Common Skin Infections: Bacterial

Types of infections:

1- BACTERIAL INFECTIONS.
2- VIRAL INFECTIONS.
3- FUNGAL INFECTIONS
4- PARASITIC INFECTIONS

1-bacterial infections

Impetigo

Epidemiology

- **Primarily affects children** (especially between 2–6 years of age).
- Impetigo is **highly contagious** and can cause epidemics in preschools or schools.
- **Impetigo is the most common bacterial skin infection among children**

Etiology

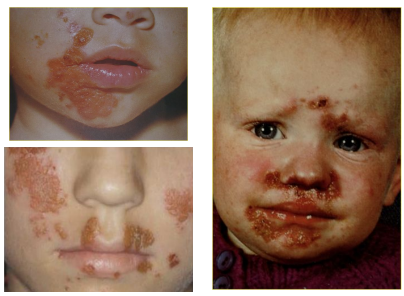
- **Staphylococcus aureus (>90%) (Most common)** > both bullous impetigo and nonbullous impetigo.
- **Streptococcus pyogenes > causes nonbullous impetigo only.**

Clinical features

"Know the descriptive term as they may come in the exam"

Nonbullous impetigo (70%):

- **Papules**, which **turn into small vesicles surrounded by erythema** and/or **pustules**.
- Negative Nikolsky sign.
- **Distribution**:
  - Face (most common), especially around the nose and mouth.

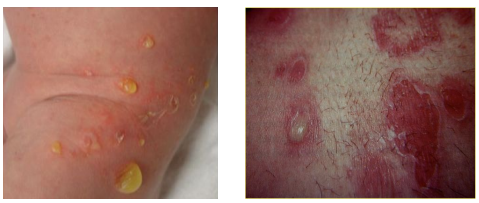


Honeycomb appearance

Perioral perinasal crusted honey colored papules.

Bullous impetigo (30%):

- **Vesicles that grow to form large, flaccid bullae**, which go on to rupture and form thin, brown crusts.
- Positive Nikolsky sign
- **Distribution**:
  - Trunk and upper extremities



Diagnosis

Generally diagnosed based on clinical presentation
DDx: Chronic bullous disease of childhood (in first 1-2 months of disease) especially if there was no response to Abx

Treatment

- **Wound care**
- **Topical antibiotics (mupirocin).**

If the patient has Fever, constitutional symptoms or is immunocompromised; give oral antibiotics: **Amoxicillin, Cephalosporin.**
If **MRSA infection**; clindamycin, **trimethoprim-sulfamethoxazole**, doxycycline

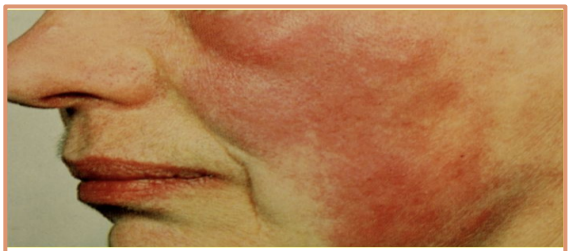
Common Skin Infections: Bacterial (Cont.)

Cellulitis & Erysipelas

Definitions	• **Erysipelas:** superficial skin infection involving the upper dermis. • **Cellulitis:** local infection of the deep dermis and subcutaneous tissue.
Etiology	• **Streptococcus pyogenes (Group A Streptococcus) (Most common)** • Less commonly: Staphylococcus aureus. H.Influenza could possibly cause it in children (but less common than strep) In both erysipelas and cellulitis, the most common point of entry for the pathogen is a small skin lesion (e.g., interdigital tinea pedis). • Diabetes and Athlete's foot are among risk factors

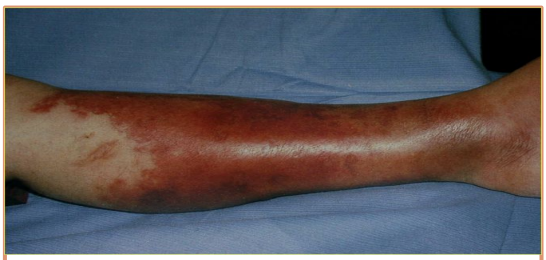
Clinical features	• **Local signs: erythema, edema, warmth, tenderness**
	  ○ **Specific to erysipelas**: raised, sharply demarcated lesion.
	  ○ **Specific to cellulitis**: poorly defined lesion with induration.
	• Cutaneous lymphatic edema (historically referred to as "peau d'orange").
	• **Common locations: lower limbs & face.**
	• Possible additional features
	  ○ Lymphangitis: red streaks radiating from the skin lesion and following the direction of the lymphatic vessels
	  ○ Lymphadenitis: swollen, tender, regional lymph nodes
	  ○ Purulent exudate
	• Systemic symptoms (in moderate/severe infections): fever, chills, confusion, nausea, headache, muscle and joint pain (+Constitutional symptoms)

Diagnosis	• Generally diagnosed based on clinical presentation.
Treatment	• Oral Penicillins. However, if you suspect MRSA (Methicillin Resistant Staph A); clindamycin, vancomycin, doxycycline or 3rd generation cephalosporins. • If the patient has signs of **septicemia or not improving after 24 hours of oral antibiotics; switch to IV Antibiotics.**



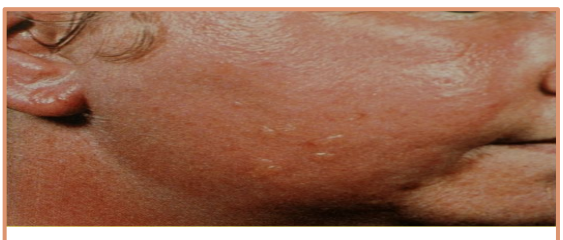
red and swollen.

Infection here is more deep ; cellulitis



Most common site for cellulitis is the leg because the leg is more prone to trauma.

More severe cellulitis erupted bullae



More swollen edematous With blisters

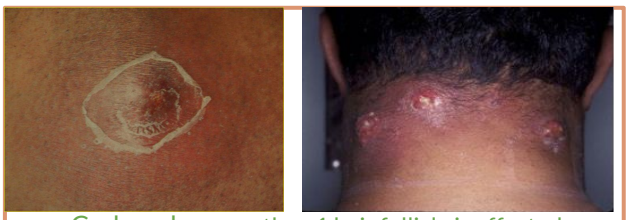
Common Skin Infections: Bacterial (Cont.)

Folliculitis

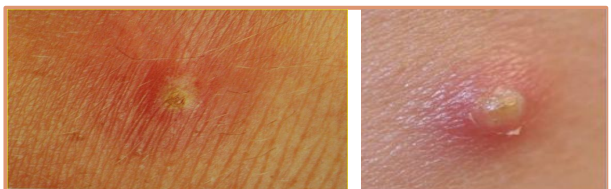
Definitions:	• **Folliculitis:**
	  ○ Localized inflammation of the hair follicle (or sebaceous glands) that is limited to the epidermis. **Basically: Infection of a hair follicle.**
	• **Furuncle:**
	  ○ Deep folliculitis beyond the dermis **in one hair follicle.**
	• **Carbuncle:**
	  ○ Confluent folliculitis that forms an inflammatory mass (**Multiple follicles**).
	Furuncles & Carbuncles are usually seen in immunocompromised pts.

Etiology	• **Staphylococcus aureus. (Most common),** usually happens when the person is shaving
	• **Others:**
	  ○ Gram negative bacteria – usually in patients with acne who are on broad spectrum antibiotics.
	  ○ Pseudomonas ("Hot tub folliculitis"). appears 8–48 hours after exposure to contaminated water
	  ○ Yeasts (candida and pityrosporum).
	  ○ Demodex.

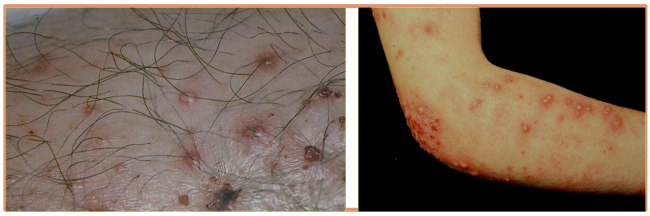
Clinical features	• **Tender papules and/or pustules, often pruritic** • **Located at the site of hair follicles** • **Possible pus drainage from follicular orifices** • **Facial furuncles can result in severe complications (e.g., periorbital cellulitis, cavernous sinus thrombosis).**
Diagnosis	• Generally diagnosed based on clinical presentation.
Treatment	• Topical antiseptics such as Chlorhexidine • **Topical antibiotics, such as Fusidic acid, Mupirocin or clindamycin.** • More resistant cases may need oral antibiotics (similar to impetigo). • Hot tub folliculitis: (P. aeruginosa)– usually self limited (ciprofloxacin in severe cases). • Gram negative: trimethoprim, isotretinoin. • Some patients will have **chronic folliculitis** (on and off breakouts). It is caused by being **a carrier of staph**. It mainly affects 4 areas (we apply topical Abx to these areas) : Axilla, groin, nostrils, and palms. These patients can be given rifampicin which penetrates more aggressively on tissues which is helpful in carrier state



Carbuncle; more than 1 hair follicle is affected



Furuncle ; deep folliculitis in diabetics



MCQ: Diabetic patients can develop these.

Common Skin Infections: Bacterial (Cont.) & Viral

Staphylococcal scalded skin syndrome (SSSS):

- Primarily affects infants and young children between 6 months and 5 years of age (Usually in nurseries and closed communities)
- Rare in adults: may occur in adults with predisposing conditions (e.g., impaired renal function or immunosuppression)
- **Widespread infection of staphylococcus, we need immediate I.V antibiotics to avoid septicemia**

Initially:

- Fever
- Skin tenderness
- Diffuse or localized erythema, often beginning **periorally**

After 24–48 hours:

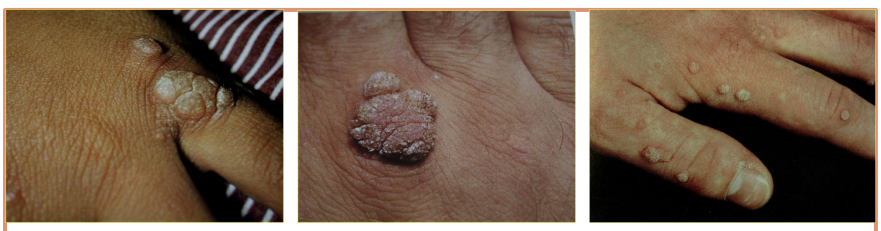
- Flaccid, easily ruptured blisters that break to reveal moist, red skin beneath (i.e., with a "scalded" appearance) → widespread sloughing of epidermal skin
- Nikolsky sign is positive
- No mucosal involvement
- Cracking, and crusting
- Signs of shock (hypotension, tachycardia)

- DDX: TEN, but the difference is TEN is due to drugs reactions, in elderly, here usually in children

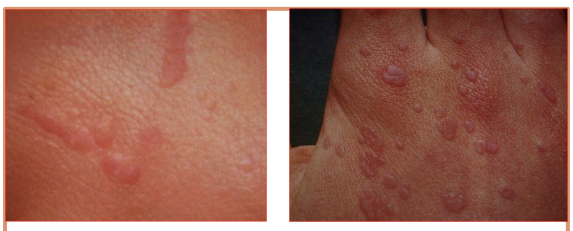
2-Viral infections

Warts / ثالول

Etiology	• Common warts are caused by HPV 2 and 4. (1 and 3 as well but it is less common) • Flat warts are associated with HPV 3 and 10 • genital warts are caused by HPV 6 and 11 and they cause cervical squamous cell carcinoma. • HPV 16,18, 31, 33 are the most aggressive in causing genital cancers.
Diagnosis	• Diagnosis of the cancer by skin biopsy • To know what subtype of Human Papilloma virus is by PCR (polymerase chain reaction)



Hyperkeratotic verrucous papules



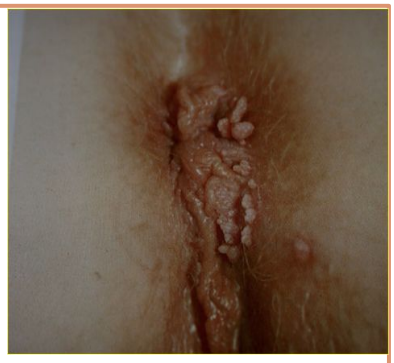
plane wart caused by HPV type 1 mainly

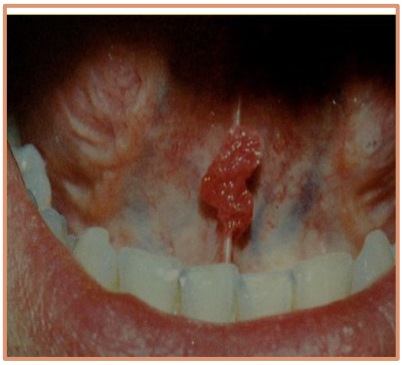
Note: Numbers of HPV are important

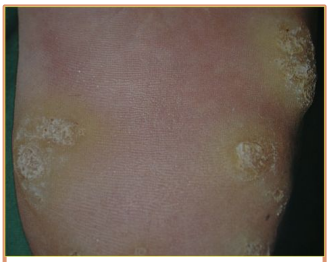
2-Viral infections

Condyloma acuminate: type of genital warts, commonly sexually transmitted.
Think of child abuse if a child has genital warts.

Description: Multiple Soft convoluted (finger like) papules.





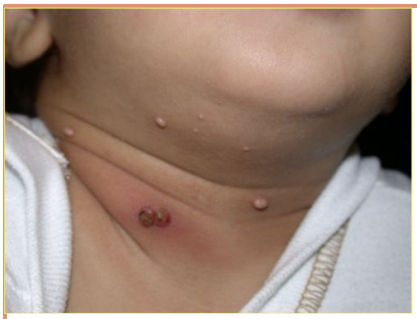


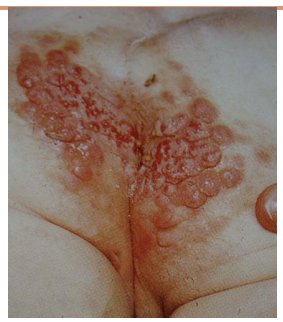
Plantar wart. (Affect sole)

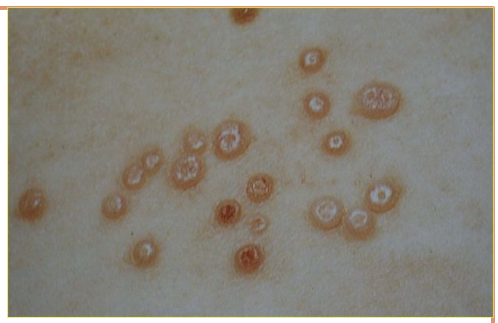
HPV: 6,11 , Usually does not cause cancer, Tx: **imiquimod**

Molluscum Contagiosum (Poxvirus):

Etiology & Epidemiology	• DNA poxvirus (molluscum contagiosum virus) • **Mostly in children** rarely with adults (in immunocompromised or as a STD) • **In genital warts in children it can be cause by autoinoculation or Abuse.** ○ **Autoinoculation: secondary infection originating from the site of an infection already present in the body.**
Diagnosis	• Diagnosis of the cancer by skin biopsy







Dome shaped shiny yellowish-whitish papule with central umbilication.

Management of Warts and Molluscum Contagiosum (Poxvirus):

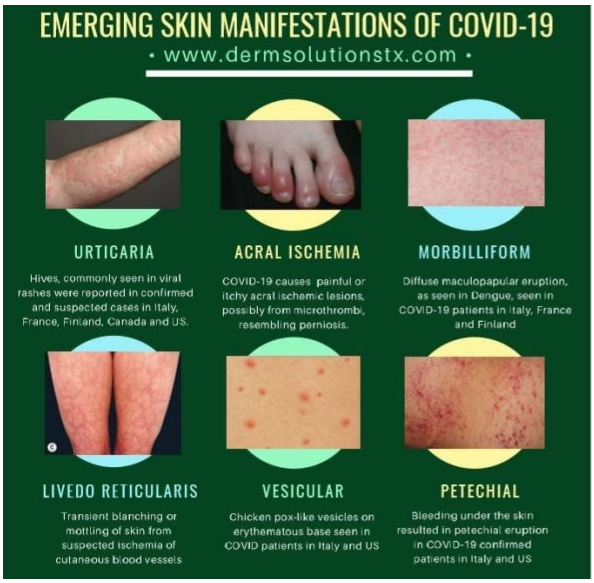
- **Both Involute spontaneously.**
- Liquid nitrogen
- Electric cautery
- Keratolytic e.g. salicylic acid

Genital Warts	• In genital warts it is painful to use the previous treatments so **Imiquimod(cream)** is the treatment of choice.
Molluscum Contagiosum	**Most effective treatment of molluscum is curettage** but you can't use that for warts because warts are deeper in the skin.

Common Skin Infections: Viral (Cont.)

COVID-19 "يمكن نجيب منه سؤال ولا اثنين"

- Can cause any skin manifestation
- Exanthematous (morbilliform) rash, predominantly involving the trunk has been reported as the most common cutaneous manifestation of COVID-19
- Acral ischemia could occur due to inflammatory processes, like any virus



Important

Monkeypox

Etiology & Epidemiology	• Caused by **Monkeypox virus**, from family **Poxviridae** (same as smallpox) • Originally in monkeys, but then transmitted to human • Endemic in West and Central Africa "Congo kinshasa" any country deals with monkeys
Clinical features	• The manifestation could be the same as chickenpox (العنقز), papules with vesicles, can be pustule
Risk factors	• **Homosexuals** • Exposure to animal reservoirs
Transmission	• Human-to-human transmission, through cutaneous or mucosal lesions or body fluids **(e.g., sex, kissing, hugging, massaging)**, Respiratory droplet, vertical or fomite transmission (e.g., from contaminated clothes, bed sheets) • **Animal-to-human transmission**: scratch or bite from an infected animal
Prevention	• By smallpox vaccines (الجدري), but since smallpox is eradicated, the vaccine is not given anymore, that's why the virus start to be endemic in these countries
Diagnoses	• Clinically & PCR • Laboratory tests can identify individuals with severe disease who have indications for inpatient management and/or antiviral therapy.
Management	• Self-limiting disease, resolve within 2 weeks • Supportive care • Isolation to prevent the spread of the disease

Common Skin Infections: Viral (Cont.)

Herpes Viruses	

Herpes Simplex	• **Usually present as a group of small blisters.**
	
	• **HSV-1(H. labialis)**
	  ○ **Mostly affects Orolabial mucosa.**
	  ○ **80% of general population** aged 18 had HSV-1 whether it was clinical or subclinical. So, if you test them with IGG for HSV-1, they'll be positive
	  ○ Infection with HSV-1 usually is acquired in childhood via saliva.
	  ○ Recurring, erythematous vesicles that turn into painful ulcerations, also known as cold sores; oral mucosa and lip borders
	  ○ **Normally self-limiting**, but sometimes it causes Primary severe Gingivostomatitis and you should give systemic antiviral.
	  ○ **Stays latent in trigeminal ganglia**. (If it affects the ophthalmic division we must urgently refer the patient to ophthalmology)
	
	• **HSV-2 (genital herpes)**
	  ○ **Mostly affects genital.**
	  ○ **Sexually transmitted.**
	  ■ Patients need counseling to teach them (not to spread the virus).
	  ■ **You should treat the partner.**
	  ○ Lesions with a punched-out appearance that ulcerate after several days in the anogenital area
	  ○ Lesions may appear as single or disseminated, painful red bumps or white vesicles.
	  ○ Stay latent in sacral ganglia
	
	• **Herpetic whitlow.**
	• **Eczema herpeticum:**
	  ○ **Infection with HSV in patients with previous skin disease (eg: atopic dermatitis, pemphigus, Darrier disease) - or any condition that breaks the integrity of the skin.**
	  ○ **Serious complication that needs admission and systemic antiviral.**
	  ○ **Any patient with active eczema and herpes should be given systemic antiviral to prevent Eczema Herpeticum.**

Diagnosis	• Tzanck Smear • Direct fluorescent antibody(DFA) • **Viral culture- most definitive**
Treatment	• Oral /IV acyclovir for: ○ **Genital, Recurrent, immunosuppressed, neonatal, Eczema Herpeticum.** • **Prophylaxis: indicated in the case of frequent (4 to 5 times) or severe relapses; 6 months - 1 year Acyclovir.**

Common Skin Infections: Viral (Cont.)

Herpes Viruses (Cont.)

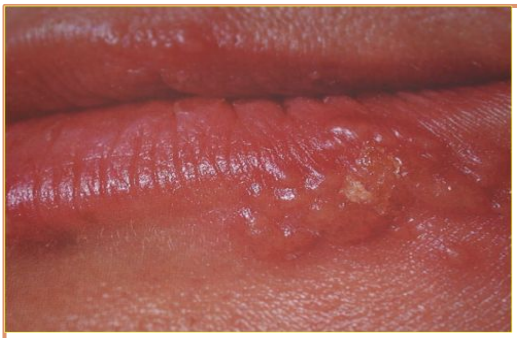
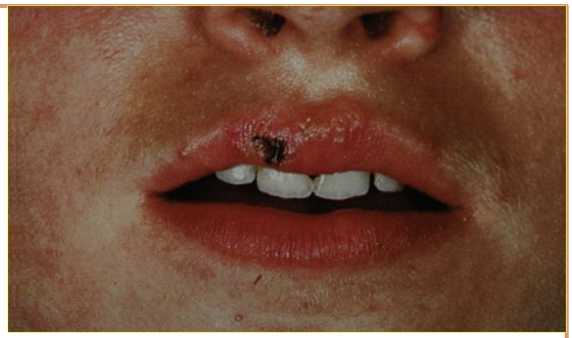
Varicella (Chicken pox)	• **Initial infection with varicella zoster virus (VZV)** which is HSV-3
	• **Highly contagious**
	• **The whole illness : 3 weeks**
	  ○ **Incubation period : 2 weeks.**
	  ○ **Prodrome of respiratory coryza.**
	  ○ **Disseminated red macules with central vesicles or pustules.**
	• Papules→ superficial vesicles filled with **clear fluid** on an erythematous base → umbilicated and crusty pustules → scabs fall off after 1–3 weeks, (often leaving a depressed base)
	• Lesions first **manifest centrally (i.e., face, scalp, and trunk)** and spread to the extremities.
	• **The patient is contagious 5 days before and 5 days after skin eruption**
	• **Mainly affects Children.** We give antivirals to prevents scarring
	  ○ **Adults : immunosuppression, pneumonia.** More severe
	• **Varicella in pregnancy:**
	  ○ 1st and 2nd trimester : risk of varicella embryopathy syndrome & abortion.
	  ○ 3rd trimester congenital varicella
	  ○ Pregnant patients with varicella should receive VZ immunoglobulin and antiviral therapy.
	• Severe varicella infection is characterized by the prolonged eruption of vesicles, which are sometimes hemorrhagic, high fever > 1 week, and dissemination of VZV to the brain (encephalitis), liver (hepatitis), and/or lungs (pneumonia).

Herpes Zoster (Shingle)	• **Adults, elderly.** > 50 Yo
	• **Following initial varicella infection VZV remains latent in sensory ganglia; when reactivated it will affects skin dermatome supplied by this ganglia.**
	• **Phases:**
	  • **Prodromal pain**
	  • **Dermatomal (grouped blisters and vesicles on background of erythema)**
	  • **Post-herpetic neuralgia**

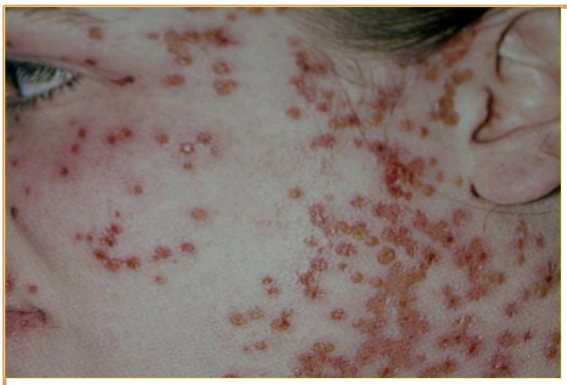
Diagnosis	• Tzanck Smear • Direct fluorescent antibody (DFA) • **Viral culture- most definitive**

Treatment	• **Varicella**
	  ○ Symptomatic for itching.
	  ○ Systemic antiviral in immunocompromised patients
	• **Zoster**
	  ○ Analgesia
	  ○ **ANTIVIRAL**(acyclovir, or "cyclovir" group in general) **(within 72 hours of skin eruption).** > To minimize the disease duration **& may help decrease Post herpetic neuralgia.**

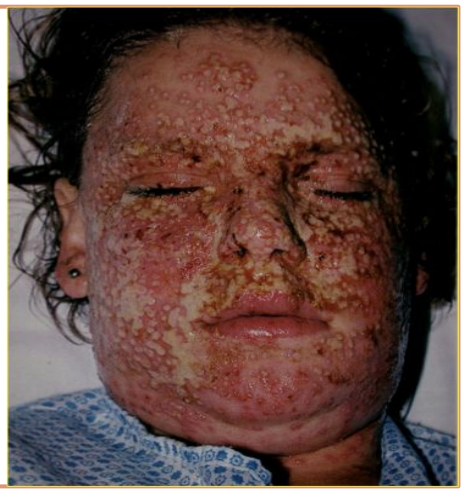
Common Skin Infections: Viral (Cont.)

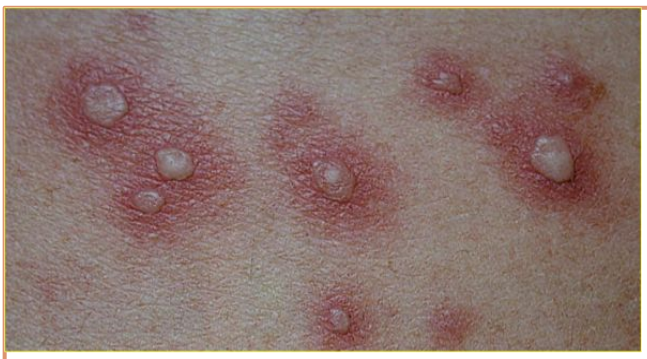
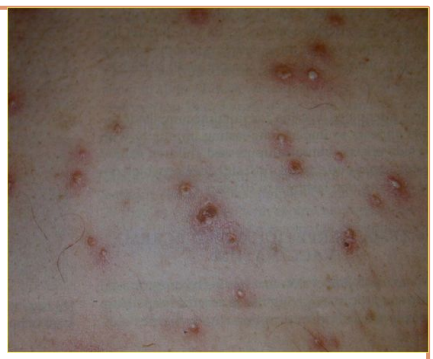



HSV-1: Multiple grouped erythematous vesicles

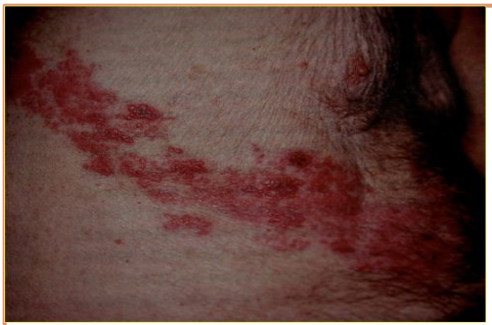
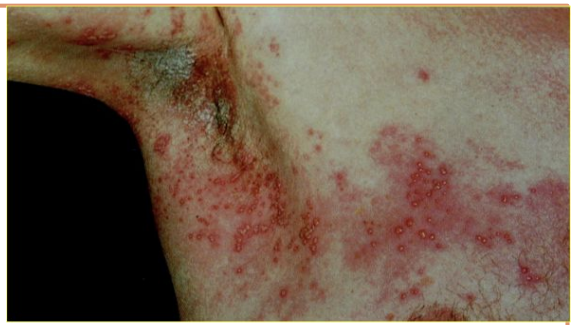


Eczema Herpeticum



Varicella: Multiple vesicles on erythematous base (dew drops)

Zoster

Common Skin Infections: Fungal

3- Fungal infections

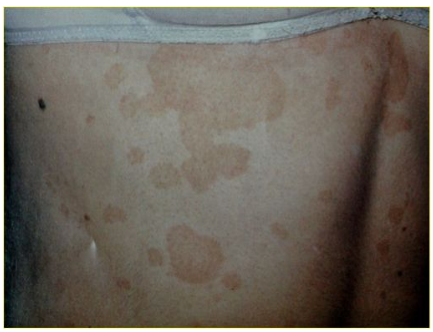
All Tinea infections are caused by dermatophytosis except tinea Versicolor caused by Malassezia Furfur and its part of our normal skin flora

Tinea Versicolor

- **Most common fungal infection in adults & adolescents. It is chronic and mostly affects the truncal area & upper extremities.**
- **Caused by Malassezia Furfur**
- **Pityriasis versicolor alba:** pale patches (hypopigmentation).
- **Pityriasis versicolor rubra:** reddish-brown (hyperpigmentation).
- **Diagnosis: Wood's lamp: coppery-orange fluorescence).**

Treatment:

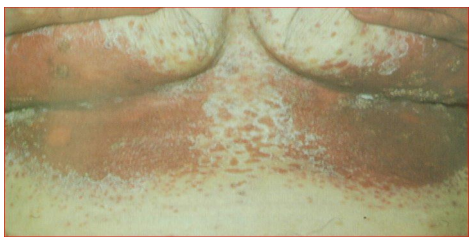
- **Topical** antifungal (e.g. ketoconazole shampoo) systemic antifungal can be used also (e.g. itraconazole).



Well-defined brownish scaly patches.

Candida Infection (intertrigo)

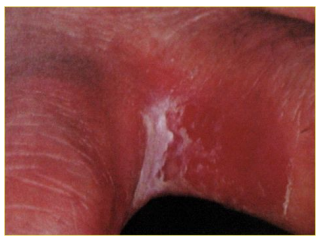
- **Affects moist and flexures**
- **BUT diabetic, obese, immunocompromised & bedridden patients are at a higher risk.**
- **Treatment:**
  - **topical antifungal +/- steroid if the patient has eczema.**

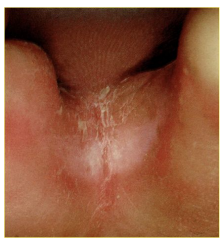


Well defined erythematous scaly eroded patches with satellite lesion.

Tinea Pedis (Athlete feet)

- Fungal infection caused by superficial **dermatophytes**.
- It affects mainly adults, (patients with moist skin in between the toes like athletes and diabetics are at higher risk).
- **Treatment:**
  - Education to dry up the skin.
  - Topical antifungal. (Azoles, Terbinafine, Nystatin)
  - In severe cases systemic antifungal.

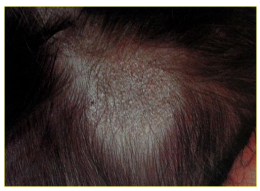


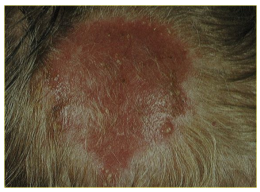


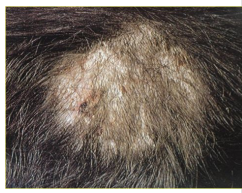
Painful erosions.
Note: If patient comes with cellulitis, check their feet as tinea pedis lesions may be an entry point for bacteria

Tinea Capitis

- Mostly in **children**
- May mimic seborrheic dermatitis
- Treatment:
  - Systemic antifungal
  - **Mainly Griseofulvin**, then Terbinafine, itraconazole
- Cats, birds, squirrels are common sources of infection



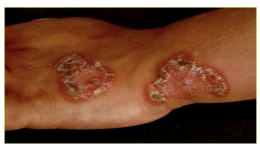


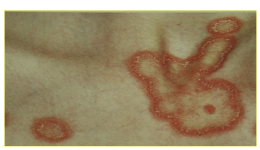


Well-defined erythematous scaly alopecic patches.
There is crust & papules w/o inflammation, unlike alopecia

Tinea Corporis

- Caused by superficial dermatophytes
- **Treatment:**
  - Single lesion > topical antifungal
  - Multiple lesions > systemic
  - antifungal (like Itraconazole)





Annular scaly active border with central clearing. In some cases it can have severe inflammation so instead of center will be red but it less than the borders

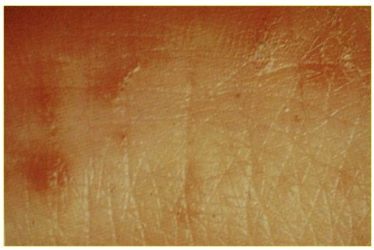
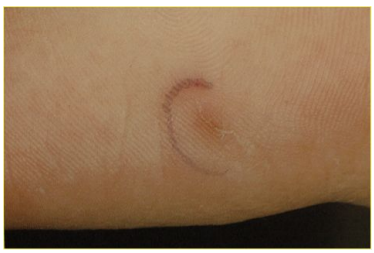
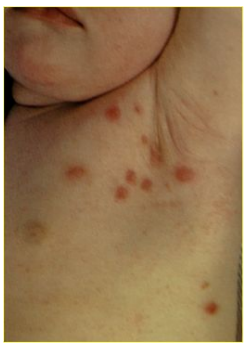
Common Skin Infections: Infestations

4- Parasitic Infestations

Infestations

Scabies
الجرب

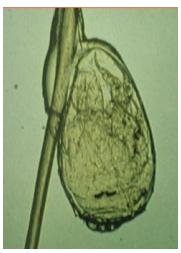
- **Causative organism:**
  - **Sarcoptes scabiei var. homini**
- Usually in groins / body folds / around nipples /genitalia.
- Affects all age group and became more common in crowded close lived people like in, shelters,travellers, homeless, prisoners,etc.
- **Intense pruritus** that increases **at night**
- **Characterized by Tunnels or Burrows (as seen in left pic).**
- **Treatment:**
  - **Topical: Permethrin / lindane cream**
  - they apply it on the whole body for 8 hours. They need to apply it again after one week and one more time after two weeks, 3 in total **to kill the newly hatched eggs**
  - Oral treatment can be used specially in epidemic situation or in severe and immunocompromised patients: Ivermectin
- Cleaning everything e.g. (clothes, blanket, pillows, etc) is required to prevent re-infection

Pediculosis
القمل

- **Affect scalp or and sometimes groin.**
- **Usually in children and homeless people**
- **Same sources as scabies**
- **May lead to secondary bacterial infection**
- **Treatment:**
  - **Topical: Permethrin / lindane** (Same as scabies) **but in shampoo formulation** to apply it over the scalp for 15 minutes then rain it with water, this can be repeated in 3 consecutive days to make sure all insects are killed.
  - Close contacts should be involved in assessment and treated if needed.

MCQ: Pediculosis in the past usually transmits a disease from one patient to another, what is it ? know it. (Epidemic typhus)

Answer from CDC: Body lice are known to transmit disease (*epidemic **typhus**, Bartonella quintana infection, and epidemic relapsing fever*).

Eczema & Dermatitis

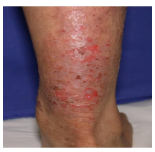
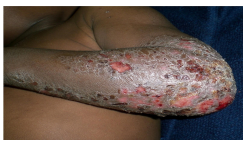
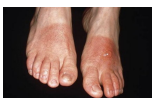
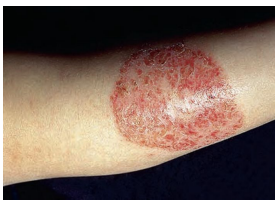
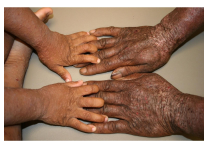
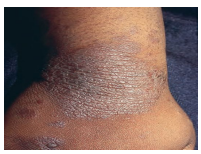
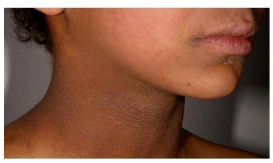
Eczema:

Definition:

- Inflammation of the skin.

Eczema VS Dermatitis:

- Eczema is a general word.
- Atopic dermatitis is a specific type of eczema and there are other types (contact dermatitis and others).

Eczema		
Acute eczema	**Subacute eczema**	**Chronic eczema**
Erosion, oozing and vesicles. The primary lesion of eczema is vesicles - Oozing = "Fluids" The secondary lesion of eczema is erosion    Acute red erosions on top of chronic with crust	**Redness + Swelling crust + Scale + infection** 	Lichenification, dark pigmentation and thick papules and plaques. Lichenification: Thickening of skin due to chronic rubbing, increase skin marking    Child with adult pattern (neck)

Dermatitis types:

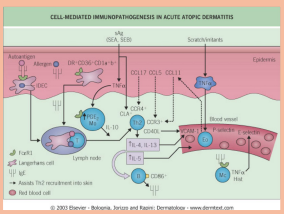
Atopic	**Seborrheic**	**Contact**	
Nummular	**Asteatotic**	**Stasis**	**Neurodermatitis/ Lichen Simplex Chronicus**

Atopic Dermatitis (AD):

Introduction

Definition: chronic relapsing itchy skin disease in genetically predisposed patients e.g: family Hx of asthma, nose or eye allergy.
Associated diseases: bronchial asthma, allergic rhinitis, allergic conjunctivitis.
Incidence: up to 15% in developed countries. Up to 15% - 20% in early childhood. More in males
Age of onset: 60% within the first 2 months, 30% by the age of 5, 10% between age of 6-20
Grow out tendency!

Pathogenesis



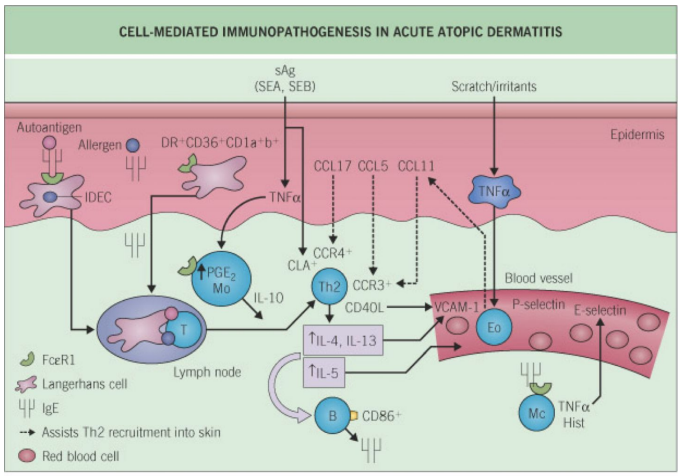
Multifactorial;

- **"Atopy": genetic predisposition**
- **Dry (atopic) skin** (decrease human B-defensin 3 predisposing patients to frequent skin infections : colonized by S aureus. infection with S aureus often causes a flare of AD) (decrease production of moisturizing lipids; sebum)
- **Allergy, increased tendency to certain allergens. AD and Food! minor role**
- Mutation of FLG (encodes filaggrin) disturbed skin barrier function dry skin, decrease moisturizing lipid production
- T-Cell (elevated Th2 cytokines and increased IgE production.)
- Recent studies showed a potential role for the Th17 pathway, with increased circulating Th17 cells in atopic patients, & increased Th17 in acute eczematous lesions. A decreased Th17 in chronic eczema argues for a dynamic role for the Th17 pathway.

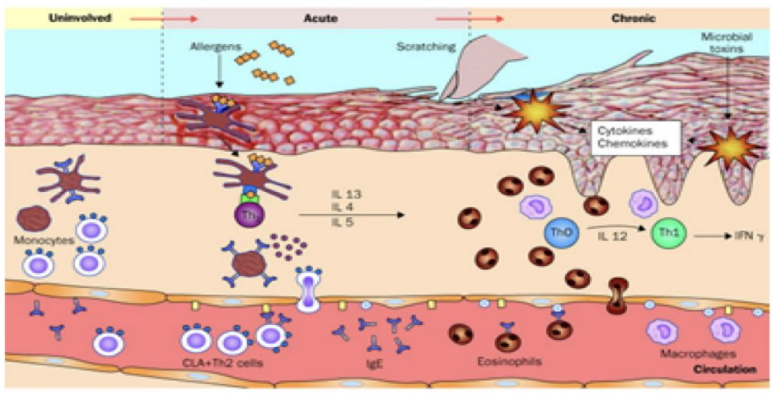
Prevalence and association with other atopic disorders

- Prevalence is almost 20% in US, representing a marked increase during the past several decade.
- Studies before 1960 estimated the prevalence to be up to 3%.
- **AD is often the 1st manifestation of the "atopic march";**
  - **AD → Asthma → Allergic rhinitis**
  - Asthma occurs in up to 50% of children who develop AD during the first 2 years of life;
  - Allergic rhinitis develop in 43-80% of children with AD.
  - In general children showing more severe dermatitis have a higher risk of developing asthma, as well as sensitization to foods and environmental allergens.
- **AD occurs more frequently in urban areas than in rural areas, in smaller families, and in higher socioeconomic classes.**
- Ultimately 80% of patients will develop increased IgE levels.
- **Loss-of-function mutations in profilaggrin (FLG)** (induce moisturizing of the skin) **cause ichthyosis vulgaris, a common genetic disorder characterized by dry, scaling skin** and hyperlinear palms that has long been known to be **common in individuals with AD**.
- **Distinct mutations in FLG** have been discovered in the European and Japanese populations, but all are strongly linked with AD, particularly of early onset.

Notes on Pathogenesis



-The immune system is divided into 2 parts: Innate (langerhan cells, antigen presenting cells(APC),etc..) & Acquired.
-Firstly the APC receives antigen “Recognition”(viral, bacterial,allergen, auto-antigen)
-The innate immune system is always first to react (through adhesion molecules, cytokines..) if not enough-> activation of the acquired immune system.
- APC and T Cells will meet in the **lymph node**-> **APC** presents the allergen antigen and ACTIVATE **T helper 2** (**Th2**) (responsible for allergic reaction)
- Th2 will:
1. Increases IL-5: Increases Eosinophils (migrate from blood to epidermis)
2. Increases IL-4 & IL-13: Activate the Vascular-Endothelial system > Inflammation (WBC, Cytokines..etc).
- usually: IgM-> acute infection, IgG-> chronic infection, in this situation (allergy) the blood IgE will increase in the chronic phase
- persistence of inflammation is why we call it “ immunodysregulation”.



- as time passes the immune system will try to balance the high Th2 => Th1 will increase and Th2 will decrease.
- when Th1 appears (chronic eczema) it is often mixed with psoriasis (both have Th1 activation).

- Allergic reaction types:
  - type 1 => urticaria (tested w skin prick test takes 15-30min)
  - type 4 => delayed hypersensitivity reaction (skin patch test requires 48-72hr)

Atopic Dermatitis (AD):

Histology

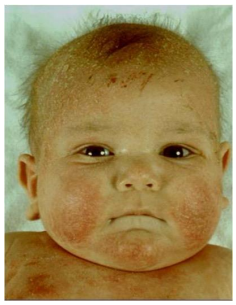
- **Edema within the epidermis (spongiosis)** and infiltration with lymphocytes and macrophages in the superficial dermis (no need to take a biopsy in AD).

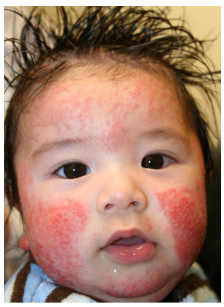
Clinical Variants of Atopic Dermatitis (AD) :

according to morphology when they first appeared

Infantile Atopic Dermatitis

- **60% of case AD present in the first year of life,** after 2 months of age.
- **Begin as itchy erythema of the cheeks.**
- **Distribution**:
  - Includes **scalp, neck, forehead, wrist, and extensors.**
  - **Diaper area is usually spared**
- Well demarcated, Ill defined (eczema always ill defined, psoriasis we'll defined), erythematous plaques(raised cause of inflammation), crusty and non-scaley.
- Red skin, tiny vesicles on "puffy " surface. Scaling, exudate with wet crust and fissures.

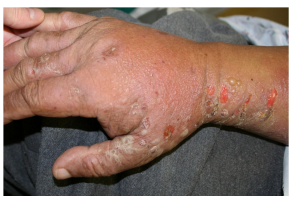


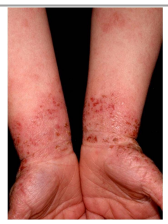


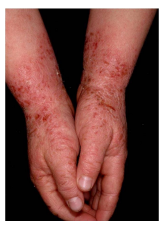
Baby looks well
No fever, not crying

Childhood Atopic Dermatitis

- Characterized by **less acute lesions.**
- **Distribution**:
  - **Antecubital and popliteal fossae, flexor wrist, eyelids, and face.**
- Severe atopic dermatitis involving more than 50% of body surface area is associated with growth retardation.
- May be generalized
- Papular, lichenified plaques, erosions, crusts.



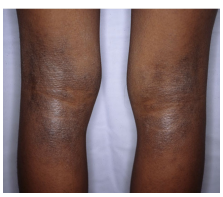


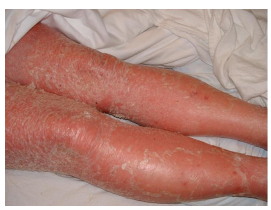


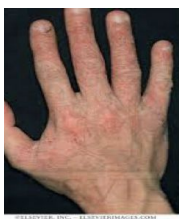
Adult Atopic Dermatitis

Can be localized or generalized

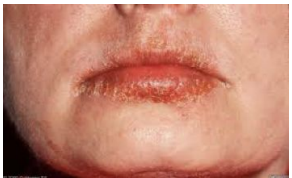
- **Distribution**:
  - **Antecubital and popliteal fossae, the front side of the neck, the forehead, and area around the eyes.**
- Atopic individuals are at greater risk of developing hand dermatitis than are the rest of the population.
- 70% develop hand dermatitis some times in their lives.
- Ill demarcated hyperpigmentation with lichenification.

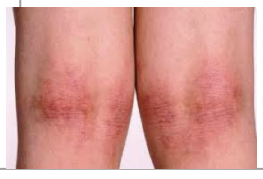


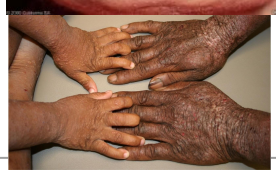




This is Erythroderma, a very rare complication of atopic dermatitis.



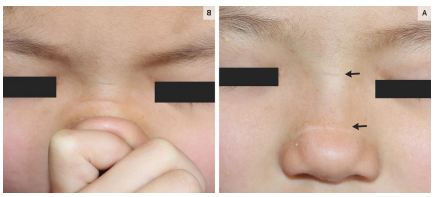




Atopic Dermatitis (AD):

Sequelae

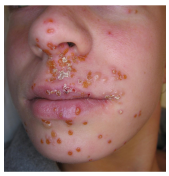
- Atopic individuals have a distinct tendency toward an extra line or groove of the lower eyelid, so called ”atopic pleat”, is present at birth or shortly after and usually retained throughout life, referred to as “Dennie-Morgan fold.
- Another feature, an exaggerated linear nasal crease, caused by frequent rubbing of the nasal tip (allergic salute), although not a specific sign of AD.

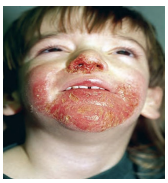


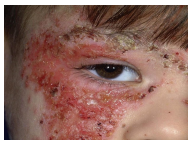
Complications of Atopic Dermatitis:

Secondary infections

- **Impetigo, a bacterial infection** caused by s. Aureus or streptococcus.
- If seen assume infection over subacute state and take swab, start Abx

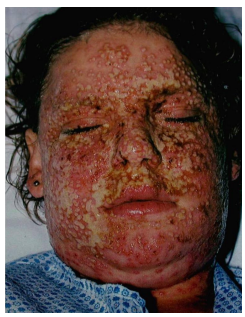




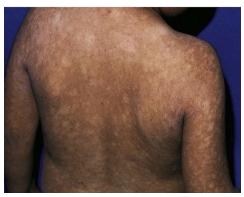


Eczema herpeticum

Eczema Herpiticum is a serious complicaiton caused by herpes simplex virus on a eczemarous patient that needs admission and systemic antiviral (V acyclovir) analgesia and an ophthalmologist.

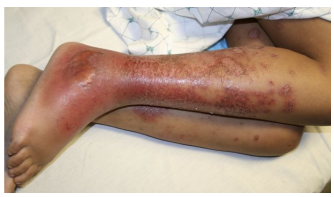


Post Inflammatory Hyper/Hypo-pigmentation (PIH)



Cellulitis

Skin infection
Why it’s not eczema?
- Because it’s deep “subcutaneous”
- Larger
- Painful



Growth retardation

Psychological

Table 5.I. Revised criteria for the diagnosis of atopic dermatitis[4]

a. Must have:
- Pruritus

b. Plus 3 or more of the following:
- History of involvement of skin creases (front of elbows, back of knees, front of ankles, neck, around the eyes)
- History of a generally dry skin in the past year
- Personal history of asthma or hay fever
- Onset under the age of 2 years
- Visible flexural dermatitis

The diagnosis of atopic dermatitis in adults is primarily clinical; special investigations only contribute in identifying external aggravating factors.

DIAGNOSTIC FEATURES OF ATOPIC DERMATITIS

Major features (3 of 4 present)
- Pruritus
- Typical morphology and distribution of skin lesions
- Chronic or chronically relapsing dermatitis
- Personal or family history of atopy

Minor features (3 of 23 present)
- Xerosis
- Ichthyosis/palmar hyperlinearity/keratosis pilaris النقرن (جلد الدجاج)، المسام متقاربة وقاسية
- Immediate (type I) skin test reactivity
- Elevated serum IgE
- Early age of onset
- Tendency towards cutaneous infections/impaired cell-mediated immunity
- Tendency towards non-specific hand or foot dermatitis
- Nipple eczema
- Cheilitis
- Recurrent conjunctivitis
- Dennie–Morgan infraorbital fold
- Keratoconus
- Anterior subcapsular cataract
- Orbital darkening
- Facial pallor/erythema
- Pityriasis alba
- Anterior neck folds
- Pruritus when sweating
- Intolerance to wool and lipid solvents
- Perifollicular accentuation
- Food intolerance
- Course influenced by environmental/emotional factors
- White dermographism/delayed blanch

Atopic Dermatitis (AD):

Investigations

- Atopic dermatitis is purely clinical; **No investigations are needed.**
- Please don't order IgE level, it's costly & helpless

Management of Atopic Dermatitis (AD):

Education! Education! Education! | **Psychological Support!**

Skin care:

Topical therapy (topical steroids, Tacrolimus, Pimecrolimus)

Topical steroids:

Classification of Topical Corticosteroids

Class	Potency	Examples (Not exclusive)	Caution
1	Superpotent	Clobetasole Propionate, Halobetasole Propionate	*Avoid in children, face, folds, near genitals.*
2	Potent	Betamethasone dipropionate, Halcinonide, Flucinonide	*Avoid in children, face, folds, near genitals.*
3	Upper Mid Strength	Betamethasone Valerate	*Use cautiously in children. Avoid on face, folds, near genitals*
4	Mid Strength	Mometasone, Beclomethasone, Fluocinolone 0.25%, Triamcinolone acetonide, Methyl Prednisolone acetonate	*They may be used in children for a short duration. Not to be used on face and body folds.*
5	Lower Mid Strength	Hydrocortisone butyrate, Fluticasone propionate	*Can be used in all ages and on the face and folds for a short duration*
6	Mild	Desonide, Flucinolone 0.1%	*Can be used in all ages and on the face and folds for a short duration*
7	Least Potent	Hydrocortisone 1%	*This can be used in all, the only one that may be bought over the counter.*

Local cutaneous side-effects
- Atrophy
- Striae
- Periorificial granulomatous dermatitis
- Acne
- Telangiectasia
- Erythema
- Hypopigmentation

Ocular effects
- Cataracts
- Glaucoma

Systemic side-effects
- Hypothalamic-pituitary-adrenal axis suppression

Phototherapy

using UV type B, it has anti- inflammatory effect, used specially when most of the body is affected, exposed to the ight twice a week

Sedative antihistamine (Oral H1 antihistamine) to control itching and help sleep

Antibiotics--- Antistaphylococcal drugs

Systemic therapy: Steroids rare, **Cyclosporine** nephrotoxic and can cause HTN, **Methotrexate, Azathioprine**

New biologics such as dupilumab

Pharmacological intervention

- Topical calcineurin inhibitors level of recommendations is A
- Efficacy:

1. Tacrolimus ointments(0.03% and 0.1% strengths)
   a. Approved for moderate to severe disease
   b. 0.1% as effective as the mid potency TCS hydrocortisone butyrate 0.1%.
   c. 0.03% is less effective than hydrocortisone butyrate 0.1% but more effective than the low potency TCS hydrocortisone acetate 1%
2. Pimecrolimus cream (1% strength)
   a. indicated for mild to moderate AD
   b. Less effective than mid and high potency TCS direct compression made

AD & food

Minor role

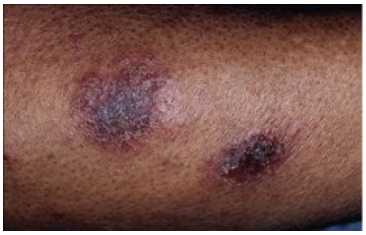
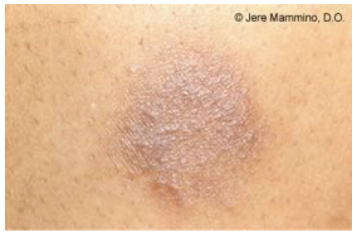
Prognosis

- Half of the cases improve by 2 years of age. Most improve by teenage years
- <10% of patients have lifelong problems
- 30-50% will develop BA or hay fever

Nummular Dermatitis & Regional Eczema

Nummular dermatitis

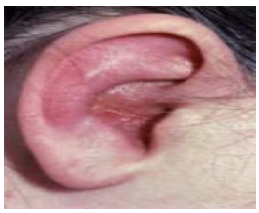
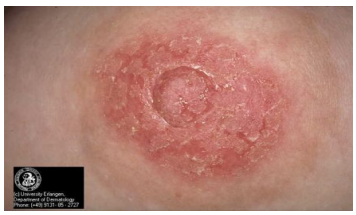
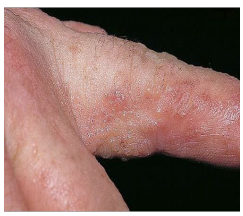
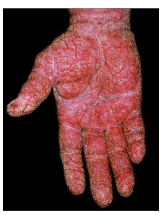
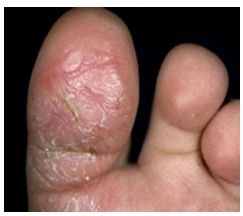
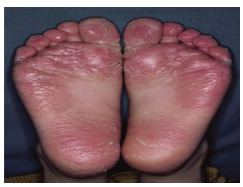
- **Coin shaped patches and plaques.**
- **Secondary to xerosis cutis.**
- **Primary symptom itch.**

Notice the surrounding xerosis

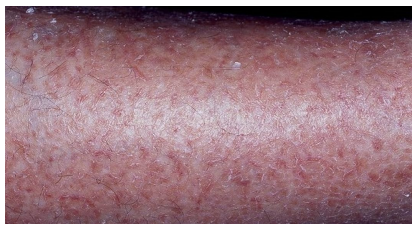
Regional Eczema

Regional Eczema:

Ear eczema Due to earring	• Most frequently caused by seborrheic or atopic dermatitis. • **Staph, Strep, or Pseudomonas.** • Earlobe is pathognomonic of nickel allergy.	
Nipple eczema Due to breastfeeding	• Painful fissuring, seen especially in nursing mothers • Maybe an isolated manifestation of atopic dermatitis. • If it persists more than 3 month, and/or unilateral, biopsy is mandatory to rule out **Paget's disease.**	
Hand Eczema Hand sensitizer	• **Spongiosis** histologically. • Irritant hand dermatitis seen in homemakers, nurses. • **Resulting from excessive exposure to soaps.** • Pompholyx- tapioca vesicles, on sides of fingers, palms, and soles • **Irritant** vs **allergic**.	  Ddx: scabies.
Juvenile plantar dermatosis	• Begins as a patchy symmetrical, smooth, red, glazed macules on the base of the great toes the pressure zone • Affect age 3 to puberty. • Symmetrical lesions on weight bearing area • Virtually always resolve after puberty Bilateral Ill defined erythematous shiny plaques with scales and fissures More in summer, heat, sock wearing Can happen in palm too (palmo-plantar dermatosis); problem with sweat glands. Treat with proper ventilation and moisturizer	  
Eyelid dermatitis due to makeup		
Diaper dermatitis		

Xerotic eczema & Contact Dermatitis

Xerotic / Asteototic eczema



- Aka: **winter itch** due to dryness, nummular eczema, eczema craquele, and asteototic eczema.
- Anterior shins, extensor arms, and flank
- **Elderly person predisposed.**
- Use of bath oils in bath water is recommended to prevent water loss
- Moisturizers – urea or lactic acid.

Contact Dermatitis

Definition: dermatitis results from contact with external materials.

Pathogenesis:

Irritant like detergent,chemicals, acid vs. allergic dye, henna, latex : (cytotoxic vs type IV)

Common irritants: detergent, acids, dust, burning chemicals, etc

Common allergens: perfumes, hair dyes, nickels, leathers, metals, rubbers, latex, cosmetics, etc

Allergic contact dermatitis

- **Type 4 Hypersensitivity Response.**
- Classically well demarcated/patterned.
- **First exposure does not cause a reaction**
- Begins 24 h after subsequent exposure if already allergic
- Exposure can be infrequent (once a month).
- **Commonest: Nickel i.e. like a jeans button**, chromates, rubber, preservatives, topical Abx, topical cs
- **Patch testing is gold standard for diagnosis**
  (read at 48, 96 h)

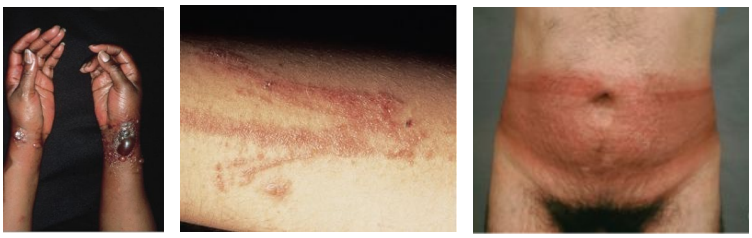
Management

- Identification removal of causes.
- **Patch testing:**

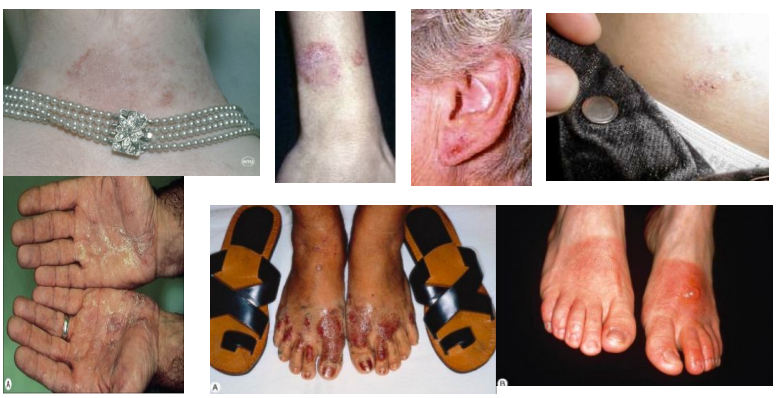
for allergic contact dermatitis not for irritant

Avoidance allergens

Topical corticosteroids



poison Ivy/ oak/ sumac



Potassium dichromate in leather

TOP TEN ALLERGENS AS IDENTIFIED BY THE NORTH AMERICAN CONTACT DERMATITIS GROUP

Test substance	Allergic reactions (%)	Relevant reactions (%)
Nickel sulfate	14.2	49.1
Neomycin sulfate	13.1	46.2
Balsam of Peru	11.8	82.9
Fragrance mix	11.7	86.9
Thimerosal 10.9		16.8
Sodium gold thiosulfate	9.5	40.6
Formaldehyde 9.3		63.2
Quaternium-15 9.0		88.7
Cobalt chloride	9.0	55.1
Bacitracin 8.7		50.4

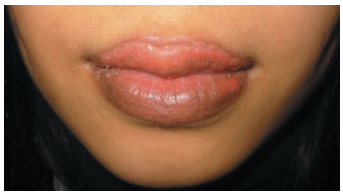
Xerotic eczema & Contact Dermatitis

Irritant contact dermatitis

- All people will react to an irritant if applied in a high enough concentration
- At 1st exposure
- **Most contact dermatitis is irritant in nature.**
- **Occupational morbidity.**
- **Prevention is key!**

Common causes:

- Hands repeatedly exposed to water, cleansers
- Lip-licking habit – wetting and drying caused by saliva
- Napkin dermatitis



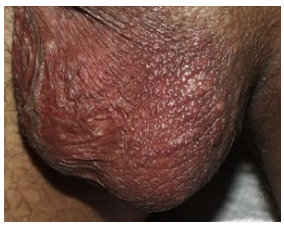
IRRITANTS AND MECHANISMS OF TOXICITY

Irritant	Mechanisms of toxicity
Detergents	Solubilization and/or disruption of barrier lipids and natural moisturizing factors in the stratum corneum Protein denaturation Membrane toxicity
Acids	Protein denaturation Cytotoxicity
Alkalis	Barrier lipid denaturation Cytotoxicity through cellular swelling
Oils	Disorganization of barrier lipids
Organic solvents	Solubilization of membrane lipids Membrane toxicity
Oxidants	Cytotoxicity
Reducing agents	Keratolysis
Water	If barrier is disrupted, cytotoxicity through swelling of viable epidermal cells

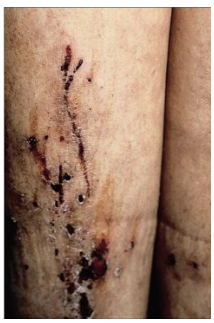
Neurodermatitis/Lichen Simplex Chronicus

- Paroxysmal pruritus.
- Habitual excoriating or rubbing.
- Skin thickens to defend.
- Consider underlying disease.

Increased skin markings



No fungus on the scrotum!

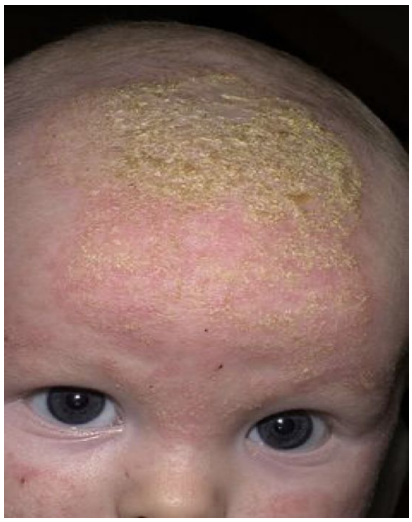


Prurigo simplex

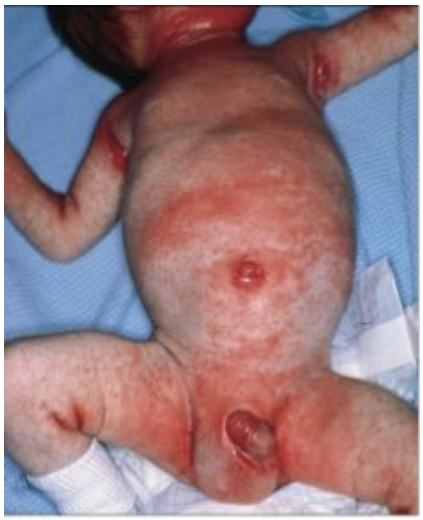
Seborrheic Dermatitis

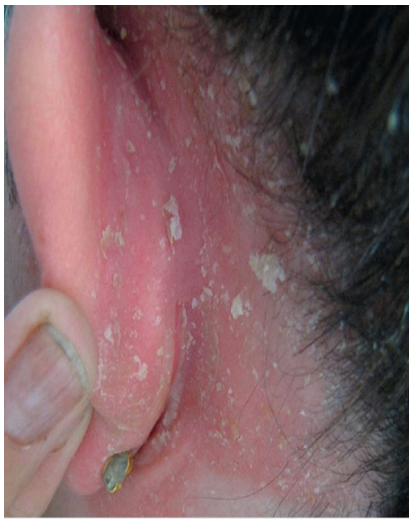
- **Definition:** redness and scaling in regions where the sebaceous glands are most active as the face, scalp, presternal area and body folds. **Very common chronic dermatosis.**
- **Age:** infancy, puberty , old age. More in **male**
- **Pathogenesis:**
  Increased Sebum!(seborrheic state), Tendency, **Pityrosporum ovale (Maalassezia furfur)** overgrowth, More in Parkinson, HIV/AIDS patients.
- **Distribution:**
  Hairy are of head, cradle cap
  Face: forehead, nasolabial folds , glabella and eyebrows.
  Trunk: DDx: PR vs pityriasis versicolor
  Body folds: axillae, groins, anogenital area, submammary areas, umbilicus and diaper area (infants
  sharply marginated erythematous eruption, erosions and fissures
  Genitalia: with yellow crust and psoriasiform lesion

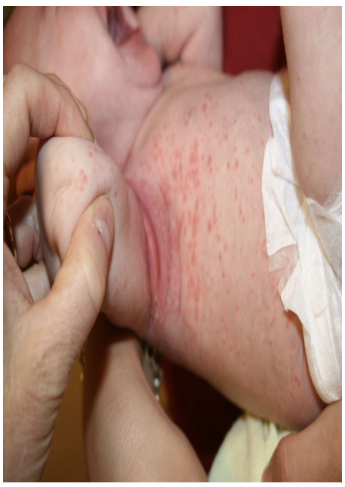
Seborrheic Dermatitis

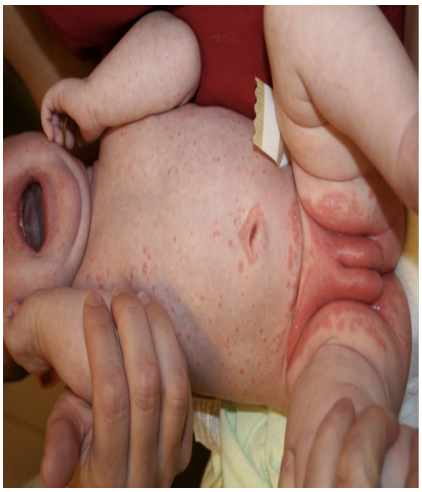


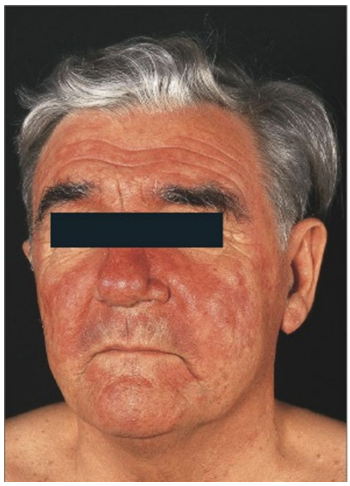
Cradle cap of oily scales on red scalp

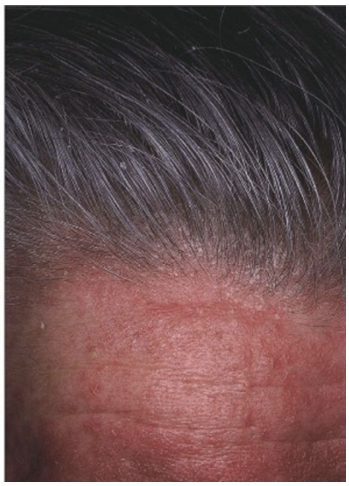


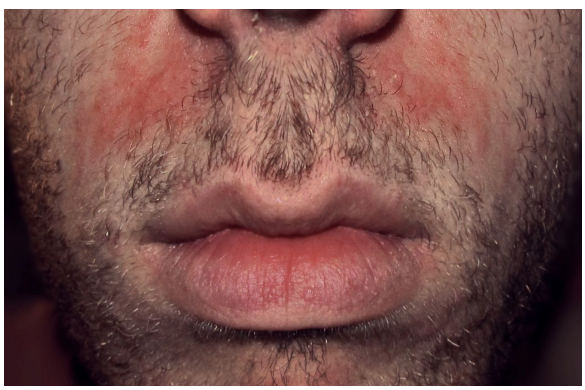


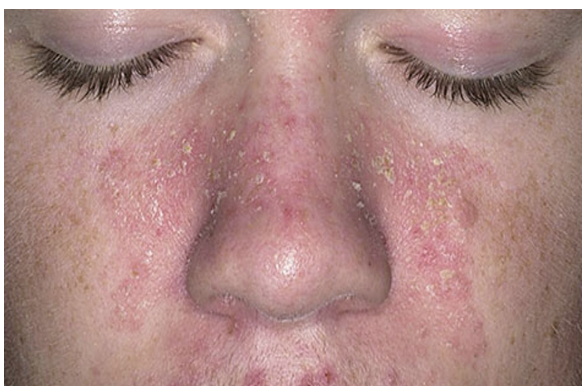


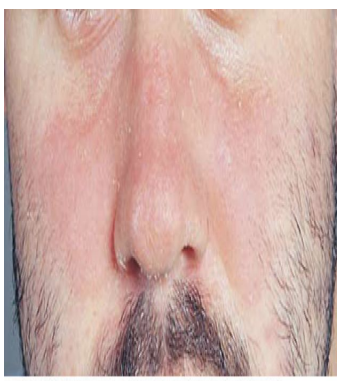












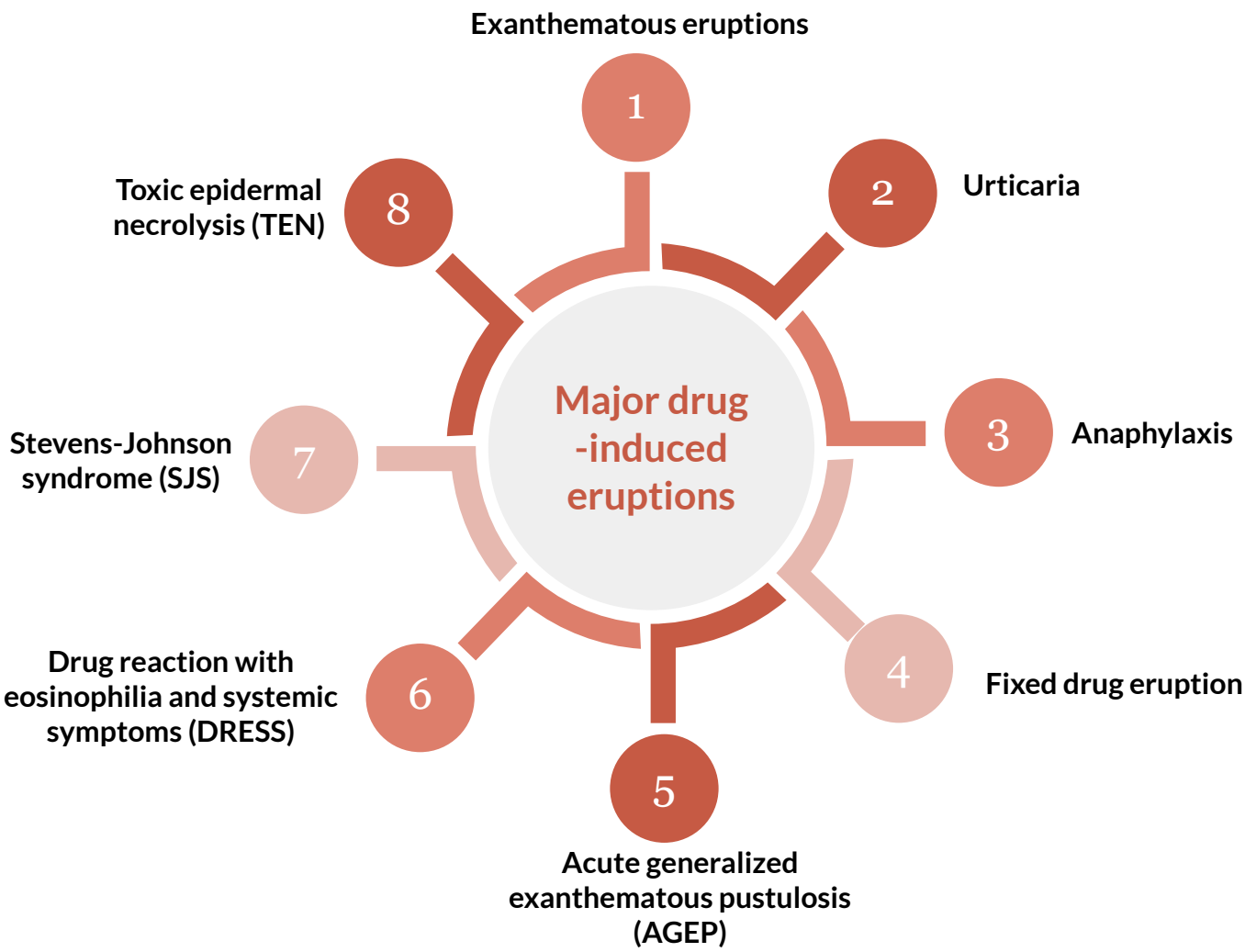
Drug Eruptions

Introduction:

- The skin is one of the most common targets for adverse drug reactions.
- 1-5% of patients receiving antibiotics and anticonvulsants may develop a drug eruption.
- ~2% of all drug-induced skin reactions are considered ''serious''.
- Skin reactions to drugs are responsible for ~3% of all disabling injuries that occur during hospitalizations.
- Either due to:
  - **Immunologic response.**
  - Non-immunologic (Overdose, side effect, drug-drug interaction, metabolism…etc).

Diagnostic approach for drug eruptions:

1. **Clinical characteristics:** (history, Examination)
   - Type of primary lesion.
   - Distribution and number of lesions (each drug have different distribution and lesions).
   - Mucous membrane involvement (to determine a benign vs. non benign skin reaction), facial edema.
   - Associated signs and symptoms fever , SOB, arthralgia
2. **Chronological factors:**
   - Document all drugs to which the patient **has been exposed**.
   - Date of eruption, time interval.
3. **Literature search:** (to be updated because all kinds of new drug reactions are published on a daily basis).



Exanthematous Drug Eruptions and Urticaria

Exanthematous Drug Eruptions

Clinical features

- The most common drug reaction affecting the skin.
- Classically begins **7 to 14** days after the start of a new medication.
- Begins as **erythematous macules** (symmetric) that sometimes becomes palpable (maculopapular eruptions).
- Begins on the trunk and upper extremities and progressively becomes confluent (start as multiple separated lesions and merge together to one big lesion).
- Mucous membranes are usually **spared.**
- Pruritus and low-grade fever(due to cytokines) and often present.
- The eruption disappears spontaneously after **1-2 weeks** without complications (it is not serious drug reaction).
- The following classes of drugs have a significantly higher incidence: **Aminopenicillins, Sulfonamides, Cephalosporins and anticonvulsants,** allopurinol, NSAIDs**.** names of the drugs will come in the exam
- **Always look for the following:**
  - Edema of the face + blood eosinophilia (DRESS).
  - Mucous membrane lesions or painful dusky skin (SJS, TEN) (usually spared in exanthematous drug eruptions).

Histology

- Nonspecific changes, eosinophils may be present.

The major DDx

- Viral exanthem (often indistinguishable) (history of respiratory tract infections).
- Drug etiology favored in adults, viral favored in pediatric patients.
- The presence of peripheral blood eosinophilia favors a drug reaction. Drug allergy

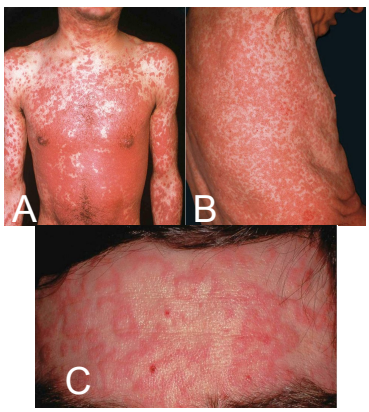
If a child came ddx —> viral

Treatment

- **Supportive** (Mostly). Depending on the symptoms
- Discontinue the offending drug. (risk vs benefit).
- Topical antipruritics and corticosteroids may help to alleviate pruritus.
- Systemic glucocorticoids

Pictures

- **(A)** Numerous pink erythematous maculopapular eruption on the trunk that is scattered and as we go down it coalesce and become confluent. (may be due to cephalosporin). major DDx: viral infection but it is more common in children unlike Drug eruption which is more in adult.
  Female note: diffuse numerous erythematous macules and patches over the trunk and extremities
- **(B)** Confluence of lesions on the trunk.
- **(C)** annular plaques on the forehead may be secondary to phenobarbital. Palpable plaque bright pink erythema



Urticaria

Clinical features

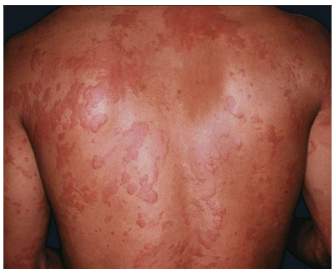
- **Transient erythematous and edematous papules and plaques that are usually associated with pruritus.**
- They can appear anywhere in the body including palms, soles and scalp.
- Duration is usually a few hours to 24 hours (sometimes stays for minutes)
- Skin is normal after they resolve.
- Acute: Less than 6 weeks. Chronic: Persist longer.
- Drugs associated with <10% of all cases of urticaria (acute > chronic)
- Mostly antibiotics (Penicillins, cephalosporins, ACE inhibitors, CCB).
- **Tx:** Discontinue drug, Antihistamines, Systemic glucocorticoids.

(Don't get confused, in acute case, the condition lasts 6w, the duration of the episode is 24h)

Urticaria, Angioedema, Anaphylaxis and Photosensitivity

Urticaria (cont')

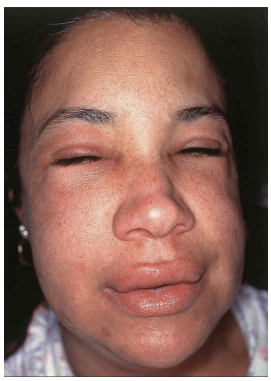
Pictures



- Erythematous Raised edematous papules or plaques (also we can call it hives or wheels). Diffuse numerous erythematous edematous ill defined blanchable plaques over the back , after few minutes this will appear as normal back
- Urticaria secondary to penicillin.
- Several of the lesions have a figurate appearance.

Angioedema

Clinical features



- Transient edema of the dermal, subcutaneous and submucosal tissue.
- Associated with urticaria in 50% of cases.
- May be complicated by life-threatening anaphylaxis.
- **ACE** inhibitors (1 day to several years after starting).
- Usually on the face (eyelids, lips), less often on genitals and extremities.
- Unilateral or asymmetric.
- Can involve the larynx, epiglottis, oropharynx and intestinal wall (in severe cases).
- ACE inhibitors, Penicillins and NSAIDs.
- Picture : Airway closure due to mucosal edema and muscle spasm , swelling in nose, lips and eyelids

Anaphylaxis

Clinical features

- An acute life-threatening reaction that can results from exposure to a number of drugs.
- Penicillin (1 per 5000).
- Combines skin with systemic manifestations (hypotension, tachycardia).
- Serious cases tend to appear within minutes and more common with parenteral administration as compared to oral ingestion.

Treatment

- Discontinue drug and strict avoidance in the future.
- Systemic steroids.
- **SubQ**(Subcutaneous) **epinephrine** in cases of life-threatening angioedema or anaphylaxis. Must go to the ER

Photosensitivity

INFO

- Cutaneous photosensitivity may be:
  - Idiopathic.
  - Due to endogenous photosensitizers (Porphyrins).
  - Due to Exogenous photosensitizers (Medications).

- The photosensitivity drug reactions are classically divided into 2 major types:
  i. Phototoxic (more common).
  ii. Photoallergic.

Photosensitivity and vasculitis

Photosensitivity

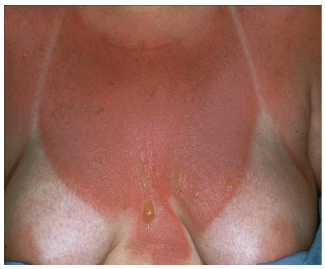
Phototoxicity

"to happen you need medication (sufficient) + light exposure"

- Fairly common and predictable. The drugs are known
- Can **occur** in any person who receives a **sufficient amount of a phototoxic drug together with sufficient exposure to UVR.**
- Clinically: an exaggerated sunburn in a shorter than expected time.
- Limited to sun-exposed areas and followed by hyperpigmentation.
- **Most common drugs: Tetracyclines (doxycycline)** (we give it often when treating acne), **NSAIDs, Fluoroquinolones**.
- Administering a short half-life drug in the evening decreases the risk.

Phototoxicity Picture

- Erythema and bullae are obviously limited to sun-exposed sites and resemble an exaggerated sunburn. Female notes: Diffused tensed moderate so severe it's showing blisters . V neck , photo distribution
- Phototoxic reaction in a patient receiving methotrexate. Patients on methotrexate can also experience a "sunburn-recall" phenomenon.

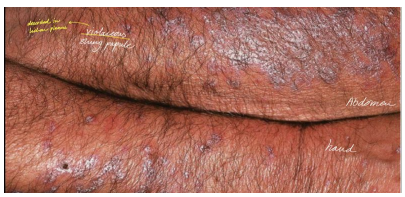


Photoallergy

- Occur as a result of cell-mediated hypersensitivity (to an allergen activated or produced by the effect of light on a drug).
- UVR is required to convert the drug into an immunologically active compound (Photo-allergen) that induces the immune response.
- More chronic than phototoxic.
- Clinically: Pruritic and resemble dermatitis or lichen planus but primarily in sun-exposed sites. (clinically differ from phototoxicity)
- Most common drugs: Thiazide diuretics, Sulfonamides antibiotics, Sulfonylureas and phenothiazines (all contain sulfur).
- **Tx**: Drug withdrawal, Topical steroids, physical barriers, reduce sun exposure + broad-spectrum sunscreens.

Photoallergy Picture

- resemble lichen planus or eczematous reaction.
- Photolichenoid drug eruption due to Hydrochlorothiazide. The lesions favored the extensor surfaces of the forearms.

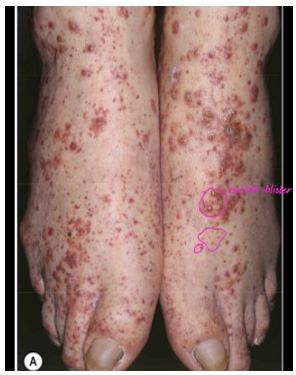


Vasculitis

Clinical features

Type 3 sensitivity can be caused by infection, drugs, or autoimmune. Examples : small —> HSP , medium—> polyarthritis nodusa

- ~10% of the cases are due to drugs.
- Clinically: Purpuric papules on the lower extremities.
- Systemic involvement is very unusual.
- Occurs 7-21 days (almost all the durations mentioned in this lecture are **important**) after drug administration and less than 3 days following re-challenge (if you give the drug again).
- Most common drugs: Penicillins, NSAIDs, Sulfonamides and cephalosporins.



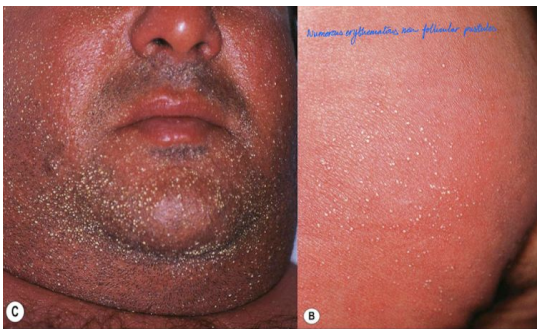
Neutrophilic drug eruptions and DRESS

Neutrophilic drug eruptions

Acute generalized exanthematous pustulosis (AGEP)

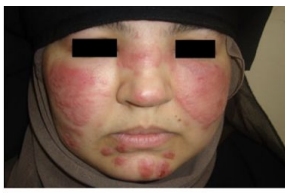
- Acute febrile drug eruption.
- Numerous small, non-follicular, sterile pustules (neutrophils are attracted to pustules) (Non-infectious), arising within large areas of edematous erythema.
- More than 90% of cases are drug-induced. imp for you
- The onset is usually within 2 days (very fast) of starting the medication.
- Lesions begin on the face or intertriginous zones (groin, axillae) and then disseminate within a few hours.
- The lesions last for 1 to 2 weeks and are followed by a superficial **desquamation**.
- Lab: leukocytosis with high neutrophils
- **DDx**: Acute pustular psoriasis.
- Drugs: **Antibiotics** (Beta-lactam and macrolides), **CCB** and **Antimalarials**.

AGEP Picture



- Hundreds of tiny 1-2 mm sterile pustules in background of erythema.
- positive patch test result 4 days following the application of 0.75% metronidazole in a patient with a previous pustular drug eruption to that medication.
- Diffuse erythema of the buttock (due to cephalosporin, **B**) and face (due to metronidazole, **A**) studded with sterile pustules.
- Spongiform pustules are seen within the epidermis of lesional skin.

Sweet's syndrome (Acute febrile neutrophilic dermatosis)

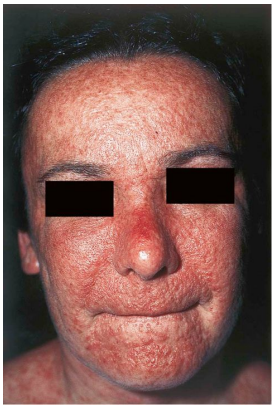


- This syndrome is characterized by fever,
- peripheral blood neutrophilia, and painful erythematous plaques that favor the face and upper extremities.
- Neutrophils migrate from the bone marrow to the skin
- Drugs represent <5% of all cases
- It starts about a week after the onset of drug administration.

Drug reaction with eosinophilia and systemic symptoms (DRESS)

INFO

- Delayed hypersensitivity (after two months)
- AKA Drug-induced hypersensitivity syndrome (DIHS)
- Due to alteration in the metabolism of drugs + immune mechanisms.
- Possible role for viruses HHV-6 and HHV-7.
- Drugs: **Anticonvulsants** (phenobarbital, Carbamazepine and phenytoin) and **sulfonamides**.



Multiple erythematous and edematous facial papules are present.

DRESS and Bullous Eruptions

Drug reaction with eosinophilia and systemic symptoms (DRESS) (Cont')

Clinical features

- Starts **2-6 weeks** after drug initiation.
- Fever (85%) and a cutaneous eruption (75%) are the most common symptoms.
- Begins as a morbilliform eruption, which later becomes edematous, with follicular accentuation (Prominence).
- The face, upper trunk and extremities are the initial sites of involvement.
- **Edema of the face is the hallmark of DRESS.**
- Lymph nodes are often enlarged.
- **The most common and most severe site of visceral involvement is the liver** (majority of deaths associated with this syndrome). Worst kind of hepatitis occurs with DRESS
- Other organs involved: Heart, lungs, kidneys and thyroid.
- Prominent eosinophilia is a very characteristic feature. Serious reaction

Treatment

- Early withdrawal the offending drug. (may not be sufficient for obtaining a full recovery)
- Topical steroids for mild cases.
- Systemic steroids for life-threatening heart and lung involvement. To go to the organs

Bullous Eruptions

- **Fixed drug eruption.**
- **Linear IgA bullous dermatosis.**
- **Drug-induced bullous pemphigoid.**
- **Drug-induced pemphigus.**
- **Steven-Johnson syndrome and TEN.**

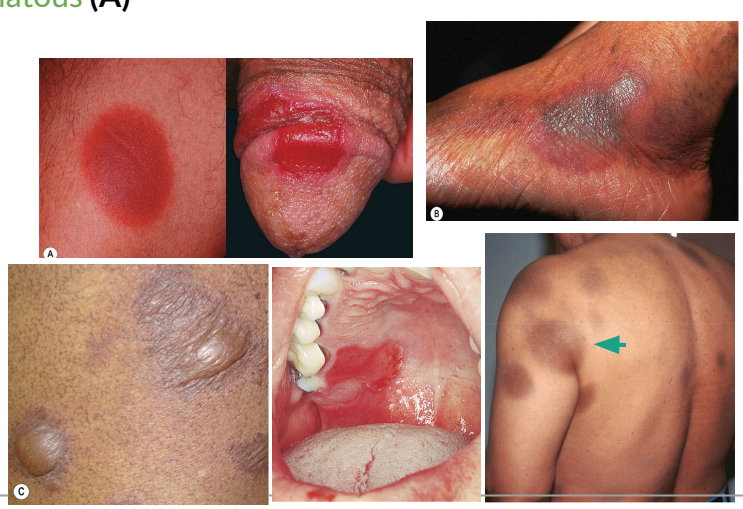
Fixed drug eruption

- Lesions develop **1-2 weeks** after a first exposure and within **24 hours within subsequent exposures.**
- **One or a few round, sharply demarcated, erythematous and edematous plaques are seen.**
- Sometimes a dusky, violaceous hue and a central blister may be seen. (violaceous = purple)
- Favors the lips, face, hands, feet and genitalia.
- The lesions progressively fade over several days (**leaving** Post inflammatory hyperpigmentation **(PIH) behind**). (not painful or itchy)(not necessarily permanent)
- **Lesions recur at exactly the same sites upon re-administration of the drug.**
- There is a generalized form of FDE (similar clinically to EM/SJS).(rare)
- A non-pigmenting variant of FDE occurs mainly with pseudoephedrine.
- Drugs: Sulfonamides, NSAIDs, Barbiturates, Tetracyclines and Carbamazepine.

Fixed drug eruption Pictures

"It's easy to remember because it is a single lesion"

- Round oval Well-demarcated erythematous **(A)** to violet–brown plaques that can develop a detached epidermis **(B)**, Bulla or blister **(C)** or erosion **(D)** centrally. As lesions heal, circular or oval areas of hyperpigmentation are commonly seen **(E).**
- Histologically, serous crust, a few necrotic keratinocytes, mild vacuolar changes at the dermo–epidermal junction, papillary dermal edema and melanophages can be seen as well as a mononuclear infiltrate.

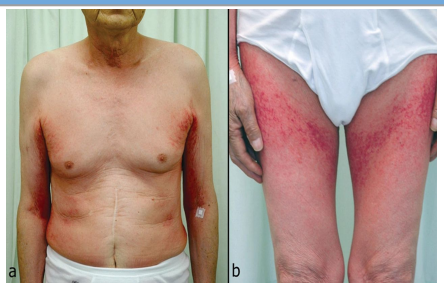


Bullous Eruptions and Other Drugs Eruption

Bullous Eruptions

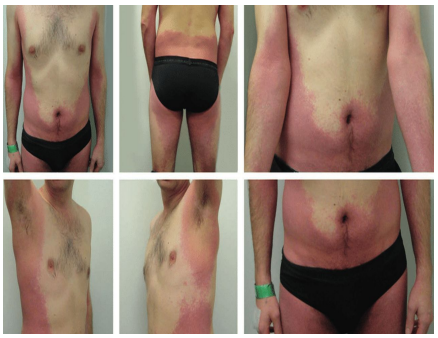
Symmetrical drug-induced intertriginous and flexural exanthema (SDRIFE)
skipped by the doctor

- Sharply demarcated, symmetrical areas of erythema over the anogenital region after exposure to systemic drugs.
- Aminopenicillin & Cephalosporin are the most common drugs.
- There is usually involvement of at least one flexural site.



SYMMETRICAL DRUG-RELATED INTERTRIGINOUS AND FLEXURAL EXANTHEMA (SDRIFE) – CLINICAL CRITERIA

- Exposure to a *systemically* administered drug*, occurring with either the initial or a repeated dose (excluding contact allergens)
- Sharply demarcated erythema of the gluteal/perianal area and/or V-shaped erythema of the inguinal/perigenital area
- Involvement of at least one other intertriginous site/flexural fold
- Symmetry of affected areas
- Absence of systemic symptoms and signs



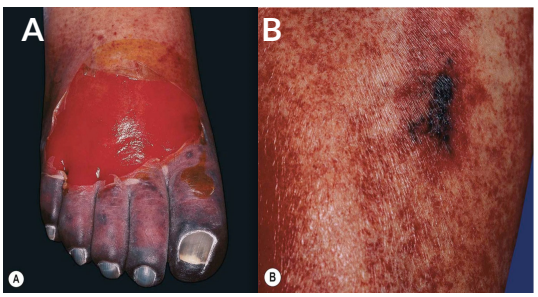
Other Drug Eruptions

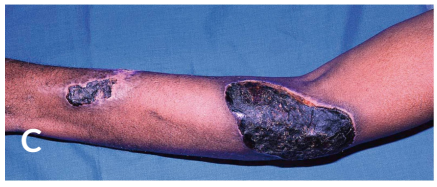
- **Anticoagulant-induced skin necrosis.**
- **Serum sickness-like eruption.**
- **Drug-induced lupus.**
- **Drug-induced psoriasis.**
- **Acneiform eruptions.**
- **Pigmentary changes.**
- **Pseudolymphoma.**
- **Chemotherapy reactions.**

Anticoagulant -induced skin necrosis

- Rare, sometimes life-threatening (emergency).
- Induced by **Warfarin or Heparin**.
- Begins 2 to 5 days after therapy.
- Erythematous, painful plaques evolve into hemorrhagic blisters and necrotic ulcers.
- Mainly over the breasts, thighs and buttocks. (fat areas)
- Patients with hereditary **deficiency of protein C** are at highest risk.
- **Tx:** Discontinue warfarin & start Vitamin K + I.V infusion of protein C.

- Heparin-induced thrombocytopenia with thrombosis syndrome.
- **(A)** Ischemia and necrosis of the foot.
- **(B)** Petechiae due to thrombocytopenia and an irregular area of cutaneous necrosis due to thrombosis.
- **(C)** Painful necrotic ulcer.





Other Drugs Eruption

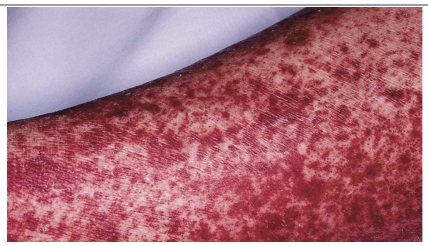
Other Drug Eruptions

Serum sickness-like eruption

- Type 3 complement mediated reaction
- Mainly in **children**.
- Fever, Arthralgias, arthritis, rash and lymphadenopathy.
- 1 to 3 weeks, after drug exposure.
- Unlike true serum sickness, hypocomplementemia, vasculitis and renal disease are absent.
- Occurs in approximately 1 in 2000 children given **cefaclor.**

Serum sickness-like eruption Pictures

- Serum sickness due to antithymocyte globulin.
- The purpuric lesions are due to small vessel **vasculitis** in this patient with aplastic anemia.



Drug-induced Lupus Involvement 75% Joints 90% Skin

Drug-induced systemic lupus:

- Fever, weight loss, pericarditis, pulmonary inflammation.
- Skin involvement is rare but includes: malar-erythema, photo eruption and discoid lesions.
- Vasculitis, renal and neurologic involvement is rare.
- Starts **over a year** after the medication is initiated (the time here is variable).
- +ve anti-histone Abs in 95% of cases (-ve DsDNA). MCQ
- Clinical symptoms resolve within 4 to 6 weeks.
- **Procainamide, hydralazine, chlorpromazine, isoniazid, methyldopa, quinidine, D-penicillamine and Minocycline**. (It's very important to know the medications)

Drug-induced subcutaneous Lupus:

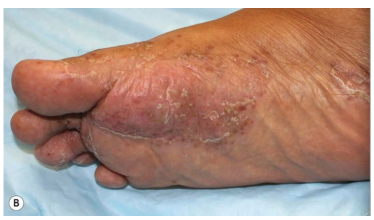
- Psoriasiform and annular lesions on the upper trunk and extensor arms.
- Hydrochlorothiazide, CCBs, Terbinafine (commonly used antifungal), NSAIDs, Griseofulvin (antifungal).
- Resolution of the rash may or may not occur after discontinuation of the responsible drug.

Drug-induced Psoriasis

- Drugs can affect a patient in 3 different ways: (no need to know about this)
  1. Exacerbation of **pre-existing** psoriasis
  2. Induction of lesions of psoriasis in clinically **normal skin in a patient w psoriasis.**
  3. De novo psoriasis.
- **Terbinafine** (antifungal), **NSAIDs**, **Antimalarials used for lupus**, ACE inhibitors, **Lithium (very common) and B-blockers.**
- Common treatment of Psoriasis can also cause it.
- Lesions of drug-induced psoriasis usually regress within weeks to a few months of discontinuing the inciting drug.

Drug-induced Psoriasis pictures

- Psoriasiform eruptions due to TNF-α inhibitors.
  -usually in palms & soles-.
- A Widespread papulosquamous lesions in a patient being treated with infliximab for gastrointestinal GVHD. Histologically, there was no evidence of cutaneous GVHD. this is Sterile pustulosis of the plantar surface developed in this patient with rheumatoid arthritis who had received infliximab for the previous 5 years. Neither patient had had a reduction in immunosuppression prior to the onset of the psoriasiform eruption.

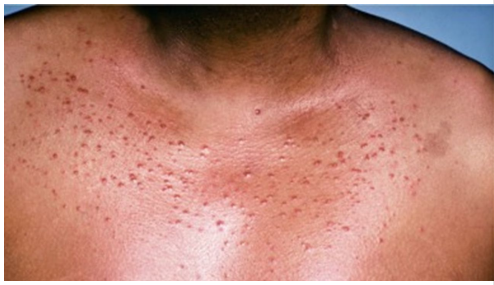


Other Drugs Eruption

Other Drug Eruptions

Acneiform eruptions

- Represent ~1% of drug-induced skin eruptions.
- Clinically, just like acne but comedones are absent.
- **Corticosteroids**, **Androgens** (male bodybuilders), hydantoins, lithium, progestin-containing OCPs.
- Tx: stop the offending agent (benefits > risk) and treat the like acne (with antibiotics)



Monomorphic, and it involves the trunk more commonly, unlike the usual acne

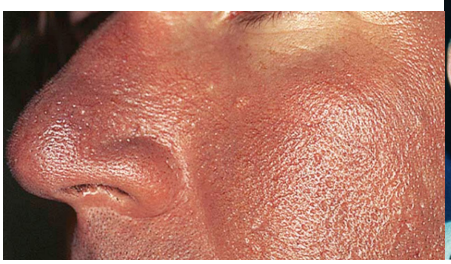
Pigmentary changes

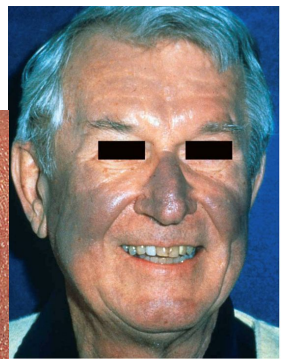
Hyperpigmentation:

- Usually more pronounced in sun-exposed areas (each one has a different type of pigmentation reaction).
- Minocycline (brown-black photosensitive) → subacute lupus.
- Antimalarials (hydroxychloroquine = grey-blue) used for SLE.
- Amiodarone (blue-grey).
- Silver, gold and arsenic.
- Bleomycin chemotherapy.

Hypopigmentation:

- Chronic use of topical steroids.





Pigmentary changes Pictures

- Gray–violet discoloration of the face due to amiodarone.
- Biopsy specimens demonstrate yellow–brown granules within dermal macrophages. Note sparing of the lower eyelid.
- Gray–violet Amiodarone induced pigmentation.

Lecture Summary (436 team)

Type of eruptions	Onset	Clinically	Causes
Exanthematous Drug Eruptions	7 to 14 days	erythematous macules (symmetric), sometimes palpable on the trunk and upper extremities, Pruritis	Aminopenicillins, Sulfonamides, Cephalosporins and anticonvulsants
Urticaria	few hours to 24 hours	Transient erythematous and edematous papules and plaques associated with pruritis. palms,soles and scalp.	antibiotics (Penicillins, cephalosporins)
Angioedema	ACE inhibitors (1 day to several years after starting)	Transient edema of the dermal, subcutaneous and submucosal tissue. on the face (eyelids, lips)	ACE inhibitors, Penicillins and NSAIDs
Anaphylaxis	within minutes	Combines skin with systemic manifestations (hypotension, tachycardia).	Penicillins
Phototoxic	sunburn in a shorter than expected time.	The erythema and bullae are obviously limited to sun-exposed sites and resemble an exaggerated sunburn	Tetracyclines (doxycycline), NSAIDs, Fluoroquinolones.
Photoallergy	-	Pruritic and resemble dermatitis or lichen planus	Thiazide diuretics, Sulfonamides antibiotics, Sulfonylureas and phenothiazines
Vasculitis	7-21 days	Purpuric papules on the lower extremities	Penicillins, NSAIDs, Sulfonamides and cephalosporins.
AGEP	2 days	Numerous small, non-follicular, sterile pustules, arising within large areas of edematous erythema	Antibiotics (Beta-lactam and macrolides), CCB and Antimalarials.
Sweet's syndrome	1 week	fever, peripheral blood neutrophilia, and painful erythematous plaques that favor the face and upper extremities	-
DRESS	2-6 weeks	morbilliform eruption, which later becomes edematous, with follicular accentuation. The face, upper trunk and extremities are the initial sites of involvement. Edema of the face is a hallmark of DRESS.	Anticonvulsants (phenobarbital, Carbamazepine and phenytoin) and sulfonamides.
FDE	1-2 weeks	One round, sharply demarcated, erythematous and edematous plaques. Sometimes a dusky, violaceous hue and a central blister.	Sulfonamides, NSAIDs, Barbiturates, Tetracyclines and Carbamazepine.
SDRIFE	-	Sharply demarcated, symmetrical areas of erythema over the anogenital region	Aminopenicillin & Cephalosporin
Anticoagulant-induced skin necrosis	2 to 5 days	Erythematous, painful plaques evolve into hemorrhagic blisters and necrotic ulcers. Mainly over the breasts, thighs and buttocks	Warfarin or Heparin
Serum sickness-like eruption	1 to 3 weeks	Mainly in children. Fever, Arthralgias, arthritis, rash and lymphadenopathy.	Cefaclor
Drug-induced Lupus	4 to 6 weeks	Fever, weight loss, pericarditis and pulmonary inflammation	Procainamide, hydralazine, chlorpromazine, isoniazid, methyldopa, quinidine, D-penicillamine and Minocycline
Drug-induced Psoriasis	weeks to a few months	-	erbinafine, NSAIDs, Antimalarials, ACE inhibitors, Lithium and B-blockers. TNF-induced Psoriasis.
Acneiform	-	Acne but comedones are absent.	Corticosteroids, Androgens, hydantoins, lithium, progestin-containing OCPs.
Hyperpigmentation	-	-	Minocycline, Antimalarials, Amiodarone, Silver, gold and arsenic, Bleomycin
Hypopigmentation	-	-	Chronic use of topical steroids

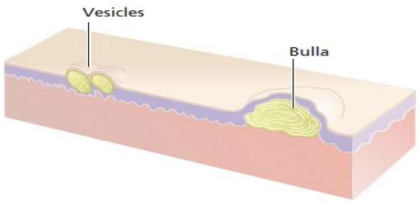
Blistering Diseases

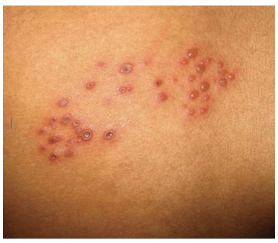
CONTENT OF THIS LECTURE:

- PEMPHIGUS VULGARIS
- BULLOUS PEMPHIGOID)
- CHRONIC BULLOUS DISEASE OF CHILDHOOD
- PARANEOPLASTIC PEMPHIGUS (Present with Cancer)

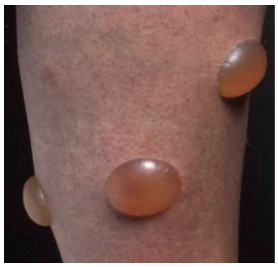
Definition:

- Vesicles and bullae are raised lesions that contain fluid.
- A **vesicle** is **less than 0.5** cm in diameter.
- A **bulla** is l**arger than 0.5** cm in diameter.



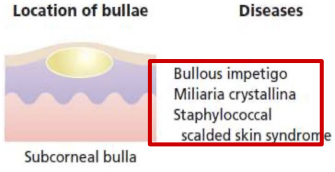
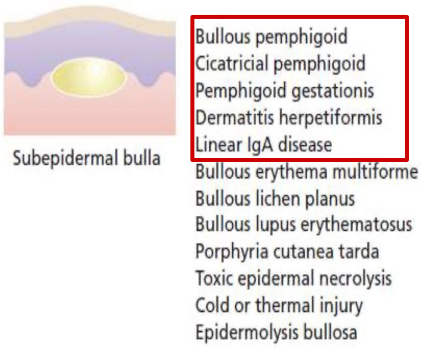


Multiple grouped vesicles on erythematous base (Vesicle is <5mm)



Multiple Bullae (> 5mm)

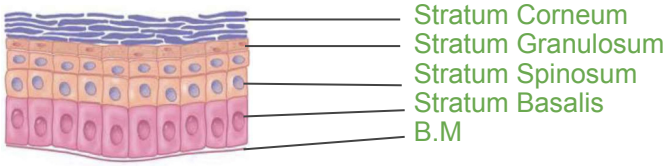
CLASSIFICATION OF VESICULOBULLOUS DISEASES:

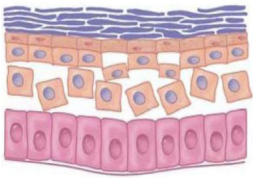
Subcorneal blister:	Intra-epidermal blister:	Subepidermal blister blister:
- Just beneath the stratum corneum. Very superficial. - Have the thinner roofs - Ruptured easily & leave an oozing denuded surface. - Not caused by autoimmune diseases. - Pathogen in subcorneal are prone to rupture so, often the presentation is Erosions not Bullae or vesicle, as is the case with Pemphigus Vulgaris in the intraepidermal Blister Group. • Bullous impetigo: Staph-Strep infection. • Miliaria crystallina: sweat duct obstruction causes prickly heat rash. • SSSS: present with peeling of the skin. SSSS: Staphylococcal scalded skin syndrome  	- within the prickle cell layer on the epidermis - Have thin roofs - Ruptured easily & leave an oozing denuded surface - Viral vesicles like: HSV, Chicken Pox virus.  	- Between the dermis and epidermis - Their roofs are relatively thick - Tend to be tense - May contain blood - Below the B.M of the epidermis, so it will present with tense bullae. 

Blistering Diseases

Dr. Note:

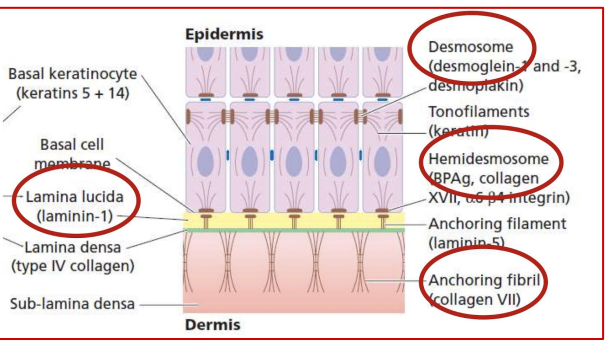
- In these autoimmune diseases, the Autoantibodies attack specific Ag in the Skin cells, the cells (layer) that are attacked, will lose the attachment and cohesion with other cells and among itself. The Cells will end up more rounded and floated.
- This process is called **Acantholysis** (totally detached) → vesicle, these cells are called acantholytic cells.

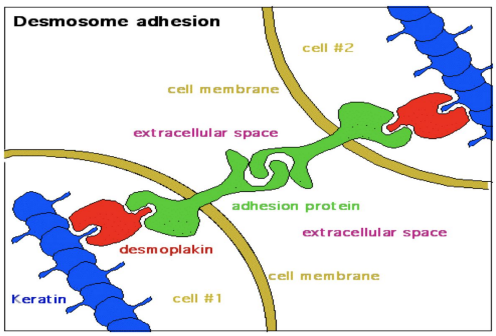




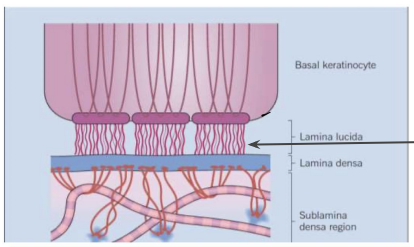
Dermo-epidermal junction: IMPORTANT

- **Desmosome**: Between the spinous layer of the epidermis, attach cells together in multiple direction, composed of **Desmoglein-1 and -3, & Desmoplakin.**
- **Hemidesmosome**: Attach cells in one direction to the B.M, (connects the epidermis to the dermis). Composed of: **BPAg** & **α6 β4 integrin** & collagen XVII.
- Lamina densa: The B.M itself.
- Anchoring fibrils: Attach the B.M to the dermis. Composed of collagen VII.
- All these structure can be affected, either genetically absent or attacked by Ab in Autoimmune.
- **Pemphigus group:** the antibodies will target **Desmoglein-1** and/or **Desmoglein -3** → level of separation is high, separation is between the basal keratinocytes themselves **(intra-epidermal)** resulting in "**flaccid** blisters" = easily ruptured.
- **Pemphigoid group:** the antibodies will target **BPAg 1 and BPAg 2** → level of separation is under the basal keratinocytes **(subepidermal)** resulting in "**tense** blisters" = hardly ruptured.
- Congenital Vesicular Blistering disease: as in the case when collagen VII absent "epidermolysis bullosa dystrophica" which is characterized by extremely fragile skin (mechanical fragility), B.m and epidermis is in surface of the blister.

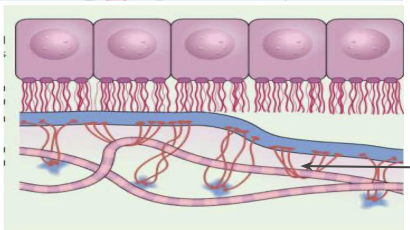




Here the adhesion molecule is desmoglein-1, -3 it is affected in Pemphigus Vulgaris



Hemidesmosome

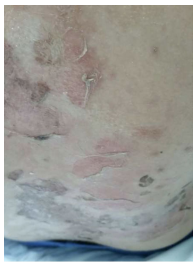
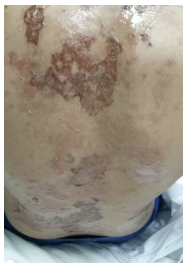


Anchoring fibrils

- Hemidesmosome: work as a strong attachment for cells, without the skin would develop blister. In Bullous pemphigoid the effect is on hemidesmosome.
- This is important clinically because we do biopsy and we check the result: if it's Bullous pemphigoid then we will not see the b.m in the surface of the bullous. But in Epidermolysis bullosa acquisita, you will see the b.m in the surface and the dermis in the floor.

Blistering Diseases

Multiple erosions with erythematous base on the back.

Since the skin is thin, then the pathology is intraepidermal (in the intra-spinosum layer). so, this is most likely is desmosome pathology. In **Pemphigus vulgaris** (you will see deeper erosion because all the epidermis is gone, unlike the bullous pemphigoid).

Blistering Disorders

- In Adults: the main group of blistering disorders is associated with autoantibody formation.
- In Children: the main cause of blistering disorders is Genodermatosis (epidermolysis bullosa):
  - Epidermolysis Bullosa is a group of mechanobullous genodermatosis. Rare, present at birth or infancy. Range from localized relatively mild trauma induced blisters to life threatening/debilitating conditions
  - Diagnosis is made based on family history, clinical examination, light and electron microscopy

Diagnostic test:

Accurate pathological diagnosis requires 2 biopsies (1 histopathology + 1 IF) of a small newly formed lesion and perilesional skin for immunopathological studies.

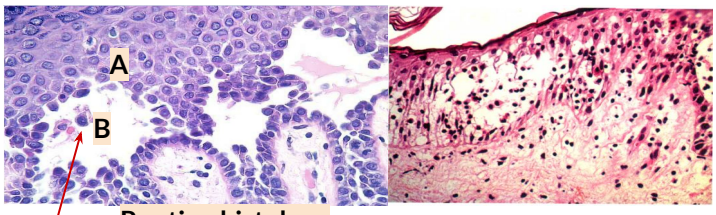
The first biopsy on the lesion to know the level of separation, while the second biopsy on the intact skin to do direct immunofluorescence.

Routine histology:

Lesional sample
(small bulla or edge of large one)

A;; The desmosomes present in the small spaces between cells

B: cell without cytoplasm, the desmosomes connect cells together will lead to stretching of cells, which is lost here



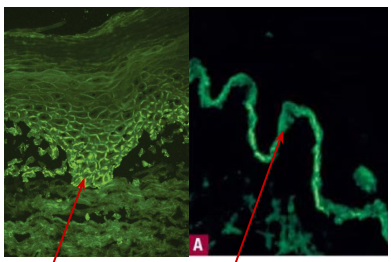
Routine histology

Acantholysis(small cytoplasm & large nucleus)

Direct immunofluorescence:

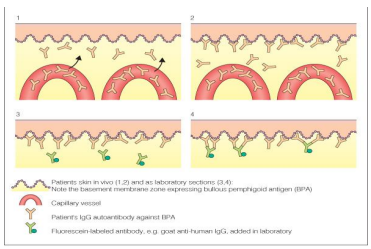
- Perilesional sample (away from inflammation).
- IgG and C3: in Pemphigus vulgaris and Bullous pemphigoid.
- IgA: in linear igA bullous Diseases.

You have to know where the cleavage is in the IF to know your DDx.



Spinosum

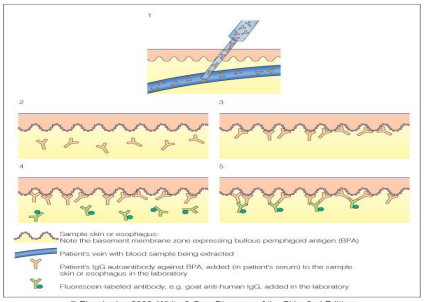
Basement membrane



Indirect immunofluorescence:

Patient's serum is added to specific substrates that express antigen of interest

mostly used in research, we don't do it usually



Electron microscopy:

Used for congenital diseases mainly

Gives you the specific place of pathology due to it's ultra structural features

Used in Genodermatosis because it's not an autoimmune disease

Blistering Diseases

Autoimmune bullous disease (438)

Loss of intraepidermal adhesion (pemphigus group)	Loss of subepidermal adhesion
I. Pemphigus vulgaris (PV): • Classic • Pemphigus vegetans	I. Pemphigoid: • Bullous pemphigoid • Cicatricial pemphigoid • Pemphigoid gestationis
II. Pemphigus foliaceus: • Classic • Fogo selvagum • Pemphigus erythematosus (Senear- Usher Syndrome)	II. Dermatitis herpatiformis
III. Drug induced pemphigus	III.linear IgA disease: • Of childhood • Adult form
IV. Paraneoplastic pemphigus	
V. IgA pemphigus	IV. Epidermolysis bullosa aquisita

Pemphigus group

Definition:

A group of disorders with loss of intraepidermal adhesion due to autoantibodies directed against proteins of the desmosomal complex that hold keratinocytes together

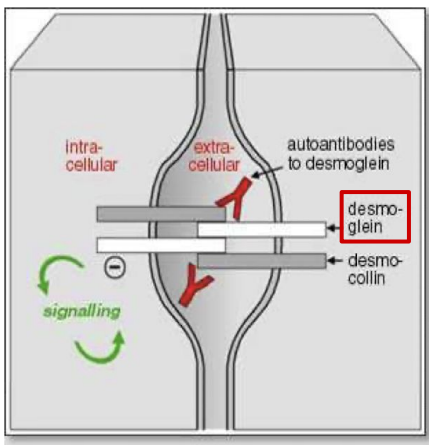
Pemphigus is a group characterized by blistering of the skin and mucous Membranes.

- **Auto-antibodies against DESMOSOMES in epidermis and mucosal surface.**
- Specifically Desmoglein -1, desmoglein -3. Dg-1 is usually superficial, while -3 is found in the cells of the mucous membrane and is Usually affected more hence, the prominent presentation of PV is oral erosion.

Four sub-clinical variants :

- Pemphigus Vulgaris: is the **most common** Pemphigus variant, and the form usually responsible for **oral lesions.** (Pt. Usually presents w/ dysphagia & painful oral lesions) (oral lesion seen in paraneoplastic syndrome too).

- Other types include: Folacious (superficial, affect Desmoglein -1 only, no mucous membrane involvement), vegetens (localized, no mucous membrane involvement), erythematosus (can be confused with lupus).



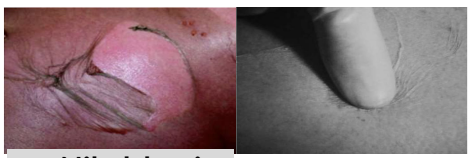
Blistering Diseases

Pemphigus group

Disease	Type of immunoglobulin	Against...
Pemphigus vulgaris (PV)	IgG	Mucosal type → desmoglein 3 Mucocutaneous type → desmoglein 3 & desmoglein 1 (PV almost always starts in the mucus membrane thus the first target is always desmoglein 3 ± desmoglein 1)
Pemphigus foliaceus (PF)	IgG	Desmoglein 1 ONLY (purely cutaneous)
paraneoplastic pemphigus	IgG	plakin molecules in addition to autoantibodies against desmogleins

1. Pemphigus Vulgaris:

- Severe, potentially fatal disease with intraepidermal blister formation of the skin and oral mucosa caused by IgG autoantibodies against "desmogleins"
- Begins with erosions on mucous membrane then other skin areas.
- **Very painful.**
- Not a self-limiting disease, it could be fetal within days
- +ve Nikolsky's sign: Twisting pressure on normal skin shears skin.
- Age: middle-age 40-60 years (in Bullous pemphigoid 65+).
- Secondary infection and disturbance of fluid and electrolyte balance are common complications.



+ve Nikolsky sign

Pathogenesis:

- Genetic predisposition: HLA-DRQ402- DQ0505
- IgG autoantibodies against desmoglein 3 (Dsg 3) and later desmoglein1(Dsg 1). The bound antibodies activate proteases that damage the desmosome, leading to acantholysis = floating cells.
- Serum antibody titer usually correlates with severity of disease and course

Clinical features:

Mucous membrane:

- lesions usually present as painful erosions

- Intact blisters are rare

- Sites: oral mucosa, vermillion lip, throat, esophagus, conjunctivae, nasal mucosa, vagina, penis, anus, labia

- Most common sites: buccal & palatine mucosa

- Vermillion lip -> thick fissured hemorrhagic crust

- throat ->hoarseness, difficulty swallowing

- 70%, anti-Dsg3 (Dsg 3 is the main desmoglein in mucosal surfaces)

- Always check the scalp when confronted with unexplained oral erosions

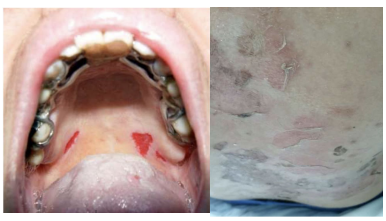
Blistering Diseases

1. Pemphigus Vulgaris (cont'):

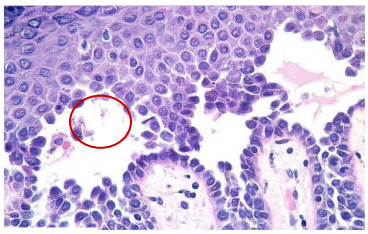
Skin

- Primary skin lesions of PV are flaccid,
- Thin-walled, easily ruptured blisters They could arise on either
- Normal-appearing skin or erythematous base
- The blisters are fragile and soon rupture to form painful erosions that ooze and
- Bleed easily, later forming crusts Can become generalized
- Lesions that heal often leave hyperpigmented patches with NO scarring
- More generalized disease due to the development of IgG autoantibodies against Dsg1 which is present in the skin along with Dsg3

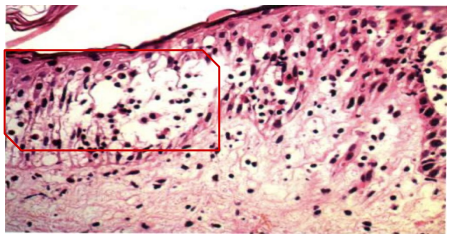
Findings:



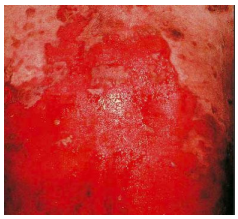
Erosion of the mucous membrane in the mouth → PV

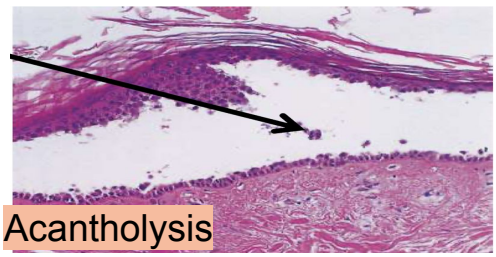


Keratocyte **acantholytic** cells, due to loss of desmosome.

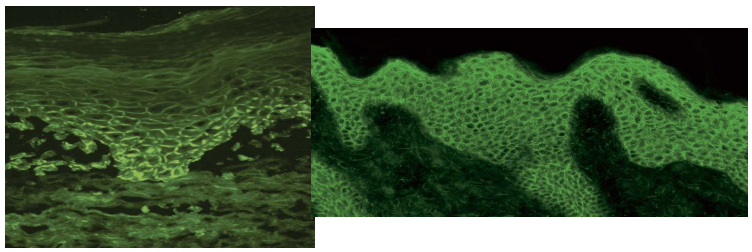


Interspinous layer with vesicle due to loss of dermosome.





Acantholysis pointed by the arrow, also notice how the B.M is not a part of the Bullae (below the blister). It's a Acantholysis without keratinocyte necrosis **(unlike Stevens-Johnson syndrome which has keratinocyte necrosis)**



IgG and **C3**: All are found in the interspinous area in the desmosome unlike the Bullos where discussed later.
The wide spread flaring of Abs response demonstrate the severity of PV which is more than Bullous Pemphigoid.
I.e. PV needs higher dose of steroids and often involves all the body, including: muscosa

Diagnostic approach:

History (always ask medication Hx)

Physical examination (skin, mucous membranes, nails)

- Nikolsky sign à because of an absence of cohesion within the epidermis, its upper layers easily move laterally with slight pressure or rubbing in active patients with pemphigus
- Asboe-Hansen signà " bulla- spread phenomenon" gentle pressure on an intact bulla forces the fluid to spread under the skin away from the site of pressure

Investigation

- Skin biopsy: from lesional skin, intact vesicles if found
- DIF: from perilesional skin shows deposition of IgG (100%), C3 (80%)
- Indirect IF
- ELISA: to identify anti-Dsg3,1

Blistering Diseases

Differential Diagnosis;

When skin is involved:
- Bullous impetigo
- Dyskeratotic acantholytic disorders
- Hailey-Hailey
- Grover disease

When mucus membrane is involved:
- Denture intolerance
- Erosive candidiasis
- Chronic recurrent apothecary
- Erythema multiforme
- Erosive lichen planus
- Herpetic gingivitis

Treatment:

Nonbiological:

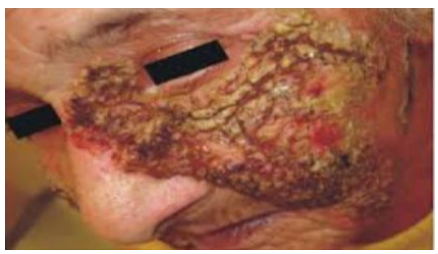
- High dose **systemic steroids 60-100 mg** of prednisolone.
- Immunosuppressive agent such as **azathioprine cyclophosphamide, Methotrexate or mycophenolate** -to decrease the uses of steroids-. (usually, Rituximab: for severe cases & mycophenolate: for mild cases.
- Patient will probably have to remain on systemic steroids for long time.
- Antibiotics; to treat superinfection only.

Biological Rx:

1. **Rituximab:** IV 86% free of disease after 3 yrs. it's an Anti-CD-20: against B-lymphocytes
2. **IVIG** (intravenous immunoglobulin).

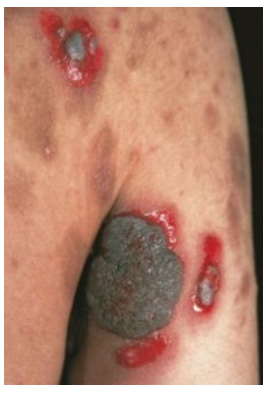
- If not treated leads to dramatic drop in QoL, like inability to speak and erosion all over the body (Poor prognosis if not treated).
- 1st line High dose steroid, then we give mycophenolate or azathioprine to decrease the steroid dose, steroid is lifelong sometimes.
- **Rituximab** is reserved for resistant cases but, **IF SEVERE**, RITUXIMAB should be given in conjunct with steroids usually gives long remission.
- **Rituximab** has 2 protocol, one for RA, and the other is Lymphoma dose (weekly) Almost always in PV we use the RA dose which is: 1000 mg twice with 2 wks apart.

2. Pemphigus vegetans:



Clinical features:

- It's a vegetative variant of pemphigus vulgaris.



- Characterized by flaccid blisters that become erosion and then form **fungoid vegetations**, especially in **intertriginous areas, the scalp and face**

- **Early lesions start as pustules (rather than vesicles)**, then they soon progress to vegetative plaques
- treatment same as pemphigus vulgaris

3. Pemphigus foliaceus:

- Is a form of pemphigus in which patients develop scaly, crusted cutaneous erosions often on an erythematous base
- Disease of middle-aged and older patients
- In this form of pemphigus they do not have mucosal involvement even with widespread disease u Lesions have a seborrheic distribution (face, scalp, and upper trunk).
- IgG autoantibodies against desmoglein 1
- More often drug induced than pemphigus vulgaris
- Patients with pemphigus foliaceus are not severely ill

Diagnostic approach:

History (always ask medication Hx)

Physical examination (skin, mucous membranes, nails)

- Nikolsky sign present

Investigation

- DIF: from perilesional skin shows superficial deposition of IgG
- ELISA: to identify IgG antibodies against Dsg 1

Treatment:

- Same as pemphigus vulgaris but usually more responsive to therapy
- Dapsone maybe helpful

4. Drug-induced PV

- Drugs can induce PV
- Drugs reported most significantly in association with PV are:
  - Penicillamine.
  - Captopril.
  - Anti-epiliptic: phenytoin and carbamazepine.

Drugs that induce pemphigus can be devided into 2 groups

Agents containing the sulfhydryl group:

- Penicillamine
- Captopril
- Piroxicam
- Penicillamine —> PF is seen more than PV, ratio 4:1
- Sulfhydryl group of these drugs interact with the sulfhydryl group of Dsg1 & Dsg 3 (acantholysis without antibody formation)

Agent without sulfhydryl group:

-Beta-blockers
- Cephalosporins
- Penicillins
- Rifampin
- Induce acantholysis via immune mechanism

Most patients with drug-induced pemphigus go into remission after the offending drug is discontinued

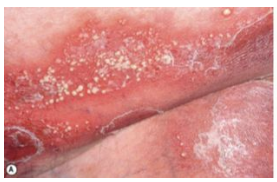
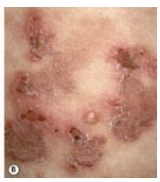
5. IgA pemphigus:

Represents a group of autoimmune intraepidermal blistering disease

Presenting with:
1- **Vesicopustular** eruption
2- **Neutrophilic** infiltration of the skin
3- Circulating **IgA** autoantibodies against the cell surface of keratinocytes, but with NO IgG autoantibodies

Two distinct types:
1- Subcorneal pustular dermatosis (SPD)
2- Intraepidermal neutrophilic type (IEN)

- Both types present with flaccid vesicles or pustules that coalesce to form an annular pattern with central crusting
- Sunflower-like configuration of pustules is a characteristic sign of the IEN type
- Most common site: axilla, groin, trunk
- NO mucous membrane involvement Pruritus is a significant symptom
- Pruritus is a significant symptom

Diagnostic approach:

History

Physical examination (skin, mucous membranes, nails)

Investigation
- DIF: **IgA** autoantibodies directed against keratinocyte cell surface (not desmoglein)

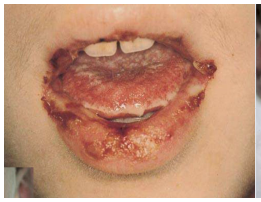
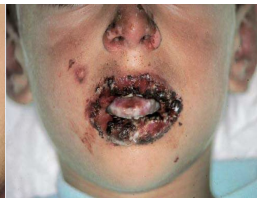
Treatment:
Most cases are responsive to dapsone, if not ,corticosteroids & other immunosuppressive agents

6. Paraneoplastic Pemphigus:

- The least common and most severe type of pemphigus is **paraneoplastic pemphigus** (PNP).
- This disorder **is a complication of** cancer usually **lymphoma,** non- Hodgkin lymphoma, Chronic lymphocytic leukemia and **Castleman's disease.**
- It may precede the diagnosis of the tumor.
- **Painful sores appear on the mouth, lips, and the esophagus.**
- Complete removal and/or cure of the tumor may improve the skin disease.
- IF you have a case of:
  - A: severe oral involvement.
  - B: IF it shows +ve for everything in serology: Anti-Desmoglein, plaqin, etc.
  - If you treat the cause (cancer) it goes away and it will be treated.

Blistering Diseases

Clinical features:

When you see this picture, the first thing you should think about is steven-johnson syndrome
but in this case it is a child so you have to think of Castleman disease.

- The most constant clinical feature is the presence of intractable stomatitis

- The Stomatitis consists of erosions and ulcerations that affect all layers of the oropharynx and characteristically extend onto the Vermilion lip

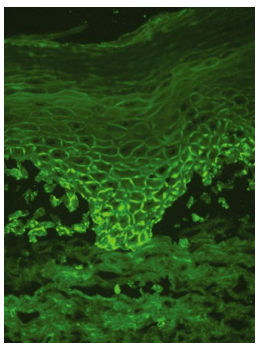
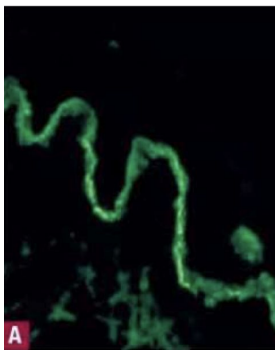
- Stomatitis is usually the earliest presenting sign and, after treatment, is the one that persists and is extremely resistant to therapy

- Pseudomembranous conjunctivitis à scarring, blindness Could also affect: esophagus, nasopharynx, vagina, labia, penis

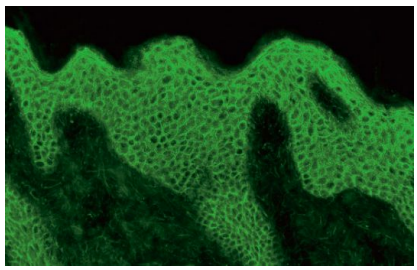
- Cutaneous findings are "polymorphic"

- Erythematous macule
- Flaccid blisters and erosions (resembling pemphigus)
- Tense blisters (resembling pemphigoid)
- Erythema multiforme like lesion
- Lichenoid eruption

Findings:

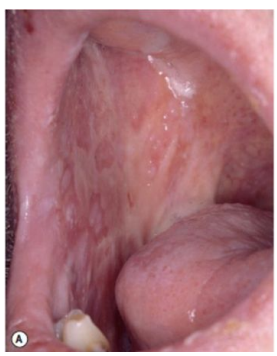
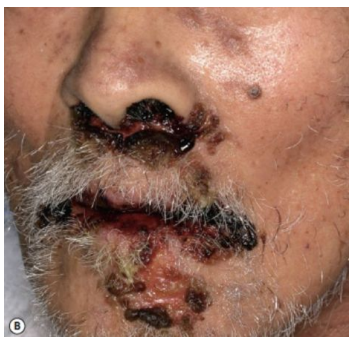
- **IF** → IgG and C3 and IgA
  → linear flaring of B.M if IgG:
  Epidermolysis bullosa acquisita Bullous pemphigoid.
  → linear flaring of B.M if IgA:
  Linear IgA bullous dermatosis



Treatment:

Treat the underlying tumor Benign tumors: it may take 6-18 months to see complete resolution of lesions after excision of benign neoplasms Malignant tumors:

1. No consensus on a standard effective therapeutic regimen
2. Cutaneous lesions respond more rapidly than the stomatitis, which is refractory to treatment

- Prognosis of paraneoplastic pemphigus is poor due to its resistant nature to treatment

Blistering Diseases

Pemphigoid group

1. Bullous Pemphigoid:

It's completely opposite to pemphigus Vulgaris

- The most common autoimmune subepidermal blistering disease, caused by autoantibodies to components of hemidesmosomes in the basement membrane zone (BMZ)
- Characterized by large blisters on an erythematous base.
- Mainly in older age group more than 60 y. **Elderly patients.**
- The **prognosis** is usually **good**.

Clinical features:

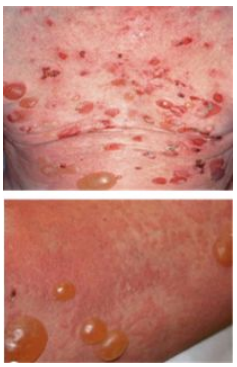
- Elderly patients
- Large **tense** blisters on upper arms and Thighs. unlike Vulgaris, which is flaccid
- Eczematous base with no clear erythema.
- Itch rather than pain. (too itchy to the point that sometimes it presents as eczema).
- Oral lesions are less frequent than pemphigus.
- Has:
  - Tense blister hard to rupture (pathology below b.m).
  - NOT Painful but Urticaria.

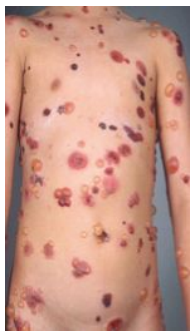
Pathology:

- **Sub epidermal between epidermis and dermis the epidermis forms the roof of the blister.**
- Immunoglobulin and complement are deposited in the lamina lucida of the basement membrane in a linear band.
- Antigens identified are BP 1 "BP230' and BP 2 "BP180" which is most likely to be more involved in the

- Drug-induced bullous pemphigoid:

1. Diuretics (furosemide)
2. D-penicillamine
3. Antibiotics (amoxicillin, ciprofloxacin)
4. Potassium iodide





Clinical features:

BP is an **intensely pruritic** eruption with widespread blister formation

In early stages and atypical variant: excoriated, eczematous, urticarial lesions

Blisters are stable and tense

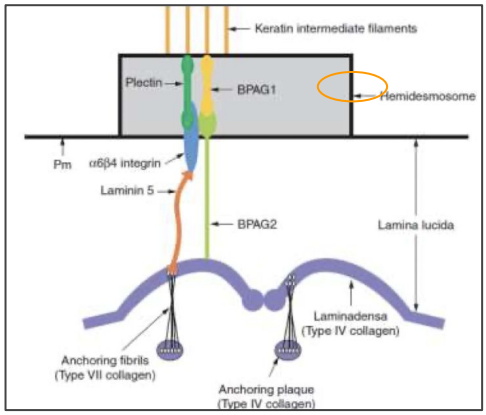
Mucosal involvement in < 20 %

Non-bullous phase: cutaneous manifestations are non-specific & polymorphic (pruritus, excoriations, eczematous, urticarial lesions)

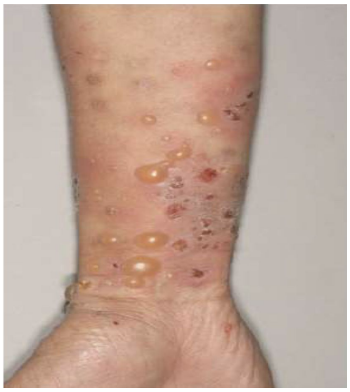
Bullous phase: characterized by the development of vesicles and bullae on normal or erythematous skin along with urticarial lesions

- Bullae predominate on the flexural aspects of the limbs and the lower trunk

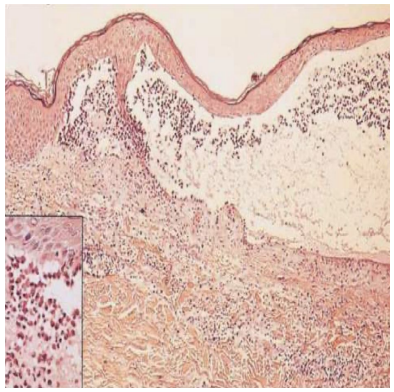
Blistering Diseases



BPAG1: Intracellular binds BPAG2 to hemidesmosome.
BPAG2: Extracellular attach hemidesmosome to the papillary dermis.
Pm, lamnin, a6B4 integrin: all target for congenital diseases



Extensive erythema and deeper erosion and the blister are most tense and often present with blisters



Eosinophils

Diagnostic approach:

The diagnosis of BP is based upon the clinical presentation, histologic features, and positive findings on direct and indirect immunofluorescence

History

Physical examination

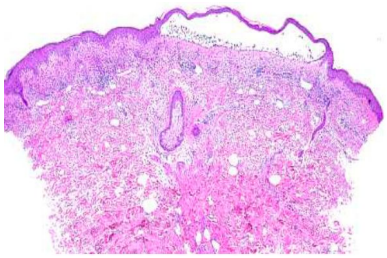
Investigation

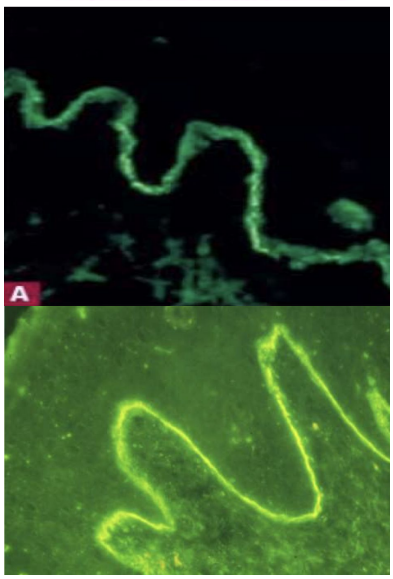
- CBC & Differential —> ↑eosinophils
- ESR↑
- IgE ↑ eosinophils, ESR & IgE are elevated in 60% of patients with BP
- Skin Biopsy:

• Non-bullous phase → non- specific, eosinophilic inflammatory infiltrate

• Bullous phase → subepidermal blister, accompanied by a dermal inflammatory infiltrate composed of eosinophils

- DIF → from perilesional, uninvolved skin, linear, continuous deposits of IgG and C3 along the epidermal basement membrane





In Bullous pemphigoid the IF shows **linear** band.

Treatment:

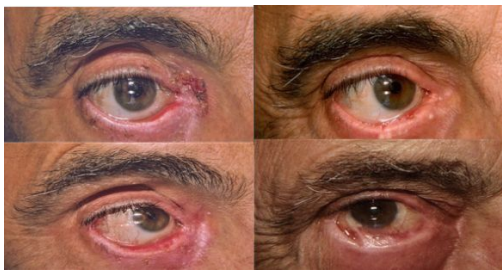
- Mild may also respond very well to potent or moderately potent topical steroids alone.
- Severe pemphigoid :Systemic steroids , but unlike pemphigus, it may be possible to discontinue.
- The addition of either azathioprine enable the oral steroid dose to be reduced more rapidly.
- Potent steroid moderate dose is enough… Even if severe topical high potency steroid is enough.
- So, the good thing here you don't use orals steroids and you don't get the complications especially for the elderly, but it's hard because it need to be topically applied for the whole body, if oral 1/2 mg of dose is enough we add azathioprine if not recovered enough.
- Some physician use doxycycline and niacinamide and say they have anti-inflammatory effect.

2. Cicatricial Pemphigoid:

Is a chronic, autoimmune, subepithelial blistering disorder characterized by a predominant involvement of the external mucosal surfaces (mainly oral & conjunctival mucosa, but it could affect any mucosal site) and a tendency for **scarring**

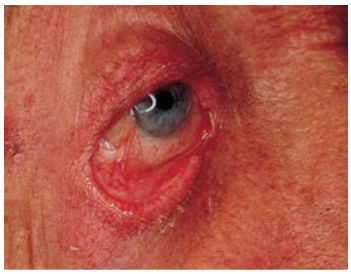
- Patients > 65 years

Clinical features:



Oral mucosa → lesions less painful than PV

Conjunctiva:
- affected in 75% of cases.
- Starts unilaterally, within 2 years becomes bilateral
- adhesions, ectropion, corneal damage



Esophagus & larynx → can develop strictures that may require surgery

Genitalia → narrowing of vaginal orifice, adhesions between glans & foreskin

Skin: only involved in 25% , face, scalp and upper trunk, atrophic scarring

Diagnostic approach:

History

Physical examination

Investigation
- DIF → IgG autoantibodies directed against the basement membrane of mucosa and/or skin
- Indirect IF → salt-split skin

Treatment:

- Local therapy such as potent topical corticosteroids is crucial and, in some cases, maybe sufficient
- Oral lesions → topical steroids (mouthwash, topical preparations),
- Nasal, pharyngeal, esophageal disease → steroid sprays/ inhalers
- Ocular → topical / systemic cortecosteroids, ophthalmology referral
- Severe disease: Oral corticosteroids, Dapsone, Cyclophosphamide, Azathioprine, Surgical therapy

3. Pemphigoid Gestationis:

- Synonym: « herpes gestationis » was previously termed herpes gestationis because the morphology of the blisters was similar to that of herpes, however it's not herpetic.
- A form of BP occuring during pregnancy
- Occurs in 1/10000-40000 pregnancies
- No maternal risk, no increase in birth defects. However, pregnancy complications and fetal death occurs in 15-30%
- Erythematous urticarial plaques, alone or with papules, vesicles, blisters in sub-epidermal area, erosions
- Intense pruritus
- Sites: abdomen, proximal extremities
- Rarely appears postpartum, resolve within 3 months
- Occasionally recurs with menses or ingestion of OCP, tends to be worse in next pregnancy
- The antibodies cross the placenta, the newborn can have blisters for a few weeks

Diagnostic approach:

History

Physical examination

Investigation

- Cbc & differential eosinophilia
- DIF & indirect IF

Treatment:

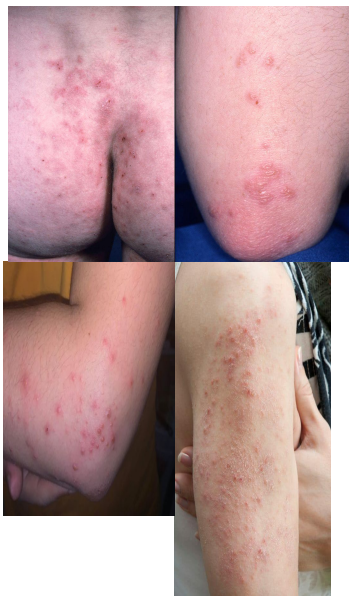
Topical steroids

- Systemic steroids: avoid in 1st trimester
- Skin care to prevent infection
- Antihistamines for tx of pruritus

4. Dermatitis Herpetiformis

Herpetiformis means "herpes-like lesion", which is a group of vesicles

- A chronic, **recurrent intensely pruritic** Although, they're tense, pts. Remove'em due to their itchiness
- 30-40 year old
- Grouped vesicles, papules on extremities and buttocks
- Associated with Gluten sensitive enteropathy
- **IgA autoantibodies against transglutaminase**
- **Exacerbated by Iodide and Gluten ingestion**
- DH is a cutaneous manifestation of celiac disease and is associated with gluten sensitivity in virtually all cases
- DH and celiac disease are genetic disorders strongly associated with HLA-DQ2 genotype, in which IgA antiendomysial antibodies are directed against tissue transglutaminases (in the skin → epidermal transglutaminase)



Clinical features:

Sites : extensor surfaces of elbows/knees, sacrum, buttocks, scalp

Grouped 'herpetiform' papules/vesicles/urticarial wheals over an erythematous base, associated with intense pruritus, burning, stinging and **excoriations**

Spontaneous remissions may occur, but disease often lifelong

DH other symptoms include Malabsroption, Iron deficiency anemia, Steatorrhea

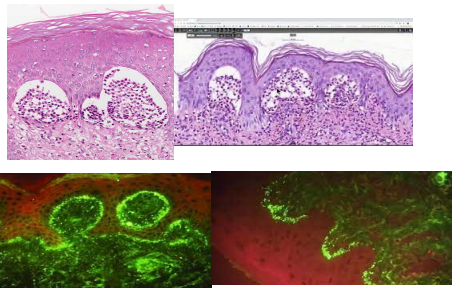
Diagnostic approach:

History

Physical examination

Investigation

Skin biopsy: **subepidermal blister, with neutrophilic microabscesses in the papillary dermis is the hallmark of the disease**

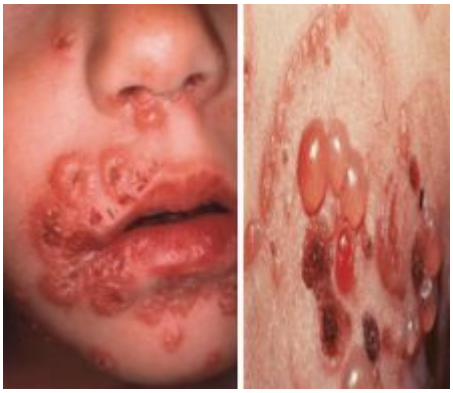


- DIF → **Granular deposits of IgA in the dermal papillae** (Confirmatory test)
- Indirect IF
- ELISA identifies IgA against transglutaminase in 80% of cases
- Jejunal Biopsy flattening of the villi

Treatment:

- **Dapsone** 100-150 mg/d works by inhibiting the adhesion between neutrophils and IgA
  - **Quick** response within hours
  - It can precipitate G6PD or methemoglobin
- Sulfapyridine 1-1.5 grams/d if dapsone not tolerated. Monitor kidney function
- **Gluten free diet is slow, and usually not enough** but can lower doses of medications

5. Linear IgA Disease:



- Subepidermal blistering disease caused by deposits of IgA along BMZ
- Linear IgA disease is characterized by on linear IgA deposition at the basement membrane
- Maybe identical to DH but WITHOUT GI involvement , or resemble BP
- Over 50% have mucosal involvement

Diagnostic approach:

History

Physical examination

Investigation

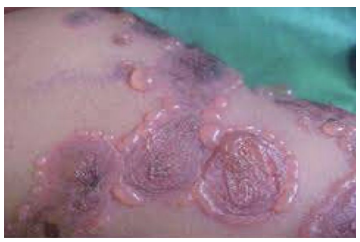
- DIF → linear IgA deposits along the basement membrane
- Indirect IF

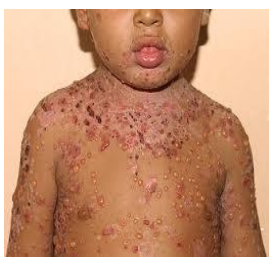
Treatment:

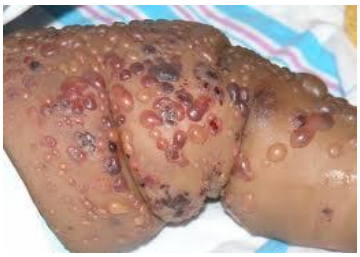
- Dapsone
- Sulfapyridine
- Antibiotics: tetracycline, erythromycin, dicloxacillin
- Antibiotics are a good treatment for the childhood form, and were found to be better than dapsone in this age group

6. childhood form "Chronic bullous disease of childhood":

Clinical Feature:







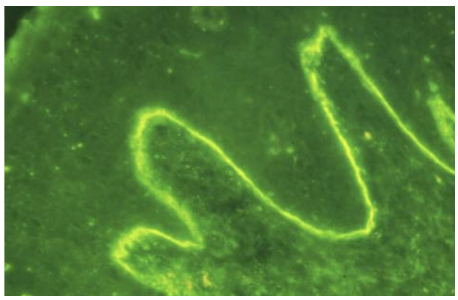
- Occurs in children "preschool", and resolves spontaneously
- **Circular clusters of large blisters like the type seen in pemphigoid (cluster of jewels).**

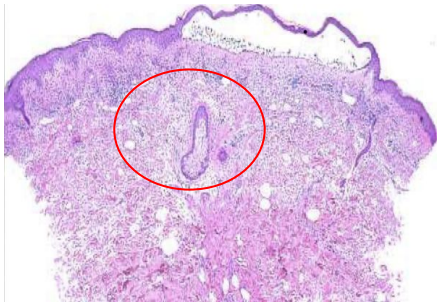
  (similar target of Bullous pemphigoid).
- It involves the perioral area, lower trunk, inner thighs and genitalia.
- Blistering may spread all over the body.

Blistering Diseases

Investigations:

- Skin Biopsy will show subepidermal splits
- Direct IF reveals IgA along the BM of the epidermis in a linear pattern (similar to BP except in BP it's IgG).





Neutrophils unlike BP which is eosinophils

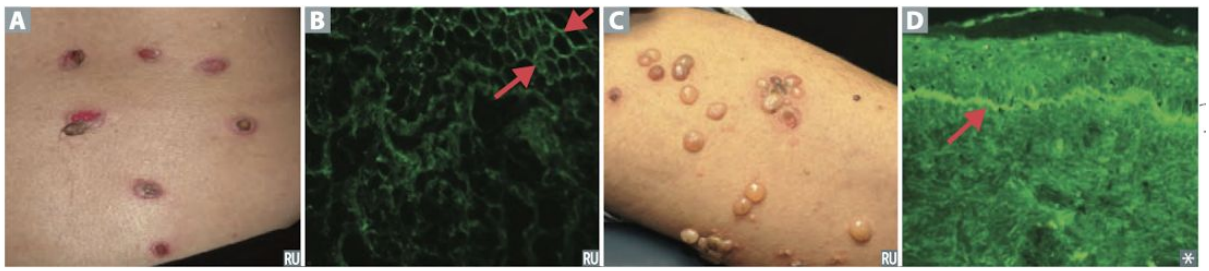
Treatment:

- Oral **dapsone** 50-200 mg daily (Ad/E) (dapsone works greatly on Neutrophils).
- Sulphonamides and immunosuppressants.
- Erythromycin. (in case of sulfa allergy)
- **Flucloxacillin** : 7 cases reported excellent response from KKUH.
- We can use steroid but as last option

Summary regarding the differences between P. Vulgaris & Bullous P. "Dr slides"

Autoimmune blistering skin disorders

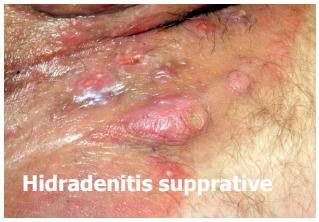
	Pemphigus vulgaris	Bullous pemphigoid
PATHOPHYSIOLOGY	Potentially fatal. Most commonly seen in older adults. Type II hypersensitivity reaction. IgG antibodies against desmoglein-1 and/or desmoglein-3 (component of desmosomes, which connect keratinocytes in the stratum spinosum).	Less severe than pemphigus vulgaris. Most commonly seen in older adults. Type II hypersensitivity reaction. IgG antibodies against hemidesmosomes (epidermal basement membrane; antibodies are "bullow" the epidermis).
GROSS MORPHOLOGY	Flaccid intraepidermal bullae A caused by acantholysis (separation of keratinocytes, "row of tombstones" on H&E stain); oral mucosa is involved. Nikolsky sign ⊕.	Tense blisters C containing eosinophils; oral mucosa spared. Nikolsky sign ⊖.
IMMUNOFLUORESCENCE	Reticular pattern around epidermal cells B.	Linear pattern at epidermal-dermal junction D.

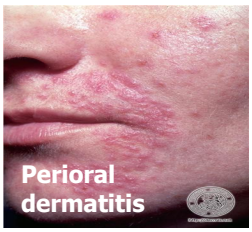


Nikolsky sign: is a skin finding in which the top layers of the skin slip away from the lower layers when rubbed.

Acne vulgaris and related disorders

Main subtopics





A)Acne Vulgaris

- Acne is an old disease, the problem dated back to the pharaohs in the Egypt 4000 years ago
- Multifactorial disease pilosebaceous unit
- Affects both male & female
- The most common dermatological disease
- Mostly prevalent between 12-24 yrs.
- affects 8% between 25-34, 4% between 35-44.
- it's a chronic disease originating within the pilosebaceous follicles.

Four interrelated processes are involved:

- ➔ Sebum overproduction
- ➔ Abnormal shedding of follicular epithelium
- ➔ Follicular colonization by Cutibacterium acnes (previously called Propionibacterium acnes)
- ➔ Inflammation

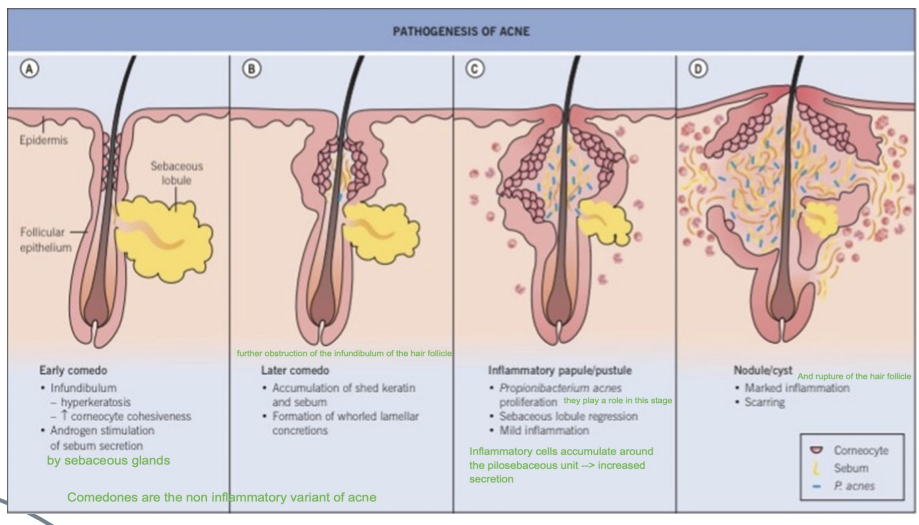
Pathogenesis:

-Ductal cornification occlusion **(micro-comedo),** it is pathognomonic of acne (characteristic). due to altered keratinization (micro-pathogenesis).

-Increased sebum secretion (Seborrhoea). Altered keratinization due to increase cell production (cornification) that lead to occlusion, dilation of sebaceous gland and increase sebum production (non inflammatory acne).

-Ductal colonization with propionibacterium acnes. Manipulation and scratching of comedone lead to bacterial colonizations that lead to inflammation (it is non infectious inflammation).

-Rupture of sebaceous gland and inflammation. Inflammation characterized by redness and pus (inflammatory acne).



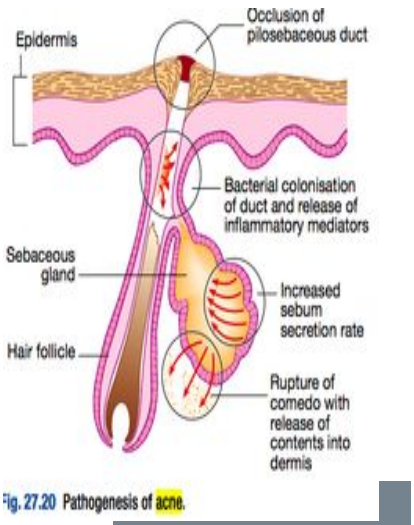
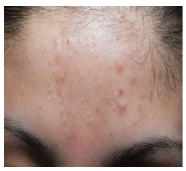
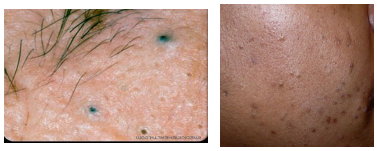


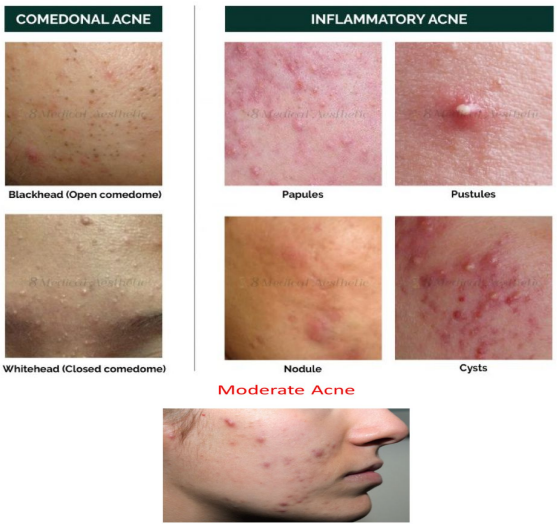
Fig. 27.20 Pathogenesis of acne.

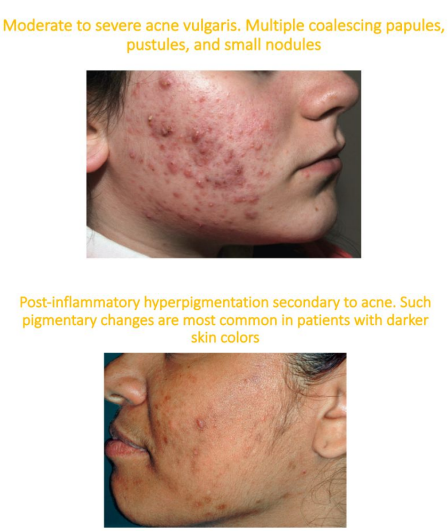
Acne vulgaris

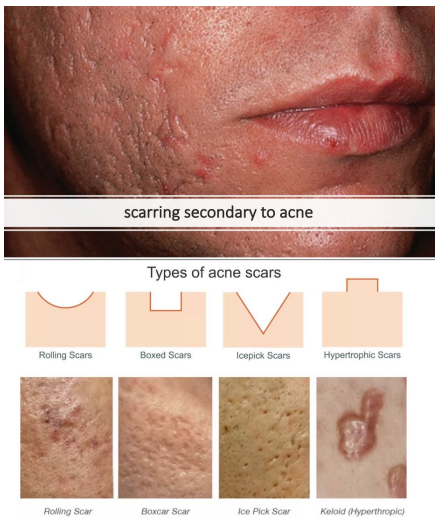
Microcomedone: (Pathognomonic)
Hyperkeratotic plug made of sebum and keratin in follicular canal.

Close vs Open comedone (MCQ)

Closed comedone (white head)	Open comedone (Black head)
• Closed follicular orifice, accumulation of sebum and keratin. 	• Open follicular orifice with melanin and oxidized lipid due to exposure to O_2 that lead to karatin oxidation. 





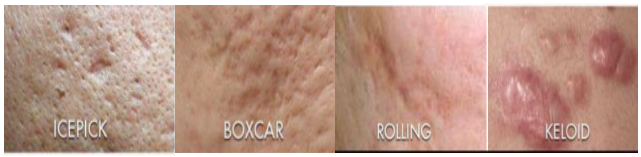


Clinical features

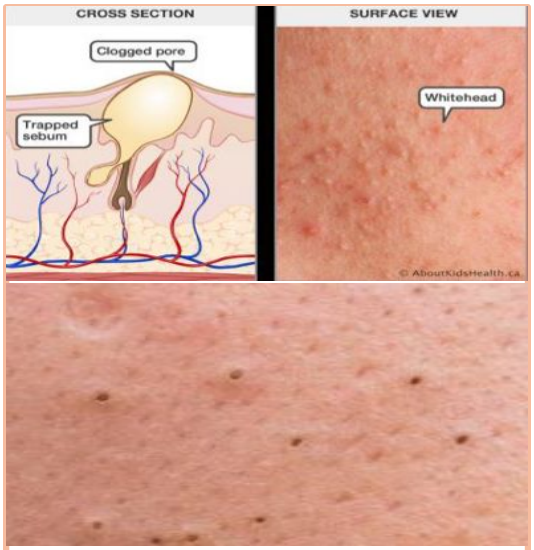
- **Acne lesions are divided into:**
  1- Inflammatory lesion (papules, pustules, nodules, cyst).
  2 - non inflammatory lesion (open, closed comedones).
- **The comedones are the pathognomonic lesion.**
- **Seborrhea.**
- **Post inflammatory hyperpigmentation.**
- **Scaring (Atrophic and hypertrophic)**
- Lesion predominate in sebaceous rich gland including **face,chest, upper arm and upper back.**
- When follicles rupture into surrounding tissues they result in inflammatory lesion (we treat acne early to avoid these things):
  1-papules. 2-pustules. 3-nodules. 4- cyst.
- The severity of acne ranges from mild, moderate, severe according to the predominant lesion.
- **Comedon predominance is considered to be mild,** while extensive papulopustules and nodules or **cysts are considered severe.**
- Acne has psychosocial impact which is involved in determining the severity.

Types of scar

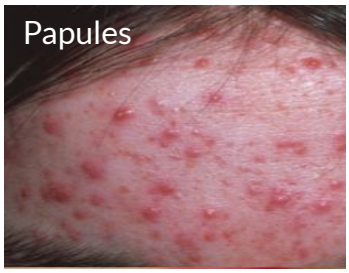
- **Ice pick scar.**
- **Boxcar scar.**
- **Rolling.**
- **Keloid.**

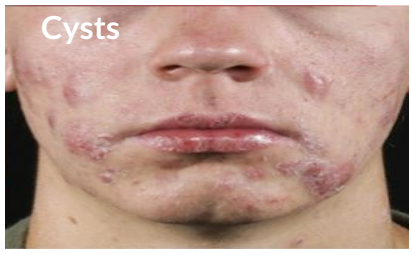


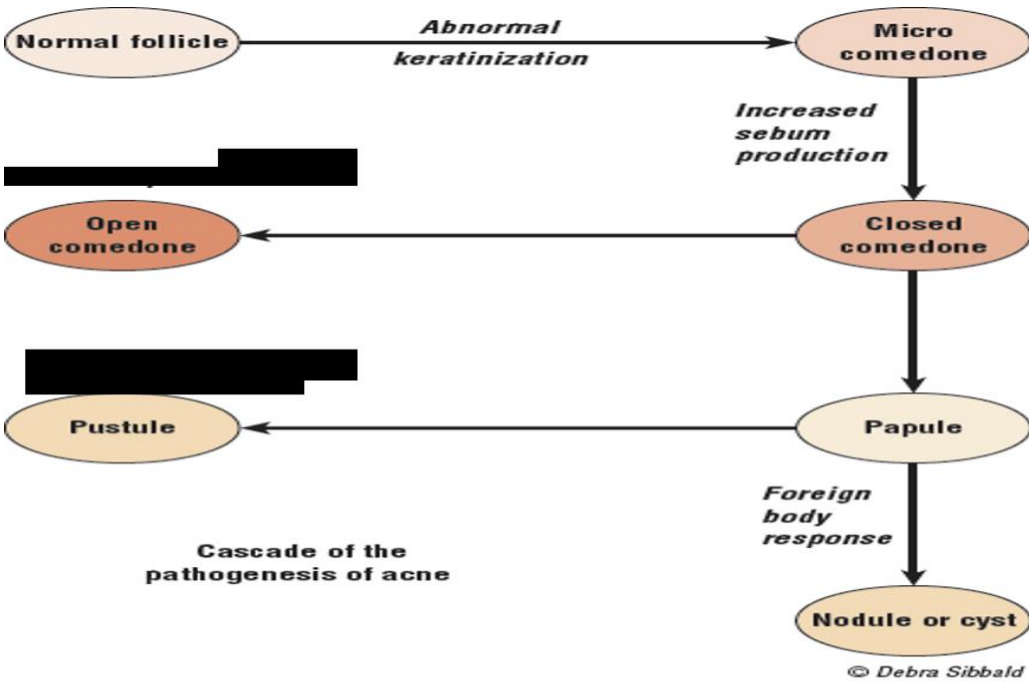
Acne vulgaris



Non inflammatory lesions
closed and open comedones







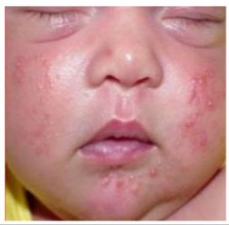
Cascade of the pathogenesis of acne

Source: J.T. DiPiro, R.L. Talbert, G.C. Yee, G.R. Matzke, B.G. Wells, L.M. Posey: Pharmacotherapy: A Pathophysiologic Approach, 10th Edition, www.accesspharmacy.com

Acute subtypes

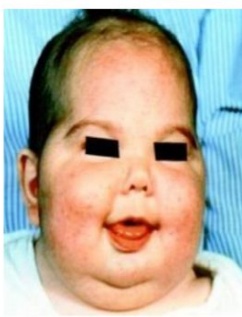
Neonatal acne

- Onset between 0-6 w of age.
- Characterized by closed comedones.
- Resolve spontaneously within 1-3 months.
- No relation with later development of acne.



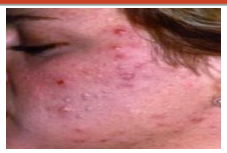
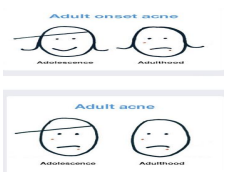
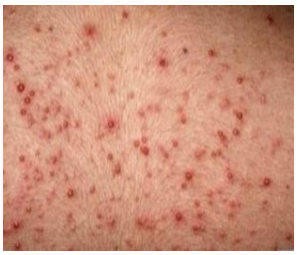
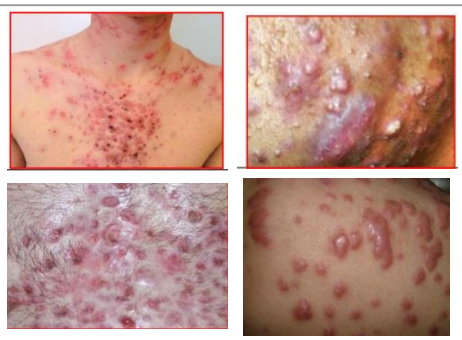
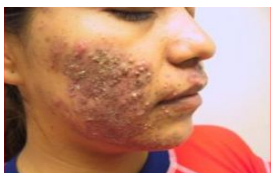
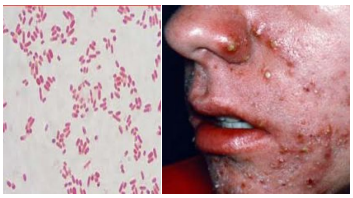
Infantile acne

- Onset between 3-6 m.
- Characterized by inflammatory lesions.
- Can be associated with precocious androgen secretion to **brain (hamartoma and astrocytoma).**
- Think of hormonal issues that could continue with him throughout his life, must be treated.
- **Endocrinology examination (LH)** and **bone age** is important.
- There is increased risk of development of severe acne later in life.



Acne vulgaris

Acute subtypes (cont')

Teenage acne	• More in boys. (Most common disease derma) • Mainly comedonal. • May be the first sign of puberty. 
Adult acne	• Affects adults above 25 years. • Can be continuation of teenage acne or start denovo. • IF associated with hirsutism, irregular periods evaluate for hyper secretion of ovarian androgens (e.g. **Polycystic ovary syndrome**). 
Drug induced acne	• Steroids, Iodides, Bromides, INH, Lithium, Phenytoin, Epidermal growth factor inhibitors (cetuximab) cause acneiform eruption. • The characteristic feature of **steroids acne is the absence of comedones** and **monomorphic lesions** as small pustules and papules all looking alike. It has a predilection to the chest & back 
Acne conglobata	• Highly inflammatory (severe form of acne); with comedones, nodules, abscesses, draining sinuses, over the back and chest. • Often persist for long periods. • Affect males in adult life (18-30 years). • **Heal with scars (Depressed or Keloidal).** • **No systemic involvement in acne conglobata.** 
Acne Fulminans	• Sudden massive inflammatory tender lesions with ulceration Heals with scarring. • Associated with fever, increased ESR & CRP, polyarthralgia, Leukocytosis. Systemic involvement. • The patient might needs admission. 
Occupa -tional acne	• Due to contact with **oils – tars –chlorinated hydrocarbons** used in the synthesis of insecticides and solvents. • Lesions appear at site of contact including large comedones, papules,pustules, nodules. • The most serious form is the chloracne due to systemic effect (liver damage, CNS involvement, decrease lung vital capacity).
Gram negative folliculitis	• Infection with G –ve organisms (Klebsiella, proteus, E.coli). • Seen in patients under chronic antibiotic acne treatments. • Superficial pustules without comedones or even cysts involving from intranasal area to chin and cheeks. • Response to ampicillin, Isotretinoin and TMP-SM. 

Aggravating Factor

01 **Diet has not relation to acne**

02 **Pre menstrual flare**

03 **Sweating**

04 **UV Radiation**

05 **Stress**

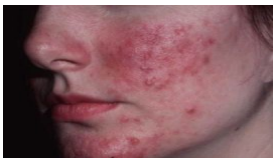
06 **Friction**

07 **Cosmetics**

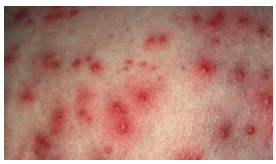
Acne vulgaris

Differential diagnosis for acne vulgaris

Rosacea

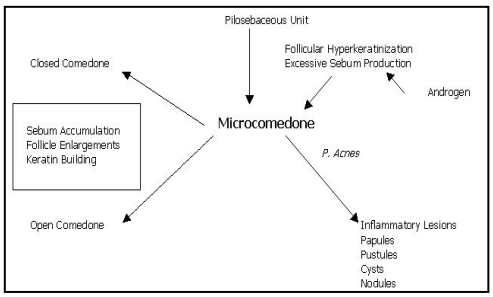


Folliculitis



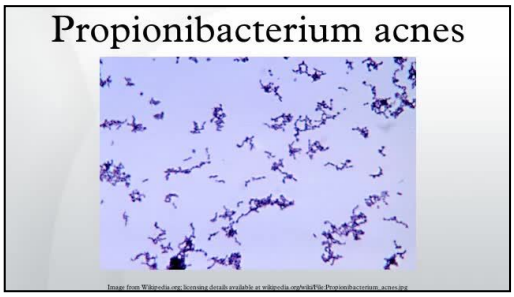
Acne treatment goals

- **Decrease scarring** + Hyperpigmentation.
- Decrease unsightly appearance.
- Decrease psychological stress.
- Explain length of treatment, may be several months and initial response may be slow but must persevere.



Principle in treating acne

- Reverse the altered keratinization.
- Decrease the intra-follicular P.acnes.
- Decrease sebaceous gland activity.
- Decrease inflammation.

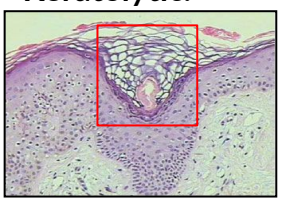


Treatments

Oral Oral therapy used To kill the bacteria	Topical Topical therapy used to alter keratinization	Miscellaneous
Antibiotics:	Benzoyl peroxide	Laser resurfacing
Doxycycline	Retinoic acid	Chemical peel
Minocycline	Adaplene Tazarotene	Comedo extraction
Erythromycin	Resorcinol, Sulfer	Dermaberasion
Retinoids:	Azeliac acid	Intralesional steroid
Isotretinoin	**Antibiotics:**	CROSS
Hormons:	Clindamycin	-
Antiandrogens	Erythromycin	-
OCP		

Acne vulgaris

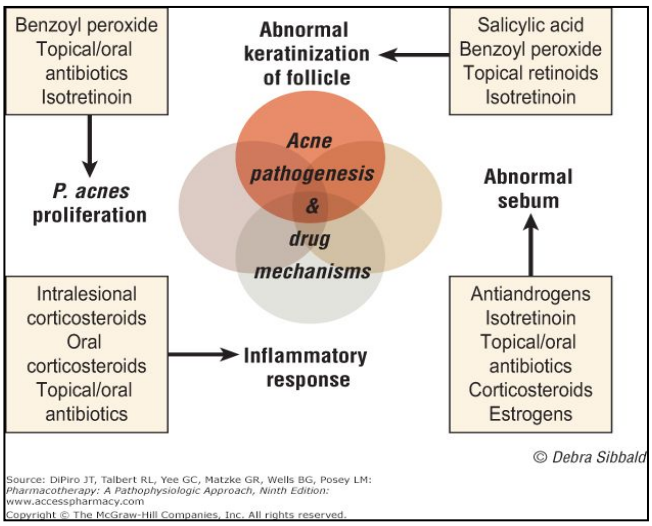
Topical therapy (Result is noticed within 2 month)

Benzoyl peroxide	Retinoic acid	Salicylic Acid	Resorcinol and sulfur	Azelaic acid
- High **antibacterial** activity. - Drying effect. - Could cause irritation and contact dermatitis.	- **Comedolytic** activity. - Advice patient not to expose to sun as it may lead to burn.	- **Comedolytic**, less potent than retinoic acid.	- **Keratolytic.** 	- **antibacterial** and **bleaching**.

Oral therapy

Drug	Dose	Recommendation & duration
Tetracycline	0.5 BD	• Taken on empty stomach to promote absorption. • Not to be taken with milk or antacid. • Not to be given to pregnant women.
Erythromycin	0.5 g BD	• For **pregnant women** with bad acne.
Azithromycin	250 mg	• 3 consecutive days/w for pregnant women.
Doxycycline	100 mg/day	• Can be taken with food, photosensitivity.
Minocycline	100 mg/day	• Drug could cause blue–black pigmentation in scars, lupus, hepatitis, photosensitive drug rash.
Clindamycin	—	• Could cause pseudomembranous colitis.
Trimethoprim/ Sulphamethoxazole	—	• Used only in resistant cases .
Isotretinoin	0.5-1 mg/kg	• Give long term remission. • Given in resistant acne.

- Systemic antibiotic have to be used for **3 months to avoid resistance.**



Acne vulgaris

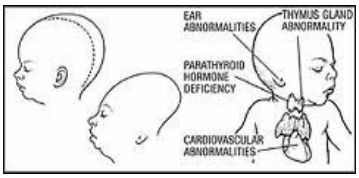
Side effects: (very common)

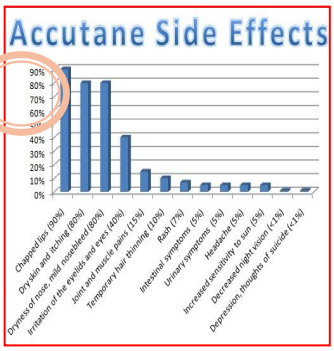
- Dryness of mucous membranes (Cheilitis, Conjunctivitis).
- **Headache** and increased intracranial pressure (Pseudotumor cerebri).
- Contact lens intolerance.
- Isotretinoin should not be given with tetracycline.
- **Bone** and joint pains.
- Increases triglycerides and cholesterol (most important investigation we do with patient on Isotretinoin) or LFT.
- Patients should avoid pregnancy 4 week after discontinuation of drug because of teratogenicity.
- Depression and mood swing.

Isotretinoin (Accutane)
Vitamin A analogue

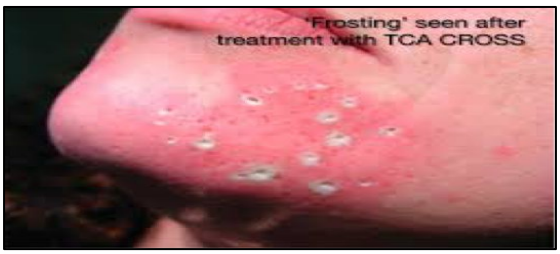
Hormonal

- OCP consider less androgenic progestogen, eg: marvelon/cilest, but increased risk of DVT.
- Consider cyproterone acetate (antiandrogen). With oestrogen (dianette). flutamide (antiandrogen).
- Used in polycystic Ovarian syndrome (POS). Think about female with hirsutism and acne.

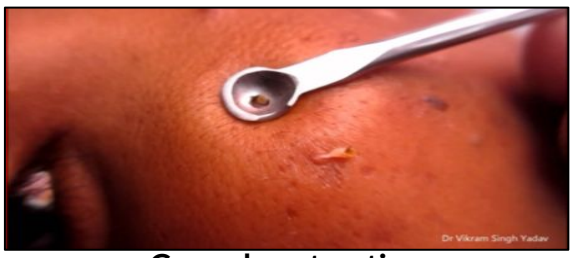




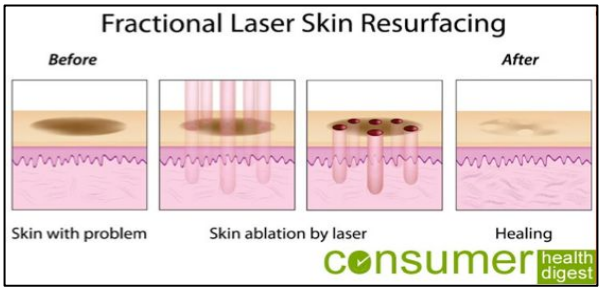
Other Treatments:

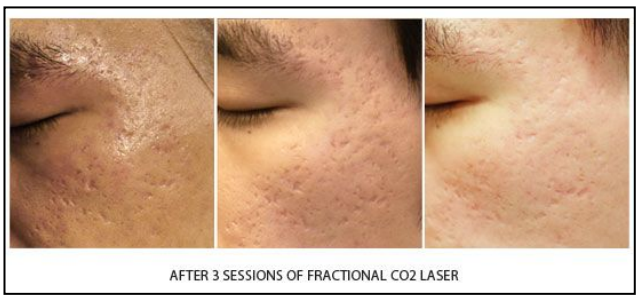


CROSS (chemical reconstruction of skin scars)



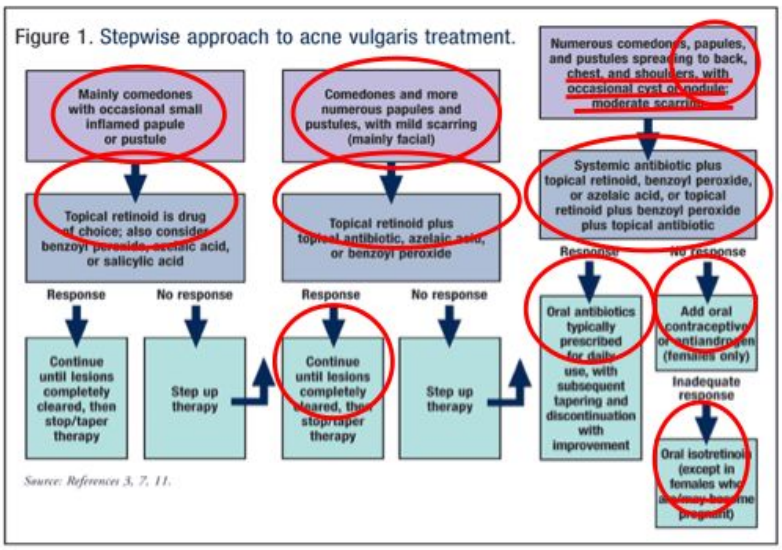
Comedo extraction





Take Home Massage:

- **A** avoid squeezing and manipulation.
- **C** comply with medication.
- **N** no cosmetics and moisturizers.
- **E** early treatment to avoid scaring.

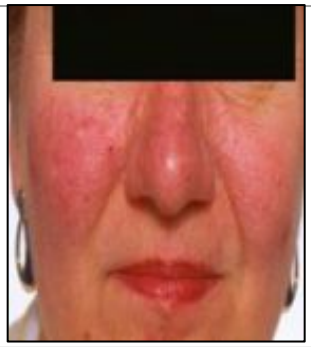


Acne related disorders

B)Rosacea

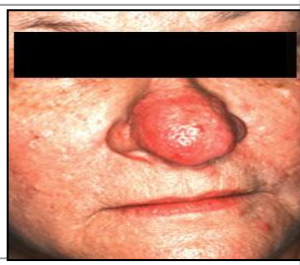
Definition

- A chronic skin rash involving the central face
- Papules and Papulo-pustules in the **center of the face and nose** against vivid erythematous background with **telangiectasia**. (pathognomic feature).



Incidence

- Common in 3rd and 4th decade, Peaks between 40-50.
- Starts between the age of 30 and 60 years.
- Common in fair skin.
- Women are affected more than men **but rhinophyma is more in men.**



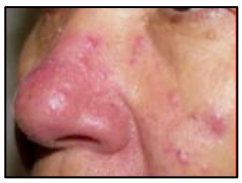
Pathogenesis

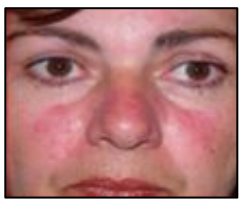
- Unknown.
- Genetic predisposition (38% have a relative).
- Sunlight and heat (in kitchen and crowded places).
- Constitutional predisposition to flushing & blushing.
- **Demodex folliculorum mite.**
- H. Pylori infection.

Clinical Findings

The Hallmark Is:

- **Episodes of flushing and erythema in butterfly distribution**. (MCQ)
- Papules and pustules.
- **Erythema** (flushing on the face) and telangiectasia.
- **Telangiectasia is only in rosacea not in acne.**
- **Absent comedones.**
- **Granulomas** (firm papules).
- 438 only:
- **Stage 1: persistent erythema and telangiectasia**
- **Stage 2: persistent erythema and telangiectasia , papules and pustules**
- **Stage 3: Solid edema and rhinophyma**
- **Ocular Rosacea : blepharitis , conjunctivitis , episcleritis**



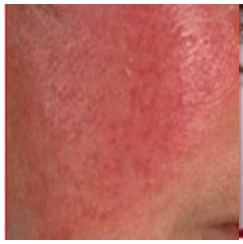


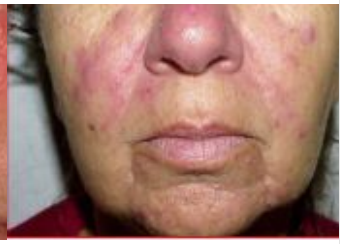
Localization:

- The **nose, cheeks**, chin, forehead and glabella (between eyebrows).
- May involve ears and chest.

Types of Rosacea

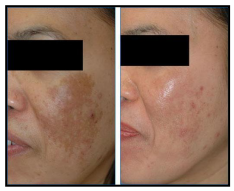
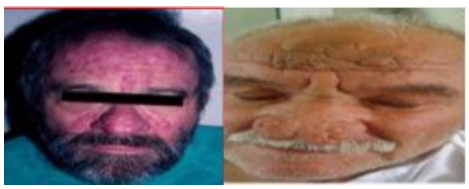
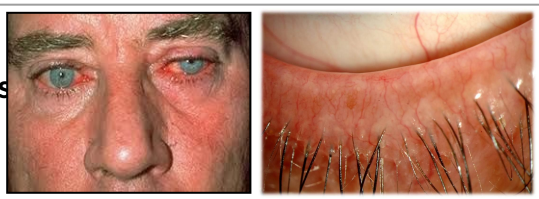
- Erythematotelangiectatic.
- Papulopustular.
- **Ocular** (it develops conjunctivitis).
- Phymatous.

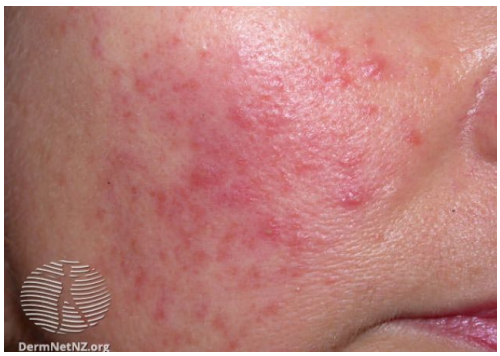


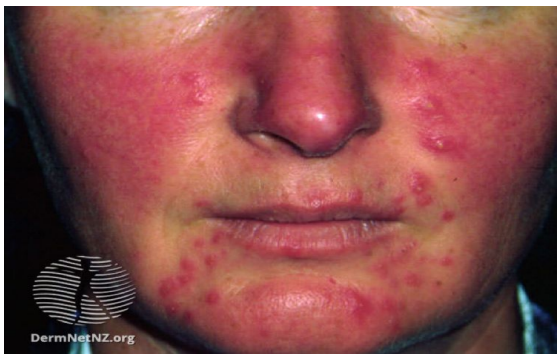


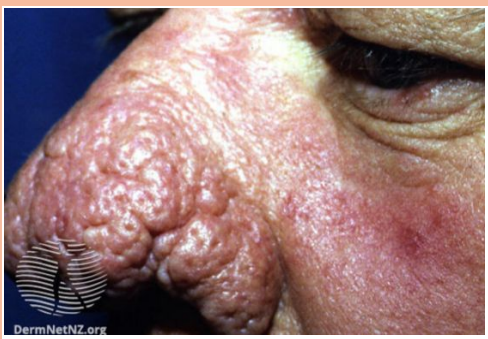
Acne related disorders

B)Rosacea

Triggers	• Hot or cold temperatures, Wind. • Hot drinks, Caffeine, Spicy food and Alcohol. • Exercise, Emotions. • Topical products that irritate the skin and decrease the barrier. • Medications that cause flushing (nicotinamide). • UVR
Associated diseases	• **MARSH syndrome:** Melasma + Acne + Rosacea + Seborrheic dermatitis + Hirsutism. 
Phymatous complication	• **Rhinophyma**: Swelling of the nose due to sebaceous gland hyperplasia. • Other phymatous complications include: gnathophyma, otophyma, blepharophyma and metophyma. 
Eye complications	**Occurs in 50% of cases including:** • **Blepharitis (the most common), conjunctivitis Keratitis, Iritis and Eyelid telangiectasia.** 

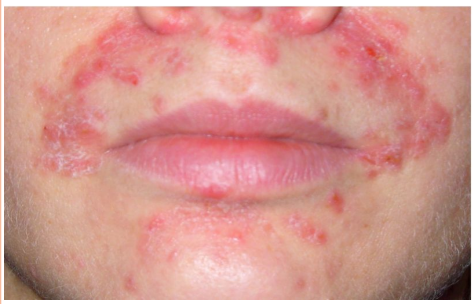






stage 3: rhinophyma --> thickening of the skin over the nose (treatment: surgery & resurfacing laser)

Perioral dermatitis



Another variant of rosacea exactly like rosacea: same triggers & pathogenesis -- only difference is distribution.. here: around the mouth

Psoriasis

Introduction:

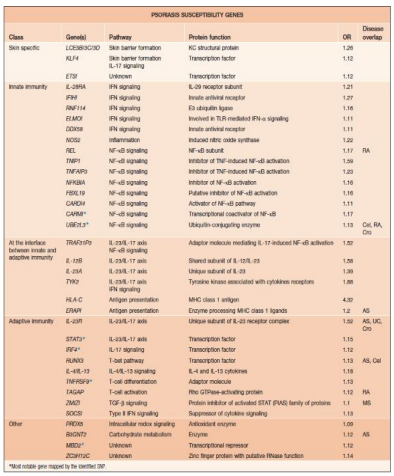
- Psoriasis is an **Complex** (Genetic + environmental factors) **immune-mediated polygenic** (Multiple genes involved) **skin disorder** (Multisystemic mainly involves the skin and joints). Various environmental triggering factors, e.g. trauma , stress, infections and medications, may elicit disease in genetically predisposed individuals.

Epidemiology:

- 2% of population (LP is less than 1%) (0.7% of Asian/African).
- 0.7% juvenile psoriasis.
- Only 25% have severe psoriasis.
- Bimodal disease (20-30s/50-60s).
- Two third of patients have family history of psoriasis (Strong family history in comparison to LP).
- Child risk : one parent 14% two parent 40%

Genetics: very imp

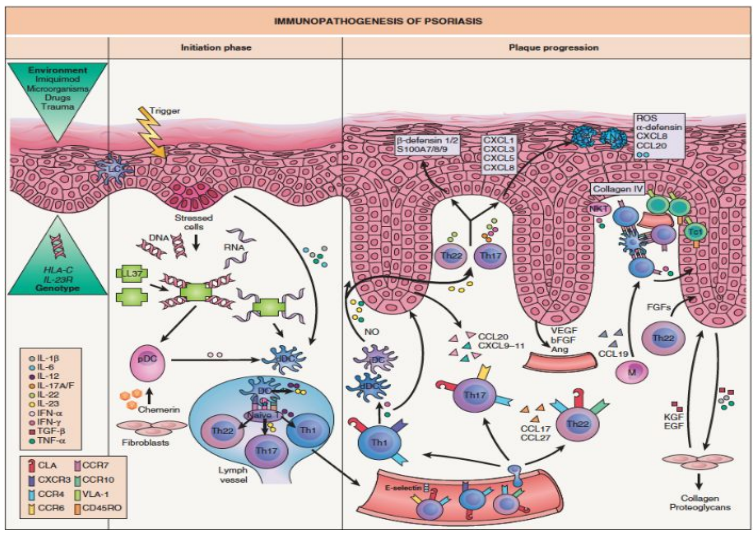
- Nine psoriasis susceptibility regions **(PSORS1–9)** in different chromosomal locations.
- **PSORS1** (on chromosome 6p), account for up to 50% of psoriasis risk.
- **PSORS1** contains genes such as **HLA-Cw6** which is important protein in immune system (from every two patients, one has this gene).
- **HLA-Cw6** is strongly linked to the age of onset of psoriasis.
  - 90% of the patients with early-onset psoriasis.
  - 50% of the patients with late-onset psoriasis.
- Early-onset psoriasis, positive family history and expression of HLA-Cw6 **(type I psoriasis).** (Aggressive type)
- Late-onset disease, no family history and a lack of expression of HLA-Cw6 **(type II psoriasis)**


PSORIASIS SUSCEPTIBILITY GENES

Class	Gene(s)	Pathway	Protein function	OR	Disease overlap
Skin specific	*LCE3B/3C/3D*	Skin barrier formation	KC structural protein	1.26	
	KLF4	Skin barrier formation	Transcription factor	1.12	
		IL-17 signaling			
	ETS1	Unknown	Transcription factor	1.12	
Innate immunity	*IL-28RA*	IFN signaling	IL-29 receptor subunit	1.21	
	IFIH1	IFN signaling	Innate antiviral receptor	1.27	
	RNF114	IFN signaling	E3 ubiquitin ligase	1.16	
	ELMO1	IFN signaling	Involved in TLR-mediated IFN-α signaling	1.11	
	DDX58	IFN signaling	Innate antiviral receptor	1.11	
	NOS2	Inflammation	Induced nitric oxide synthase	1.22	
	REL	NF-κB signaling	NF-κB subunit	1.17	RA
	TNIP1	NF-κB signaling	Inhibitor of TNF-induced NF-κB activation	1.59	
	TNFAIP3	NF-κB signaling	Inhibitor of TNF-induced NF-κB activation	1.23	
	NFKBIA	NF-κB signaling	Inhibitor of NF-κB activation	1.16	
	FBXL19	NF-κB signaling	Putative inhibitor of NF-κB activation	1.16	
	CARD14	NF-κB signaling	Activator of NF-κB pathway	1.11	
	*CARM1**	NF-κB signaling	Transcriptional coactivator of NF-κB	1.17	
	*UBE2L3**	NF-κB signaling	Ubiquitin-conjugating enzyme	1.13	Cel, RA, Cro
At the interface between innate and adaptive immunity	*TRAF3IP2*	IL-25/IL-17 axis NF-κB signaling	Adaptor molecule mediating IL-17-induced NF-κB activation	1.52	
	IL-12B	IL-23/IL-17 axis	Shared subunit of IL-12/IL-23	1.58	
	IL-23A	IL-23/IL-17 axis	Unique subunit of IL-23	1.39	
	TYK2	IL-23/IL-17 axis IFN signaling	Tyrosine kinase associated with cytokines receptors	1.68	
	HLA-C	Antigen presentation	MHC class I antigen	4.32	
	ERAP1	Antigen presentation	Enzyme processing MHC class I ligands	1.2	AS
Adaptive immunity	*IL-23R*	IL-23/IL-17 axis	Unique subunit of IL-23 receptor complex	1.52	AS, UC, Cro
	*STAT3**	IL-23/IL-17 axis	Transcription factor	1.15	
	*IRF4**	IL-17 signaling	Transcription factor	1.12	
	RUNX3	T-cell pathway	Transcription factor	1.13	AS, Cel
	IL-4/IL-13	IL-4/IL-13 signaling	IL-4 and IL-13 cytokines	1.16	
	*TNFRSF9**	T-cell differentiation	Adaptor molecule	1.13	
	TAGAP	T-cell activation	Rho GTPase-activating protein	1.12	RA
	ZMIZ1	TGF-β signaling	Protein inhibitor of activated STAT (PIAS) family of proteins	1.1	MS
	SOCS1	Type II IFN signaling	Suppressor of cytokine signaling	1.13	
Other	*PRDX5*	Intracellular redox signaling	Antioxidant enzyme	1.09	
	BIN3NT2	Carbohydrate metabolism	Enzyme	1.12	AS
	*MEDI1**	Unknown	Transcriptional repressor	1.12	
	ZC3H12C	Unknown	Zinc finger protein with putative RNase function	1.14	

*Most notable gene mapped by the identified SNP.

Pathogenesis:



Color Index:
Pathogenesis
Pathology
Clinical feature

1- A Trigger (auto antigen or exogenous source) will cause protein changes in epidermis in susceptible people (who have defect in some genes) start to present some of its antigen to APC.
2- Antigen Presenting cells (langerhans cells and keratinocytes) in the skin will recognize the antigen and present it to the naive lymphocyte.
3- APC will make the T helper cell attack the antigen which is your own epidermis (Whenever this triggers come back again it will trigger the immune system continuously).
This will lead to superficial perivascular infiltrate.
4-Lymphocyte will secret cytokines and this will lead to vasodilation (erythema).
5- Too much cytokines will stimulate the epidermis and it will lead to Acanthosis (which is elongation of rete ridges in the papalis) (induration and Plaque).
6- Continuous stimulation of cytokines will accelerate the journey of Immature cells in basal layer to epidermis from 14 days to 3-4 days which will lead to Parakeratosis (the cells are not mature enough to become Corneocytes) (scale).

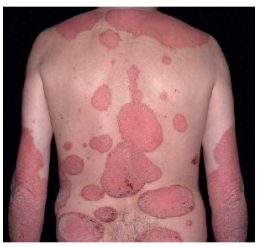
Psoriasis

Triggers:

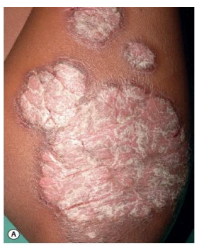
- Trauma
- Stress (emotional stress eg. alopecia areata/vitiligo)
- Infections: e.g. Streptococcal infections (group A), especially pharyngitis (most common infection to cause psoriasis).
- Drugs: e.g. lithium, IFNs, β-blockers, and antimalarial (IFNs and antimalarial drugs cause **lichen planus**).
- Hypocalcemia has been reported to be a triggering factor for generalized pustular psoriasis (happen in pregnancy).

1- Chronic Plaque Psoriasis: (~90%)

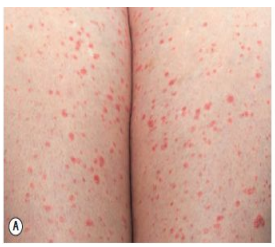
- Symmetric sharply defined erythematous plaques with thick silvery scale over the scalp, elbows, knees and lumbosacral area which is associated sometimes with hyperkeratosis of the hands and feet.
- Has these signs:
  - **Auspitz sign:** when removing a scale pinpoint bleeding occurs which represents the dilated capillaries.
  - Candle sign.
  - Woronoff sign: hypopigmented rim due to topical steroids use.
- **Types chronic plaque psoriasis:**
  - **Guttate psoriasis** looks like rain (**more common in children** and adolescents and preceded by an upper respiratory tract infection "strep") ; **REMEMBER IN CHILDREN**
  - **Flexural psoriasis** affects Axillae, groin and genital areas (humid areas masks the scales presented mistakenly as a resistant fungal infection> suspect psoriasis) and presents as well demarcated erythematous plaque without scales.
  - **sebopsoriasis:** indeterminate stage. (seborrheic dermatitis and psoriasis in the same patient)



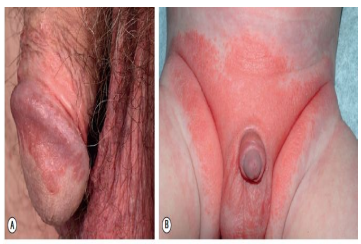
Classic Chronic Plaque type Psoriasis



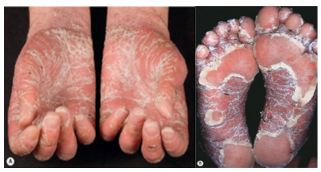
If scratched causes candle sign If peeled causes auspitz sign

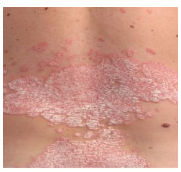


Guttate Psoriasis.



Flexural psoriasis, Notice there isn't any scaling

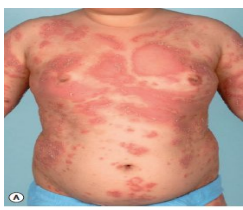




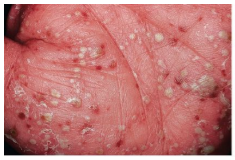
2- Pustular Psoriasis: (~9%)

- All are the same but named according to site of involvement.
- **Generalized pustular psoriasis** (von Zumbusch pattern):
  - ill patient with **constitutional symptoms** present with generalized abrupt painful eruption with erythema and **pustulation** starting over the intertriginous areas and trunk.
- **Palmoplantar pustulosis** (localized):
  - Associated with SAPHO syndrome (**S**ynovitis, **A**cne, **P**ustulosis, **H**yperostosis and **O**steitis).
- **Acrodermatitis continua of Hallopeau :**
  - Pustules over the distal portions of the fingers followed by scaling and crust formation. Pustules may also form subungual which **might cause shedding of nail plates.**

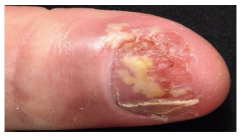
Pustular psoriasis. sheets of erythema with pustules



Palmoplantar pustulosis.



Acrodermatitis Continua of hallopeau (sama as Pustular Psoriasis but in the fingers) lead to anonychia.



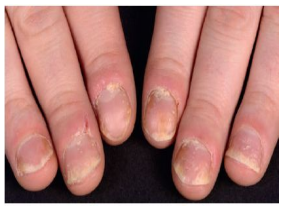
Psoriasis

3- Erythrodermic Psoriasis (EMERGENCY) (~1%). Confirm by skin biopsy

Involvement of >85-90% of body surface area with erythema>temp/electrolyte imbalance and risk of infection psoriasis is one of the pathologies that can develop into erythroderma

Nail: (more than ¾ of pt have nail involvement, ¼ of pt have joint involvement)

- Involved in 80% of patients (Thick and yellow nails).
- Patients with nail involvement appear to have an increased incidence of psoriatic arthritis.
  - **Pitting** (parakeratosis of the nail matrix).
  - **Oil-spot** (leukocytes beneath the nail plate).
  - **Onycholysis** (parakeratosis of the distal nail bed).



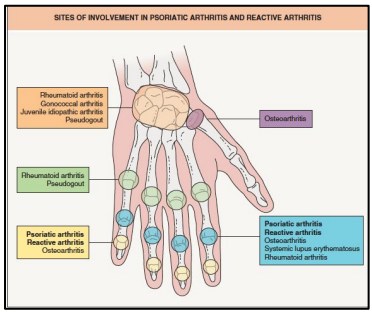
Pitting, Oil-spot, Onycholysis, Subungual hyperkeratosis and thickening of the nail

Oral mucosa: (not common in comparison to LP)

- Migratory annular erythematous lesions with hydrated white scale over the tongue **(geographic tongue)** observed mainly in pustular psoriasis patients.

Psoriatic Arthritis:

- 25% of patients
- Asymmetric distal mono-oligoarthritis (most common type) Inflammation of the DIP and PIP joints of the hands and feet (small joints). Involvement of both the DIP and PIP joints of a single digit can result in **"sausage" digit**.
- Least common presentations:
  - Rheumatoid arthritis-like:
    Symmetric polyarthritis that involves small and medium-sized joints.
  - Arthritis Mutilans (severe deformity in joints could cause shortening of digits).
  - Spondylitis and Sacroiliitis.

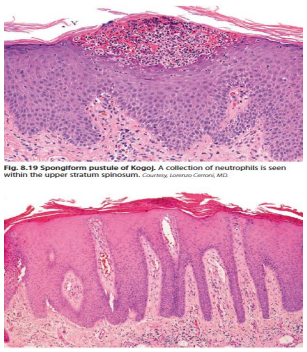


Associations: (psoriasis can increase risk of the following and vice versa)

- **Hyperlipidemia and metabolic syndrome.**
- **Diabetes Mellitus**
- **Atherosclerosis.**
- **Non-alcoholic steatohepatitis** we can't give methotrexate to Psoriatic arthritis patients because it might jeopardize the liver and cause further complications.
- **Depression and anxiety** that might lead to substance use.
- **Substance addiction.**
- **Parkinsonism.**

Pathology:

- Classically, Superficial perivascular lymphocytic infiltrate with even elongation of rete ridges ,dilated capillaries in papillary dermis which associated with spongiosis, acanthosis and parakeratosis.
- In late lesions (Secondary phenomenon, not always happening), accumulation of neutrophils within a spongiotic pustule "spongiform pustule of Kogoj" or sub-corneal accumulation of neutrophils "microabscess of Munro" (exaggerated in pustular psoriasis).



Superficial perivascular infiltrate (lymphocyte), Dilated vessels and Elongation

Psoriasis

Treatment:

1. **Focal disease:**
   a. Topical corticosteroids.
   b. VitD3 analogues (calcipotriene). **The top treatment is Combination of vit D3 + Topical Corticosteroids. (Duobrii is a medication that combines steroid with vit d3 analogous)**
   c. Coal tar.
   d. Anthralin.
   e. Tazarotene.
   f. 10% salicylic acid.
   g. We apply peeling agents to increase the absorption of corticosteroids

2. **Widespread disease:**
   Systemic steroids are contraindicated for treating psoriasis because of conversion (turns chronic plaque type into pustular). can be used in pustular psoriasis of pregnancy for safety (biologic therapy is safer).

Widespread Disease Treatment	
Chronic plaque type	Pustular type
MTX First line	Retinoids First line
Anti-TNF	Cyclosporine
NBUVB/PUVA	MTX
Anti-IL 12/23	NBUVB/PUVA
Anti-IL 17A	
Cyclosporine "consider renal toxicity"	
Retinoids (acitretin) Kept in fat tissue for years; avoid it in child bearing age due to its teratogenicity	In contrast to isotretinoin (hydrophilic)which is cleared in a month

Lichen planus

Introduction:

- Lichen Planus is an Complex immune-mediated polygenic skin disorder. Various environmental triggering factors, e.g. Stress, infections and medications may elicit the disease in genetically predisposed individuals.

Epidemiology:

- Types of Lichen planus : we can have 2 types at the same time
  - Cutaneous: it goes away usually after 4-5 years
  - Cutaneous Lichen planus affects **less than 1% of population** (Rare).
    - 75% of cutaneous Lichen planus have mucosal involvement specifically Oral.
  - Mucosal: Oral (Mucosal) Lichen planus (1-5%) more common and it's more resistant and chronic (Dentist encounter these patients more).
    - 25% of Oral Lichen planus have cutaneous Lichen planus.
  - Follicular.
- It usually affect **adult (30-60 years)** but it can rarely affect children.
- It doesn't have any gender/race predilection.
- Familial cases are underestimated (some about 10%).
- **Some experts consider them as separate disease.**

Causes:

- Idiopathic complex polygenic condition.

Lichen planus

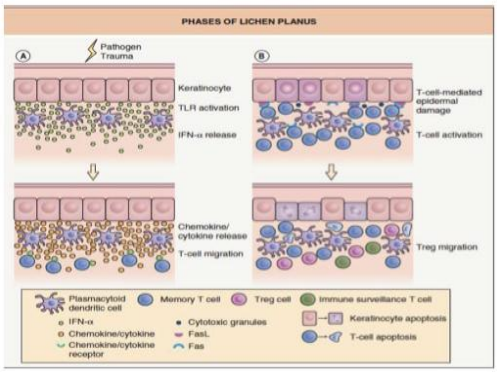
Genetic Predisposition: skipped by dr

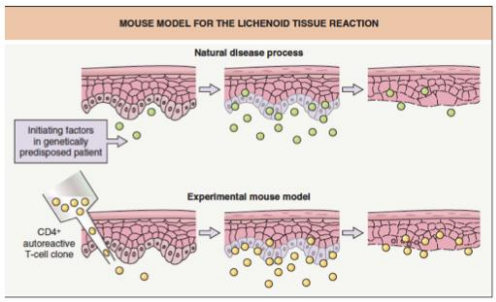
- Six single nucleotide polymorphisms (SNPs) were found to be associated the **HLA- DQB1**.
- 05:01 haplotype associated with Lichen planus.
- HLA-A5 ,HLA-A3,147,148, HLA-B7,143 HLA-DR1,149,150.
- HLA-DR10 in Arab population.
- **HLA-DRB1** 01:01 in Sardinien & Mexican population.

Antigenic Triggers:

- **Pathogens (Viral hepatitis-HCV)** (strongly associated mainly with cutaneous LP/order HCV panel).
- Geographic variation.
- **IFN therapy initiate or worsen LP.**
- Liver disease e.g. sclerosing cholangitis chronic liver disease.
- **Vaccination.**
- **Medication** (Lichenoid drug eruption e.g. antimalarials and IFNs).
- **Contact sensitizer** e.g. **mercury amalgam** حشوة الأسنان الزئبقية (it causes a lot of cases of LP, changing it to ceramic will improve the disease 50% will cure), color film developers, methacrylic acid esters, dimethyl fumarate in sofas and radiotherapy.

1- Superficial Perivascular infiltrate.
2- Sever inflammation cause thinning of epidermis (Sao tooth).
3- Retention of cells (immature).





An immune-mediated mechanism involving activated T cells (By the trigger), particularly CD8+ T cells (cytotoxic cells which will kill the keratinocytes), directed against basal keratinocytes has been proposed (In Psoriasis T helper CD4+ cell will be activated and it will cause inflammation). Upregulation of intercellular adhesion molecule-1 (ICAM-1) and cytokines associated with a Th1 immune response, such as interferon (IFN)-gamma, tumor necrosis factor (TNF)-alpha, interleukin (IL)-1 alpha, IL-6, and IL-8, may also play a role in the pathogenesis of lichen planus. The target in psoriasis and lichen planus is basal cells, the difference is what comes after. In psoriasis excessive cell division and differentiation, lichen planus the cells die and undergo macular degeneration.

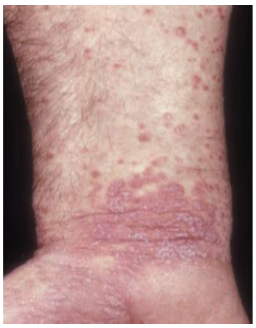
Clinical presentation: (5 Ps)

- Itchy (rubbing) not scratching **P**ruritic **P**olygonal **P**urple flat-topped (**plane**) **P**apule & **P**laques with **Wickham's striae** (Pathognomonic (wedge shaped hypergranulosis) it is a whitish lines visible in the papules of LP) over flexural surface of extremities ,wrist, legs, lower abdomen and genitalia.
- Pruritic well defined flat topped violaceous plaques and papules.

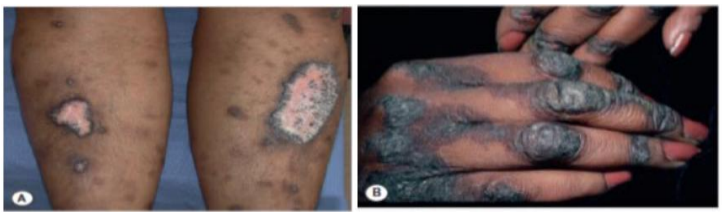
Variants: It's a littel advanced for you

By morphology	By configuration
Hypertrophic-leg	Annular-penis
Atrophic	Liner
Ulcerative-palm/soles	
Ballous	

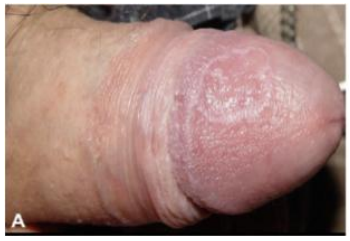
Lichen planus



Pruritic flat topped violaceous plaques and papules in the wrist.



Lichen planus pigmentosus (generalized) papules in the wrist and actinicus (sun exposed areas) Well defined slate gray patches sometimes with violaceous rim or hypopigmented halo, but it's not in the picture.

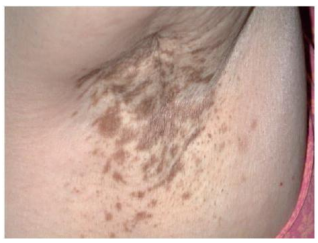


Annular Lichen planus of penis (never progress).
More common gentalia involvement in comparison to Psoriasis.

Types of LP: (by Presentation)

1- Lichen planus Pigmentosus:

- Not the same clinical features. Pigmentation is the prominent feature
- It is more common in dark skin people and it presents as **well- defined brown to slate-gray patches** with/without **violaceous** indurated border or hypopigmented halo over **axilla/groin** & proximal limbs (may come on the face).



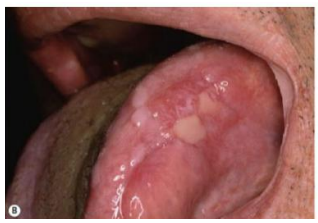
Pigmentosus (no rim neither halo).

2- Lichen planus actinicus: same as #1, but when it only affect the sun exposed area

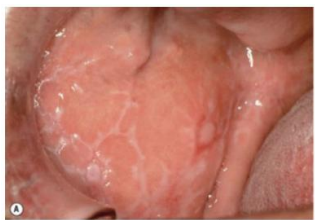
- Sun exposed area (same disease and presentation as Lichen planus Pigmentosus but named according to site of involvement).

3- Mucosal Lichen planus: more common variant

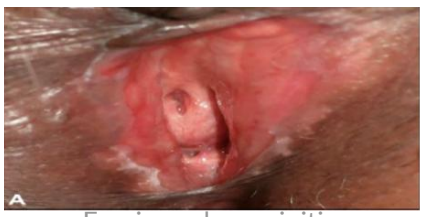
- The most common site of involvement is the oral mucosa which usually present as **well-defined reticulated violaceous plaques over buccal mucosa, lips and gingiva** (oral involvement is rare).
- **Varintes:**
  - **Reticulated.**
  - **Erosive (less than 1% risk of SCC)** If there is an oral ulcer you should take biopsy. This risk increased by smoking
  - **Atrophic.**
  - **Hypertrophic.**
- very itchy (genitalia+anal area) It can affect other mucosal surfaces e.g. vulvar, vaginal and penile- Vulvovaginogingival syndrome sever erosive.



reticulated



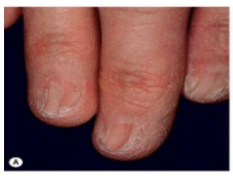
erosive

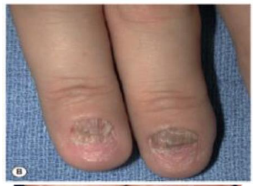


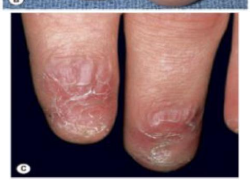
Erosive vulvovaginitis.

4- Nail Lichen planus: (Cutaneous)

- Nail involvement usually occur in 20% and it is more common in children
  - **Dorsal Pterygium** (Very specific to LP, but not pathognomonic) it happened when hyponychium attached to the Proximal nail fold.
  - **Lateral thinning.**
  - **Longitudinal ridging.**
  - **Distal splitting.**
  - Thinning of the nail.
  - 20 Nail Dystrophy when all 20 nails are destroyed. Can be caused by other diseases.





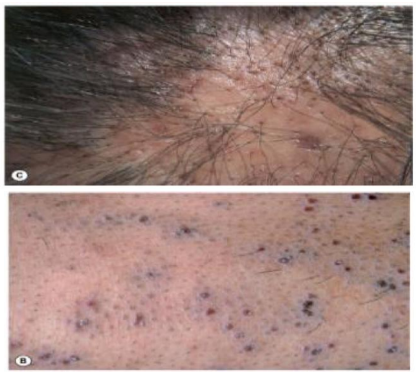


Lichen planus

Types of LP (cont'):

5- Lichen Planopilaris-LPP: (Follicular, scarring alopecia)

- It usually present as multiple, keratotic plugs surrounded by a narrow ill defined violaceous rim are observed primarily on the scalp around follicles, although other hair bearing areas can also be affected.
- The inflammatory process usually result in scarring alopecia when it doesn't cause scarring it's called lichen spinulosus.



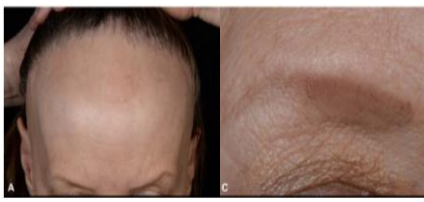
Lichen planopilaris Perifollicular
(Later causes scarring)

6- Graham-little-piccardi-lassueur syndrome:

- **Is a Triad of:**
  a. Non-scarring alopecia of pubic and axillary hairs and disseminated spinous or acuminated follicular papules.
  b. Typical cutaneous or mucosal LP.
  c. Scarring alopecia of the scalp.

7- Frontal fibrosing alopecia: (it was called Postmenposal frontal fibrosing alopecia)

- It usually affect **postmenopausal** female. >50 yo
- **It presents as frontal hairline scarring alopecia with eyebrows thinning.**



Frontal fibrosing alopecia
2ed Pic: Thinning of eyebrows

8- Lichenoid drug eruption:

- It is a drug eruption that resemble Lichen planus with the **following clinical differences:** imp
  - **Morphology:** more psoriasiform/eczematous.
  - **Distribution:** start as photo-distributed then generalized.
  - **Usually no mucosal** involvement and **Wickham's striae.**
- It can appear anytime between weeks and years after exposure (commonly diuretics cause it).

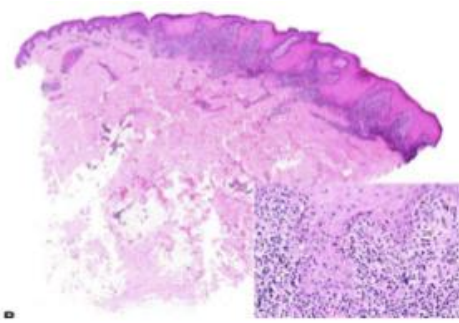
Pathology:

- **Classic Lichen planus pathology:**

  Superficial lymphocytic infiltrate with **vacuolar interface reaction at the DEJ with dyskeratotic keratinocyte** (Civatte bodies) & colloid bodies which is associated with **"wedge-shaped" hypergranulosis** (Wickham's striae) **and "saw- tooth" rete ridges.**

  There's parakeratosis like psoriasis but (absence of microabscess and collection of neutrophils within epidermis)

  If shaggy band of fibrogen along with DEJ and colloid bodies staining with immunoglobulins at the papillary dermis



- **Lichenoid drug eruption:** The infiltrate is more deep with **eosinophils**/plasma cell with the presence of **parakeratosis** (which is Not in LP).

Lichen planus course:

- It follow a relatively **short course with relapse/remit nature rarely chronic** that self-limit usually within 1-2 years except for oral and follicular LP which tend to be more chronic Leave very bad pigmentation.

Lichen planus

Treatment:

- **Focal:**
  - topical corticosteroids.
  - Intralesional corticosteroids -LPP.
- **Generalized**:
  - Systemic therapy:
    - Systemic Corticosteroids The first line of therapy for generalized.
    - Steroid sparing agents:
      - Systemic Retinoids e.g. **Acitretin** (avoid in female childbearing age)
      - Anti Malaria- Hydroxychloroquine- LPP.
      - Immunosuppressive therapy- MTX, Cyclosporine.
  - Phototherapy: not commonly used
    - NBUVB/PUVA

Pityriasis Rosea النخالة الوردية

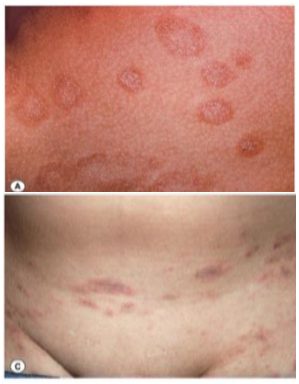
Epidemiology :

- Pityriasis Rosea is a **common acute self-limiting** (Viral) **exanthematous** eruption that usually affect adolescent (10-30 years) (Presented usually with prodrome). (Ones in your life)
- It doesn't have any gender/race predilection.
- Although, PR can be seen all year around, it is more frequent in winter, fall and spring.

Etiology :

- The etiology of PR is unknown but most experts believe that the **reactivation of HHV 6/7** play a significant role in the pathogenesis of the disease.

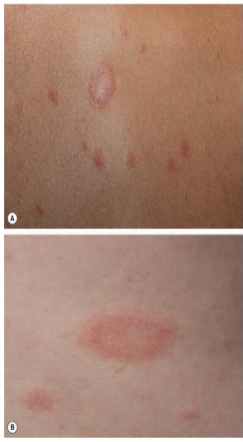
Typical pityriasis rosea: (Common)



Oval pinkish collarette scales pointing inwards.

- Single **well-defined oval** (4cm) **pink-erythematous patch** (or thin plaque) **with collarette scale** over the **trunk**/proximal limbs **(Herald patch** 50%). **(mother lesion) /common clinically diagnosed**
- followed **after average of 2 weeks** with similar **daughter lesions** on the **trunk**/proximal limbs satellite linear papules called **(christmas tree)** with whole illness ranging between **6-12 weeks**.
- The Scale in Psoriasis is **thick** whereas in PR is **thin**.
- 75% complain of pruritus.
- 75% complain of viral prodrome.
- 10% oral lesions: erosion/ulcer (most common), purpura and erythematous patch.

Atypical Pityriasis rosea: (50% present with this type)



- Herald Patch: mother patch
  - No HP.
  - Multiple HP.
  - **When we don't see clear herald patch we have to rule out secondary syphilis**
- Morphology
  - **papular** common in dark skin people and children **vesicular**.
  - Some PR have purpura or Targetoid lesion.
- Distribution
  - PR **Inversa "within skin folds"**affect axilla, groin and distal extremities sparing trunk

Pityriasis rosea النخالة الوردية

Course and duration:

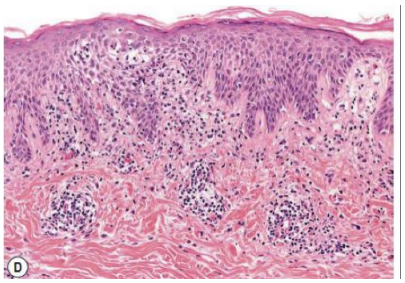
- **Persistent PR:** duration longer that 12 weeks and usually up to 6 months with aggressive course and presentation.
- **Relapsing PR: more than estimated (~5%) but carry a mild and shorter course with few attacks over 3-5 years duration (usually due to the time the immune system take to gain full control over HHV 6/7)**
- **Shall we look for HHV 6/7? we don't why would we? 1- it's not always there 2- it's a clinical diagnosis if in doubt do a biopsy to rule out other diseases.**

PR & Pregnancy: SKIPPED BY DR

- Since pregnancy is a state of altered immune response, a risk of viral reactivations and intrauterine transmission of HHV-6/7 exists.
- On the whole, the total abortion rate among women with pregnancy PR is the same as that of the general population but noteworthy, when PR develops within the 15th gestational week, the abortion rate is higher probably because the risk of intrauterine transmission of HHV-6 (or less commonly HHV-7) is increased. Doesnt affect the course of the pregnancy

Histopathology:

- **focal parakeratosis** (it's focal so that's why we have scalcing only on the edges, not like psoriasis where we have homogenous), spongiosis and acanthosis of the epidermis with superficial perivascular lymphohistiocytic infiltrate accompanied by some extravasated RBC.



PR-like eruption: SKIPPED BY DR

- An eruption that resemble PR with the following differences:
  - **lacking herald patch and viral prodrome.**
  - Papular morphology.
  - Acrofacial distribution.
  - Histology: Superficial perivascular lymphocytic infiltrate with eosinophil and vacuolar interface reaction and necrotic keratinocytes within the epidermis.
  - **HHV6/7 serology negative.**

Triggers:

- **Gold can lead to psoriasis**
- **Medications:**
  - Barbiturates, methopromazine, captopril, clonidine, **gold**, metronidazole, **D–penicillamine,** isotretinoin, levamisole, Pyribenzamine, NSAID, omeprazole, **terbinafine**, ergotamine tartrate, tyrosine kinase inhibitors & **Adalimumab**.
- **Vaccination:**
  - diphtheria, smallpox, pneumococcal, hepatitis B virus, BCG and HPV.

Treatment of PR:

- Symptomatic with **topical corticosteroids** and antihistamine (if there is Pruritus).
- Antiviral treatment (Acycolvir 800mg 5 times for 10 days) indicated in the following settings: (rarely used)
  - **Persistent PR.**
  - **Relapsing PR.**
  - Severe PR at the first trimester of pregnancy.

Dermatological Emergencies

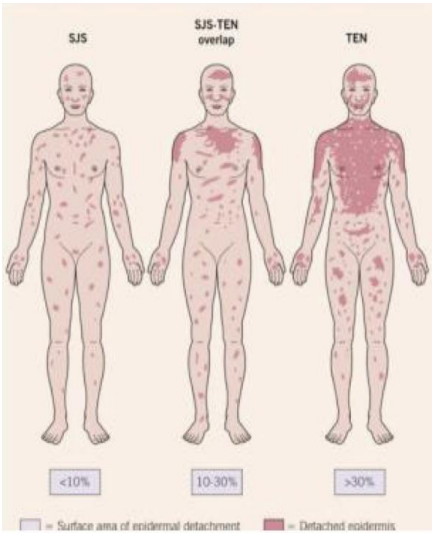
SJS/TEN | **Erythroderma** | **Purpura** | **Bullous disease** | **Urticaria/angioedema/anaphylaxis**

Alarming morphological patterns

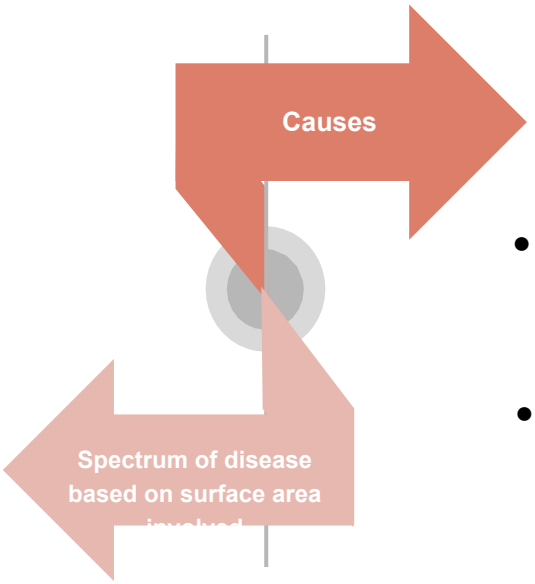
1. **Urticaria/Angioedema**
2. **Purpura/Ecchymosis**
3. **Bullae/Sloughing**
4. **Necrosis/Gangrene**
5. **Exfoliative Erythroderma syndrome**
6. **Generalized/Widespread in the acutely ill febrile patient**

Steven Johnson Syndrome (SJS) & Toxic Epidermal Necrolysis (TEN)

- Rare, acute, life-threatening **mucocutaneous** disease.
- Nearly always drug-related.
- Keratinocyte death lead to separation of skin at the dermal epidermal junction.
- **Characteristic symptoms: High fever, skin pain, anxiety and asthenia** (which is abnormal physical weakness or lack of energy).
- It is crucial to diagnose it early so the causal drug can be **discontinued.**
- SJS and its variant, TEN, involve the skin as well as mucus membranes.
- **Mortality:**
  - 5% for patients with SJS.
  - **25%-50% for patients with TEN.**



SJS and TEN are variants of an identical pathologic disease and differ only in the percentage of body surface involved.



1. Medications

- More than 100 drugs have been identified to date as being associated with SJS/TEN! (we have to be updated).
- **Most common:**
  - Allopurinol
  - Antibiotics: (Trim-sulfa, Sulfonamides)
  - NSAIDs
  - Anticonvulsants.

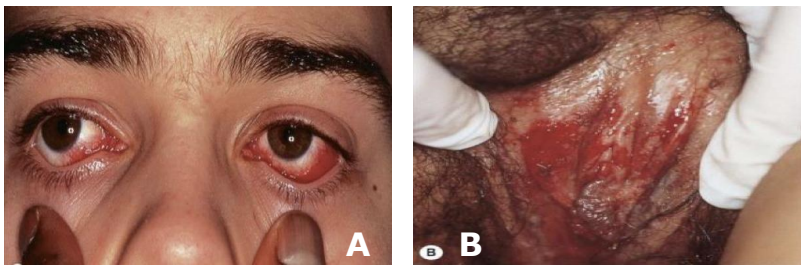
2. Infections and Immunizations (rare):

(Covid-19 vaccine-induced SJS TEN).

SJS/TEN

Clinical features of SJS/TEN

- Initially: Fever, Stinging eyes, and pain upon swallowing.
- These symptoms precede cutaneous manifestations by 1 to 3 days (you have to catch it early on).
- Skin lesions first appear on the trunk, spreading to the neck, face and proximal upper extremities.
- Distal arms and legs are relatively spared (but not the palms/soles).
- Erythema/erosions of the buccal, ocular and genital mucosa are present in more than 90% of patients (if this is absent it is unlikely to be SJS).
- TEN involvement of epithelium of the respiratory and G.I tract can also occur.
- Skin lesions are usually tender & mucosal erosions are very painful.



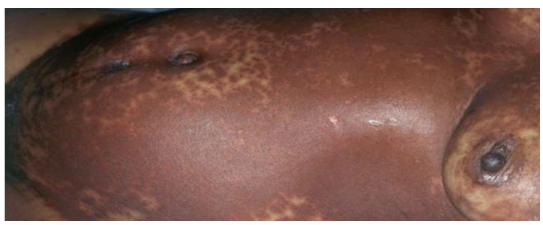
- Mucosal involvement in Stevens Johnson syndrome.

A) Erythema and conjunctival erosions.

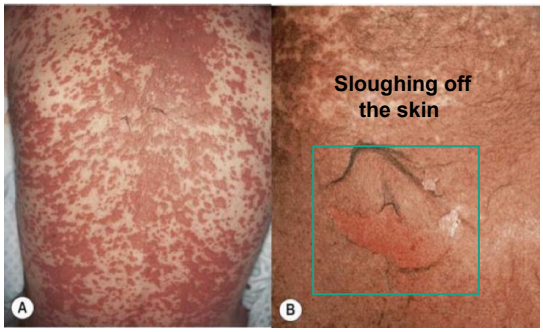
B) Erosions of the genital mucosa.

Morphology of skin lesions in SJS/TEN

- First: **erythematous, dusky red** or purpuric macules of irregular size and shape, they have a tendency to coalesce. Coalesce is when multiple single lesions combine to form one big lesion.
- **+ve Nikolsky sign** (It is dislodgement of intact superficial epidermis by a shearing force, indicating a plane of cleavage in the skin at the dermal-epidermal junction).
- Some lesions have a dusky center (**Target-like** appearance).
- Later: Full-thickness necrosis can develop (can be very rapid).
- The necrotic epidermis detaches from the dermis, fluid fills the space, **giving rise to blisters** (**flaccid** blisters) you can see erosions as these blisters break easily.
- **The blisters can be extended sideways by slight pressure of the thumb (Asboe-Hansen sign).**
- The skin resembles wet cigarette paper.



Cutaneous features of toxic epidermal necrolysis (TEN). Characteristic **dusky red color** of the early macular eruption in TEN.
Lesions with this color often progress to full-blown necrolytic lesions with dermal–epidermal detachment. (sloughing of skin)

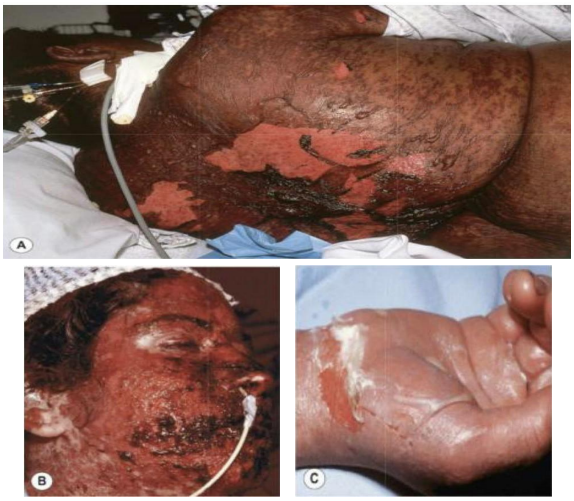


Stevens–Johnson syndrome (SJS) versus SJS–TEN overlap.

A) In addition to mucosal involvement and numerous dusky lesions with flaccid bullae, there are areas of coalescence and multiple sites of epidermal detachment. Because the latter involved >10% body surface area, the patient was classified as having SJS–TEN overlap.

B) Close-up of epidermal detachment, whose appearance has been likened to wet cigarette paper.

SJS/TEN



Later on changes.
Clinical features of toxic epidermal necrolysis (TEN)

A) Detachment of large sheets of necrolytic epidermis (>30% body surface area), leading to extensive areas of denuded skin. A few intact bullae are still present.
B) Hemorrhagic crusts with mucosal involvement.
C) Epidermal detachment of palmar skin.

SCORTEN A prognostic scoring system for patients with TEN

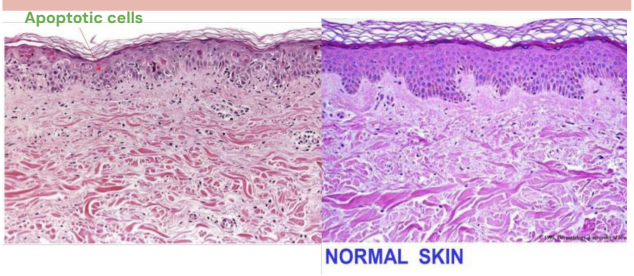
- Age > 40 years.
- HR > 120 bpm.
- Cancer or hematologic malignancy.
- BSA involved on day 1 above 10%.
- Serum urea level > 10 mmol/l.
- Serum bicarbonate level < 20 mmol/.l
- Serum glucose level > 14 mmol/l.

Mortality rate	
0-1	3.2%
2	12.1%
3	35.8%
4	58.3%
5 or more	90%

Toxic Epidermal Necrolysis (TEN)

- **Death occurs in 1/3 of pts with TEN (mainly due to infections).**
- Best managed in the **ICU/Burn unit.**
- Eliminating the culprit medication is the most important **first step.**
- SJS/TEN usually occurs **7-21 days** after the initiation of the drug (first exposure) and **within 2 days in the case of re-exposure** to a drug that previously caused SJS or TEN
- We transfer the patients to a burn unit.
- Know the duration to exclude medications outside that period.

Histology

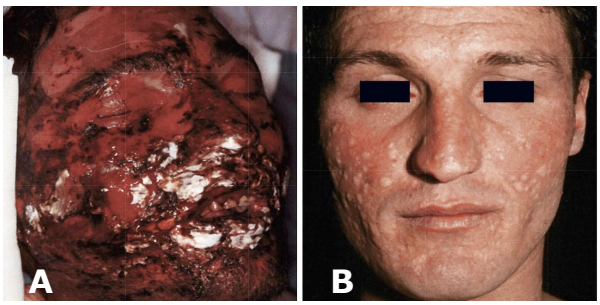


Toxic epidermal necrolysis – histopathologic features. Apoptotic keratinocytes are present individually and in clusters within the epidermis. Subtle vacuolar changes along the basal layer are accompanied by minimal inflammation, with scattered lymphocytes within the epidermis.

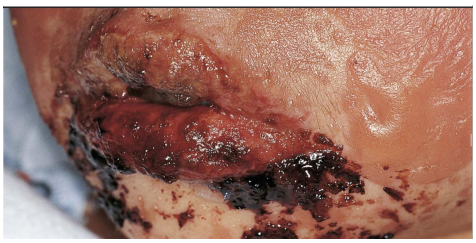
Treatment

- Supportive care in a burn unit: wound care, hydration, nutritional support..etc
- Regular examination by an ophthalmologist (for eye manifestations) it can cause **blindness** if left untreated.
- To date, no specific therapy has shown efficacy in prospective, controlled clinical trials.
- Cyclosporine
- Cyclophosphamide
- Systemic steroids
- IVIG (Good evidence on

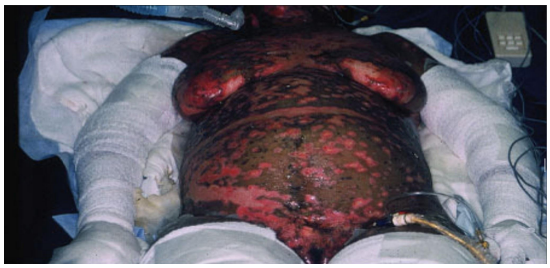
SJS/TEN & Erythroderma

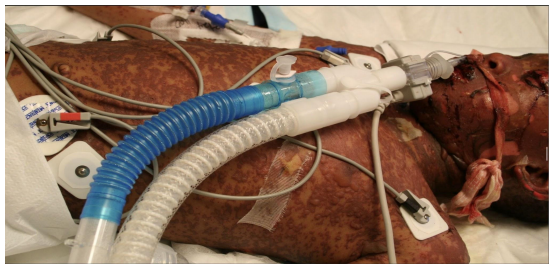


- Treatment of toxic epidermal necrolysis (TEN).
- Facial involvement of a patient with TEN (50% body surface area involvement) before (A) and 3 weeks after (B) treatment with IVIG(0.75 g/kg/day for 4 days).
- This a picture of a patient treated with IVIG.



- Childhood Stevens–Johnson syndrome secondary to **trimethoprim–sulfamethoxazole** therapy.
- Note the hemorrhagic crusts and denudation of the lips as well as bullous cutaneous lesions.





❖ Erythroderma

- Erythroderma is not a diagnosis. It's a clinical presentation
- **Generalized redness and scaling of >90% of the skin surface**.
- Considered a serious, at times life-threatening condition.
- It does not represent a disease but rather a clinical presentation of a variety of Diseases.
- **M > F (average age is ~50 yrs).**

Causes Of Erythroderma :

1) **Pre-existing dermatosis (psoriasis, eczema) 50% Most common.**
2) Undetermined 25%.
3) Drugs 15%.
4) Lymphoma, leukemia 10%.

Causes in adults VS **Causes in children**

- **Idiopathic.**
- **Atopic Dermatitis.**
- **Psoriasis.**
- **Drug reaction.**
- **Cutaneous T cell lymphoma (CTCL).**
- **Pityriasis rubra pilaris (PRP).**

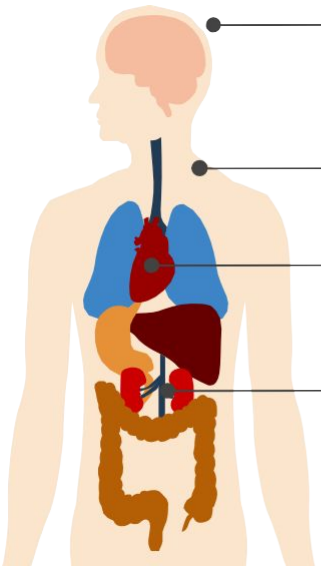
- Ichthyoses
- Immunodeficiencies , infections
- Dermatitis, Psoriasis.

Erythroderma

Clinical features of erythroderma

- Erythema precedes exfoliation by 2-6 days.
- Pruritis in 90% of patients.
- Palmoplantar keratoderma. (Thickness and redness of palms and soles)
- Nail changes in 40%.
- Diffuse non-scarring alopecia.

Systemic manifestations:

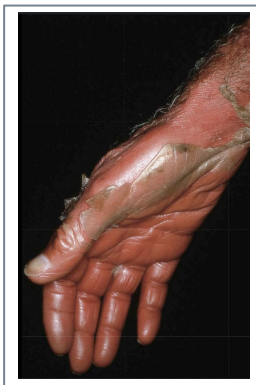


Thermoregulatory disturbances (hyper- hypothermia)

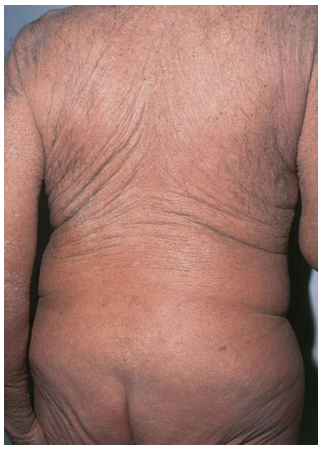
Generalized peripheral lymphadenopathy (50%)

Tachycardia, risk of t of high output cardiac failure (esp. in the elderly)

Pedal or pretibial edema in ~50% of patients



- Erythroderma with desquamation.
- Obvious exfoliation of scale with underlying erythema.

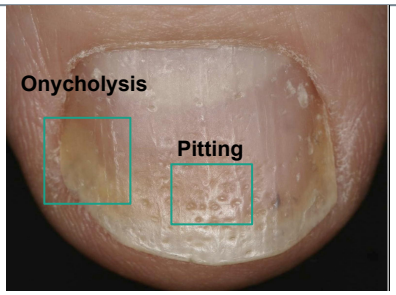


- Redness all over not normal skin.
- Idiopathic erythroderma.
- This is the type of patient that requires longitudinal evaluation to exclude the development of cutaneous T-cell lymphoma.

Manifestations based on causative disease

1) Psoriasis:
   - **Nail changes** (Oil-drop, onycholysis, nail pits).
2) Atopic dermatitis:
   - **Pruritus is intense**.
   - Lichenification (Lichenification is a skin condition that occurs in response to excessive itching or rubbing of the skin and results in thick, leathery patches of skin).
3) Drug reactions:
   - Morbilliform or scarlatiniform exanthem (The term morbilliform refers to a rash that looks like measles. The rash consists of macular lesions that are red and usually 2–10 mm in diameter but may be confluent in places).
4) Idiopathic erythroderma:
   - Elderly men.
   - Lymphadenopathy and extensive palmoplantar keratoderma.
   - Peripheral edema.

Erythroderma

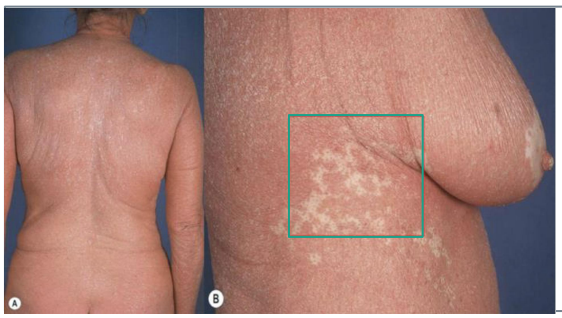


- Psoriatic erythroderma.
- Nail findings (pitting and onycholysis with a proximal rim of inflammation) point to the diagnosis of psoriasis.

Manifestations based on causative disease (cont'd):

5) CTCL (cutaneous T-cell lymphoma) : CTCL (More Benign), Sezary syndrome (malignant)
- Sezary syndrome: Erythroderma, Malignant T lymphocytes and generalized lymphadenopathy.
  If you see CTCL and Erythroderma think about Sezary syndrome.
- **Painful fissured keratoderma, diffuse alopecia, leonine facies.**

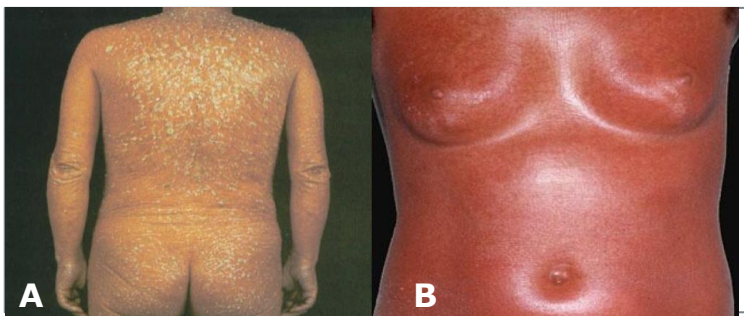
5) PRP (Pityriasis rubra pilaris) :
- **Salmon to orange color.**
- Follicular keratotic papules on the knees, elbows and dorsal fingers.
- Islands of sparing.



- Erythroderma secondary to pityriasis rubra pilaris.
- A few **islands of sparing** are noted on the upper back **(A)**, but are more noticeable on the flank and breast **(B)**. **Note the salmon color.(orange-like)**

Treatment

- Hospitalization may be required.
- Regardless of cause: Nutritional assessment, correction of fluid and electrolyte imbalance, prevention of hypothermia and tx of secondary infections.
- Idiopathic: Topical and systemic corticosteroids. Anti-histamines.
- **Treat the cause of erythroderma.**



- **(A)** A patient with Psoriasis.
- **(B)** 100% Erythroderma involvement of the skin.

Cutaneous Manifestations Of Systemic Diseases

- Skin is the gate of the body, you have to diagnose it early to prevent complications.
- Detection of Systemic disease or internal maligna through skin presentation.
- Systemic diseases associated with skin diseases.
- **the lecture contents will be classified into:**

- Connective Tissue Disease:
- Lupus
- Dermatomyositis
- Scleroderma

- GIT:
- Chronic Liver Disease (CLD)
- Acrodermatitis entropathica
- Peutz Jeghers Syndrome
- Pyoderma Gangrenosum

- Neurocutaneous diseases:
- Neurofibromatosis
- Tuberous Sclerosis

- Nutritional deficiency disorders:
- Scurvy
- Pellagra

- Cutaneous manifestations of internal malignancy.
- Acanthosis Nigricans
- Dermatomyositis

- Metabolic:
- Hyperlipidemia

- Endocrinological Diseases:
- Diabetes Mellitus
- Hyperthyrodism
- Hypothyeodism
- Cushing's Syndrome
- Addison's disease

- Behcet's Syndrome

- Causes of Generalized pruritus without skin lesions

- Nails:
- Clubbing
- Koilonychia
- Splinter haemorrhages

When to do HIV testing for skin Disease ?

Dr note: To describe any skin lesions you should mention:
1- If it is single / few / multiple / numerous.
2- Well / ill defined (if you can hold your pin and drow around it).
3- Configuration (e.g. Annular).
4- Color: erythematous / brown / blue
5- Hypo / Hyper / de (pigmented).
6- Secondary lesion if present.
7- Primary lesion.
8- Site of predilection.

Cutaneous Manifestations Of Systemic Diseases

Connective Tissue Diseases

Lupus

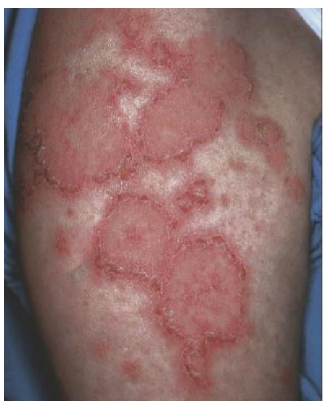
- **SLE:**
  - Facial photosensitivity.
  - Butterfly erythema (malar rash).
  - Multisystem disease (Renal, CNS, Cardiac, Blood, etc ...).
  - Positive ANA and Anti-dsDNA tests.
  - Oral and nasopharyngeal ulcers.
  - Scarring Alopecia.

- **Discoid Lupus (DLE):**
  - Round scarring lesions on light exposed areas.
  - No Systemic involvement.

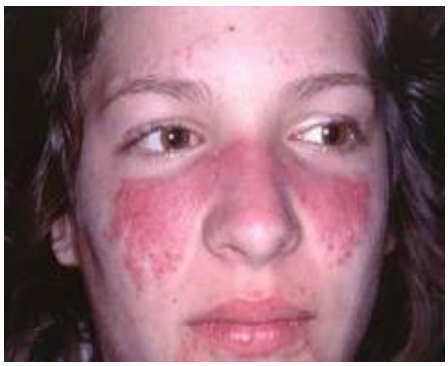
- **Subacute Cutaneous Lupus (SCLE):**
  - Papulosquamous or annular presentation.
  - Photosensitivity.
  - Does not cause scarring.
  - Usually **ANA negative but anti Ro positive.**

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

- **Drug-induced Lupus:**
  - **Procainamide and Hydralazine.**
  - Anti Histone positive.



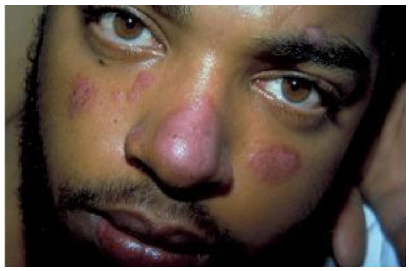
Multiple well defined Polycyclic or annular erythematous plaques with scaly border and some central clearing **(SCLE)**.



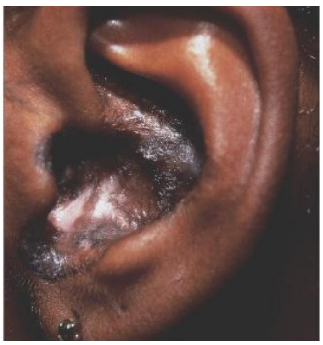
Well defined Erythematous patches and plaques over the cheeks (malar eminence) and over the nose sparing nasolabial fold.

Cutaneous Manifestations Of Systemic Diseases

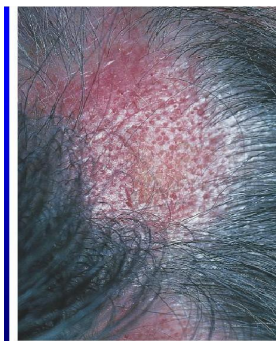
Lupus (cont'):



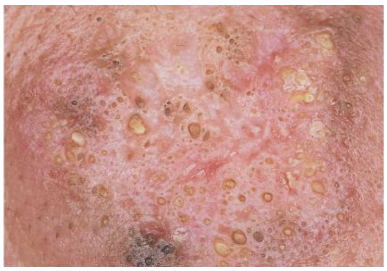
Few well defined erythematous to violesious discoid (Round not annular) plaques with loss of hair over the eyebrows **(DLE).**



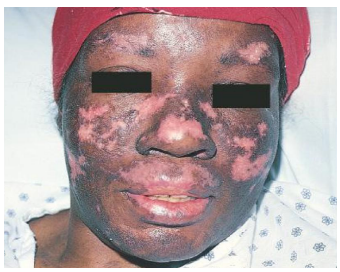
Discoid lesion with hyper & hypopigmentation.



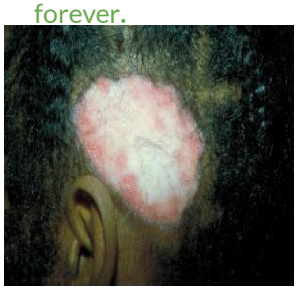
Follicular bulging (keratotic plugging), indicate early **(DLE),** so if you don't the patients earlier they well get scar and they will lose their hair maybe forever.



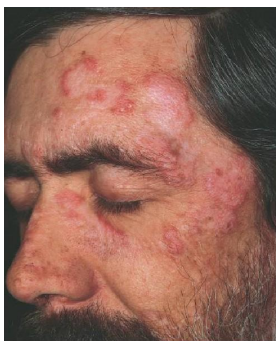
Extensive Follicular bulging.



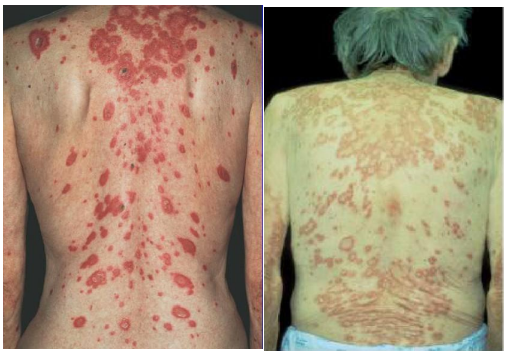
Dyspigmentation (hypo & hyper) with scaring, loss of vermilion border of the lip, also scarring alopecia on the eyebrow **(Aggressive DLE).**



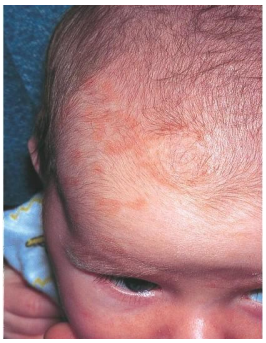
Big scarring alopecia with depigmentation and erythema .



Multiple polycyclic and annular scaly plaques **(SCLE).**



Psoriasiform annular scaly red lesions **(SCLE).**

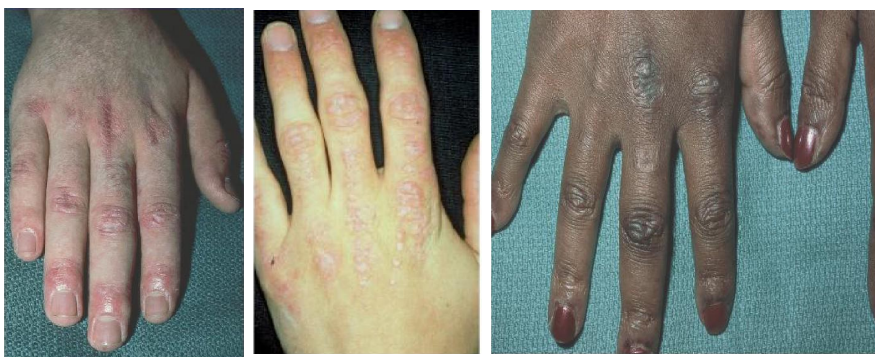


Annular lesions **(Neonatal lupus)**
Risk of heart block, so we have to check by ECG

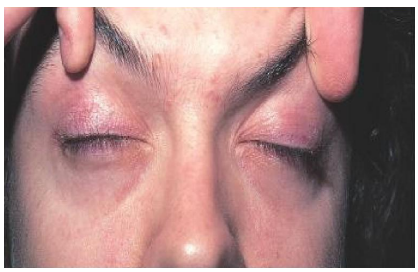
Connective Tissue Diseases (cont')

Dermato -myositis (Skin Rash + Muscle Weakness)

- **Heliotrope:** Violaceous color over the upper eyelids. .
- **Gottron's papules:** Flat- topped violaceous papules over knuckles of hands.
- Calcifications especially in kids.
- **Bilateral proximal muscle weakness** (with high CPK, positive EMG and muscle biopsy).
- In adults (especially over 50 years) associated with internal malignancy e.g. GI, Prostate, Ovary & breast. (A female above 50 newly diagnosed with dermatomyositis, you must rule out ovarian cancer first, then other types of cancer).



Violicious Gottron's papules



Heliotrope rashes

Cutaneous Manifestations Of Systemic Diseases

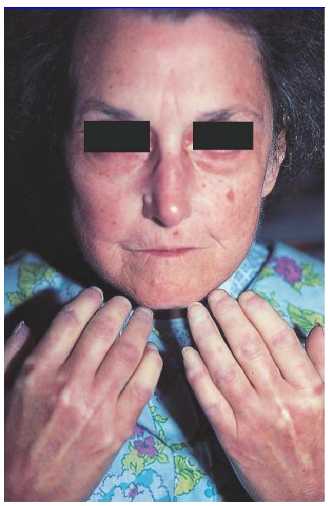
Connective Tissue Diseases (cont')

Scleroderma (systemic sclerosis)

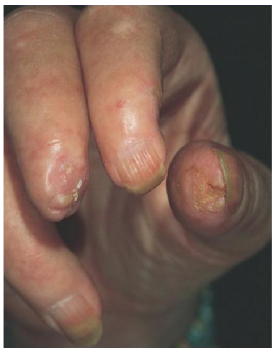
- **Scleroderma (Systemic sclerosis):**
  - Tight and thickened skin. Due to excessive collagen deposition
  - Sclerodactyly: fibrotic thickening and tightening of the skin of the fingers and hands
  - Face: Loss of forehead lines, beaked nose, small mouth, radial furrowing around the mouth.
  - Telangiectasia and calcification.
  - In diffuse type there is more systemic involvement (Lung, GI, Kidneys) and positive anti scl-70.

Other types of scleroderma include:

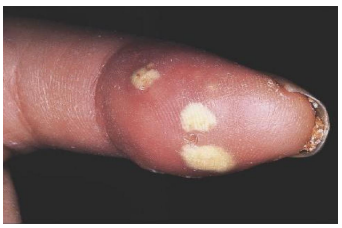
- **CREST:**
  - A milder type of scleroderma, **C** = **C**alcification, **R** = **R**aynaud's phenomenon, **E** = **E**sophageal dysfunction, **S** = **S**clerodactyly, **T** = **T**elangiectasia.
  - **Positive anti-centromere** with less systemic involvement.
- **Morphea:**
  - A localized scleroderma without systemic involvement, there is a firm, white patch of skin surrounded by violaceous ring.
- **En coup de sabre** (ضربة بالسيف) **:**
  - Linear scleroderma on the scalp and face which may give scarring alopecia and it may affect muscles or even bones.



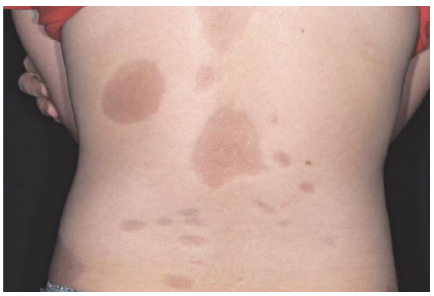
Minimal forehead wrinkle, very thick tight skin, peaked nose, small mouth, Sclerodactyly, Raynaud Phenomenon.



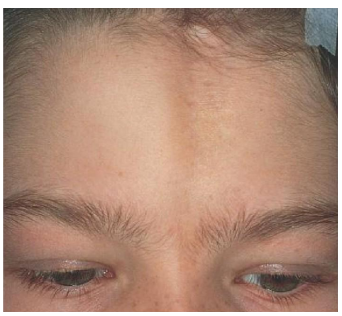
Sclerodactyly with infarction and loss of the tips of fingers.



Calcinosis cutis



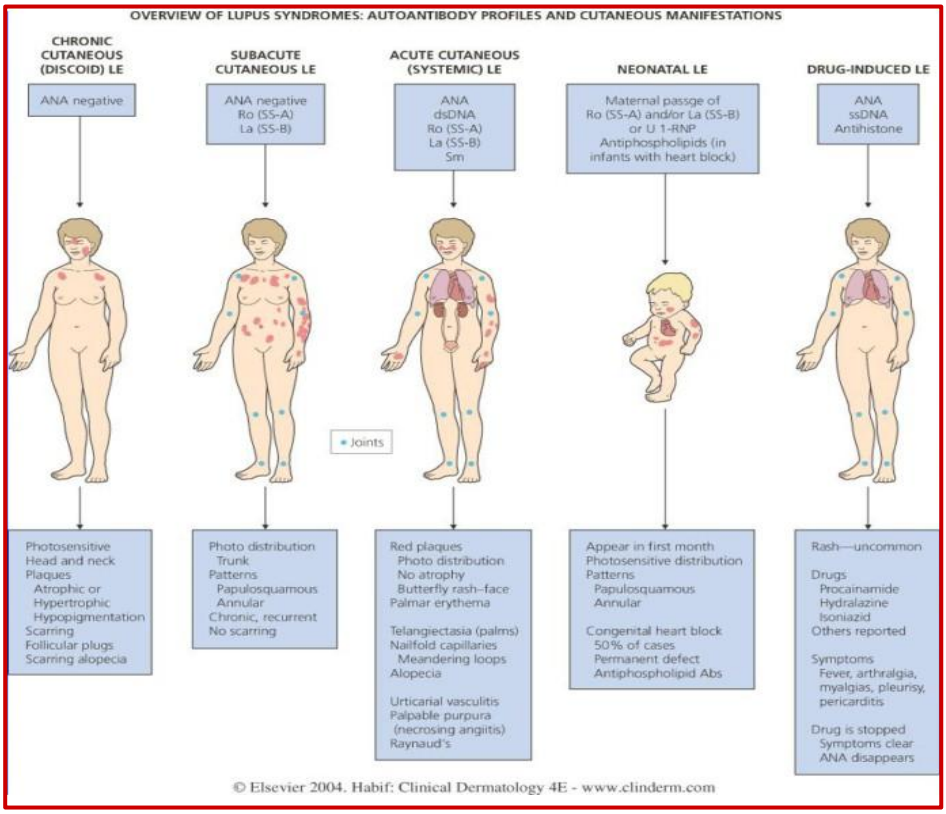
Well defined hyperpigmented atrophic plaque **(morphea).**



Deep morphea **(En coup de sabre).**

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
Anti-Ro	Neonatal lupus, SCLE
Scl-70 Antibody	For Scleroderma
Anti dsDNA	For SLE

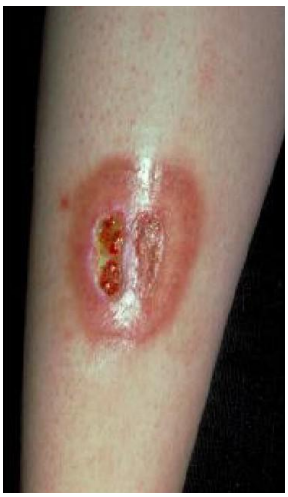
Cutaneous Manifestations Of Systemic Diseases

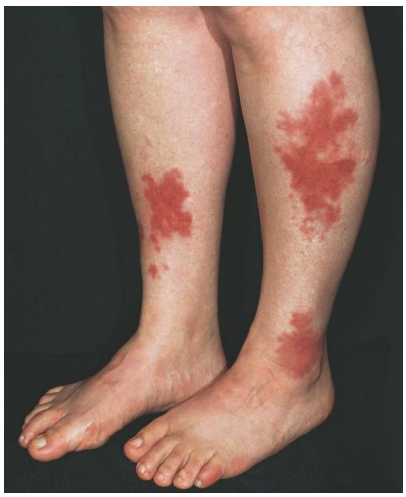


Endocrine system

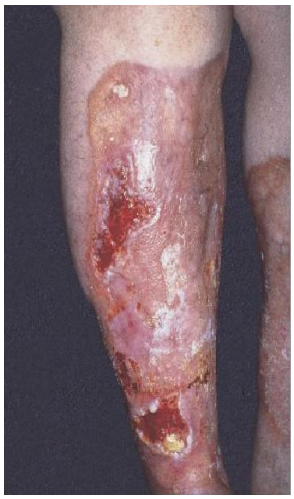
Diabetes mellitus

- **Necrobiosis lipoidica diabeticorum (NLD):**
  - Asymptomatic, usually seen on the shins. may progress to atrophy or ulcers)
  - May predate frank development of diabetes by several years (or with the onset DM).
  - **Shiny atrophic red or yellowish plaques with telangiectasia over their surface + ulceration.**
  - Severity of NLD is not directly related to severity of diabetes.
  - Increased risk of fungal and bacterial infection
  - Histopathology: shows tiered granulomatous Reaction.





Painless erythematous **orange** color plaques with **atrophy +** Telangiectasia and it will end up with ulceration.



Advanced NLD.

Cutaneous Manifestations Of Systemic Diseases

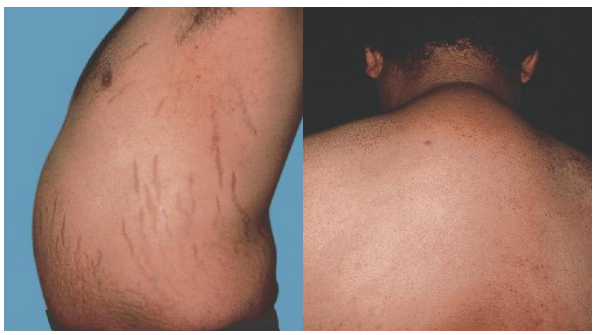
Endocrine system

Thyroid disorders

- **Hyperthyroidism:**
  - Smooth, warm, moist (due to increase sweating) skin and pruritus.
  - Pretibial myxedema (asymptomatic red plaques over shins).
  - Thin & fine hair.
  - Onycholysis (Brittle nails).
  - Clubbing.
  - Hyperpigmentation or vitiligo
- **Hypothyroidism:**
  - Dry and cold skin and pruritus.
  - Edematous skin (myxedema).
  - Hair loss of lateral third of eyebrows.
  - Brittle hair or nails.
  - A yellowish hue to the skin due to carotenaemia.
  - Delayed wound healing.

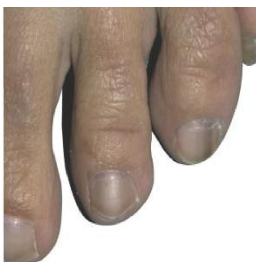
Cushing's Syndrome

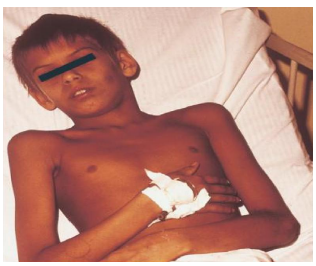
- Rounded face with fullness of cheeks (Moon face).
- Buffalo hump (fat deposit over upper back).
- Central obesity with thin arms & legs "lemon with sticks".
- Atrophy of skin & Striae.
- Purpura.
- Hirsutism & Acne.
- Clitoromegaly and male pattern alopecia (Hamilton pattern).



Addison's disease

- **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
- Patients usually present with lethargy, postural hypotension, and hyperpigmentation





GIT

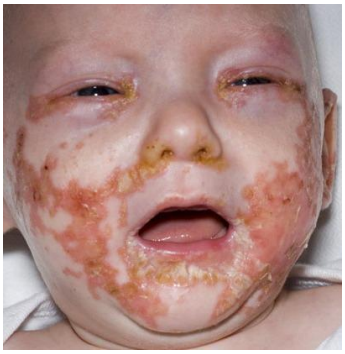
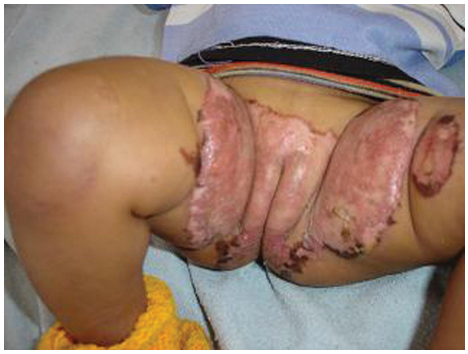
Chronic Liver Disease

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

Acrodermatitis enteropathica (Genetic disease)

- Due to **zinc** deficiency (a rare autosomal recessive disorder that impairs dietary zinc absorption in the jejunum and ileum).
- Seen in infants as inflammatory erythematous erosive scaly rash (patches and plaques similar to atopic dermatitis, but progress to vesicles, crusts, erosions, and pustules) around orifices (mouth, ears, anus) also on hands & feet.
- Alopecia and nail dystrophy.
- **Diarrhea** or abdominal pain.
- Treated with lifelong zinc supplementation (Pt will improve after 2,3 days

Cutaneous Manifestations Of Systemic Diseases

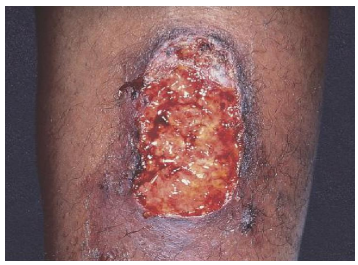



Multiple well defined crusted honey color erosions around the mouth and groins and it will be treated with zinc supplements.

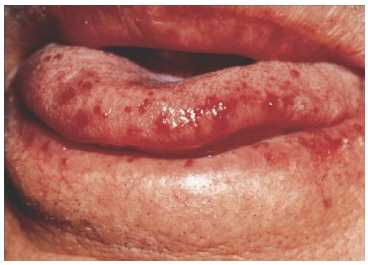
GIT

Peutz Jeghers syndrome	• Small **brown macules** on lips, buccal mucosa and small intestinal polyps. (Asymptomatic except for skin manifestations) • The skin findings first appear in infancy or early childhood. • Rarely polyps can be pre malignant. (Request colonoscopy)
Pyoderma gangrenosum	• Acute painful leg ulceration, surrounded by violaceous border. • Start as small pustules, which subsequently burst and expand to form the larger noninfectious ulcer. • Associated with Inflammatory bowel diseases, rheumatoid arthritis and leukemia.
Hereditary hemorrhagic Telangiectasia	• Telangiectasia (dilated capillaries) over lip, nose, tongue, fingers and toes. • Hx of recurrent epistaxis. • Associated with recurrent upper GI bleed.

Peutz-jeghers syndrome.



Single well defined ulcer with violaceous border.

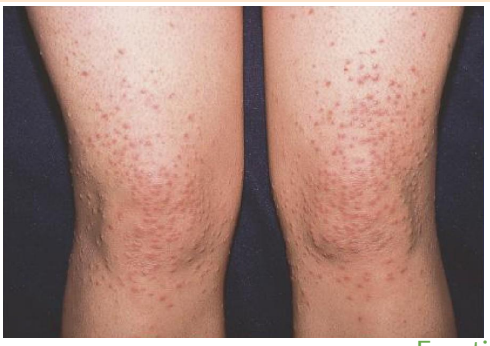
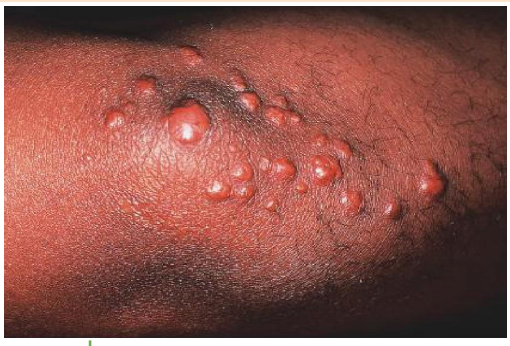


Small telangiectasia with bleeding.

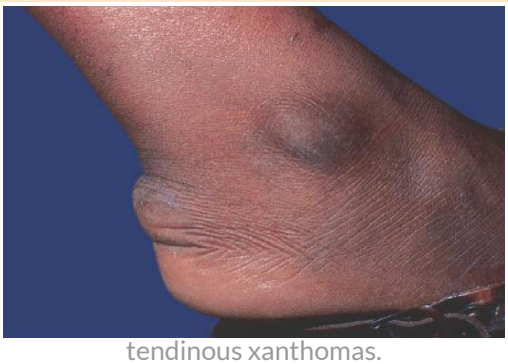
Hyperlipidemia

Hyper -lipidemia	• 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.**
Types of Xanthoma	• **Eruptive:** small papules appear in crops over buttocks & extensors. • **Tendinous:** Nodules over tendons e.g. extensor tendons of hands & feet and Achilles tendon • **Palmar crease xanthoma:** on palms. • **Tuberous:** Papules & nodules over knees and elbows. • **Xanthelasma:** Bilateral symmetrical over both eyelids.

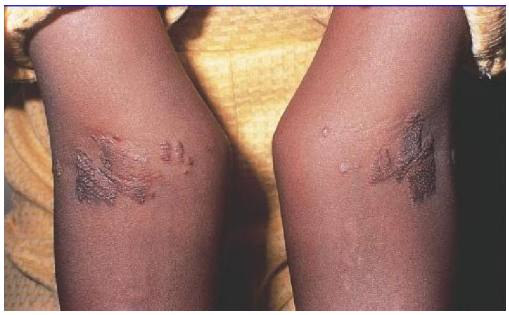
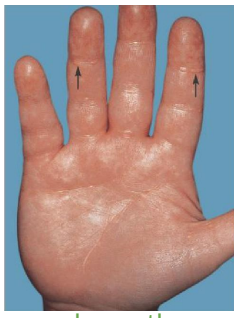
Cutaneous Manifestations Of Systemic Diseases

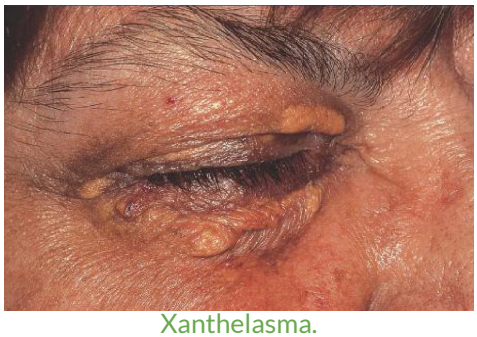
Eruptive papules.



tendinous xanthomas.

Orange color on the creases.

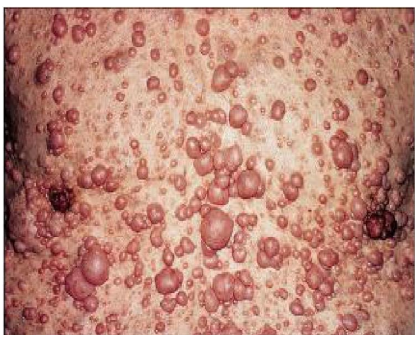


Xanthelasma.

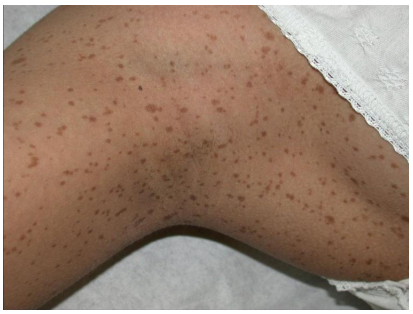
Neurocutaneous Disorders

Neuro -fibromatosis

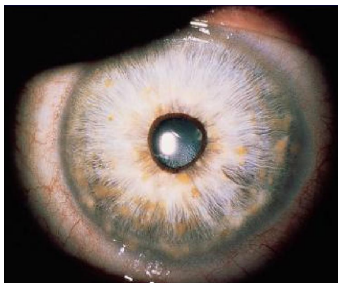
- Autosomal dominant.
- Café-au-lait macules (light brown) can be seen in other disorders but if big size and number suspect neurofibromatosis.
- Neurofibromas (soft pink or skin- colored papules and nodules).
- Axillary freckling (Crowe sign), the presence of the macules on the axillae.
- Optic glioma.
- Lisch nodules (iris hamartoma, seen by slit-lamp examination).
- Associated with Neurological complications e.g. tumors, seizures and mental retardation.



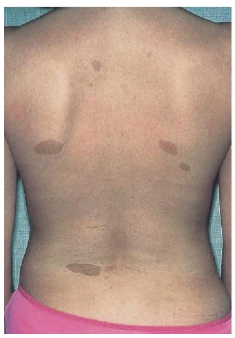
Soft innumerous well defined pink papules and nodules.



Axillary freckling.



Lisch nodules



Café-au-lait macules

Neurocutaneous Disorders (cont')

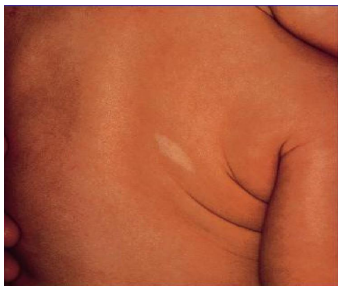
Tuberous Sclerosis (Epiloia)

- **Epi** = Epilepsy / **Loi** = Low intelligence / **A** = adenoma sebaceum.

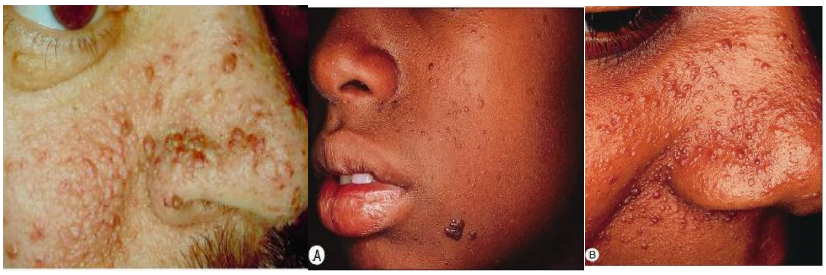
Skin Features:

- Adenoma sebaceum (angiofibroma): red papules around the nose and on chin.
- Ash-leaf hypopigmentation: oval area of hypopigmentation **(This is the earliest sign of TS).**
- **Periungual fibroma:** multiple papules & nodules around the nail **(Pathognomonic)**.
- Shagreen patch: skin colored plaque on the trunk with "orange-peel" Surface.

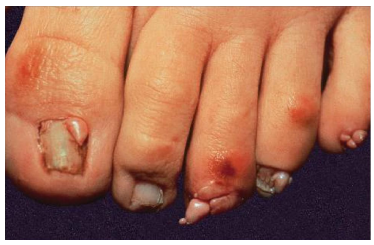
Cutaneous Manifestations Of Systemic Diseases



Ash-leaf hypopigmentation.



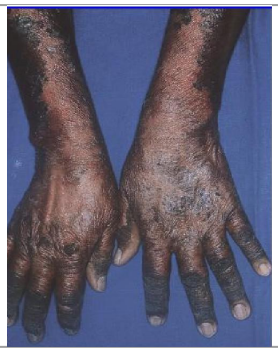
Adenoma sebaceum (angiofibroma).



Periungual angiofibroma.

Others

Behcet's syndrome	• Oral ulcer (the most common). Painful • Genital ulcers (mainly scrotal). • Iritis and arthropathy (May lead to blindness). • May have CNS involvement.
Scurvy اسقربوط	• 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. • Perifollicular hemorrhage and corkscrew hairs (Very brittle hair).
Pellagra	• Nicotinic acid deficiency. **4 "D" s :** • Dermatitis (Photodermatitis). • Diarrhea • Dementia • Death (if not treated)



Causes of Generalized Pruritus Without Skin Lesions (Important)

Causes of Generalized Pruritus Without Skin Lesions	• **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 dorsalis. • **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

Dr says: Labs are important

Cutaneous Manifestations Of Systemic Diseases

Erythema Nodosum

Erythema Nodosum

- Multiple ill-defined bilateral tender erythematous subcutaneous nodules over shins.
- More common in females.

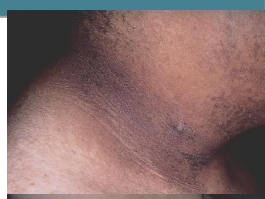
Causes:

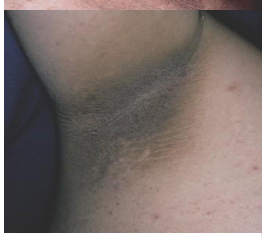
- Infectious: Streptococcus, Tuberculosis, Hepatitis, Chlamydia.
- Sarcoidosis.
- Drugs: Oral contraceptive pills, sulfonamides.
- Lymphoma & leukemia.
- Pregnancy.
- Behcet's disease.
- Idiopathic.

Acanthosis nigricans

Acanthosis nigricans

- Ill defined Brown hyperpigmentation & increased thickening of skin with **velvety texture** at neck, axillae and groin (seen more in body folds).
- Treat the underlying disease (bleaching agents do not help)
- Whenever you see Acanthosis nigrican extensively involving The palms think of malignancy, we call it trip palm





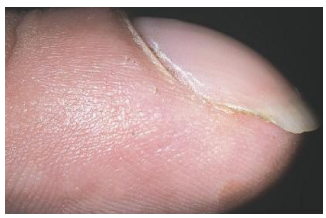
Causes:

- Obesity.
- Endocrinopathy: Diabetes, Thyroid disease, Insulin resistance.
- Internal malignancy: the most common is adenocarcinoma of stomach.
- Drugs: Nicotinic acid.
- Familial.
- Idiopathic.

Nails

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.

Causes of clubbing, From KSUMSC basic clerkship guide

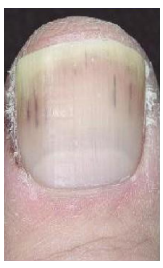
CLUBBING:

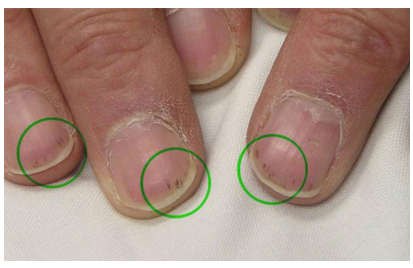
- **C**yanotic congenital heart disease
- **L**ung abscess
- **U**lcerative colitis & crohn's disease
- **B**ronchiectasis, Bronchogenic carcinoma
- **I**nfective endocarditis
- **N**othing (Idiopathic)
- **G**raves

Splinter Haemorrhages

Causes:

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



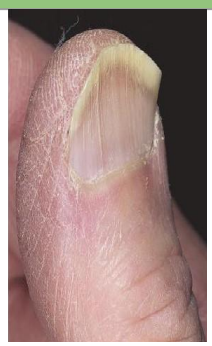


Cutaneous Manifestations Of Systemic Diseases

Nails (cont')

Koilonychia

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



Some mucocutaneous disorders in which you need to do HIV testing

Oral hairy leukoplakia

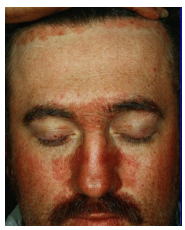
- Corrugated white plaques on the lateral aspect of the tongue.

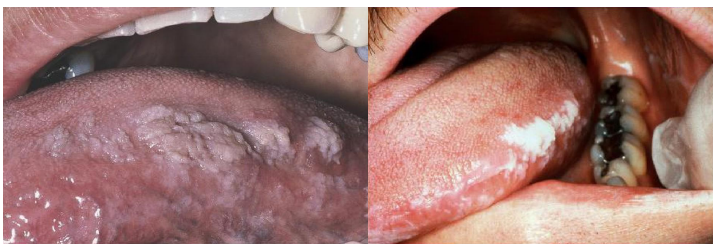
Kaposi Sarcoma

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

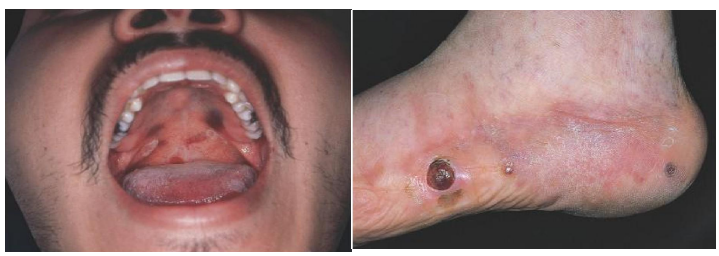
Others

- Multiple mollsucum contagiosum in adult (on face).
- Any STD.
- Seborrheic Dermatitis (extensive & refractory to therapy).
- Severe extensive recalcitrant aphthous ulceration.





Oral hairy leukoplakia



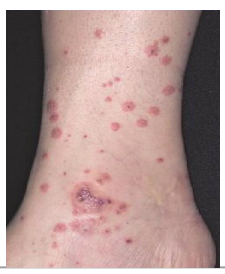
Kaposi sarcoma

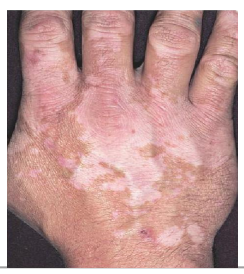
Examples of some skin diseases where you may find systemic associations:

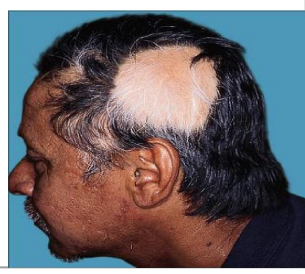
Examples of some skin diseases where you may find systemic associations

- **Lichen planus**; associated with Hepatitis B and C.
- **Vitiligo and Alopecia Areata**: both associated with autoimmune diseases like: Autoimmune Thyroiddis, Diabetes mellitus, Pernicious anemia, Myasthenia gravis, etc.

Lichen planus







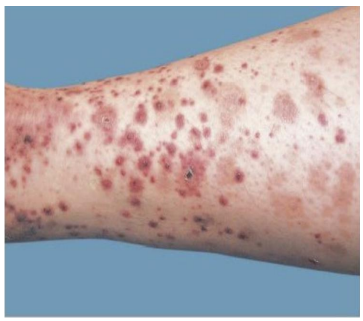
Purpura And Vasculitis

❖ Purpura

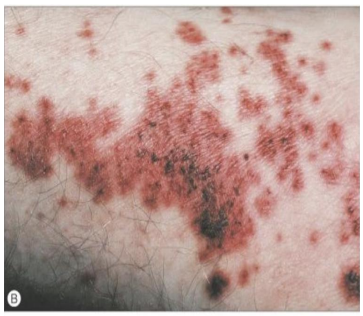
- **Definition**: Visible hemorrhage into the skin or mucous membrane.
- It's a condition of red (Dusky red) or purple discolored spots on the skin that do not blanch (doesn't disappear) on applying pressure .
- if the red spot is blanchable (goes away), then the diagnosis will be Erythema (Dilated vessels).
- You have to use glass, because you will not be able to see it if you apply pressure by your hand.
- The spots are caused by bleeding underneath the skin secondary to platelet disorders, vascular disorders,coagulation disorders or other causes.

They are subdivided as a follow:

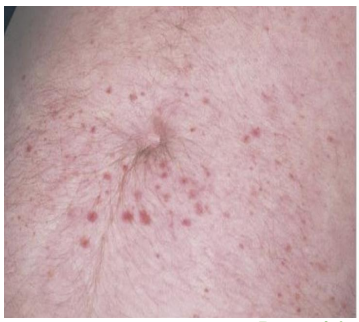
- **Petechiae:** less than or equal 3 or 4 **mm**.
- **Purpura:** (>3 or 4 **mm** - <1 **cm**) which can be either Palpable or nonpalpable (macular)
  Palpable purpura is vasculitis until proven otherwise. الدكتور يقول لو ما تطلع من المحاضرة هذي إلا بهذه المعلومة لكفتك. (مجازاً طبعاً لا تصدق)
- **Ecchymoses:** > or equal to 1 **cm**.

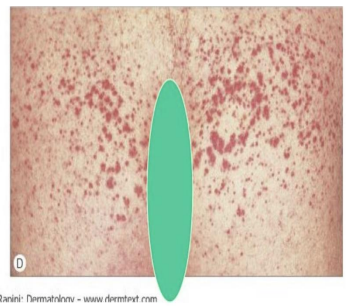


Purpura



Ecchymoses: تكون كبيرة





Petechiae: تكون صغيرة

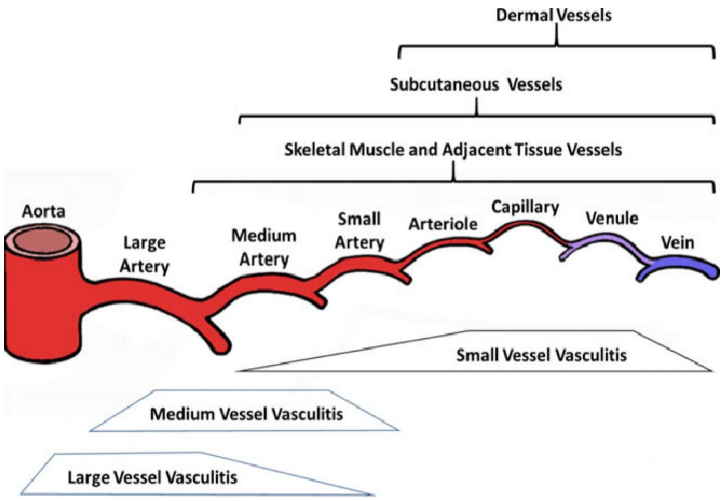
Causes	
Platelet Disorders	- Thrombocytopenia. - Platelet dysfunction.
Coagulation Factor Deficiency	• **Congenital:** - Factor VIII Deficiency. - Factor IX Deficiency. - Von Willebrands disease. • **Acquired:** - Disseminated Intravascular. - Coagulopathy. - Liver disease. - Uremia. - Vitamin K deficiency
Vascular factors	• **Congenital:** - Hereditary Hemorrhagic Telangiectasia. - Ehlers-Danlos Syndrome (Type IV). • **Acquired**: - Inflammation (Vasculitis). - Trauma. - Vitamin c deficiency (scurvy).

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.
- palpable purpura : If you closed your eyes and put your hands you can feel it

- **Classification:**
  - **Large-vessel vasculitis :** Aorta and the great vessels (subclavian, carotid) Claudication, blindness, stroke.
  - **Medium-vessel vasculitis :** Arteries with muscular wall, Mononeuritis multiplex (wrist/foot drop), mesenteric ischemia, cutaneous ulcers.
  - **Small-vessel vasculitis :** Capillaries, arterioles, venules Palpable purpura, glomerulonephritis, pulmonary hemorrhage.



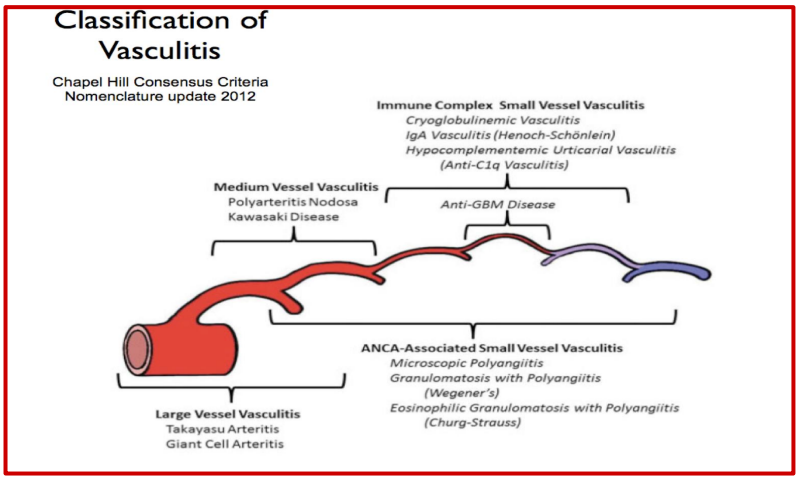


Table 26.2 Chapel Hill consensus classification.

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

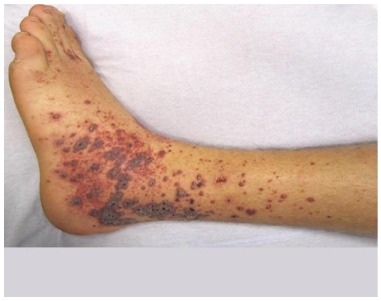
Table 3. Causes of cutaneous vasculitis[5,8]

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

More important than your name
Dr: لا تقولون محد علمنا

Purpura And Vasculitis

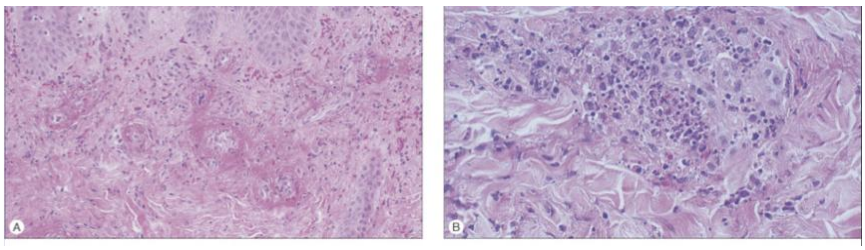
Cutaneous small vessel vasculitis :



Hemorrhagic blisters and Palpable Purpura on lower extremities

- Most common type of vasculitis and it primarily affect post-capillary venules.
- **Pathogenesis:**
  - Many forms of small-vessel vasculitis are felt to be caused by circulating immune complexes.
  - These lodge in vessel walls and activate complement.
- Palpable purpura is the hallmark.
- Pinpoint to several centimeters (Can present as erosion and ulceration).
- 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.
- 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 (may lead to ESRD).
- Renal involvement present as glomerulonephritis.
- The prognosis is good in the absence of internal involvement

- **Histology :**
  - Angiocentric segmental inflammation, endothelial cell swelling, fibrinoid necrosis of blood vessel walls and a cellular infiltrate composed of neutrophil with RBC extravasation.
  - inflammatory Cells inside and outside the blood Vessels.



- **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 & CAST
  - Skin biopsy most important tool to confirm vasculitis.

LABORATORY EVALUATION IN KNOWN OR SUSPECTED VASCULITIS	
ystem	Technique
leme	Complete blood count with differential and platelet count, erythrocyte sedimentation rate (ESR), C-reactive protein
enal	Urinalysis, BUN, creatinine
iver	Abnormal liver function tests, hepatitis B and C antibody, cryoglobulins
mmunologic	Serum complement, rheumatoid factor, antinuclear antibody, anti-dsDNA, extractable nuclear antigen, antineutrophil cytoplasmic autoantibodies (ANCA)
nfectious	Blood and cultures
lead and neck	Sinus radiographs and CT
ulmonary	Chest radiograph or CT
Cardiovascular	Electrocardiogram, creatine phosphokinase, echocardiogra
Neurologic	Nerve conduction studies
Musculoskeletal	Electromyography

DIAGNOSTIC WORKUP

Laboratory investigations

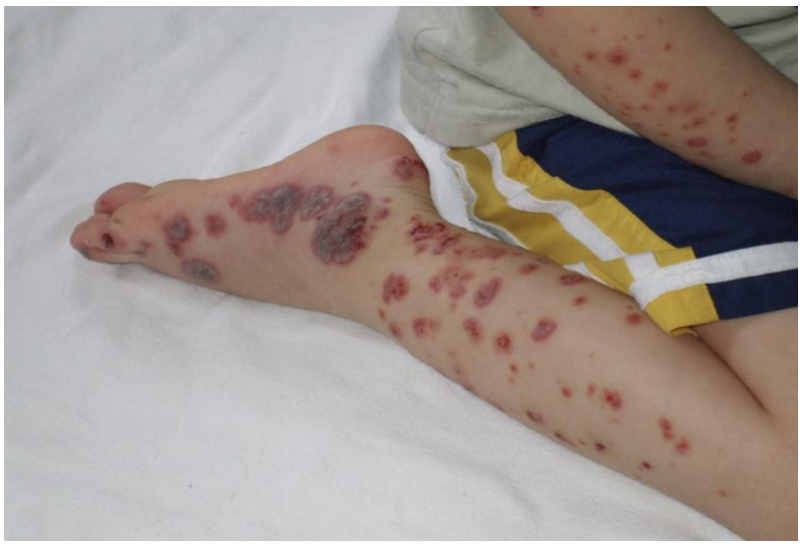
- Full blood count with differential white cell count
- Markers of inflammation: ESR,CRP
- Electrolytes and hepatic transaminases, glucose
- Urinalysis for protein and blood
- Blood cultures (if pyrexial)
- Serology—ANA ,dsDNA , ANCA,C3 and C4,ASLO titre, viral titres (e.g. hepatitis B and hepatitis C, possibly HIV, CMV, parvovirus B19 and others if recent infection).
- Others-rheumatoid factor, electrophoresis, immune complexes.

- **Treatment:**
  - Treatment of cause
  - Symptomatic treatment (if skin is only involved): rest, NSAIDS, Antihistamine.
  - Severe visceral involvement may require high doses of Systemic corticosteroids with or without an immunosuppressive agent.
  - Immunosuppressive agents for rapidly progressive course and severe systemic involvement e.g Kidney.

Purpura And Vasculitis

❖ Henoch -Schön lein purpura HSP

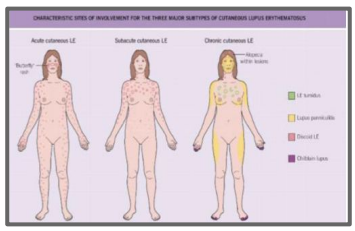
- Primarily occurs in male children (peak age 4-8 years).
- Adults may be affected
- A viral infection or streptococcal pharyngitis is the usual triggering event.
- In about 40 % of the cases the cutaneous manifestations are preceded by mild fever, headache, joint symptoms, and abdominal pain for up to 2 weeks.
- **Characterized by** intermittent purpura, arthralgia, abdominal pain and renal disease.
- Typically, purpura appears on the extensor surfaces of the extremities.
- 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 you have to do urine analysis even if skin manifestations subsides (Good prognosis unless the kidney is affected).
- IgA, C3 and fibrin depositions have been demonstrated in biopsies of both involved and uninvolved skin by immunofluorescence techniques.
- **Treatment**: supportive (bed rest, pain relieve, etc).



lupus Erythematosus

1. Lupus Erythematosus
2. Dermatomyositis
3. Scleroderma (systemic sclerosis)
4. Morphea

- LE is as an autoimmune diseases associated with antibodies directed against components of cell nuclei.
- A multisystem disorder that predominantly affects the skin.
- Its course and organs involvement are unpredictable (Great mimicker).
- It ranges from life threatening manifestation of SLE to the limited and exclusive skin involvement in chronic cutaneous lupus.
- Our concern here is the systemic involvement that might happen in Cutaneous lupus.
- There are several variants of cutaneous lupus, defined in part by the location and depth of the inflammatory infiltrate
- Lupus may affect any tissue, skin, kidneys, CNS, lungs and others.



Classification:

1. **Systemic form (SLE):**

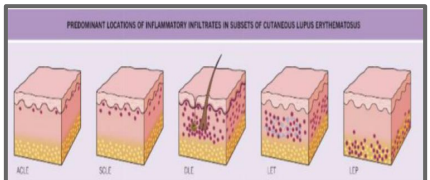
almost always associated with skin manifestations.

2. **Cutaneous form (CLE)**:

There are several variants of cutaneous lupus, defined in part by the location and depth of the inflammatory infiltrate.

further divided base on histopathological findings:

- **A. Histopathologically specific CLE:** (the dermo-epidermal junction is the site affected the most).
  - **Acute cutaneous lupus:** (Key Words: Malar rashes, non scarring, photodistributed)
    - → involves primarily the epidermis and upper dermis and is usually associated with systemic disease.
  - **Subacute cutaneous lupus:** (K.W: non scarring, types of lesions: annular, papulosquamous)
    - → involves primarily the epidermis and upper dermis and is associated with anti- Ro/SSA autoantibodies and photosensitivity.
    - → The majority of patients do not have significant systemic disease.
  - **Chronic cutaneous LE (CCLE):** (most common)
  - **i. Discoid lesions of lupus:** (K.W: scarring, follicular bulging, involve face, scalp and ears)
    - → involve the epidermis, upper and lower dermis, and adnexal structures, and they can scar.
    - → the majority of patients do not have significant systemic disease.
  - **ii. Lupus erythematosus tumidus** (rare)**:** (K.W: non scarring (no epidermal changes))
    - → Involves the dermis (minimal elevation) put there is no prominent epidermal or adnexal involvement.
  - **iii. Lupus panniculitis:**
    - → Involves the subcutaneous tissue and may result in disfiguring depressed scars.
  - **iv. Chilblain LE:**
    - → deep nodules, cold exposure, violaceous & erythematous distal toes.
- **b. Histopathologically nonspecific LE- skin manifestations:**
  - **1- which are not exclusive to LE disease.**
  - **2- Raynaud's, livedo reticularis, palmar erythema, periungual telangiectasia, vasculitis,diffuse non scarring alopecia and ulcers.**
- Note: SLE and CLE can occur simultaneously or separately.



lupus Erythematosus

Cutaneous Findings (Non-specific) Of SLE:

- Diffuse non-scarring alopecia.
- Raynaud's phenomenon.
- Nailfold telangiectasias and erythema.
- Vasculitis (might change the prognosis):
  - Urticarial vasculitis.
  - Small vessel vasculitis (e.g. palpable purpura).
  - Polyarteritis nodosa-like lesions.
  - Ulcerations.
- Cutaneous signs of antiphospholipid syndrome:
  - Livedo reticularis.
  - Ulcerations.
  - Acrocyanosis.
  - Atrophie blanche-like lesions.
- Livedoid vasculopathy.
- Palmar erythema.
- Papular and nodular mucinosis.

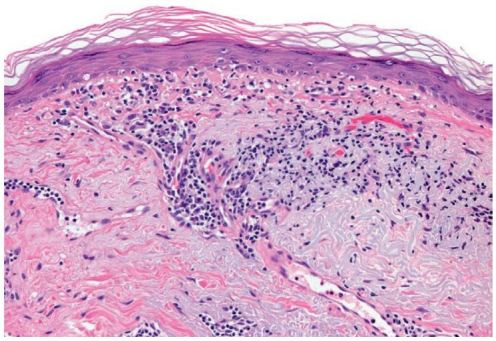
Evaluation For Lupus Erythematosus:

- **HISTORY**

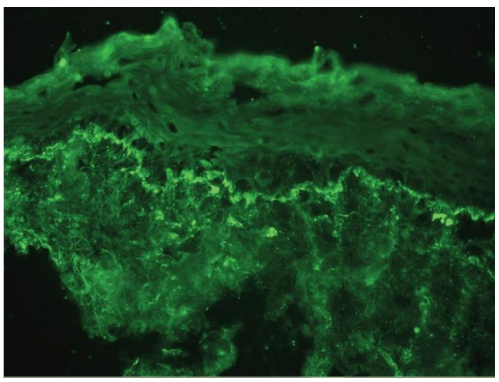
- **PHYSICAL EXAMINATION:**
  - Specific cutaneous lesions.
  - Nonspecific cutaneous lesions.
  - Lymphadenopathy, arthritis.

- LABORATORY TESTS:
  - ANA with profile (anti-dsDNA, -Sm).
  - Urinalysis.
  - CBC with differential, platelet count.
  - Chemistries (BUN, creatinine).
  - Erythrocyte sedimentation rate.
  - Complement levels (C3, C4) The lower the complement level the higher the chance of having nephritis.
  - Skin biopsy (+/- DIF). Almost all cases will need skin biopsy.

- The pathogenesis of cutaneous LE is complex, and it involves an interaction between genetic and environmental factors.
- The latter include **ultraviolet radiation (UVR)**, **medications**, **and possibly viruses**.
- This interplay triggers a complex inflammatory cascade of cytokine, chemokine and inflammatory cell responses that include cells residing within as well as recruited to the skin.
- Overall, **the lichenoid tissue reaction**, defined as epidermal basal cell damage and a bandlike lymphocytic infiltrate in the upper dermis, characterizes most subsets of cutaneous LE.
- Acute cutaneous LE will show interface dermatitis and vacuolization of basal keratinocytes (white halo) and sparse superficial lymphoid infiltrates (near the epidermal-dermal junction).
- Chronic discoid LE will show focal dense interface dermatitis with perivascular and periadnexal lymphoid infiltrates throughout the entire dermis (dark areas). A thickened basement membrane is a characteristic finding and can be highlighted by PAS staining.



Inflammation in cutaneous lupus mainly in the dermis and dermoepidermal junction (Perivascular).
Perifollicular inflammation more with discoid lupus.



- Direct immunofluorescence of cutaneous lupus:
  - Will show granular deposits of IgM are present at the dermal–epidermal junction within lesional skin. In Lesional DIF: Granular deposition of IgG/IgM in the DEJ (Dermoepidermal junction) and around hair follicles. However, in Non-lesional DIF (Normal skin) is referred to as ''Lupus band'' test, Positive reaction usually indicates systemic SLE.
  - In Lupus Band Test It's preferred to be done on non lesional non exposed skin.

lupus Erythematosus

CLE Histopathology:

- Focal or continuous epidermal atrophy (thinning) + Follicular keratin plugs (around hair follicles) + Vacuolar degeneration along the dermo-epidermal junction zone (we will see a gap) + Individual necrotic keratinocytes + Thickening of basement membrane + Abundant interstitial mucin deposits in the reticular dermis + Moderate to dense superficial and deep perivascular and periadnexal lymphocytic + melanin incontinence (the dermis will be pigmented because the keratinocytes are destroyed).

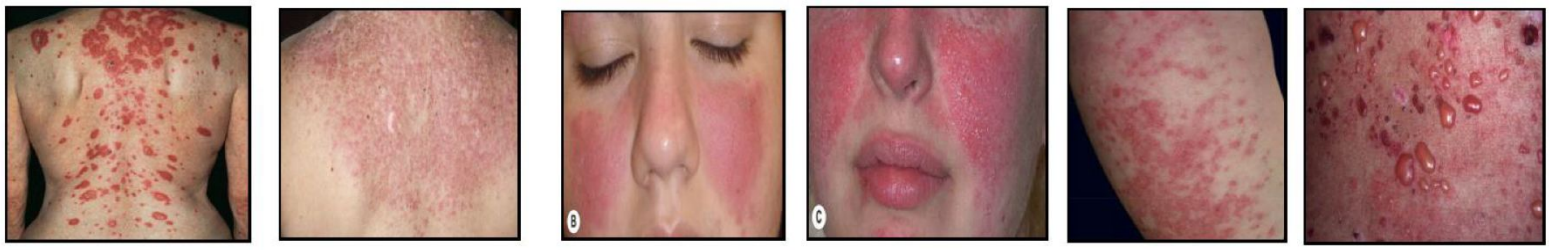
The American College Of Rheumatology 1982 Revised Criteria For Classification Of Systemic Lupus Erythematosus (not always precise)	
Malar rash	• Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds.
Discoid rash	• Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions.
Photosensitivity Skin rash	• as a result of unusual reaction to sunlight, by patient history or physician observation.
Oral ulcers	• Oral or nasopharyngeal ulceration, usually **painless**, observed by physician.
Arthritis	• Non-erosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling or effusion.
Serositis	• a) **Pleuritis** – convincing history of pleuritic pain, rubbing heard by a physician, or evidence of pleural effusion. **OR** • b) **Pericarditis** – documented by ECG, rub or evidence of pericardial effusion.
Renal disorder	• a) **Persistent proteinur**ia greater than 0.5 g/day or greater than 3+ if quantitation not performed. **OR** • b) **Cellular casts** – may be red cell, hemoglobin, granular, tubular or mixed.
Neurologic disorder	• a) **Seizures** – in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance. **OR** • b) **Psychosis** – in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance.
Hematologic disorder	• a) **Hemolytic anemia** with reticulocytosis. **OR** • b) **Leukopenia** – less than 4000/mm3 total WBC on two or more occasions. **OR** • c) **Lymphopenia** – less than 1500/mm3 on two or more occasions. **OR** • d) **Thrombocytopenia** – less than 100 000/mm3 in the absence of offending drugs.

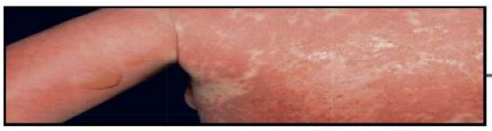
Immunologic disorder	• a) **Anti-DNA antibody** to native DNA in abnormal titer. **OR**
	• b) **Anti-Sm**: presence of antibody to Sm nuclear antigen. **OR**
	• c) Positive finding of **antiphospholipid antibodies** based on:
	  ○ (1) an abnormal serum level of IgG or IgM anticardiolipin antibodies;
	  ○ (2) a positive test result for lupus anticoagulant using standard methods; **or**
	  ○ (3) a false-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test (FTA-ABS).

Antinuclear antibody	• An abnormal titer of antinuclear antibody by immunofluorescence (or an equivalent assay) at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome.

lupus Erythematosus (ALL THE SLIDE IS EXTRA!!)

- These patients must be **evaluated carefully for evidence of internal disease.** ACLE usually indicate systemic disease.
- **Bilateral Malar erythema (Butterfly rash). Sparing of the nasolabial folds** helps differentiate lupus from rosacea. (malar is the best presentation for ACLE).
- The lesions tend to be transient, **follow sun exposure** and resolve without scarring.
- The morphology ranges from **mild erythema** (hard to be noticed by the physician) to **intense edema.**
- **Telangiectasias, erosions, dyspigmentation and epidermal atrophy** help distinguish the malar erythema from other facial rashes. Could be **scaly** like **picture c.**
- The duration may range from a few hours to several weeks.
- Sometimes may be more widespread in distribution. Rarely involves areas other than the face.
- **Pic B:** bilateral patch affecting both cheeks with fainting over the nose, with nasolabial fold sparing.
- **Pic next to picture C:** multiple erythematous papules.
- **Pic 6:** clear fluid filled tense bullae, (tense indicates deeper involvement, superficial bullae are more fluctuant and less tense).

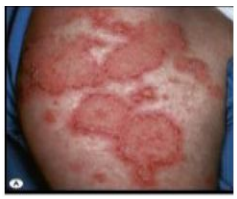




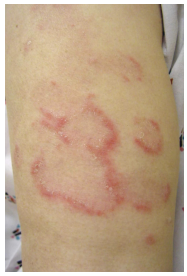
Toxic epidermal necrolysis-like eruption of acute lupus erythematosus.This presentation has also been referred to as a form of acute syndrome of apoptotic pan-epidermolysis (ASAP)

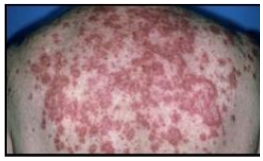
Subacute cutaneous lupus erythematosus (SCLE):

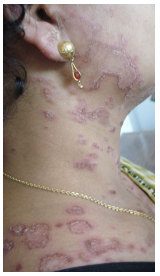
- Non-itchy dry rash appears on the upper back and chest typically **photosensitive**, lesions confined to sun-exposed skin.
- The **midfacial skin is usually spared** (difference between SCLE and ACLE), while the sides of the face, upper trunk and extensor aspects of the upper extremities are commonly involved.
- Subacute LE does not scar does not involve hair follicles.
- Systemic involvement is not usually severe.
- Can be mild, with only a few small scaly patches appearing after sun exposure.
- Lesions may have a:
  - **Annular configuration:** (**first picture:** variably sized multiple annular erythematous patches with enhanced scaly borders (or crust) on sun exposed aspects with coalescence and central clearing).
  - **Papulosquamous**/Psoriasiform type**:** more likely to progress to systemic (**second picture**: Eczematous or psoriasiform appearance on the back (photosensitive area)), best presentation (annular patch with scaly borders).



Scaly and annular (with poly cyclic margin) clear center







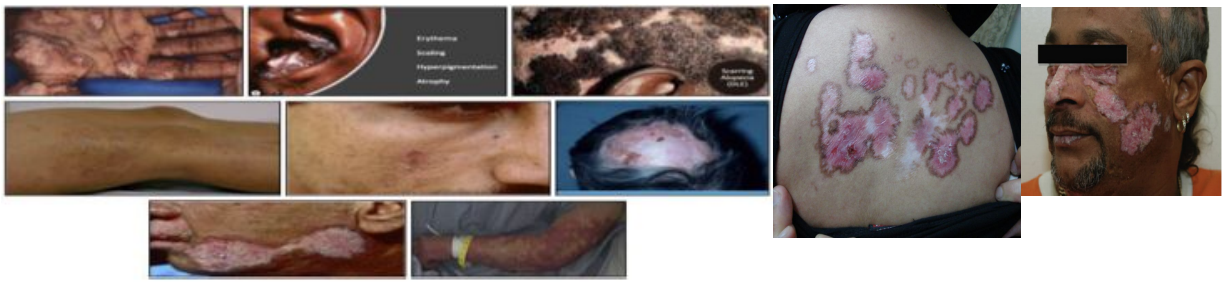
- Lesions often result in dyspigmentation (mainly hypopigmentation) but do not scar.
- The long-term prognosis of patients who have SCLE is not completely known.
- 10-15% of SCLE patients will over time develop internal disease, including **nephritis**.
- SCLE is associated with the **anti-Ro (SSA) autoantibody** and anti-la. (Approximately 70%).
- **Drug induced SCLE:**
- SCLE lesions can appear after receiving certain medications including:
  - **Hydrochlorothiazide,terbinafine,** Griseofulvin, Calcium channel blockers, NSAIDs (naproxen), Antihistamines,TNF-α inhibitors, antiepileptic,**Minocycline** and proton-pump inhibitors.
- The lesions may or may not clear once the medication is discontinued

lupus Erythematosus (ALL THE SLIDE IS EXTRA!!)

Chronic CLE:

Discoid lupus erythematosus (DLE)

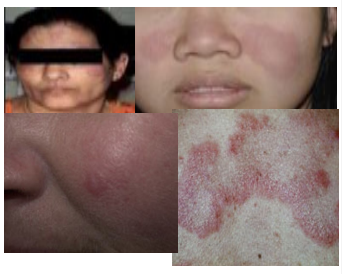
- It is the commonest form of cutaneous lupus usually presents as red scaly patches or plaques that leave dyspigmentation and **scarring** mostly hypopigmented or depigmented scars. Stuck on crust lesions
- It may be localized or widespread.
- Usually affects the cheeks, nose and ears, but sometimes involves the upper back, V of neck, and backs of hands sun exposed areas.
- Unusual to present below the neck without lesions present above the neck.
- Involvement of hair follicles will lead to scarring alopecia
- 10% of DLE patients develop SLE.
- Have a **chronic course**, less chance of remission. More difficult to control
- No clear association between sun exposure and developing DLE lesions..
- Active lesions tend to feel induration on palpation.
- Follicular plugging and scarring alopecia Irreversible hair loss.
- Dyspigmentation (Hypo in the central area and hyper at the periphery).
- Only 5-15% of DLE patients eventually develop clear-cut SLE.
- The risk is higher in patients with widespread discoid lesions.
- Remember: Discoid lesions represent 1 of the 11 ARA criteria for SLE.
- Hypertrophic DLE is an unusual variant (Thick, scaly) mostly on the arms.

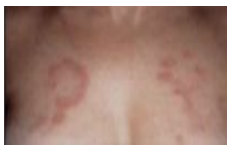


DLE Lesions which favor the head and neck region, may show erythema, scaling, atrophy and dyspigmentation in addition to scarring (and alopecia). Less common sites include the palms. 1st pic on the right: Discoid lupus lesions with dyspigmentation and scarring alopecia (well defined multiple coalescent depigmented linear patch). Hypopigmentation often develops centrally with hyperpigmentation at the periphery usually more aggressive in dark skin patients .

Lupus erythematosus tumidus (LET):

- Dermal form of lupus it's deep so it doesn't involve any epidermal changes (scales).
- The rash is characteristically photosensitive, so it affects sun-exposed sites.
- Red, swollen, urticaria-like bumps and patches or swelling.
- Induration and erythema without scaling and follicular plugging.
- Erythematous, edematous, urticarial-like plaques or nodules usually over face
- The epidermis is uninvolved but has intense dermal inflammatory infiltrate.
- Appears on the face and trunk.
- Negative serology, does not lead to systemic disease.
- multiple Annular pink–violet plaques on the chest and face
- forming arcuate configurated plaques with no scaly borders
- .None of the lesions have epidermal change.





Arcuate lesion, didn't complete a circle

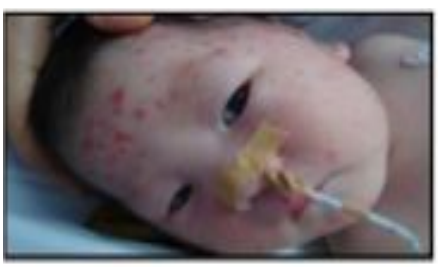
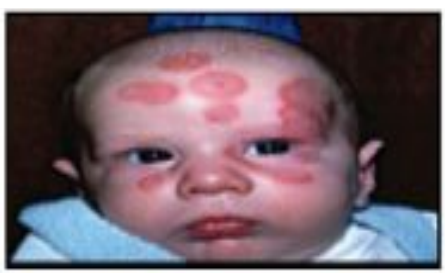
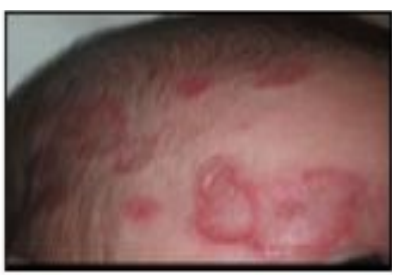
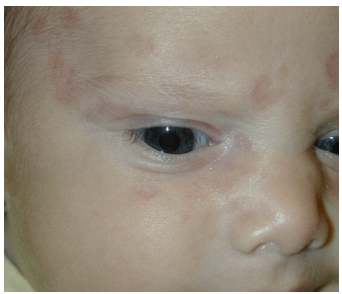
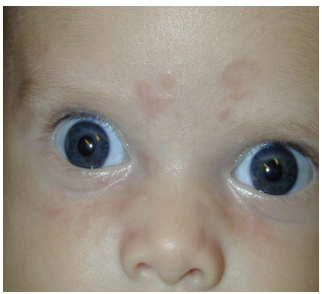
lupus Erythematosus (ALL THE SLIDE IS EXTRA!!)

Chronic CLE(Cont'd):

Lupus panniculitis (LEP)	• Involvement of deeper areas of the skin all the way down to the fat (In panniculitis the **subcutaneous tissue** is most affected) hardening of skin in areas with fat tissue (thighs & hips) leading to post inflammation atrophy • Indurated plaques that can evolve into disfiguring, depressed areas. • Occur on the face, upper arms, upper trunk, breasts, buttocks and thighs. • Some patients have discoid lesions overlying the panniculitis (Lupus Profundus). • Pic : Erythematous plaque on the upper arm. The lesions may resolve with lipoatrophy

Neonatal lupus:

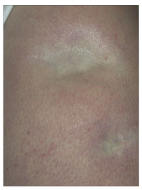
- Newborn babies born to mothers with subacute LE may develop annular rash associated with heart block so need to screen for it, that resolve spontaneously.
- May occur in infants whose mothers have **anti-Ro autoantibodies** anti-La/SSB antibodies and more rarely Ribonucleoprotein (RNP) antibodies.
- **In babies who have NLE, the SCLE-like lesions are histologically identical to those of SCLE in adults.**
- **Almost 100% of babies with NLE have anti-Ro (SSA) antibodies.**
- Unlike SCLE in adults, lesions have a predilection for the face **(Periorbital region) "raccoon or owl eye".**
- Photosensitivity is very common in NLE, but sun exposure is not required for lesions to form. (lesions can be present at birth).
- Lesions typically resolve without scarring, although dyspigmentation and residual telangiectasias may develop.
- The major extracutaneous findings are: **Congenital heart block, hepatobiliary disease and thrombocytopenia.**
- Heart block is almost always present at birth. Cardiomyopathy can occur in a small percentage of patients (neonatal period).
- Cardiac NLE has a mortality of 20% and two-thirds will require pacemakers.
- Hepatobiliary disease and thrombocytopenia, may present at birth or within the first few months of life.
- Hepatobiliary disease ranges from mild elevation of liver enzymes to liver failure.
- All NLE children should be evaluated for internal manifestations with a physical exam in addition to an ECG (cardiac changes), CBC (thrombocytopenia) and LFT (liver involvement).
- Lesions look similar to SCLE (annular). > annular erythematous plaques.
- **Third pic** : multiple annular plaques with enhanced erythematous borders.

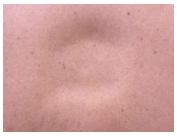






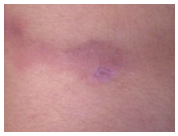
lupus Erythematosus (ALL THE SLIDE IS EXTRA!!)

Lupus Profundus

- lupus affecting the fat underlying skin lupus panniculitis.
- it may develop at any age, including children. The face is the most common area to be affected.
- Inflammation of the fat results in firm deep nodules for some months.
- The end result is deep scars on fat layer or lipodystrophy.

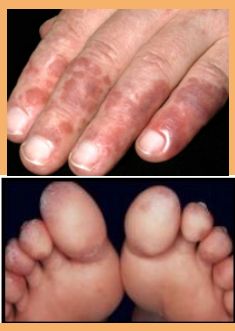






Dimpling post inflammation

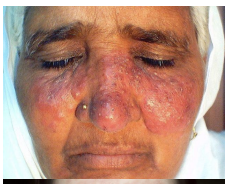
Chilblain lupus

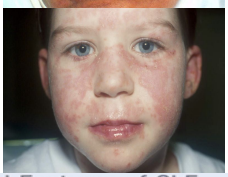


- Itchy and/or tender red or purple bumps that usually come on from cold exposure but can sometimes be precipitated by sun exposure or smoking.
- Redor dusky purple papules and plaques on the toes,fingers, and sometimes the nose, elbows, knees and lower legs.
- They are considered to be a form of skin vasculitis (blood vessel inflammation).
- Usually they have no circulating antibodies.
- The lesions are brought on or exacerbated by cold.
- Appears after exposure to cold weather.
- The lesions may represent the concurrence of ordinary chilblains with LE,although, with time, the lesions may develop a discoid lesion.
- Pic : Violaceous plaques, some with scale, on toes. If there is a family history of this disorder, the possibility of mutations in TREX1, which encodes a DNA exonuclease, can be considered.
- The main treatment is to avoid precipitating factors
- Purplish discoloration of acral areas **(toes & fingers)** worsen by cold but is there all the time, While a frost bite remits after cold is removed, Raynaud's is the range of colors (hypoxia then hypermedia) and pain.
- Now we have COVID chilblain (leads to same manifestations)
- **MCQ: mention aggravating factors for this condition? Smoking, sun exposure.**

Systemic Lupus Erythematosus:

- Only a few patients with cutaneous LE also have SLE.
- The most common presentation is with a malar eruption or butterfly.
- Other skin changes in SLE are photosensitivity, mouth ulcers, and diffuse hair loss.
- SLE may also affect joints, kidneys, lungs, heart, liver, brain, blood vessels and blood cells





Investigations

- SLE is always with positive ANA.
- antiRo/La antibodies, is nearly always present in patients with subacute LE.
- Leucopenia tends to be more pronounced in patients with systemic LE

Table 2. Clinical Features of SLE

System	Presentation
Constitutional	Fatigue, fever (in absence of infection), weight loss
Musculoskeletal	Arthritis, arthralgia, myositis
Skin	Butterfly rash, photosensitivitiy, mucous membrane lesion, alopecia, purpura, urticaria, vasculitis
Vascular	Raynaud's disease
Renal	Hematuria, proteinuria, renal casts, nephrotic syndrome
Gastrointestinal	Nausea, vomiting, abdominal pain
Pulmonary	Pleurisy, pulmonary hypertension
Cardiac	Pericarditis, endocarditis, myocarditis
Reticuloendothelial	Lymphadenopathy, splenomegaly, hepatomegaly
Hematologic	Anemia, thrombocytopenia, leukopenia
Neuropsychiatric	Psychosis, seizures, organic brain syndrome, transverse myelitis, cranial neuropathies, peripheral neuropathies

SLE: systemic lupus erythematosus.
Source: Reference 13.

Lupus:

- Skin biopsy may be diagnostic especially in discoid lupus erythematosus.
- Direct immunofluorescence tests may show positive antibody deposition along the basement membrane (lupus band test).

lupus Erythematosus

Drug induced lupus: Extra! But important

- Sex ratios are nearly equal.
- Nephritis and central nervous system features are not commonly present.
- Anti-DsDNA –ve, Anti-Histone AB +ve.
- When the drug is discontinued, the patient has resolution of clinical & laboratory abnormalities.
- Procainamide, Hydralazine, phenytoin, Carbamazepine , Lithium , Sulphonamides , Minocycline, Penicillamine, Isoniazid, Quinidine, Anti-TNF, IFN, etc.

Autoantibodies: Extra!

- Specific but not Sensitive:
  - Anti-dsDNA (lupus nephritis).
  - Anti-Sm,
- Sensitive but not specific:
  - ANA (>95%),
  - ssDNA (70%).
- Drug-induced lupus:
  - Anti-Histone Ab.

CLE Management:

- The aim of treatment for cutaneous LE is to alleviate symptoms and to prevent scarring.
- Smoking cessation will help Raynaud's phenomena and chilblain lupus . Smoking aggravates the symptoms and decreases response to treatment.
- Sun protection: Education against sun exposure + the use of sunscreen .very important!
- Topical therapy:
  - Topical steroids.
  - Topical Calcineurin inhibitors e.g. Tacrolimus.
  - Topical Retinoids.
- Oral steroids.
- Methotrexate, azathioprin, mycophenolate mofetil, cyclosporine, cyclophosphamide, IVIG, and Rituximab.
- Intralesional steroids AKA (ILK injections) more aggressive.
- **Systemic Antimalarials Therapy** (Can effect the disease course (weak disease modifying agents)):
  - Hydroxychloroquine (200 mg po qd–bid in adults; up to 6.5 mg/kg ideal body weight/day).
  - **Chloroquine** (125–250 po qd in adults; up to 3.5–4 mg/kg ideal body weight/day).
  - **Quinacrine** (100 mg po qd.
  - Combination of hydroxychloroquine or chloroquine and quinacrine (increase the efficacy of Tx).
  - Don't give Hydroxychloroquine and Chloroquine together as it leads to ocular toxicity.
  - Antimalarials side effect: xerosis, exanthematous or lichenoid drug eruptions, urticaria, blue-gray skin hyperpigmentation,ocular toxicity, gastrointestinal upset,myopathy, cardiomyopathy, and rare central nervous system side effects (dizziness, headache, insomnia, psychosis).
- **Systemic Therapy For Antimalarial-Resistant Cutaneous Disease:**
  - Retinoids (e.g. acitretin, isotretinoin).
  - **Thalidomide** (teratogenic) (50–100 mg po qd for clearing and, if necessary, 25–50 mg po qd–twice weekly for maintenance).
  - **Dapsone (primarily for bullous eruption of SLE).**
  - Immunosuppressive agents (e.g. mycophenolate mofetil, azathioprine).
  - Sulfasalazine.
  - Clofazimine.
  - **Systemic corticosteroids.**
  - Immune response modifiers (e.g., rituximab, abatacept, belimumab, anti-IL-6 Ab, anti-IL-10 Ab).

Dermatomyositis

Introduction:

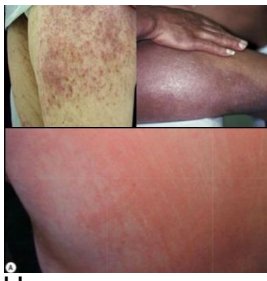
- Dermatomyositis is classified as one of the idiopathic inflammatory myopathies
- An uncommon inflammatory disease affects adults between 40-60 (females mainly) and children 5-15.
- Skin changes. A violet-colored or dusky red rash on face and eyelids and on areas around nails, knuckles, elbows, knees, chest and back. The rash, which can be patchy with bluish-purple discolorations, is often the first sign of dermatomyositis.
- Is a disease of presumed autoimmune pathogenesis (relatively rare) that presents with a symmetric, proximal extensor inflammatory myopathy and a characteristic cutaneous eruption.
- Malignancy in DM is about 10% to over 50% in adults (Most common are: Ovarian, and colon cancer but can include: breast, lung, gastric, pancreatic, lymphomas , and ¼ of adults with DM have an associated occult malignancy (unknown origin).
- The risk of malignancy may return to normal after 2-**5 years.** So, **Our concern here In DM is malignancy.**
- Skin manifestations often precede the onset of symptoms related to malignancy.
- Some pts doesn't have evidence of muscle inflammation **(Amyopathic dermatomyositis)** and Some doesn't have muscle symptoms but if you test them there is inflammation **(Hypomyopathic dermatomyositis)**.

Classification System For Dermatomyositis:

- Adult-onset:
  - Classic DM
  - Classic DM with malignancy.
  - Classic DM as part of an overlapping connective tissue disorder.
  - Clinically amyopathic DM.
  - Amyopathic DM.
  - Hypomyopathic DM
- Juvenile-onset:
  - Classic DM.
  - Clinically amyopathic DM.
  - Amyopathic DM.
  - Hypomyopathic DM.

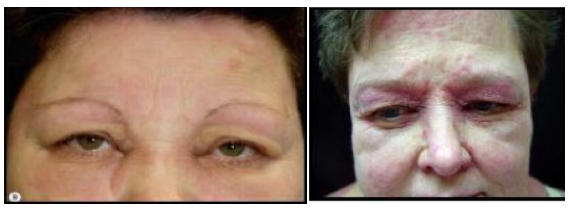
Cutaneous Manifestations Of Dermatomyositis (Uncommon) not important

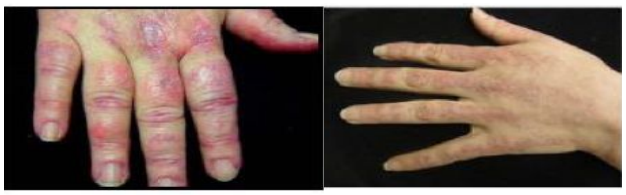
- Cutaneous erosions or ulcerations.
- Holster sign (poikiloderma of the lateral thighs) **(A)**.
- Flagellate erythema **(B)**.
- Vesiculobullous lesions.
- Exfoliative erythroderma.
- Panniculitis.
- Gingival telangiectasias.
- Pustular eruption of the elbows and knees.
- Lipoatrophy (especially in juvenile dermatomyositis).
- Small vessel vasculitis (especially in juvenile dermatomyositis).

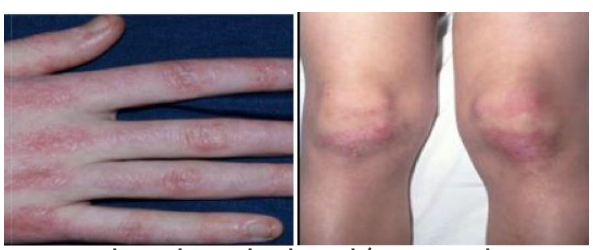


Cutaneous Manifestations Of Dermatomyositis (common) "the first 3 signs are **pathognomonic**"

Heliotrope rash	• Violaceous to dusky erythematous rash with or without edema in a symmetrical distribution involving upper palpebra skin. • Classical picture of the characteristic dermatomyositis rash.
Gottron's papules	• Slightly elevated, erythematous to violaceous papules and plaques that occur symmetrically over the extensor (dorsal) aspects of finger joints (the metacarpophalangeal (MCP) and interphalangeal (IP) joints) sometimes they are shiny.
Gottron's sign	• Symmetric, non-scaling, violaceous to erythematous macules or patches, often atrophic, in the same distribution as Gottron's papules. • Some people define them as gottron's papules, but patches not bump, and some define them as gottron's papules in areas other than the hand (no papules are present in gottron's sign).

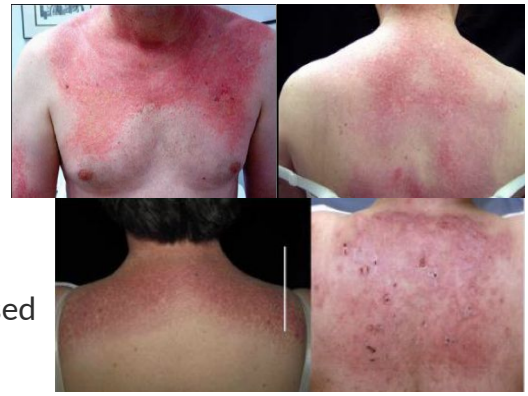
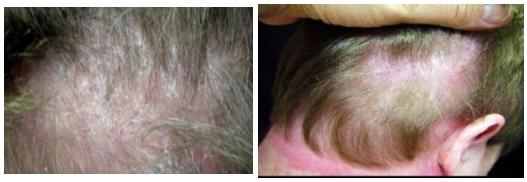
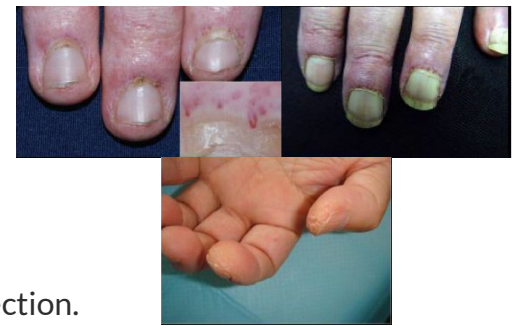
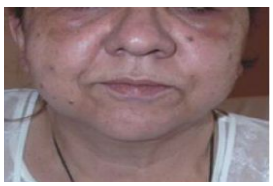






Dermatomyositis

Cutaneous Manifestations Of Dermatomyositis (common) (cont')

Photodistributed poikiloderma (includes facial erythema)	• V-sign Poikiloderma a rash that has: hyperpigmentation, hypopigmentation, atrophy, and telangiectasia • Poikiloderma over the upper back (shawl sign) Poikiloderma refers to skin that demonstrates both hyperpigmentation and hypopigmentation, as well as telangiectasias and epidermal atrophy. In DM, patients may demonstrate poikiloderma in any photo-exposed site; however, classic areas of involvement are the upper back (shawl sign). 
Scalp poikiloderma	• Erythematous to violaceous, psoriasiform dermatitis. 
Nail fold changes	• Includes ragged cuticles (Pathognomonic), nailfold telangiectasias. • Periungual and cuticular changes: Dilation of capillary loops at the proximal nailfold Ragged and thickened cuticles, cuticular overgrowth, and periungual erythema. • Fragmentation over the cuticle area breach which make pt. prone to bacteria entry and infection. • Mechanic's hand :Cracking and fissuring of the skin of dermatitis the fingertips. 
Others	• **Eyelid edema** • **Non-scarring alopecia.** • **Calcinosis cutis** (especially in juvenile dermatomyositis). 

Systemic DM manifestations:

- Myopathy: affects proximal muscle groups, mainly the extensor groups (Triceps and quadriceps) in a symmetric fashion. Progressive proximal muscle weakness involves the hips, thighs, shoulders, upper arms and neck.
- Calcinosis: More common in Juvenile DM, favors sites of trauma and can be painful (Calcinosis :stony hard papules with cheesy material , do x-ray , it might be excised)can also be found in scleroderma.
- Pulmonary disease: 15-30%, generally presents as diffuse interstitial fibrosis.
- Patients may also develop ARDS.
- Cardiac disease: Usually asymptomatic (Arrhythmias, conduction defects).
- Gastrointestinal: Symptoms such as dysphagia should prompt investigation for overlap with scleroderma.
- Photosensitivity
- Raynaud's phenomenon
- Dysphagia, gastrointestinal ulcers
- Muscle pain or tenderness
- Fatigue, fever and weight loss
- Calcinosis cutis especially in children
- Interstitial lung disease.

Dermatomyositis

Evaluation Of The Patient With Dermatomyositis:

- **HISTORY:**
  - Including potential triggers and previous malignancies, and a review of systems.

- **PHYSICAL EXAMINATION:**
  - Skin, muscle and complete general examination
  - including, in adults, breast and pelvic [women]
  - testicular and prostate [men]
  - rectal [both sexes]

- **LABORATORY EVALUATION:**
  - **Pulmonary:**
    - Pulmonary function tests (PFTs) with CO diffusion.
    - Chest X-ray and/or high-resolution chest CT.
  - **Cardiac:**
    - Electrocardiogram (EKG)
    - If symptomatic. echocardiogram and/or Holter monitor.
  - **Esophageal:**
    - If symptoms, barium swallow.
  - **General :**
    - Complete blood count.
    - Comprehensive metabolic panel.
    - Fasting levels of glucose and lipids.
    - Autoantibody panel.

- **SPECIFIC LABORATORY EVALUATION:**
  - Cutaneous: Skin biopsy (not diagnostic).
  - Muscle: Serum creatine kinase, serum aldolase, occasionally urine creatine, Electromyography (EMG)
  - Muscle biopsy (very conclusive).
  - Serum enzymes are important for diagnosis and even for management.
  - MRI or U/S (if EMG or muscle biopsy are negative)
  - SEROLOGY (ANTIBODIES) :
    High specificity: P155 (increased risk of malignancy), **Mi-2** Classical dermatomyositis (good prognosis), **Jo-1** (Antisynthetase syndrome), **SRP** (Fulminant DM, cardiac involvement).
    Low Specificity: ANA.

- **MALIGNANCY SCREEN (ADULTS):**
  - Urinalysis, stool occult blood testing.
  - Serum prostate-specific antigen (PSA) [men], Serum CA125 [women].
  - Mammogram and transvaginal pelvic U/S [women].
  - CT of chest, abdomen and pelvis.
  - Colonoscopy, if age-appropriate, iron deficiency anemia, occult blood in stool, or symptoms.
  - Upper endoscopy – if colonoscopy negative in the setting of iron deficiency anemia, occult blood in stool, or symptoms.
  - If planning chronic systemic Corticosteroids DEXA bone density scan.

TREATMENT (CUTANEOUS)

- **Sunscreens (high sun protection factor including protection against UVA).**
- **Topical corticosteroids.**
- **Topical tacrolimus.**
- **Hydroxychloroquine** as a photo protector **200 mg twice daily; increased frequency of drug eruptions in patients with dermatomyositis).**
- Hydroxychloroquine (200 mg twice daily) plus quinacrine (100 mg/day).
- Low-dose weekly methotrexate (5–15 mg weekly).
- Mycophenolate mofetil • High-dose IVIg (2 g/kg/month).
- Retinoids, Dapsone, Thalidomide.
- Leflunomide.
- Antiestrogens (e.g. tamoxifen, anastrozole).
- TNF-α inhibitors (e.g. infliximab, etanercept).
- Rituximab.

IF there a big list of treatment it means no effective treatment :)

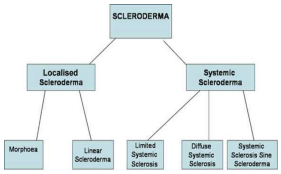
Scleroderma

Scleroderma:

- **SCLERODERMA.**
- **SYSTEMIC SCLEROSIS.**
- **PROGRESSIVE SYSTEMIC SCLEROSIS.**
- **ACROSCLEROSIS.**

SYSTEMIC SCLEROSIS:

- Systemic sclerosis (SSc, scleroderma) is an autoimmune connective tissue disease of unknown etiology that affects the skin, blood vessels and internal organs.
- The hallmark of the disease is thickening and tightness of the skin.
- characterized by fibrosis of the skin as well as internal organs, e.g. lung, heart, gastrointestinal tract (most common), and kidneys.
- The name systemic sclerosis is meant to convey the systemic nature of the disease, which has two major clinical subtypes: **limited and diffuse.**
- More common in females.
- 30-50 years.
- Not hereditary (but could be familial).
- Not invariably progressive and fatal (Our concern here is the patient Quality of life).



Classification

Limited

- Limited SSc is characterized by fibrotic skin changes that are limited to the fingers, hands and face and includes the CREST syndrome.
- Tend to develop internal involvement late in the course of disease (decades)
- **CREST Syndrome:** describes the clinical features in a subset of patients with limited SSc.
  - **C**alcinosis
  - **R**aynaud's phenomenon
  - **E**sophageal involvement
  - **S**clerodactyly
  - **T**elangiectasia

Diffuse

- In diffuse SSc, generalized fibrotic skin changes are seen and they usually start in the fingers and hands but spread to involve the forearms, arms, trunk, face and lower extremities.
- Typically associated with early internal organ involvement (within 5 yrs of onset) and a worse prognosis.
- Positive anti topoisomerase antibodies (**anti scl-70**).

Diagnostic criteria:

Either one Major criterion

- Symmetric cutaneous sclerosis proximal to the MCP or MTP joints.

Or Two or more Minor criterion:

- Sclerodactyly (localized Thickening and tightness of the skin of the fingers or toes).
- Digital pitted scars.
- Loss of substance from finger pads.

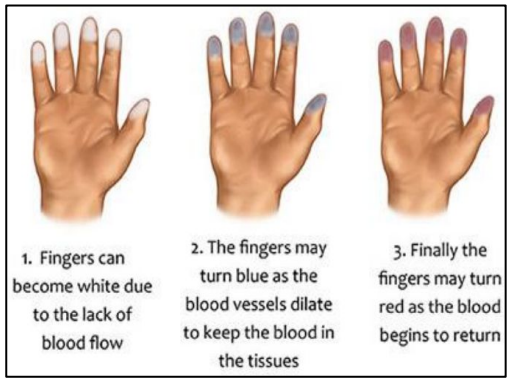
Pathogenesis:

- Individual genetic background and Exposure to environmental triggers (virus, drugs, vinyl chloride, silica and nanoparticles from traffic-derived pollution), Inducing vascular damage and fibroblast. Activate cells that have ability to give origin to endothelial cells, or collagen producing cells,These cells will migrate into injured tissues to differentiate into both endothelial cells and fibroblasts, to cause defective vasculogenesis or fibrosis or both, and to have immunomodulatory effects. The B cells in SScare activated and produced anti-topoisomerase I and anti-centromere antibodies.

Scleroderma (ALL THE SLIDE IS EXTRA!!)

Cutaneous features of systemic disease:

- Digits: Early pitting edema ,hardening, taut and shiny appearance (later on).
- Face: Beaked nose, microstomia (small mouth) and a youthful appearance.
- Dyspigmentation: Salt & pepper.
- Telangiectasias :Matted (squared off) on the Face, lips and palms.
- Nailfold capillary abnormalities: in 90%
  (Capillary drop out alternating with dilated loops).
- Dystrophic Calcinosis Cutis.
- Raynaud's phenomenon.
- Cutaneous ulcer.

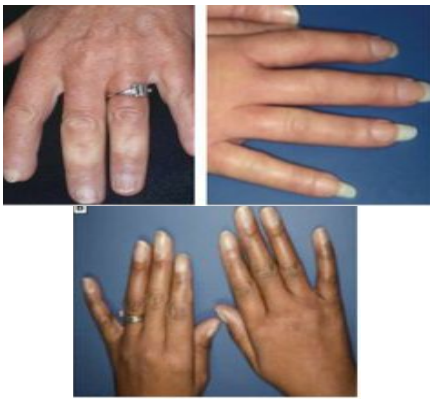


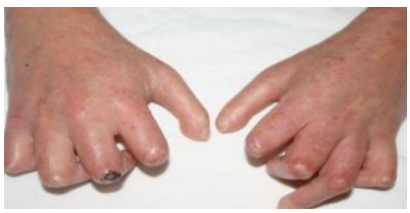
Cutaneous features of systemic disease:

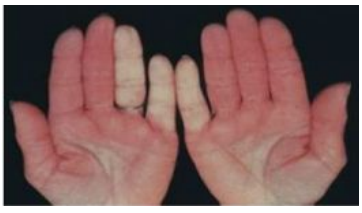
Early phase of SSc	• Early, edematous phase of systemic sclerosis • Note the demonstration of pitting edema on two of the digits. • Edematous and shiny fingers • Swelling and sclerosis reduce hand movements, so patients may be unable to make a fist, or to place the palmar surfaces together the 'prayer sign'. • Fingertips may have pitting, ulcers or loss of bulk from finger pads
Late phase	• Contractures, thick skin, ulceration and scars • Late phase of systemic sclerosis with diffuse cutaneous scleroderma. • Note the fixed flexion contractures, sclerodactyly, and the digital ulceration overlying the third proximal interphalangeal joint.

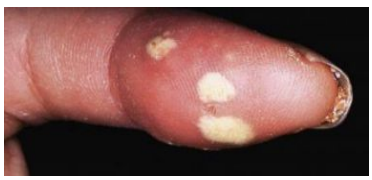
Raynaud's phenomenon	• Vasospasm of the digital microvasculature resulting in:
	  ○ Digital ischemia (pallor)
	  ○ Digital hypoxia (cyanosis)
	  ○ Digital reactive hypermedi (erythema)
	• pale then blue then red, indicates more progressive illness.

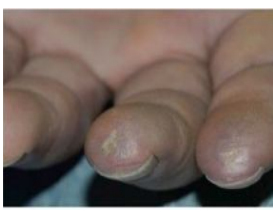
Calcinosis cutis	• white spots or ulcerations and may be quite painful.
Pitted scars	• Pitted scars of the digital pulp That form in distal areas.



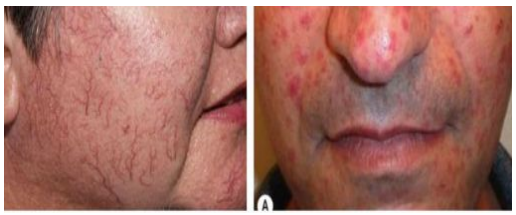








Scleroderma

Cutaneous features of systemic disease:		
Salt and pepper pigmentation	• Areas of hyper and hypopigmentation. • The "salt and pepper" sign Leukoderma with retention of perifollicular pigmentation in a patient with systemic sclerosis.	 Atrophy + Telangiectasia
Telangiectasia	• 1st picture: regular telangiectasia (long and tortuous) seen in rosacea and other skin conditions. • 2nd picture: matted telangiectasia seen in scleroderma (flat and rounded)	

WORK UP:

- Skin biopsy (histopathology): (One of the criteria to diagnose Scleroderma)
  - Compact collagen (Thick areas of collagen in the dermis), loss of subQ fat, deep lymphocytic infiltrate and trapped adnexal structures.
- **Serology (autoantibodies):** (First 3 autoantibodies are of the criteria to diagnose Scleroderma)
  - **ANA.**
  - **Anti-Scl-70 (Anti-Topoisomerase):** AKA **RNA polymerase T (Scl 70)** → diffuse disease, ILD.
  - **Anti Centromeres (ACA):** → Limited disease (CREST syndrome).
  - **Anti-RNP.**
  - **Anti-RNA Polymerase I:** → Diffuse disease.

TREATMENT:

- **"SYMPTOMATIC"**
- Most interventions focus on internal organs and unfortunately, have no significant impact on cutaneous manifestations.
- Raynaud's Phenomenon → Keep warm, CCB (Nifedipine), Angiotensin II receptor blockers (Losartan), Phosphodiesterase type inhibitors (Sildenafil). Stop smoking, decrease trauma. calcium channel blockers, aspirin and vasodilating drugs including nifedipine and iloprost infusions
- Calcinosis cutis: nifedipine, surgical or laser excision.
- Skin sclerosis: physiotherapy, phototherapy.
- GI: proton pump inhibitor, surgery for strictures.
- Kidney: ACE inhibitors.
- In severe cases: immunosuppressant , D-Penicillamine might be used.
- Cutaneous ulcers → Bosentan.
- Fibrosis.
- Morphea.
- Other skin issues: Matted Telangiectasias → Pulse dye laser, Calcinosis cutis → nifedipine, surgical or laser excision.
- Internal organs: ACE inhibitors is used to treat scleroderma renal crisis, GI → PPI or surgery for strictures, Cyclophosphamide → interstitial lung disease, Oral immunosuppressants.