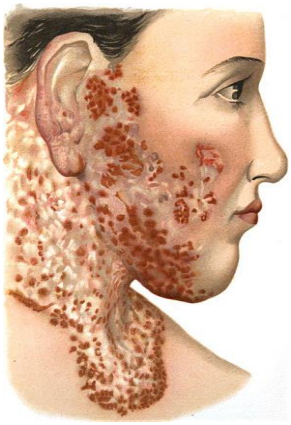
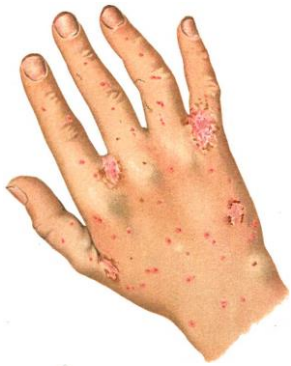
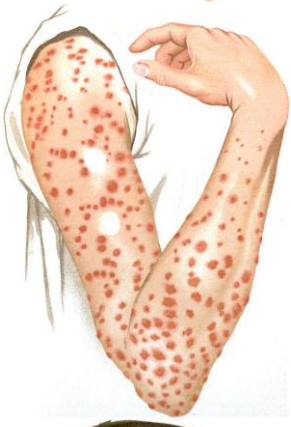
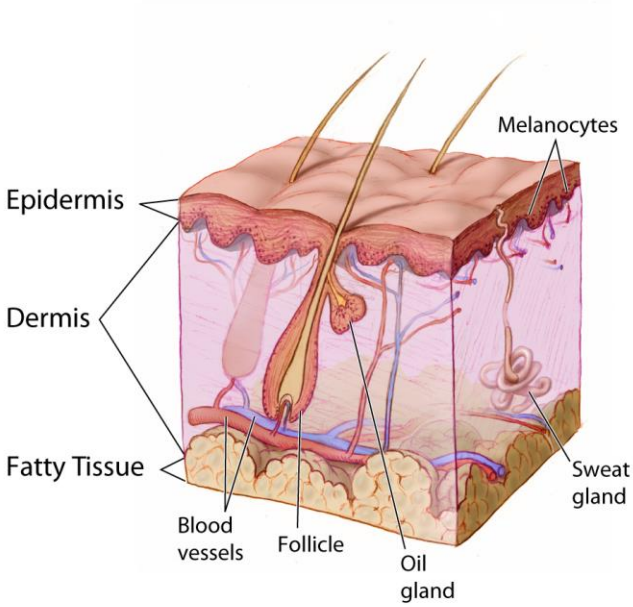
جامعة الملك سعود
King Saud University







432 Teams
Dermatology



Papulosquamous disease

Color Code: Original, Team's note, Important, Doctor's note, Not important, Old teamwork

Done by: ***Khalid*** *Alomar*

Reviewer: ***Ibrahim S. Abunohaiah***

Team Leader: ***Basil Al Suwaine***

13

Objectives

1- Define the papulosquamous disease.

2- Highlight on the pathogenesis of papulosquamous diseases.

3- Discuss the clinical features of papulosquamous diseases.

4- Highlight on the papulosquamous diseases treatment.

Headings:

1. **Psoriasis**
2. **Lichen Planus**
3. **Pityriasis Rosea**
4. **Seborrheic Dermatitis**
5. **Pityriasis Rubra Pilaris**
6. **Secondary Syphilis**
7. **Miscellaneous Mycosis Fungoides, Discoid Lupus Erythematosus, Ichthyoses**

Papulosquamous disease

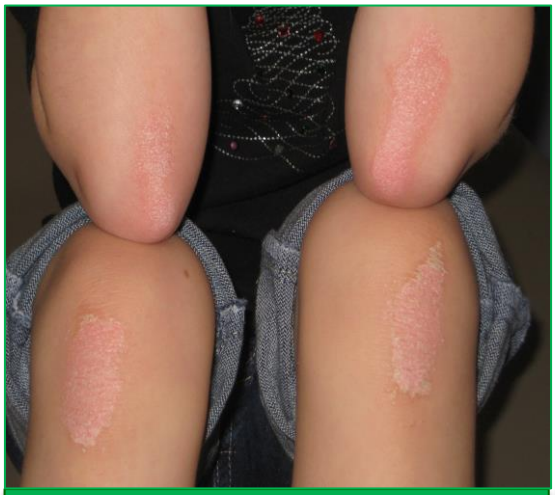
- The term *squamous* refers to **scaling** that represents thick stratum corneum and thus implies an **abnormal keratinization process**. (Papules + Scale)

↑ Production of keratinocytes or ↑ shedding

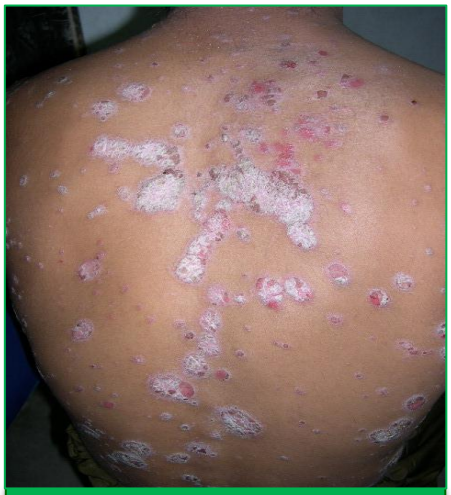
1. Psoriasis: (increased production)

- Psoriasis is a common, **chronic**, non-infectious, inflammatory skin disease.
- It affects the skin and joints.
- It causes rapid skin cell reproduction resulting in **red**, **dry patches** of thickened skin.

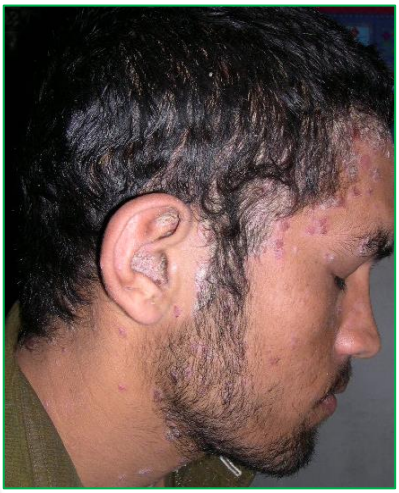
- The treatment improves some of the clinical presentation with no 100 % cure!)
- It can also affect the eye, GI & Liver but with lower incidence compared to the Skin & Joints.

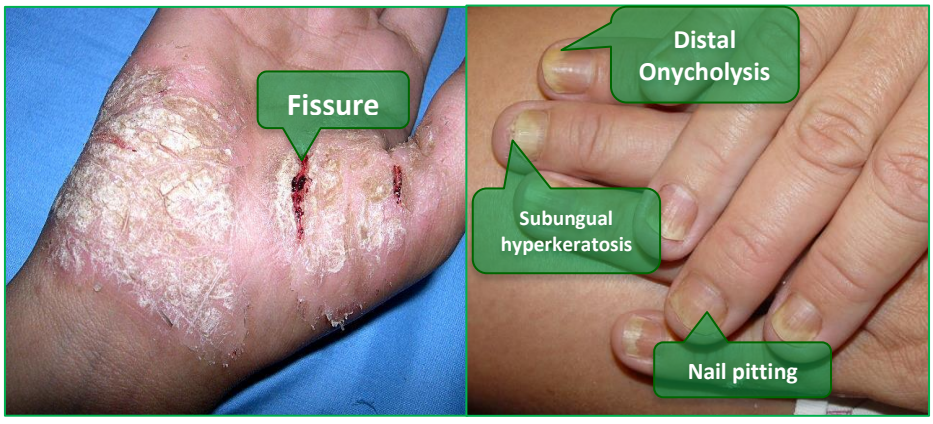


Bilateral, symmetrical, well-defined, regular, erythematous, scaly, plaques on elbows and knees.



Well-defined, generalized, dull red, scaly, papules and plaques on the back.





Fissures are an additional feature of the Psoriasis in the Palms & Soles. It develops because the palms and soles already have a thick skin, when Psoriasis occurs in it (in a thick skin) the scales accumulate; and with recurrent mechanical movements of the hands or soles the fissures develop!

- The thickest skin is in the Palms & Soles while the thinnest is in the eyelids.
- **Distal Onycholysis:** Is the separation of the distal nail plate from the nail bed.
- **Subungual hyperkeratosis**: Is scales under the nail plate.

Incidence and etiology:

- The cause of psoriasis is still **unknown**
- 1-3% (underestimate)
- F:M = 1:1
- Any age (two peak of onset) (2nd decade and around 60)
- **Race:** any race; however, epidemiologic studies have shown a higher prevalence in western European and Scandinavian populations. No case report in the Red Indians (Almost None!)

Pathogenesis:

- Exact cause is **unknown!**
- **Multifactorial causes:**

1) Genetic factor:

- Psoriasis is a multifactorial disease with a complex genetic trait.
- There are two inheritance modes:
  a- One has onset in **younger age** with family history of PS
  b- The other has onset in **late adulthood** with **NO** family history of PS
    - One affected parent……..16%
    - Both parents……..50%
    - Non-Psoriatic parents with affected child…..10%
    - Monozygotic Twins……..70%
    - Dizygotic twins……20%
    - At least 9 loci have been identified (psors-1 to 9)

2) Epidermal cell kinetics:

- The growth fraction of basal cells is increased to almost 100% compared with only 30% in a normal skin. (increase amount of production)
- The epidermal turnover time is shortened to less than 10 days compared with 30 to 60 days in normal skin. (fast production)

3) Inflammatory factors:

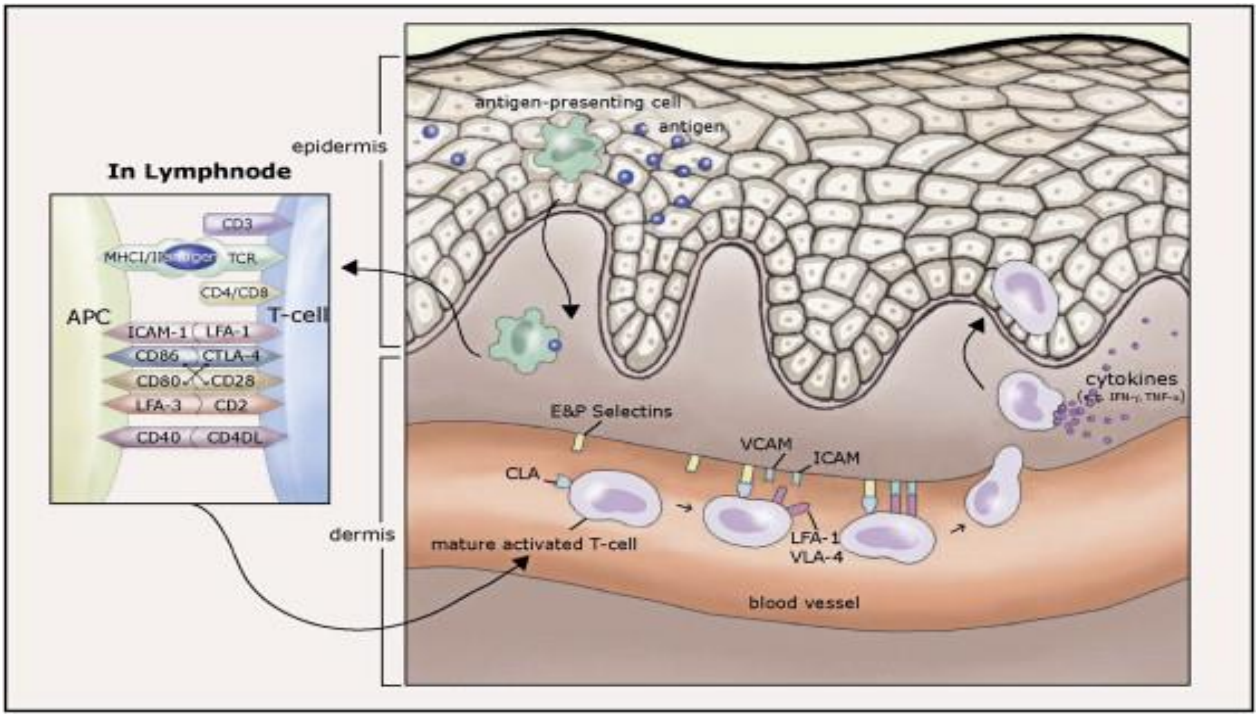
- Increase level of TNF
- TNF receptors are up-regulated
- Increase level of interferon gamma
- Increase level of interleukin 2, 12, 23 and **17**

Immunological factors:

Psoriasis is fundamentally an inflammatory skin condition with reactive abnormal epidermal differentiation and hyper proliferation.

The inflammatory mechanisms are:

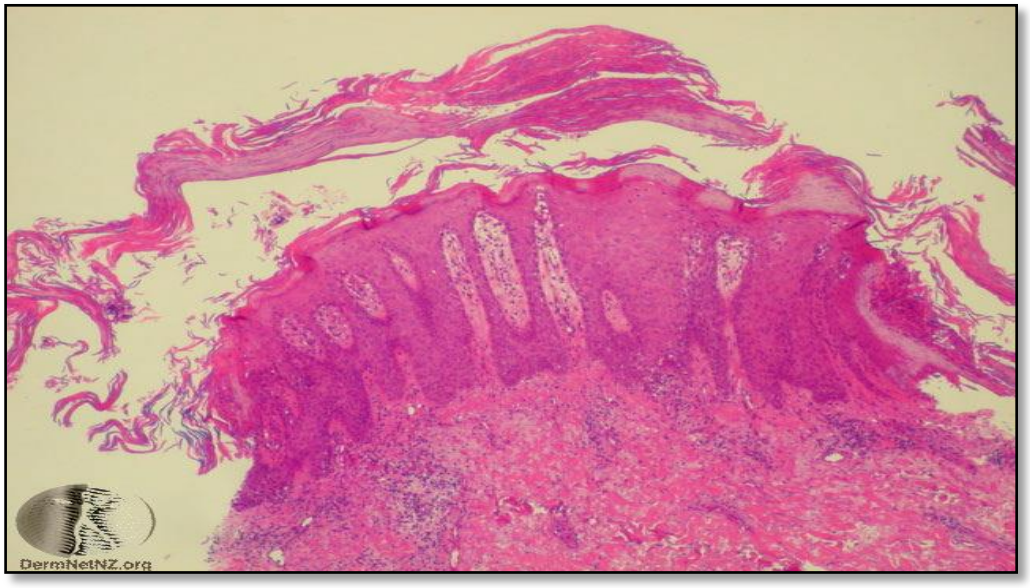
- Immune based and most likely initiated and maintained primarily by T cells in the dermis.
- Antigen-presenting cells in the skin, such as Langerhans cells.
- T-cells.
- Auspits sign.



5- Environmental factors: Triggers

- Infection (streptococcal infection) (in Guttate Psoriasis)
- Physical agents (e.g., stress, alcoholism, smoking)
- Koebner phenomenon appearance of the skin disease at site of Trauma! This phenomenon supports the immunological theory of Psoriasis!
- Drugs (lithium, anti-malarial drugs, NSAIDs and beta-blockers)

Histology:



- **Parakeratosis** (nuclei retained in the horny layer)
  Normally when the cells reach to the the horny layer it becomes **Anucleated** but in *Psoriasis* due to the rapid division of cell the cells in the horny layer retain some of its organelles including its nucleus.
- Irregular thickening of the epidermis over the rete ridges but thinning over dermal papillae. Auspit sign: when you remove the scales, a pinpoint bleeding occurs.
- Epidermal polymorphonuclear leucocyte infiltrates (Munro abscesses)
  - **Epidermo-Tropism** is the process when the neutrophils migrate from the Dermis to the Epidermis **(MCQ).**
  - If the neutrophils migrate and accumulate it will result in the formation of Micro-abscesses called Munro Abscesses.
- Dilated capillary loops in the dermal papillae.
- T-lymph infiltrate in the upper dermis.

Types of Psoriasis:

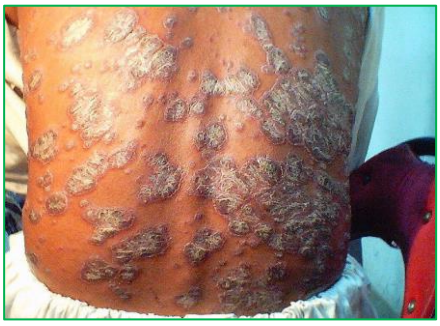
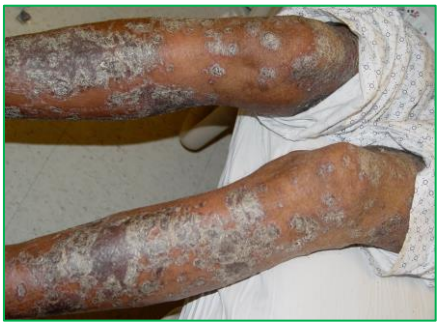
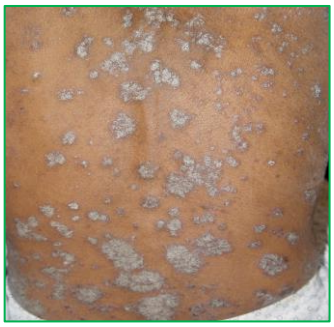
1- **Plaque**: **Most common form**.
2- **Guttate**: Appears as small red spots on the skin.
3- **Erythrodermic**: Intense redness over large areas.
4- **Pustular**: Sterile small pustules, surrounded by red skin.
5- **Inverse**: Occurs in armpits, groin and skin folds.
6- **Psoriatic Arthritis**

Psoriasis can occur on any part of the body:

- Scalp psoriasis
- Genital psoriasis
- Around eyes, ears, mouth and nose
- On the hands and feet
- Psoriasis of the nails

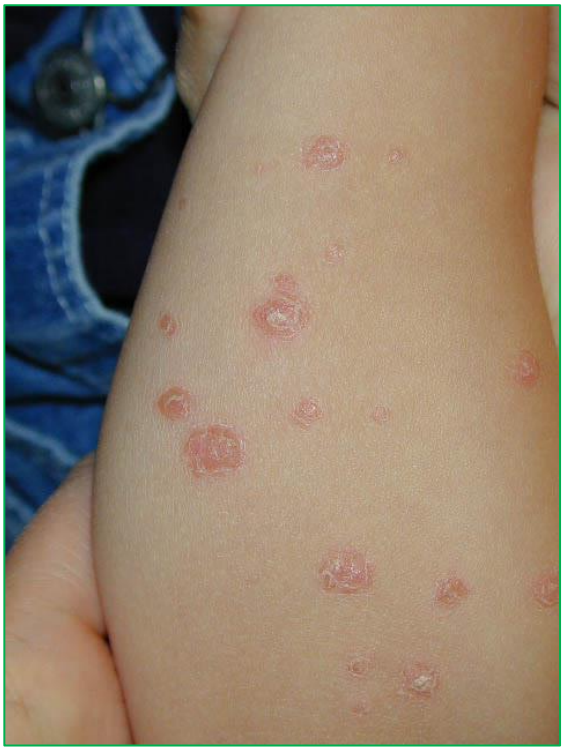
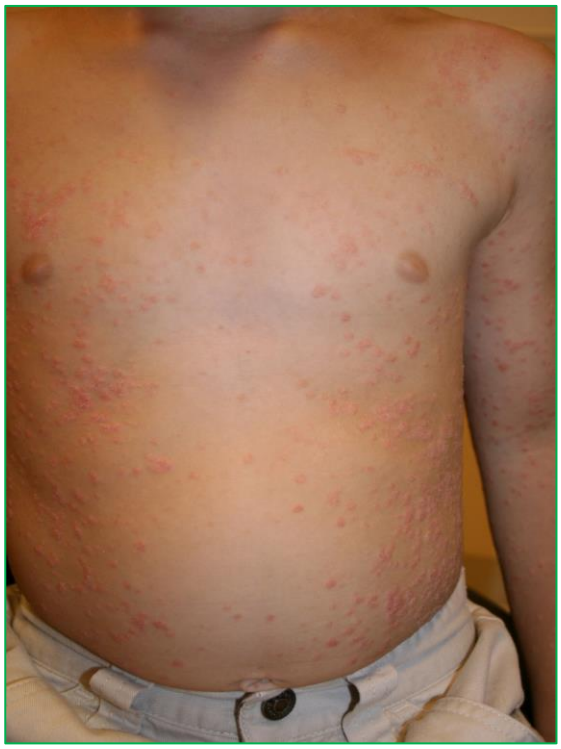
1- Plaque psoriasis (Psoriasis Vulgaris):

- By definition "vulgaris", it is the **most common** type of psoriasis.
- Characterized by round-to-oval red **plaques** distributed over extensor body surfaces and the scalp.
- Up to 10-20% of patients with plaque psoriasis may evolve into more severe disease, such as ***pustular*** or ***erythrodermic*** psoriasis

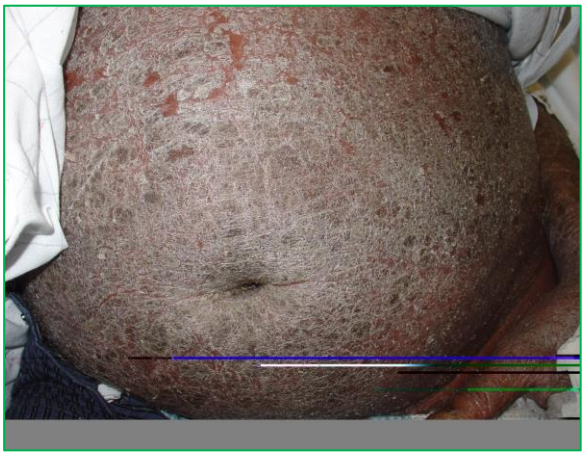
2- Guttate Psoriasis:

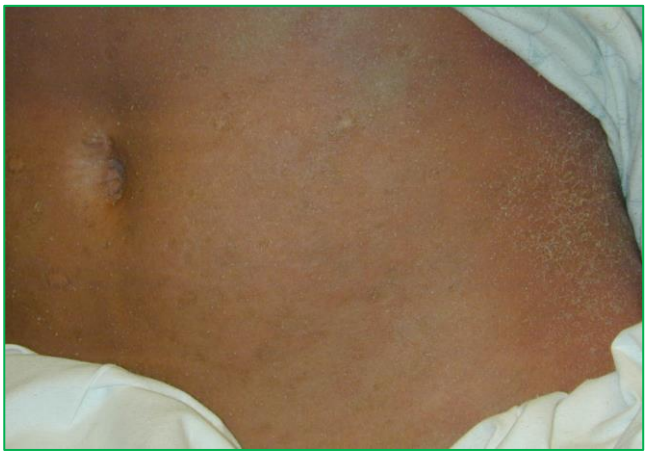
- Small, droplike, 1-10 mm in diameter, salmon-pink papules, usually with a fine scale.
- Younger than 30 years.
- Upper respiratory infection secondary to group A beta hemolytic streptococci.
- On the trunk and the proximal extremities "in the hidden areas".
- Resolution within few months.

3- Erythrodermic Psoriasis:

- Scaly erythematous lesions, involving 90% or more of the cutaneous surface.
- Hair may shed; nails may become ridged and thickened.
- Few typical psoriatic plaques.
- Unwell, fever, leukocytosis.
- Excessive body heat and hypothermia (increase heat on skin because dilatation of blood vessels but the patient will feel cold) (Low core temperature and high superficial temperature).
- Increase cutaneous blood flow (can cause heart failure).
- Increase percutaneous loss of water, protein and iron (iron deficiency anemia, because lose of keratin).
- Increase percutaneous permeability (topical drugs toxicity).





4- Pustular Psoriasis:

The pustules are due to the Murno abscess (Micro-abscess due to the Epidermo-Tropism explained earlier). If the patient is presented with Pustular Psoriasis this means it is a **severe** type of psoriasis (Huge amount of Neutrophils are invading the skin!!)

- *Uncommon form of psoriasis.*
- Pustules on an erythematous background.
- Psoriasis vulgaris may be present before, during, or after it.
- Pus is sterile.

Pustular psoriasis may be classified into several types:

1- Generalized type (von Zumbusch variant):

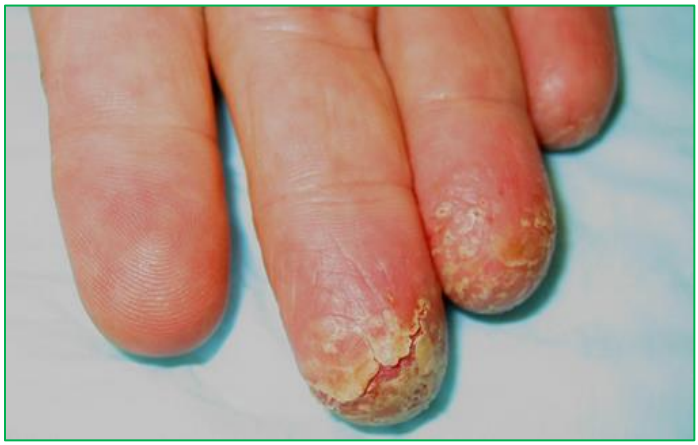
- Generalized erythema studded with interfolecular pustules.
- Fever, tachypnea and tachycardia.
- Absolute lymphopenia with polymorph nuclear leukocytosis up to 40,000/µL.

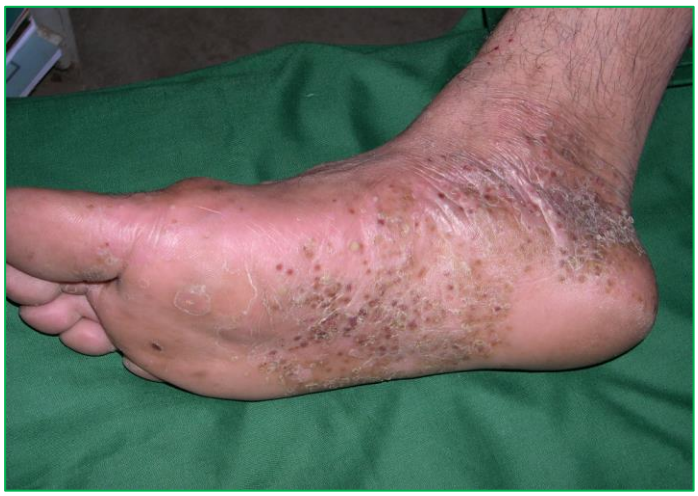
2- Localized form (in palms and soles).

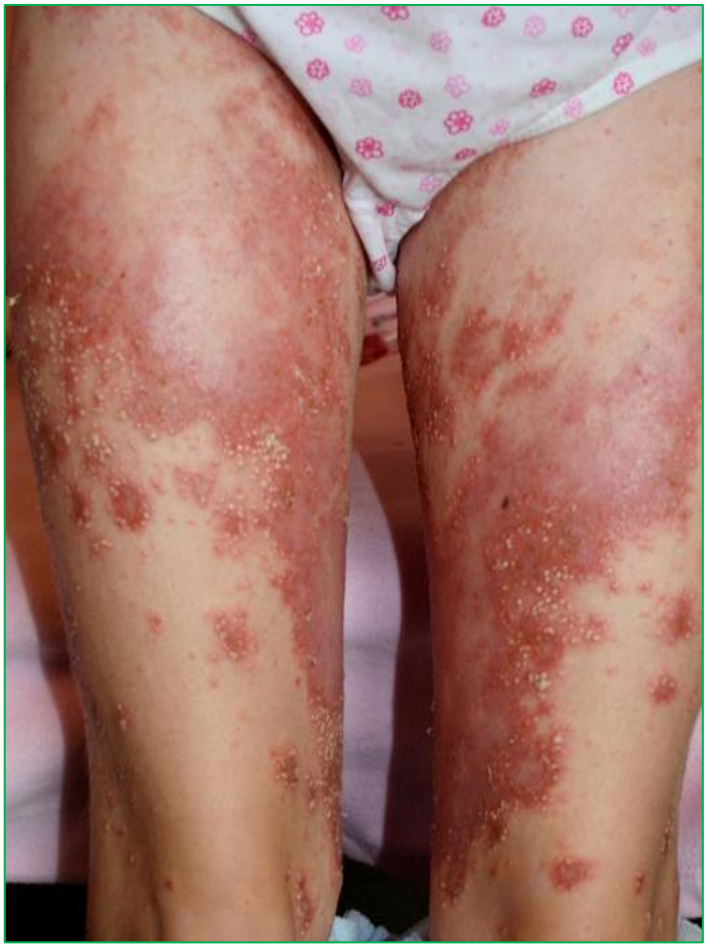
Causes of Pustular Psoriasis:

Idiopathic in many patients but can be caused by:

- Withdrawal of systemic steroids.
- Drugs; including: Salicylates, Lithium, Phenylbutazone, Hydroxychloroquine, Interferon.
- Strong, irritating topicals; including: Tar, Anthralin, Steroids under Occlusion, and Zinc Pyrithione in shampoo.
- Infections.
- Sunlight (or Phototherapy).
- Cholestatic Jaundice.
- Hypocalcemia.

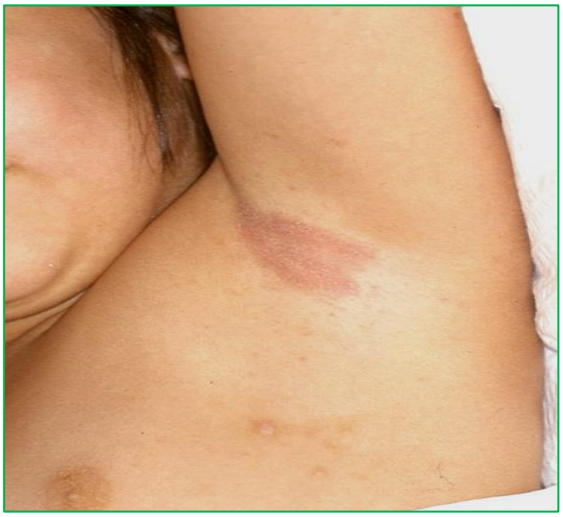


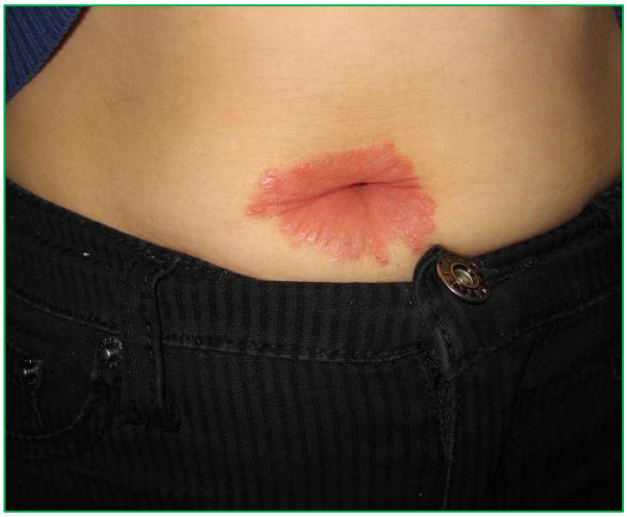




5- Psoriasis inversus (*Sebopsoriasis*):

- Over body folds.
- The erythema and scales are very similar to that seen in Seborrhoeic dermatitis (it has no or very thin scales).



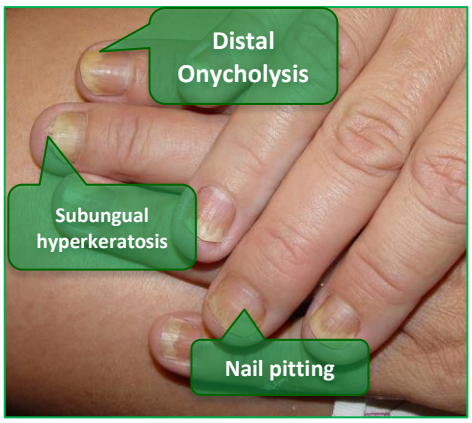


6- Psoriatic Arthritis:

- 5% of patients with psoriasis develop *Psoriatic Arthritis.*
- Most commonly a **seronegative oligoarthritis**.
- Asymmetric oligoarthritis occurs in as many as 70% of patients with psoriatic arthritis.
- DIP joint involvement occurs in approximately 5-10 of patients with psoriatic arthritis.
- *Arthritis mutilans* is a rare form of psoriatic arthritis occurring in 5% of patients with psoriatic arthritis.

7- Psoriatic nail:

- Psoriatic nail disease occurs in 10-55% of all patients with psoriasis.
- Less than 5% of psoriatic nail disease cases occur in patients without other cutaneous findings.
- Oil drop or salmon patch/nail bed Pitting.
- Subungual hyperkeratosis.
- Onycholysis.
- Beau lines (longitudinal grove).



Differential diagnosis:

- Bowes Disease
- Cutaneous T-Cell Lymphoma
- Drug Eruptions
- Erythema Annulare Centrifugum
- Extramammary Paget Disease
- Lichen Planus
- Lichen Simplex Chronicus
- Lupus Erythematosus, Discoid
- Lupus Erythematosus, Subacute Cutaneous
- Nummular Dermatitis
- Parapsoriasis
- Pityriasis Rosea
- Pityriasis Rubra Pilaris
- Seborrheic Dermatitis
- Syphilis

Investigations:

- Skin biopsy (**not needed for diagnosis** except in case there are differential diagnoses, It is preferable to do it for *documentation* because it is a chronic disease).
- Others (imaging if there is joint involvement, CBC, Hg, LFT, Renal profile, Ca, Vit. D… to asses the complications or to establish a baseline for treatment.)

Treatment of psoriasis:

If more than 20% of the body involved give systemic treatment

- What influences therapy choice?
  - Clinical type and severity of psoriasis (eg, mild vs moderate-to-severe), assessed by Psoriasis Area and Severity Index (PASI)
  - Response to previous treatment
  - Therapeutic options
  - Patient preference
- The "1-2-3" step approach is no longer generally accepted for disease more than mild in severity
  - Level 1: Topical agents—do not work
  - Level 2: "Phototherapy"—difficult; not always available
  - Level 3: Systemic therapy
- Risk in relation to benefit must be evaluated

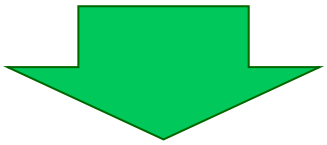
In practice, PASI score is not enough e.g.: female will marry in few next weeks and she has psoriatic lesions on her vulva. Treat systemic not topical even if less than 20%.

Topical Agents 1st Line

- Initial therapeutic choice for mild-to-moderate psoriasis
  - Emollients
  - Keratolytics (salicylic acid, lactic acid, urea)
  - Coal tar
  - Anthralin
  - Vitamin D_3 analogues (calcipotriene)
  - Corticosteroids
  - Retinoids (tazarotene, acitretin)
- Compliance can be difficult due to amount of time required to apply topicals 2 to 4 times/day

To remember the Topical Therapy of Psoriasis remember the morphology in Psoriasis:
1) **Scales** = Remove it by **Keratolytics**.
2) **Increase Mitosis in the cells** = Use Anti-Mitotic (Anthralin & Coal tar)
3) **Inflammatory cells** = Use Steroids & Immune-modulators (Tacrolimus etc.)

If ***no response*** or ***more than 20%*** of the body involved



Phototherapy: 2nd Line

- Used to treat moderate-to-severe psoriasis
- Phototherapy causes death of T cells in the skin
  - Natural sunlight
  - Ultraviolet (UV) B light
  - UVB light + coal tar (Goeckerman treatment)
    - Best therapeutic index for moderate-to-severe disease
  - UVB light + anthralin + coal tar (Ingram regimen)
  - Usually 3 treatments/week for 2 to 3 months is needed
  - Accessibility to a light box facility and compliance necessary

UVA Light with Psoralen (PUVA)

- Psoralen is a drug that causes a toxic reaction to skin lymphocytes when it is activated by UVA light
- Psoralen can be given systemically or topically
- Effective treatment—longest remissions of any treatment available
- Adverse effects
  - Nausea, burning, pruritus
  - Risk of cancer with cumulative use—both squamous cell carcinoma and melanoma
    - >160 cumulative treatments

If **no response** or **the patient has psoriatic arthritis**

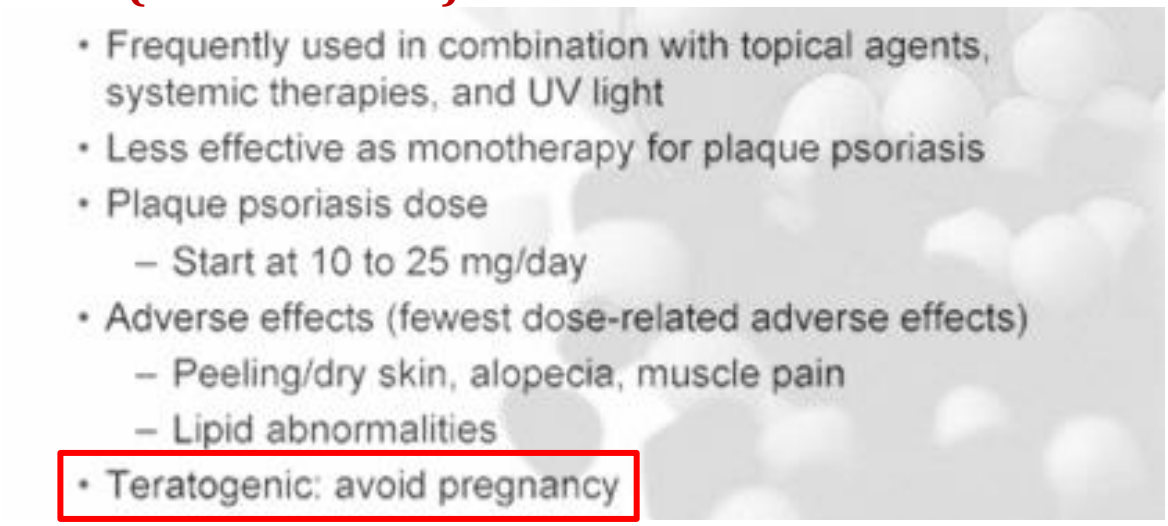
Methotrexate: 3rd Line

- Folic acid metabolite
  - Blocks deoxyribonucleic acid synthesis, inhibits cell proliferation
- Dose
  - Start at about 15 mg/week; maximum 30 mg/week
  - Can also be given intramuscularly
- Adverse effects
  - Headache, nausea, bone marrow suppression
  - Cumulative dose predictive of liver toxicity
    - Prospectively identify risk factors for liver disease
    - Guidelines recommend liver biopsy after 1.5 g
    - Teratogenic in men and women

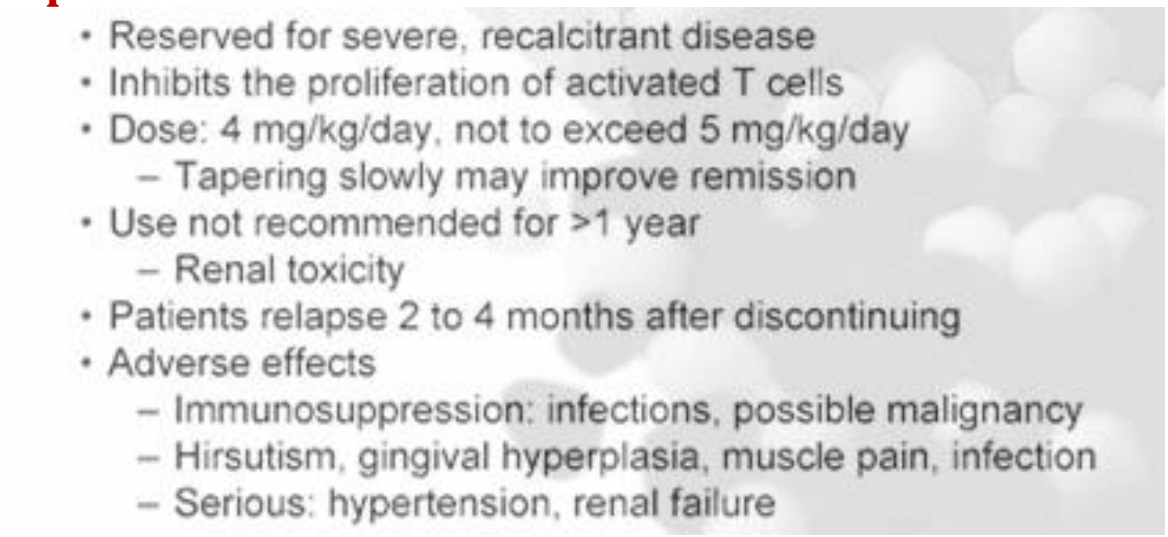
Maximum accumulative dose is 3 g

What is the indications of Systemic Therapy in Psoriasis?
1) More than 20% of skin involvement.
2) Severe.
We define it as Severe Psoriasis when its affect the Quality of Life e.g. a Female patient with Scalp Psoriasis or a Surgeon with Hand Psoriasis)

Acitretin: (Oral Retinoid)



Cyclosporine:



Biologic Therapies (for the treatment of Psoriasis)

Check for hidden infection before start treating with biologicals (TB, hepatitis…)

- Alefacept (Amevive)
- Etanercept (Enbril)
- Adalimumab (Humira)
- Infliximab (Remicade)
- Ustekinumab (Stelara) *Anti-Interleukin*
- Tofacitinip. *Janus kinase (Jak) pathway inhibitor*

Alefacept (Amevive):

- It is the first biologic agent approved by the FDA for the treatment of Psoriasis.
- It works by blocking T cell activation and proliferation by binding to CD2 receptors on T cells.
- This stops the T cells from releasing cytokines, which is the primary cause of the inflammation.
- 7.5 mg by IV injection or 15 mg by IM injection once weekly for 12 weeks.
- **S/E**: dizziness, cough, nausea, itching, muscle aches, chills, injection site pain and injection site redness and swelling.
- Infections.
- Not used nowadays because its effect is very weak.

Etanercept (Enbril):

- This molecule serves as an exogenous TNF receptor and prevents excess TNF from binding to cell-bound receptors.
- 50mg SC given twice weekly for 3 months, then 50 mg SC qwk.
- **Contraindications:** Sepsis, active infection, concurrent live vaccination.
- **S/E:** injection site reactions (most common).
- Upper respiratory tract **infections**.

Adalimumab (Humira) SC, 80 mg → 40 mg

Infliximab (Remicade) IV, 5 mg/kg

Ustekinumab (Stelara) Anti-Interleukin (injection every 3 month)

Tofacitinip: Janus kinase (Jak) pathway inhibitor

Steroid is contraindicated in psoriasis because withdrawal symptoms Except in pregnancy

Summary From 431 team work

Lines of Treatment in Psoriasis:
1- Topical Therapy.
2- Systemic Therapy (if more than 20% of surface area OR it affect the Quality of Life)
3- Phototherapy.
4- Biological Therapy
5- Cytotoxic Medications (Methotrexate, Vit A derivatives, Cyclosporine etc..)

Biological Therapies generally are safe but the most important side effect is the reactivation of chronic infections especially: TB so we need to do test for it (e.g. PPD or QuantiFERON)
PPD = Give 10 units of PPD and read it after 48 to 72 hrs.
The induration should be more than 15 to be positive, if it is from 5 - 10 = Gray area we should do QuantiFERON to confirm.

2. Lichen Planus: (الحزاز)

- Lichen planus (LP) is a **pruritic**, papular eruption characterized by its **violaceous** color; polygonal shape; and, sometimes, fine scale.
- It is most commonly found on the **flexor** surfaces of the upper extremities, on the genitalia, and on the mucous membranes.

Epidemiology:

- Approximately 1% of all new patients seen at health care clinics.
- LP can occur at any age but two thirds of patients are aged 30-60 years
- Rare in children
- F=M
- No racial predispositions have been noted

Pathophysiology:

- The cause of LP is **unknown**
- LP may be a cell-mediated immune response of unknown origin
- LP may be found with other diseases of altered immunity like ulcerative colitis, alopecia areata, vitiligo, dermatomyositis.
- An association is noted between LP and **hepatitis C virus** infection, chronic active hepatitis, and primary biliary cirrhosis.
- Familial cases.
- Drug may induce lichenoid reaction like: Thiazide, Antimalarials, Propranolol.

Clinical features:

- Most cases are insidious.
- The initial lesion is usually located on the flexor surface of the limbs.
- After a week or more, a generalized eruption develops with maximal spreading within 2-16 weeks.
- Pruritus is common but varies in severity.
- Oral lesions may be asymptomatic or have a burning sensation.
- In more than 50% of patients with cutaneous disease, the lesions resolve within 6 months, and 85% of cases subside within 18 months.
- The papules are **violaceous**, shiny, and polygonal; varying in size from 1mm to greater than 1 cm in diameter.
- They can be discrete or arranged in groups of lines or Circles.
- Characteristic fine, white lines, called ***Wickham Stria***, are often found on the papules.
- Oral lesions are classified as reticular, plaque-like, atrophic, papular, erosive, and bullous.
- Ulcerated oral lesions may have a higher incidence of malignant transformation.
- Genital involvement is common in men with cutaneous disease
- Vulvar involvement can range from reticulate papules to severe erosions

- ## Variations in LP:

1- Hypertrophic LP:

These extremely pruritic lesions are most often found on the extensor surfaces of the lower extremities, especially around the ankles.

2- Atrophic LP:

Is characterized by a few lesions, which are often the resolution of annular or hypertrophic lesions.

3- Erosive LP: risk of squamous cell carcinoma

4- Follicular LP:

- Keratotic papules that may coalesce into plaques.
-A scarring alopecia may result.

5- Annular LP:

Annular lesions with an atrophic center can be found on the buccal mucosa and the male genitalia.

6- Vesicular and bullous LP:

Develop on the lower limbs or in the mouth from preexisting LP lesions.

7- Actinic LP:

- Africa, the Middle East, and India.
- Mildly pruritic eruption.
- Characterized by nummular patches with a hypo-pigmented zone surrounding a hyper-pigmented center.

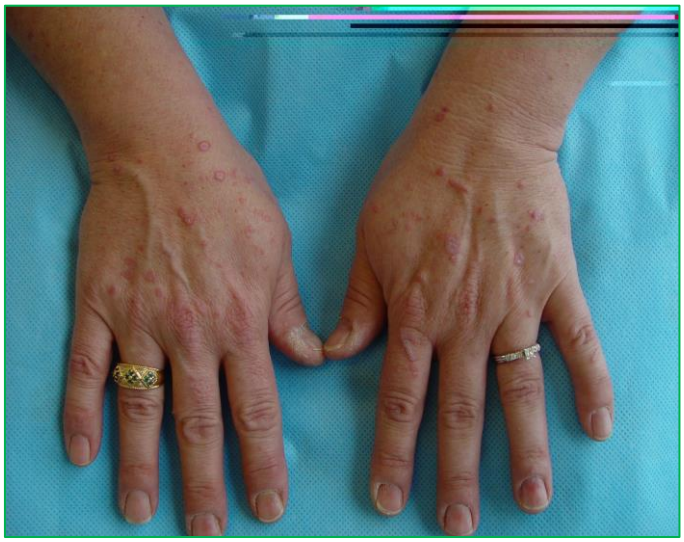
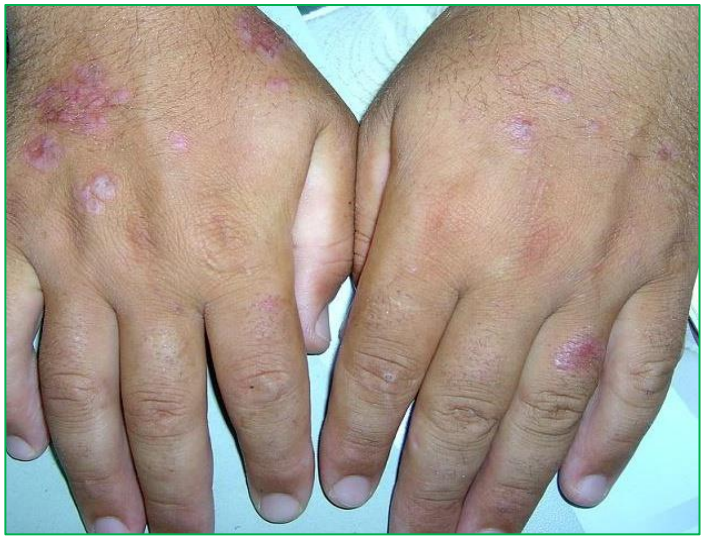
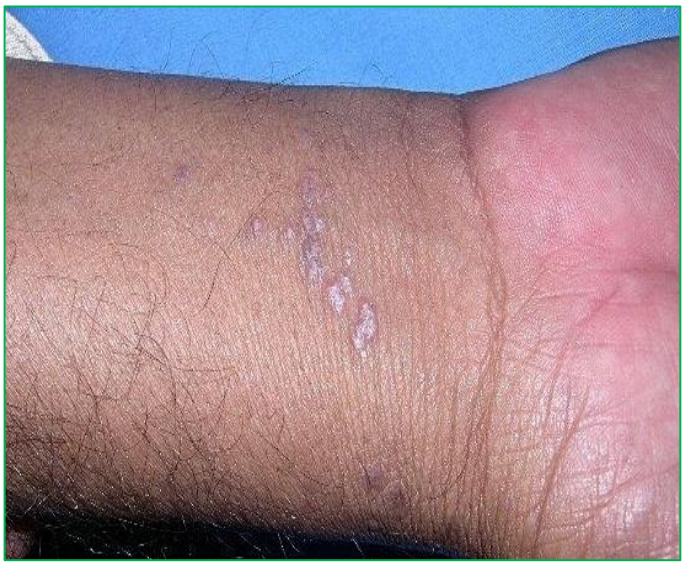
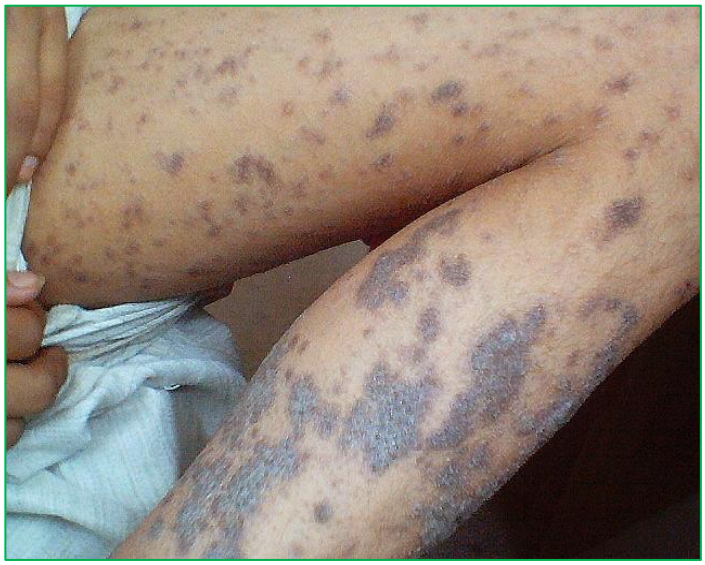
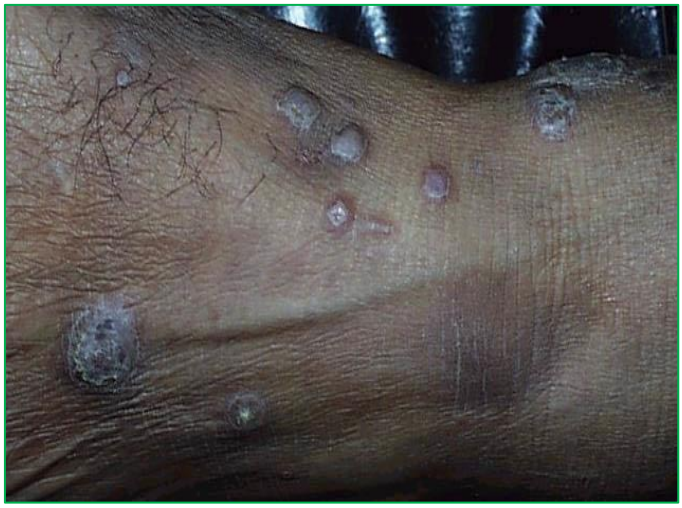
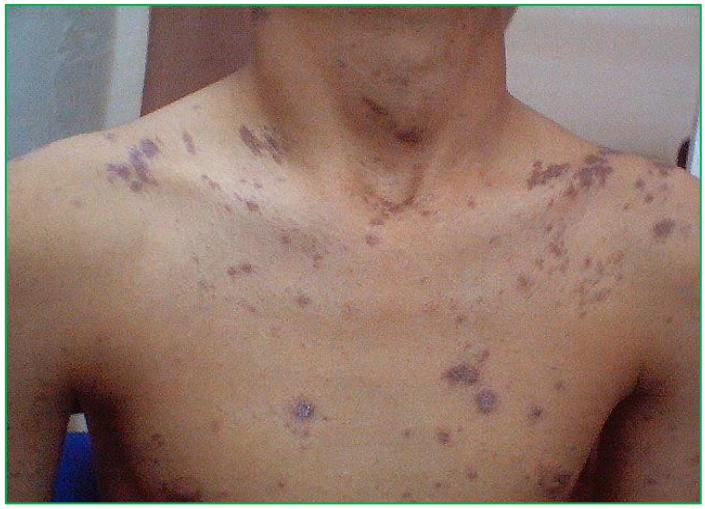
8-LP Pigmentosus:

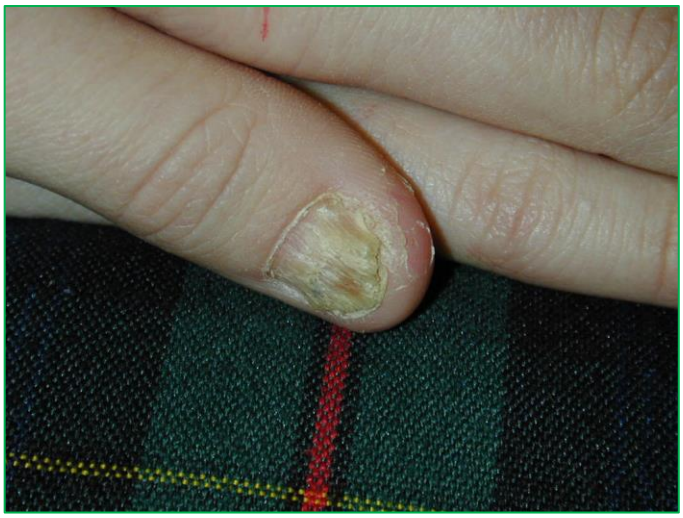
- Common in persons with darker-pigmented skin.
- Usually appears on face and neck.

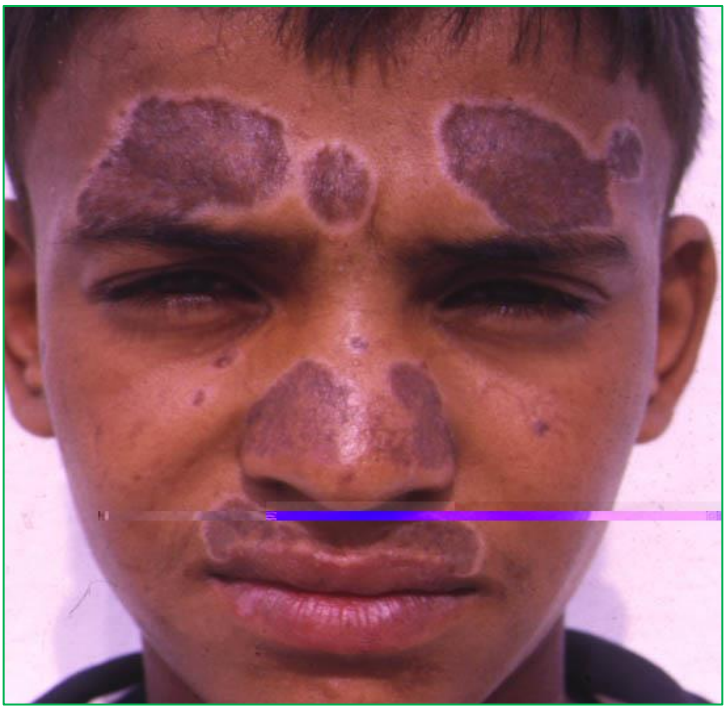
LP and nail: -

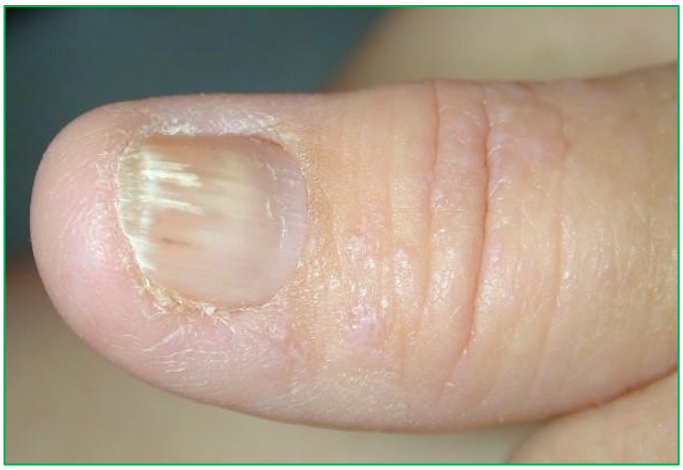
- In 10% of patients
- Nail plate thinning causes longitudinal grooving and ridging
- Subungual hyperkeratosis and Onycholysis.
- Twenty-nail dystrophy
- Rarely, the matrix can be permanently destroyed with prominent Pterygium formation.

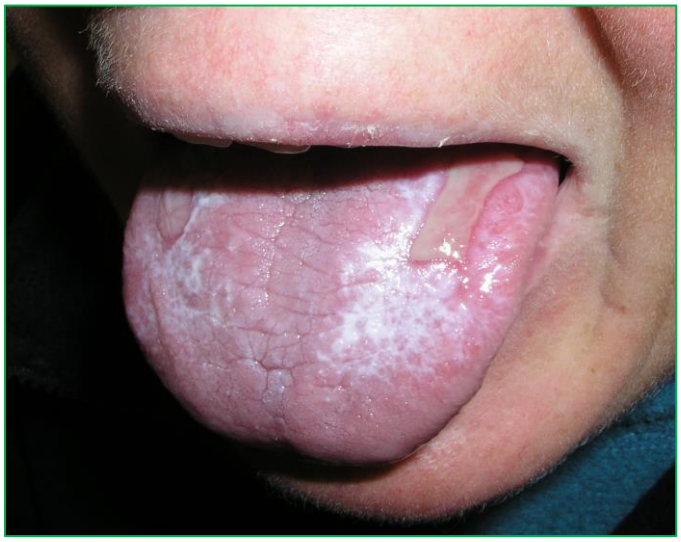
Pterygium unguis (Dorsal pterygium) forms as a result of scarring between the proximal nailfold and matrix.

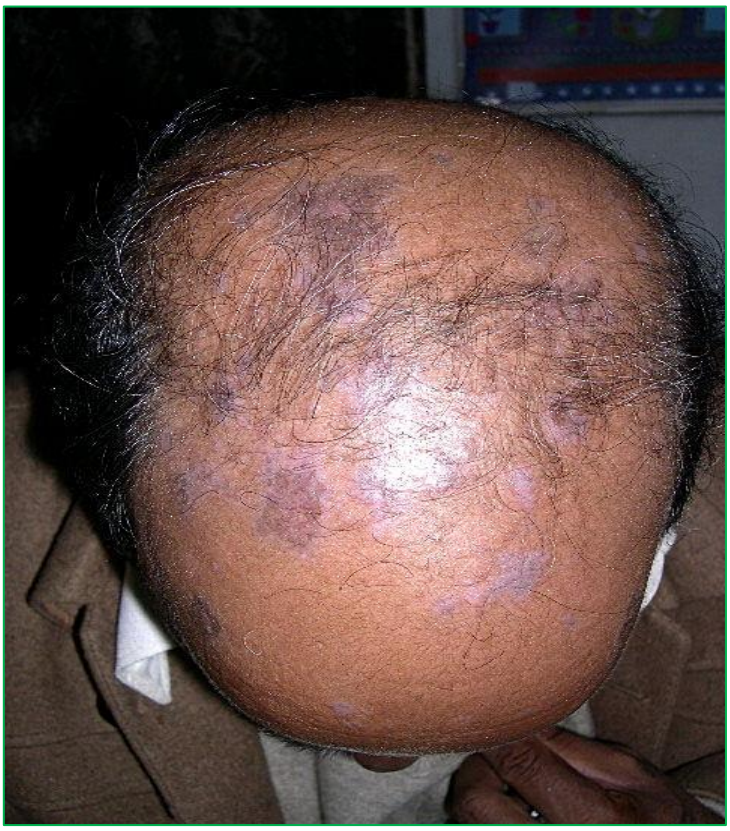

















Differentials diagnoses: (clinical diagnosis)

- Graft Versus Host Disease
- Lichen Nitidus
- Lichen Simplex Chronicus
- Pityriasis Rosea
- Psoriasis, Guttate
- Psoriasis, Plaque
- Syphilis
- Tinea Corporis

Treatment:

- Self-limited disease that usually resolves within 8-12 months.
- Treat to prevent hyperpigmentation.
- Anti-histamine (for pruritus).
- Topical steroids, particularly class I or II ointments
- Systemic steroids for symptom control and possibly more rapid resolution
- Oral Acitretin (Retinoid).
- Photo-therapy
- Others

3. Pityriasis Rosea: (النخالة الوردية)

Definition:

Exanthem is a widespread rash usually occurring in children but can occur in adults.

- Acute mild inflammtory exanthem.
- Characterized by the development of erythematous scaly macules on the trunk.

Epidemiology:

- In children and young adult (10-30)
- Increased incidence in Spring and Autumn
- PR has been estimated to account for 2% of dermatology outpatient visits.
- PR is **more common in women** than in men

Pathophysiology:

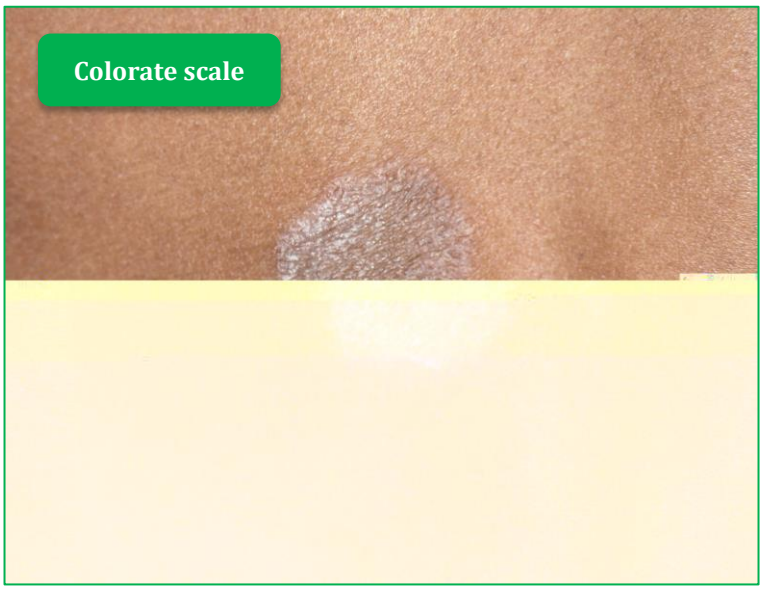
- PR is considered to be a viral exanthem
- Immunologic data suggest a viral etiology
- Families and close contacts
- A single outbreak tends to elicit lifelong immunity
- Human herpes virus (HHV)–7 and HHV-6
- PR-like drug eruptions may be difficult to distinguish from non–drug-induced cases.
- Captopril, metronidazole, isotretinoin, penicillamine, bismuth, gold, barbiturates, and omeprazole.

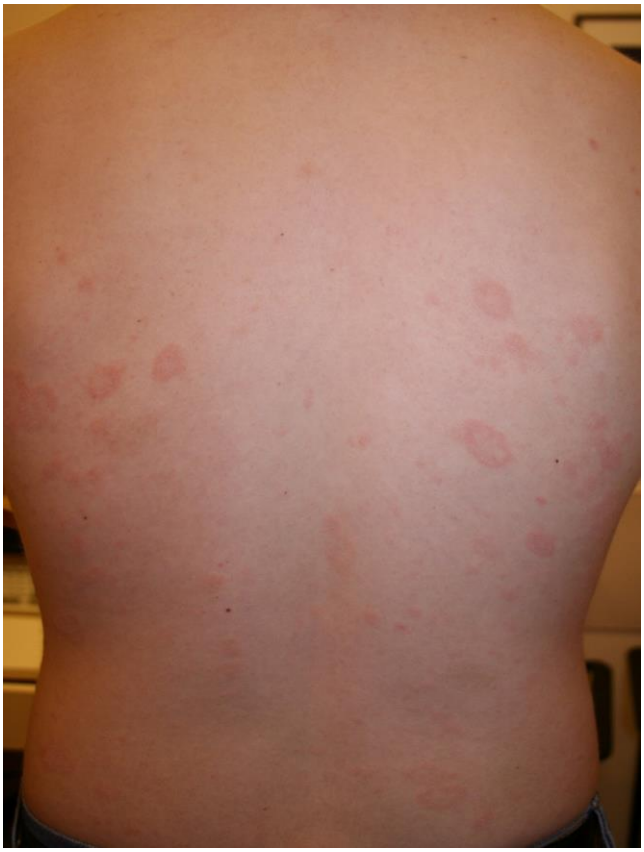
Clinical Features:

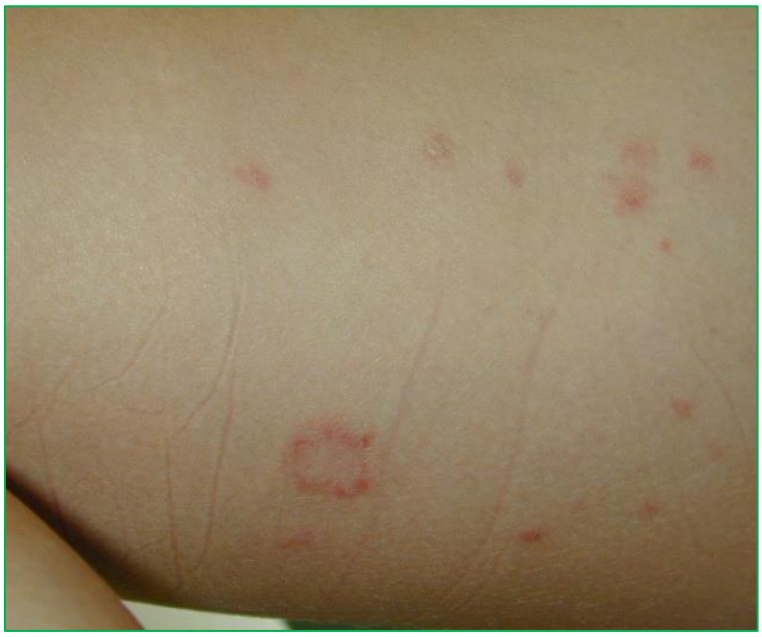
- Begins with a solitary macule that heralds the eruption (herald spot/patch).
- Usually a salmon-colored macule.
- Over a few days it become a patch with a collarette of fine scale just inside the well-demarcated border.
- Within the next 1-2 weeks, a generalized exanthem usually appears.
- Bilateral and symmetric macules with a collarette scale oriented with their long axes along cleavage lines.
- Tends to resolve over the next 6 weeks.
- Pruritus is common, usually of mild-to-moderate severity.
- Over trunk and proximal limbs.

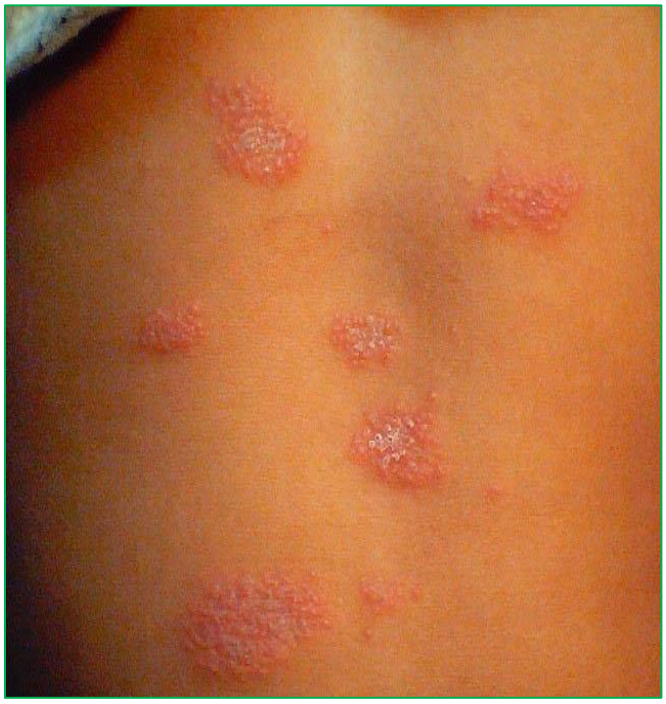
Atypical form of PR:

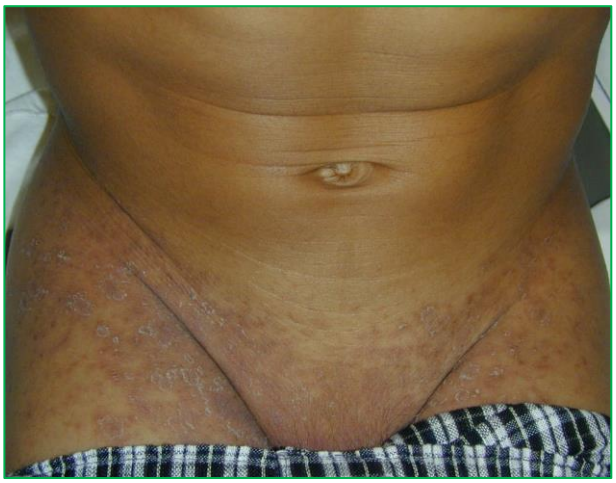
- Occurs in 20% of patients
- Inverse PR
- Unilateral variant
- Papular PR
- Erythema multiforme–like
- Purpuric PR

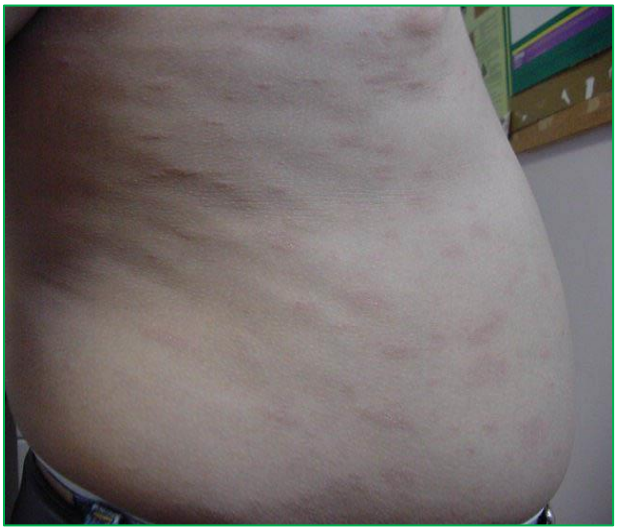












Differential diagnosis:

- Lichen Planus
- Nummular Dermatitis
- Pityriasis Lichenoides
- Psoriasis, Guttate
- Seborrheic Dermatitis
- Syphilis
- Tinea Corporis

Treatment:

- Reassurance that the rash will resolve
- Relief of pruritus
- Topical menthol-phenol lotion
- Oral antihistamines
- Topical steroids
- Systemic steroids
- Ultraviolet B (UV-B) light therapy
- Antiviral

GOOD LUCK!