Cutaneous Manifestation Of Systemic Disease

Objectives :

- To highlight the relation between skin manifestations and common systemic disorders.
- To understands various skin clues and their importance in investigating and managing different systemic diseases

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Revised by:

Sources: *doctor's slides and notes+ FITZPATRICK color atlas +433 team male + 434 team*

[Color index : Important | Notes | Extra]

Introduction

Skin is the gate of the body, some systemic diseases or malignancies can have skin manifestations.In this lecture we are going to study specific diseases and how they present in the skin, the lecture contents will be classified into:

1- Connective tissue diseases.

2- Endocrinological diseases.

3- GIT and metabolic disease.

4- Neurocutaneous diseases and Behcet's syndrome.

5- Causes of pruritus without skin diseases, nail changes, and when to do HIV testing for skin diseases.

Connective Tissue Diseases

There are 3 main connective tissue diseases:

A. Systemic Lupus Erythematosus (SLE).

B. Dermatomyositis.

C. Scleroderma.

1-Systemic Lupus Erythematosus

SLE is an autoimmune multisystem inflammatory disorder, there is genetic, environmental and hormonal factor involvement.

SLE has positive ANA and Anti-dsDNA tests.

Types of SLE include:

A. Spontaneous SLE.

B. Discoid Lupus.

C. Subacute Cutaneous Lupus. D. Neonatal Lupus.

E. Drug-induced Lupus.

Skin characteristics of SLE are:

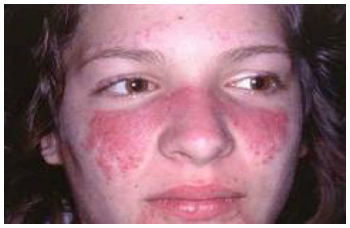
A. Facial photosensitivity.

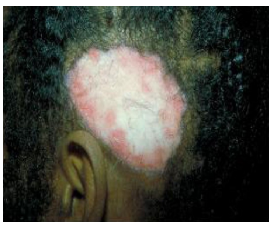
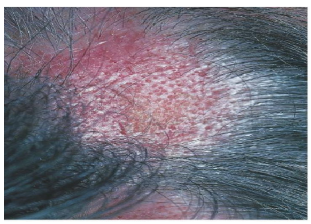
B. Butterfly erythema(malar rash).

C. Oral and nasopharyngeal ulcers.

D. Alopecia.(scarring)

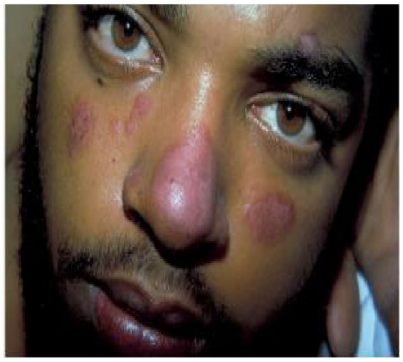
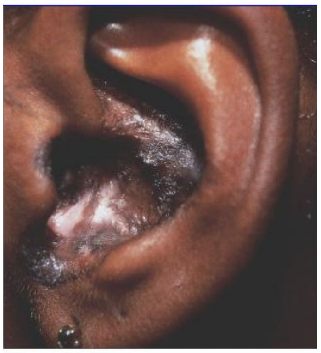
E. Raynaud's phenomenon(found in 20% of the cases).



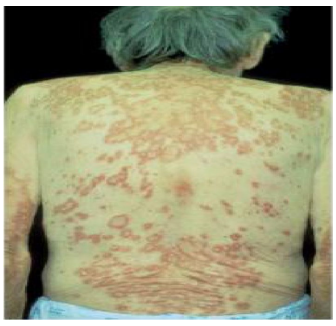
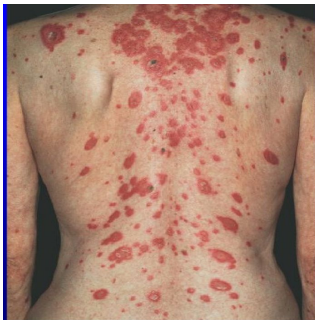
Discoid lupus:

Usually there is discoid lesions that are present in the skull, round scarring in light exposed areas and no systemic involvement.Description of lesions in discoid lupus is very important.

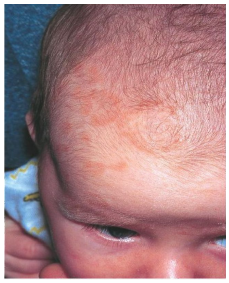
Subacute Cutaneous Lupus:

Has a papulosquamous or annular presentation, Associated with photosensitivity, does not cause scarring and usually ANA-negative but Anti Ro Positive.

Neonatal Lupus:

It appears in the first month when there is an active disease during delivery, lesions are annular or papulosquamous with a photodistribution, lesions commonly appear in the skull(neonatal lupus is the third differential in skull lesions appearing in an infant), the disease is anti Ro positive and is associated with congenital heart block (complete and permanent) the patient usually needs a pacemaker.



E. Drug-induced Lupus:

Procainamide and Hydralazine are the commonest causes for development of this condition, drug-induced lupus is usually anti-histone positive.

2-Dermatomyositis

Dermatomyositis is an idiopathic inflammatory myopathy, there is a genetic predisposition and an environmental trigger leading to humoral immune activation resulting in chronic inflammation.

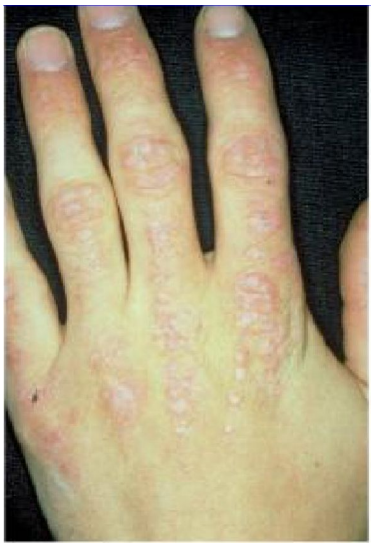
Patients present with a characteristic skin rash and proximal muscle weakness(the patient will not say there is pain, instead the patient will say i feel tired).

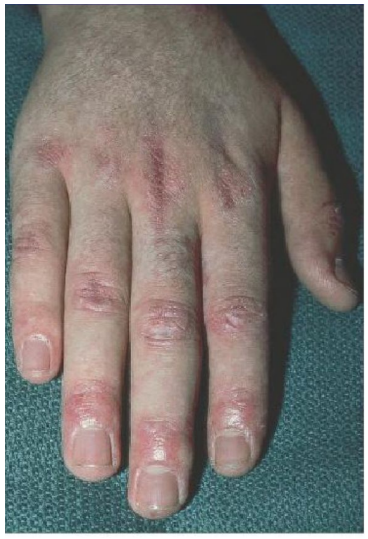
Skin features in dermatomyositis:

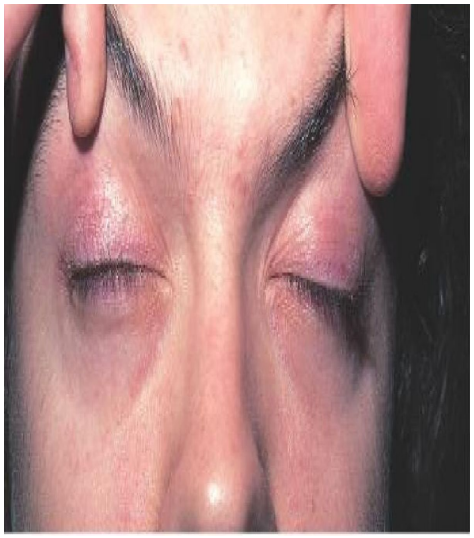
- **Heliotrope**: Violaceous color over the upper eyelids(reddish discoloration usually in the upper eyelid, sometimes it will be edematous).
- Gottron's papules: Flat- topped violaceous papules over knuckles of hands(it involves nails and joints but not the fingers).
- **Calcifications** especially in kids.

There is bilateral proximal muscle weakness with high CPK, positive EMG and muscle biopsy. In adults especially over 50 years of age it is associated with internal malignancy.

(A female above 50 newly diagnosed with dermatomyositis, you have to rule out ovarian cancer first, then other types of cancer).







3-Scleroderma

Definition: Scleroderma is a chronic connective tissue disorder with widespread fibrosis, it could be diffuse or limited.

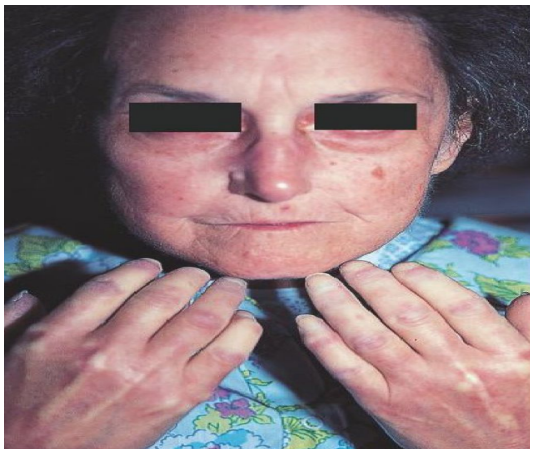
Features of Scleroderma:

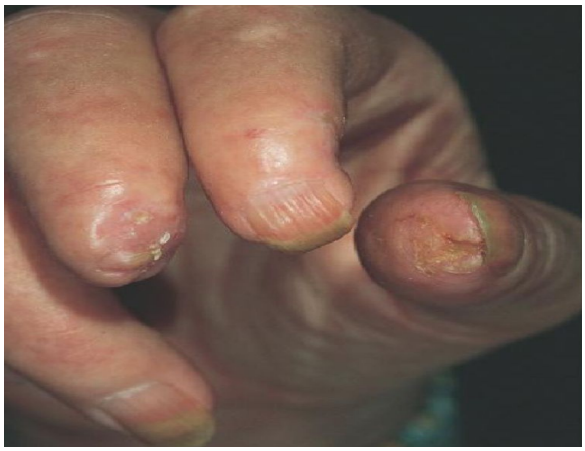
1) **A. Tight and thickened skin.**
2) **Loss of forehead lines,** beaked nose, small mouth, radial furrowing around the mouth.
3) **CREST is a milder type of scleroderma, there is Calcification, Raynaud's phenomenon, Esophageal dysfunction, Sclerodactyly, Telangiectasia and positive anti-centromere with less systemic involvement.**
4) In diffuse type there is more systemic involvement (Lung, GI, Kidneys) and **positive anti scl-70.**

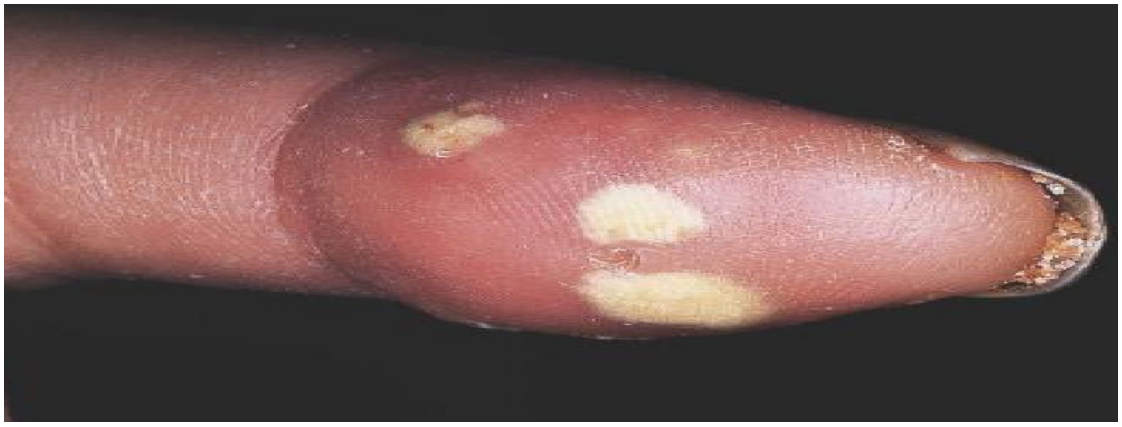
Other types of scleroderma include:

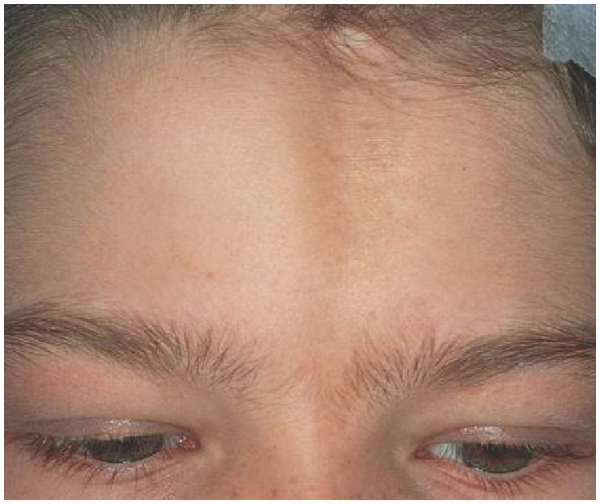
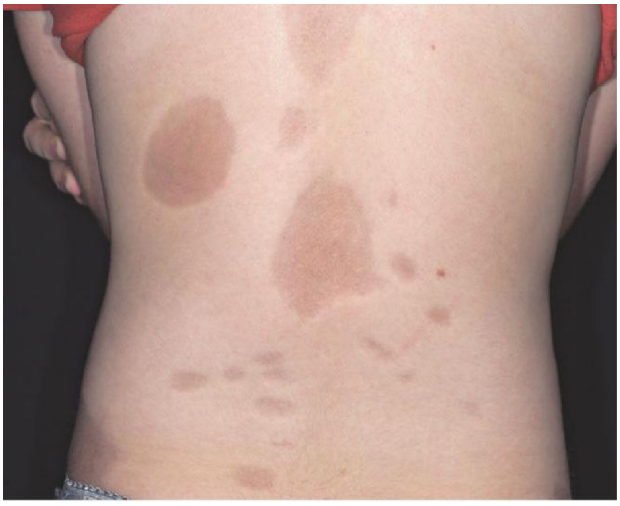
1-Morphea: A localized scleroderma without systemic involvement, there is a firm,white patch of skin surrounded by violaceous ring.

2-En coup de sabre: Linear scleroderma on the scalp and face which may give scarring alopecia and it may affect muscles or even bones.







The pic on the left en coup de sapre the pic on the right is morphea

Antibody Testing in connective tissue diseases (Important)

Antibody	Clinical Significance
ANA	Screening for SLE and other CTD
Anti-Centromere	Marker for CREST
Anti-Histone	Marker for Drug-induced Lupus
Anti-Smith	Specific for SLE
Anti-RNP	For Mixed CTD
Anto-Ro	Neonatal lupus, SCLE
Scl-70 Antibody	For Scleroderma
Anti dsDNA	For SLE

Skin and endocrine system:

A- Diabetes mellitus:

◀*Skin tags*

small, pedunculated, soft papules on the eyelids, the neck, and the axillae. Mostly associated with obesity and insulin Resistance. If numerous usually on top of acantohsis nigricans.

◀*Acanthosis nigricans*

hyperpigmented, velvety **plaques** in body folds. Increased insulin, which binds to insulin-like growth factor receptors to stimulate the growth of Keratinocytes and dermal Fibroblasts. Treatment is by weight reduction and decrease insulin resistance.

◀*Diabetic dermopathy*

Very common, atrophic, hyperpigmented **papules** and **plaques** on Shins. Men are affected more often than women. Possibly related to diabetic neuropathy and vasculopathy. No effective treatment, but it does improve with diabetic control.

◀*Bullous diabeticorum*

Rare. Spontaneous blistering of the hands and feet. Heals without scaring.

◀*Thickening of skin*

Thickening of the hands with tiny papules on fingers and stiff joints.
Pebbled knuckles (or Huntley papules) are multiple minute papules, grouped on the extensor side of the fingers, on the knuckles, or on the periungual surface Generalized asymptomatic thickening of the skin (diabetic stiff skin) Scleredema on upper back and neck.

◀*Necrobiosis lipoidica diabeticorum*

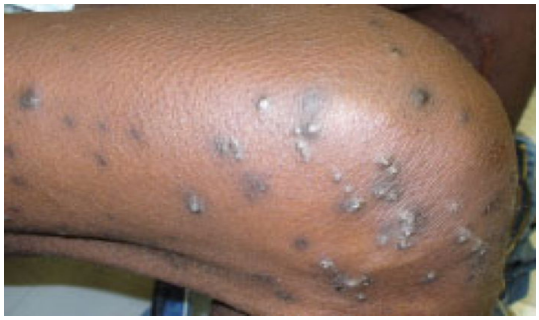
Yellow atrophic plaques on the shins. Sometimes they ulcerate. Histopathology: shows tiered granulomatous Reaction.
Treatment: topical, intralesional steroids, tacrolimus, phototherapy, cyclosporine, and rarely surgery.

◀*Bacterial and fungal infections*

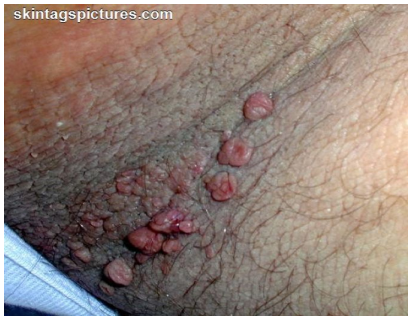
Pyodermic infections such as impetigo, folliculitis, carbuncles, furunculosis, ecthyma, and erysipelas can be more severe and widespread in diabetic patients.
Erythrasma, caused by *Corynebacterium minutissimum mostly on axillae and groin.*malignant otitis externa, often caused by *Pseudomonas aeruginosa*.
Tinea pedis (can lead to cellulitis) and onychomycosis.
Candidal infections like perleche on corners of mouth, and on vulva.
Rare infections like mucormycosis by Phycomycetes and anaerobic cellulitis by *Clostridium* species.

◀*Perforating dermatosis*

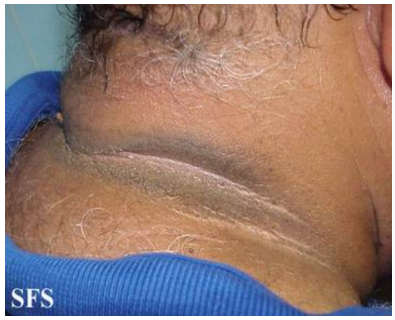
Pruritic hyperkeratotic papules on the legs and trunk.
Histopathology shows transepidermal elimination of collagen and/or elastin.
Common in patients with diabetes and renal failure.
treatments include topical keratolytics, phototherapy, topical and systemic retinoids, topical and intralesional steroids, oral antihistamines, and cryotherapy.



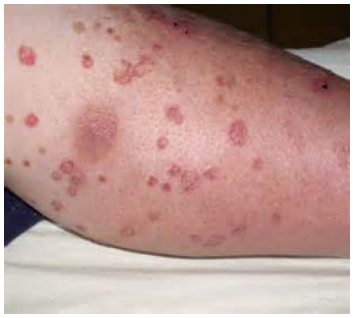
****Skin tags**

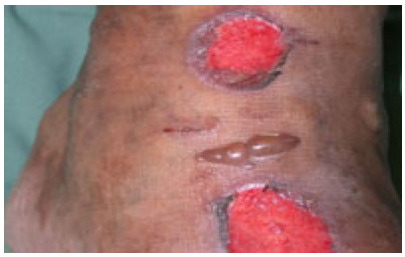


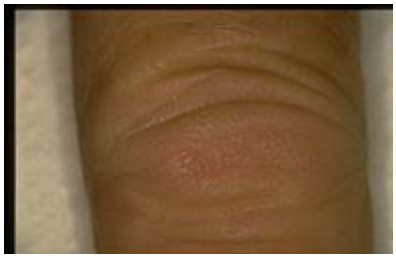
acanthosis nigricans

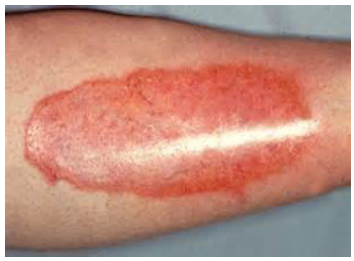


diabetic dermopathy







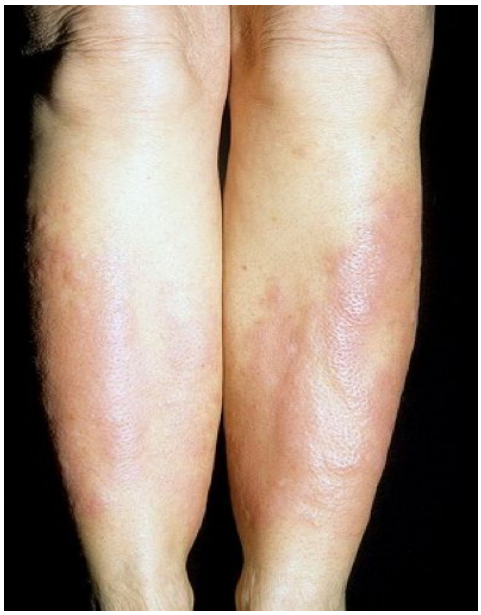


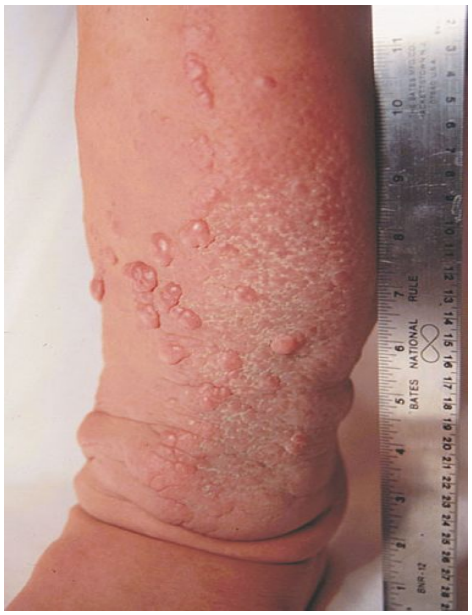
Necrobiosis lipoidica diabeticorum***Skin thickening******Necrobiosis lipoidica diabeticorum**

B- Thyroid disorders

◀ Hyperthyroidism

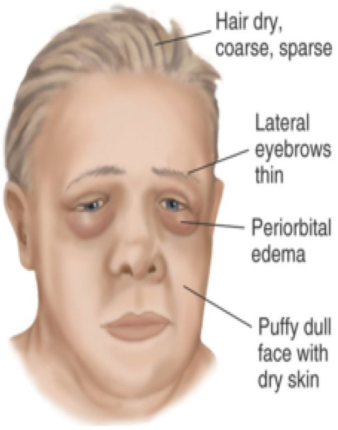
- ❖ Pretibial myxedema: is the most characteristic features of thyrotoxicosis appearing as shiny waxy papules and plaques having orange-skin appearance on the chin of the tibia.
- ❖ Warm skin and increased sweating and pruritus.
- ❖ Premature hair graying, alopecia with fine soft thinned scalp hair.
- ❖ Hyperpigmentation or vitiligo.
- ❖ Brittle nails.





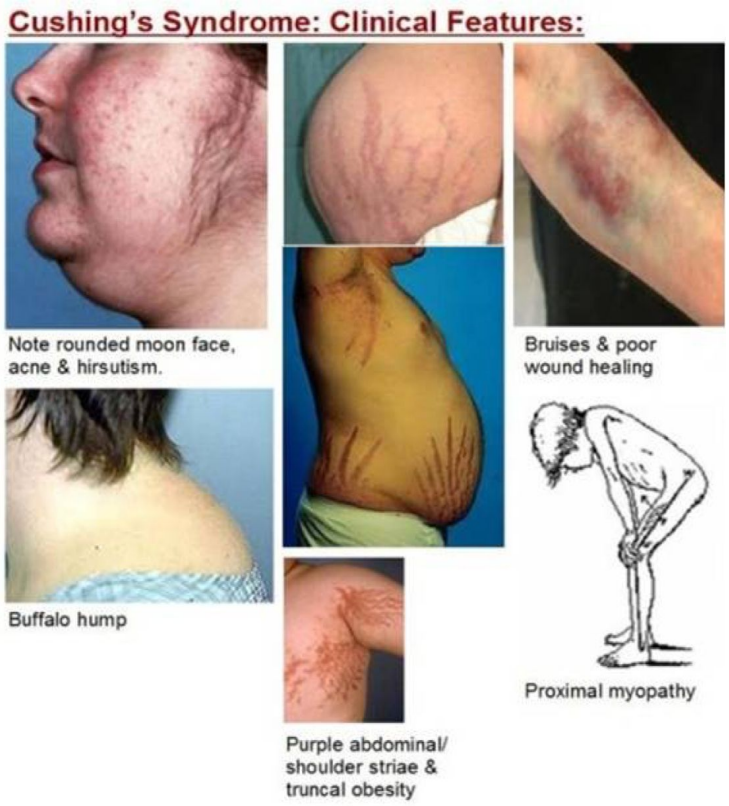
◀ Hypothyroidism

- ❖ Cold, pale and dry skin and pruritus.
- ❖ A yellowish hue to the skin due to carotenaemia. Slow growing ridged and brittle nails.
- ❖ Delayed wound healing.



C- Cushing's syndrome

- caused by prolonged exposure to high levels of plasma glucocorticoid, adrenocortical hyperplasia, benign or malignant adrenal tumours, ectopic ACTH syndrome – secretion of ACTH by malignant or benign tumours arising in structures other than the pituitary or adrenal glands, exogenous steroid administration.
- Acne and hirsutism.
- Clitromegaly and male pattern alopecia (Hamilton pattern). Striae.
- Easy bruising and purpura.
- Moon face and buffalo hump with fat redistribution.
- Telangectasia on face. Poor wound healing.



D- Addison's disease Adrenocortical hypofunction

- Hyperpigmentation at Sun exposed skin, sites of trauma, axillae, palmar creases, old scars ,nevi and mucous membranes.
- Diffuse pigmentation on skin and mucous membranes.
- Melanocytes stimulation by ACTH

#Gastrointestinal diseases

★1-Dermatitis herpetiformis

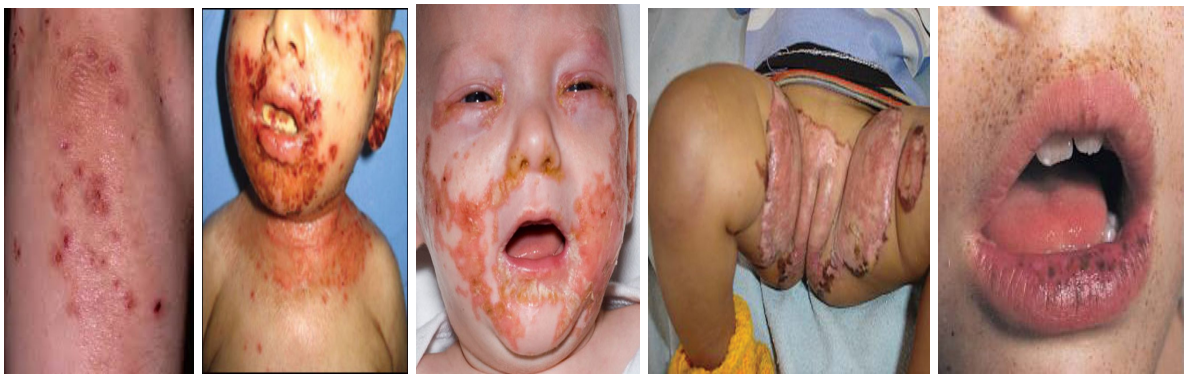
- Small severely pruritic vesicular lesions found in a symmetric distribution of both upper and lower extensor surfaces, buttocks and the scalp.
- direct immunofluorescence finding is granular deposition of **IgA** within the dermal papillae.
- celiac disease (also known as gluten-sensitive enteropathy and celiac sprue) are caused by the inability to absorb gluten from the diet.
- Treatment: gluten-free diet and dapsone.

★2-Acrodermatitis enteropathica

- a rare autosomal recessive disorder that impairs dietary zinc absorption in the jejunum and ileum.
- presents in infants several weeks after breastfeeding is discontinued.
- characterized by diarrhea, inflammatory rash, and hair loss.
- scaly, erythematous patches and plaques similar to atopic dermatitis, but progress to vesicles, crusts, erosions, and pustules on acral areas, perioral and perianal areas.
- Treatment by zinc supplementation for life.

★3- Peutz Jeghers syndrome

- autosomal dominant disorder.
- mucocutaneous hyperpigmentation together with GI polyposis.
- The skin findings first appear in infancy or early childhood and involve brown macules on the lips and buccal mucosa.
- multiple hamartomatous polyps occurring most commonly in the jejunum.
- 2-3% of patients develop GI carcinoma during their lifetimes.



- **The first pic on the left is a pic of dermatitis herpetiformis**
- **The 3 pics in the middle is for acrodermatitis enteropathica**
- **The last pic on the right is a pic of peutz jeghers**

★4- Pyoderma gangrenosum

- a painful, ulcerative lesion with a well-defined, undermined violaceous border.
- start as small pustules, which subsequently burst and expand to form the larger noninfectious ulcer.
- Positive pathergy test.
- Mostly associated with ulcerative colitis. Also with Crohn's disease, rheumatoid arthritis, and leukemia.

★5- Porphyria cutanea tarda

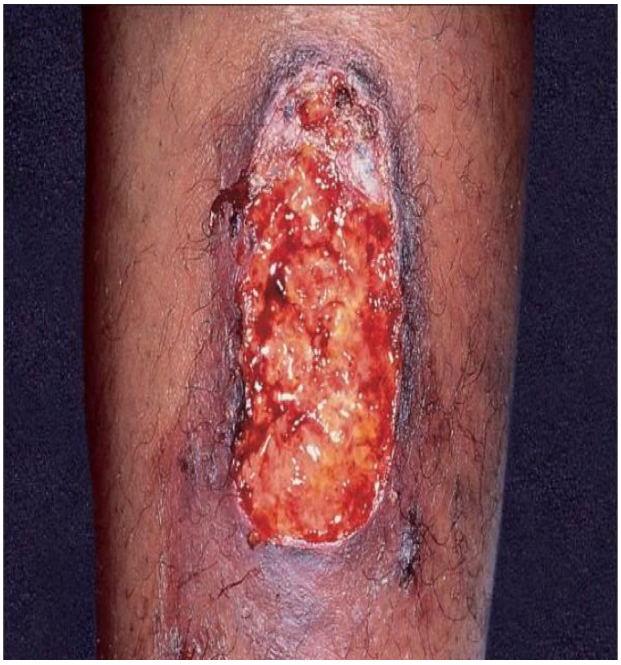
- most common porphyria occurring in adults.
- skin photosensitivity with increased skin fragility, facial hypertrichosis, blisters, scarring with milia formation, and skin hyperpigmentation on the hands and other sun-exposed areas.
- results from the decreased activity of the enzyme uroporphyrinogen decarboxylase.
- Associated with Hep C virus.
- Treatment by removal of possible triggers, including iron supplementation,alcohol, and estrogens. Also by phlebotomy and hydroxychloroquine

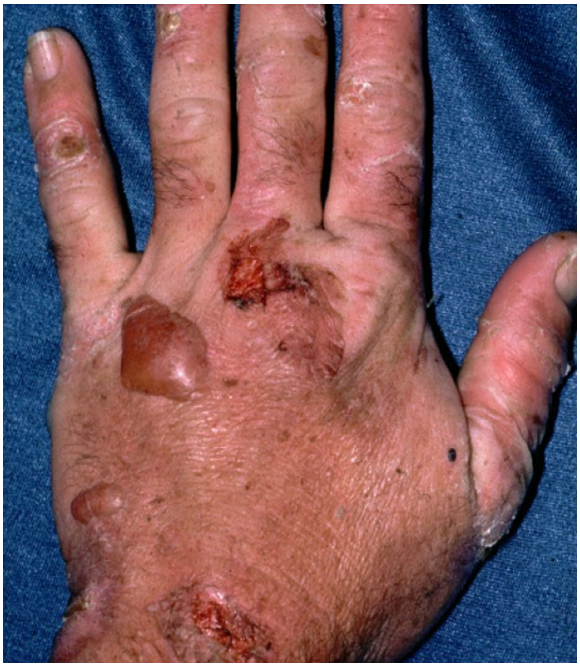
★6-Hemochromatosis

- a disorder of iron overload leading to excess deposition in multiple body organs.
- metallic gray or bronze-brown color that is generally diffuse.
- skin atrophy, ichthyosis, partial hair loss (most often in the pubic region), and koilonychia.
- cirrhosis may develop, and might lead to hepatocellular carcinoma.
- treatment involves phlebotomy and chelating agents.

★7- Liver Cirrhosis

- Clinical features: Some of the associated abnormalities are the following:• Pruritus: this is related to obstructive jaundice and may precede it.
- Pigmentation with bile pigments and sometimes melanin.
- Spider naevi: these are often multiple in chronic liver disease.
- Palmar erythema.
- White nails: these associate with hypoalbuminemia.• Porphyria cutanea tarda.
- Xanthomas: in primary biliary cirrhosis.
- Hair loss
- Generalized asteatotic eczema: it may occur in alcoholics with cirrhosis who have become zinc deficient.





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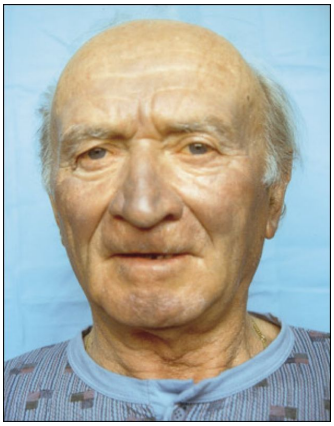
The pic on the right is a pic of **Porphyria cutanea tarda**



hemochromatosis

#Renal diseases

★ Xerosis:

- ❖ occurs in 50-92% of the dialysis population. Some patients may develop acquired ichthyosis.
- ❖ the exact cause of xerosis in ESRD remains unknown. Many patients respond to routine use of emollients

★ Pruritus:

- ❖ affects 15-49% of patients with chronic renal failure and 50-90% of the dialysis population. Uremia is the most common metabolic cause of pruritus.
- ❖ Cutaneous manifestations of pruritus include excoriations, prurigo nodularis, and lichen simplex chronicus.
- ❖ Pruritus typically resolves after transplantation.
- ❖ Treatment include sedating antihistamines, emollients, phototherapy, thalidomide, and gabapentin .

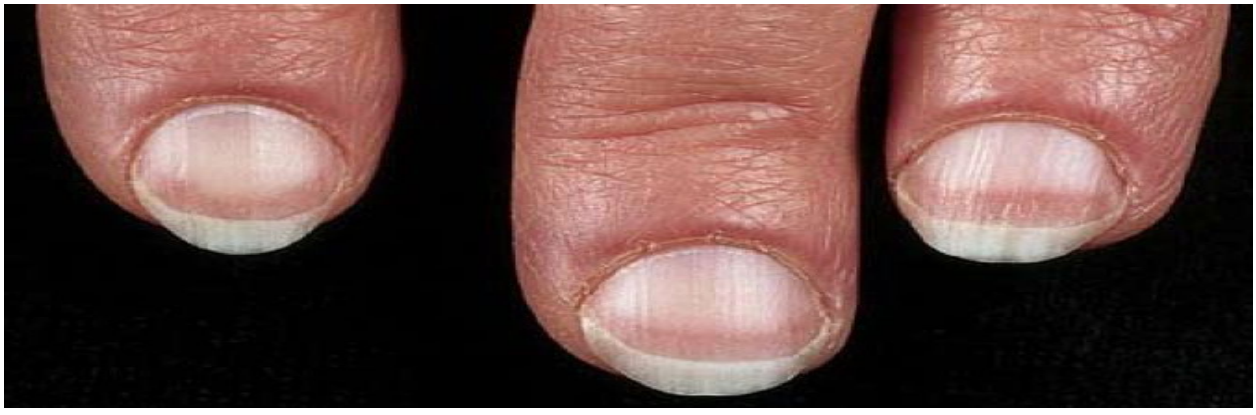
★ Half and half nails:

- ❖ occur in around 40% of patients on dialysis. Kidney transplant usually resolve this sign.
- ❖ Usually involve fingernails.

★ Nephrogenic systemic fibrosis:

- ❖ mostly seen in **ESRD** and dialysis patients.
- ❖ Presents as thick, indurated plaques on the extremities and the trunk similar to scleroderma.
- ❖ gadolinium might have a role in the pathogenesis of this condition.
- ❖ Treatment includes immunosuppressive agents, phototherapy, topical steroids, retinoids, and photopheresis.

Half and half nails



Neurocutaneous Disorders

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

★ Tuberous Sclerosis (Epiloia) :

Epi = Epilepsy/Loi = Low intellegence /A= adenoma sebaceoum

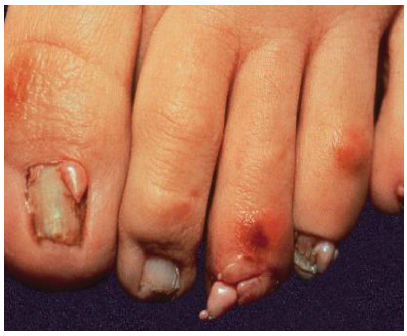
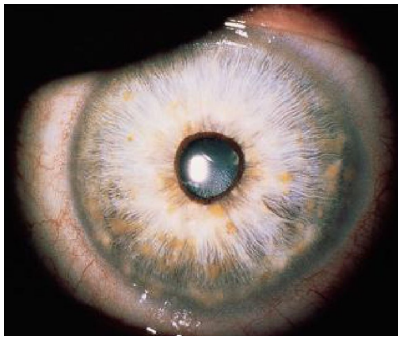
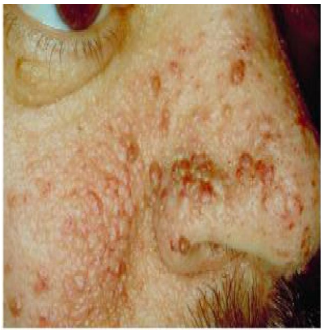
Skin Features :

Adenoma sebaceum (anigofibroma): red papules around the nose and on chin

Ash-leaf hypopigmention: oval area of hypopigmentation ***This is the earliest sign of TS***

Periungal fibroma: multiple papules & nodules around the nail

Shagreen patch: skin colored plaque on the trunk with “orange-peel” Surface

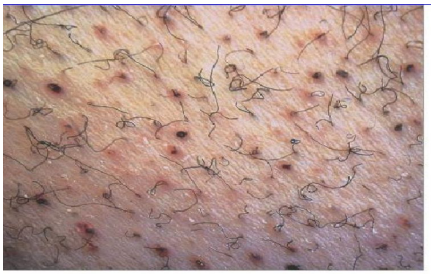
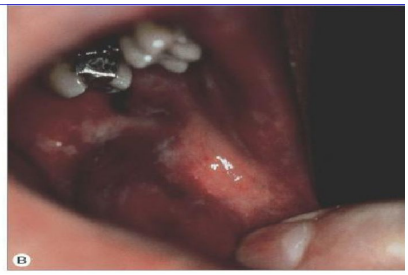
Others

★ Behcet’s Syndrome:

- Oral ulcer (the most common). Genital ulcers (mainly scrotal). Iritis and arthoropathy.May have CNS involvement.

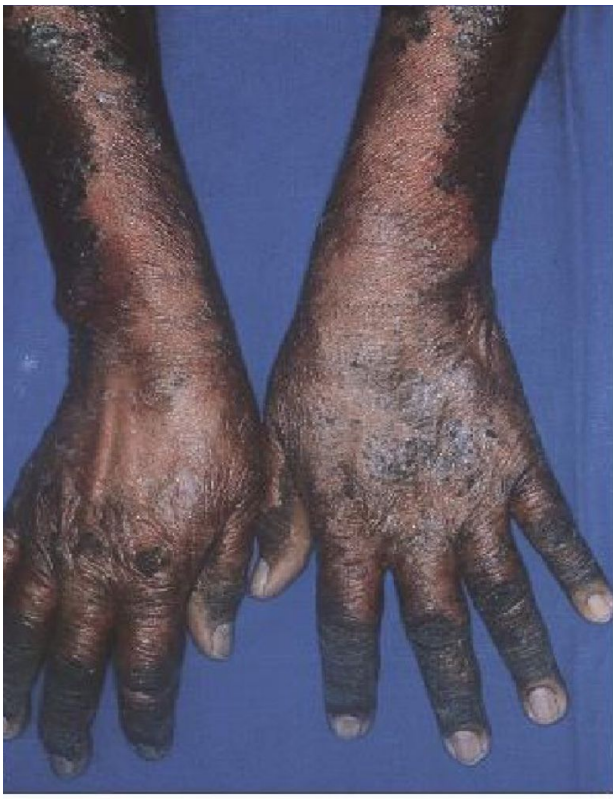
★ Scurvy :

- Vitamin C deficiency, Bleeding gums
- Can cause teeth loss (permanent complication)
- Easy bruishing
- Diagnosis : Low ascorbic acid (Vit-C) level in Leukocyte

★ **Pellagra:** Nictonic acid deficiency 4 "D"s:

- Dermatitis (Photodermatitis)
- Death (if not treated)• Diarrhea
- Dementia



Causes of generalized pruritus without skin lesions:

Endocrine: DM, hypo& hyperthyroidsm
Haematological: polycythemia rubra vera, iron def anemia Malignancy; e.g. Lymphoma ü
Hepatic: primary biliary cirrhosis Renal: CRF, The commonest manifestation of CRF is pruritus
Neurological : e.g. Tabes dorialis
Others: Psychognic, Drugs, Idiopthaic.

Nails:

★ Koilonychia:

- ❖ Spoon- shaped appearance Causes:
- ❖ Iron deficiency anemia
- ❖ Thyroid disease
- ❖ Physiological; early childhood
- ❖ Dermatosis: Lichen planus, Alopecia Areata and others

★ Clubbing :

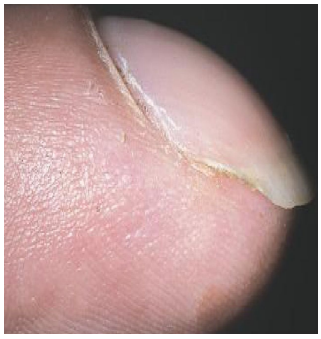
- ○ Exaggeration of the normal nail curve associated with loss of the normal angle between nail and posterior nail fold.

Causes:

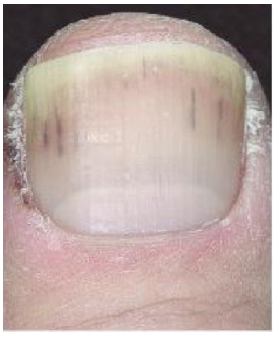
- ○ Thoracic: Lung abscess, Lung CA
- ○ CVS: Congenital cyanotic heart disease
- ○ GIT:GI carcinoma, Inflammatory bowel disease Endocrine: Thyroid disease
- ○ Idiopathic.

★ Splinter Haemorrhages Causes :

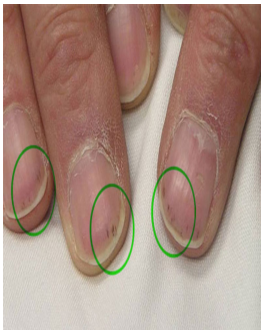
- ❖ Bacterial endocarditis
- ❖ Septic emboli
- ❖ CTD
- ❖ Trauma
- ❖ Idiopathic



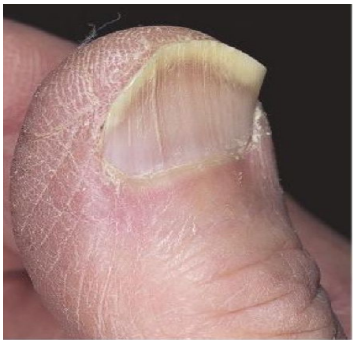
Clubbing



** splinter hemmoarage**



splinter hemmoarage



Koilonychia

Hyperlipidemia:

★ **Xanthelasma palpebrarum:**

- ❖ is the most common of the xanthomas asymptomatic and usually bilateral and symmetric.
- ❖ Can be associated with any type of primary hyperlipoproteinemia and could be without hyperlipidemia.
- ❖ often treated with topical trichloroacetic acid, electrodesiccation, laser therapy, and surgical excision.

★ **Tendinous xanthomas:**

- ❖ commonly seen on the Achilles tendon followed by the hands, feet, elbows, and knees.
- ❖ The least responsive xanthoma to treatment.
- ❖ Mostly seen in patients with familial hypercholesterolemia.

★ **Tuberous xanthomas:**

- ❖ are firm and nontender cutaneous and subcutaneous yellowish nodules on extensor surfaces.
- ❖ Mostly associated with familial dysbetalipoproteinemia.
- ❖ May resolve after months of treatment with lipid lowering agents.

★ **Eruptive xanthomas:**

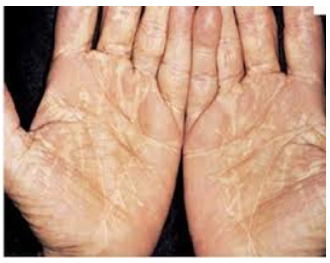
- ❖ are painless, yellowish papules on an erythematous base that present as grouped lesions on trunk, elbows and buttocks.
- ❖ Usually associated with hypertriglyceridemia.
- ❖ Could be seen in poorly controlled diabetes and acute pancreatitis.
- ❖ Usually resolve in few weeks after therapy.

★ **Planar xanthomas**

- ❖ are elevated cutaneous yellowish-orange deposits on palmar creases.
- ❖ Usually associated with familial dysbetalipoproteinemia.

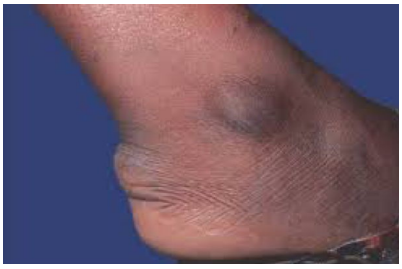
Types of Xanthomas :

1. **Eruptive**: small papules appear in crops over buttocks &extensors
2. **Tendinous**: Nodules over tendons e.g. extensor tendonsof hands & feet and Achilles tendon.
3. **Palmar crease** xanthoma: on palms
4. **Tuberous:** Papules & nodules over knees and elbows
5. **Xanthelasma:** Bilateral symmetrical over both eyelids.



Palmar

exanthelasma



tendinous xanthomas