Dermatological Manifestations of Systemic Diseases

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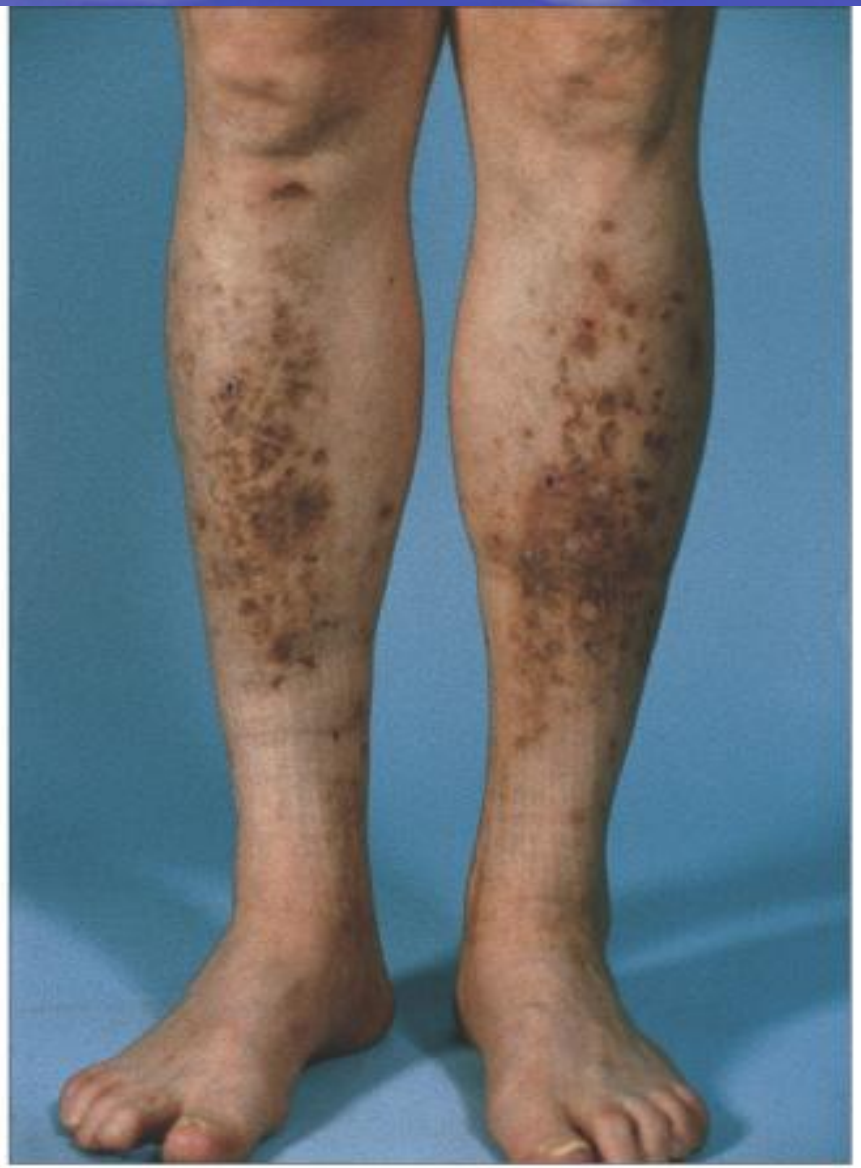
objectives

- Skin involvment can be the first sign of a systemic disease and may be a manifestation of a serious underlying disease.
- Skin manifestations of systemic disease are wide, varied, specific and nonspecific
- Common things are common
- Learn to ask the right questions
- Don’t forget to examine hair, nail and mucous membrane



Skin manifestations of Diabetes mellitus:

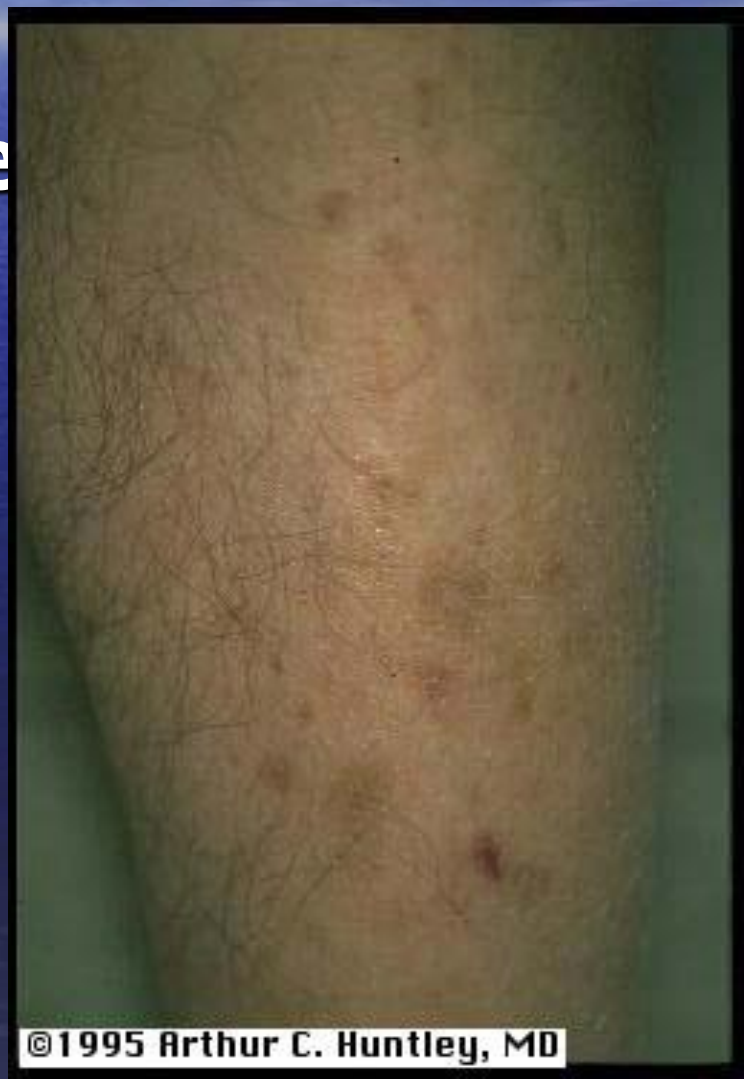
skin manifestations due to vascular abnormalities:

A- wet gangrene of the foot

B- Diabetic Bullae

C- Diabetic dermopathy" shin spots":

D- Erysiepilas- like erythema



2. Diabetic neuropathy (peripheral)

Autonomic neuropathy

3.Cutaneous infections:

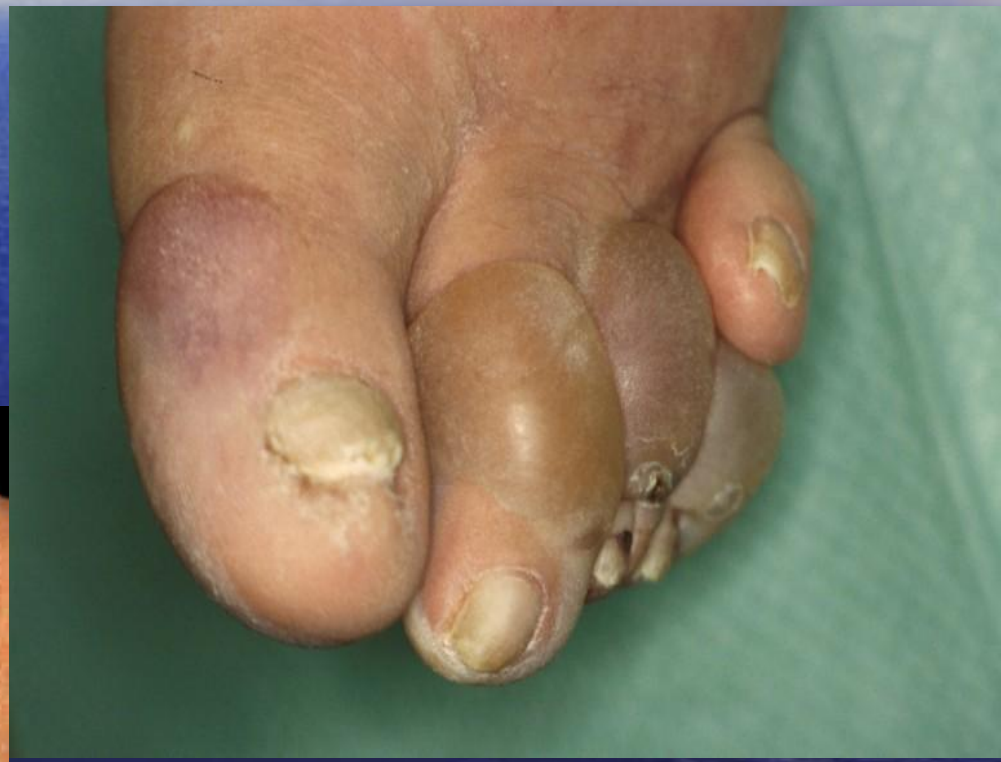
A- Staphylococcus aureus

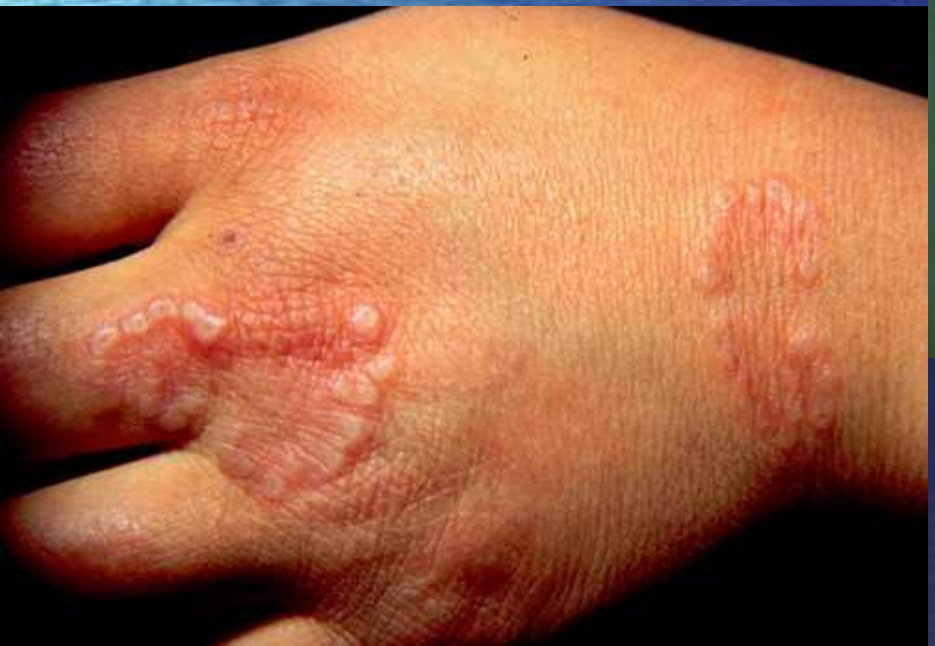
B- Non- clostridial gangrene

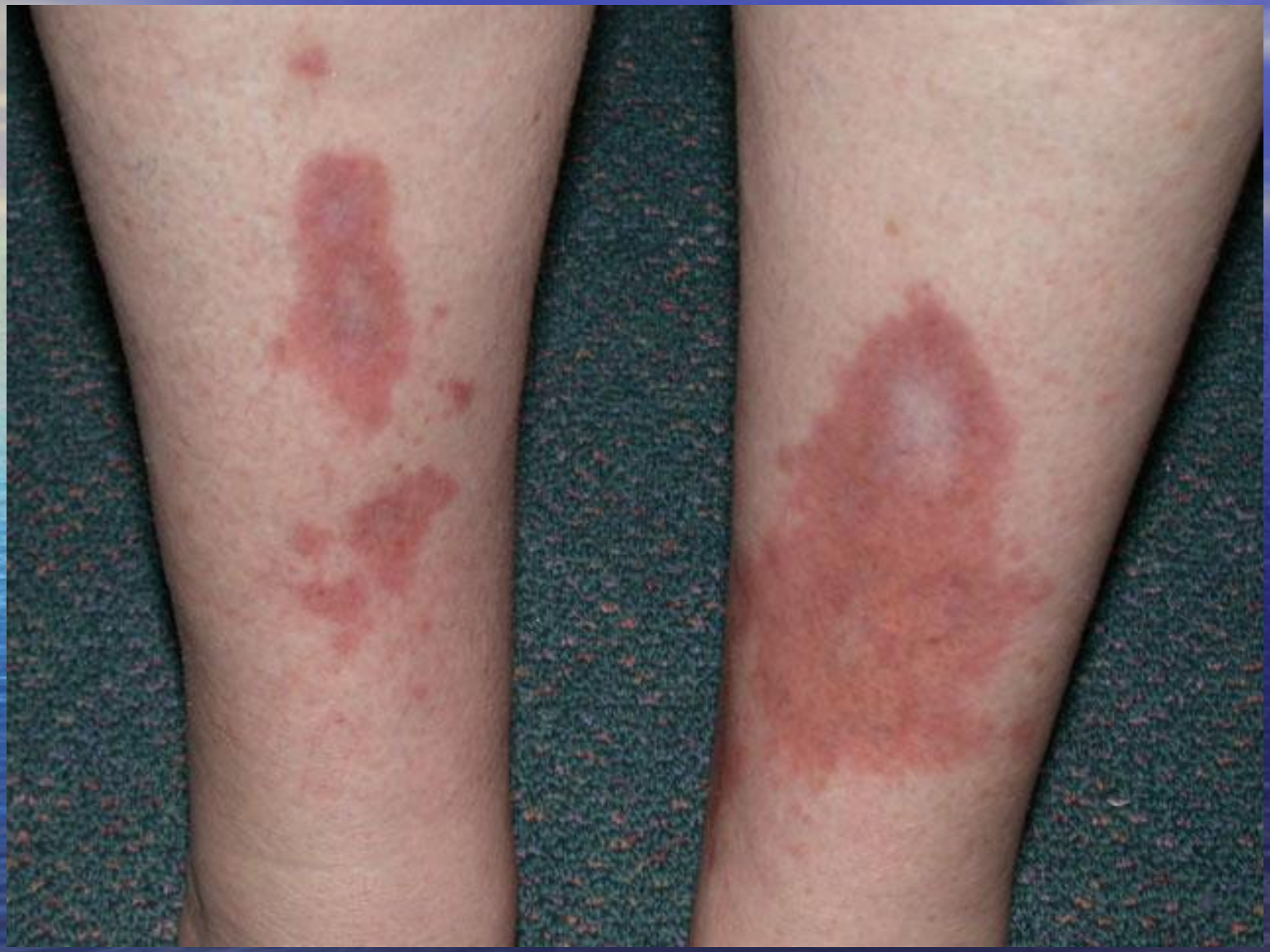
C- Candidiasis

4. Various skin disorders associated with diabetes mellitus:

- Diabetic bullae
- Pruritus
- Granuloma annulare







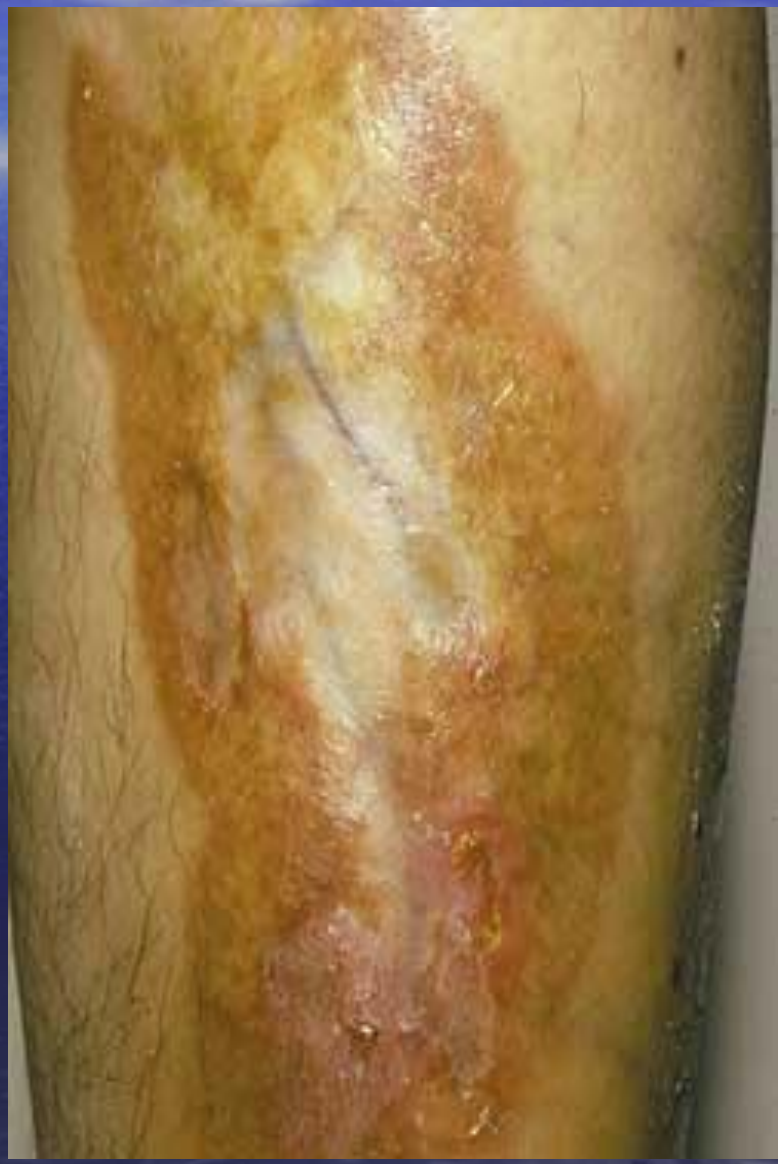
Skin problems associated with diabetes mellitus

- **Necrobiosis lipoidica**
  - Rare, insulin dependent DM
  - One or more tender yellowish brown patches develop slowly on the lower legs over several months
  - Round, oval or an irregular shape
  - The centre of the patch becomes shiny, pale, thinned
  - Prominent blood vessels (telangiectasia)
  - Often painless

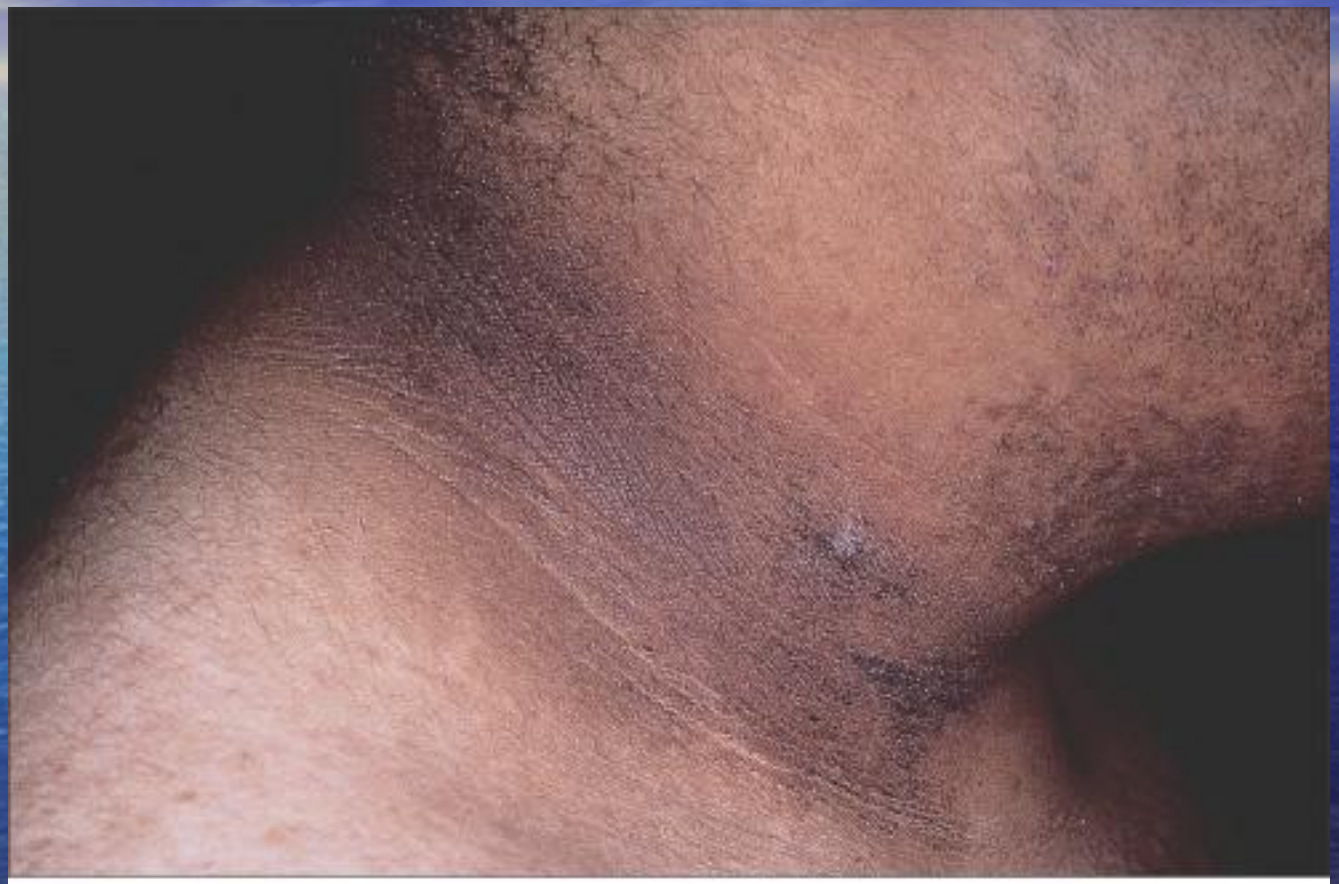
- Treatment: control of diabetes doesn't help in disappearance of the lesions.
  - Intralesional steroids.
  - Systemic aspirin: 300mg/day and dipyridamole 75 mg/day.
  - Nicotineamide
  - Ticlopidine as antiplatelet
  - pentoxyfylline.
  - Preilesional heparin injection

  - Oral cyclosporin

  - Photochemotherapy (PUVA)



Acanthosis nigricans



-Causes:

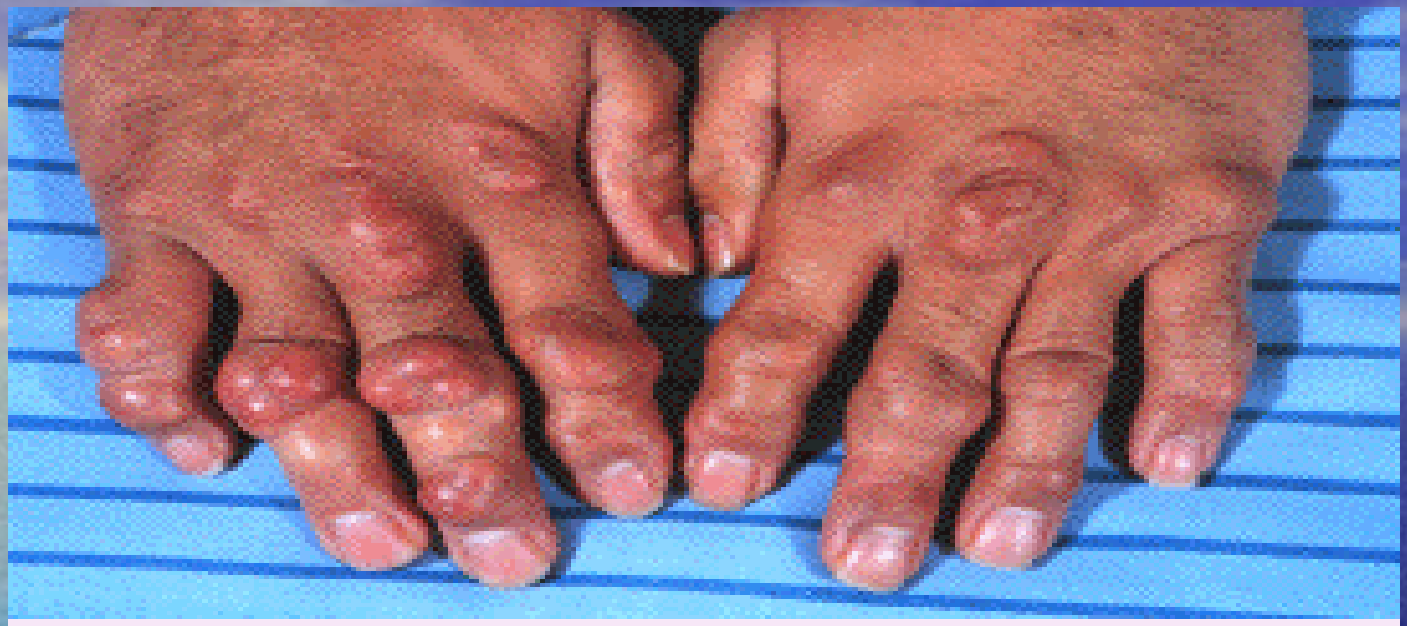
-obesity & insulin resistance & endocrinopathy
(DM, acromegaly ,cushing syndrome ,hypothyroidisim , Addison disease & hyperandrogenic state as HAIRAN syndrome (hyperandrogen, insulin resistance, acanthosis nigricans)

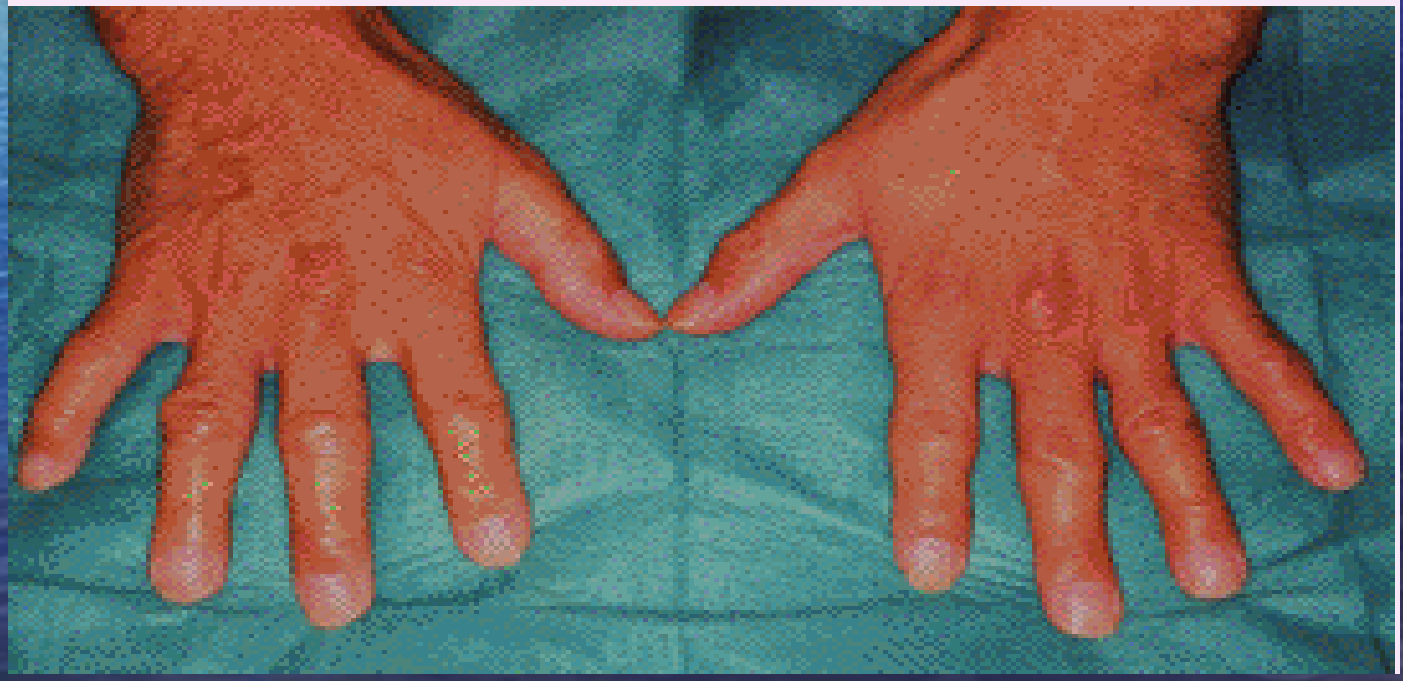
-Malignancy (esp. GIT, Lung & Breast CA)

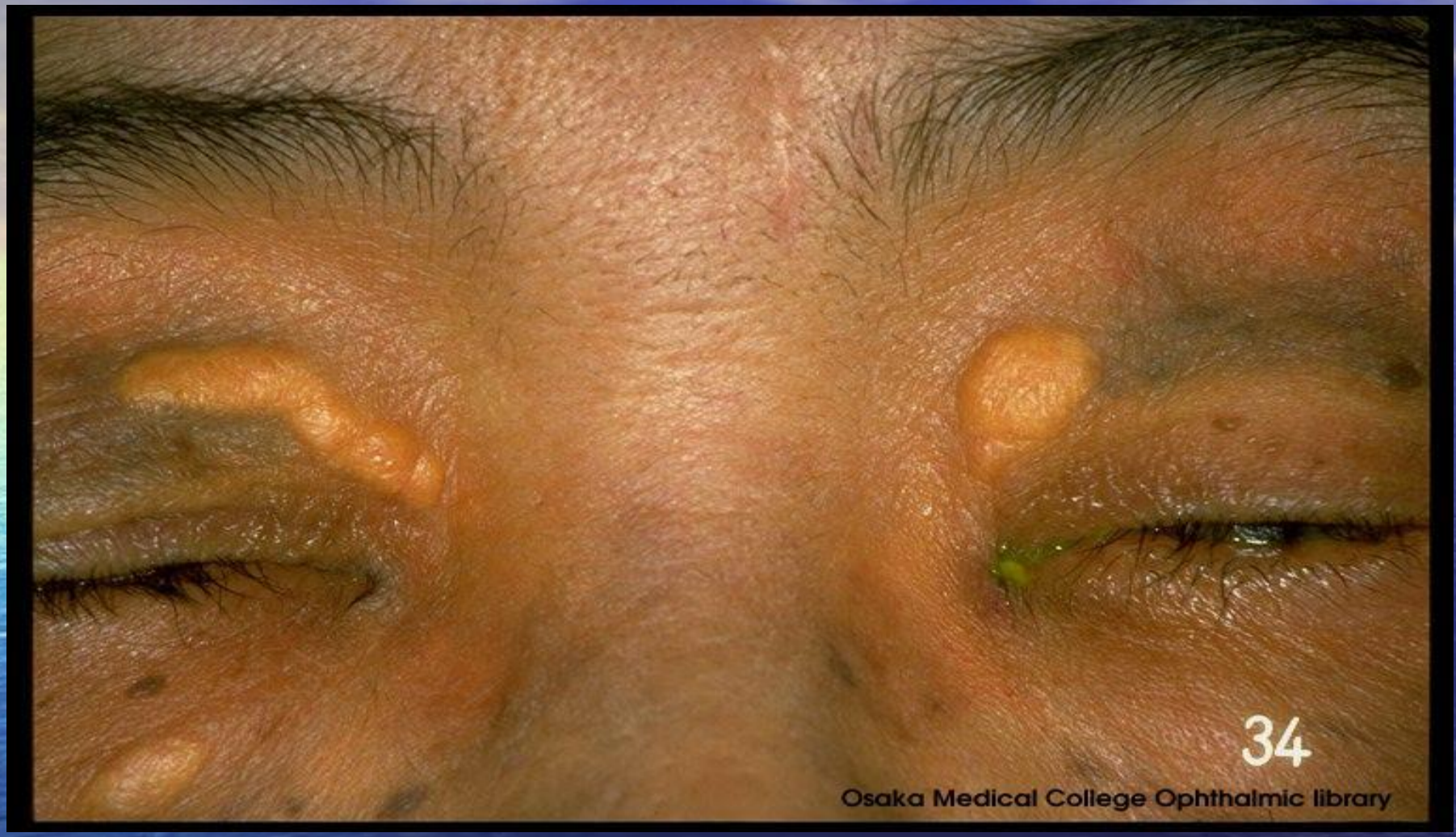
-Medications(nicotinic acid ,niacinamide , testosterone, OCP & Glucocorticoid)

Hyperlipidemia

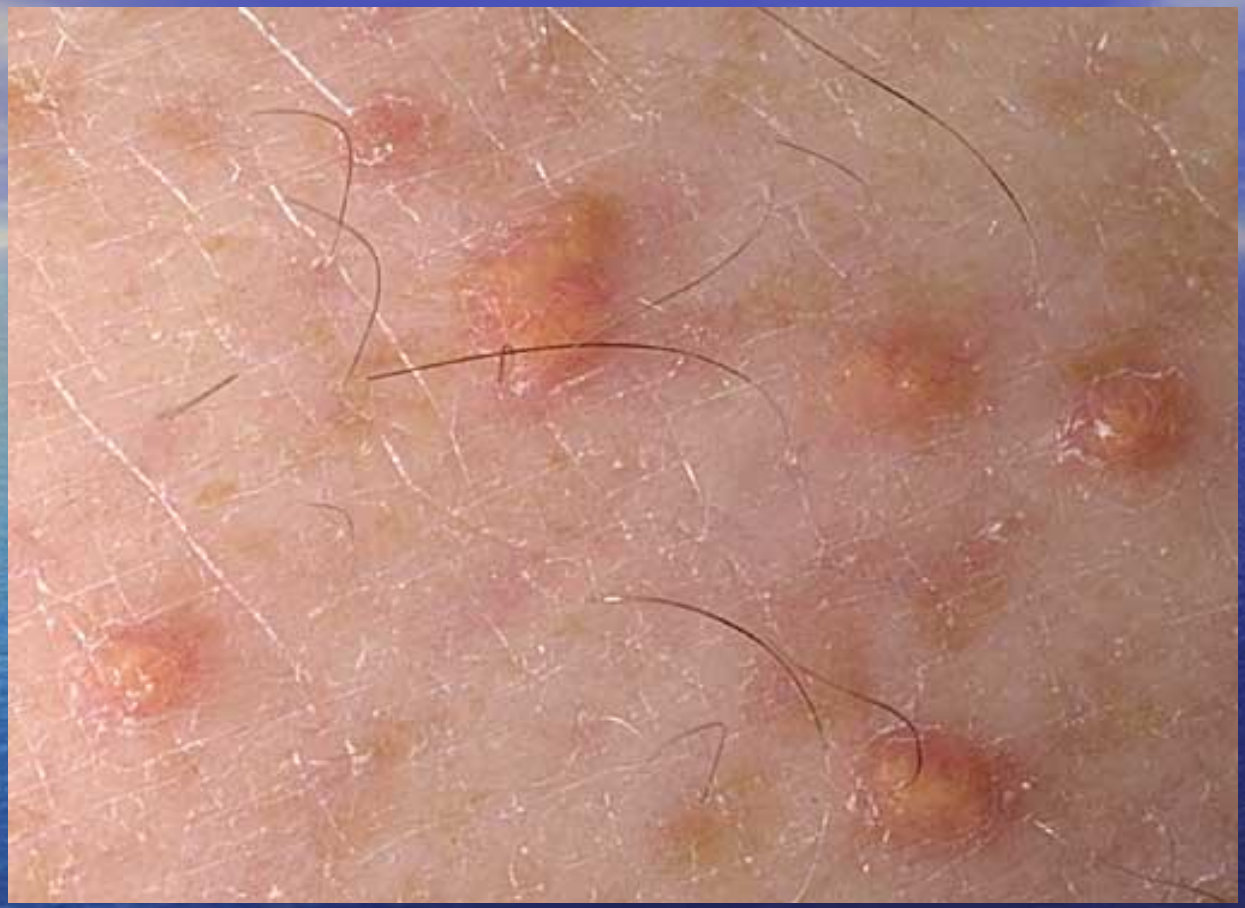
- Xanthomata
  - 4 forms : tendinous subcutaneous nodule found in fascia, ligament and extensor tendon of hand, knee and elbow
  - Planar : yellow, soft, macule or plaque found on the upper eyelids
  - Tuberous : yellow to reddish nodule at extensor surface of elbows, knees and knuckles
  - Eruptive : sudden, multiple reddish yellow papule extensor of extremities, buttock







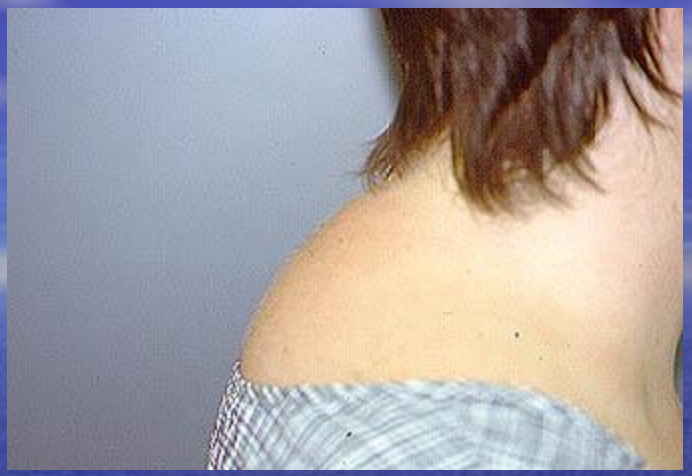
PLANAR XANTHOMA

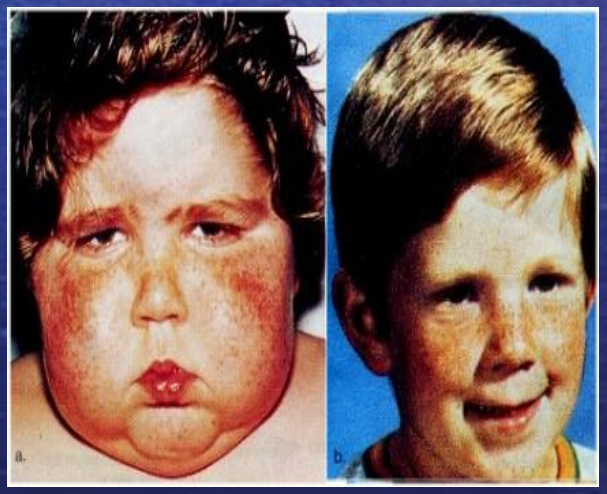


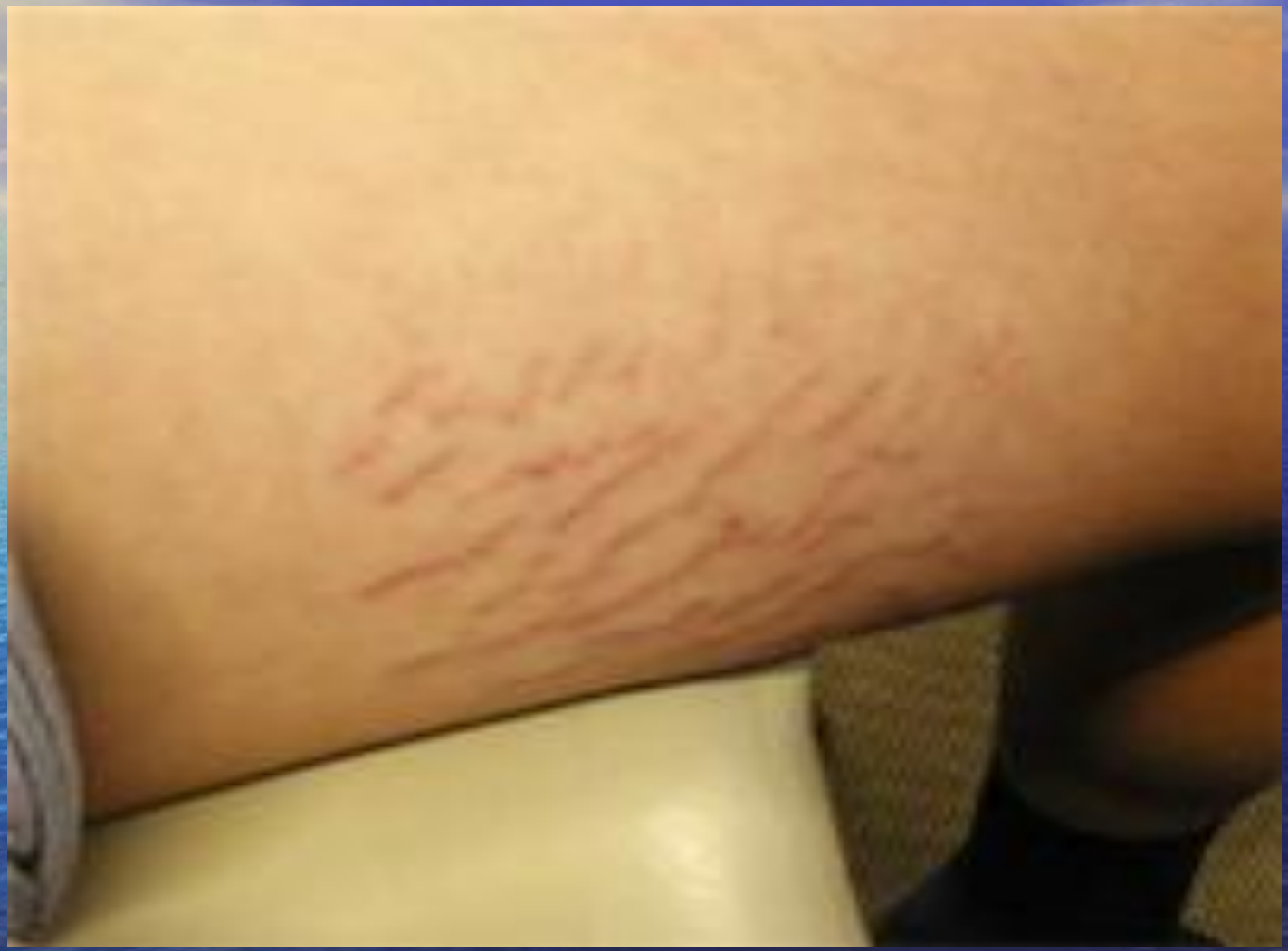
ERUPTIVE XANTHOMA

Cushing syndrome:

- Deposition of fat over the clavicles and back of the neck" Buffalo hump"
- Puffy, rounded erythematosus face with telangiectasia "Moon face"
- Trunkal obesity with slender wasting limbs.
- Striae distensae .
- Hirsutism, acneform rash, androgenetic alopecia.



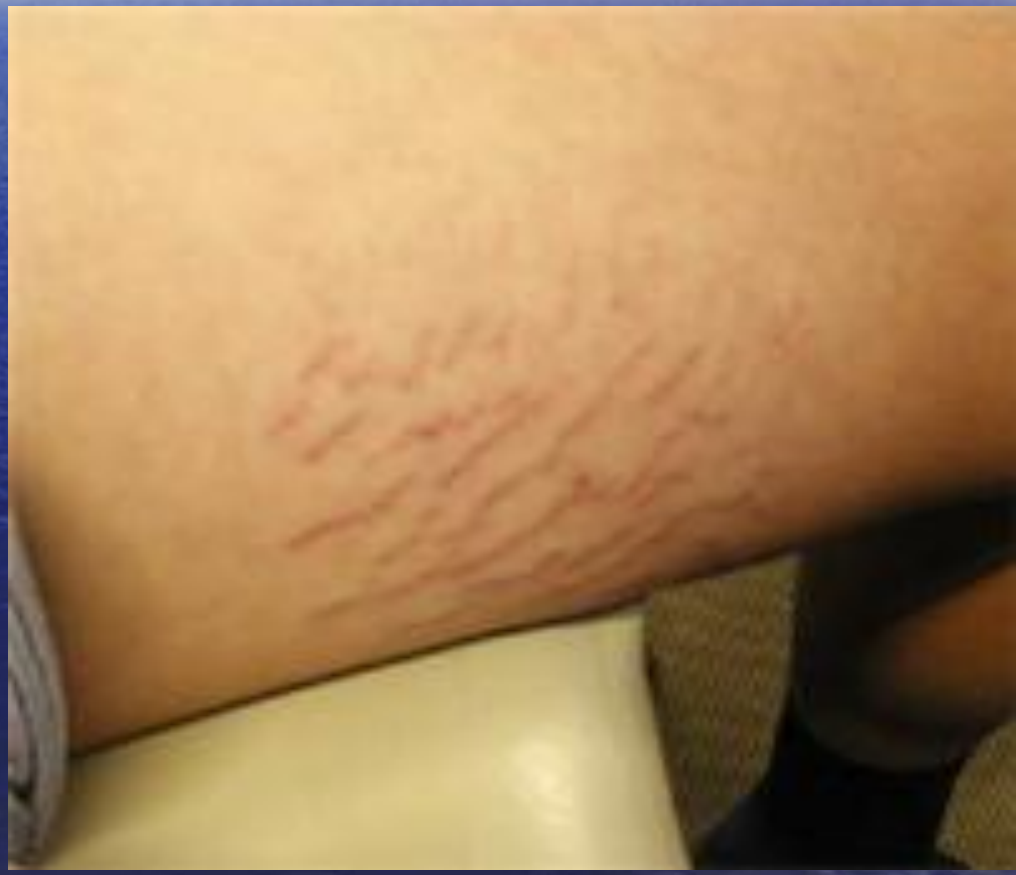




Striae distensae

Aetiology:

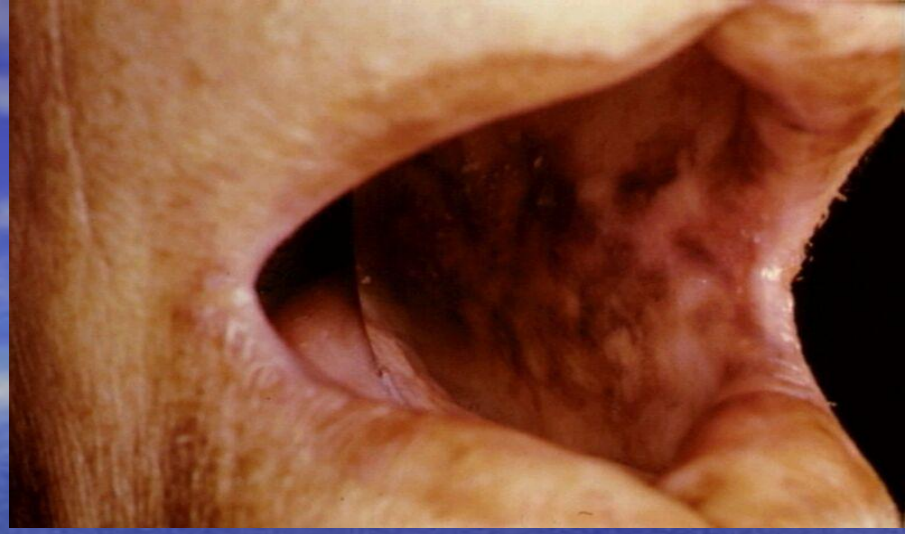
- Idiopathic
- pregnancy: Striae gravidarum
- Endocrine: cushing
- Iatrogenic: systemic or potent topical steroids, anabolic drugs or androgens.

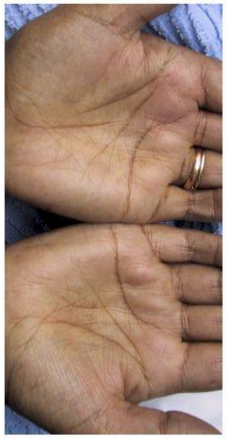


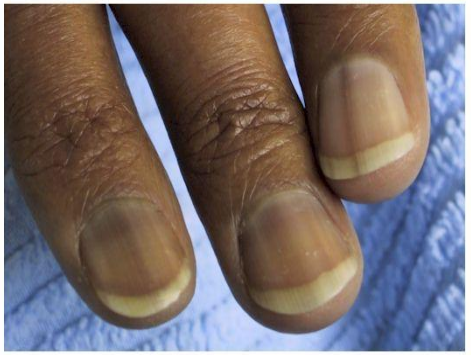
Addison,s disease:

- hyperpigmentation that is more prominent in light exposed areas, scars, genitalia, palmar and finger creases, and under the nails. The pigmentation characteristically affects the mucous membranes.

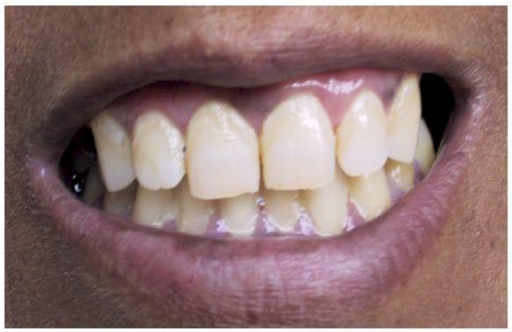
-Loss of pubic and axillary hair in females.







Addison's disease:



- Note the generalised skin pigmentation (in a Caucasion patient) but especially the deposition in the palmer skin creases, nails and gums.

- She was treated many years ago for pulmonary TB. What are the other causes of this condition?

- **Hyperthyroidism:**

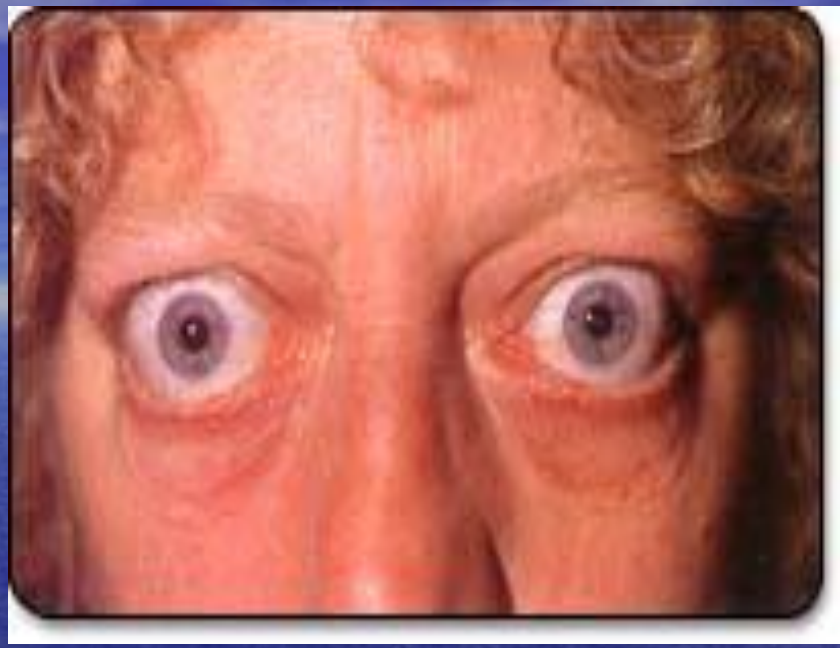
-red,soft, moist and hot skin.

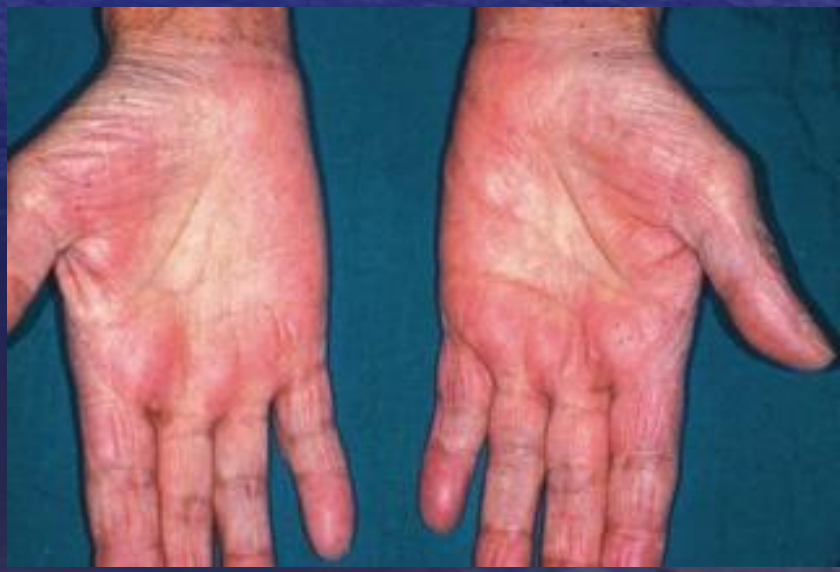
-Diffuse thinning of scalp hair

-Rapid nail growth and onycholysis.

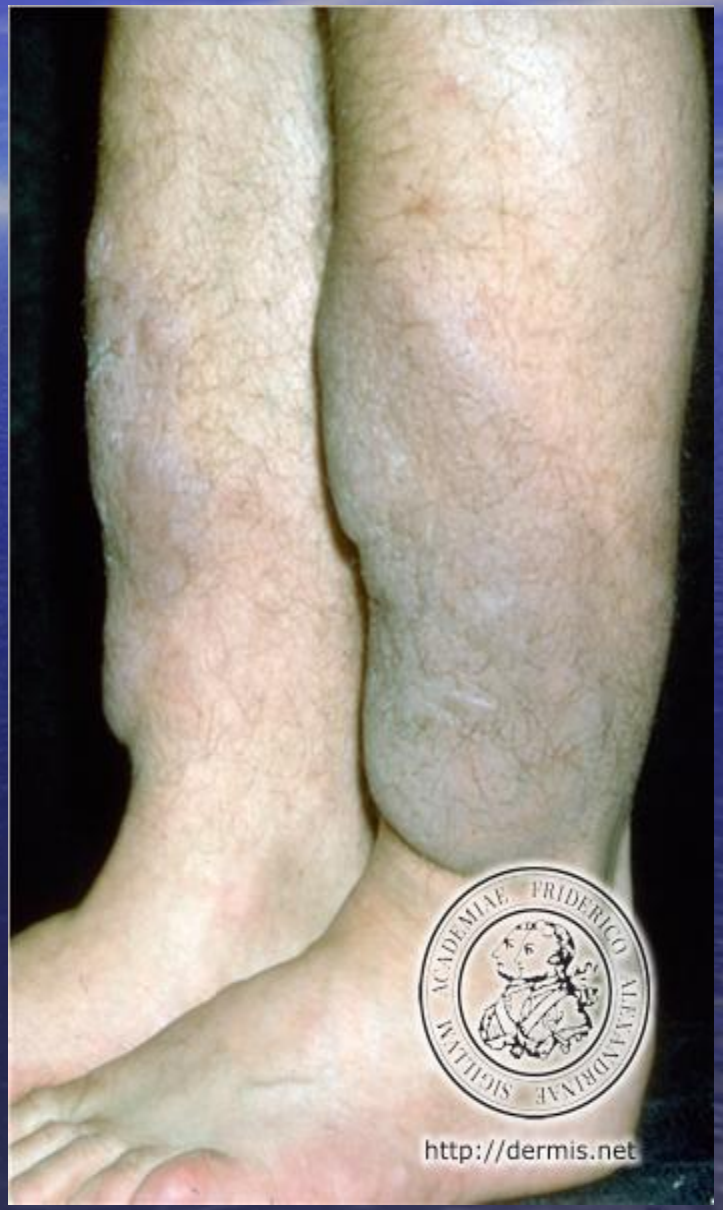
-Palmar erythema and facial flushing.

-Hyperhidrosis or increased sweating.



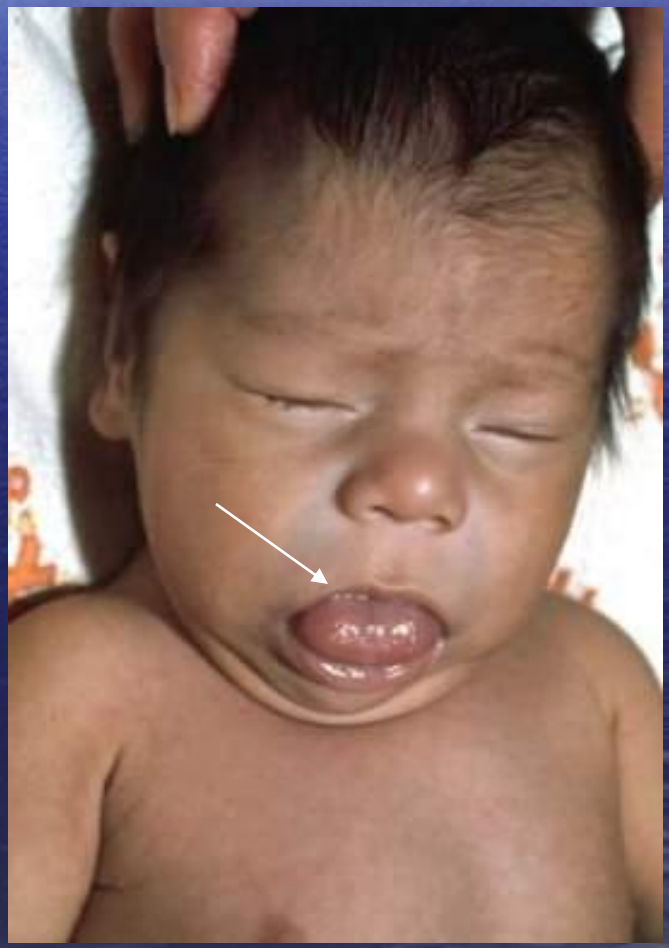


-Pretibial myxoedema: appears as small red or skin colored coalescing Nodules



- Hypothyroidism

Macroglossia

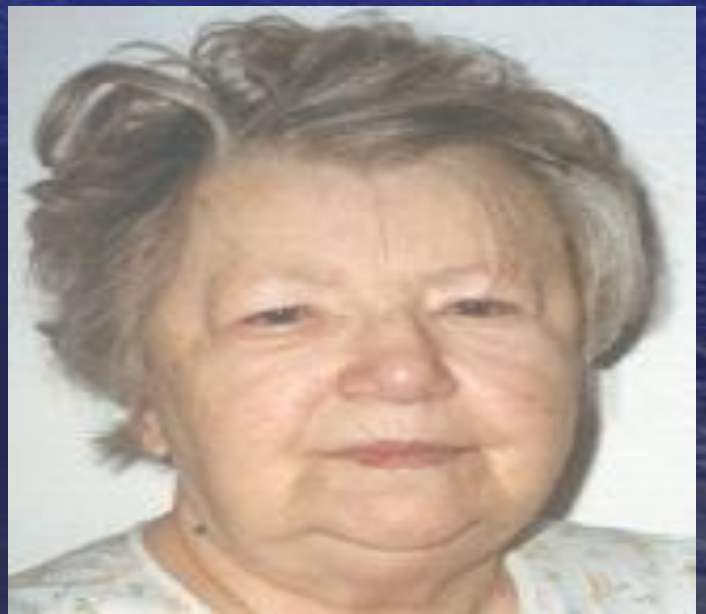


Hypothyroidism:

-Buffy face with coarse features.

- The skin is pale, thickened, cold, finely scaling and wrinkled.

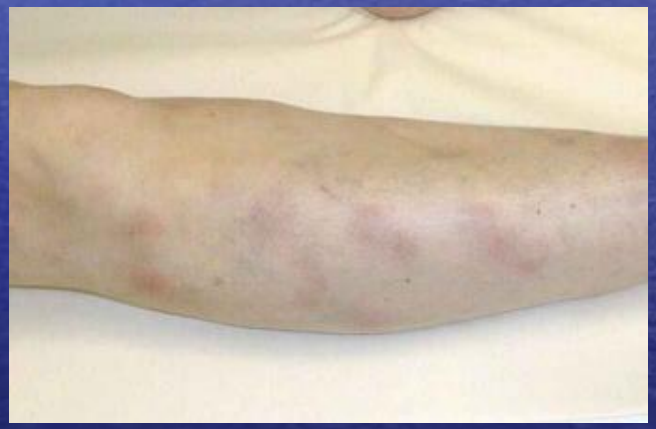
- Coarse sparse hair of the scalp with loss of the lateral third of the eyebrows.

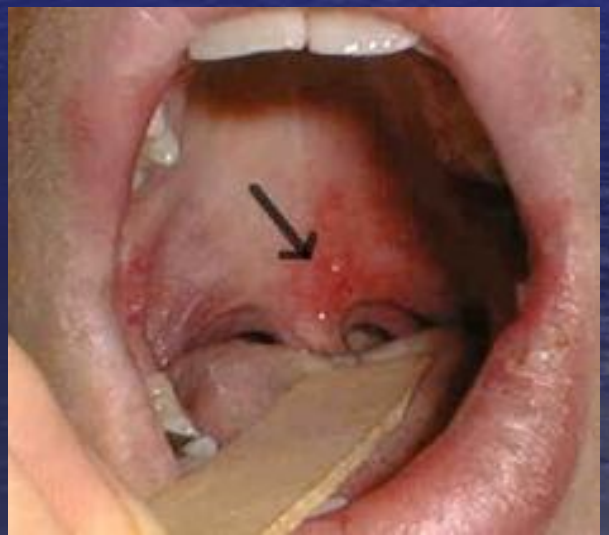


Gastrointestinal tract and the skin

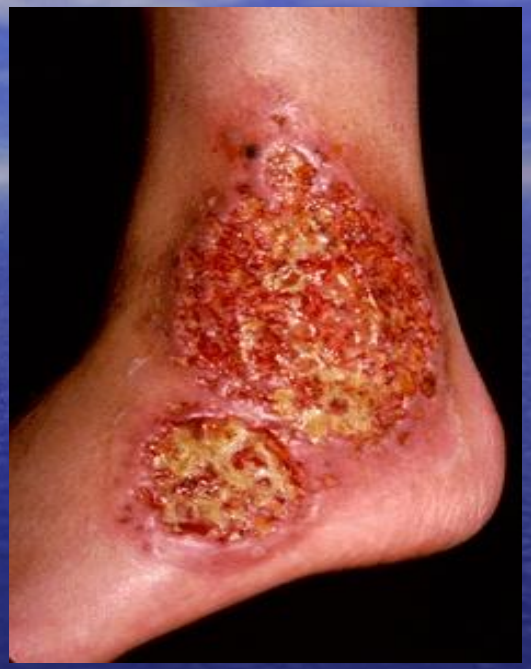
- **Crohn,s disease**

-Perianal abscess and fisulae.
-Erythema nodosum
-Erythema multiforme
-Aphthous-like stomatitis and glossitis.
-Cutaneous vasculitis.
-Epidermolysis bullousa acquisita.
-Metastatic Crohn,s disease as numerous eroded cutaneous granulomas at sites distant from the affected intestine.
-Pyoderma gangrenosum.



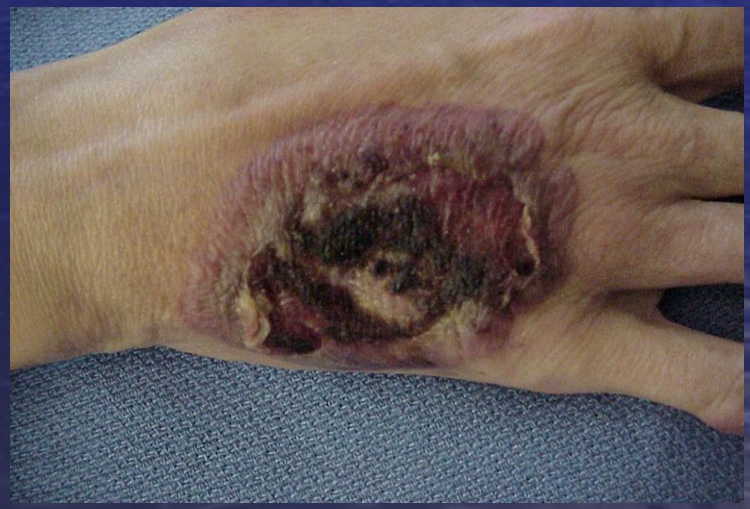


Pyoderma gangrenosum



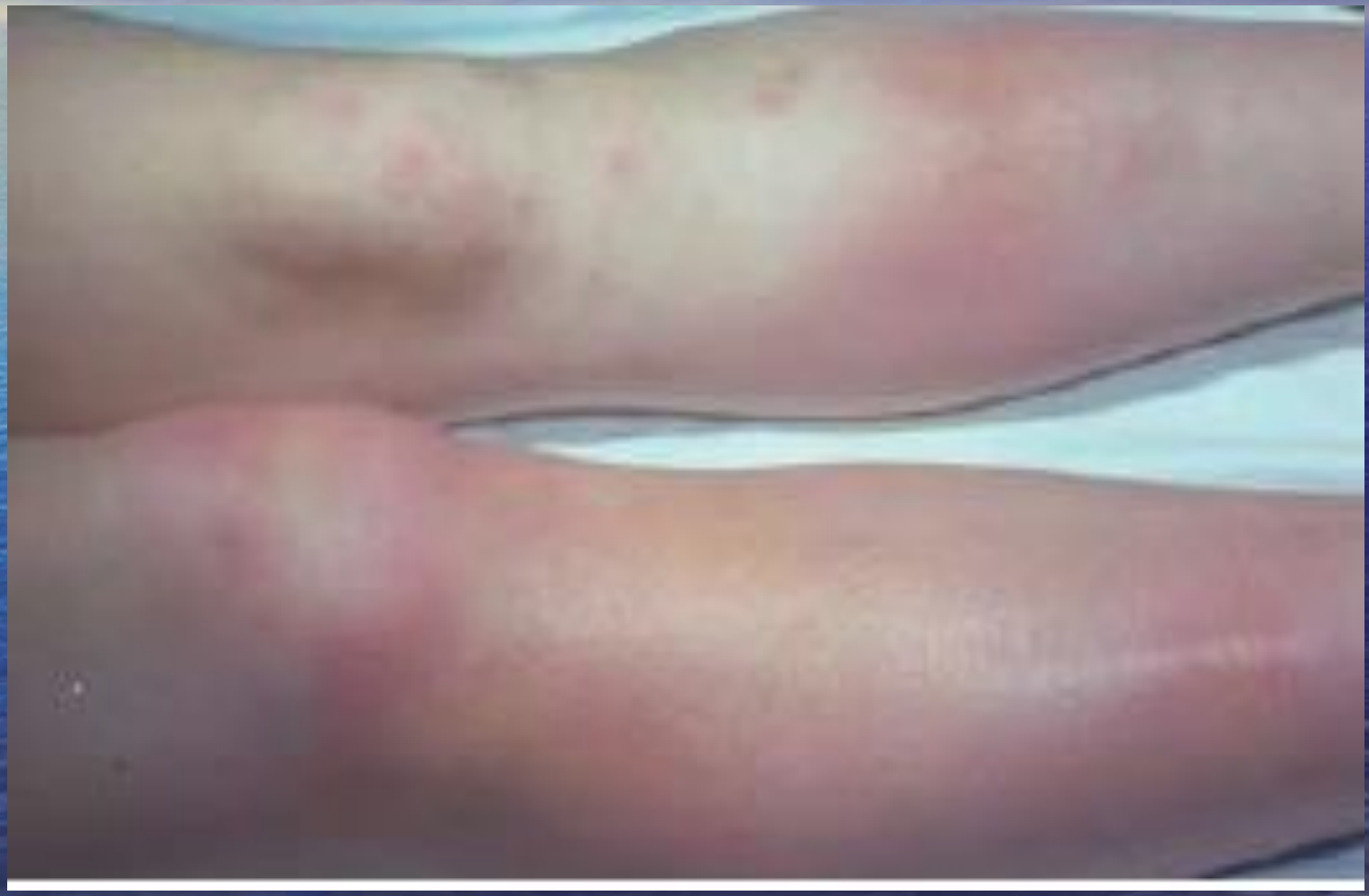
Aetiology:

- Idiopathic in 50% of the cases.
- Inflammatory bowel disease- Crohn,s disease and ulcerative colitis.
- Connective tissue diseases- Rheumatoid arthritis, SLE or Behc,et disease.
- Blood disease: Leukemia, multiple myeloma, polycythemia or monoclonal gammopathy.



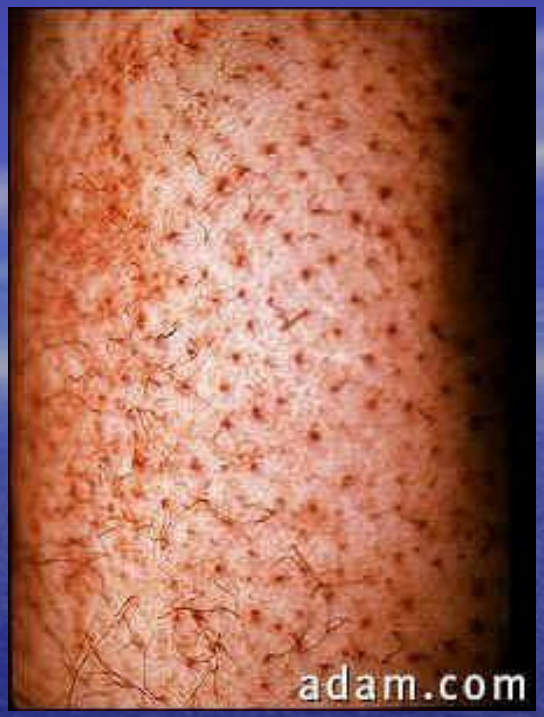
- Treatment:
  - Dealing with underlying cause.
  - Systemic steroids in high dose like 60-80 mg oral prednisolone daily and then reduce gradually.
- Azathioprime, Dapsone, or cyclosporine

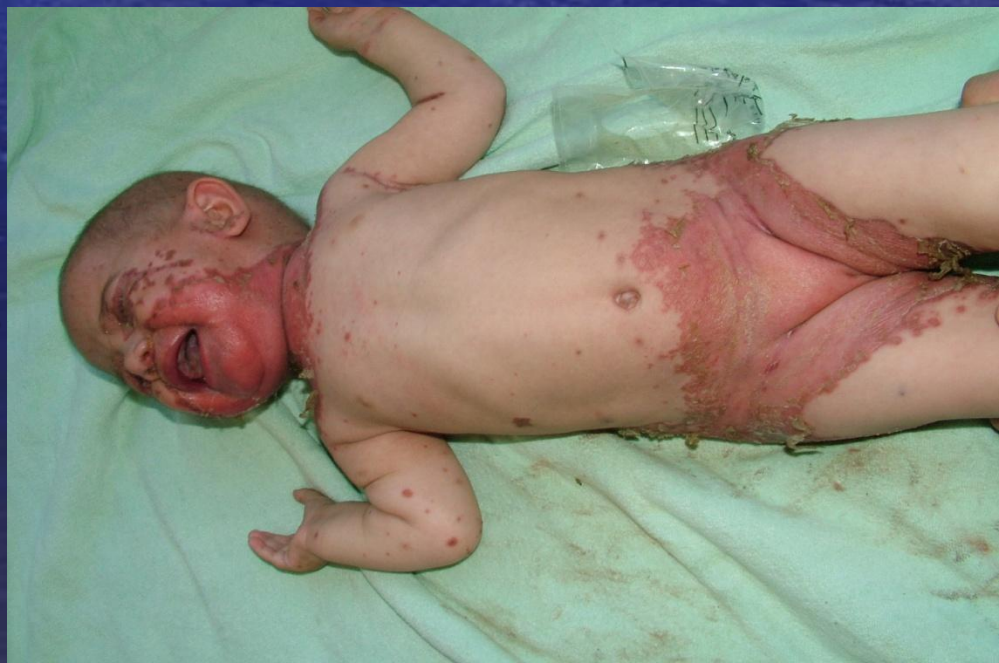
Erythema nodusom



Causes of erythema nodosum	Approach and investigations
Infections	
• Bacterial, eg. Streptococcus, Yersinia, Salmonella, Campylobacter	• Throat swab, anti streptolysin O titre (ASOT), anti-double stranded DNA antibodies
• Viral, eg. Epstein Barr virus	• Serology and stool cultures where appropriate
• Mycobacterial	• Serology where appropriate
	• Investigate if clinical suspicion – chest X-ray, Mantoux, Quantiferon gold
Sarcoidosis	Chest X-ray, serum angiotensin converting enzyme inhibitor (ACEI), calcium and referral if abnormal
Inflammatory bowel disease	History and examination
Malignancy Leukaemia, lymphoma (rare) Postradiotherapy	Full blood count and film
Pregnancy	History, βHCG level
Behcet syndrome	History of oral and genital aphthous ulcers and examination
Drugs	Recent commencement in particular oral contraceptive pill, tetracycline antibiotics, sulphur based drugs, bromides and iodides

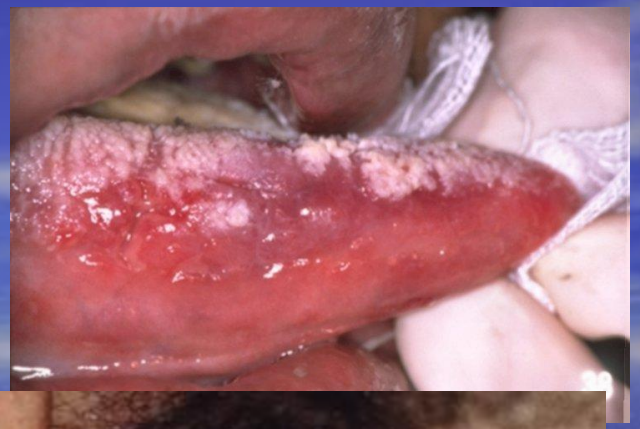
- **Ulcerative colitis**: identical to Crohn,s disease but pyoderma gangrenosum and erythema nodosum are more common in ulcerative colitis.
- **Malabsorption**: specific or non-specific features.
- **Non- specific features**: Pallor, dry skin, oedema, acquired icthyosis, Pigmentary disorders, glossitis, mouth ulcers.
- **Specific features** due to certain factor deficiency:
- e.g. – Follicular hyperkeratosis ---------- Vit. A deficiency.
- Echymosis and scurvy ---------- Vit. C deficiency.
- Acrodermatitis enteropathica ---------- Zinc deficiency.

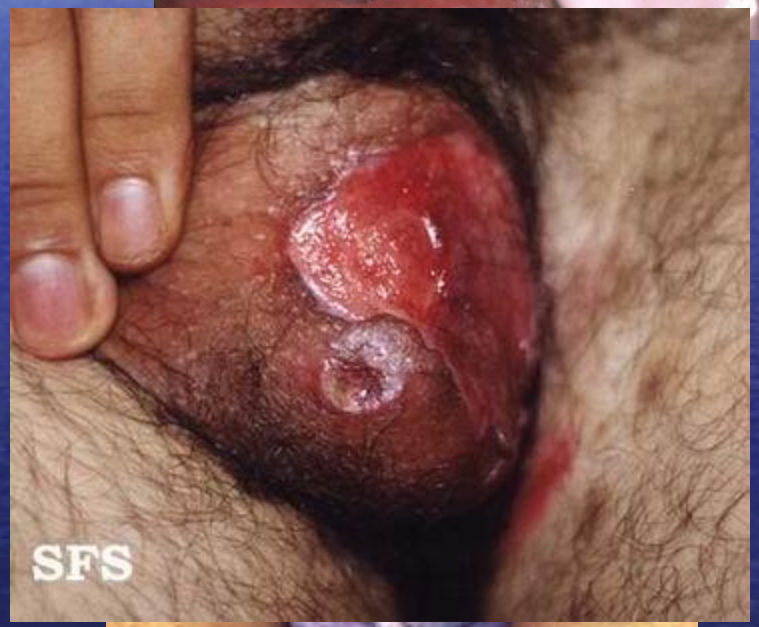


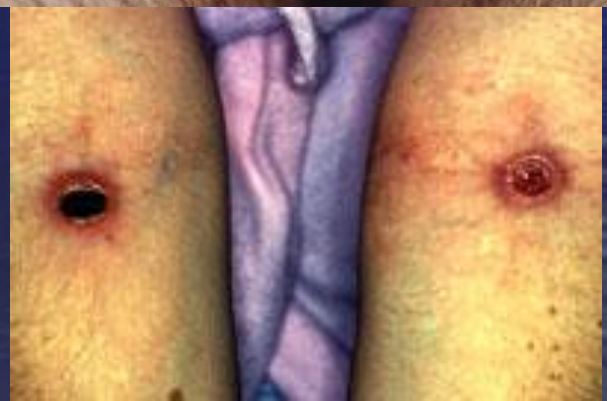


Behcet disease

- Recurrent aphthous oral ulcerations more than three times per a year is a must plus two of the following:
- Genital ulceration or other skin manifestations Erythema-nodosum like lesions, pseudofolliculitis, papulopustular lesions or acneform rash.
- Eye lesions: anterior or posterior uveitis
- Positive pathergy test







Generalised pruritus

- Generalised pruritus in the absence of a rash requires investigation and exclusion of an underlying systemic disorder

- it is important to distinguish these from an underlying primary skin disease such as scabies or eczema

Conditions that Cause Pruritus

1-Chronic Renal Disease

2-Cholestasis

3-Endocrine Disease

- Thyrotoxicosis – often due to increased skin blood flow which raises skin temperature
- Hypothyroidism – pruritus secondary to the dry skin

4-Malignancy

- Most common association: Hodgkin's disease and polycythemia rubra vera

5-HIV Infection

6-Iron deficiency anemia

7-Parasetic infection

Workup of Generalized Pruritus

- Physical exam
- CBC, diff , Blood film
- Stool for O&P, occult blood
- CXR
- Thyroid, renal, and liver function tests
- Drug history

PARANEOPLASTIC DERMATOSES

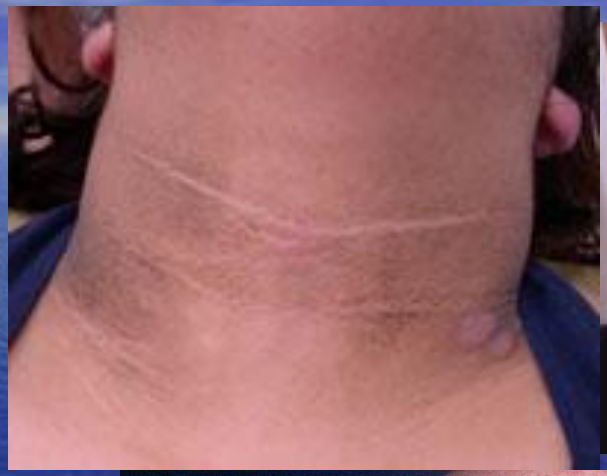
PARANEOPLASTIC DERMATOSES

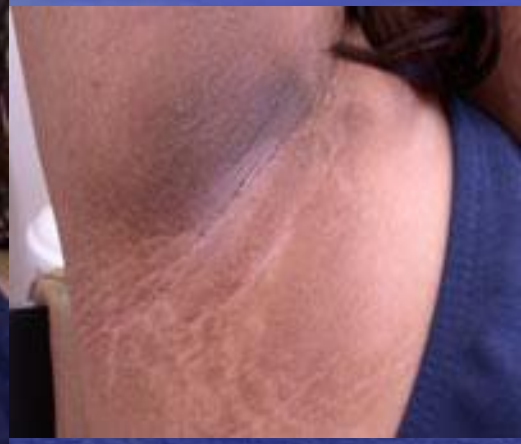
SUSPECT A PARANEOPLASTIC DERMATOSIS IF:

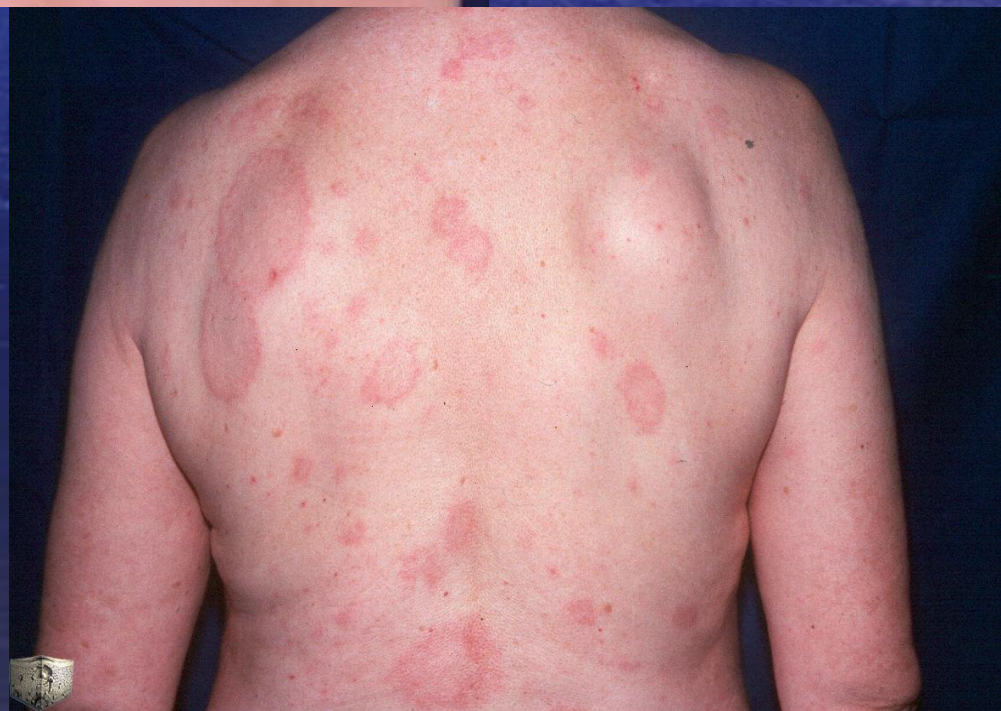
- *Abrupt onset of dermatosis in advanced age*
- *Rapid course*
- *Atypical clinical presentation*
- *More severe skin lesions*

Paraneoplastic dermatoses

1. Acanthosis nigricans
2. Dermatomyositis
3. Erythema gyratum repens
4. Erythema nodosum and erythema multiforme





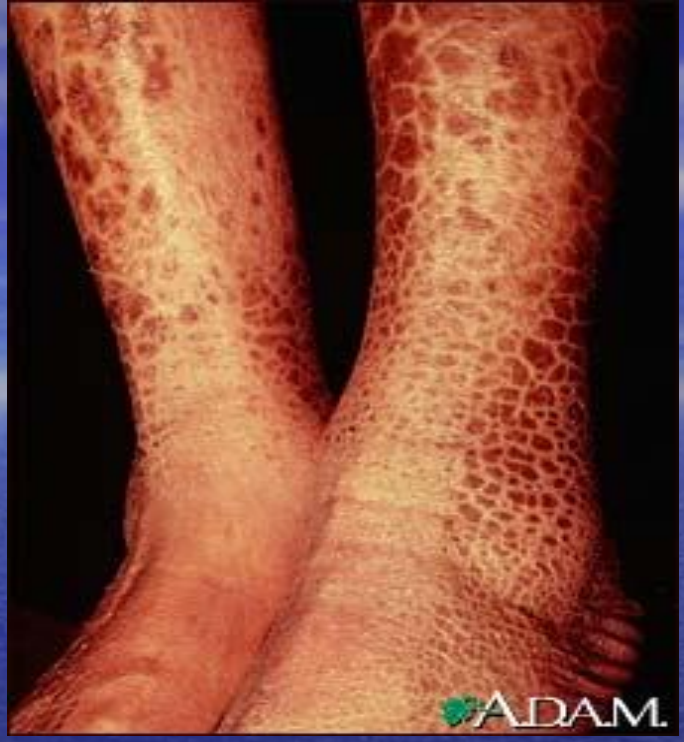


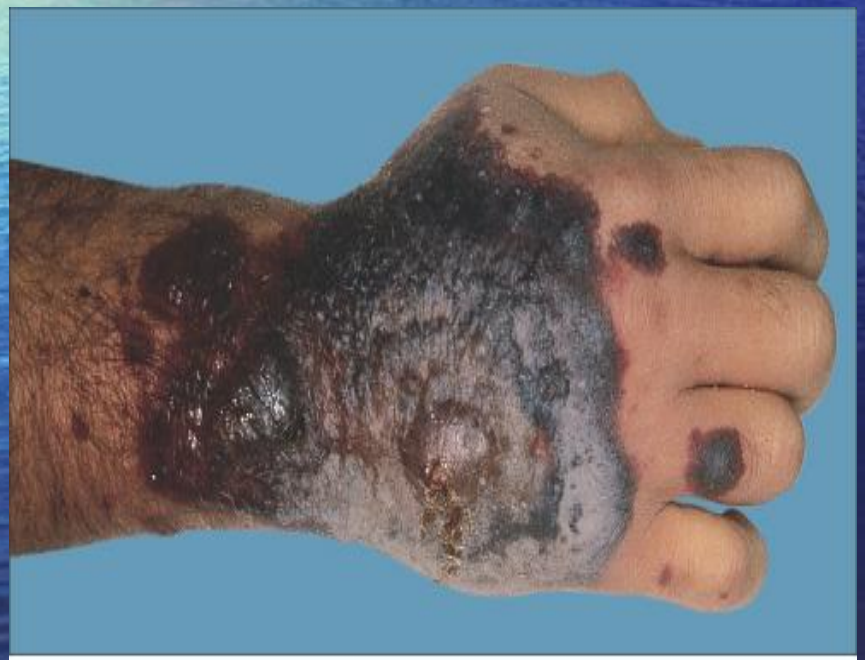
5. Acquired icthyosis

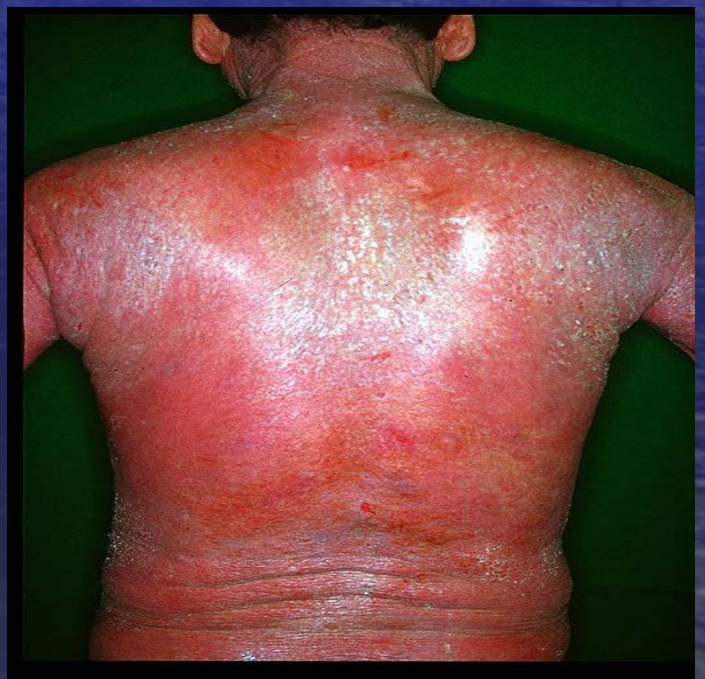
6. sweet syndrom

7. Pyoderma gangrenosum

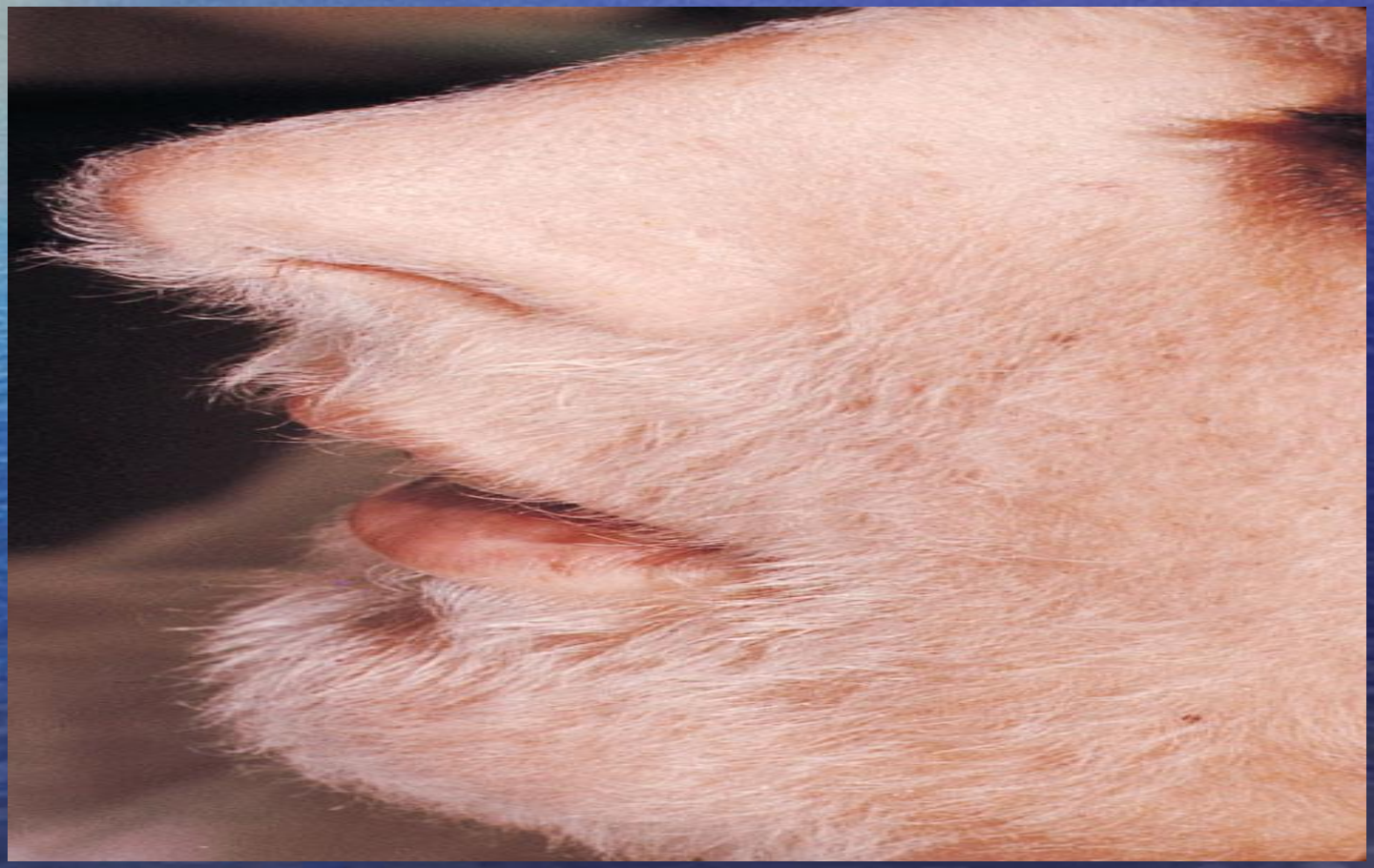
8. Erythroderma







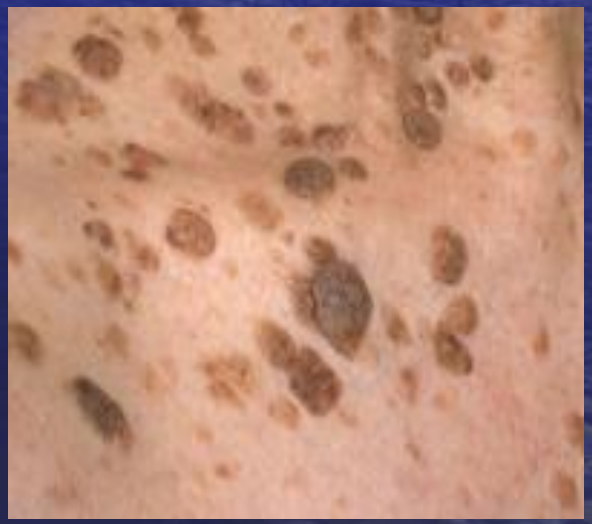
9. Acquired hypertrichosis lanuginosa



10. Tripe palms

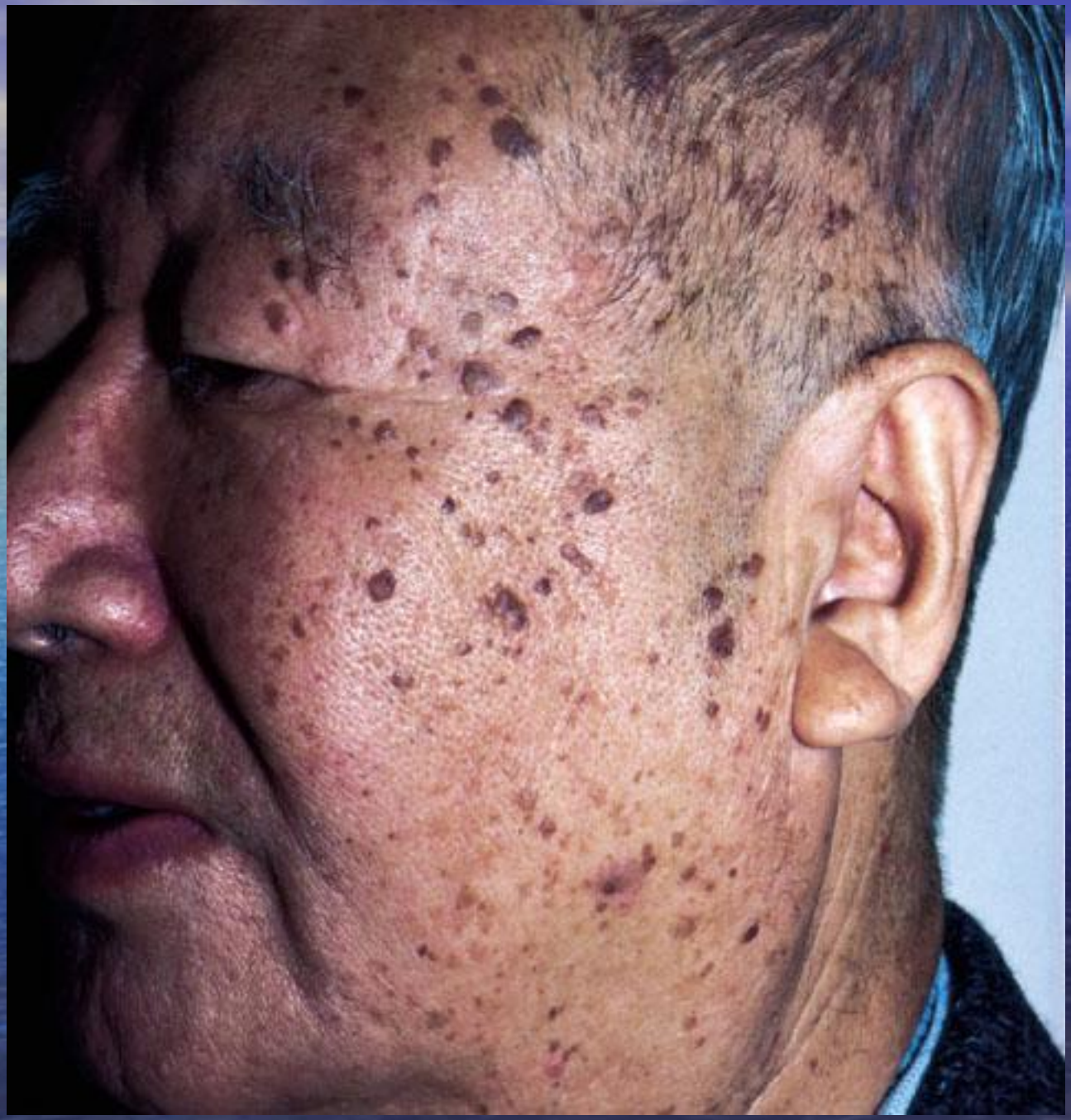
11. The sign of Leser-Telat

12. Necrolytic migratory erythema

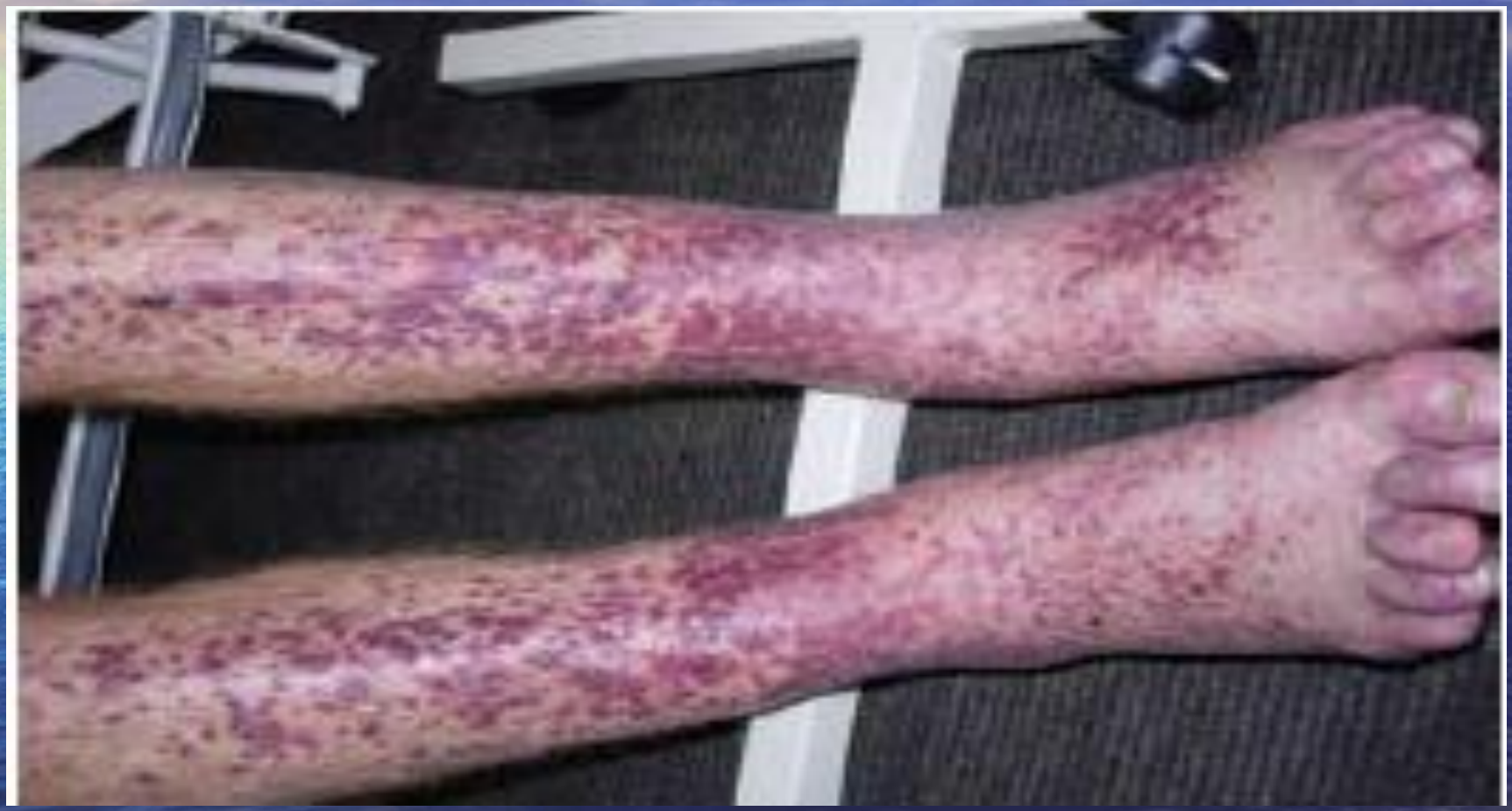


Sign of Leser-Trelat

- Sudden appearance of multiple seborrheic keratoses
- Association with internal malignancy is unproven



Purpura and vasculitis



Definition

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

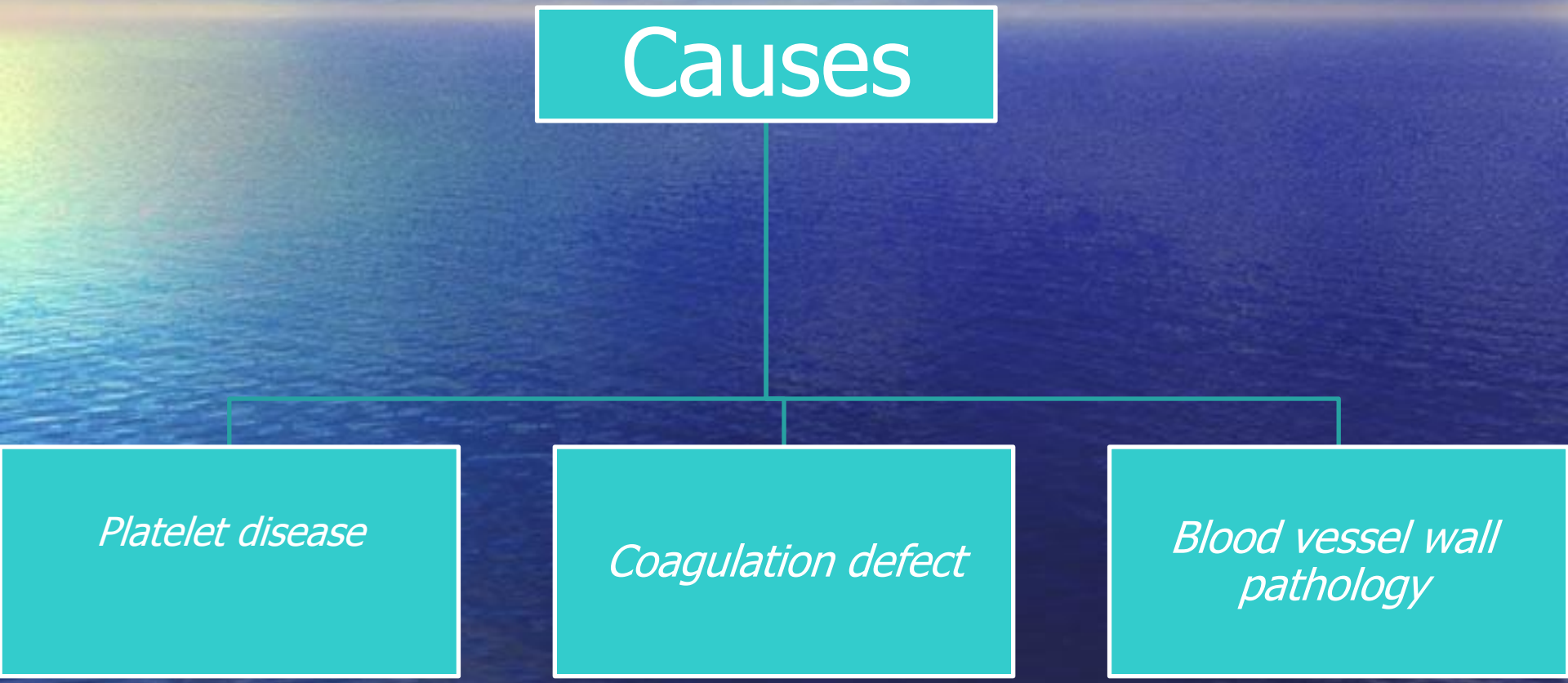
-Petechiae less than or equal 4 mm

-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

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, *primary causes*

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

Classification, secondary causes

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

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

-Is the 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

Palpable purpura is the hallmark

-Pinpoint to several centimeters

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

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

Cutaneous small vessel vasculitis

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

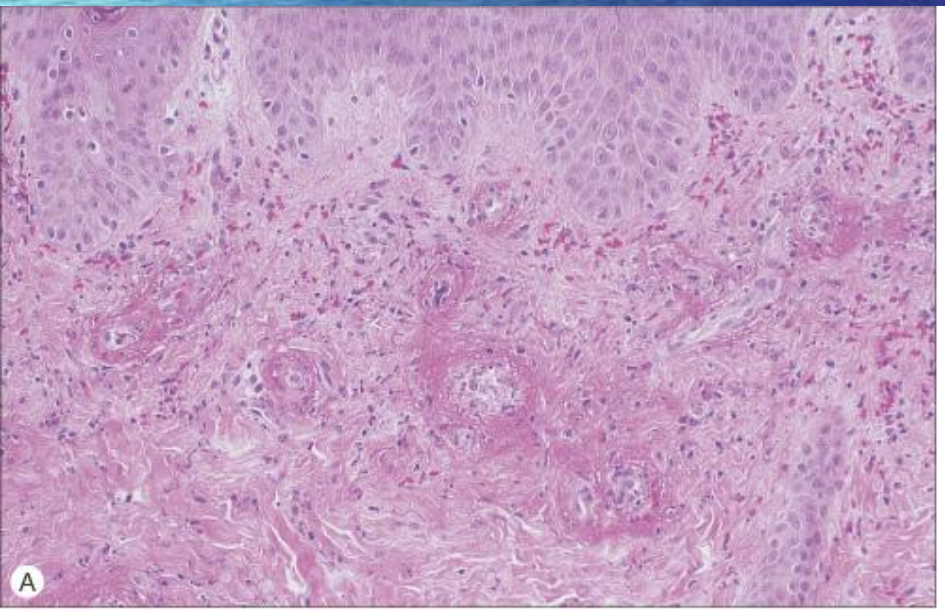
-The internal organs affected most commonly include the joints, GIT, and the kidneys.

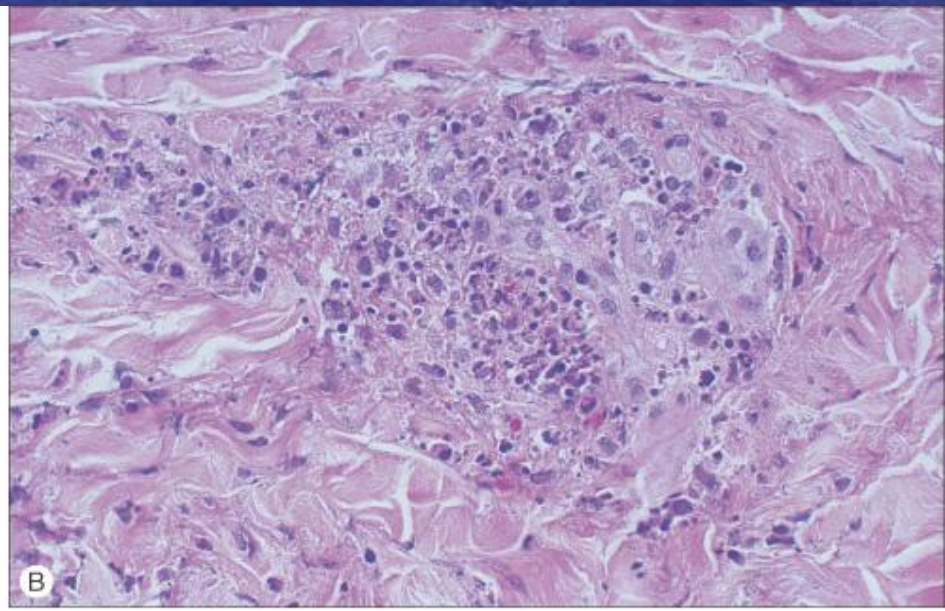
-Renal involvement present as glomerulonephritis

- 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

Treatment

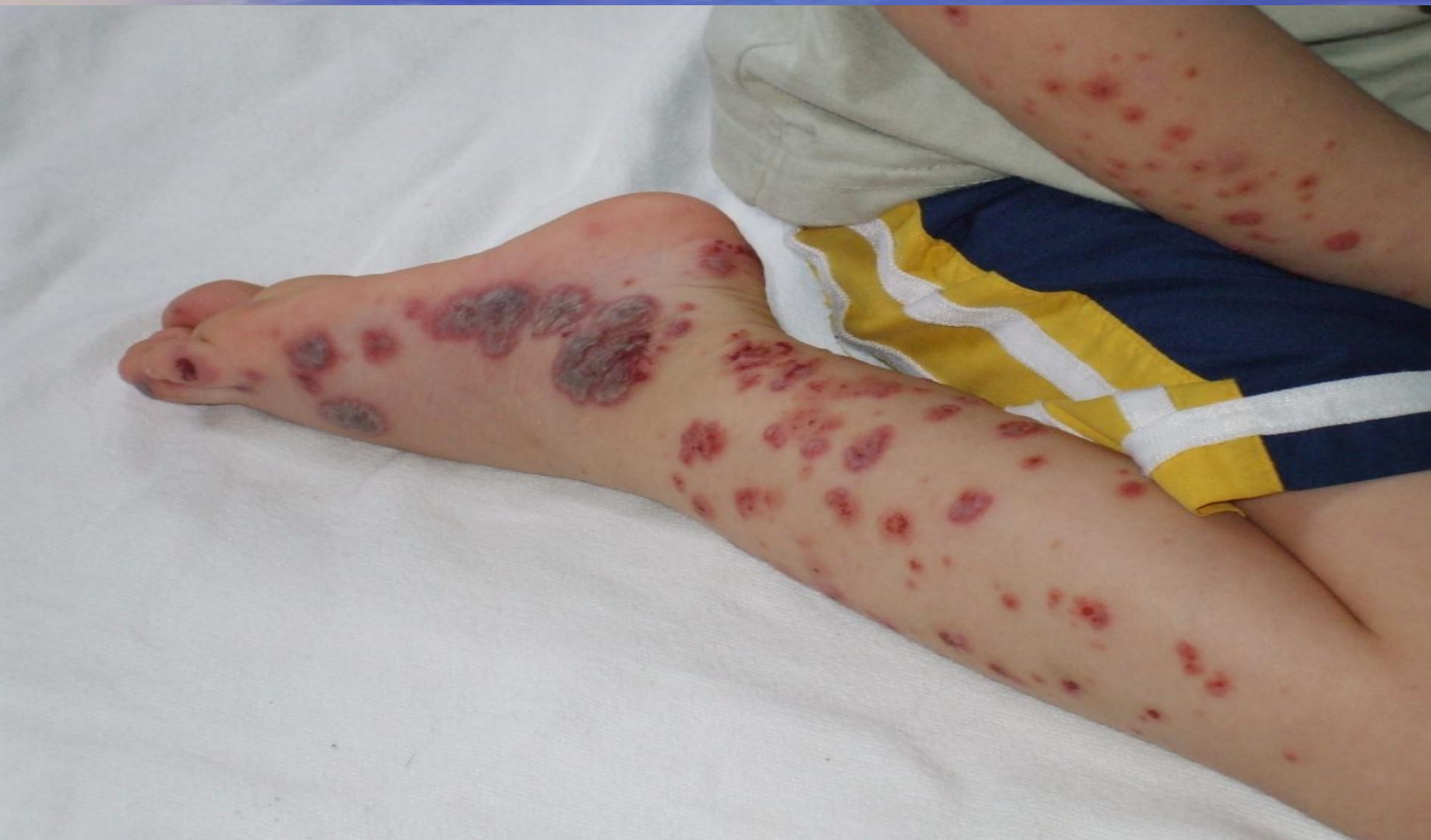
treatment of cause.

-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



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

Henoch-Schönlein purpura HSP

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

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

Henoch-Schönlein purpura HSP

Biopsy

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

Thank you