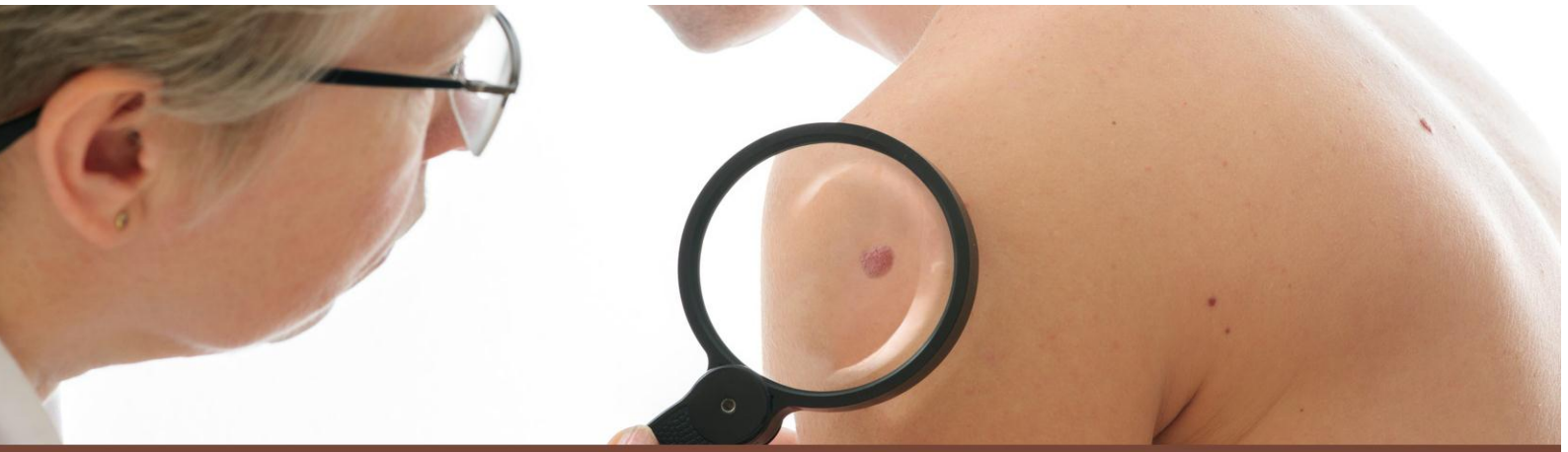


433 Teams

DERMATOLOGY

Lecture (13)

Papulosquamous diseases **(Psoriasis)**

derm433team@gmail.com

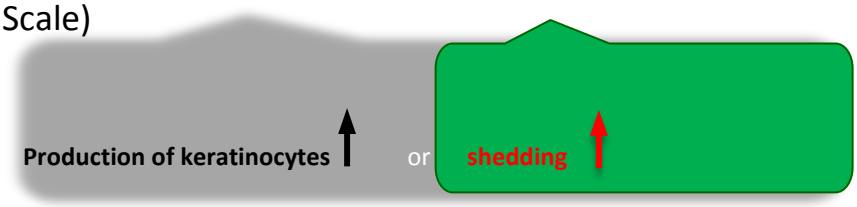
Objectives:

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.

Color index : slides, doctor notes, 432 notes

Papulosquamous disease:

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



Papulosquamous diseases :

- PSORIASIS
- Pityriasis rosea
- Lichen planus
- Seborrheic dermatitis
- Pityriasis rubra pilaris
- Secondary syphilis
- Miscellaneous mycosis fungoides, discoid lupus erythematosus, ichthyoses

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.

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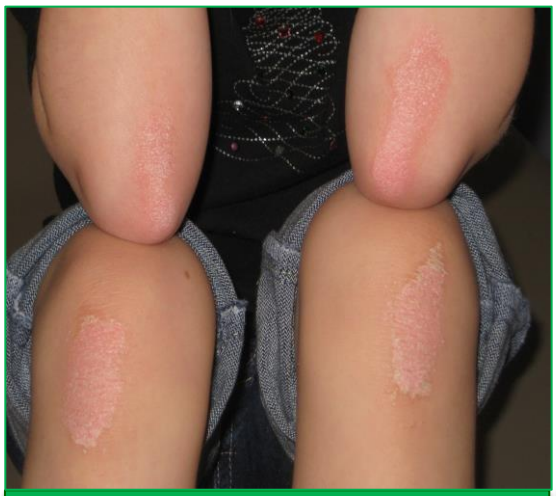
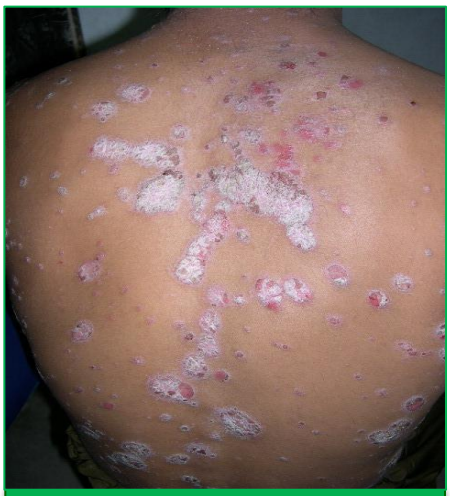
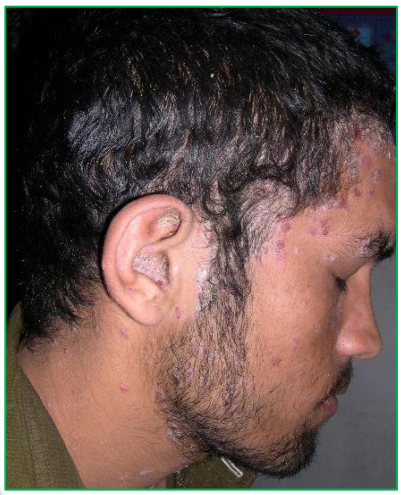
- The treatment improves some of the clinical presentation with no 100 % cure!)
- It can also affect the eye, GI & Liver but with lower incidence compared to the Skin & Joints .

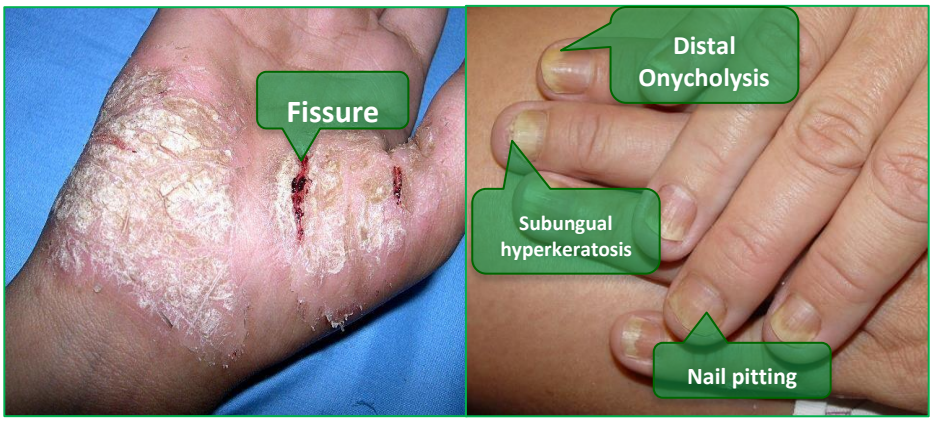


Bilateral, symmetrical, well-defined, regular, erythematous, scaly, plaques on elbows and knees.



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.

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:
  1-type I psoriasis **(Early onset**): more likely to be familial, have a severe clinical course and is associated with HLA-Cw6, −B13 and −B57
  2-type II (**Late onset**): ages 50 to 60 and is correlated with HLA-Cw2 and −B27

- One affected parent……..16%
  - Both parents……50%
  - Non-Psoriatic parents with affected child…..10%
  - Monozygotic Twins……..70%
  - Dizygotic twins……20%
  - At least 10 loci have been identified (psors-1 to 10)

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:

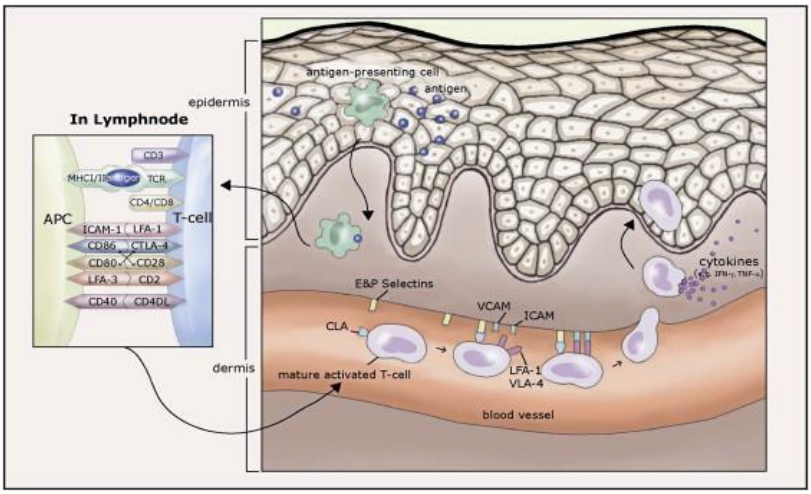
- Increase level of TNF
- TNF receptors are up-regulated
- Increase level of interferon gamma
- Increase level of interleukin 2, 12, 23 and **17**

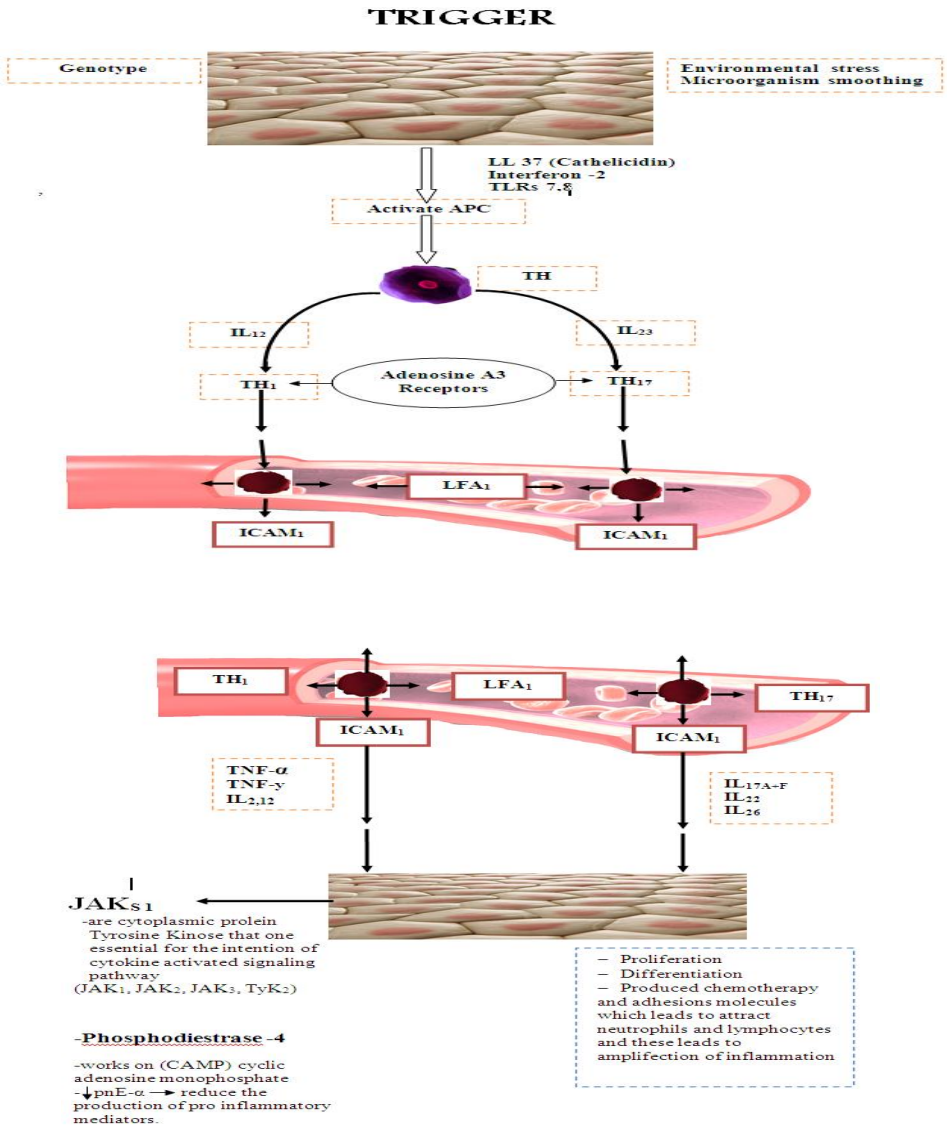
4) Immunological factors:

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.

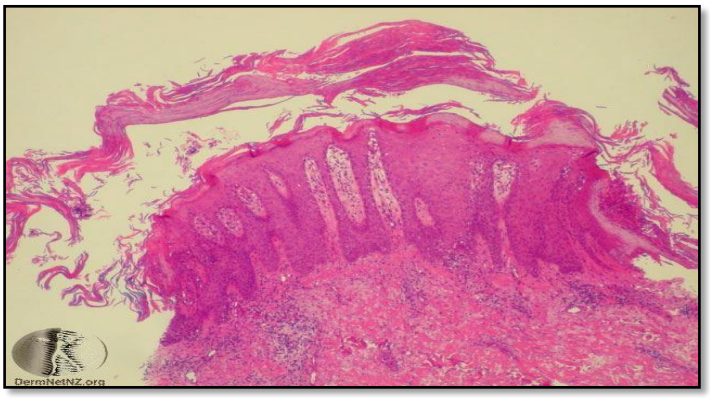




5) Environmental factors: Triggers

- 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):

- 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
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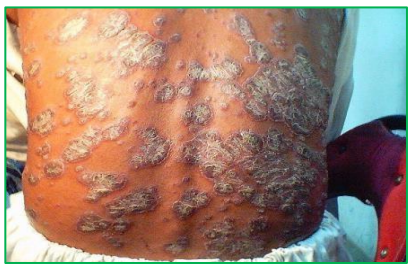
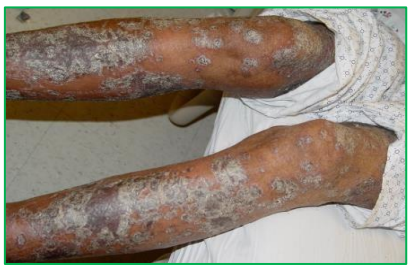
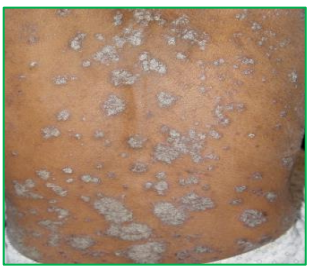
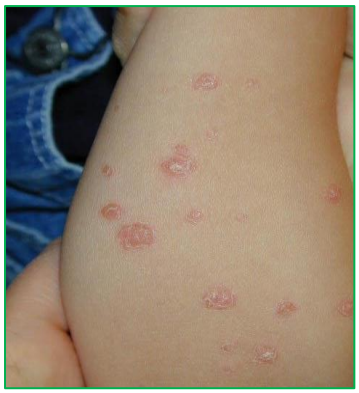
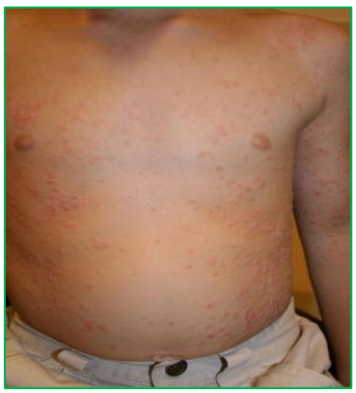




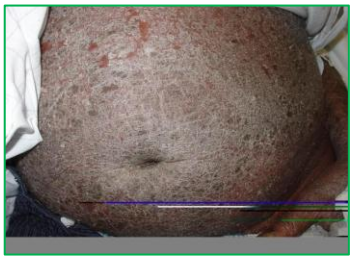
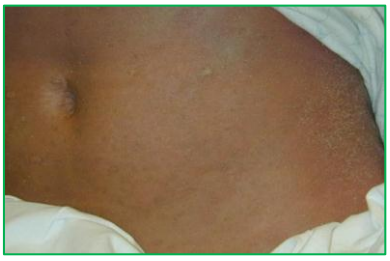
2- Guttate Psoriasis:

- 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:

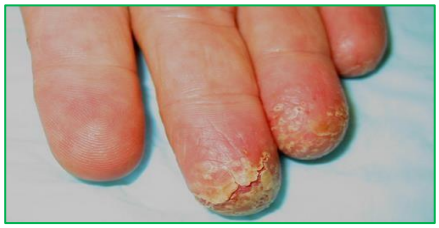
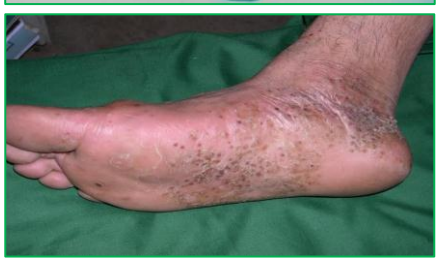
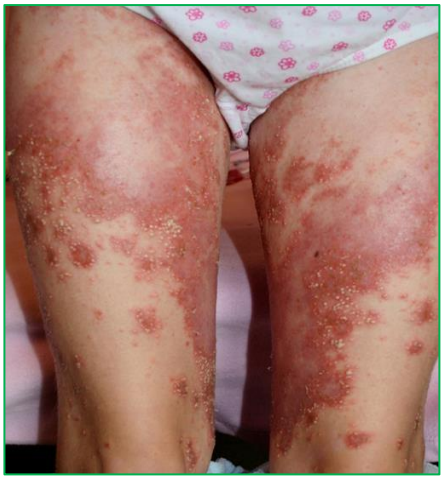
1- Generalized type (von Zumbusch variant):
   - Generalized erythema studded with interfolecular pustules.
   - Fever, tachypnea and tachycardia.
   - Absolute lymphopenia with polymorph nuclear leukocytosis up to 40,000/µL.

2- Localized form (in palms and soles).

Causes of Pustular Psoriasis:

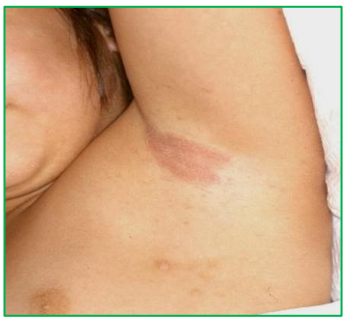
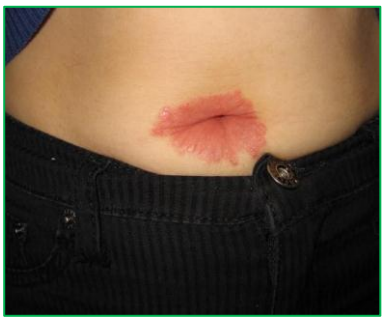
Idiopathic in many patients but can be caused by:

- 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).

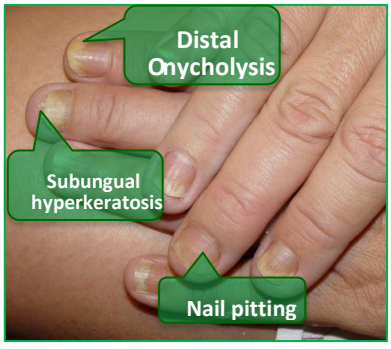



6- Psoriatic Arthritis:

- 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:

a. Psoriatic nail disease occurs in 10-55% of all patients with psoriasis.
b. Less than 5% of psoriatic nail disease cases occur in patients without other cutaneous findings.
c. **(more risk for Psoriatic arthritis)**
d. Oil drop or salmon patch/nail bed Pitting.
e. Subungual hyperkeratosis.
f. Onycholysis.
g. Beau lines (longitudinal grove).



Differential diagnosis:

1-Bowes Disease
2-Cutaneous T-Cell Lymphoma
3-Drug Eruptions
4-Erythema Annulare Centrifugum
5-Extramammary Paget Disease
6-Lichen Planus
7-Lichen Simplex Chronicus
8-Lupus Erythematosus, Discoid
9-Lupus Erythematosus, Subacute Cutaneous
10-Nummular Dermatitis
11-Parapsoriasis
12-Pityriasis Rosea
13-Pityriasis Rubra Pilaris
14-Seborrheic Dermatitis
15-Syphilis

Investigations:

h. 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).

i. 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 & Immu ne-modulators (Tacrolimus etc.)

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

phtotherapy: 2nd line

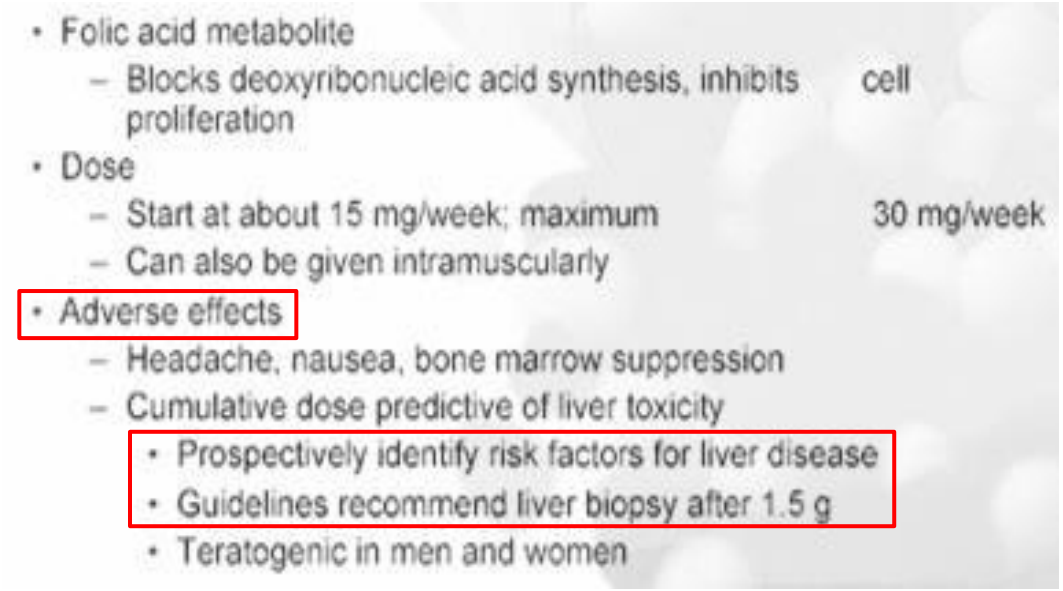
- Used to treat moderate-to-severe psoriasis
- Phototherapy causes death of T cells in the skin
  - Natural sunlight
  - Ultraviolet (UV) B light
  - UVB light + coal tar (Goeckerman treatment)
    - Best therapeutic index for moderate-to-severe disease
  - UVB light + anthralin + coal tar (Ingram regimen)
  - 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



. New maximum accumulative dose is 3 g (liver biopsy to rule out cirrhosis)

Other side effects : bone marrow suppression – oral ulcers.

Stop it for 3 months before getting pregnant

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)

- Frequently used in combination with topical agents, systemic therapies, and UV light
- Less effective as monotherapy for plaque psoriasis
- Plaque psoriasis dose
  - Start at 10 to 25 mg/day
- Adverse effects (fewest dose-related adverse effects)
  - Peeling/dry skin, alopecia, muscle pain
  - Lipid abnormalities
- Teratogenic: avoid pregnancy

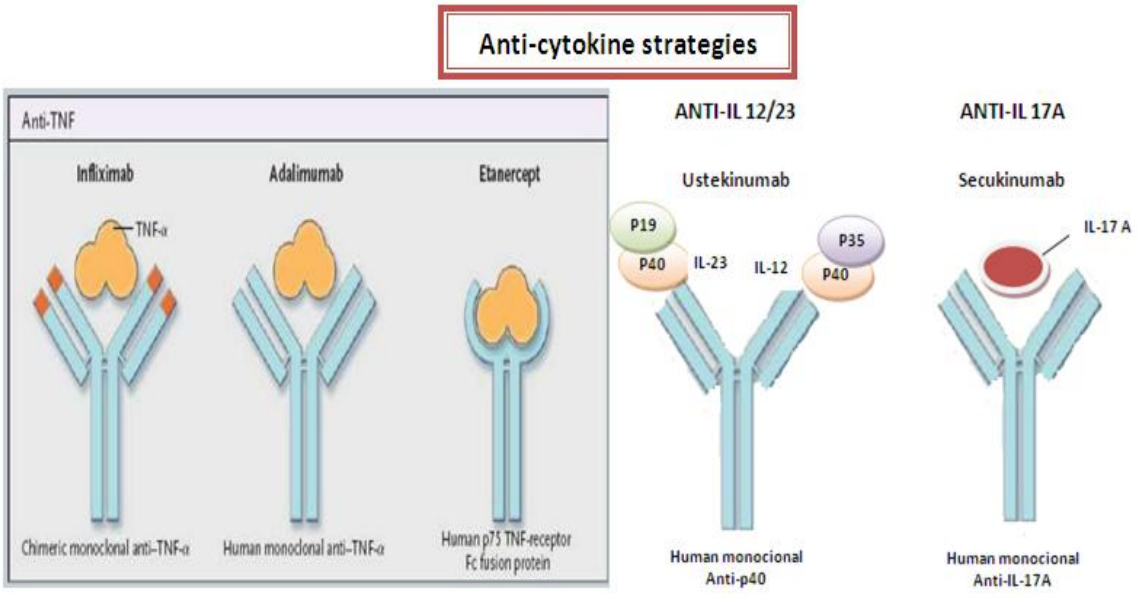
Cyclosporine:

- Reserved for severe, recalcitrant disease
- Inhibits the proliferation of activated T cells
- Dose: 4 mg/kg/day, not to exceed 5 mg/kg/day
  - Tapering slowly may improve remission
- Use not recommended for >1 year
  - Renal toxicity
- Patients relapse 2 to 4 months after discontinuing
- Adverse effects
  - Immunosuppression: infections, possible malignancy
  - Hirsutism, gingival hyperplasia, muscle pain, infection
  - Serious: hypertension, renal failure

Renal histopathological changes starts after 6 months

Biologic Therapies (for the treatment of moderate to severe Psoriasis) :

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



1-Janus kinase inhibitor

-cytokines function by binding to and activating type I and type II cytokine receptors

-These receptors in turn rely on the Janus kinase (JAK) family of enzymes for signal transduction

-drugs that inhibit the activity of these Janus kinases block cytokine signalling.

Tofacitinib AND ruxolitinib

2-Phosphodiesterase 4 (PDE4) is a key enzyme in the regulation of immune responses of inflammatory diseases through degradation of the second messenger, cyclic adenosine 3',5'-monophosphate (cAMP). Apremilast, a selective PDE4 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

Lines of Treatment in Psoriasis: **Summary From 431 team work**

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.

Done By:

Ali Alolayan	
Musab Almasry