

Drugs Used in Dermatologic Disorders

Pharmacology 3

Dr. Heba Khader

بِسْمِ اللَّهِ نَبْدُ خَتَامَ الْمَادَةِ ٥٥٥

بِسْمِ اللَّهِ
نَبْدُ خَتَامِ
الْمَادَةِ

٥٨٩ ٣٠ أيام → الفطخ الطبيعي
 * Epidermal cell Proliferation → حالة الصدفية ٣-١٥ أيام

الصدفية - Psoriasis

- Psoriasis is a **long-lasting autoimmune disease**.

مرض مناعي بطن فترة طويلة

Psoriasis manifests with **increased epidermal cell proliferation**.

- Skin cells are replaced every **3-5 days** in psoriasis rather than the usual **28-30 days**.

- Psoriasis causes cells to **build up rapidly** on the surface of the skin.

The extra skin cells form **thick, silvery scales** and **itchy, dry, red patches** that are **sometimes painful**.

- Psoriasis appears to have both **genetic factors** and **T-cell-mediated immune components**.

يمكن تظفر بسبب وراثي
 او مناعي

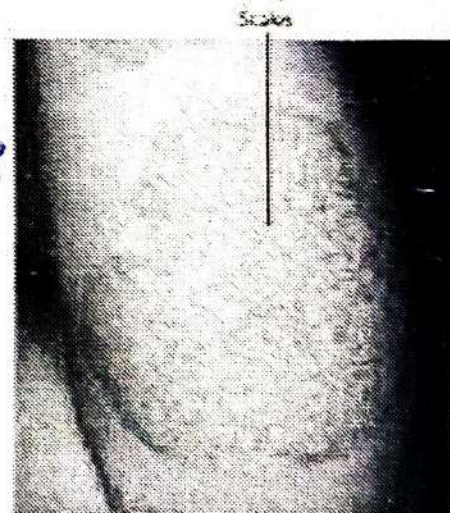
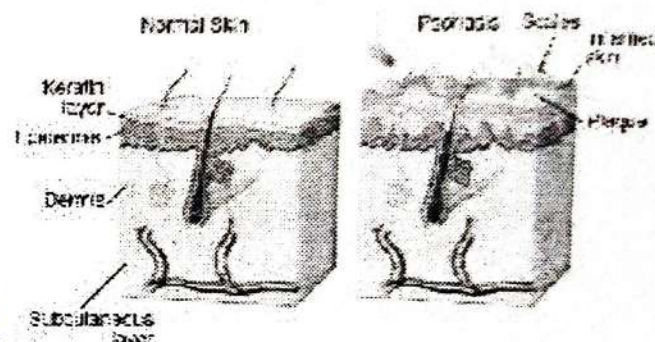


Figure 34.9
 Psoriasis. A large, scaly, erythematous plaque.

ic

السبب
 يتغير خلايا الجلد
 تتجدد بسرعة اصطناعية
 السريعة الطبيعية

اضطرابات

General approach to psoriasis treatment

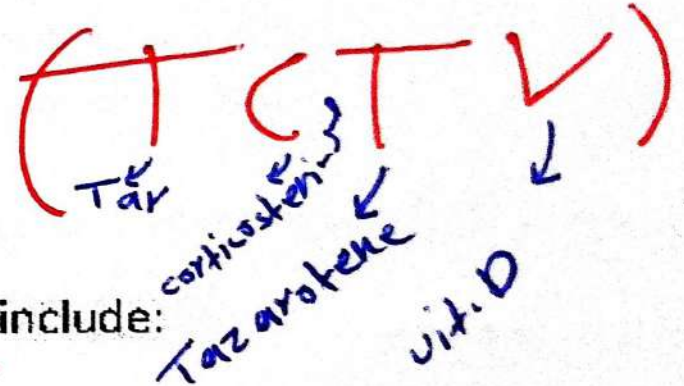
لازم المريض يستمر عليها حتى
ما يصبح جفاف

موطبان

1. Emollients are frequently used during therapy-free periods to minimize skin dryness that can lead to early recurrence. حتى ما ترجع ثاني

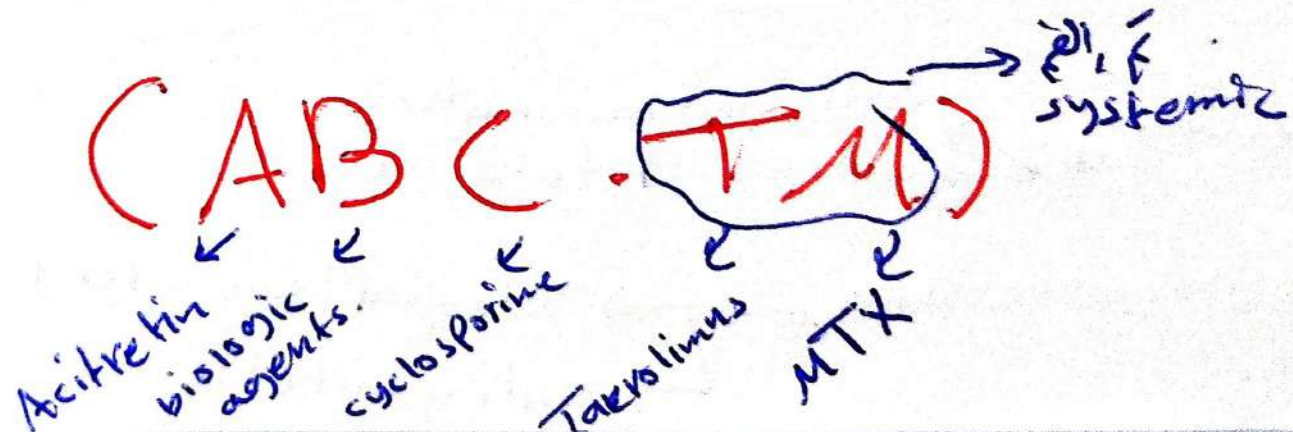
2. Topical treatments for mild to moderate psoriasis include:

- ✓ Tar
- ✓ Corticosteroids → oval و ممكن تكون oval
- ✓ Vitamin D analogues (Calcipotriene & Calcitriol)
- ✓ Tazarotene



3. Systemic treatments for moderate to severe psoriasis include:

- ✓ biologic agents
- ✓ Acitretin
- ✓ Cyclosporine
- ✓ Tacrolimus
- ✓ Methotrexate



Topical
Tar

كانوا يستخدمونه قديماً لكن المنتجات الحديثة قللت من استخدامه

- The use of tar is a time-honored modality for treating psoriasis, although newer (and less messy) treatment options have reduced its popularity.

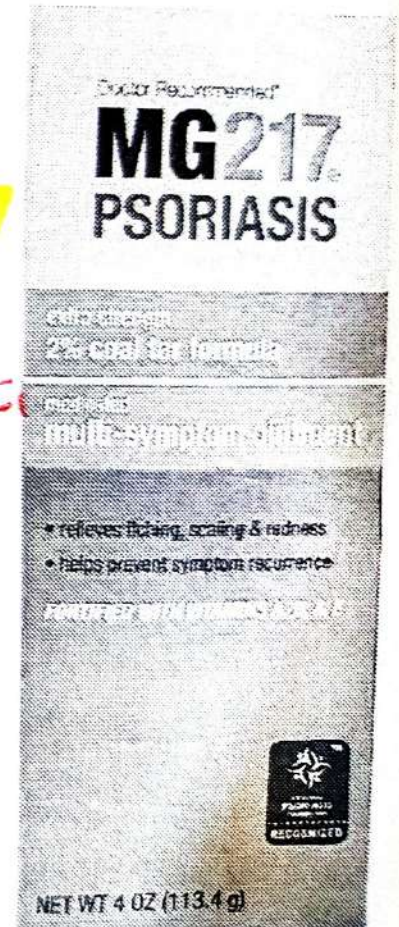
• Tar has apparent anti-inflammatory and anti-proliferative effects.
 لم يؤثر على يقلل من تكاثر السريع لـ epidermal cell

• Topical tar preparations, including shampoos, creams, and other preparations, can be used once daily.
 استخدام مرة واحدة باليوم

• Patients should be warned that tar products have the potential to stain hair, skin, and clothing.
 يمكن يوسخ الشعر

- For shampoos, the emphasis should be on making sure the product reaches the scalp. Tar shampoo should be left in place for 5 to 10 minutes before rinsing it out.

ننصح بالتأكد من وصول الشامبو لـ scalp لفروة الرأس وبعدها
بنتركه خمس عشر دقائق وبعدها يغسل الشعر .



Topical glucocorticosteroids

١/ يستعملوا بنفس الميكانيزم لـ oral

- Topical glucocorticosteroids are the most widely prescribed drugs for skin diseases.

- Like systemic glucocorticosteroids, topical glucocorticosteroids bind to cytoplasmic receptors that transport the drug to the nucleus where the complex binds to particular regions of DNA known as the glucocorticoid response element (GRE) and alters gene expression.

- Such receptors have been identified in both epidermis and dermis.

glucocorticosteroids → bind to cytoplasmic receptors → transport the drug into the nucleus

→ form complex with specific region on DNA as (GRE) → Alters gene expression

توجد هذه المستقبلات في (dermis @ epidermis) و تؤثر على جينات

Topical glucocorticosteroids

الآثار

- * The therapeutic effectiveness of topical corticosteroids is based primarily on their anti-inflammatory activity. ①
- The antimitotic effects of corticosteroids on human epidermis may account for an additional mechanism of action in psoriasis and other dermatologic diseases associated with increased cell turnover.

* السبب في زيادة الكورتيزون في الجلد هو زيادة معدل دوران الخلايا (cell turnover) وهو تأثيرها Antimitotic في psoriasis

الآثار
* Tare → anti-inflammatory
 → anti-proliferative

* glucocorticosteroids → anti-inflammatory
 → anti-mitotic

Topical glucocorticosteroids

تلك الامتصاص يكون في الطب المصاب أسرع من الطب السليم *

- Absorption:
- Corticosteroids are only minimally absorbed following application to normal skin.

جلد سليم ے امتصاص ضعیف

- Long-term occlusion with an impermeable film such as plastic wrap is an effective method of enhancing penetration, yielding a tenfold increase in absorption.

تسکین لہاء الطبقة مع تزیید امتصاصه

- Penetration is increased several fold in the inflamed skin of atopic dermatitis; and in severe exfoliative diseases, such as psoriasis.

الامتصاص أسرع بالجلد المصاب

- Ointment bases tend to give better activity to the corticosteroid than do cream or lotion vehicles.

المزهم أفضل من الكريم ومن اللوشن

- Increasing the concentration of a corticosteroid increases the penetration but not proportionately.

كل ما تم تزیید بتزید الكورتيزون ے رج یزیه ار

Penetration لہ لکن من بکل مناسب اور یحیی مکافی

أنواع

Topical glucocorticosteroids

- ① • Hydrocortisone
- ② • Betamethasone
- ③ • Acclometasone
- ④ • Triamcinolone
- ⑤ • Fluocinolone
- ⑥ • Clobetasol

Class	Potency	Generic name and strength
Class I	Very potent	Clobetasol propionate 0.05%
Class II	Potent	Betamethasone dipropionate 0.025% Betamethasone valerate 0.1% Betamethasone dipropionate 0.05% Difluocortolone valerate 0.1% Fluocinolone acetonide 0.025% Hydrocortisone butyrate 0.1% Mometasone furoate 0.1% Triamcinolone acetonide 0.1%
Class III	Moderate	Acclometasone dipropionate 0.05% Betamethasone valerate 0.025% Clobetasone butyrate 0.05% Fluocinolone acetonide 0.00525% Fluocortolone 0.25%
Class IV	Mild	Hydrocortisone 0.1%-2.5% Fluocinolone acetonide 0.0075%

BNF: British National Formulary

Vitamin D Analogues

calcipotriene

calcitriol

① أهمية فيتامين د على الكالسيوم

- Vitamin D, important in cellular and systemic calcium metabolism, also inhibits keratinocyte differentiation and proliferation, suggesting a role in the treatment of hyperkeratotic skin disease.

- However, use of vitamin D has been limited by its propensity to cause hypercalcemia.

بكون استزاده ضمن limit معين ليس ؟

- This has driven the development of analogues of vitamin D with less effect on calcium homeostasis.

سلبية التأثير ؟

- Calcipotriene** binds to vitamin D receptors as does vitamin D, but it is 100 times less active on systemic calcium metabolism because of its rapid local metabolism.

لا تم تطوير نظائر لفيتامين د ال بـتستغل نفس نفس فيتامين د ال

من ناحية ارتباطه بالـ receptor لكن - مختلف تأثيرهم على الكالسيوم

له مثال على نظير لفيتامين د ال هو calcipotriene - تأثيره على الكالسيوم

متباولينم أقل بـ ١٠٠ مرة !!!

Vitamin D Analogues

cream
scalp lotion
foam



Topical ^{موضعي} rapid local metabolism ^{كأنه}

- Calcipotriene (calcipotriol) is available as a 0.005% cream, scalp lotion, and foam.

- Is generally applied one to two times per day. ^{استخدام مرة أو مرتين في اليوم}

- On average, improvement is seen within 2 weeks of treatment with calcipotriene, with approximately 70% of patients demonstrating marked improvement after 8 weeks of therapy. <sup>خلال أسبوعين
بالبشر التحسين
ويعتدل فلان شهرين</sup>

- Adverse effects** include burning, itching, and **mild irritation**, with dryness and erythema of the treatment area.

كثير !!

- Care should be taken to avoid facial contact, which may cause ocular irritation. ^{كازم نفعه عن الوجه كأنه يسهل تهيج بالعين}

- A once-daily two-compound ointment (Taclonex) or foam (Enstilar) containing **calcipotriene and betamethasone** dipropionate are available. This combination is more effective than its individual ingredients and is well tolerated

يمكن يكون combination ويعطينا مفعول أفضل لكن بهاء الحالة

Taclonex + Enstilar ^{بصير استخدامه لمرة واحدة في اليوم مش}

Vitamin D Analogues

- **Calcitriol** is another vitamin D analogue.
- Calcitriol 3 mcg/g ointment is similar in efficacy and comparable in safety to calcipotriene 0.005% ointment and is **better tolerated in intertriginous and sensitive areas of the skin.**

منزلة

calcipotriene + calcitriol

في تشابهها من ناحية ال efficacy + safety
في مختلفها من ناحية انه ال calcitriol بقدر عادي
استخدمه مناطق حساسة بدون مايجب irritation

Tazarotene

- Tazarotene, a synthetic retinoid, is a prodrug that exerts its pharmacologic activity when hydrolyzed to its active metabolite, tazarotenic acid.

فائدة

- It modulates keratinocyte proliferation and differentiation.

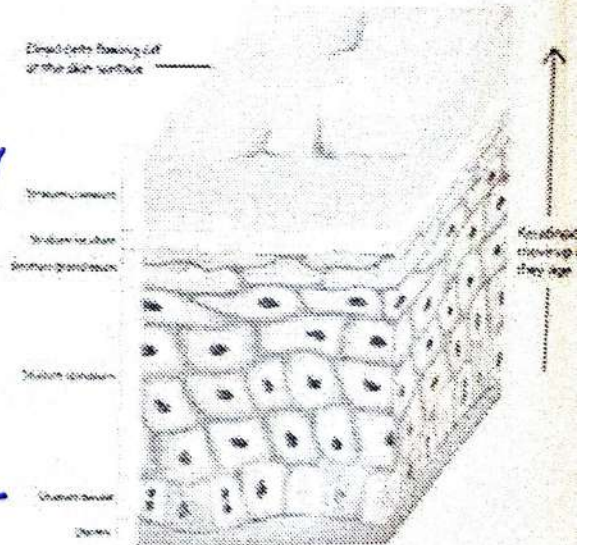
* Tazarotene hydrolysis → Tazarotenic acid

لهاد التي مع بيطين الكفون، شو الكفون

modulates keratinocyte
Proliferation and differentiation

يتني بيه كفا ر Vit.D بول Vit.D كان بول
inhibition not modulate.

Anatomy of the Epidermis



shutterstock.com - 125124725

Tazarotene

- Adverse effects (dose- and frequency-related): تبعاً لى الدور ولى كم مرة حطيت منه

1. Mild to moderate **pruritus, burning, stinging, or erythema.**

فوائد استءامه
مع الكورتيكويدون

- often used in combination with topical corticosteroids to decrease the incidence of local adverse events and to increase efficacy. (2) (1)

2. May **increase the tumorigenic potential of ultraviolet radiation.**

طى التأككده هو
داعى الشمس

- patients should be advised to avoid or minimize sun exposure and use a protective sunscreen. (2) (1)

3. Tazarotene is absorbed percutaneously, and **teratogenic systemic concentrations may be achieved if applied to more than 20% of total body surface area.**

- Women of childbearing potential must therefore be advised of the risk prior to initiating therapy, and adequate birth control measures must be utilized while on therapy.

- يجب التنبيه لكل مرأة بتخطيط للحمل قبل استءامه لانه
تتراكم فيه systemi

Biologic agents

- The biologic agents currently FDA approved for the treatment of moderate to severe psoriasis are: *2 class*
 - Tumor necrosis factor inhibitors: adalimumab, infliximab, etanercept.
 - cytokine inhibitors: ixekizumab, secukinumab, and ustekinumab

TABLE 61-2 Biologic agents for psoriasis.

Biologic Agent	Usual Adult Dosage
Adalimumab—Humira	80 mg SC x 1, then 40 mg q2 weeks
Etanercept—Enbrel	50 mg SC twice/week x 12 weeks, then once/week
Infliximab—Remicade	5 mg/kg IV at 0, 2, and 6 weeks, then q8 weeks
Ixekizumab—Taltz	160 mg at 0 weeks and 80 mg at 2, 4, 6, 8, 10, and 12 weeks, then q4 weeks
Secukinumab—Cosentyx	300 mg SC at 0, 1, 2, 3, and 4 weeks, then q4 weeks
Ustekinumab—Stelara	Either 45 mg or 90 mg SC at 0 and 4 weeks, then q12 weeks (dose for psoriasis is 45 mg for patients weighing ≤100 kg and 90 mg for those weighing ≥100 kg)

retinoid receptor
 ريتينويد ريسيپٽور

Acitretin → oral retinoid
 severe psoriasis

- Acitretin, an oral retinoid indicated for the treatment of severe psoriasis.
- It acts on retinoid receptors in the keratinocyte nucleus to correct abnormal cell differentiation.
- In contrast to the fast-acting cyclosporine and methotrexate, acitretin resolves psoriatic lesions more slowly.

* Acitretin → Keratinocyte nucleus → retinoid receptors → correct abnormal cell differentiation.

* cyclosporine + MTX ⇒ Fast acting

* Acitretin ⇒ slowly acting

تقرّيبًا هون رح نكي عن أعراض مشابهة لاستخدام
الدوكتان (isotretinoin) به نه برضو فيتامين A

Acitretin

- **Adverse effects** are dose dependent. They include:
 - **Hypervitaminosis A** (i.e., dry lips/cheilitis, dry mouth, dry nose, dry eyes/conjunctivitis, dry skin, pruritus, scaling, and hair loss)
 - **Hepatotoxicity**
 - **Hypercholesterolemia and hypertriglyceridemia.**
 - To counteract hyperlipidemic effects, gemfibrozil has been studied for concomitant use with acitretin.
 - **Teratogenic** and thus is contraindicated in females who are pregnant or who plan pregnancy within the 3 years following drug discontinuation.
- ❖ Patients **must not donate blood** during treatment and for 3 years after acitretin is stopped.

أعراض سمية
فيتامين A
"جفاف"

لازم ما يصير حمل وة بترجى بالدم دة بعد ٣ سنين
من إيقاف الدواء

The End



هائے ار enel اُحار من سک استبائت
موفقین ...

Marion Yacoub _____
17/11/2024