Skin & Systemic Disease

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INTRODUCTION

Systemic Disease: a disorder that can affect a few organs and tissues or even the whole body.

Skin often mirrors changes in the internal milieu; therefore, skin changes may be the first sign of an internal problem.

Why is it important to be familiar with the cutaneous manifestations of such disorders?

- Diagnosis
- Treatment

01

INTERNAL MALIGNANCY

You could enter a subtitle here if you need it

PARANEOPLASTIC DERMATOSES

Symptoms that are not caused directly by the tumor but rather as a reaction to it

GENODERMATOSIS

Heritable syndromes with a cutaneous component that predispose at-risk individuals to develop cancer

NONPARANEOPLASTIC

tumoral infiltration into the skin

- Metastasis
- Leukemia cutis

PARANEOPLASTIC DERMATOSES

Hyperkeratotic & Proliferative:

- Bazex syndrome
- Extramammary Paget disease
- Tripe palm
- Acanthosis nigricans
- Acquired ichthyosis
- Palmoplantar keratoderma

Inflammatory:

- Exfoliative erythroderma
- Erythema gyratum repens
- Dermatomyositis
- Sweet syndrome (Acute Febrile Neutrophilic Dermatosis)
- Necrolytic migratory erythema
- Pancreatic panniculitis

Bullous:

- Paraneoplastic pemphigus
- Mucous membrane pemphigoid (antiepiligrin variant of cicatricial pemphigoid)

Hormonal

- Ectopic Cushing's syndrome (ectopic ACTH)
- Carcinoid syndrome
- Multiple endocrine neoplasia syndrome
- Glucagonoma syndrome

Hair & Nail Changes:

- Hypertrichosis languinosa

ASSOCIATION WITH MALIGNANCY

most/all cases

- Bazex syndrome
- Carcinoid syndrome
- Erythema gyratum repens
- Ectopic ACTH
- Paget's
- Breast CA
- Paraneoplastic pemphigus
- Tripe palms
- Aquired hypertrichosis lanuginosa

strong association

- Acanthosis nigricans
- Dermatomyositis
- Anti-epiligrin cicatricial pemphigoid
- Extramammary Paget disease
- Sweet's syndrome

may be associated

- Acquired ichthyosis
- Exfoliative erythroderma
- Necrobiotic xanthogranuloma
- Porphyria cutanea tarda

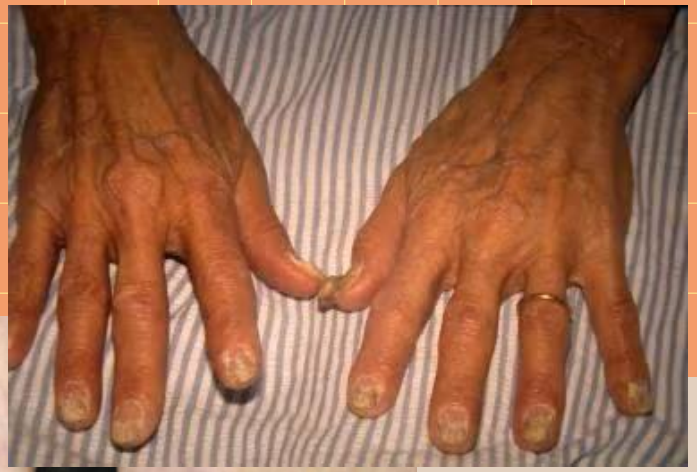
When is it more likely to be maglinancy? Curthe's Postulates

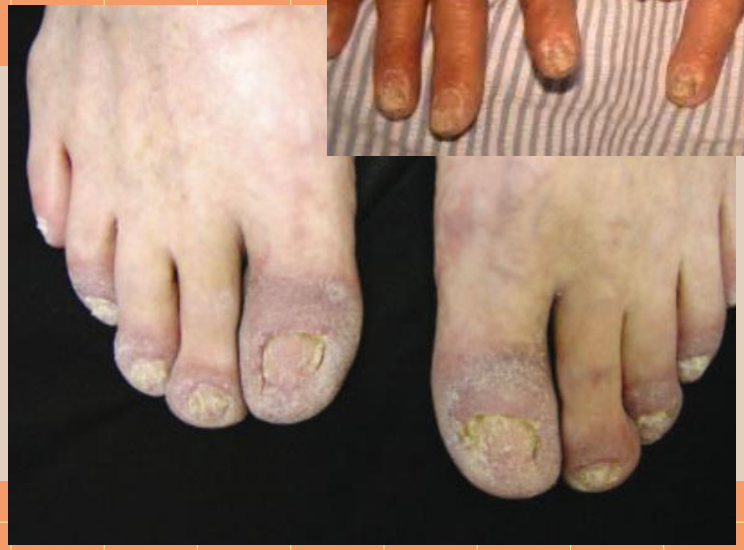
- concurrent onset
- parallel course
- relation between the skin disease and the malignancy is uniform
- genetic or statistically significant association

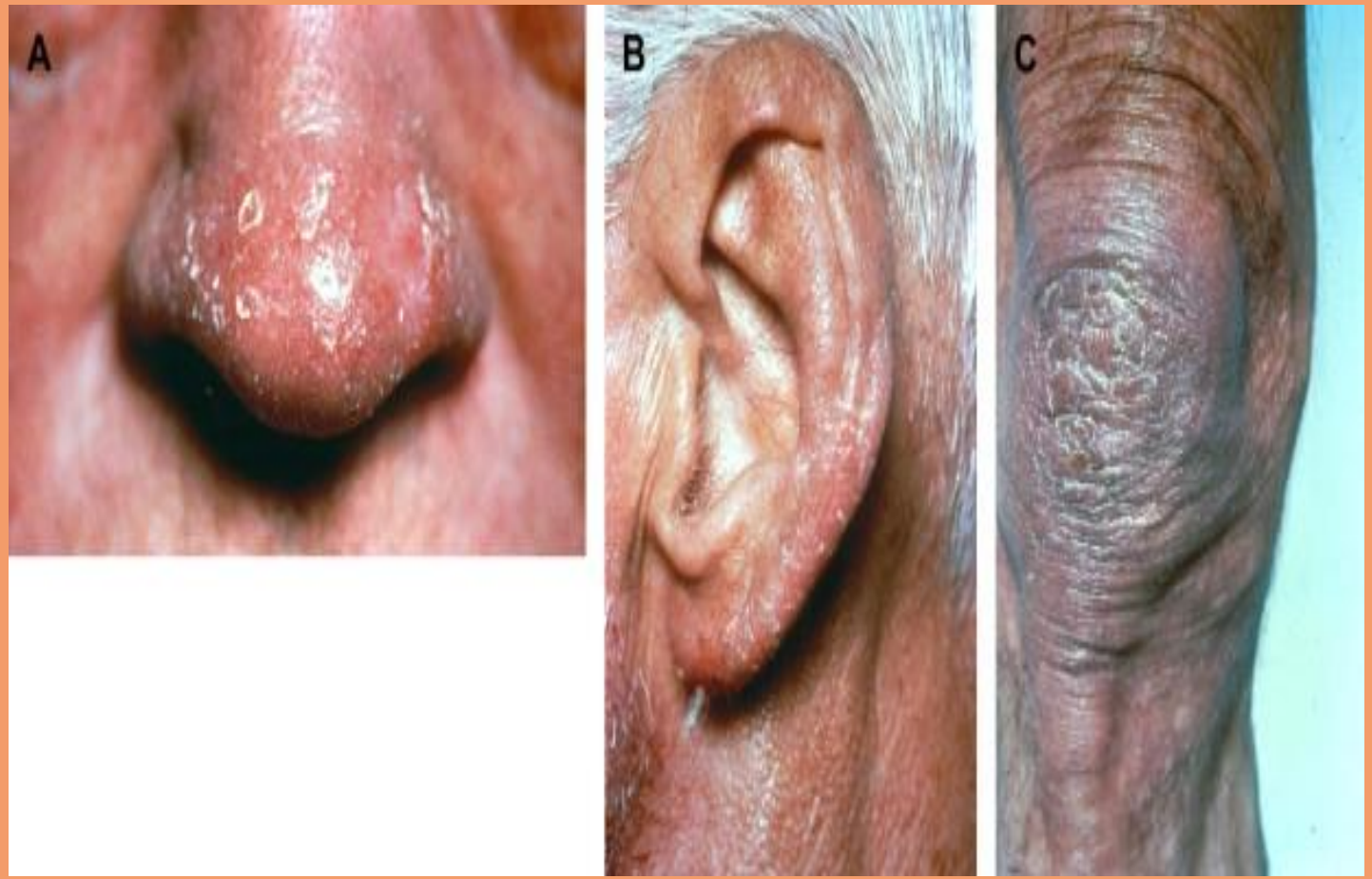
BAZEX SYNDROME

AKA acrokeratosis paraneoplastica

- violaceous, psoriasis-like plaques predominantly located in acral areas (especially the fingers, toes, nose, and helices ie rim of the ear)
- Ass/w painful paronychia, keratoderma, paraneoplastic pruritus
- strongly associated with squamous cell carcinoma of the upper aerodigestive tract
- usually resistant to targeted therapies, but treatment of the neoplasm usually leads to resolution of the cutaneous findings



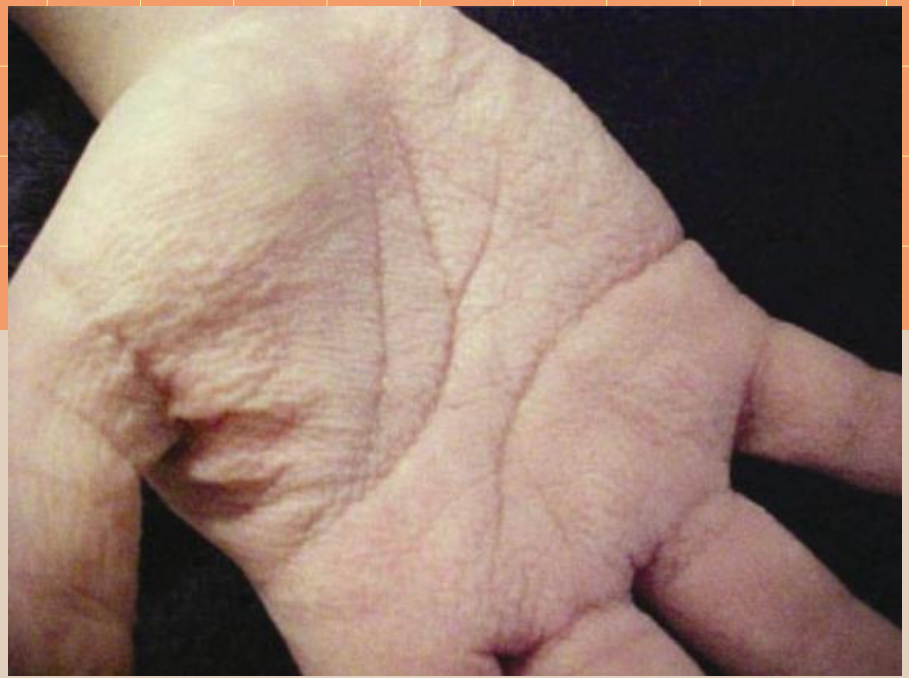



A
B
C

TRIPE PALM

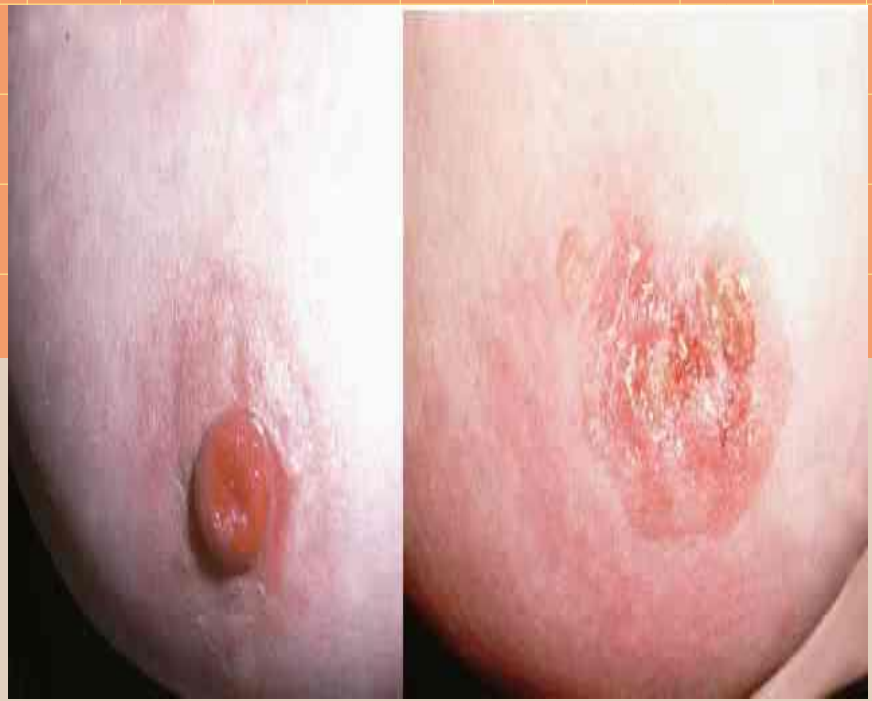
AKA acanthosis palmaris or acquired pachydermatoglyphia

- characteristic velvety thickening of the palms (and sometimes soles) with a ridged/rugose (wrinkled) appearance
- “predominantly associated with gastric or lung cancer
- Concurrent acanthosis nigricans is often present
- Improvement/resolution occurred in 1/3 of patients after beginning treatment for malignancy



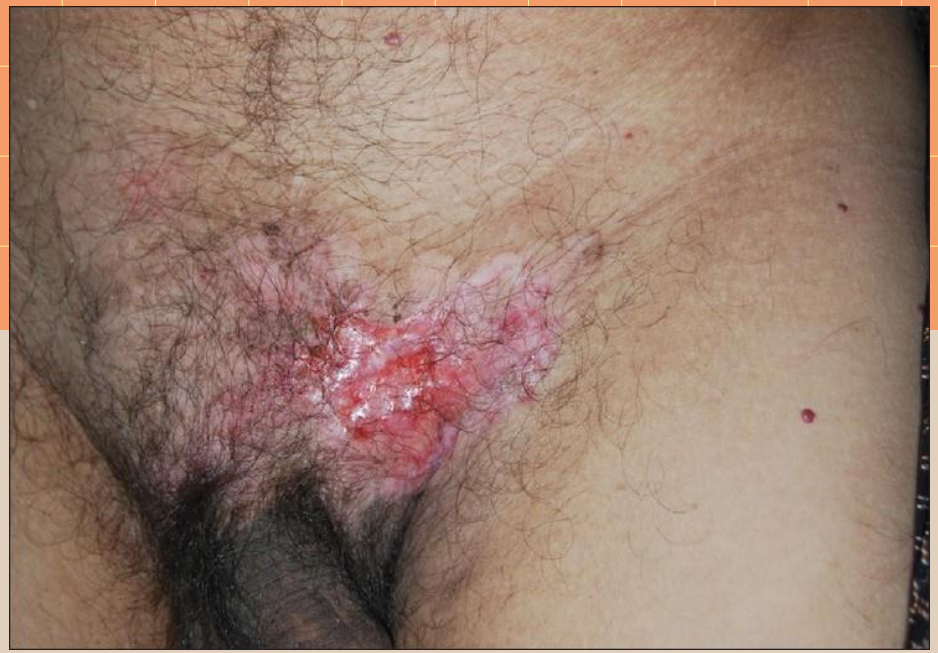
MAMMARY PAGET'S DISEASE

- pruritic eczema-like rash involving the nipple and areola
- flaking and scaling of the nipple skin and there may be nipple retraction
- In advanced stages, there can be crusting, ulceration, skin erosion, and discharge.
- The differential diagnosis includes eczema, contact dermatitis, duct ectasia



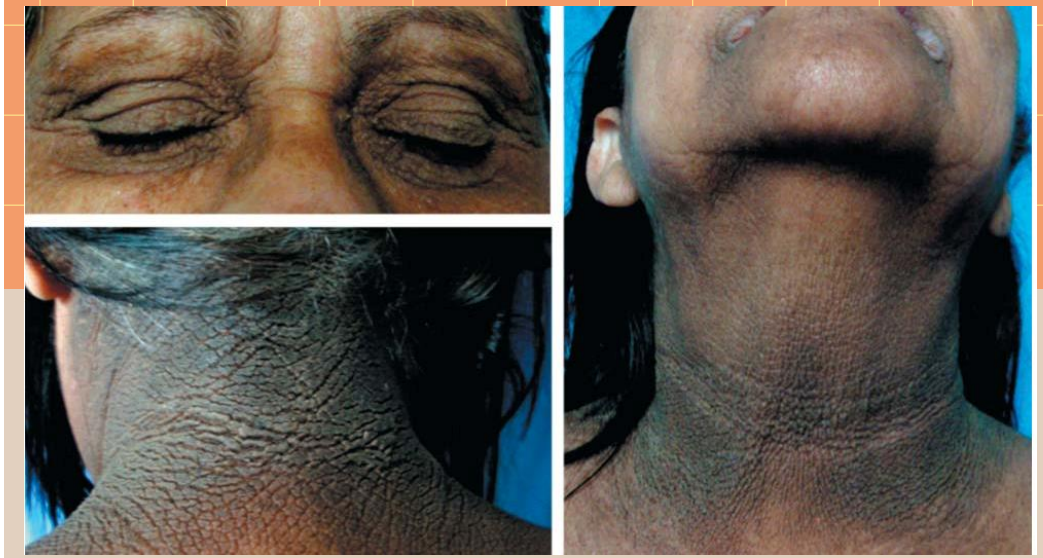
EXTRAMAMMARY PAGET'S DISEASE

- clinically indistinguishable from that of Paget disease, except for its location—typically appears on the apocrine gland–bearing perianal or vulvar skin



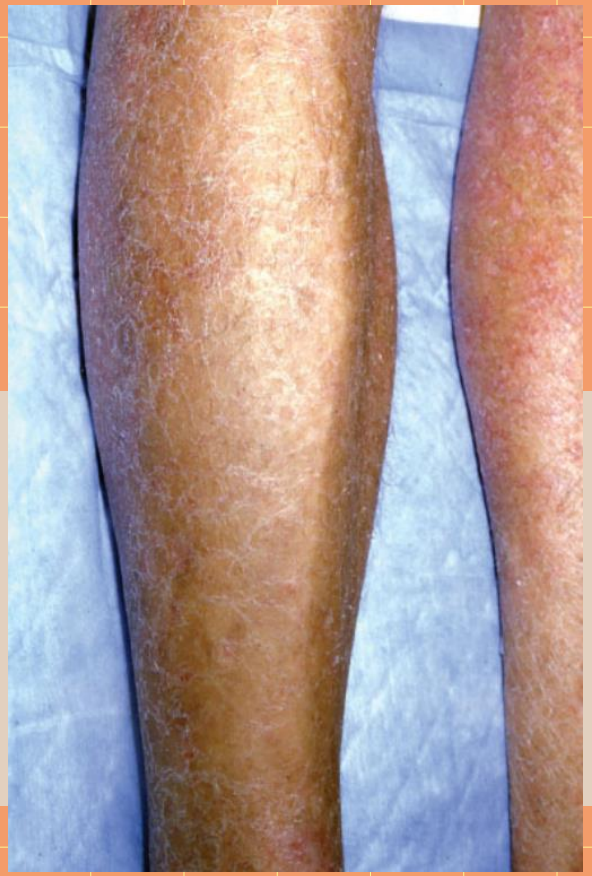
ACANTHOSIS NIGRICANS

- velvety to verrucous hyperpigmented plaques in intertriginous areas
- majority are benign and associated with obesity and insulin resistance, but the disease also can herald the onset of malignancy, usually gastric, with a more striking clinical presentation→
  - patients tend to be older, are generally not obese, and have often experienced recent unintentional weight loss leading to a cachectic appearance
  - cutaneous plaques are florid and may develop in unusual locations (eg, oral cavity, palms and soles)
  - Ass/w tripe palm and sign of Leser-Trélat



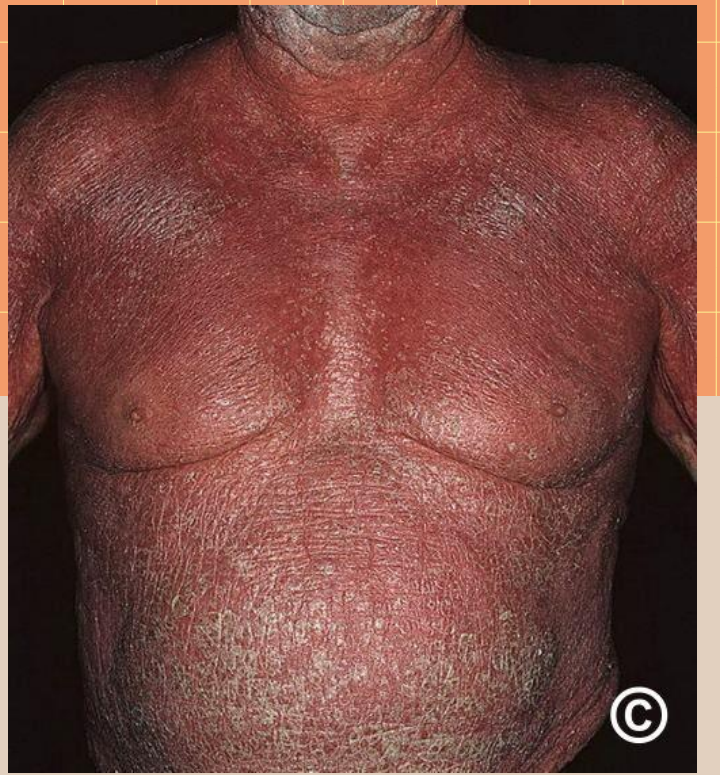
ACQUIRED ICHTHYOSIS

- can be congenital or acquired
- acquired can be associated with inflammatory, endocrinologic, or neoplastic processes
- presentation is similar to the inherited condition ichthyosis vulgaris, with prominent fish-like, relatively large scales adherent to the skin; however, the scaling in acquired disease may also be present on the palms and soles and in skin flexures
- Hodgkin lymphoma is the most common malignancy associated with acquired ichthyosis



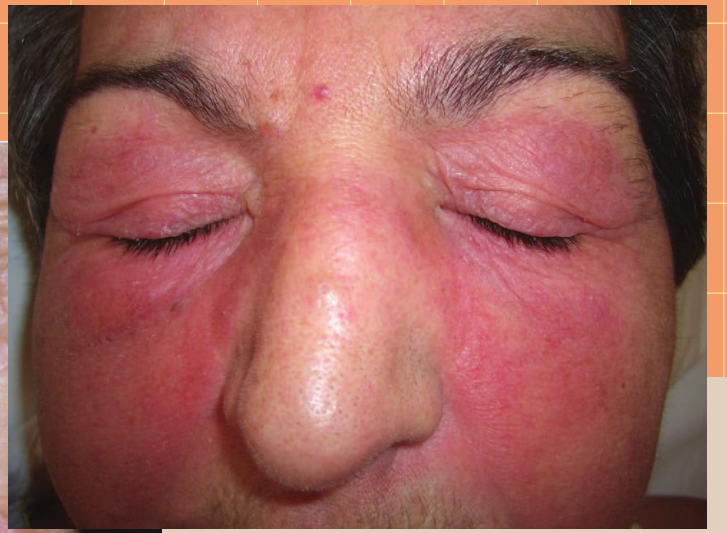
EXFOLIATIVE ERYTHRODERMA/DERMATITIS

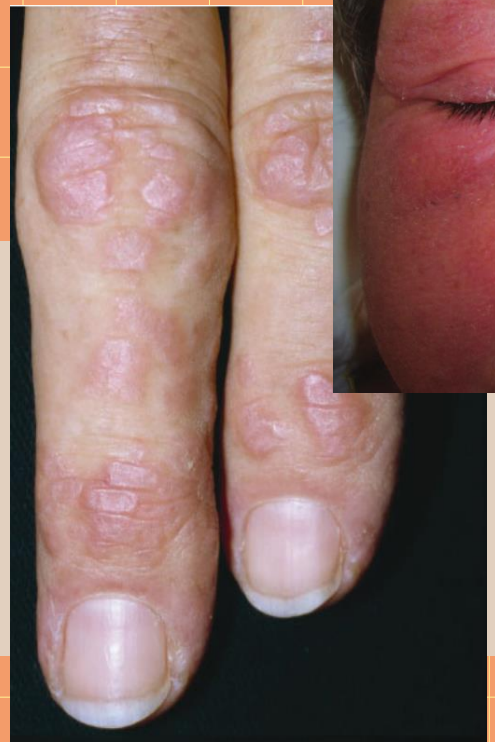
- diffuse and generalized erythema of the skin, may involve >90% of the BSA
- Severe pruritus, ectropion, and generalized lymphadenopathy are not uncommon; superficial desquamation usually ensues
- most common cause is a preexisting skin disease—atopic dermatitis or psoriasis, followed by drug hypersensitivity reactions
- erythroderma linked to malignancy are associated with lymphoid malignancies, particularly cutaneous T cell lymphoma
- usually resolves with treatment of the associated malignancy



DERMATOMYOSITIS

- **skin findings**: scaly violaceous papules overlying hands' bony prominences (Gottron papules), violaceous patches on periorbital skin (heliotrope eruption); less specific: photosensitivity, poikiloderma, scaly plaques on the scalp and lateral thighs, periungual telangiectasia
- **myopathy**: progressive, symmetric, proximal weakness
- risk of malignancy: older age, male, cutaneous necrosis, ↑ESR and CRP
- muscle disease is more likely to improve with treatment of underlying cancer than skin disease

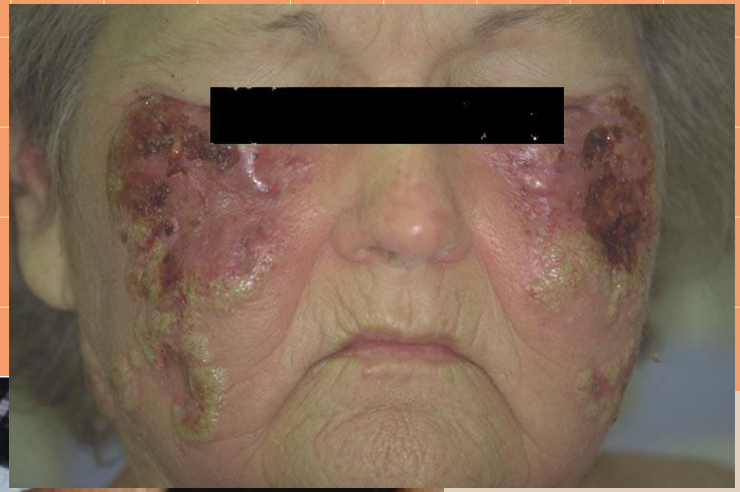


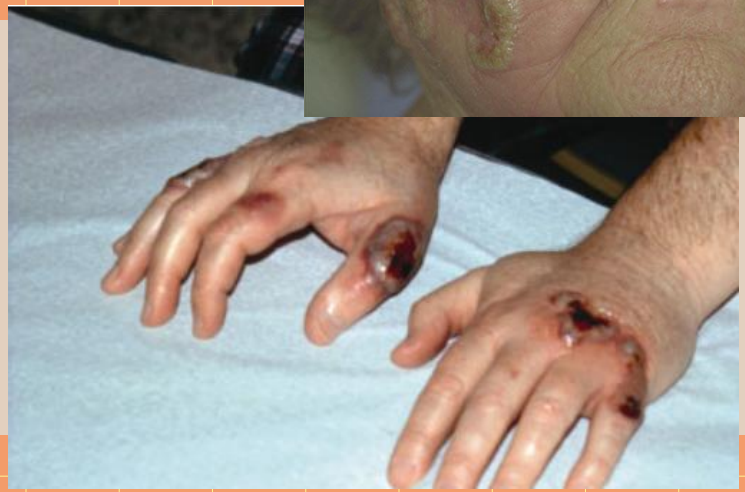


SWEET SYNDROME

AKA acute febrile neutrophilic dermatosis

- characterized by a dermal neutrophilic infiltration and fever
- well-demarcated, erythematous to violaceous papules + plaques with an irregular pseudo-vesiculated surface
- pustulation and blistering can occur, may cause pain and burning sensation, but usually not pruritic.
- most often found on the face, neck, and upper extremities
- pathergy
- Most common malignancy is AML, distinguished by severe anemia

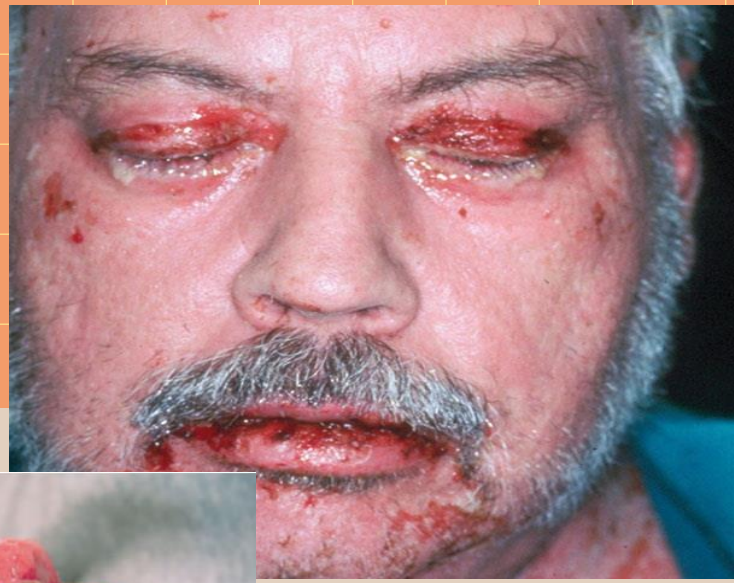


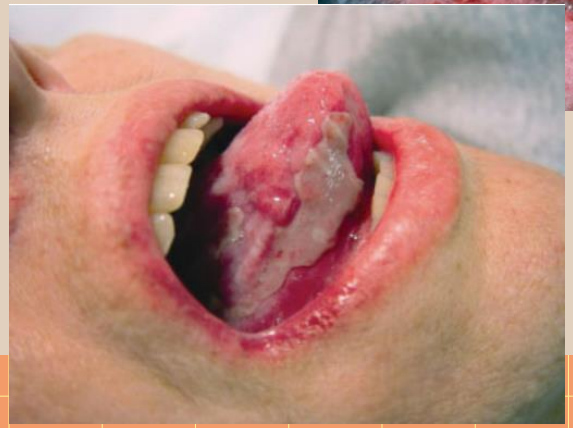


PARANEOPLASTIC PEMPHIGUS

AKA paraneoplastic autoimmune multiorgan syndrome

- most consistent clinical feature is a painful stomatitis
- cutaneous manifestations: tense bullae or lesions resembling erythema multiforme or lichen planus
- ocular complications, muscle weakness, myasthenia gravis, and severe involvement of the airways
- non-Hodgkin lymphoma is the most frequent associated disorder
- treatment by removal of tumor; immunosuppressants may be helpful

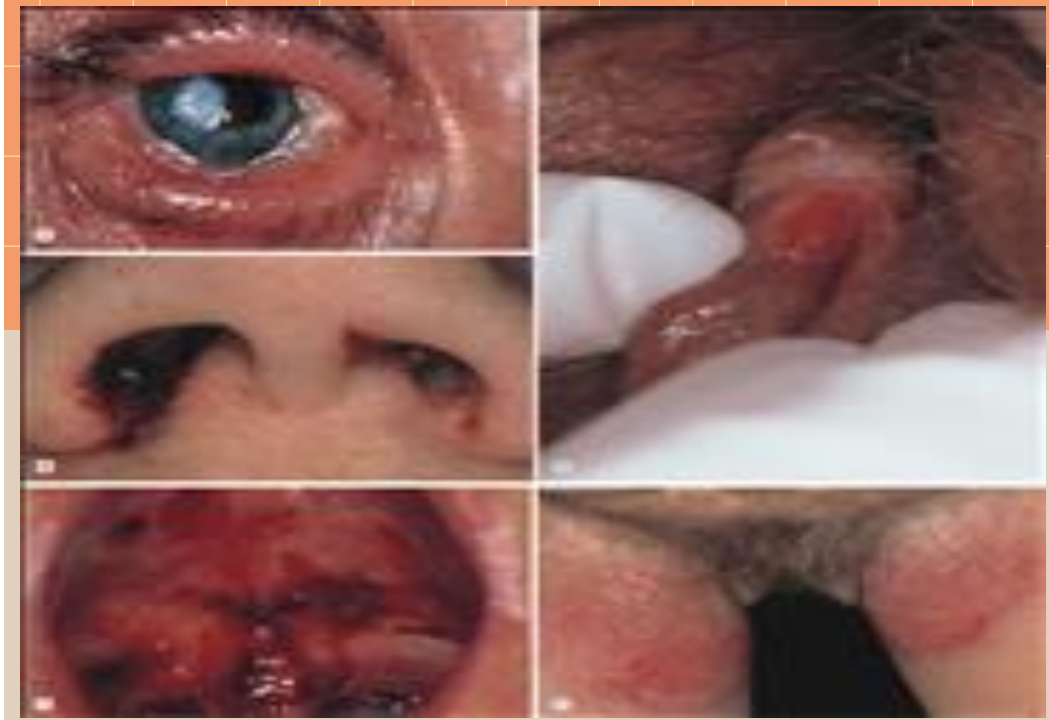




ANTI-EPILIGRIN CICATRICIAL PEMPHIGOID

mucous membrane pemphigoid with antibodies against laminin 332 (epiligrin)

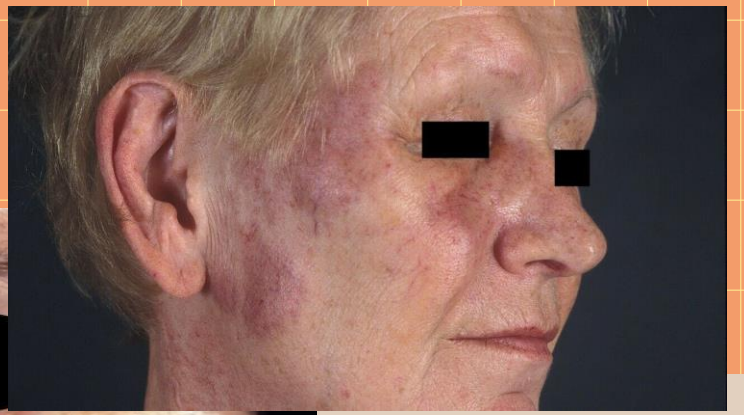
- autoimmune disease→antibodies against laminin 332 (epiligrin) in the dermal-epidermal junction→
- severe, painful blisters and erosions on the oral mucosa, and skin manifestations consisting of bullae and erosions on an erythematous base
- Immunosuppressive therapy may be effective for improving symptoms; however, the disease course often is progressive

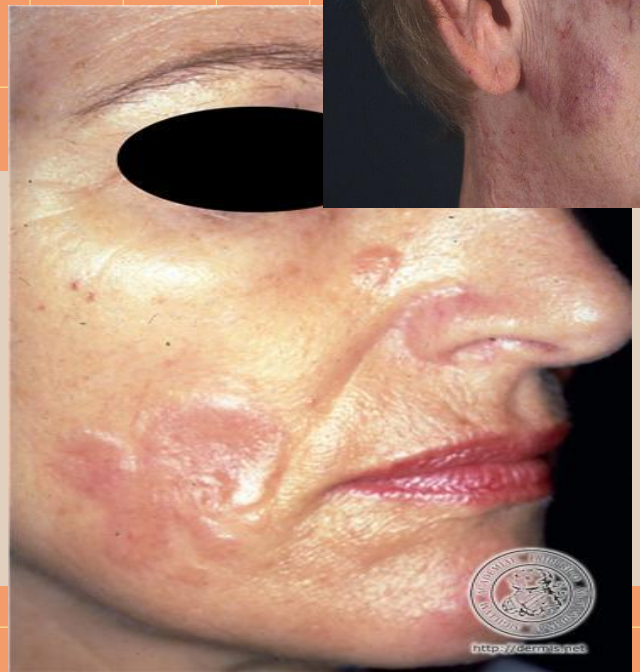


NECROBIOTIC XANTHOGRANULOMA

With paraproteinemia (monoclonal gammopathy)

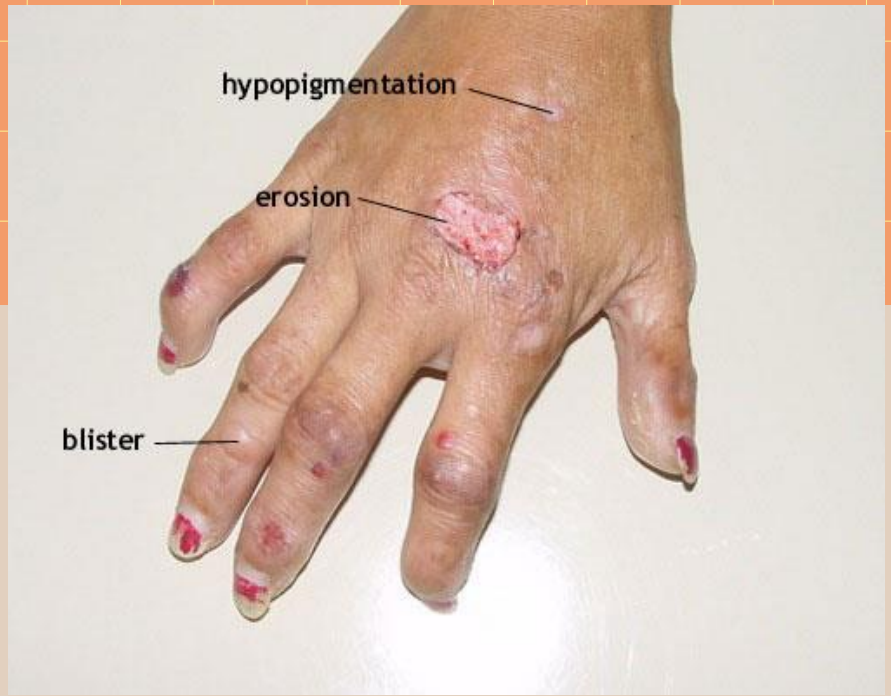
- multiple yellowish plaques and subcutaneous nodules located in the periorbital region and on the head, the neck, the flexures of the extremities, and the trunk.
- Ulceration and scarring are common
- Associated malignancies include lymphoproliferative diseases, myeloma, chronic lymphoid leukemia, and lymphoma





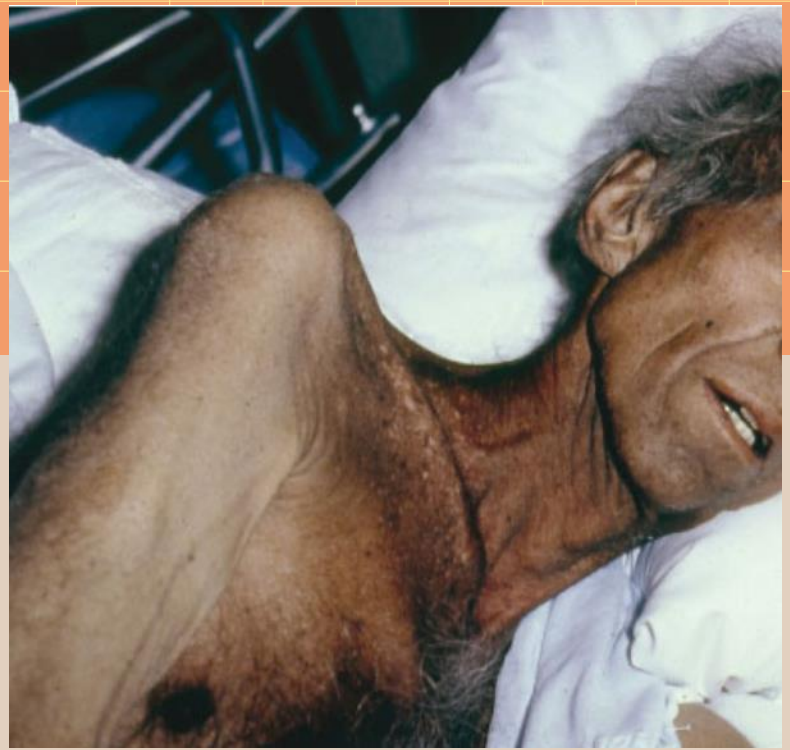
PORPHYRIA CUTANEA TARDA

- common porphyria caused by decreased activity in the uroporphyrinogen decarboxylase enzyme, leading to the accumulation of porphyrins
- Cutaneous photosensitivity → fluid-filled vesicles on sun-exposed areas, friable skin, wounds heal slowly and hyperpigmentation
- Higher incidence of hepatocellular carcinoma



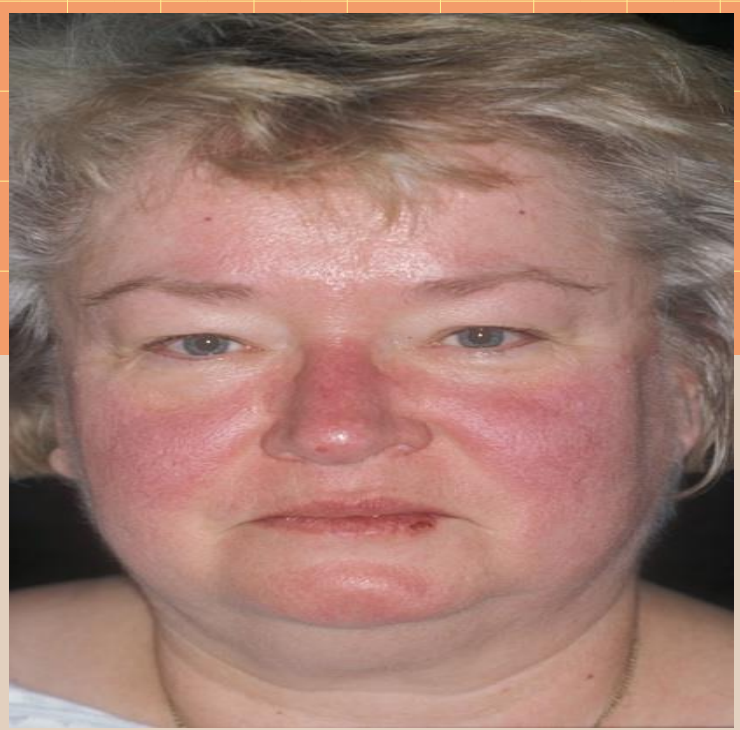
ECTOPIC CUSHING'S (ACTH) SYNDROME

- most common hormonally induced paraneoplastic syndrome associated with internal malignancy
- generalized hyperpigmentation (cutaneous+mucosal), muscle wasting, proximal muscle weakness, abnormal fat distribution, peripheral edema, hypokalemic metabolic alkalosis, abnormal glucose tolerance, and hypertension
- most common cause is lung carcinoma, specifically the small cell neuroendocrine type



CARCINOID SYNDROME

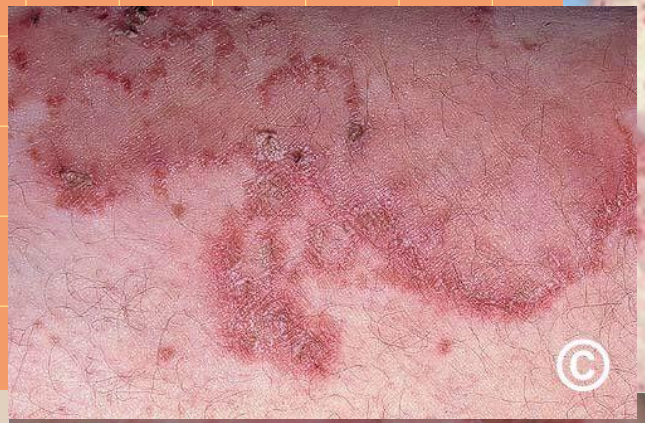
- Carcinoid tumors can produce a variety of vasoactive substances→episodes of flushing initially lasting 10-30 minutes and involve only the upper half of the body
- Successive attacks eventually lead to a more permanent facial cyanotic flush with associated telangiectasia, resembling rosacea
- Classical carcinoid syndrome occurs primarily with intestinal carcinoids metastatic to the liver or with extraintestinal tumors.

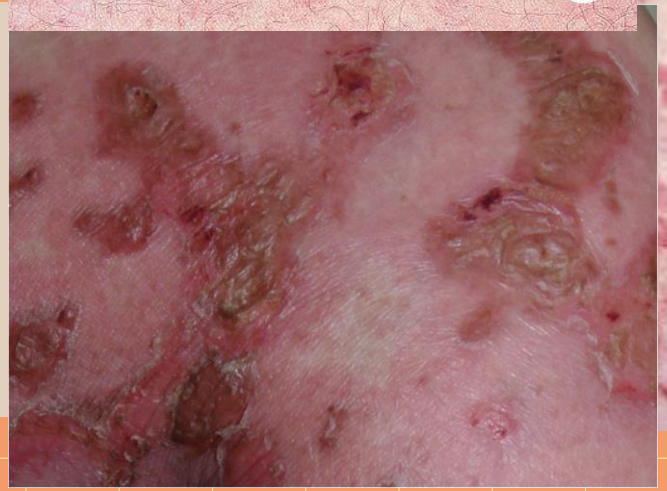


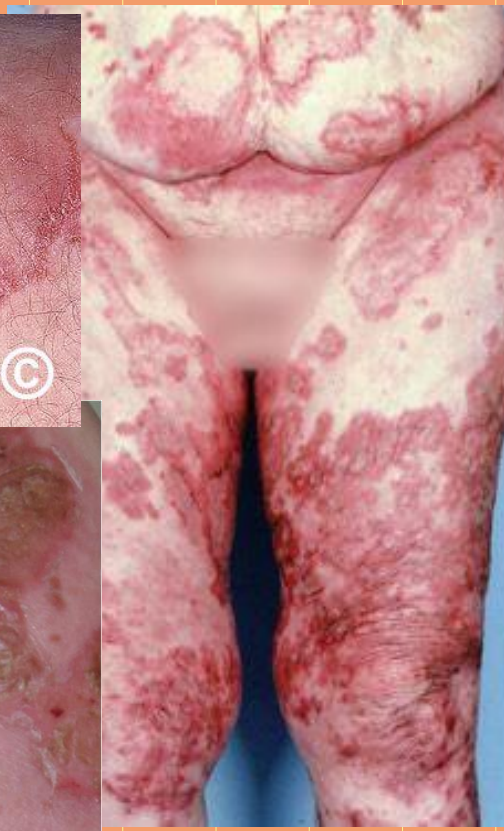
GLUCAGONOMA SYNDROME

Necrolytic migratory erythema

- transient, weeping eczematous or psoriasiform eruption that occurs in approximately 70% of patients with glucagon-secreting pancreatic islet cell tumors (glucagonomas)
- begins as erythematous papules or plaques involving the face, perineum, and extremities
- 7-14 days: lesions enlarge and coalesce. Central clearing then occurs, leaving bronze-colored, indurated areas centrally, with blistering, crusting, and scaling at the borders; affected areas are often pruritic and painful

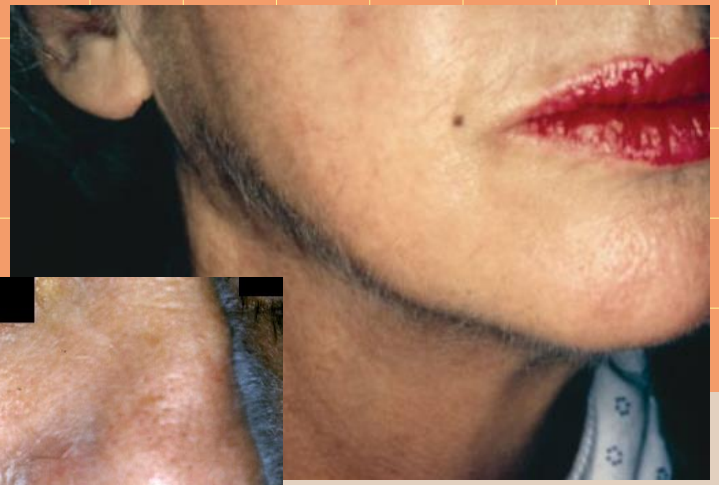


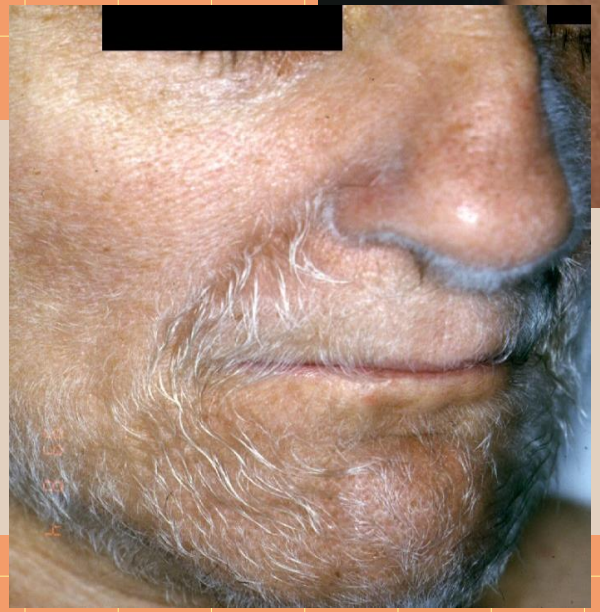




ACQUIRED HYPERTRICHOSIS LANGUINOSA

- appearance of silky, non-pigmented lanugo hair growth, which is predominantly localized to the head and neck but may spread to the torso, arms, and legs
- strong association with adenocarcinomas arising in the large bowel, breast, lung, and kidney
- usually presents in patients with advanced or metastatic cancer
- Removal of the malignancy may lead to resolution of the excess hair growth





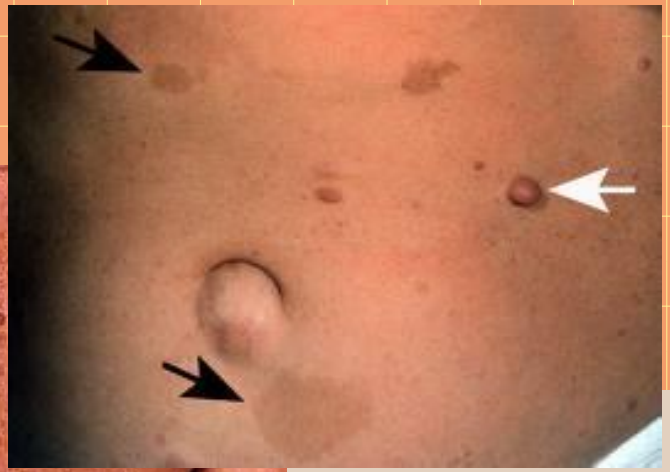
GENODERMATOSES (HEREDITARY)

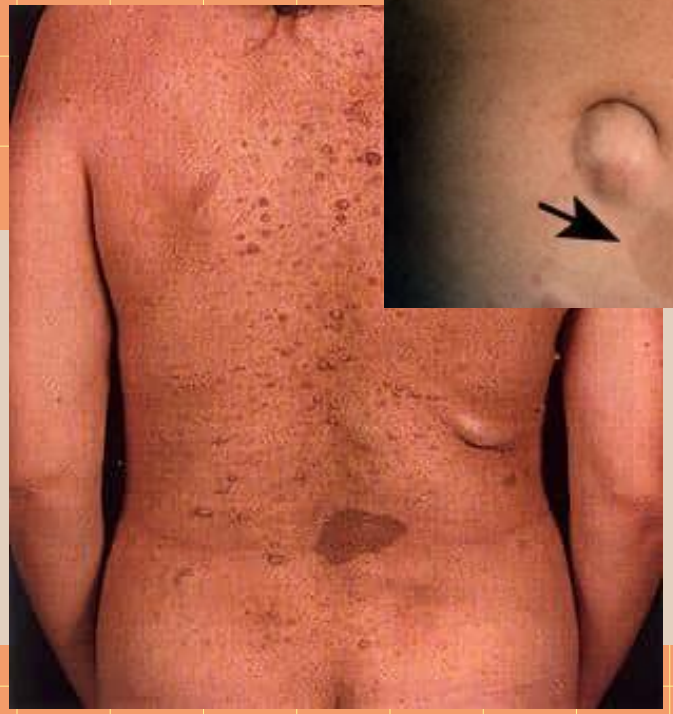
- Cowden syndrome: a multiple hamartoma syndrome
  - Associated malignancies: breast, thyroid, urogenital, GIT, neurologic
- Gardner syndrome: familial adenomatous polyposis (FAP)
  - extracolonic malignancies, including neoplasms of the thyroid, pancreas, liver, central nervous system, gallbladder, biliary tract, duodenum, and stomach
- Muir–Torre syndrome: Lynch syndrome variant
  - Associated malignancies: colorectal and genitourinary cancers
- Ataxia-telangiectasia
  - Associated malignancies: non-Hodgkin lymphoma, leukemia, and gastric cancer
- Neurofibromatosis type 1
  - Brain and kidney tumors

NEUROFIBROMATOSIS TYPE 1

AKA von Recklinghausen's disease

- autosomal dominant neurocutaneous disorder with nervous system, skeletal, and dermatologic manifestations, caused by mutations in the *NF1* gene, encoding the protein neurofibromin
- Characteristic findings:
  - Six or more café-au-lait macules of greatest diameter >5 mm in prepubertal and >15 mm in postpubertal individuals
  - Two or more neurofibromas of any type or one plexiform neurofibroma
  - Freckling in the axillary or inguinal regions (Crowe sign)





02

ENDOCRINE DISEASES

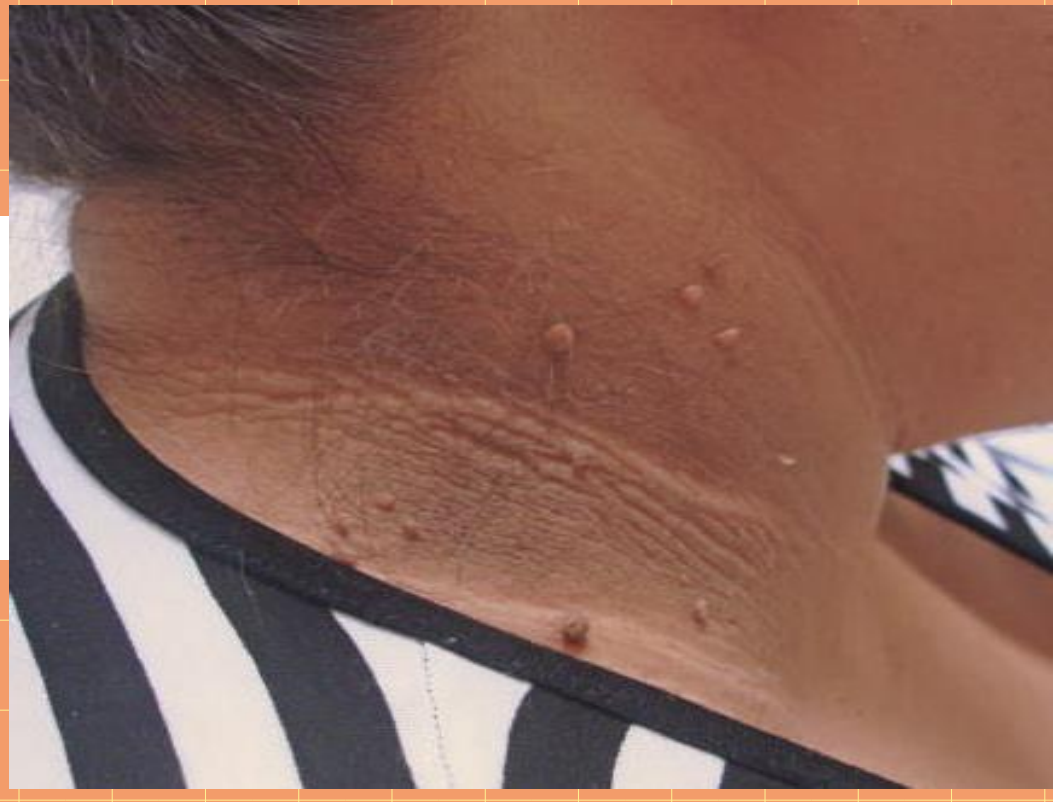
DM
Thyroid diseases,
Adrenal diseases

DIABETES MELLITUS

- Acanthosis nigricans
- Acral dry gangrene
- Diabetic bullae
- Diabetic cheiroarthropathy
- Disseminated granuloma annularae
- Eruptive xanthoma
- Necrobiosis lipoidica diabeticorum,
- Diabetic dermopathy-
- Neuropathic ulcer
- Rubeosis: chronic flush of neck, face, and upper extremities
- Scleredema adultorum of buschke
- Hemochromatosis, bronzing of the skin due to melanin
- Perforating skin disorder

ACANTHOSIS NIGRICANS

Velvety hyperpigmentation + thickening of skin, could be associated with skin tags

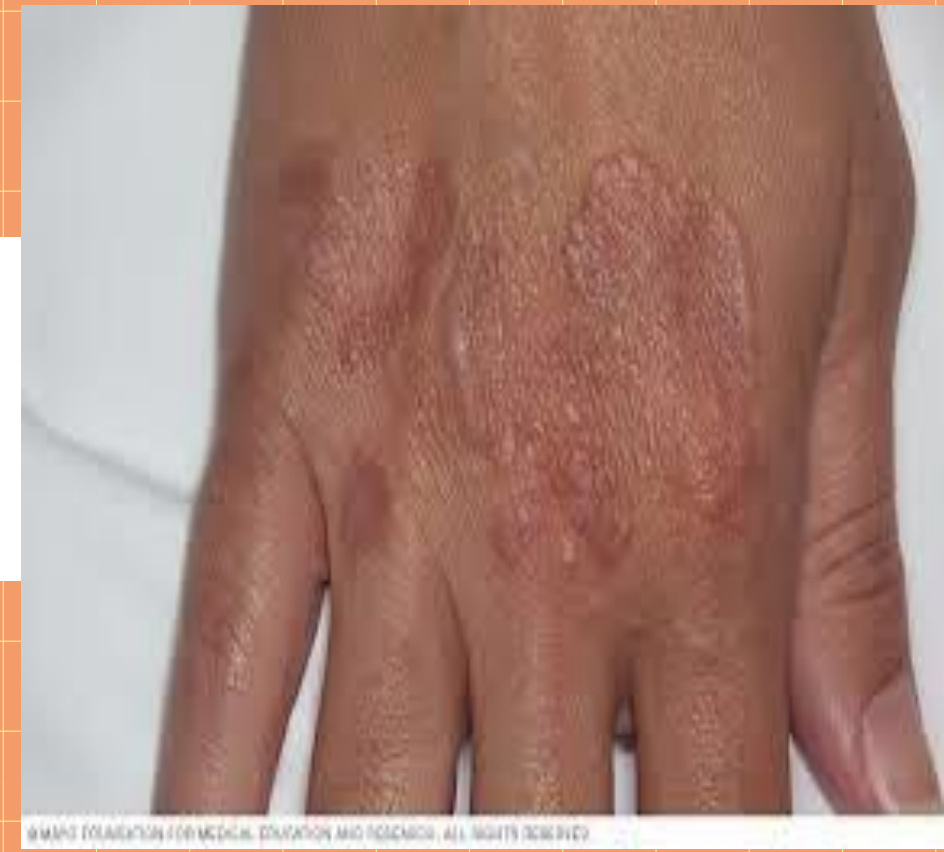


DIABETIC BULLAE

Large, few (1-2) on acral sites

GRANULOMA ANNULARE

Discolored plaques + papules
in a ring patter

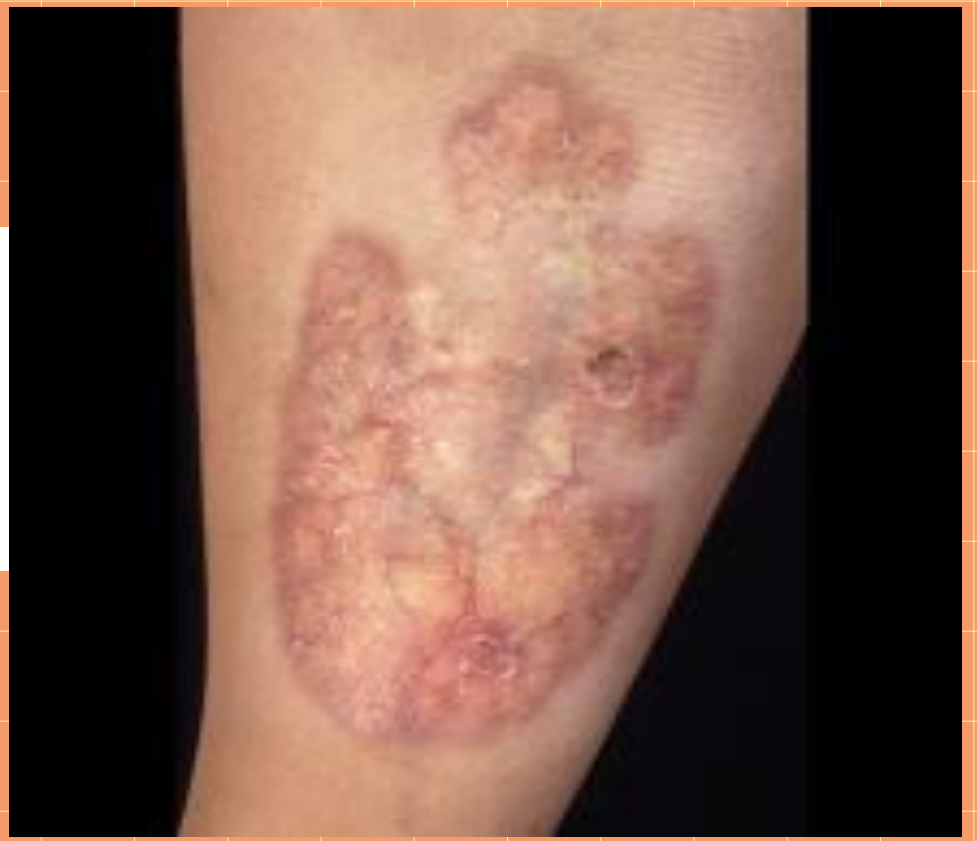


DIABETIC CHEIROARTHROPATHY

Inability to fully flex or extend the fingers

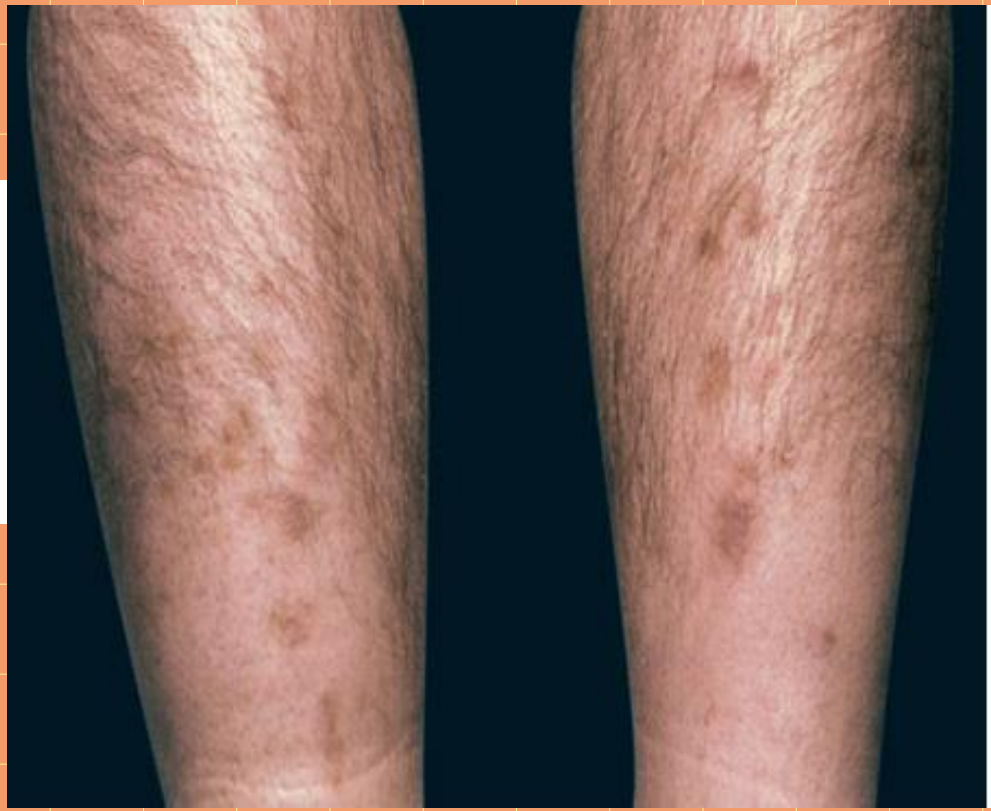
NECROBIOSIS LIPOIDICA DIABETICORUM

Erythematous yellowish plaques with telangiectasia and atrophic centers on the shins, could ulcerate



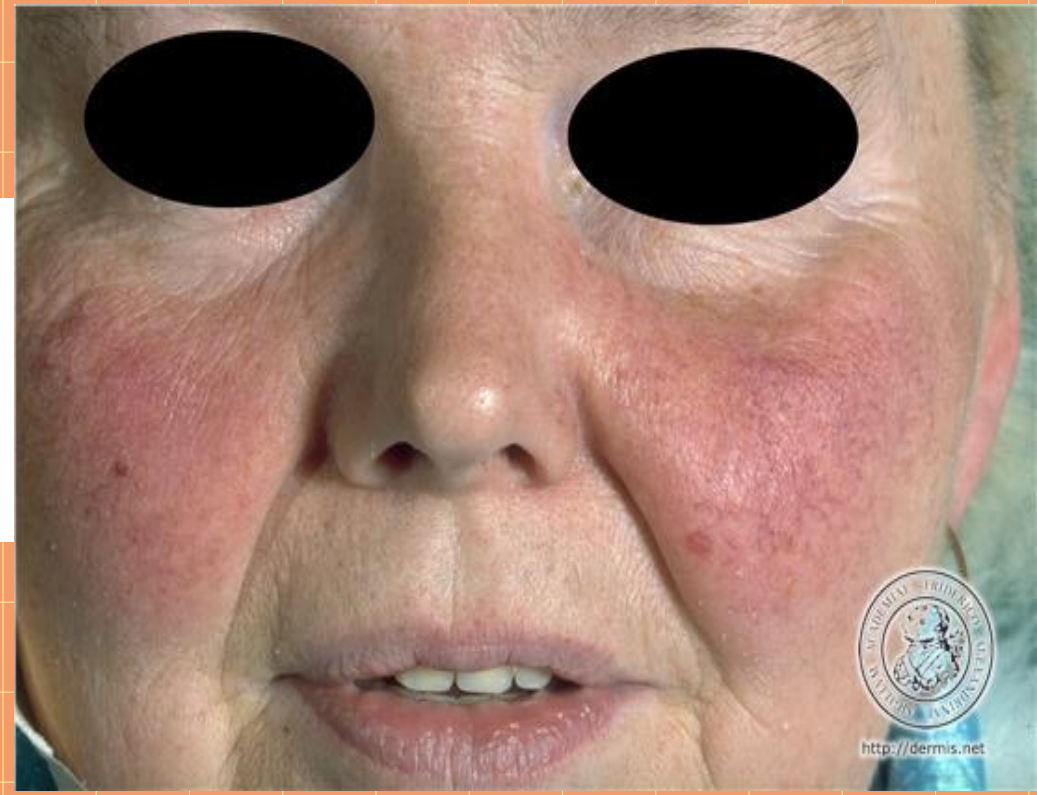
DIABETIC DERMOPATHY

Asymptomatic brown scar-like lesions on the shins



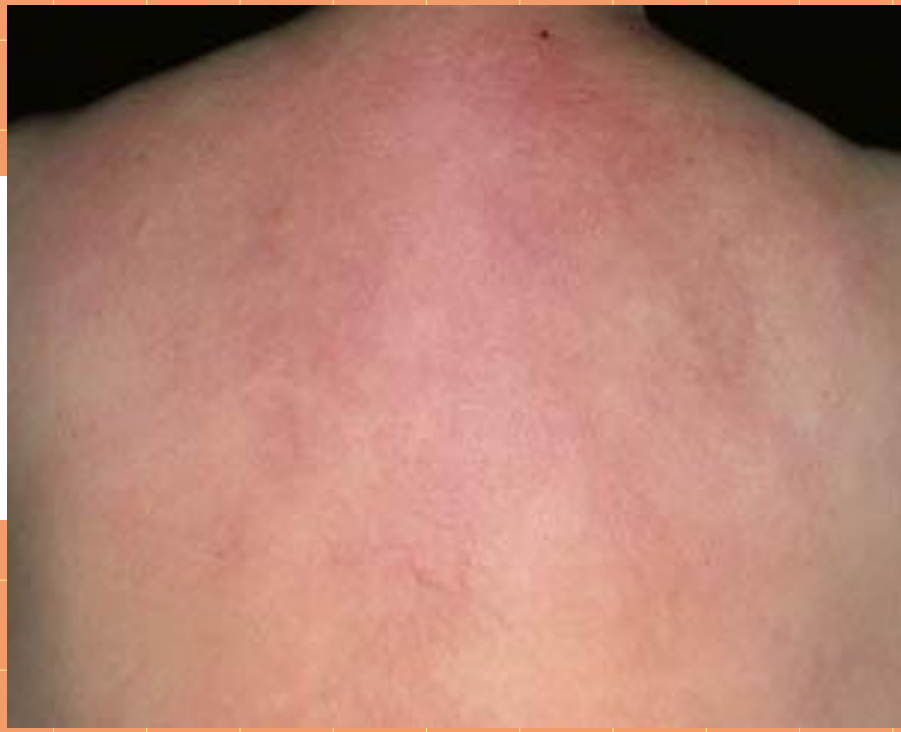
RUBEOSIS FACIEI DIABETICORUM

Facial flushing, could present on the neck and upper extremities



SCLEREDEMA ADULTORUM OF BUSCHKE

Erythema + thickening of the skin due to mucin accumulation on the back, chest, and face

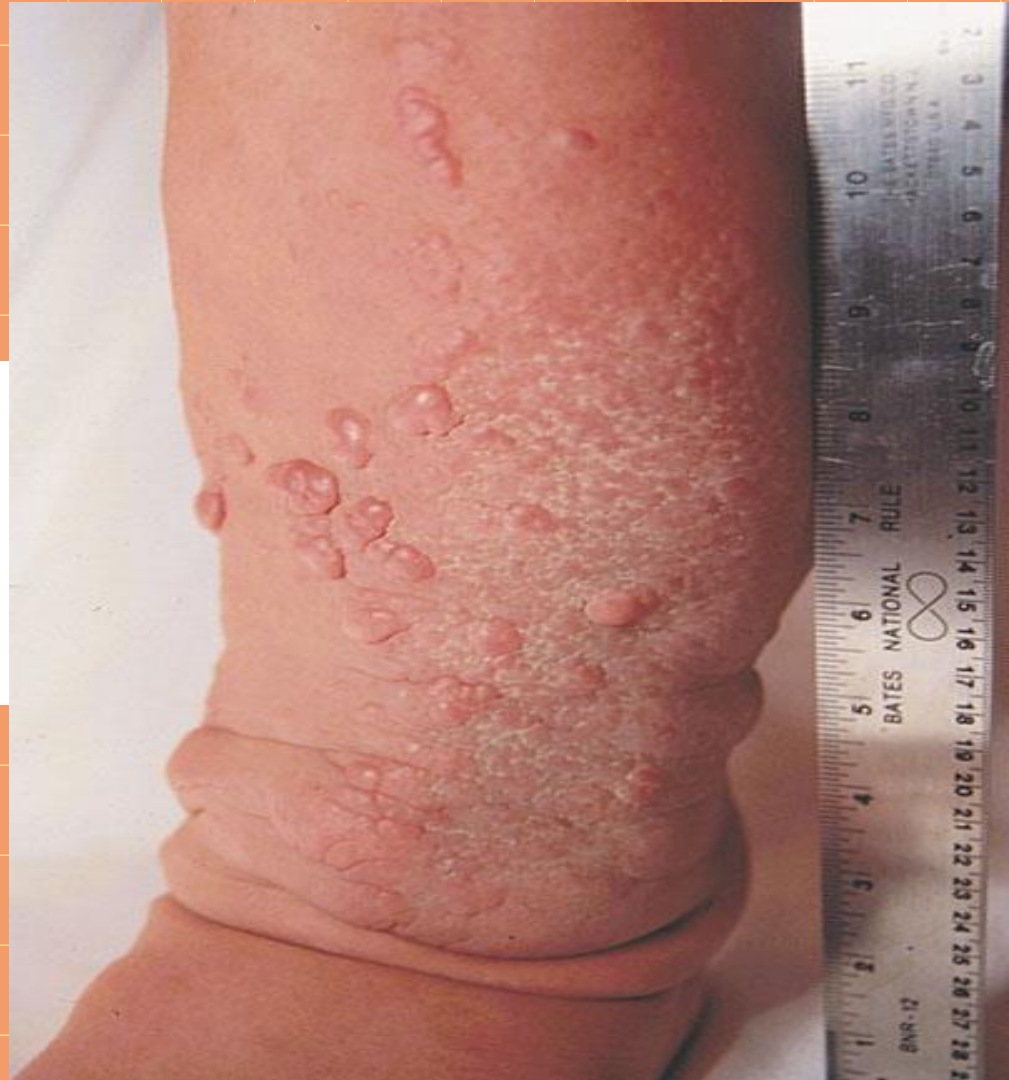


HYPERTHYROIDISM

- Cutaneous changes: fine, velvety, smooth warm, and moist (increased sweating), hyperpigmentation, pruritus
- Cutaneous disease: pretibial myxedema, thyroid acropachy (clubbing), urticaria, dermographism and vitiligo
- Hair changes: fine, thin; mild diffuse alopecia
- Hair disease: Alopecia areata
- Nail changes: onycholysis, koilonychia, clubbing
- Investigation: TSH, T3, T4 , anti-thyroperoxidase + anti-Thyroglobulin antibodies

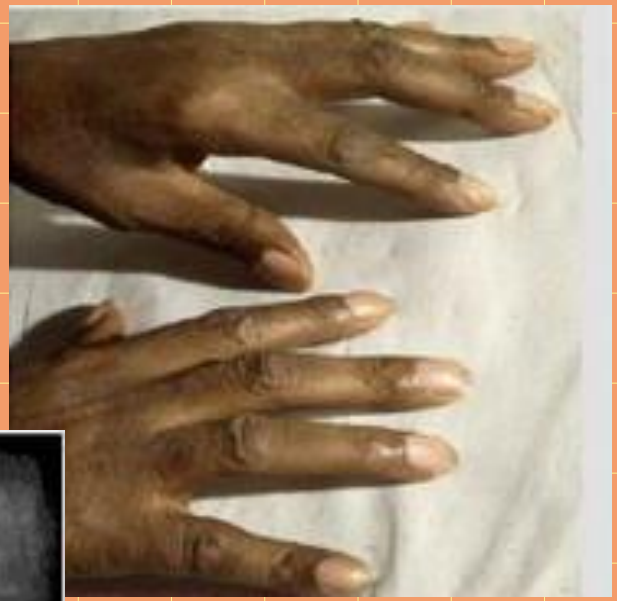
PRETIBIAL MYXEDEMA

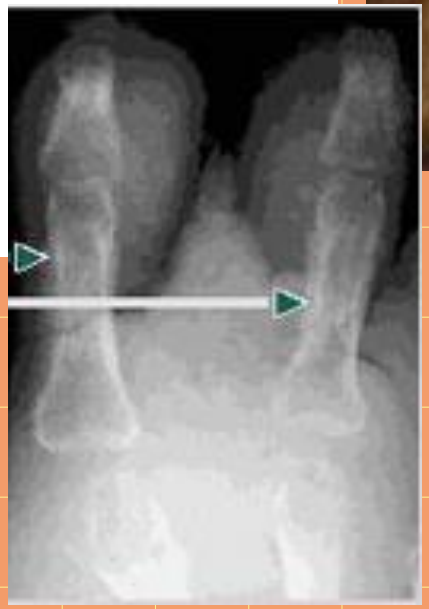
Thickened skin with verrucous lesions due to mucin depostion

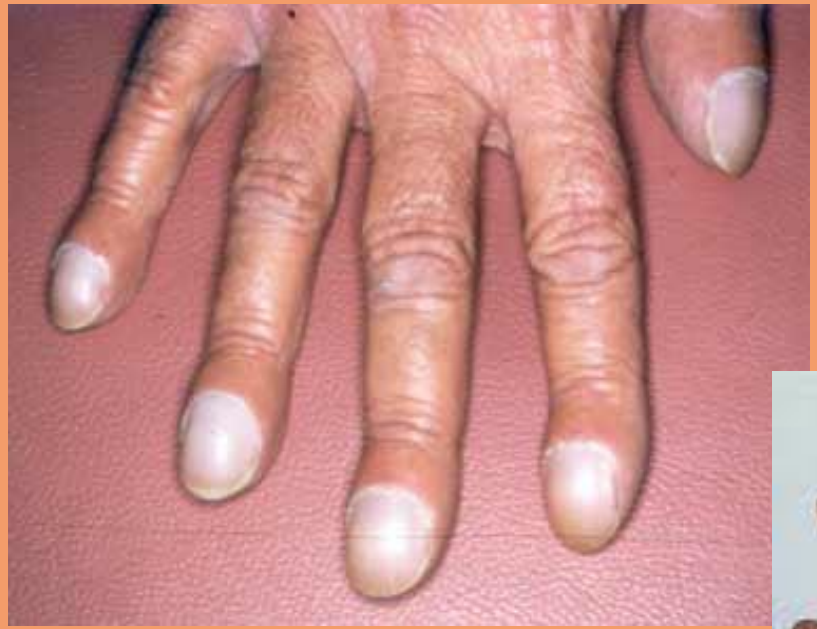


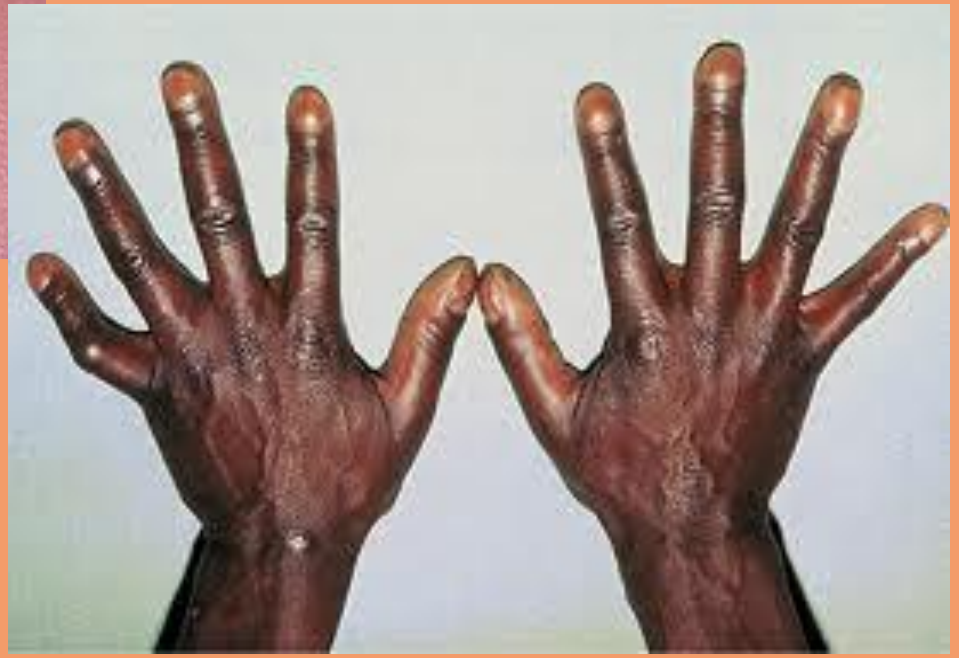
PRETIBIAL MYXEDEMA

Painless clubbing, periosteal bone formation + periosteal proliferation, soft tissue swelling that is pigmented and hyperkeratotic







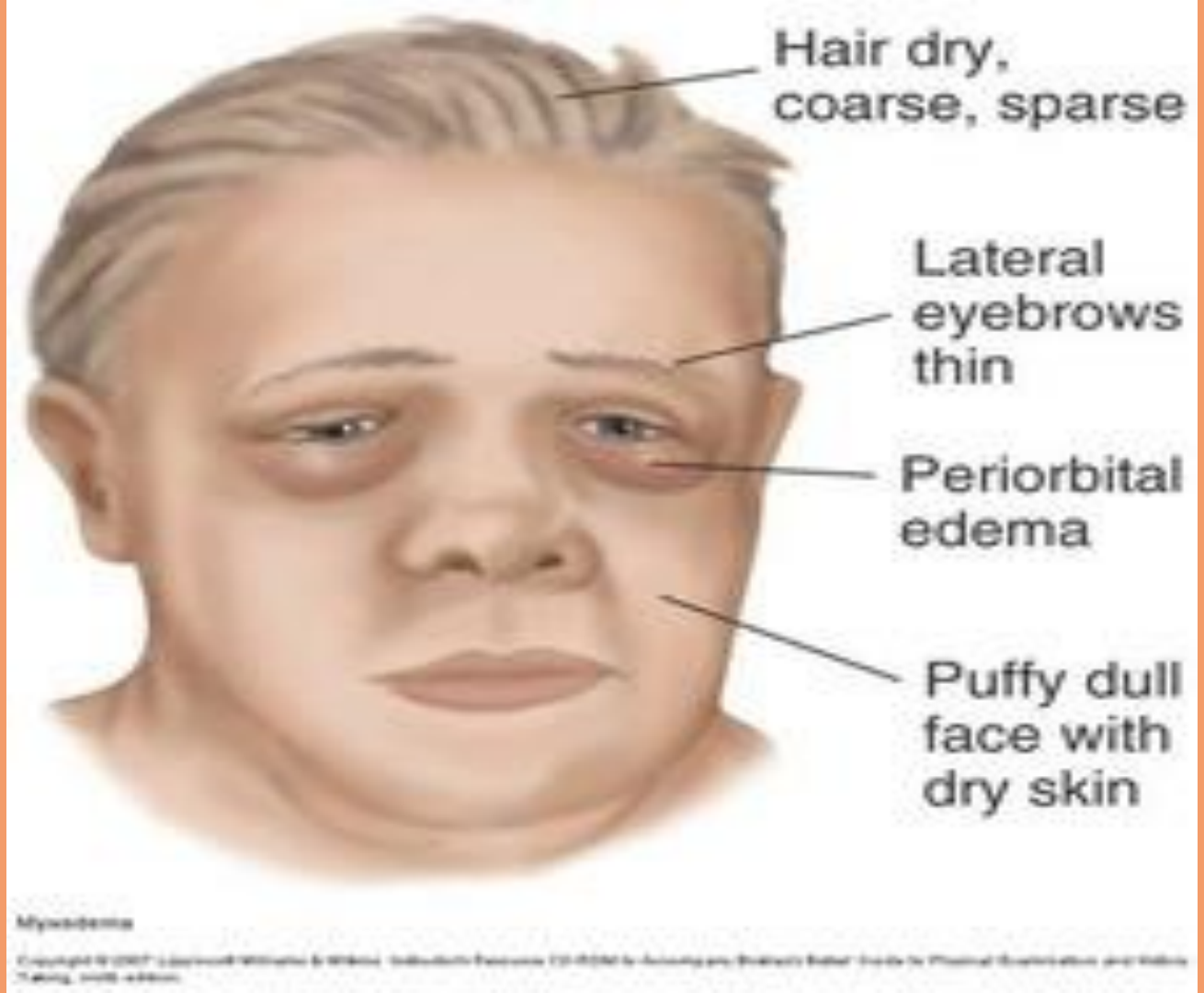


ONYCHOLYSIS

ALOPECIA AREATA

HYPORTHYROIDISM

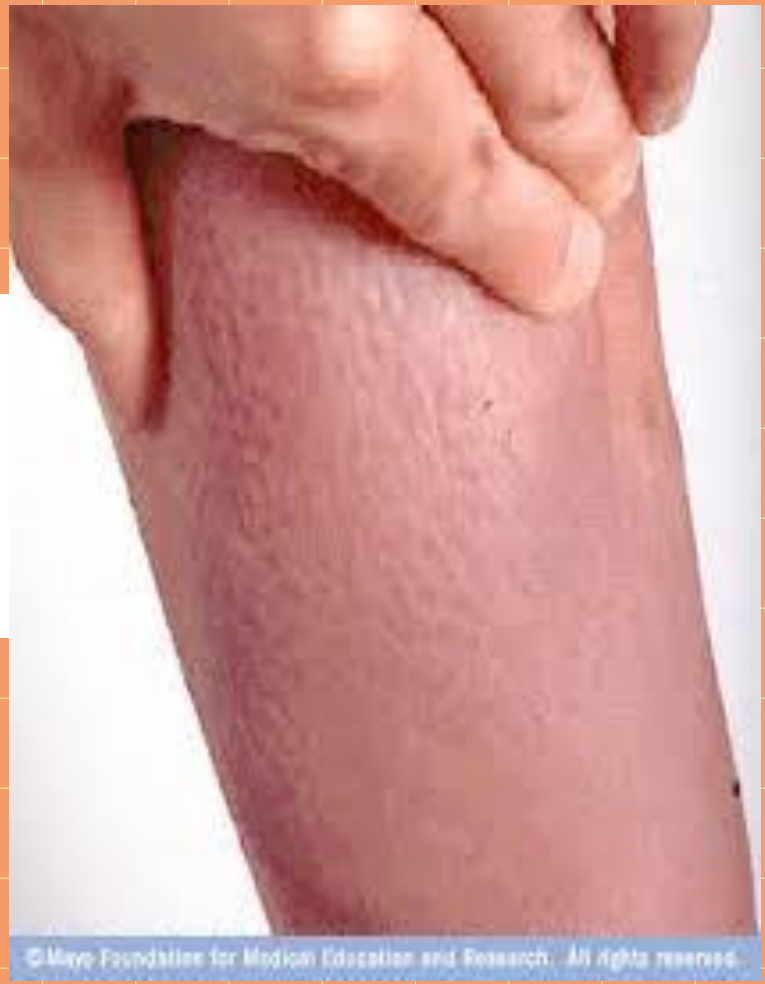
- Cutaneous changes: dry, rough, coarse skin, cold and pale, boggy and edematous skin (myxedema), yellow discoloration (carotenemia), easy bruising (capillary fragility)
- Cutaneous disease: ichthyosis, palmoplantar keratoderma, eruptive and tuberous xanthoma
- Hair changes: dull, coarse, brittle hair, slow growth, alopecia of lateral eyebrows
- Nail changes: thin, brittle, striated nails, slow growth, onycholysis
- Investigations: TSH,T3,T4, Anti-Thyroperoxidase, anti-Thyroglobulin antibodies


Hair dry, coarse, sparse
Lateral eyebrows thin
Periorbital edema
Puffy dull face with dry skin

Myxedema

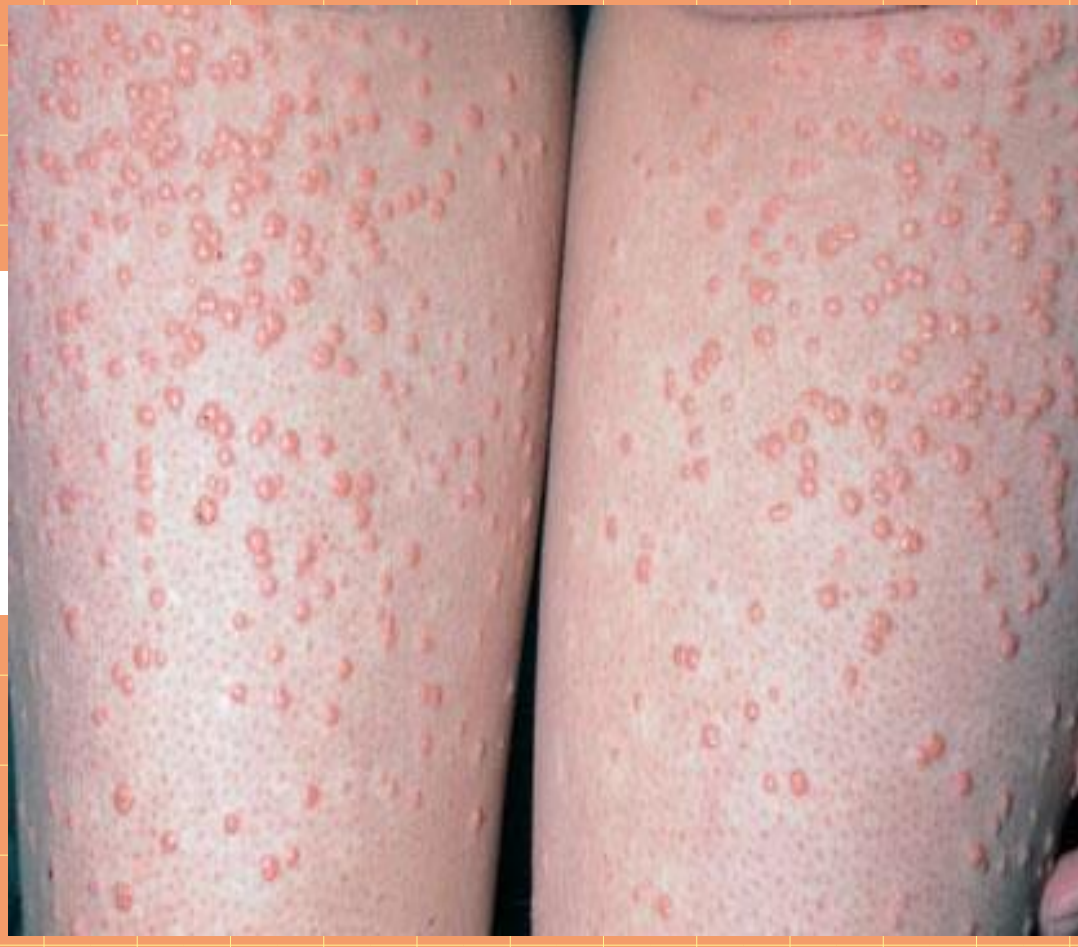
MYXEDEMA

Thick skin due to mucin depostion



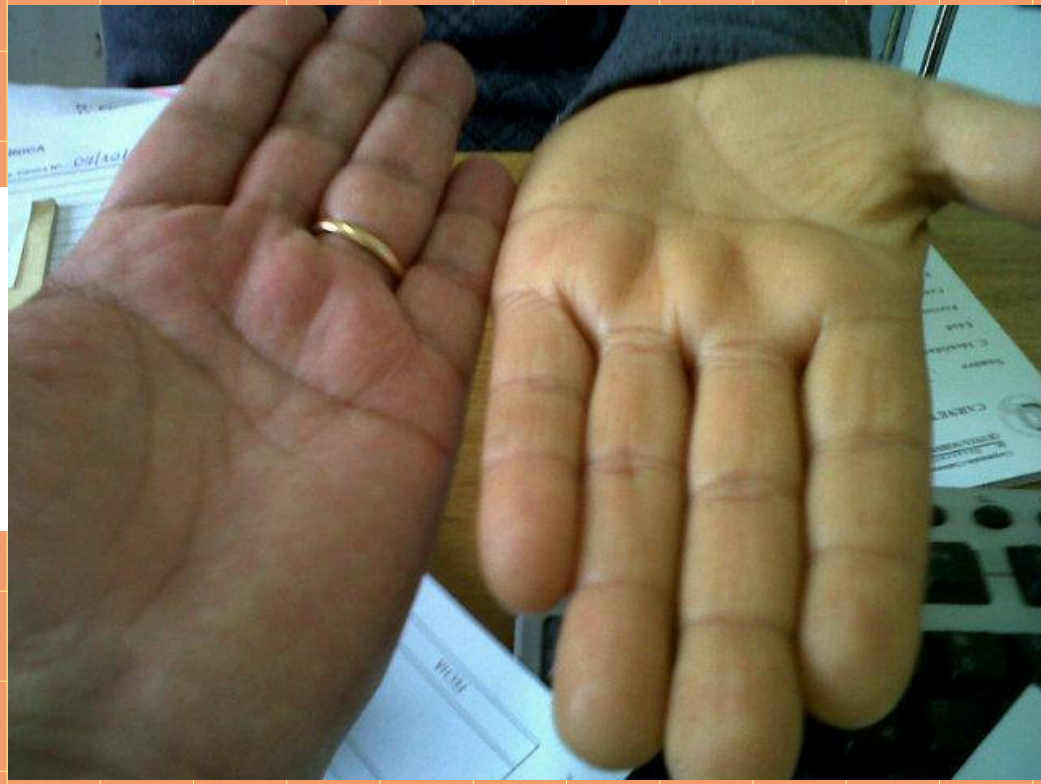
ERUPTIVE XANTHOMA

Yellowish papules



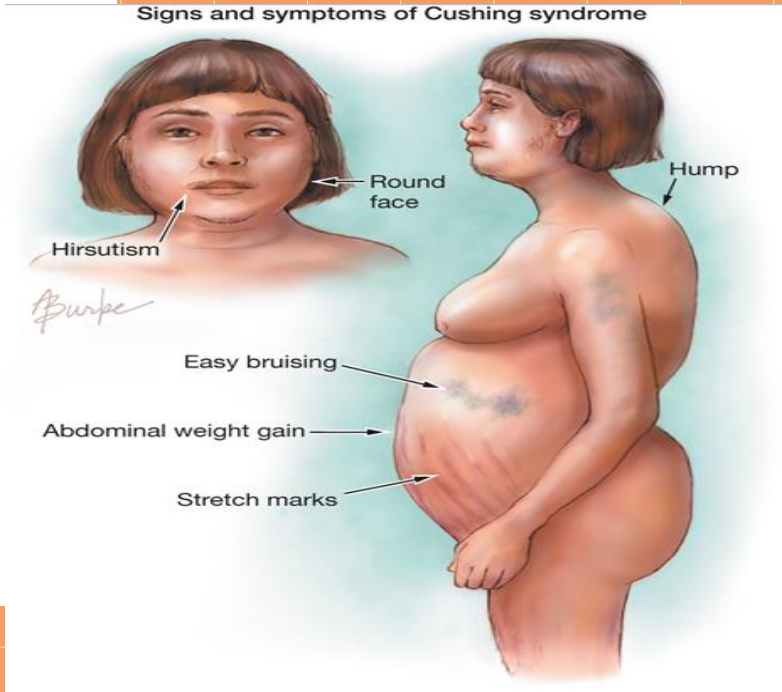
CAROTENEMIA

Yellow discoloration in thick skin (palms + soles)



CUSHING'S SYNDROME

- Moon face
- Buffalo hump
- Pelvic girdle fat deposition, reduced fat on arms and legs
- Striae, purpura after minor trauma
- Skin infections: TV, dermatophytosis, candidiasis
- Acne, hirsutism
- Investigations: ACTH, Dexamethasone suppression test



ADDISON'S DISEASE

- Hyperpigmentations (MSH-like effect due to secretion of ACTH), diffuse, more on sun-exposed areas, palmar creases, mucous membranes, nails, axillae, nipples, and perineum
- Vitiligo
- Investigations: ACTH

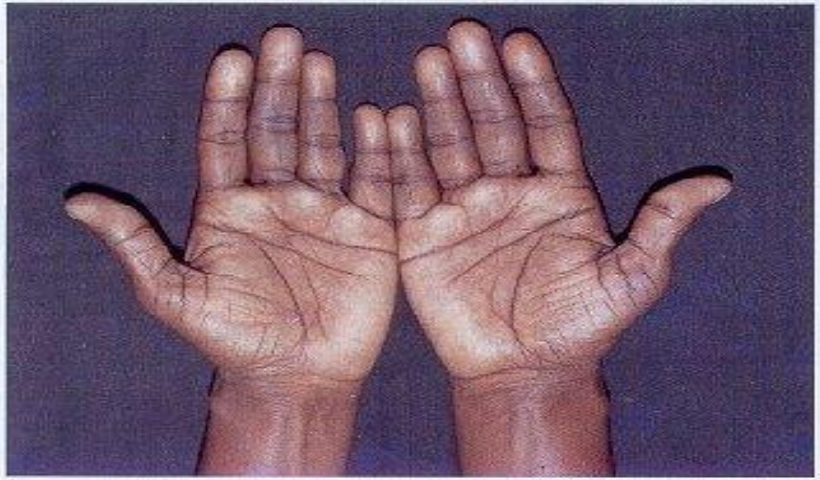
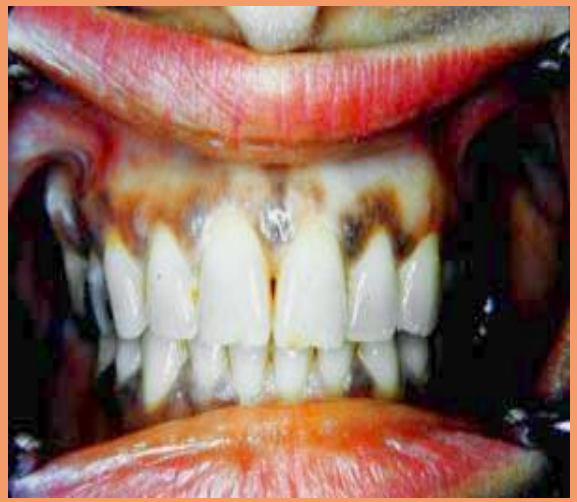


Fig. 2 Addison's disease – hyperpigmentation involving the palms of the hand.



03

CONNECTIVE TISSUE DISEASES

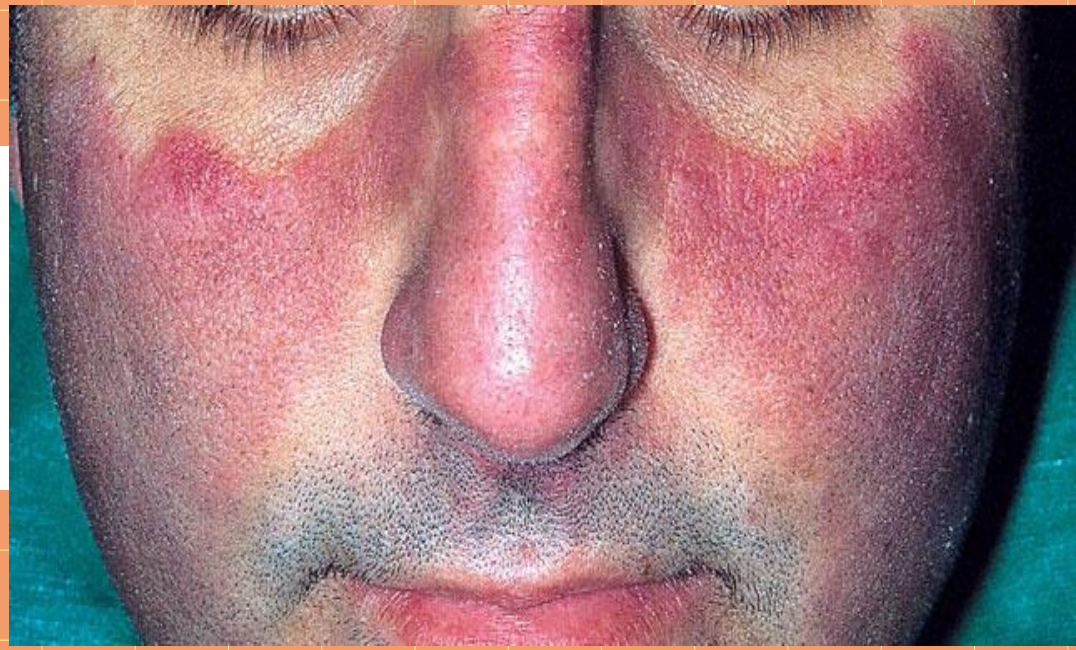
SLE, RA, DM, SS

SLE

- Malar Erythema
- Photosensitivity
- Discoid skin lesions
- Livedo reticularis, ulcers
- Urticaria , urticarial vasculitis
- Periungual telangiectasia and erythema

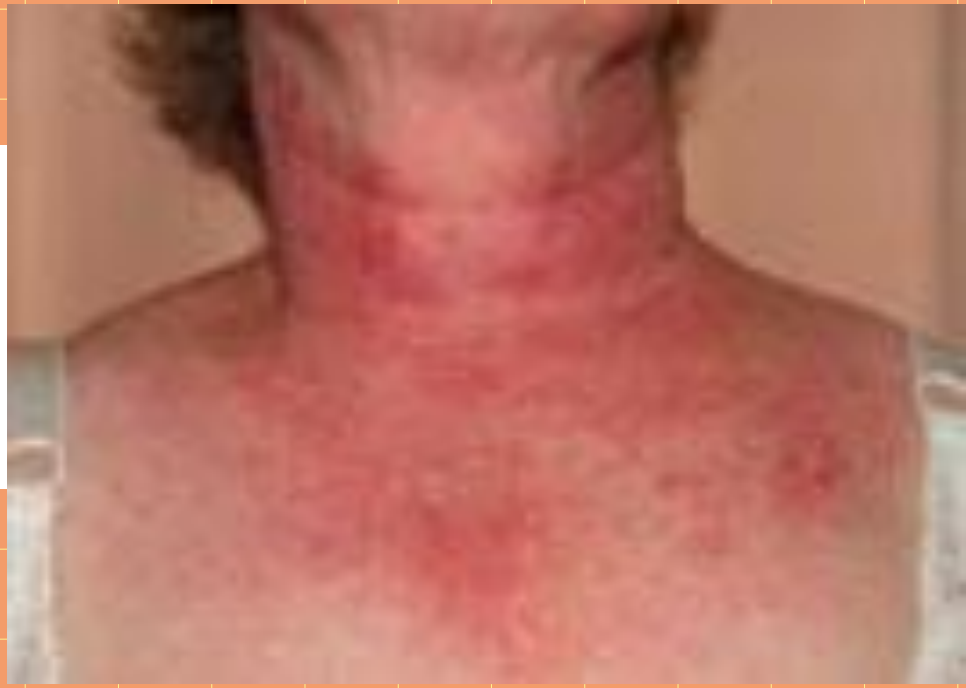
MALAR RASH

Erythematous rash affecting the cheeks and nose bridge



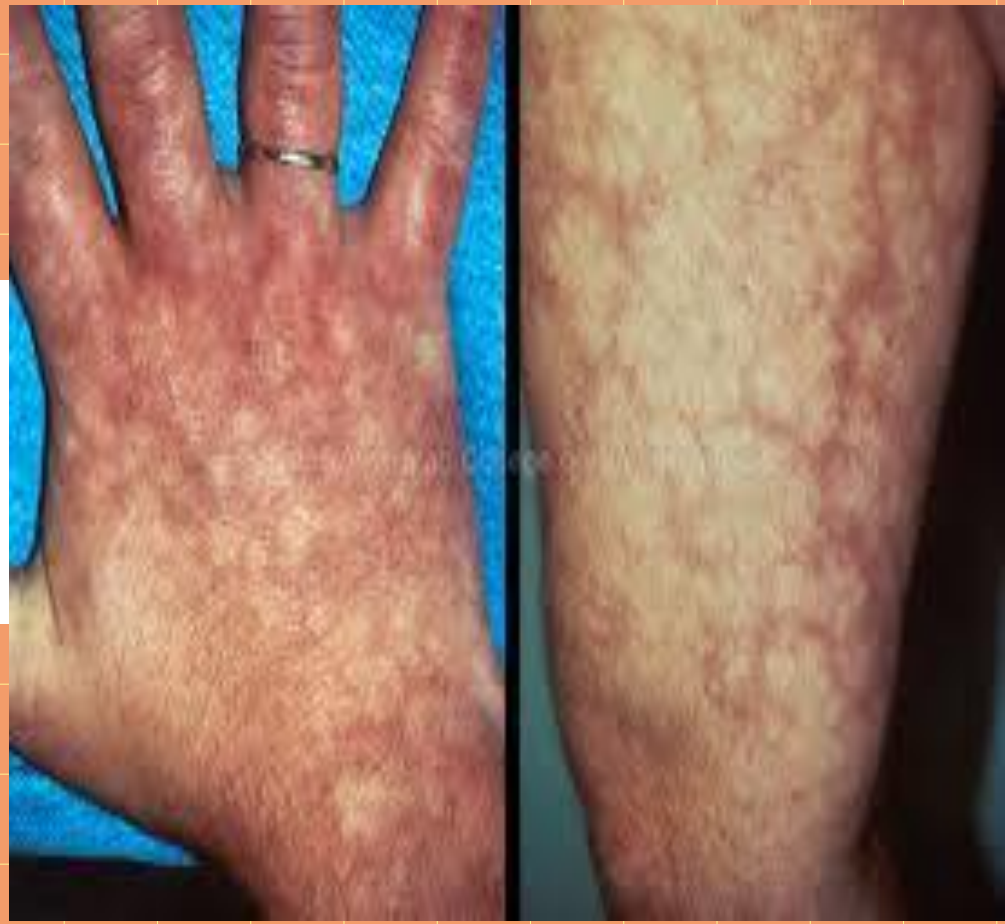
PHOTOSENSITIVITY

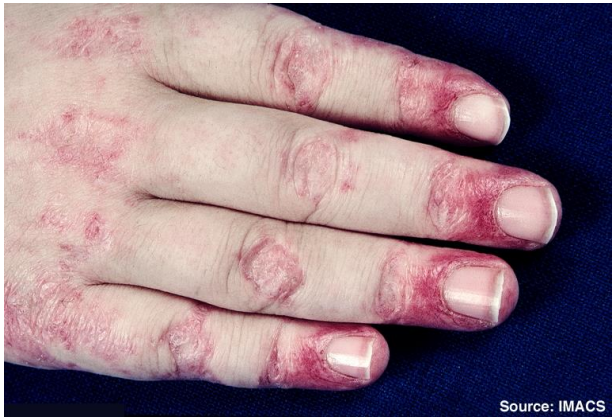
Eczematous lesions with erythema and itching on sun-exposed areas



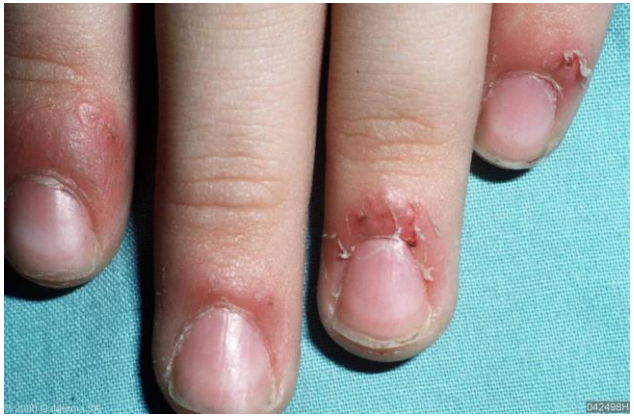
LIVIDO RETICULARIS

Lace-like pattern of erythema due to thromboembolic event →vascular compromise; occurs on CT diseases and hypercoagulable states

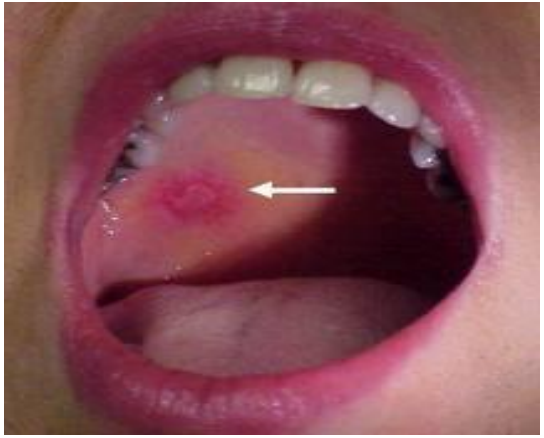




Periungal erythema + telangeictasia

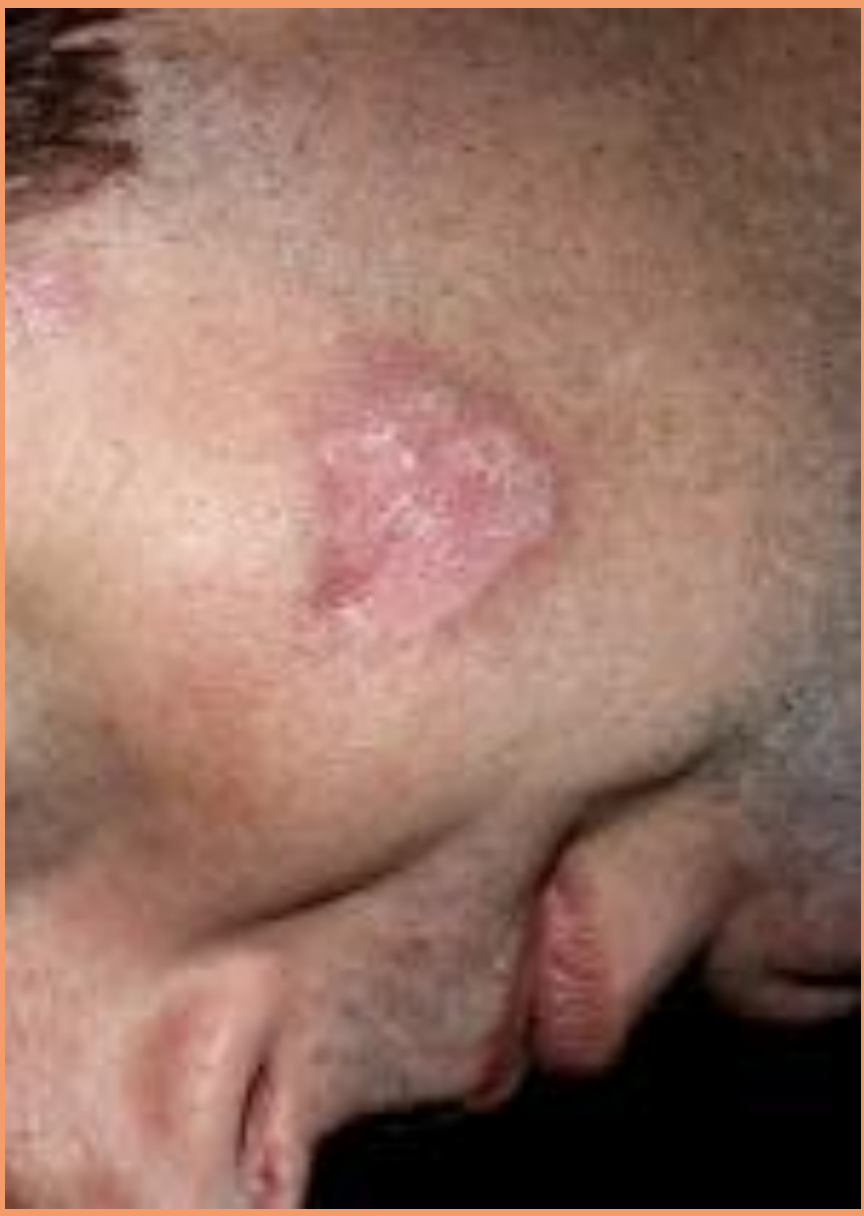


Periungal erythema + necrotic area



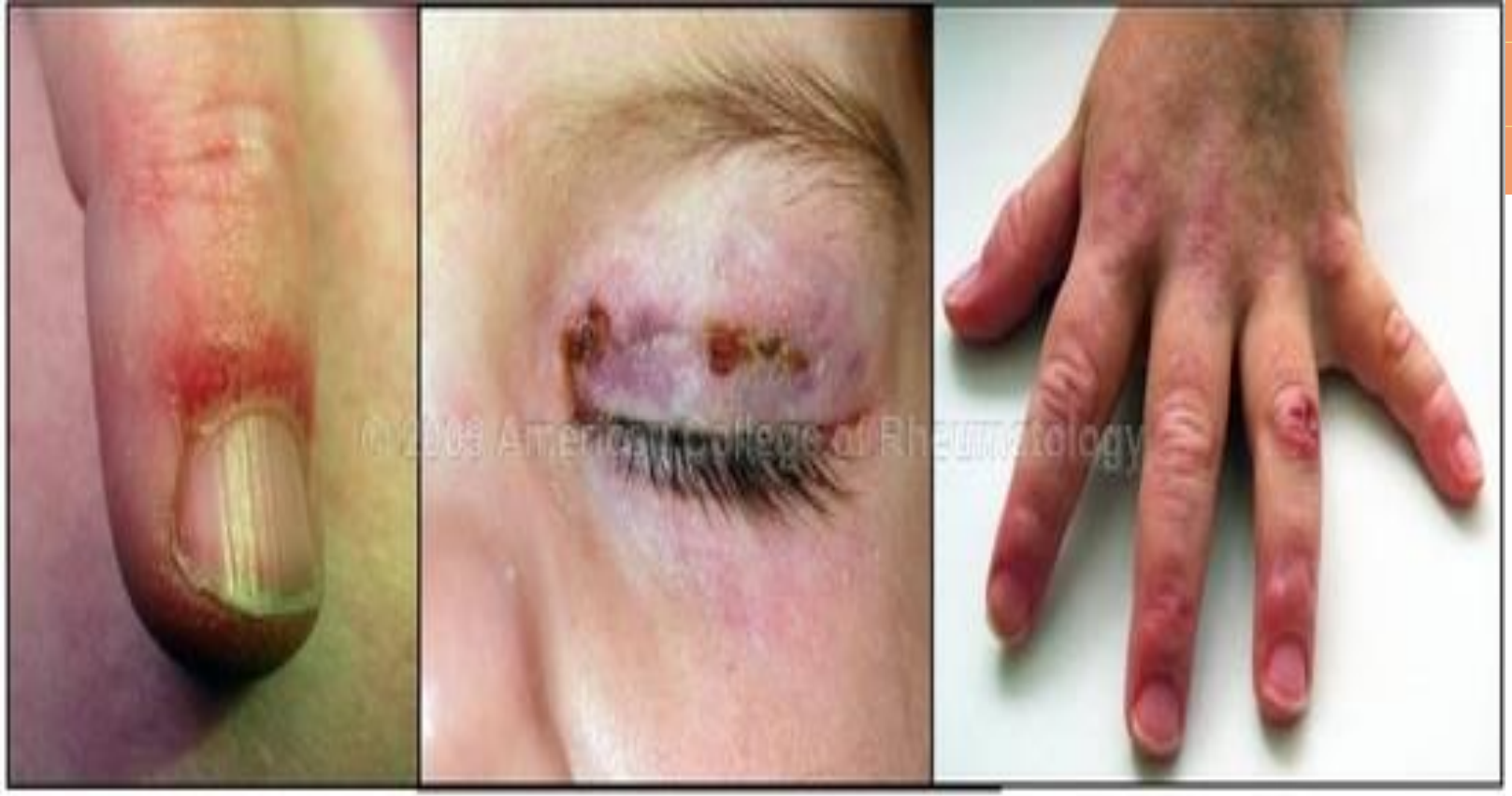
Oral ulcer

Discoid scarring lesion



DERMATOMYOSITIS

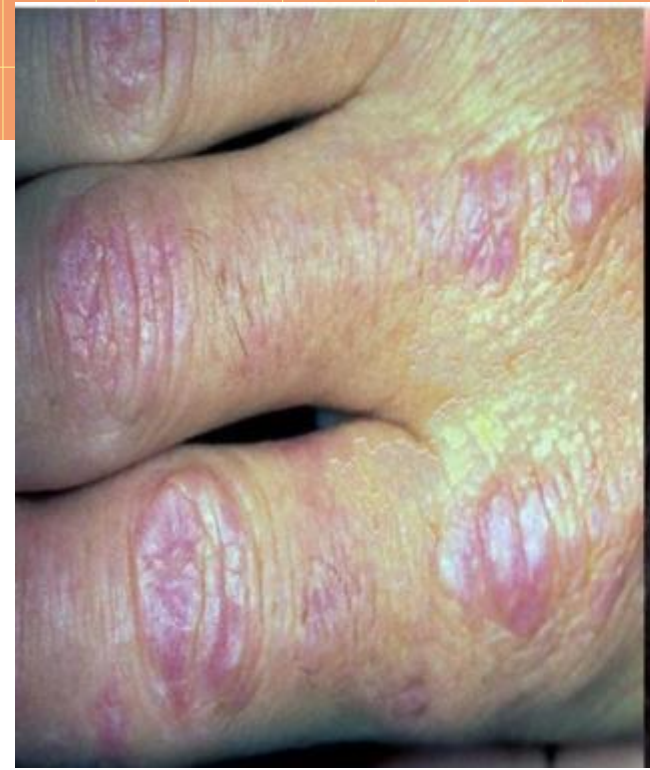
- Gottron’s papules
- Heliotrope erythema
- Photodistributed poikiloderma
- Periungual telangiectasia and erythema



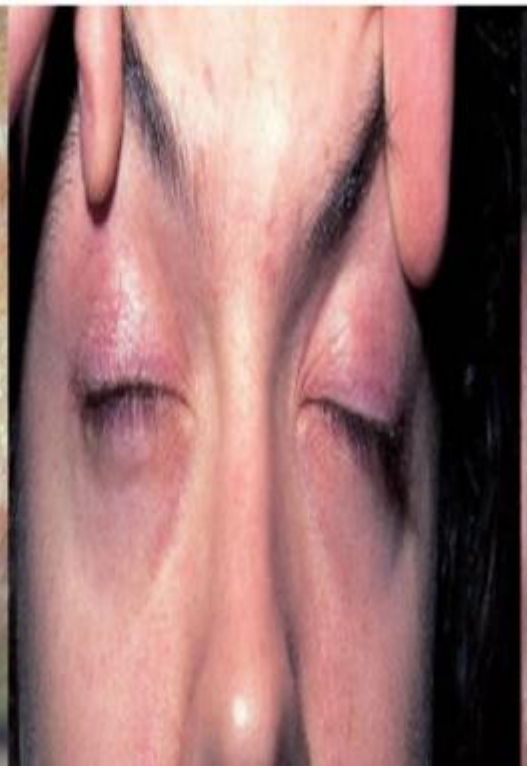
Periungal erythema + telangeictasia

Heliotrope rash + eyelid edema

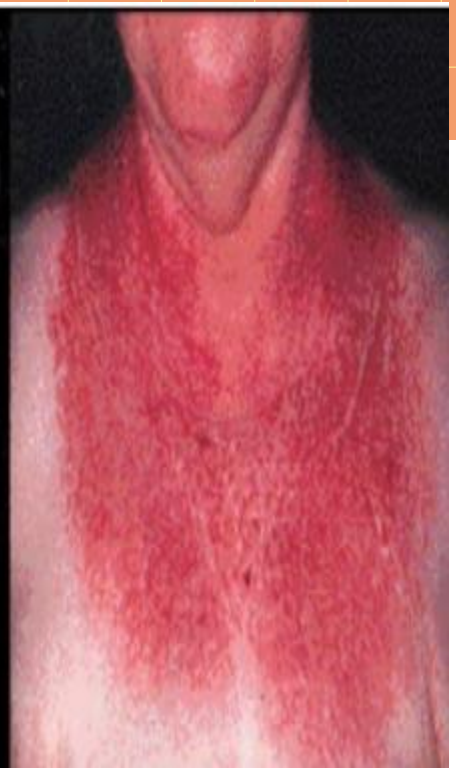
Gottron’s papules



Gottron’s papules



Heliotrope rash + eyelid edema

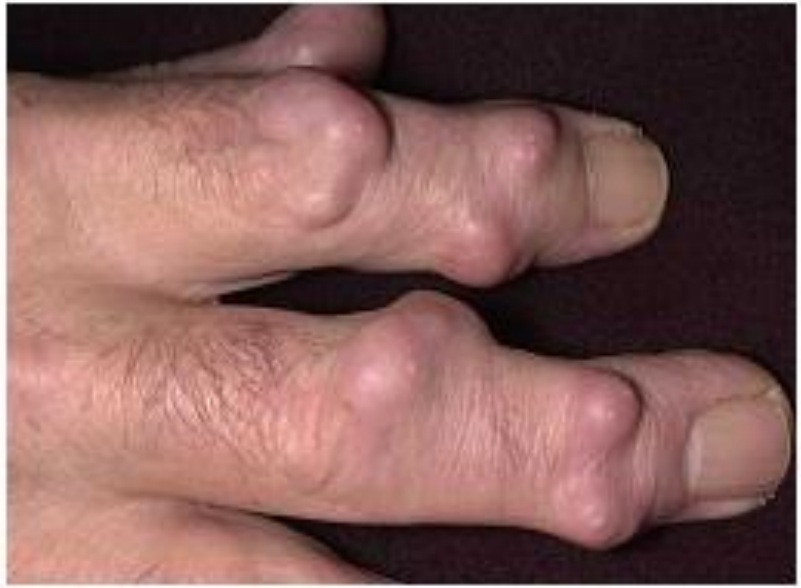


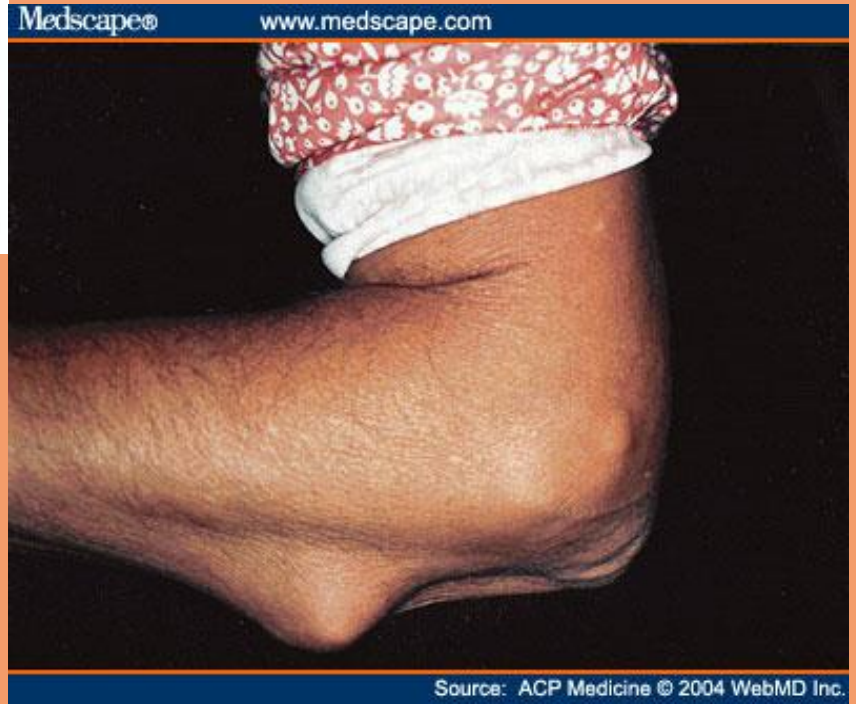
Poikiloderma
triad: atrophy, telangiectasia, hyperpigmentation

RHEUMATOID ARTHRITIS

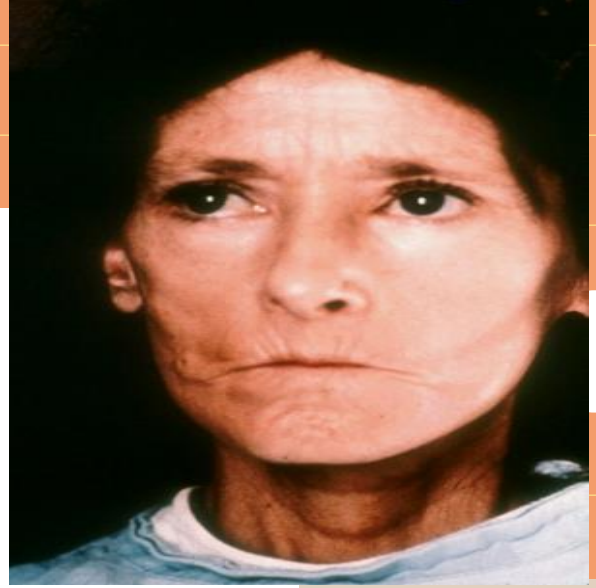
- Rheumatoid nodules
- Vasculitis
- Erthema elevatum diutinum
- Pyoderma gangrenosum (CT diseases, malignancy, IBD)
- Sweet`s Syndrome
- Purpuric papules on distal digits
- Periungual telangiectasia and erythema

RHEUMATOID NODULES

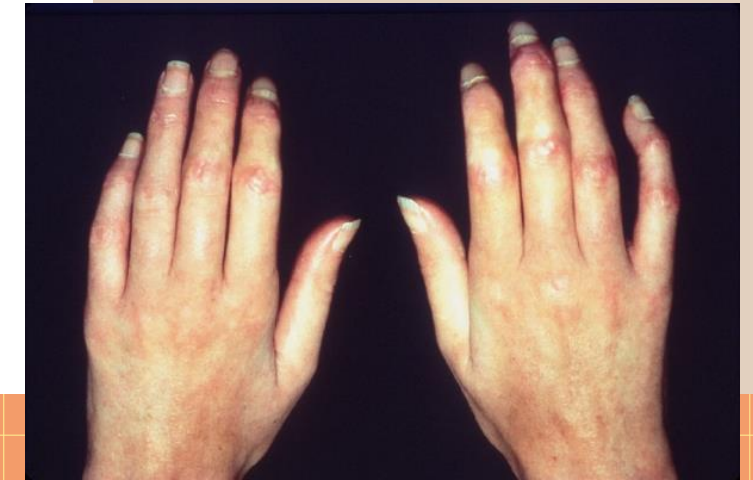




SCLERODERMA



- Skin sclerosis, tight bound skin
- Peaked nose
- Perioral farrows
- Periungual telangiectasia and erythema
- Sclerodactyly

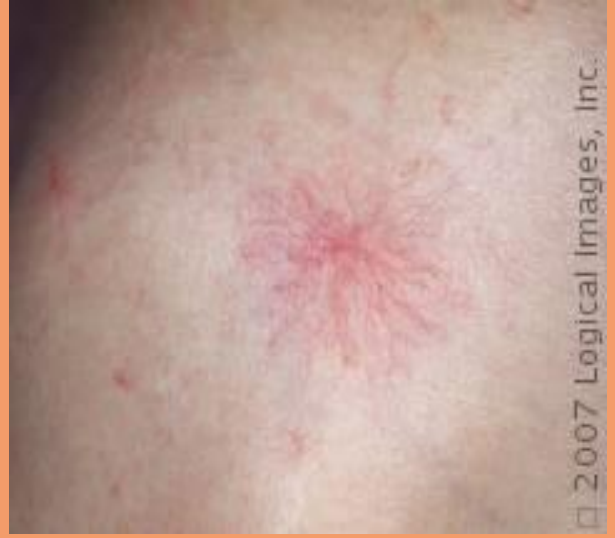


04

LIVER DISEASES

You could enter a subtitle here if you need it

- Pruritus, obstructive jaundice
- Hyperpigmentations due to bile and melanin
- Spider nevi, multiple
- Palmar erythema
- White nails (Terry's nails) due to hypoalbuminemia
- Lichen planus
- Polyarteritis nodosa
- PCT
- Xanthoma, primary biliary cirrhosis
- Hair loss and generalized asteatotic eczema
- Gynecomastia (in cirrhosis)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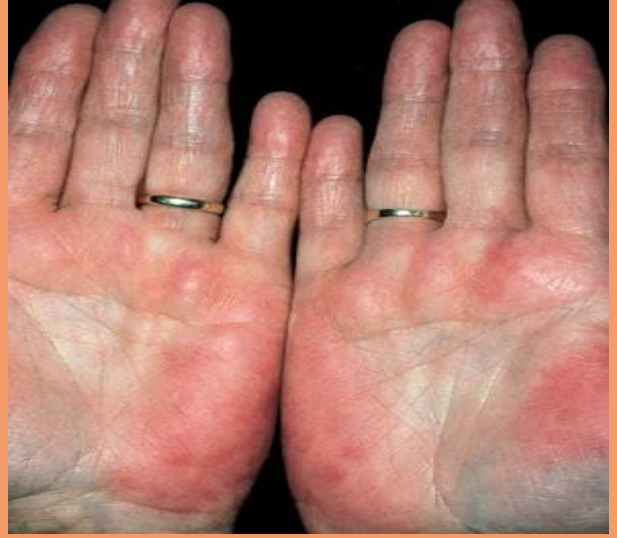
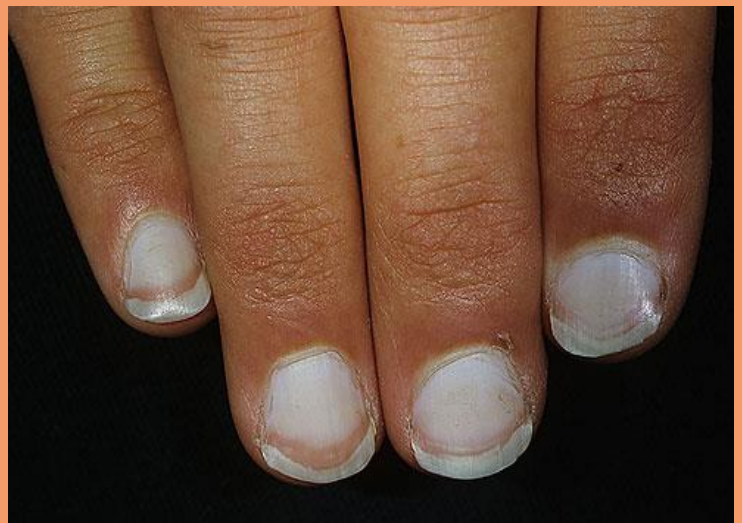
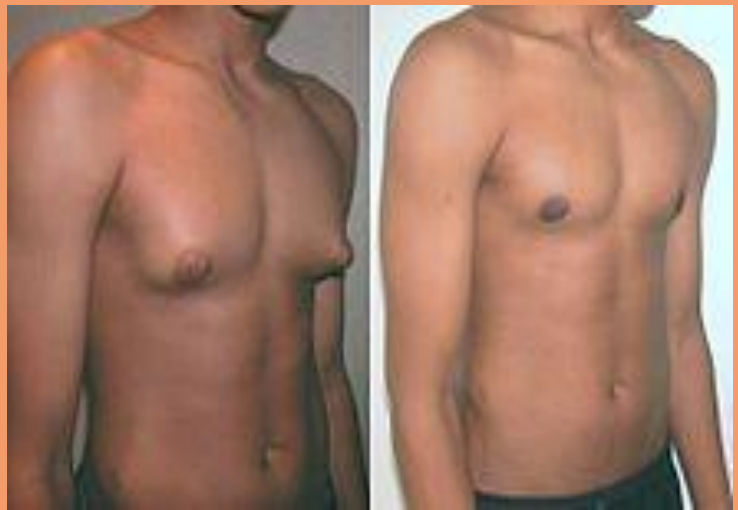




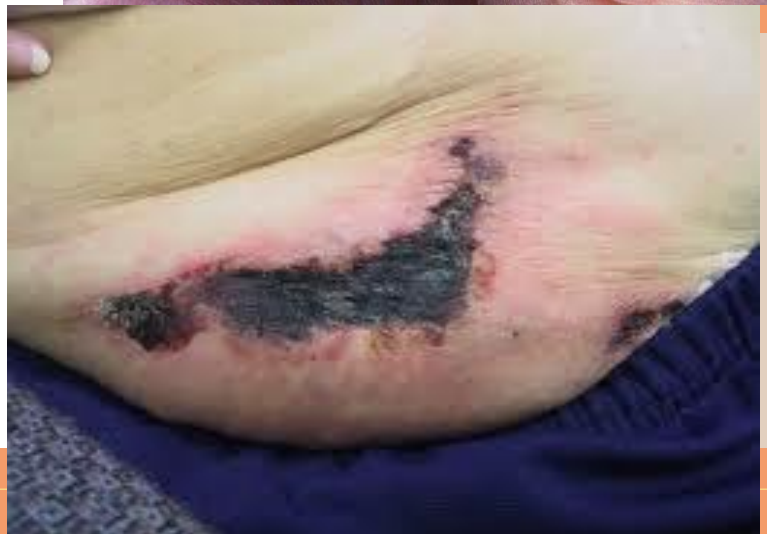


05

RENAL DISEASES

You could enter a subtitle here if you need it

- Pruritus and dry skin
- Pigmentations, yellowish sallow, pale skin
- Half and half nails (white l red/ Lindsay’s nails)
- Perforating disorder, folliculitis
- Pseudoporphyria
- Calciphylaxis: skin necrosis due to intravascular wall calcification



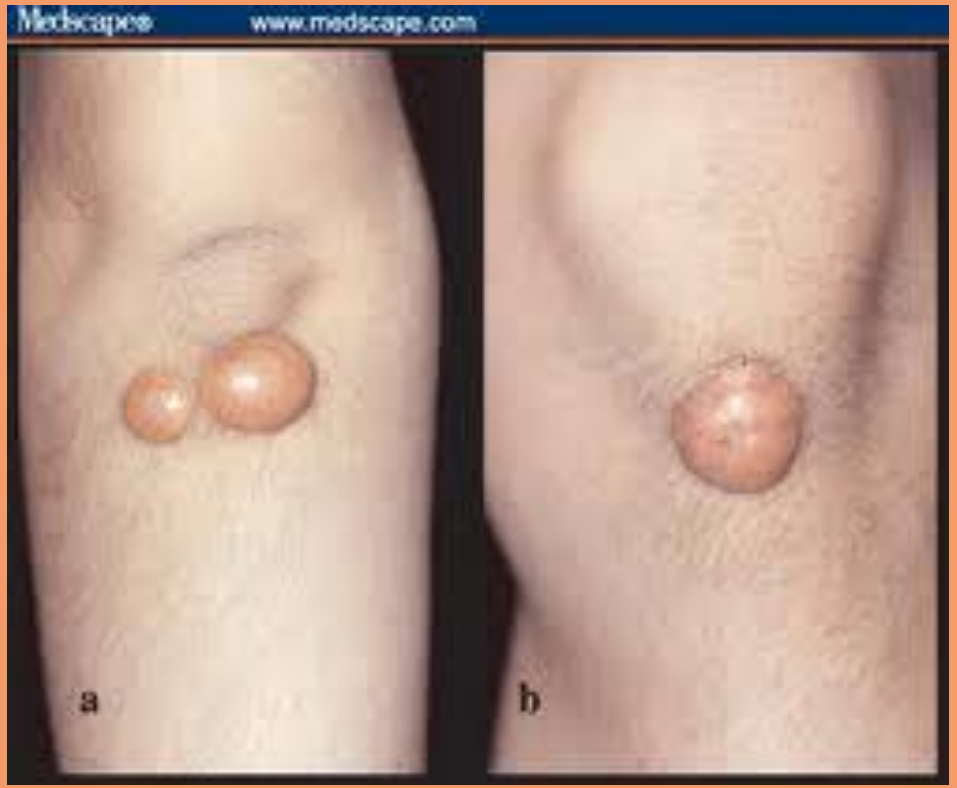
06

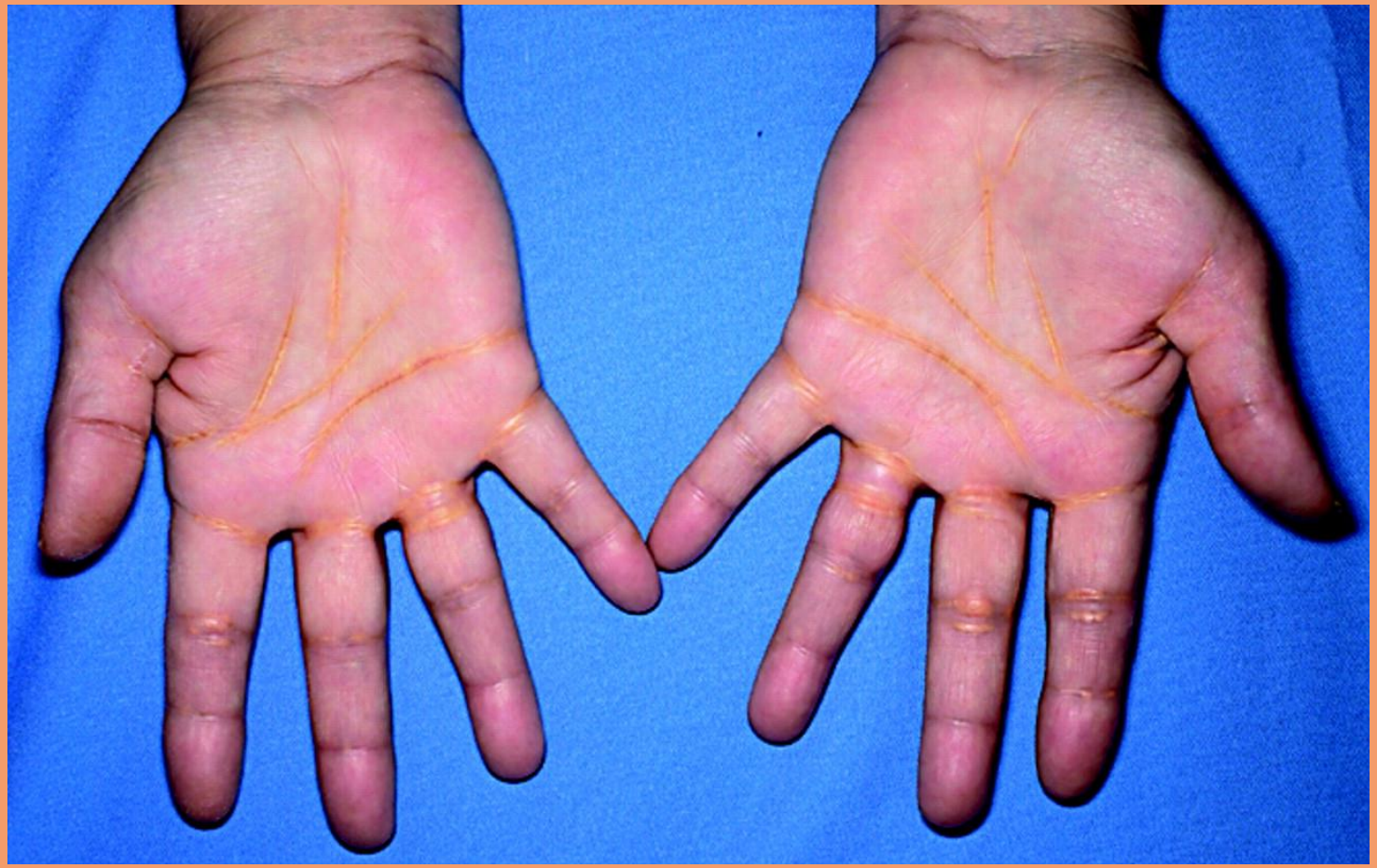
XANTHOMA

You could enter a subtitle here if you need it

- Primary hyperlipidemia: genetic, six groups
- Secondary hyperlipidemia:
  - Diabetes mellitus
  - Cirrhosis
  - Nephrotic syndrome
  - Hypothyroidism
- Three types, diagnosed clinically or by biopsy

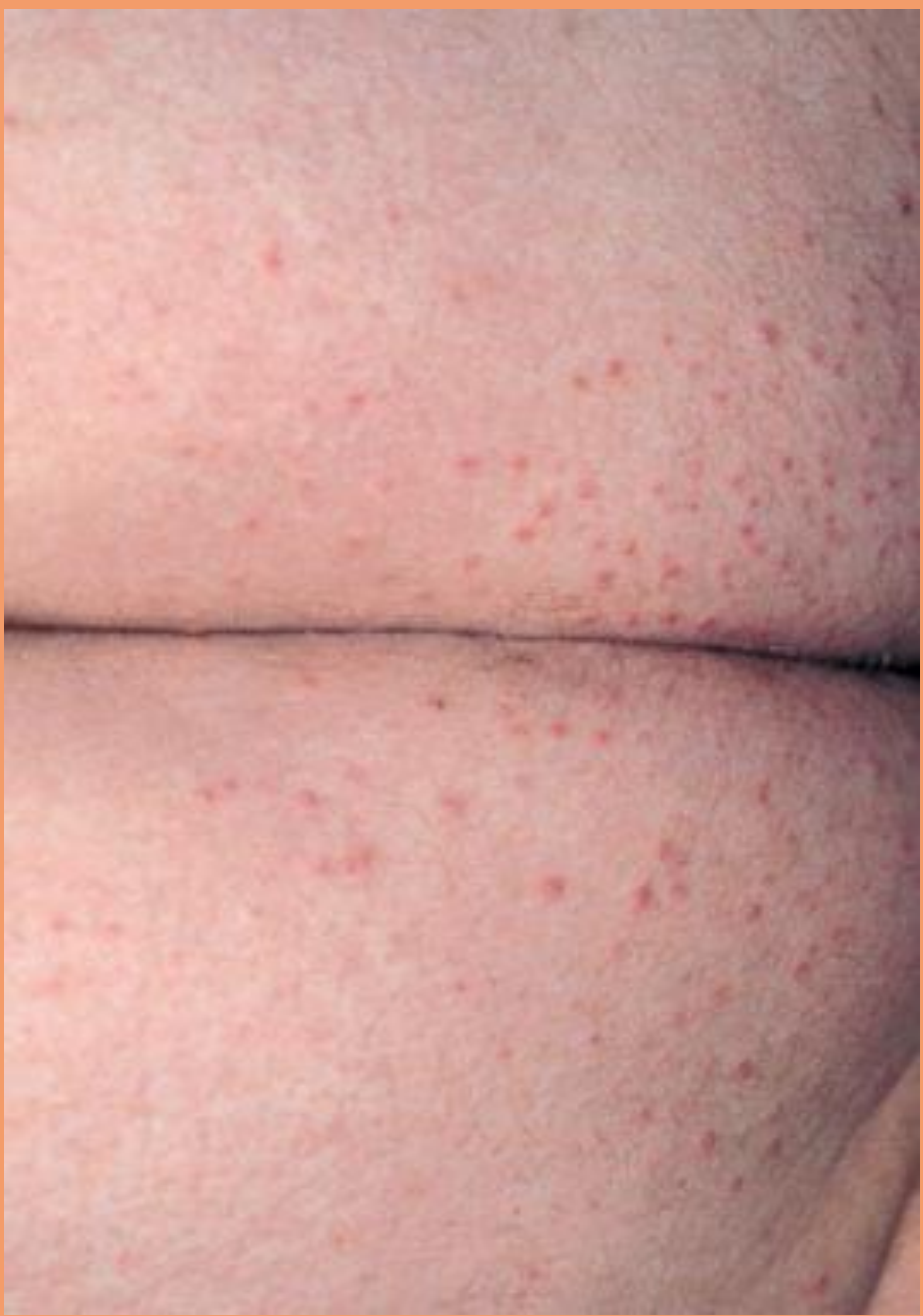
NODULAR / TUBEROUS



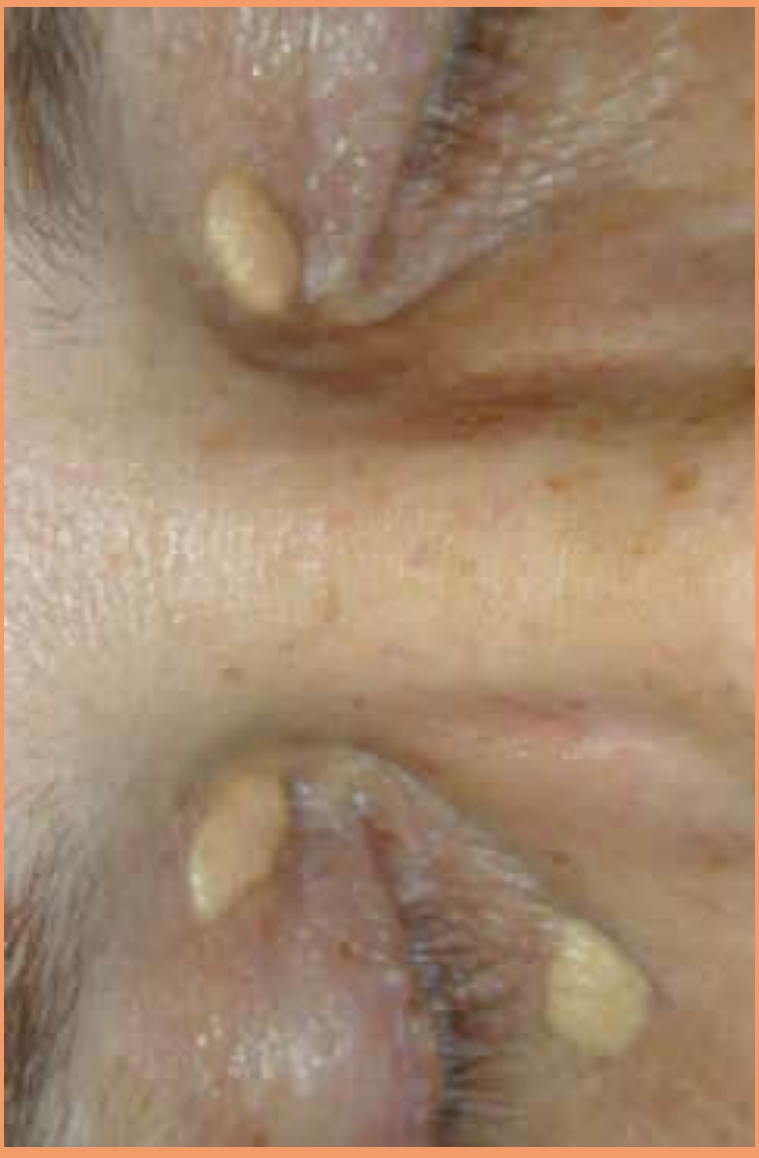


LINEAR

ERUPTIVE PAPULES



XANTHELASMA



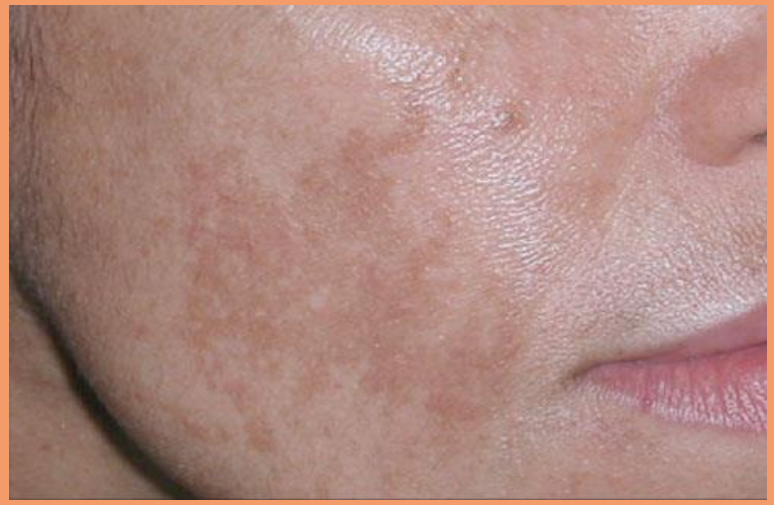
07

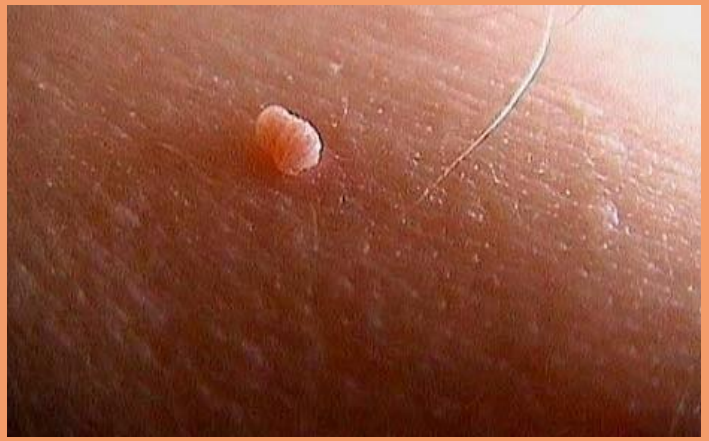
PREGNANCY

Physiologica hormonal changes
Dermatoses

HORMONAL CHANGES

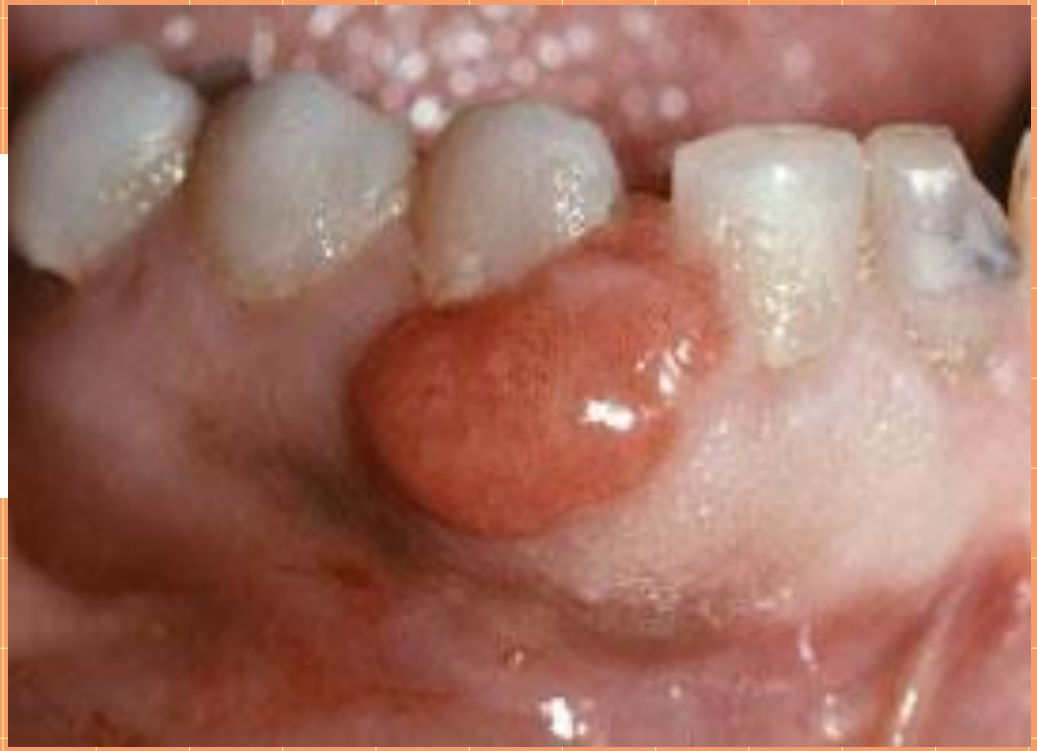
- Linea nigra
- Darkening of areola and nipples
- Palmar erythema
- Telangiectasia
- Striae
- Hair loss, especially after delivery (telogen effluvium)
- Skin tags
- Melasma
- Pyogenic granuloma, mouth





PYOGENIC GRANULOMA

Vascular proliferations in the mucos membranes



DERMATOSES OF PREGNANCY

- Pruritis of pregnancy
- Urticarial plaques and papules of pregnancy
- Impetigo herpetiformes (generalized pustular psoriasis of pregnancy)
- Pemphigoid gestations
- prurigo of pregnancy
- CholesTasis of pregnancy

08

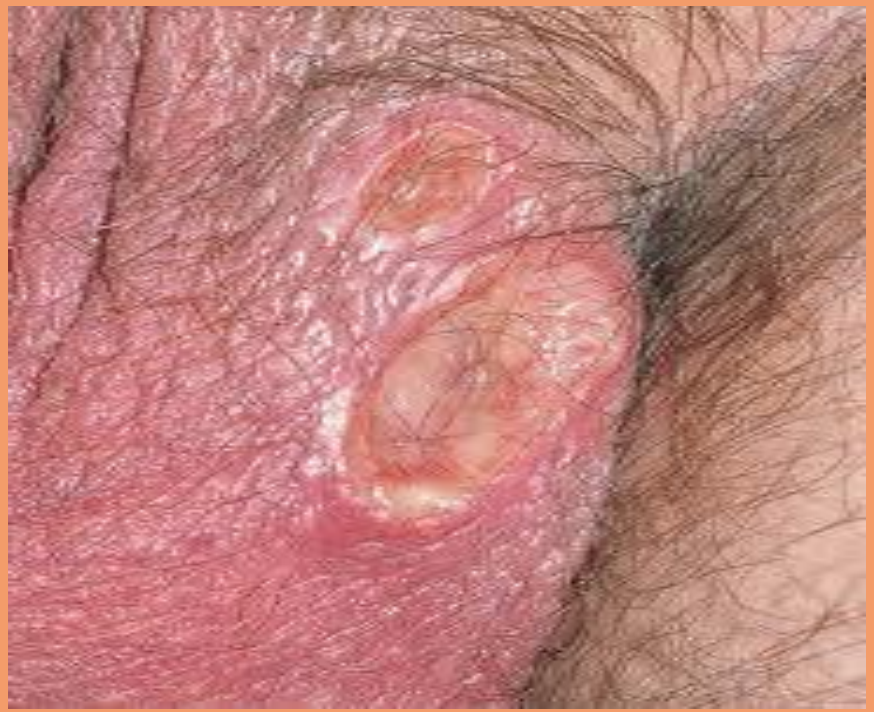
OTHER

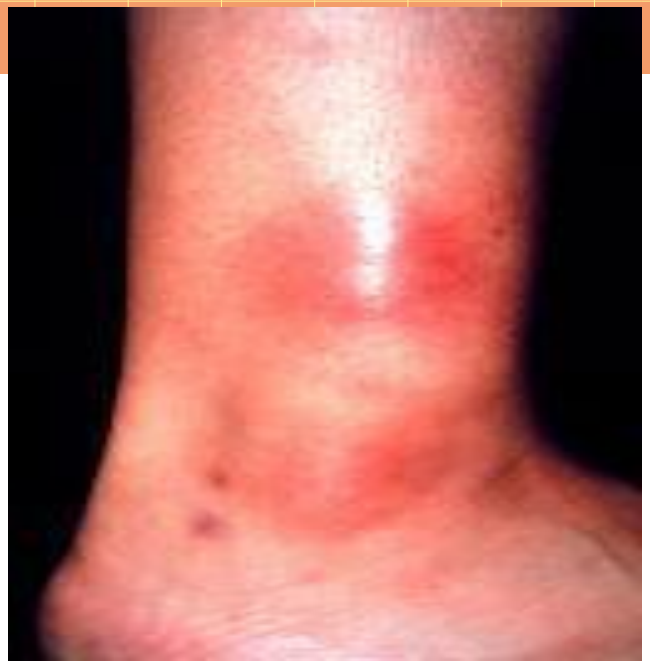
Behcet Disease
Bacterial Endocarditis
Malabsorption + malnutrition
Misc

BEHCET'S DISEASE

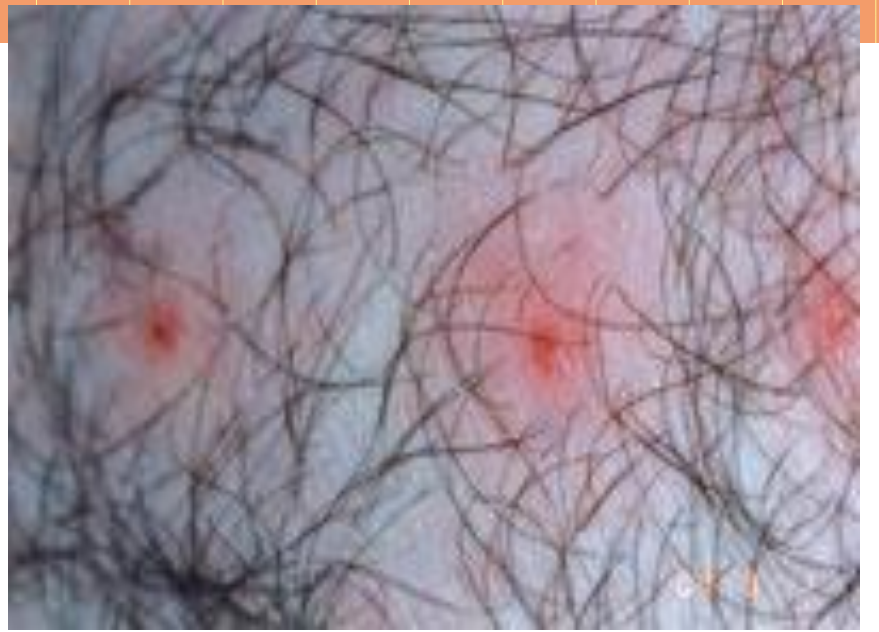
- Painful oral ulcers with yellowish base
- Painful genital ulcers with yellowish base
- Pathergy reaction
- Erythema nodosum–like lesions
- Erythema multiforme-like lesions
- Acne form skin rash

ORAL ULCERS





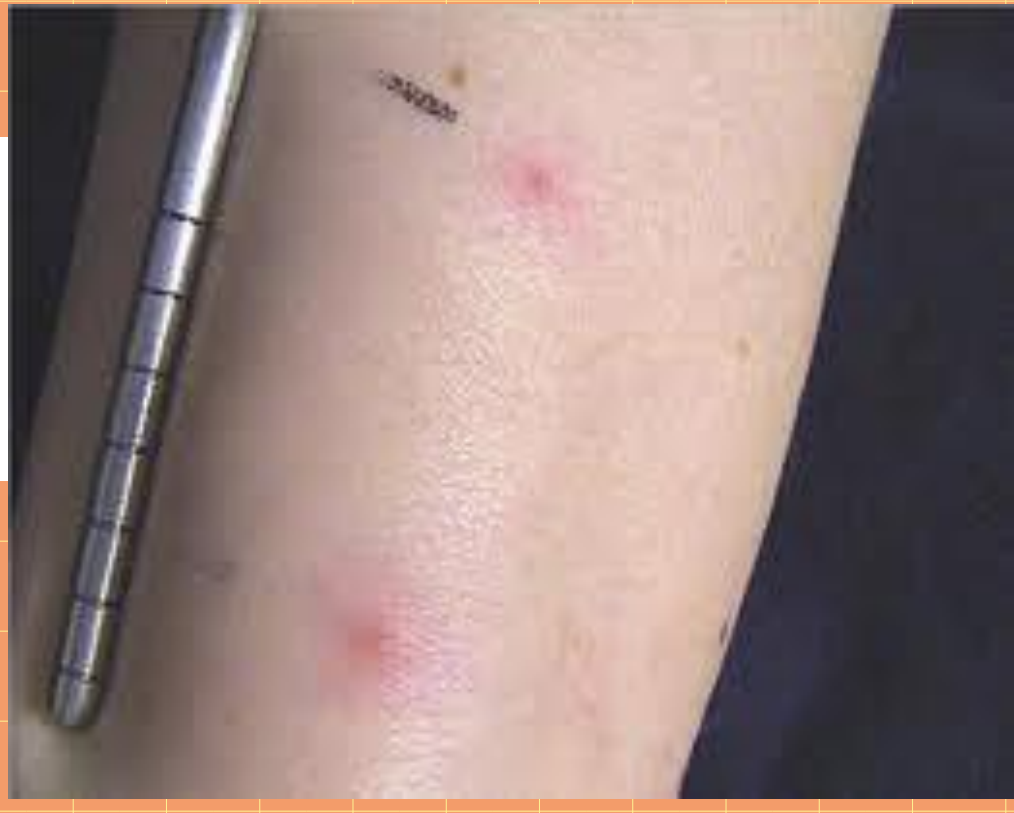
Erythema nodusum-like lesions



Folliculitis and acneform rash

PATHERGY REACTION

Development of pustule at the site of a needle prick

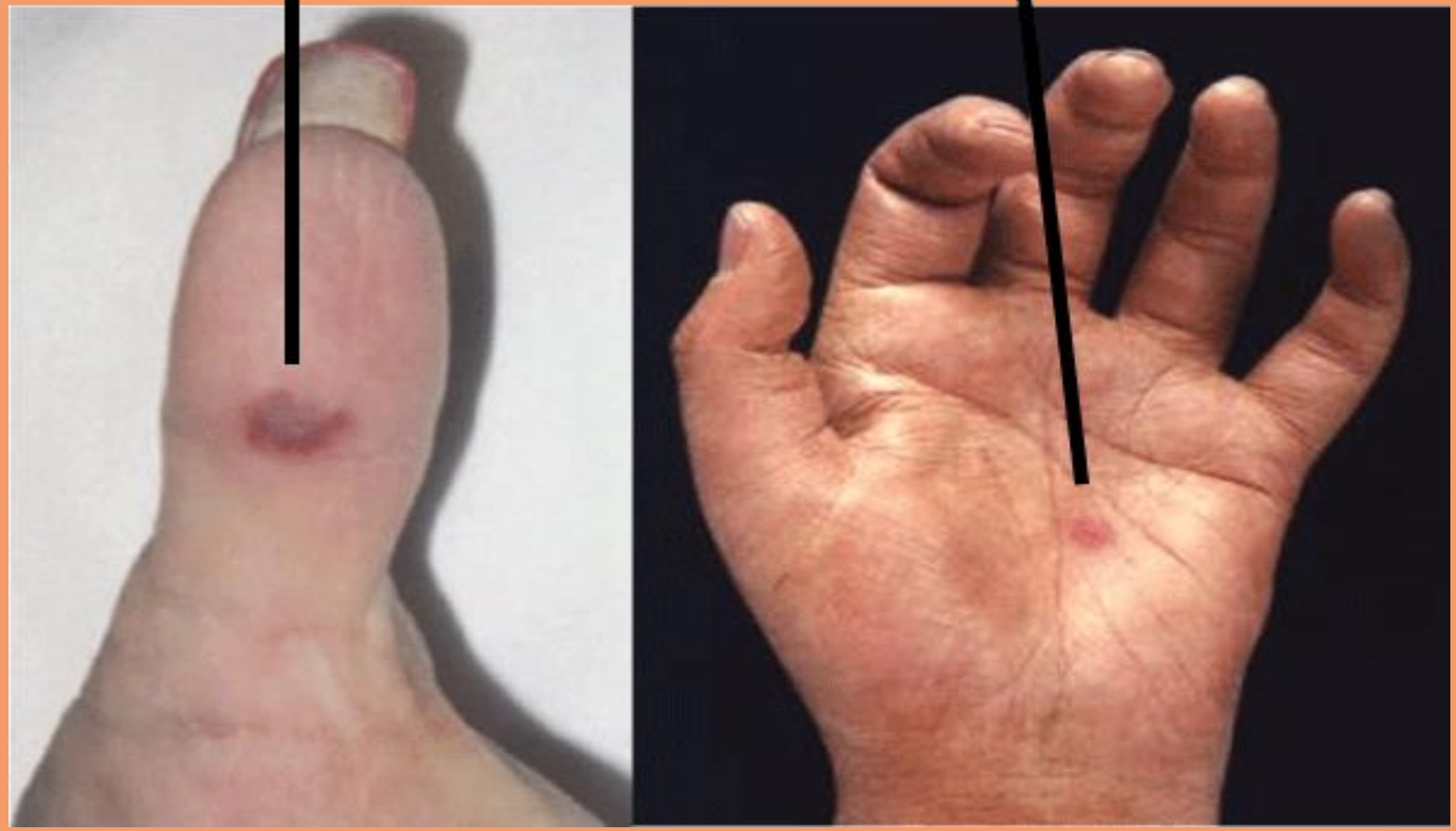


BACTERIAL ENDOCARDITIS

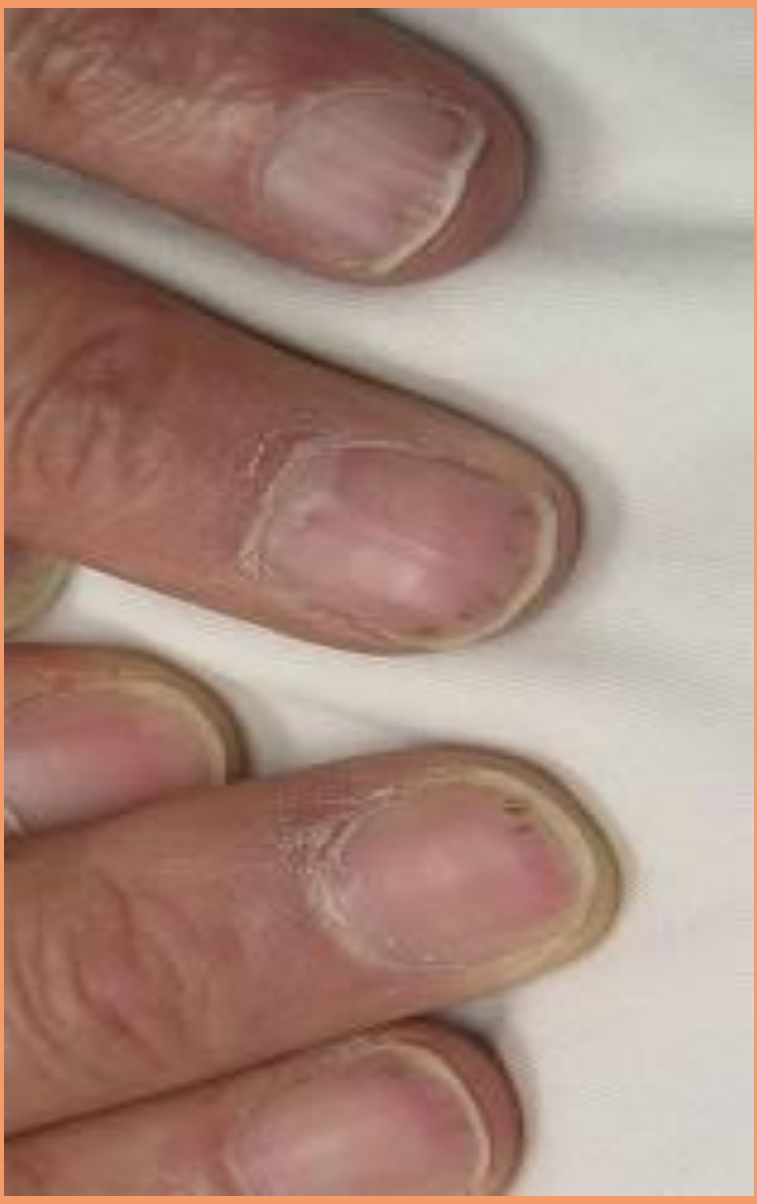
- Purpura
- Nail fold infarction
- Janeway lesions
- Osler’s nodules

Osler Node

Janeway Lesion



SPLINTER HEMORRHAGES



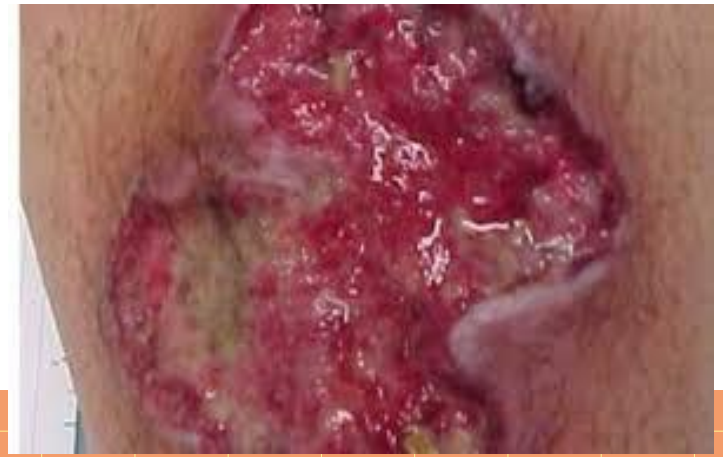
MALABSORPTION & MALNUTRITION

- Itching, dryness, pigmentations
- Brittle nails and hair
- Kwashiorkor: dry red-brown hair
- Iron deficiency: pallor, itching, diffuse hair loss, koilonychia
- Vit. A deficiency: dry skin, follicular hyperkeratosis, xerophthalmia
- Vit. C deficiency: scurvy

MISC

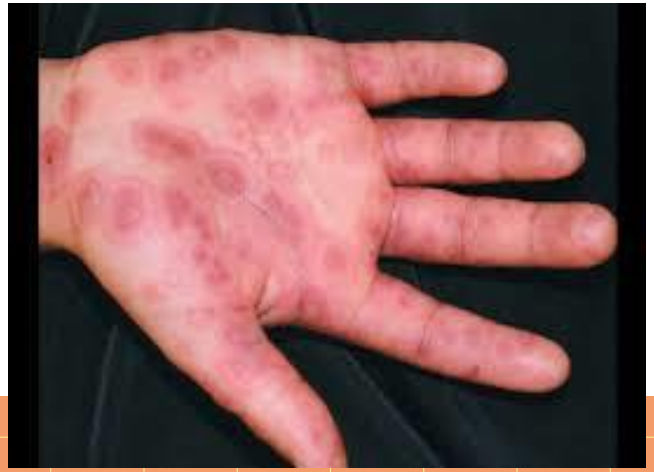
PYODERMA GANGRENOSUM

- inflammatory bowel disease
- Malignancy
- Connective tissue disorders



ERYTHEMA MULTIFORME

- Infections
- Drugs
- Connective tissue diseases
- Pregnancy and others



ERYTHEMA NODOSUM

- TB, Strep. infections,
- Sarcoidosis
- Connective tissue diseases
- Malignancy and others