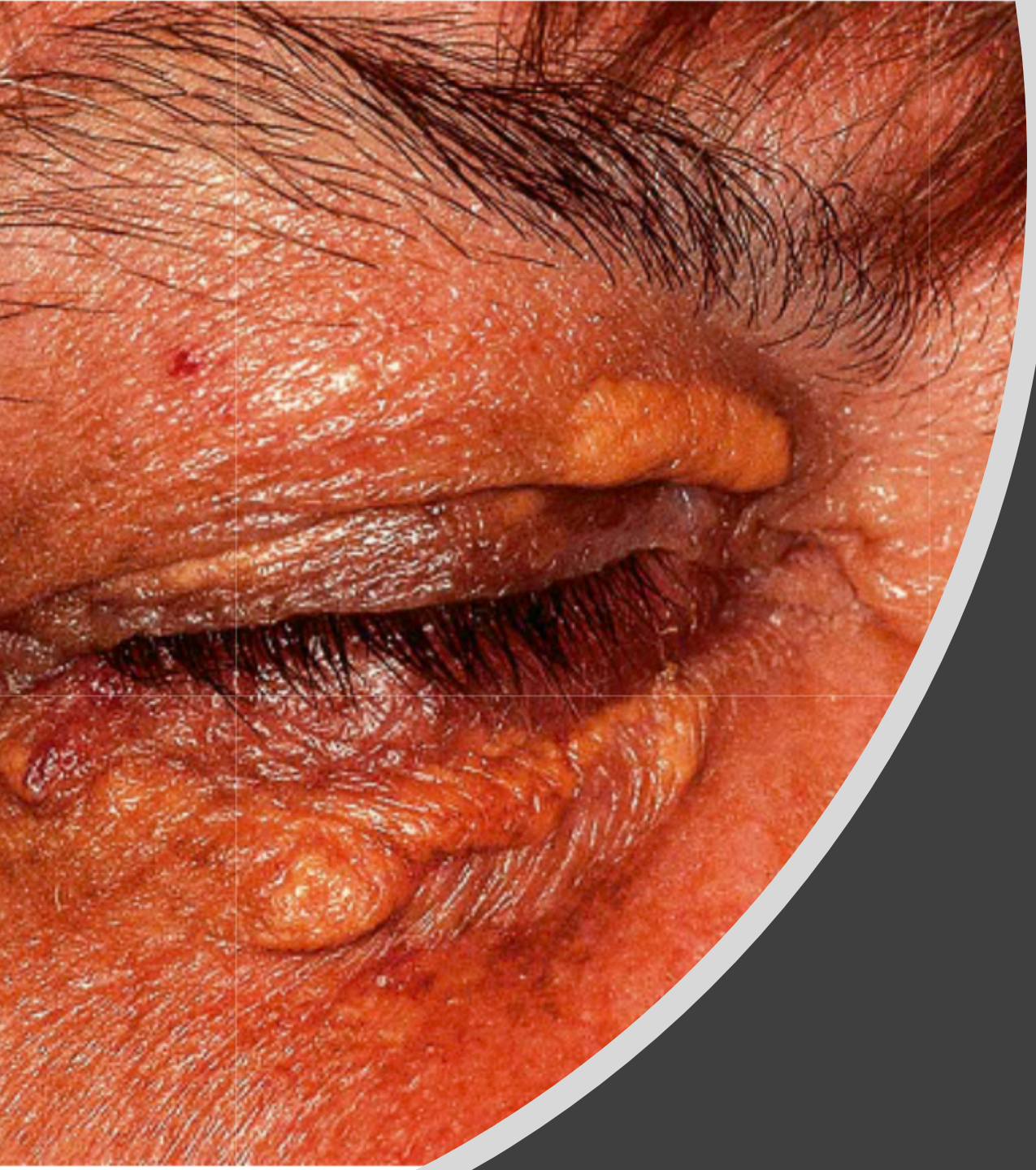


Cutaneous manifestations of systemic diseases

Abdulaziz Madani, M.D

Assistant Professor

Department of Dermatology, College of Medicine

King Saud University

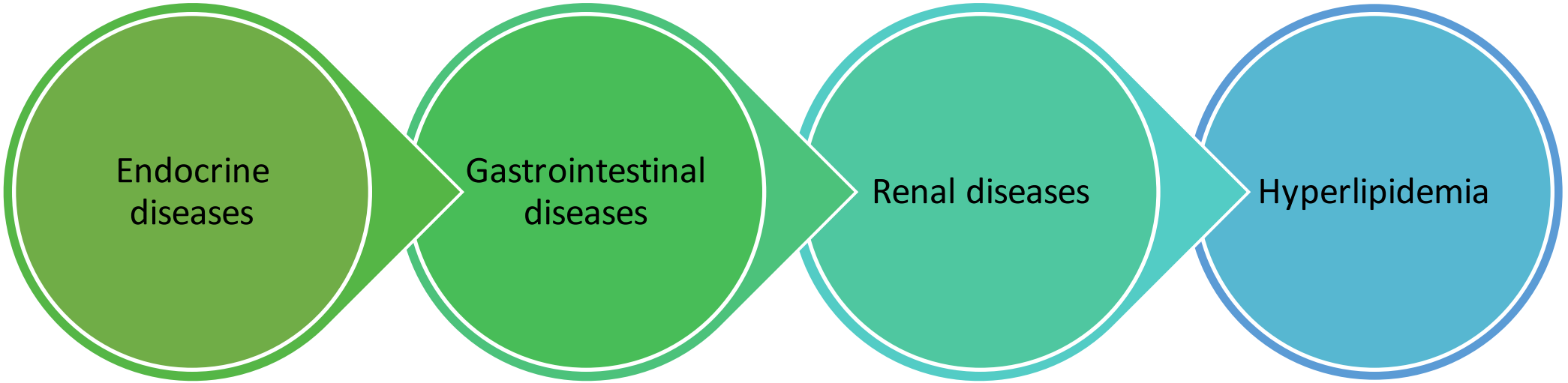
Objectives

To highlight the relation between skin manifestations and common systemic disorders.

To understand various skin clues and their importance in investigating and managing different systemic disease

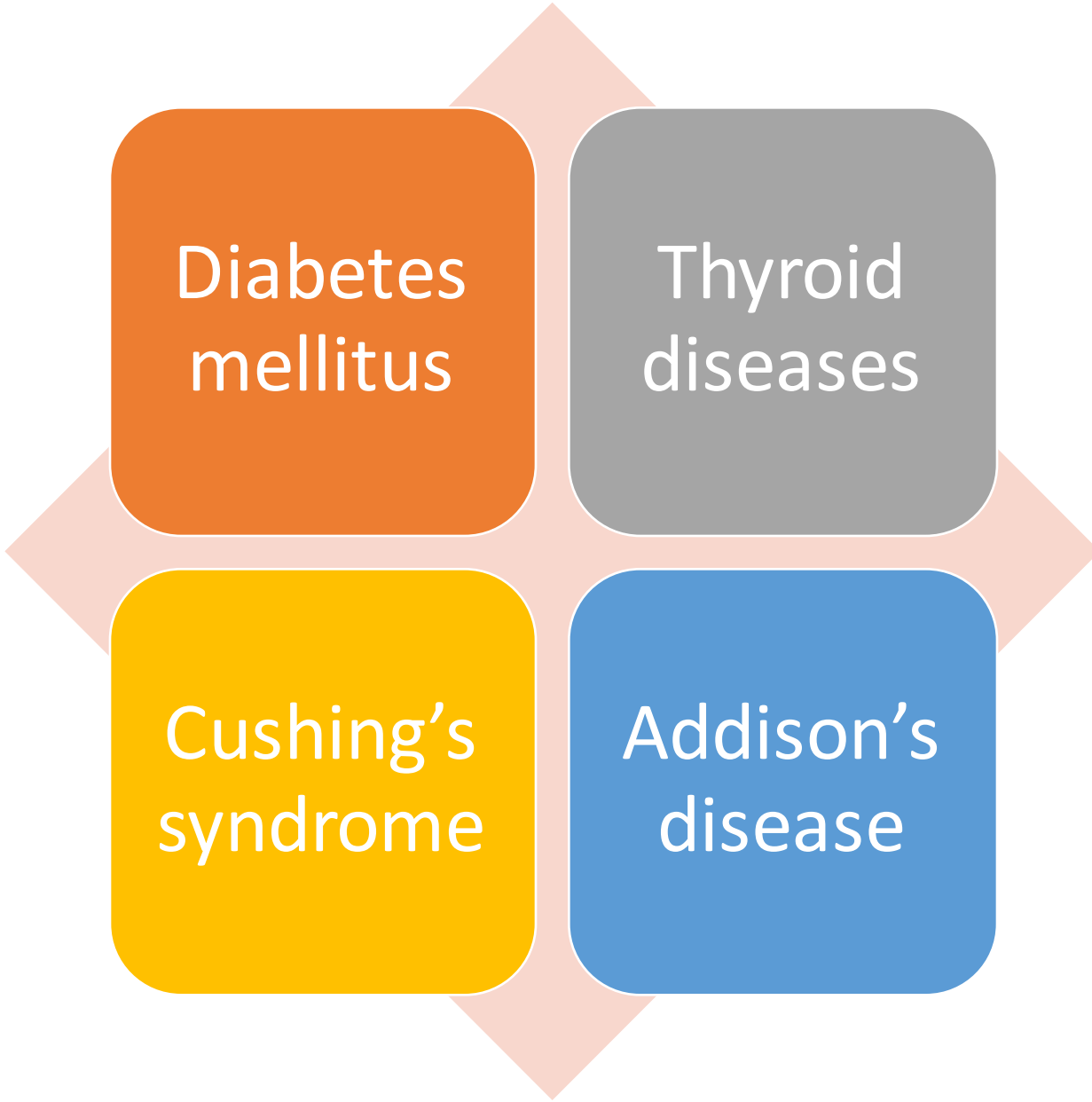
This lecture is not meant to be inclusive but to highlight important aspects in their diagnosis and management

Systemic diseases



Endocrine Diseases

Cutaneous manifestations of endocrine diseases



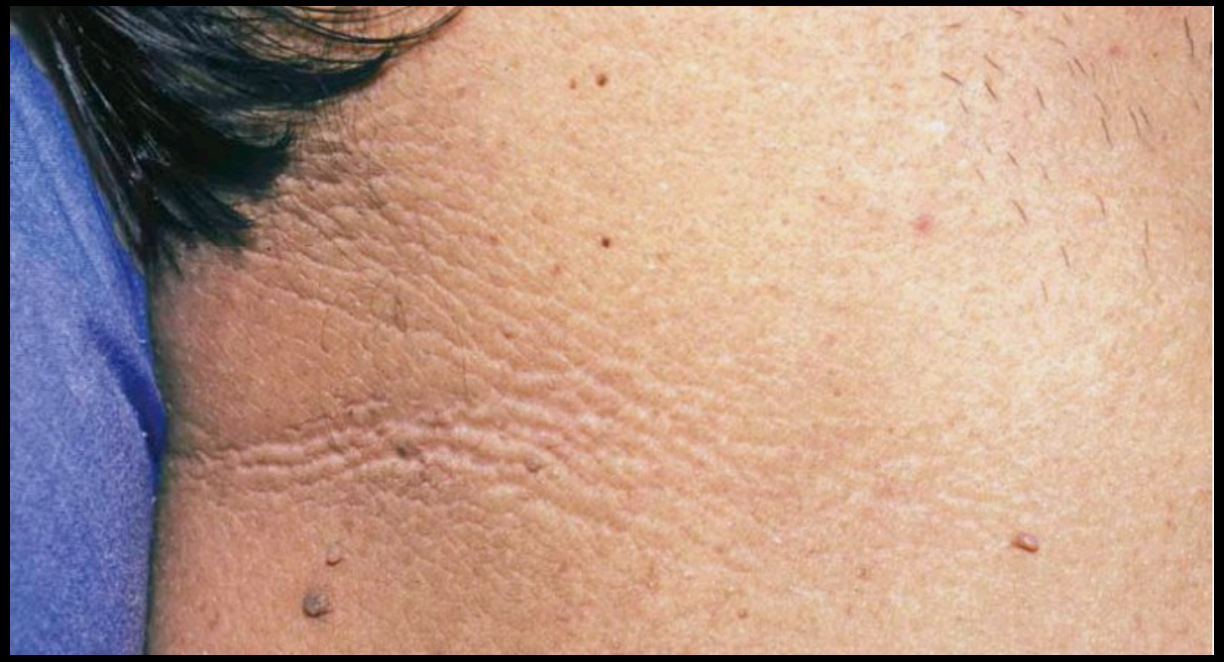
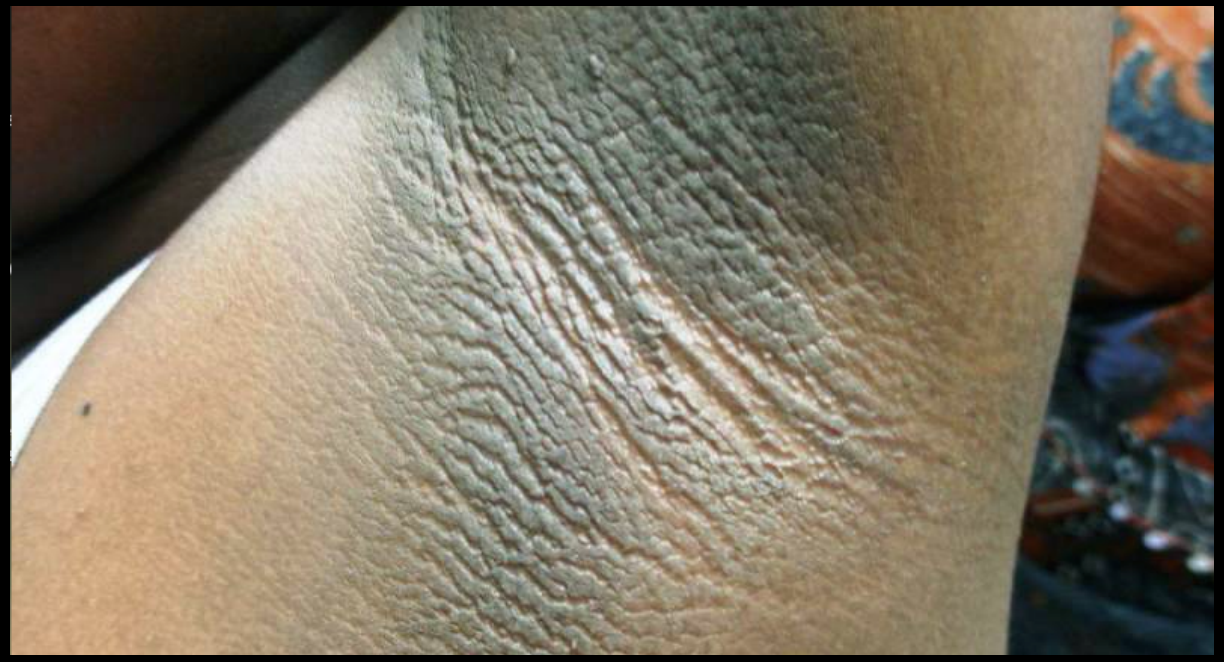
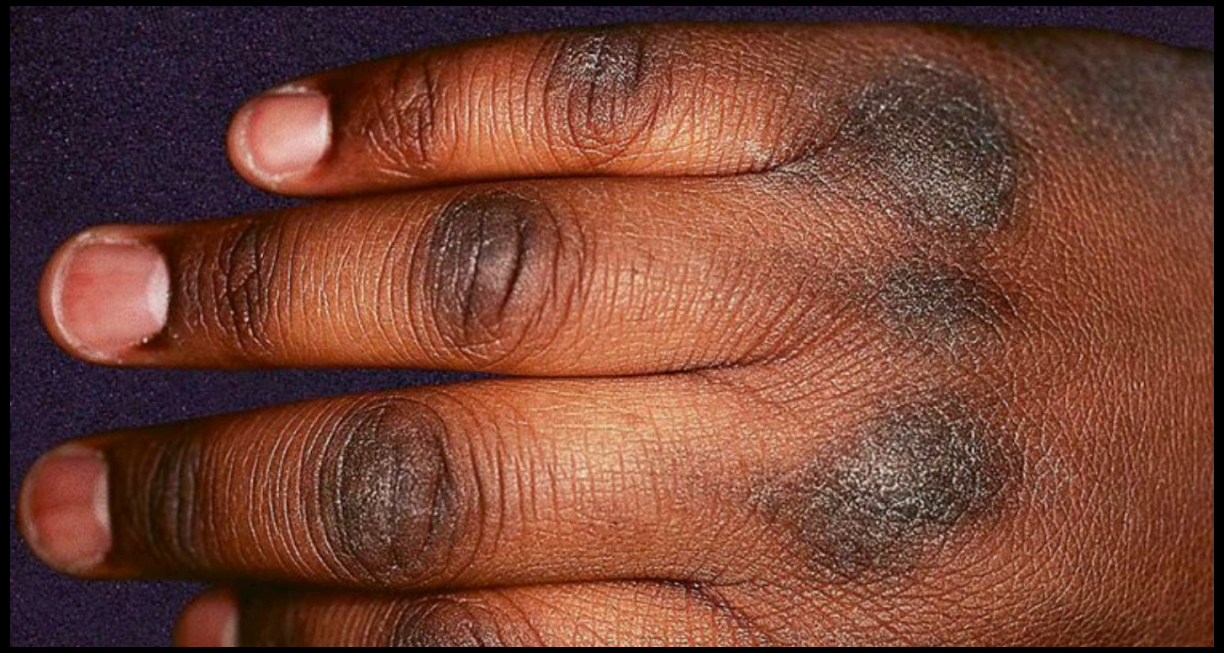
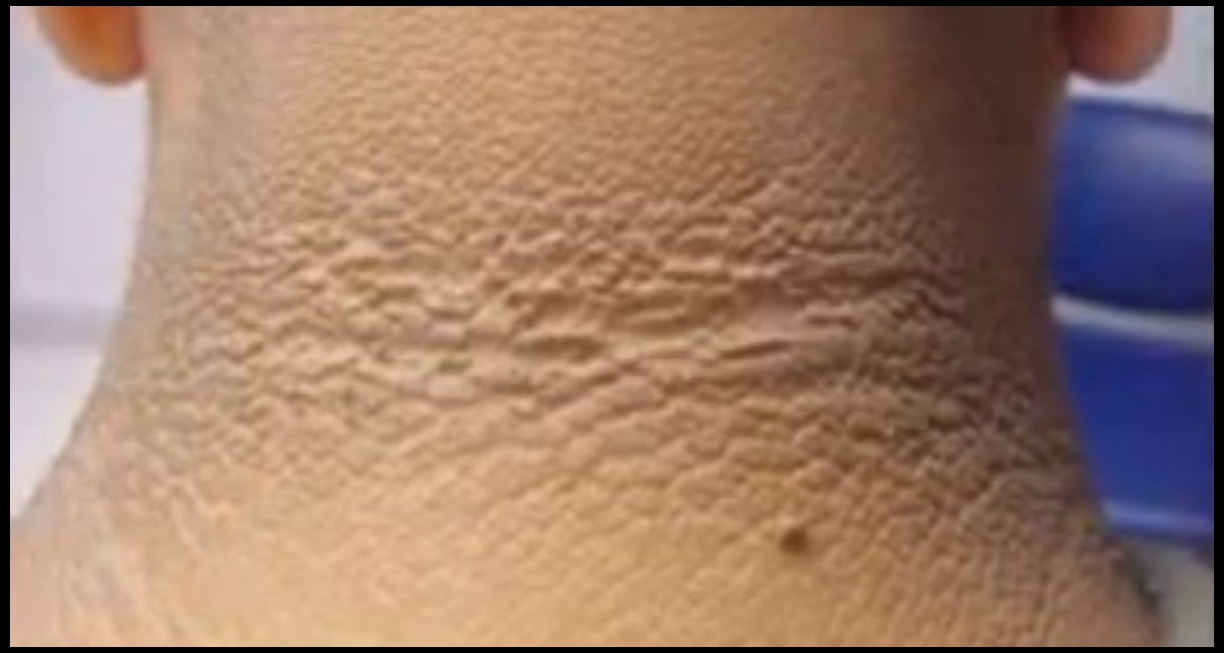
Diabetes Mellitus

Diabetes Mellitus

Acanthosis Nigricans	Acrochordrons “ skin tags”	Diabetic Dermopathy	Necrobiosis Lipodica Diabeticorum
Bullous Diabeticorum	Scleredema Diabeticorum	Acquired Perforating Dermatosis	Bacterial and Fungal infections

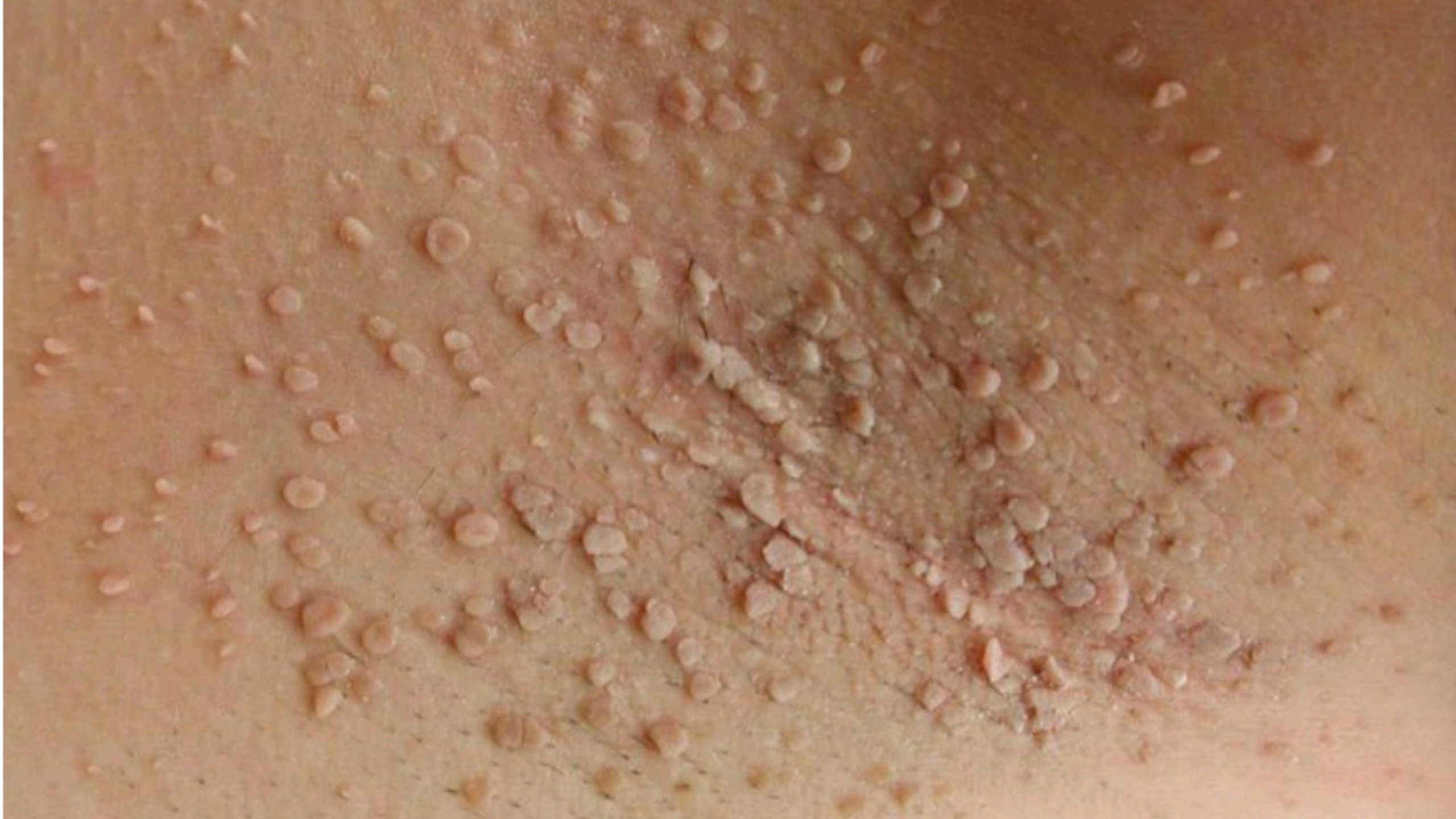
Acanthosis Nigricans

- Velvety hyperpigmentation of the intertriginous/flexural areas (body folds and creases) and less often, extensor surfaces.
- Commonly associated with insulin resistance and Obesity.
- More common in Hispanics and people of African descent.
- Can be associated with an internal malignancy (gastric adenocarcinoma).
- Tx: Weight reduction and treat the underlying cause.

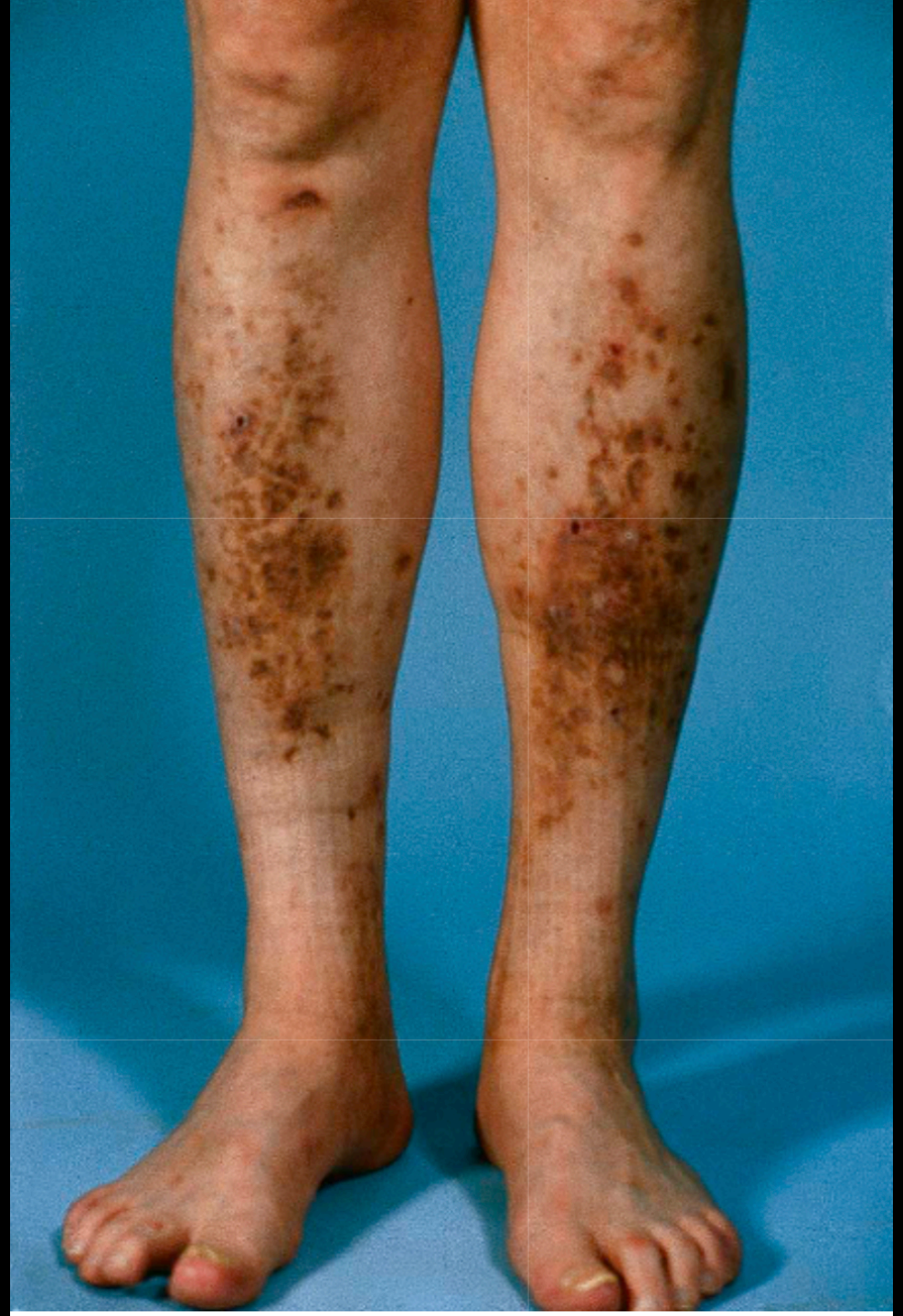
Acrochodrons “Skin Tags”

- Very common.
- Soft, skin colored, pedunculated papules.
- Neck, axilla and groin.
- Asymptomatic.
- Can get irritated or infracted.
- Tx: Cosmetic removal.



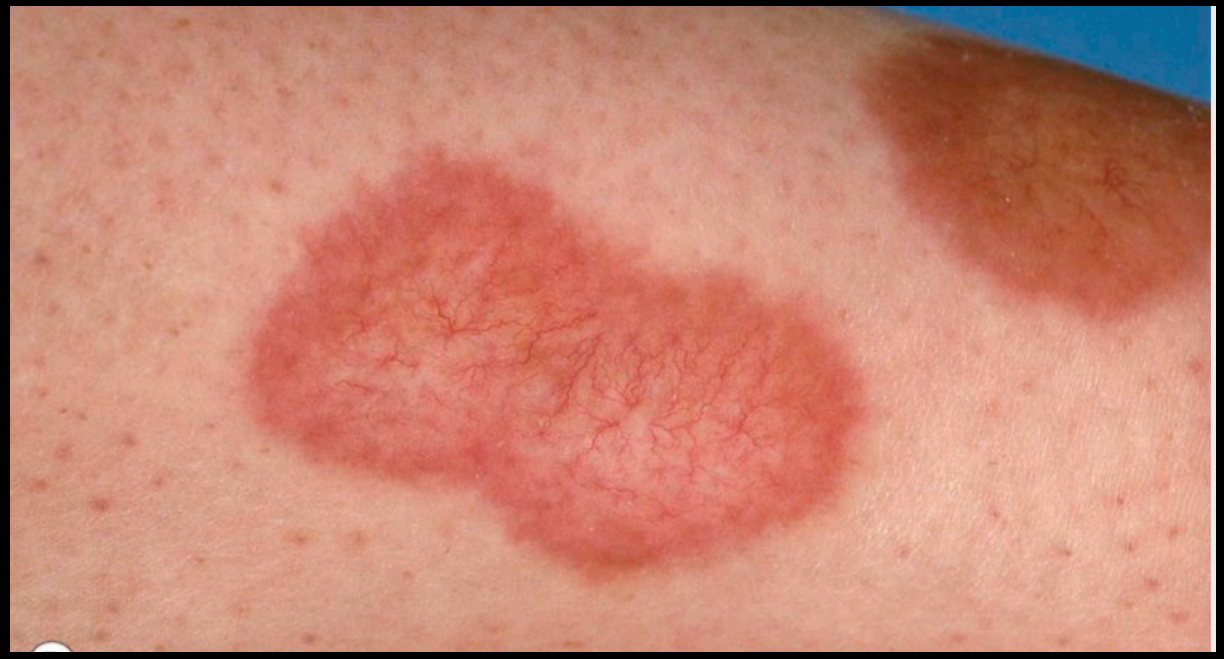
Diabetic Dermopathy

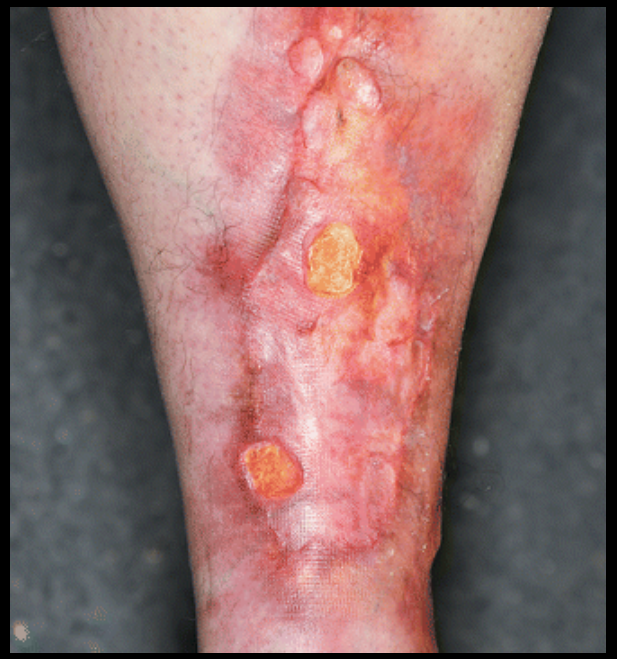
- The most common cutaneous sign of DM.
- Brown atrophic macules and patches on the legs.
- Possibly precipitated by trauma.
- They usually do not require treatment and tend to resolve after a few years with improved blood glucose control.

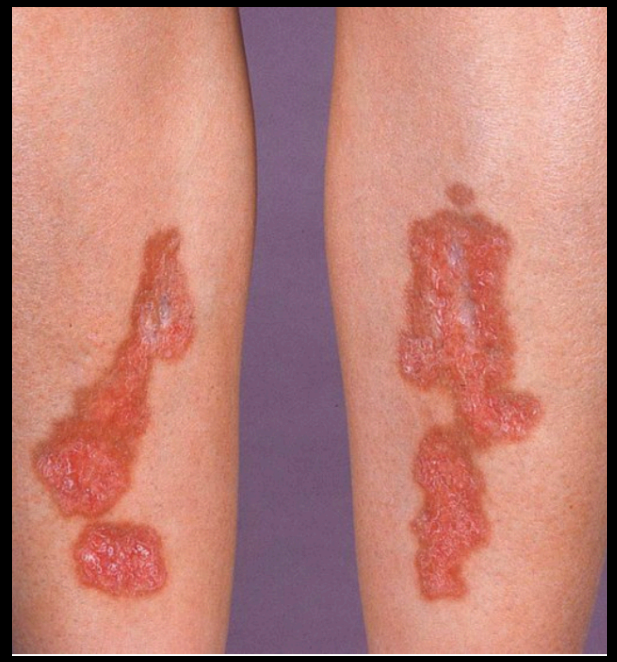


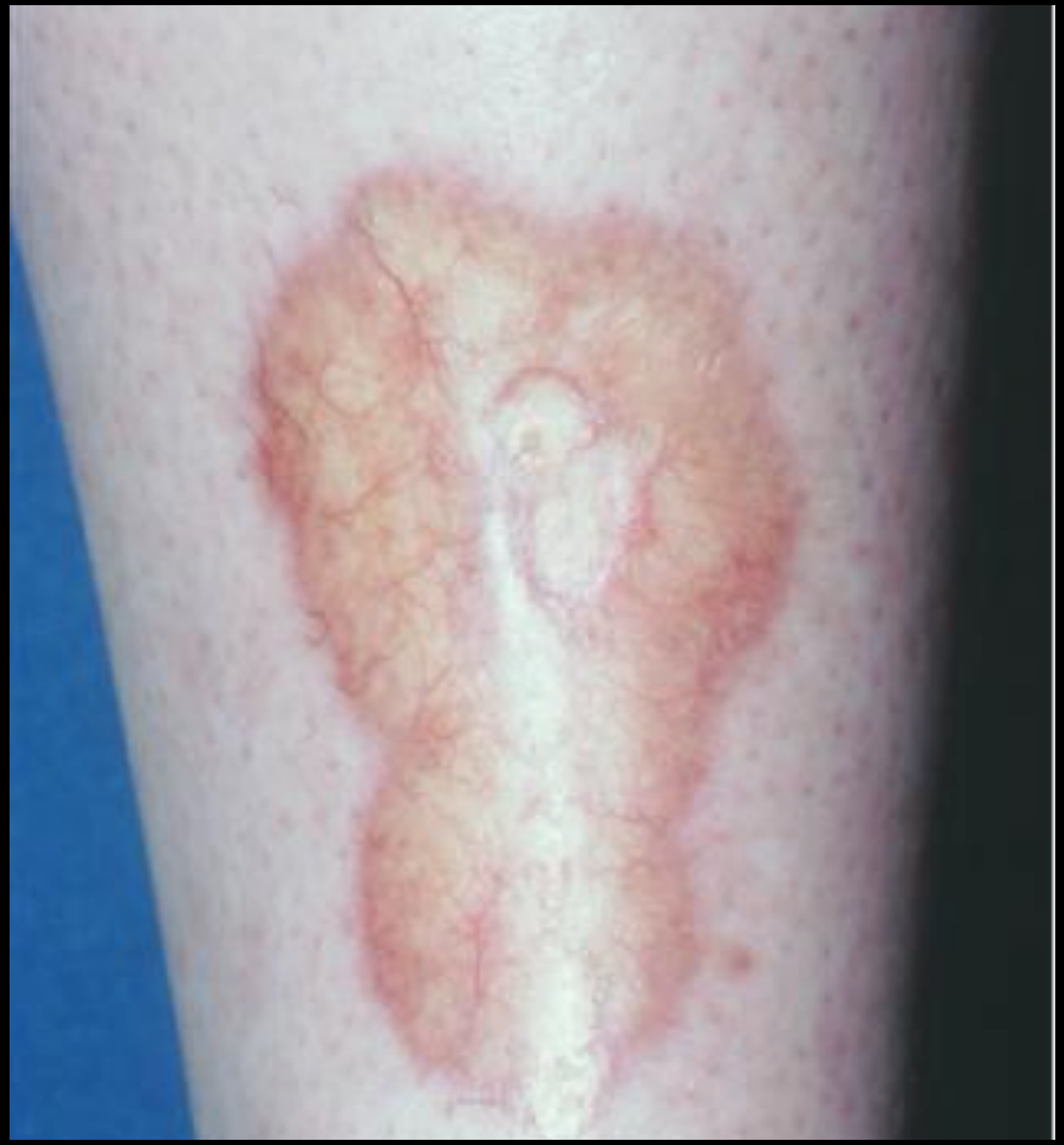
Necrobiosis Lipodica Diabeticorum

- Plaque with violaceous to red-brown, palpable peripheral rims and yellow-brown atrophic centers with telangiectasis.
- The most common site is the shins.
- Ulceration can occur following trauma.
- The proportion of patients with DM varies from 15% to 65%.
- Only 0.03% of patients with DM have NLD.
- Pathogenesis is unknown.
- Tx: Control of blood glucose does not have significant effect. Can improve with topical/intralesional steroids.



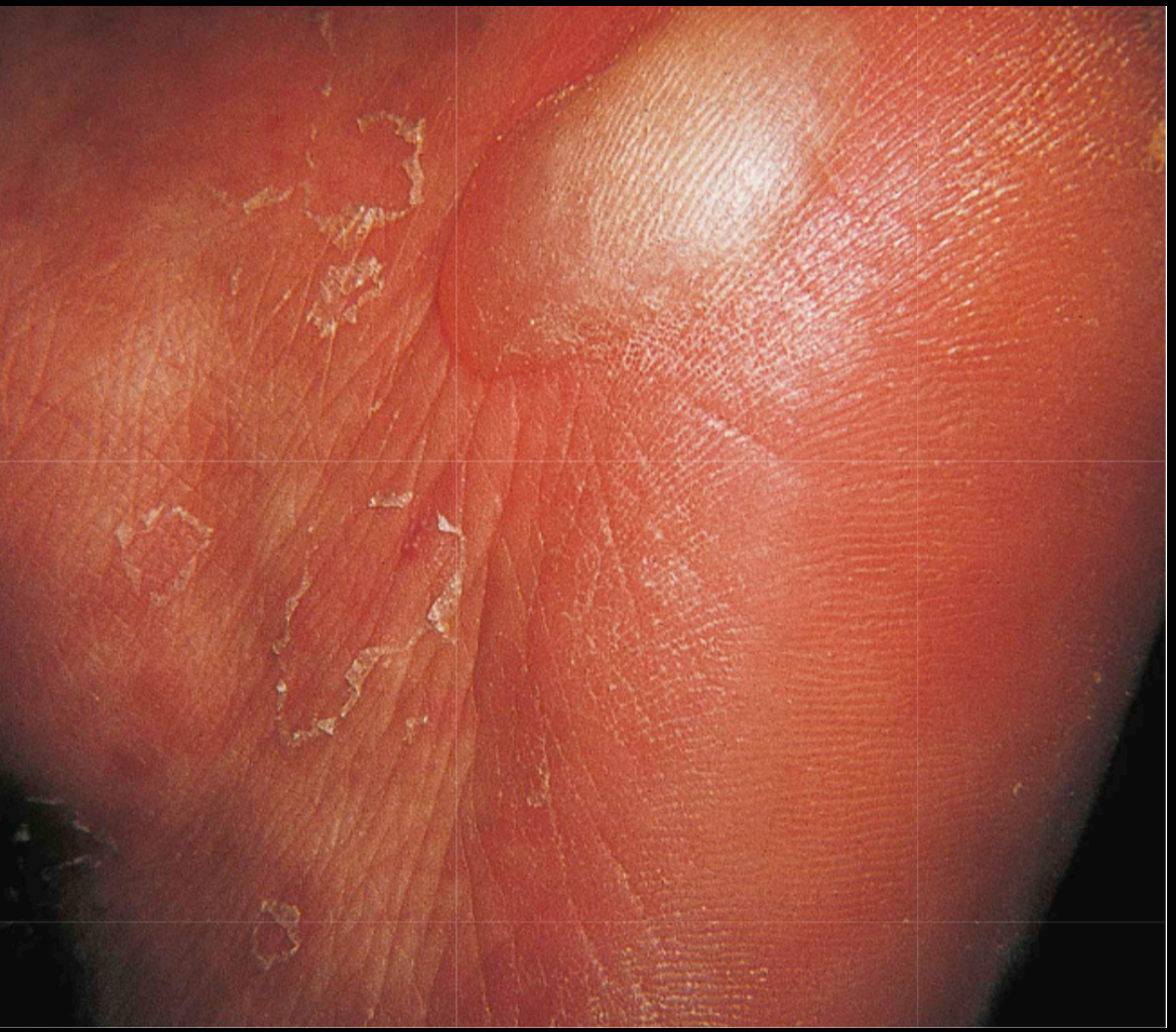


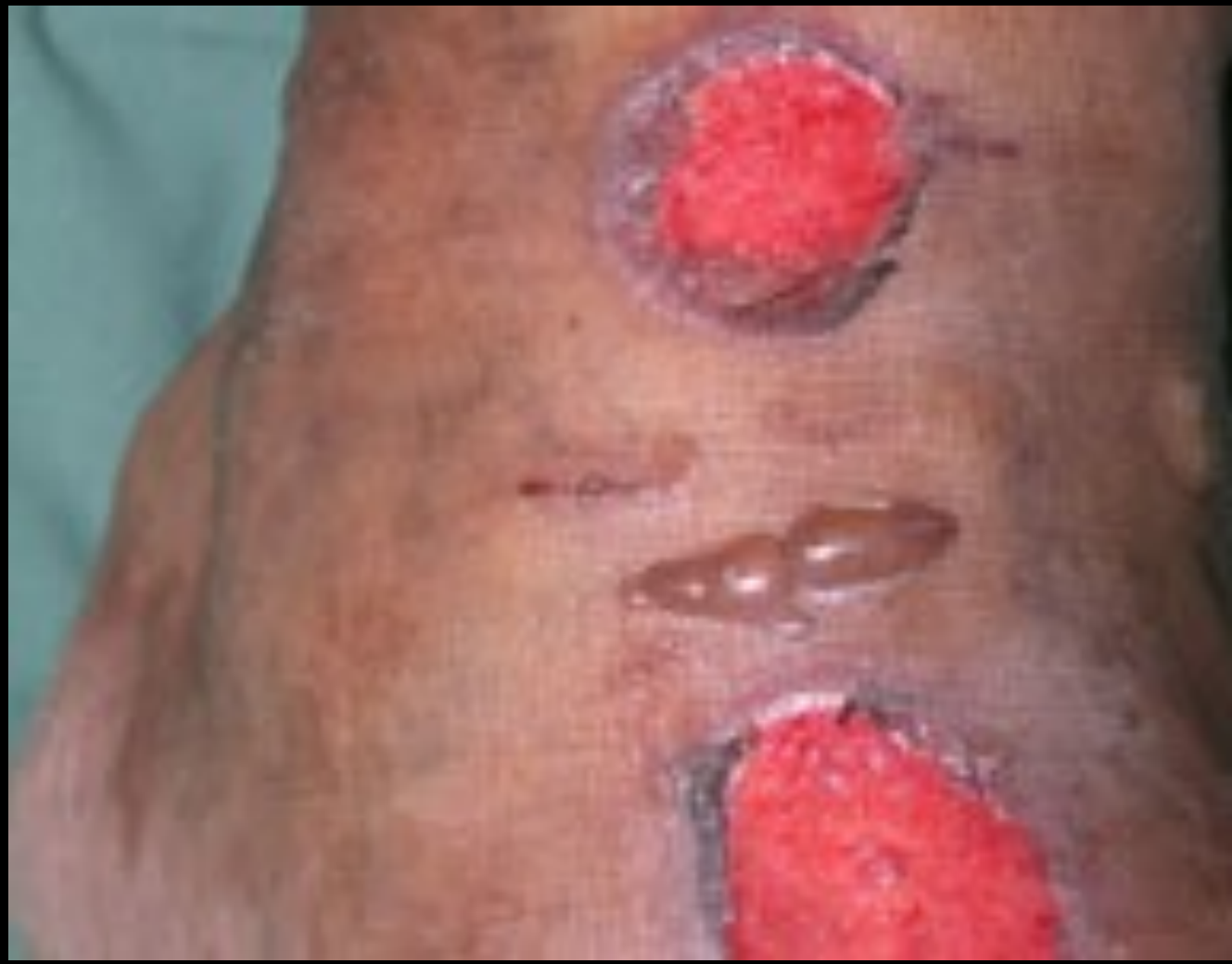




Bullous Diabeticorum

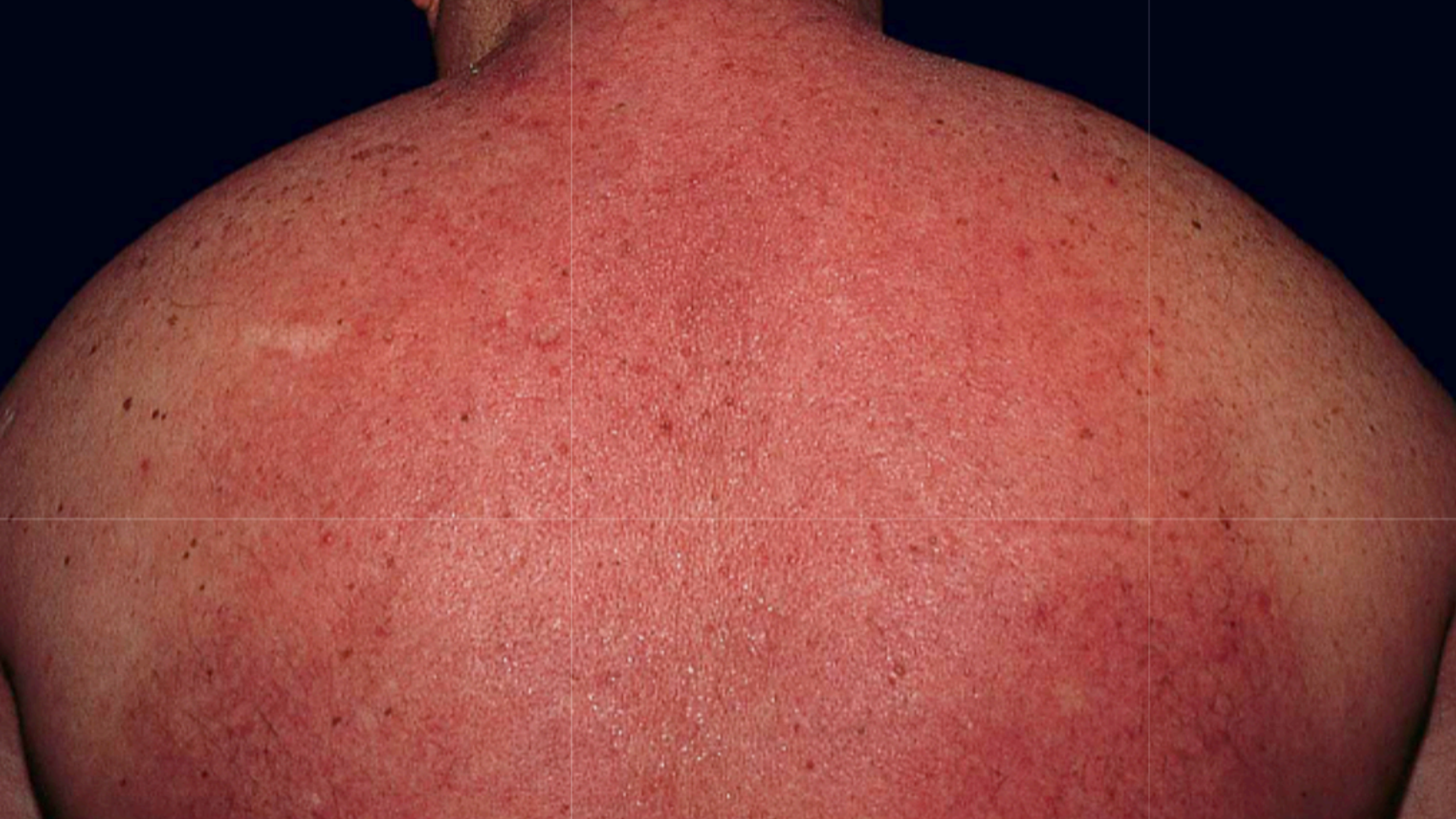
- A rare condition associated with DM.
- Tense blisters develop on normal-appearing skin in acral sites (feet, lower legs, hands).
- There is frequently an association with peripheral neuropathy.
- Spontaneous healing usually occurs within 2 to 6 weeks.





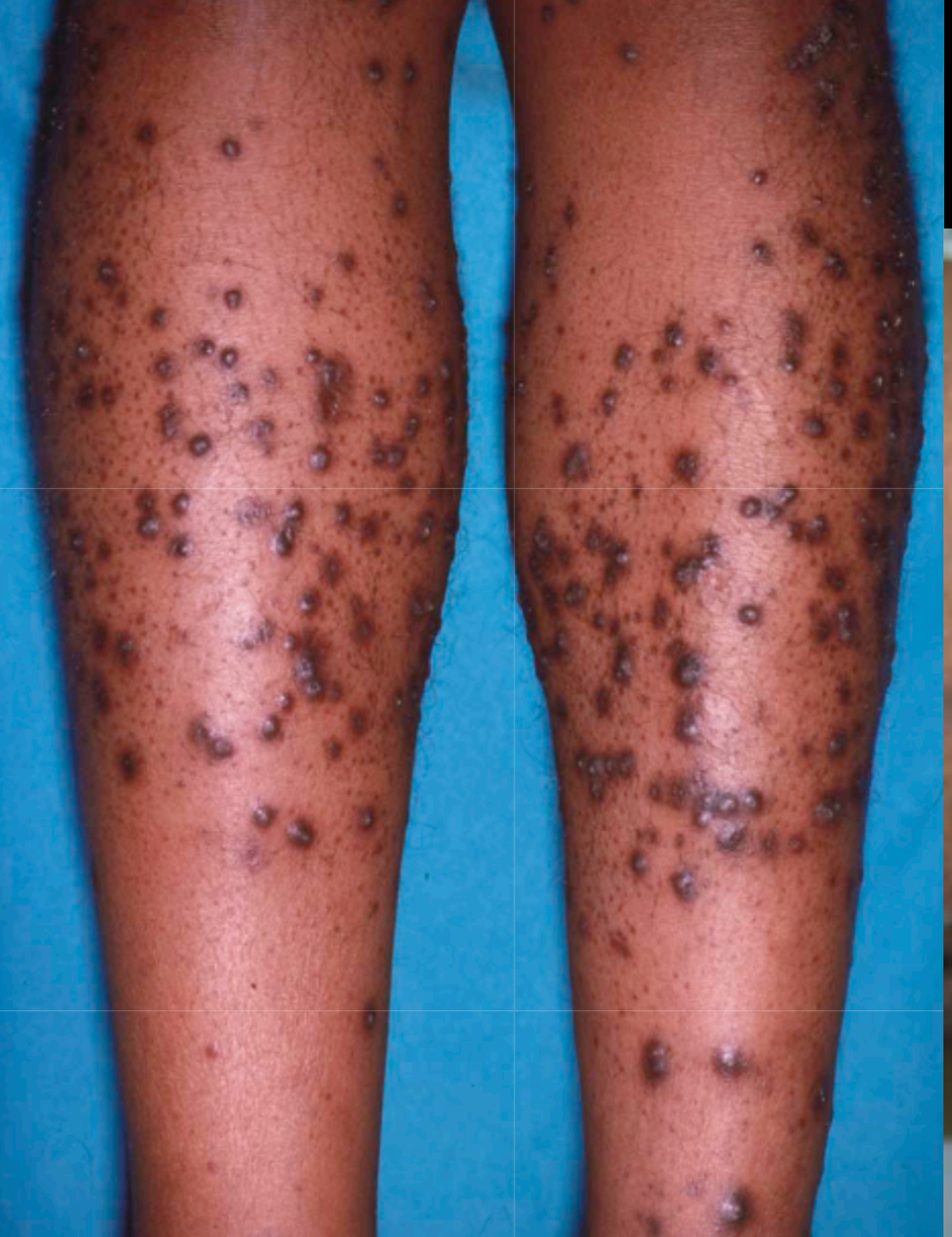
Scleredema

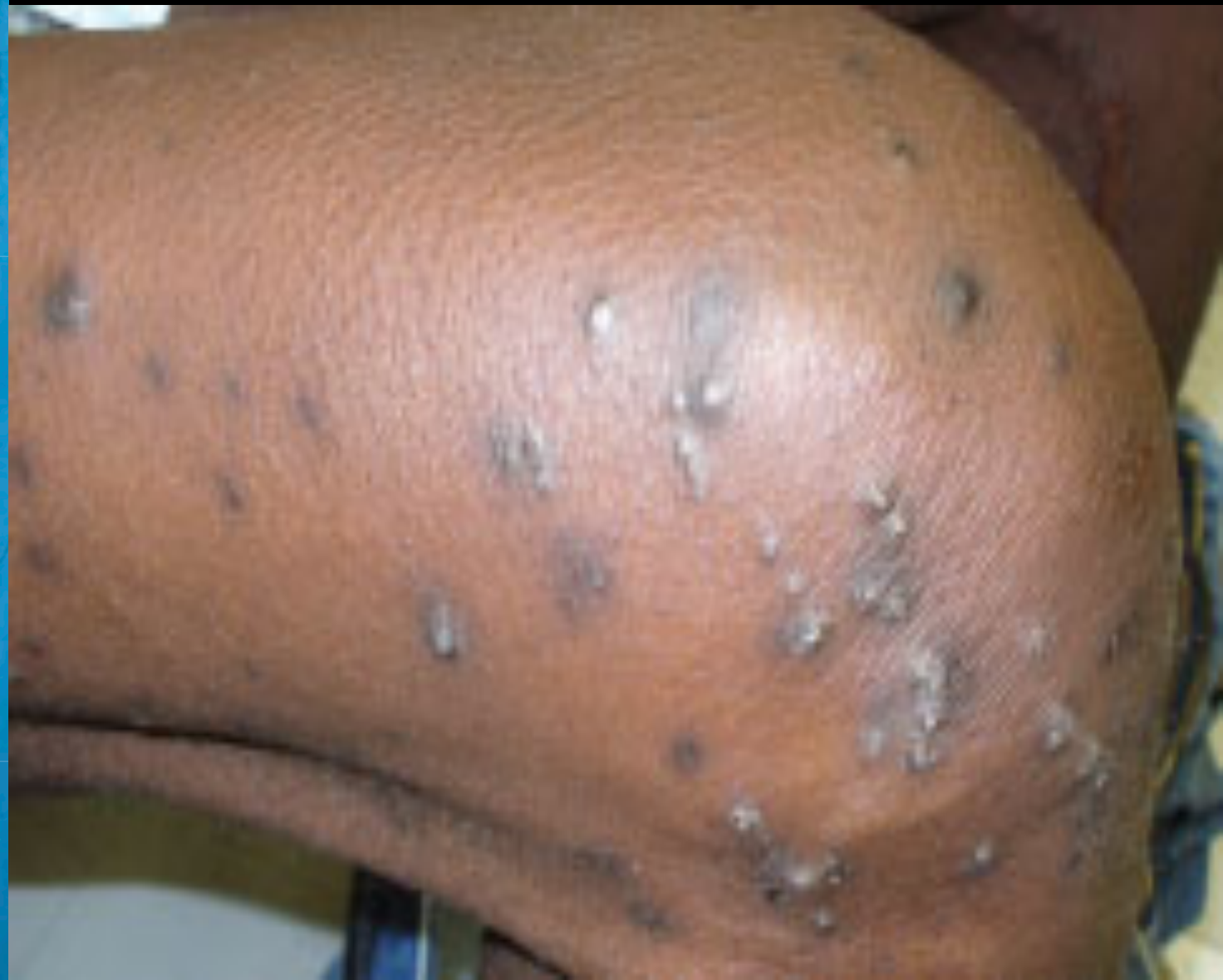
- More common in males, often obese, with longstanding, uncontrolled diabetes, that have frequently suffered complications of diabetes (neuropathy, nephropathy, retinopathy, atherosclerosis).
- Presents as woody induration and thickening of the skin of the mid upper back, neck, and shoulders.
- Can be associated with infection and monoclonal gammopathies.
- Control of diabetes does not affect the course of scleredema



Acquired Perforating Dermatosis

- A skin disorder occurring in patients with chronic renal failure, DM or both.
- Characterized by the transepidermal elimination of both collagen and elastic fibers.
- They present as 2-10 mm, firm, hyperkeratotic, often umbilicated papules occurring on the trunk and extremities.
- Tx: Topical keratolytics, phototherapy, topical/systemic retinoids, topical/intralesional steroids.





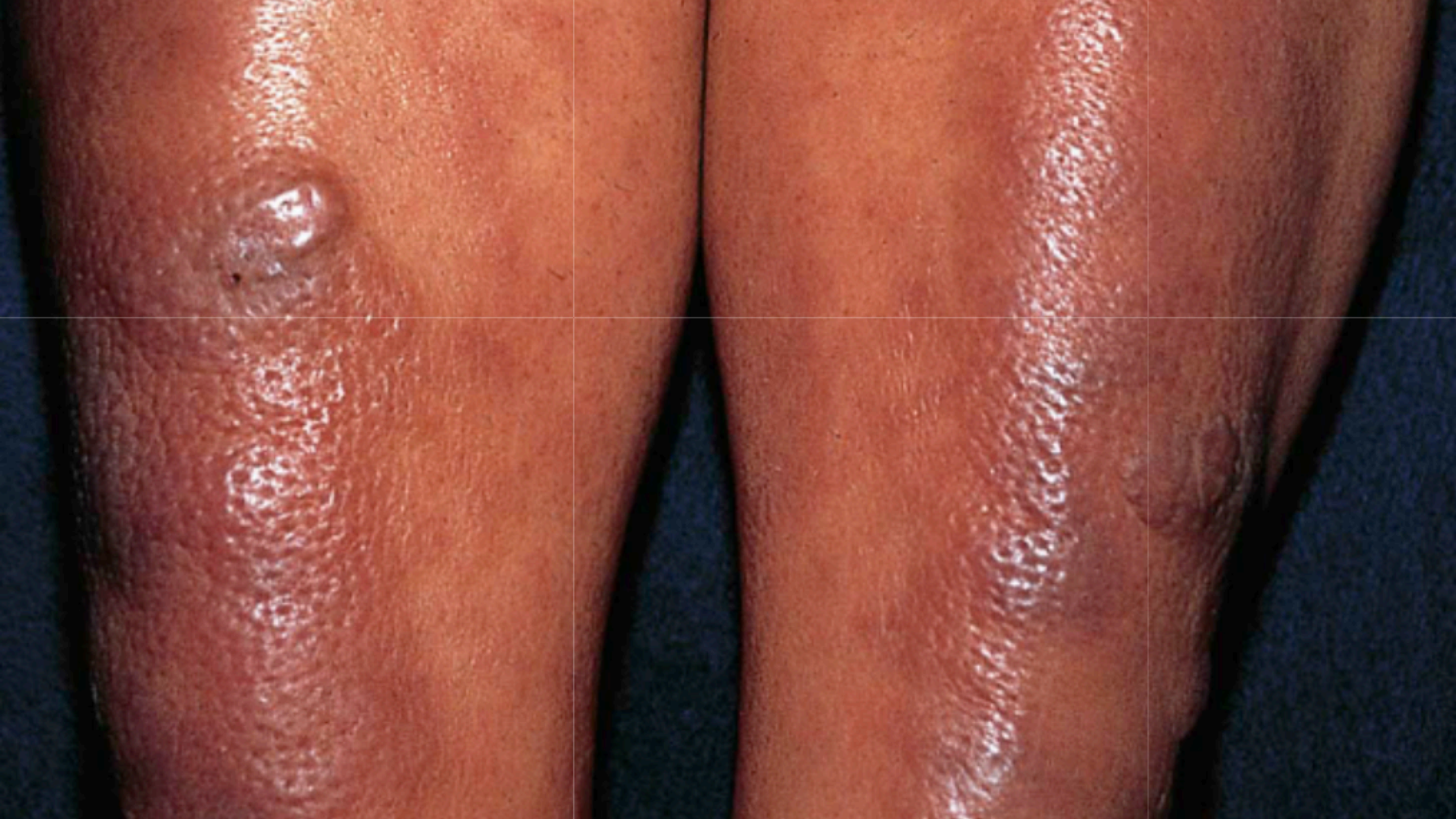
Thyroid Diseases

Hyperthyroidism

- Warm, moist skin.
- Palmoplantar hyperhidrosis.
- Pruritis.
- Diffuse, non-scarring alopecia. Increased risk of alopecia areata.
- Facial flushing.
- Hyperpigmentation of the skin, vitiligo.
- Nail changes: Plummer's nails, onycholysis, clubbing.

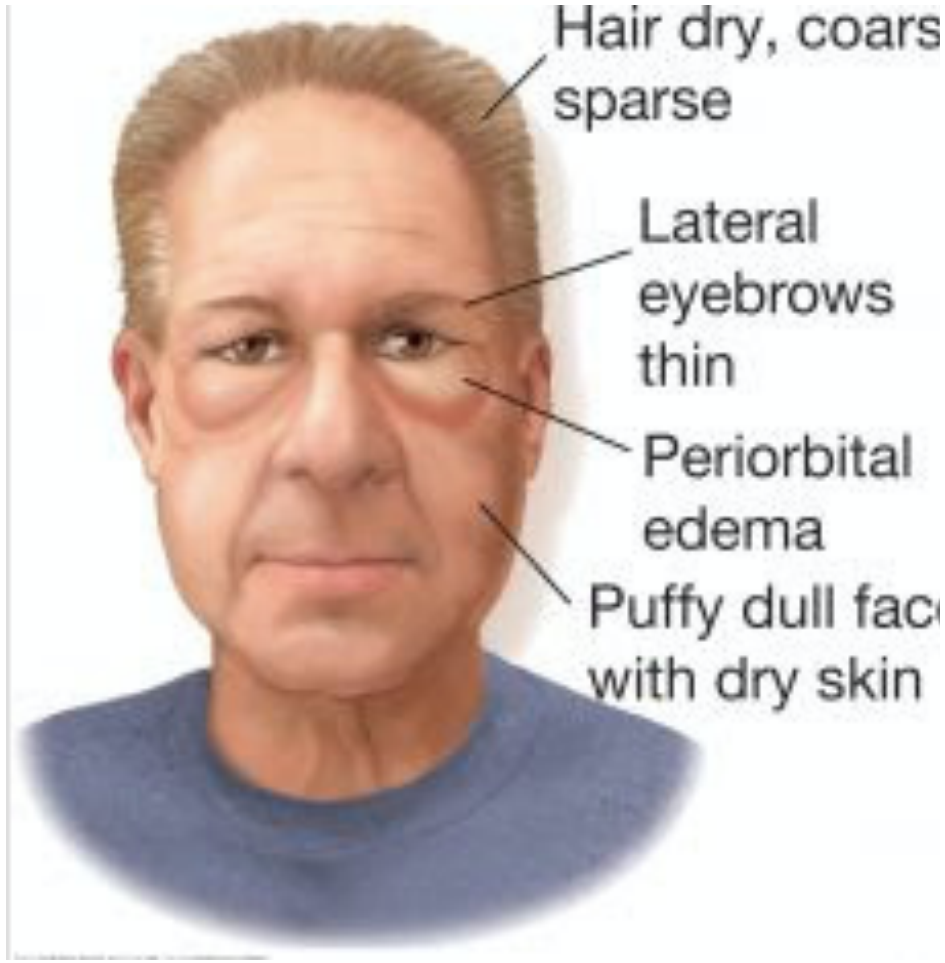
Pretibial myxedema:

- Cutaneous induration of the shins due to mucin deposition.
- Most commonly associated with Graves disease.
- Skin-colored to brown, waxy, indurated nodules/plaques with characteristic peau d'orange appearance.



Hypothyroidism

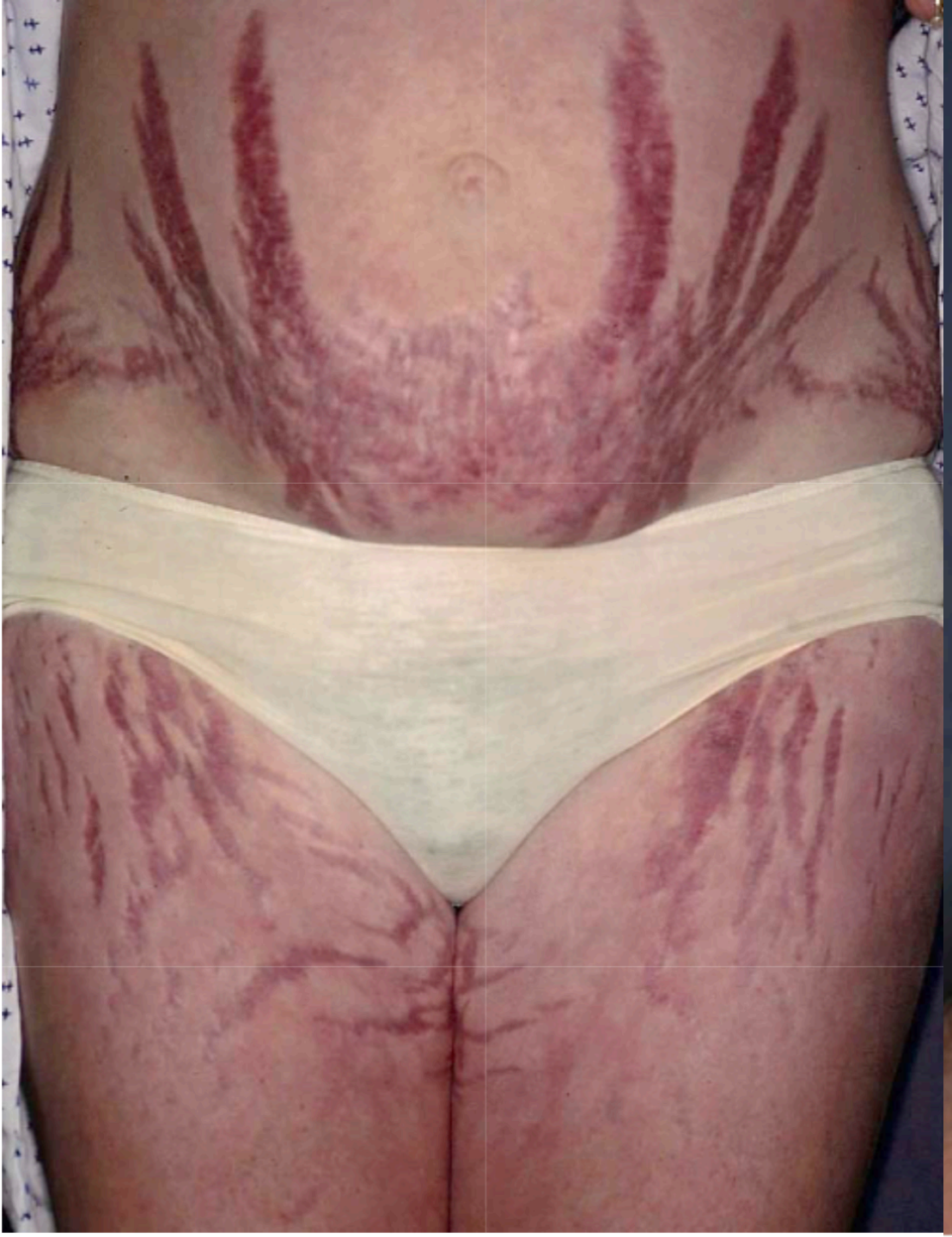
- Coarse, rough, dry skin.
- Pallor.
- Pruritis.
- Carotenemia.
- Diffuse hair loss with dull, coarse, brittle hair.
- Loss of the lateral 1/3 of the eyebrow.
- Myxedematous facies.
- Autoimmune disease – vitiligo, alopecia areata.

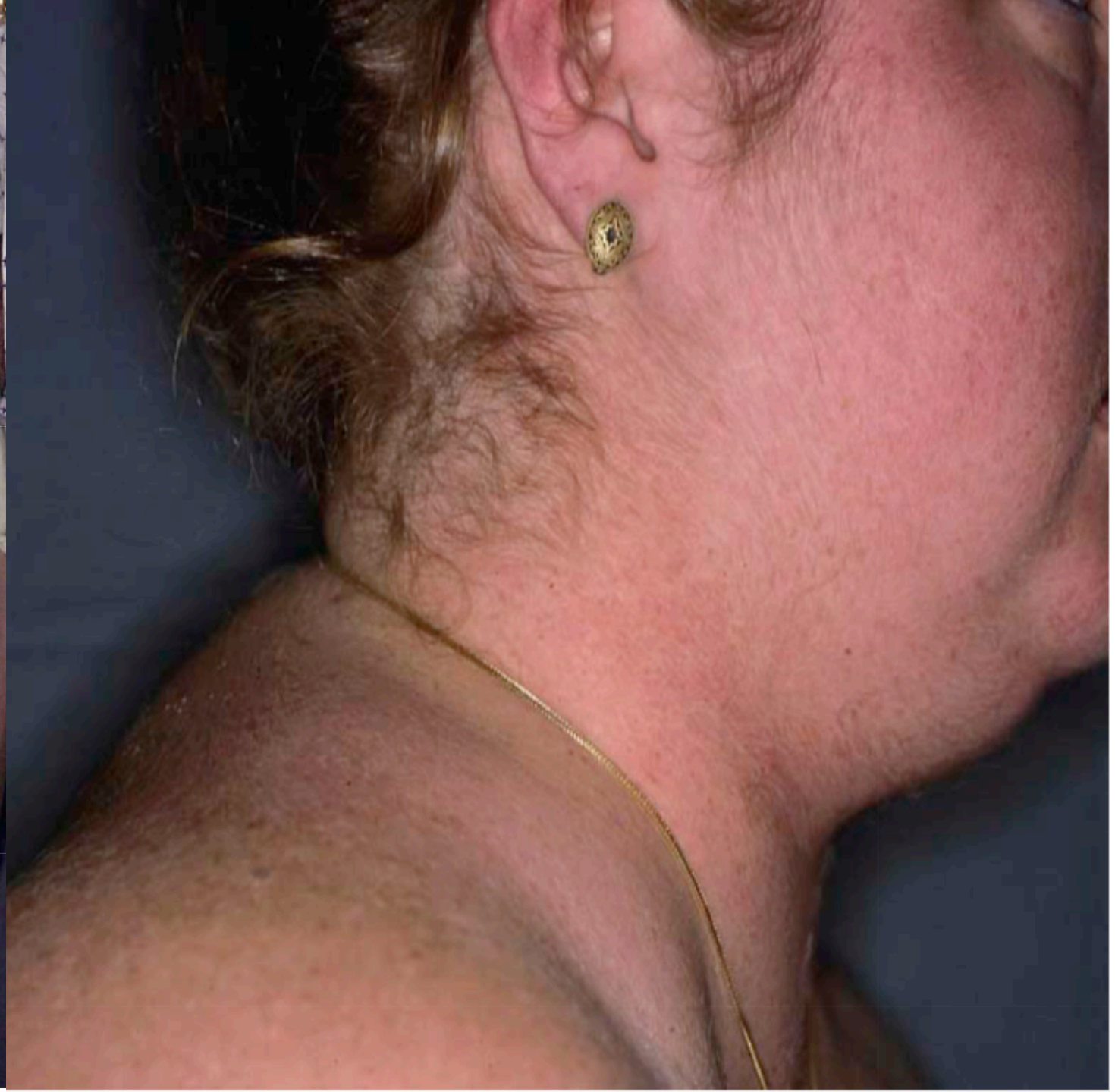

Hair dry, coars
sparse
Lateral
eyebrows
thin
Periorbital
edema
Puffy dull fac
with dry skin

Cushing Syndrome

Cushing's Syndrome

- Excessive glucocorticoid activity.
- Altered subcutaneous fat distribution: Moon facies, buffalo hump.
- Skin atrophy: Striae, prolonged wound healing, purpura.
- Infections: Tinea versicolor, onychomycosis, candidiasis.
- Adnexal effects: Corticosteroid-related acne, hirsutism.

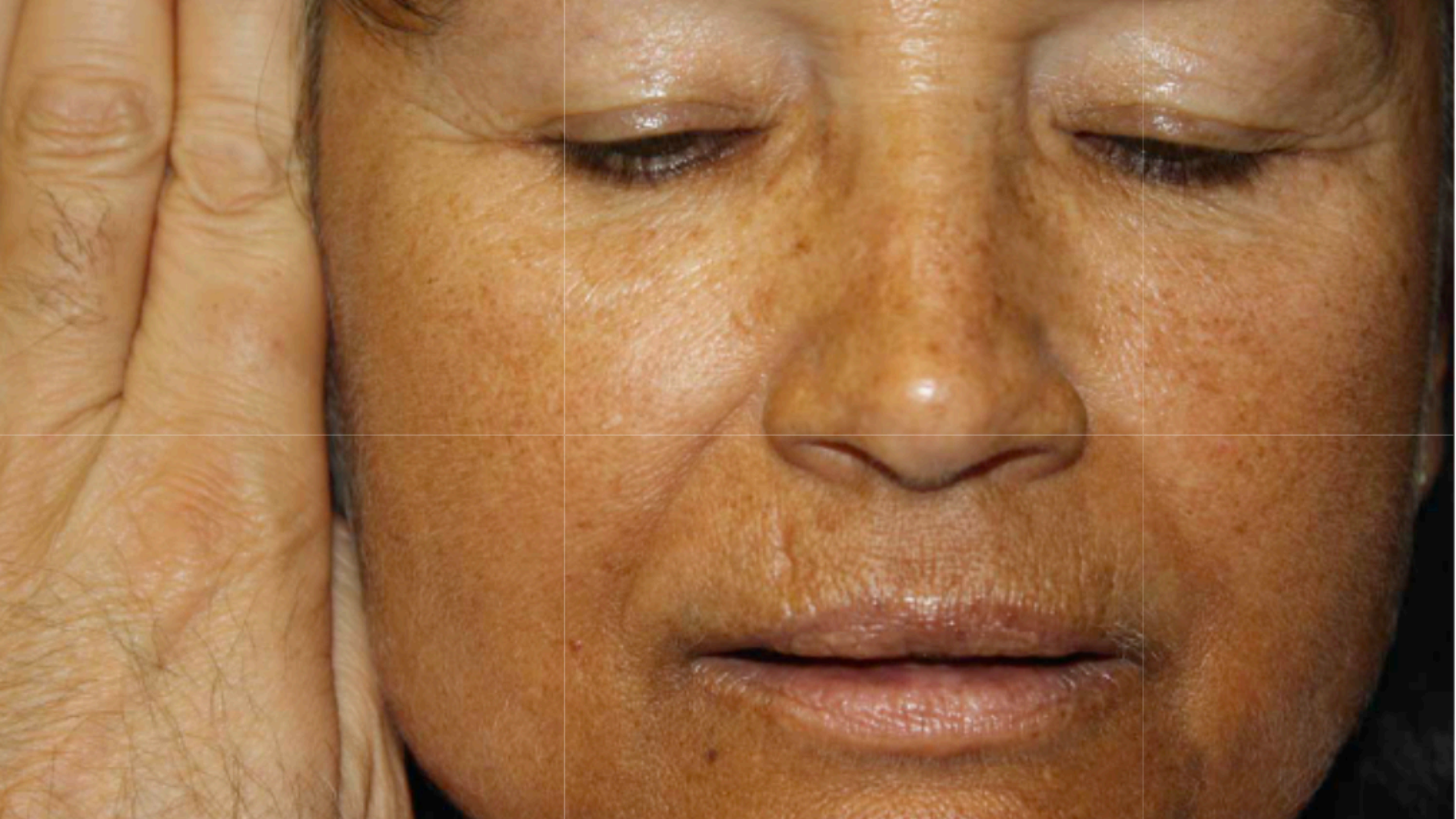




Addison’s Disease

Addison's Disease

- Insufficient glucocorticoid activity.
- Hyperpigmentation of the skin and mucous membranes due to high levels of circulating ACTH that binds to Melanocortin-1 receptor on the surface of the dermal melanocytes.
- Loss of ambisexual hair in post-pubertal women.
- Fibrosis and calcification of cartilage including the ear (rare).



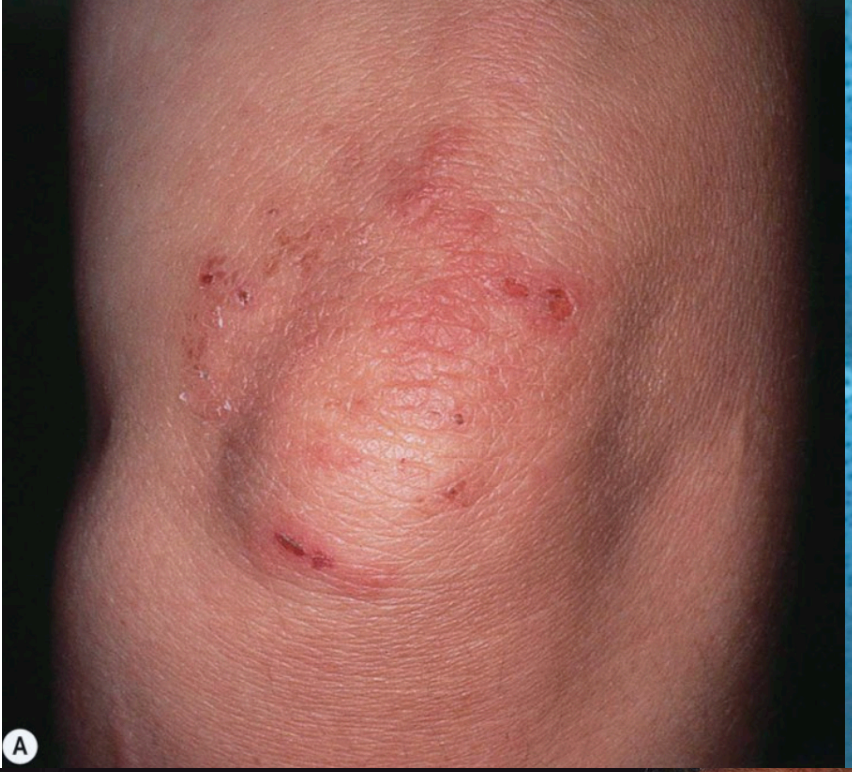
Gastrointestinal Diseases

Cutaneous Manifestations of Gastrointestinal Diseases

- Dermatitis herpetiformis
- Acrodermatitis enteropathica
- Pyoderma gangrenosum
- Peutz Jeghers syndrome
- Porphyria cutanea tarda
- Hemochromatosis
- Liver cirrhosis

Dermatitis herpetiformis

- An autoimmune blistering disorder that is often associated with a gluten-sensitive enteropathy.
- Small, severly pruritic, clustered vesicular papules or plaques that are symmetrically distributed over the extensor surfaces (elbows, knees, buttocks and shoulders).
- Worsening of the disease with dietary intake of gluten.
- Considered a cutaneous manifestation of celiac disease.
- Direct immunofluorescence (DIF) of prelesional skin shows granular IgA deposits in the dermal papillae.
- Tx: Dapsone, Gluten-free diet.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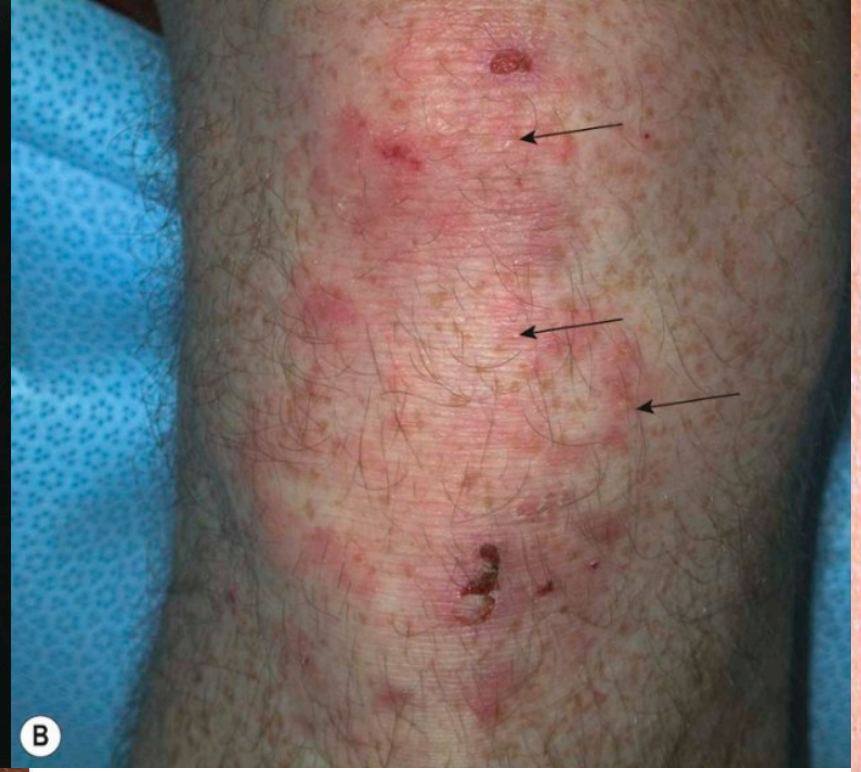
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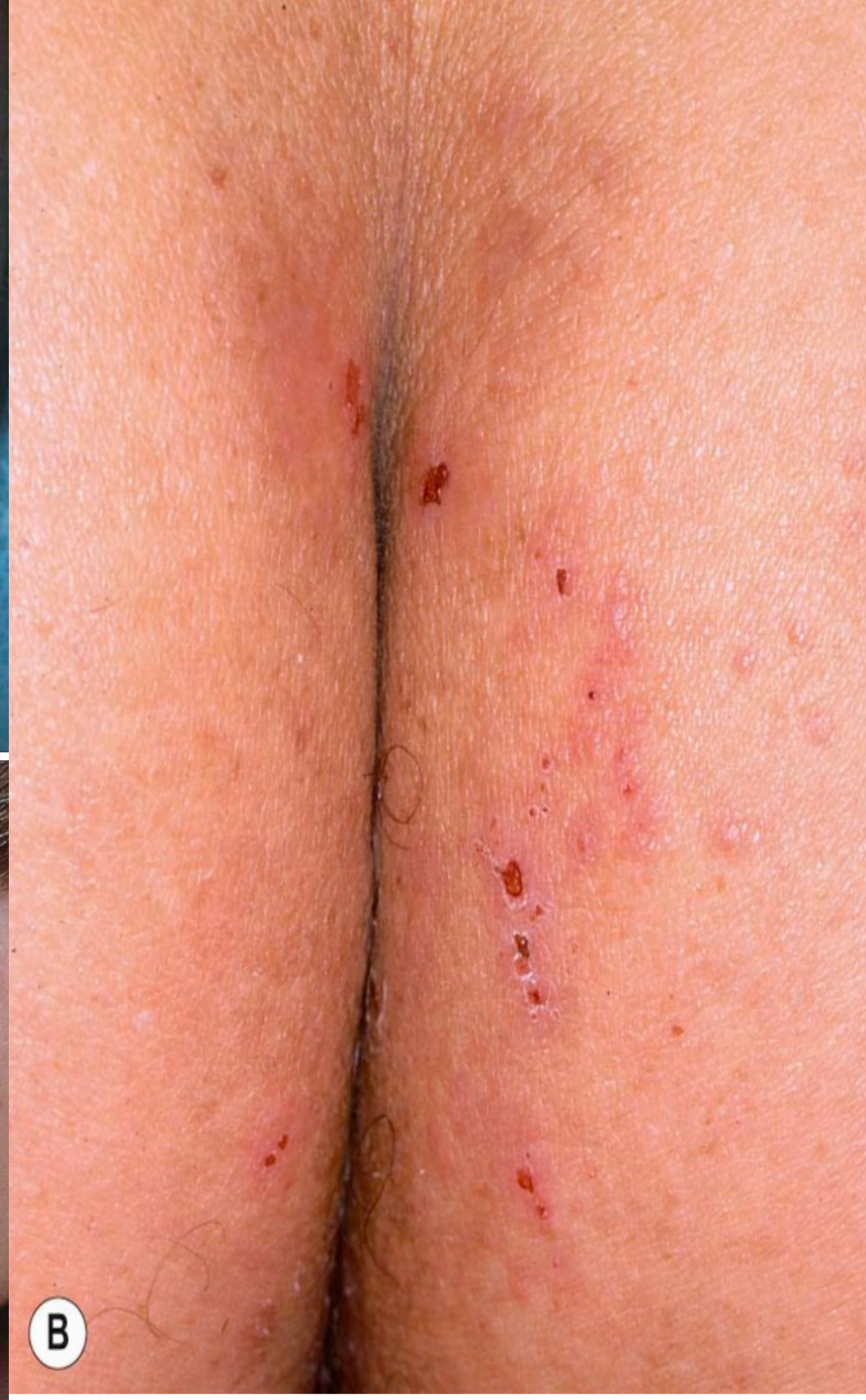
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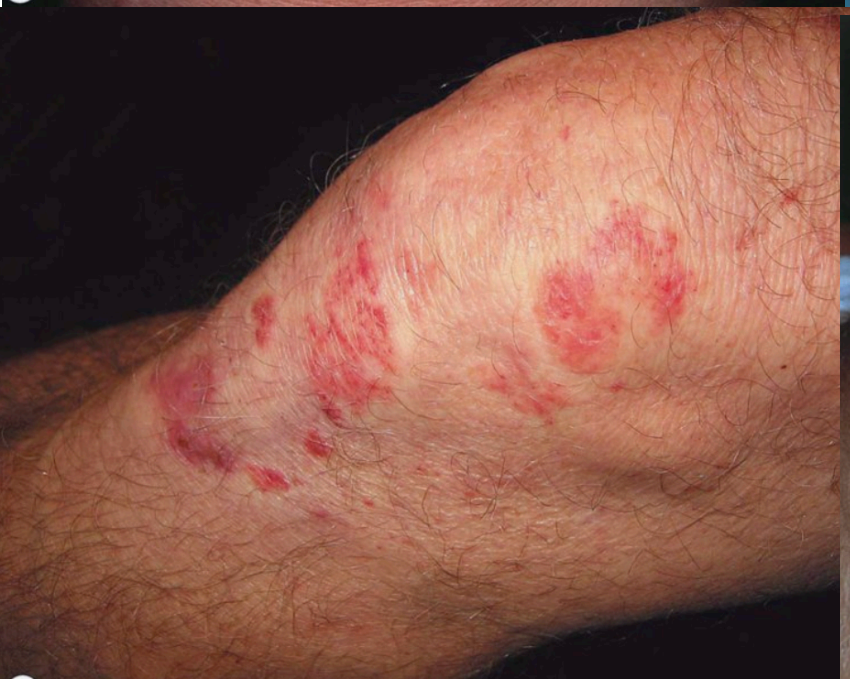

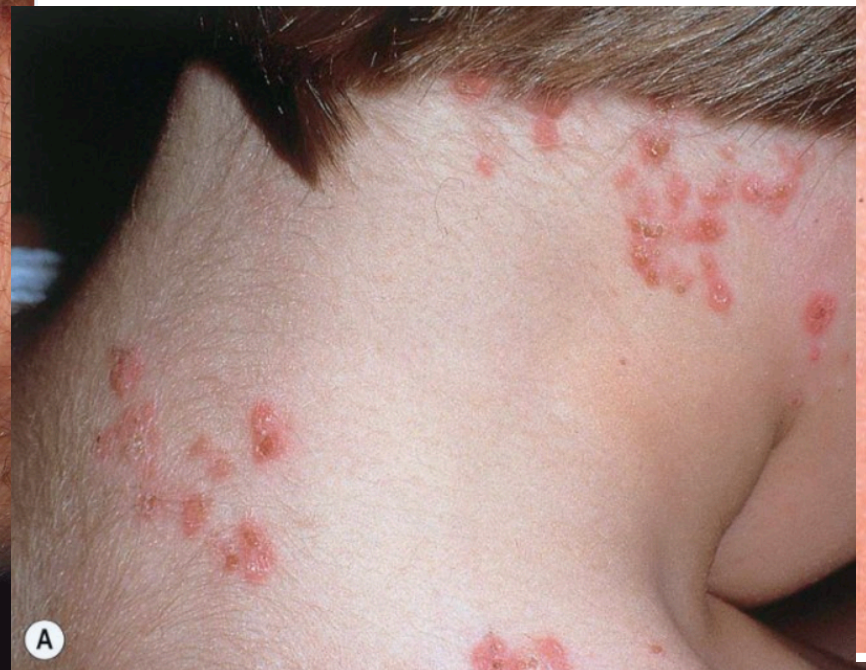
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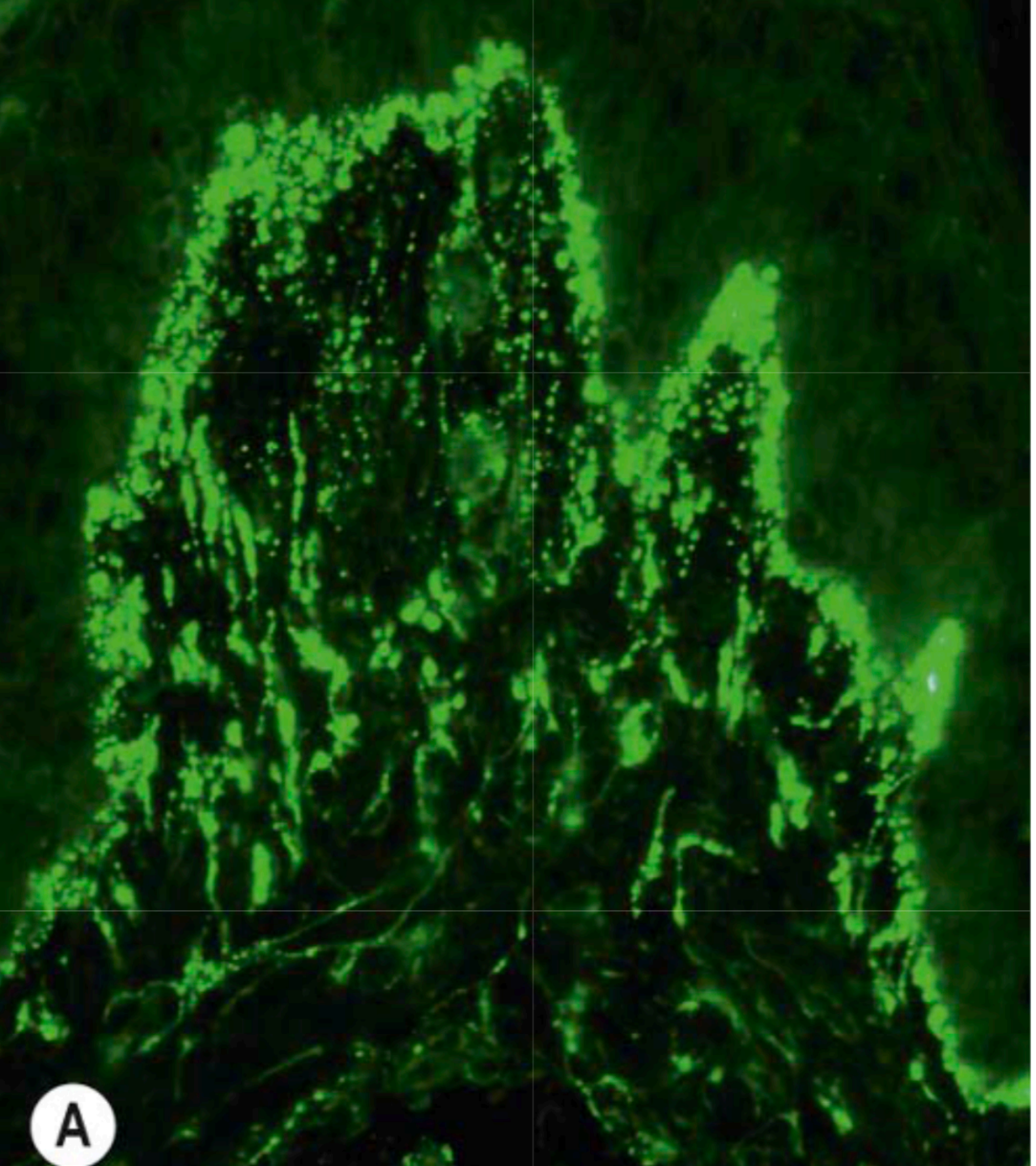
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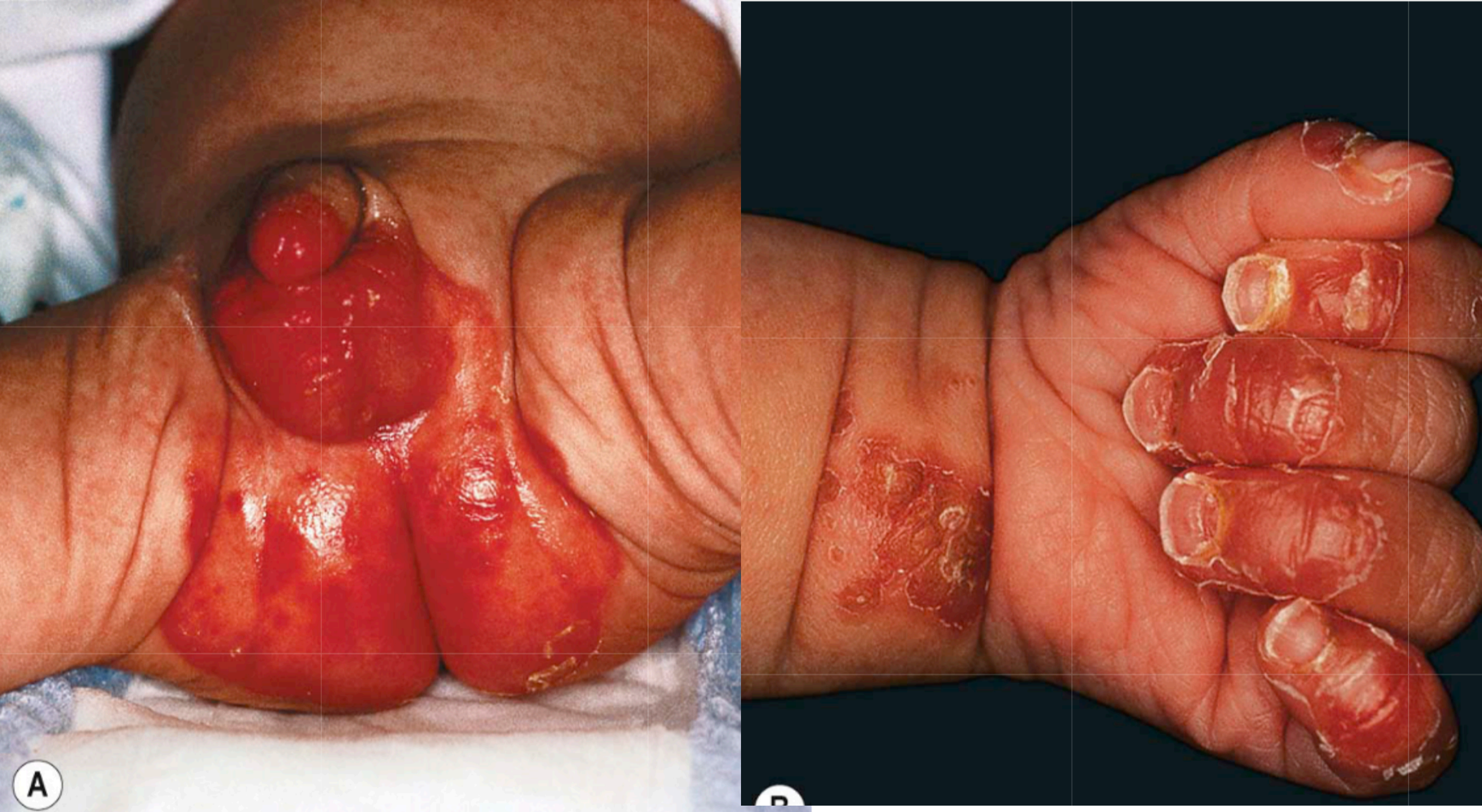
Acrodermatitis Enteropathica

- A rare autosomal recessive disorder that impairs dietary Zinc absorption in the GI tract.
- Usually starts manifesting as the infant is weaned from breast milk.
- Characterized by periorificial and acral dermatitis, alopecia.
- Scaly, erythematous patches and plaques similar to atopic dermatitis but progress to vesicles, crusts, erosions and pustules on the acral, perioral and perianal areas.
- Tx: Lifelong dietary Zinc supplementation.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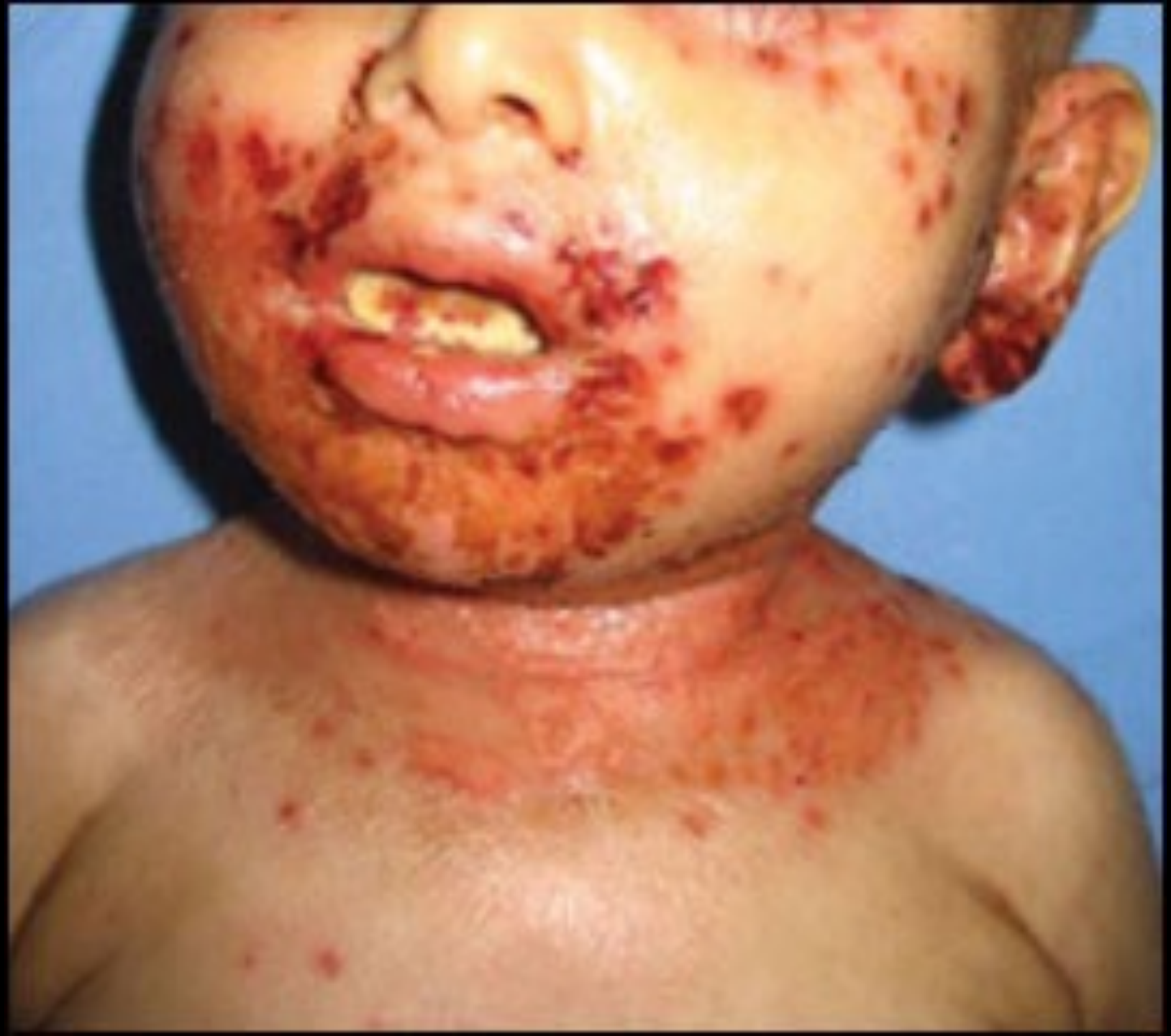
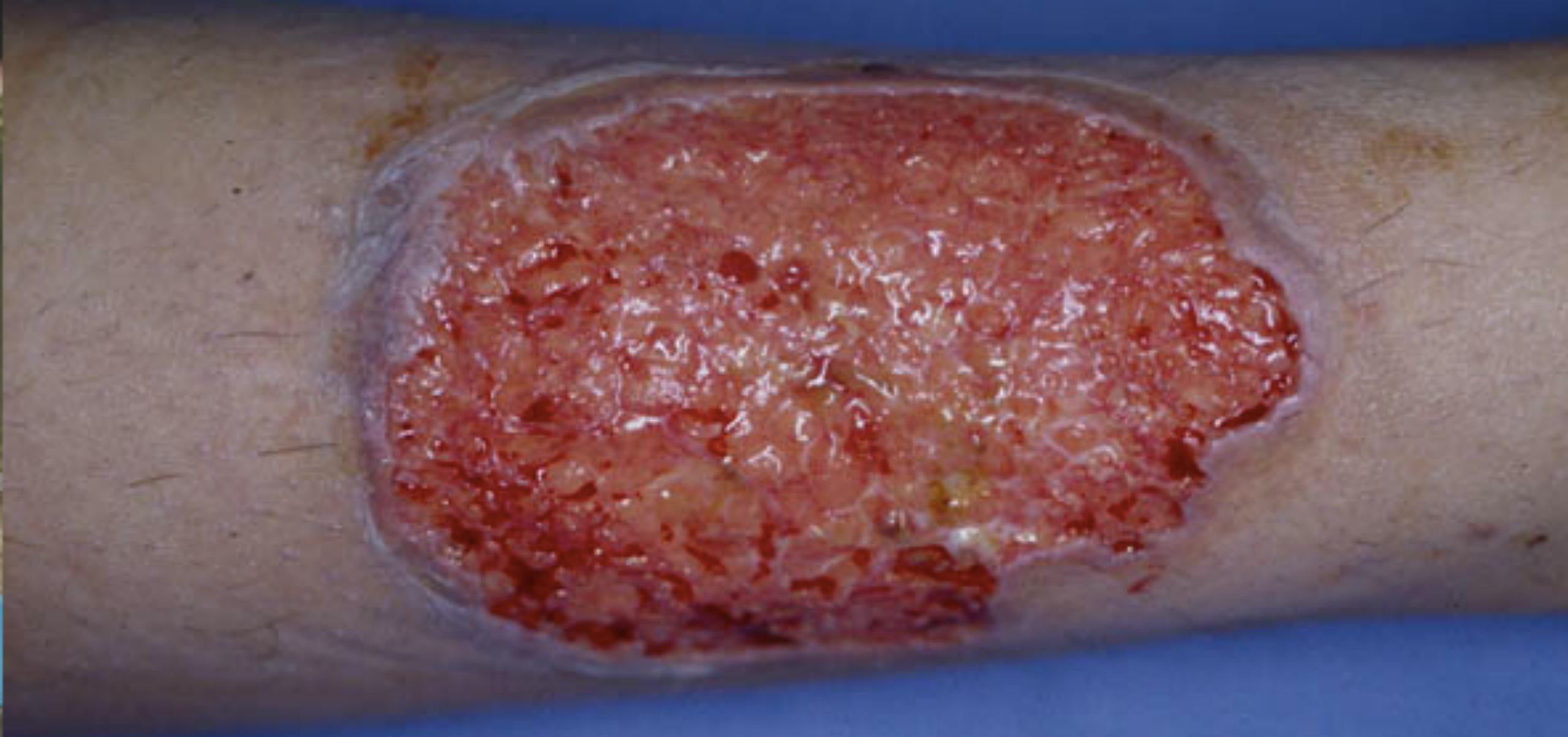
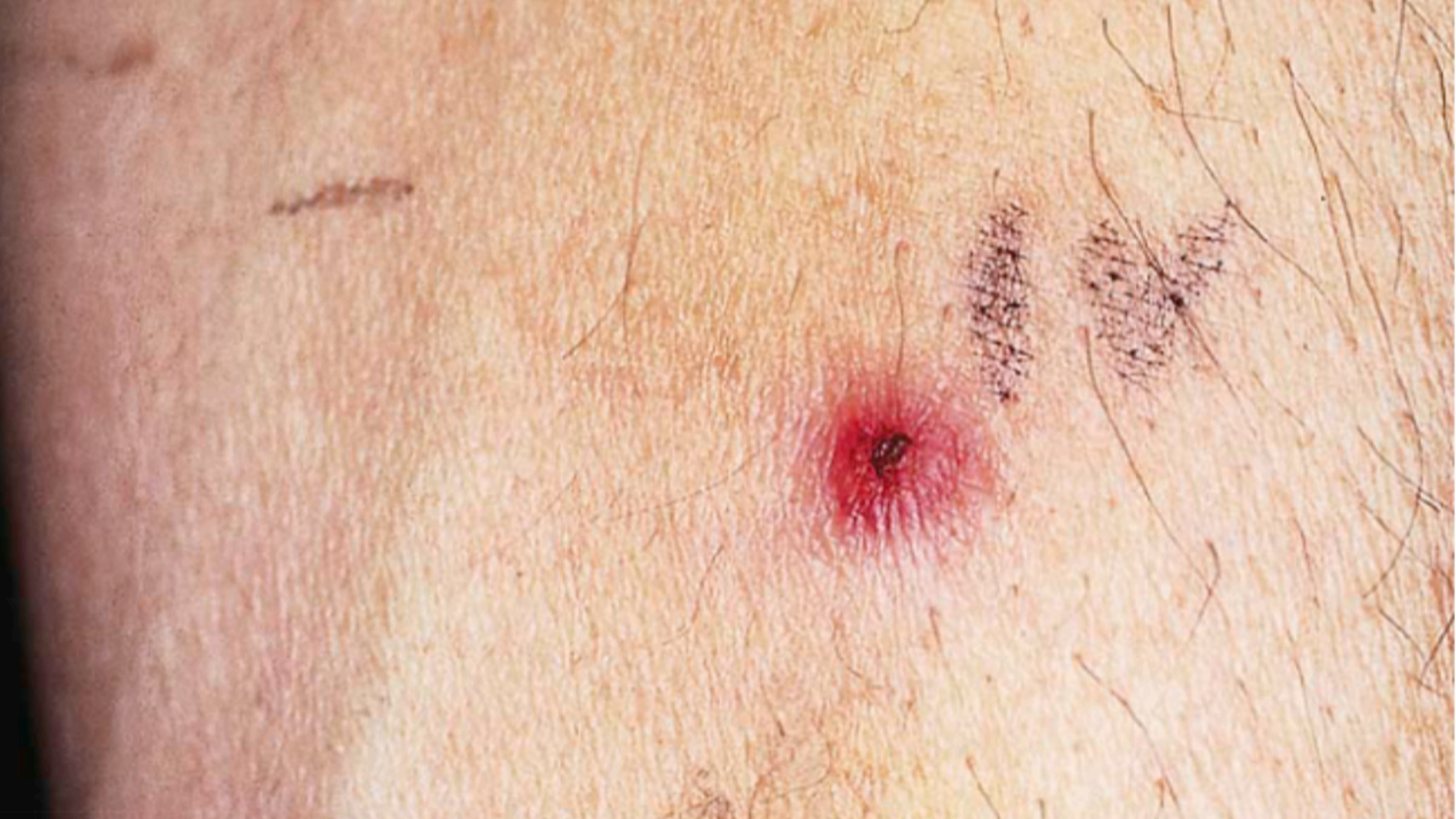


Pyoderma gangrenosum

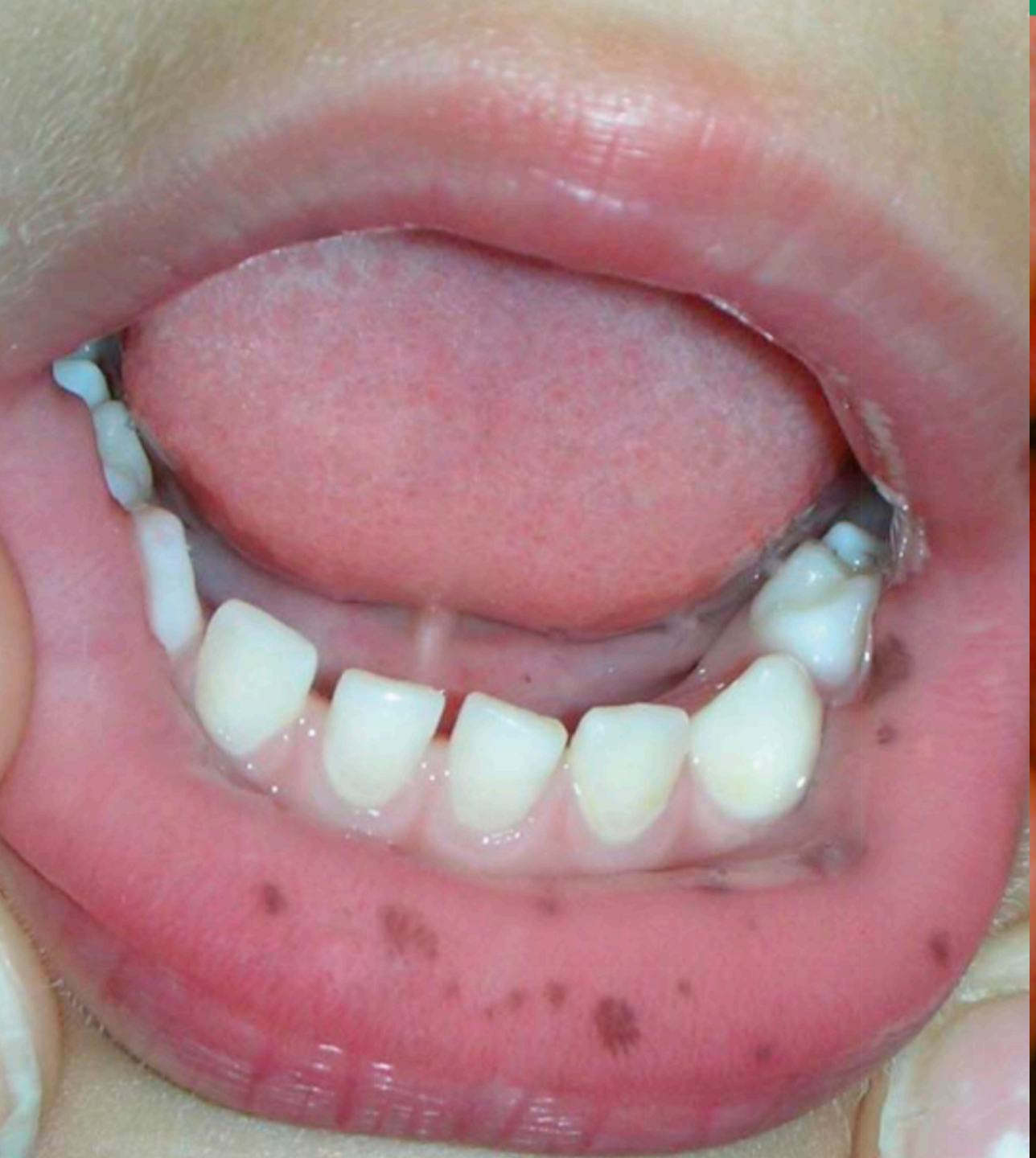
- Painful ulcerative lesions with a well-defined undermined, violaceous border.
- Starts as a small red papule or pustule, that subsequently expands to form a large non-infectious ulcer.
- Positive pathergy test.
- Mostly associated with ulcerative colitis, Crohn's disease, Rheumatoid arthritis and leukemia.
- Tx: topical/intralesional steroids, systemic immunotherapy, biologics.
- Surgery is contraindicated.

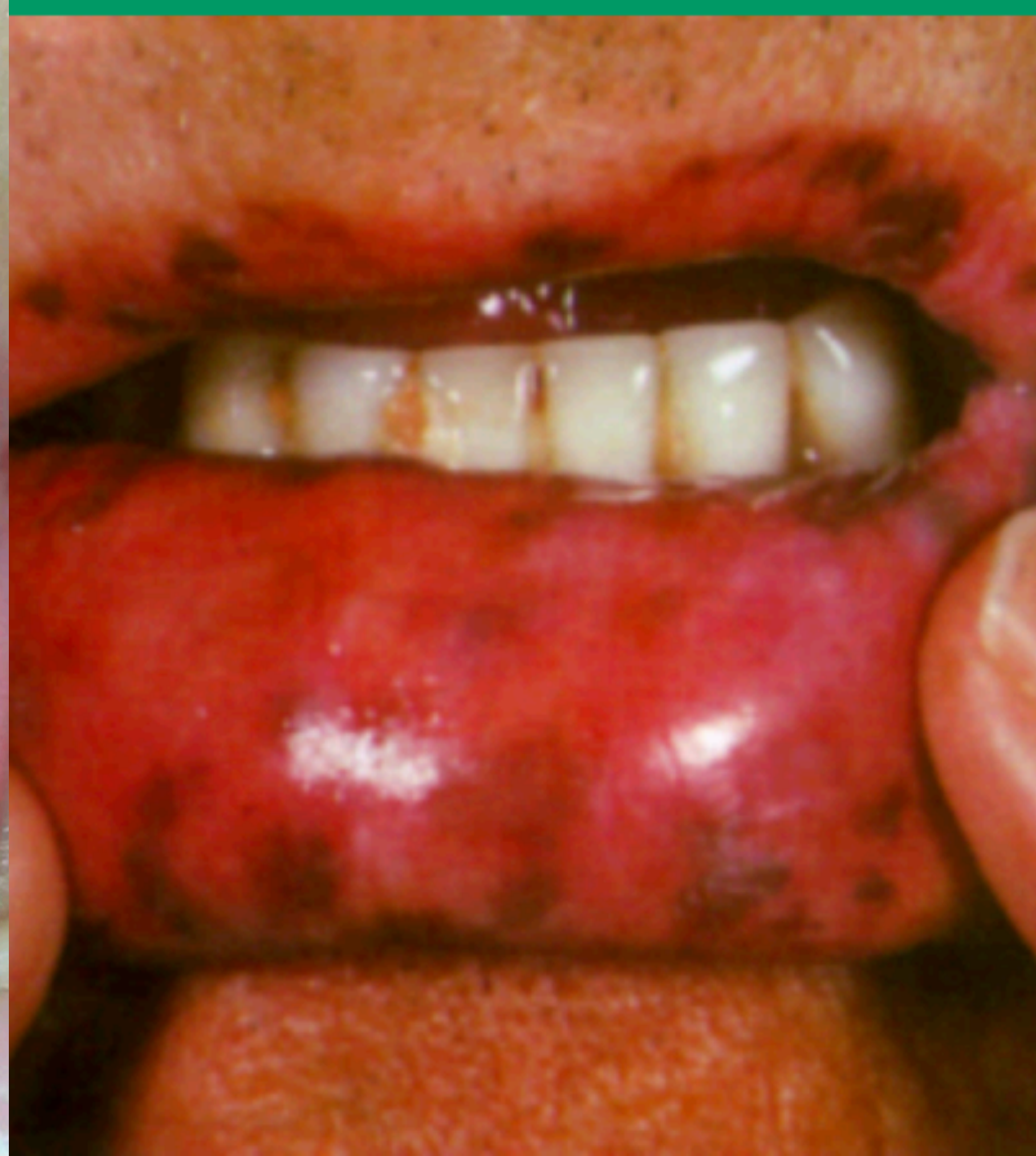




Peutz Jeghers syndrome

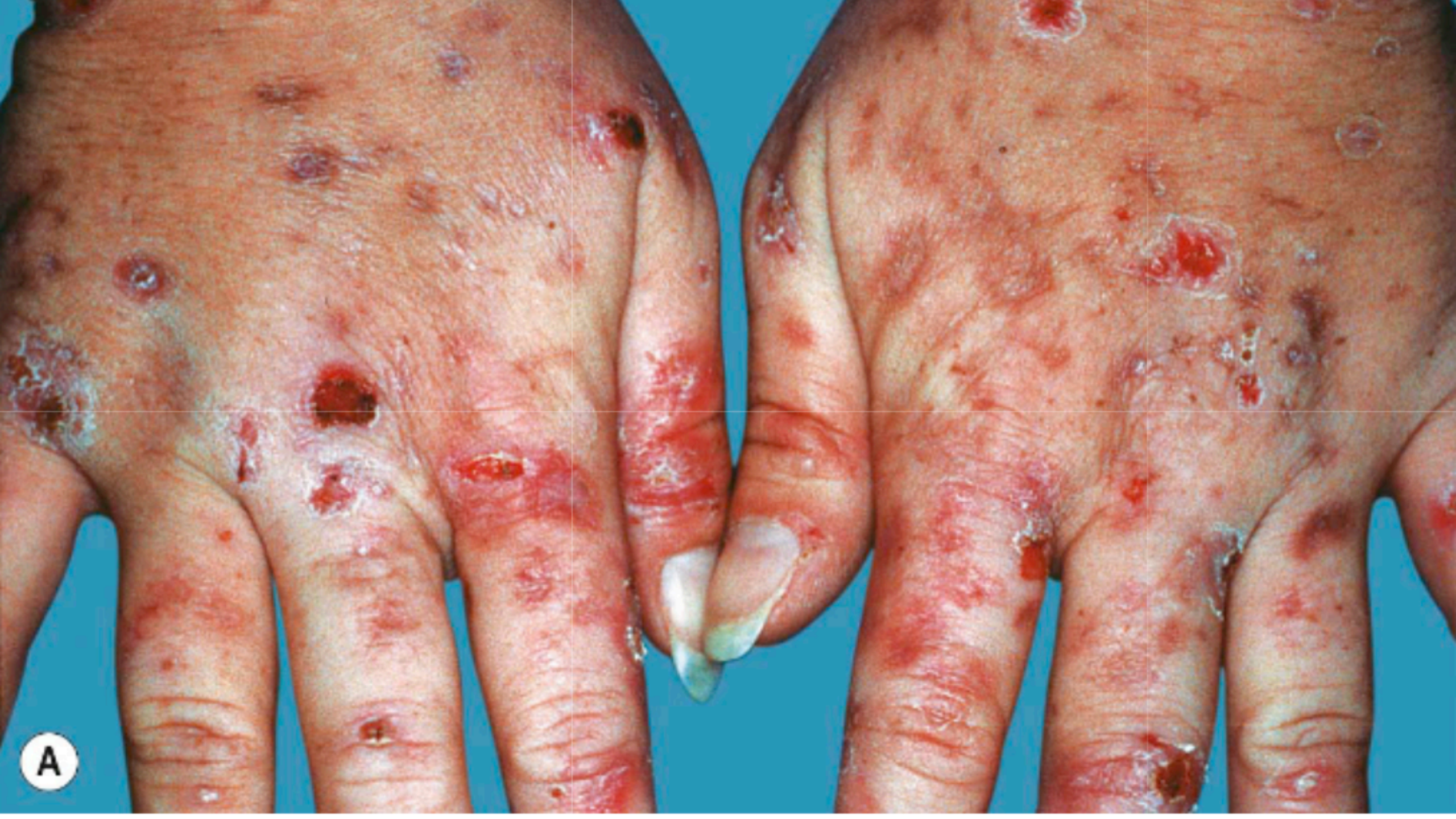
- Autosomal dominant due to mutations in the STK11 gene.
- Skin: Melanotic (brown) macules on mucosal surfaces and less often on acral or perioral skin that first appear very early in life.
- GI: Hamartomatous polyps throughout the GI tract. Bleeding may occur.
- Increased incidence of breast, ovarian and GI cancers.





Porphyria cutanea tarda (PCT)

- Porphyrias are inherited metabolic disorders resulting from a deficiency of an enzyme in the heme production pathway.
- PCT is the most common porphyria occurring in adults.
- Deficiency in ‘’ Uroporphyrinogen decarboxylase’’
- Photosensitivity, skin fragility of sun-exposed skin after mechanical trauma, leading to erosions and bullae on the hands mainly.
- Healing of crusted erosions and bullae leaves milia, hyperpigmentation, and atrophic scars.
- Facial Hypertrichosis.
- Frequently associated with Hepatitis C infection.
- Tx: Phlebotomy, hydroxychloroquine, sun avoidance.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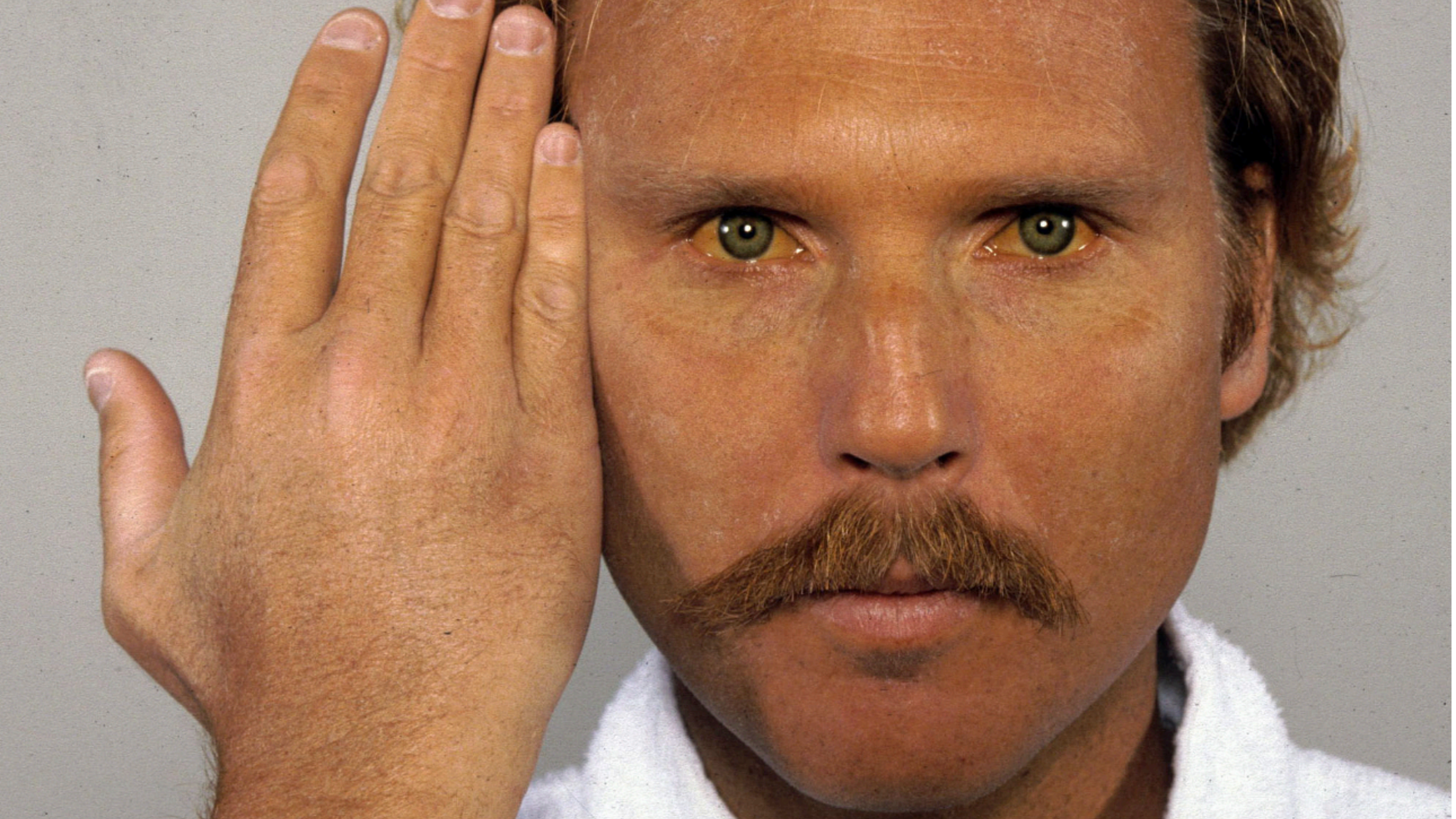
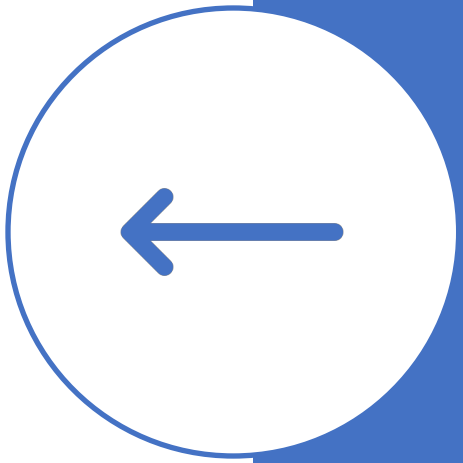
Hemochromatosis

- Autosomal recessive disorder characterized by the abnormal accumulation of iron in several organs leading to organ toxicity.
- Cutaneous pigmentation is one of the earliest signs of the disease, most pronounced on sun-exposed areas (face).
- Appears as brownish bronze or at times slate gray.
- Other findings: ichthyosis-like changes, koilonychia and hair loss.
- Tx: Phelebotomy.



Liver cirrhosis

- Jaundice
- Pruritis
- Spider angioma
- Palmar erythema
- Purpura
- Petechiae
- Caput medusae
- Loss of body hair.



Renal Diseases

Cutaneous Manifestations of Renal Disease

MANIFESTATIONS ASSOCIATED WITH UREMIA

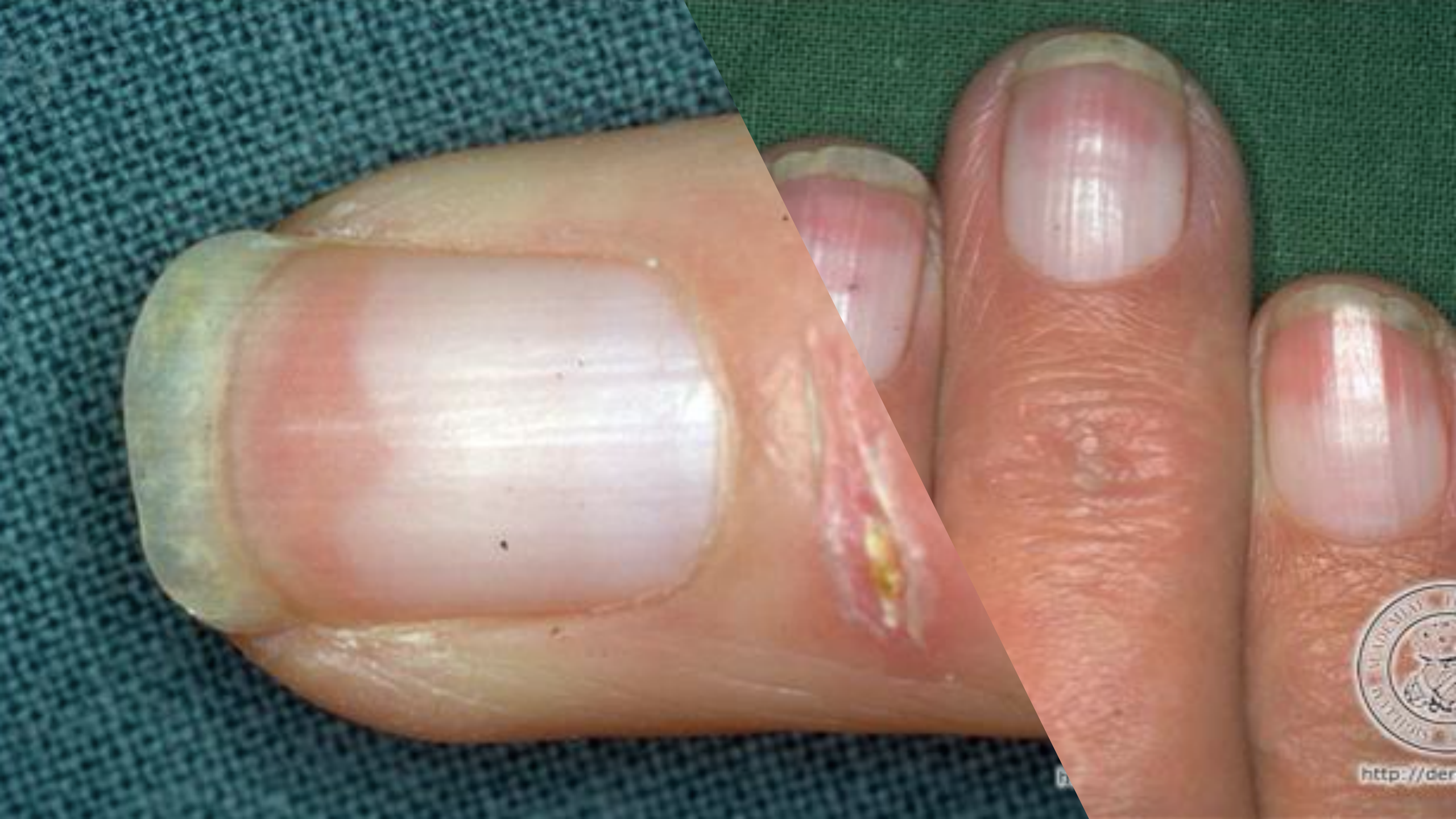
NEPHROGENIC SYSTEMIC FIBROSIS

Manifestations associated with uremia

- **Xerosis:**
- 50-90% of dialysis patients
- Can improve with routine use of emollients.

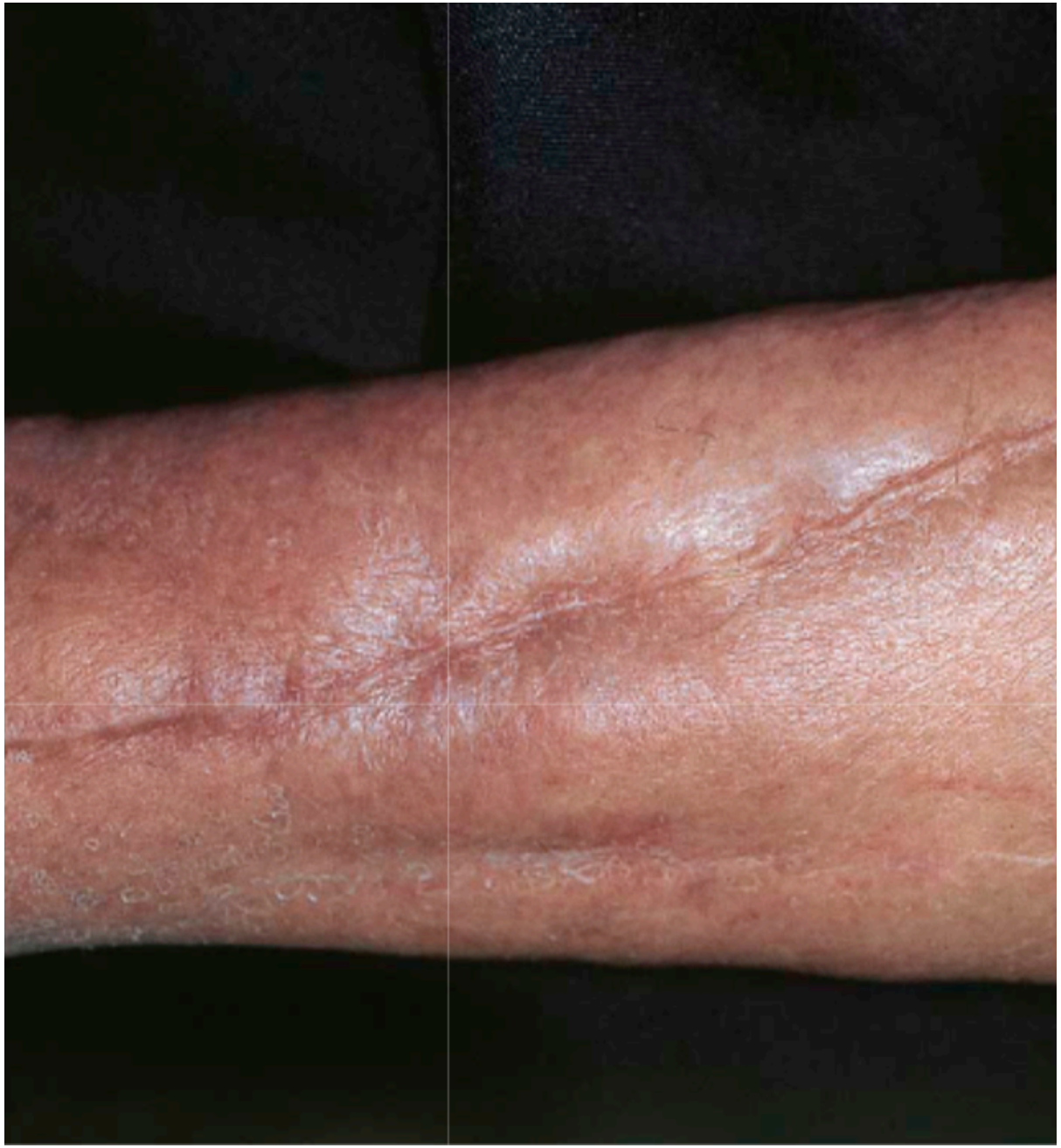
- **Pruritis:**
- The most common metabolic cause of pruritis.
- Manifestations of pruritis include: Excoriations, prurigo nodularis, lichen simplex chronicus.
- Resolved after transplantation.
- Tx: Antihistamines, emollients, phototherapy, thalidomide, gabapentin…

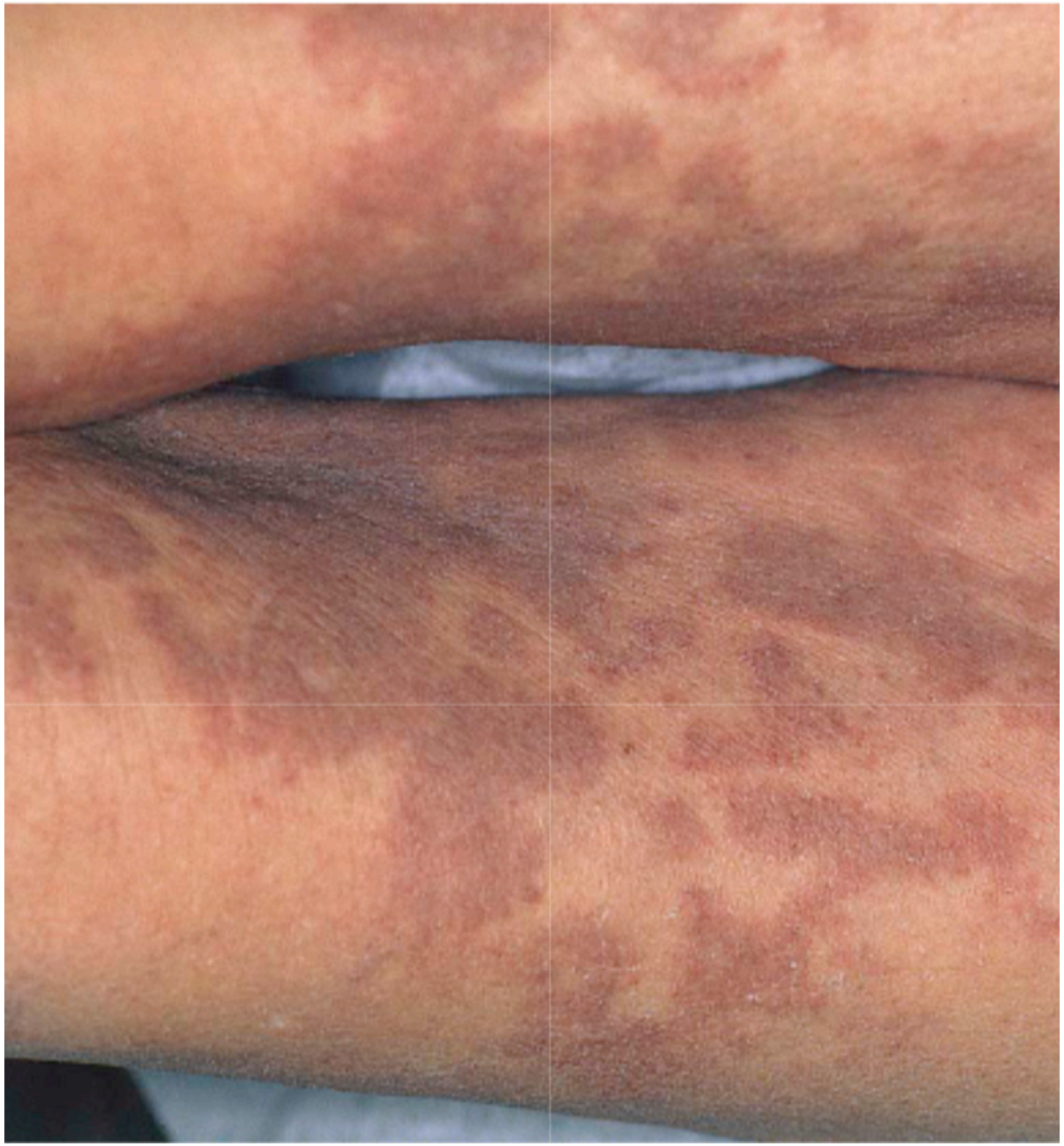
- **Half-and-Half nails:**
- 40% of patients on dialysis.
- Disappears several months after transplantation.
- Dark (Reddish-brown) distal band and a white proximal band.
- More common on fingernails but could be seen on the toenails.



Nephrogenic Systemic Fibrosis

- Fibrosis of the skin and internal organs.
- Caused by exposure to gadolinium-based contrast agents used in imaging in patients who have renal insufficiency on dialysis.
- Large areas of thick, woody, indurated skin with fibrotic nodules and plaques on the extremities and trunk.
- Tx: Extracorporeal photochemotherapy, immunosuppressive therapy, phototherapy, IVIG.

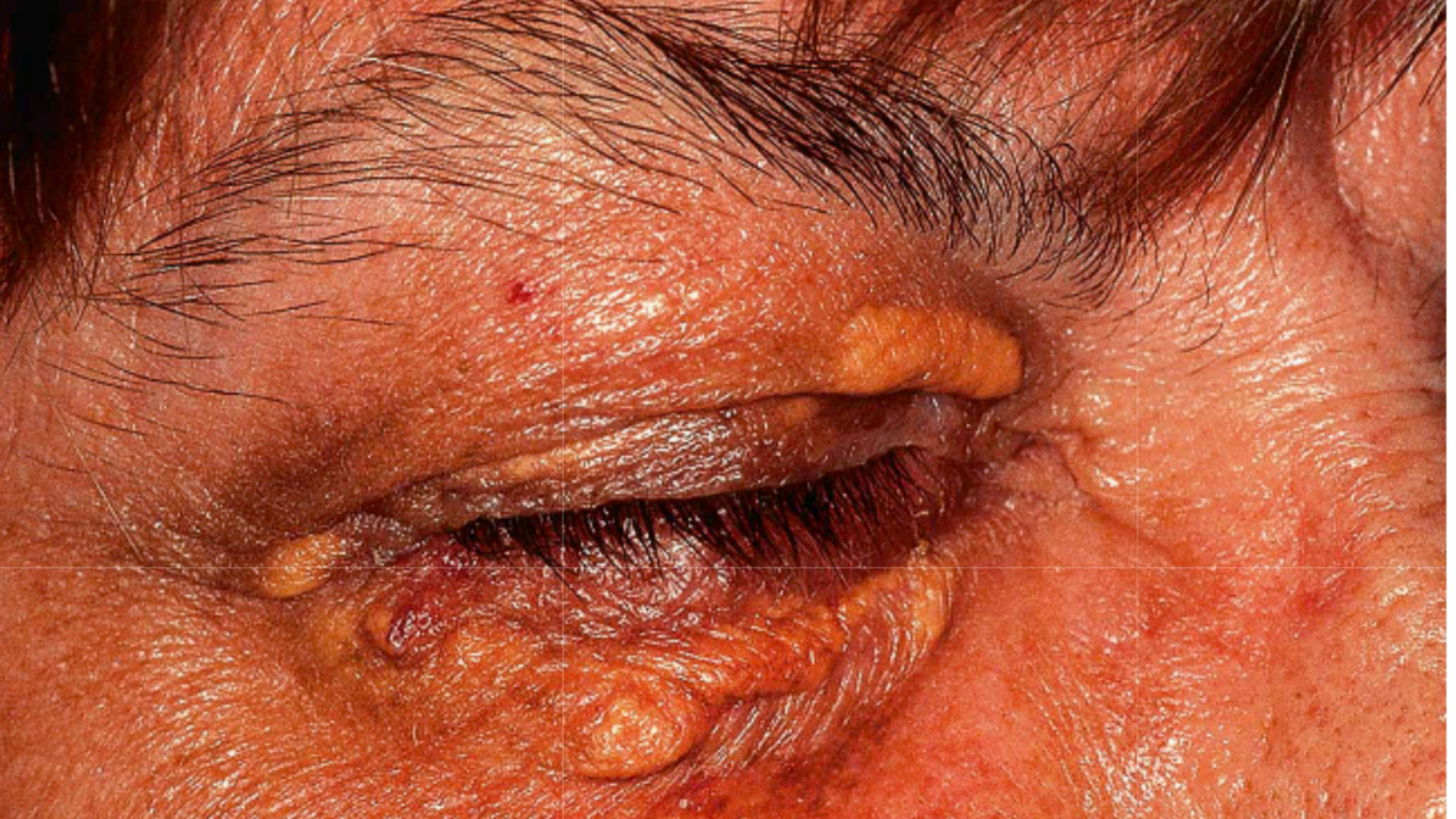




Hyperlipidemia

Xanthelasma Palpebrarum

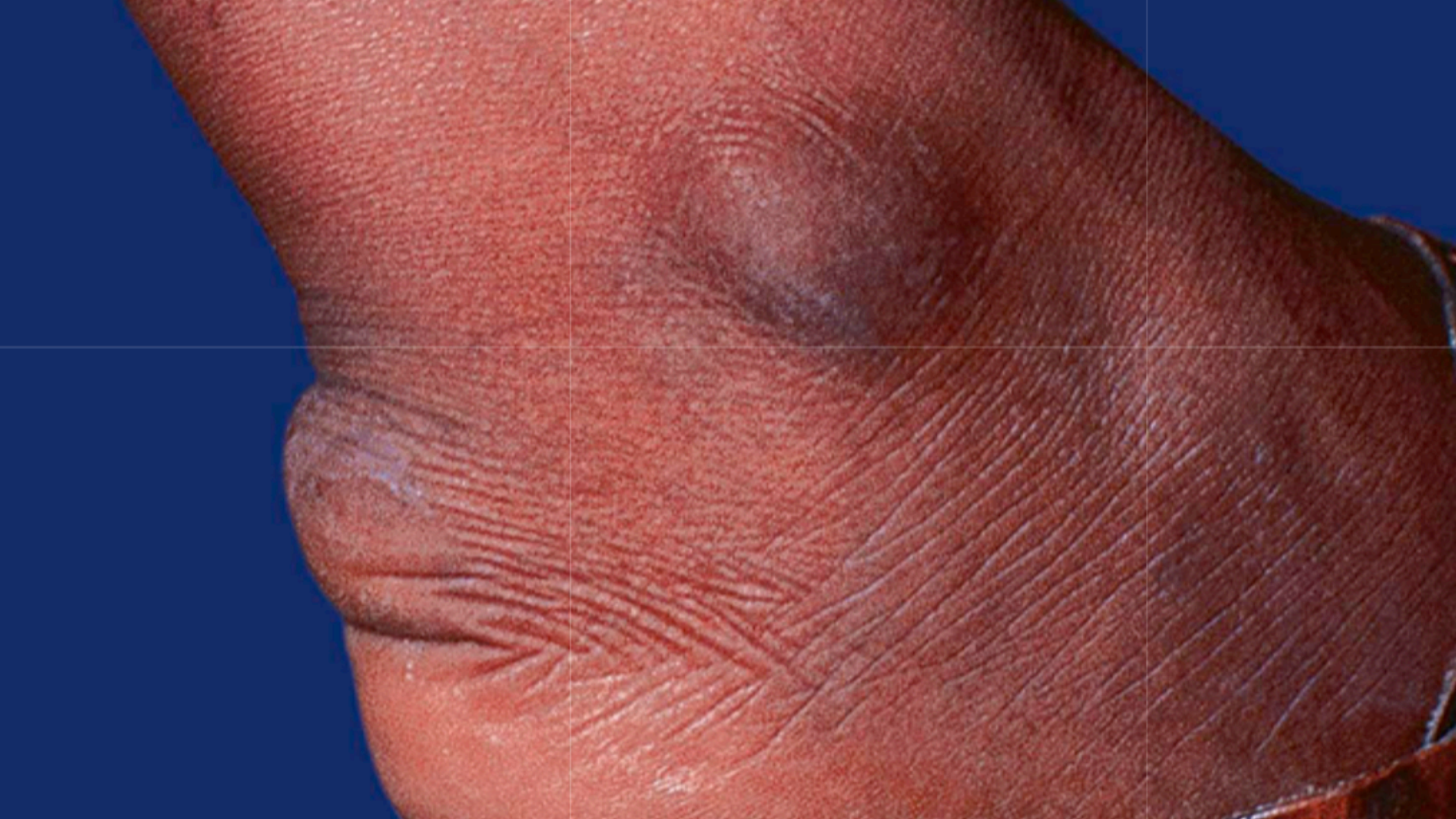
- Most common cutaneous xanthoma.
- Occurs mostly near the inner canthus (upper > Lower eyelid)
- Asymptomatic, bilateral.
- Can be associated with any type of primary hyperlipoprotenemia but can also occur without hyperlipidemia (50%).
- Tx: Surgical excision, laser, cryotherapy.

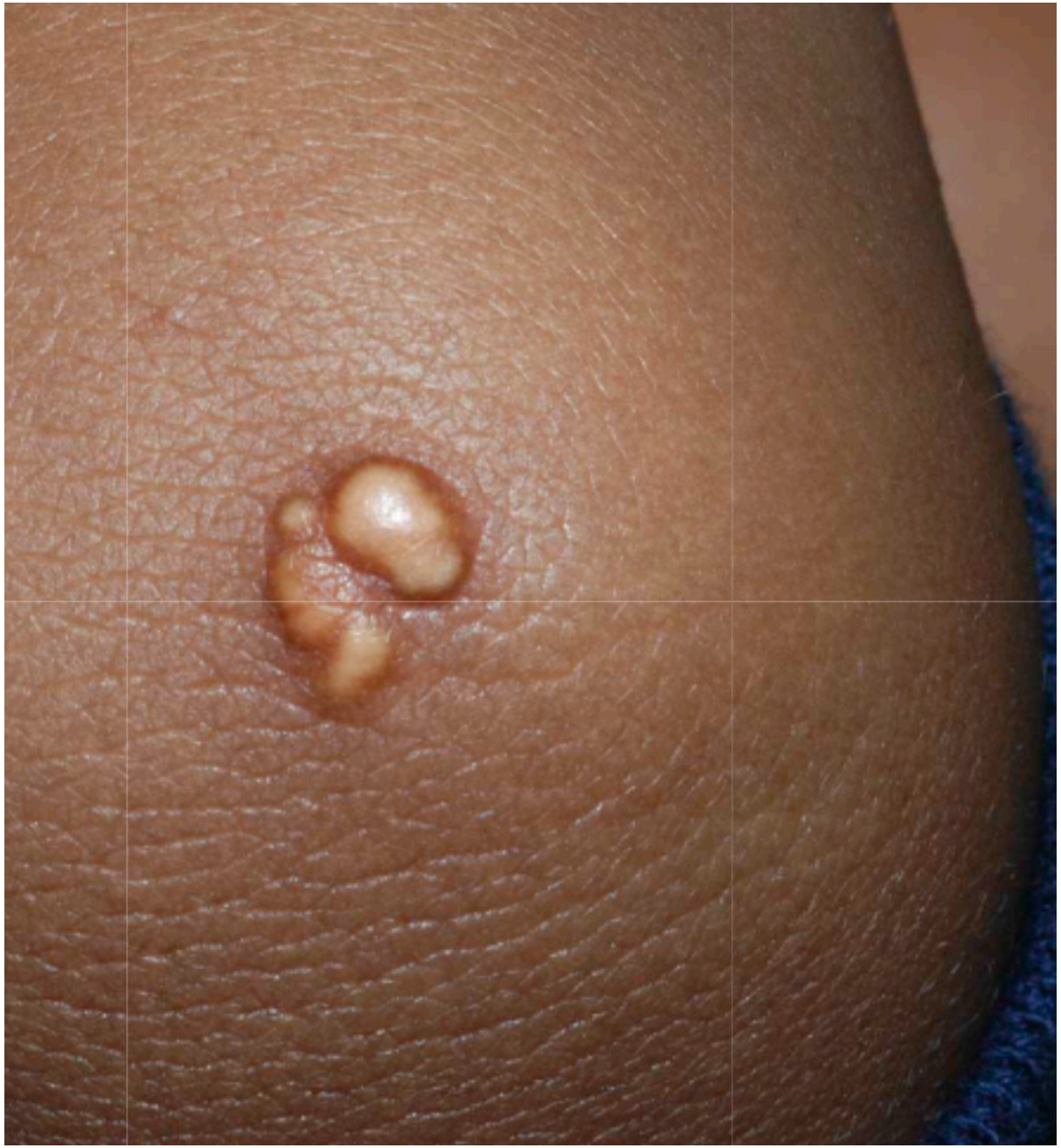


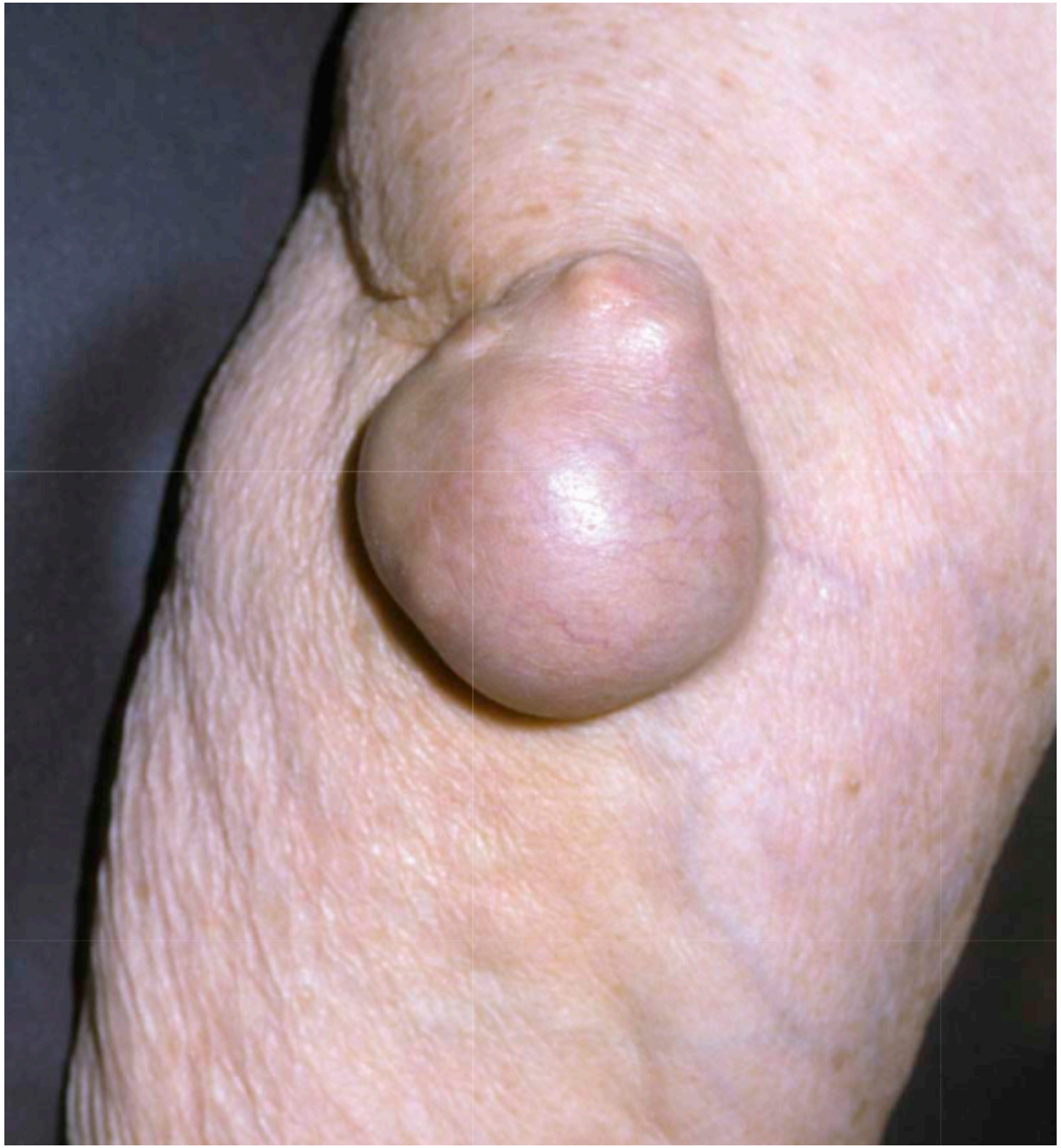
Tendinous/Tuberous Xanthomas

- **Tendinous xanthoma:**
- Commonly seen on the achilles tendon, followed by the hand/feet, elbows/knees.
- The least responsive to treatment.
- Most seen in patients with familial hypercholesterolemia.

- **Tuberous Xanthoma:**
- Firm, non-tender, cutaneous and subcutaneous yellowish nodules on the extensor surfaces.
- Mostly associated with familial dyslipoprotenemia.
- May resolve after months of treatment with lipid lowering agents.

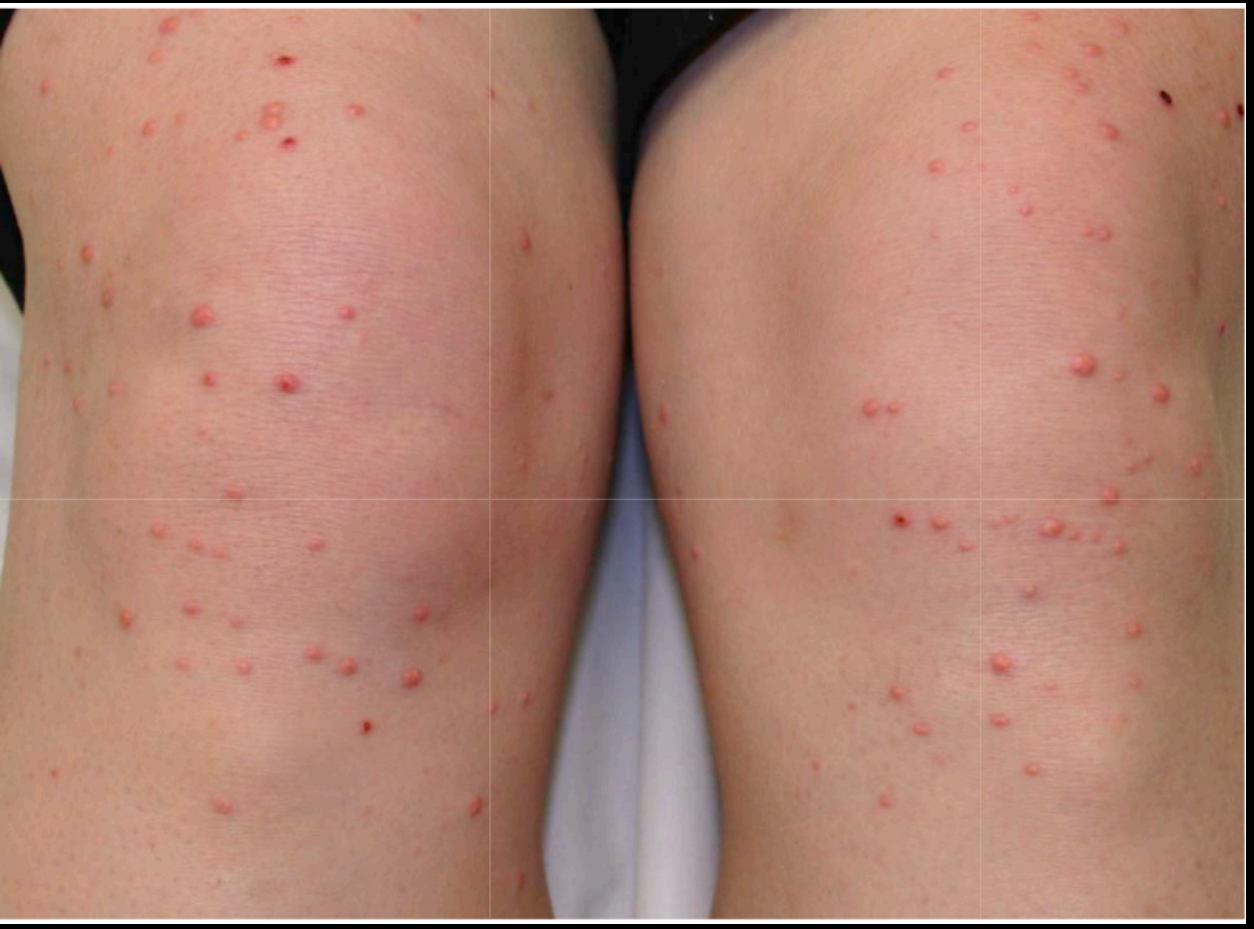


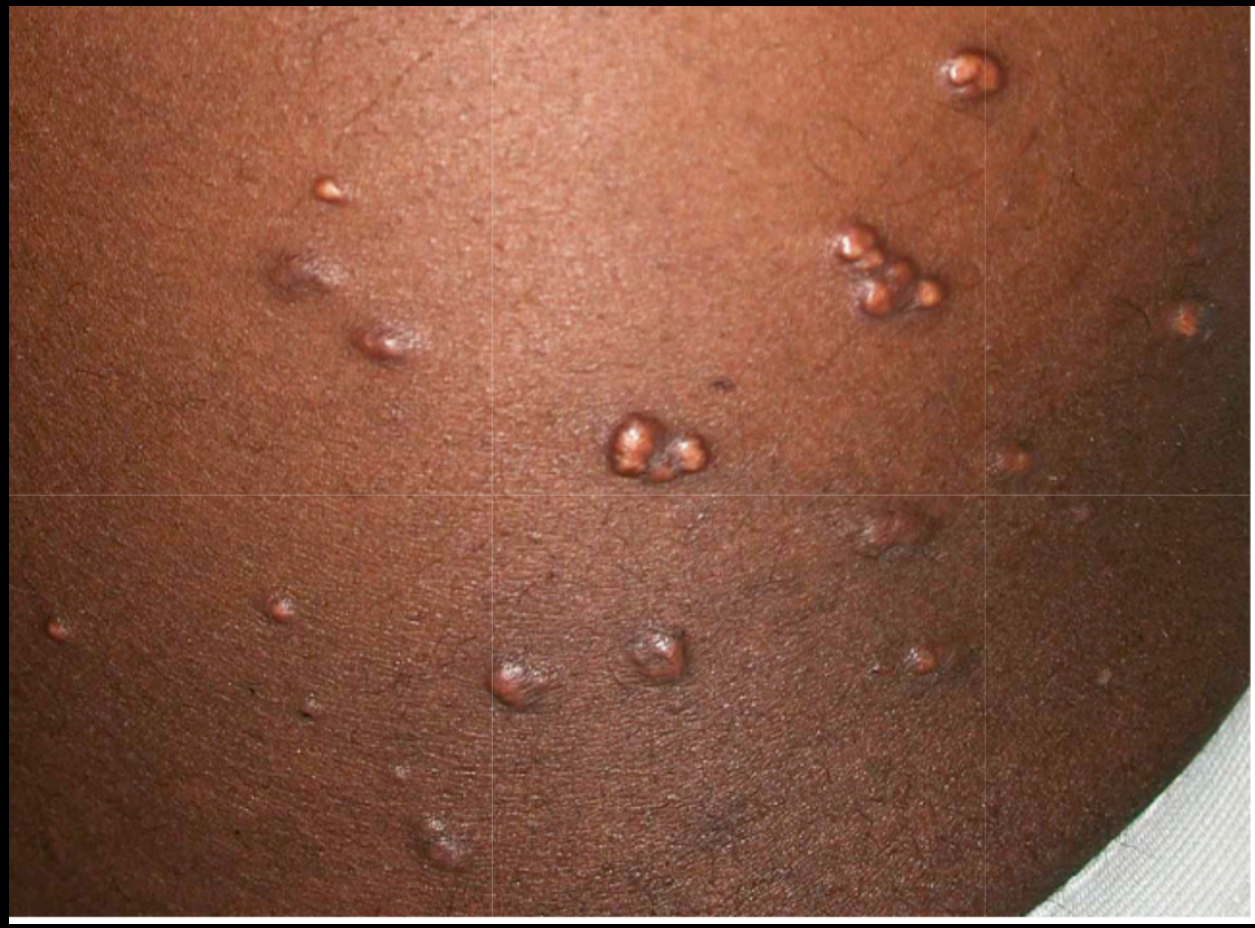




Eruptive Xanthomas

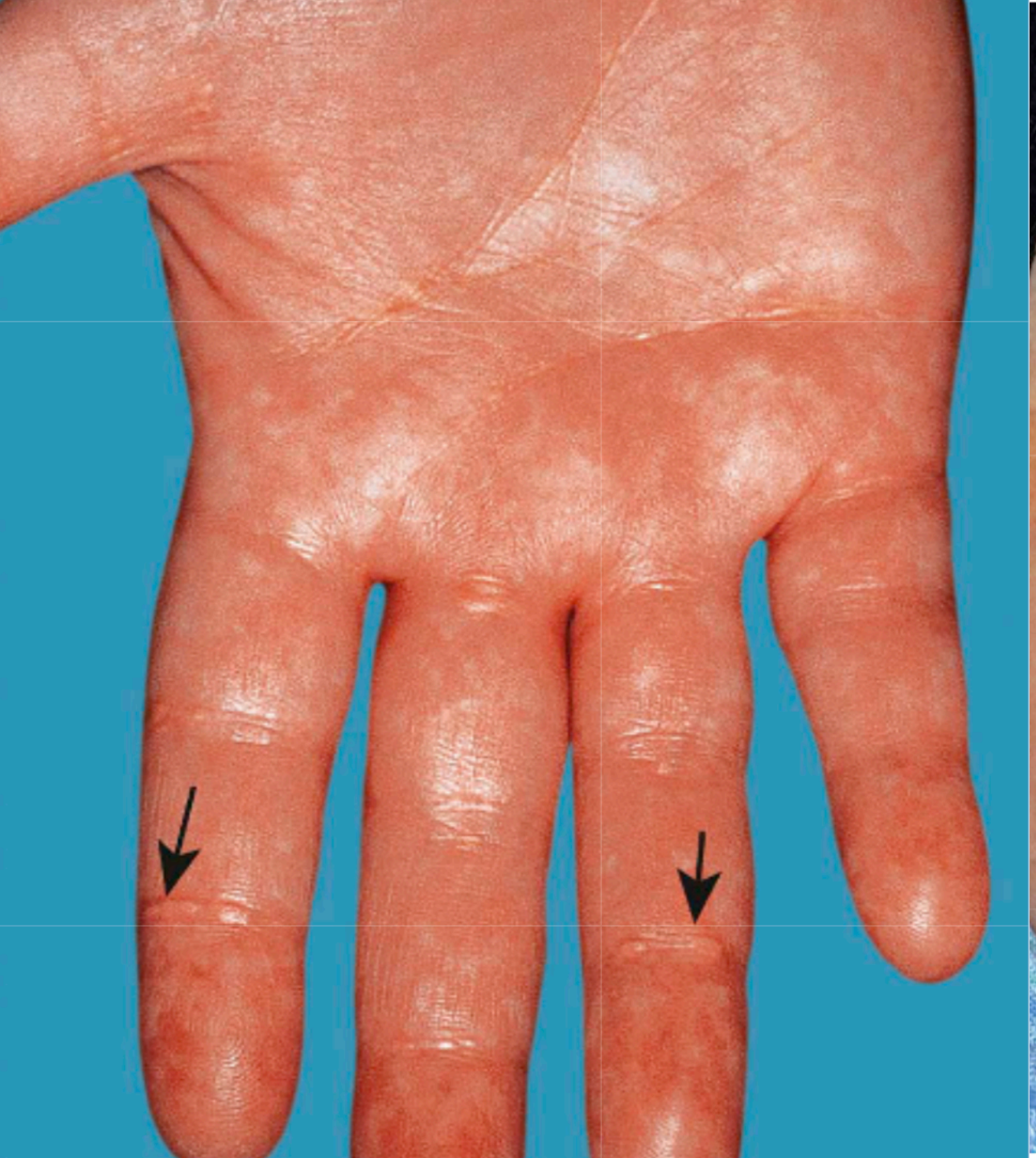
- Painless, yellowish papules on an erythematous base, that present as grouped lesions on the extremities (knees), trunk, elbows and buttocks.
- Usually associated with hypertriglyceridemia.
- Could be seen in poorly controlled diabetes and acute pancreatitis.
- Usually resolves in a few weeks after therapy.

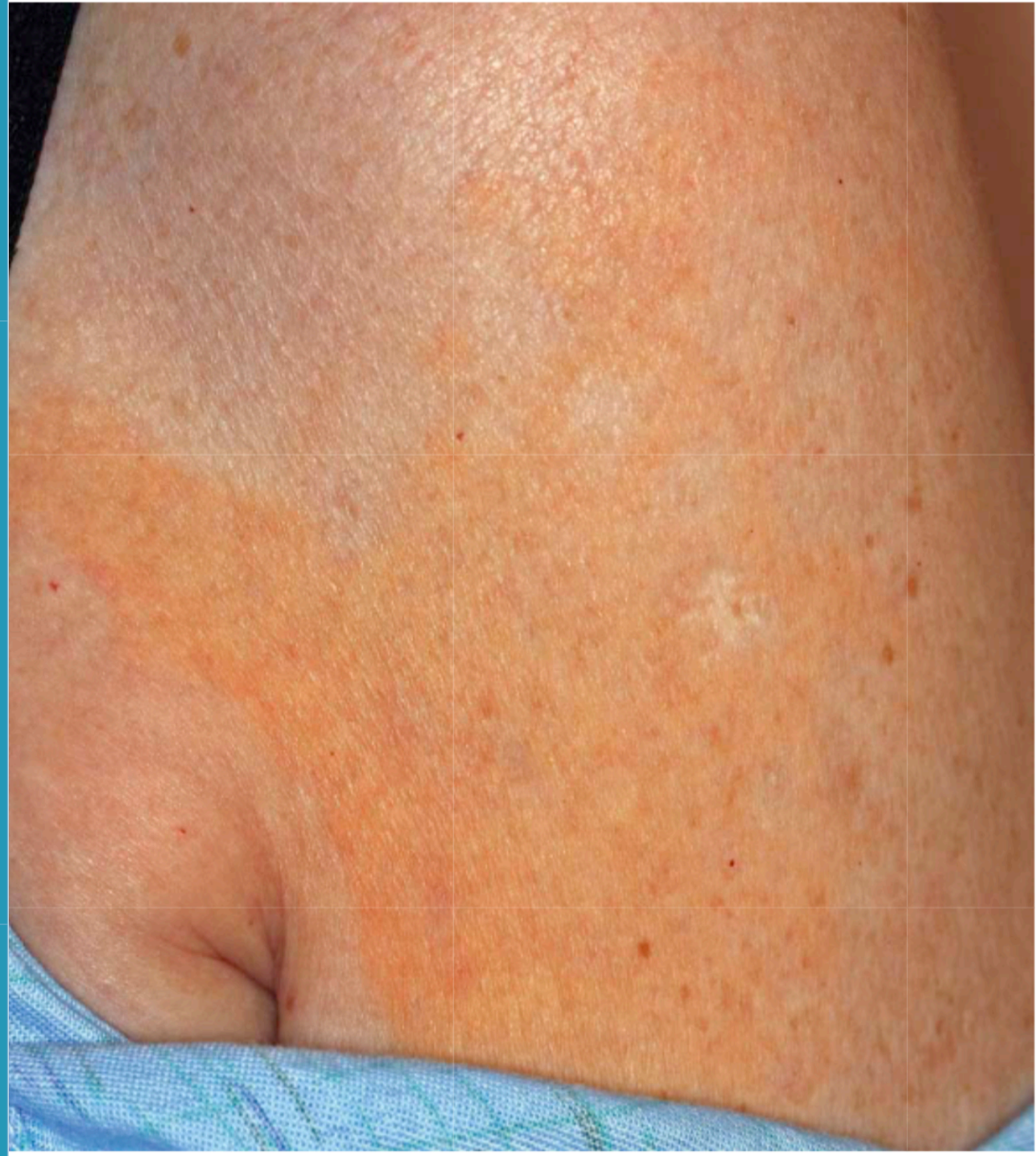




Planar Xanthomas

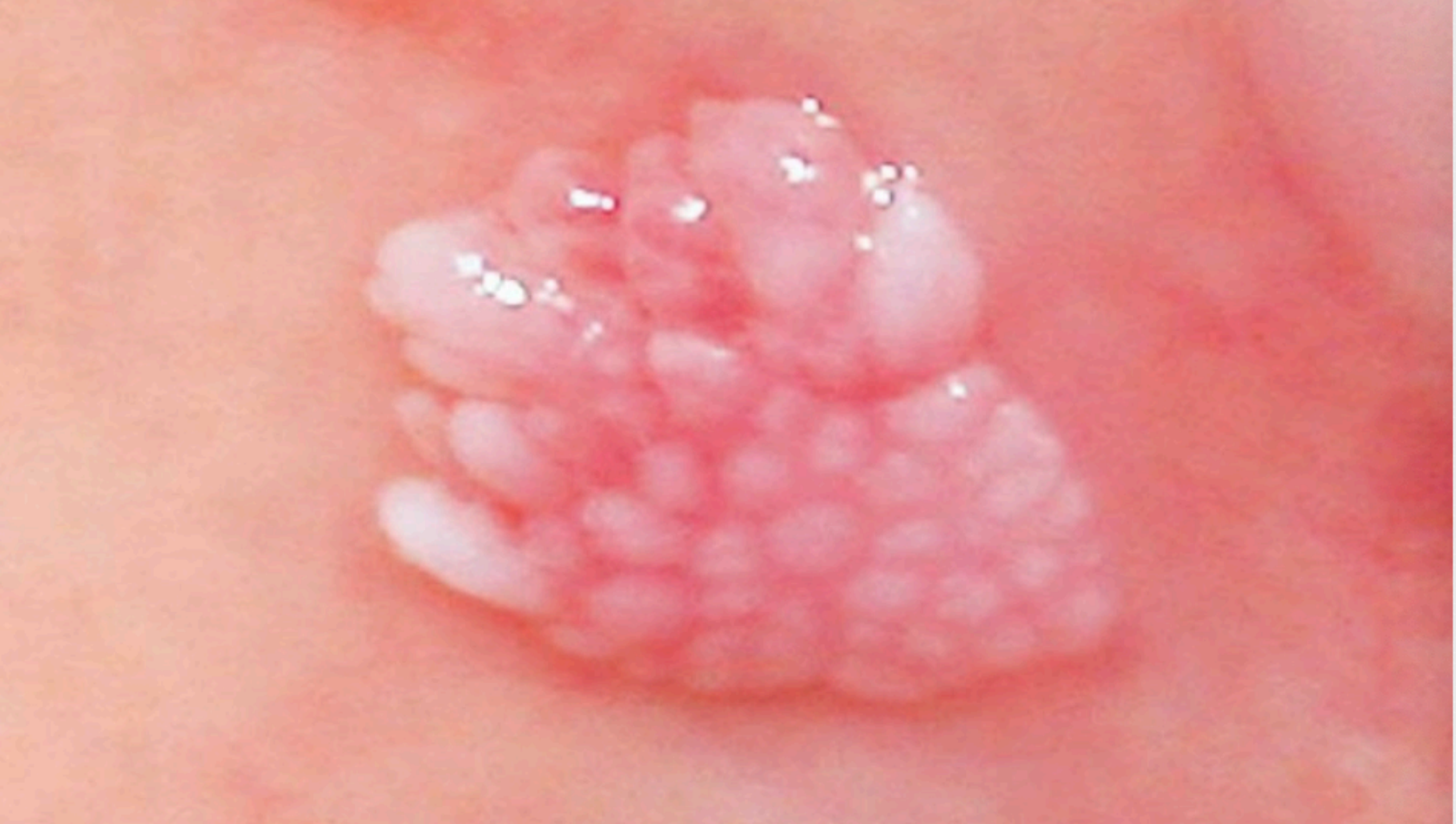
- Yellowish-orange papules, patches or plaques.
- Plane xanthomas of the palmar creases (**Xanthoma striatum palmare**) are almost diagnostic of dysbetalipoprotenemia.
- Plane xanthomas of cholestasis may occur as as complication of liver disease (plaques on the hands and feet).
- Plane xanthomas can occur in a normolipemic patient and could signal the presence of an underlying monoclonal gammopathy.





Verruciform Xanthomas

- Asymptomatic solitary plaques averaging 1 to 2 cm in diameter.
- Occur primarly in the mouth but sometimes in anogenital sites.
- Usually no associated hyperlipidemia.
- Lesions persist for years.



Amadani1@ksu.edu.sa