Topical therapies for PSORIASIS

Peter Foley MBBS, BMedSc, MD, FACD
Associate Professor of Dermatology, The University of Melbourne, Department of Medicine (Dermatology), St Vincent’s Hospital Melbourne
Dermatology Investigation, Biological Therapies and Photobiology Clinics, St Vincent’s Hospital Melbourne
Biological Therapies and Phototherapy Clinics, Skin and Cancer Foundation Inc
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- Celgene - I
- Australian Ultraviolet Services - C
- Aspen - SP
- BMS - I
TREATMENT OPTIONS - PSORIASIS

• Do nothing
• Topical therapy
• Phototherapy
• Systemic therapy
• Biological therapy
Definition of treatment goals for moderate to severe psoriasis: a European consensus

U. Mrowietz · K. Kragballe · K. Reich · P. Spuls · C. E. M. Griffiths · A. Nast · J. Franke · C. Antoniou · P. Arenberger · F. Balieva · M. Bylaitė · O. Correia · E. Daudén · P. Gisondi · L. Iversen · L. Kemény · M. Lahfa · T. Nijsten · T. Rantanen · A. Reich · T. Rosenbach · S. Segaert · C. Smith · T. Talme · B. Vole-Platzer · N. Yawalkar
Tools

- Before defining treatment goals, a consensus about the definition of psoriasis severity using the tools was necessary.
Definition of mild psoriasis (I)

- BSA ≤10 and PASI ≤10 and DLQI ≤10
- In accordance with existing guidelines, it is recommended to treat mild psoriasis with topical agents

Definition of mild psoriasis (II)

- If BSA ≤10 and PASI ≤ 10 indicates mild disease but DLQI >10 indicates significant impact on quality of life, psoriasis can be considered moderate to severe and systemic therapy may be initiated when the patient’s disease cannot be controlled by topical treatment.
Mild → moderate to severe

- Involvement of visible areas
- Involvement of major parts of the scalp

Mild → moderate to severe

- Involvement of genitals
- Involvement of palms and/or soles

Mild → moderate to severe

- Onycholysis or onychodystrophy of at least two fingernails

Mild → moderate to severe

- Pruritus leading to scratching
- Presence of single recalcitrant plaques
Treatment options

- **Available treatments:**
  - topical therapies
  - phototherapies
  - systemic agents

- **Approximately 70–80% can be treated adequately using topical therapy; 20–30% by phototherapy, systemic agents or biological therapies.**

- **Topical therapy is the preferred first-line treatment for psoriasis,** and:
  - should be tailored to individual needs
  - should take into account the site and extent of the lesion, the patient’s age and likely compliance with treatment

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Psoriasis treatment in pregnancy

- Teratogenic systemic therapies are contraindicated\(^1\)
- Avoid topical retinoids\(^2\)
- Potent topical corticosteroids to be used with caution\(^3\)

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TOPICAL THERAPIES FOR PSORIASIS

• General skin care
  - Soap free cleansers
  - Moisturiser/emollient

• Keratolytics
  - Salicylic acid

• Corticosteroids

• Vitamin D analogues

• Retinoids

• Tar

• Dithranol

• Calcineurin inhibitors
TOPICAL THERAPIES FOR PSORIASIS

• Choice of treatment depends on the extent and pattern of psoriasis, and patient preference\textsuperscript{1}

• Effective in short term (6–8 weeks) with a 2 point improvement on a 12 point severity scale\textsuperscript{2}

• Poor adherence to topical therapy in psoriasis may be common\textsuperscript{3}

First line

Topical corticosteroids (limited duration?)

Topical vitamin D derivative (calcipotriol)

Topical calcipotriol/steroid combination

Topical tazarotene (usually combined with topical steroid)

Topical calcineurin inhibitors (on flexural aspects/face)

Targeted phototherapy (for use on limited, resistant plaques)

Second line

Systemic agents (short-term use)

Creams vs Ointments

**Cream**
- Oil in water
- Runnier
- Contains preservatives
  - stings

**Ointment**
- Water in oil
- Thicker and greasier
- Less preservatives
- More moisturising
Creams vs Ointments vs Lotions

- Ointments are used on dry areas to moisturise.
- Lotions are used in scalp (elocon, diprosone, advantan).
- Creams are used on hairy areas to reduce occlusion folliculitis.
Three Factors Determine the Potency of Topical Drugs

1. **Activity of the drug**
2. **Delivery of the drug by the vehicle**
3. **Compliance** Whether patients actually apply the product
Use Enough Topical Steroid

- 1 finger-tip unit of cream = covers 2 x palmar surface area
- Tip: Prescribe enough topical steroid through authority if required
Potency of Topical Corticosteroids

Weak
- Hydrocortisone 1% (Sigmacort, Cortef, Egocort)
- Desonide (Desowen)
- Clobetasone (Eumovate)

Medium (100g tubes)
- Triamcinolone acetonide (Aristocort)
- Bethamethasone valerate (Celestone, Betnovate)

Potent (15g tubes)
- Methylprednisolone aceponate (Advantan)
- Mometasone Furoate (Elocon/Novasone)
- Bethamethasone dipropionate (Diprosone/Eleuphrat)

Superpotent
- Diprosone OV
- Clobetasol dipropionate
Topical Corticosteroids

• The mechanisms of action of corticosteroids include:
  - anti-inflammatory
  - antiproliferative
  - immunosuppressive
  - vasoconstrictive effects

• These effects are mediated through their binding to intracellular corticosteroid receptors and regulation of gene transcription of numerous genes, particularly those that code for proinflammatory cytokines
Topical Corticosteroids

- Local cutaneous side effects, which occur more frequently than systemic side effects, are more commonly seen at steroid-sensitive sites, including the face and intertriginous areas.
Topical Corticosteroids

- Skin atrophy
- Telangiectasia
- Striae distensae
- Acne
- Folliculitis
- Purpura

- May exacerbate preexisting or coexistent dermatoses
  - rosacea
  - perioral dermatitis
  - tinea infections

- May on occasion cause contact dermatitis
Topical Corticosteroids

- Systemic side effects, although infrequent, may occur when locally applied corticosteroids become absorbed through the skin and enter the circulatory system.
- The greatest risk of systemic side effects occurs when potent or superpotent corticosteroids are used over a large surface for a prolonged period or are used under occlusion.
- Systemic effects have also been observed with widespread and extended use of mid-potency corticosteroids.
Topical Corticosteroids

- Well-known but relatively uncommon systemic side effects of topical corticosteroid usage include:
  - Hypothalamic-pituitary-adrenal (HPA) axis suppression
  - Cushing’s syndrome
  - Osteonecrosis of the femoral head
  - Cataracts and glaucoma
Other topicals

• Vitamin D analogues
  - Calcipotriol
    • Monotherapy = Daivonex
    • Combination therapy = Daivobet

• Retinoids
  - Tazarotene

• Calcineurin inhibitors
  - Pimecrolimus
  - Tacrolimus
Other topicals

• Tar
  - Extemporaneous
  - Proprietary
    • Exorex
    • Linotar
    • Hamilton Laboratories Eczema Cream

• Dithranol
  - Extemporaneous
  - Proprietary
    • Dithrasal
    • Micanol
Calcipotriol

- The mechanism of action of the vitamin D analogues in psoriasis is believed to be mediated by their binding to vitamin D receptors, which leads to both the inhibition of keratinocyte proliferation and the enhancement of keratinocyte differentiation.
Calcipotriol

- Calcipotriol inhibits epidermal proliferation and inflammation and enhances normal keratinisation,\(^1\) making descaling or the concomitant use of keratinising agents unnecessary while patients are undergoing treatment.

Calcipotriol

Local side effects
• Burning
• Pruritus
• Oedema
• Peeling
• Dryness
• Erythema

Systemic side effects
• Hypercalcemia
• Parathyroid hormone suppression
• Rare unless patients:
  - are applying more than the recommended dosage of 100 g/wk
  - have underlying renal disease
  - have impaired calcium metabolism
Tar

- Obtained by destructive distillation of bituminous coal at very high temperatures
- Over 10,000 different compounds make up coal tar but only 400 or so identified
  - Main groups of compounds making up crude coal tar are 48% hydrocarbons, 42% carbon and 10% water
- Thick, nearly black, viscous liquid with a characteristic smell
- Most often obtained in solution form (0.1 - 20%)
Tar

- The mechanism of action of coal tar is not well understood
- Known to suppress DNA synthesis
- Antimicrobial, antipruritic (reduce itching) and keratoplastic (normalise keratin growth in the skin and reduce scaling) effects
- May initially cause mild stinging or irritation
- When used on the scalp, it may temporarily discolour bleached, tinted, light hair
- Stains skin and clothing - the stain on the skin will wear off after cessation
- Coal tar may cause photosensitivity
- Controversy over the carcinogenic potential of coal tar
Dithranol

- Anthralin
- Hydroxyanthrone, anthracene derivative
  - tricyclic aromatic hydrocarbon consisting of three fused benzene rings
- Anti-proliferative effects
  - inhibition of DNA synthesis
  - strong reducing properties
- Prevention of T-lymphocyte activation and normalisation of keratinocyte differentiation may occur by a direct effect on mitochondria
Dithranol

- More dithranol penetrates into impaired skin in 30 min than into intact skin during about 16 hr
- Creams, ointment or pastes in 0.1 - 2%
Dithranol

- Slower onset of action, typically several weeks, but without potential for rebound
- Cannot be used on face or genitalia
- Temporarily stains skin yellowy-brown
- Permanently stains clothing fabrics
- May cause a local burning sensation and irritation
  - may be minimised by careful attention
  - gradually stepping up strength
- Surrounding skin can be protected using soft white paraffin
Tazarotene

• Functions by:
  - Normalising abnormal keratinocyte differentiation
  - Diminishing hyperproliferation
  - Decreasing expression of inflammatory markers
Tazarotene

• Pregnancy category X
• The most common side effect of tazarotene is local irritation in lesional and perilesional skin
  - Irritation may be reduced by use of the cream formulation, use of the lower concentration product, combination use with moisturisers, application on alternate days, short-contact (30 to 60 minutes) treatment and applying in combination with topical corticosteroids
Daivobet - what's the hook?

- Combination therapy
- Once daily
- Ointment
- Rapid onset
- Transition to Daivonex
# Common psoriasis treatment options

<table>
<thead>
<tr>
<th>Agent</th>
<th>Efficacy</th>
<th>Relapse rate</th>
<th>Side effects</th>
<th>Cosmetic problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emollients</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Keratolytic agents</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Coal tar</td>
<td>++</td>
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<tr>
<td>Dithranol</td>
<td>+++</td>
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<tr>
<td>Corticosteroids (potent/very potent)</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>-</td>
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<tr>
<td>Vitamin D$_3$ analogues</td>
<td>+++</td>
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<tr>
<td>Corticosteroids/ vitamin D$_3$ analogues</td>
<td>+++</td>
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<tr>
<td>Tazarotene</td>
<td>++</td>
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</tbody>
</table>

-, little or none; +, depending on the number of +s, denotes intensity, frequency, or severity.
Cochrane review

Topical treatments for chronic plaque psoriasis:

- Vitamin D is more effective than coal tar
- The relative effectiveness of vitamin D and dithranol varies but the effectiveness of dithranol and tazarotene is probably similar to that of vitamin D products
- Vitamin D products are more effective than emollients alone
- Vitamin D and corticosteroids are equally effective for treating psoriasis of the body, but corticosteroids appear to be more effective than vitamin D for treating psoriasis of the scalp
- Combined treatment with vitamin D and corticosteroids is more effective than either vitamin D alone or corticosteroids alone for both body and scalp psoriasis
Reasons for poor adherence

- Long-term treatment required\(^1\)
- Difficulties with treatment
  - not convenient to apply\(^2\)
  - not easy to use\(^2\)
  - side effects\(^1\)
- Quality-of-life issues\(^2\)
- Psychosocial disability\(^3\)
- Unrealistic expectations\(^4\)
- Lack of time in discussion with the healthcare professional\(^4\)
- Lack of suitable management programme\(^4\)

Strategies to improve adherence

Individualised therapy maximises outcomes

- Appropriately personalised therapy\(^1\)
- Patient education\(^2\)
- Managing patient expectations\(^3\)
- Positive patient-healthcare professional relationship\(^1\)
- Psychological support\(^1\)
- Sympathetic approach\(^2\)
- Cognitive behavioural therapy\(^2\)

Optimising topical therapy for psoriasis

• Positive patient–healthcare professional relationship

• Manage patient expectations

• Maximise adherence
  • Provide individualised, safe treatment
  • Achieve long-term control/remission
  • Improve quality of life
  • Patient education
  • Empower patient
Special sites

- Scalp
- Nails
- Flexures
- Face
- Genitals
Scalp

- OTC shampoos: coal tar shampoos, ketoconazole, ciclopirox olamine, zinc pyrithione
- Leave-on applications for more severe cases:
  - topical corticosteroid lotion
  - calcipotriol
  - salicylic acid and coal tar creams
  - dithranol
DAIVOBET® 50/500 GEL
How to use Daivobet® 50/500 gel
(calcipotriol/betamethasone dipropionate)

1. Shake the bottle before removing the cap, so that the gel mixes well. Comb your hair to remove any loose scales, and part your hair before applying the gel.

2. Apply some Daivobet® gel to your index finger, from the tip of the finger to the first crease in the finger. This is called a fingertip unit (FTU). Usually, an amount between 2 and 8 FTUs a day is enough to treat your scalp.

3. Gently rub the gel only on the areas of the scalp affected by psoriasis. Wash your hands thoroughly after applying the gel. Avoid getting the gel on other parts of the body (especially the face, mouth, and eyes).

   If you get the gel in your eyes, rinse your eyes with clean water, and tell your doctor. Wipe off any gel that has accidentally come into contact with skin that is not affected by psoriasis.

4. To get the best results, do not wash your hair immediately after applying the gel. Let the gel remain on your scalp for a few hours, for example, overnight, or during the day, or between returning home from work and going to bed. Do not bandage, cover, or wrap the treated area. Avoid contact with fabric that is easily stained by grease (e.g., silk).

5. While your hair is still dry (prior to wetting your hair), rub a mild shampoo into the areas where the gel was applied. This will allow the gel to wash out easily. Leave the shampoo on the scalp for a couple of minutes.

6. After you have applied the shampoo to dry hair and left it for a few minutes, e.g., while cleaning your teeth, rinse the gel from your hair, then wash and style it as usual.
Nails

- Avoid trauma
- Keep nails short
- Topical corticosteroid lotions
- Combination topical corticosteroid/calcipotriol gel
- Iontophoresis
  - Dexamethasone
  - Methotrexate
Flexures

- Topical corticosteroids
- Topical calcineurin inhibitors
- Low strength tar preparations
Face

- Topical corticosteroids
- Topical calcineurin inhibitors
- Low strength tar preparations
Genitals

- Topical corticosteroids
- Topical calcineurin inhibitors
- Low strength tar preparations
Topical Therapies for Psoriasis

- May be effective as monotherapy
- Often used in combination with photo- or systemic therapies
- Choice depends on nature and extent of disease
- Compliance - adherence and/or persistence may be poor
Questions?