Derma Team 436

PAPULOSQUAMOUS DISORDERS (PSORIASIS, LICHEN PLANUS & PITYRIASIS ROSEA)

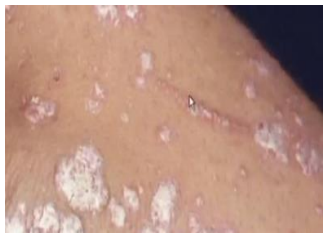
Objective of the lecture:

- To know the definition of papulosquamous pattern.
- To know the group of diseases known as papulosquamous diseases.
- Psoriasis pathogenesis, clinical presentation, and management.
- Lichen planus pathogenesis, clinical presentation, and management.
- Pityriasis rosea pathogenesis, clinical presentation, and management.

Done by **team leader: Ghada Alhadlaq**
members: Rawan Alwadee & Deena AlNouwaiser.
Revised by: Shrooq Alsomali

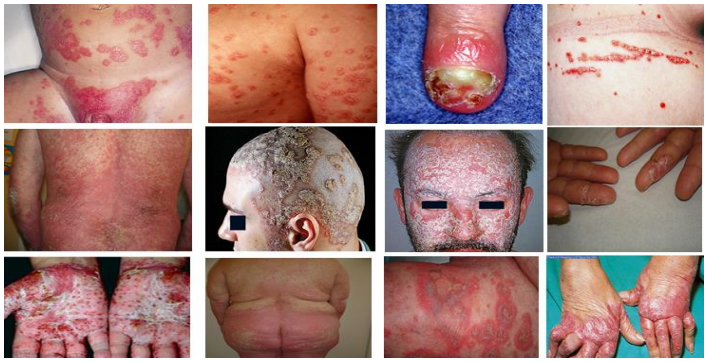
Before you start.. CHECK THE EDITING FILE
Sources: doctor's slides and notes + Group B teamwork
[Color index: Important | doctor notes | Extra]

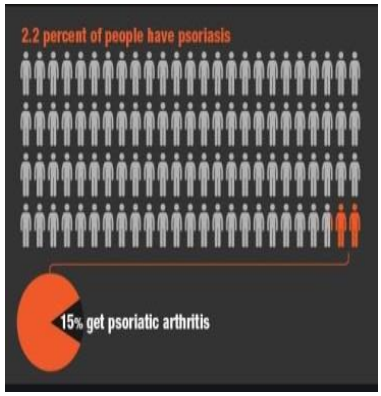
Papulosquamous diseases:



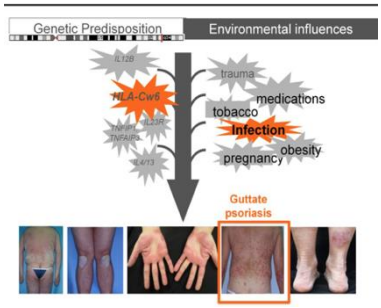
- The term squamous refers to scaling that represents thick Stratum Corneum and thus implies an abnormal keratinization process.
  - Keratinization is the differentiation of basal keratinocytes.
  - The basal keratinocytes as they move upward, they accumulate keratin inside them & their organelles totally die.
- Papulosquamous diseases are typically characterized by scaly papules (papule = elevated lesion).
- It could be papule or plaque, but the papulosquamous is **the reaction pattern** of the disease which means a reaction (inflammation) inside the skin (within the epidermis & dermis) to a specific thing that presents itself on the surface of the skin with a certain morphology.
- Other disease patterns include psoriasiform, lichenoid, bullous, pustular as well as papulosquamous pattern & each has many differential diagnoses.

Psoriasis (الصدفية):





- Chronic non-contagious polygenic multisystem inflammatory disease.
- Psoriasis can be triggered by infections, trauma, stress and medications.
- The characteristic lesion (classical psoriatic lesion) is a sharply demarcated erythematous scaly plaque that may be localized or generalized.
- The natural history follows a chronic course with intermittent remissions.
- Has two peaks in age of onset (bi-model age presentation): one at 20-30 years and a second at 40-50.



Genetic factors **play a role in psoriasis proved by:**

- Positive family history by 36-91%.
- There are multiple susceptibility genes called (PSORS 1-9).
- HLA studies showed high risk of psoriasis with HLA-Cw6 (also called PSORS 1 & is present on chromosome 6).
- **HLA type influences the type of psoriasis and the course of the disease.**

TYPE	HLA
Pustular psoriasis	B27
Guttate psoriasis	B13, B17
erythrodermic	B13, B17

COURSE	HLA
Early onset (positive family history).	Cw6 (type 1 psoriasis) 90% of psoriasis patients have this kind of HLA typing
Late onset (negative family history, negative Cw6).	(type 2 psoriasis)

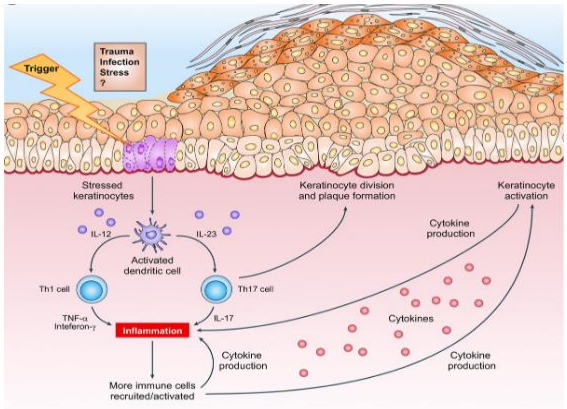
- One affected parent: 16%.
- Both parents: 50%.
- Non-psoriatic parents with sibling: 10%.
- Monozygotic twins: 70%.
- Dizygotic twins: 20%.

Triggering factors:

- Trauma (25% of patients) sunburn, viral exanthem or physical trauma.
  - If psoriasis is induced by trauma, it is called koebnerization (also called isomorphic phenomenon).
  - Ddx of keobnerization: psoriasis, lichen planus or warts.
  - Trauma-induced psoriasis occurs in patients **already having psoriasis.**
- Infections (streptococcal pharyngitis).
- Drugs: lithium, β-blockers, antimalarials, IF (interferon).
  - Antimalarias can either trigger or exacerbate psoriasis. Triger psoriasis means that after taking anti-malarias, psoriasis develops; however, exacerbation of psoriasis means it makes the condition worse in patients already having psoriasis.
- Irritating topicals like tar and dithranol.
- Hypocalcemia.
- Pregnancy.
- Obesity.

Pathogenesis of psoriasis:

- The trigger acts on the basal keratinocyte → keratinocytes become stressed & start to present some of its antigen to dendritic cells → the dendritic cells get activated → IL-23 & IL-12 under the effect of dendritic cell stimulate Th17 cell & Th1 cell respectively → both of them induce inflammation & recruit more cells from the endothelium to keep the inflammation going on.
- Th17 cells will also cause excessive proliferation of the basal keratinocytes. The elevated lesion results from the cells building up. All of the basal keratinocytes underneath the lesion are contributing to the proliferation. This is what we call growth fraction.



Epidermal cell kinetics:

- The growth fraction of basal cells is increased to almost 100% (in psoriatic patients) compared with 30% in normal skin.
  - Growth fraction is a ratio of dividing cells over the population cells.
  - 100% growth fraction means all the population cells are dividing.
- The epidermal turnover time is shortened to less than 10 days compared with 30 to 60 days in normal skin.

Tools to measure severity index:

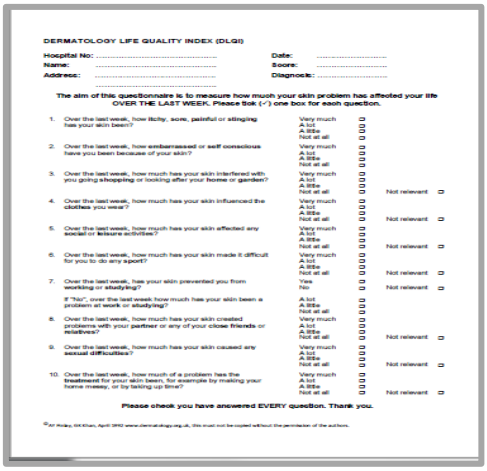
- **Psoriasis is a disease of 10**
- Psoriasis Area and Severity Index (PASI).

- It is an equation that measures the erythema, scaling & induration of the lesion.
- We sum the 3 measures & multiply them to the surface area involved.
- It ranges from 0-72; **anything above 10 is a severe psoriasis.**

- Physician global assessment (PGA).

Psoriasis		
0	Clear	No signs of psoriasis, but postinflammatory discoloration may be present
1	Almost clear	Only minimal plaque elevation, scaling, and erythema
2	Mild	Slight plaque elevation, scaling, and erythema
3	Moderate	Moderate plaque elevation, scaling, and erythema
4	Severe	Very marked plaque elevation, scaling, and erythema

- Dermatology life quality index (DLQI)
  - 10 questions, covering the following topics: symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, sex, treatment.
  - Each question refers to the impact of the skin disease on the patient's life over the previous week.
  - **>10 is considered severe psoriasis.**



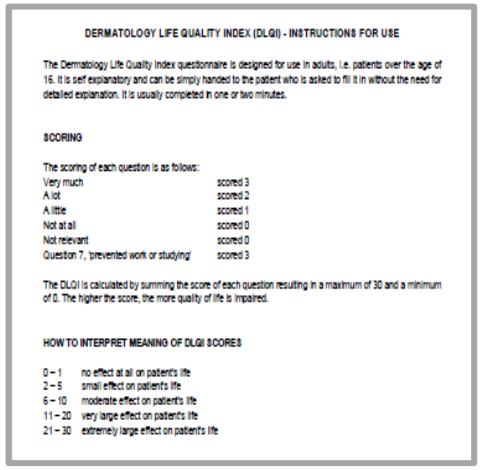
DERMATOLOGY LIFE QUALITY INDEX (DLQI)

Hospital No: ..... Date: .....
Name: ..... Score: .....
Address: ..... Diagnosis: .....

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick (✓) one box for each question.

1. Over the last week, how itchy, sore, painful or stinging has your skin been? — Very much / A lot / A little / Not at all
2. Over the last week, how embarrassed or self conscious have you been because of your skin? — Very much / A lot / A little / Not at all
3. Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden? — Very much / A lot / A little / Not at all / Not relevant
4. Over the last week, how much has your skin influenced the clothes you wear? — Very much / A lot / A little / Not at all / Not relevant
5. Over the last week, how much has your skin affected any social or leisure activities? — Very much / A lot / A little / Not at all / Not relevant
6. Over the last week, how much has your skin made it difficult for you to do any sport? — Very much / A lot / A little / Not at all / Not relevant
7. Over the last week, has your skin prevented you from working or studying? — Yes / No / Not relevant
   If "No", over the last week how much has your skin been a problem at work or studying? — A lot / A little / Not at all
8. Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives? — Very much / A lot / A little / Not at all / Not relevant
9. Over the last week, how much has your skin caused any sexual difficulties? — Very much / A lot / A little / Not at all / Not relevant
10. Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time? — Very much / A lot / A little / Not at all / Not relevant

Please check you have answered EVERY question. Thank you.



DERMATOLOGY LIFE QUALITY INDEX (DLQI) - INSTRUCTIONS FOR USE

The Dermatology Life Quality Index questionnaire is designed for use in adults, i.e. patients over the age of 16. It is self explanatory and can be simply handed to the patient who is asked to fill it in without the need for detailed explanation. It is usually completed in one or two minutes.

SCORING

The scoring of each question is as follows:

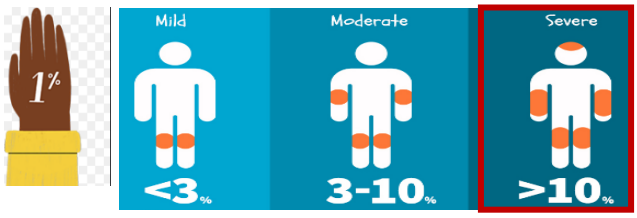
Very much	scored 3
A lot	scored 2
A little	scored 1
Not at all	scored 0
Not relevant	scored 0
Question 7, 'prevented work or studying'	scored 3

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

HOW TO INTERPRET MEANING OF DLQI SCORES

0 – 1	no effect at all on patient's life
2 – 5	small effect on patient's life
6 – 10	moderate effect on patient's life
11 – 20	very large effect on patient's life
21 – 30	extremely large effect on patient's life

- **Patient global assessment.**
  - How the patient is assessing the severity of psoriasis. For example, the patient may have psoriasis limited to his hands, but is very distressing him.
- Body surface area (BSA) affected: role of hand.
  - Hand = Equal 1% BSA **(the patient's hand).**



There are five types of psoriasis:

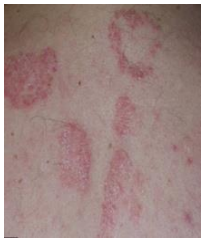
- Plaque (most common).
- Guttate.
- Pustular.
- Erythrodermic.
- Psoriatic arthritis.

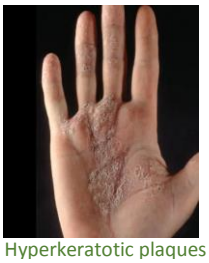
Special locations:

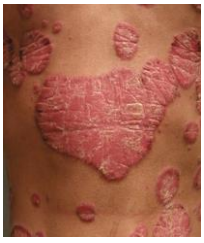
- Nail psoriasis.
- Palmoplantar pustulosis.
- Flexural psoriasis.
  - Flexures = الثنيات (ابغاكم تعرفوها).
  - Flexural areas in the body: axilla, under the breasts & the groin.
- Oral psoriasis.

- Napkin psoriasis.
- At any point of time different variants may coexist.

Chronic plaque psoriasis:



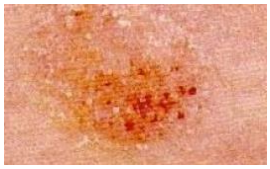


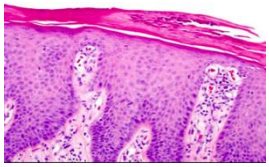


Hyperkeratotic plaques

- Characterized by sharply demarcated scaly erythematous plaques.
- Relatively symmetric distribution.
- Scalp, elbows, knees, hands and presacrum are sites of predeliction.
- When healing occurs, it starts in the center producing **annular lesions.**
- The most common type of psoriasis ranges from mild to severe.
- 65% complain of itching.
- The disease may worsen in winter improve in summer.
- The major symptom is disfigurement that affects the quality of life.
- Signs of exacerbation and unstable disease include pinpoint papules surrounding existing plaques or expansion of the lesion with more intense erythema and tenderness.
- Koebner phenomenon is positive.

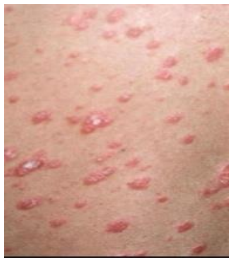
Auspitz sign is positive:





- The appearance of small bleeding points (pin-point bleeding) after removal of scale from the surface of psoriatic papules or plaques.
  - This sign is characteristic but NOT pathognomonic.
- It is a reflection of dilated vessels of the papillary dermis and thinning of the suprapapillary epidermis.

Guttate psoriasis (guttate = drop)



- Small papules over the trunk and extremities.
- Seen commonly in children and adolescent preceded by URTI.
- In over half of patients an elevated antistreptolysin O titer indicating recent streptococcal infection.

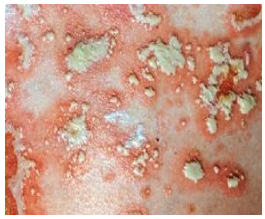
Pustular psoriasis

Generalized

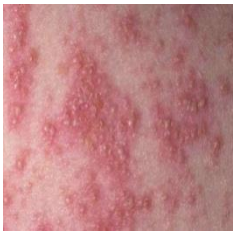
Localized

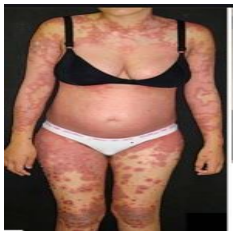
Palmoplantar pustulosis

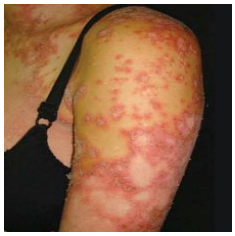
Acrodermatitis continua of hallopeau



Pustular psoriasis: Generalized





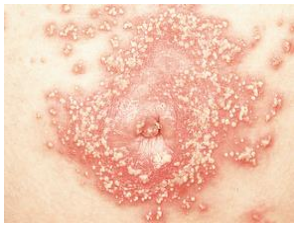


- Von Zumbusch.
- Impetigo Herpitiformis in pregnancy.

- **Generalized pustular psoriasis Von Zumbusch:**
  - Pustules over the body including nail beds, palms, soles.
  - Skin is tender and may proceed to erythroderma.

- Fever, malaise and leukocytosis occurs.
- May form annular plaques.
- Resolves with extensive scaling.
- Onycholysis, shedding of the nails and hair loss (telogen effluvium) may follow 2-3 months later.
- Tongue may show circinate desquamation.

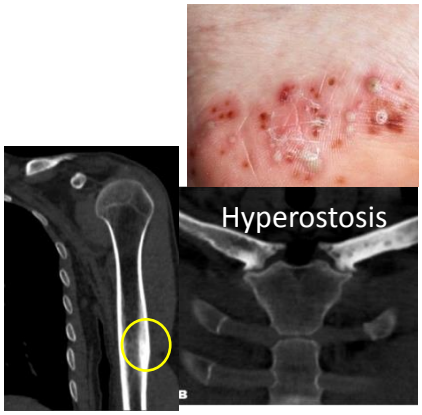
- **Generalized pustular psoriasis impetigo Herpitiformis:**
  - Acute onset of pustules with annular configuration during the third trimester associated with hypocalcemia.
    - It may start in the 1st trimester.
  - There is no personal history or familial psoriasis.



Annular pustules on the umbilicus

Localized pustular psoriasis:

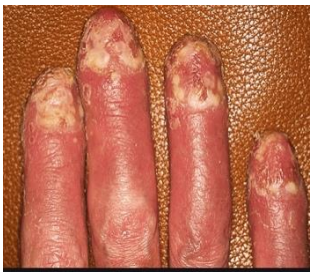
- **Palmoplantar Pustulosis.**
  - Sterile deeply-seated pustules admixed with yellow brown macules.
    - Pustules sharply localized to the palms & soles (cannot extend further).
  - Triggered by stress or infection.
  - May be associated with bone lesions SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis).
    - Hyperostosis in the medial ends of clavicle presented by tenderness. It can be erythematous & it is recurrent.
  - Minority of patients have plaque or pustular psoriasis.



Periosteal reaction indicating osteitis

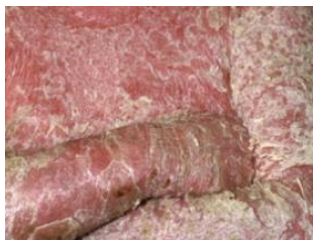
Acrodermatitis Continua of Hallopeau

- Acro = pointed ends of the body such as the nose, ears & extremities.
- Pustular eruption of distal portions of fingers or toes that extends proximally.
- Most commonly affects the thumb.
- The phalanx becomes red, scaly and studded with pustules. Later the pustules burst leaving glazed painful skin and another bout of pustules appear.
- Can result in nail dystrophy or loss of nail.

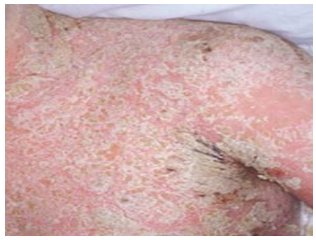


Erythrodermic psoriasis

- Erythroderma is any skin lesion that is present in ≥90% of body surface.
- Erythroderma is a descriptive term characterized by erythema & scaling that can be caused by medications, lichen planus, ectopic dermatitis as well as psoriasis.
  - How to differentiate? by ruling out previous diagnosis of psoriasis or family hx of psoriasis.
- It affects all body sites ≥90%.
- Erythema is most prominent feature with **scaling**.
- Erythroderma is a state of skin failure in which the skin loses its thermo-regulatory function & becoming poilkothermic.
- Patients suffer from hypothermia due to vasodilation.

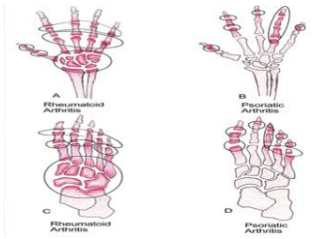


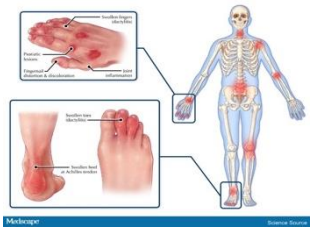
- Lower limb edema secondary to vasodilatation and loss of proteins (due to loss of keratin from the skin & it should be compensated by high protein diet).
- High-output cardiac failure and impaired liver and renal functions also occur thus it is a systemic disease.
- Onset may be gradual or acute.
- Clues to diagnosis of psoriatic erythroderma include **facial sparing** (not always but most of the cases), **characteristic** psoriatic **nail changes** and **previous plaques** in classic location.



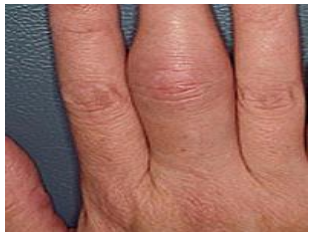
Psoriatic arthritis

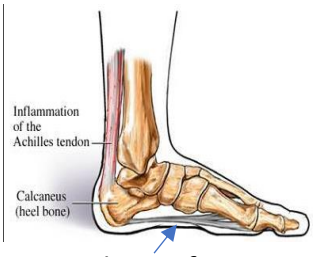
5 types:





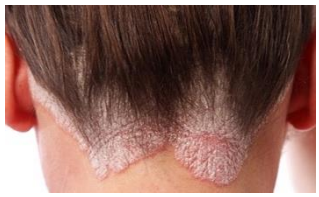
- Mono- and asymmetric oligo arthritis (oligo = 2-4).
- Arthritis of distal interphalangeal joints (a typical finding in psoriasis).
  - It can also affect the middle & proximal inter-phalangeal joints.
- Rheumatoid arthritis like.
- Arthritis mutilans; it results in deformity of the hand.
- Spondylitis and sacroilitis.
- The most common presentation is inflammation of the distal (DIP mainly) and proximal (PIP) interphalangeal joints.
- Sausage digit if both DIP&PIP affected.
- Early diagnosis is important to avoid loss of function.
- **Radiology shows:**
  - Enthesitis is inflammation of the tendon insertion points (very important to ask about joint pain to prevent loss of joint function).
  - Periosteal bone formation and erosions (the only disease that can cause **both** bone erosions & formation is psoriasis).
  - Pencil in cup deformity.

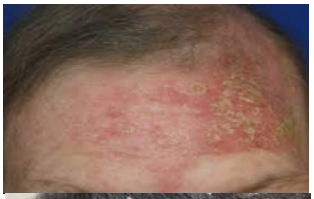


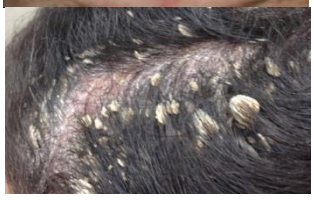


Plantar fasciitis

Scalp psoriasis





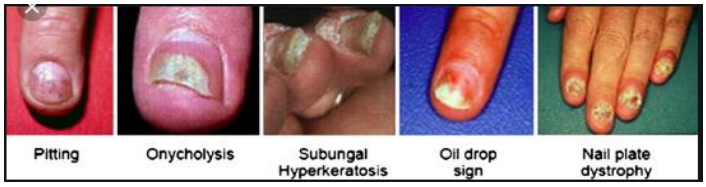


- The back of the head is a common site.
- May involve the whole scalp.
- Appears as well-defined erythematous plaques with thick **silvery** white **scale.**
- May extend beyond the hairline.
- May coexist with seborrheic dermatitis called sebopsoriasis.
  - Scales of seborrheic dermatitis is greasy yellowish scales.
- Sebopsoriasis the lesions are localized to seborrheic areas.
- Scales sometimes are asbestos like (thick) and attached to the hairs (Pityriasis amintecea).
  - Pityriasis amintecea can be seen in seborrheic dermatitis; secondary infected atopic dermatitis and T. capitis (ask about contact with animals).
  - Pityriasis amintecea in seborrheic dermatitis occurs in seborrheic areas such as the nasolabial folds, the eyebrows, behind the ears & chest.
  - In atopic dermatitis, we should ask about hand eczema.

Nail psoriasis

- Psoriatic nail disease occurs in 10-70% of all patients with psoriasis.
- Less than 5% of psoriatic nail disease cases occur in patients without other cutaneous findings.
- **Fingernails are more affected than toenails.**

- Psoriasis affects nail matrix (pitting), nailbed (oil drop) and hyponychium (subungual hyperkeratosis).
  - > 25 pits are more in favor of psoriasis.

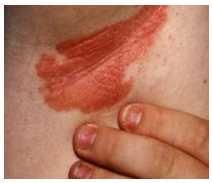


Pneumonic (STOP)

- **S**: Subungual hyperkeratosis, Splinter hemorrhage
- **T:** Thickening
- **O**: Onycholysis, Oil spots
- **P**: Pitting

Inverse psoriasis

- Psoriasis of the axilla



no scales because the area is wet

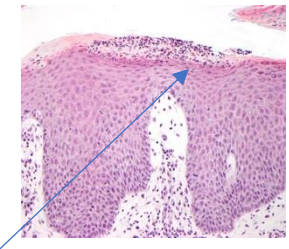
Napkin psoriasis

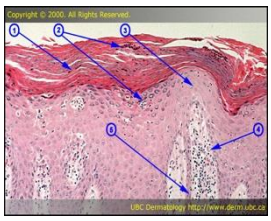
- Ddx of napkin psoriasis: irritant contact napkin dermatitis or candidal napkin dermatitis.
- How to differentiate?
  - Well-defined papules or plaques of psoriasis.
  - Erythema in psoriasis is severe (vivid color).

If you leave the area open for some time, it will show scales.

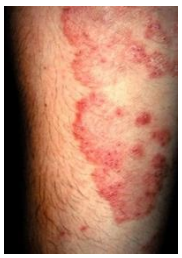
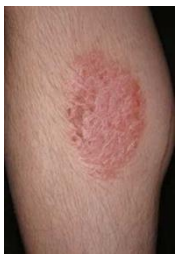
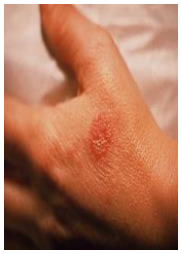
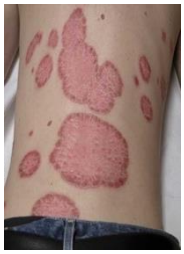
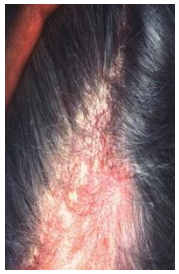
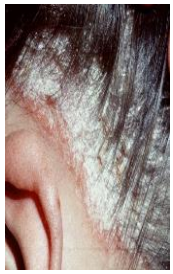
Psoriasis pathology

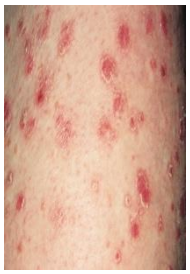
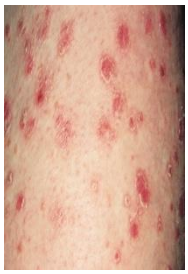
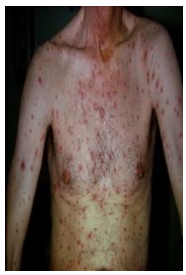
- Parakeratosis (nuclei retained in the horny layer).
  - Normally, there should be NO nuclei in stratum cornea.
  - The nuclei had no time to disappear (the turnover time of keratinocytes is shortened to 10 days in psoriatic patients).
- Irregular thickening of the epidermis over the rete ridges (to accommodate all the dividing cells) but thinning over dermal papillae
- Epidermal polymorphonuclear leucocyte infiltrates (munro micro abscesses).
  - It is neutrophils in the stratum corneum; **This is a feature of psoriasis** in which you can diagnose psoriasis once you see it.
- Dilated capillary loops in the dermal papillae.
- T-lymph infiltrate in the upper dermis.

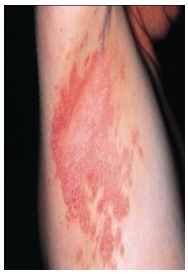
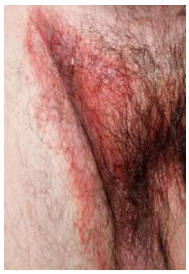
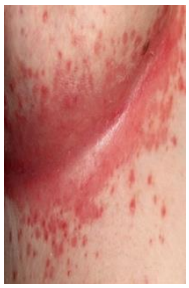
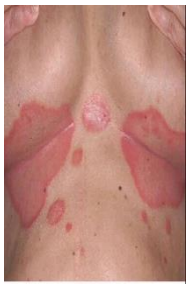


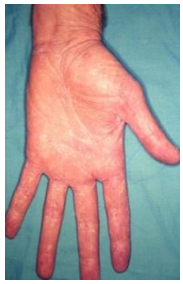
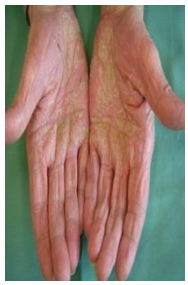
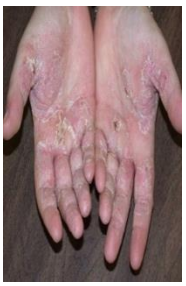
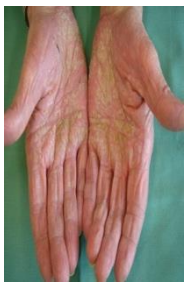
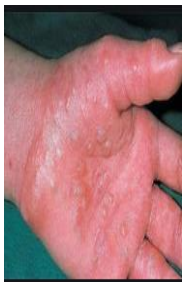
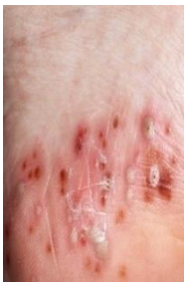


Differential diagnosis	
Localized plaques • Tinea • Eczema • Seborrhoeic dermatitis	**Flexural** • Tinea • Eczema • Candidiasis • Seborrhoeic dermatitis
Guttate • Pityriasis rosea • Drug eruption • Secondary syphilis	**Erythrodermic** • Eczema • Lichen planus • Drug
Palmoplantar • Tinea	

Localised patches/plaques		
Tinea corporis	• Affects body. • Lacks symmetrical lesions. • Presence of peripheral scale (active edge) and central clearing. • How to differentiate between this condition & annular lesions of psoriasis? The color of the psoriatic lesions is more intense. Take scales & examine it under microscope; if there are fungi, it indicates fungal infection.	 **Tinea corporis**  **Psoriasis**
Discoid eczema	• Individualized ill-defined plaques more pruritic (itchy) than psoriasis. • Lacks silvery scale. • Less vivid color than psoriasis.	 **Discoid eczema**  **Psoriasis**
Seborrhoeic dermatitis	• Characterized by yellowish greasy scaling and erythema. - Scales of psoriasis is whitish slivery scales & is usually thick. • Localized to many of the same areas as psoriasis. • Affects furrows of face. • **Generally restricted to hairline.**	 **Seborrhoeic dermatitis**  **Psoriasis**

Guttate psoriasis		
Pityriasis rosea	• Difficult to distinguish from acute guttate psoriasis. • Presents first as single large patch called herald patch. • Progresses within hours/days to a truncal rash of multiple red scaly plaques (**'Christmas tree' distribution**).	 **Guttate psoriasis**  **Pityriasis rosea**
Secondary syphilis	• Search for characteristic primary syphilitic lesion (called chancre which is an ulcer in the genital area or oral mucosa), lymphadenopathy, and lesions on face, **palm and soles (always affected).** - The palms & soles develop copper-color macules. • Conduct serology (+ve VDRL) and skin biopsies to confirm diagnosis. - Skin biopsy shows endarteritis with plasma cells.	 **Guttate psoriasis**  **Secondary syphilis**

Flexural psoriasis		
Tinea cruris	• Affects groin area. • Characterised by central clearing with advancing edge with fine scale.	 **Flexural psoriasis**  **Tinea cruris**
Candidiasis	Characteristic peripheral pustules (satellite pustules) and scaling different from psoriasis. - Lesions from candidiasis are red, glazing with no scales. But **unlike** the well-demarcated psoriatic lesions, they **are not** well-demarcated & have satellite pustules. • Yeast cultures are diagnostic.	 **Candida intertrigo**  **Psoriasis**

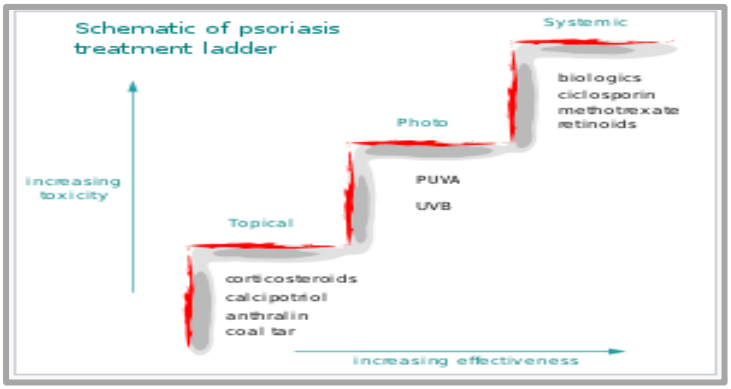
Palmoplantar psoriasis		
Tinea manum	• Fungal infection of the hand. • Ringworm of hands. • Fine powdery scale, particularly involving palms and palmar Creases. • Usually asymmetrical.	 **Tinea manum**  **Palmoplantar psoriasis**
Hand and foot eczema	• Hyperkeratotic forms difficult to distinguish from psoriasis. • Biopsies may assist diagnosis. - If there is monru micro abscess → psoriasis. • Look for history of atopy, a lack of psoriasis elsewhere on body, and evidence of eczema elsewhere on skin.	 **Hand eczema**  **Palmoplantar psoriasis**
Pompholyx of palms and soles (dyshidrotic eczema).	• The ducts of the sweat glands get obstructed due to any reason thus preventing the sweat from being excreted. • Presents as clear vesicles contrast to white/yellow pustules in pustular psoriasis. - It lacks the yellowish-brown macules seen in pustular psoriasis. • Accompanied by intense pruritus.	 **Pompholyx**  **Pustular psoriasis**

Comorbedities:

- Cardiovascular disease.
- Metabolic syndrome and its individual components (i.e., hypertension, obesity, impaired glucose regulation, and low HDL levels).
- Malignancies including lymphoma, and non-melanoma skin cancer such as basal cell carcinoma & squamous cell carcinoma (PUVA, systemic therapy).
- Autoimmune diseases (e.g., inflammatory bowel disease, multiple sclerosis).
- Psychiatric conditions including anxiety and depression.

Treatment:

Topical	Biologic therapy	Phototherapy	Systemic
• Corticosteroids. • Vitamin D analogs. • Retinoids. • Calcineurin inhibitors. • Anthralin. • Coal tar.	• TNF inhibitors: adalimumab, Etanercept, Infliximab • IL-12/IL-23: ustekinumab.	• UVB • UVA • PUVA	• Acetretin. • MTX (methotrexate). • Cyclosporin.



Psoriasis topical therapy	
Topical Corticosteroids	**-Indication:** Plaque psoriasis <10 %. **-Dosing**: monotherapy 1-2 times daily. -Combined with other topical agents, UV light, and systemic agents. -Toxicity of topical steroid: • Local—skin atrophy, telangiectasia, striae, purpura, contact dermatitis, rosacea/acne if used on the face. • Systemic—HPA axis suppression may occur with use of medium- and high-potency topical steroids causing Cushing syndrome, DM or HTN. This will be lessened by intermittent or localized use. • Increased IOP, glaucoma, and cataract have been reported with use around eye.
Vitamin D analogues	**Indication:** Plaque-type psoriasis. **Dosing:** Twice daily. Calcitriol, calcipotriol, tacalcitol, maxacalcitol are used. Combination of calcipotriene and betamethasone ointment available. **Adverse reactions:** • Transient irritation in lesional and perilesional skin. • Elevation of serum calcium more likely to occur in patients treated with > 100 g/wk in adults and >50 g/wk in children. • Photosensitivity.

	• Since calcipotriene is inactivated by UVA, it is important to apply calcipotriene **after and not** before UVA exposure.
TAZORETENE Vitamin A analogues	• Best used in combination with topical corticosteroids. Once daily for 12 weeks. • Probably best reserved for thick, recalcitrant plaques of psoriasis. **Adverse reactions:** • Skin irritation in lesional and perilesional skin. • Photosensitizing. • Pregnancy and nursing: Category X.
Calcinurin inhibitors (tacrolimus and pimecrolimus)	**-Indication:** Intertriginous and facial psoriasis to avoid using steroids on the face because of its side-effects (acne/rosacea/eye complications). **-Side effects:** stinging, burning, itching. - Better not used below 2 years of age.
Anthralin	**Indications:** Use has been declined these days. **Dosing:** short-contact therapy for 2h once dialy. • 2% dithranol in Lassar's paste applied for 2 h once daily recommended as optimal for home use. Adverse reactions: skin irritation and staining of skin and clothing.

Psoriasis systemic therapy			
Agent		**Administration (route; frequency)**	**Side effects**
Acitretin	Vitamin A derivative (retinoid); has immunomodulatory and anti-inflammatory activity and modulates epidermal proliferation and differentiation.	Oral; once daily.	• Mucocutaneous changes; hypertriglyceridemia, elevated LFT. • Enhanced efficacy when combined with UVB/ PUVA. • Pregnancy category X.
Cyclosporine	Calcineurin inhibitor; blocks inflammatory cytokine production and T-cell activation.	Oral; twice daily.	• Nephrotoxicity, hypertension. - HTN secondary to cyclosporine is treated only by calcium-channel blockers (nifedipine); other classes of anti-hypertensive medications increase the toxicity of cyclosporine. • Limited duration of continuous treatment (1 year). • Risk of skin cancer if history of PUVA. • Reversible changes in serum lipids. • Pregnancy category C (it can be used in pregnant women, but you have to weigh the risk against benefits).

Methotrexate	Competitive inhibitor of dihydrofolate reductase; interferes with nucleic acid synthesis, thereby inhibiting lymphoid proliferation.	Oral, SC, or IM; once weekly.	• Myelosuppression, hepatotoxicity, pulmonary fibrosis. - You have to monitor the liver & bone marrow. • Parenteral administration may minimize GI side effects. • Folate supplementation may be recommended. • Pregnancy category X (can NOT be used).

Psoriasis systemic therapy:

- **Retinoids /Acitretin:**
  - VIT A analogue.
  - Inhibits abnormal keratinization.

Indication:

- Severe plaque type psoriasis.
- HIV-positive patients with severe psoriasis.
  - Why used for HIV patients? It works only on keratinocytes & their differentiation & has no role in the immunity.
- 10-75 mg/d given as a single dose.
- The preferred schedule is acitretin monotherapy for 2 weeks followed by the addition of phototherapy.

Adverse events:

- Dry eyes and lips, lipid derangements, pancreatitis, hyperostosis, pseudotumor cerebri, hepatotoxicity, and teratogenicity (**only female**:3 years for wash out).

- **Methotrexate**:
  - Folic acid antagonist blocks dihydrofolate reductase leading to inhibition of folic acid metabolism.
  - Antiproliferative, induces apoptosis and an immune and anti-inflammatory modulator.

Indication:

- Severe, recalcitrant, disabling psoriasis not adequately responsive.
- Often used as the primary agent to treat psoriatic arthritis.

Dosing:

- Weekly single oral dose, 7.5-25mg weekly oral/IM.
- Low-dose folate supplementation may reduce the hematologic, GI, and hepatic side effects of methotrexate without decreasing the efficacy.

Absolute contraindications:

- Pregnancy.
- Nursing mothers.
- Alcoholic liver disease or other chronic liver disease.
- Immunodeficiency syndromes.
- Bone-marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia.

Relative contraindications:

- Abnormalities in renal function.
- Abnormalities in liver function.
- Active infection (because it's an immune modulator).
- Obesity.
- Diabetes mellitus.

Toxicity of methotrexate:

- Elevated LFT results - Minor elevations of LFT results are common; if elevation exceeds 2x normal, must check more frequently; if exceeds 3x normal, consider dose reduction; if exceeds 5x Discontinue.
- Anemia, aplastic anemia, leukopenia, thrombocytopenia.
- Interstitial pneumonitis or lung fibrosis.
- Ulcerative stomatitis. GI ulceration and bleeding.
- Nausea, vomiting, diarrhea.
- Malaise or fatigue, dizziness.
- Chills and fever.
- Decreased resistance to infection.
- Alopecia.
- Pregnancy: category X; **men and women** considering conception should be off methotrexate for 3 months before attempting to conceive.

How to monitor for methotrexate induced liver fibrosis:

- Procollagen 3 N terminal peptide (P3NP) unreliable in PsA (psoriatic arthritis).
  - High level of P3NP in a blood sample indicates underlying fibrosis.
- Transient elastography (fibroscan).
  - US shows elastic tissue of the liver.
  - A result of F2/F3 indicates underlying fibrosis.
- MRI elastography.
- Liver biopsy. High risk and low risk?
  - High risk: diabetes, liver disease, obesity & alcohol.
  - In high risk patients, baseline liver biopsy should be done & repeated when the dose is 1-1.5 g.
  - While in low risk patients, liver biopsy is done when the dose 3.5-4 g **only if needed.**

- **Cyclosporin:**
  - Inhibits calcineurin phosphorylation.
  - 2 to 5mg/kg/day for 12 to 24 weeks (maximum) to limit cumulative nephrotoxicity.
    - Shows quick improvement of the condition.

Indication:

- Erythrodermic psoriasis, Generalized pustular psoriasis, and Palmoplantar psoriasis, Severe recalcitrant plaque psoriasis.
  - In other words, we use cyclosporin for severe entities of psoriasis.
- Do baseline creatinine **repeat twice.**
- Monitor creatinine **(very important).**
  - **If increased by 30% or less, you should decrease the dose by 1 mg.**
  - **If increased by >30%, you should discontinue the medication.**
- Monitor blood pressure for secondary HTN.

Toxicity:

- Renal impairment (Acute, chronic).
- Hypertension.
- **Malignancies**.
- Lymphoproliferative.
- Headache, tremor, paresthesia.
- Hypertrichosis.
- Gingival hyperplasia.
- Worsening acne.
- Nausea/vomiting/diarrhea.
- Myalgias.
- Flu-like symptoms.
- Lethargy.
- Hypertriglyceridemia.
- Hypomagnesemia.
- **Hyperkalemia**.
- Hyperbilirubinemia.
- Increased risk of infection.
- May increase risk of cancer.

Drug interactions:

- Inducers/inhibitors of cytochrome P450 3A4.
- Cyclosporine may reduce clearance of digoxin, colchicine, prednisolone, statins (increased risk of rhabdomyolysis).
- Potassium-sparing diuretics cause hyperkalemia (spironolactone must NOT be given).
- Thiazide diuretics increase nephrotoxicity.
- Grapefruit juice (increases toxicity of cyclosporine).

- **Phototherapy**
  - Broadband ultraviolet B: 290-313 nm.
  - Narrowband ultraviolet B: 311 nm.
  - PUVA (psoralen ultraviolet A): 320-400 nm.
    - Psoralen is an oral medication taken 2 hours before being exposed to UV light.
    - Psoralen stays in the blood for 8 hours at least thus patients have to wear goggles even after the session to protect the eyes.
    - Side-effect of psoralen: gastric upset, patient should avoid sunlight for the whole day after receiving the treatment.
  - NB-UVB most commonly used due to: easier use, and fewer side effects when compared with BB-UVB or PUVA.
  - NBUVB leads to rapid clearance of lesions than BB-UVB.

Indications:

- Unresponsive generalized psoriasis/chronic plaque psoriasis (including guttate and seborrhoeic).
- May aggravate psoriatic erythroderma and generalized pustular psoriasis.
- Contraindications: Patients with known LE (lupus), H/O melanoma or NMSC (non-melanoma skin cancer).

Mode of action NBUVB:

- Locally immunosuppressive.
- Inhibition of epidermal hyperproliferation and angiogenesis.
- Selective reduction in T lymphocytes within psoriatic skin via apoptosis.

Toxicity of NBUVB:

Acute:

- Erythema, pruritus, burning, blister (NBUVB).

Long term:

- Photoaging, lentigines, telangiectasias, cataract (especially patients using psoralen).
- Theoretical risk of cancer. However numerous studies have failed to show photocarcinogenesis.
- Advise use of protective goggles and genital shields during treatment.
- NB-UVB therapy should be considered first-line therapy in pregnant patients with plaque and guttate psoriasis who need systemic therapy.
- Can be used with emollients, topical corticosteroid or VIT D analogues or systemic treatment like retinoids and MTX.

PUVA mode of action:

- Has effects on epidermal keratinocytes and **Langerhans cells** (antigen-presenting cells) (similar to UVB irradiation).
- Has effects on dermal cells including granulocytes and T Lymphocytes.
- Psoralen intercalates between DNA base pairs and, on exposure to UVA, forms psoralen DNA cross-links that prevent DNA replication.
- Death of antigen presenting cells.
- Dosing: 8-MOP (Methoxypsoralen) 0.4-0.6 mg/kg, taken 1-2 h before exposure to UVA. Treatment 2-3 times/wk

- UV protective eye wear when outdoors for 12 hrs post ingestion.
- Combination therapy such as calcipotriol, retinoids is safe but not with **cyclosporin as the risk of squamous cell carcinoma increases.**
  - Patients who are receiving more 200 sessions of PUVA are at risk of skin cancer.

Topical PUVA:

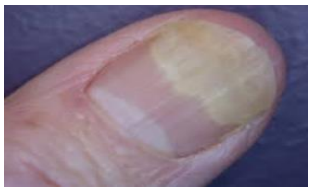
- For localized psoriasis to palms and feet.
- Use 0.1% 8-methoxypsoralen in emollient and treat 2-3 /wk.
- Apply 30 min before UVA.
- Bath PUVA-50 mg of 8-Methoxypsoralen in 100 L of water, 20-30 min pre-exposure.

Toxicity of PUVA:

Acute:

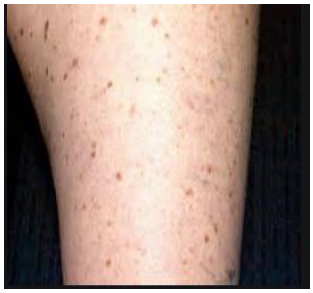
- Nausea and vomiting are common.
- Dizziness and headache are rare.
- Burns & erythema: peaks at 48-96 h (in UVA) while in narrowband in 8 hours (UVB).
- Pruritus.
- Tanning: starts 1 wk after PUVA.
- Blisters, photo-onycholysis, melanonychia.

Melanonychia



Chronic:

- Photocarcinogenesis (SCC, BCC, and possible melanoma).
- Increased risk of photocarcinogenesis Caucasians with skin types I-III after 200 treatments; this risk not present for non-Caucasians.
- Photoaging and lentigines are common, especially in patients of skin types I-III and are cumulative UVA dose dependent.



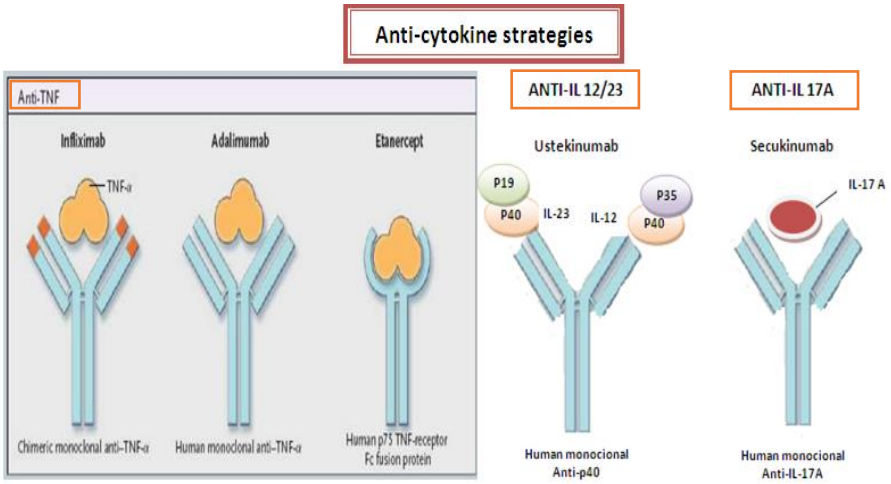
Excimer laser

- Used for resistant localized psoriasis such as scalp and palmoplantar psoriasis.

New oral medications:

- **Apremilast:**
  - Is a phosphodiesterase 4 (PDE4) inhibitor.
  - Promotes **anti-inflammatory processes.**
  - Used for moderate-to-severe plaque psoriasis.
  - 30 mg BID for 16 weeks.
  - Adverse events: nausea, diarrhea, nasopharyngitis, headache, suicidal thoughts, depression.

Biologic therapy



Indications of biologics:

- Severe disease: Psoriasis Area Severity Index (PASI) score of 10 or more (or a body surface area (BSA) of 10% or greater) AND a Dermatology Life Quality Index (DLQI) of >10.
- Phototherapy and alternative standard systemic therapy are contraindicated or cannot be used.
- Unresponsive to standard systemic therapy.

- **Complete blood cell count including platelet count.**
- **Liver function tests.**
- **Renal panel.**
- **Hepatitis panel.**
- Tuberclin test or **Quantiferon Gold assay** (especially for anti-TNF to exclude TB).
- **HIV.**
- **Pregnancy test.**
- **Avoid vaccination with live vaccines** (varicella; mumps; measles; rubella; oral typhoid; yellow fever).
- **Avoid live-attenuated vaccines** (including intranasal influenza and the herpes zoster vaccine).

Biologic therapy:

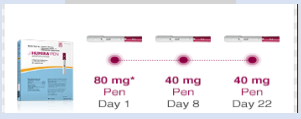
Target key parts of immune system that drive psoriasis.

Biological agents include:

- Tumor necrosis factor-α inhibitors:
  - Etanercept.
  - Adalimumab.
  - Infliximab.
- Non TNF inhibitors-α inhibitors:
  - Interleukin (IL-12 / IL-23) inhibitor (Ustekinumab).
  - Interleukin (IL-17) inhibitor (Secukinomab).

Contraindications:

- Patients with active, serious infections.
- New York Heart Association class III or higher congestive heart failure.
- History of demyelinating disease (e.g. multiple sclerosis).
- Serious hematologic disease (e.g. aplastic anemia).
- **Current** malignant tumor or **prior** malignant disease.
- Immune-compromised by congenital or acquired immunodeficiency syndrome.

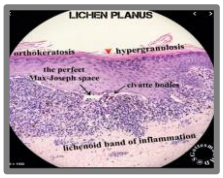
TNF inhibitors	Dose	Side effects
Etanercept Moderate-to-severe psoriasis	**1st Line therapy** 50 mg twice/week given **SC** x 3 months followed by 50 mg once/week.	• Mildly pruritic injection site reactions. • Rare cases of serious infections (i.e., TB) and malignancies. - Flare up of TB even if quantiferon is normal. - Patients with +ve quantiferon are referred to ID clinic for INH prophylaxis.
Adalimumab 	**1st Line therapy** Induction dose: 80 mg at the start and 40 mg at week one. Then maintenance dose: 40 mg every other week. • **SC.**	• Mildly pruritic injection site reactions • Rare cases of serious infections (i.e., TB) and malignancies.

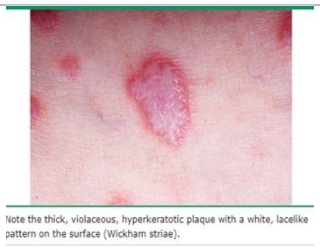
Infliximab Severe psoriasis	5 mg/kg at weeks 0, 2, and 6 weeks then every 8-week intervals to maintain disease control up to 1 year **(IV).** • Only one given IV & the patient should be admitted.	• Infusion reactions and rare cases of **serious infections (i.e. TB)** and malignancies including hepatosplenic T-cell lymphoma (in children). • There are rare reports of drug-induced, reversible side effects including lupus without renal, or CNS complications.
Biologic	**Dose**	**Side effect**
Secukinomab Selectively binds and neutralizes interleukin (IL) 17-A Moderate-to-severe plaque psoriasis	Second-line biologic therapy 300 mg SC injection with initial dosing at weeks 0, 1, 2, and 3 followed by 300 mg every 4 weeks.	• Nasopharyngitis, Diarrhea, URTI, Candida infections (localized mucosal, or cutaneous) • Good therapeutic option in patients with **PsA and who are at increased risk of TB.**
Ustekinumab Prevents the interaction of IL12 /IL23 with their cell surface receptors, blocking Th-1/IL12 and Th-17/IL23 pathways	Second-line biologic therapy for psoriasis 45 or 90 mg SC at week o and 4 then every 12 weeks.	• Lower SAE rates, and lower infectious and serious infectious compared to the TNF antagonists • Good therapeutic option in patients with latent TB.

Summery:

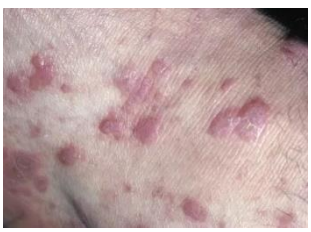
- Psoriasis is a common chronic inflammatory skin.
- It is a complex immune-mediated disease. Multiple genes have been associated with susceptibility to psoriasis.
- Chronic plaque psoriasis, the most common form of psoriasis. the scalp, extensor elbows, knees, and gluteal cleft are common locations for chronic plaque psoriasis. Other major subtypes include guttate, pustular, and erythrodermic psoriasis.
- Individuals with psoriasis are at risk for psoriatic arthritis and multiple other comorbidities such as obesity, metabolic syndrome, hypertension, diabetes, and atherosclerotic disease.

Lichen planus الحزاز المسطح:

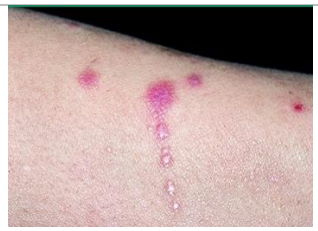




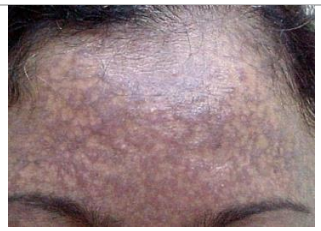
Classical



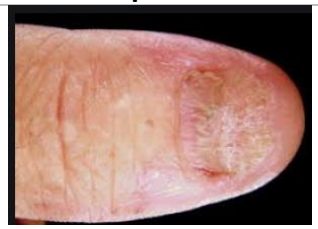
Classical



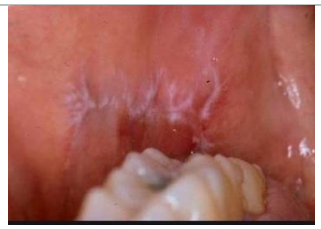
Koebner phenomenon



Variants



Nail LP



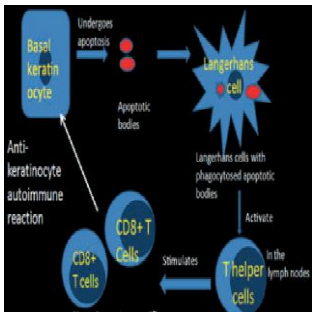
Oral

- An idiopathic inflammatory disease of the skin and mucous membranes.
  - If there is an underlying cause, it is called lichenoid reaction.
- Classic LP is characterized by pruritic, violaceous papules that favor the extremities.
  - 5 P's of lichen planus: papule, pruritic, polygonal, planar (flat-topped) & purple (violation).
- The onset of LP occurs most commonly during the 5-6th decade. 2/3rd of patients developing the disease between the ages of 30 and 60 years.
- Increased prevalence of Hepatitis C.
- Exposures to infections (hepatitis c), trauma (koebnerization), drugs, and contact allergens (amalgum) as well as autoimmune disorder have been proposed as contributing factors in genetically proposed individuals.

Causes:

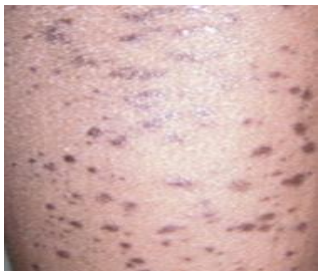
- Idiopathic complex polygenic condition.
- Genetic predisposition:
  - Six single nucleotide polymorphism (SNPs) were found to be associated with HLA-DQB1*05:01 Haplotype associated with LP.
  - (HLA-A5, HLA-A3, 147,148, HLA-B7,143, HLA-DR1, 149,150 in the Arab population).
- Pathogens.
- Liver disease like sclerosing colangitis, chronic liver disease, Hepatitis C or biliary cirrhosis.
- Vaccination and drugs (IF, Antimalarials).
- Contact sensitizer (mercury amalgam, color film developers, methylacrylic esters).

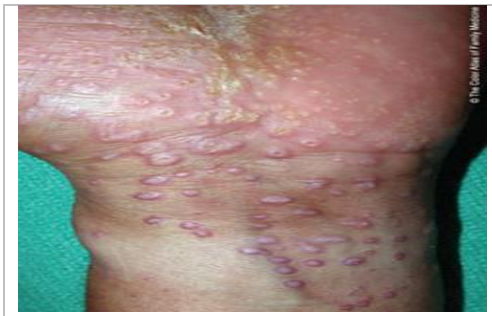
- The etiology of lichen planus is unknown.
- An immune-mediated mechanism involving activated T cells, particularly CD8+ T cells (cytotoxic cells which will kill the keratinocytes), directed against **basal keratinocytes** has been proposed.
- Upregulation of intercellular adhesion molecule-1 (ICAM-1) 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.



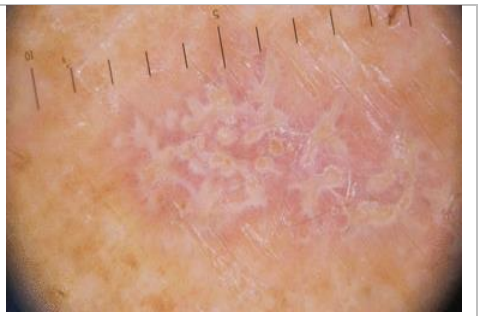
Clinical presentation of lichen planus:

- The extremities, **particularly the ankles and the volar surface of the wrists, are common sites** for cutaneous involvement.
- Lesions heal with **post-inflammatory hyperpigmentation** (it is deep thus may take years to disappear, thus you need to hit hard from the beginning to avoid it).





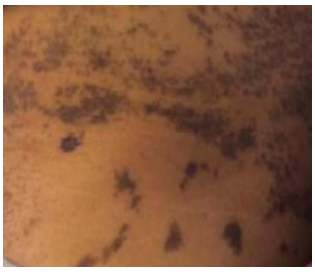
Flat topped polygonal violaceous papules



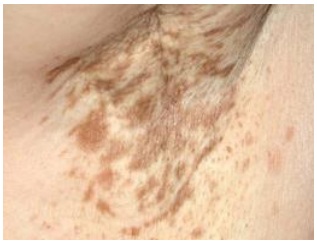
Dermoscopy showing Wickham's striae (WS)

Clinical Variants of lichen planus:

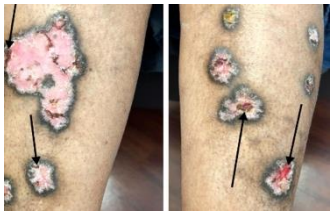
- **Lichen planus pigmentosus**
  - Presents with gray-brown or dark brown macules or patches (has NO papular element before) that are most commonly found in sun-exposed or flexural areas (if happens in the flexures, it is called lichen planus inversus).
  - Pruritus is minimal or absent.
  - The term "lichen planus pigmentosus-inversus" is used to describe patients with primarily flexural involvement.

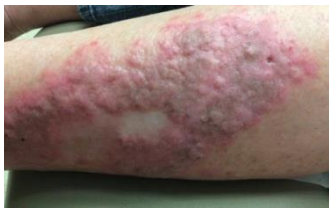


- **Inverse lichen planus**
  - Characterized by flat-toped erythematous to violaceous papules and plaques in intertriginous sites, such as the axillae, inguinal creases, inframammary area, or limb flexures.
  - Associated (post-inflammatory) hyperpigmentation is common.

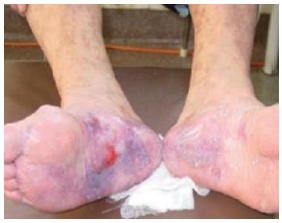


- **Hypertrophic lichen planus**
  - Characterized by intensely pruritic, flat-topped plaques (the lesions are hypertrophic).
  - Involving typically the anterior lower legs.
  - Cutaneous squamous cell carcinoma has been reported in patients with longstanding hypertrophic lichen planus lesions.

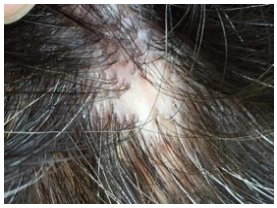




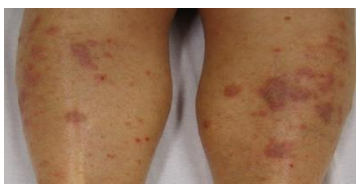
- **Additional variants include**
  - Palmoplantar lichen planus (a variant that may demonstrate ulceration).
    - It may cause blisters.
  - Perforating lichen planus.

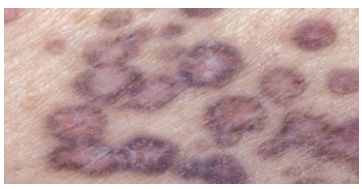


- **Lichen planopilaris (follicular lichen planus)**
    - Pilar means hair follicles.
  - The scalp is the classic site for lichen planopilaris.
    - It causes scarring alopecia; you have to hit hard in such cases. otherwise, the involved area becomes fibrotic.
  - However, other body sites, particularly in patients with the Graham-Little-Piccardi-Lasseur syndrome (GLPL).
  - GLPL presents with:
    - Multifocal cicatricial alopecia of the scalp.
    - Non-cicatricial (scarring) alopecia of axilla and groin.
    - Follicular lichen planus eruption on the body, scalp, or both.

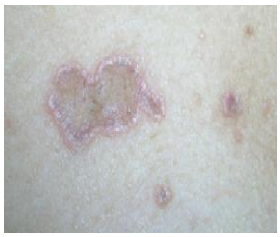


- **Atrophic lichen planus**
  - Violaceous, round or oval, atrophic (depressed) plaques.
  - The legs are a common site of involvement.

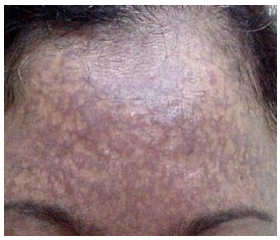




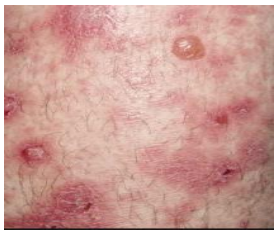
- **Annular lichen planus**
  - Characterized by the development of violaceous plaques with central clearing.
  - The penis, scrotum, and intertriginous areas are common sites of involvement.
  - Annular lesions may occur in other areas.
  - Central atrophy may be present.

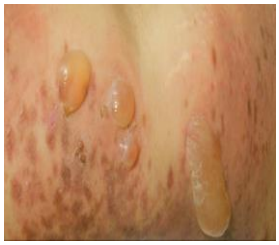


- **Actinic lichen planus** (actinic = photodistributed)
  - known as lichen planus tropicus, presents with a photodistributed eruption of hyperpigmented macules, violaceous or annular papules, or plaques.
    - Photodistribution areas are the face, neck & upper trunk.
  - Most commonly seen in the Middle East, India, and east Africa.



- **Bullous lichen planus**
  - Vesicles or bullae within the sites of existing cutaneous lichen planus lesions.
    - Appear on **diseased skin** but NOT normal skin.
  - The legs are a common site of lesion development.

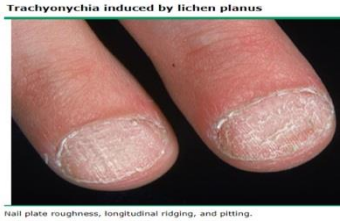




- **Nail lichen planus:**
  - Longitudinal ridging.
  - Fissuring.
  - Pterygium.
  - Thinning
  - 20 nail dystrophy/syndrome (when both fingernails & toenails are affected).
  - When nails are involved, the disease spectrum varies from minor dystrophy to total nail loss
  - The disease process in lichen planus of the nails primarily occurs in the nail matrix.

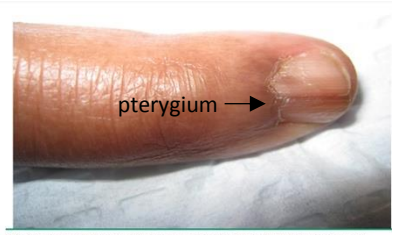
Lichen planus of the nail may present with nail plate thinning, longitudinal ridging (trachyonychia), fissuring, and rarely, pterygium. Nail plate thinning and longitudinal ridging are visible on this patient's nails.

Fissuring



Nail plate roughness, longitudinal ridging, and pitting.

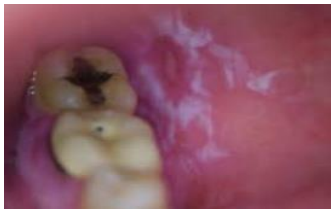
Trachyonychia (roughness of the nail)

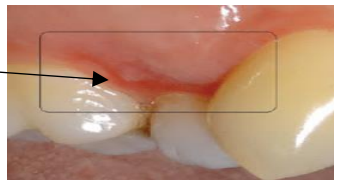


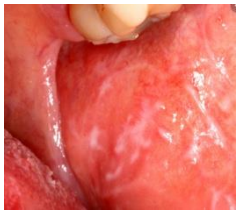
The proximal nail fold is adherent to the nail bed (pterygium). Longitudinal melanonychia (brown bands in the nail plate) is also present.

Pterygium (when proximal nail fold progress/adheres into the nail)

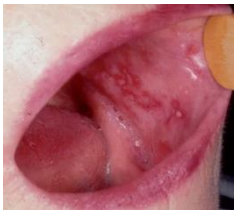
- **Oral lichen**
  - Lichen planus of the mucous membranes can occur in conjunction with cutaneous disease or independently.
  - Mucous membrane disease may consist solely of lacelike Wickham's striae (reticular type)/white patches that are particularly evident on the buccal mucosa.
  - Papular.
  - Atrophic may lead to (desquamative gingevitis)
    - Other ddx: configus vulgaris, Bullous pemphigoid, contact allergens.
  - Erosive lesions.



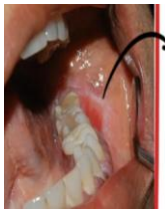




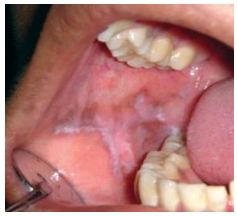
Lace like

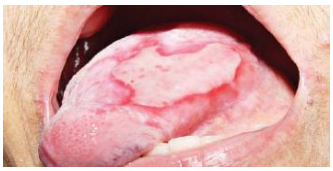


Ulcerative LP



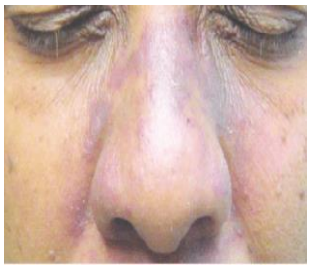
Atrophic erythematous



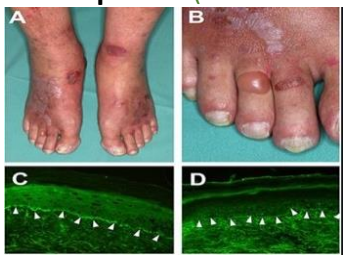


- **Overlap syndromes:**
  - Are disorders that are characterized by the presence of features of cutaneous lichen planus and a second disease.
  - Lichen planus pemphigoides and lichen planus-lupus erythematous overlap syndromes.

- **Lichen planus-lupus erythematosus overlap syndrome**
  - Rare condition, patients develop skin lesions with clinical, histologic, and/or immunopathologic features of both diseases.
  - Clinically, patients often present with **discoid lupus erythematosus** or malar erythema and cutaneous lichen planus.



- **Lichen planus pemphigoides overlap syndrome**
  - Patients develop **bullae in normal appearing skin and on top of lesions of lichen planus** (abnormal lesion).
    - The presence of both the bullae & lichen planus lesions means it is NOT a pure lichen planus.
  - Similar to bullous pemphigoid, direct immunofluorescence studies of LPP demonstrate linear deposition of **IgG and C3 at the dermal-epidermal junction.**
  - The natural history of most cases of cutaneous lichen planus is to remit within one to two years in up to two thirds of patients.
  - Oral, genital, scalp, and nail lichen planus tend to be more persistent.



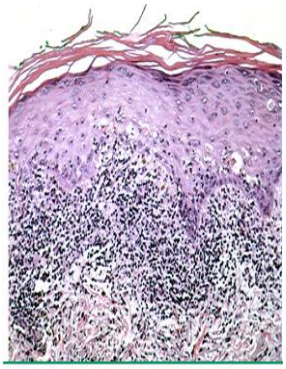
Complication of lichen planus:

- Squamous cell carcinoma in oral erosive LP & hypertrophic LP.
- Scaring alopecia in lichen planopilaris.
- Post inflammatory hyperpigmentation.

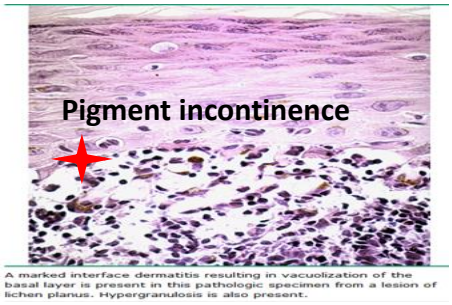
Histopathological features:

- Hyperkeratosis (thickening of stratum corneum) without parakeratosis.
- Vacuolization of the basal layer.
- Civatte bodies (apoptotic keratinocytes) in the lower epidermis.
- Wedge-shaped hypergranulosis, "saw-tooth" shaped rete ridges.

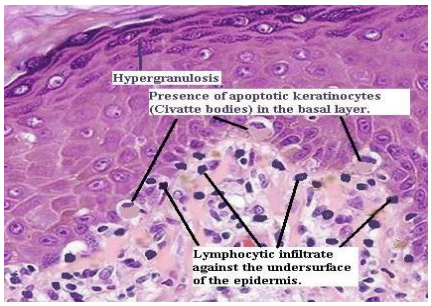
- Small clefts at the dermal-epidermal junction (Max-Joseph spaces).
  - This separation is caused by liquefactive degeneration resulting in bullae formation.
- Band-like lymphocytic infiltrate at the dermal-epidermal junction.
- Eosinophilic colloid bodies (apoptotic keratinocytes) in the papillary dermis.
- Pigment incontinence (most prominent in dark-skinned individuals).
  - Because the melanosomes are phagocytosed by melanophages.



This specimen from a lesion of cutaneous lichen planus demonstrates a band-like lymphocytic infiltrate, saw-tooth rete ridges, multiple apoptotic keratinocytes, and wedge-shaped hypergranulosis.



A marked interface dermatitis resulting in vacuolization of the basal layer is present in this pathologic specimen from a lesion of lichen planus. Hypergranulosis is also present.

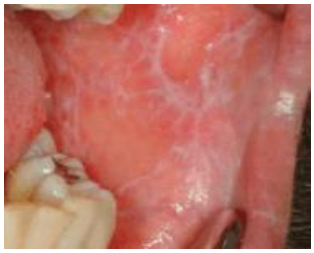
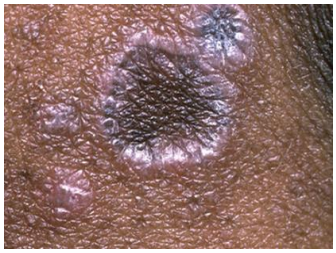
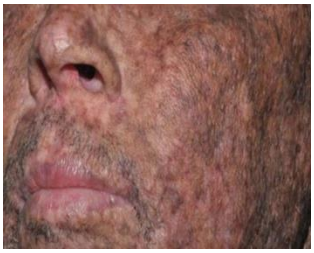


Differential diagnosis:

- Lichenoid drug eruption (drug-induced lichen planus) should always be considered so that the offending agent can be withdrawn when possible.
  - Always take history of medications in patients with lichen planus because it is difficult to differentiate between drug-induced & classic lichen planus except pathologically (there will be eosinophils in drug-induced).
- The cutaneous manifestations closely resemble idiopathic lichen planus.
- The patient's history of drug exposure and a skin biopsy can aid in distinguishing lichenoid drug eruptions from idiopathic lichen planus.
- Lichenoid drug eruptions usually develop insidiously and can affect any area of the body surface.

Group of drug	
Antimicrobial substances	Aminosalicylate sodium, ethambutol, griseofulvin, ketoconazole, streptomycin, tetracycline, trovafloxacin, isoniazid
Antihistamines (H_2-blocker)	Ranitidine, roxatidine
Antihypertensives/antiarrhythmics	**ACE-inhibitors** (captopril, enalapril), doxazosin, **beta blockers** (propranolol, labetalol, sotalol), **methyldopa**, prazosin, nifedipine, **quinidine**
Antimalarial drugs	**Chloroquine**, **hydroxychloroquine**, quinine
Antidepressives/antianxiety drugs/antipsychotics/anticonvulsants	Amitriptyline, carbamazepine, chlorpromazine, levomepromazine, methopromazine, imipramine, lorazepam, phenytoin
Diuretics	**Thiazide diuretics** (chlorothiazide and hydrochlorothiazide), furosemide, spironolactone
Antidiabetics	Sulfonylureas (chlorpropamide, glimepiride, tolazamide, tolbutamide, glyburide)
Metals	**Gold salts**, arsenic, bismuth, mercury, palladium, lithium
Nonsteroidal-antiinflammatory drugs (NSAIDs)	Acetylsalicylic acid, benoxaprofen, diflunisal, fenclofenac, flurbiprofen, ibuprofen, indomethacin, naproxen, sulindac
Proton pump inhibitors	Omeprazole, lansoprazole, pantoprazole
Lipid lowering drugs	Pravastatin, simvastatin, gemfibrozil
Tumor necrosis factor-alpha antagonists	Infliximab, adalimumab, etanercept, lenercept

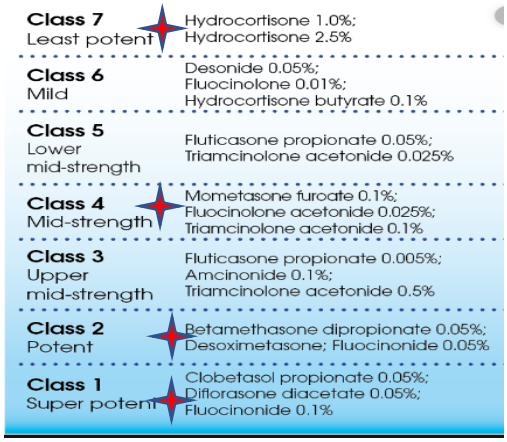
- **Chronic graft-versus-host disease:**
  - Chronic graft-versus-host disease can produce a lichenoid eruption with clinical and histologic findings similar to lichen planus. The history of preceding hematopoietic cell transplant is helpful for diagnosis.

Lichen planus treatment:

Treatment: The standard therapies include topical, intralesional, systemic corticosteroids, phototherapy, retinoids.

- Topical corticosteroids
  - Are the mainstay of treatment for patients with localized disease. Efficacy should be assessed after two to three weeks.
  - Cutaneous lesions on the trunk and extremities use a high potency or super high potency topical corticosteroid (eg, 0.05% betamethasone dipropionate).
  - For intertriginous or facial skin, mid-potency or low-potency corticosteroid creams or ointments should be used.



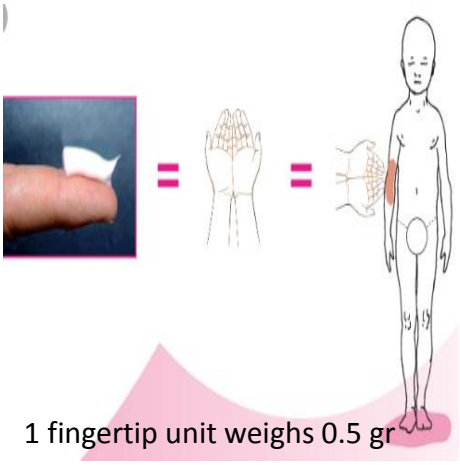
Golden role for topical steroid usage:

- For thick skin use potent to super potent.
- For thin skin like eyelids use least potent.
- Maximum use of steroid is 2 weeks.

Side effects of topical steroid:

Side effects of Topical Steroids

Striae	Contact dermatitis
Telangiectasia	Tachyphylaxis
Stellate pseudoscars	Facial hypertrichosis
Hypopigmentation	Folliculitis
Fragile skin, purpura	Miliaria
Impaired wound healing	Increased susceptibility to bacterial fungal and viral inf.
Steroid dependency	Perioral Dermatitis
Glaucoma and cataract	Rosacea
Atrophy	

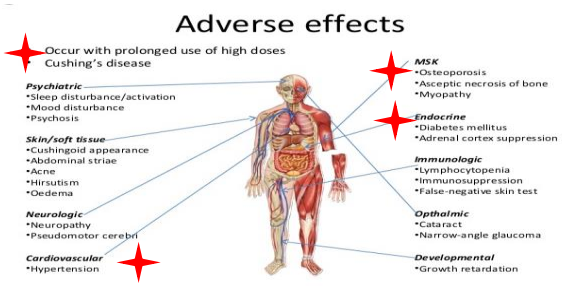


Tachyphylaxis = loss of response to corticosteroids.

- **Oral glucocorticoid**
  - Short course of an oral glucocorticoid when acute control of cutaneous lichen planus is necessary for patients with extensive disease.
  - Continued, long-term treatment with systemic glucocorticoids is less favorable due to the serious side effects associated with long-term therapy.
  - 30 to 60 mg daily for **four to six weeks** followed by a **taper** of the dose to discontinuation over the next **four to six** weeks.

- **Intralesional corticosteroids**
  - For the thick lesions of hypertrophic lichen planus.
  - Triamcinolone acetonide in a concentration of 2.5 to 10 mg/mL.
  - Repeated after four to six weeks.

Side effects of systemic corticosteroids:



- **Phototherapy**
  - Narrowband UVB (three times per week for six weeks).
  - The frequency of narrowband UVB treatment once an adequate response is achieved is tapered. If no response is observed after three to four months, discontinue treatment.
  - PUVA.

Contraindication to phototherapy

- Xerodema pigmentosum.
- Systemic lupus erythematosus.
- History of skin cancer.

Acitretin.

- **Other treatments**
  - Oral antihistamines (eg, Hydroxyzine hydrochloride 10 to 50 mg four times a day, as necessary) to control pruritus.
  - Other medications that have been reported to be of benefit in some patients with cutaneous lichen planus include:
  - Methotrexate, Thalidomide, Cyclosporin, Dapsone/sulfasalazine, Hydroxychloroquin, Mycophenolate mofetil.

Genital lichen planus

- Topical corticosteroids or topical calcineurin inhibitors are often used in the treatment of genital lichen planus.

Lichen planopilaris

- The treatment of lichen planopilaris (LPP) can be difficult.
- Topical corticosteroids or intralesional corticosteroids are often used as first-line therapies.

Oral lichen planus

- High potency topical corticosteroid. Applied 3-4 times/ day using a fingertip or Q-tip. As symptoms improve, the frequency of application is reduced as tolerated.
- Dry the affected areas (with gauze) prior to application.
- Eating or drinking should be avoided for at least 30 minutes after application.

Topical calcineurin inhibitors

- Pimecrolimus 1% and Tacrolimus 0.03, 0.1% are effective for oral LP.
- Used in same way as corticosteroid.

Side effects:

- Burning sensation.

Oral elixirs or suspensions

- 5 mL dexamethasone [0.5 mg/5 mL] used as a mouth rinse up to six times per day) for patients with widespread oral disease and who have difficulty applying topical corticosteroids to the affected areas.
- Intralesional steroid (painful) in concentrations between 10 and 40 mg/mL.

Side effects:

- Oropharyngeal candidiasis is a common side effect. Can be prevented or treated with antifungal therapy.

Topical cyclosporine

- Topical cyclosporine (5 mL of a 100 mg/mL solution, swished for five minutes and then spit) three times daily.

Pain management

- Nonsteroidal anti-inflammatory agent or actaminophen.
- Intraoral topical anesthetics (viscous lidocaine 2% solution, lidocaine 2% gel) before meals.
- Potential risks of topical anesthetics include systemic absorption with potential toxicity and suppression of gag reflex with increased risk of aspiration.

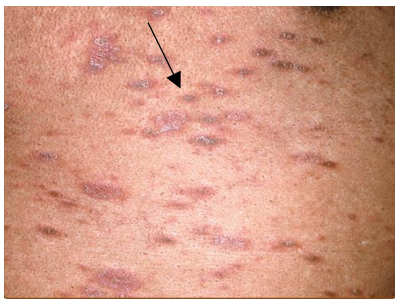
Nonpharmacologic

- Minimize Exposure to factors that exacerbate the disease (acidic, salty, spicy, hot, sharp, or rough foods).
- Maintenance of good oral hygiene.
- Elimination of mechanical irritation from dental restorations, appliances, or sharp teeth.
- Avoidance of trauma (eg, chewing on lips or mucosa).
- Cessation of smoking.

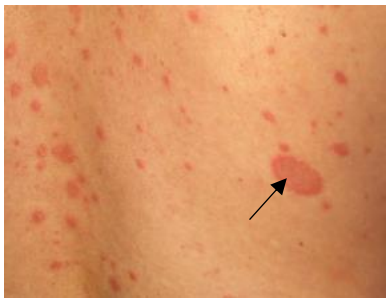
Summery

- Lichen planus may affect the skin, nails, or mucous membranes.
- Typically presents as pruritic, polygonal, violaceous papules and/or plaques with an overlying white, lacelike pattern (Wickham's striae).
- May also present with hypertrophic or vesicobullous lesions.
- Lichen planopilaris affects the scalp and can lead to scarring alopecia.
- Significant post-inflammatory hyperpigmentation is common.
- Further studies are necessary to determine if HCV screening should be performed in patients with lichen planus.
- High potency topical corticosteroids as initial treatment of localized cutaneous lichen planus on the trunk or extremities.
- Patients with widespread cutaneous disease may benefit from phototherapy, acitretin, or a short course of systemic glucocorticoid therapy.

Pityriasis rosea النخالة الوردية:



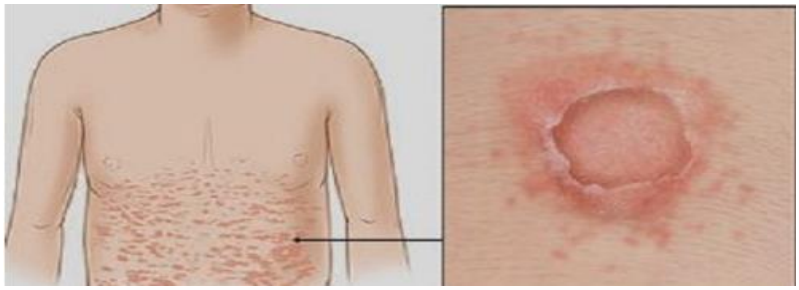
Colarette scale



Herald patch

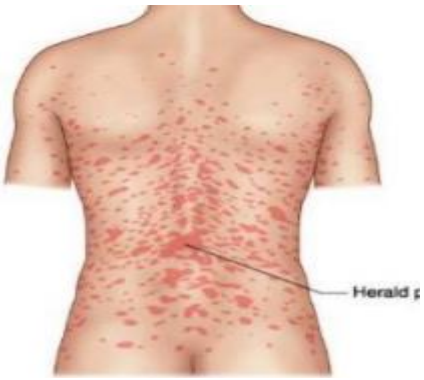
- Distributed bilaterally over trunk and proximal extremities in christmas tree pattern.
  - The long axis of the lesion follows the langer's lines.
- Common, "acute", self-limited (lasts for 2 months) papulosquamous eruption that favors healthy adolescents and young adults.
  - Classical lesion: erythematous papules with Colarette scale.
- The classic presentation is readily recognized.
- Generally, it only appears once throughout life.
- Atypical forms may present a greater challenge.
- Persistent PR up to 6 months.
- Relapsing PR: 5%, mild shorter course, few attacks over 3-5 years.
- A viral etiology has been postulated, but this remains unproven.

- Seasonal variation.



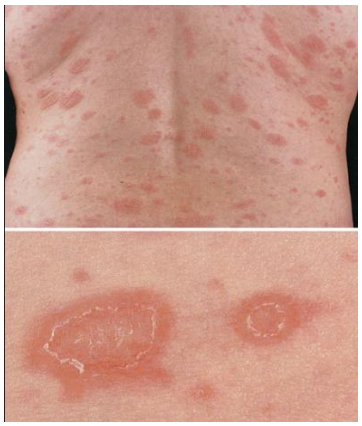
Pathogenesis:

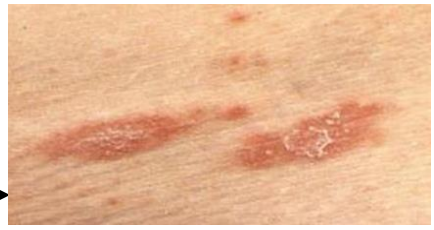
- The precise cause of pityriasis rosea unknown.
- A viral etiology is frequently proposed.
- Human herpesvirus-7(HHV-7) and, less so, on HHV-6.
- Attempts to identify HHV-7 DNA within cutaneous lesions have been unsuccessful.



Clinical presentation

- Most patients with pityriasis rosea are asymptomatic.
- However, 25% of patients, pruritus ranges from mild to severe.
- Mild prodrome with headache, malaise, fever, arthralgia in 5% of patients.
- The classic situation, a solitary lesion "herald patch" appears on the trunk and enlarges over several days.
- Less often, this initial lesion is seen on the neck or proximal extremities.
- It predates the remainder of the eruption by hours to days.
- The herald patch incidence varies from 12% to 94%, but in most series, it has been seen in over 50% of cases.
- Multiple herald patches have also been reported.
- The herald patch is a skin- to pink- to salmon-colored patch or plaque with a slightly raised advancing margin.
- The size of herald patch varies from 2-4 cm, but it can be as small as 1 cm or large as 10 cm.
- Within the next few days, there is a blossoming of lesions on the trunk and proximal extremities.
- The lesions are usually round to oval papules or plaques, with their long axis following Langer's lines of Cleavage, characteristic collarette scale.
- On the posterior trunk, the lesions show a "fir tree" or "Christmas tree "pattern.
- Minute pustules can also be seen during this initial phase of pityriasis rosea.
- The face, palms and soles are usually (but not always) spared.
- Oral lesions are uncommon.
- The eruption of pityriasis rosea usually persists for 6–8 weeks and then spontaneously resolves; however, occasional patients have lesions that may last 5 months or longer.
- In the latter situation, the possibility of pityriasis lichenoides chronica arises. Almost same presentation as pityriasis rosea but the duration differs.

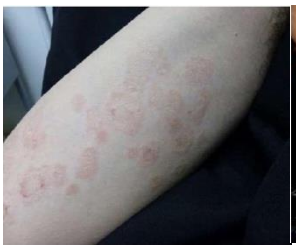


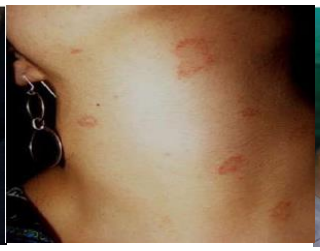


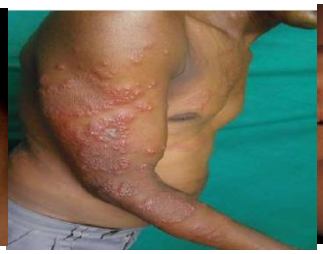
Atypical forms of pityriasis rosea

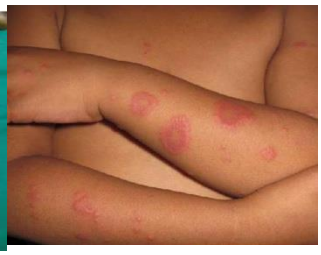
Lacks herald patch, different morphology (purpuric, targetoid) and distribution (inverse over axilla, groin, distal extremities)

- Inverse.
  - Involves the axillae and inguinal areas and sometimes the face.
  - It is more common in younger children and in those with darkly pigmented skin.
- Urticarial.
- Erythema multiforme like (Targetoid).
- Vesicular.
- Pustular.
- Purpuric.

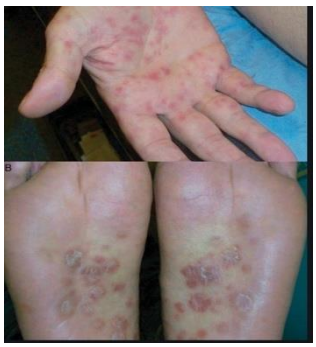

Urticarial


Purpuric

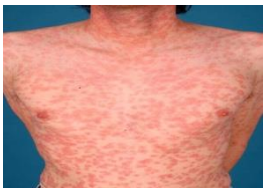

Vesicular


Erythema multiform like (targetoid)

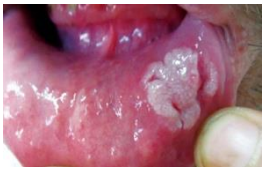
Differential Diagnosis:



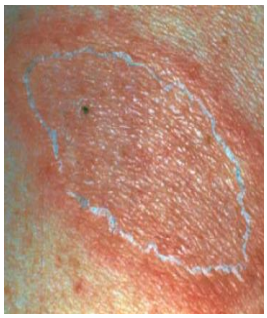
- **Secondary syphilis:**
  - Meticulous history taking, history of chancre, lymphadenopathy.
  - Lesions are monomorphous and always asymptomatic; almost always affect palms and soles.
  - Positive VDRL test.
  - Histology showing plasma cells.

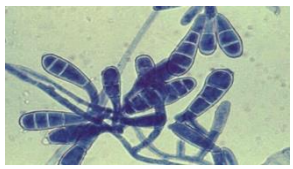


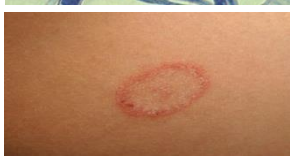

Condyloma lata


Condyloma lata

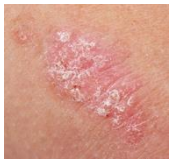
- **Dermatophytosis:**
  - Difficult to differentiate from herald patch. However, a mycotic lesion expands progressively and shows a clear center (activity in the periphery).
  - Positive KOH mount.

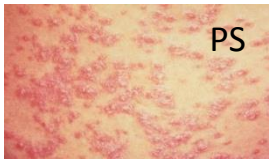


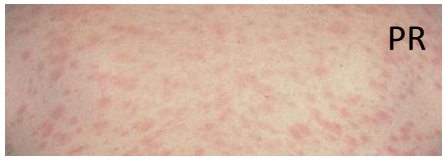




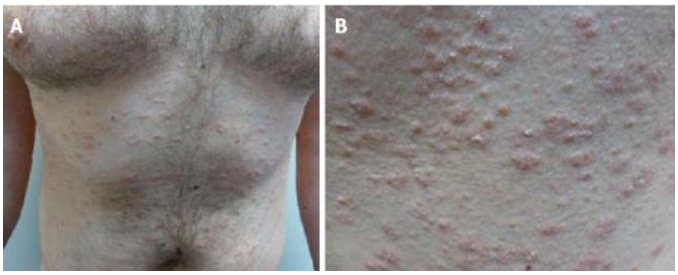
- **Guttate psoriasis:**
  - History of sore throat.
  - Presence of rain-drop pattern and histology are important clues.
  - Scales are thicker and silvery-white.

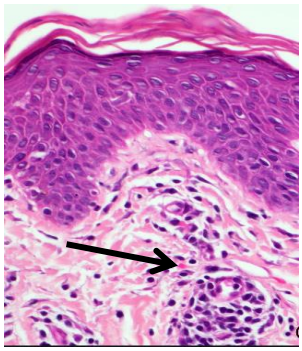






- **PR like drug eruption:**
  - Ac converting enzyme (ACE) inhibitors, metronidazole, isotretinoin, gold, arsenic, non-steroidal anti-inflammatory, terbinafin, omeprazole, bismuth, imatinib and clonidine, as well as etanercept, tripelennamine, ketotifen, salvarsan and BCG vaccine.
  - The lesions are usually monomorphic and **lack herald patch.**
  - Slower to resolve than the idiopathic form.





- Most patients with pityriasis rosea don't have biopsies because the clinical picture is characteristic, and the histopathology is relatively nonspecific.
- Small mounds of parakeratosis, spongiosis (epidermal edema), and a mild lymphohistiocytic perivascular and interstitial papillary dermal infiltrate.
- There may be mild erythrocyte extravasation.

Treatment:

- Because pityriasis rosea is often asymptomatic and self-limited, patient education and reassurance is sufficient.
- Symptomatic treatment with antihistamines and topical steroid.
- NBUVB.
- Acyclovir 400mg TDS x7 days. When to use?
  - Persistent PR.
  - Relapsing PR.
  - PR occurring in the 1st trimester of pregnancy.
- Short course oral steroids in severe cases.

Questions:

1- Which of the following is the primary lesion for lichen planus?

A. Papule
B. Nodule
C. Pustule
D. Macule

2- Pityriasis rosea is (associated) caused by reactivation of?

A. herpes 1
B. herpes 2
C. herpes 6
D. herpes 8

3- Most common nail change in lichen planus

A. Pitting
B. Oil drop
C. Longitudinal striations
D. Subungual hyperkeratosis

4- 30 years old male presents with multiple silvery white scaly plaques on his extensors. Which of the following is a common associated manifestation?

A. nephritis
B. Arthritis
C. Conjunctivitis
D. Interstitial pneumonitis

5- A skin lesion with a change in color and is more than 1 cm without elevation is called:

A. Papule
B. Macule
C. Plaque
D. Patch

6- which one type of psoriasis is considered serious or emergency?

A. Erythematous psoriasis
B. Pustular psoriasis
C. Psoriasis vulgaris
D. Guttate psoriasis

7-Which of the following organs is affected the most when using Cyclosporine as treatment for psoriasis?

A) Liver
B) Brain
C) Kidney
D) Heart

8- A 30 y/o male presented to you with multiple well-defined flat topped violaceous polygonal papules and plaques crossed with fine white lines over the trunk and extremities. What is your diagnosis?

a) Psoriasis
b) Lichen planus
c) Pityriasis rosea
d) Atopic dermatitis

9- Continued use of methotrexate will mostly likely cause damage to which of the following?

a) Liver
b) Kidneys
c) Joints

10- Elevated lesion less than 0.5cm what is the name of this lesion?

a) Macule
b) Patch
c) Papule
d) Plaque

11- What's the most common type of psoriasis

a) Plaque psoriasis
b) Erythrodermic Psoriasis
c) Pustular psoriasis
d) Plantopalmar Psoriasis

12- Pityriasis rosea is associated with which one of the following?

a) Herpes 1
b) Herpes 2
c) Herpes 7
d) Herpes 8

13- Which one of the following is present in nail lichen planus?

A- Splinter hemorrhage.
B- Oil drop.
C- Pterygium.
D- Clubbing.

14- Which one of the following is associated with lichen plans?

A- Hepatitis C.
B- HIV.
C- HPV.
D- HHV.

15- What is the clinical term that describes the presence of nucleated cell in the stratum corneum seen is psoriasis?

A- Parakeratosis.
B- Hyperkeratosis.
C- Acanthosis.

16- Old Patient who is in renal dialysis which one of the following is contraindication to give?

A- Cyclosporine.
B- Methotrexate.
C- Retinoid.

17- Erosive lichen planus has a risk of causing which of the following?

A- basal cell carcinoma
B- Squamous cell carcinoma

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
A	C	D	B	D	B	C	B	A	C	A	C	C	A	A	A	B