CUTANEOUS MANIFESTATIONS OF SYSTEMIC DISEASES

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Contents:

- Introduction:
  - ConnectiveTissue Diseases
    - Lupus
    - Dermatomyositis
    - Scleroderma
  - Endocrinological Diseases
    - Diabetes Mellitus
    - Hyperthyrodism
    - Hypothyeodism
    - Cushing's Syndrome
    - Addison's disease

- GIT:
  - Chronic Liver Disease (CLD)
  - Acrodermatitis entropathica
  - Peutz Jeghers Syndrome
  - Pyoderma Gangrenosum
  - Hereditary hemaorrghic Telangectasia
- Metabolic:
  - Hyperlipidemia

- Neurocutaneous diseases
  1. Neurofibromatosis
  2. Tuberous Sclerosis
- Behcet's Syndrome
  - Nutritional deficiency disorders
    - Scurvy
    - Pellagra
- Causes of Generalized pruritus without skin lesions

- Cutaneous manifestations of internal malignancy.
  - Acanthosis Nigricans
  - Dermatomyositis
- Nails:
  - Clubbing
  - Koilonychia
  - Splinter haemorrhages
- When to do HIV testing for skin Disease ?

- Introduction:
  - Skin is the “Gate of the Body”
  - Detection of Systemic disease or internal malignancy through skin presentation.
  - Systemic diseases associated with skin diseases

- SLE:
  - Facial Photosensitivity
  - Butterfly Erythema
  - Multisystem disease (Renal, CNS, Cardic, Blood, etc….)
  - Positive ANA and anti-ds DNA

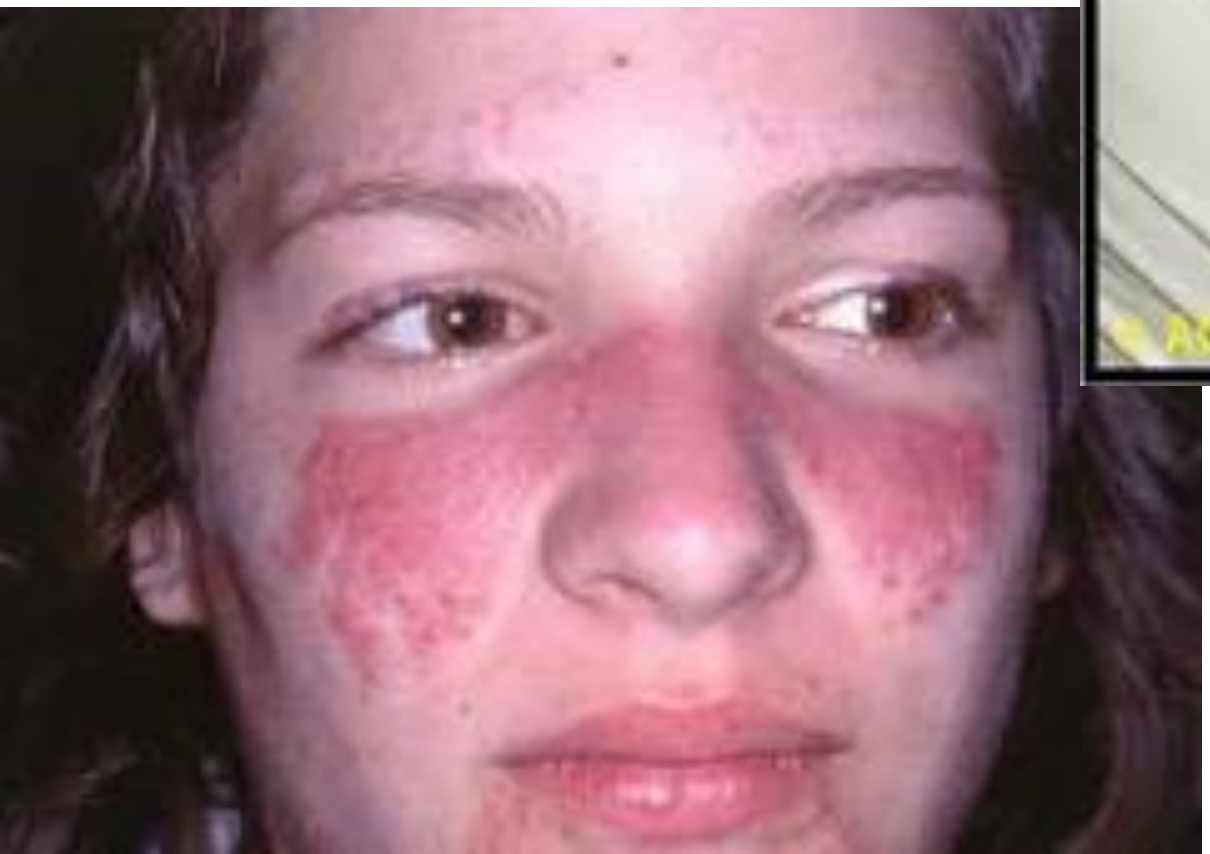
Discoid Lupus (DLE)

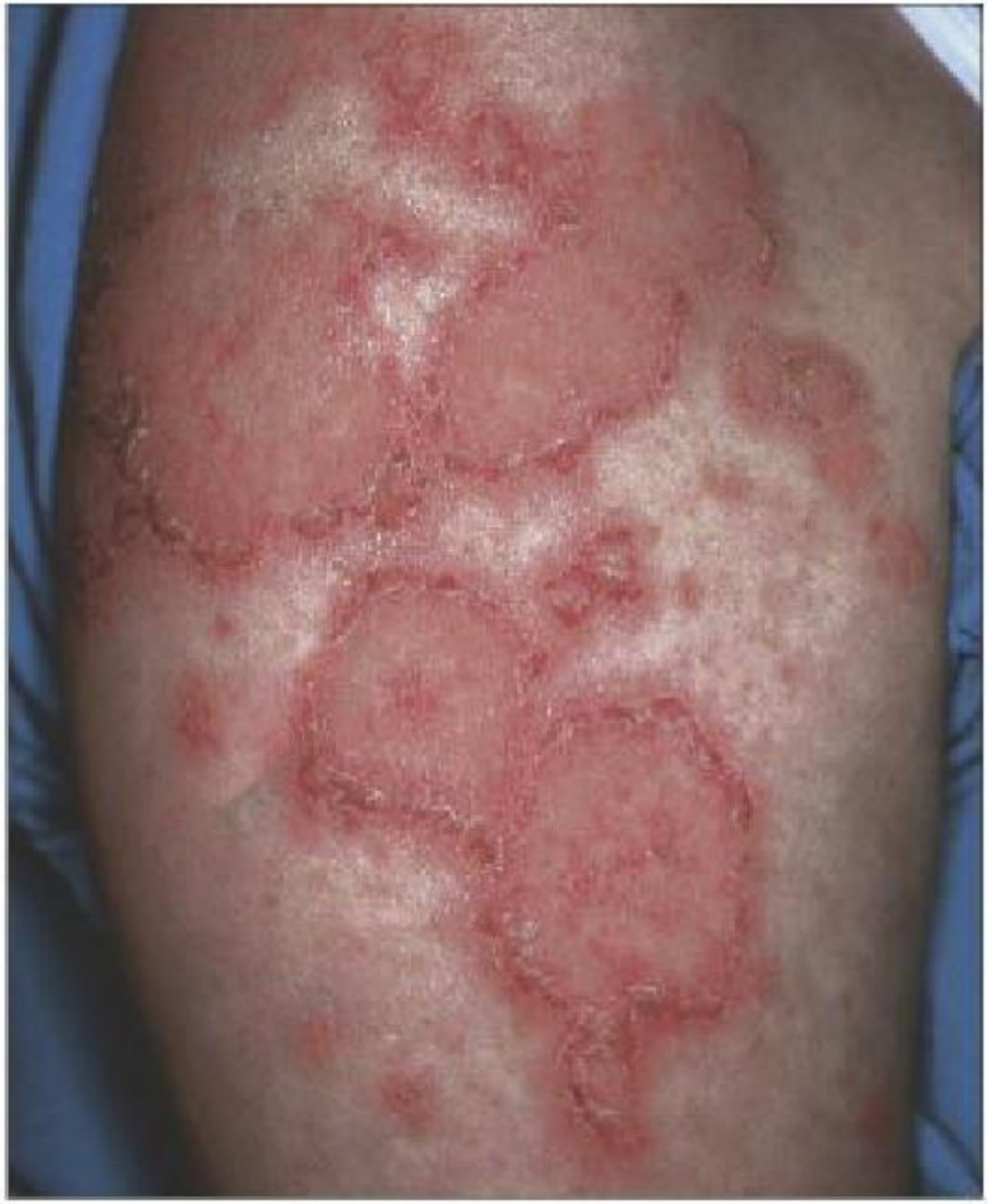
- round scarring lesions on light exposed areas
- No Systemic involvement

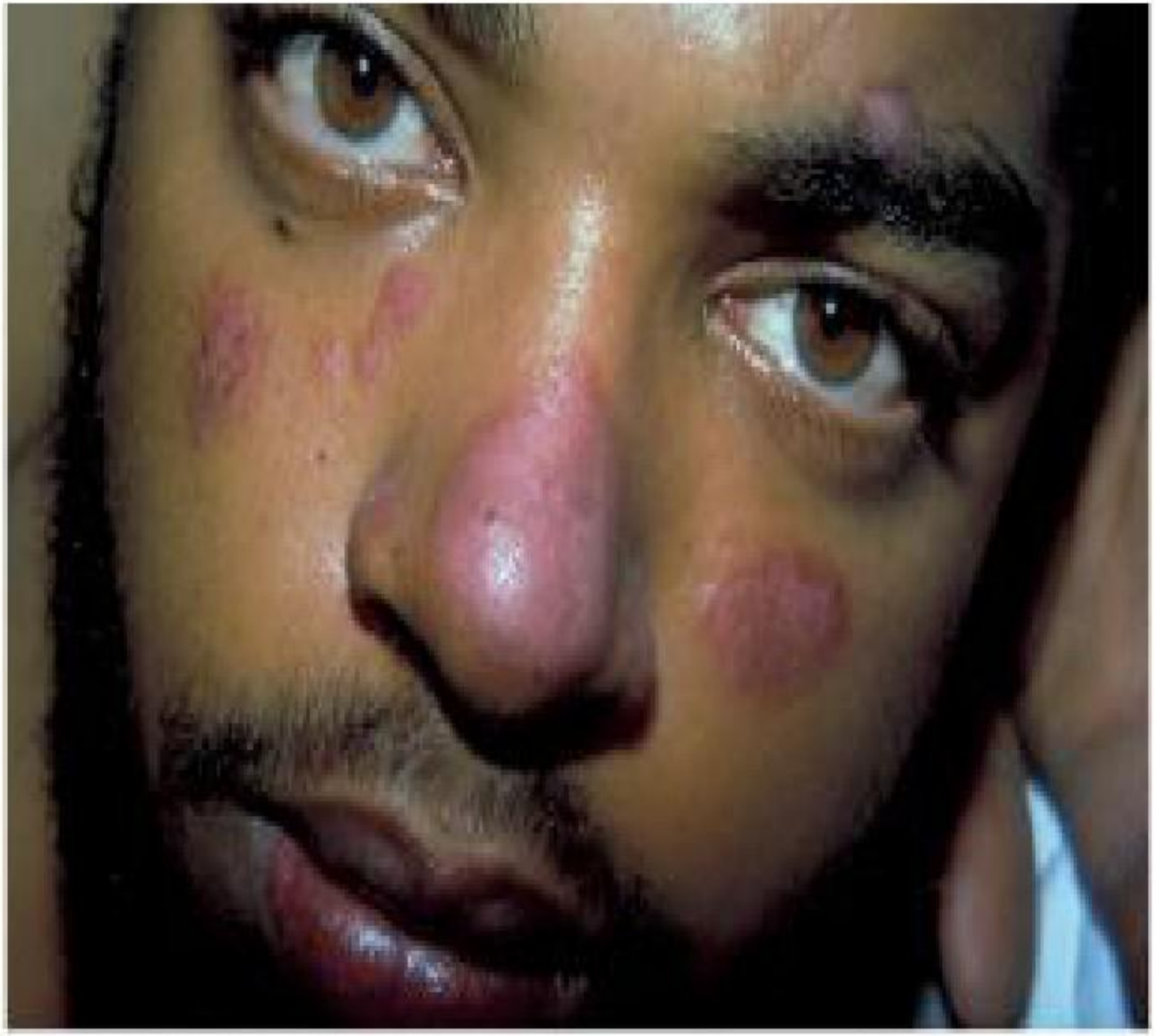
- Subacute Cutaneous Lupus (SCLE)
  - papulosqamous or annular presentation
  - Photosensitivity
  - Dose not cause scarring
  - Usually ANA negative but anti Ro positive.

Neonatal Lupus:

- Appears in the first month in a photo-distribution
- Patterns : Papulosqamous and annular
- Congenital heart block (complete & permanent) usually needs pacemaker
- anti Ro positive







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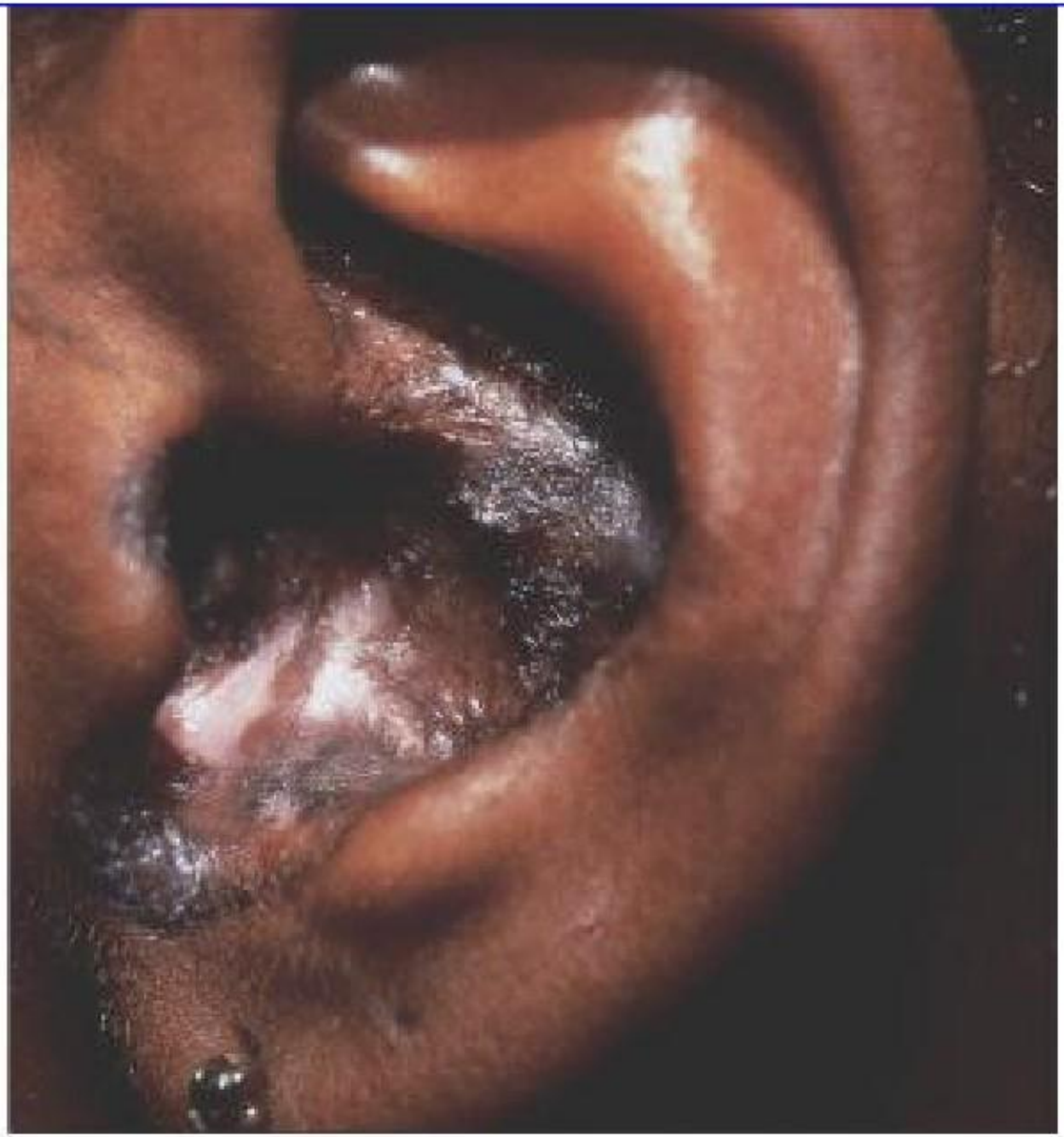

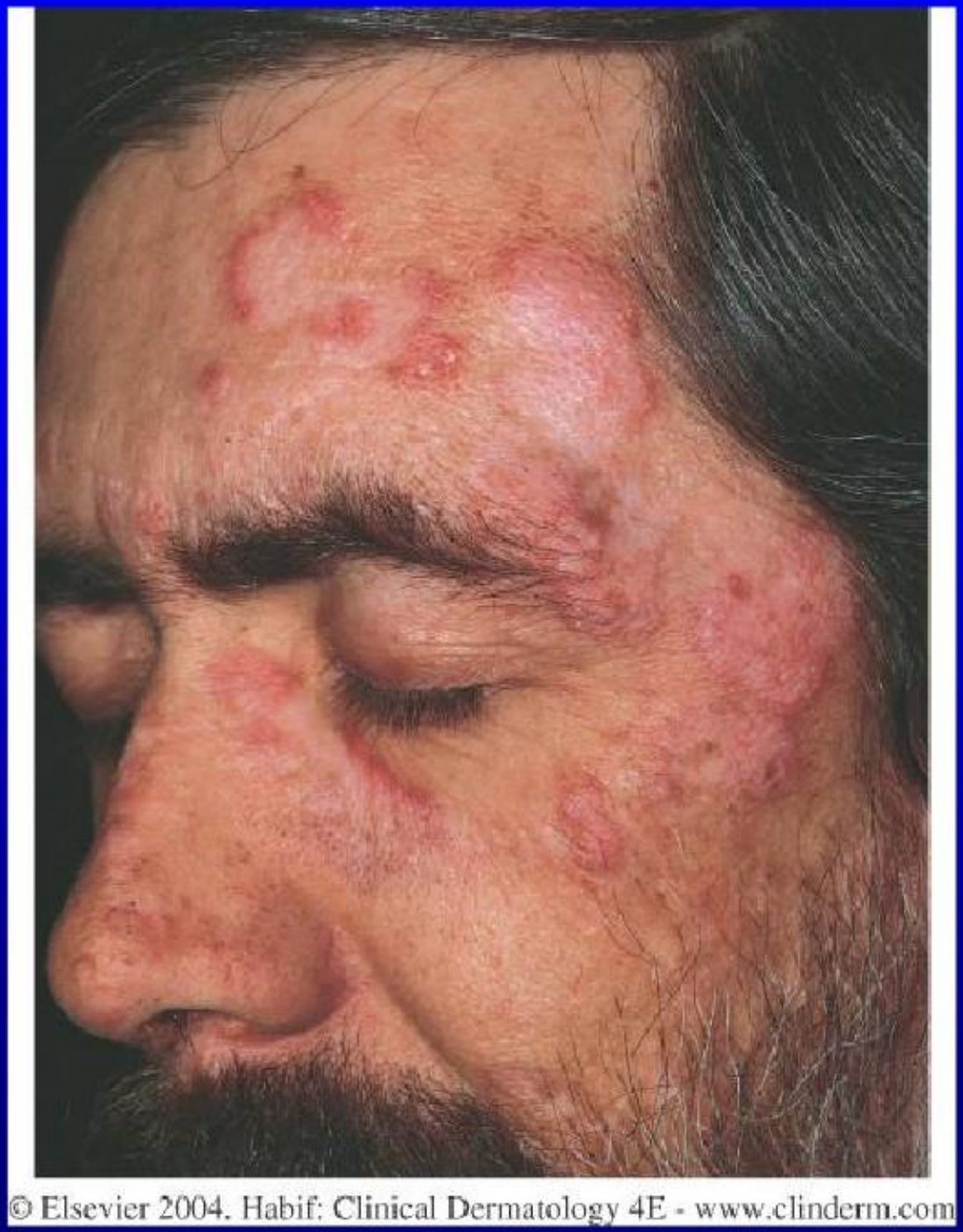

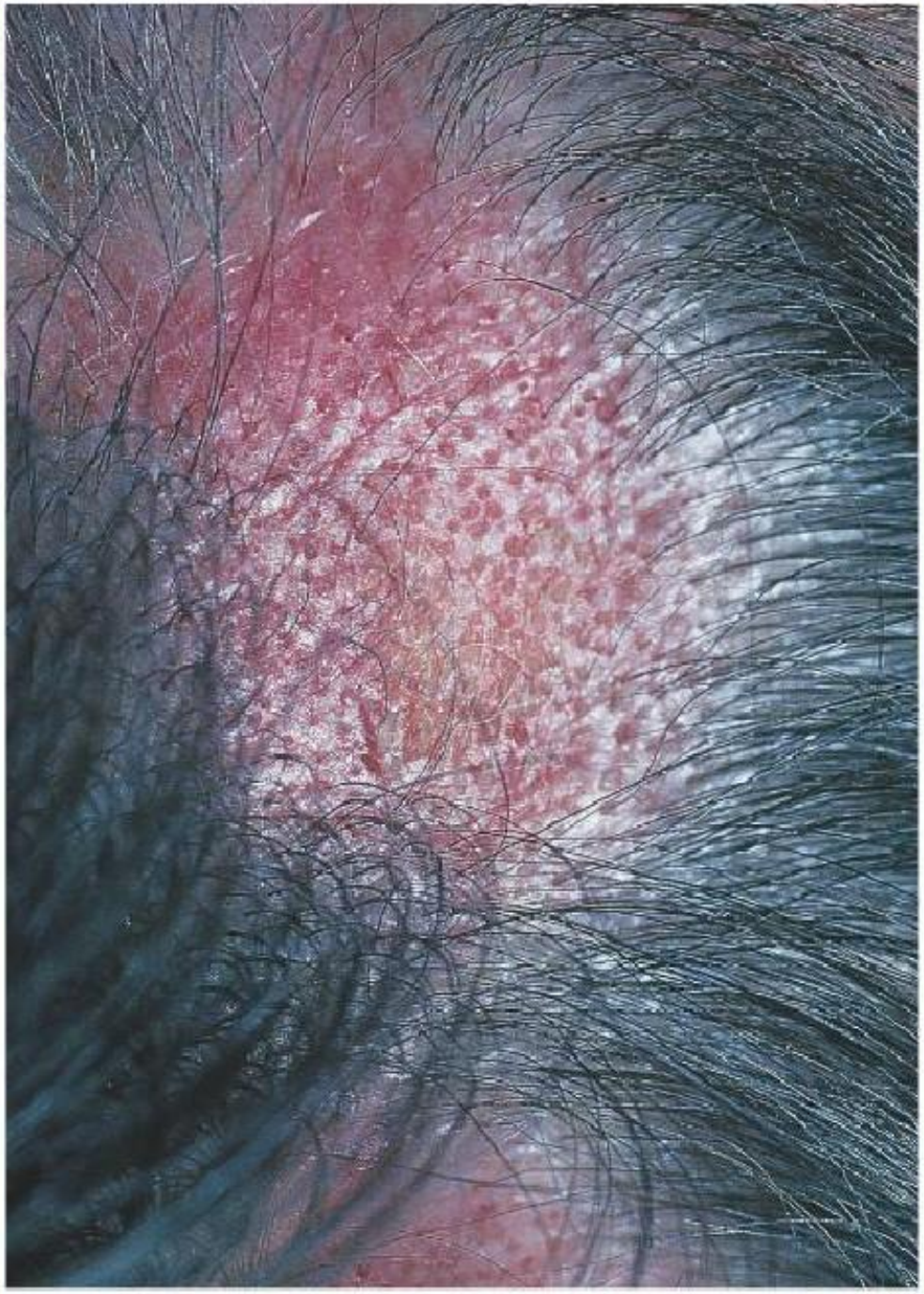

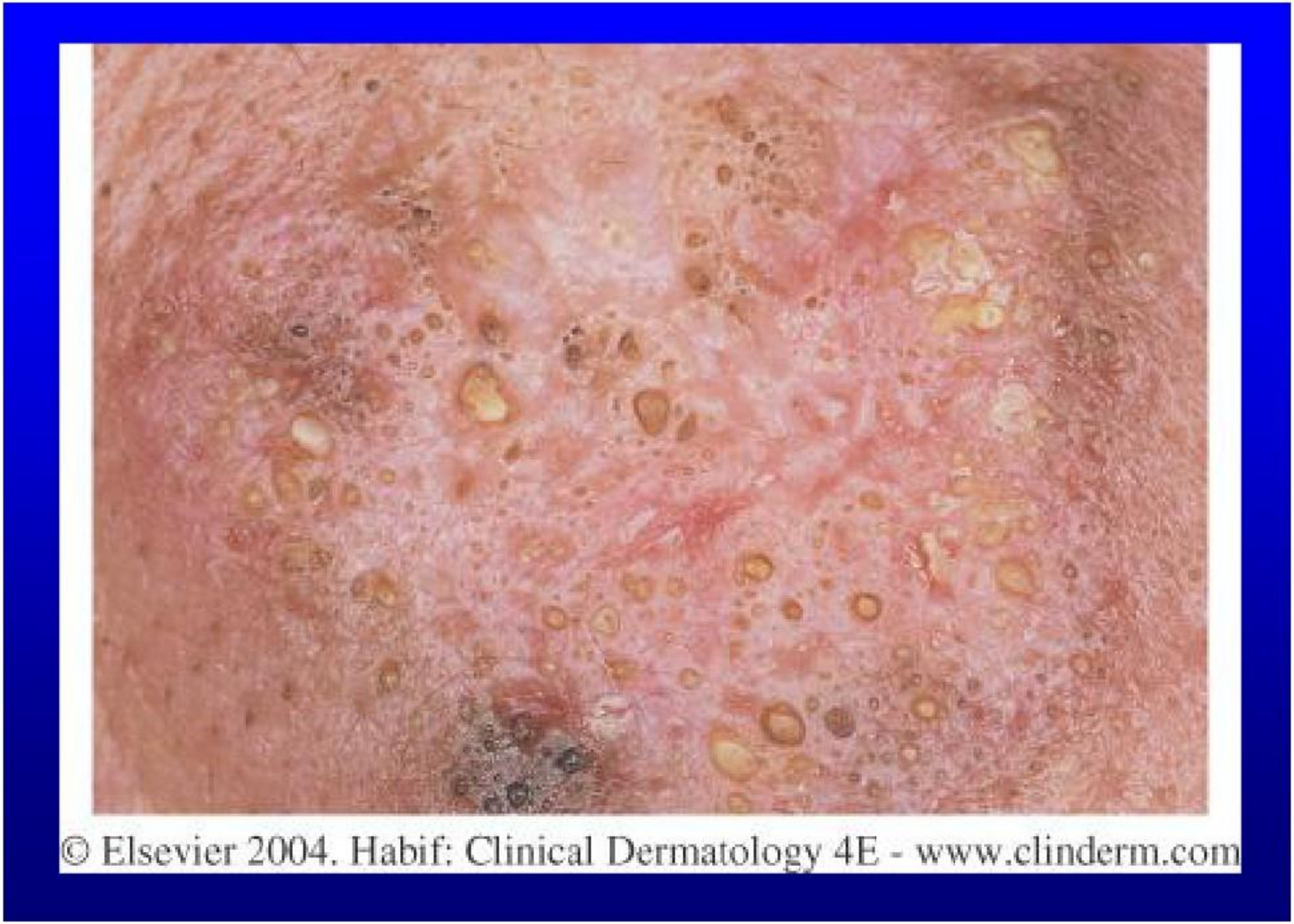

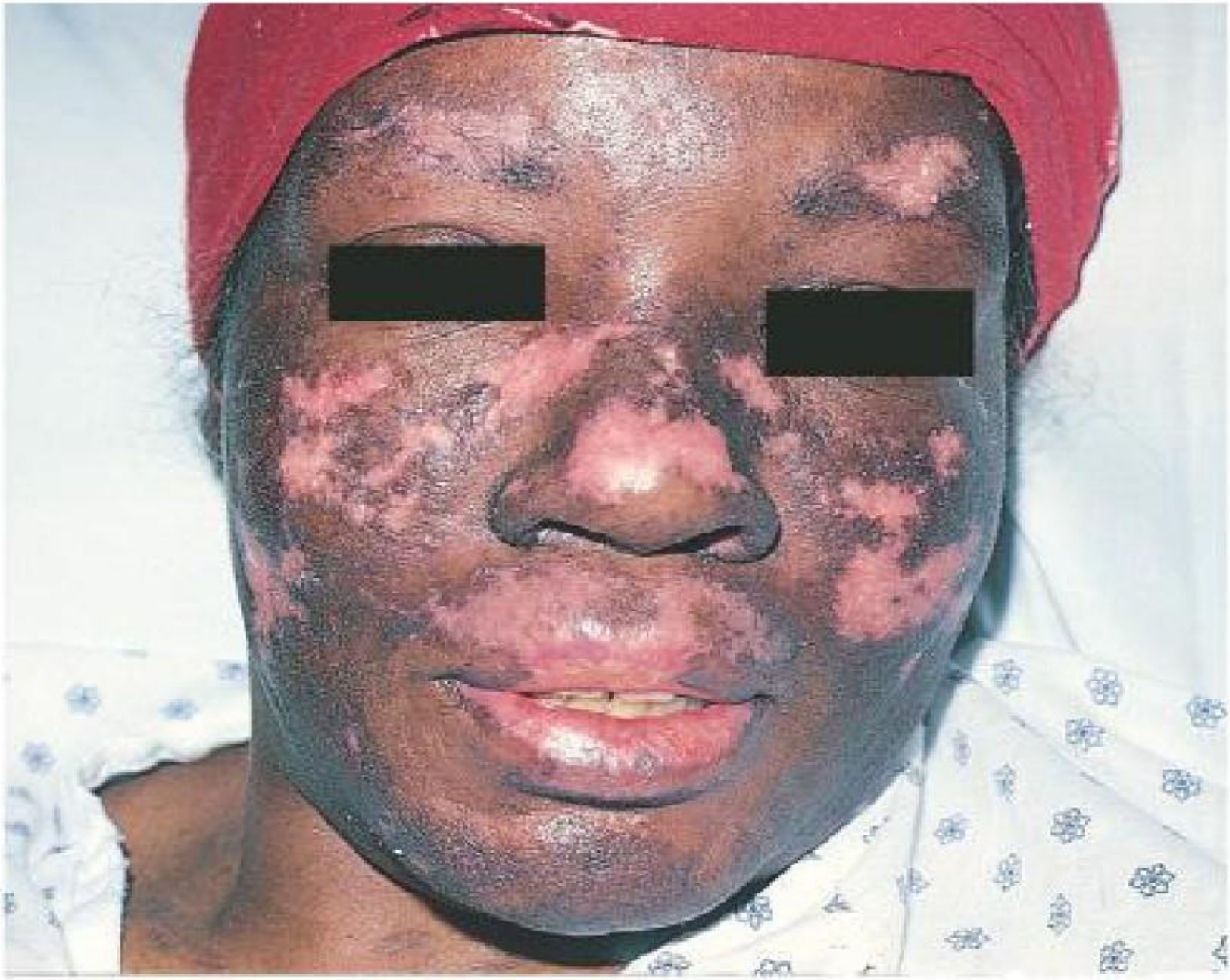

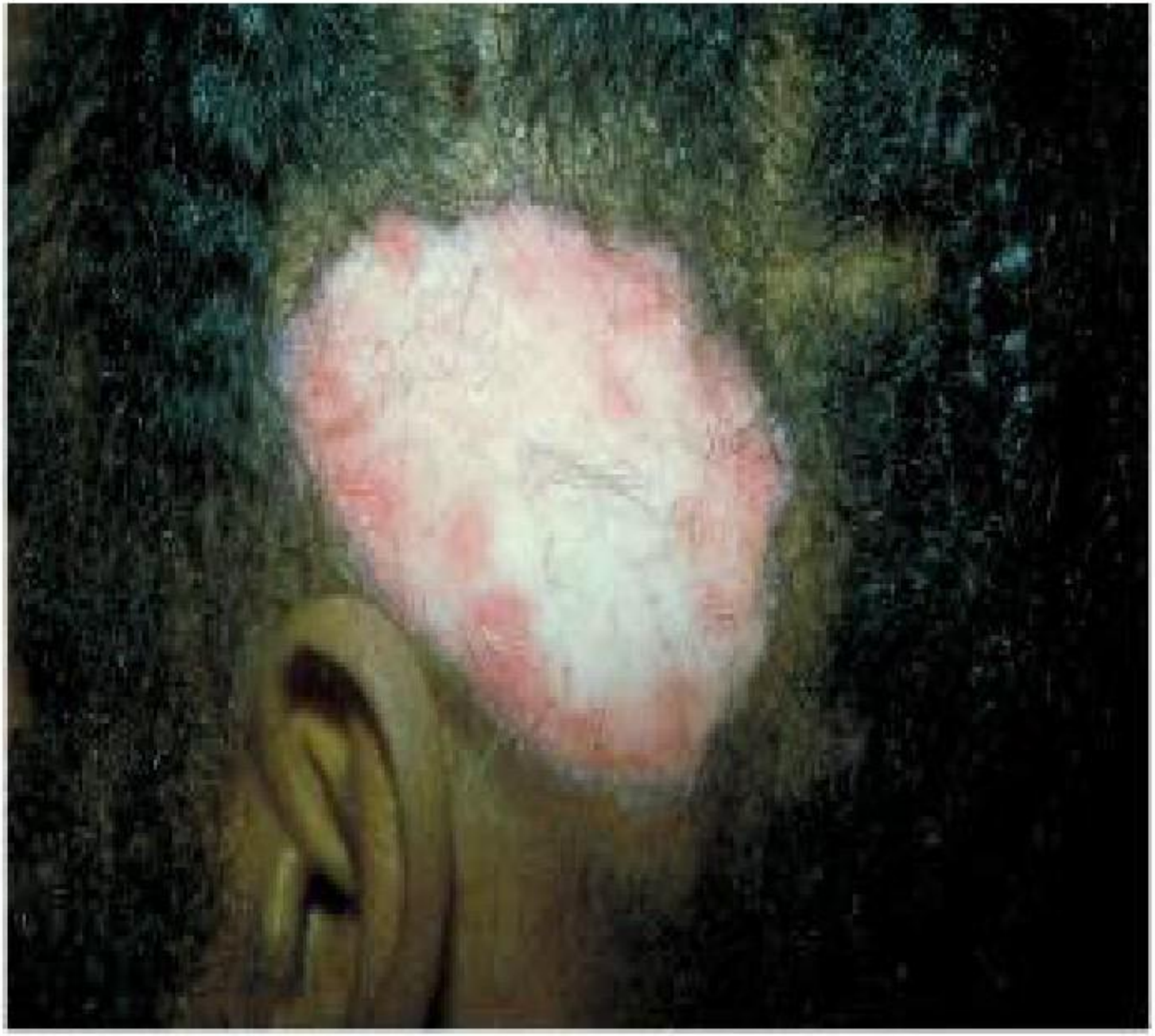

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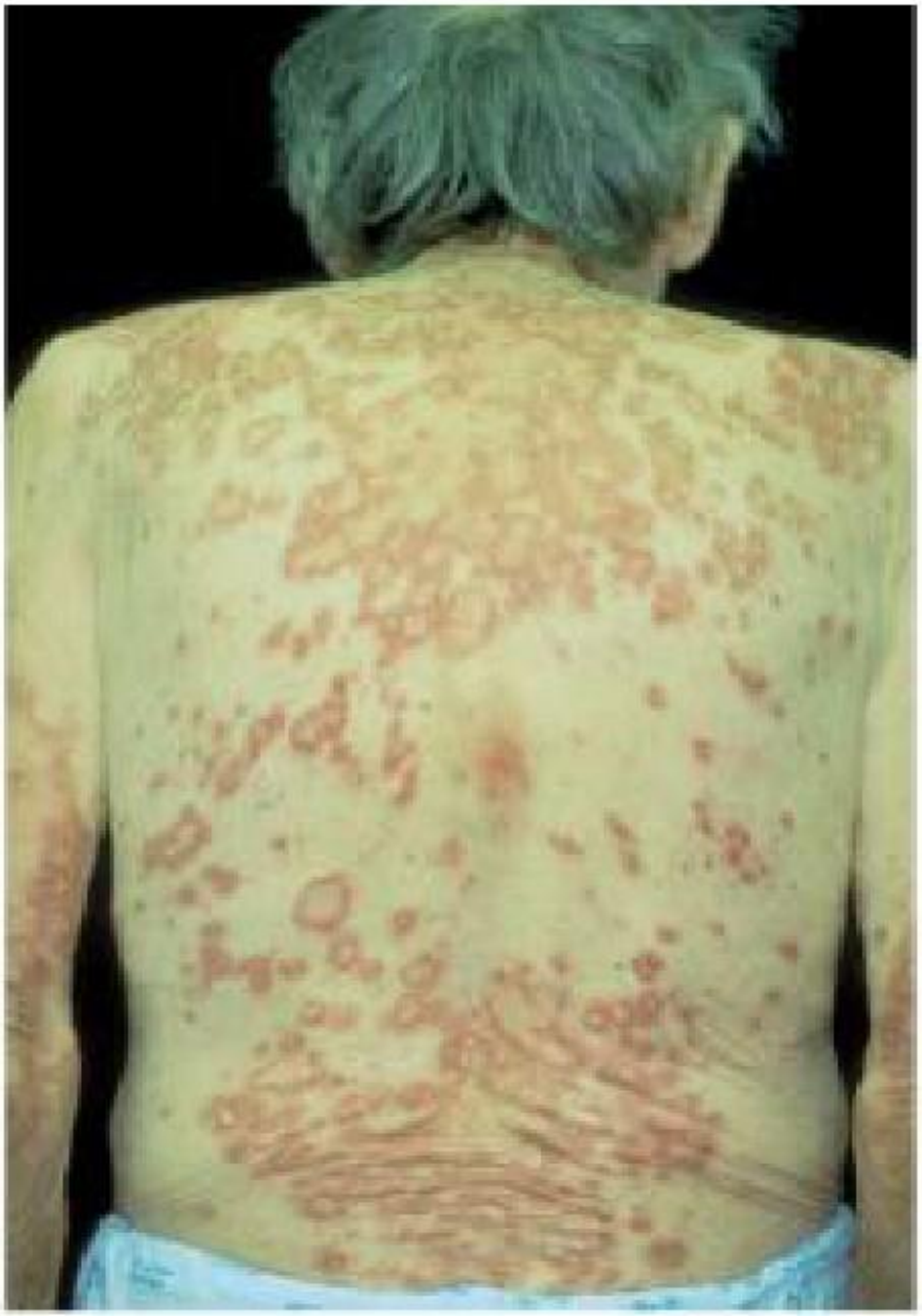

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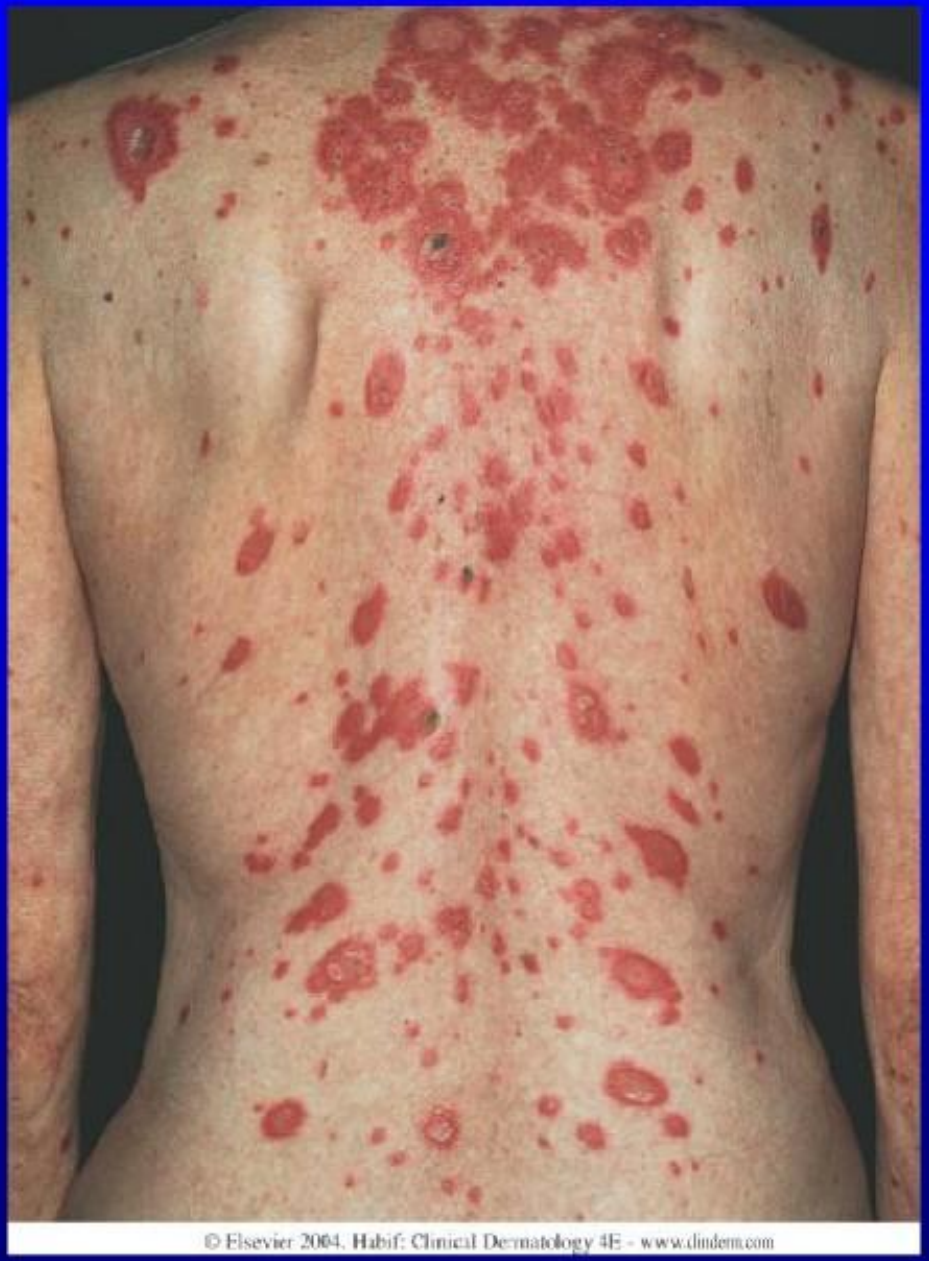
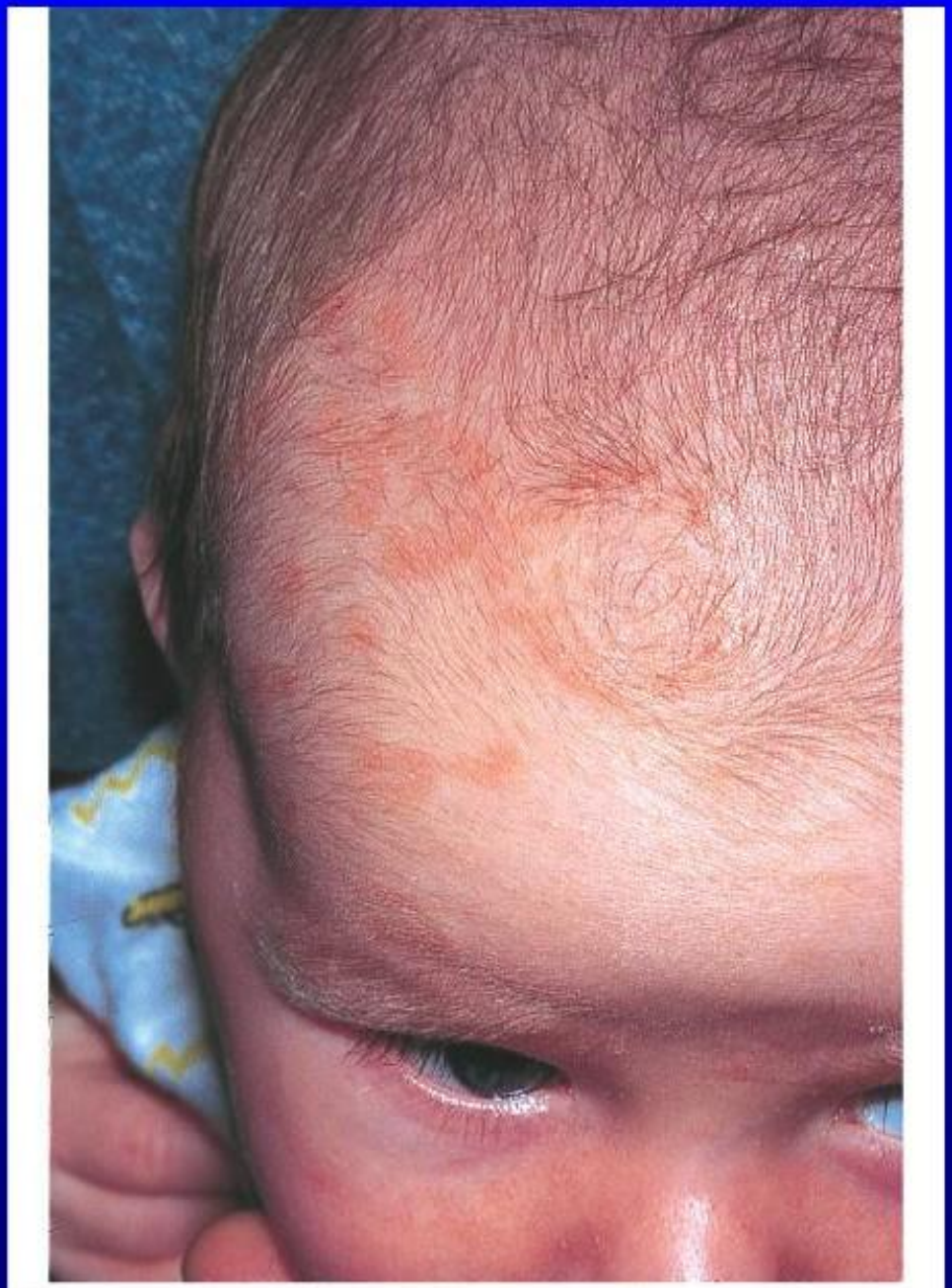
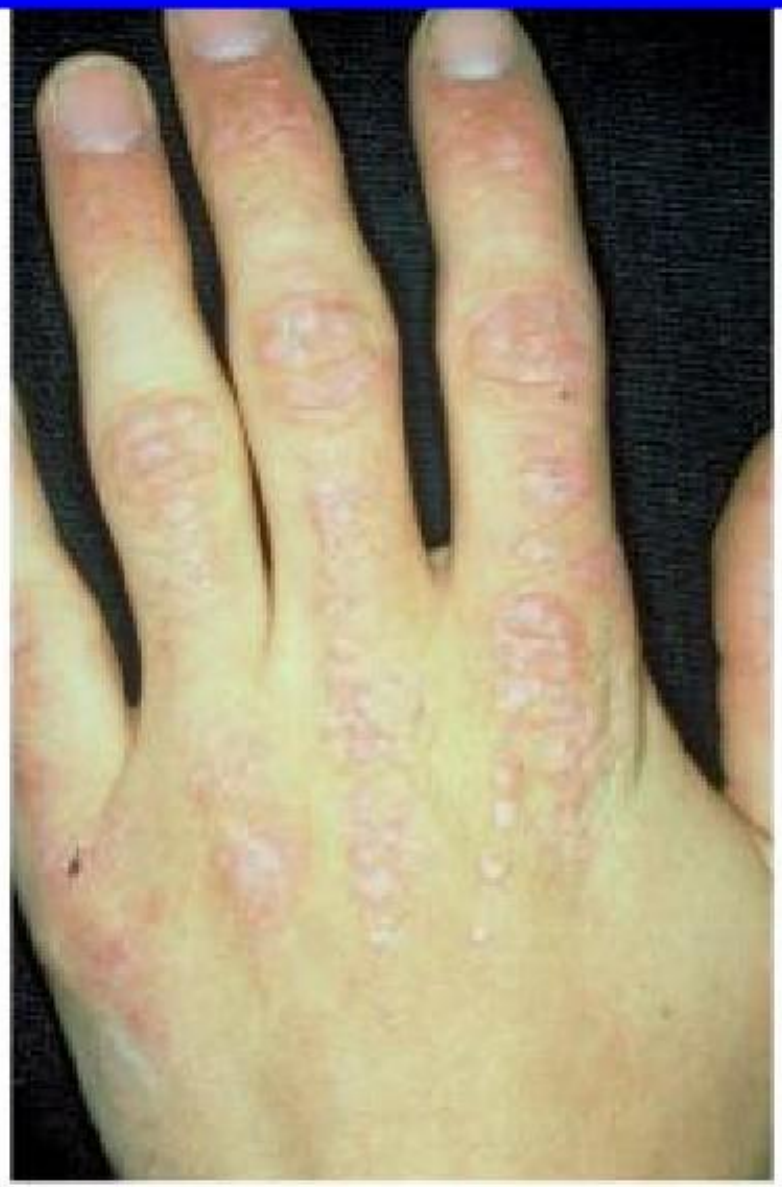
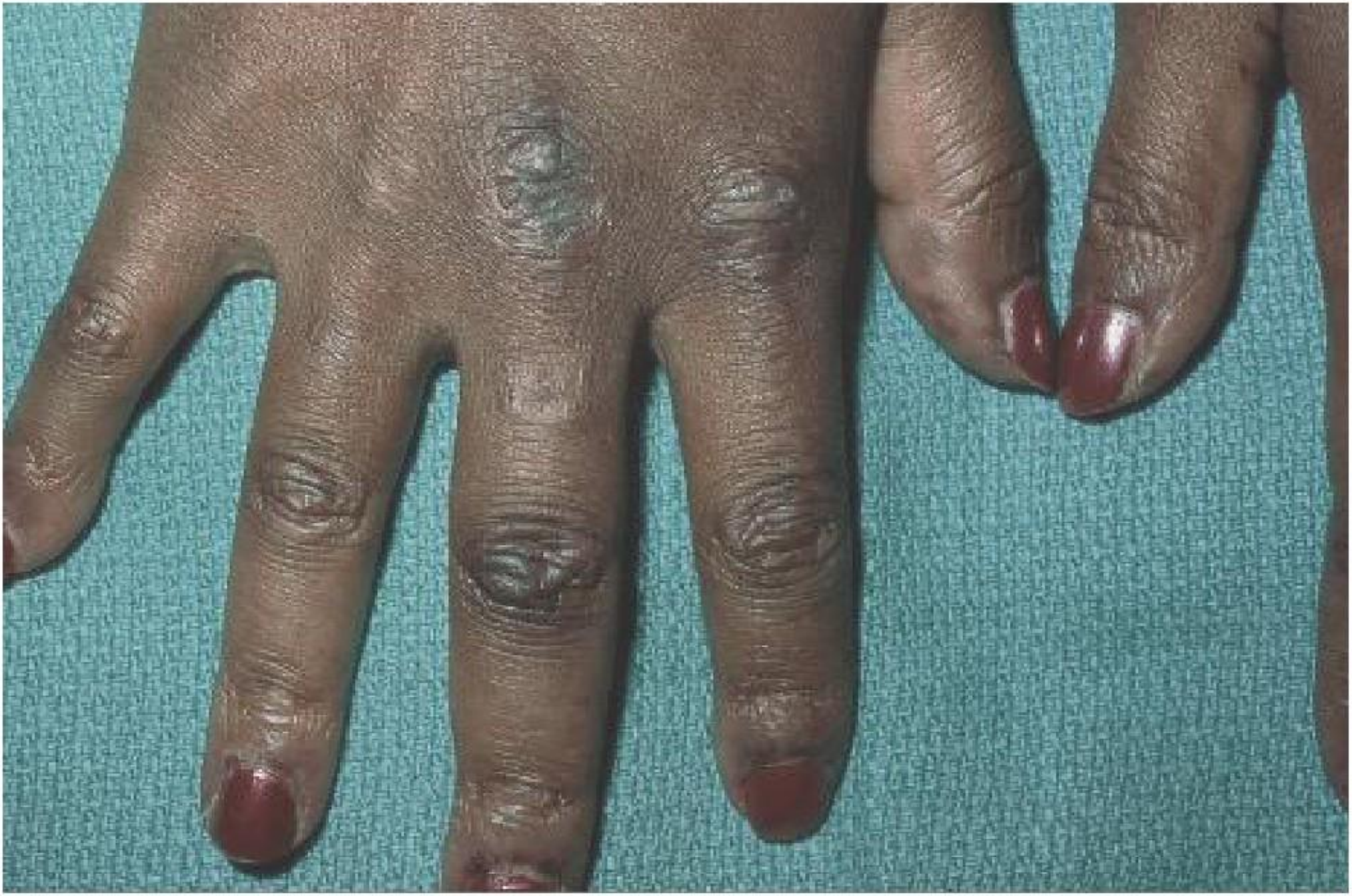




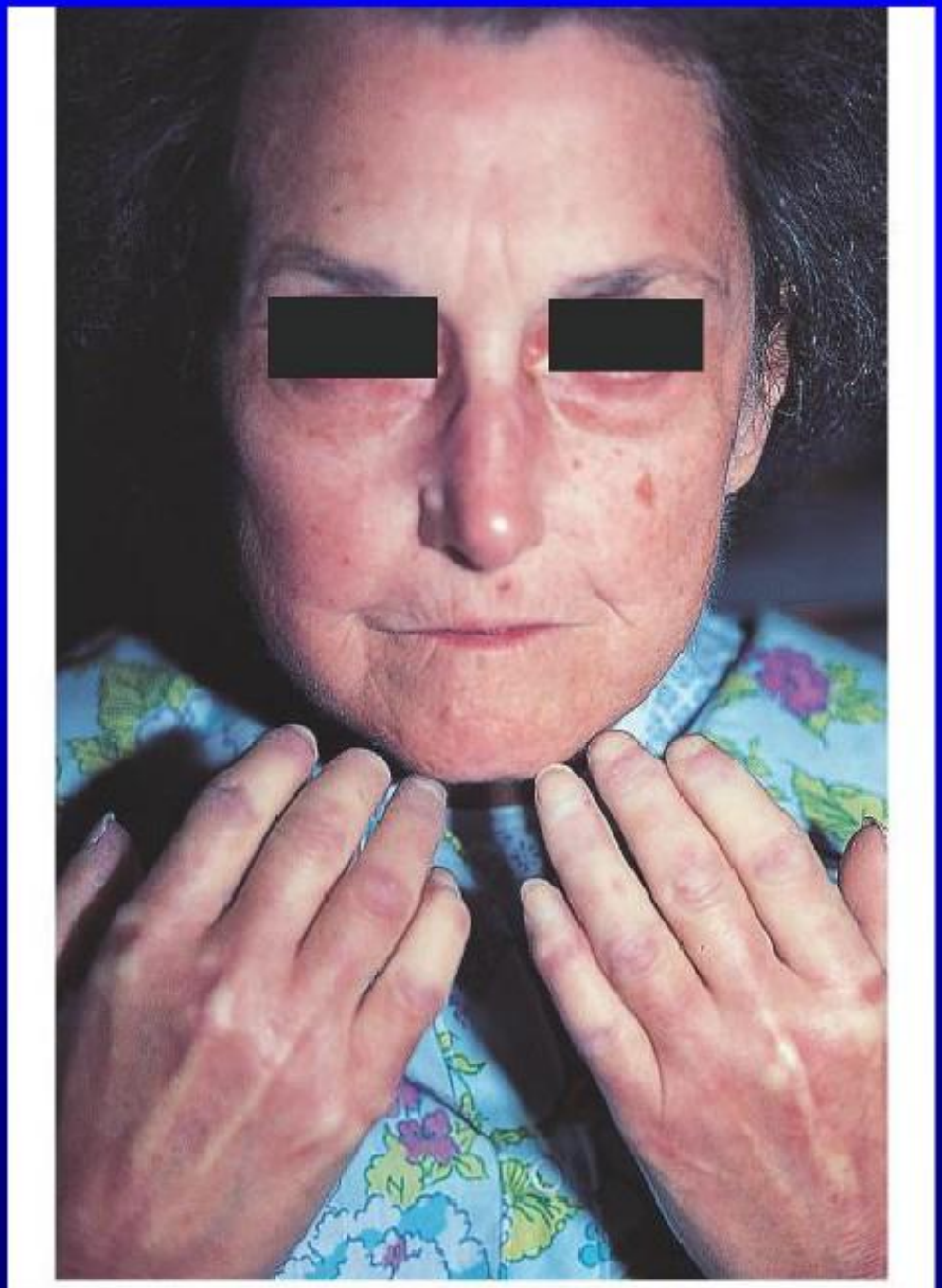
- Drug - Induced Lupus:
  - Cause:
    - Procainamide
    - Hydralazine
    - Others
  - Antihistone positive

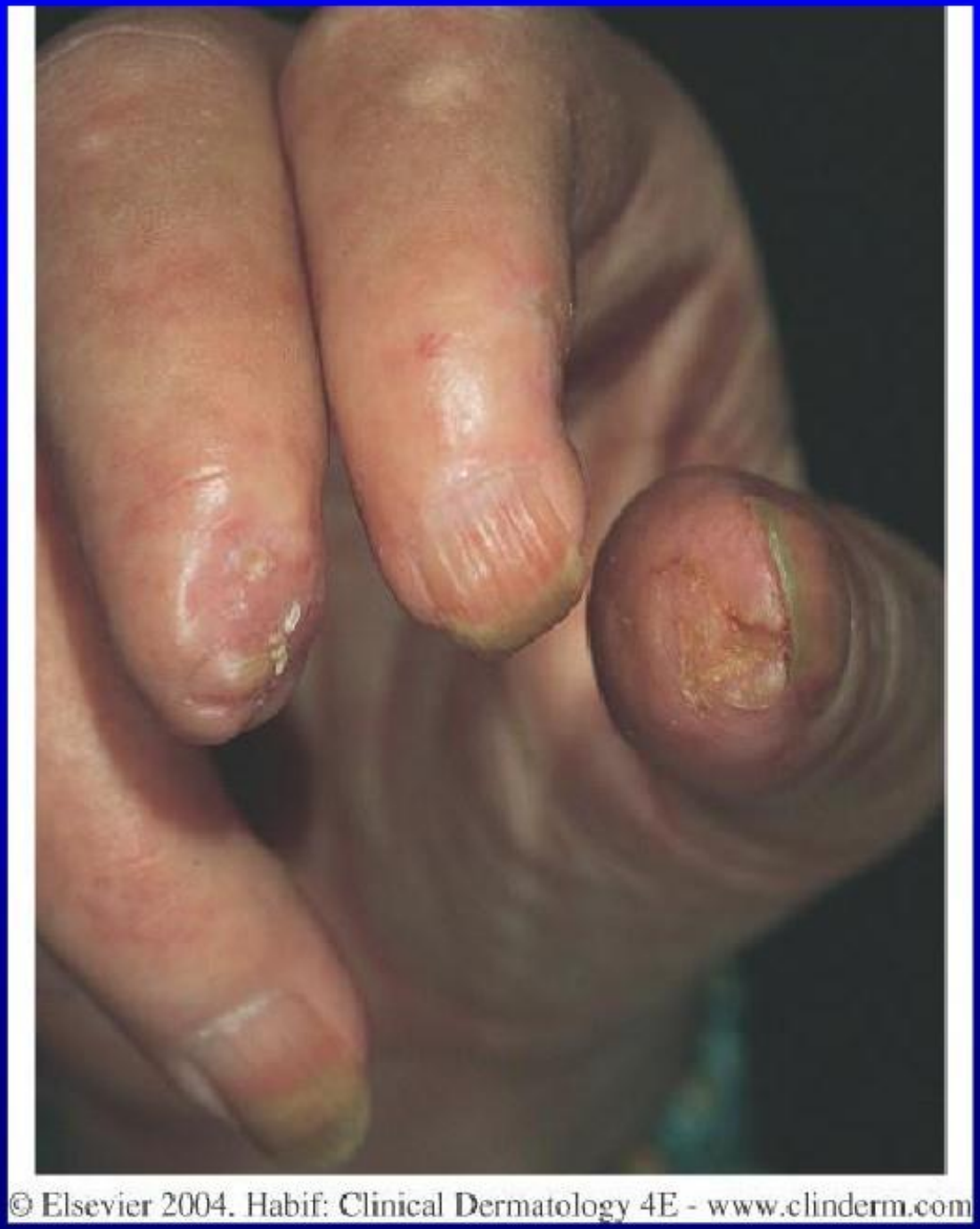
- Dermatomyositis (Skin Rash + Muscle Weakness):
  - Heliotrope : Violeceous color over the upper eyelids
  - Gottoron's papules: Flat- topped violaceous papules over knuckles of hands
  - Calcifications especially in kids
  - Bilateral proximal muscle weakness (with high CPK, Positive EMG and Muscle biopsy)
  - In adults (especially over 50 yrs) associated with internal malignancy (e.g. GI, Prostrate, ovary & breast)

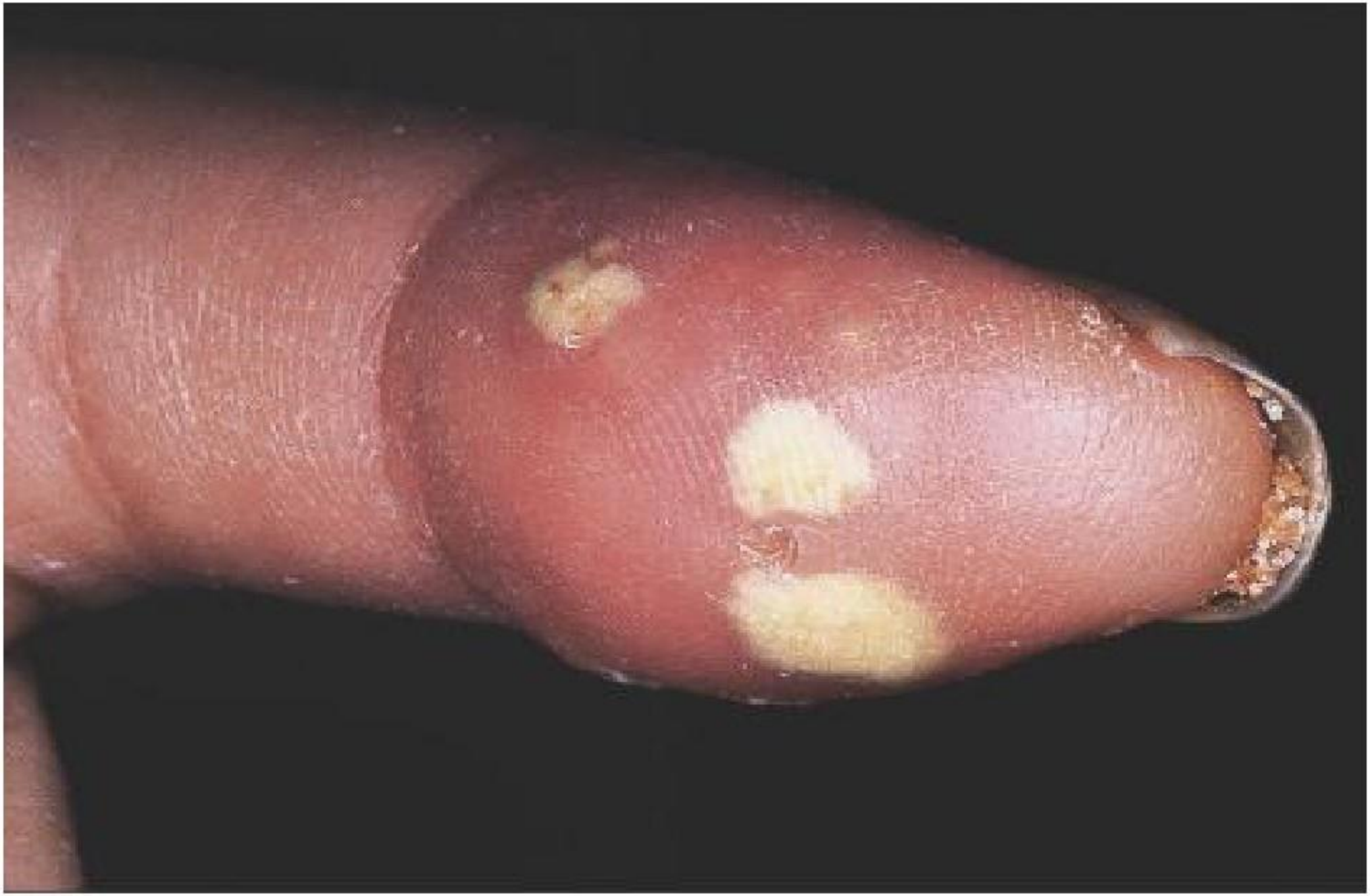




- Scleroderma (Systemic Sclerosis)
  - Thickened & tight skin
  - Sclerodactyly
  - Face: loss of forehead lines
  - beaked nose, small mouth, radial furrowing around the mouth)
  - Telangectasia and calcification
  - Systemic involvement:
    - Lung, GI, Kidneys
    - Positive anti scl-70

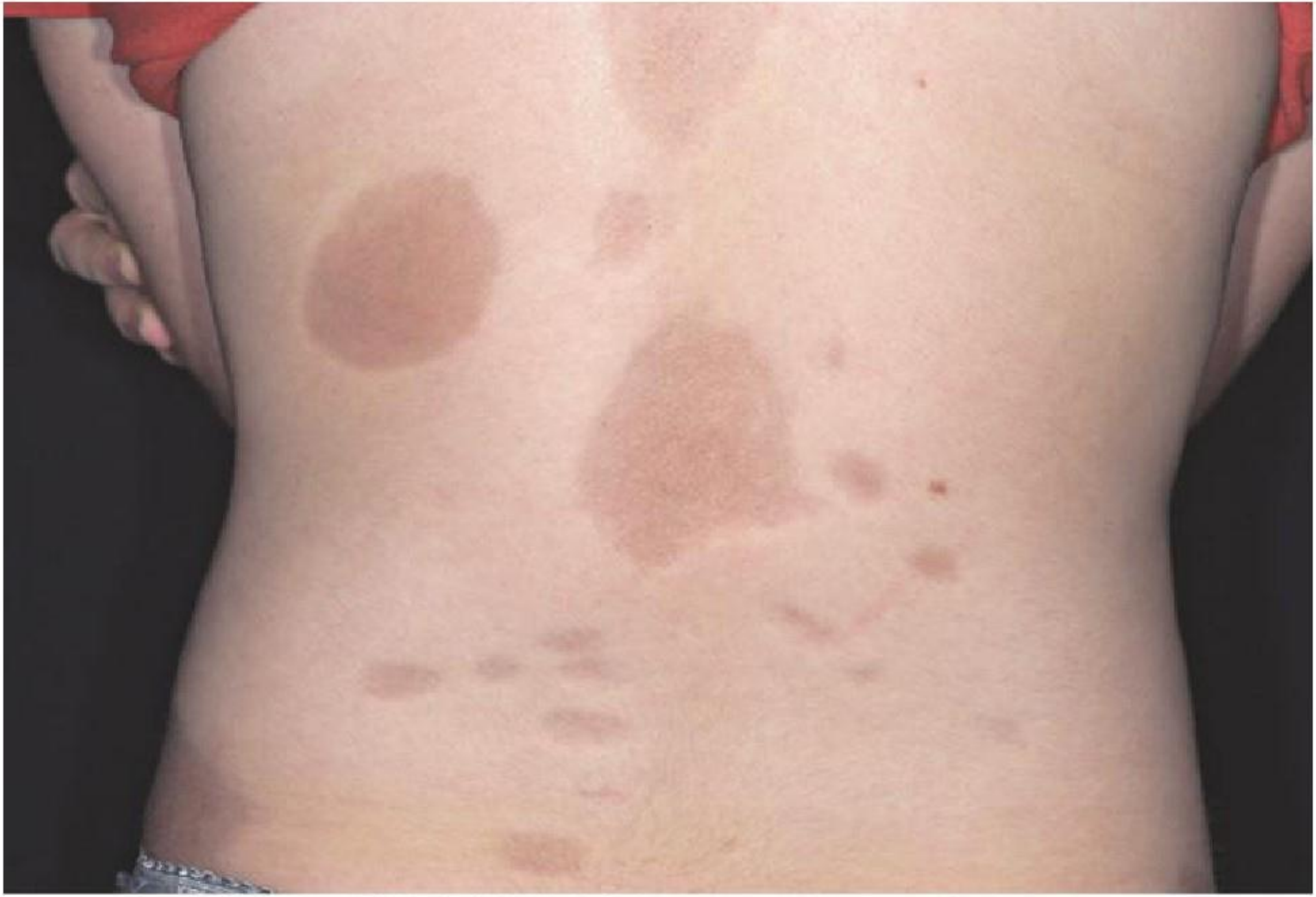


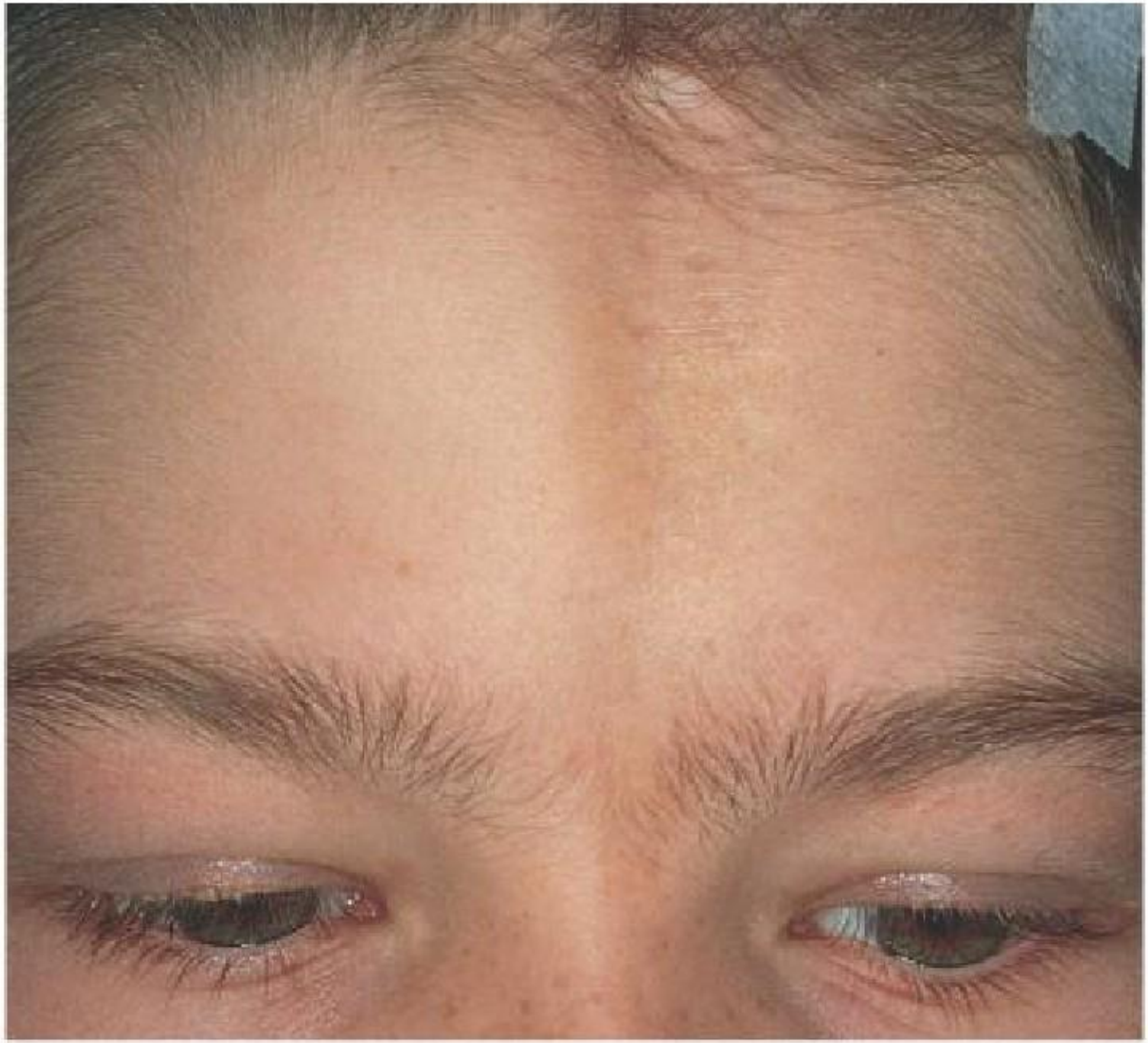




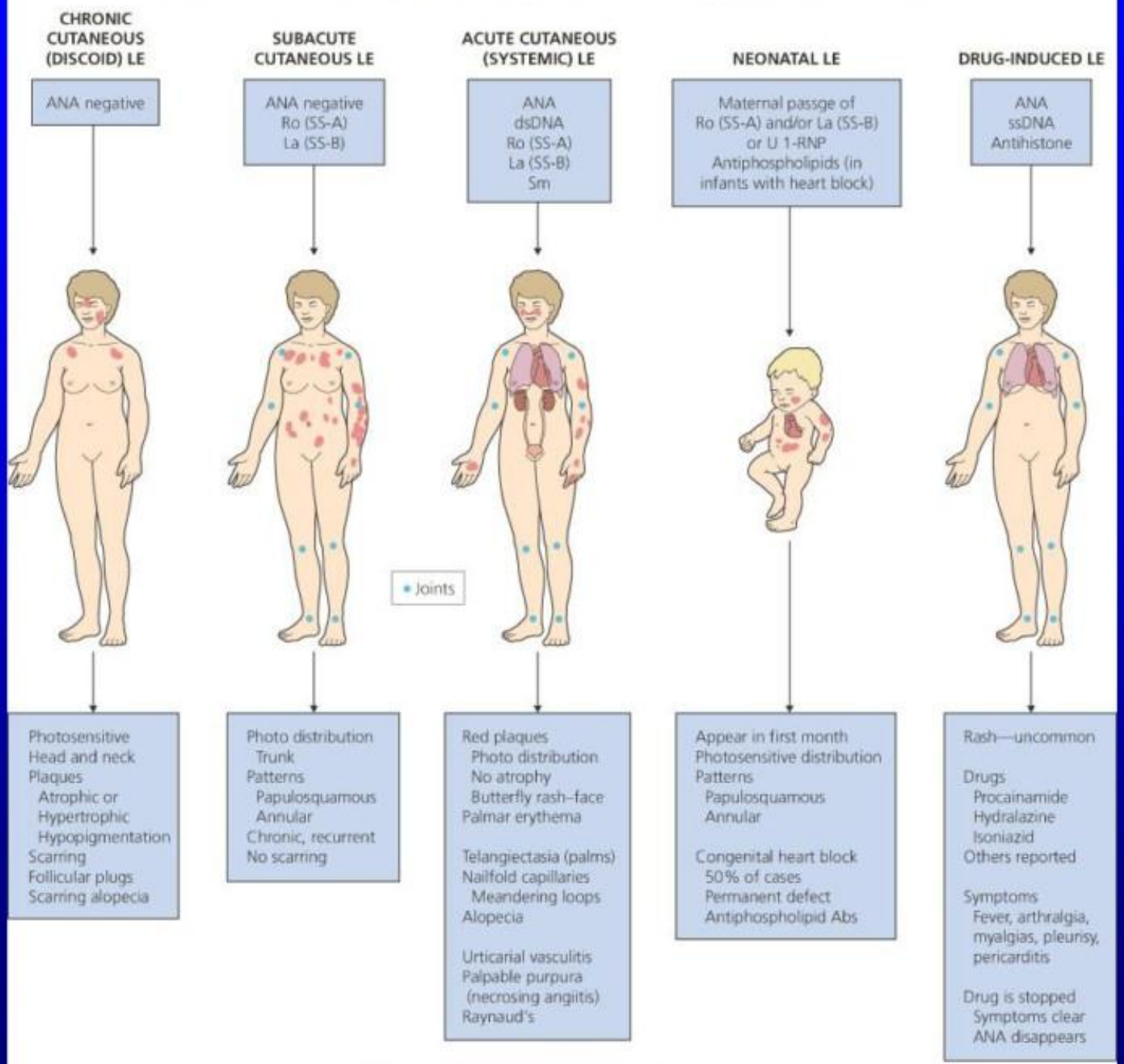
- CREST (milder variant of scleroderma)
  - C=Calcification
  - R =Raynand's
  - E =Eosopheagal dysfunction
  - S= Sclerodactasia
  - T=Telangectasia
  - Positive anti- centromere
  - Less systemic involvement.

- Morphea:
  - Localized scleroderma without systemic involvement.
    - Firm,white patch of skin surrounded by violaceous ring
- En coup de sabre
  - Linear scleroderma on the scalp and face which may give scarring alopecia + it may affect muscle or even bone





OVERVIEW OF LUPUS SYNDROMES: AUTOANTIBODY PROFILES AND CUTANEOUS MANIFESTATIONS



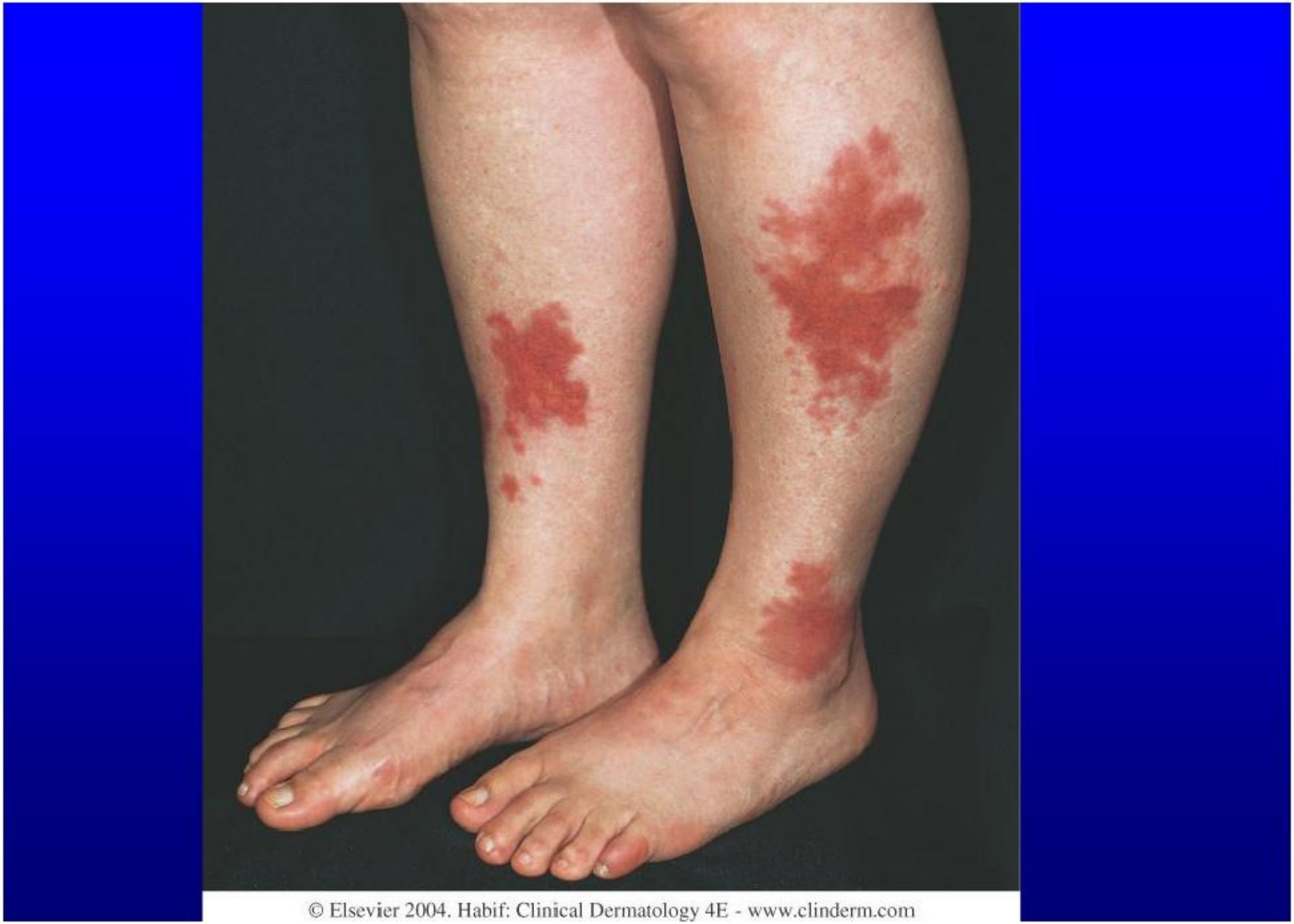
Antibody testing for CTD (table)

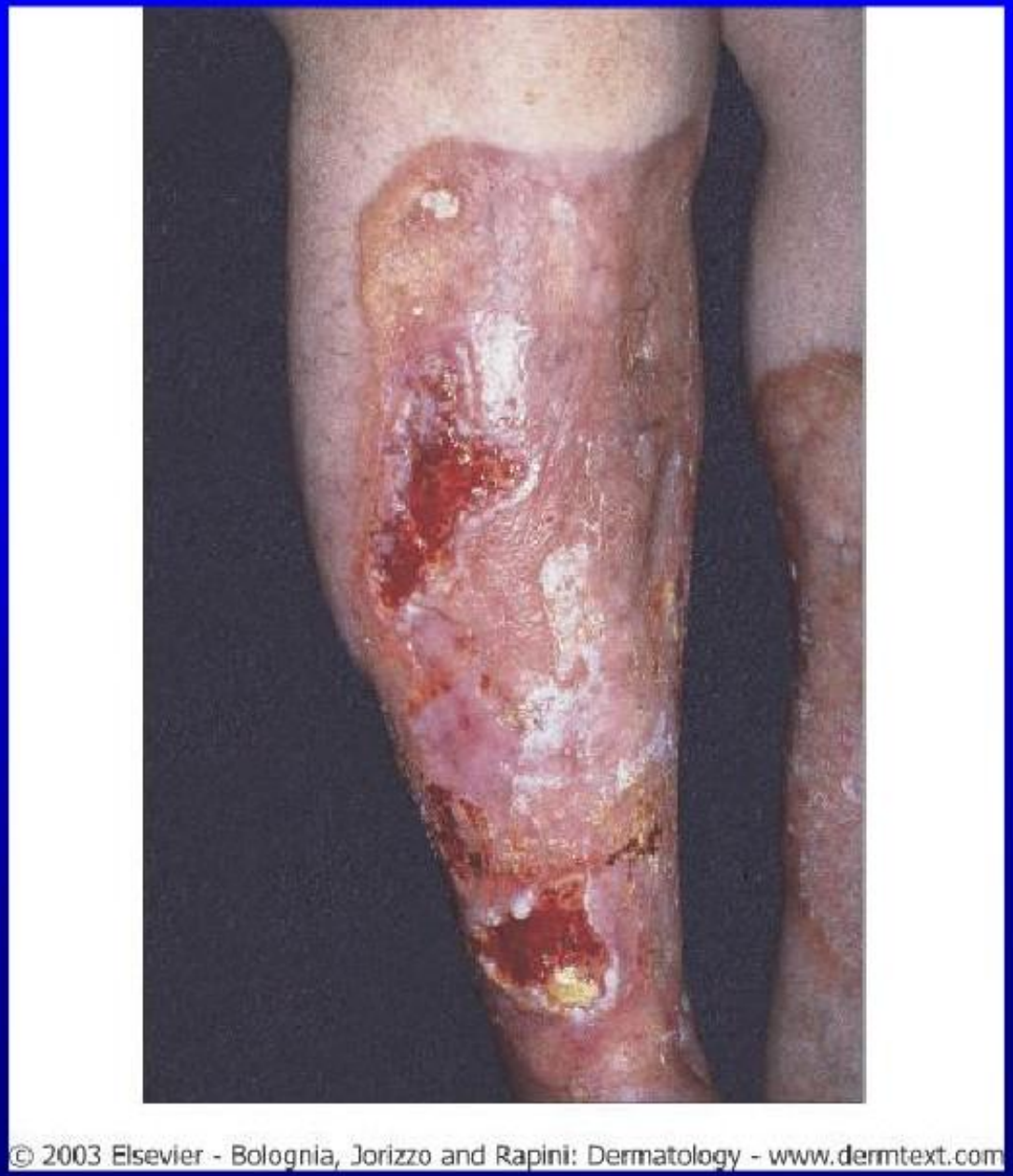
Antibody	Clinical significance
ANA	Screening for SLE and other CTD
Anti-Centromere	Marker for CREST
Anti-histone	Marker for Drug-Induced Lupus
Anti-Smith	Specific for SLE
Anti - RNP	For MCTD
Anti - Ro	Neonatal Lupus, SCLE
Scl - 70 antibody	For Scleroderma
Anti ds- DNA	For SLE

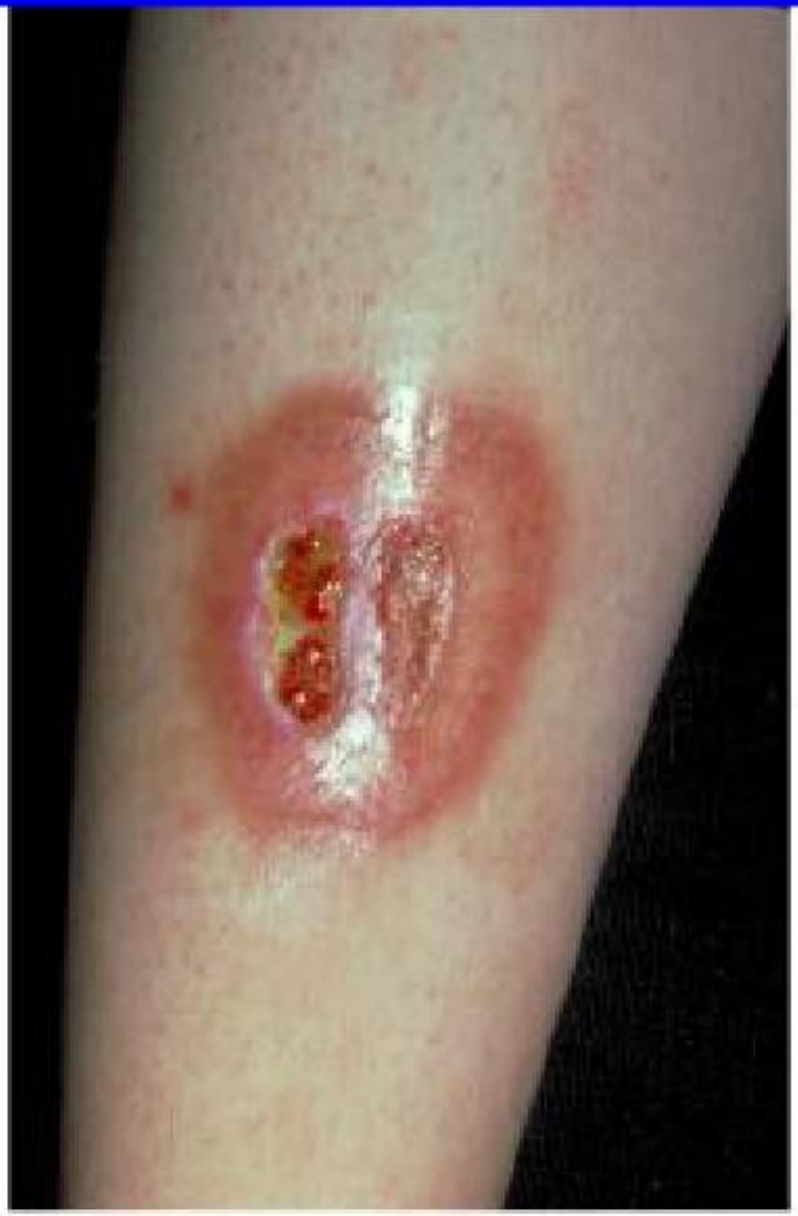
Endocrine :

- Diabetes
  - Necrobiosis Lipoidica diabeticorum (NLD) :Asymptomatic
  - Usually seen on the shins
  - May predate frank development of diabetes by several years
  - Shiny atrophic red or yellowish plaques with telangectasia over their surface + ulceration
  - Severity of NLD is not directly related to severity of diabetes.

**Increased risk of fungal and bacterial infection*

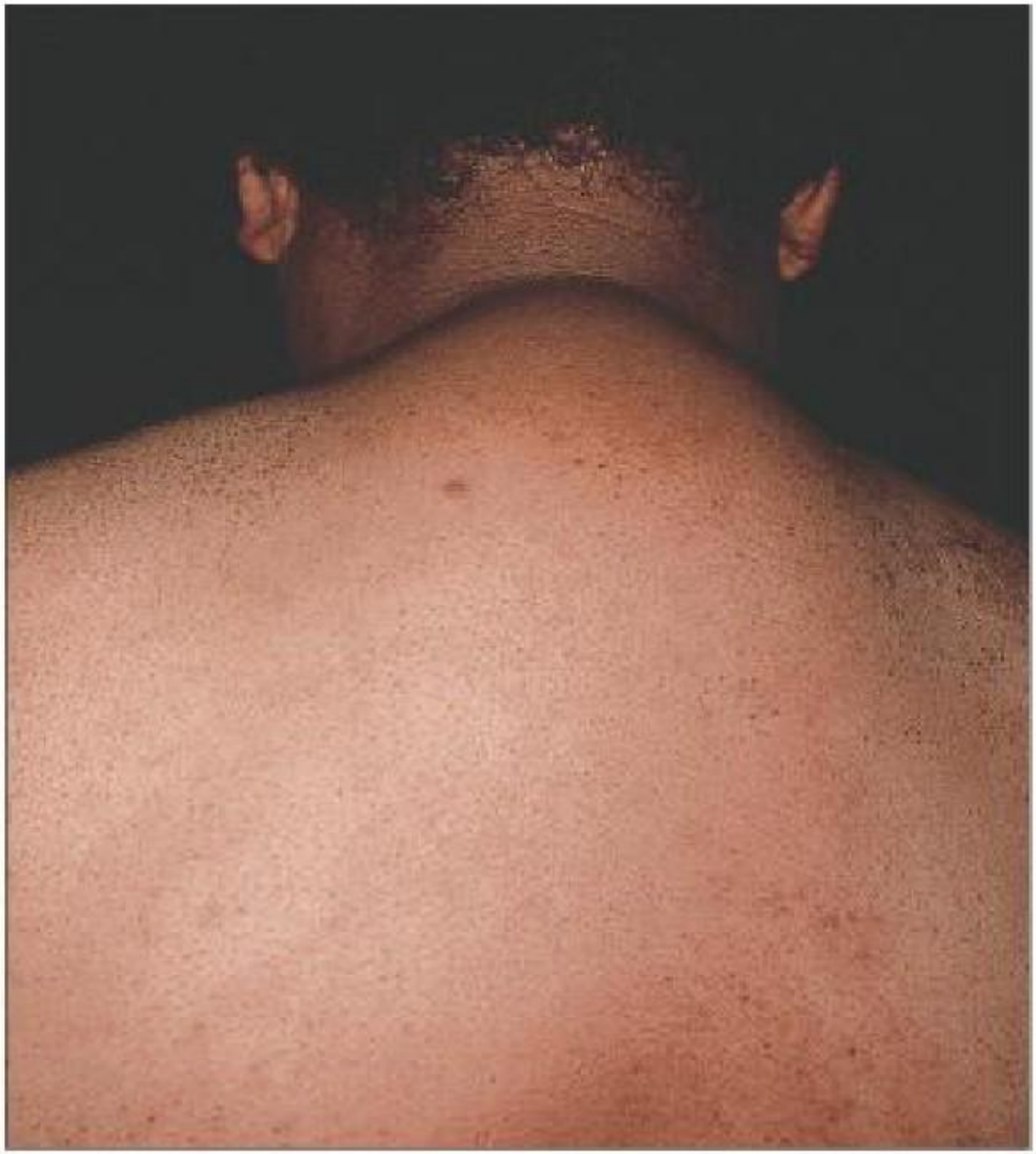


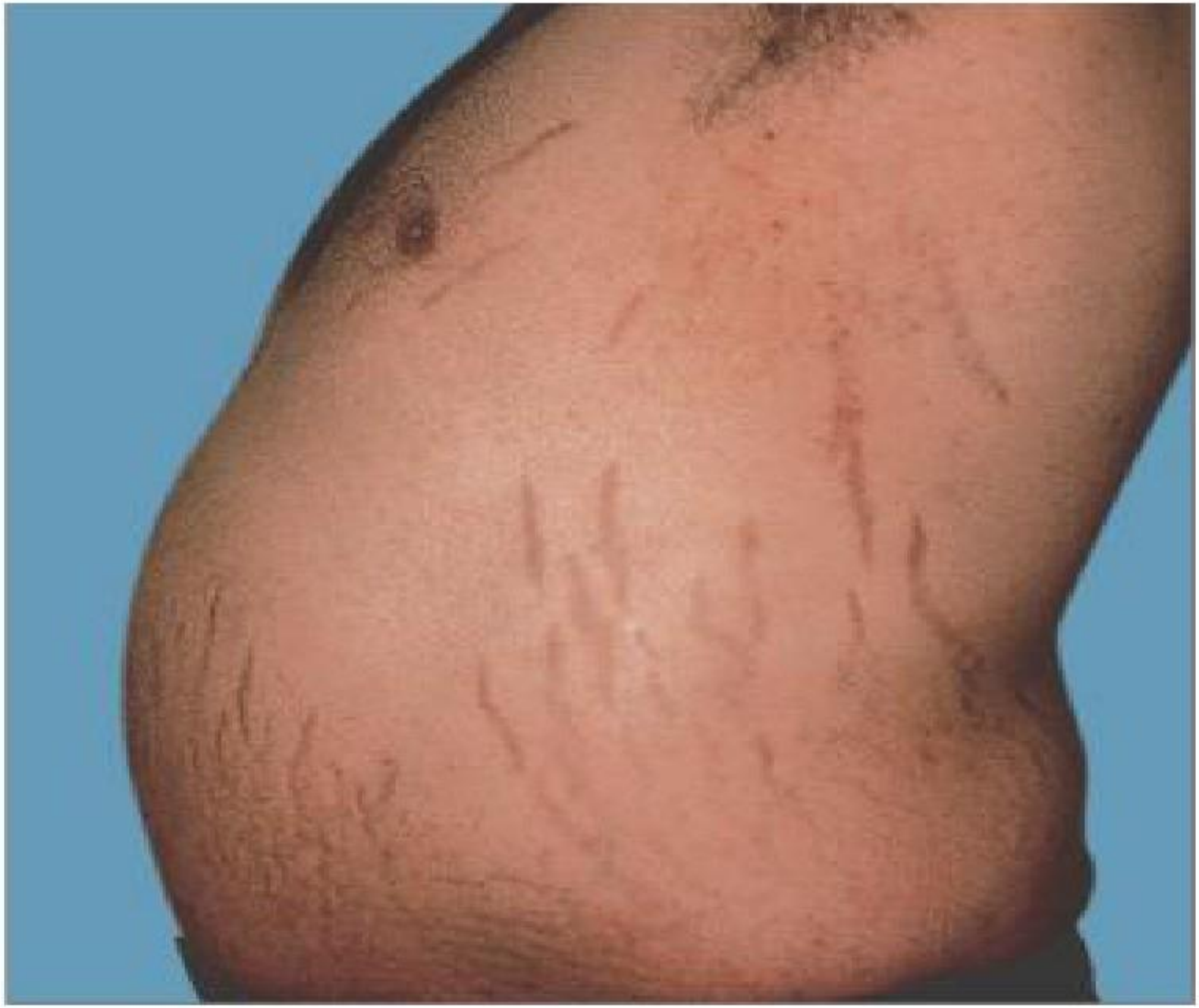




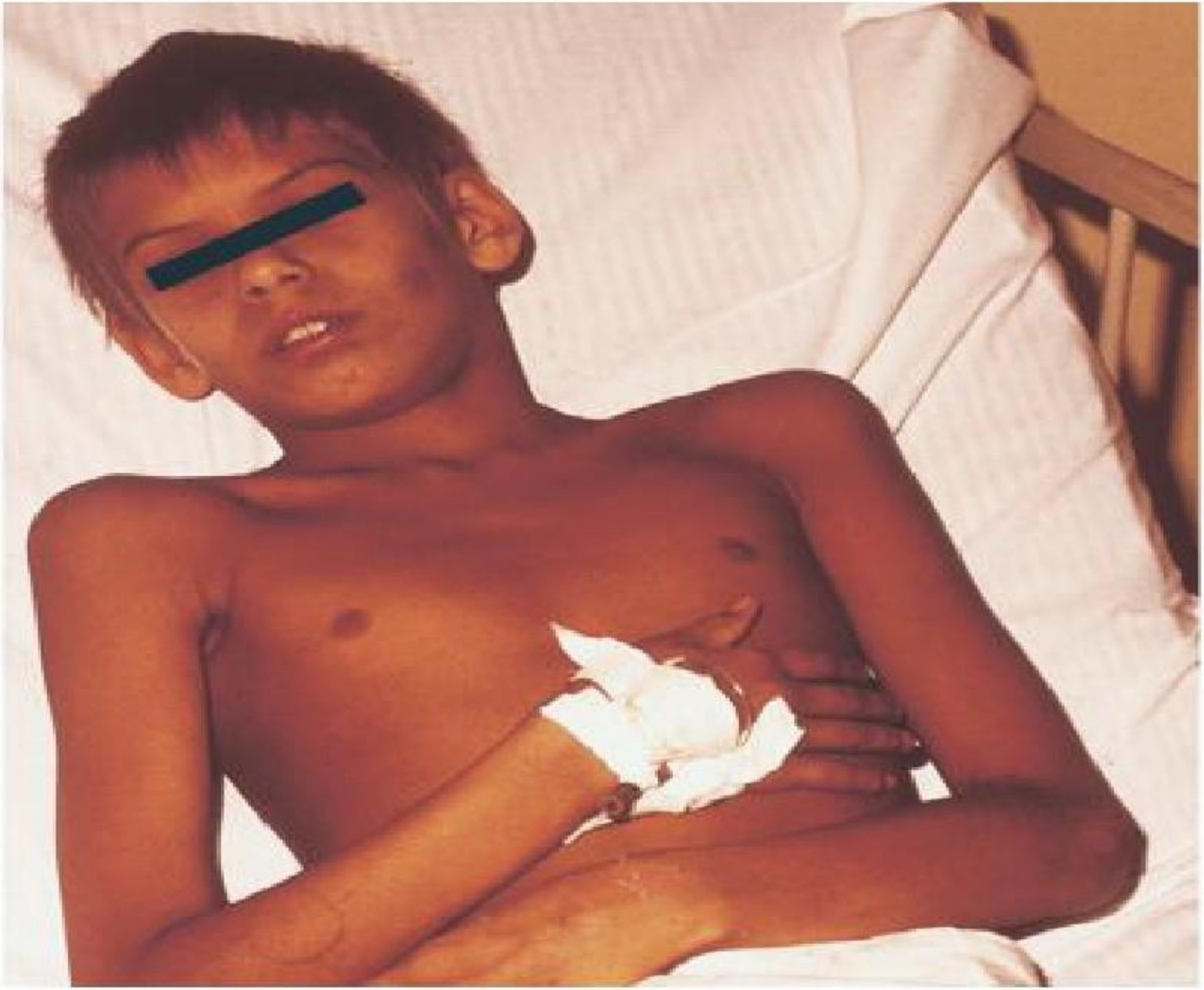
- Hyperthyrodism:
  - Smooth, warm, moist (due to increase sweating) skin
  - Peritibial myxedema (asymptomatic red plaques over shins)
  - Thin & fine hair
  - Onycholysis
  - Clubbing.
- Hypothyrodism
  - Dry, cold, skin
  - Edematous skin (myxedema)
  - Hair loss of lateral third of eyebrows
  - Brittle hair or nails

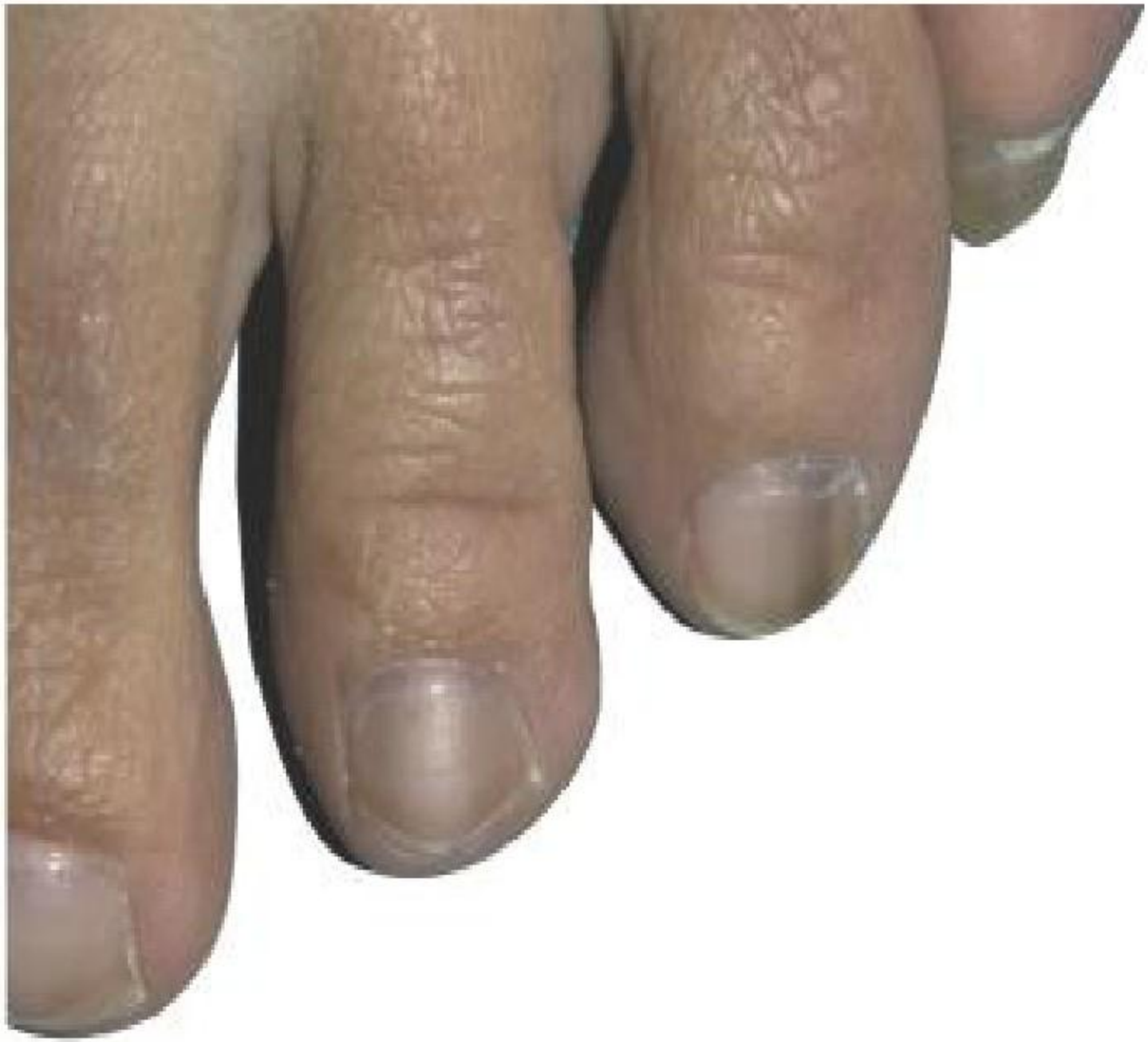
- Cushing's Syndrome:
  - Rounded face with fullness of cheeks (Moon face)
  - Buffalo hump (fat deposit over upper back)
  - Central obesity with thin arms & legs & "lemon with sticks"
  - Atrophy of skin
  - Striae
  - Purpura
  - Hirsutism
  - Acne





- Addison’s disease:
  - Hyperpigmentation:
    - at Sun exposed skin, sites of trauma, axillae, palmar creases, old scars ,nevi and mucous membranes

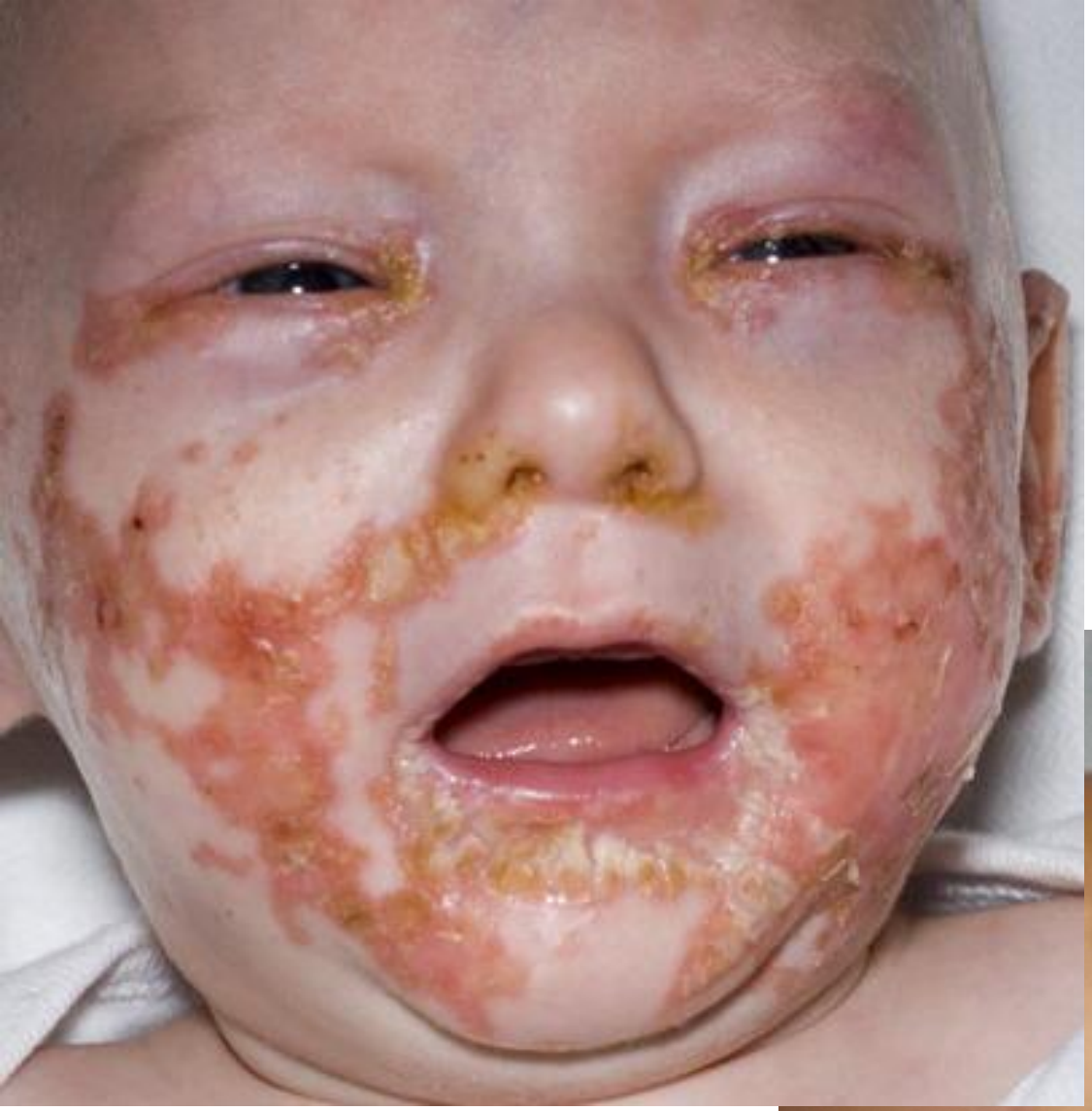


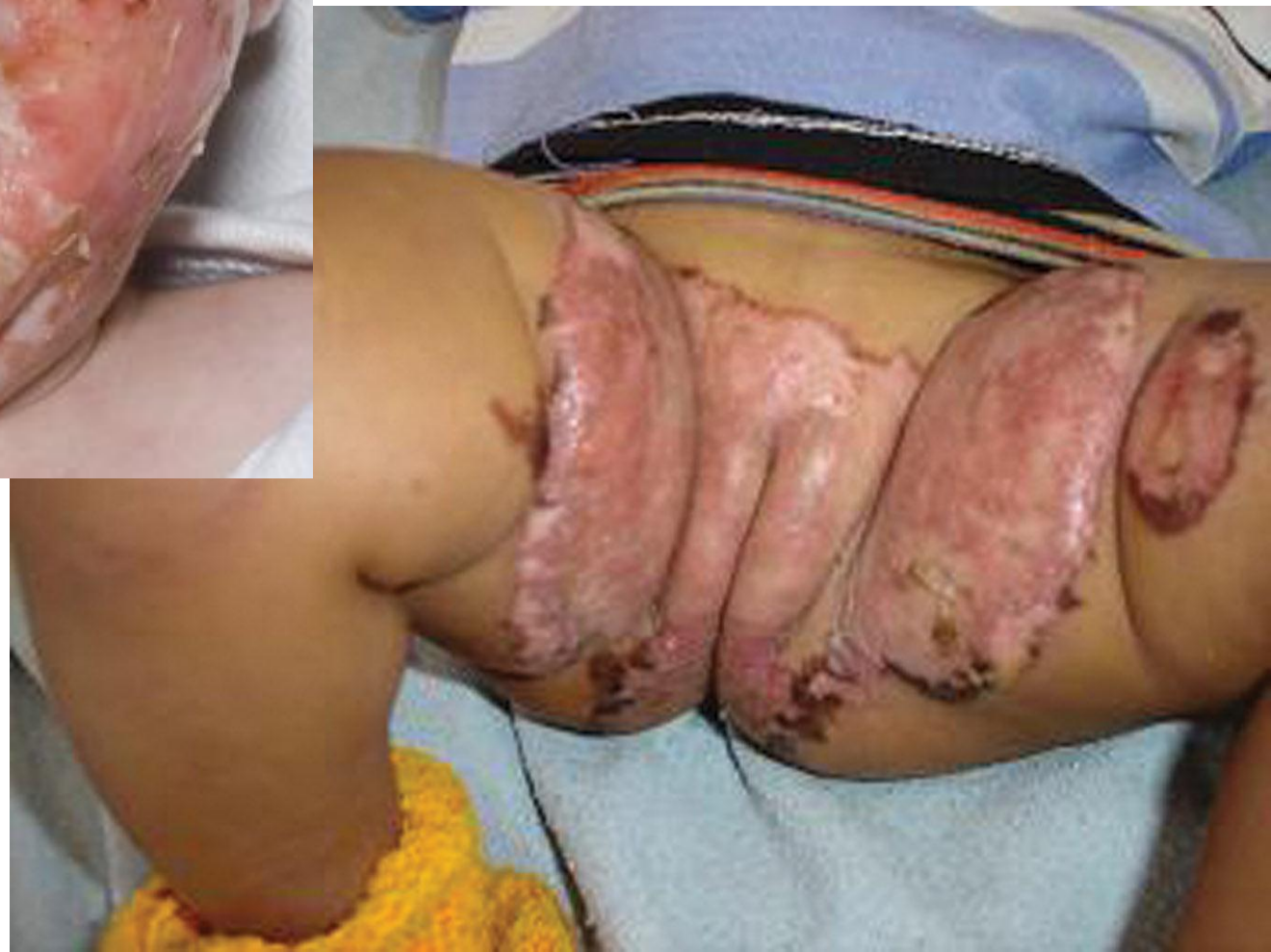


GIT

- Chronic Liver Disease
  - Jaundice
  - Spider telangectasia
  - Acne
  - Gyneacomastia
  - Purpura
  - Collateral viens
  - Striae
  - Palmer erythema
  - Dupuytren's contracture
  - White nails.

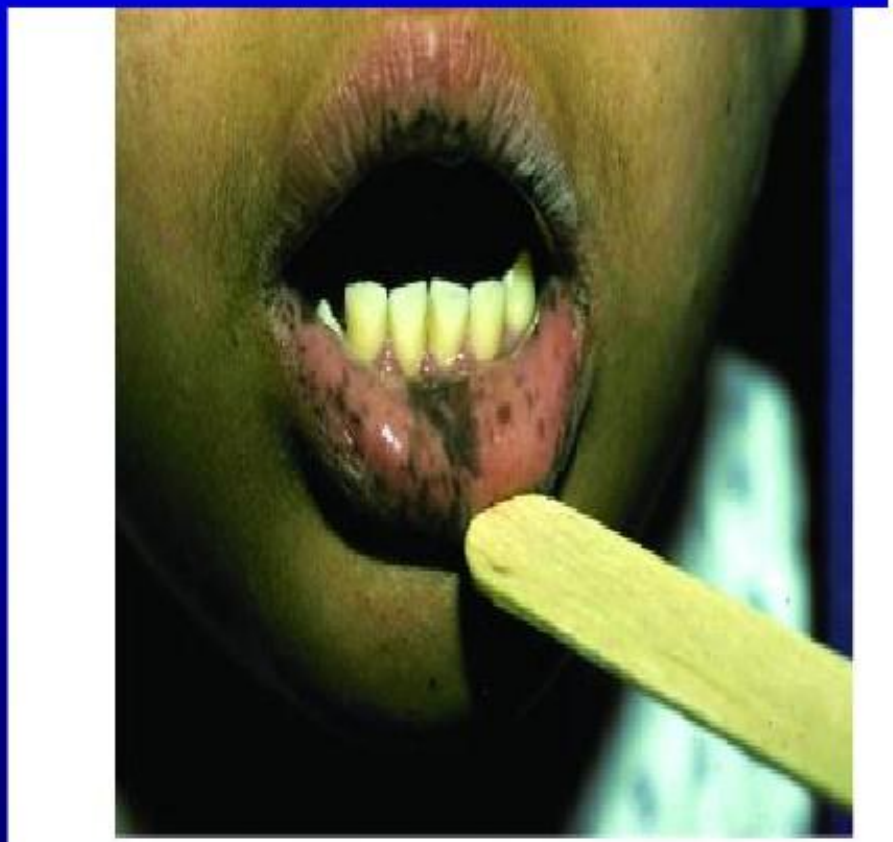
- Acrodermatitis enteropathica (genetic disease)
  - Due to zinc deficiency
  - Seen in infants as erythematous erosive rash around orifices (mouth, ears, anus)also on hands & feet.
  - Alopecia and nail dystrophy
  - Diarrhea or abdominal pain.

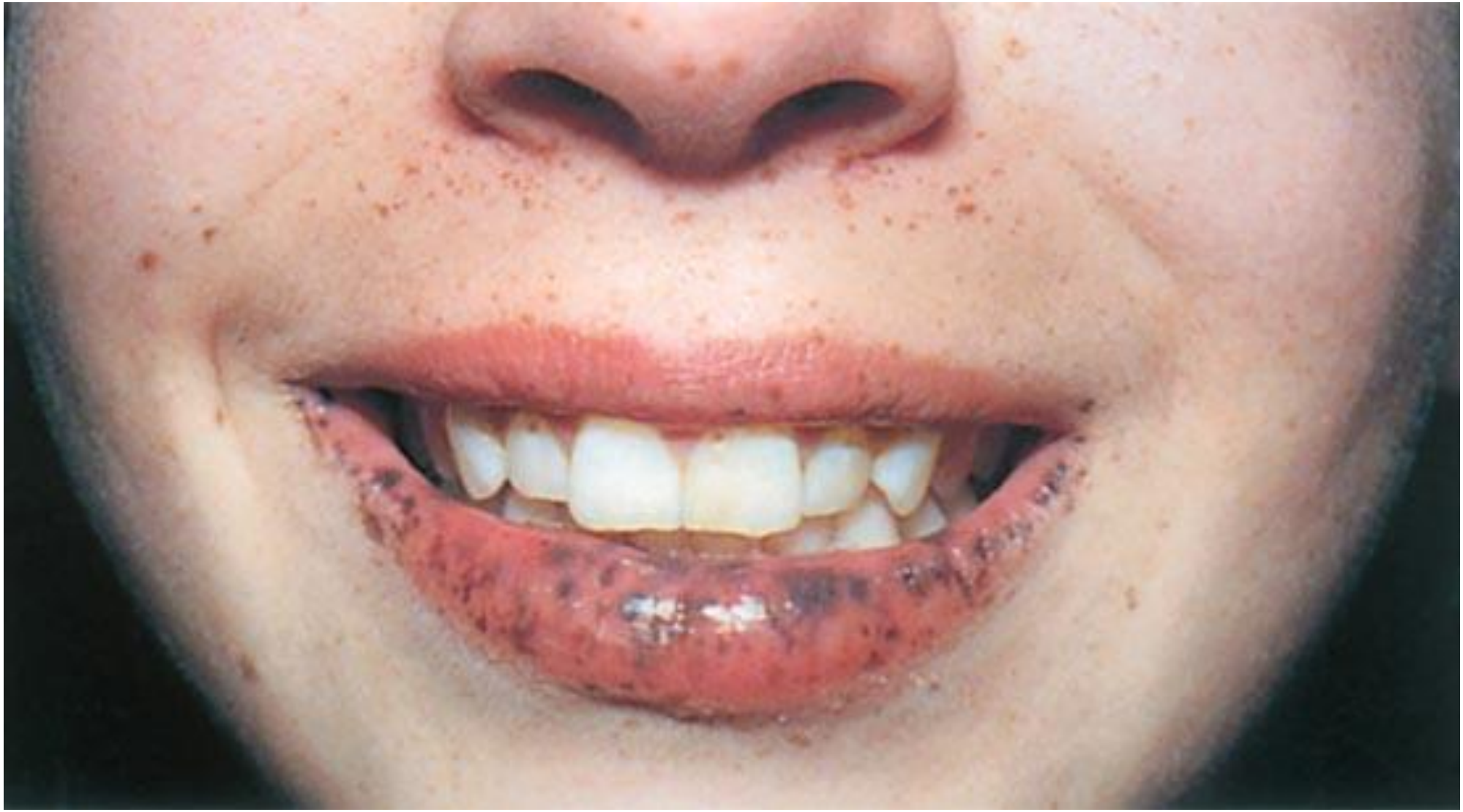




Peutz-Jeghers Syndrome

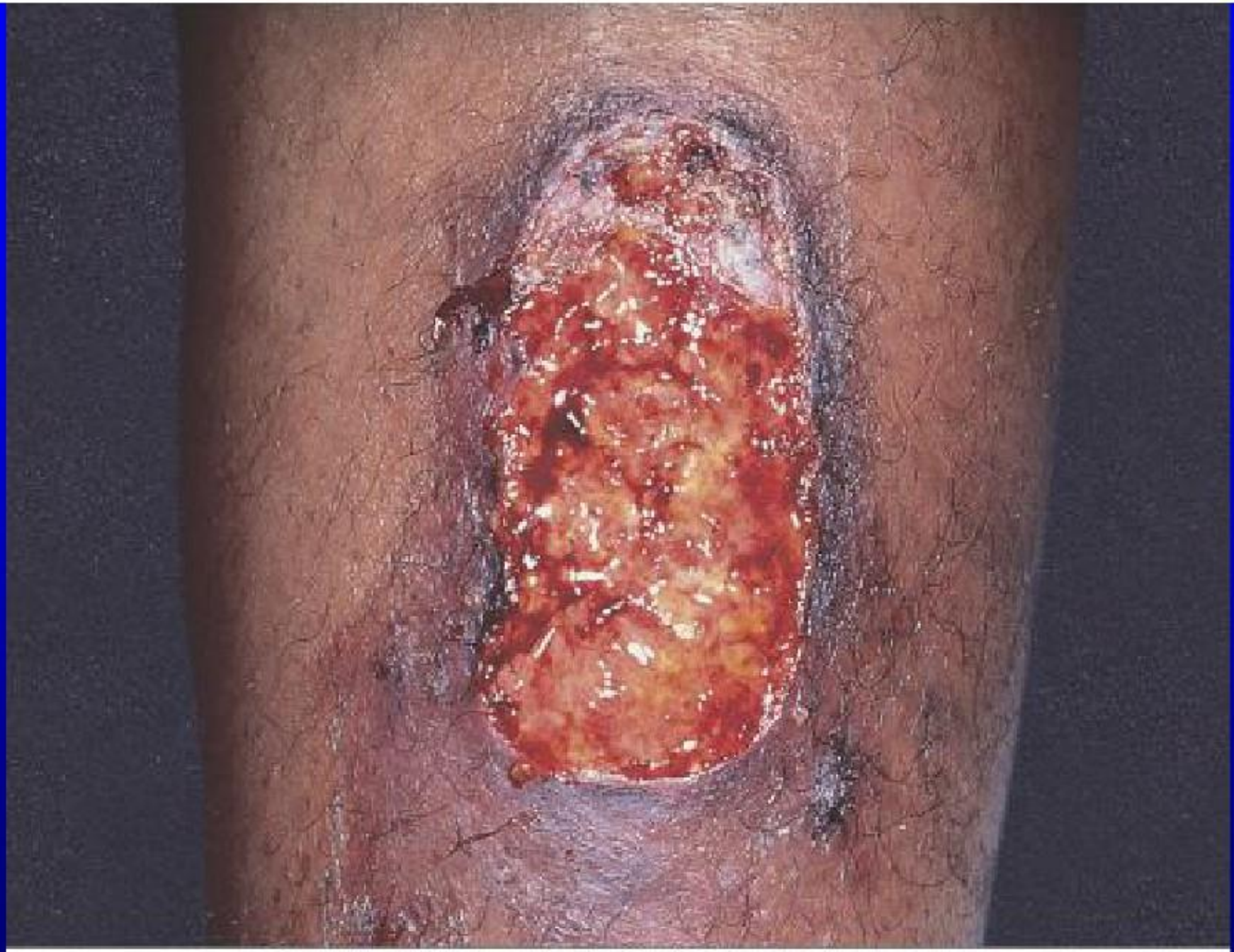
- Small brown macules on lips, buccal mucosa and small intestinal polyps
- rarely polyps can be premalignant.



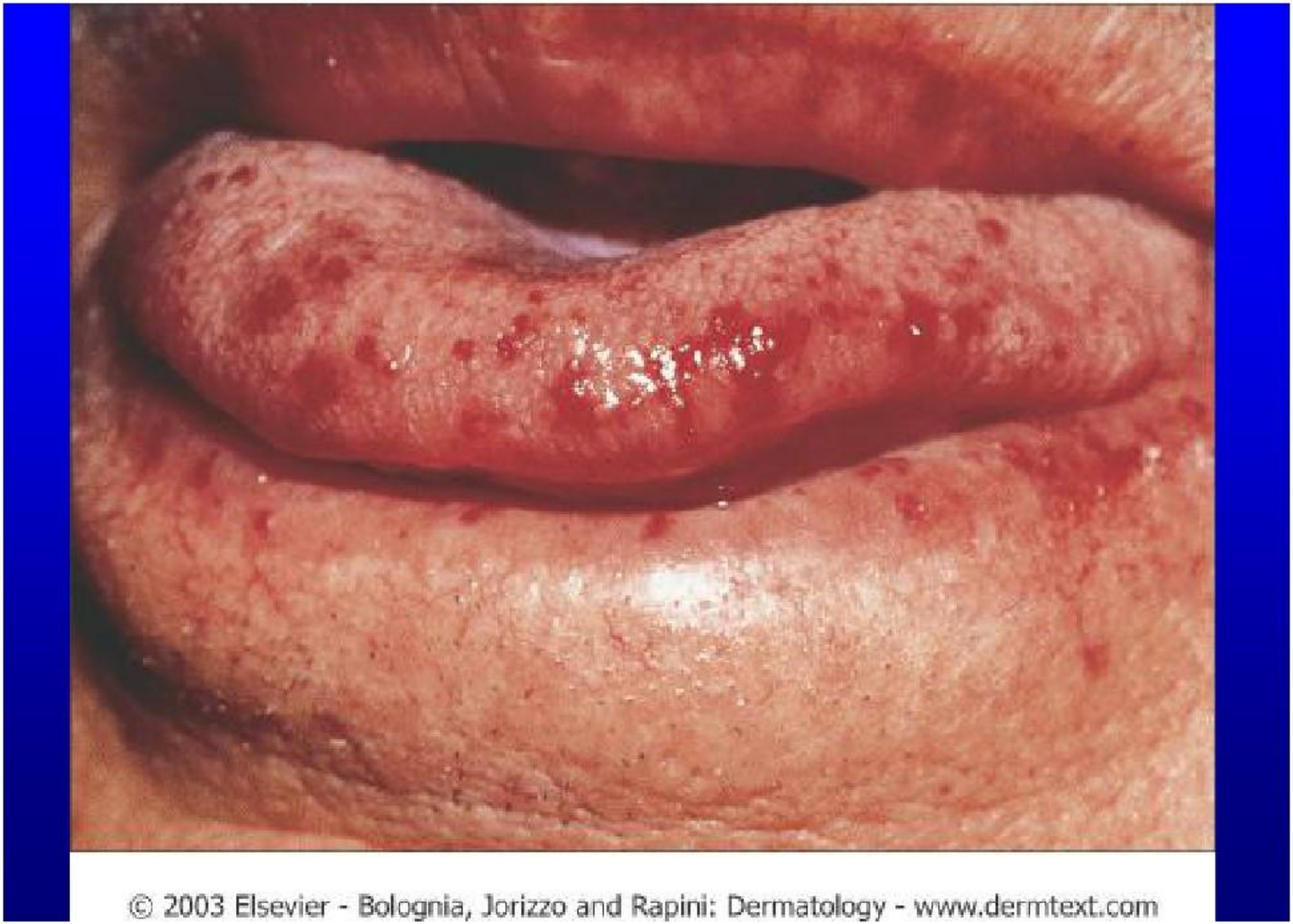


Pyoderma Gangrenosum:

- Acute painful leg ulceration, surrounded by violaceous border
- Associated with inflammatory bowel disease
- Other associations; Rheumatoid Artharitis and leukemia



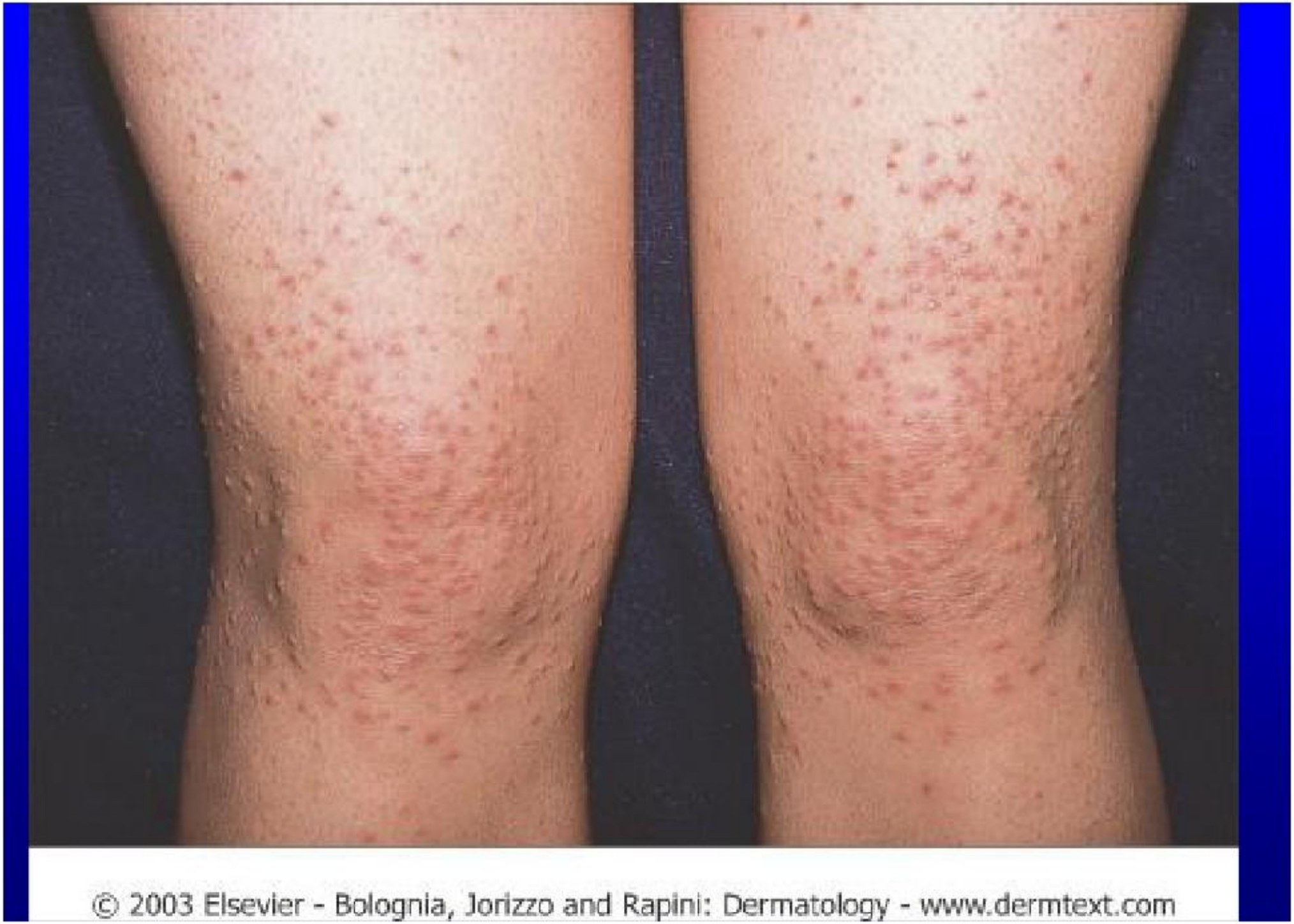
- Hereditary haemorrghic Telangectasia
  - Telangectasia (dilated capillaries) over lip,nose, tongue, fingers and toes.
  - Hx of recurrent epistaxis
  - Associated with recurrent upper GI bleed

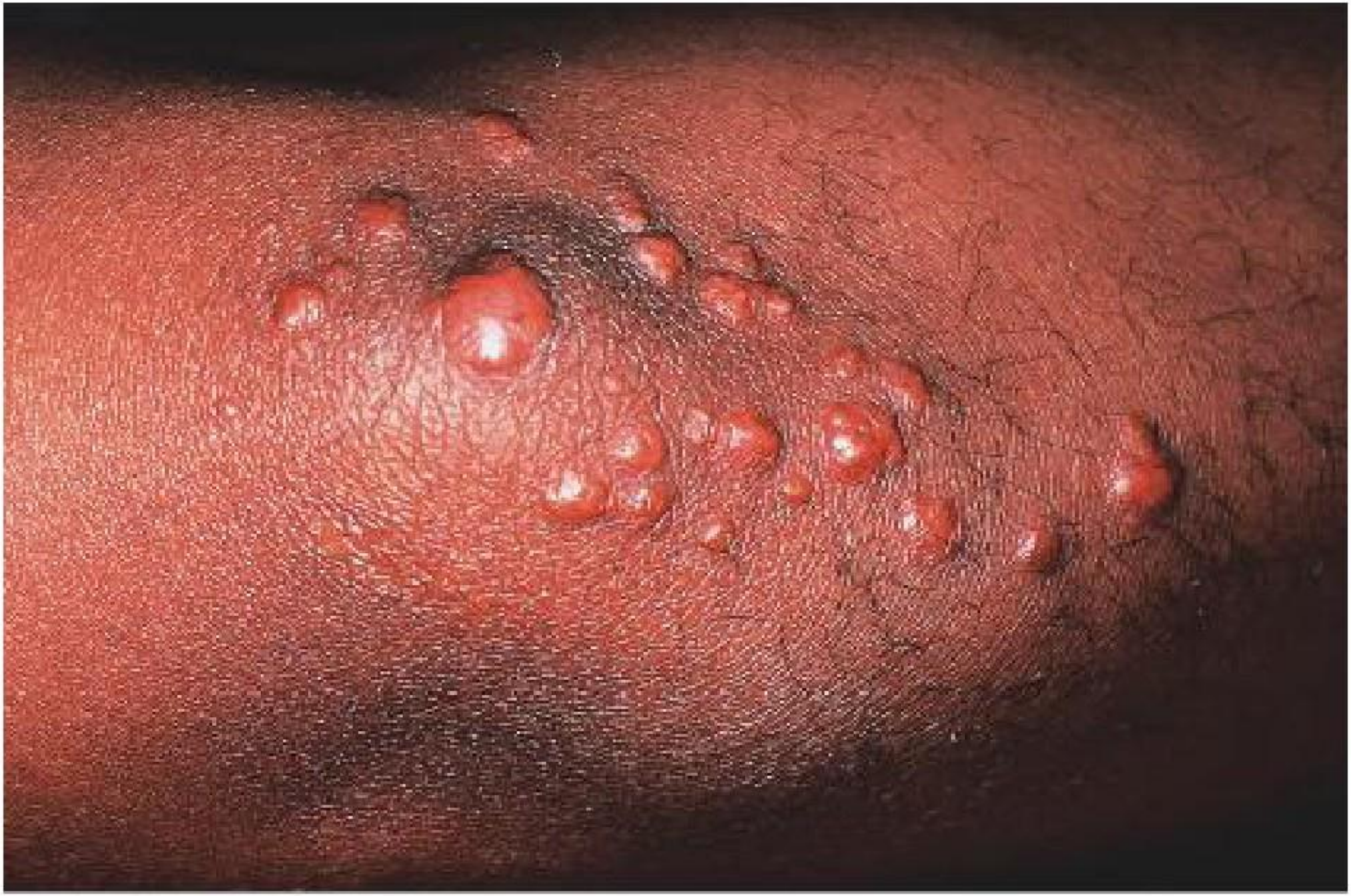


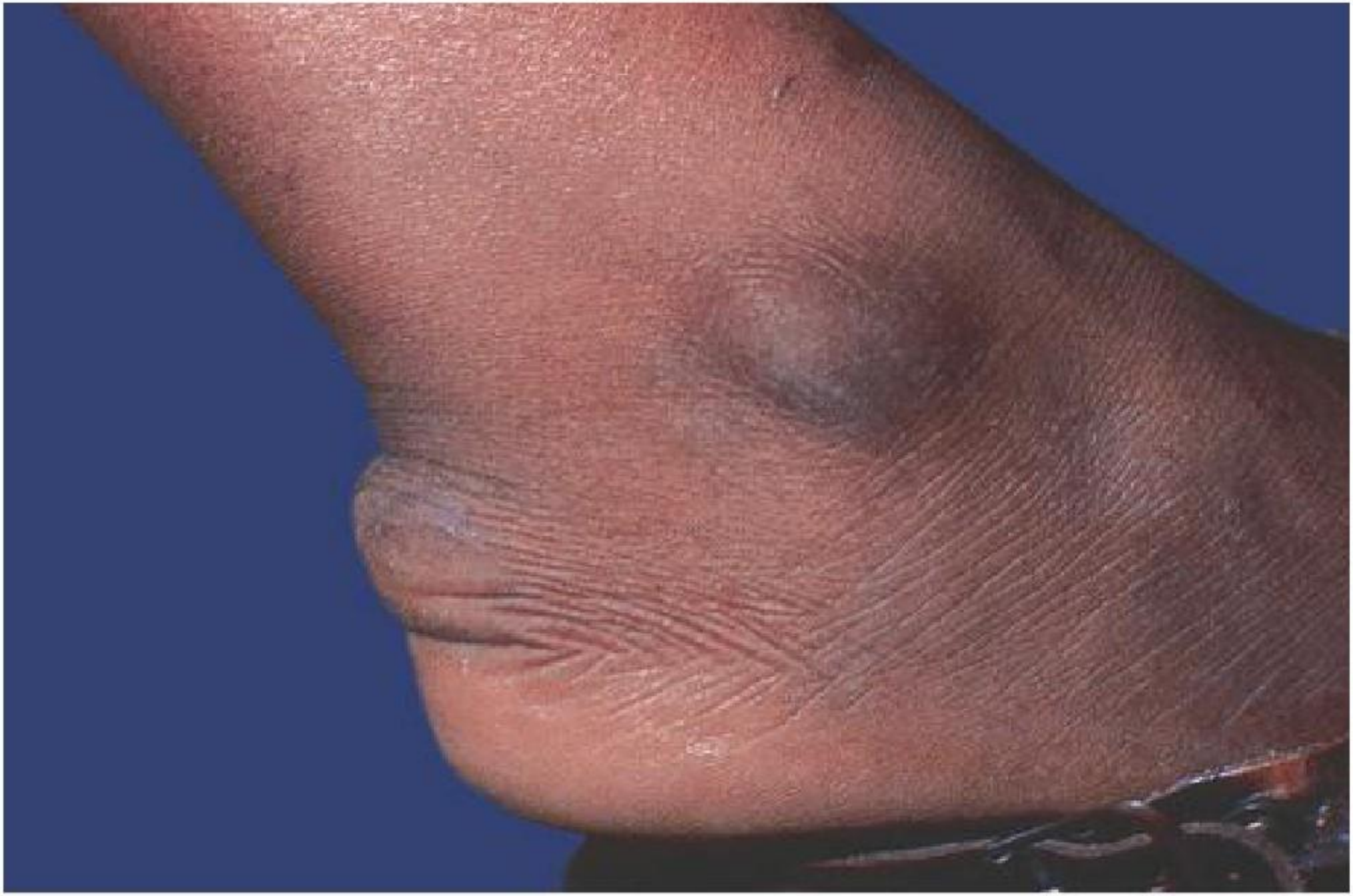
Hyperlipidemia:

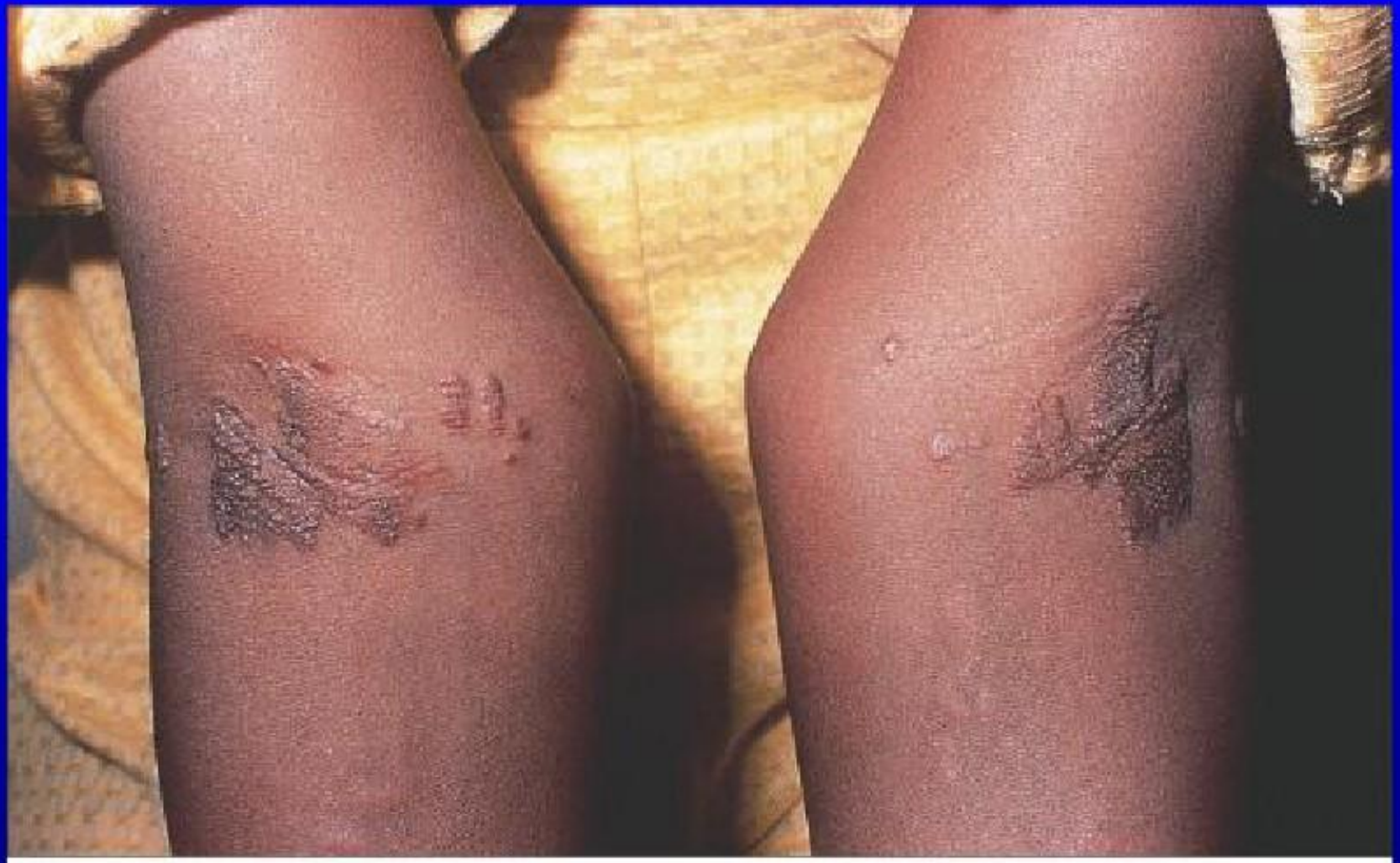
- Present with different types of xanthomas
- Yellow color is characteristic

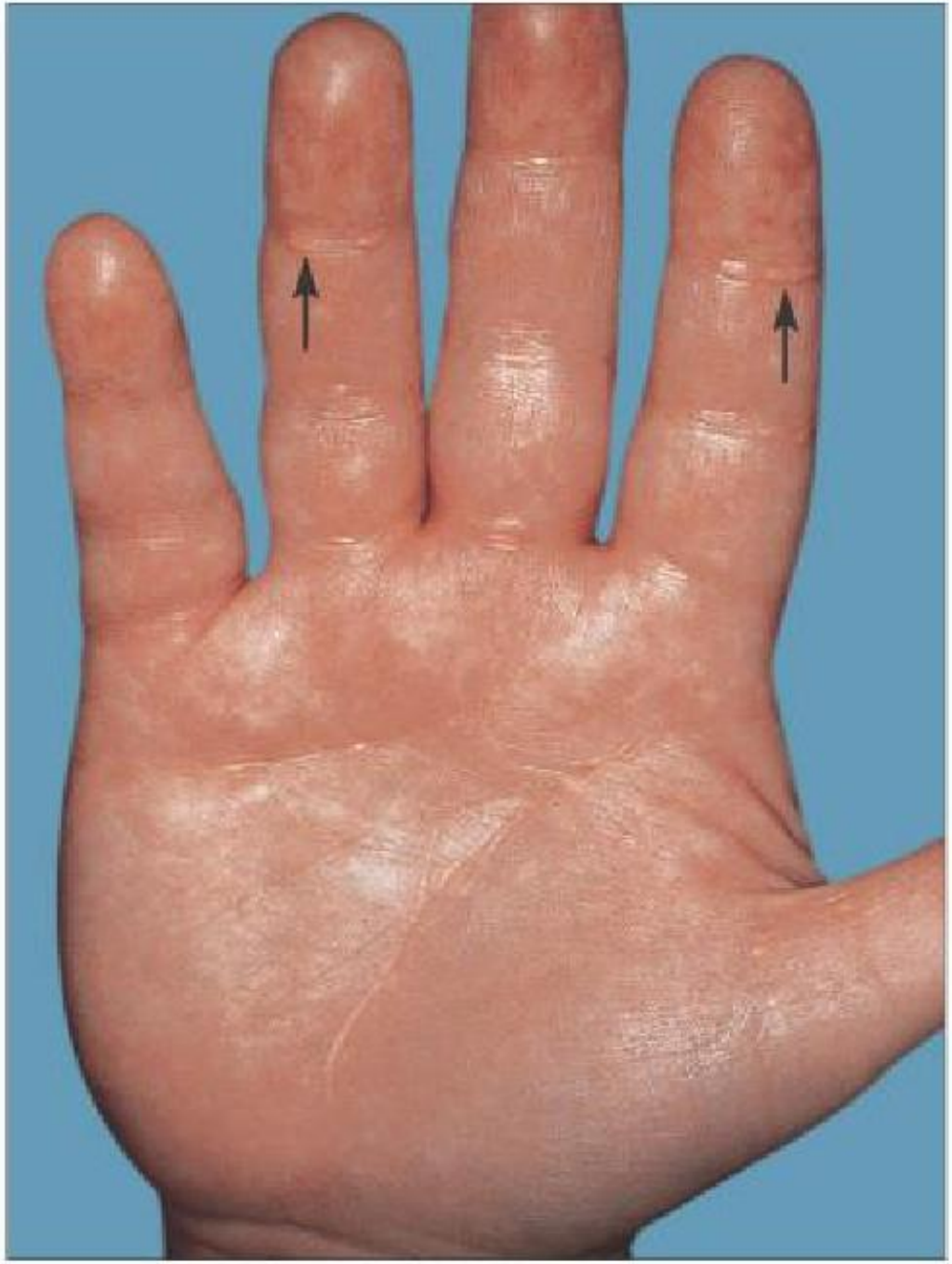
- Types of Xanthomas
  - **Eruptive**: small papules appear in crops over buttocks & extensors
  - **Tendinous**: Nodules over tendons e.g. extensor tendons of hands & feet and Achilles tendon.
  - **Palmar crease** xanthoma: on palms
  - **Tuberous:** Papules & nodules over knees and elbows
  - **Xanthelasma:** Bilateral symmetrical over both eyelids.

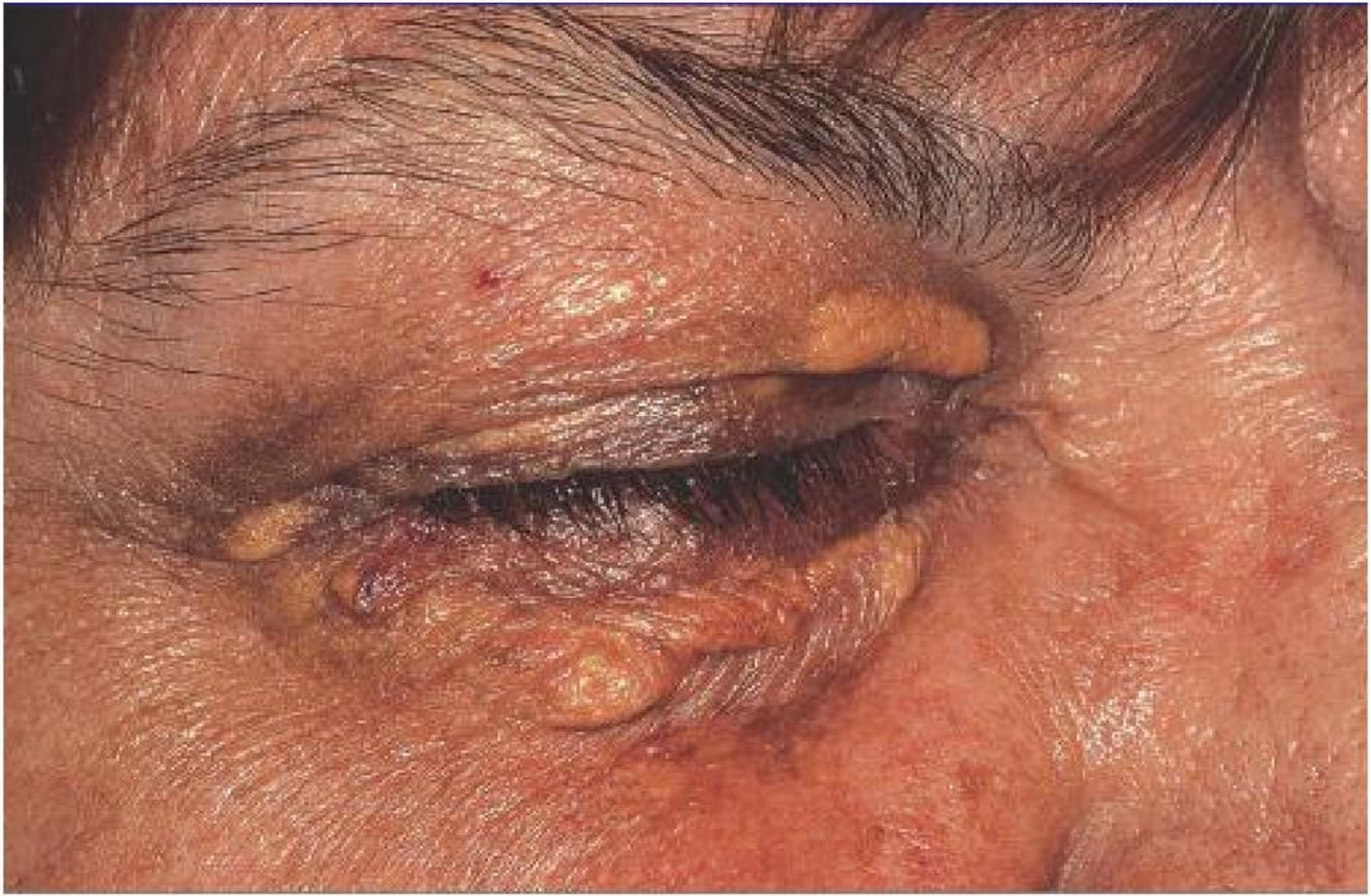








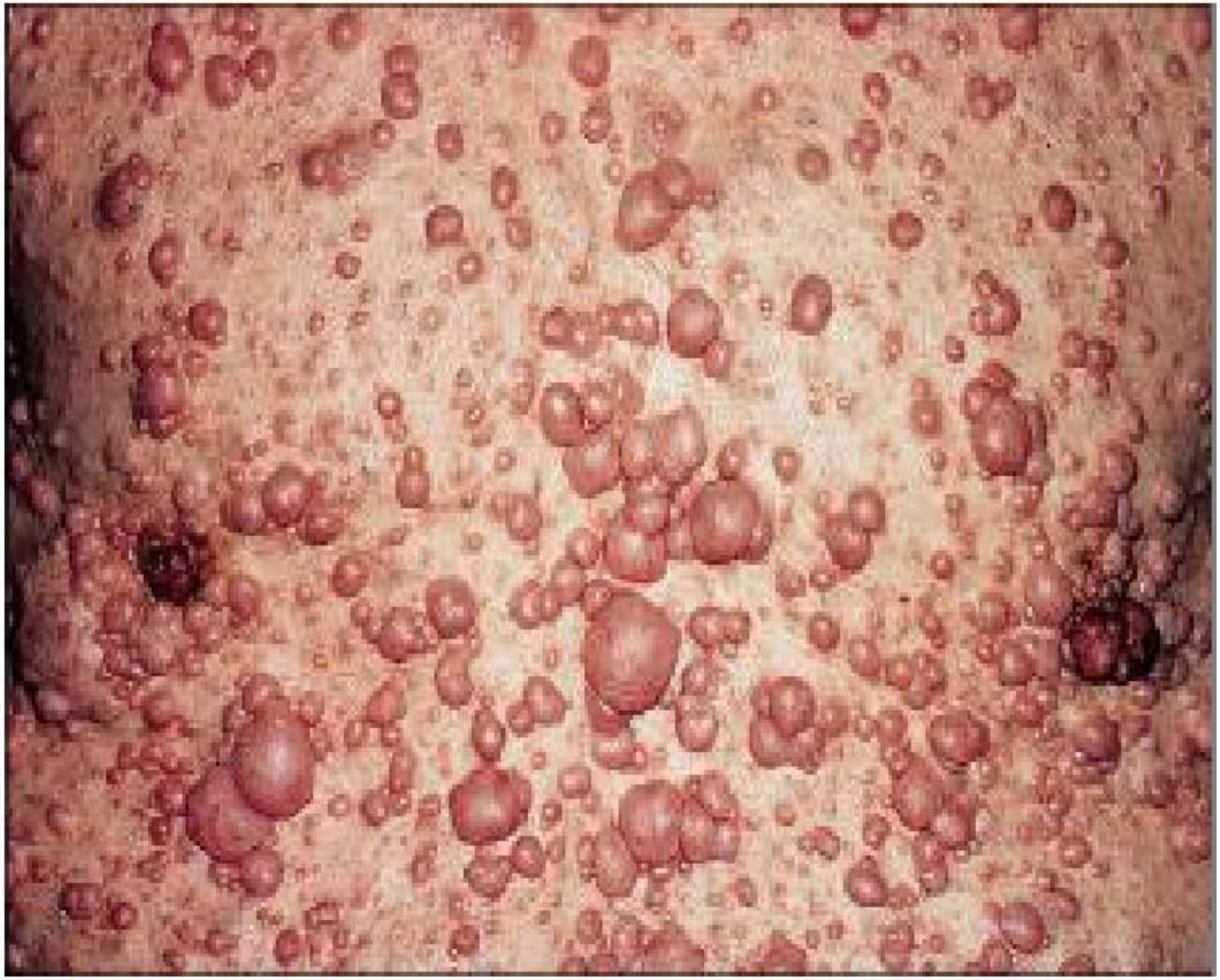


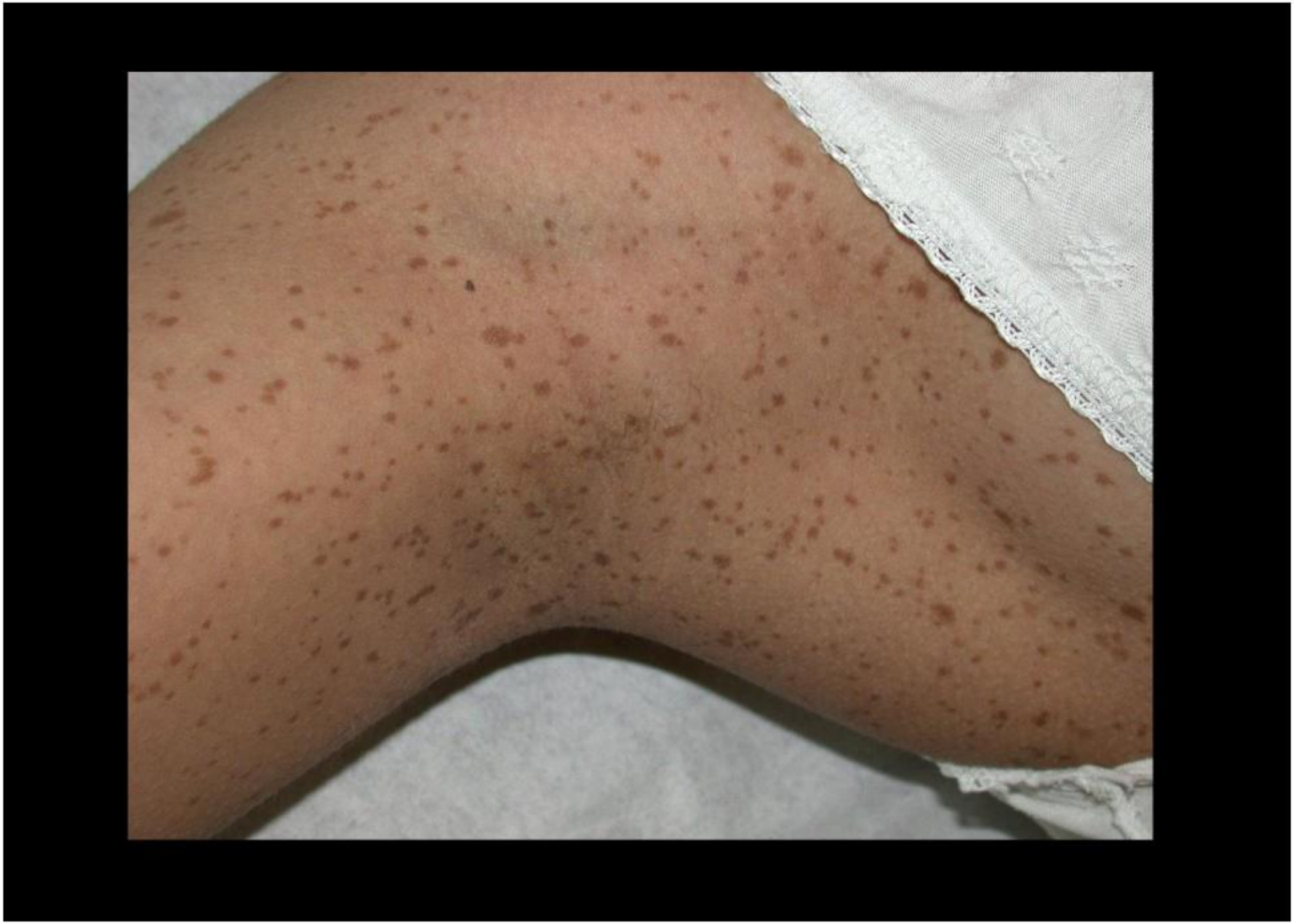


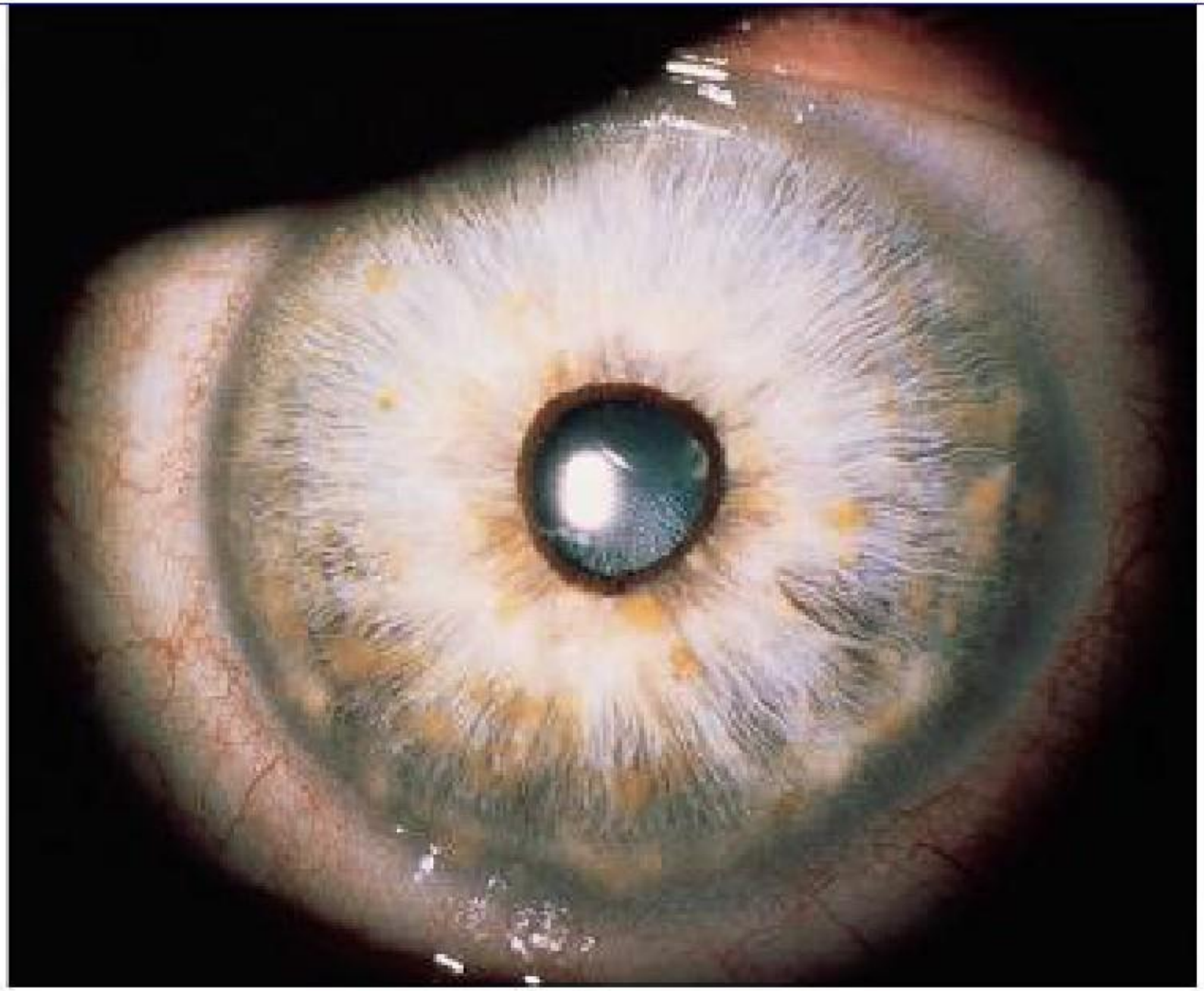
- Xanthoma may be a pointer to:
  - Primary hyperlipemic status due to genetic abnormality
  - Secondary hyperlipemic status due to renal, hepatic, endocrine or pancreatic disease
  - Normo-lipemic status.

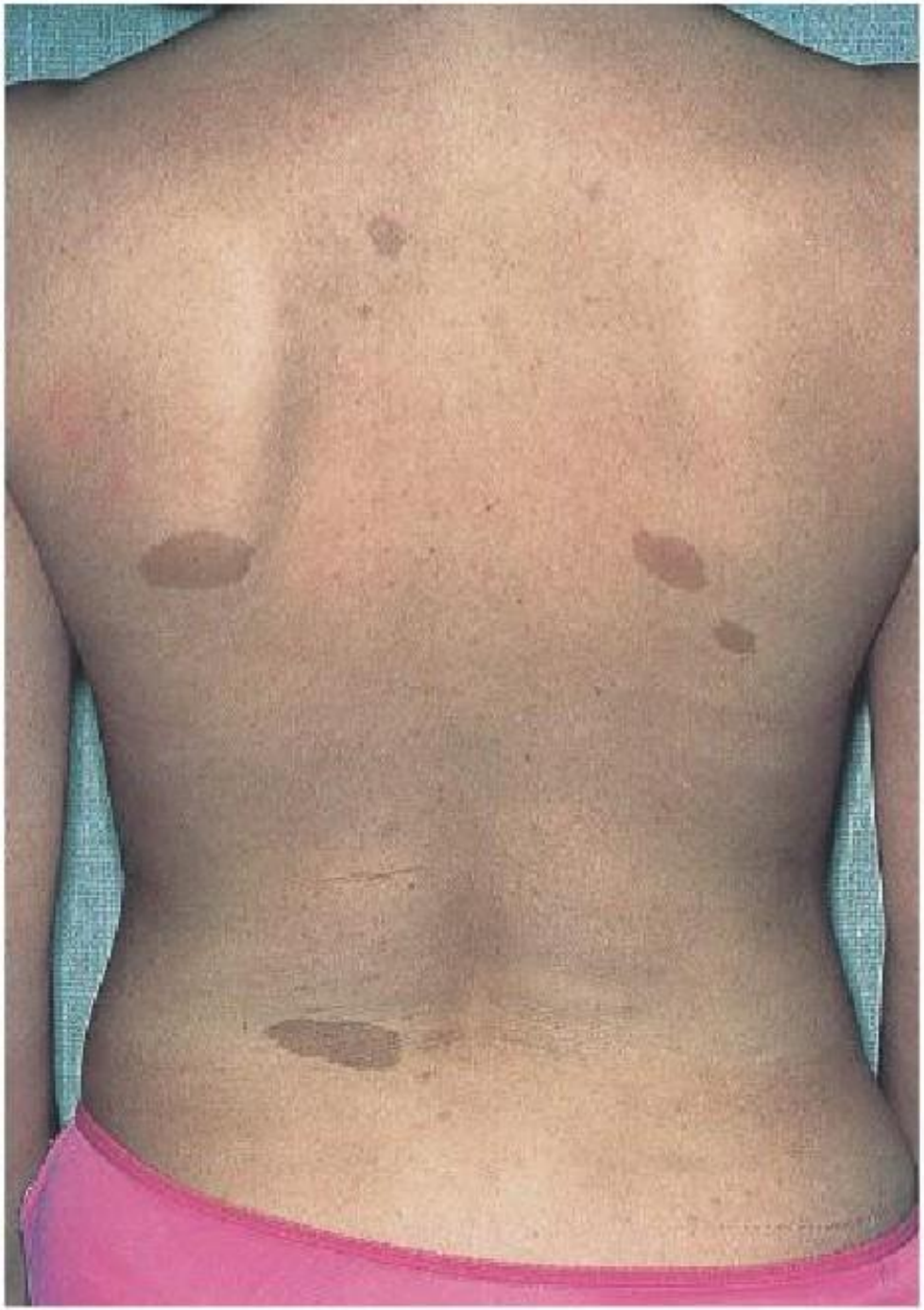
Neurocutaneous Disorders

- Neurofibromatosis:
  - Autosomal dominant
  - Café-au-lait macules(light brown)
  - Neurofibromas(soft pink or skin- colored papules and nodules)
  - Axillary freckling
  - Optic glioma
  - Lisch nodules (iris hamartoma, seen by slit-lamp examination)
  - Associated with Neurological complications e.g. tumors, seizures and mental retardation.



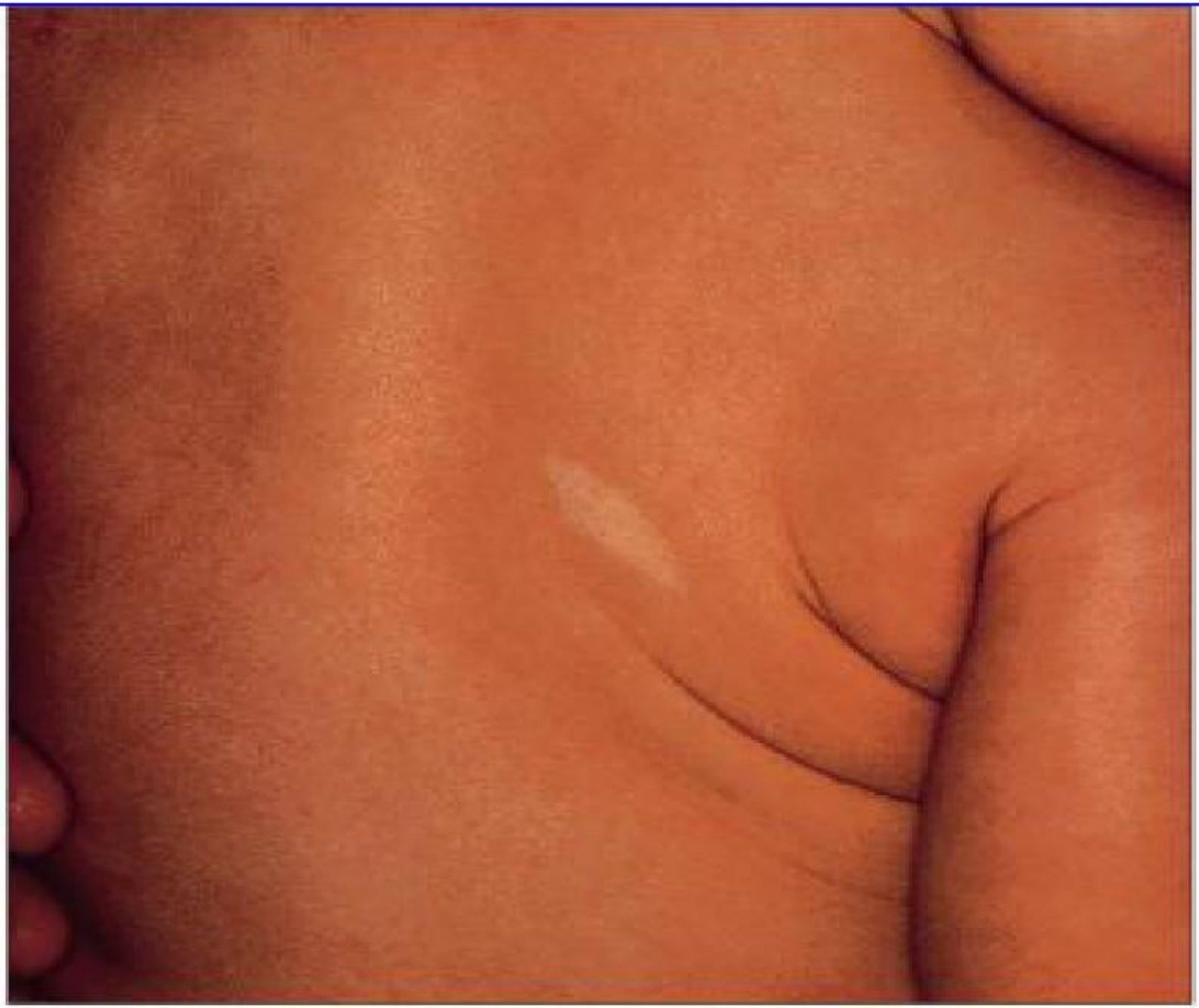


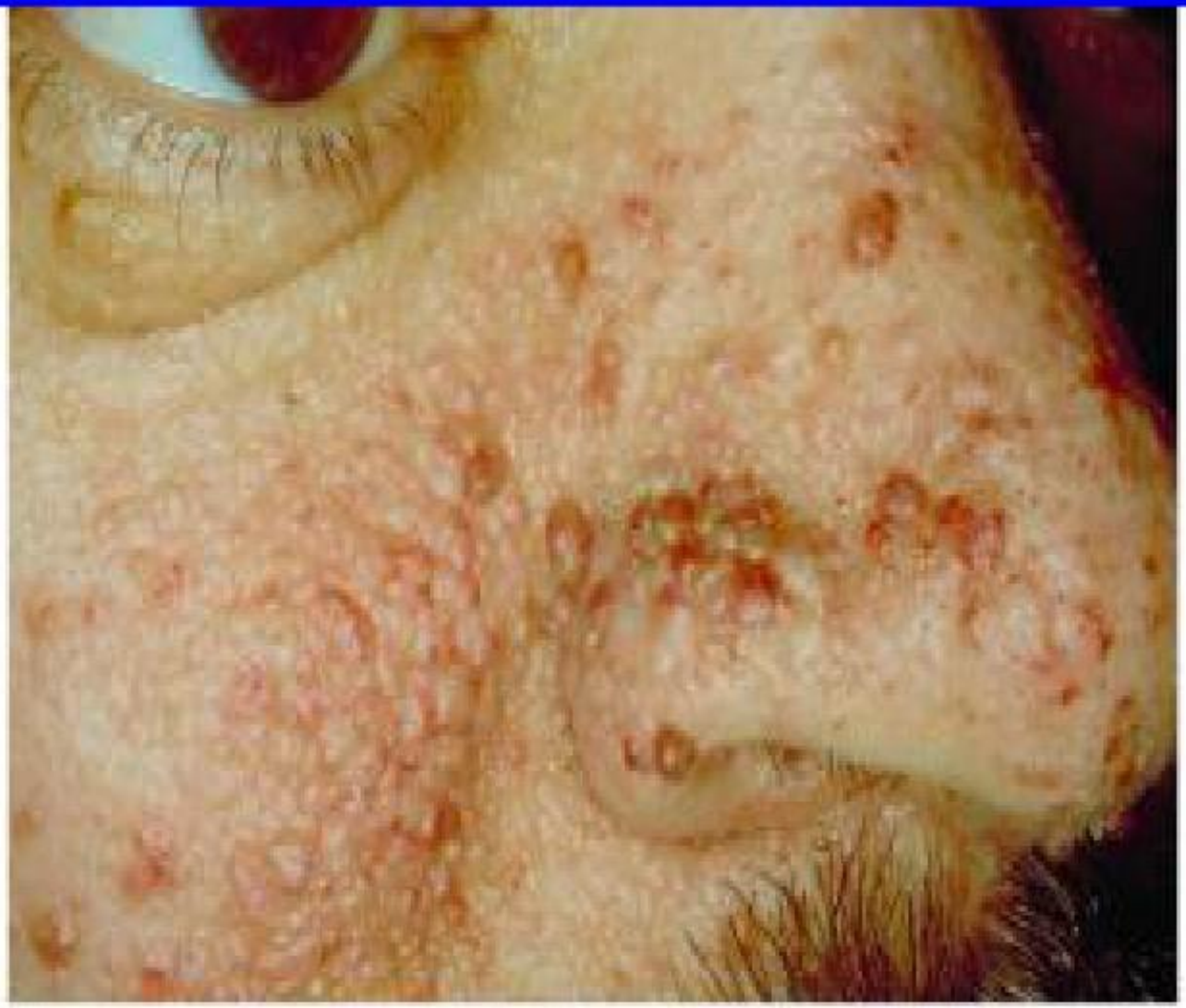


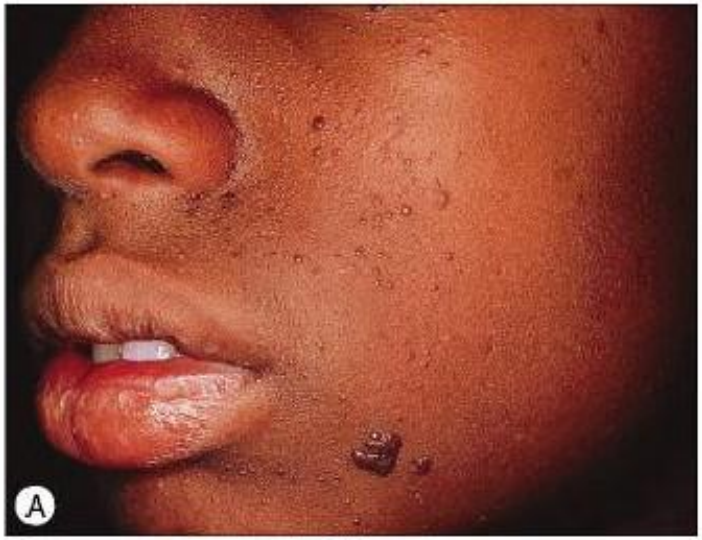


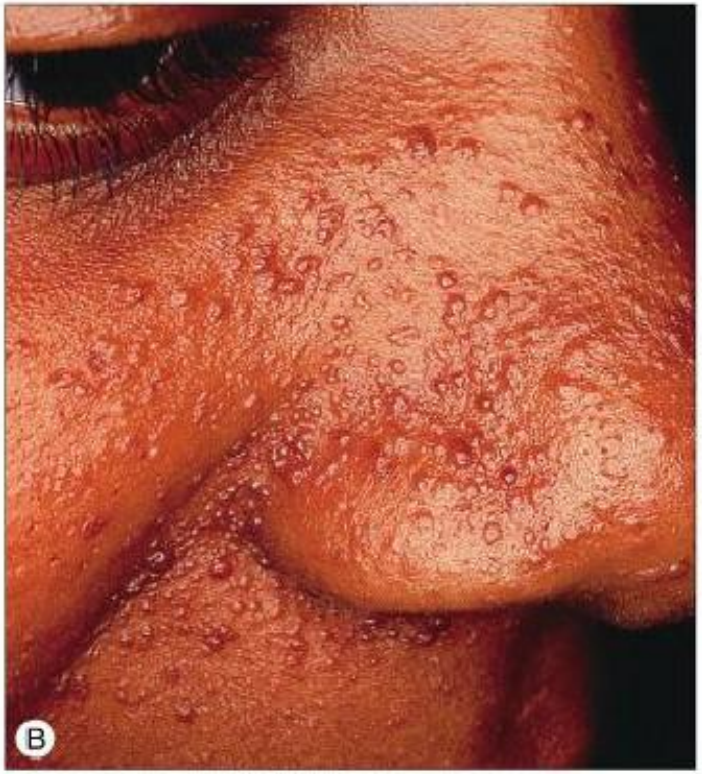
- Tuberous Sclerosis (Epiloia) :
  - Epi = Epilepsy
  - Loi = Low intellegence
  - a = adenoma sebaceoum
- Skin features

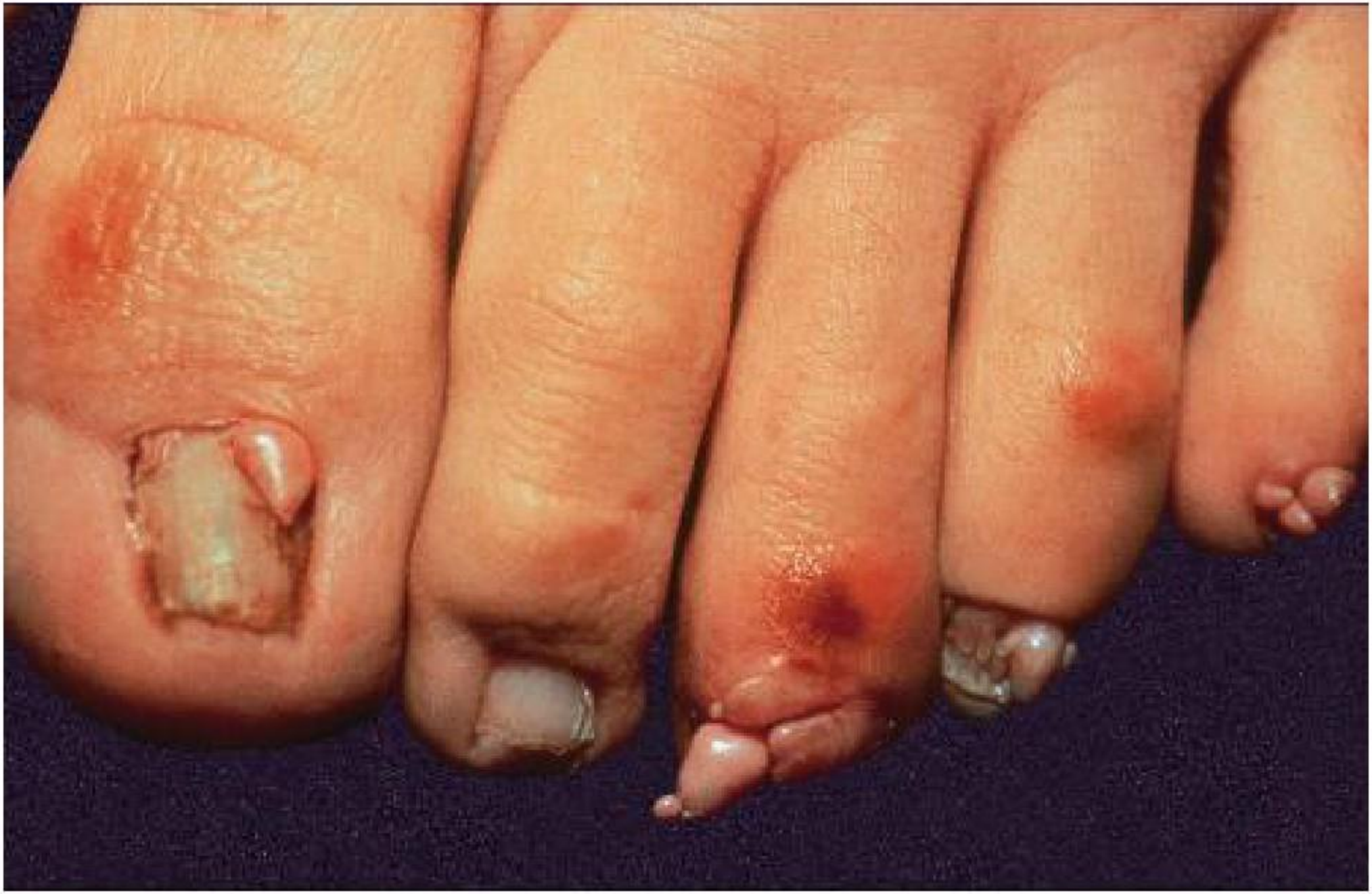
1. Adenoma sebaceoum (anigofibroma): red papules around the nose and on chin
2. Ash-leaf hypopigmention: oval area of hypopigmention ***This is the earliest sign of TS***
3. Periungal fibroma: multiple papules & nodules around the nail
4. Shagreen patch: skin colored plaque on the trunk with "orange-peel" surface











- Behcet's Syndrome:
  - Oral ulcer (the most common)
  - Genital ulcers (mainly scrotal)
  - Iritis and arthoropathy
  - May have CNS involvement
- Scurvy :
  - Vitamin C deficiency
  - Bleeding gums
  - Can cause teeth loss (permanent complication)

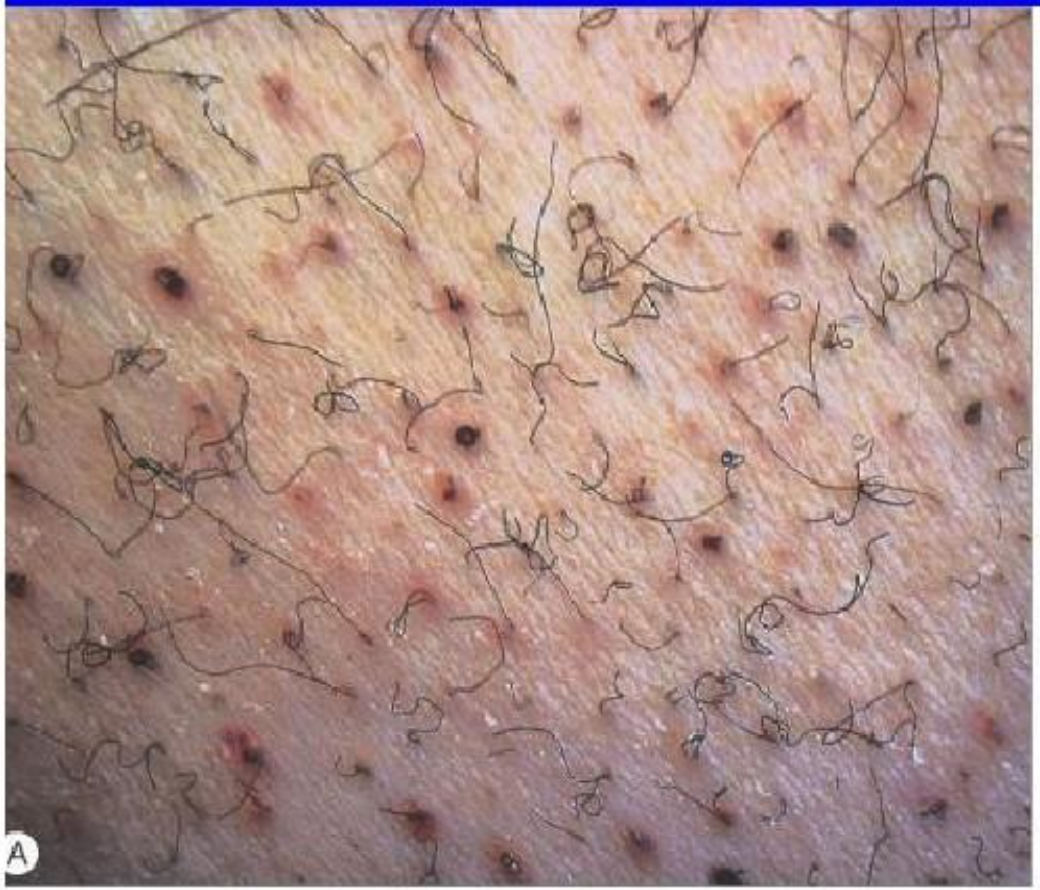
- Scurvy(cont'd)
  - Easy bruishing
  - Diagnosis : Low ascorbic acid (Vit-C) level in Leukocyte
- Pellagra:
  - Nictonic acid deficiency
  - 4 "D"s

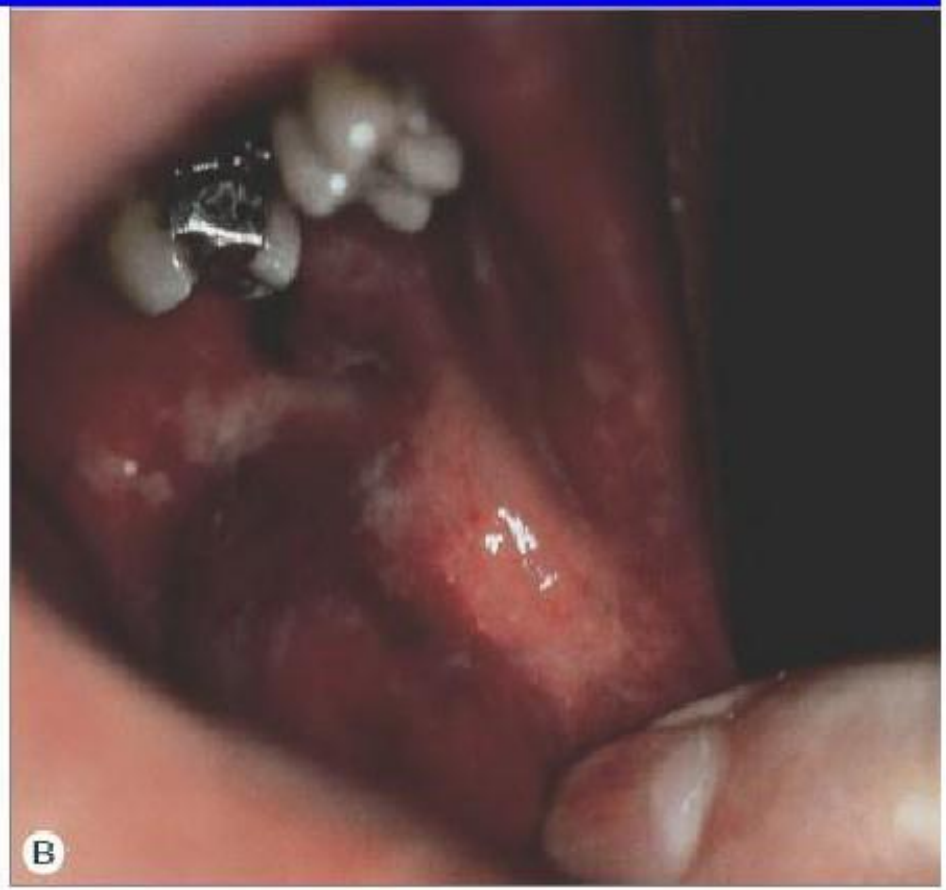
    Dermatitis (Photodermatitis)

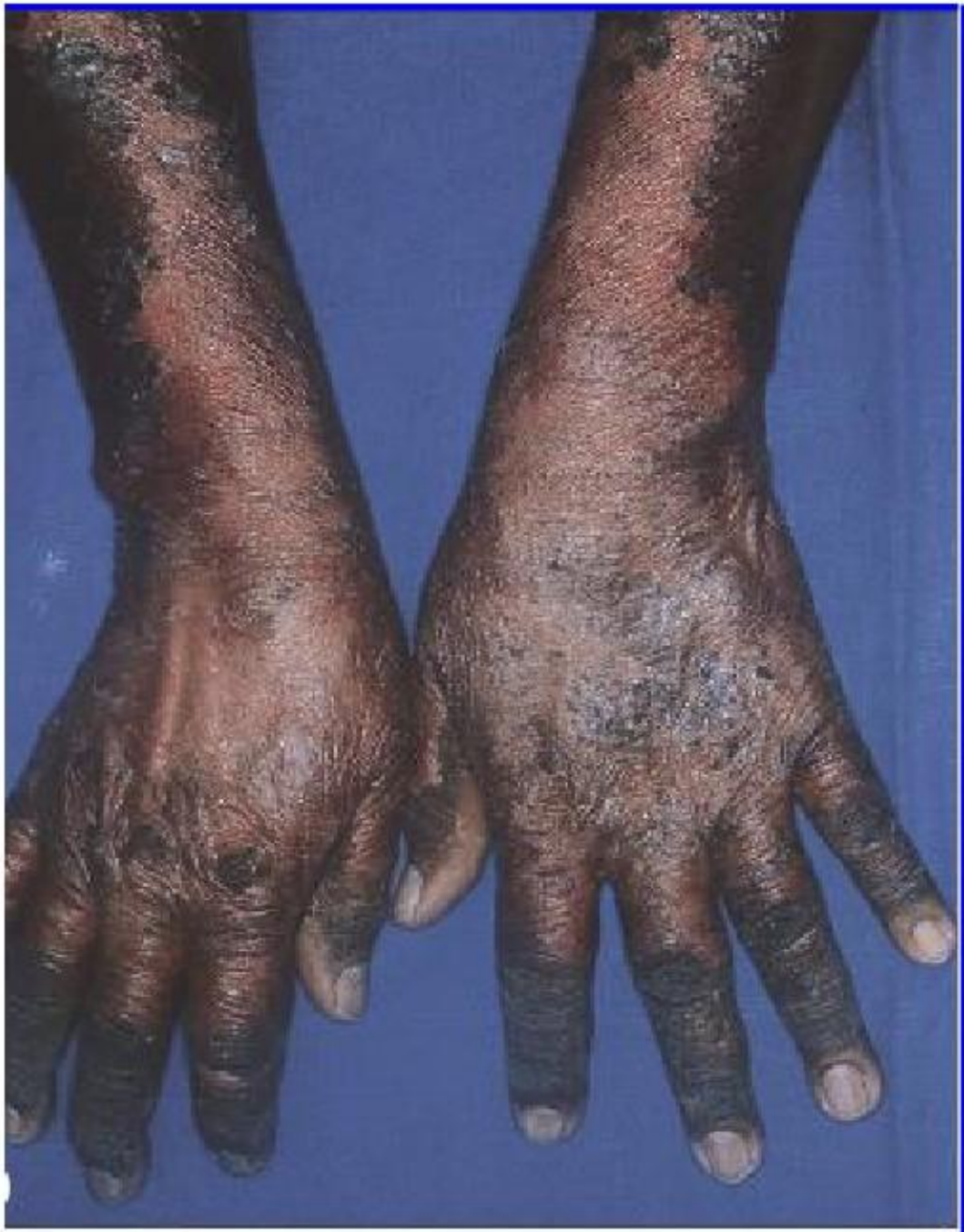
    Diarrhea

    Dementia

    Death (if not treated)







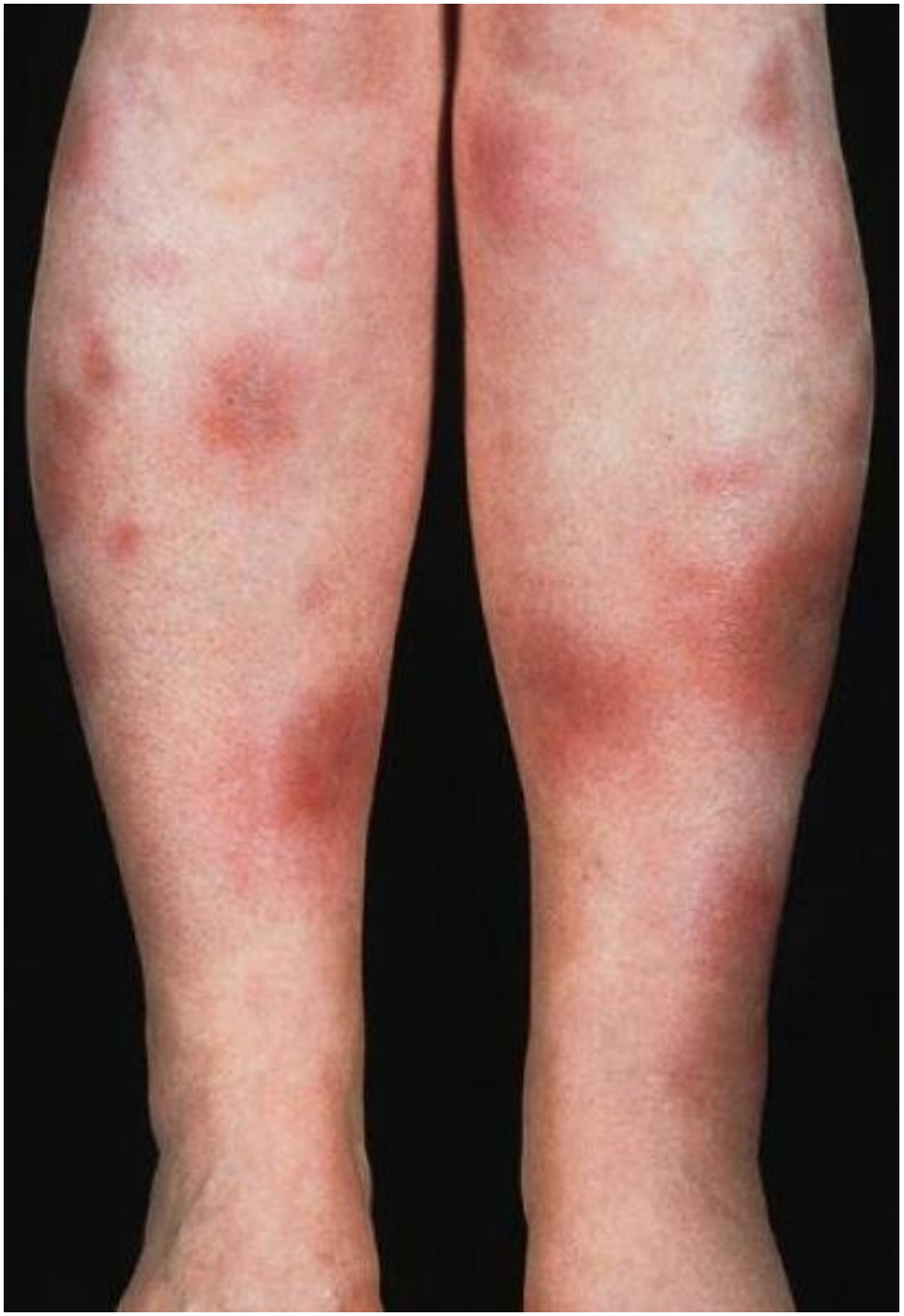
Pellagra

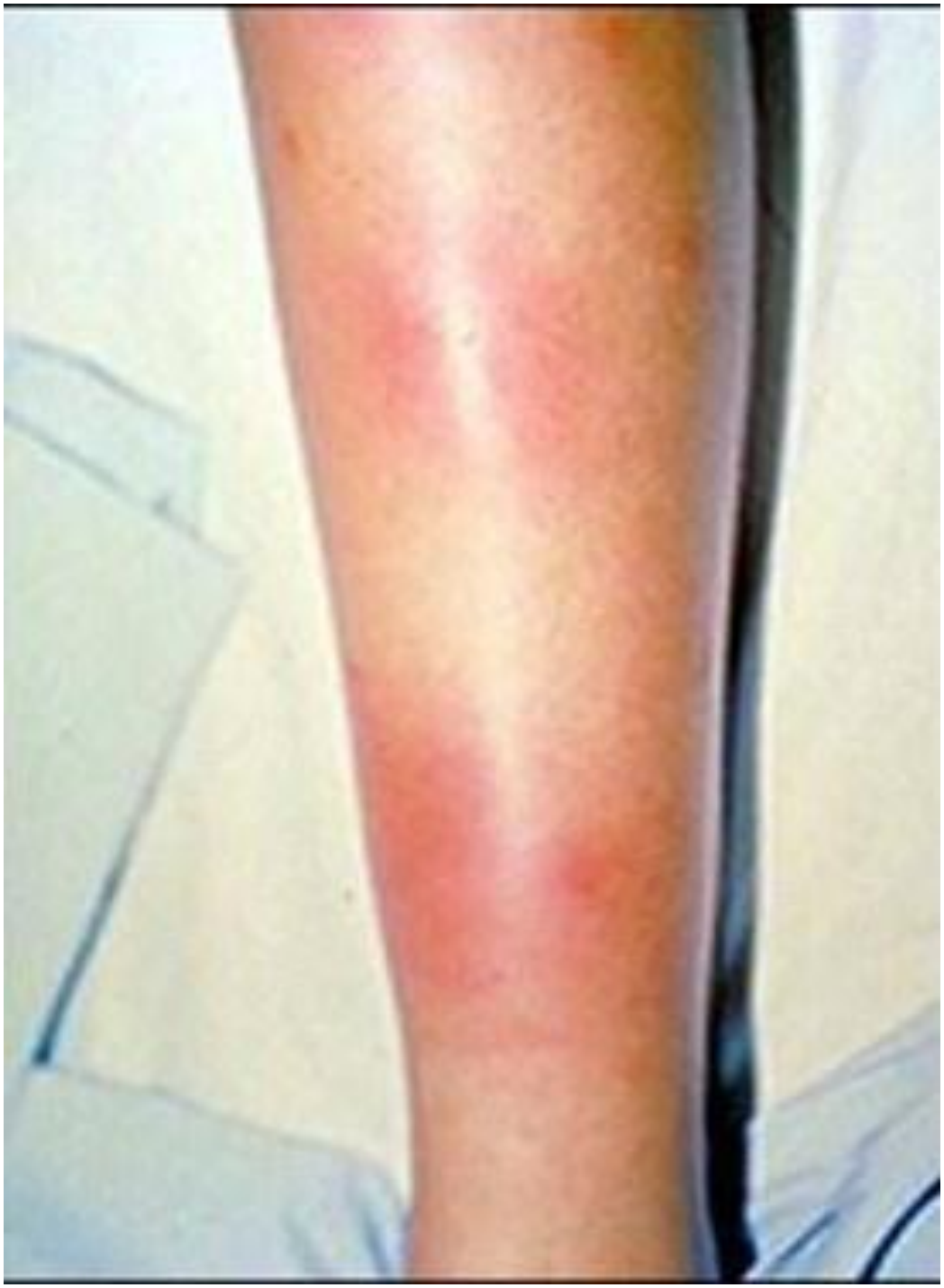
- Causes of generalized pruritus without skin lesions:
  1. Endocrine: DM, hypo& hyperthyroidsm
  2. Haematological: polycythemia rubra vera, iron def anemia
  3. Malignancy; e.g. Lymphoma
  4. Hepatic: primary biliary cirrhosis
  5. Renal: CRF

  The commonest manifestation of CRF is pruritus
  6. Neurological : e.g. Tabes dorialis
  7. Others:
     - Psychognic
     - Drugs
     - Idiopthaic

Erythema Nodosum

- Multiple bilateral tender erythematous subcutaneous nodules Over shins
- More common in females
- Causes:
  - Infectious: Streptococus, Tuberculosis, Hepatitis ,Chlamydia
  - Sarcoidosis
  - Drugs : Oral contraceptive pills, sulfonamides
  - Lymphoma & leukemia
  - Pregnancy
  - Behcet's disease
  - Idiopathic

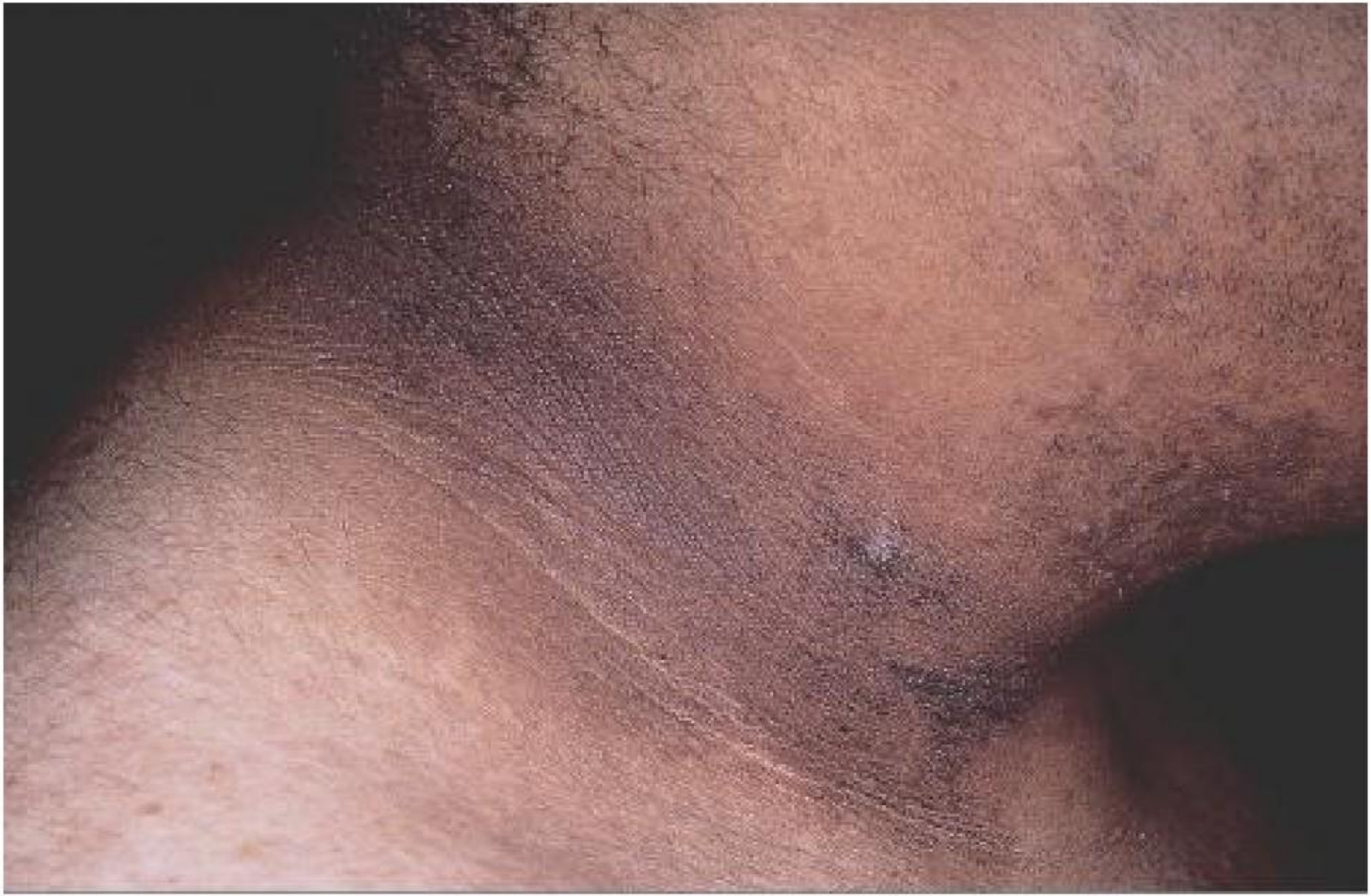


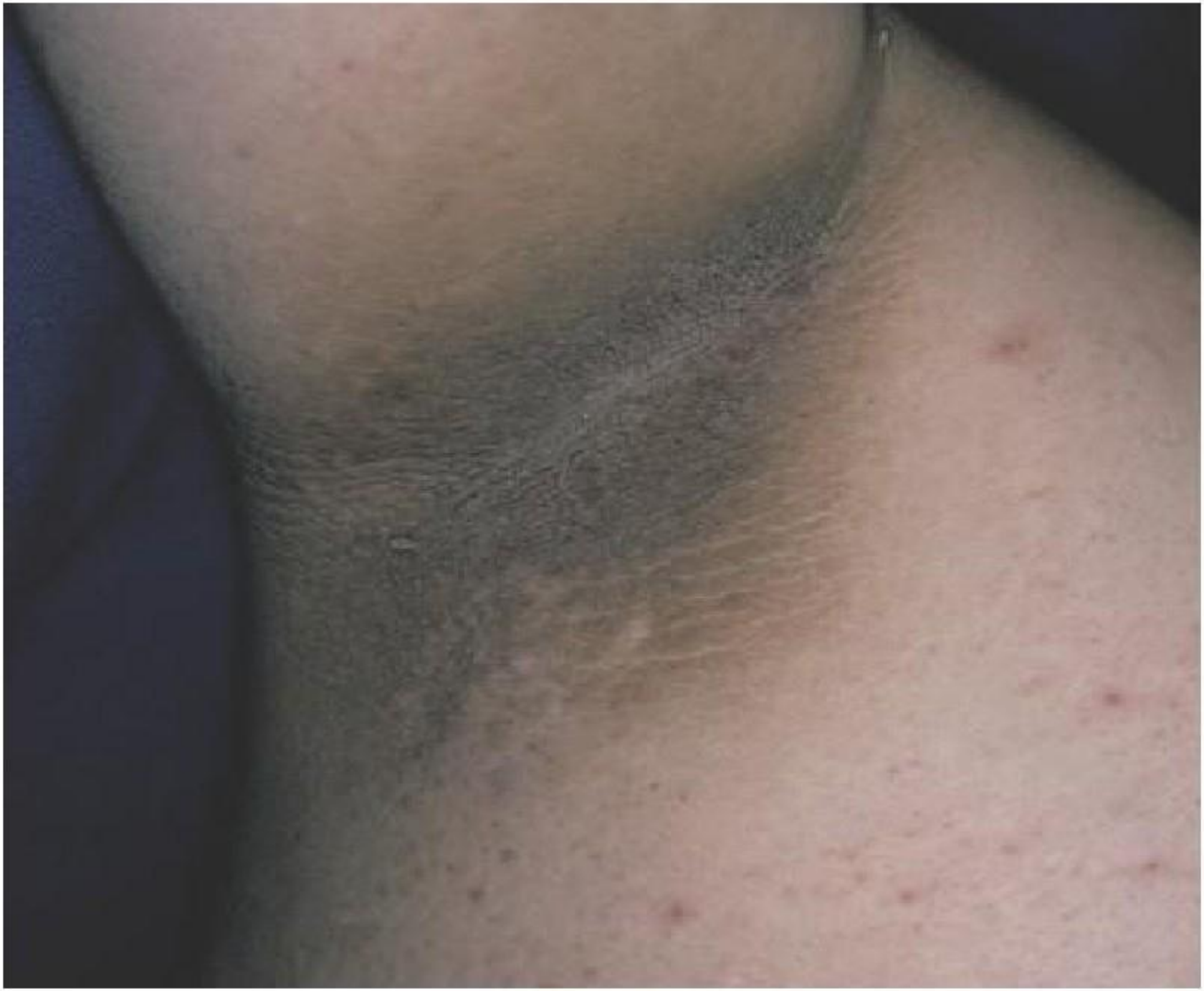


Acanthosis Nigricans:

- Brown hyperpigmentation & increased thickening of skin with velvety texture at neck, axillae and groin

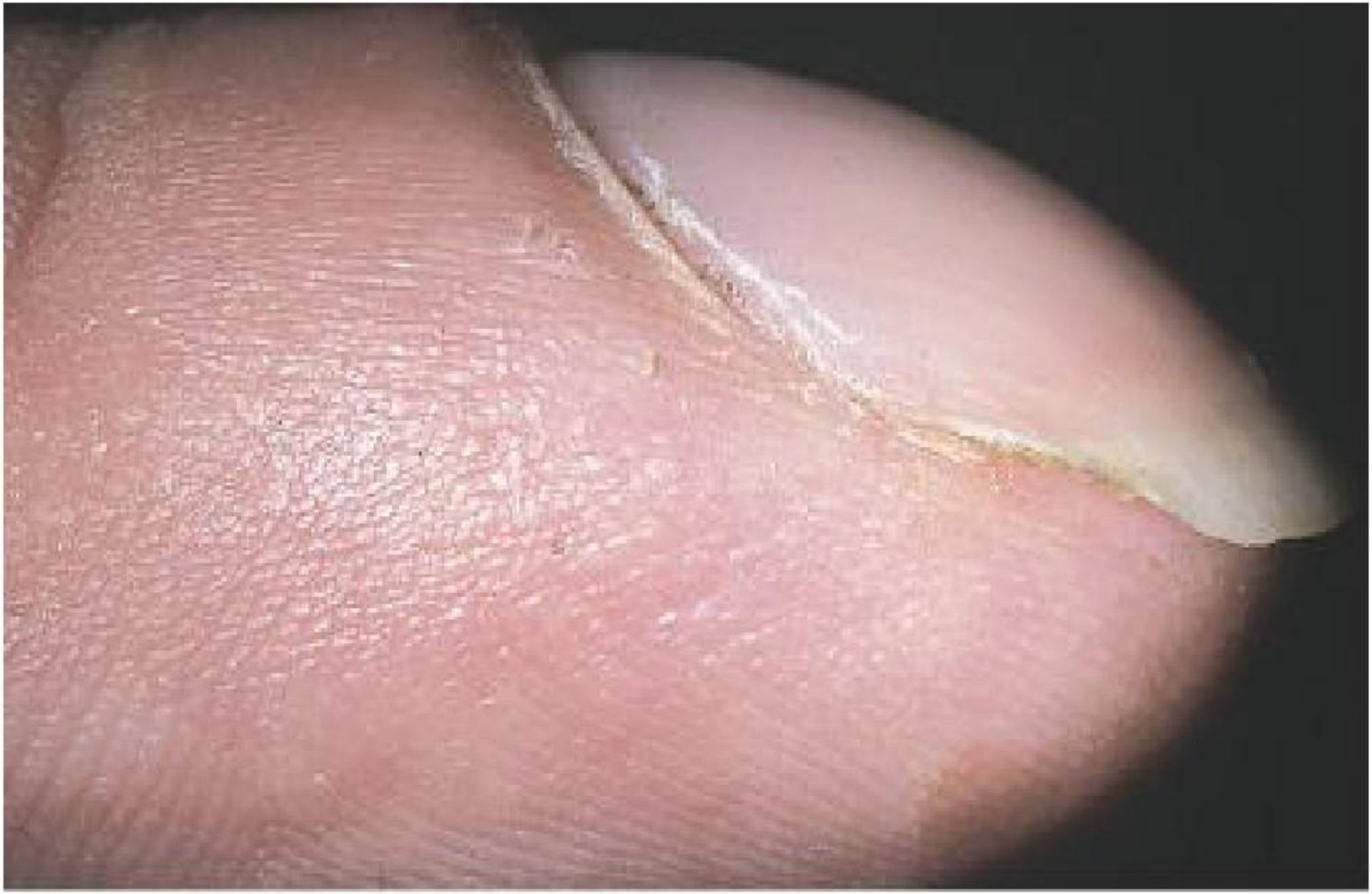
- Causes:
  - Obesity
  - Endocrinopathy : Diabetes, Thyroid disease, Insulin resistance
  - Internal malignancy: the most common is adenocarcinoma of stomach
  - Drugs: Nicotinic acid
  - Familial
  - Idiopathic





Nails

- Clubbing :
  - Exaggeration of the normal nail curve associated with loss of the normal angle between nail and posterior nail fold
  - Causes:
    1. Thoracic: Lung abscess, Lung CA
    2. CVS: Congenital cyanotic heart disease
    3. GIT:GI carcinoma, Inflammatory bowel disease
    4. Endocrine: Thyroid disease
    5. Idiopathic:



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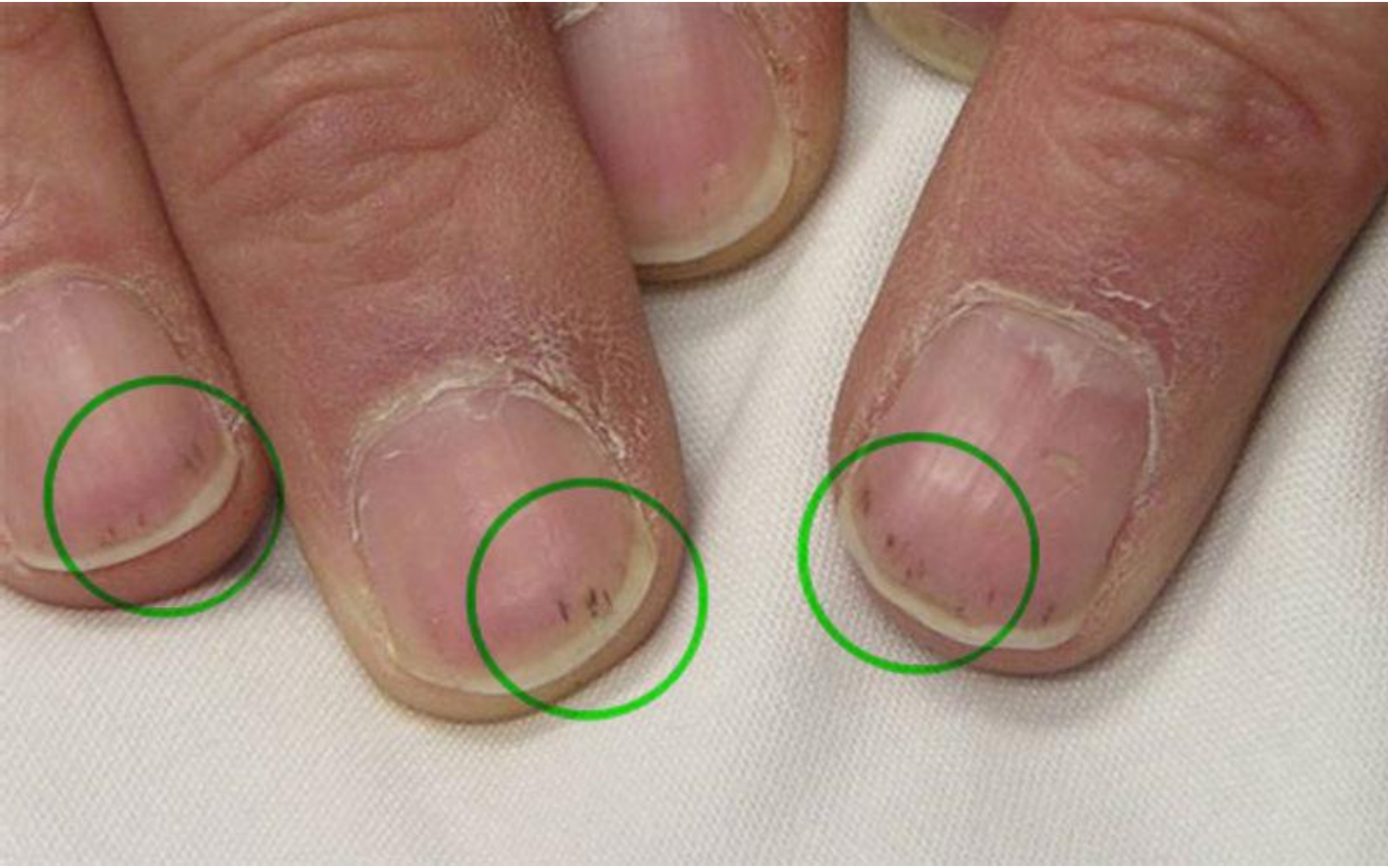
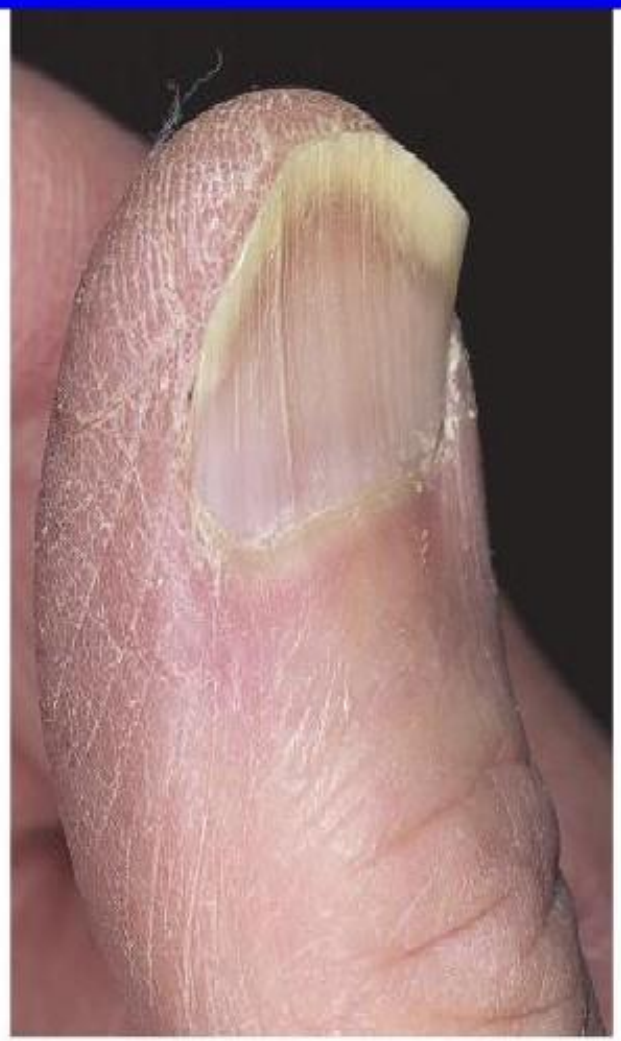
- Splinter Haemorrhages :
  - Causes :
    1. Bacterial endocarditis
    2. Septic emboli
    3. CTD
    4. Trauma
    5. Idiopathic





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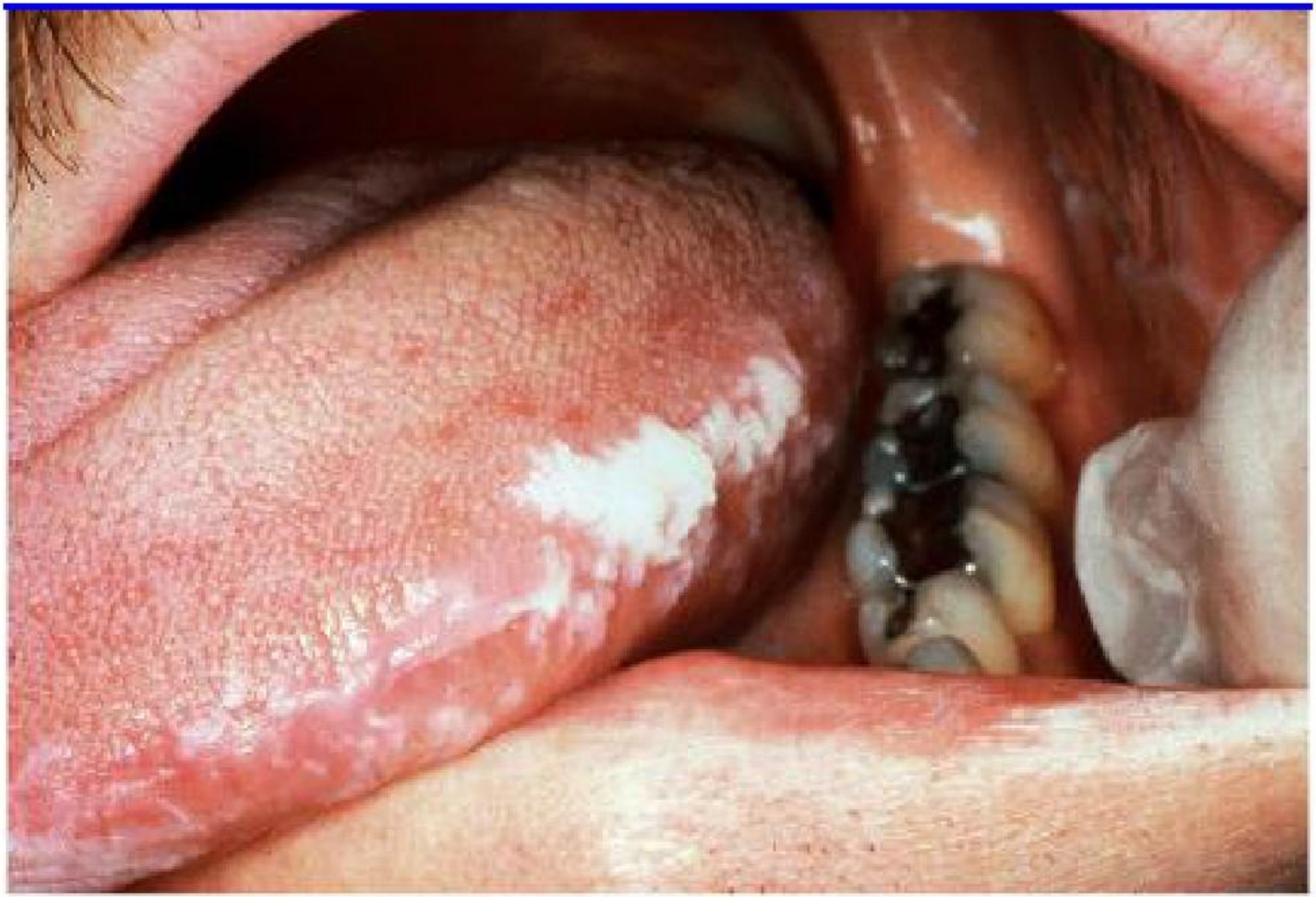
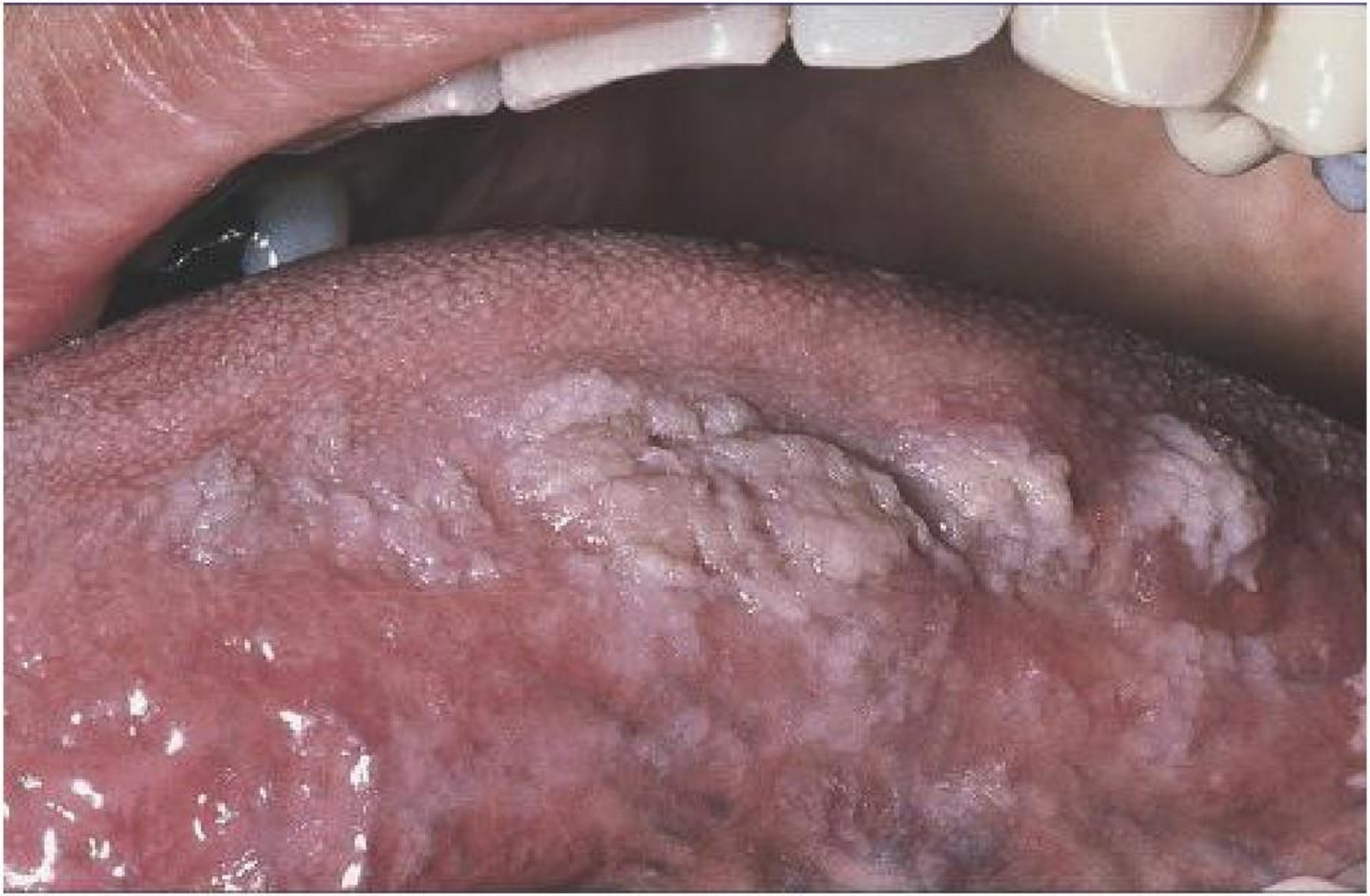
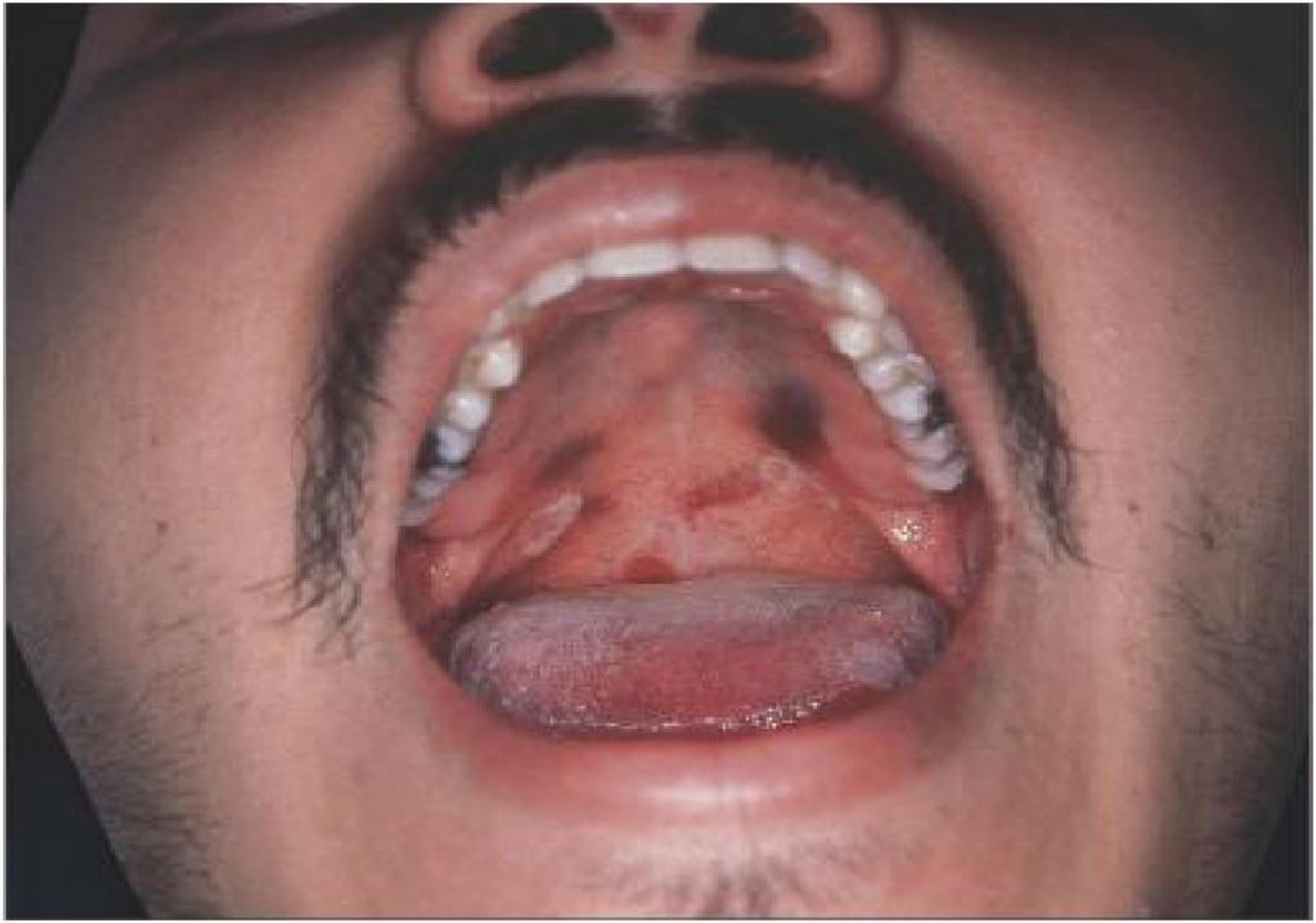
- Koilonychia :
  - Spoon- shaped appearance
  - Causes:
    1. Iron deficiency anemia
    2. Thyroid disease
    3. Physological; early childhood
    4. Dermatoses: Lichen planus
       Alopecia Areata and others

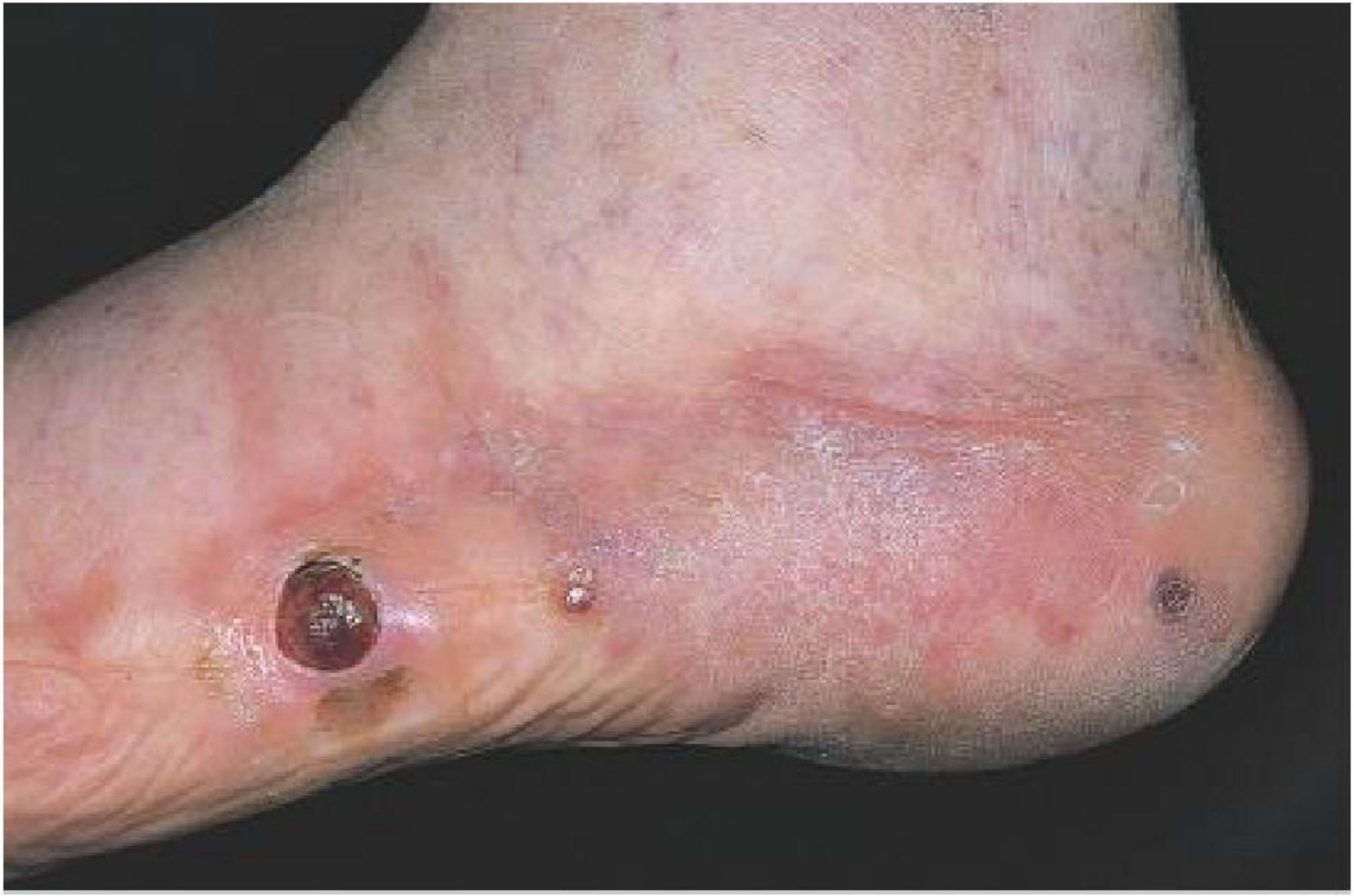
Some mucocutaneous disorders in which you need to do HIV testing?

- Oral hairy leukoplakia:
  - Corragated white plaques on the lateral aspect of the tongue.
- Kaposi Sarcoma:
  - Caused by HHV -8
  - Blue macules ,patches or nodules which is in essence a vascular tumor
  - Associated with low CD4 count
  - May resolve or diminish if CD4 count rises
  - Types of Kaposi sarcoma :Classic type (in elderly),Immunosupperssion associated ,HIV associated ,and African endemic type
  - Metastasis to Lymph nodes , and Viscera









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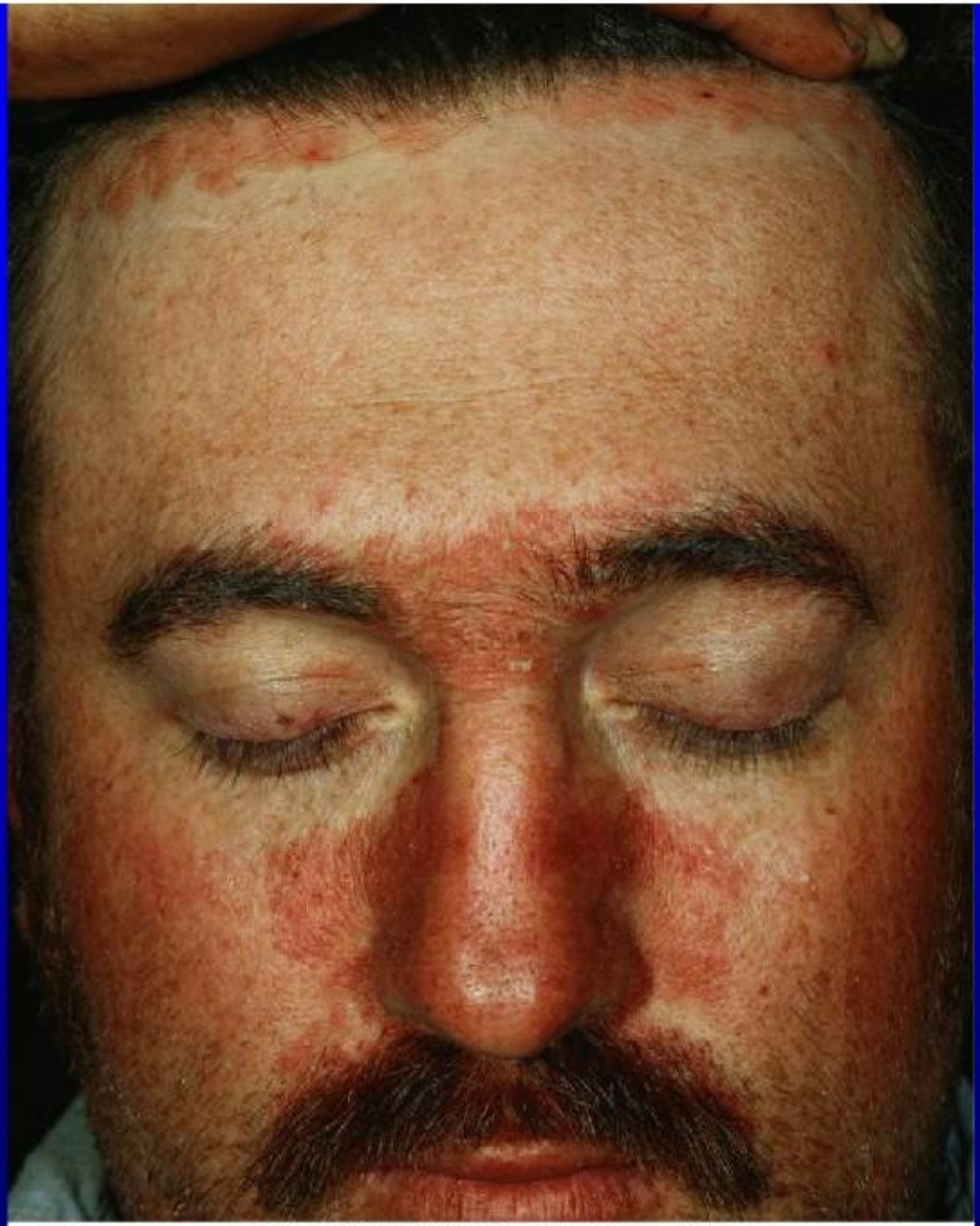


*Multiple mollsucum contagiosum in adult (on face)

*Any STD

*Seborrheic Dermatitis (extensive & refractory to therapy)

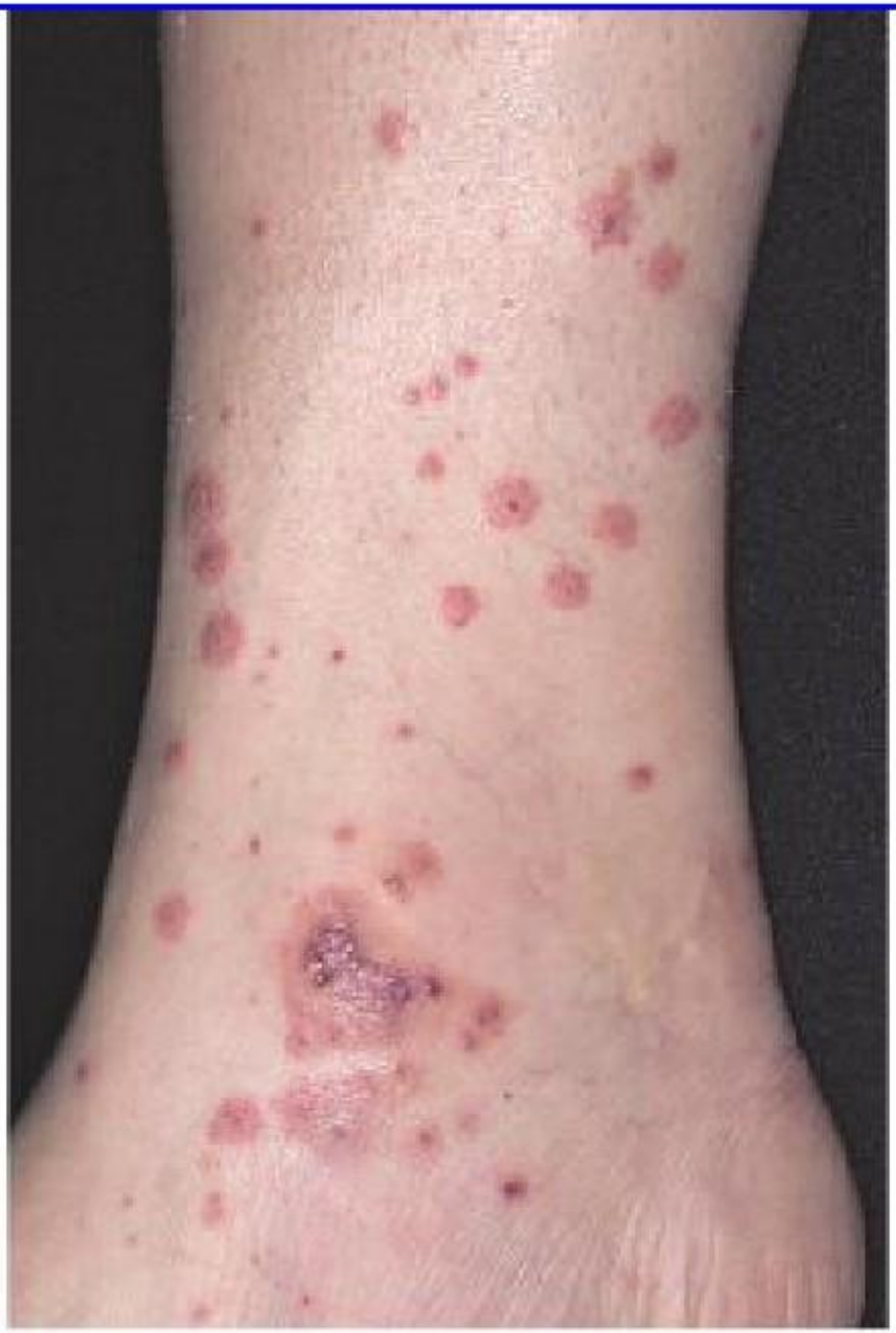
*Severe extensive relacitrant apthous ulceration

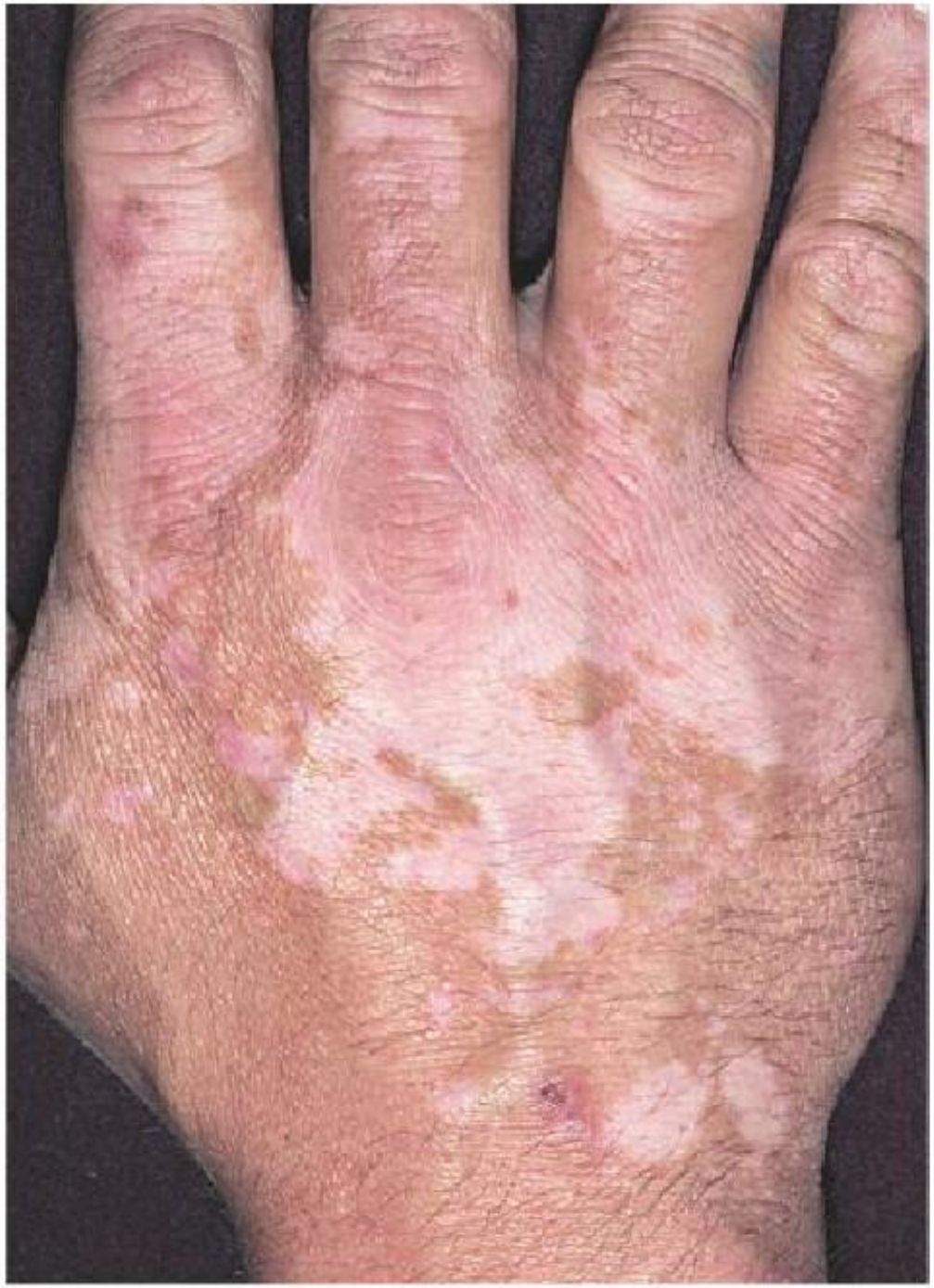
Examples of some skin diseases where you may find systemic associations:

1. Lichen planus;associated with Hepatitis B and C
2. Vitiligo and
3. Alopecia Areata :

both associated with autoimmune diseases like: Autoimmune

Thyroid dis,Diabetes mellitus ,Prenicious anemia,Mysthina gravis etc





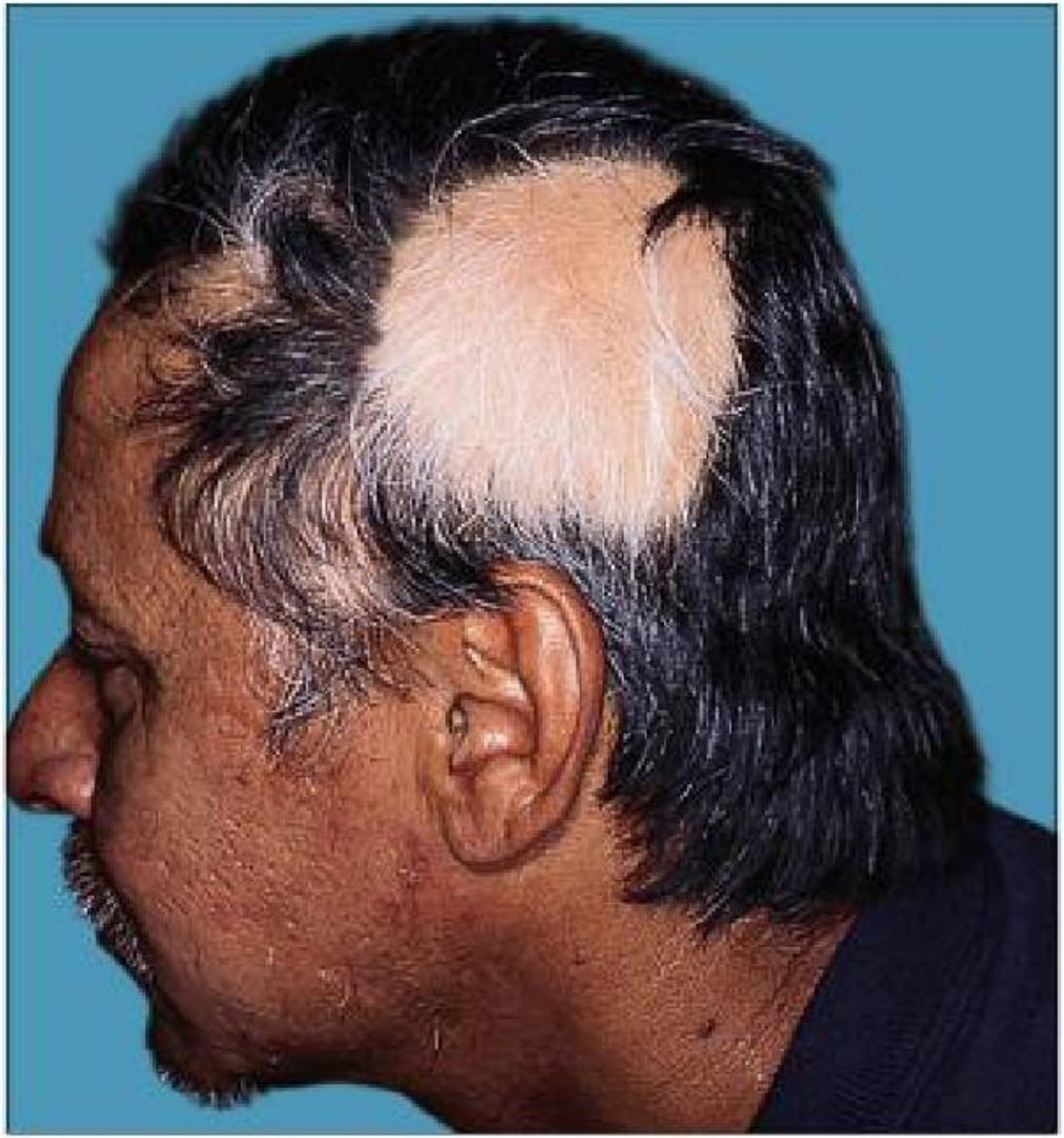


Table 7.2 Possible laboratory studies in the evaluation of pruritus. These laboratory tests should be performed according to the patient's history, in particular in cases of generalized pruritus of unknown etiology.

POSSIBLE LABORATORY STUDIES IN THE EVALUATION OF PRURITUS
• Erythrocyte sedimentation rate (ESR) • Complete blood cell count (CBC) with differential and platelet count • Blood urea nitrogen, creatinine • Liver transaminases, alkaline phosphatase, bilirubin • Fasting glucose • Thyroid function tests (thyroid stimulating hormone (TSH) and thyroxine levels) • Parathyroid function (calcium and phosphate levels) • Serum iron, ferritin • Chest radiograph • Stool for ova, parasites and occult blood
• Viral hepatitis screen • Serum protein electrophoresis • Serum immunofixation • Antinuclear antibodies (ANA), antimitochondrial antibodies
• Human immunodeficiency virus (HIV) • Allergy panel: total IgE, histamine, serotonin (plasma) • Prick tests of major atopy antigens and additives, patch tests • Urine for sediment, 5-hydroxyindolacetic acid (5-HIAA) and mast cell metabolites • Additional radiographic studies, e.g. abdominal CT scan • Anti-tissue transglutaminase antibody • Anti-smooth muscle antibody

Purpura and Vasculitis

- **Purpura** is a condition of red or purple discolored spots on the skin that do not blanch on applying pressure.

- The spots are caused by bleeding underneath the skin secondary to platelet disorders, vascular disorders, coagulation disorders, or other causes.

- They measure 3–10 mm,whereas petechiae measure less than 3 mm, and ecchymoses greater than 1 cm.

Definition

Visible hemorrhage into the skin or mucous membrane subdivided as a follow:

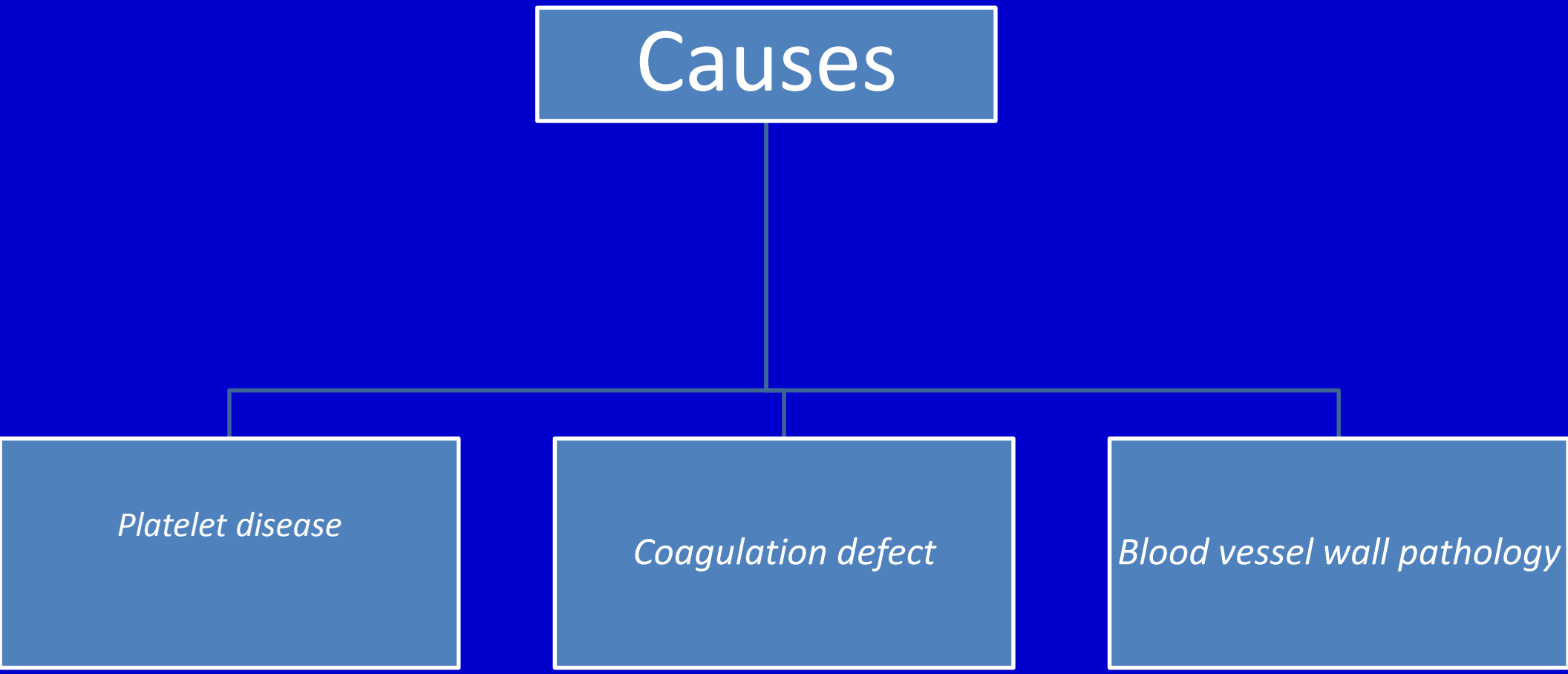
-Petechiae less than or equal 4 mm

-Purpura (>4mm - < 1cm)

which can be either Palpable or non-palpable(macular)

-Ecchymoses > or equal to 1 cm

Purpura


Causes
Platelet disease
Coagulation defect
Blood vessel wall pathology

Causes

1-Platelet Disorders

Thrombocytopenia

Platelet Dysfunction

2-Coagulation Factor Deficiency

Congenital

Factor VIII Deficiency

Factor IX Deficiency

Von Willebrands disease

Acquired

Disseminated Intravascular Coagulopathy

Liver disease

Uremia

Vitamin K deficincy

3-Vascular Factors

Congenital

Hereditary Hemorrhagic Telangectasia

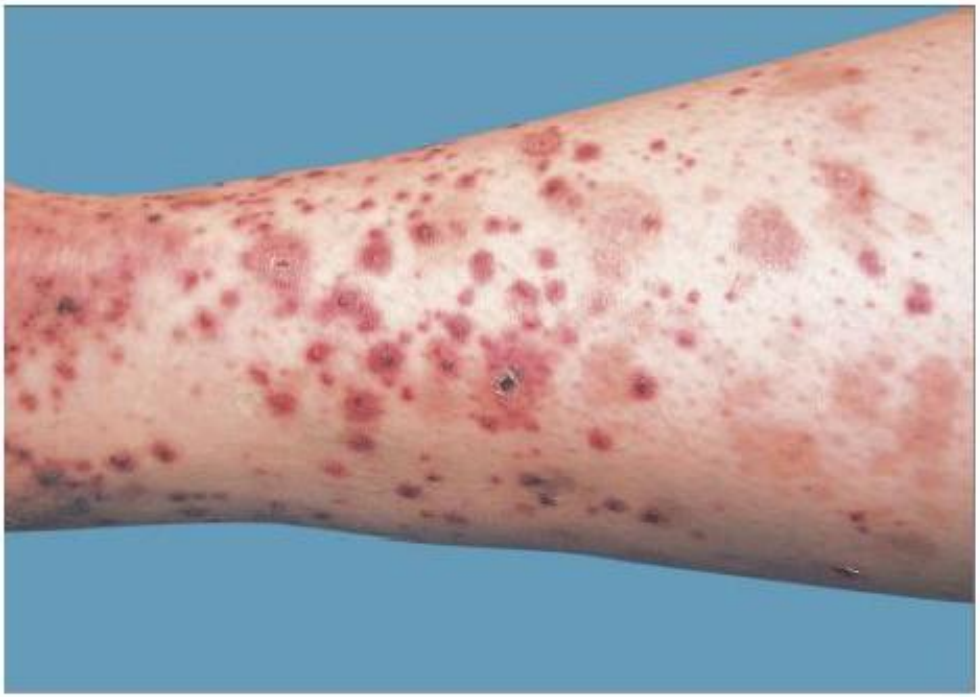
Ehlers-Danlos Syndrome (Type IV)

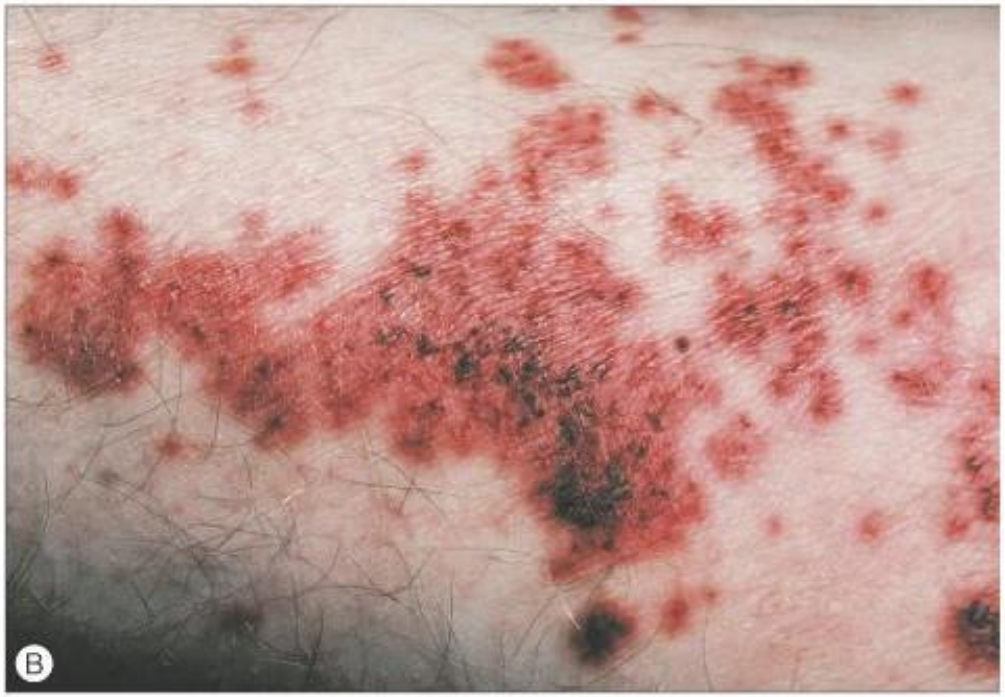
Acquired:

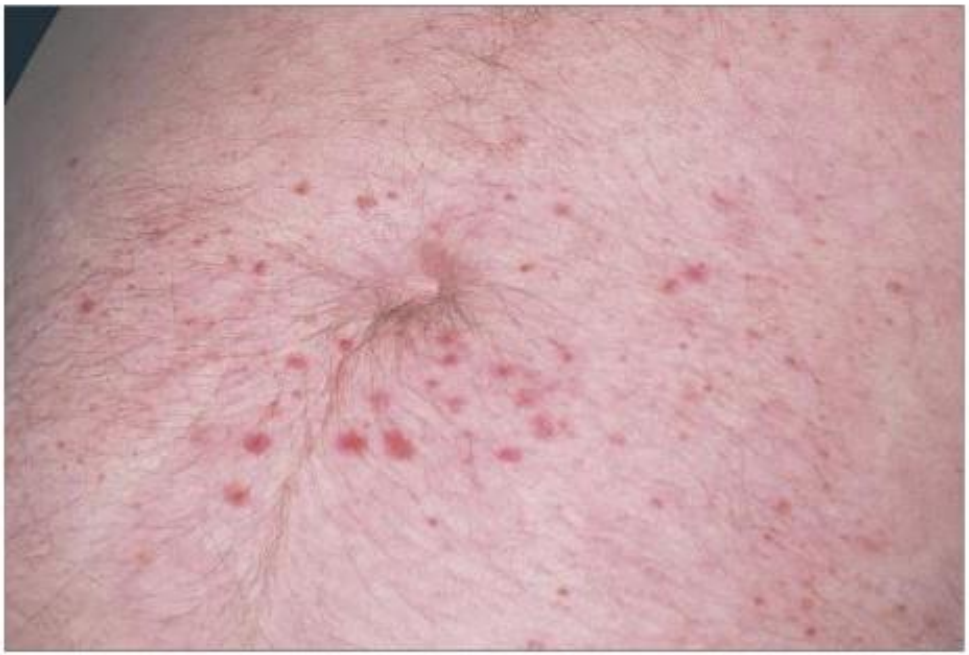
Inflammation(Vasculitis)

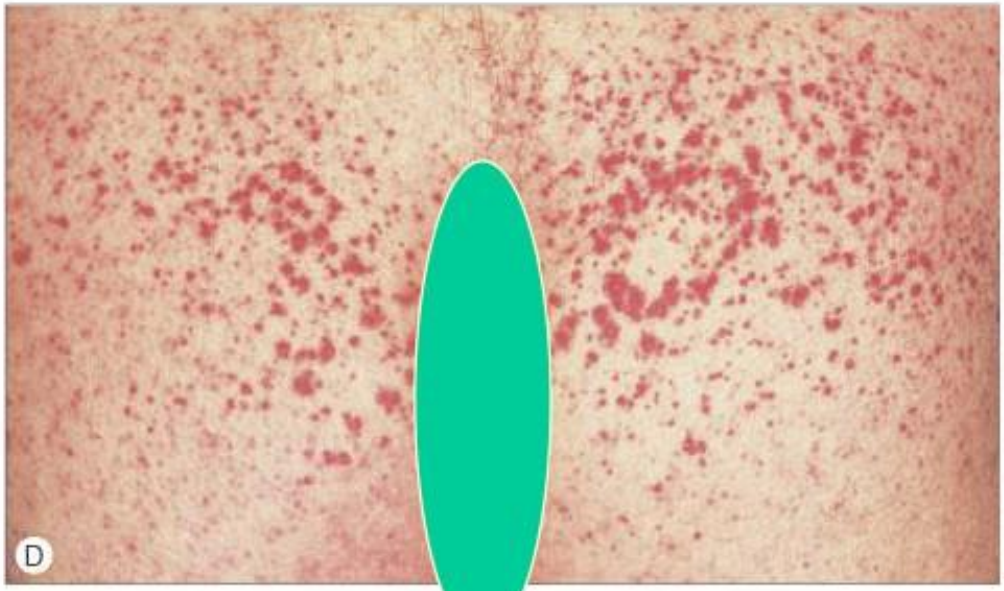
Trauma

Vitamin c deficiency (scurvy)

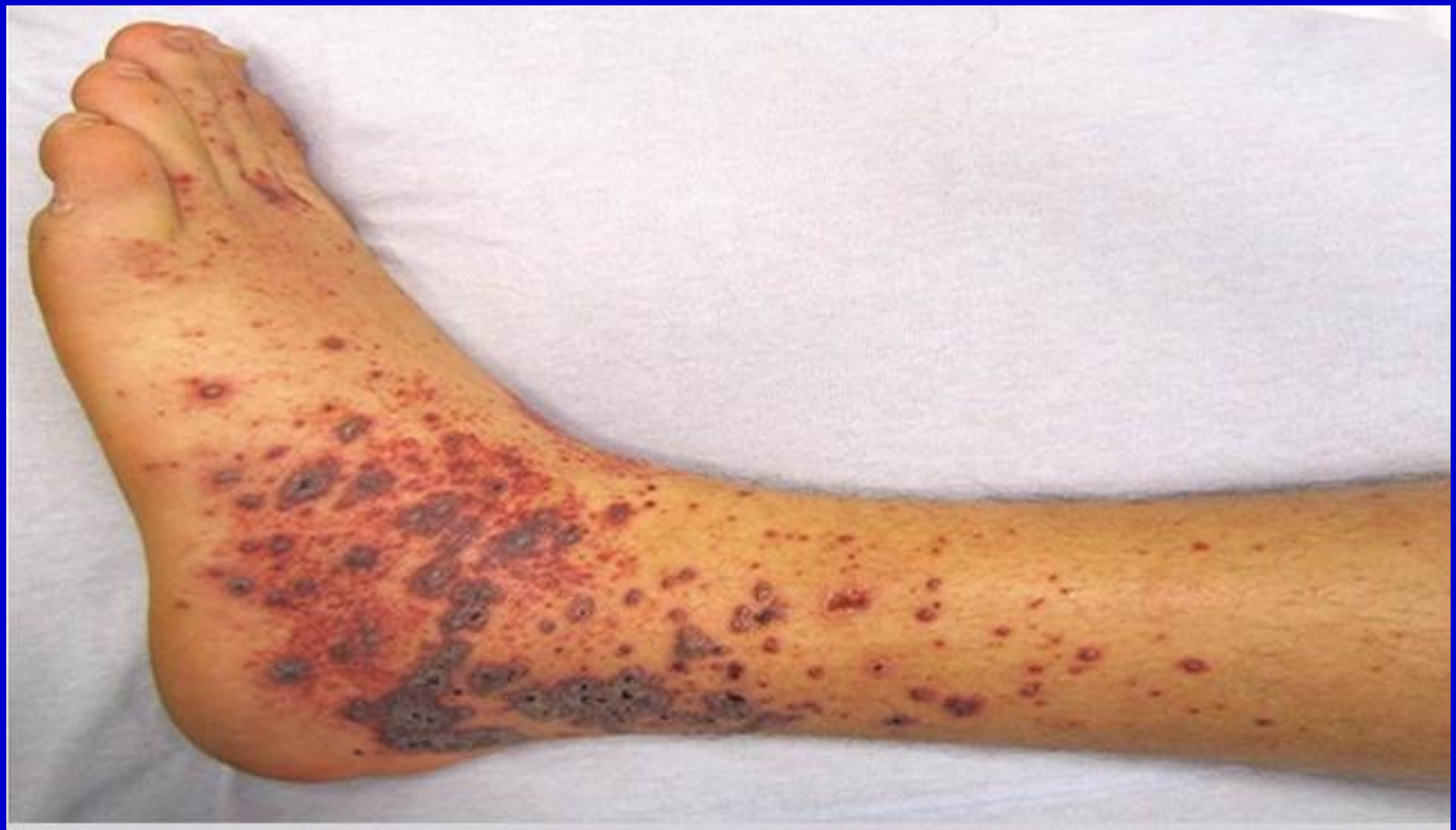








vasculitis



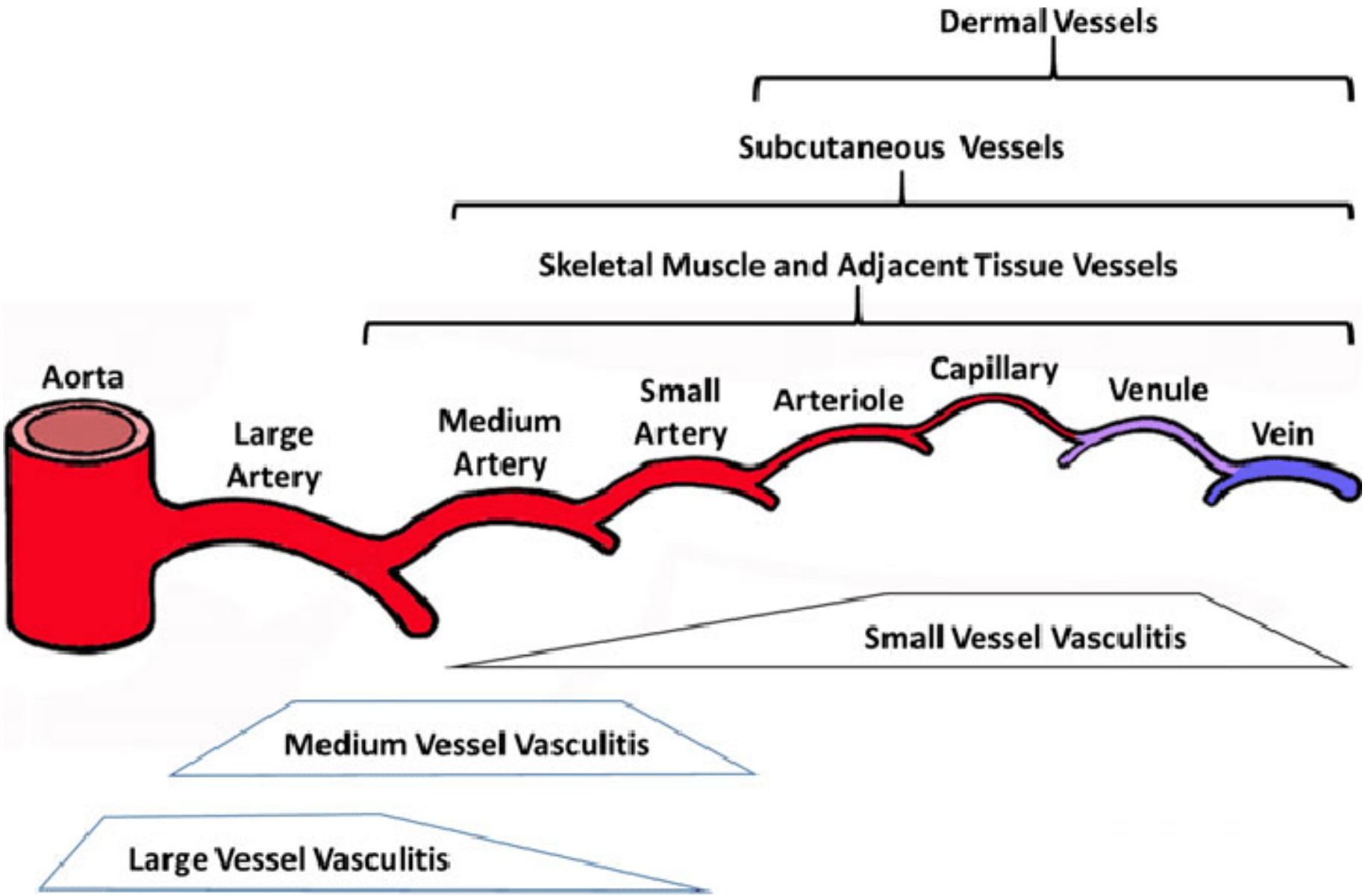
Definition

A clinicopathologic process characterized by inflammatory destruction of blood vessels that results in occlusion or destruction of the vessel and ischemia of the tissues supplied by that vessel.

classification

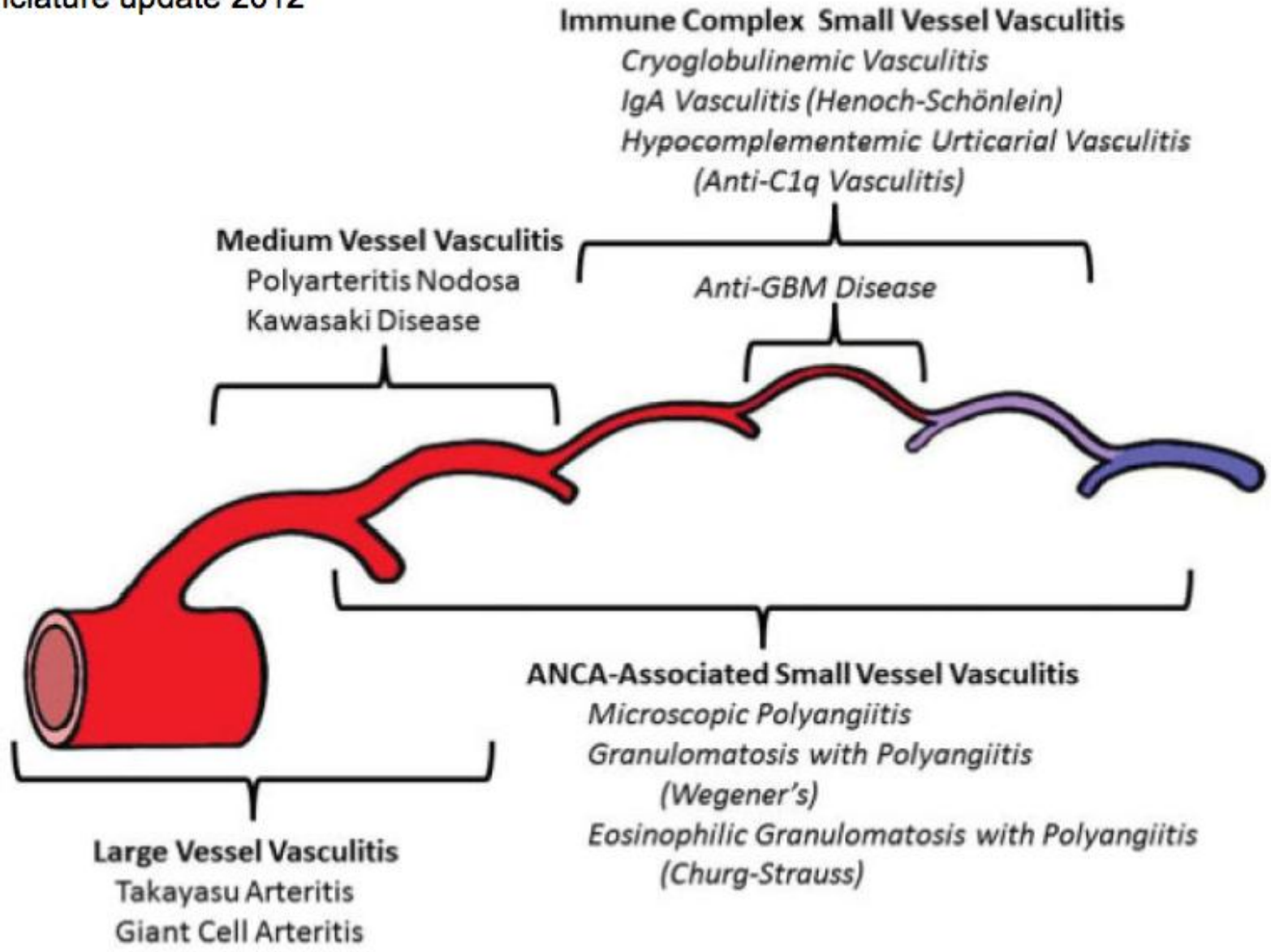
Table 26.2 Chapel Hill consensus classification.

CHAPEL HILL CONSENSUS CLASSIFICATION
Large-vessel vasculitis
• Giant cell arteritis • Takayasu's arteritis
Medium-vessel vasculitis
• Classic polyarteritis nodosa • Kawasaki disease
Small-vessel vasculitis
• Wegener's granulomatosis • Churg–Strauss syndrome • Microscopic polyangiitis (polyarteritis) • Henoch–Schönlein purpura • Essential cryoglobulinemia • Cutaneous leukocytoclastic vasculitis


Dermal Vessels
Subcutaneous Vessels
Skeletal Muscle and Adjacent Tissue Vessels
Aorta
Large Artery
Medium Artery
Small Artery
Arteriole
Capillary
Venule
Vein
Small Vessel Vasculitis
Medium Vessel Vasculitis
Large Vessel Vasculitis

Classification of Vasculitis

Chapel Hill Consensus Criteria
Nomenclature update 2012



Classification

-***Large-vessel vasculitis***

Aorta and the great vessels (subclavian, carotid)

Claudication, blindness, stroke

-Medium-vessel vasculitis

Arteries with muscular wall

Mononeuritis multiplex (wrist/foot drop), mesenteric ischemia, cutaneous ulcers

-Small-vessel vasculitis

Capillaries, arterioles, venules

Palpable purpura, glomerulonephritis, pulmonary hemorrhage

Cutaneous small vessel vasculitis

- most common type of vasculititis and it primarily affect post-capillary venules

Cutaneous small vessel vasculitis

Pathogenesis:

-Many forms of small-vessel vasculitis are felt to be caused by circulating immune complexes

-These lodge in vessel walls and activate compliment

Cutaneous small vessel vasculitis

Table 3. Causes of cutaneous vasculitis[5,6]

Infections	
Bacterial	• Streptococcal, meningococcal, urinary tract infections
Viral	• Hepatitis B and C, HIV
Mycobacterial	• Tuberculosis
Connective tissue disorders	• SLE and related conditions • Rheumatoid arthritis • Systemic sclerosis, Sjogren syndrome • Dermatomyositis • Medium vessel vasculitides (Wegener granulomatosis, polyarteritis nodosa, Churg-Strauss syndrome)
Malignancy	• Haematologic — myeloproliferative — lymphoma — monoclonal gammopathy — multiple myeloma
Drugs	Including antibiotics, antihypertensives
Idiopathic	Henoch-Schonlein purpura

Cutaneous small vessel vasculitis

Palpable purpura is the hallmark

-Pinpoint to several centimeters

-Early on lesion may not be palpable,Papulonodular, vascular, bullous, pustular or ulcerated forms may develop

-Predominate on the ankles and lower legs i.e dependent areas

-*may be localized to the skin or may manifest in other organs.*

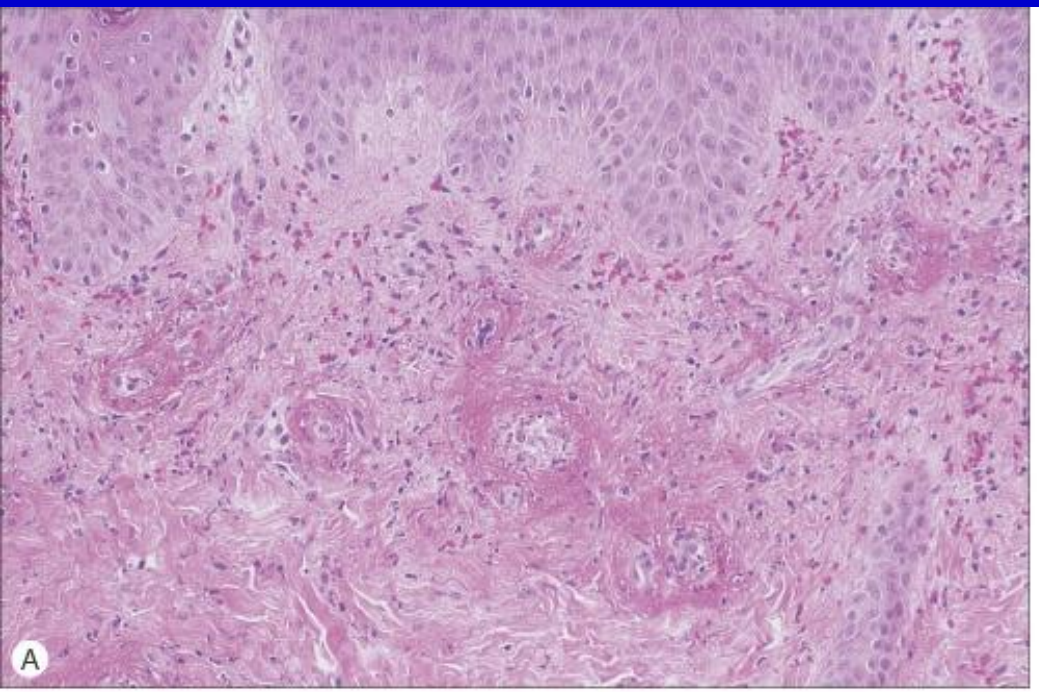
-*The internal organs affected most commonly include the joints, GIT, and the kidneys.*

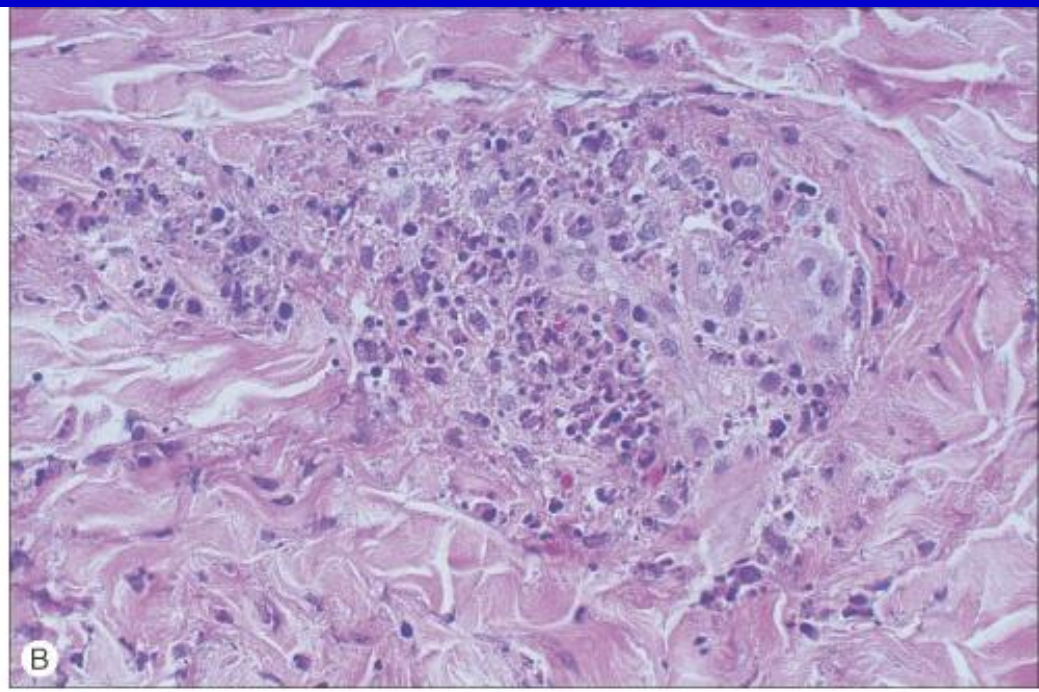
-*Renal involvement present as glomerulonephritis*

- *The prognosis is good in the absence of internal involvement*

Histology

- *Agiocentric segmental inflammation, endothelial cell swelling, fibrinoid necrosis of blood vessel walls and a cellular infiltrate composed of neutrophil with RBC extravasation.*





Work up

-Detailed history and physical examination

-History should focus on possible infectious disorders, prior associated diseases, drugs ingested, and a thorough review of systems

-CBC, strep throat culture or ASO titer, Hep B & C serologies and ANA are a reasonable initial screen,renal profile

-URINALYSIS FOR RBC , PROTIEN & CAST

- Skin biopsy

ble 26.4 Laboratory evaluation in known or suspected vasculitis.

LABORATORY EVALUATION IN KNOWN OR SUSPECTED VASCULITIS	
ystem	Technique
leme	Complete blood count with differential and platelet count, erythrocyte sedimentation rate (ESR), C-reactive protein
enal	Urinalysis, BUN, creatinine
iver	Abnormal liver function tests, hepatitis B and C antibody, cryoglobulins
mmunologic	Serum complement, rheumatoid factor, antinuclear antibody, anti-dsDNA, extractable nuclear antigen, antineutrophil cytoplasmic autoantibodies (ANCA)
nfectious	Blood and cultures
lead and neck	Sinus radiographs and CT
ulmonary	Chest radiograph or CT
Cardiovascular	Electrocardiogram, creatine phosphokinase, echocardiogram
Neurologic	Nerve conduction studies
Musculoskeletal	Electromyography

DIAGNOSTIC WORKUP

Laboratory investigations

- Full blood count with differential white cell count
- Markers of inflammation: ESR,CRP
- Electrolytes and hepatic transaminases, glucose
- Urinalysis for protein and blood
- Blood cultures (if pyrexial)
- Serology—ANA ,dsDNA , ANCA,C3 and C4,ASLO titre, viral titres (e.g. hepatitis B and hepatitis C, possibly HIV, CMV, parvovirus B19 and others if recent infection).
- Others-rheumatoid factor, electrophoresis, immune complexes.

Treatment

treatment of cause.

-Symptomatic treatment (if skin is only involved): rest ,NSAIDS ,Antihistamine

-severe visceral involvement may require high doses of corticosteroids with or without an immunosuppressive agent

-Immunosuppressive agents for rapidly progressive course and severe systemic involvement

Henoch-Schönlein purpura HSP

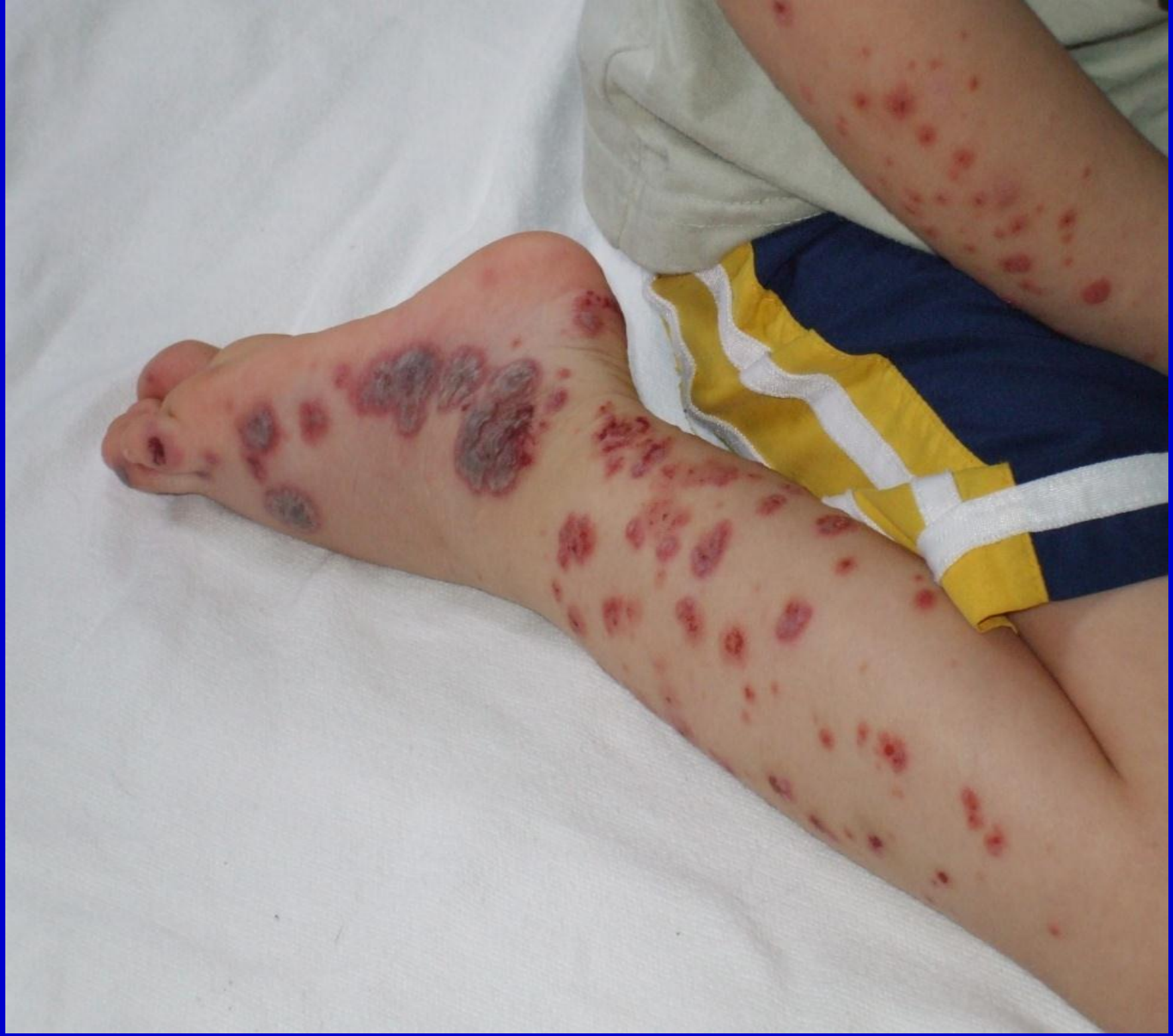
-Primarily occurs in male children

-peak age 4-8 years

-Adults may be affected

-A viral infection or streptococcal pharyngitis are the usual triggering event

-In about 40 % of the cases the cutaneous manifestations are preceded by mild fever, headache, joint symptoms, and abdominal pain for up to 2 weeks



*-Characterized by **intermittent purpura, arthralgia, abdominal pain, and renal disease***

-Typically purpura appears on the extensor surfaces of the extremities

-Become hemorrhagic within a day and fades in 5 days

-New crops appear over a few weeks

May be associated with:

pulmonary hemorrhage

Abdominal pain and GI bleeding

-GI radiographs may show "cobblestone" appearance

-Renal manifestations may occur in 25% or more but only 5% end up with ESRD

- *The long-term prognosis in children with gross hematuria is very good; however, progressive glomerular disease and renal failure may develop in a small percentage*

- *IgA, C3 and fibrin depositions have been demonstrated in biopsies of both involved and uninvolved skin by immunofluorescence techniques*

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