

PASSION ACADEMIC TEAM

YU - MEDICINE

MUSCULOSKELETAL SYSTEM

Sheet#6 - Pharmacology

Lec. Title : Topical Anti-Inflammatory &
Antipruritic Agents

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Topical anti-inflammatory and Antipruritic agents

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Psoriasis

- chronic inflammatory disease characterized by recurrent exacerbations and remissions of thickened, erythematous, and scaling plaques.
- relatively asymptomatic, but about 25% of patients complain of pruritus



#psoriasis

_auto immune disease

_our immune system attack skin's layer (age of skin cells is a month after that regeneration happens (start) for skin cell.) and increase the proliferation (as well increase rate of keratinocytes which produce keratin) with chronic inflammation.

_silent disease (asymptomatic).

_accompanied with cardiovascular problem or arthritis
"psoriatic arthritis".

_المرضى الي بصيبيهم وعمرهم اقل من 25 ما يكملو لعمر ال 60 ولكن الي بصيبيهم بعمر فوق ال 25 يكملوا لفوق ال 60 سنة.

_يكون على شكل وجود طبقات من الكيراتين على الجلد في البداية مع تقشرات الجلد.

_but suddenly start episodes of pain in this lesion ,so acute exacerbation happens with 1-thickened 2-erythematous 3-scaling plaques.

Treatment of Psoriasis

1. First-line topical pharmacotherapy:

- Moderate to ~~high potency topical steroid creams~~, gels and ointment.
- ~~Topical calcipotriene~~
- Topical ~~coal tar~~-derivatives (~~anthralin~~/LCD) and ~~retinoids~~ (Tazorac)

2. Phototherapy with narrowband UVB and PUVA ("psoralen and ultraviolet light A")

3. Second line-systemic pharmacotherapy :

- Methotrexate, a potent antimetabolite and immune suppressant.
- Cyclosporine, a potent immune suppressive drug

#treatment of psoriasis which divide into:

1_topical:keratolytic (detachment of keratinocytes &slow its proliferation)

A-Vit A &its derivatives (tazarotene)

B-salicylic acid (keratolytic effect)

C-coal tar

D- steroid creams

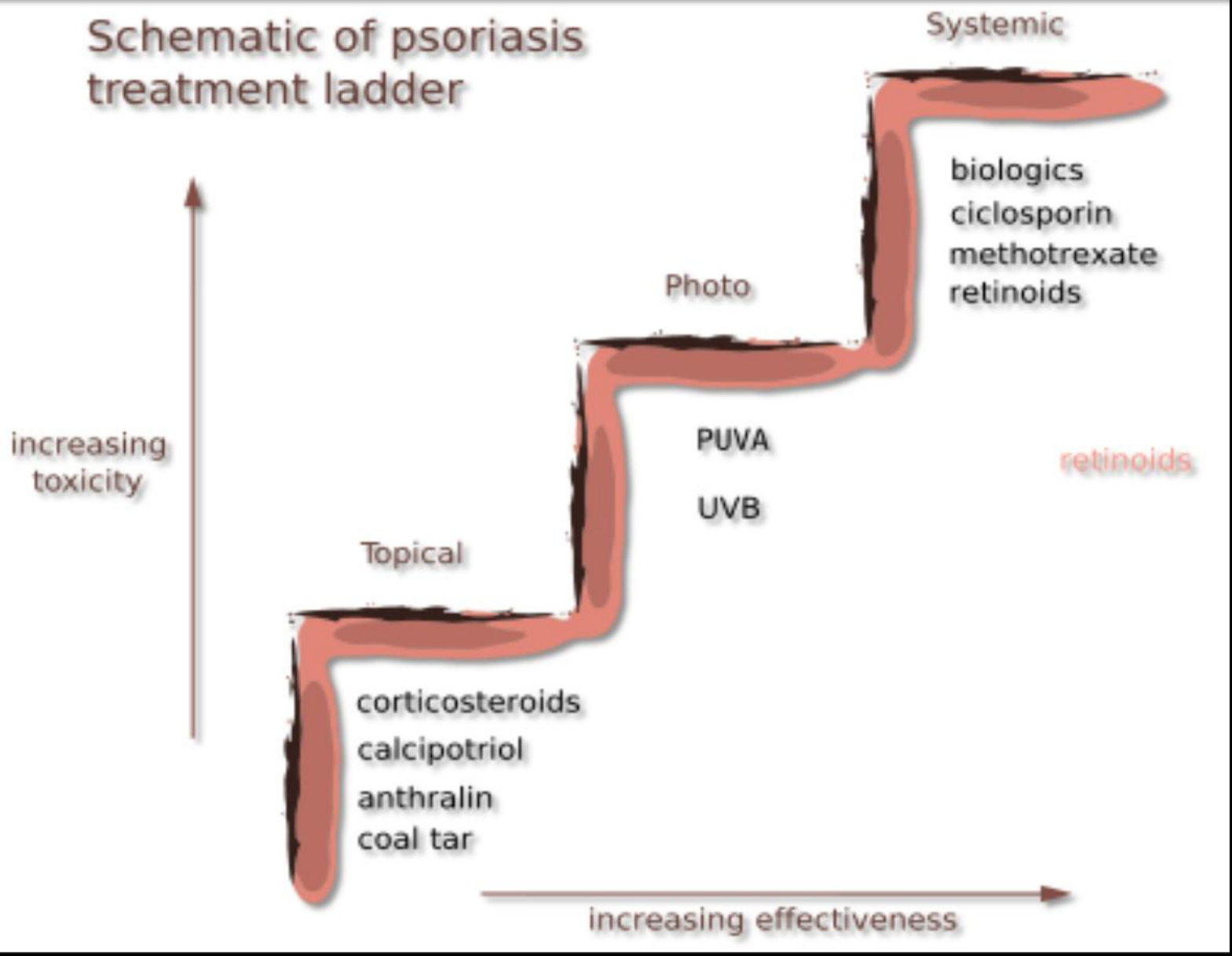
2_phototherapy

_psoralen and ultraviolet light –A

3_systemic

_as immune suppressant :-methotrexate –cyclosporine - tacrolimus .

Schematic of psoriasis treatment ladder



First-line topical pharmacotherapy

Keratolytics

1. **Salicylic acid:** is one of the most commonly used keratolytics.

- It remove scales, smooth the skin, and decrease hyperkeratosis.
- The keratolytic effect enhances penetration and efficacy of some other topical agents such as **corticosteroids**

#first line topical:

-keratolytics

1_salicylic acid :is one of the most commonly used keratolytics .

- remove scales

- ↓ smooth the skin .

-decrease hyperkeratosis

_the keratolytic effect enhances penetration & efficacy of some of the topical agent such as corticosteroids .

_لأنه تأثيره هو انه يعمل تحليل لطبقات الجلد المتراكمة نتيجة زيادة الكيراتين وبالتالي يسهل دخول corticosteroids to inflamed area.

First-line topical pharmacotherapy

2. Corticosteroids

- Topical corticosteroids: gel , cream and ointment
- Low-potency products:
 - Hydrocortisone, Methylprednisolone, Alclometasone, **Dexamethasone**, Flumethasone
- Medium-potency products:
 - **Beclomethasone dipropionate** , Fluocinolone acetonide
- High-potency preparations :
 - Clobetasol propionate, **Betamethasone**

#corticosteroids(gel,cream,ointment)

_potency جميعهم متشابهون ولكن يختلفون فقط بال
كلما زادت كان تاثير الدواء بكمية قليلة اكبر ,جرعة قليلة من الدواء : _potency
كافية لبدء التاثير .

Topical Corticosteroids

- **Adverse effects:**
 - local tissue atrophy.
 - Thinning of the epidermis
 - Systemic consequences: hyperglycemia, Tachyphylaxis and ~~rebound flare of psoriasis after abrupt cessation of therapy can also occur.~~

#adverse effect of corticosteroids :

1_local tissue atrophy &necrosis

2_thinning of epidermis

-وهو المطلوب من العلاج لازالة الطبقات المتراكمة ولكن الاستخدام الزائد بعمل
thinning الي من مسبباته

Corticosteroid → ↑ protein catabolism

3_systemic consequences

-if systemically absorbed :hyperglycemia ,tachyphylaxs

&rebound flare of psoriasis os terabrupt cessation of therapy
can also occure .

وبناخذ ستيرويد فما بصير نوقفه فجأة لانه رح يرجع chronic_لانه المرض
المرض اشد واسوا من اول.

Calcipotriene

a synthetic vitamin D analog used for moderate to severe plaque psoriasis and scalp.

Tazarotene

a synthetic ~~retinoid~~ that is hydrolyzed to its active metabolite, tazarotenic acid. **Tazarotene is often used with topical corticosteroids to decrease local adverse effects and increase efficacy.**

Coal Tar



- MOA: Tar can help ~~slow the rapid growth of skin cells~~ it can help ~~reduce the inflammation~~, itching and scaling of psoriasis.
- Generally, ~~the higher the concentration of tar, the more potent the product.~~
- It is usually ~~applied directly to lesions in the evening and allowed to remain in skin contact through the night.~~
- It may also be used in bathwater.
- ~~No quick onset~~ but longer remission
- Often combined with SA, UV light therapy



Anthralin



- Anthralin: antiproliferative activity on keratinocyte
- 2 treatment approach:
 - **long contact (LCAT)** Cream and ointment formulations are usually applied in the evening and allowed to remain overnight
 - **short contact (SCAT)** :Alternatively, short-contact anthralin therapy with application for 10 to 20 minutes
- Anthralin products must be applied ~~only to affected areas~~ because contact with uninvolved skin may result in excessive irritation and staining
- ~~Staining of affected plaques indicates a positive response because cell turnover has been slowed enough to take up the stain.~~

#Anthralin as well as coal tar:

_proliferation. يتم امتصاصه من قبل الجلد والذي بدوره يؤدي الى وقف ال
_يتم التاكيد من مفعول الدواء اذا كانت النتيجة ممتازة ام لا من خلال لون المنطقة
المصابة ,اذا تلونت يعني انها امتصت الدواء ويوجد نتائج .

Second-line systemic pharmacotherapy

1. **Biologic therapies :Infliximab, Adalimumab**
2. **Acitretin** is a retinoic acid
3. **Cyclosporine demonstrates immunosuppressive activity by inhibiting of T-cell**
4. **methotrexate**
5. **Tacrolimus, an immunosuppressant that inhibits T-cell activation,**

second line (systemic):

1_biological therapies

_infliximab &adalimamb → TNF-a inhibitor

2_immune suppressive

- methotrexate :may cause hepatotoxic &liver cirrhosis .

3_cyclosporine

-immunosuppressive by inhibiting of T-cell ,while
corticosteroid inhibite both T&B-cell.

4_systemic Vit.A

-Vit.A like tazarotene 'topical'

- acitretin:systemic retinoic acid

Second-line systemic pharmacotherapy

Hydroxyurea

- **MOA: inhibits cell synthesis**
- used selectively in the treatment of psoriasis, especially in those with liver disease who would be at risk of adverse effects with other agents.
- Adverse effects include bone marrow toxicity ,cutaneous reactions, leg ulcers, and megaloblastic anemia.

#Hydroxy urea:

_anti cancer drug

_the main drug to treatment of sickle cell anemia with
adverse effect (megaloblastic anemia)

Anti-pruritics

- There are several ingredients that have been approved by the FDA for treating itch.
 1. **calamine lotion:** zinc oxide. It has a mild drying action on the skin
 2. **Topical hydrocortisone** (a weak steroid),
 3. **Menthol/Camphor.** Menthol provides a sensation of coolness by acting on the skin's receptors
 4. **Oral antihistamine:** diphenhydramine