Drugs Used in Dermatologic Disorders

Pharmacology 3

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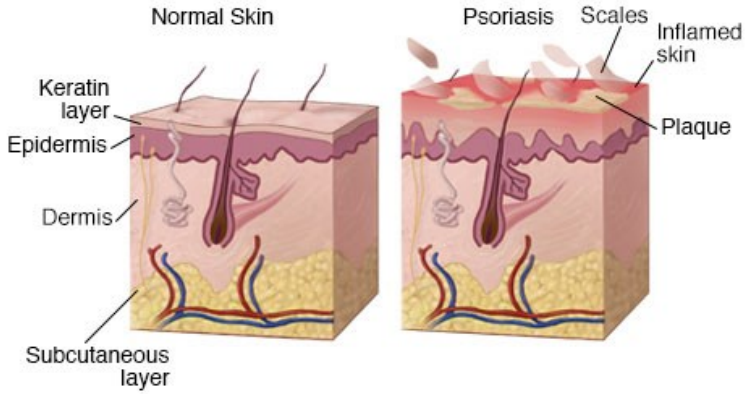
Psoriasis

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



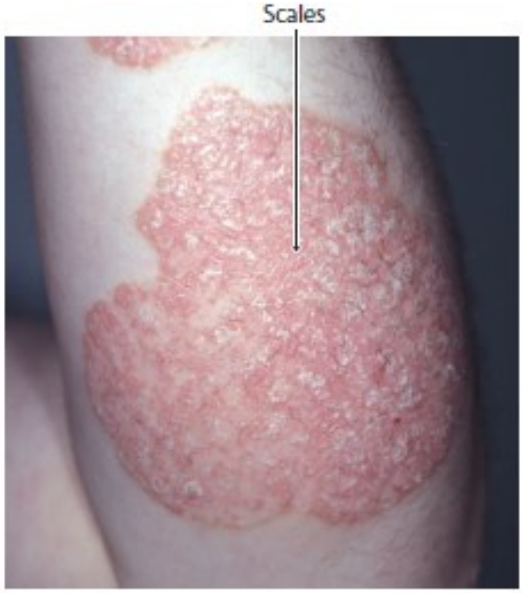
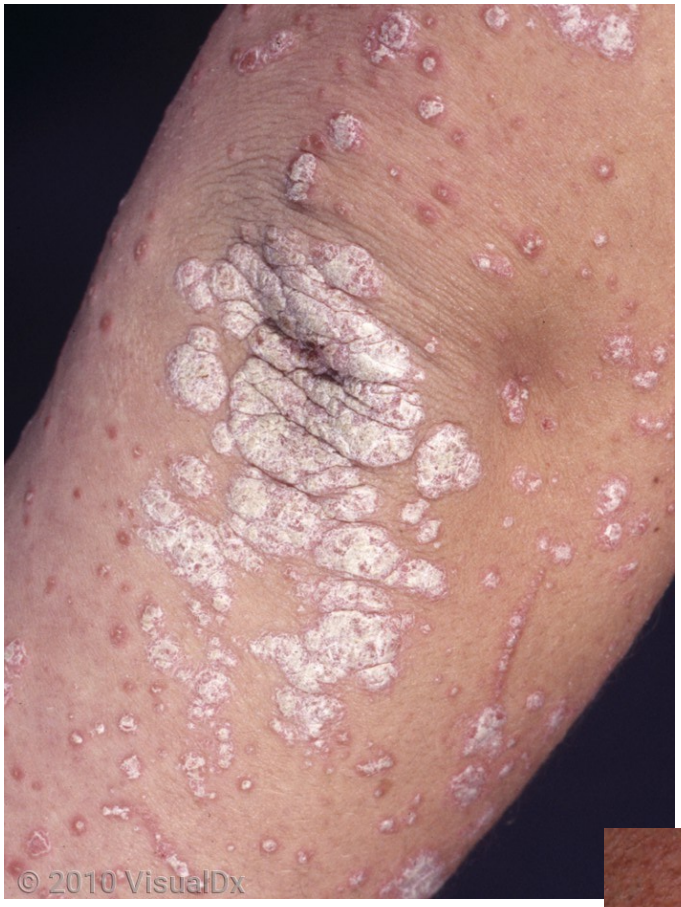


Figure 34.9
Psoriasis. A large, scaly, erythematous plaque.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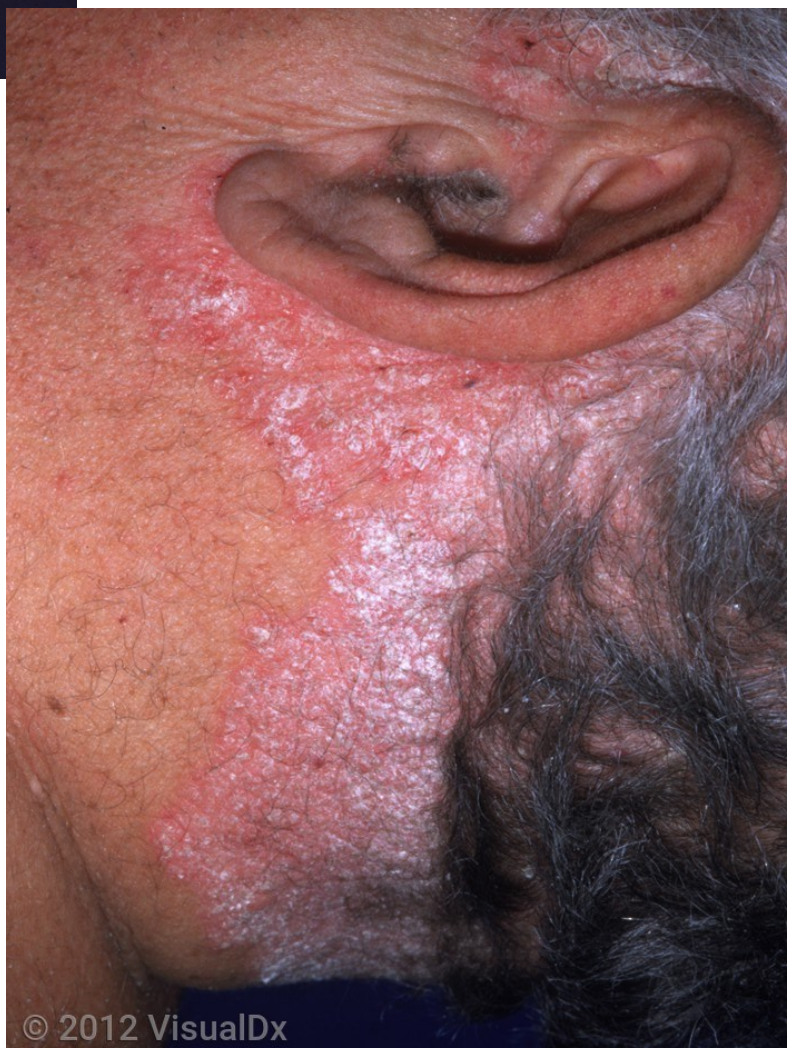
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General approach to psoriasis treatment

1. Emollients are frequently used during therapy-free periods to minimize skin dryness that can lead to early recurrence.
2. Topical treatments for mild to moderate psoriasis include:
   - Tar
   - Corticosteroids
   - Vitamin D analogues (Calcipotriene & Calcitriol)
   - Tazarotene
3. Systemic treatments for moderate to severe psoriasis include:
   - biologic agents
   - Acitretin
   - Cyclosporine
   - Tacrolimus
   - Methotrexate

Tar

- 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.
- Topical tar preparations, including shampoos, creams, and other preparations, can be used once daily.
- Patients should be warned that tar products have the potential to **stain hair, skin, and clothing.**
- 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.

Topical glucocorticosteroids

- 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.

Topical glucocorticosteroids

- The therapeutic effectiveness of topical corticosteroids is based primarily on their anti-inflammatory activity.
- 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.

Topical glucocorticosteroids

- Absorption:
- Corticosteroids are only minimally absorbed following application to normal skin.
- Long-term occlusion with an impermeable film such as plastic wrap is an effective method of enhancing penetration, yielding a tenfold increase in absorption.
- Penetration is increased several fold in the inflamed skin of atopic dermatitis; and in severe exfoliative diseases, such as psoriasis.
- Ointment bases tend to give better activity to the corticosteroid than do cream or lotion vehicles.
- Increasing the concentration of a corticosteroid increases the penetration but not proportionately.

Topical glucocorticosteroids potency

- Hydrocortisone
- Betamethasone
- Aclometasone
- Triamcinolone
- Fluocinolone
- Clobetasol

Class	Potency	Generic name and strength
Class I	Very potent	Clobetasol propionate 0.05%
Class II	Potent	Beclometasone dipropionate 0.025%
		Betamethasone valerate 0.1%
		Betamethasone dipropionate 0.05%
		Diflucortolone valerate 0.1%
		Fluocinolone acetonide 0.025%
		Hydrocortisone butyrate 0.1%
		Mometasone furoate 0.1%
		Triamcinolone acetonide 0.1%
Class III	Moderate	Alclometasone dipropionate 0.05%
		Betamethasone valerate 0.025%
		Clobetasone butyrate 0.05%
		Fluocinolone acetonide 0.00625%
		Fluocortolone 0.25%
Class IV	Mild	Hydrocortisone 0.1%-2.5%
		Fluocinolone acetonide 0.0025%

BNF: British National Formulary

Table 1 – Corticosteroids for psoriasis

Agent	Potency	Target area	Available vehicles
Hydrocortisone	Class 7, very low	Face	Cream, lotion
Desonide	Class 6, low	Face	Cream, lotion, ointment
Hydrocortisone valerate	Class 5, low to mid	Body	Cream, ointment
Triamcinolone acetonide	Class 4, mid	Body	Cream, lotion, ointment
Halcinonide	Class 3, mid to high	Body, caution in intertriginous areas	Cream, ointment, solution
Betamethasone valerate	Class 3, mid to high	Body, caution in intertriginous areas	Aerosol foam, cream, lotion, ointment
Fluocinonide	Class 2, high	Body except for intertriginous areas	Cream, gel, ointment, solution
Clobetasol propionate	Class 1, ultra-high	Body except for intertriginous areas	Aerosol foam, cream, gel, ointment, solution

Adapted from Scheinfeld NS. *Consultant.* 2005.[68]

Vitamin D Analogues

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

Vitamin D Analogues

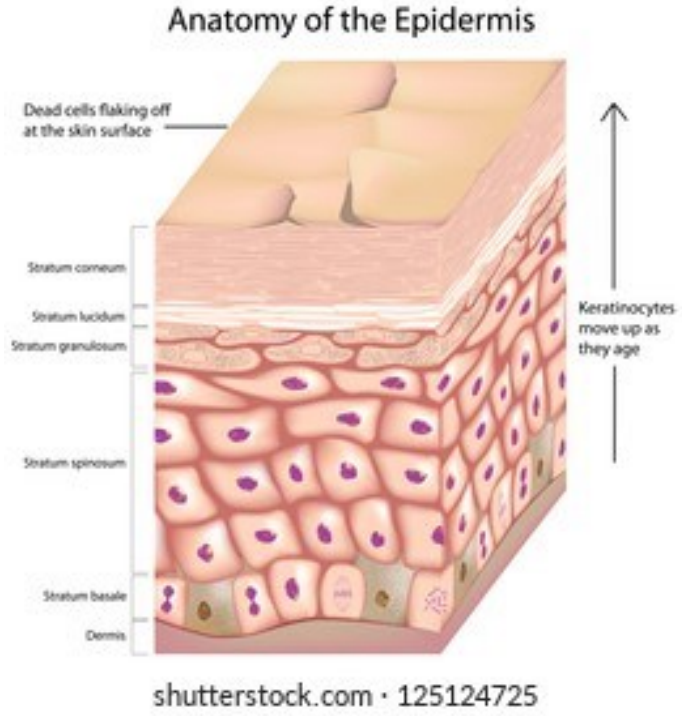
- **Calcipotriene (calcipotriol)** is available as a 0.005% cream, scalp lotion, and foam.
- Is generally applied one to two times per day.
- On average, improvement is seen within 2 weeks of treatment with calcipotriene, with approximately 70% of patients demonstrating marked improvement after 8 weeks of therapy.
- **Adverse effects** include burning, itching, and mild irritation, with dryness and erythema of the treatment area.
  - Care should be taken to avoid facial contact, which may cause ocular irritation.
- 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

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.**

Tazarotene

- Tazarotene, a synthetic retinoid, is a prodrug that exerts its pharmacologic activity when hydrolyzed to its active metabolite, tazarotenic acid.
- It <u>modulates keratinocyte proliferation and differentiation.</u>



Tazarotene

- Adverse effects (dose- and frequency-related):
  1. Mild to moderate **pruritus, burning, stinging, or erythema.**
     - often used in combination with topical corticosteroids to decrease the incidence of local adverse events and to increase efficacy.
  2. May **increase the tumorigenic potential of ultraviolet radiation**.
     - patients should be advised to avoid or minimize sun exposure and use a protective sunscreen.
  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.

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Biologic agents

- The biologic agents currently FDA approved for the treatment of moderate to severe psoriasis are:

1. Tumor necrosis factor inhibitors: **adalimumab, infliximab**, **etanercept.**
2. cytokine inhibitors: **ixekizumab, secukinumab,** and **ustekinumab**

TABLE 61–2 Biologic agents for psoriasis.

Biologic Agent	Usual Adult Dosage
Adalimumab—*Humira*	80 mg SC × 1, then 40 mg q2 weeks
Etanercept—*Enbrel*	50 mg SC twice/week × 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)

Acitretin

- **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

- **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.

The End