7-Cutaneous Manifestations of Systemic Diseases (Purpura & Vasculitis)

Objectives:
Not given

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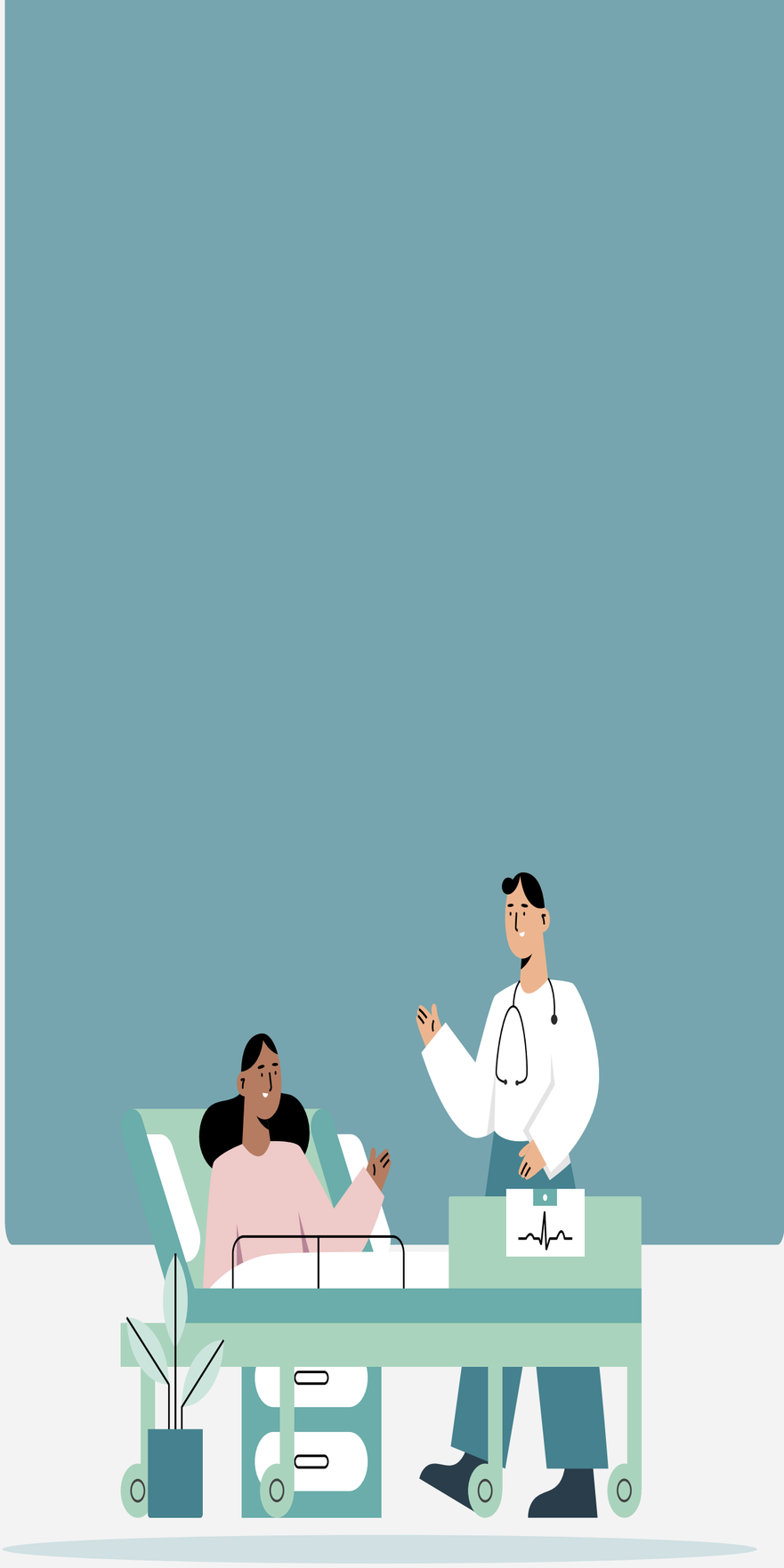
AlJouharah AlShunaifi, AlHanouf AlJaloud, Nouf AlOtaibi.
Revised by: Saif Al Meshari, Rotana Khateeb

References: Doctor slides, Team 436

Color Index:

- Important
- Doctor's Notes
- Extra

Editing File

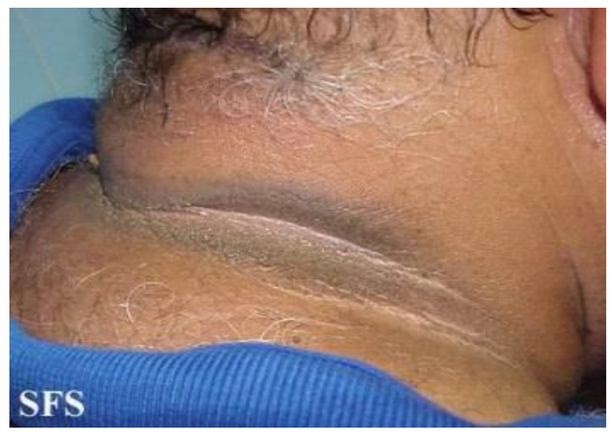


Cutaneous manifestations of Endocrine disorders

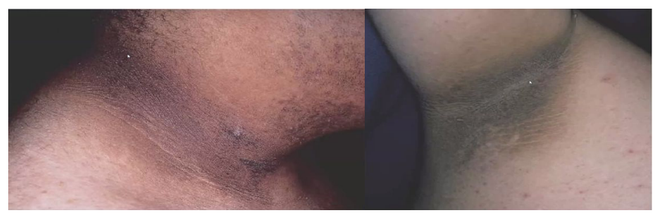
Diabetes Mellitus

1. Acanthosis Nigricans (AN)

- Hyperpigmented velvety plaques of the flexures. The face, external genitalia, medial thighs, dorsal joints, lips and umbilicus can be involved in extensive cases.
- Brown color is an increase in thickness + Velvety texture (Velvety : ملمس مخملي)



- **Causes:**
  - Obesity.
  - Endocrinopathy:
    - Diabetes, thyroid disease, insulin resistance, acromegaly, cushing syndrome, hypothyroidism, and hyperandrogenic states such as HAIRAN syndrome (hyperandrogenism, insulin resistance, and acanthosis nigricans)
  - Internal malignancy (GIT, lung, and breast) the most common is adenocarcinoma of stomach.
    - The process is paraneoplastic, they usually have very extensive effects on the eyelids, knuckles, and palms (tripe palms) like the lining of a sheep's stomach.
  - Medications:
    - Nicotinic acid, niacinamide, testosterone, OCP, and glucocorticoids.
  - Familial.
  - Idiopathic.
- **Pathogenesis:**
  - Genetic sensitivity of the skin to hyperinsulinemia aberrant keratinocyte and fibroblast proliferation stimulated by excess growth factor (e.g., Insulin like growth factor)
- **Treatment:**
  - Treat the underlying cause:
  - Tight blood glucose control,
  - Treatment of underlying malignancy,
  - Weight control if obese
  - Discontinuation of offending agent
  - Do you think that the hyperpigmentation is due to increased melanin? No its due to thickening. So, if someone comes to the clinic using a bleaching agent won't work here.
  - We can give keratolytic agent to reduce the thickness of the skin.

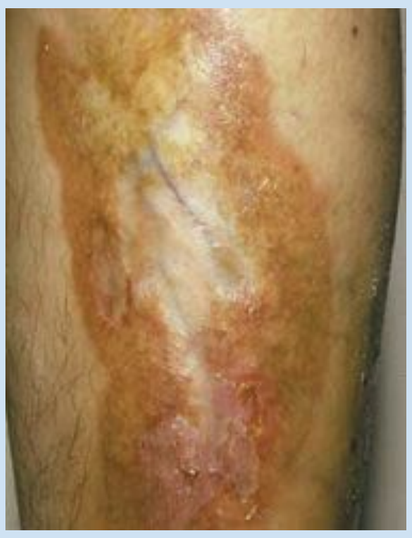


- **Skin tag** (pedunculated skin papule) :
  - Has the same causes/pathogenesis as acanthosis nigricans due to obesity and insulin resistance
  - Its **thickening of the epidermis** in the flexures area.

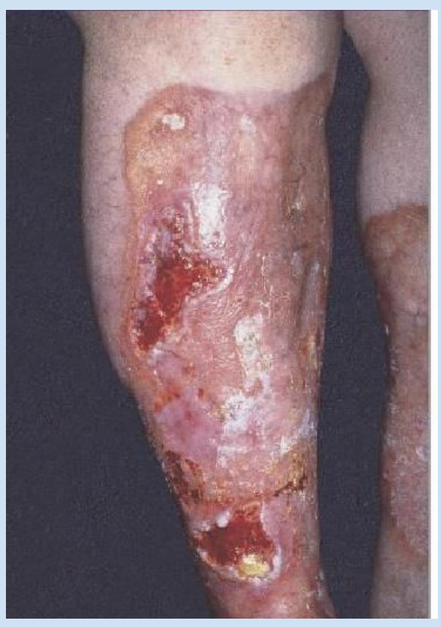
Cutaneous manifestations of Endocrine disorders

Diabetes Mellitus

2. Necrobiosis Lipoidica Diabeticorum (NLD)



Well demarcated atrophic plaque erythematous yellowish orange telangiectasia and ulcer.



From the name:

Necrobiosis: it's a necrosis of the collagen.

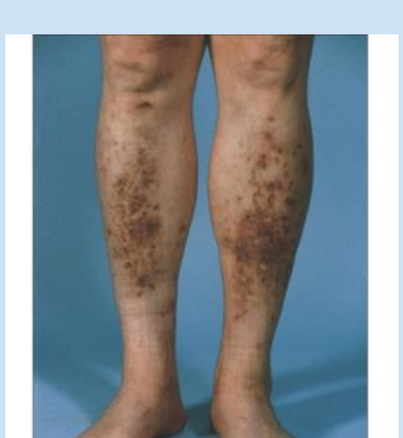
Lipoidica : lipid deposition in the dermis.

Diabeticorum :because it's caused by DM.

Asymptomatic seen in the shins of the leg, may progress to atrophy or ulcers

- Patients classically present with **single or multiple red brown papules**, which progress to sharply demarcated yellow-brown/orange **atrophic**, **telangiectatic** plaques with a **violaceous, irregular border.**
- Commonly they developed secondary erosion or ulcers.
- Common sites include **shins** followed by ankles, calves, thighs and feet.
- **Ulceration** occurs in about 35% of cases.
  - Cutaneous anesthesia, hypohidrosis and partial alopecia can be found.
- **Pathology:**
  - Palisading granulomas containing degenerating collagen (necrobiosis). With lipid deposition giving lesion yellowish hue
  - Pathogenesis is thought to involve the nonenzymatic glycosylation of dermal collagen and elastin
- Approximately 60% of NLD patients have diabetes & 20% have glucose intolerance. Conversely, up to 3% of diabetics have NLD. So not very common.
  - Women are more affected than men.
- **Treatment:**
  - Ulcer prevention.
  - No impact of tight glucose control on likelihood of developing NLD.
  - **Intralesional steroids**
  - Aspirin
  - Antiplatelet
  - Pentoxifylline.
  - Perilesional heparin injection to improve vasculopathy

3. Diabetic Dermopathy or "Shin Spots"

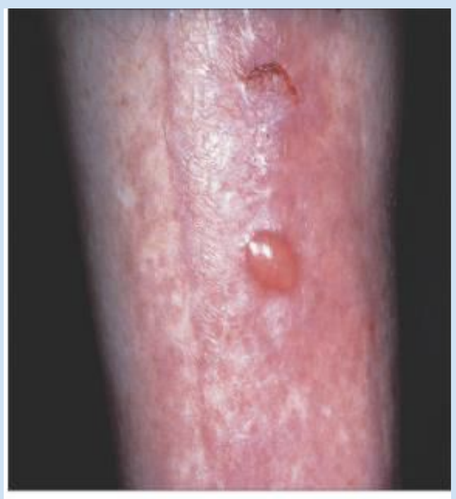


- Most common cutaneous manifestation of diabetes.
- M >F, males
- Over age 50 years with long standing diabetes.
- Possibly related to **diabetic neuropathy** and **vasculopathy**
- There are **bilateral asymptomatic red-brown atrophic macules** on **shins**
- There is no effective treatment.
  - Even tight control of diabetes won't improve it .
- **Describe the lesion:**
  - Start from outside to inside, so bilateral, asymmetrical (symmetrical means mirror like) , primary lesion is flat and small lesion 'macule'. So this is one of the commonest cutaneous manifestation of DM and this is one of the commonest sites.

Cutaneous manifestations of Endocrine disorders

Diabetes Mellitus

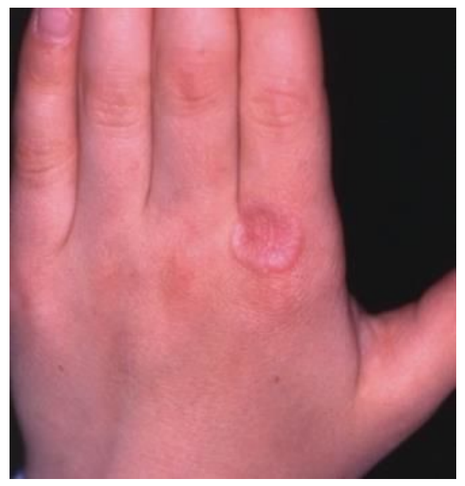
4. Diabetic Bullae or Bullae Diabeticorum



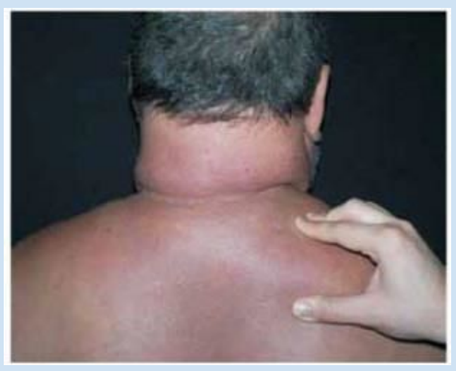
- Rarest cutaneous complications of diabetes.
- M > F, long standing diabetics.
- Trauma and **microangiopathy** may play a role
- **Clinical:**
  - Rapid onset overnight, of painless usually tense blisters on the hands and feet.
  - What type of bullae is this (tense or flaccid)?
    - It's a **tense bullae**, usually flaccid won't present to you at the clinic they will rupture and will present with erosions so you will be lucky if you see one at the clinic.
- **Pathology:**
  - Intraepidermal and/or subepidermal split without acantholysis. DIF "direct immunofluorescence" is negative (to differentiate it from other types of bullae)
- **Treatment:**
  - Spontaneous healing without scarring or treatment

5. Granuloma Annulare

- Why is it called "granuloma annulare"? because it's annular and in biopsy we will see granuloma.
- Association between granuloma annulare and diabetes is controversial.
- Generalized form of GA is the most closely associated with DM. not the solitary ones.
- It has a chronic and relapsing course
- **Treatment:**
  - IL steroid or topical steroids
  - Systemic steroid
  - PUVA "phototherapy"
- **PIC:** Asymptomatic erythematous, red-purple dome shaped papules arranged in annular configuration.



6. Scleredema Diabeticorum



- Thickening of the skin of the upper of the neck and the back.
- **Irreversible.**
- Due to deposition of **myosin** or **hyaluronic acid** in the **dermis**.
- Occurs diabetics with poorly controlled, long-standing disease, and obese men
- Painless, **symmetric woody "peau d'orange" induration** the upper back and neck.
- No specific treatment is available
- Control of hyperglycemia afterward does not improve the scleredema

Cutaneous manifestations of Endocrine disorders

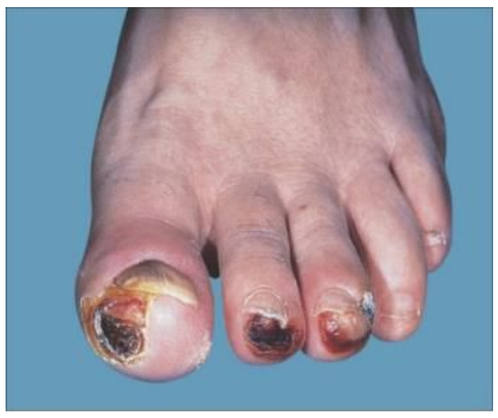
Diabetes Mellitus

7. Cutaneous Infections

Diabetic patients are predisposed to develop cutaneous infections due to poor microcirculation

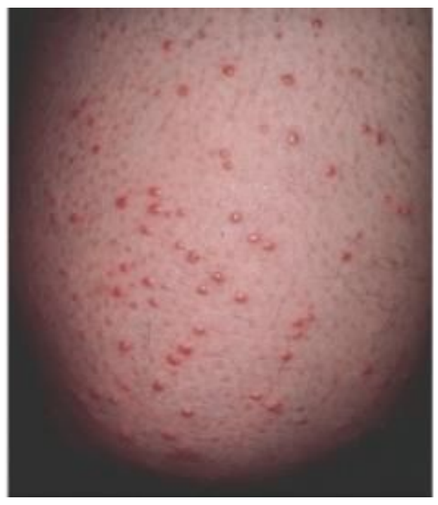
- Bacterial
- Fungal

8. Other Manifestations of DM:



Diabetic neuropathy (peripheral), neuropathic ulcers

What are the type of ulcers? Arterial, neuropathic, venous.

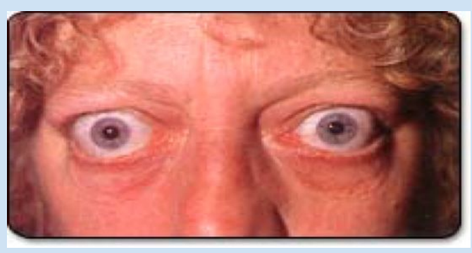


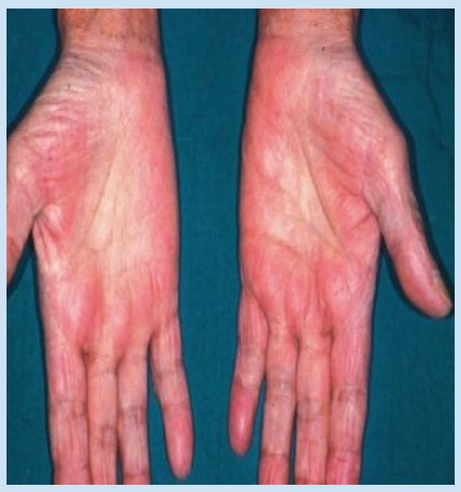
Eruptive Xanthomas

Multiple eruptive erythematous orangish to yellowish papules

Thyroid Disease

Non-specific features of Hyperthyroidism



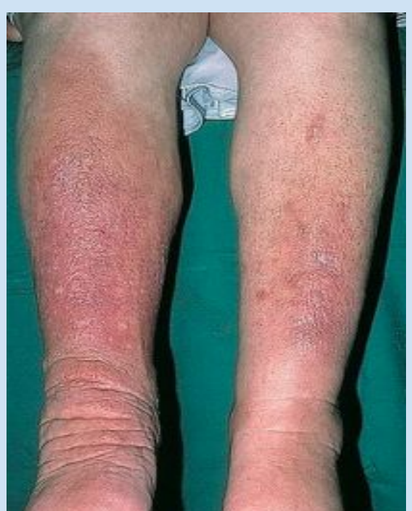


- **Skin:**
  - Warm, and moist
  - Palmar erythema
  - Flushing of head/neck, trunk
- **Hair**
  - Soft/fine/straight
  - Diffuse reversible (Non scarring) alopecia (Telogen effluvium)
- **Nails:**
  - Faster rate of growth
  - Onycholysis
  - Plummer nails: concave deformity with distal onycholysis
- **Pigmentation:**
  - Focal or generalized hyperpigmentation
  - Vitiligo

Table 53.5 Dermatologic manifestations of hyperthyroidism.

DERMATOLOGIC MANIFESTATIONS OF HYPERTHYROIDISM	
Cutaneous changes	Fine, velvety, or smooth skin Warm, moist skin due to increased sweating Hyperpigmentation – localized or generalized
Cutaneous diseases	Vitiligo Urticaria, dermatographism Pretibial myxedema and thyroid acropachy
Hair changes	Fine, thin Mild, diffuse alopecia
Hair disease	Alopecia areata
Nail changes	Onycholysis Koilonychia Clubbing from thyroid acropachy

Thyroid Dermatopathy: Pretibial Myxedema



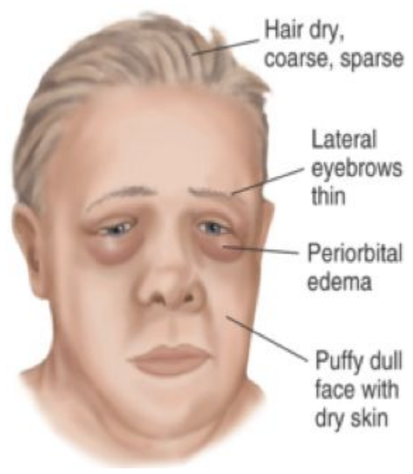
- The most common characteristic features of thyrotoxicosis appearing as Bilateral non-pitting **shiny *waxy* red papule and plaque** having **orange-like appearance** on the shin of tibia 'pretibial area'.
- Due to deposition of **myosin** as in Scleredema Diabeticorum.
- Occurs in **Grave's disease**
  - Remember: General manifestations of Grave's disease are:
    1. Goiter
    2. Exophthalmos
    3. **Pretibial myxedema**
- Clinical findings are due to **increase in hyaluronic acid within the dermis**
- **Treatment** includes:
  - High potency topical steroids
  - And/or intralesional steroid injection

Cutaneous manifestations of Endocrine disorders

Thyroid Disease

Non-specific features of Hypothyroidism

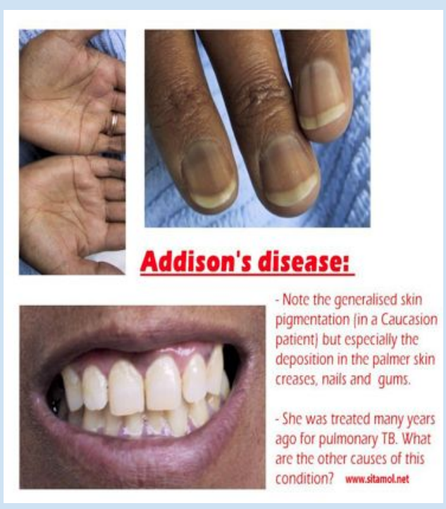
- Remember: hypothyroidism could be associated with other autoimmune conditions such as vitiligo and alopecia areata
- **Skin:**
  - Cool and pale
  - Xerosis (dryness of skin)
  - Pruritus (itching)
  - Hypohidrosis (diminished sweating)
  - Yellowish hue secondary to carotenemia. Slow growing ridged and brittle hair and nails.
  - Swollen lips, broad nose, puffy dull face , macroglossia
  - Generalized myxedema: swollen waxy appearance
  - Purpura secondary to poor wound healing
  - Periorbital edema



- **Hair:**
  - Dry, brittle, coarse hair
  - Diffuse alopecia, telogen effluvium
  - Loss of the lateral third of eyebrow (madarosis)

Other endocrine disorders

Hypocorticism (Addison disease)
Primary adrenal insufficiency



- **Generalized hyperpigmentation**
  - (why? ACTH has same precursor as MSH)
  - that is more prominent in **light exposed areas**, scars, genitalia, palmar and finger creases, nevi and under the nails. The pigmentation characteristically affects the mucous membranes.
- Loss of **pubic** and **axillary** hair in females. Adrenal synthesize androgen
- **Improvement of acne** Adrenal synthesize androgen

So if a patient presents with similar symptoms,
what lab investigations should you order?

1. Cortisol levels
2. Electrolytes (hyponatremia/hyperkalemia)

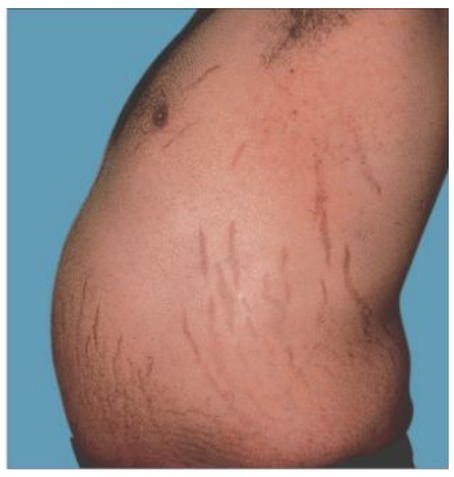
DERMATOLOGIC MANIFESTATIONS OF HYPOTHYROIDISM	
Skin changes	Dry, rough, or coarse; cold and pale, boggy and edematous (myxedema) Yellow discoloration as a result of carotenemia Easy bruising (capillary fragility)
Cutaneous diseases	Ichthyosis and palmoplantar keratoderma Eruptive and/or tuberous xanthomas
Hair changes	Dull, coarse, and brittle Slow growth (increase in telogen hair phase) Alopecia of the lateral third of the eyebrows
Nail changes	Thin, brittle, striated Slow growth Onycholysis (rare)

SELECTED DERMATOLOGIC MANIFESTATIONS OF ADDISON'S DISEASE

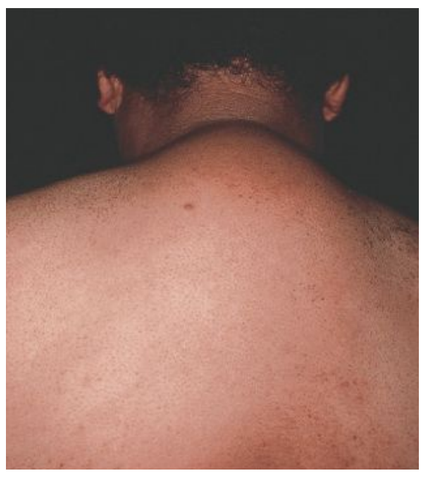
- Hyperpigmentation (MSH-like effect due to secretion of ACTH)
  - Diffuse with sun-exposed accentuation
  - Sites of trauma
  - Axillary, perineum, and nipples
  - Palmar creases
  - Nevi
  - Mucous membranes
  - Hair
  - Nails
- Loss of ambisexual hair in postpubertal women
- Fibrosis and calcification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

Cushing's Syndrome

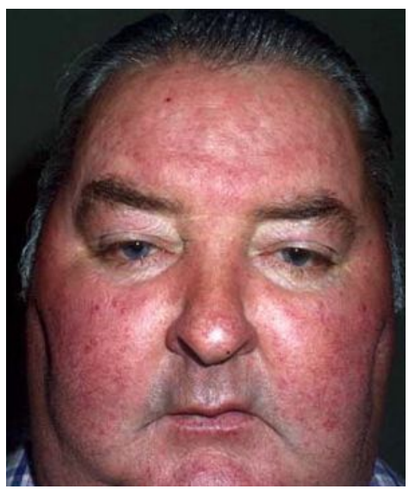
- Endogenous or exogenous (as side effect of steroid)
- **Buffalo hump**
  - Deposition of fat over the clavicles and back of the neck
- **Moon face**
  - Rounded erythematosus face with telangiectasia
- **Truncal /central obesity** with slender wasting limbs.
- Dermal atrophy in form of (**Striae** rubrae distensae)
- **Hirsutism**, **acneiform rash,** rosacea , androgenetic alopecia.
- **Easy bruising** of the skin on simple trauma.
- **Clitoromegaly** and male pattern alopecia (Hamilton pattern).
- Purpura due to delayed wound healing . and increase risk of infections



Striae distensae



Buffalo hump



DERMATOLOGIC MANIFESTATIONS OF CUSHING'S DISEASE (SYNDROME)
Altered subcutaneous fat distribution*
• Rounded facies • Fullness of the cheeks ('moon' facies) • Dorsal cervical vertebral fat deposits (buffalo hump) (Fig. 53.20) • Pelvic girdle fat deposition • Reduced fat in the arms and legs
Skin atrophy
• Global atrophy with epidermal and dermal components affected • Multiple striae on abdominal flanks, arms, and thighs (Fig. 53.21) • Cutaneous fragility and prolonged wound healing • Purpura with minor trauma due to reduced connective tissue support
Cutaneous infections
• Pityriasis (tinea) versicolor • Dermatophytosis and onychomycosis • Candidiasis
Appendageal effects
• Corticosteroid-related acne • Hirsutism

Metabolic disorders

Hyperlipoproteinemia

Type I

- Familial lipoprotein lipase deficiency (AR) or apoprotein CII deficiency
- Increased chylomicrons
- Associated with hepatomegaly, pancreatitis

Type IIa

- Familial hypercholesterolemia, common hypercholesterolemia (AD)
- Increased LDL

Type IIb

- Familial hypercholesterolemia (AD)
- Increased LDL and VLDL

Type III

- Familial Dysbetalipoproteinemia (AR)
- Increased IDL

Type IV

- Familial hypertriglyceridemia (AD)
- Increased VLDL

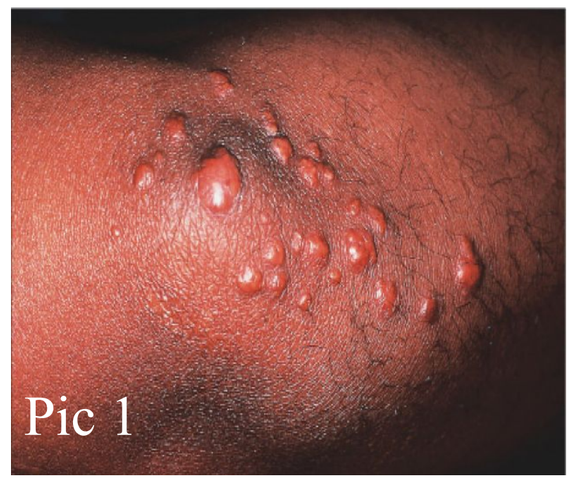
Type V

- Familial type V hyperlipoproteinemia, familial lipoprotein lipase deficiency (AD)
- Increased chylomicrons and VLDL

Xanthomatosis:

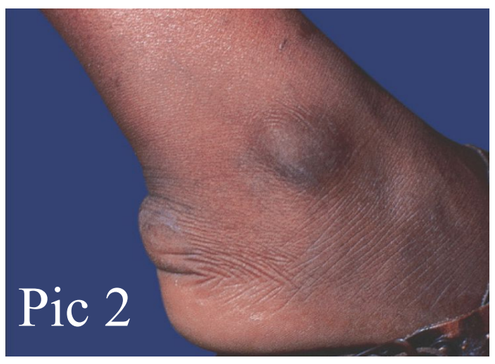
1. Tuberous Xanthoma

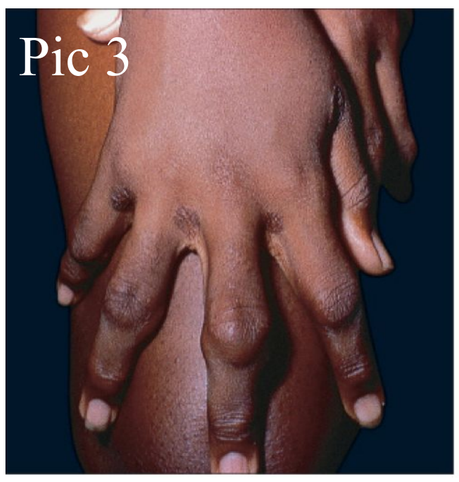
- Flat or elevated, rounded, grouped, yellowish-orange nodules over joints (particularly elbows and knees)
- Types II, III, and IV
- Biliary cirrhosis
- **Pic1:** Tuberous xanthomas of the knee, note the yellowish hue.


Pic 1

2. Tendinous Xanthoma

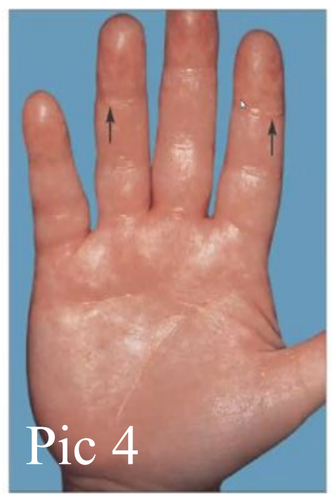
- Papules or nodules over tendons:
  - extensor tendons on dorsum of hands, feet, and **achilles**
- Types II, III
- **Pic 2:** Linear swelling of the Achilles area representing a tendinous xanthoma in a patient with dysbetalipoproteinemia.
- **Pic 3:** Tendinous xanthomas of the fingers in a patient with homozygous familial hypercholesterolemia.


Pic 2


Pic 3

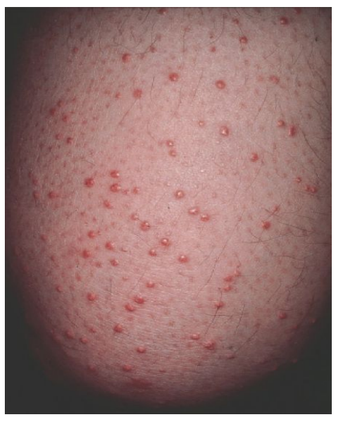
3. Palmar Xanthoma

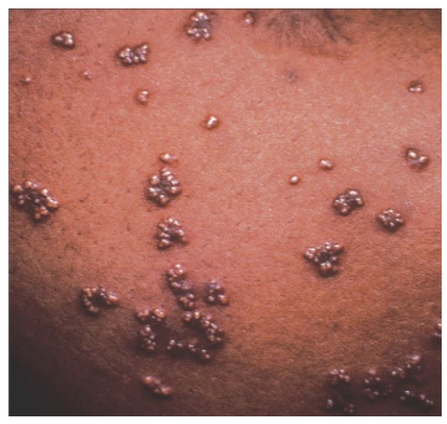
- Nodules and irregular plaques on palms and flexural surfaces of fingers
- Type III
- **Pic 4:** Plane xanthomas of the palmar creases in a patient with dysbetalipoproteinemia (arrows).

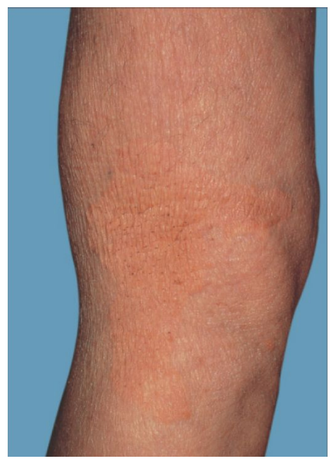
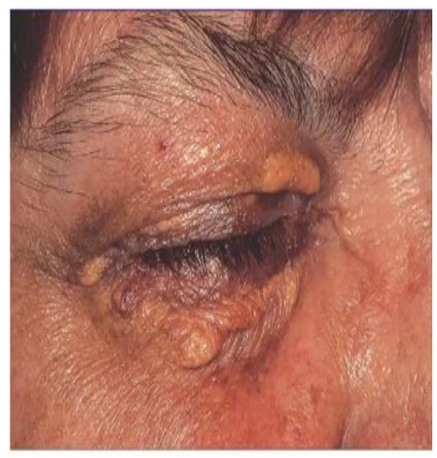

Pic 4

4. Eruptive Xanthoma

- Painless Small yellow/orange/red papules appearing in crops over entire body → buttocks, flexor surfaces, arms, thighs, knees, oral mucosa and **may koebnerize**
- Associated with markedly elevated or abrupt increase in **triglycerides** (elevated **chylomicrons**)
- Types l ,lll , lV , and V
- **Causes:**
  - **Diabetes**, obesity, pancreatitis, chronic renal failure, hypothyroidism, estrogen therapy, corticosteroids, isotretinoin, acitretin

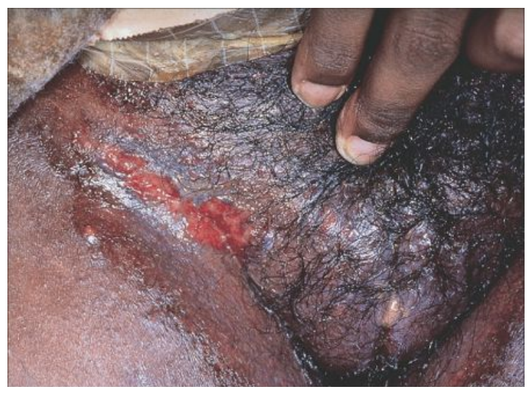




5. Planar Xanthoma	• Flat macules or slightly elevated plaques, yellow/tan color • Associated with biliary cirrhosis, biliary atresia, myeloma, monoclonal gammopathy, lymphoma. • Characteristically around eyelids, neck, trunk, shoulders, or axillae • Types ll,lll • **Pic:** Plane xanthoma in a patient with a monoclonal IgG gammopathy 
6. Xanthelasma does not necessarily means there is hyperlipidemia, however, u should check the lipid).	• Most common type of xanthoma • **Eyelids** • Usually present without any other disease, but can occur in types II and III • Common among women with hepatic or biliary disorders, also seen in myxedema, diabetes • Best treated with surgical excision or laser • **Pic:** Xanthelasma palpebrarum with typical yellowish hue. ○ Yellow plaques around the eye 

Cutaneous manifestations of Gastrointestinal disorders

Manifestations of Inflammatory Bowel Disease (IBD)

Fissures and Fistula	CD > UC	Commonly involves perineum and groin area associated with edema and inflammation
Oral Crohn	CD	Edema, cobblestone, ulcerations, nodules
Metastatic Crohn's	CD	Nodules, plaques, ulcerations; commonly on extremities or intertrigenous regions mimics Erythema Nodosum When you do biopsy you will find finding similar to intestinal crohn's disease 
Erythema Nodosum	UC > CD	Tender red nodules on anterior lower legs; precedes or occurs simultaneously with IBD flares
Pyoderma Gangrenosum	UC > CD	Papules, pustules, hemorrhagic blisters -> enlarge, ulcerate with dusky undermined edges; exacerbated by trauma; frequently on legs
Pyoderma Vegetans	UC	Vegetating plaques, vesiculo-pustules of intertriginous areas; heal with hyperpigmentation; when process involves mucosa =Pyostomatitis vegetan
Chronic Aphthous Ulcers	UC > CD	Identical to common aphthous ulcers; develop with IBD flares
Other less common manifestation: Epidermolysis bullosa acquisita, erythema multiforme, urticaria, clubbing, psoriasis, vitiligo. Note: CD = Crohn's disease, UC = Ulcerative Colitis		

Cutaneous manifestations of Gastrointestinal disorders

Manifestations of Inflammatory Bowel Disease (IBD)

Erythema Nodosum:

- Erythematous, tender subcutaneous nodules on commonly anterior shins;
- also seen on thighs, lateral aspects of lower legs, arms, and face, bilateral, symmetrical.
- **Very painful** by history and **very tender** by examination.
- Often accompanied by:
  - fever, chills, malaise, and leukocytosis
  - 70% have associated arthropathy of the adjacent joint .
- Occurs at any age, but most prevalent **between 20 and 30 years** of age Usually in teenagers and early twenties and more in female. If you work with pediatric you will see it there
- **Cause:**
  - MNEMONIC: **SHOUT BCG**

    S= Sarcoid, Sulfa drugs, Strept.

    H= Histoplasmosis

    O= Oral contraceptives, pregnancy

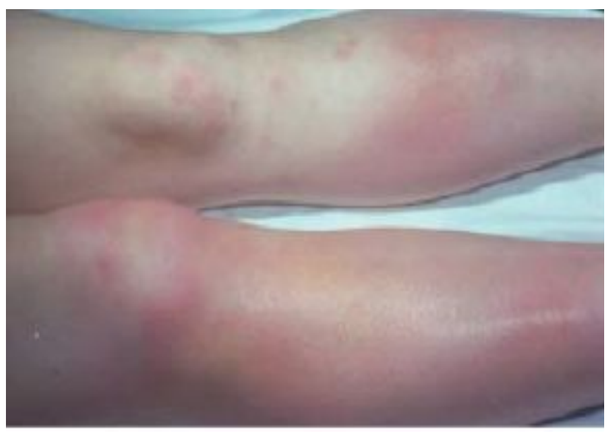
    U= Ulcerative colitis

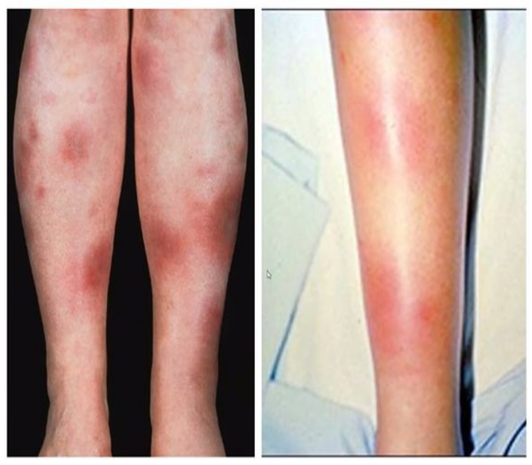
    T= TB

    B= Behcet's

    C= Crohn's , Chlamydia

    G= GI (Yersinia, salmonella)
  - + lymphoma and leukemia





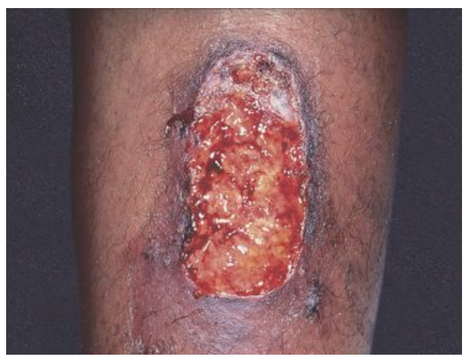
- **Work up:**
  - Hx (exclude drugs , hx of infection & GI symptoms)
  - CBC, diff. x
  - ESR x
  - Throat swab
  - ASO titre
  - CXR
  - PPD
  - Stool for occult blood
  - **Histology:** very deep skin biopsy as its inflammation of the subcutaneous tissue
    - Septal panniculitis without vasculitis
- **Treatment:**
  - Bed rest, **Spontaneous resolution** usually occurs within three to six weeks **without scarring.**
  - NSAIDs such as indomethacin or naproxen
  - Systemic steroids effective **in severe cases** and resistant and can be dangerous if infection is etiology
  - Potassium iodide. *In chronic cases*

Cutaneous manifestations of Gastrointestinal disorders

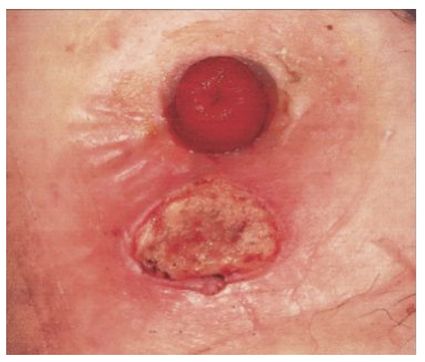
Manifestations of Inflammatory Bowel Disease (IBD)

Pyoderma gangrenosum

- **Acute painful leg ulceration** lesion with a **well-defined, undermined violaceous** border.
- start as small pustules, which subsequently burst and expand to form the larger noninfectious ulcer.
- 1.5-5% of patients with **IBD** develop PG
  - Mostly associated with ulcerative colitis. Also, with Crohn's disease
- Associated with leukemia, myeloma, monoclonaL gammopathy (IgA), polycythemia, chronic active hepatitis, HCV, HIV, SLE & pregnancy
- Associated with PAPA syndrome:
  - Pyogenic arthritis, pyoderma gangrenosum, severe cystic acne
- May be associated with arthritis
- Positive **pathergy test.**
  - Patient with PG have one finding called pathergy sign or test. it means they may develop PG at the site of trauma or surgery.



- **Four Types:**
  - Ulcerative, Pustular, Bullous, Vegetative
- **Pic:** Distinct rolled edges and show satellite violaceous papules that break down and fuse with central ulcer (Single Well demarcated ulcer with violaceous (بنفسجي) border with central slough materials)
- **Histology:** Massive dermal edema with epidermal neutrophilic abscesses. (Not specific. so its diagnosis of exclusion you have to exclude all other causes of ulcers like infections and malignancy)
- **Treatment:**
  - Treat the underlying cause
  - Potent topical steroids or IL steroids
  - Topical tacrolimus
  - Systemic steroids
  - Cyclosporine ,Sulfapyridine, sulfasalazine, and dapsone
  - Infliximab
  - Other agents:
    - thalidomide, SSKI, azathioprine, cyclophosphamide, chlorambucil

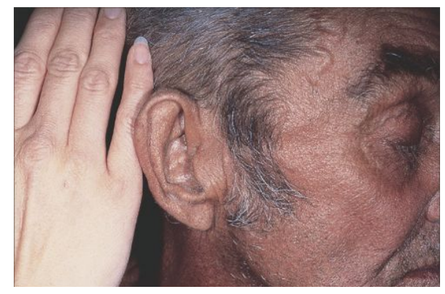


Peristomal Pyoderma Gangrenosum

Cutaneous Manifestation of Liver diseases

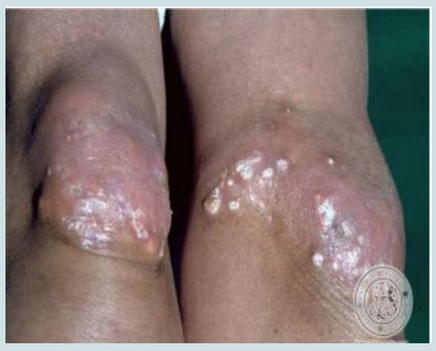
- **Pruritus:**
  - Generalized itching especially in the presence of biliary obstruction or jaundice.
  - Check thyroid,LFT, renal profile Jaundice.
- **Spider naevi:** small telangiectatic blood vessels especially on the face and upper chest.
- **Palmar erythema.**
- **Thinning of the hair** and sometime loss of sexual hair in the axillary and pubic areas.
  - because liver usually metabolize estrogen it won't be metabolized . these areas are androgen dependent and those patients will have high estrogen.
- **Porphyria cutanea tarda.**
- **Xanthoma**
- Acne, gynaecomastia, purpura, collateral veins, striae, palmar erythema, dupuytren's contracture, and white nails.

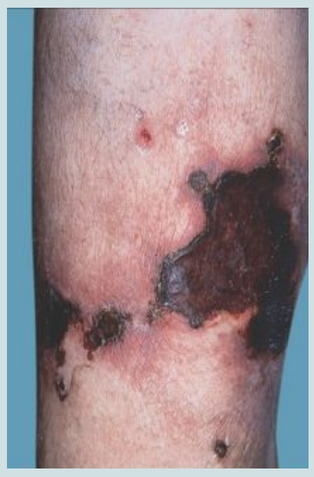
Cutaneous Manifestation of Liver diseases

Hemochromatosis	Inherited disorder with impaired iron metabolism so they have iron overload resulting is liver cirrhosis and diffuse bronzing of the skin (darkening of the skin) 

End Stage Renal Disease (ESRD) and Dialysis

Pruritus	the most common cutaneous manifestation of ESRD
Half and half (Lindsay's) nails	Edema of the nail bed and capillary network and give the **proximal half** of the nail an **opaque white** appearance and **redness of the distal part**. 
Metastatic Calcification	Deposition of calcium within tissue secondary to abnormal calcium and or phosphate metabolism. They develop **secondary** and **tertiary hyperparathyroidism.** It can manifest in the skin as benign nodular calcifications (calcinosis cutis as in picture) or as a more serious condition (calciphylaxis) with an associated mortality rate between 60-80% • **Calciphylaxis:** ○ Calciphylaxis presents as **painful purpuric plaques** and **retiform purpura** with progression to **ulceration** and **necrosis**. ○ A dialysis patient with picture of necrosis you have to think of calciphylaxis.it's a serious disease up to 60% mortality rate due to secondary staph infection, a deep biopsy will show calcification of the media of the blood vessels. ○ Distribution of the lesions may predict prognosis; ■ patients with acral lesions have a better outcome that those with proximally located lesions ○ **Histological finding**: ■ Medial calcification, **intimal hyperplasia** of **small arteries** and arterioles ○ **Management** of these patients includes ■ Total or subtotal parathyroidectomy (if PTH levels are elevated) ■ Wound care ■ And avoidance or precipitating factors. ○ Mortality is related to Staphylococcal superinfection of ulcers with resultant sepsis
Porphyria Cutanea Tarda (PCT)	• Pathogenesis may be related to the **suboptimal clearance of uroporphyrins** (product of heme synthesis pathway) from the circulation which is a photosensitizer. • Photodistributed, blisters, bullae, skin fragility, hyperpigmentation and hypertrichosis. • Usually it Is inherited disease but can be a accrued as in renal and liver failure. • **Vampire therapy:** the patient when they go to the sun the develop severe cutaneous finding and need frequent blood transfusion because they have defective heme synthesis pathway. just a way to remember, they go out and night and look for blood. • **Pseudo-PCT:** ○ Similar clinical and histological findings of PCT, in setting of **normal porphyrin profile.** ○ Usually due to certain medications such as **furosemide**, naproxen, tetracycline, nalidixic acid, or amiodarone or renal disease.





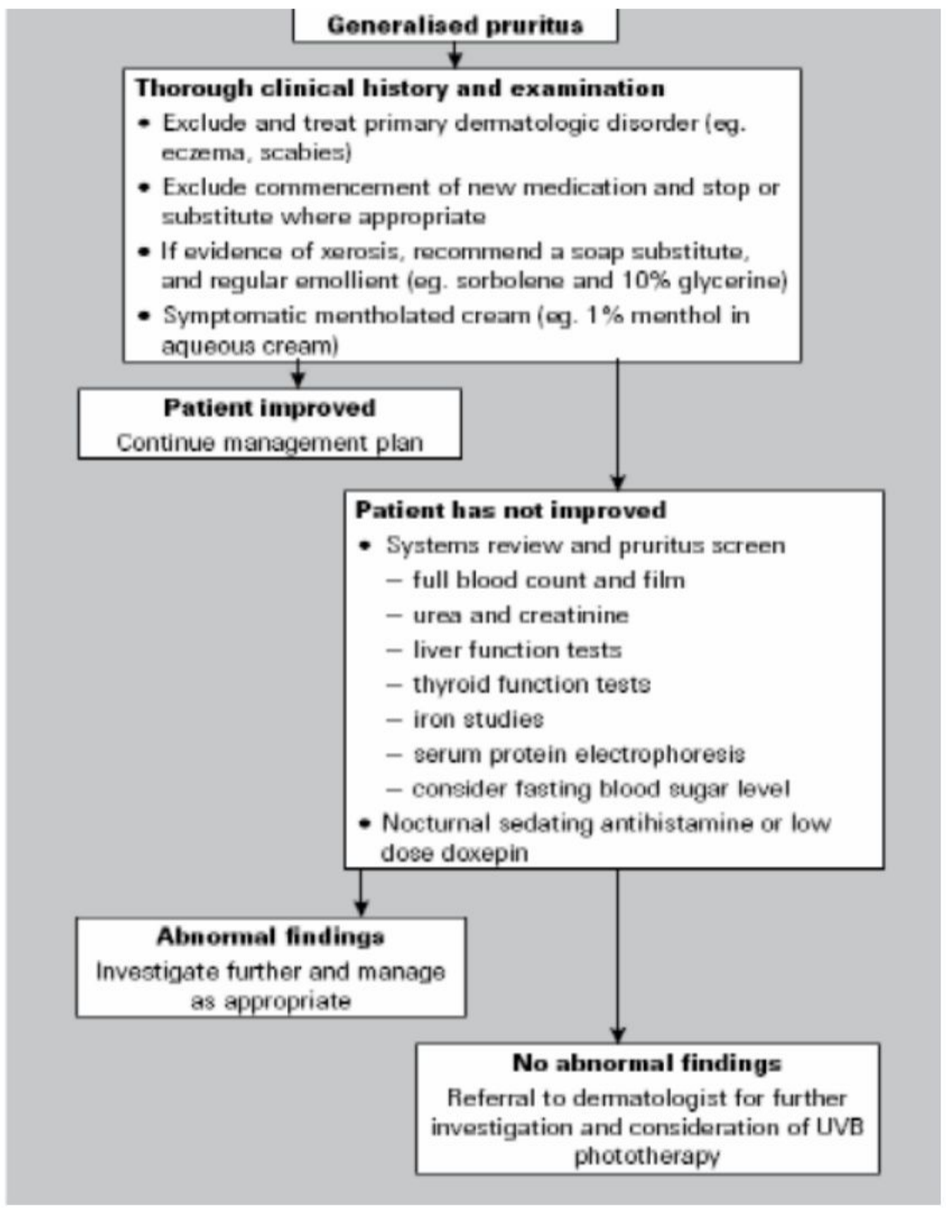
Calciphylaxis

Generalized Pruritus

- Generalised pruritus in the absence of a rash requires investigation and exclusion of an underlying systemic disorder .
- They don't have primary or secondary lesion that helps in diagnosing the disease
- It is important to distinguish these from an underlying primary skin disease such as scabies or eczema
- **Conditions that cause pruritus:**
  - Chronic Renal Disease (Most common manifestation CRF is pruritus) uremia is also the **most common metabolic cause of pruritus**
  - **Cholestasis** (primary biliary cirrhosis)
  - Endocrine Disorders:
    - **Thyrotoxicosis** – often due to **increased skin blood** flow which raises skin temperature
    - **Hypothyroidism** – pruritus **secondary to the dry skin**
    - DM
  - **Malignancy:**
    - Most common association: **Hodgkin's** disease and **polycythemia rubra vera**, Even solid malignancy as paraneoplastic syndrome
  - HIV infection
  - Iron deficiency anemia , can cause severe itching and when u treat it the puriritis will go
  - Chronic infection, Parasitic infection
  - **Neurological:** tabes dorsalis
- **Workup for Generalised Pruritus:**
  - History and Physical exam. Ask for symptoms of Thyroid, renal, and liver disease
  - CBC, diff, Blood film to rule out hematological malignancy
  - Stool for O&P 'ova and parasite', occult blood
  - CXR
  - Thyroid, renal, and liver function tests

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.

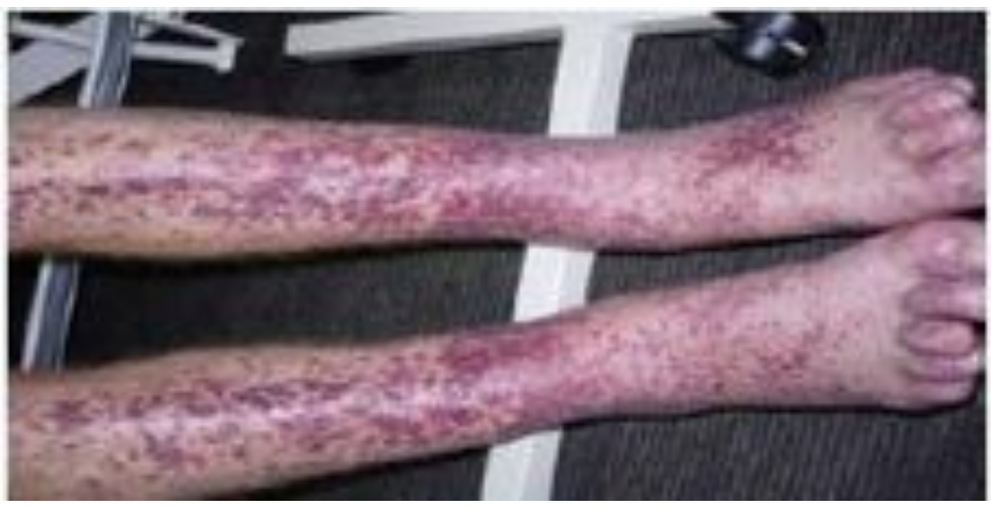
POSSIBLE LABORATORY STUDIES IN THE EVALUATION OF PRURITUS
• Erythrocyte sedimentation rate (ESR) • Complete blood cell count (CBC) with differential and platelet count • Blood urea nitrogen, creatinine • Liver transaminases, alkaline phosphatase, bilirubin • Fasting glucose • Thyroid function tests (thyroid 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

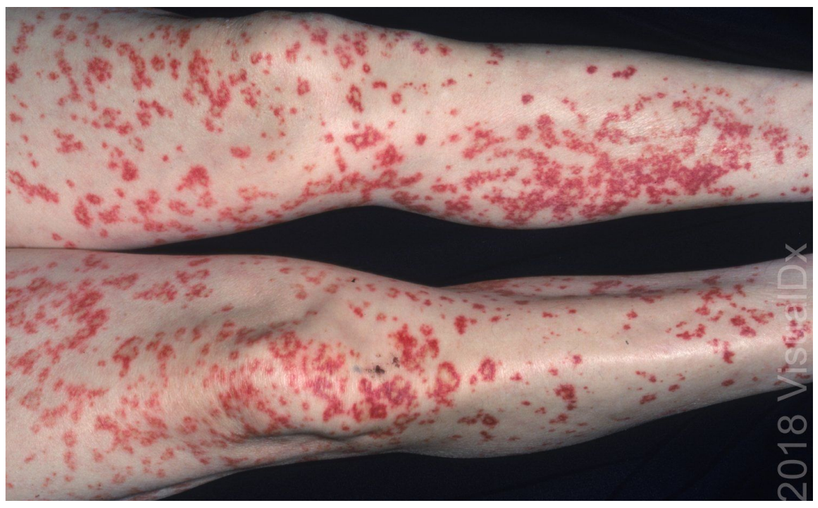


Part 2 Purpura and vasculitis

Purpura:

- **Definition:**
  - Visible hemorrhage into the skin or mucous membrane its a condition of red or purple discolored spots on skin that do not blanch (doesn't disappear) on applying pressure
    - Using glass if blanchable → Erythema (dilated vessel), if not blanchable → purpura.
- Subdivided as a follow:
  - Petechiae less than or equal 4 mm
  - Purpura (>4mm - < 1cm), which can be either Palpable or nonpalpable(macular)
    - What we care about here is palpable purpura caused by inflammation (vasculitis)
  - Ecchymoses > or equal to 1 cm
- **Causes:**
  - **Platelet disease**
    - **Platelet Disorders**
      - Thrombocytopenia
      - Platelet Dysfunction
  - **Coagulation defect**
    - **Coagulation Factor Deficiency**
      - **Congenital**
        - Factor VIII Deficiency
        - Factor IX Deficiency
        - Von Willebrand's disease
      - **Acquired**
        - Disseminated Intravascular Coagulopathy
        - Liver disease
        - Uremia
        - Vitamin K deficiency
  - **Blood vessel wall pathology**
    - **Congenital**
      - Hereditary Hemorrhagic Telangiectasia
      - Ehlers-Danlos Syndrome (Type IV)
    - **Acquired:**
      - Inflammation (Vasculitis)
      - Trauma
      - Vitamin c deficiency (scurvy)





Part 2 Purpura and vasculitis

Vasculitis:

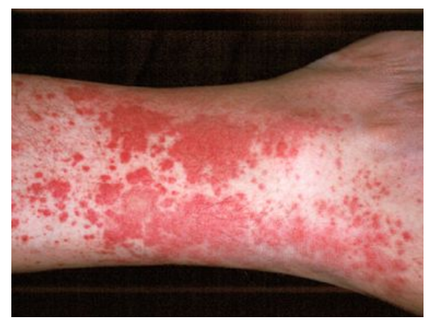
- **Definition:**
- A clinicopathologic process characterized by inflammatory destruction of blood vessels that results in occlusion or destruction of the vessel and ischemia of the tissues supplied by that vessel. Vasculitis could present with either one of these : purpura, nodules, ulceration, livedo reticularis.
- **Classification**:
  - **Large-vessel vasculitis** we don't care about it they don't present to dermatologist
    - Aorta and the great vessels (subclavian, carotid) Claudication, blindness, stroke
  - **Medium-vessel vasculitis** they don't present to dermatologist.
    - Arteries with muscular wall organ blood vessels like renal arteries, coronary arteries Mononeuritis multiplex (wrist/foot drop), mesenteric ischemia, cutaneous ulcers.
  - **Small-vessel vasculitis** what we care about and present to us
    - Capillaries, arterioles, venules, Palpable purpura, glomerulonephritis, pulmonary hemorrhage

Table 26.2 Chapel Hill consensus classification. IMP

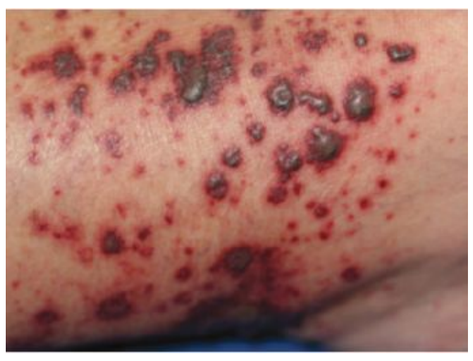
CHAPEL HILL CONSENSUS CLASSIFICATION
Large-vessel vasculitis
• Giant cell arteritis • Takayasu's arteritis
Medium-vessel vasculitis
• Classic polyarteritis nodosa • Kawasaki disease
Small-vessel vasculitis
• Wegener's granulomatosis • Churg–Strauss syndrome • Microscopic polyangiitis (polyarteritis)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

Cutaneous small vessel vasculitis

- Is the most common type of vasculitis and it primarily affect post-capillary venules in the skin
- **Pathogenesis:**
  - Many forms of small-vessel vasculitis are felt to be caused by circulating **immune complexes type 3 immune reaction.**
  - These lodge in vessel walls and activate complement



- **Palpable** purpura is the hallmark
- Pinpoint to several centimeters not the size of the lesion it means the involved area.
- The commonest cause esp in pediatric is post Streptococcal infection
- 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** buttocks too
- Mild pruritis, fever, malaise, arthralgia and/or myalgia may occur
- 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
- **Describe this lesion:** multiple dusky , red papule And blood fluid vesicle and haemorrhagic bulla. You can simply say it's palpable purpura instead of dusky red papule.



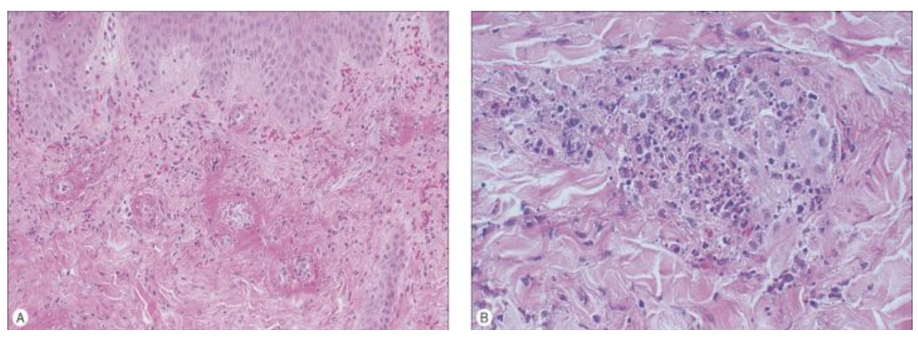
- Hemorrhagic vesicles or bullae may develop

Part 2 Purpura and vasculitis

Vasculitis:

Cutaneous small vessel vasculitis Cont.

- **Course:**
  - Typically resolve in 3 to 4 weeks
  - Residual post-inflammatory hyperpigmentation may be seen
  - Self-limiting if only skin
  - May recur or become chronic
  - The prognosis is **good in the absence of internal involvement.**
- **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 , Protein & casts.**
  - **Histology** We need 2 biopsies
    - Angiocentric segmental inflammation, endothelial cell swelling, fibrinoid necrosis of blood vessel walls and a cellular infiltrate composed of neutrophil with RBC extravasation.



- **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
  - Referral for nephrology or pediatrics

The doctor went through them:

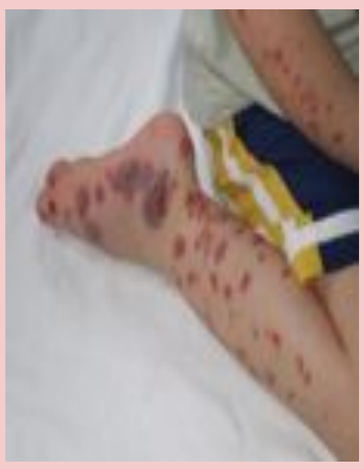
Table 3. Causes of cutaneous vasculitis[5,8]

Infections Bacterial Viral Mycobacterial	• Streptococcal, meningococcal, urinary tract infections • Hepatitis B and C, HIV • 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

- **If 12 years old patient present with purpura in the ER .what will you do?**
  - Ask about history of infection, review medication like antibiotic .
  - all the features of CTD (joint pain)
- What is your next step after history and examination?
  - We need to two set of investigation:
    - **to know the cause:**
      - CBC, strep throat culture or ASO titer, Hep B & C serologies and ANA
    - **to look for complication (small vessels are also present in organs):**
      - Renal profile and urine analysis , if kidney is affected they will present RBC cast
    - Then take biopsy (2 biopsy) one for histology and one for immunofluorescence" from fresh lesion with 48 hours to rule out Henoch-schonlein purpura, (they will have IGA).
  - Even if urine analysis comes negative don't release the patient they may develop cast later on repeat the analysis after one month.

Part 2 Purpura and vasculitis

Vasculitis:

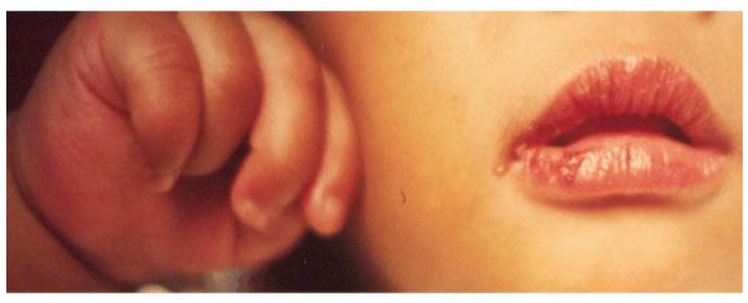


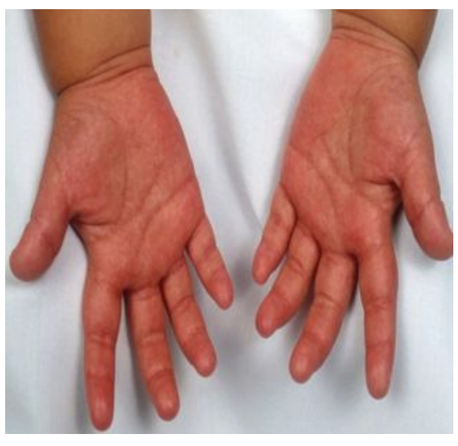
Henoch Schönlein purpura (HSP)
IgA Vasculitis

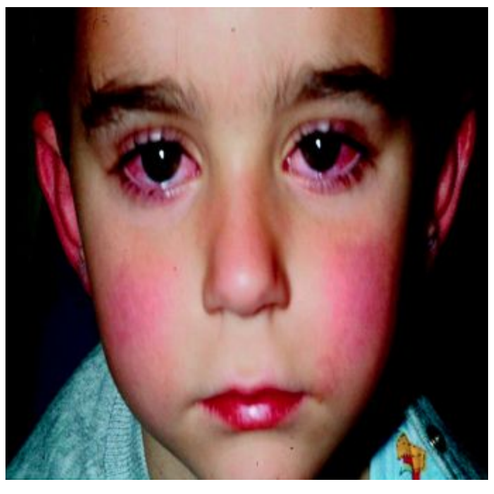
- Primarily occurs in male children
- One of the forms of idiopathic Small vessels vasculitis
- peak age 4-8 years
- Adults may be affected
- A viral infection or streptococcal pharyngitis are the usual triggering event, Group A Streptococcus
- In about 40 % of the cases the cutaneous manifestations are preceded by mild fever, headache, joint symptoms, and abdominal pain for up to 2 weeks
- **Characterized by:**
  - Intermittent palpable purpura
  - Arthralgia
  - Abdominal pain
  - Renal disease
- Typically, purpura appears on the extensor surfaces of the extremities dependent area
- 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
- Add up the investigation :IgA, C3 and fibrin depositions have been demonstrated in **biopsies** of both involved and uninvolved skin by immunofluorescence techniques.
  - IgA Immune complex deposition in vascular walls
- **Treatment:**
  - Supportive (bed rest, pain relieve,etc).

Mucocutaneous lymph node syndrome (Kawasaki's disease).

- It's not vasculitis its mentioned here because they do have coronary artery disease.you are the one will inform pediatrician about it.
- Predominantly seen in children less than 5 years of age.
- Occurs most often in Japan .but I have seen it here
- To make the diagnosis a patient should have a **fever** above 38.3 C for **5 days** plus **4 of the 5 following criteria:**
  1. **Edema of hands and feet**
  2. **Polymorphous** rash exanthem
  3. **Nonpurulent** bilateral **conjunctival injection**
  4. Changes in the lips and oral cavity shape
     - Strawberry tongue
     - Cracked and red lips
  5. Acute, nonpurulent **cervical adenopathy**
- **Coronary arterial disease occurs** and thrombocythemia may occur
- In combination **vessel occlusion may occur and the subsequent MI**, which occur as the child is recovering from the acute illness
- **Treatment:**
  - **IVIG** is the cornerstone of treatment
  - Antiplatelet therapy with aspirin in high doses is recommended.







Questions:

1. **Which of the following skin rashes is associated with diabetes mellitus?**
   - **A.** Acanthosis nigricans
   - **B.** Palpable purpura
   - **C.** Pretibial myxedema
   - **D.** Striae

2. **A Henoch-Schönlein purpura scenario, which type of reaction?**
   - **A.** type 1
   - **B.** type 2
   - **C.** type 3
   - **D.** type 4

3. **What is the pathognomonic sign for small vessel vasculitis:**
   - **A.** Vesicles
   - **B.** Bulla
   - **C.** Scars
   - **D.** Purpura

Questions:

3. **Which of the following is the most common site of Henoch schonlein purpura?**
   - **A.** Face and scalp
   - **B.** Extensor surface of limb and back
   - **C.** Palms and soles
   - **D.** Flexor surface of limbs

4. **A 6-year old boy presented with palpable purpuric papules and plaques over the shins and buttoks for 5 days associated with abdominal pain. If you send skin biopsy for direct immunofluorescence, which of the following is typical for this disease?**
   - **A.** C2 and C4 Deposition
   - **B.** IgG and IgM deposition
   - **C.** IgG deposition
   - **D.** IgA and C3 deposition

5. **A 15-year-old boy presented to the emergency department with purpuric papules and plaques over the shins for one day associated with pain of the ankle joints, there symptoms were preceded by upper respiratory tract infection. Which of the following investigation is helpful to rule out internal organ involvement by vasculitis?**
   - **A.** Urine analysis for RBC casts
   - **B.** Renal function test
   - **C.** Chest X-rays
   - **D.** CBC

6. **What is the best treatment for cutaneous small vessel vasculitis without systemic involvement?**
   - **A.** Bed rest
   - **B.** Methotrexate
   - **C.** Steroid

7. **Pruritis:**
   - **A.** Could indicate thyroid anomaly
   - **B.** Pure cutaneous
   - **C.** Always treated with topical steroids
   - **D.** Not due to underlying disease

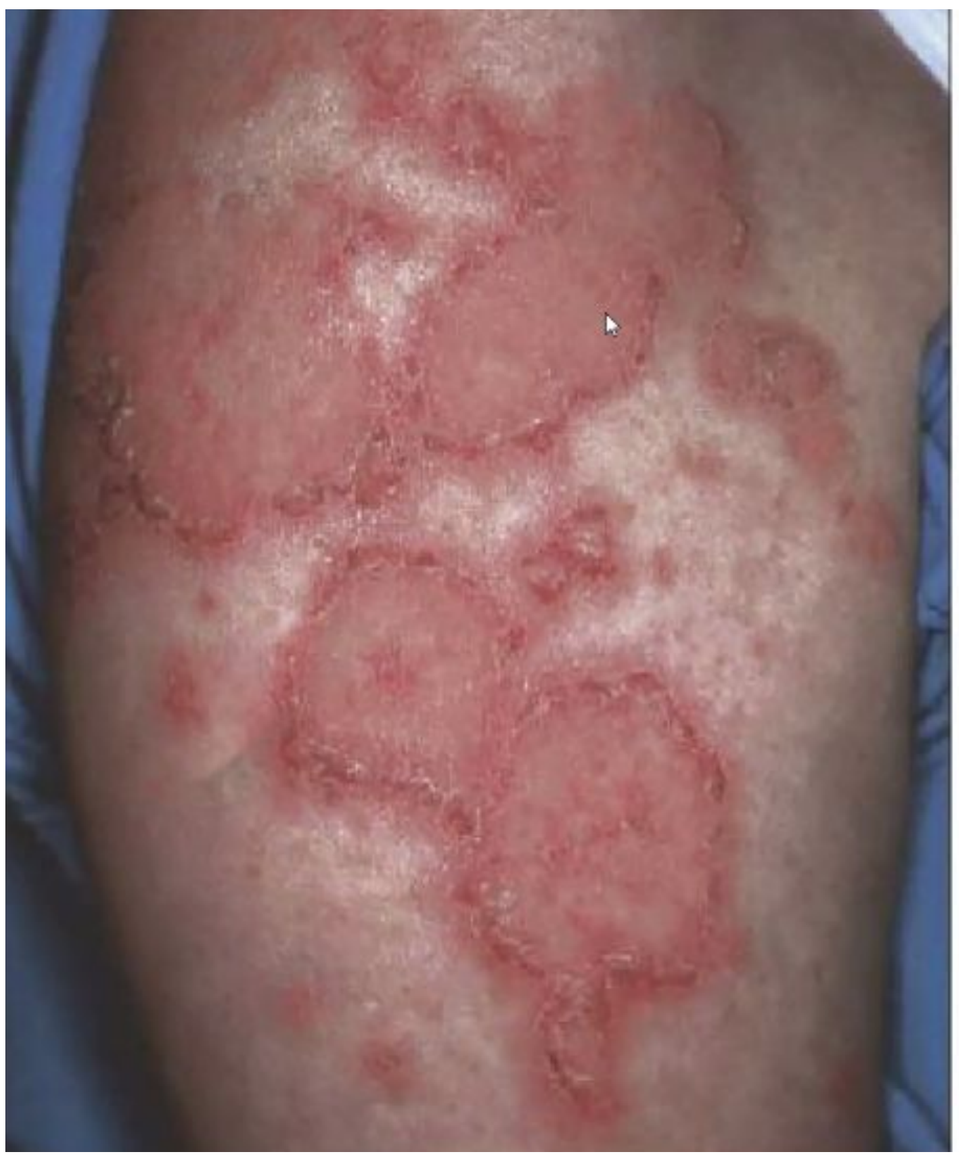
8. **14- Erythema nodosum lesion is**
   - **A.** It is subcutaneous nodules
   - **B.** Affect men more than women
   - **C.** Most commonly involved the upper back
   - **D.** Internal malignancy

1:A
2:C
3:D
4:B
5:D
6:B
7:A
8:A
9:A

Male slides

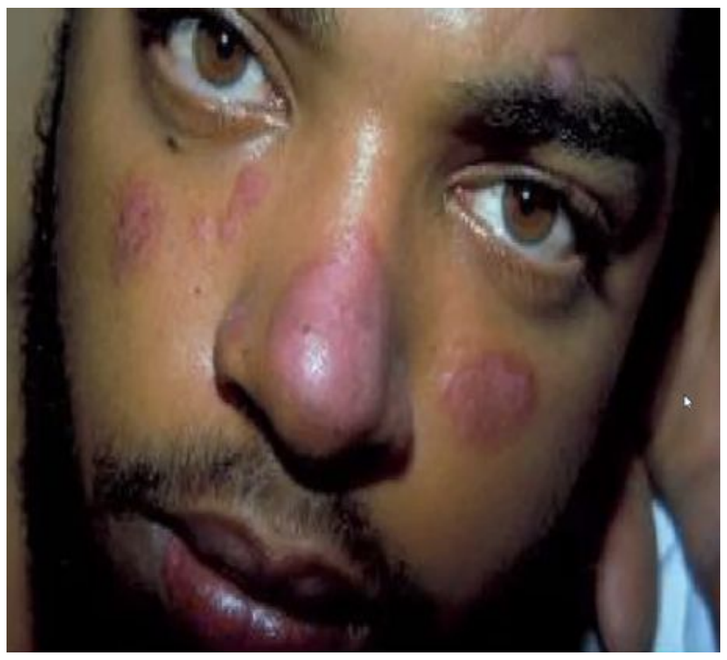
Doctor’s notes about connective tissue disease

1. Lupus



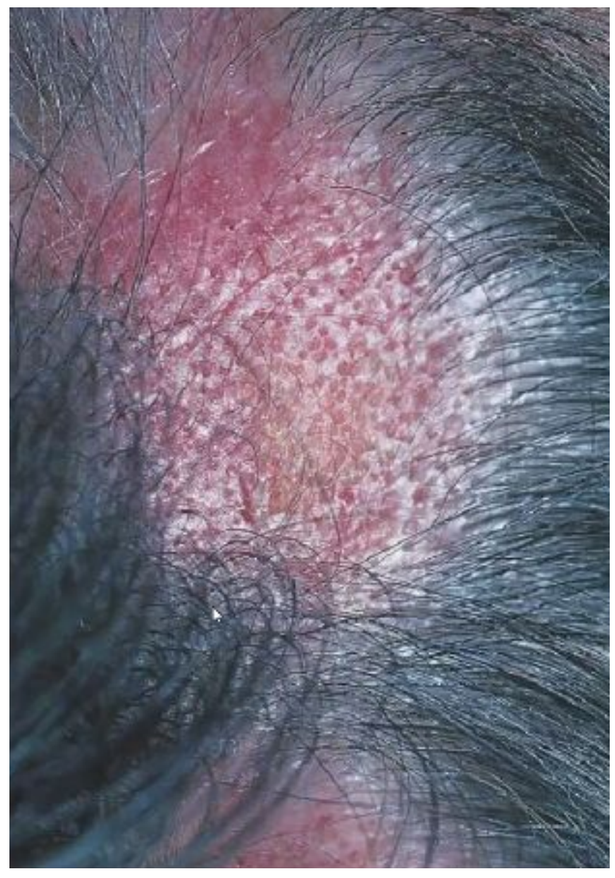
Few well demarcated erythematous scaly annular plaques *with central clearing*

This is subacute

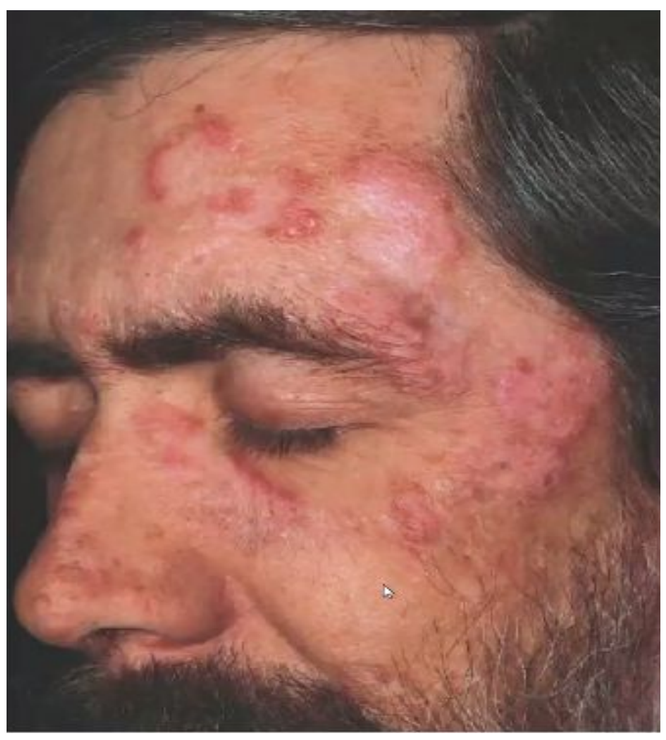


Few well demarcated oval/discoid erythematous scarring plaques on the nose and the eyebrow.

- (Loss of hair means there is scarring)
- This is Discoid lupus

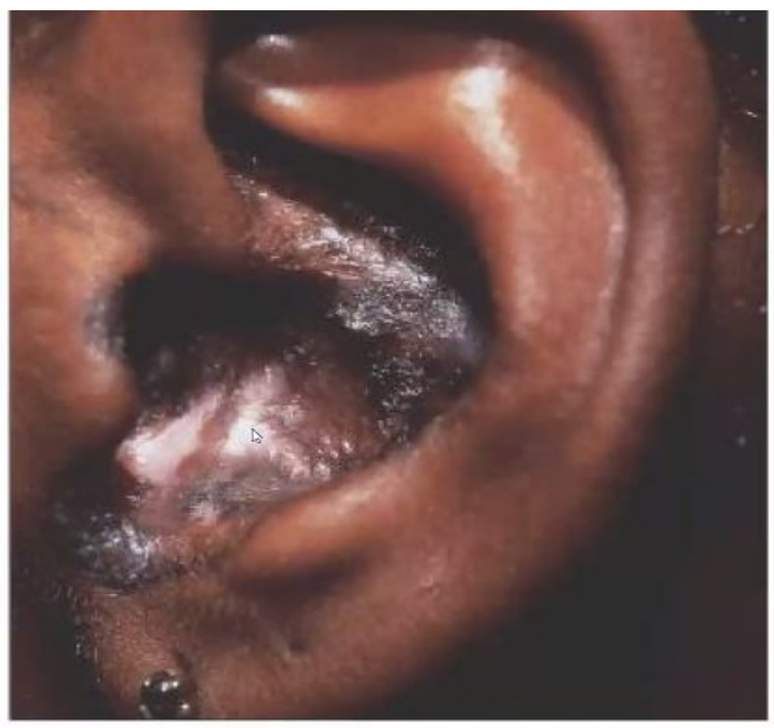


Loss of hair and erythematous with follicular plugging (a sign indicating an upcoming discoid)



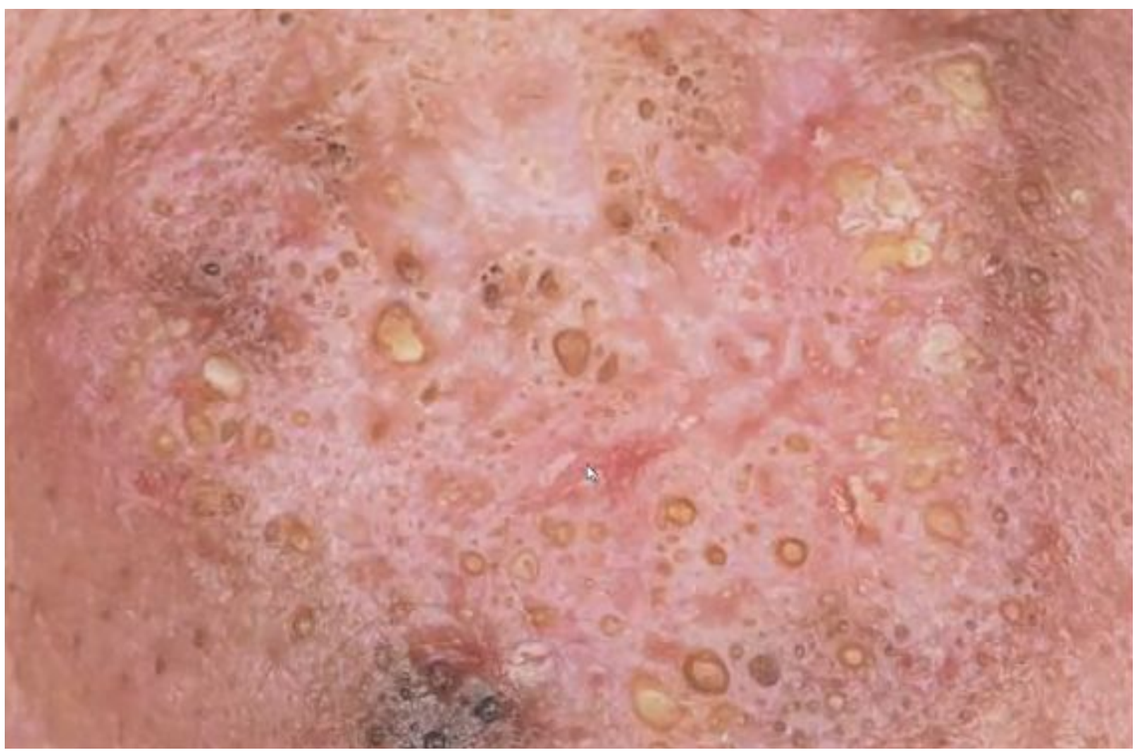
Multiple erythematous papules and plaques with raised border annularity and polycyclical and hypopigmentation in the center. (no scarring)

- This is subacute cutaneous lupus



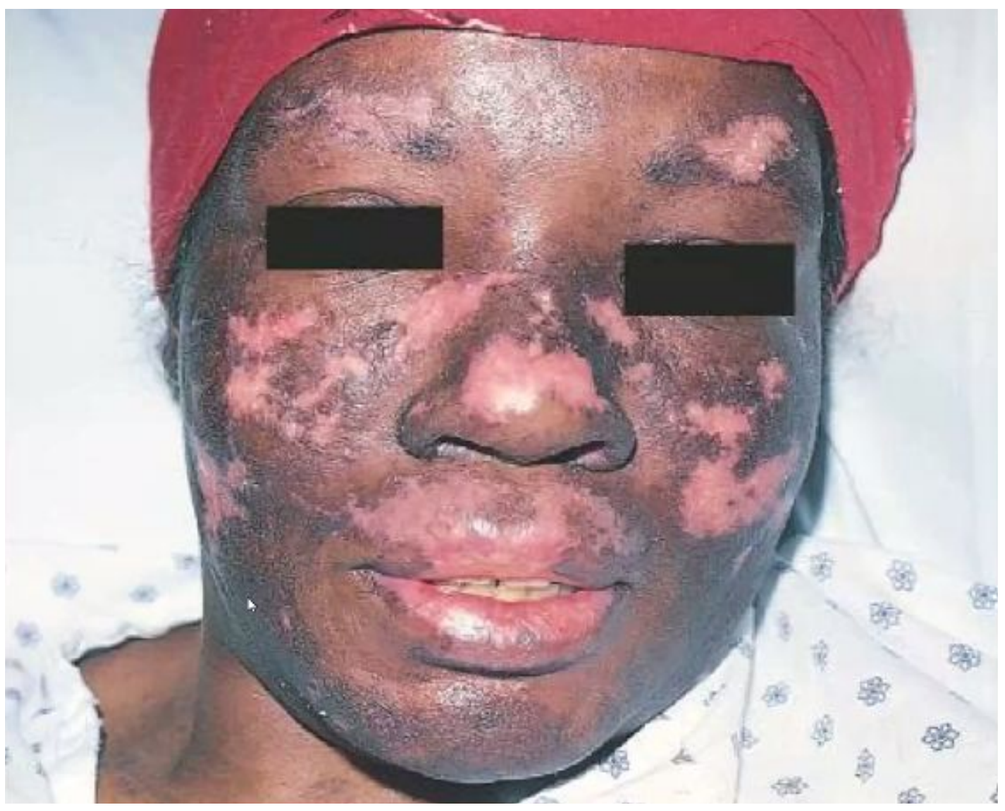
- Annular
- Scarring with hyper pigmentation and depigmentation
- This is discoid (a common place is the ear)

Male slides

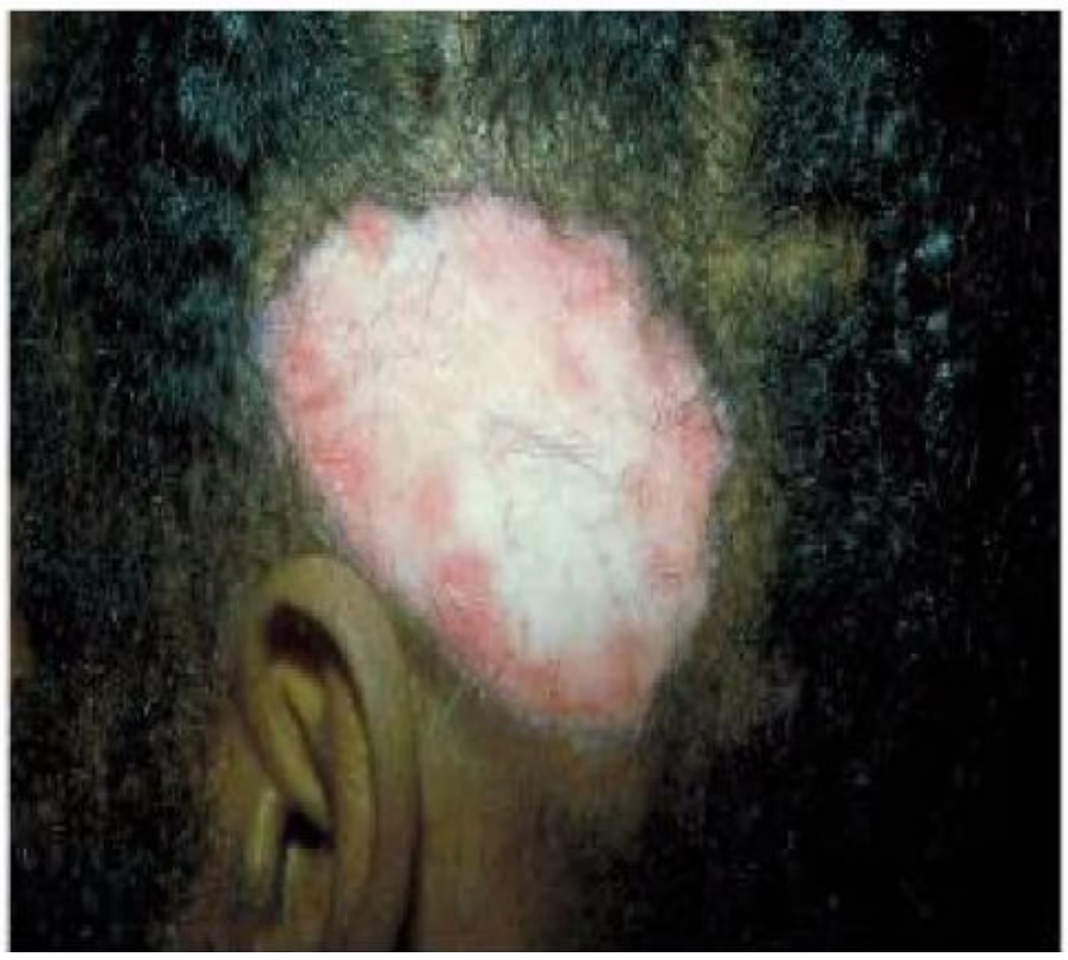


A more severe pic of follicular plugging

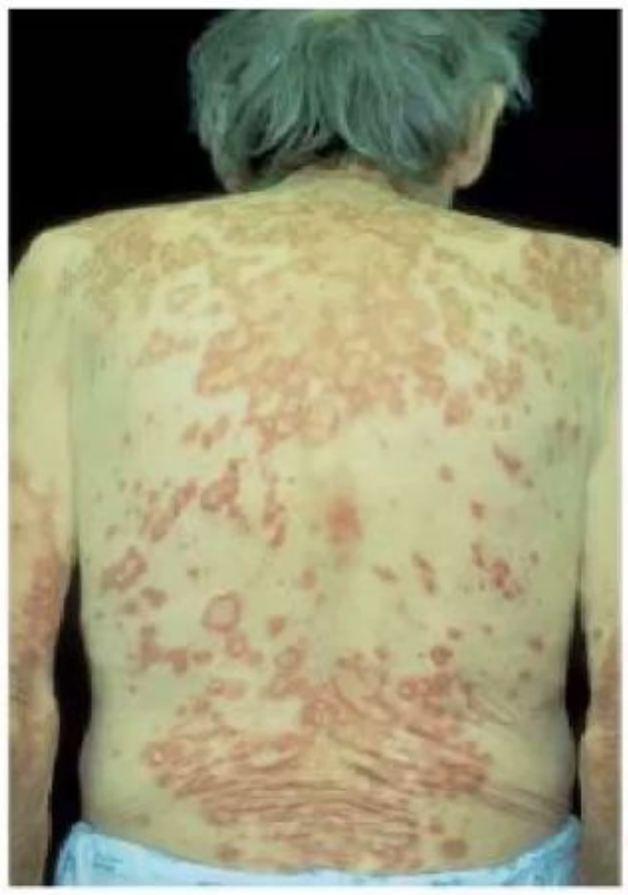
- كانك جايب سدادة وحاطها فيه
- This is Stage 4 discoid lupus



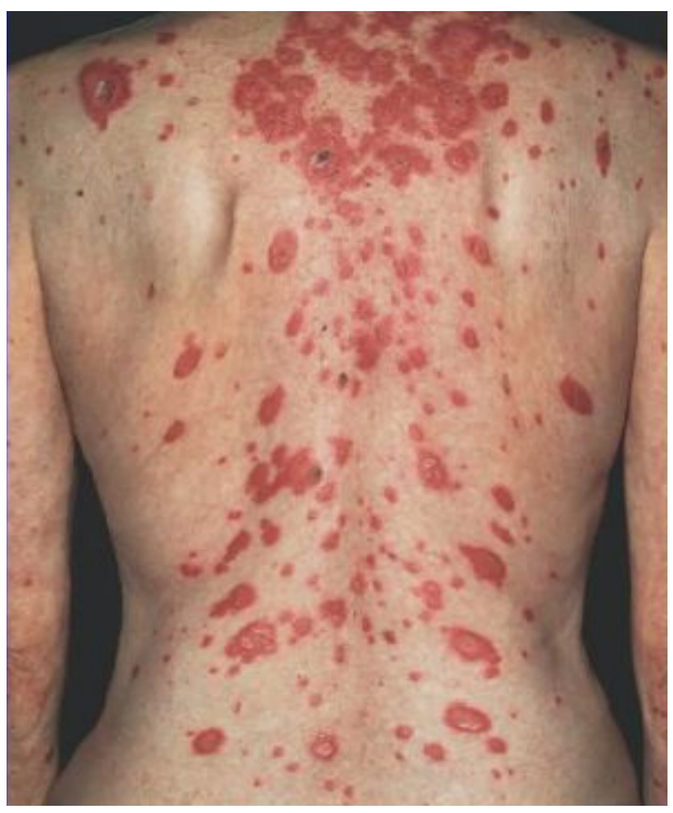
- Multiple irregular patches spread out over the face with scars + (hypo pigmentation erythematous *with surrounded hyper pigmentated).*
- (look at the eyebrows there is loss of hair which means there is scarring)
- This is a case of discoid lupus



Single erythematous hairless plaque/scar with white center, this is severe discoid.

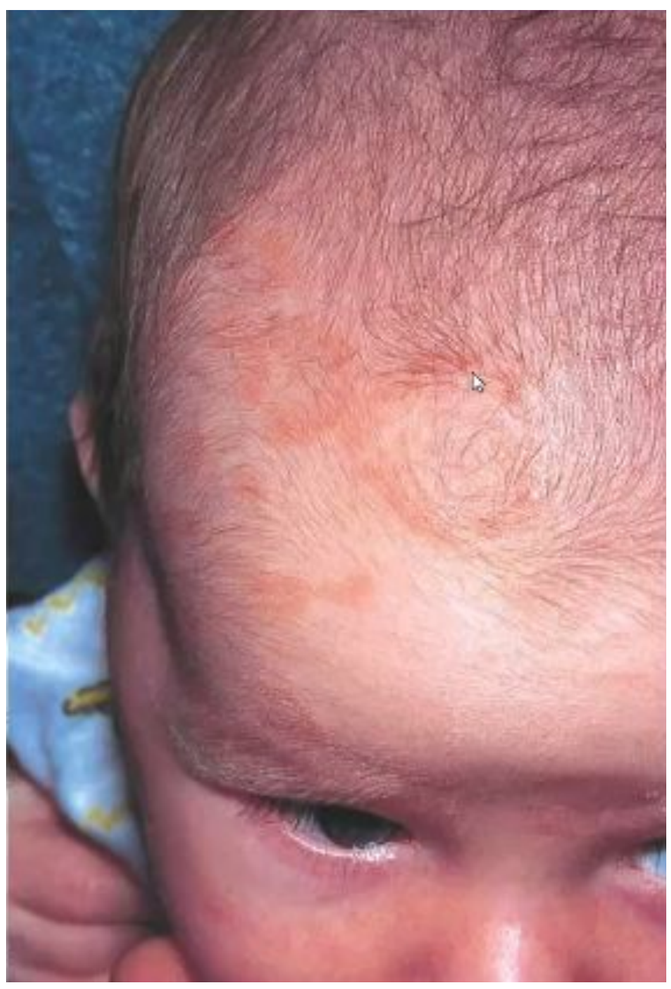


- Innumerable well demarcated erythematous irregular annular plaques and some of them polycyclic involving the upper and lower back with the posterior of the arm.
- There is no scarring
- This is *subacute*



Psoriasiform multiple scaly annular plaque and some of them are oval plaques.

How to identify a scar? A scar is a permanent change in the skin texture could be in the same level, atrophic, hypertrophic, keloid….

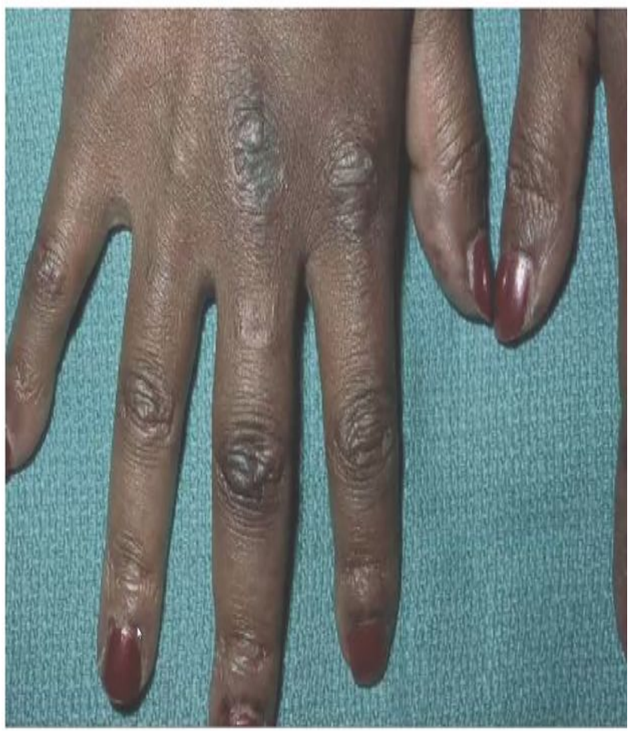


Neonatal lupus

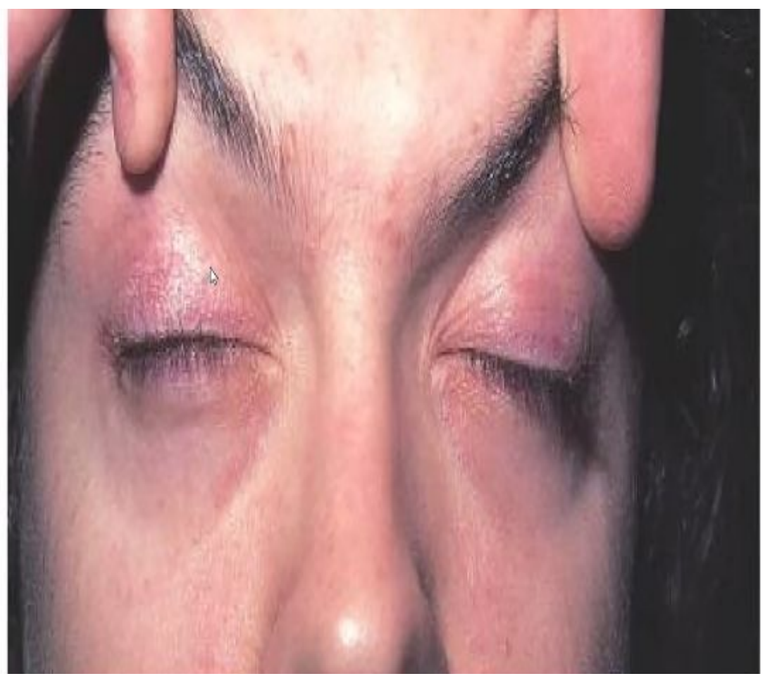
What is the most important thing to check?

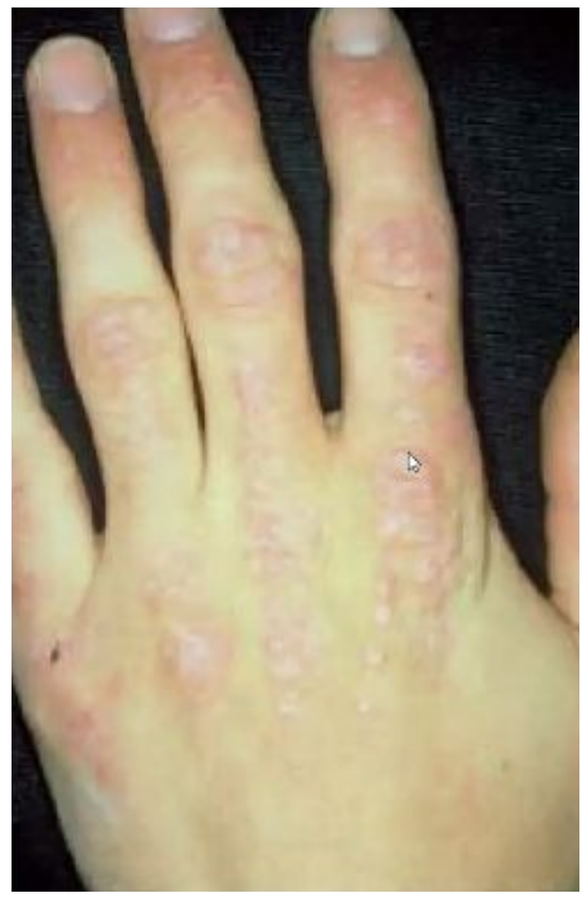
Heart block (by ECG)

2. Dermatomyositis

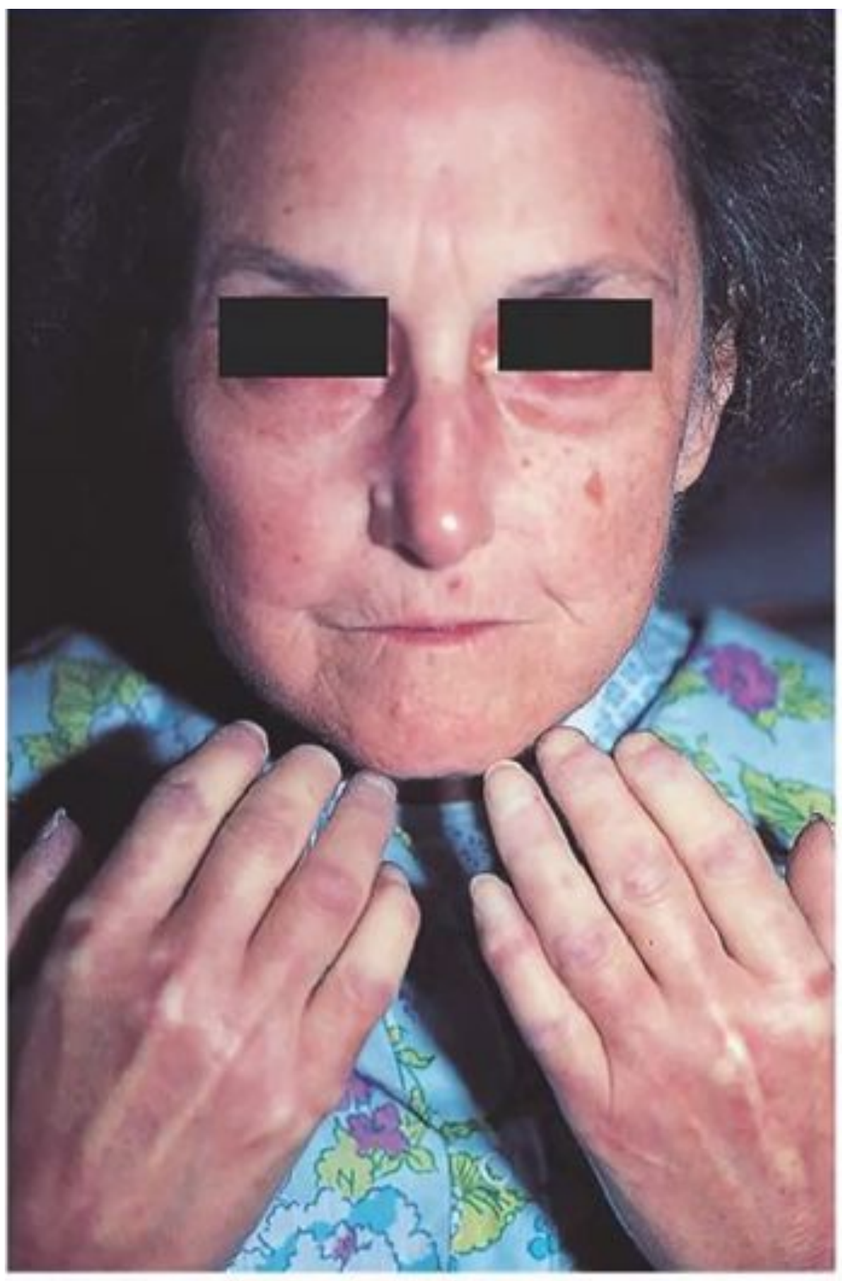


Male slides

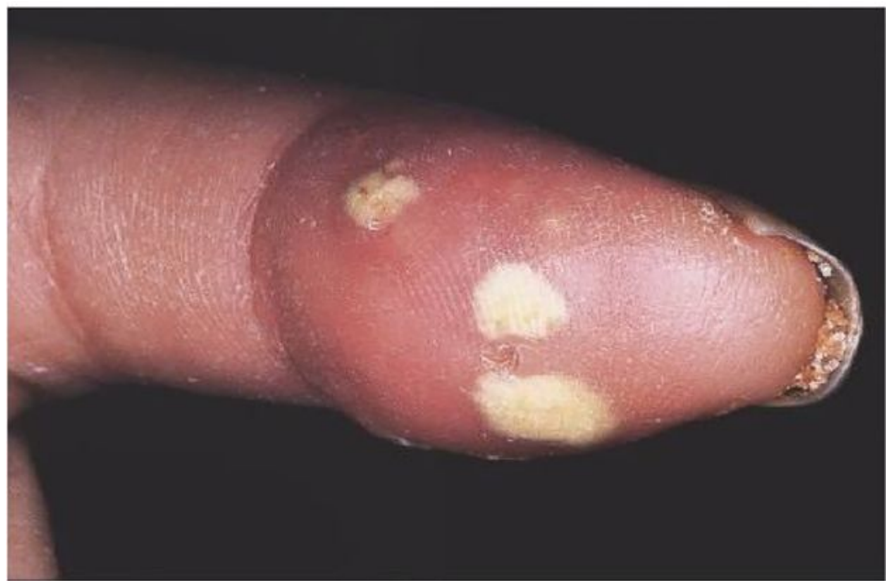




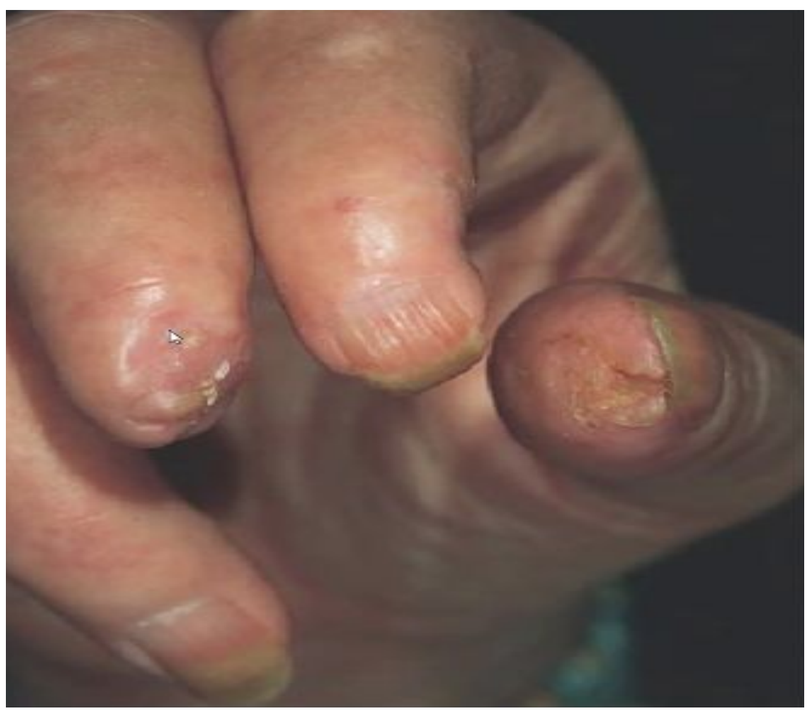
3. Scleroderma



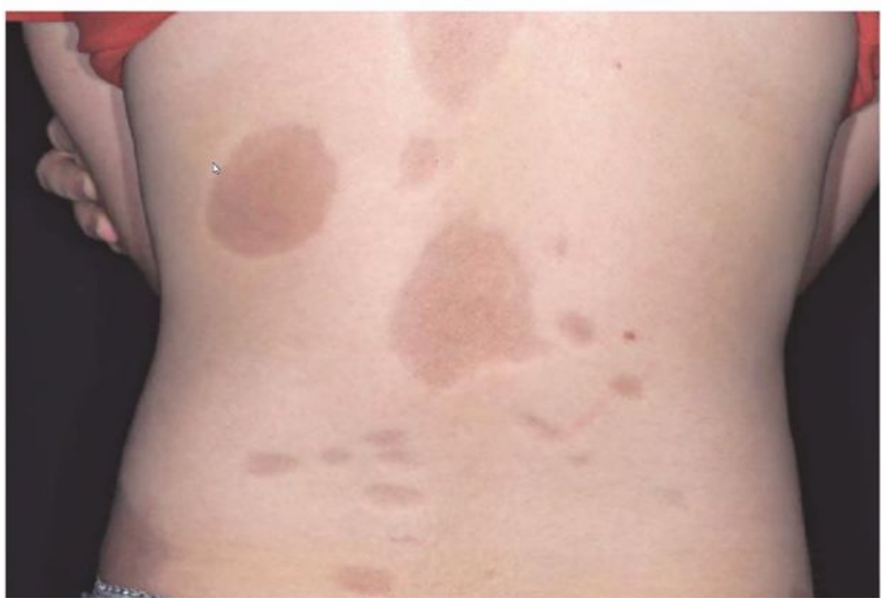
1. Skin tightening on both hands (difficult to pinch because its hard and thick) and the lips as well
2. No wrinkles/loss of wrinkles (even though she is 70)
3. Opening of the mouth is small (due to tightness)
4. Peak nose
5. Sclerodactyly
6. Raynaud's phenomenon
7. Tight skin



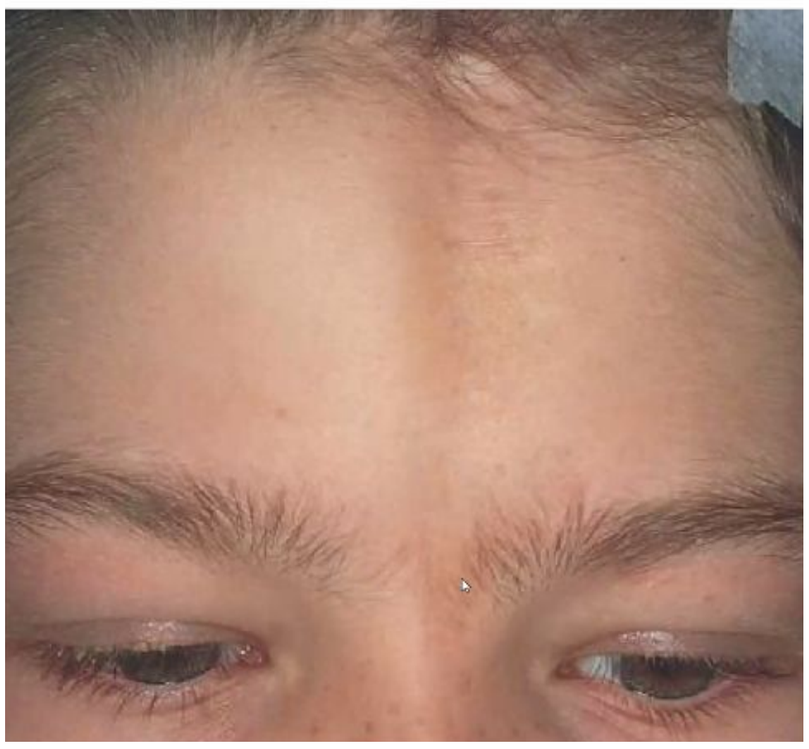
Calcification



Loss of blood supply + Renaud phenomena = Loss of the tip of the fingers



- *Describe: Circular well demarcated patches ..*
- There is some depression (atrophy) and sclerosis of the skin = morphea
- Morphia is localized scleroderma تصلب موضعي بالجلد



En coupe de sabre ضربة بالسيف

Atrophy skin muscle bone

Linear scleroderma