Derma Team 436

cutaneous manifestation of systemic diseases

Objectives:

Not given

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Before you start.. CHECK THE EDITING FILE

Sources: doctor's slides and notes + FITZPATRICK color atlas +435 team

[Color index: Important | doctor 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 Generalized 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: round scarring lesions on light exposed areas, No Systemic involvement.

C. Subacute Cutaneous Lupus: papulosqamous or annular presentation Photosensitivity, Dose not cause scarring, Usually ANA negative but anti Ro positive.

D. Neonatal Lupus: Congenital heart block (complete & permanent) usually needs pacemaker, anti Ro positive, Appears in the first month in a photo-distribution, Patterns (Papulosqamous and annular).

E. Drug-induced Lupus: Procainamide and Hydralazine, Antihistone positive.

Skin characteristics of SLE are:

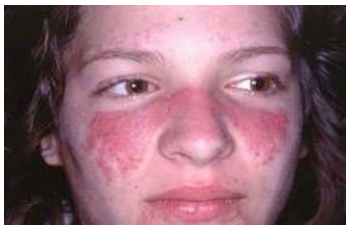
A. Facial photosensitivity.

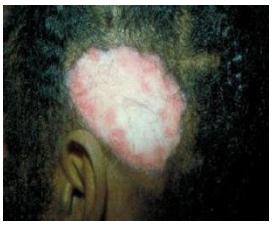
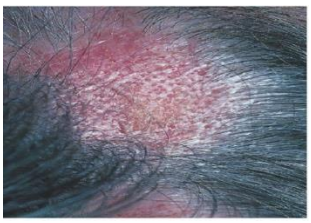
B. Butterfly erythema (malar rash).

C. Oral and nasopharyngeal ulcers.

D. Alopecia. (scarring)

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



Pic1&2: butterfly erythema indicates (ACLE).
Pic3&4: discoid lopus with scarring alopecia (pic 3 there is dyschromia: loss of pigmentation).
Pic4(notice the follicular plugging).

2-Dermatomyositis

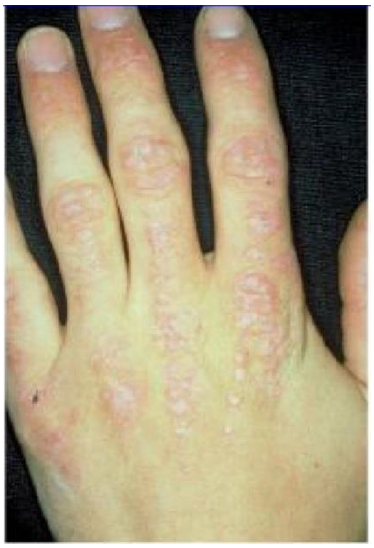
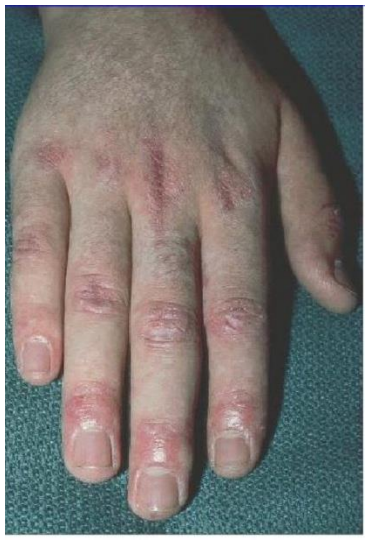
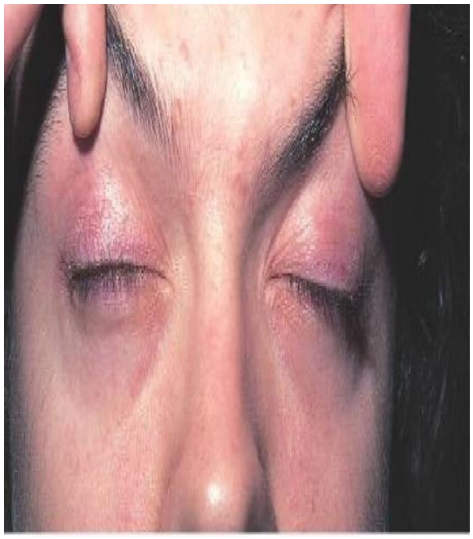
Dermatomyositis is an idiopathic inflammatory myopathy, there is a genetic predisposition and an environmental trigger leading to humoral immune activation resulting in chronic inflammation.

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 must 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.

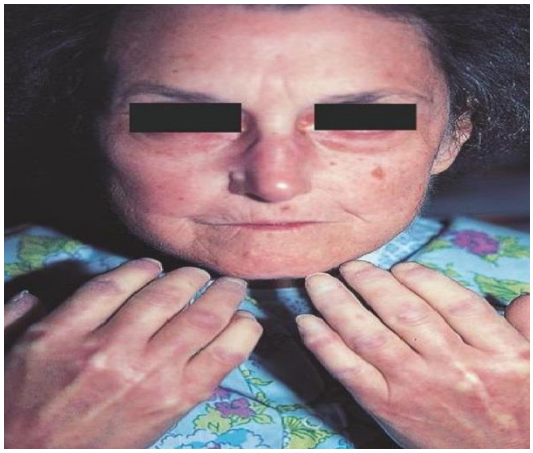
Features of Scleroderma:

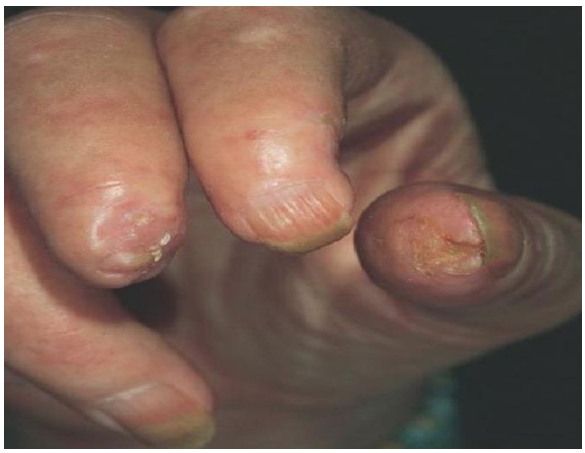
1) **A. Tight and thickened skin.**
2) **Loss of forehead lines,** beaked nose, small mouth, radial furrowing around the mouth.
3) **CREST is a milder type of scleroderma, there is Calcification, Raynaud's phenomenon, Esophageal dysfunction, Sclerodactyly, Telangiectasia and positive anti-centromere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

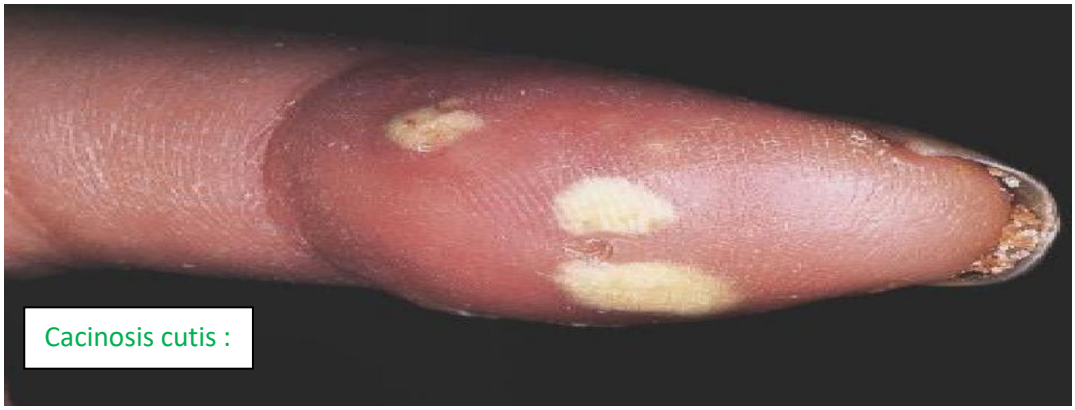
Other types of scleroderma include:

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.

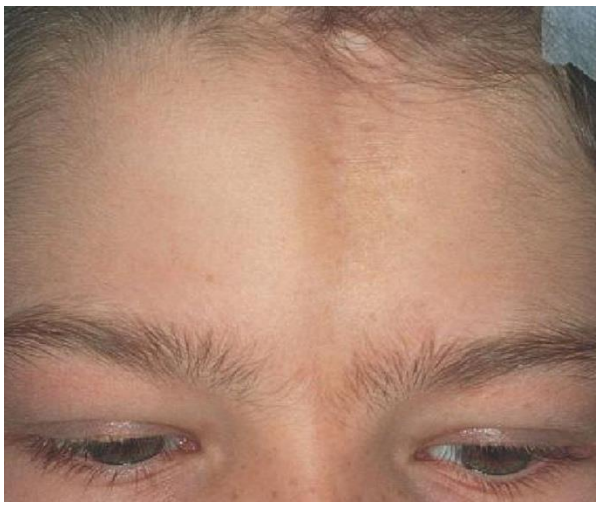




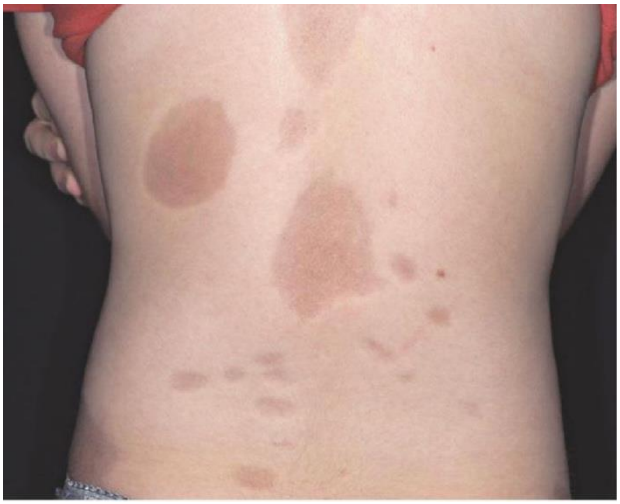


Cacinosis cutis :

Deep atrophy seen in linear localized scleroderma, goes deep.



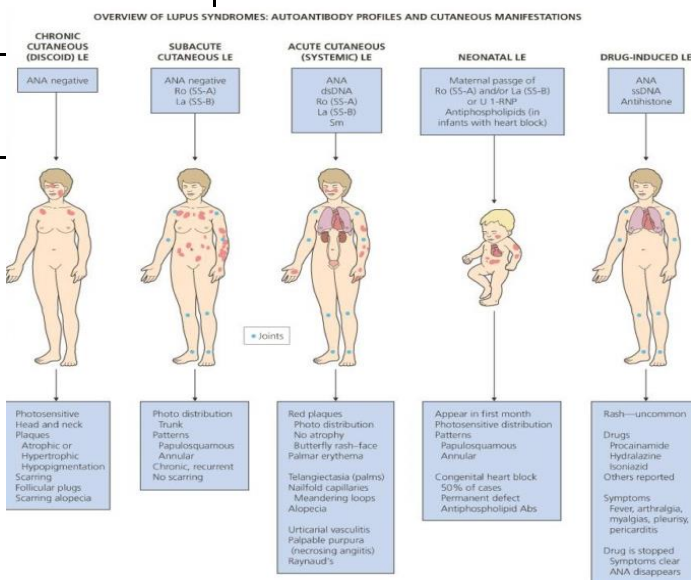
coup de sapre



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



Endocrine system:

A- Diabetes mellitus:

◄ *Acanthosis nigricans*

- Brown hyperpigmentation & increased thickening of skin with velvety texture at neck, axillae and groin, usually have velvety appearance, seen more in body folds.
- Causes:

1. Obesity.
2. Endocrinopathy: Diabetes, Thyroid disease, Insulin resistance.
3. Internal malignancy: the most common is adenocarcinoma of stomach.
4. Drugs: Nicotinic acid.
5. Familial.
6. Idiopathic.

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.

◄ *Necrobiosis lipoidica diabeticorum* (asymptomatic seen in the shins of the leg, may progress to atrophy or ulcers)

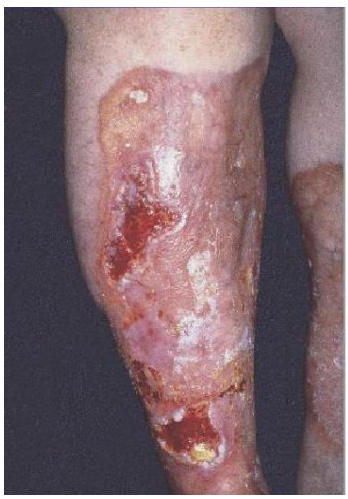
Shiny red or yellowish atrophic plaques on the shins with telangiectasia over their surface.

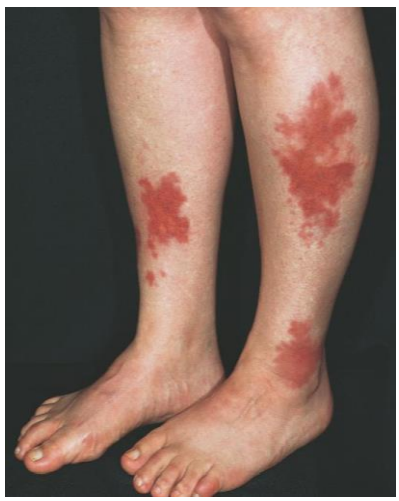
Sometimes they ulcerate. Histopathology: shows tiered granulomatous Reaction.

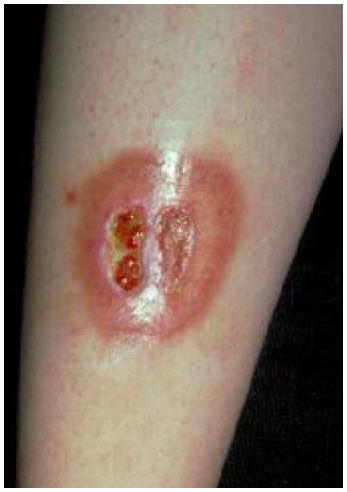
Severity of NLD is not directly related to severity of diabetes.

May predate frank development of diabetes by several years.

**Increased risk of fungal and bacterial infection*



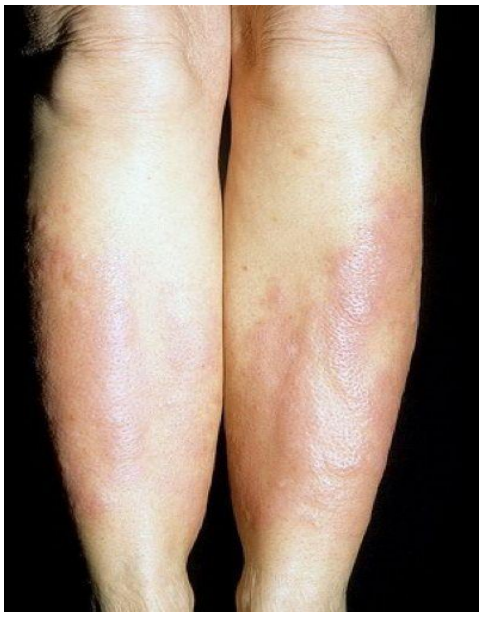


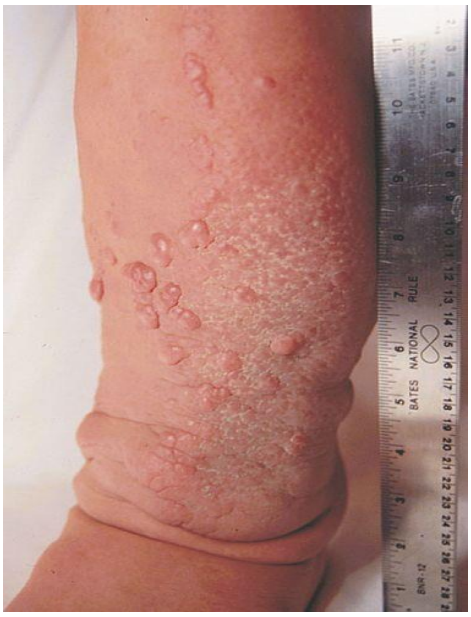


B- Thyroid disorders

◀ Hyperthyroidism

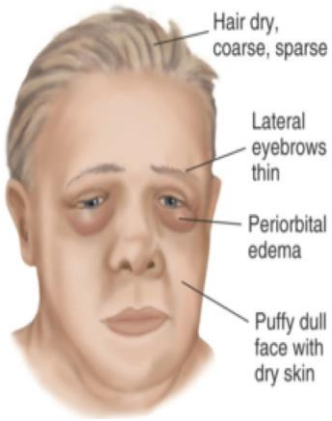
- Pretibial myxedema: is the most characteristic features of thyrotoxicosis appearing as shiny waxy red papules and plaques having orange-skin appearance on the shin of the tibia.
- Warm skin and increased sweating and pruritus.
- Premature hair graying, alopecia with fine soft thinned scalp hair.
-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





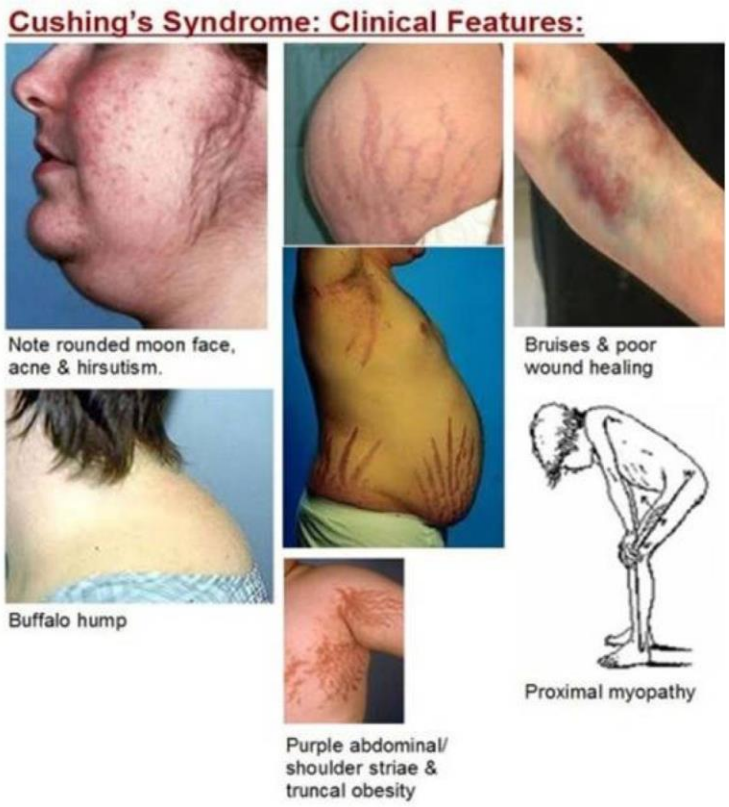
◀ Hypothyroidism

- Cold, pale and dry skin and pruritus.
- Edematous skin (myxedema).
- A yellowish hue to the skin due to carotenaemia. Slow growing ridged and brittle hair and nails.
- Hair loss of lateral third of eyebrows.
- Delayed wound healing.



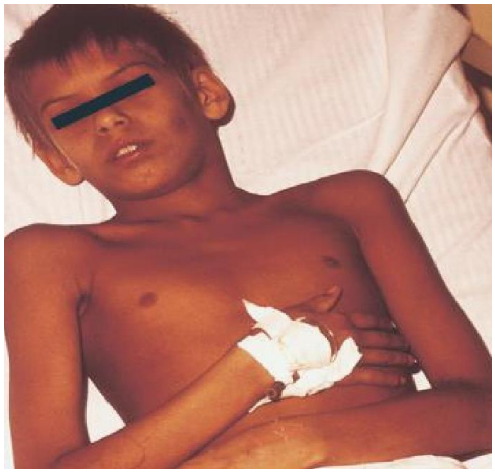
C- Cushing's syndrome

- caused by prolonged exposure to high levels of plasma glucocorticoid, adrenocortical hyperplasia, benign or malignant adrenal tumors, ectopic ACTH syndrome – secretion of ACTH by malignant or benign tumors arising in structures other than the pituitary or adrenal glands, exogenous steroid administration.
  - Acne and hirsutism.
  - Clitoromegaly and male pattern alopecia (Hamilton pattern). Striae.
  - Easy bruising and purpura.
  - Moon face and buffalo hump with fat redistribution.
  - Telangiectasia on face. Poor wound healing. Purpura.
  - Central obesity with thin arms & legs. Atrophy of skin.



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



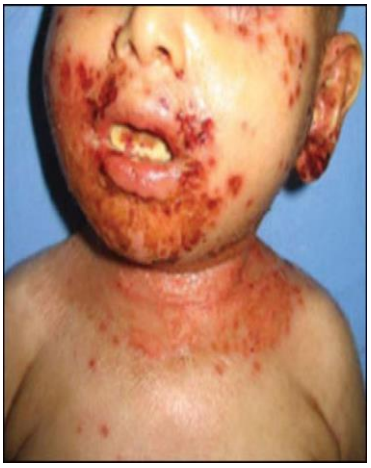
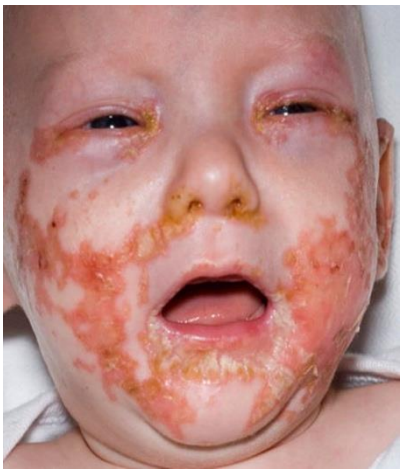
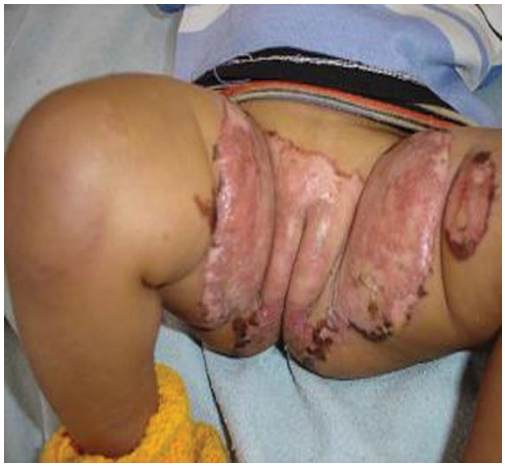
Gastrointestinal diseases

1- Chronic Liver Disease

- Jaundice, spider telangiectasia, acne, gynaecomastia, purpura, collateral veins, striae, palmer erythema, dupuytren's contracture, and white nails.

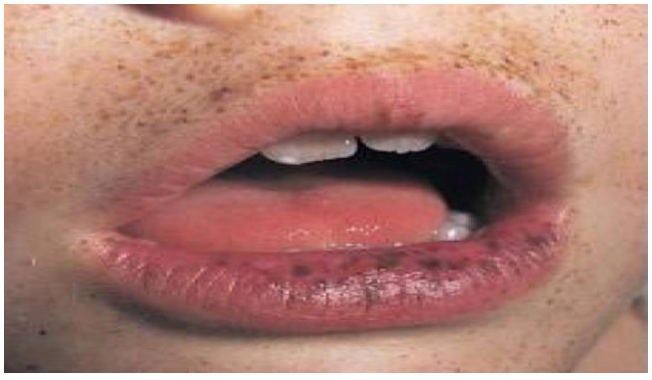
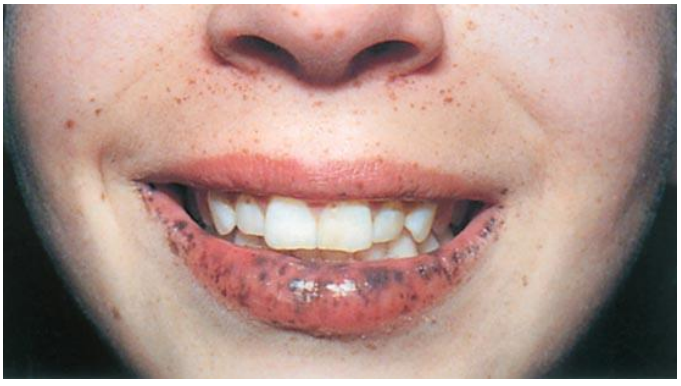
2-Acrodermatitis enteropathica (eczema like, around orifices).

- a rare autosomal recessive disorder that impairs dietary zinc absorption in the jejunum and ileum.
- presents in infants several weeks after breastfeeding is discontinued, they also have gi symptoms like diarrhea and abdominal pain.
- characterized by diarrhea, inflammatory rash, nail dystrophy, abdominal pain, 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.

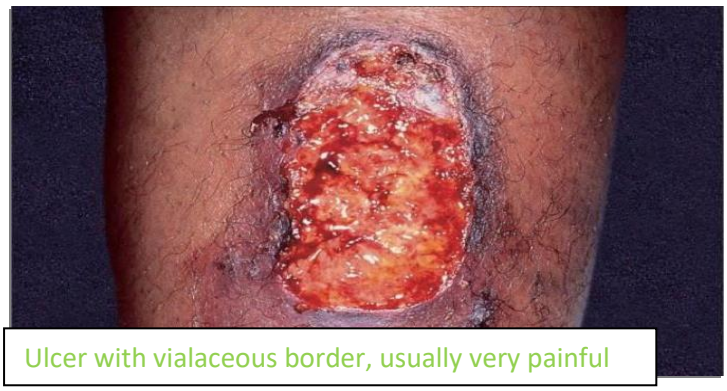
3- Peutz Jeghers syndrome

- autosomal dominant disorder.
- mucocutaneous hyperpigmentation together with GI polyposis.
- rarely polyps can be premalignant may progress to malignancy.
- 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
-

4- Pyoderma gangrenosum

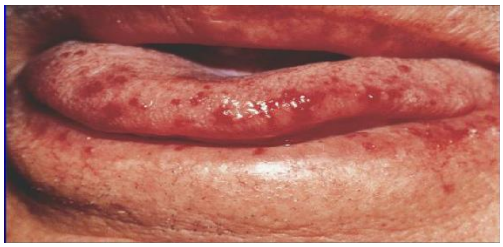
- Acute painful leg ulceration lesion with a well-defined, undermined violaceous border.
- start as small pustules, which subsequently burst and expand to form the larger noninfectious ulcer.
- Positive pathergy test.
- Mostly associated with ulcerative colitis. Also, with Crohn's disease, rheumatoid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



Ulcer with vialaceous border, usually very painful

5-Hereditary haemorrghic Telangiectasia

- Telangectasia (dilated capillaries) over lip, nose, tongue, fingers and toes.
- Hx of recurrent epistaxis.
- Associated with recurrent upper GI bleed.

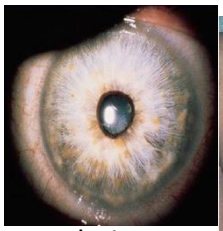


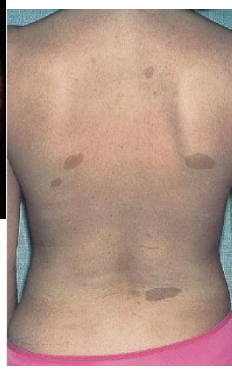
Neurocutaneous Disorders

Neurofibromatosis:

Autosomal dominant.

- Café-au-lait macules (light brown) can be seen in other disorders but if big size and number suspect neurofibromatosis
- 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

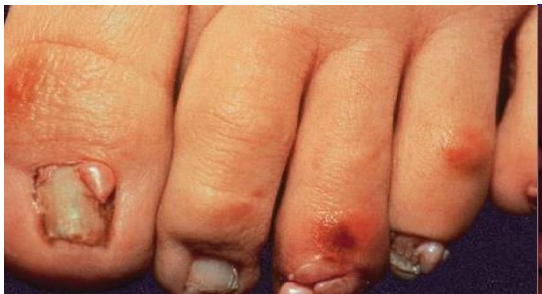
Skin Features:

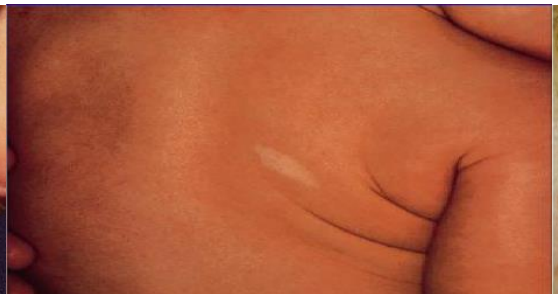
Adenoma sebaceum (anigofibroma): red papules around the nose and on chin.

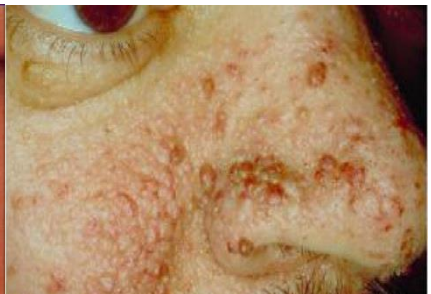
Ash-leaf hypopigmention: oval area of hypopigmentation ***This is the earliest sign of TS.***

Periungal fibroma: multiple papules & nodules around the nail

Shagreen patch: skin colored plaque on the trunk with "orange-peel" Surface.







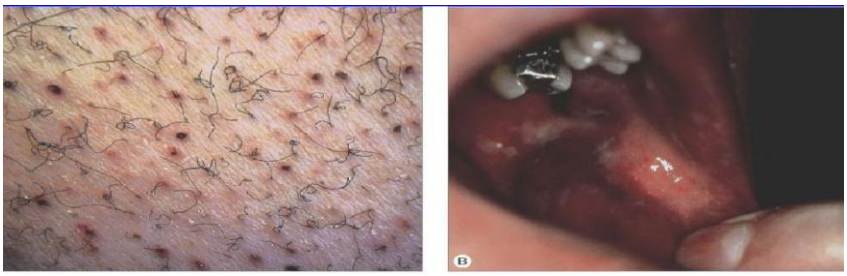
Others:

Behcet's syndrome:

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

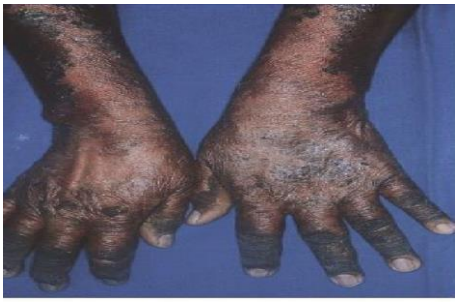
Scurvy:

- Vitamin C deficiency, Bleeding gums.
- Can cause teeth loss (permanent complication).
- Easy bruising, they bleed easily through their gum.
- Diagnosis: Low ascorbic acid (Vit-C) level in Leukocyte.
- Very brittle hair.



Pellagra: Nictonic acid deficiency 4 "D" s:

- Dermatitis (Photodermatitis)
- Death (if not treated)
- Diarrhea
- Dementia
- Vitamin deficiency.



Causes of Generalized Pruritus Without Skin Lesions

Generalized Pruritus can indicate internal disease:

- Endocrine: DM, hypo& hyperthyroidism.
- Hematological: polycythemia rubra vera, iron def anemia.
- Malignancy; e.g. Lymphoma.
- Hepatic: primary biliary cirrhosis.
- Renal: CRF. (The commonest manifestation of CRF is pruritus).
- Neurological: e.g. Tabes dorialis.
- Others: Psychogenic, Drugs, Idiopathic.

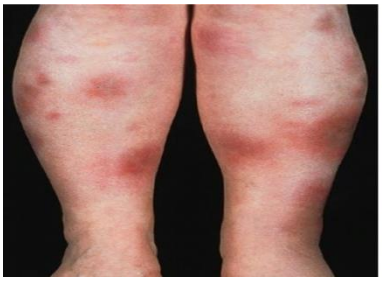
Table 7.2 Possible laboratory studies in the evaluation of pruritus. These laboratory tests should be performed according to the patient's history, in particular in cases of generalized pruritus of unknown etiology.

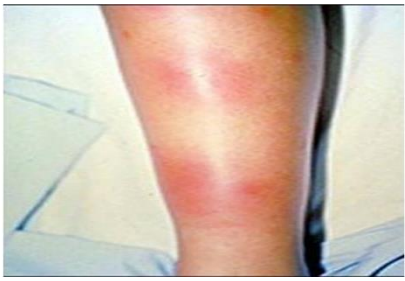
POSSIBLE LABORATORY STUDIES IN THE EVALUATION OF PRURITUS
• Erythrocyte sedimentation rate (ESR) • Complete blood cell count (CBC) with differential and platelet count • Blood urea nitrogen, creatinine • Liver transaminases, alkaline phosphatase, bilirubin • Fasting glucose • Thyroid function tests (thyroid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

Erythema Nodosum

- ❖ Multiple ill-defined bilateral tender erythematous subcutaneous nodules over shins
- ❖ More common in females
- ❖ Causes:

1. Infectious: Streptococcus, Tuberculosis, Hepatitis, Chlamydia.
2. Sarcoidosis.
3. Drugs: Oral contraceptive pills, sulfonamides.
4. Lymphoma & leukemia.
5. Pregnancy.
6. Behcet's disease.
7. Idiopathic.





Nails:

Koilonychia:

- Spoon- shaped appearance
- Causes:

1. Iron deficiency anemia
2. Thyroid disease
3. Physiological; early childhood.
4. Dermatosis: Lichen planus, Alopecia Areata and others

Clubbing:

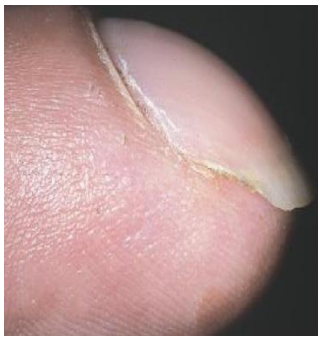
- Exaggeration of the normal nail curve associated with loss of the normal angle between nail and posterior nail fold.

Causes:

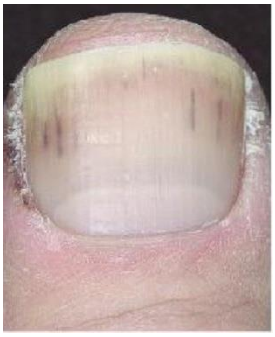
- Thoracic: Lung abscess, Lung CA
- CVS: Congenital cyanotic heart disease
- GIT:GI carcinoma, Inflammatory bowel disease Endocrine: Thyroid disease
- Idiopathic.

Splinter Haemorrhages Causes:

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

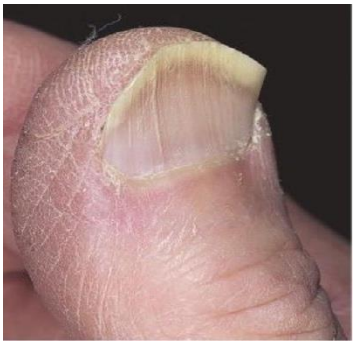


Clubbing



splinter hemmoarage

splinter hemmoarage



Koilonychia

Hyperlipidemia:

(Present with different types of xanthomas, Yellow color is characteristic)

Xanthoma may be a pointer to: Primary hyperlipemic status due to genetic abnormality, Secondary hyperlipemic status due to renal, hepatic, endocrine or pancreatic disease, Normo-lipemic status.

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:

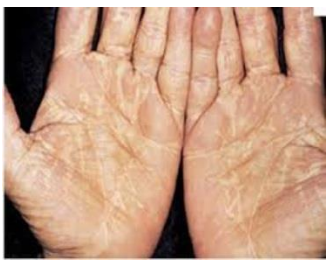
- are painless, yellowish papules on an erythematous base that present as grouped lesions on trunk, elbows and buttocks.
  - Usually associated with hypertriglyceridemia.
  - Could be seen in poorly controlled diabetes and acute pancreatitis.
  - Usually resolve in few weeks after therapy.

Planar xanthomas:

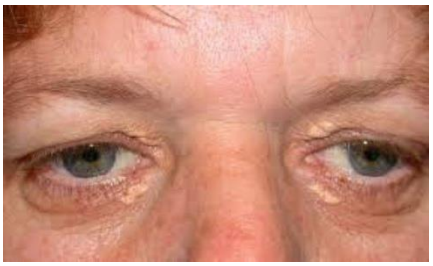
- are elevated cutaneous yellowish-orange deposits on palmar creases.
- Usually associated with familial dysbetalipoproteinemia.

Types of Xanthomas:

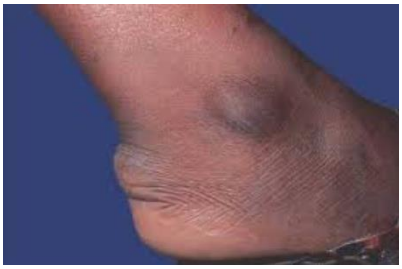
1. **Eruptive**: small papules appear in crops over buttocks &extensors
2. **Tendinous**: Nodules over tendons e.g. extensor tendons of hands & feet and Achilles tendon.
3. **Palmar crease** xanthoma: on palms
4. **Tuberous:** Papules & nodules over knees and elbows
5. **Xanthelasma:** Bilateral symmetrical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



Palmar



exanthelasma

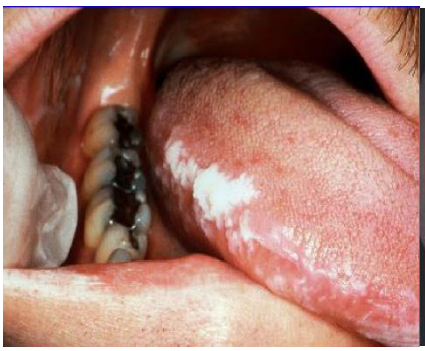
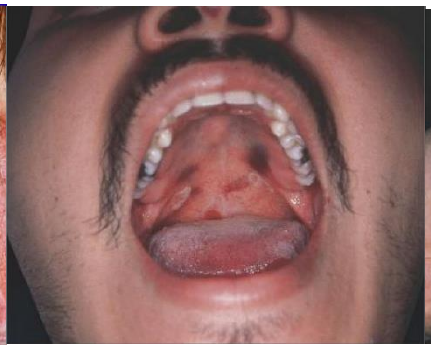
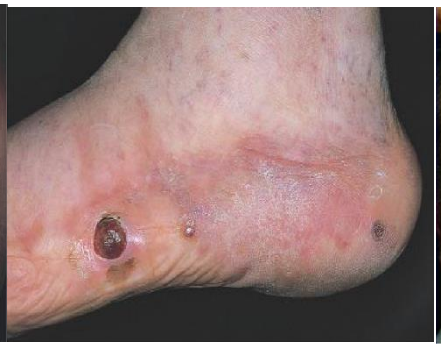
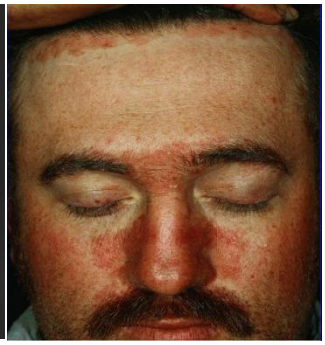


tendinous xanthomas

Some mucocutaneous disorders in which you need to do HIV testing?

- Oral hairy leukoplakia: Corrugated white plaques on the lateral aspect of the tongue.
- Kaposi Sarcoma not all associated with HIV:

1. Caused by HHV -8.
2. Blue macules, patches or nodules which is in essence a vascular tumor.
3. Associated with low CD4 count.
4. May resolve or diminish if CD4 count rises.
5. Types of Kaposi sarcoma: Classic type (in elderly), Immunosuppression associated, HIV associated, and African endemic type.
6. Metastasis to Lymph nodes, and Viscera.
7. Severe seborrheic dermatitis not responding to medications.

Examples of some skin diseases where you may find systemic associations:

- Lichen planus; associated with Hepatitis B and C
- Vitiligo and Alopecia Areata: both associated with autoimmune diseases like: Autoimmune Thyroid dis, Diabetes mellitus, Prenicious anemia, Mysthina gravis etc.