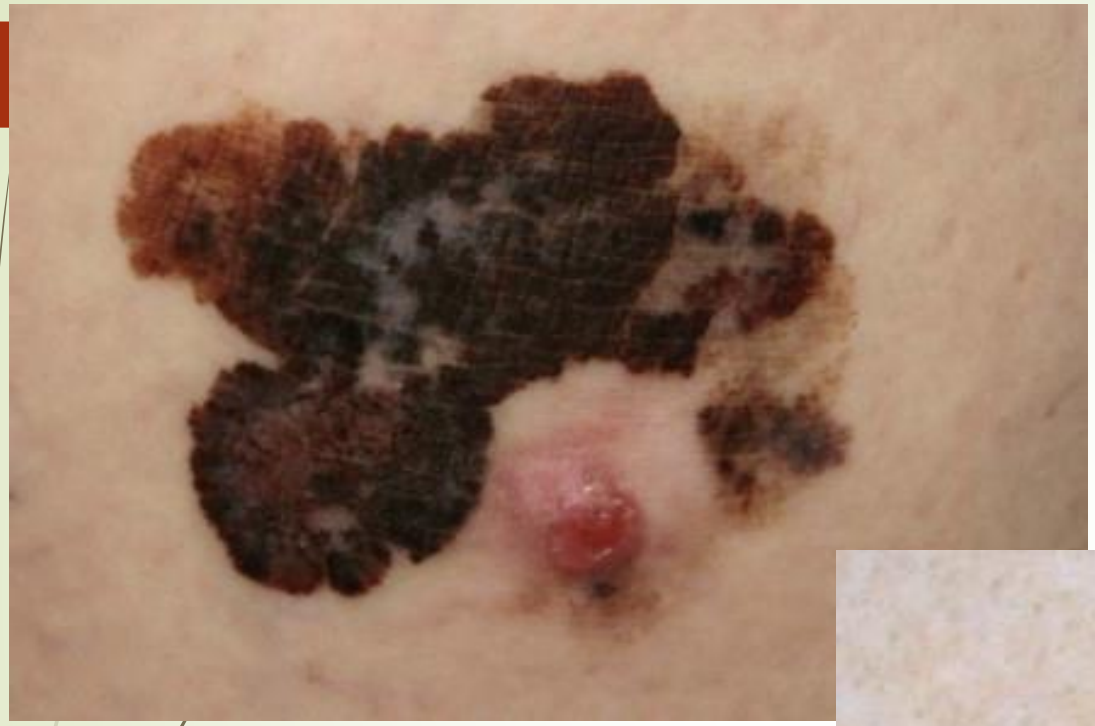
Melanoma statistics

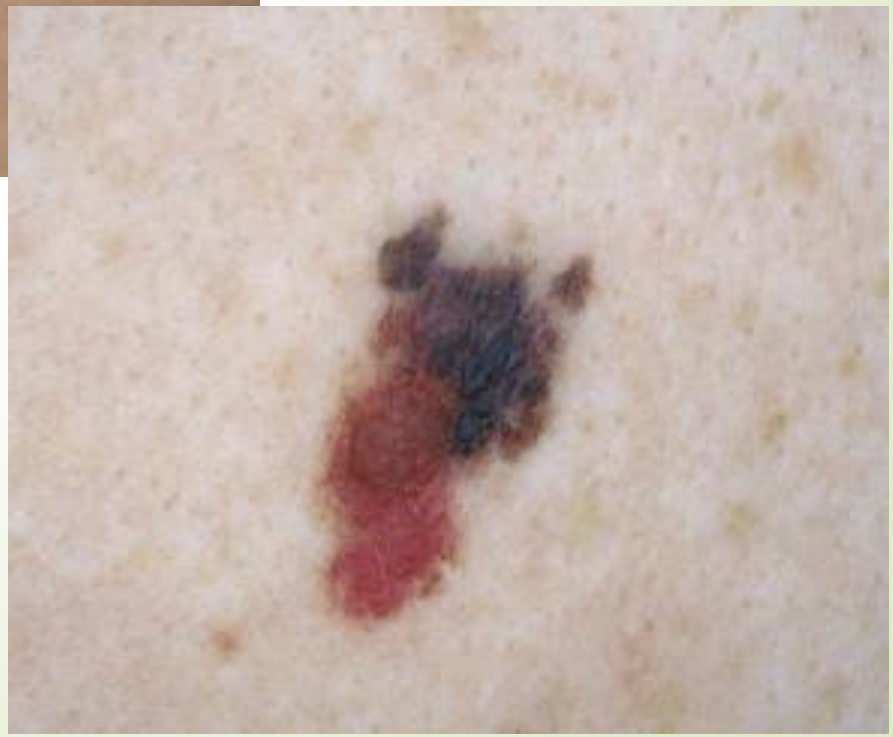
- Approximately 75% of skin cancer deaths are from melanoma
- On average, one American dies from melanoma every hour
- In 2018, it is estimated that 10,130 deaths will be attributed to melanoma
- WHO estimates 65,000 people/year worldwide die from melanoma
- Lifetime risk of melanoma
  - 1935: 1 in 1500
  - 2009: 1 in 57 (M), 1 in 81 (F)
  - 2013: 1 in 35
  - 2018 1 in 30
  - Melanoma rates have doubled from 1982 to 2011


Asymmetry.
One half is unlike the other half.
Border.
An irregular, scalloped, or poorly defined border.
Color.
Is varied from one area to another; has shades of tan, brown, or black; is sometimes white, red, or blue.
Diameter.
Melanomas are usually greater than 6mm (the size of a pencil eraser) when diagnosed, but they can be smaller.
Evolving.
A mole or skin lesion that looks different from the rest or is changing in size, shape, or color.

DIFFERENT TYPES OF PRIMARY CUTANEOUS MELANOMA

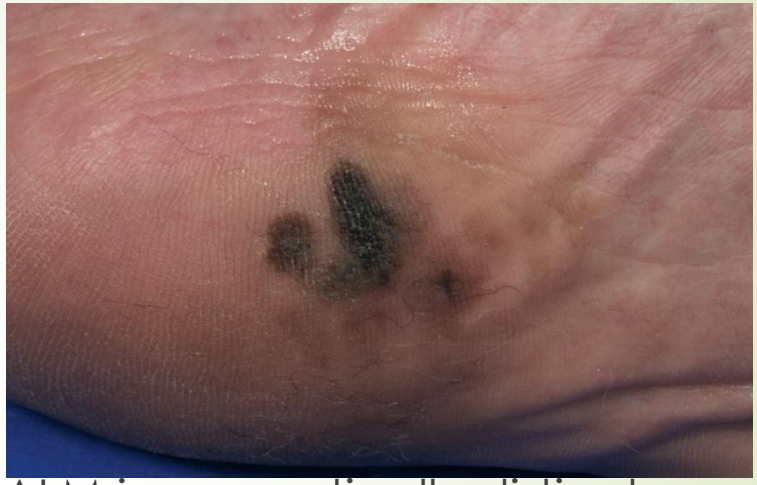
Type of melanoma	Frequency (%)	Site	Radial growth	Special features
Superficial spreading melanoma	**60–70**	Any site, preference for **lower extremities (women), trunk (men and women)**	Yes	More **pagetoid spread**, less solar elastosis **May have regression 50% arise in pre-exsisting nevi**
Nodular melanoma	15–30	Any site, preference for trunk, head, neck	**No (VERTICAL)**	Nodule with more rapid vertical growth
Lentigo maligna melanoma	5–15	**Face,** especially nose and cheeks	Yes	Slower growth over years within **sun-damaged skin**
Acral lentiginous melanoma	5–10	**Palms, soles,** nail unit	Yes	Most common melanoma type in patients with **darker skin types**





Acral Lentiginous Melanoma

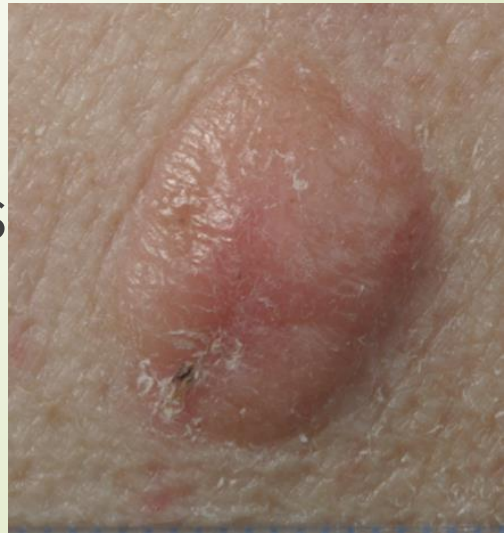
- Onset: 7th decade
- Palms, soles, nails
- 5% of all melanomas
  - Similar incidence amongst all races and ethnicities
  - Blacks (70%), Asians (45%)
- Asymmetric, brown to black macule with color variation and irregular borders
- Often, diagnosed at an advanced stage



- ALM is a genetically distinct subtype of melanoma
  - More and different genetic mutations than other types of cutaneous melanoma
  - Activating KIT mutations

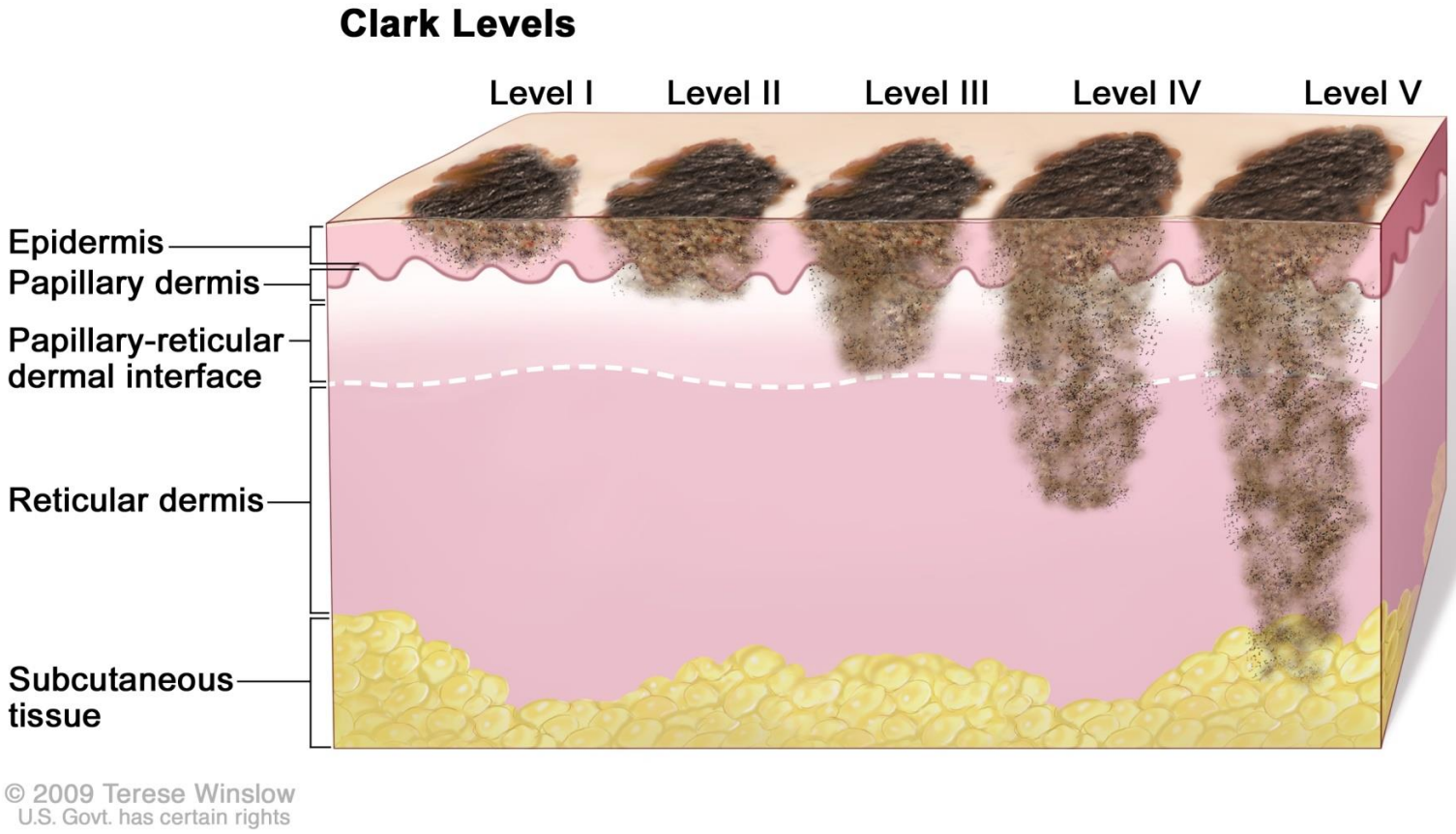
Amelanotic Melanomas

- All four of the cutaneous melanoma subtypes can occur as amelanotic variants
- Amleanotic SSMs, nodular melanomas and LMMs often biopsied due to clinical suspicion of BCC
- Amelanotic AMLs may be mistaken for warts or SCC
- Same prognosis and therapy as pigmented melanomas



Clark Levels

Invasion based on anatomic layers



TNM Classification

Melanoma TNM Classification		
T classification	**Thickness**	**Ulceration Status/Mitoses**
Tis	N/A	N/A
T1	≤ 1.0 mm	a: w/o ulceration and mitosis <1/mm²
		b: with ulceration or mitoses ≥ 1/mm²
T2	1.01 - 2.0 mm	a: w/o ulceration
		b: with ulceration
T3	2.01 - 4.0 mm	a: w/o ulceration
		b: with ulceration
T4	> 4.0 mm	a: w/o ulceration
		b: with ulceration
N classification	**# of Metastatic Nodes**	**Nodal Metastatic Mass**
N0	0 nodes	N/A
N1	1 node	a: micrometastasis*
		b: macrometastasis**
N2	2-3 nodes	a: micrometastasis*
		b: macrometastasis**
		c: in-transit met(s)/satellite(s) without metastatic nodes
N3	4 or more metastatic nodes, or matted nodes, or in-transit met(s)/satellite(s) with metastatic node(s)	
M classification	**Site**	**Serum LDH**
M0	0 sites	N/A
M1a	Distant skin, subcutaneous, or nodal mets	Normal
M1b	Lung metastases	Normal
M1c	All other visceral metastases	Normal
	Any distant metastasis	Elevated

*Micrometastases are diagnosed after sentinel lymph node biopsy and completion lymphadenectomy (if performed).

**Macrometastases are defined as clinically detectable nodal metastases confirmed by therapeutic lymphadenectomy or when nodal metastasis exhibits gross extracapsular extension.

Table 1a: TNM Criteria for Cutaneous Melanoma (2010)
Adapted from Melanoma of the skin. In: Edge SB, Byrd DR, Compton CC, eds. AJCC Cancer Staging Manual. 7th ed. New York, NY.: Springer, 2010. (Used with permission)

- T: Thickness, Mitotic rate, ulceration
- N
  - Number of metastatic lymph nodes
  - Micro vs macroscopic nodal tumor burden
  - Presence of satellite or in-transit mets
- M: Metastatic disease
  - Anatomic site of distant mets
  - Serum LDH

Melanocytic Nevus with architectural features…

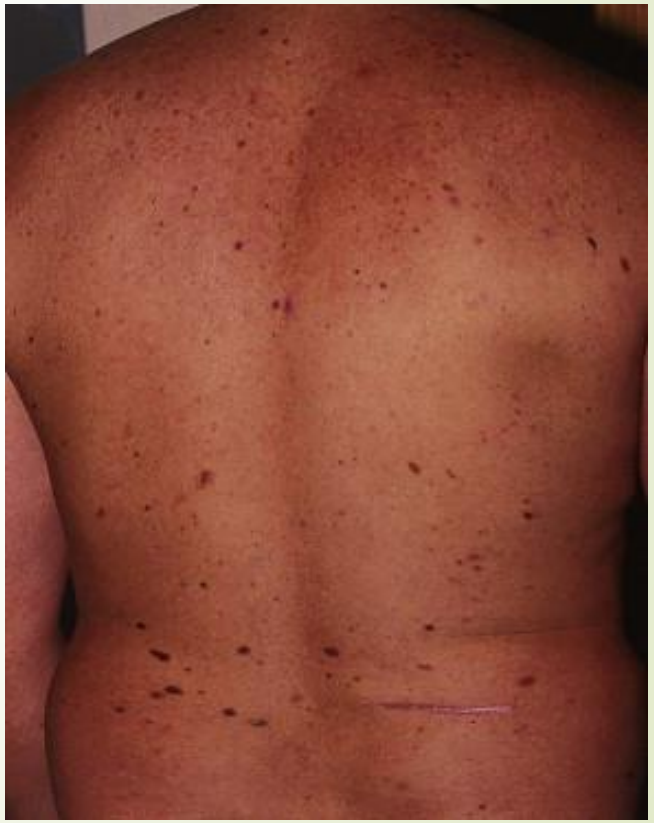
- Warning – controversial!
- Formally termed dysplastic nevus
- 5-10 mm or larger, irregular, macular lesion with various colors primarily on trunk but can occur anywhere
- histologically usually reveals basilar melanocytic hyperplasia and cytologic atypia
- potential melanoma precursor and marker for increased risk of melanoma

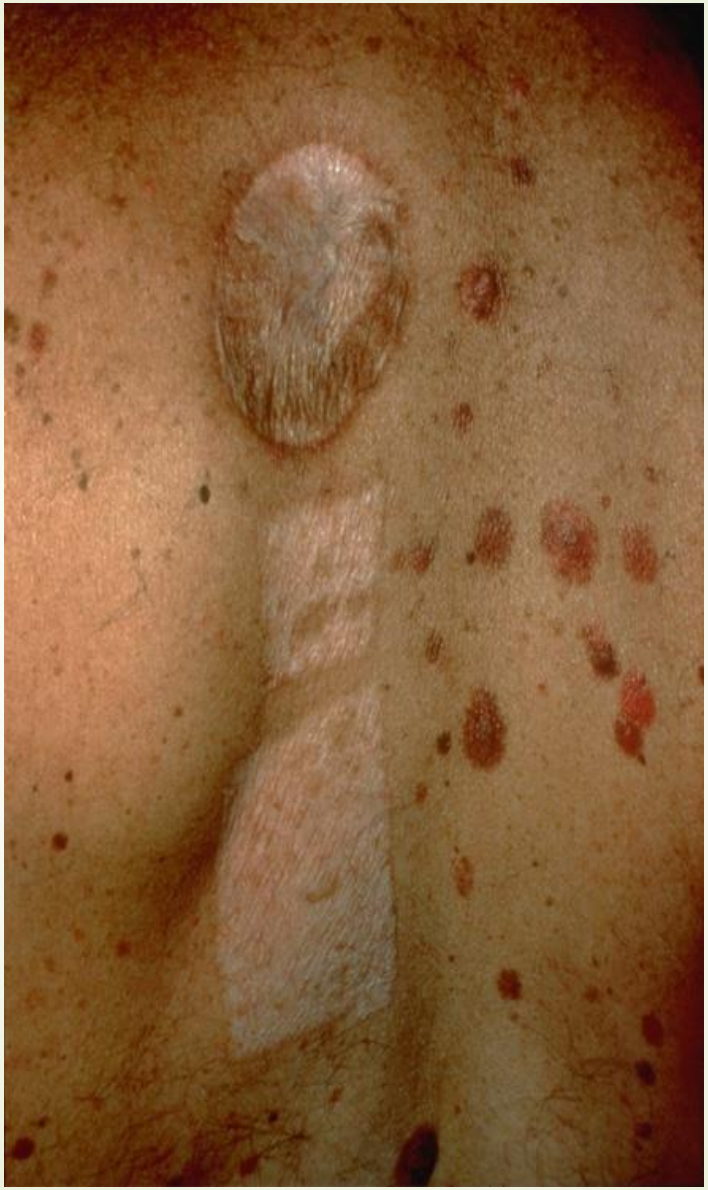
Dysplastic Nevus

- Occurrence: 5% -20% of pts have at least one clinically dysplastic nevus.
- Importance:
  1. Careful history and evaluation of family members.
  2. DNs provide another risk factor for melanoma predisposition. >3 lesions increases the risk of melanoma from 3 to 43 times.
  3. Increased risk of melanoma in the DN AND in the rest of epidermis

Dysplastic Nevus

- Fried Egg appearance
- Generally larger than are common nevi
  - usually 5–12mm, with irregular borders.
- Develop new lesions over a lifetime.
- Sun protected areas.



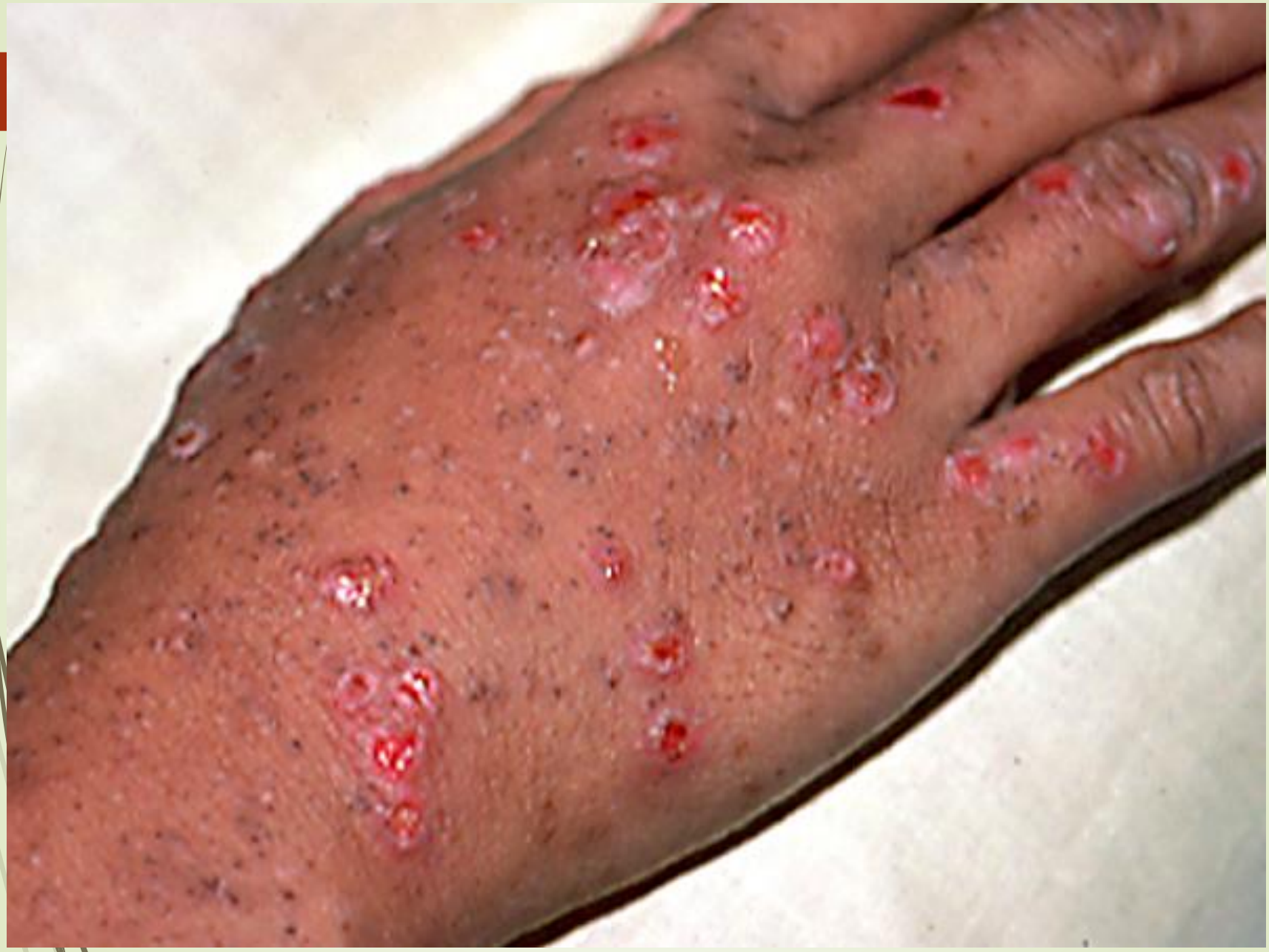


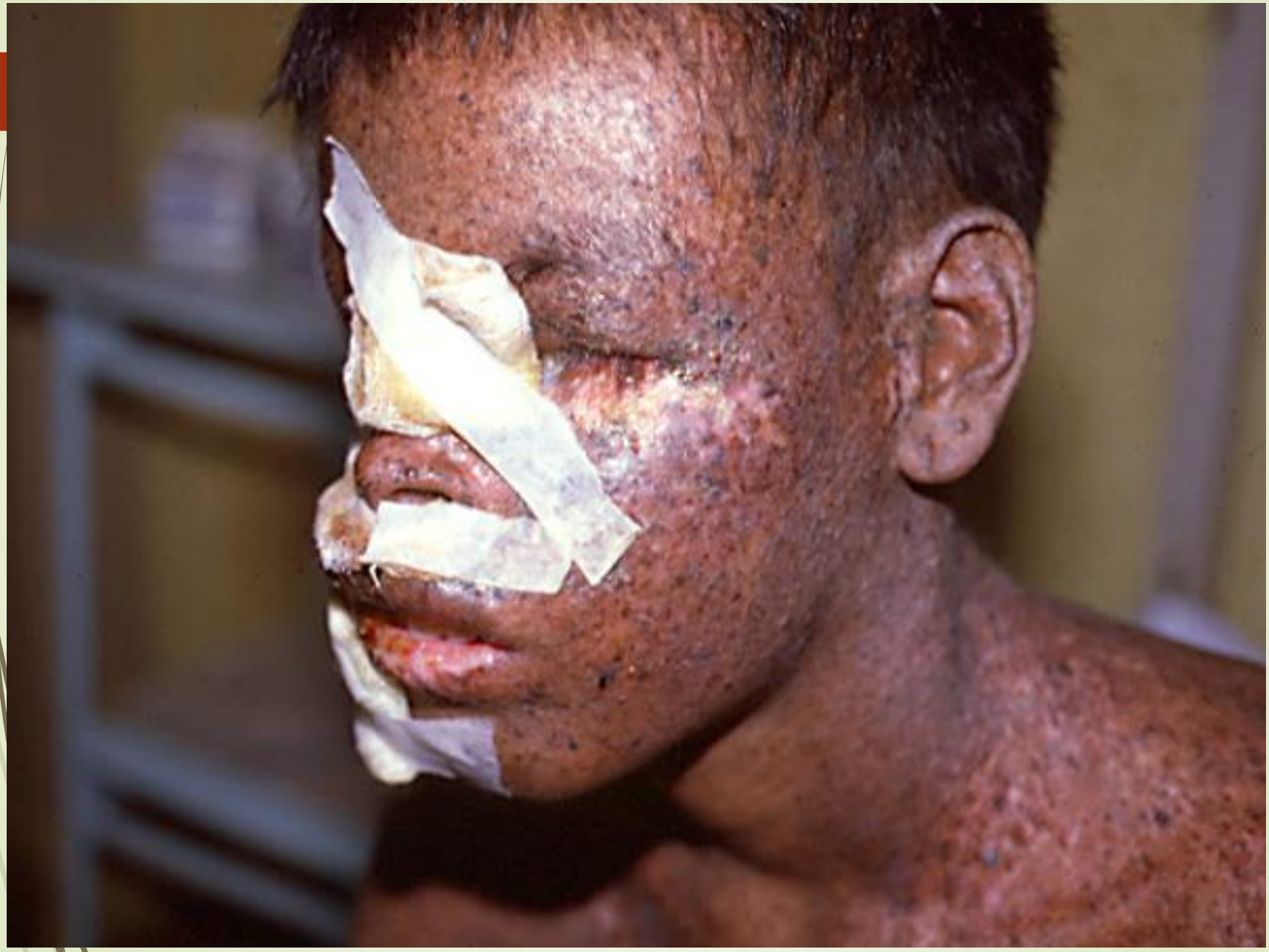
Dysplastic Nevus Syndrome

- Risk of melanoma:
  - Normal = 1 %.
  - DN, no family with MM = 6% lifetime risk.
  - DN, (+) family history of MM = 15 %
  - DN, (+) two or more 1st degree relatives with MM, lifetime risk approaches 100%.

XERODERMA PIGMENTOSA

- Rare autosomal recessive genodermatosis
- Enhanced cellular photosensitivity to UV radation and early onset of cutaneous malignancies
- Multiple malignancies include melanoma, basal cell, squamous cell, fibrosarcoma, and angiosarcoma
- Defect in the DNA repair (now 8 different types)
- The basic defect is in the endonuclease repair
- Prognosis poor usually die in early life
- Management-avoid UV exposure





Cutaneous lymphoma

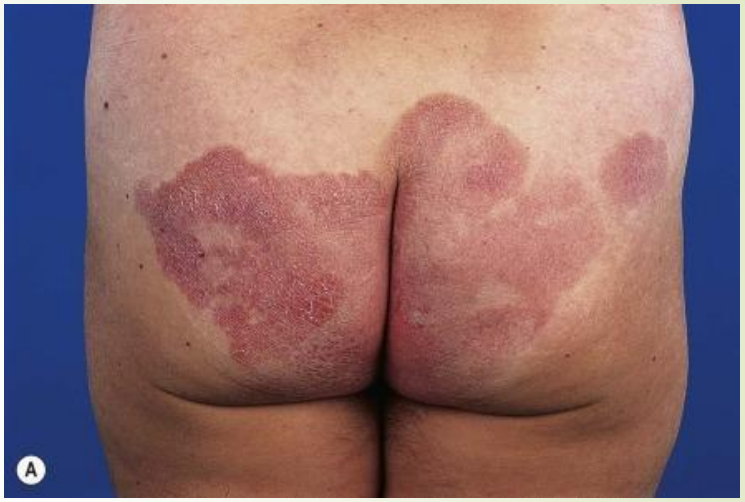
- **Primary** (occur in the skin without evidence of extracutaneous involvement) or **secondary** (simultaneous or preceding evidence of extracutaneous involvement)
- Classified based on their cell type of origin
  - B-cell and T-cell lymphomas
  - Histologic features used in the classification system include:
    - cell size (large versus small)
    - nuclear morphology (cleaved or non-cleaved)
    - Immunophenotype
- CTCL represents 75–80% of all primary cutaneous lymphomas, whereas primary cutaneous B-cell lymphomas (CBCL) account for 20–25%

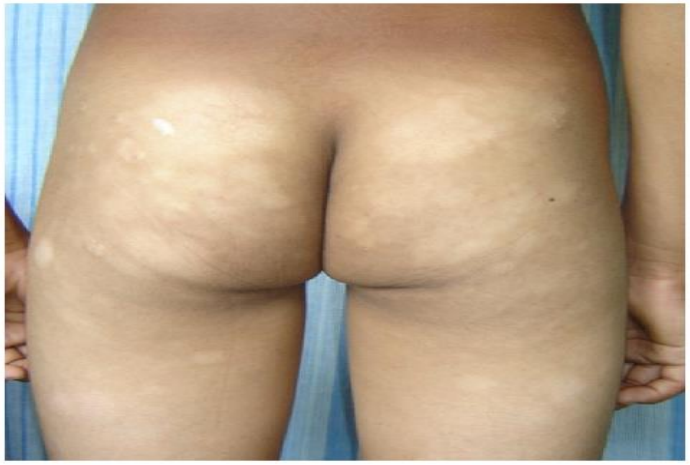
Mycosis Fungoides

- Classical MF progresses from patch stage (can have severe pruritus) to plaque stage and finally to tumor stage disease (and some progress to erythroderma), with a protracted clinical course over years or even decades
- Generally affects elderly patients, M>F, and has a long evolution
  - Can also occur in children and adolescents
- Median duration from onset of skin lesions to the diagnosis of MF is 4–6 yrs
- Eventually, some patients may develop noncutaneous involvement (lymph nodes MC, peripheral blood and visceral organ involvement)
- Many patients die of other conditions but once tumors develop or lymph node involvement occurs the prognosis is guarded
- Early aggressive chemotherapy is not indicated secondary to excessive morbidity and mortality

MF

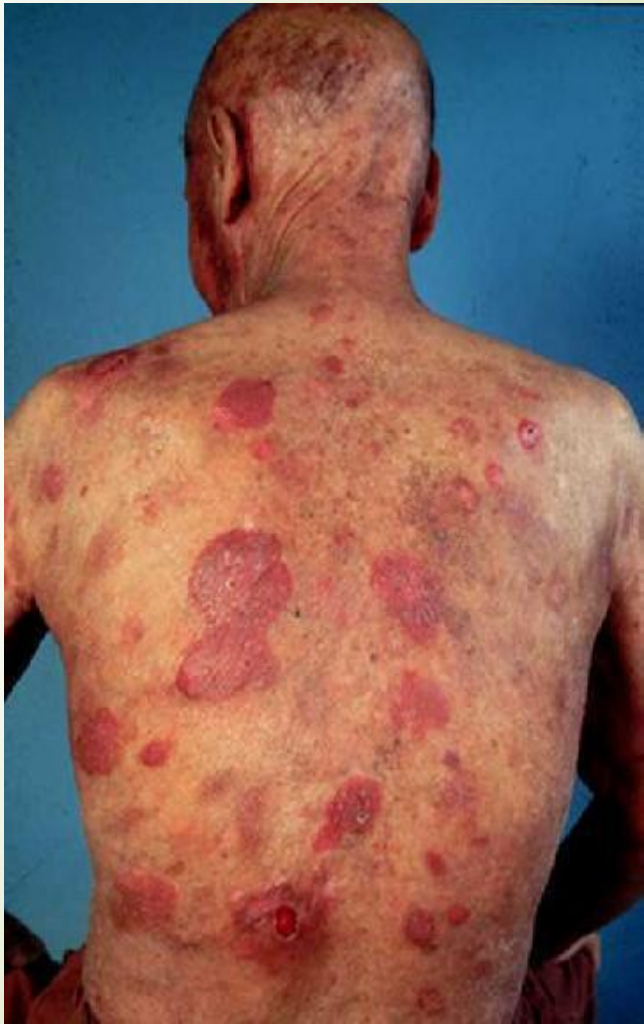
- Patch stage
  - Macular lesions, generally look like eczema, that may be generalized or localized to one area and then spread
  - Lower abdomen, buttocks, upper thighs, breasts of women are common locations
  - May present with an atrophic surface, poikiloderma, verrucous, hypopigmented (MC in darker races or kids), lesions that resemble pigmented purpura, and the vesicular, bullous, or pustular form
  - Small /large plaque parapsoriasis with poikilodermatous change are early patch stage lesions of MF, but this is debated (Bologna states about 10% of lg plaque parapsoriasis progresses to MF)





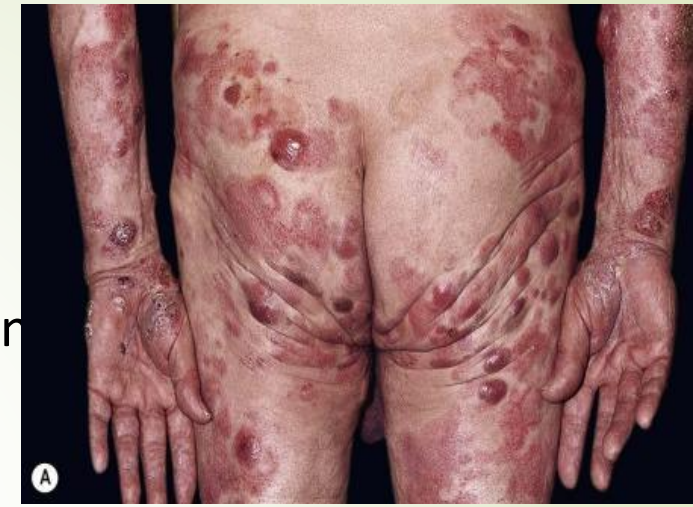
MF

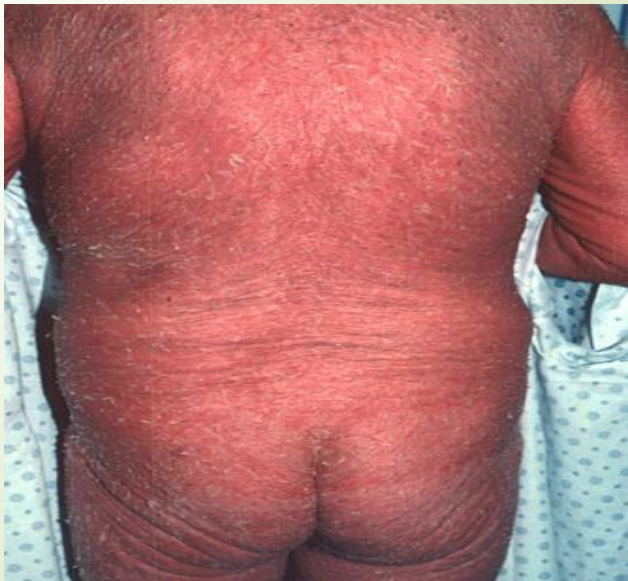
- Plaque stage
  - With progression, more infiltrated reddish-brown, scaling plaques develop, which gradually enlarge and may have an annular, polycyclic or typical horseshoe-shaped configuration
    - may resemble psoriasis, a subacute dermatitis, or a granulomatous dermal process
  - Many patients never progress beyond the plaque stage
  - Palms and soles may be involved with hyperkeratotic, psoriasiform, and fissuring plaques
  - Various plaques eventually coalesce and the involvement becomes widespread with patches of normal skin interspersed
  - Advanced lesions will feature superficial ulcerations that are painful and may be accompanied by enlarged lymph nodes



MF

- Tumor stage
  - Large, various sized and shaped nodules on infiltrated plaques and apparently normal skin
  - Nodules tend to break down early and form deep oval ulcers with based covered by a necrotic grayish substance with rolled edges
  - Predilection for the trunk but may appear anywhere including the mouth and upper respiratory tract
  - Uncommonly, may be the first sign
- Erythrodermic variant
  - Generalized exfoliation, universal erythema
  - Scanty hairs, dystrophic nails, hyperkeratotic palms and soles
  - May be the first sign





MF

- Systemic manifestations
  - Lymph node involvement is MC → it predicts progression of the disease in at least 25%, reduces survival to about 7 years
  - Any other evidence of visceral involvement is a grave prognostic sign
  - Any abnormality on CT/bone marrow bx → survival is 1 year
- Pathogenesis
  - MF is a neoplasm of memory helper T-cells
  - Events leading to the development of malignant T cells is unknown
  - Possibly due to chronic exposure to an antigen, but not confirmed
    - Patients with atopic derm are at increased risk (persistent stimulation of T cells may lead to a malignant clone)
  - Immunologically "activated" skin
    - MF cells express cutaneous lymphocyte antigen (CLA) – the ligand for E selectin, expressed on endothelial cells of inflamed skin
      - Allows malignant cells to traffic into the skin from peripheral blood
    - CCR4 – homing molecule expressed on MF cells and the ligand is basal keratinocytes

MF Treatment

Treatment – skin directed therapies for early MF (stage IA-IIA) and limited tumor disease (IIB)

- **Topical corticosteroids**
  - Superpotent class 1, complete remission in up to 60%, important adjunct tx in advanced disease
- **Topical chemo-**→ nitrogen mustard and carmustine
  - Complete remission in 60-80%
  - Side effects: cutaneous intolerance, allergic contact dermatitis, development of skin CA with longterm use
- **UV therapy**
  - PUVA: 80-90% complete remission→ many relapse even with maintainence tx
  - Broadband UVB→ up to 75% complete response.
  - Narrowband UVB and UVA_1
  - Extracorporeal photochemotherapy→ useful in erythrodermic MF or Sezary
    - Circulating cells are extracted and treated with UVA outside the body – the patient ingests psoralen prior to treatment
- **Radiation**

  Total skin electron beam irradiation
  - Very effective in stage IA-B (>80% complete remission), but not used commonly for these stages
  - Most useful for tumor stage (40% complete remission)
  - Side effects: erythema, edema, worsening of lesions, temporary loss of hair, nails and sweat gland function.

  Local radiotherapy with Xray or electron beam→ used for single tumor or as adjunct tx

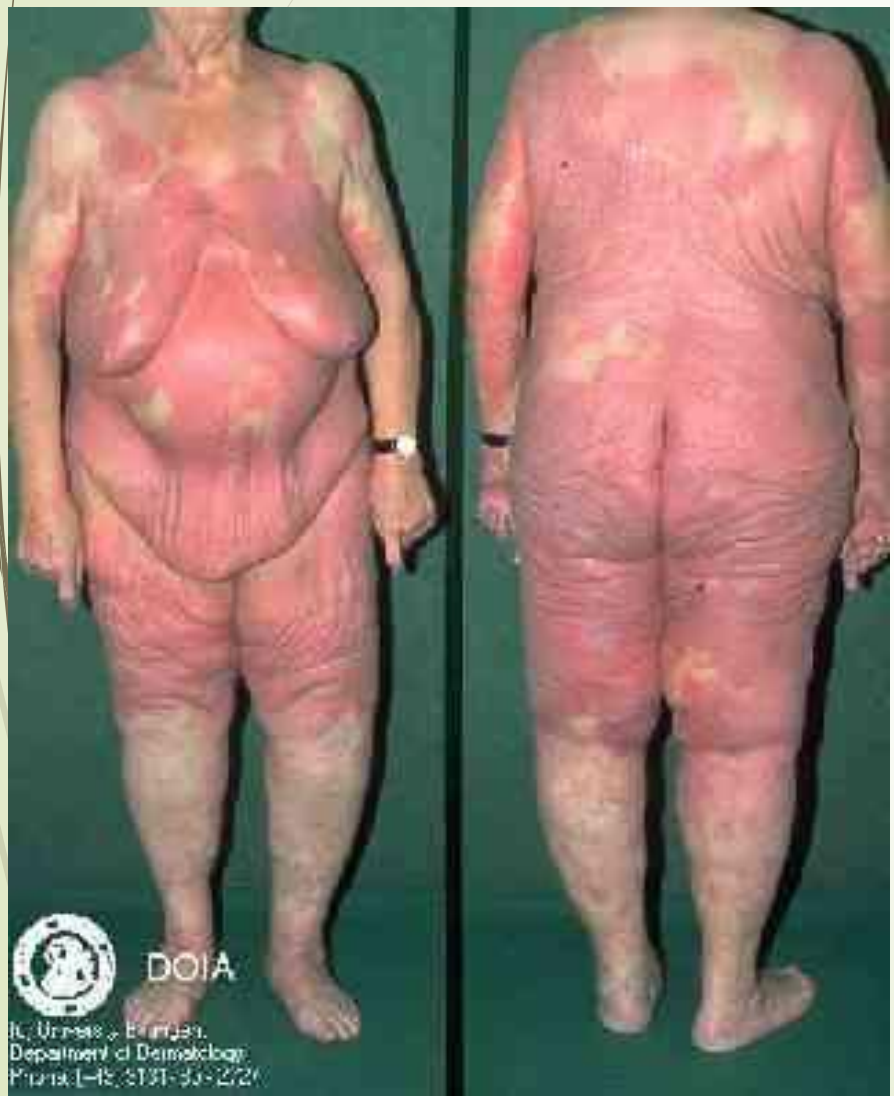
MF Treatment

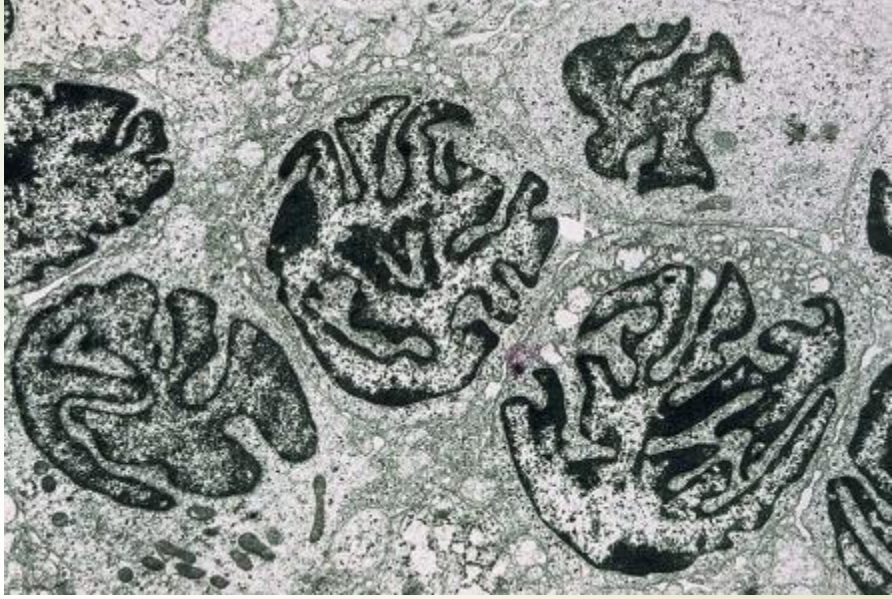
- **Biologic response modifiers** – IFN alpha, gamma, GMCSF, IL2 / 12
  - IFN α most commonly used. Works best in combo with PUVA
    - SEs: flu-like symptoms, hair loss, nausea, depression and bone marrow suppression.
- **Retinoids**
  - Isotretinoin (1-3 mg/kg/day)-44% response
  - Bexarotene (RXR) – 1% topical gel and oral tablet
    - SEs: hyperpercholesterolemia, hypertriglyceridemia, central hypothyroidism, leukopenia
  - All work best when combined with PUVA
- **Systemic chemotherapy**
  - Should only be used in patients with LN or visceral involvement, or in patients with progressive skin tumors that have failed other therapies
  - Standard is 6 cycles of CHOP
- **Fusion toxin**
  - Denileukin diftitox, a fusion of a portion of the diptheria toxin to recombinant IL-2
  - Selectively binds to cells expressing the IL-2 receptor→ inhibits protein synthesis→ cell death
  - SEs: capillary leak syndrome, fever, and fluid retention
- **Histone deacetylase inhibitors**
  - Vorinostat and depsipeptide→ overall response 35%, complete response rare

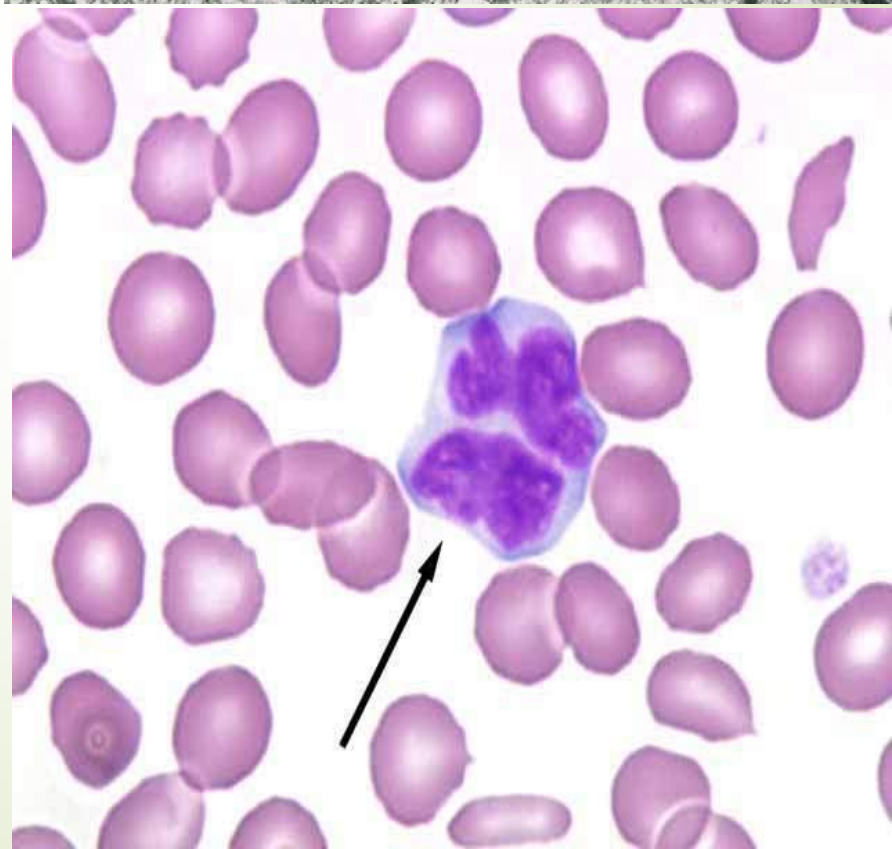
Sezary syndrome

- Leukemic phase of MF, less than 5% of CTCL
- **Triad**: erythroderma, generalized lymphadenopathy, and the presence of neoplastic T cells (Sézary cells) in the skin, lymph nodes and peripheral blood
- Skin shows a fiery red color, can also have leonine facies, eyelid edema, ectropion, diffuse alopecia, palmoplantar hyperkeratosis, dystrophic nails
- Severe pruritus and burning, episodes of chills
- Leukocytosis and helper T cells with deeply convoluted nuclei (Sezary cells)
- Histologically appears similar to MF
- **Criteria recommended for the diagnosis**:
  - Demonstration of a T-cell clone in the peripheral blood by molecular or cytogenetic methods,
  - Demonstration of immunophenotypical abnormalities (expanded $CD4^+$ T-cell population → CD4/CD8 ratio > 10 and/or aberrant expression of pan-T-cell antigens)
  - Absolute Sézary cell count of least 1000 cells per µl
- T cell gene rearrangement studies can confirm the dx
- Poor prognosis, average survival is 5 years

Sezary syndrome



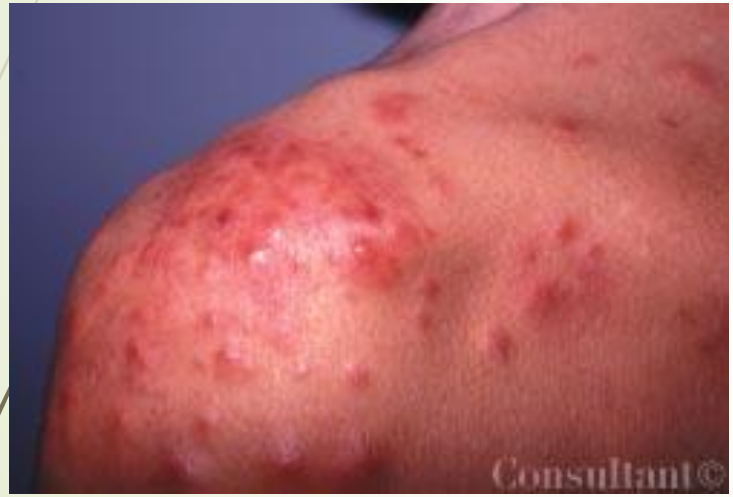


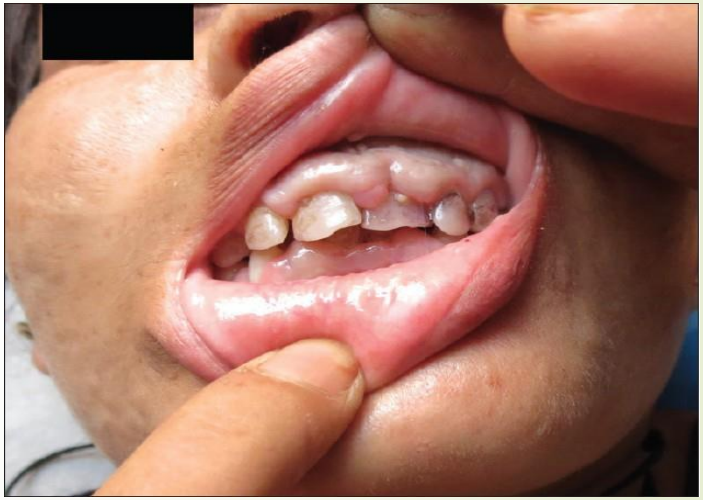


Leukemia Cutis

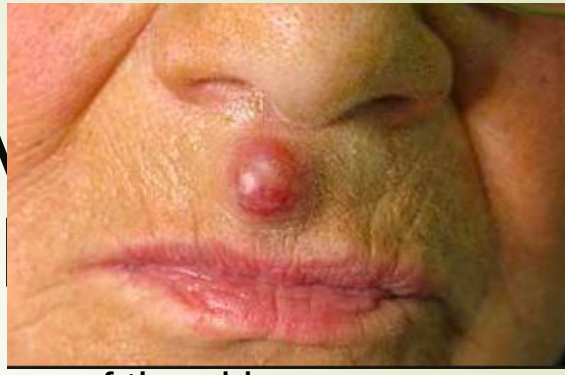
- Cutaneous eruptions of leukemia accounts for 30% of all skin biopsy specimens in patients with leukemia
- Vast majority of derm manifestations are seen in patients with AML or MDS
  - Only 25% will have a positive biopsy
  - In contrast, 50% of ALL, CML, and CLL biopsies are positive for leukemia cutis
- Various presentations, can get firm papules and nodules that are frequently hemorrhagic (from thrombocytopenia)
- Can develop in any location, but head, neck and trunk mc
  - Rubbery texture, extensive facial involvement may lead to leonine facies
- Leukemic infiltrates may arise at sites of trauma or scars.
- Gingival infiltration causing hypertrophy is common in patients with AML
- MC occurs concomittantly with the dx of leukemia or following the dx
- Leukemia cutis is a poor prognostic finding with 90% of patients having extramedullary involvement and 40% having meningeal infiltration

Leukemia cutis





MERKEL CELL CARCINOM
(TRABECULAR CARCINO



Rare, aggressive, malignant primary neuroendocrine carcinoma of the skin

- **AAD 2018: SEER-18 registry --> Number of reported cases of Merkel cell carcinoma increased by 95% between 2000 and 2013**
  - Believed to be related to aging population; sun exposure and fair skin are also risk factors

Cell of origin is thought to be the merkel cell

- Slow-acting mechanoreceptor in the basal layer

90% occur over the age of 50

Clinical presentation:

- Rapidly growing red to violaceous nodule with a shiny surface and overlying telangiectases
- Preferentially affects sun-exposed areas
  - Head and neck (36%)
  - Leg (15%)
  - Arm (22%)
  - Trunk (11%)

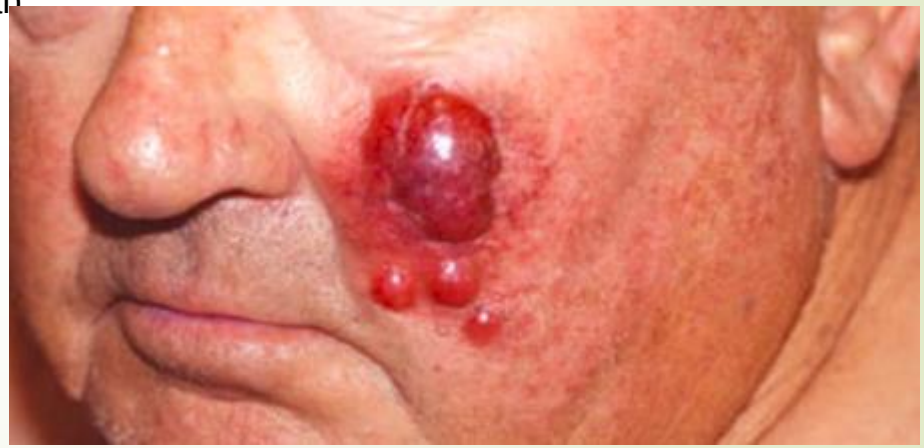
MERKEL CELL CARCINOMA

~80% of MCCs in North America and 25% in Australia are associated with Merkel cell **polyomavirus (MCPyV)**

- Better prognosis (25% vs 15% at 5-year survival)

A E I O U (Increased suspicion of MCC)

- A→ Asymptomatic
- E → Expanding rapidly
- I → Immune suppression
- O → Older than 50
- U → UV exposed skin in fair person



TREATMENT

Wide excision 2-3 cm margins

- "The current National Comprehensive Cancer Network (NCCN) guidelines recommend excision with 1- to 2-cm margins down to fascia or periosteum (level III evidence)" Tello et al. JAAD CME March 2018.

Mohs micrographic surgery– yielding lowest local recurrence rates

Adjuvant treatment

Radiation

Chemotherapy*- Considered palliative in the setting of metastatic MCC

PET and CT scanning of the relevant nodal region, chest, and liver should be performed

Sentinel lymph node biopsy

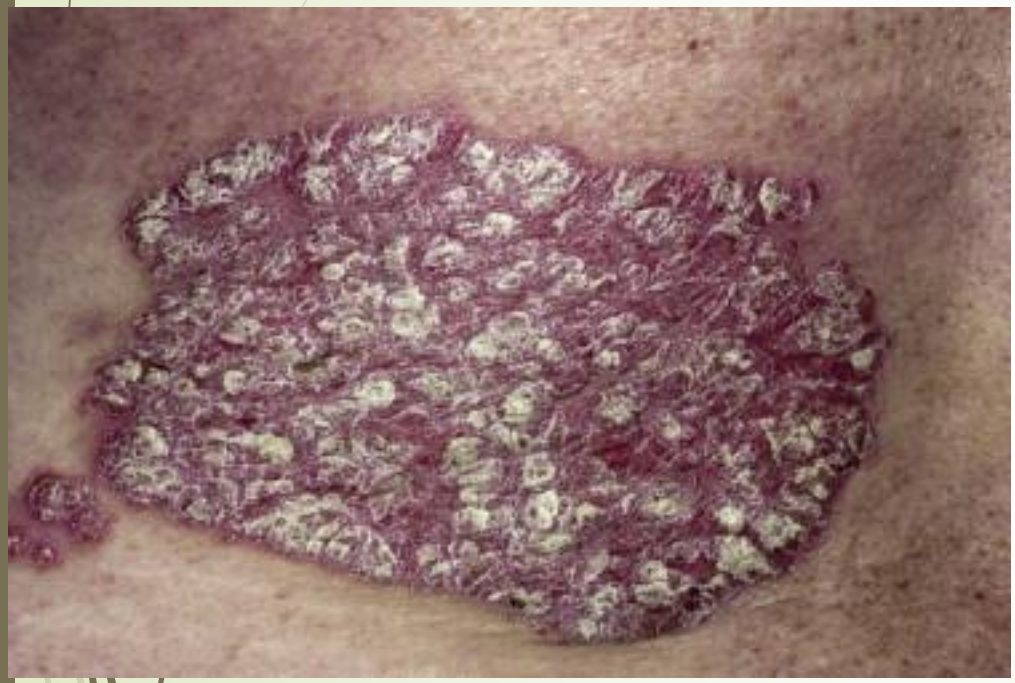
- SLNB-positive patients have a 0% survival rate if not given additional therapy for the lymphatic involvement
- "SLNB should be considered in all patients with MCC who do not have clinically detectable nodes unless surgery is contraindicated or declined"- Tello et al. JAAD March CME 2018.

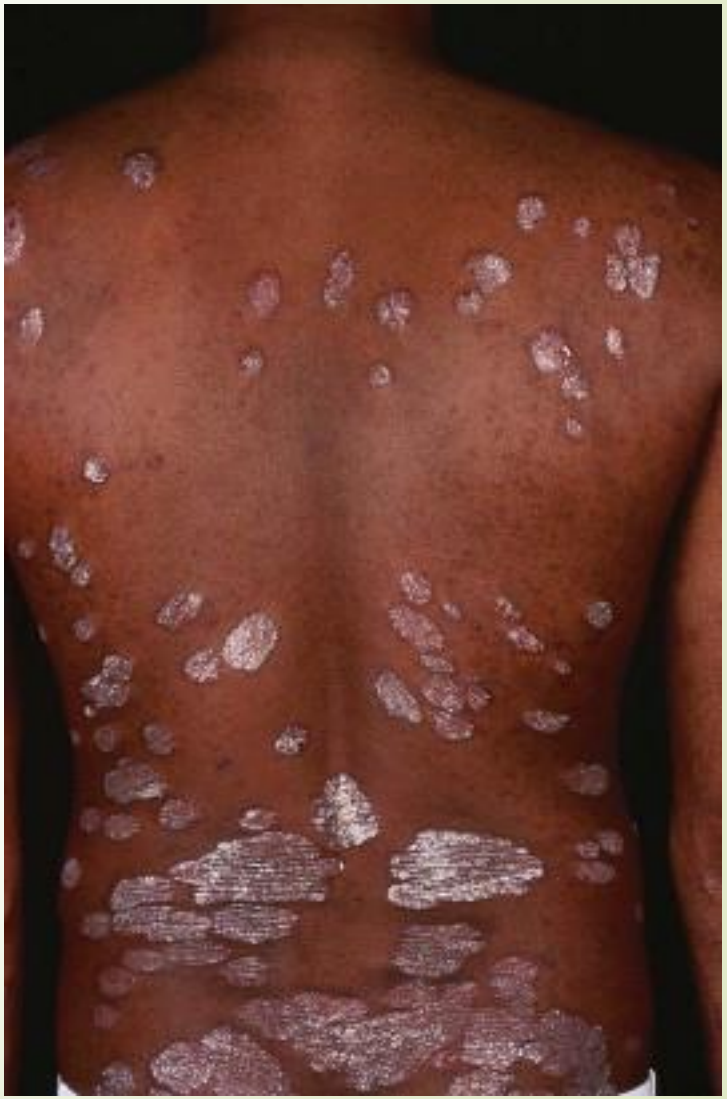
Metastases incidence at diagnosis

Lymph nodes – 27%→

Distant hematogenous – 7% (liver, bone, brain, lung)

Psoriasis





Generalized plaque psoriasis – Sharply demarcated plaques with silvery scale

Psoriasis

- 2% of Population affected in the US
- Begins 3rd decade of life

  Bimodal peak: 29 and 55
- Increased incidence in offspring of parents with Psoriasis
- Comorbid Associations

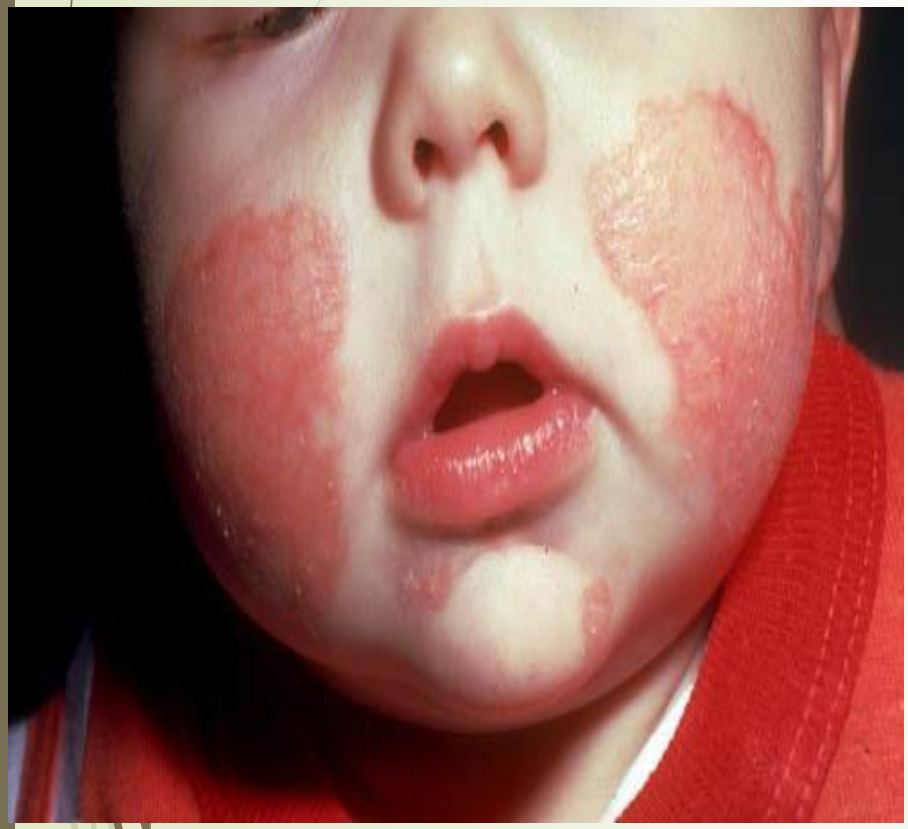
  HTN Obesity Psa

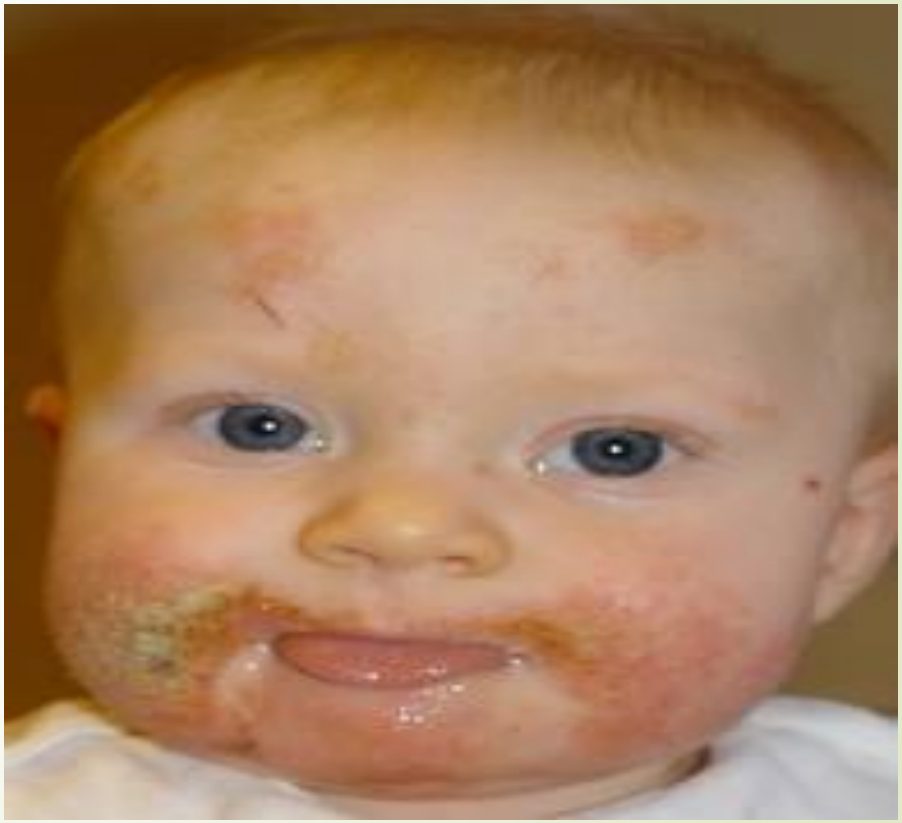
  Diabetes Increased risk of cardiovascular disease

  Depression Metabolic Syndrome

  Crohns Ulcerative colitis
- 71% have 1 comorbid conditions and 47% have 2

Atopic dermatitis





Atopic dermatitis

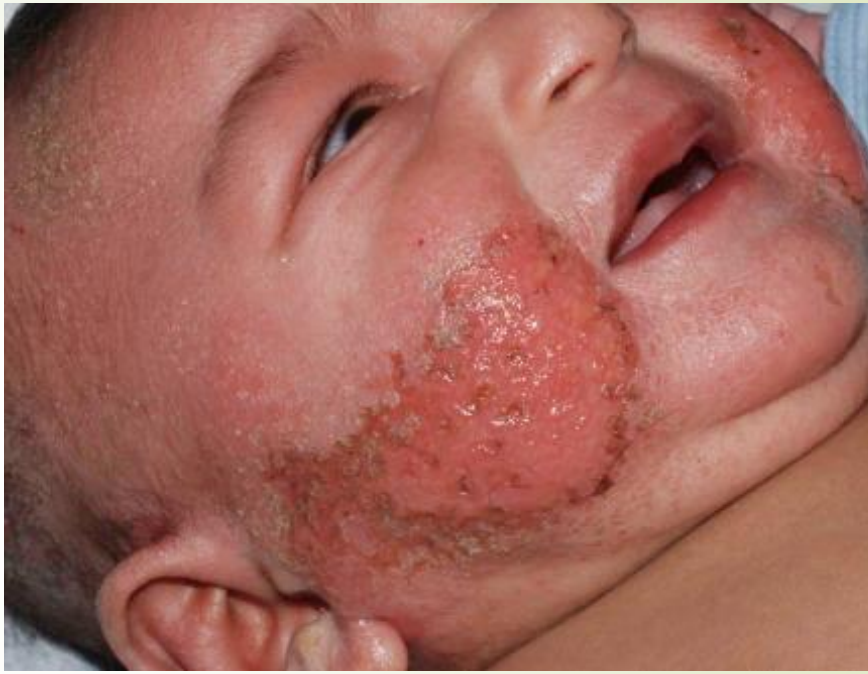
- *The itch that rashes*
- 30% kids, 0.9% adults
- Triad of Asthma, Allergies, and Atopic Dermatitis
- Chronic, pruritic eczematous disease that nearly always starts in childhood and follows a remitting / relapsing course
- Pruritus is the hallmark in all stages
- Complex interrelationship of environmental, immunologic, genetic, and pharmacologic factors
- Exacerbated by infection, stress, climate changes, irritants, and allergens
- Approximately 60% of atopic children will have some degree in adulthood in the form of hand dermatitis
- Prevalence is less in rural areas compared to urban (increasing rates)
- 45% of cases begin before 6 months old, 60% before 1 y.o.
- **Atopic triad: eczema, asthma, allergies**

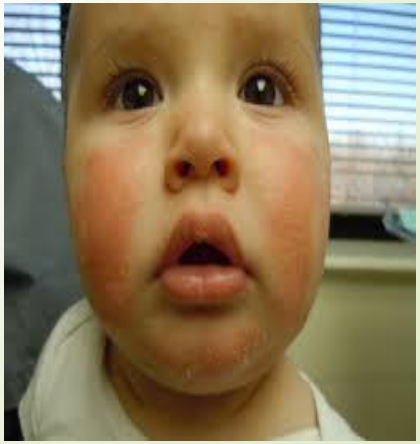
Atopic dermatitis

- Path
  - Epidermal barrier dysfunction
  - Increased IgE levels
  - Serum eosinophilia
  - Aeroallergens
    - House dust, mites, cockroaches, mold, grass
  - Reduced cell mediated immunity
    - Can have severe, widespread HSV (eczema herpeticum)
- Unfavorable prognostic factors
  - Persistent dry or itchy skin in adult life
  - Widespread dermatitis in childhood
  - Allergic rhinitis
  - Family history of atopic dermatitis
  - Asthma
  - Early age of onset
  - Female gender

Atopic dermatitis

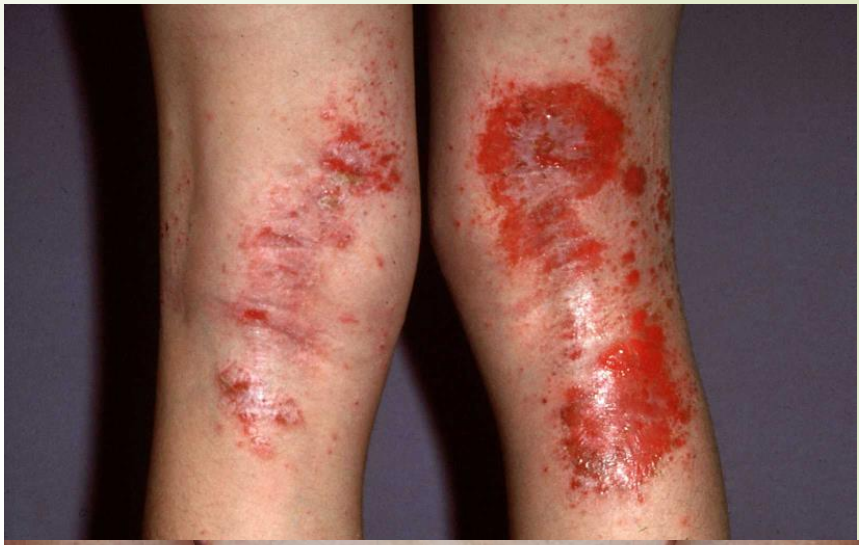
- **Infant phase**
  - Birth to 2 years old
  - MC occurrence is a baby during the winter months develops dry, red, scaling areas confined to the cheeks with perioral and perinasal sparing
  - Extensor surfaces common (crawling to relieve itch)
  - Diaper area is often spared
  - Prolonged AD features increasing amounts of discomfort, disrupts sleep for both parents and patient
  - Height is correlated with the surface area of skin affected by eczema

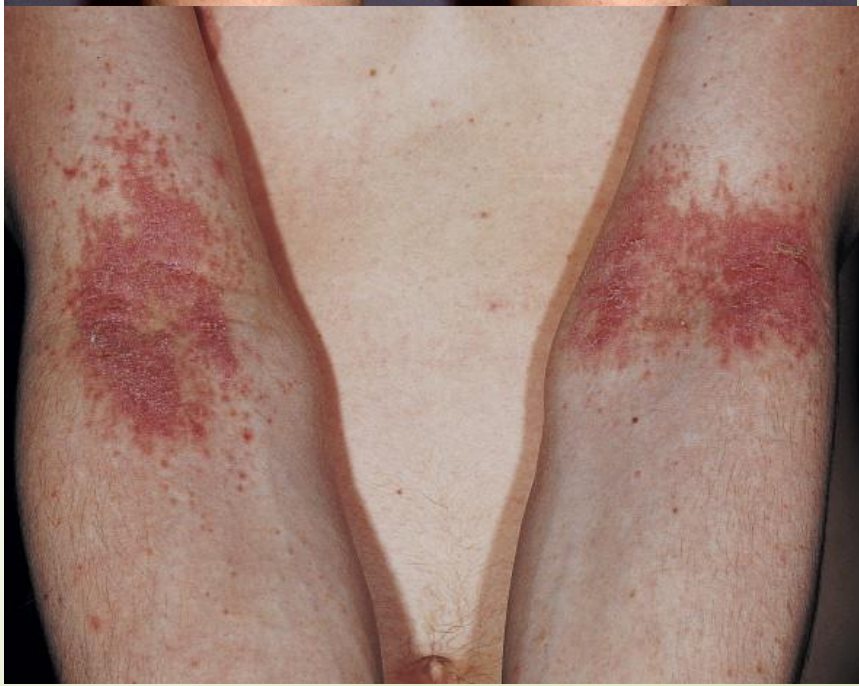


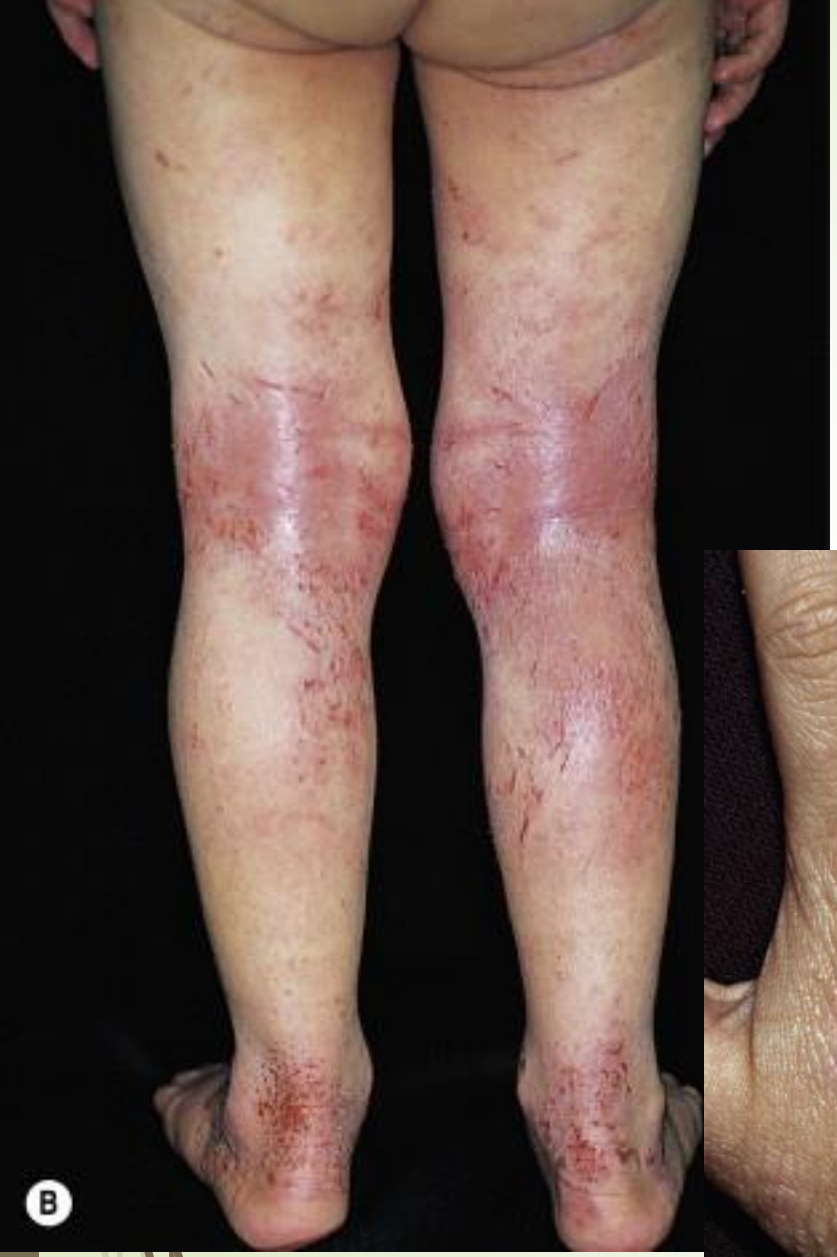


Atopic Dermatitis

- **Childhood phase (2 to 12 y.o.)**
  - MC and characteristic appearance of inflammation is in ***flexural*** areas
    - Antecubital fossae, neck, wrists, ankles
  - These areas of repeated flexion / extension perspire -> stimulates burning and intense pruritus -> initiates the itch – scratch cycle
  - Tight clothing makes it worse
  - Hypopigmentation can result from scratching -> destruction of melanocytes
  - The inflammation affects life -> duration of sleep cannot be maintained -> school, work, job performance suffers
  - The dermatitis is a lifelong ordeal



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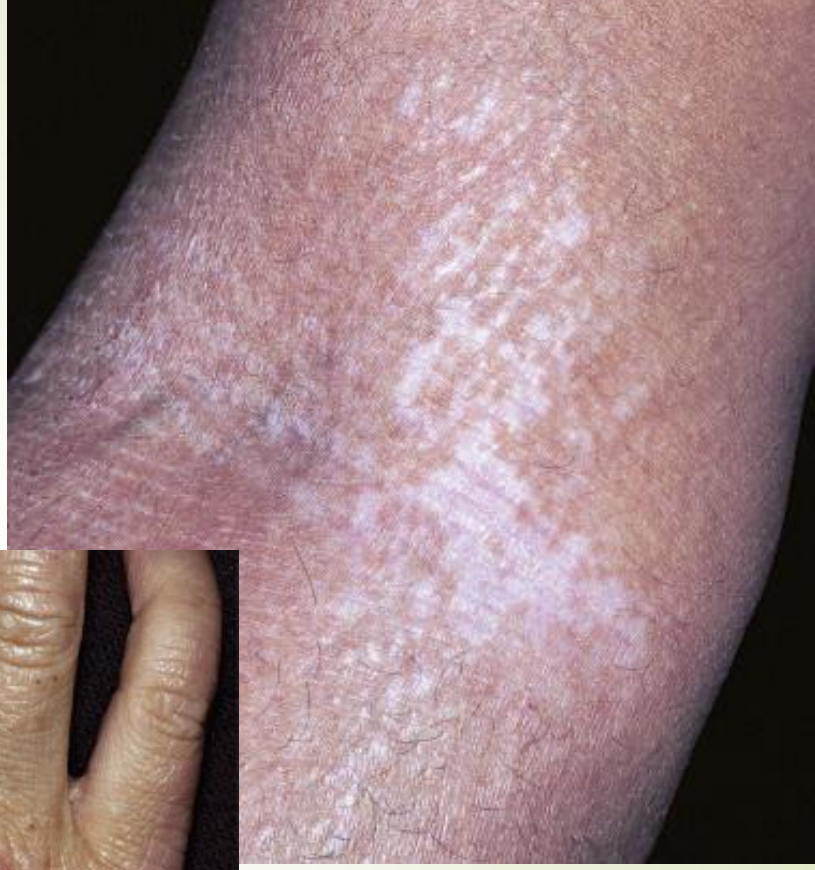

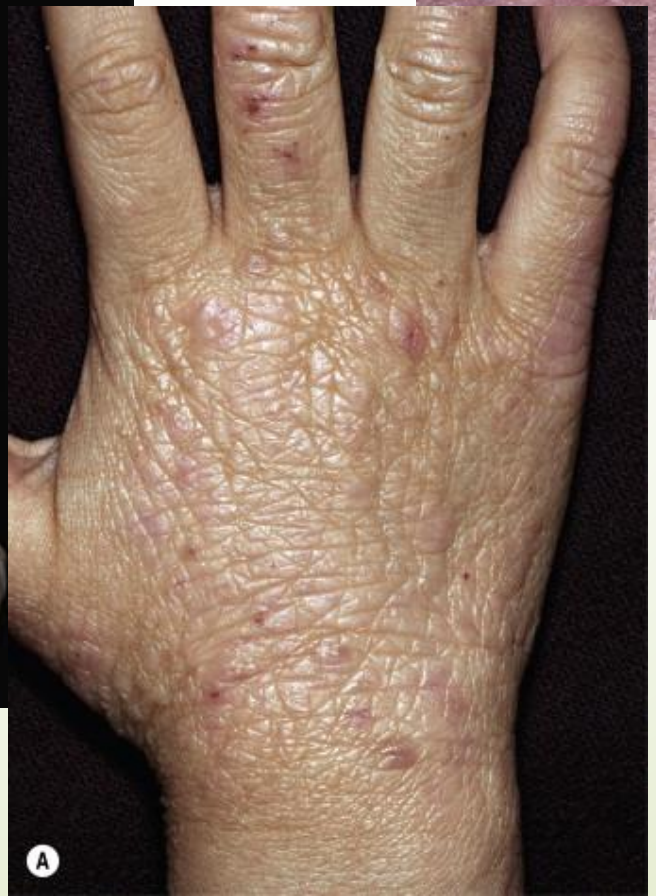
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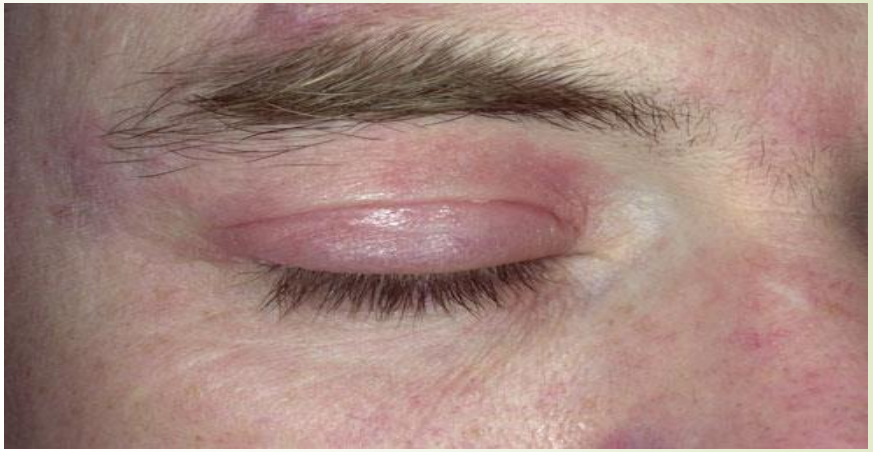
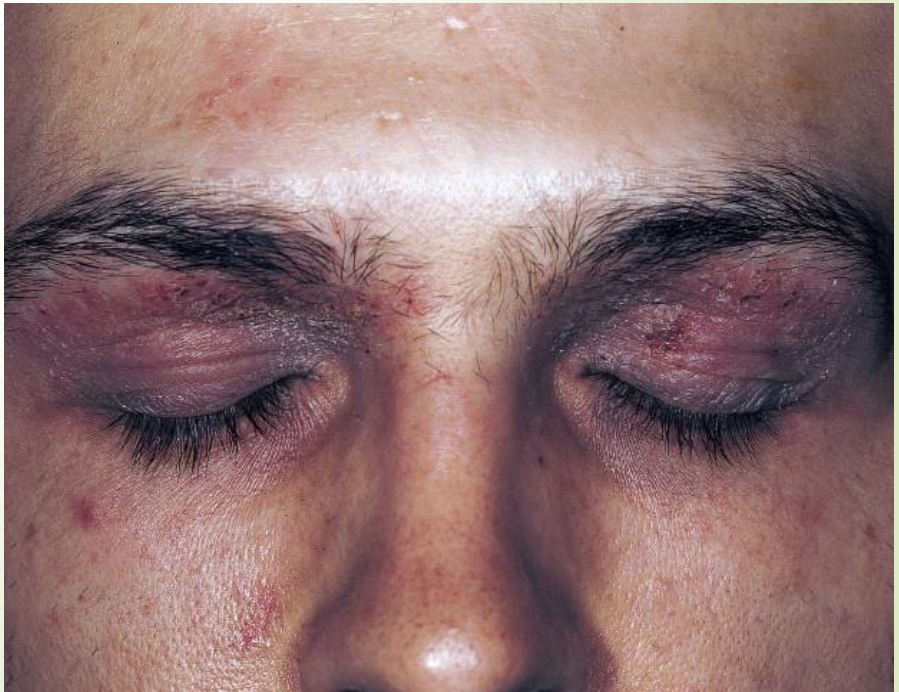
Atopic dermatitis

- Adult phase (12 y.o. to adult)
  - Onset near puberty
  - Localized inflammation with lichenification is MC
  - Hand dermatitis is MC form of AD in adults
    - Dorsal aspect of hand MC
  - Upper eyelids common
  - Dennie-Morgan fold: below the lower eyelid

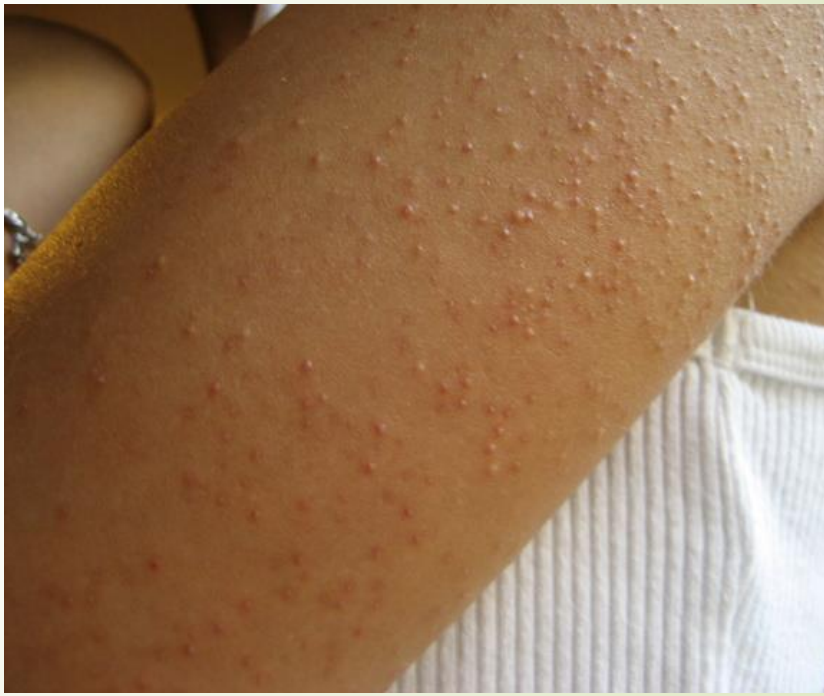




Dennie-Morgan Line

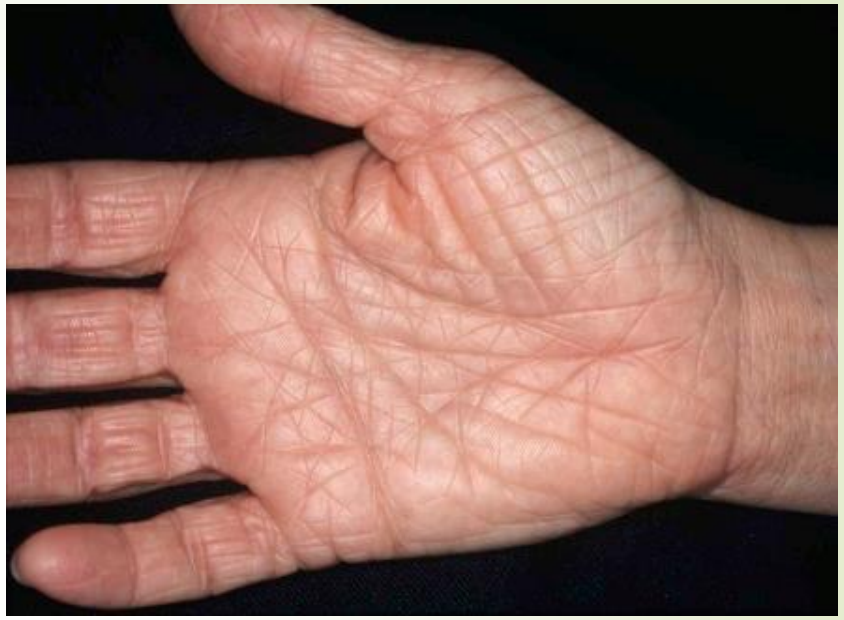
AD – Associated features

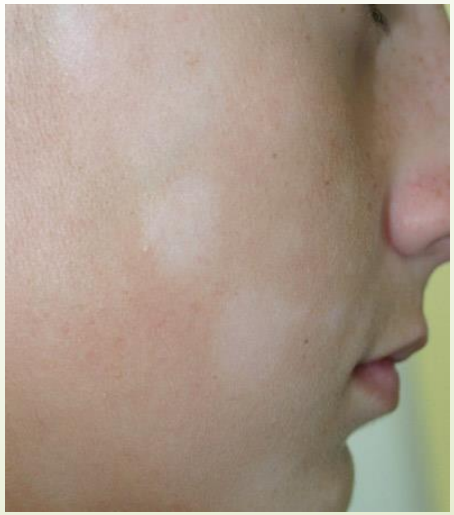
- Keratosis pilaris
  - Very common, but more common and extensive in patients with AD
  - Small, rough, follicular papules along the posterolateral aspects of the upper arms and anterior thighs MC, but can occur anywhere except palms and soles
  - Cause: excess keratin trapped around base of hair follicle
  - Can appear pustular, resemble acne on the face
  - Systemic steroids may worsen
  - Treatment
    - Topical retinoids
    - Short courses of topical steroids can reduce erythema
    - Lac-hydrin, Amlactin, Urea cream, and salicylic acid can reduce roughness

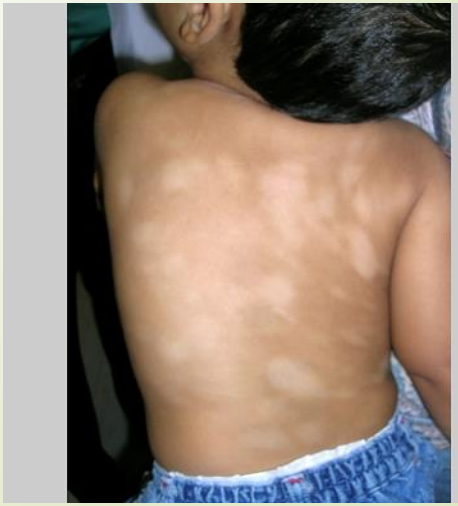


AD- Associated features

- Hyperlinear palmar creases
  - Accentuated skin creases of the palms
  - Initiated by rubbing or scratching
- Pityriasis alba
  - Asymptomatic, hypopigmented , scaling plaque with indistinct borders
  - Common on face, lateral upper arms, thighs
  - Appears in children, usually disappears by adulthood
  - More obvious in the summer when the areas do not tan
- Cataracts
  - Incidence ~ 10% in AD patients
  - Possibly related to corticosteroid use, but true etiology still unknown

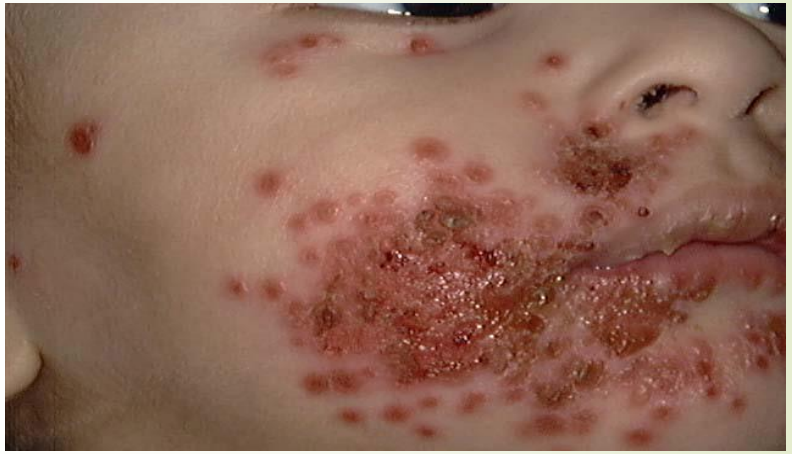


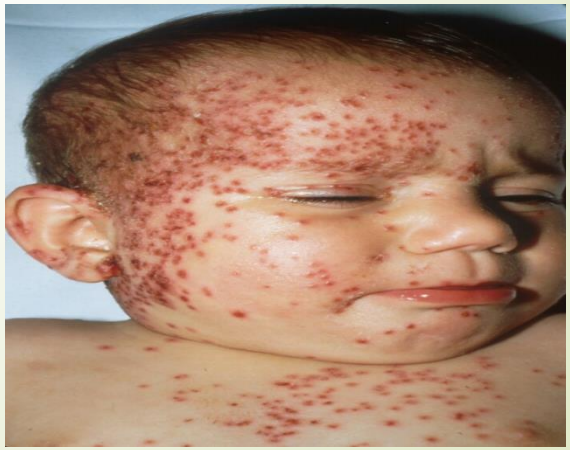




AD - complications

- Eczema herpeticum
  - HSV infection in patients with AD
  - Rapid onset of diffuse cutaneous HSV
  - Ranges in severity
    - Viremia with internal organ dissemination can be fatal
  - MC in areas of active or recently healed dermatitis, particularly the face
  - Secondary staph infection is common
- Treatment
  - Young infant: emergency, early Acyclovir can be life saving
  - Cool, wet compresses
  - Acyclovir po 30 mg/kg/day
  - Antibiotics





CONTACT DERMATITIS

ALLERGIC CONTACT DERM

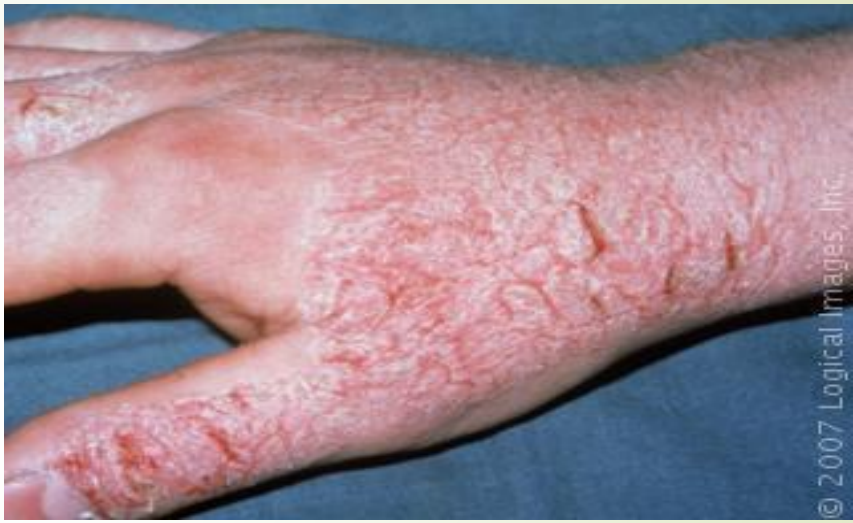
- IMMUNOLOGIC RESPONSE TO ALLERGAN

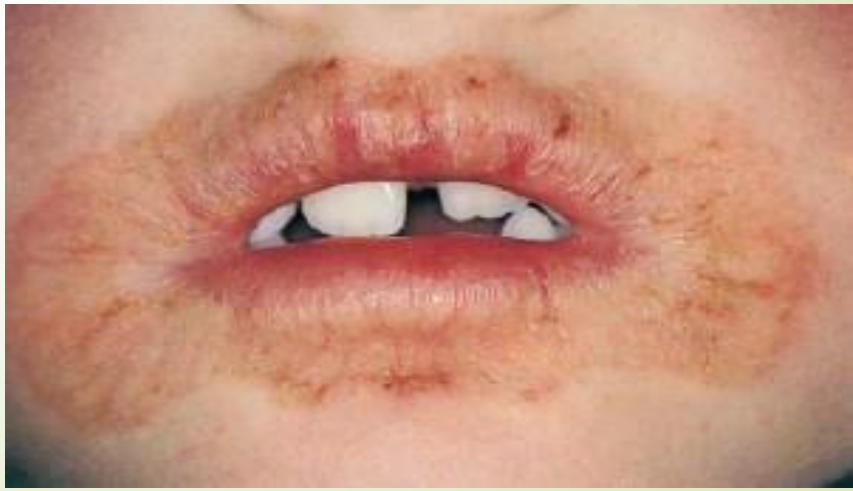
IRRITANT CONTACT DERM

- NON-IMMUNOLOGIC RESPONSE TO ALLERGAN
- MOST COMMON TYPE

Contact dermatitis

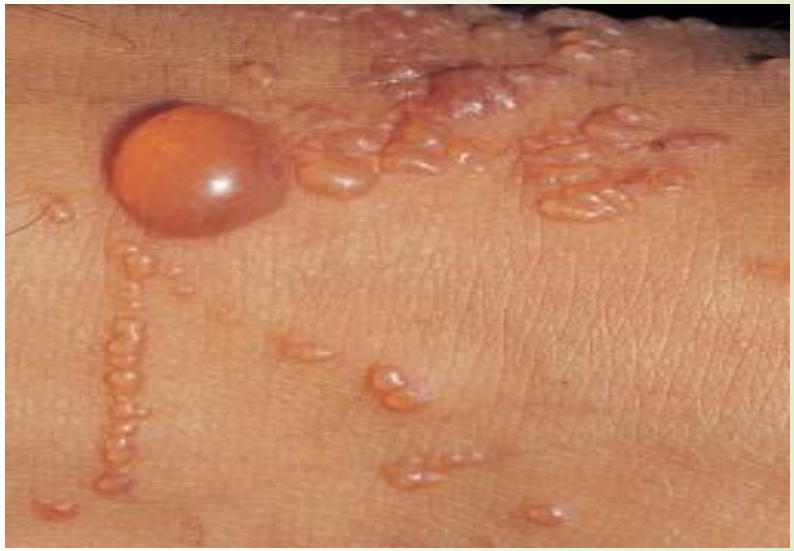
- Irritant contact
  - MCC of contact derm
  - Any process that damages any component of the skin barrier compromises its function -> non-immunologic eczematous response may result
  - Patients vary in their ability to withstand exposure to irritants
  - Management
    - Avoid exposure to irritants
    - Topical steroids if inflammation present
    - Moisturizers
    - Barrier creams
    - Cool compresses if inflammation present
    - Wash hands in cool water
    - Takes ~ 4 months for barrier function to normalize after the skin appears normal





Contact dermatitis

- Allergic contact
  - Less common than ICD
  - Inflammatory reaction following absorption of previously sensitized, antigen-specific T lymphocytes
  - Most contact allergens are weak, require multiple exposures before sensitization occurs
  - Stronger antigens (poison ivy) require only 2 exposures
  - Cross sensitization
    - Occurs when allergens with similar chemical structures are not differentiated by the immune system
      - Poison ivy, cashew nuts, mango rind, japanese lacquer tree



Contact dermatitis

Clinical presentation

- Allergic contact dermatitis
  - Shape and location of the rash are the best clues for diagnosis
    - Plants produce linear lesions
    - Pattern of inflammation may correspond exactly to the shape of the offending substance
    - Location (under wristband, ring finger, ear lobe, umbilicus)
  - ***Nickel*** is MC allergy worldwide
  - Intensity of inflammation depends on:
    - Degree of sensitivity
    - Concentration of the antigen

Distribution diagnosis

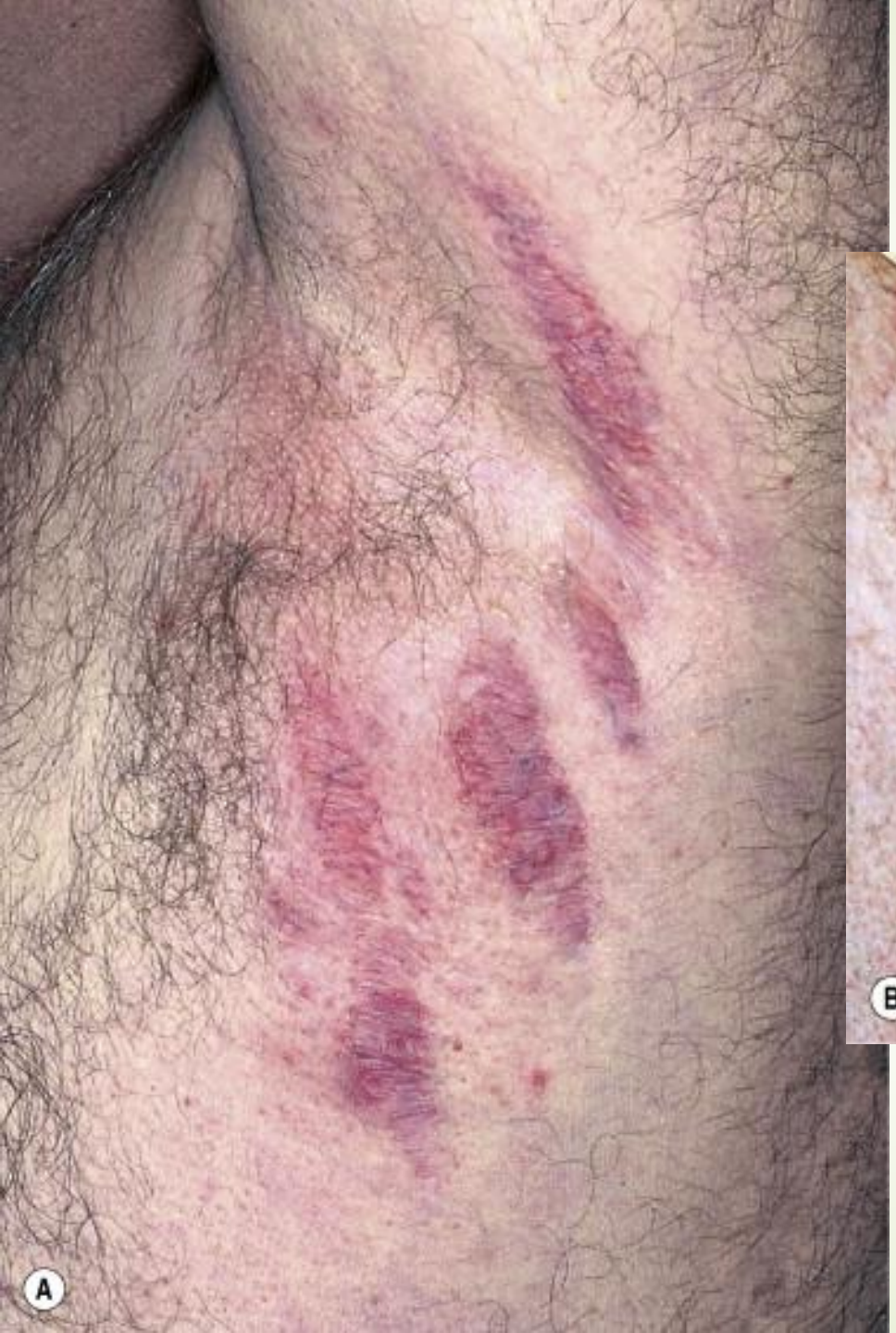
- Scalp, ears
  - Shampoos, hair dye, glasses
- Eyelids
  - Nail polish, cosmetics, contact lens solution
- Neck
  - Jewelry (nickel MC), perfume
- Trunk
  - Formaldehyde, fragrances, azo-aniline dyes (colored clothes), nickel (umbilicus)
- Arms
  - Soaps, sunscreens, industrial solvents, oils
- Fingertips
  - Glutaraldehyde (disinfectants), methylmethacrylate (glue), PPD (p-phenylenediamine)
- Axillae
  - Deodorant, clothing
- Hands
  - Soaps, detergents, foods, spices,

Topical Corticosteroids

Medscape® www.medscape.com

Class	Generic Name	Formulation
Class 1 Very High Potency		
	Betamethasone dipropionate	0.05% G O (diprolene)
	Clobetasol	0.05% C F G L O
	Diflorasone diacetate	0.05% O
	Halobetasol propionate	0.05% C O
Class 2 High Potency		
	Amcinonide	0.1% O
	Betamethasone dipropionate	0.05% C (diprolene)
	Desoximetasone	0.05% G, 0.25% C O
	Fluocinonide	0.05% C G O S
	Halcinonide	0.1% C
	Mometasone furoate	0.1% O
Class 3 High Potency		
	Amcinonide	0.1% C L
	Betamethasone dipropionate	0.05% C (non-diprolene)
	Betamethasone valerate	0.1% O
	Desoximetasone	0.05% C
	Diflorasone diacetate	0.05% C
	Fluticasone propionate	0.005% O
	Halcinonide	0.1% O S
	Triamcinolone	0.1% O
Class 4 Mid Potency		
	Betamethasone valerate	0.12% F
	Flucinolone acetonide	0.025% O
	Flurandrenolide	0.05% O
	Hydrocortisone valerate	0.2% O
	Mometasone furoate	0.1% C
	Triamcinolone	0.1% C
Class 5 Mid Potency		
	Betamethasone dipropionate	0.05% L
	Betamethasone valerate	0.1% C
	Flucinolone acetonide	0.025% C
	Fluticasone propionate	0.05% C
	Flurandrenolide	0.05% C
	Hydrocortisone butyrate	0.1% C
	Hydrocortisone valerate	0.2% C
Class 6 Low Potency		
	Alcometasone dipropionate	0.05% C O
	Betamethasone valerate	0.1% L
	Desonide	0.05% C L O
	Flucinolone acetonide	0.01% C S
Class 7 Low Potency		
	Hydrocortisone acetate	0.5% C L O, 1% C O F
	Hydrocortisone hydrochloride	0.25% C L, 0.5% C L O S, 1% C L O S, 2% L, 2.5% C L O S

C = Cream, F = Foam, G = Gel, L = Lotion, O = Ointment, S = Solution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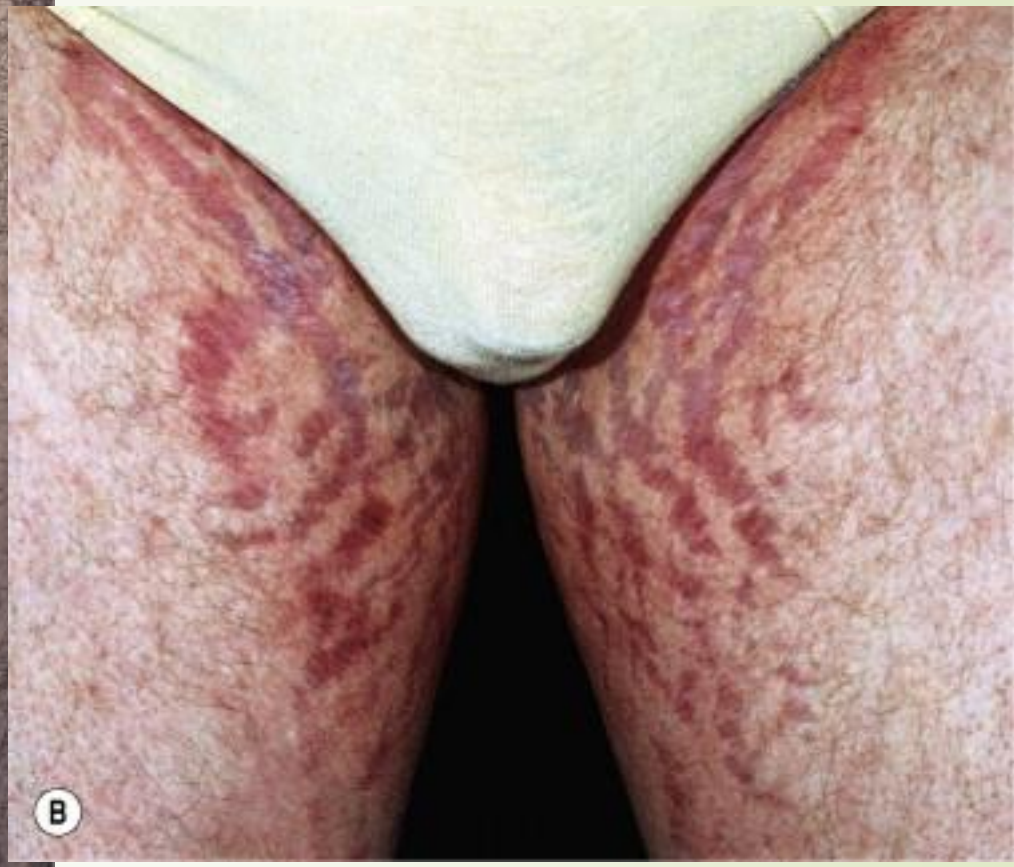
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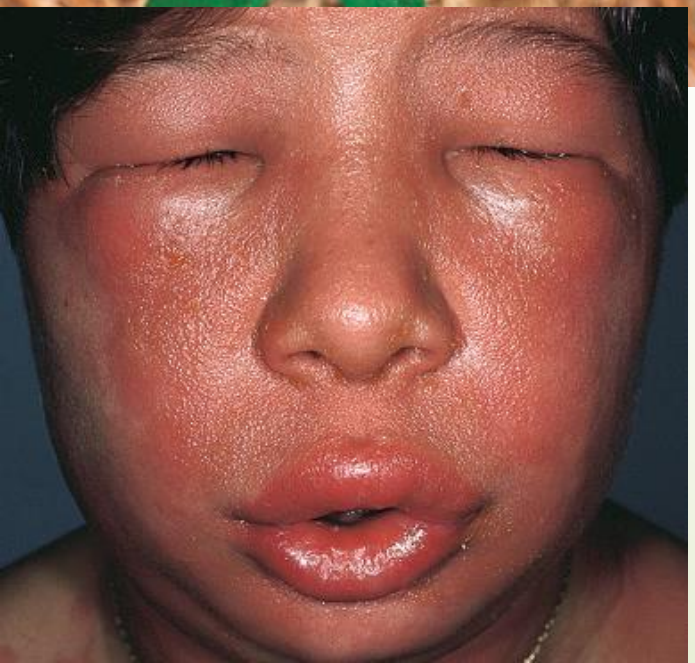
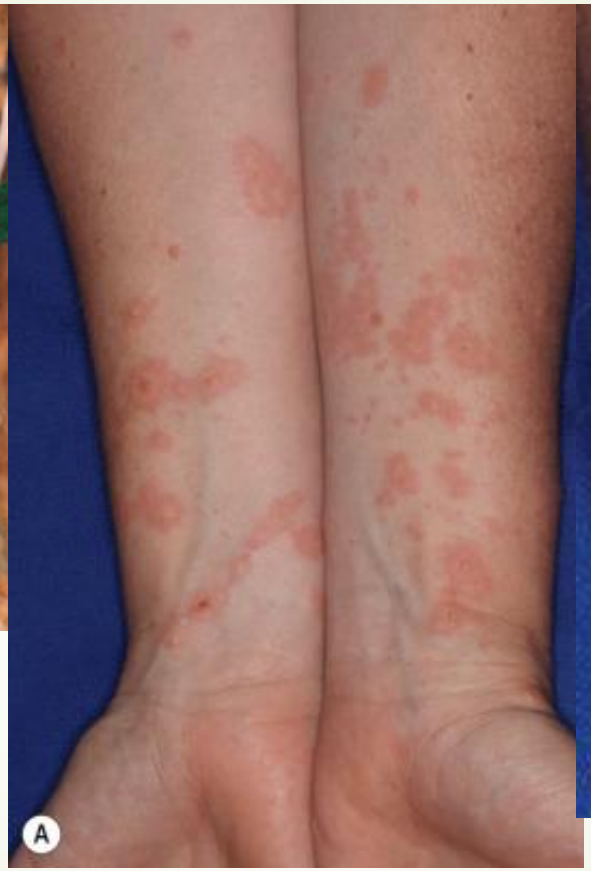
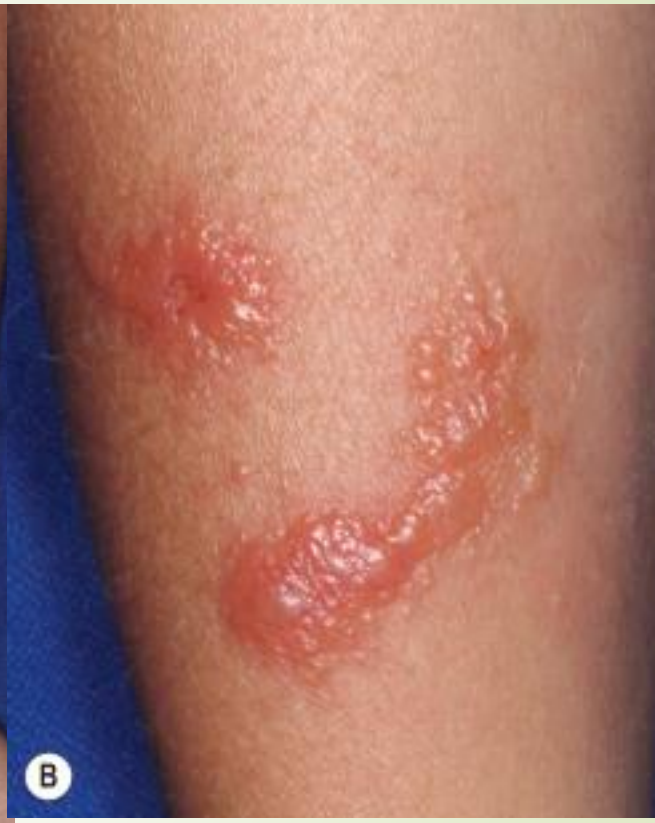
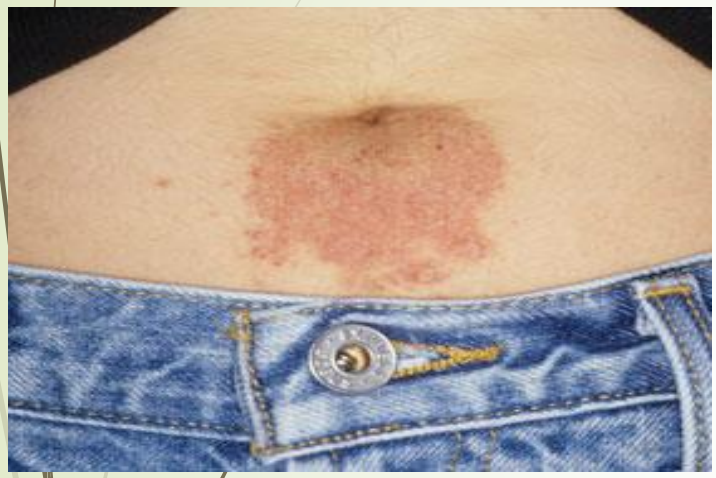
Rhus Dermatitis- Poison Ivy

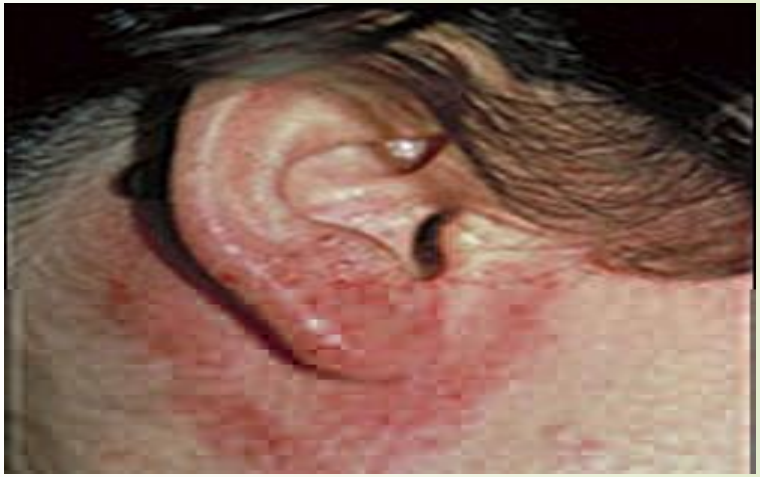


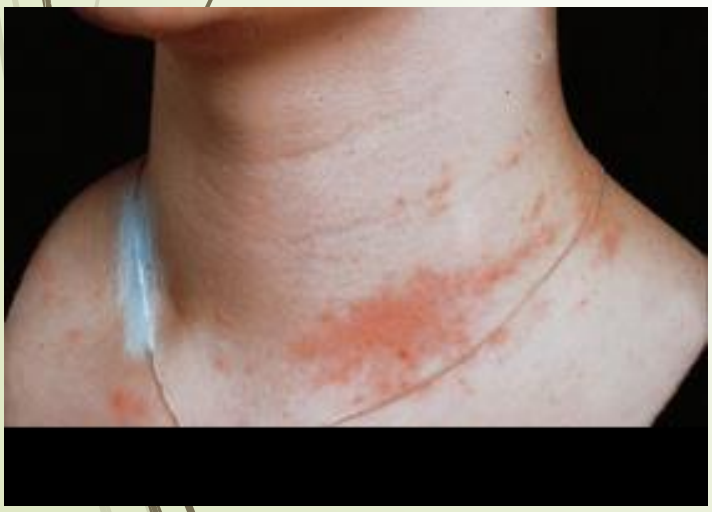


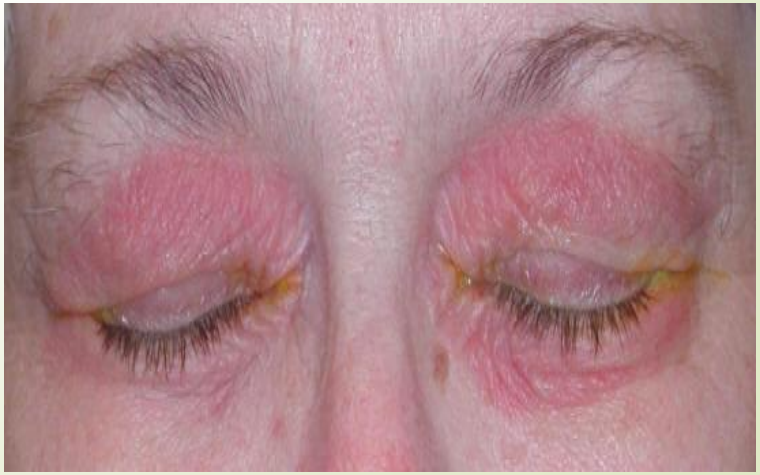


Contact dermatitis



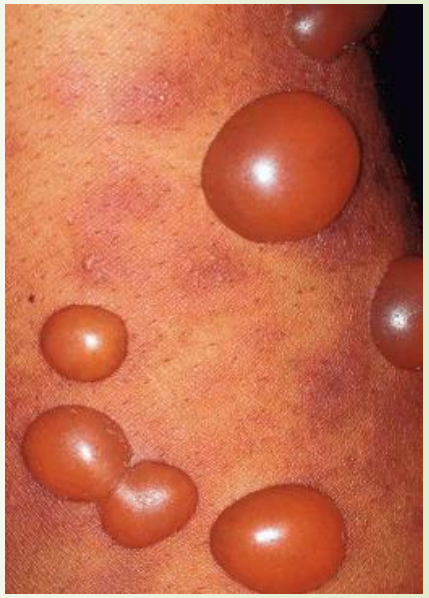






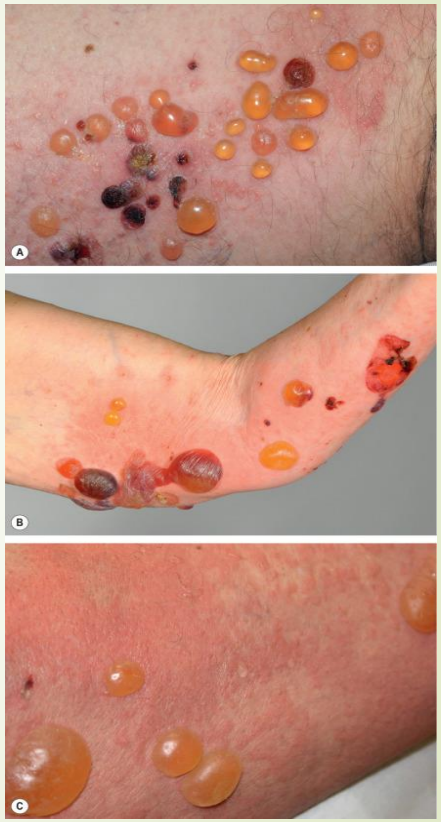
Bullous Pemphigoid

- MOST COMMON blistering disease
- Demographics
  - Elderly: > 60 yrs
- Etiology
  - Circulating *basement membrane zone* antibodies of IgG present in 70%
  - Autoantibodies- identified in 90%
    - Bullous pemphigoid antigen 1 (BPAG1) 230KD
    - Bullous pemphigoid antigen 2 (BPAG2) 180KD
- Associations
  - Dementia, parkinson disease, epilepsy, and multiple sclerosis



Bullous Pemphigoid

- Often starts as urticarial wheals
  - May be misdiagnosed as urticaria
- Evolve into large, tense bullae over medial thighs, groin, abdomen, and legs
  - "Bullae on an urticarial base"
- Nikolsky's sign negative → deeper process
- Rupture → large denuded areas that heal spontaneously
- +/- pruritus with subsequent tenderness
- Young girls may be initially seen with localized vulvar erosions and ulcers that resemble signs of child abuse



Bullous Pemphigoid

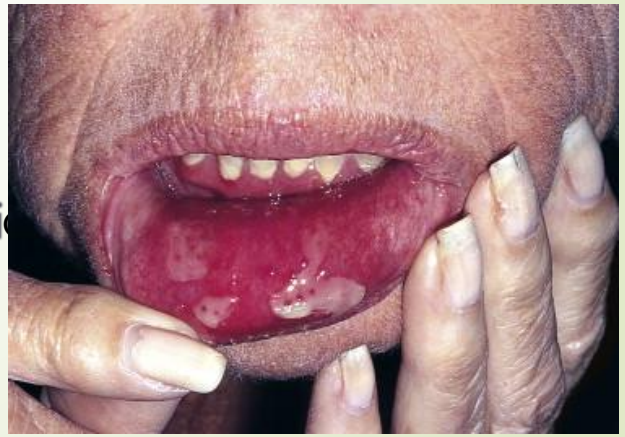
- First line: topical and systemic corticosteroids
  - Prednisone 0.5-0.75mg/kg per day
- ±Tetracycline with nicatinamide TID
- Steroid sparing agents
  - Azathioprine, dapsone, mycophenolate mofetil, methotrexate, rituximab, chlorambucil
- Usually good prognosis

Pemphigus

- Greek pemphix: bubble or blister
- Rare group of autoimmune diseases involving skin and mucous membranes
  - Autoantibiodies to desmoglein 1→ mucocutaneous
  - Autoantibodies to desmoglein 3 → mucosal
- Differentiated based upon level of the split
  - Pemphigus vulgaris
  - Pemphigus foliaceous
  - Pemphigus erythematosus
  - Drug induced pemphigus
  - Paraneoplastic pemphigus

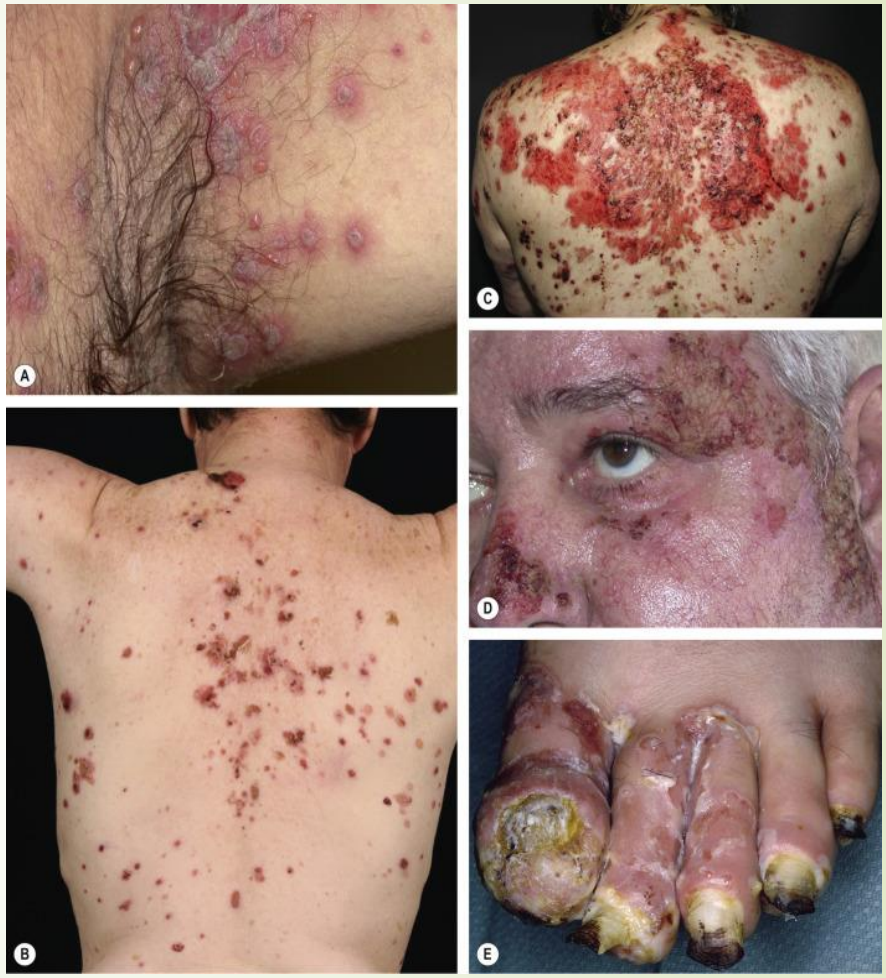
Pemphigus Vulgaris

- Potentially fatal autoimmune bullous disease of the skin and mucous membranes; intraepidermal
- MC form of pemphigus
- M=F; 40-60yo; Jewish ancestry a/w 10x inc. risk
- Nonpruritic, flaccid blisters vary in size on normal or erythematous skin
  - Appear first in the mouth (esp. palatine and buccal mucosa)→ the groin, scalp, face, neck, axillae, or genitals
  - Heal with brown hyperpigmentation
  - No scarring
- Secondary fluid imbalance and bacterial infecti
- Esophagitis dissecans superficialis may occur
- + Nikolsky and Asboe-Hansen sign



Pemphigus Vulgaris

- May be drug induced:
  - Penicillamine (esp. if treating rheumatoid arthritis)
  - Captopril, enalapril, lisinopril
  - Piroxicam
  - Penicillin derivatives



What you really need to know about…
Hidra Hidradenitis Suppurativa (HS) (Acne Inversa)

- aka Hidradenitis Suppurativa, Acne Inversa, Pyoderma Fistulans Significa, Verneuil's disease or Smoker's Boils
- First described in 1839
- Intertriginous skin with terminal hairs and apocrine glands
  - Axillary, inguinal, perineal, buttock, submammary areas
  - Most frequently **axillae of young women**
  - Men more frequently in groin and perianal areas
- Tender, firm red nodules → fluctuant, suppuration, sinus tract formation, extensive scarring
- Average of 2- 5 painful abscesses per month
- Associated with follicular occlusion triad

H Suppurativa

- Prevalence from less than 1% to 4%
- Most common in second and third decades of life and not usually before puberty
- Female to Male ratio is approx. 3.3:1
- Highest incidence in women ages 20-29
- Men have more atypical and severe presentations

What you really need to know about…
HS Suppurativa

- Pathogenesis of HS in unclear
- Risk Factors
  - Smoking
  - Obesity
  - Mechanical Friction
- Genetics (1/3 have 1st degree relatives with the disease)
- Bacteria (may produce occlusive biofilm and inflammatory response)

HS

- Delay of diagnosis from symptom onset to diagnosis is approx. 7 years
- Delay diagnosis and treatment leads to more severe and debilitating disease
- Significant negative on Quality of Life (DLQI)
- Patients often have significant feelings of Shame, Isolation and Stigmatization
- Substantial diminished sexual health

HS Suppurativa

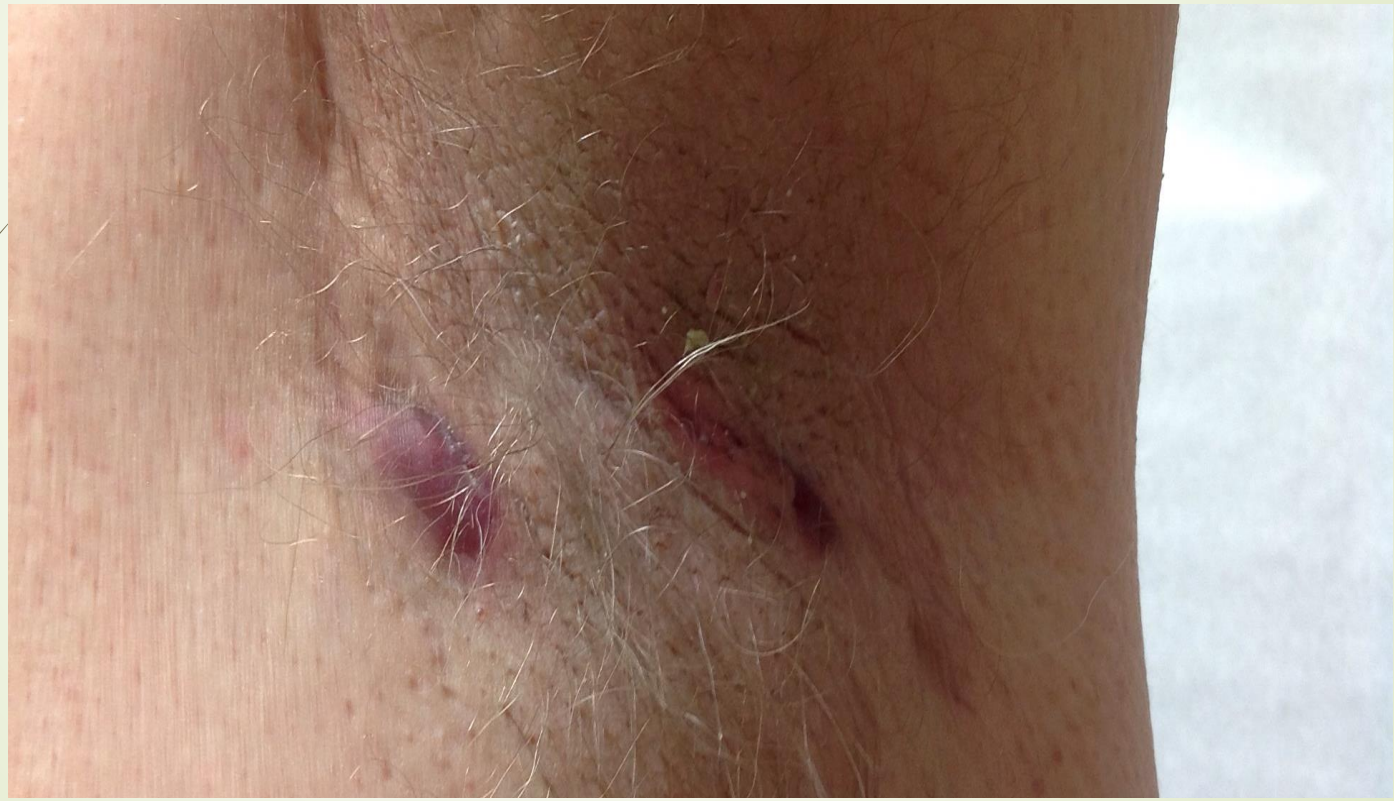
Associated Comorbidities

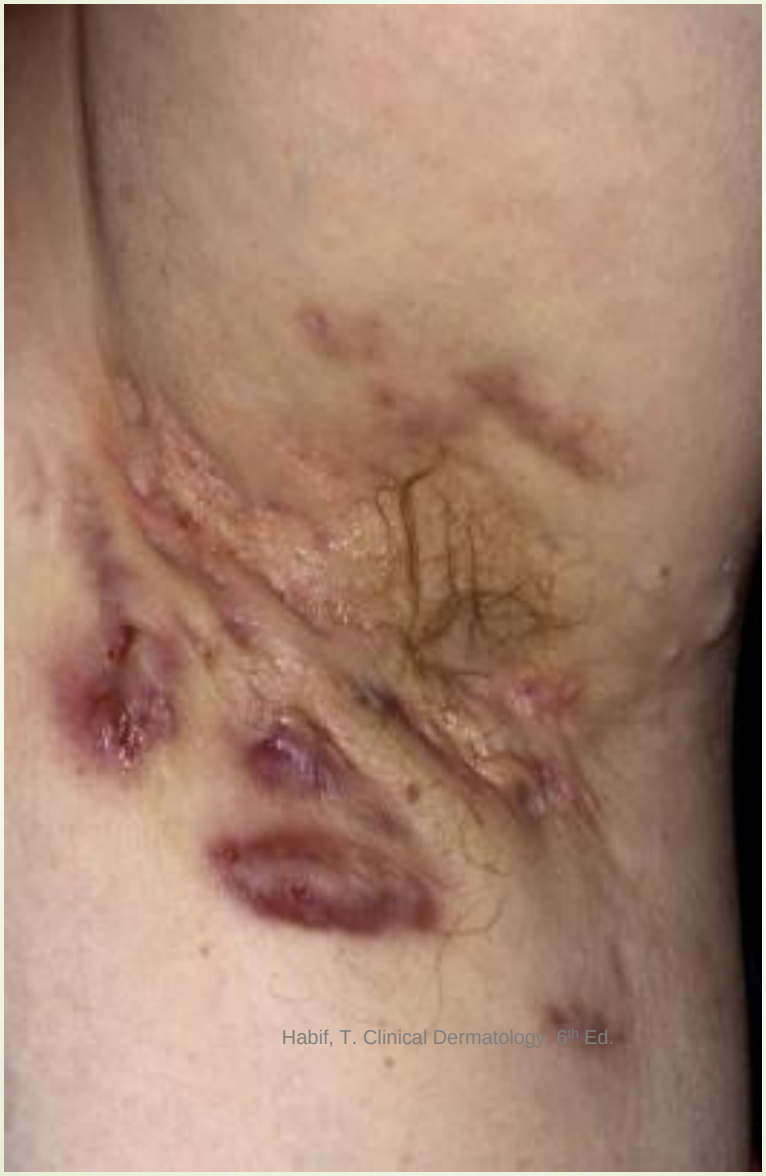
- Dyslipidemia
- Metabolic Syndrome
- Inflammatory bowel disease
- Arthropathies
- Polycystic Ovarian Syndrome
- Psychiatric Disorder and Depression
- Diabetes
- Thyroid Disease
- Lymphoma
- Alcohol and Drug use and Dependence

Treatment for (HS) Hidradenitis Suppurativa

Lifestyle modifications are needed to improve symptoms

- Smoking Cessation
- Weight loss
- Wearing loose fitting clothing
- Friction reduction
- Avoid Topical Irritants
- Dietary Modification





Habif, T. Clinical Dermatology, 6th Ed.

Hidradenitis Suppurativa