

Topical treatments in dermatology

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Abstract

Topical medications are key agents in treating a range of skin conditions, as they allow affected areas to be targeted while avoiding systemic side effects. Although there is a wide range of topical agents available, it is helpful to be familiar with a few commonly used formulations. This article describes how to select appropriate agents, prescribe appropriate quantities, and counsel patients on safe and effective treatment regimens.

Key words: Acne; Eczema; Emollients; Topical antimicrobials; Topical corticosteroids; Topical immunomodulators; Topical retinoids

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Introduction

After an inpatient dermatology review, it is often the junior doctor who prescribes the suggested treatment plan. The plethora of available topical formulations, sometimes with similar sounding names (but different strengths and actions), can cause confusion among trainees. It is also essential to know how to advise patients on effective application techniques and expected side effects. This article gives trainees more confidence with this. The focus is on topical treatments for common inflammatory dermatoses and pre-cancerous and cancerous skin conditions. Topical antimicrobial agents are beyond the scope of this article.

Understanding topical agents

Vehicles

Topical formulations have an active ingredient in an inactive base (vehicle). The choice of vehicle depends on several factors, including which areas of the body are affected, the type of skin condition and patient preference. In general, ointments are greasier preparations that have high potency, as they are the most occlusive and therefore have the most significant penetration. This is followed by creams, lotions, solutions, gels, foams, sprays and shampoos (Chen and Obayan, 2015). **Table 1** describes different vehicles along with examples.

Emollients

Emollients are used in a wide variety of skin conditions. They are moisturisers which primarily hydrate dry, itchy skin and are available in different vehicles including ointments, creams, lotions, gels or sprays.

Table 1. Vehicles for topical agents

Vehicle	Description	Examples
Ointments	Greasy preparations: their occlusive effect leads to greater percutaneous absorption of the active ingredient (Chen and Obayan, 2015)	Hydromol ointment: a greasy emollient
Lotions, oils and foams	Easy to apply formulations in a liquid or foamy base	Dermol 500 lotion: an emollient with antiseptic properties that can also be mixed with water to use as a soap substitute
Creams	Emulsions of oil in water which are generally well absorbed	Zerobase cream

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A commonly used emollient is white soft paraffin along with liquid paraffin, which is available as a:

- Cream (Zerobase cream with white soft paraffin 10%/liquid paraffin 11%, 500 g)
- Ointment (50:50 ointment with white soft paraffin 50%/liquid paraffin 50%, 500 g)
- Spray (Emollin 50:50 spray with white soft paraffin 50%/liquid paraffin 50%, 240 ml).

They can be plain with no added ingredients (eg Hydromol, Cetaban) or can contain ingredients such as urea to soften keratin (eg Balneum), antiseptics (eg Dermalol), or lauromacrogols with itch-relieving properties (eg E45 Itch plus).

They should be applied liberally at least once daily, with more frequent applications (two to four times daily) for patients with very dry skin, and should be used even when the skin appears clear. Approximately 250–500 g will be needed every week for an adult of average size (National Institute of Health and Care Excellence, 2021). Emollients are best applied to the skin in the direction of hair growth (rather than rubbing them in) to avoid occlusion or irritation of the hair follicles, which could lead to folliculitis (Burge et al, 2016).

It is important to remember that all paraffin-based emollients, such as white soft paraffin in liquid paraffin (white soft paraffin/liquid paraffin 50:50), have an associated risk of burns (regardless of paraffin concentration) as they act as an accelerant when cloth with dried emollients is ignited (Medicines and Healthcare products Regulatory Agency, 2018). This risk also exists with paraffin-free emollients. Patients must be warned about this risk and counselled on smoking cessation when prescribing emollients.

Emollients can also be used as soap substitutes. Patients with conditions such as eczema should avoid using soap as recommended by the National Institute of Health and Care Excellence (2018) guidelines. Many commercially available soaps contain surfactants such as sodium lauryl sulphate, which can cause damage as a result of their emulsifying effects on the lipids of the skin. Instead, emollients such as Hydromol or Dermalol 500 lotion dissolved in warm water can be used as soap substitutes.

Dermatological conditions and their treatments

Eczema

The terms eczema and dermatitis (inflammation of the skin) tend to be used synonymously. Eczema refers to a cutaneous reaction pattern with variable signs depending on whether it is acute, sub-acute or chronic. In cases of acute eczema, cutaneous signs include ill-defined areas of erythema, oedema, and areas of exudation and crusting (if infected). Features of chronic eczema include lichenification (thickened skin with increased skin markings) and hyper- or hypo-pigmented post-inflammatory changes (Burge et al, 2016).

Along with emollients, topical corticosteroids are widely used in the management of eczema. They are classified based on their strength. Some commonly used trade names are given in [Table 2](#).

Super potent and potent topical corticosteroids should be avoided in areas where the skin is thin (face and neck) or in intertriginous locations (axilla, inframammary and groin areas) where there is greater penetration and absorption of medication.

Table 2. Topical corticosteroids

Strength	Chemical name	Commonly used trade names
Mild	Hydrocortisone 0.5%, 1%, 2.5%	Hydrocortisone
Moderately potent	Betamethasone valerate 0.025%	Betnovate RD*
	Clobetasone butyrate 0.05% [†]	Eumovate, Clobavate
Potent	Betamethasone valerate 0.1%	Betnovate*
	Mometasone furoate 0.1%	Elocon
Super potent	Clobetasol propionate 0.1% [†]	Dermovate

*Betnovate RD 0.025% (ready diluted) is a moderately potent topical corticosteroid whereas Betnovate 0.1% is a potent topical corticosteroid. [†]Clobetasone and clobetasol have similar sounding names but the latter is super potent and they should not be confused



Figure 1. One fingertip unit.

Local adverse effects include thinning of the skin, bruising, stretch marks, folliculitis, acne, loss of skin pigment, and worsening of untreated fungal infections (Burge et al, 2016). It is important to counsel patients on safe quantities of topical corticosteroids to try to avoid some of these side effects. These are often measured in fingertip units – the amount of cream or ointment that covers the end of an adult finger from the distal interphalangeal joint to the tip of the finger when squeezed from a tube with a 5 mm nozzle (Figure 1). This is enough to cover an area of skin the size of two palms with the fingers together (Burge et al, 2016).

The National Institute of Health and Care Excellence (2018) guideline recommends the following for control of an acute flare of eczema.

For the body (excluding face, axillae and genitalia):

- Prescribe a topical corticosteroid according to the severity of the eczema (usually a moderately potent or potent topical corticosteroid)
- Advise the patient to apply once daily until clear, and then for 48 hours after the eczema has cleared (up to 14 days in total)
- To avoid the long-term side effects of topical corticosteroids, clinicians can counsel patients to use them for up to 2 weeks at a time, and then step down to intermittent use 2 days a week (eg Saturday and Sunday). This is also known as weekend therapy, and involves applying topical corticosteroid to previously active sites. This is one of the most clinically useful evidence-based approaches for treating chronic or relapsing eczema (Phillips et al, 2016)
- To avoid dilution, topical corticosteroids should be applied 20–30 minutes before or after any emollient (Burge et al, 2016).

For the face, axillae and genitalia:

- Only a mild to moderate potency topical corticosteroid should be prescribed, usually for up to 5 days at a time.

The above durations of treatment are recommended by the National Institute of Health and Care Excellence (2018) guidelines, but in clinical practice, topical corticosteroids are sometimes used for longer periods. Table 3 outlines the average quantities of topical corticosteroids needed for once-daily application for an average adult over a 2-week period and Figure 2 illustrates the approximate number of fingertip units required for each body part on an average adult. Clinical scenario 1 discusses a patient and suggested treatment options.

Table 3. Average quantities of topical corticosteroids needed for once-daily application for an average adult for 2 weeks

Area	Quantity
Face and neck	15–30g
Both hands	30g
Scalp	30g
Both arms	30–60g
Both legs	100g
Trunk	100g
Groin and genitalia	15–30g

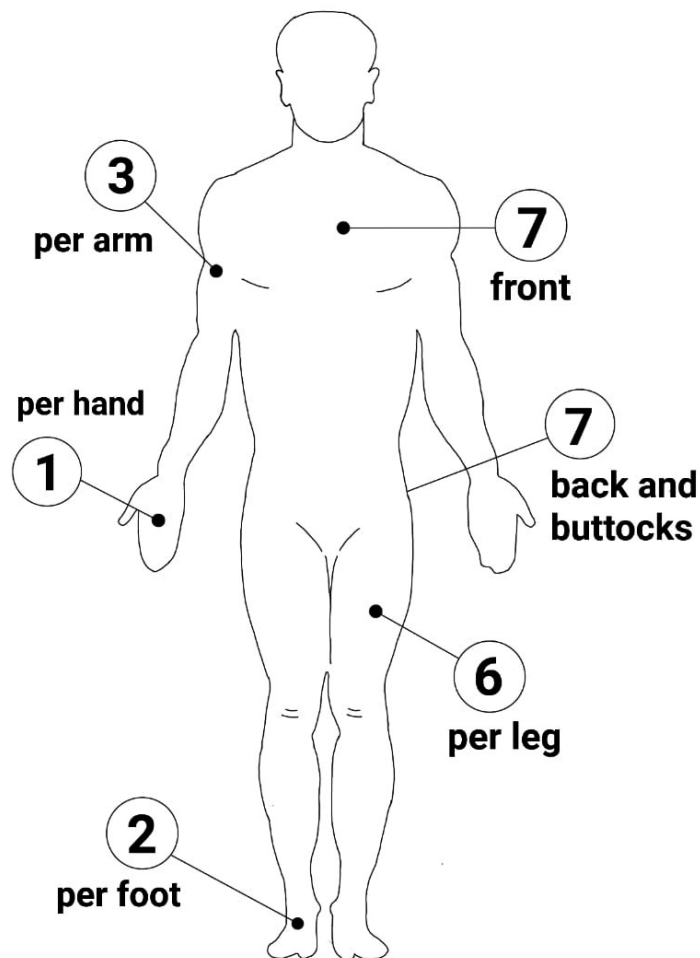


Figure 2. The approximate number of fingertip units required for each body part on an average adult man.

Clinical scenario 1

Mrs Y is concerned about her legs as they feel dry, itchy and appear slightly red. On examination, she has multiple varicose veins bilaterally. There are areas of ill-defined, dry, erythematous plaques with excoriations suggestive of an eczematous process. The skin does not appear infected. The diagnosis is venous eczema.

- What could be prescribed to help?
- What should she avoid using and what could be prescribed instead?

Answers

An example of a management regimen would include the following agents:

Emollient – for example Hydromol ointment (500 g), Cetraben cream (500 g) or Aproderm gel (500 g) to use at least twice daily

Topical corticosteroids – mometasone ointment (100g tube x 1) to be used once daily on affected areas of the legs until clear (up to 2 weeks at a time), then step down to use on Saturday and Sunday for a few weeks and then stop.

Steroid-sparing agent – for recurrent flares, she could use tacrolimus 0.1% ointment once daily as a steroid-sparing agent during the week, with topical mometasone ointment on Saturday and Sunday to maintain control.

She should avoid using soaps or shower gels and use a soap substitute to wash with instead, eg Dermal 500 lotion.

Steroid phobia is fear and anxiety about using topical corticosteroids which may be accentuated by the common misconception that topical corticosteroids are analogous to anabolic steroids or oral steroids (Charman et al, 2000). This can lead to poor compliance and failure to achieve adequate control of the skin condition. It is important to take the time to educate patients on the safe and effective use of topical steroids and reassure them that topical corticosteroids rarely cause serious adverse effects if used correctly (National Institute of Health and Care Excellence, 2018).

Topical calcineurin inhibitors can be used as steroid-sparing agents in eczema (see below).

Psoriasis

Sharply demarcated, scaly erythematous plaques are the cutaneous hallmark of chronic plaque psoriasis. Topical treatment options for psoriasis include topical corticosteroids and topical vitamin D analogues (Van de Kerkhof and Nestle, 2018). Combination therapy with a topical vitamin D analogue (eg calcipotriol) and topical corticosteroids (eg betamethasone) is more effective than either alone (National Institute of Health and Care Excellence, 2012). For example, a calcipotriol and betamethasone combination is available as a gel (Dovobet gel), ointment (Dovobet ointment) or foam (Enstilar foam).

In patients with calcium metabolism disorders, topical vitamin D analogues must be used cautiously as they can cause severe hypercalcaemia when more than 300 g per week is used, but are generally safe at doses of less than 100 g per week (Jabbar-Lopez et al, 2014).

Before moving on to other inflammatory dermatoses, it is important to mention the role of topical calcineurin inhibitors, which act as topical immunomodulators and are mainly used as steroid-sparing agents in conditions such as eczema and psoriasis (especially in areas such as the face and intertriginous areas). Examples include tacrolimus ointment (0.1% or 0.03%) or pimecrolimus cream (1%).

Tacrolimus is available as Protopic 0.1% ointment (for use in patients aged >16 years) and 0.03% ointment (for use in patients aged >2 years). Pimecrolimus 1% is available as Elidel cream. The most commonly reported side effects are burning, stinging or a sensation of warmth at sites of application, and it is important to counsel patients on this (Fox et al, 2018). This usually settles after a few days of continued applications.

A Cochrane review by Cury Martins et al (2015) found that tacrolimus 0.1% ointment was more effective than mild potency topical corticosteroids, tacrolimus 0.03% ointment and pimecrolimus 0.1% cream. A meta-analysis from Svensson et al (2011) found tacrolimus 0.1% ointment had similar efficacy to potent topical corticosteroids for treating atopic dermatitis. **Clinical scenario 2** discusses a patient and suggested treatment options.

Acne vulgaris

Acne is a chronic inflammatory skin condition characterised by blockage and inflammation of the pilosebaceous unit (the hair follicle, hair shaft and sebaceous gland). It can present with inflammatory lesions (papules, pustules or nodules), non-inflammatory lesions (open comedones – whiteheads, or closed comedones – blackheads), or a mixture of both.

Topical agents alone can be used to treat mild acne (predominantly non-inflamed lesions, with a few inflamed lesions) or can be used in combination with systemic agents for moderate or severe acne (widespread inflammatory lesions) (National Institute of Health and Care Excellence, 2020).

Targeted topical agents for acne include benzoyl peroxide and azelaic acid, which have a bacteriostatic effect against *Propionibacterium acnes* (a Gram-positive bacteria implicated in the pathogenesis of acne) (Carley et al, 2018). Benzoyl peroxide is also available in combination with other topical antibiotics such as clindamycin (Duac).

Other topical formulations for acne include topical retinoids, which are analogues of vitamin A. Examples of these formulations include first generation topical retinoids such as tretinoin and newer third generation retinoids such as adapalene (Differin 0.1% gel/cream) and tazarotene (Zorac 0.05% or 0.1% gel). Topical retinoids are available in combination with benzoyl peroxide, eg Epiduo gel 0.1%/2.5%, which contains adapalene 0.1% and benzoyl peroxide 2.5%. Patients should be advised to spread a thin layer to cover the whole affected area, not just over visible spots (National Institute of Health and Care Excellence, 2020).

Clinical scenario 2

Just after 5 pm on a Friday, you are asked to see Mrs X with a 'worsening rash'. Realising that the inpatient dermatology service only resumes on Monday, you approach her. She is a 62-year-old woman with a background of well-controlled psoriasis. She has used a 'few creams and ointments' in the past but has not needed any treatment for the last 10 years. She is an inpatient for the treatment of community-acquired pneumonia and is starting to feel much better from a respiratory point of view. However, she feels her psoriasis has flared during this admission.

On examination, you note around 10–15, well-defined, pink plaques with a silvery-white scale over her trunk (Figures 3a and b) and upper limbs. Given her previous history and typical appearance of the plaques, you confirm that this is a moderate flare of psoriasis. She thanks you for confirming this and requests some treatment.

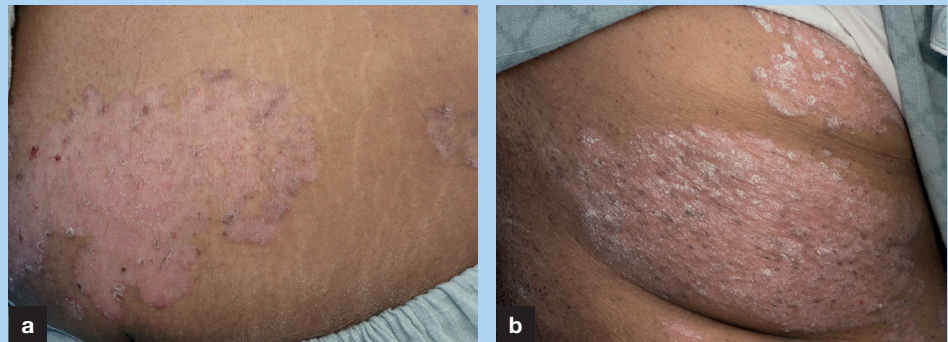


Figure 3. Clinical photographs showing the typical appearance of chronic plaque psoriasis over (a) the abdomen and (b) back.

- What could you prescribe to help?
- What quantity would you prescribe and how frequently would you advise application?

Answers

First, she would benefit from an emollient. Ask if she has any particular preferences and offer options such as a greasy but very hydrating ointment like Hydromol or a less greasier preparation such as Cetraban cream. Prescribe 500g quantities that can be used as needed. Ask for her smoking history and counsel her on the fire risk associated with emollients.

Combination therapy with a vitamin D analogue (eg calcipotriol) and corticosteroid (eg betamethasone) is more effective than either alone, so this can be offered as a gel, ointment (Dovobet gel/ointment) or foam (Enstilar foam). Example prescriptions:

- Dovobet ointment 100g tube x 1 to be applied once daily to affected areas over the body until clear, up to 8 weeks initially (maximum 15 g/day) or
- Enstilar foam (120g can x 1) to be applied once daily to affected areas of the body until clear, up to 4 weeks at a time (maximum 15 g/day).

After 4–8 weeks, she can be followed up to review if the treatments have worked or if referral to secondary care is needed.

Adverse effects include skin irritation, which can be minimised by advising patients to apply a thin layer two or three times a week initially, working up to daily applications as tolerated (National Institute of Health and Care Excellence, 2020). Oral retinoids are contraindicated in pregnancy and the use of topical retinoids is not justified in pregnancy, as the benefits do not outweigh the risks (Kaplan et al, 2015).

Rosacea

This is another chronic inflammatory condition of the face, with a constellation of clinical signs and symptoms including a tendency to develop facial flushing with the eventual development of persistent facial erythema and telangiectasia, along with inflammatory

papules and pustules. There can be associated eye symptoms (burning, itching, dryness, gritty sensation) or bulbous enlargement of the nose (rhinophyma) as a result of hypertrophy of the sebaceous glands. Management includes the use of sunscreen to avoid photoexacerbation, along with topical agents used alone or in combination with systemic agents such as oral antibiotics or oral retinoids (Burge et al, 2016).

Topical formulations for rosacea are targeted at different features of the disease:

- If facial erythema is the main concern, once-daily brimonidine tartrate gel (an alpha2-adrenoreceptor agonist) can be helpful as a result of its vasoconstrictive action (Van Zuuren et al, 2015). This is available as Mirvaso gel (3 mg/g) with the maximum daily recommended dose being 1 g of gel (approximately five pea-sized amounts) (Electronic Medicines Compendium, 2020a)
- For papulopustular disease, topical antimicrobial agents such as metronidazole 0.75% gel, 15% azelaic acid gel or 1% ivermectin are effective, with ivermectin being slightly more effective than metronidazole (Van Zuuren et al, 2015).

Pre-cancerous and cancerous conditions

Pre-cancerous conditions of the skin amenable to treatment with topical agents include actinic (solar) keratosis and Bowen's disease. Actinic keratosis refers to discrete or confluent patches of erythema, scaling or hyperkeratosis, predominantly on sun-exposed skin. These are premalignant lesions that indicate chronic sun damage and are associated with a low risk of progression to squamous cell carcinoma (Burge et al, 2016).

Bowen's disease is another premalignant lesion, also known as squamous cell carcinoma in situ, in which the full thickness of the epidermis is dysplastic with atypical keratinocytes, but they have not yet breached the basement membrane to become a squamous cell carcinoma (Mohandas et al, 2020). Both actinic keratoses and Bowen's disease can be treated with a topical chemotherapeutic agent called 5-fluorouracil, available as Efudix cream. The British National Formulary (2020) recommends application once to twice daily for 3–4 weeks, but in clinical practice treatment regimens can vary. When applied, 5-fluorouracil causes a localised inflammatory response, with the skin going through stages of erythema, crusted erosions, followed by re-epithelialisation (Electronic Medicines Compendium, 2020b). The aim is to destroy the pre-cancerous cells and to prevent progression to squamous cell carcinoma of the skin. Patient information leaflets with photographs of the vigorous inflammatory reaction expected with treatment can be helpful to make patients aware of this reaction.

Imiquimod is another topical agent for the treatment of actinic keratosis and Bowen's disease and is also licensed for treating superficial basal cell carcinomas. It is available in two strengths: 3.75% (Zyclara) and 5% (Aldara), with the former licensed for treating actinic keratosis and the latter for low risk basal cell carcinoma and actinic keratosis. Along with local application site reactions, influenza-like symptoms are a commonly reported side effect as a result of its immunomodulatory effects (Thomson et al, 2020).

Conclusions

Although numerous topical agents are available, it can be helpful to be familiar with a few commonly used preparations and their correct application techniques in order to guide patients appropriately. Written instructions in the form of a care plan can help patients to

Key points

- Topical treatments are the mainstay of therapy in many dermatological conditions as they allow affected areas to be targeted while avoiding systemic side effects.
- Emollients, steroids, calcineurin inhibitors, retinoids, vitamin D analogues and topical immunomodulatory agents are some of the commonly used agents for treatment.
- It is important to consider not only the active agent, but also the vehicle, concentration, and characteristics of the skin of the affected area when choosing appropriate therapy.

Curriculum checklist

This article addresses the following requirements from the general internal medicine training curriculum:

- Managing patients in an outpatient clinic, ambulatory or community setting, including management of long-term conditions
- Providing continuity of care to medical inpatients, including management of comorbidities and cognitive impairment
- Managing medical problems in patients in other specialties and special cases.

carry out treatment effectively at home. Patient information leaflets are available on the British Association of Dermatology website. They can be helpful sources of information for both patients and clinicians.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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