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Topical Management of Recalcitrant Psoriasis & Eczema

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Introduction

Psoriasis and eczema, especially atopic eczema, are two of the most common cutaneous conditions seen by family physicians and dermatologists. Although the etiology of both conditions is unknown, immunologic abnormalities with an increase in immune mediators are thought to play major roles. These skin disorders are not curable, but can be controlled with proper topical therapy. However, psoriasis and eczema can at times be recalcitrant to conservative topical treatment. As such, it may be helpful for family physicians to be aware of more aggressive or innovative topical options for recalcitrant cases. Patients unresponsive to aggressive topical therapy may require systemic treatment or phototherapy, which carry a greater potential for adverse effects. Such cases are best managed by dermatologists with more experience in using these therapies.

Overview of Topical Corticosteroids

Due to their anti-inflammatory, immunosuppressive, and anti-proliferative properties, corticosteroids are effective for treating a variety of inflammatory dermatoses, including psoriasis and atopic eczema.

Potency

- The potency rating of a topical corticosteroid describes the intensity of the agent's clinical effect.¹ Seven groups of topical steroid potencies have been developed, these are ranked from superpotent (Group 1) to low potency (Group 7). Table 1 lists the topical corticosteroid potencies and gives available examples in Canada.

Vehicle Considerations

- Ointments are water-in-oil emulsions and are more hydrating to the stratum corneum. They provide an occlusive barrier, and because of an increased depot effect, drug penetration is enhanced, leading to greater potency.
 - For example, Table 1 shows the same chemical compound, triamcinolone acetonide 0.1%, can be Class 4 potency as an ointment, but only Class 5 as a cream. Therefore, an ointment can be useful in treating refractory dermatoses, especially for thick, fissured, and lichenified skin lesions.

Administration and Dosing

- Localized recalcitrant conditions may benefit from using a corticosteroid ointment under occlusion (e.g., plastic wraps and hydrocolloid dressings), which can increase the drug permeability up to 10 times.²
- Topical corticosteroids are usually applied once or twice daily. The duration of daily use of ultra-potent formulations should not exceed 3 weeks.³ Medium and high strength topical corticosteroids can be used up to 3 months.³ It can be difficult to adhere to these guidelines, as psoriasis and atopic eczema are chronic, requiring long-term therapy for management.

ALSO IN THIS ISSUE: Topical Management of Rosacea (page 5) & The Role and Topical Management of *Staphylococcus aureus* in Atopic Dermatitis (page 9)

Overview of Topical Corticosteroids (continued)

- In general, it is best to treat active disease more aggressively and then taper to the lowest strength that can maintain disease control.
- Use of superpotent topical corticosteroids should not exceed 50 grams per week in order to avoid excessive absorption and adrenal suppression.

Adverse Effects from Overuse or Prolonged Use

- Risks from long-term topical corticosteroid use include tachyphylaxis - a diminished pharmacologic response after repeated drug administration.¹

- There is a potential for rebound - a severe exacerbation of the dermatosis after abrupt discontinuation.⁴
- Systemic complications include suppression of the hypothalamic-pituitary axis, Cushing's syndrome, hyperglycemia, and avascular necrosis.⁴
- Local adverse effects associated with prolonged use of potent topical corticosteroids include skin atrophy, striae, purpura, telangiectasia, acneiform eruptions (steroid-induced acne, perioral dermatitis, and rosacea), hypopigmentation, and hypertrichosis.⁴

Topical Treatment of Psoriasis Vulgaris

Psoriasis vulgaris is a common, chronic, inflammatory skin disease affecting 2% of the population.⁵ Most psoriatic patients have limited disease (<5% body surface area) and can be successfully treated with topical agents.⁵ Plaque psoriasis (PPs) and psoriasis involving the scalp, palms or soles can be particularly refractory to topical therapy.

Topical agents used to treat psoriasis include corticosteroids, vitamin D analogue (calcipotriol), retinoids (tazarotene), tar, anthralin,⁶ salicylic acid, and topical calcineurin inhibitors (TCIs). Also, combination therapies are available and may be useful because of their increased potency, decreased side-effects, and increased adherence due to less frequent dosing. A systematic review of topical treatments for chronic PPs included 131 randomized controlled trials with 21,448 participants concluded.⁷

- Vitamin D analogue (calcipotriol) was significantly more effective than placebo.
- Potent (betamethasone dipropionate) and very potent (clobetasol propionate) topical corticosteroids were better than placebo, with very potent preparations working better than weaker ones.
- Dithranol (anthralin) and tazarotene worked better than placebo.
- Combination therapies with a vitamin D analogue (calcipotriol) and a potent corticosteroid were more effective than either product alone.
- Potent topical corticosteroids were less likely than calcipotriol to cause local adverse events.

Recalcitrant Plaque Psoriasis

For recalcitrant PPs, a well-tolerated first-line regimen would normally be a combination of a vitamin D analogue (calcipotriol) and potent steroid (betamethasone dipropionate 0.05%) applied daily at bedtime.

- Resistant patients can also be treated with a potent corticosteroid, such as clobetasol propionate 0.05% cream or ointment, twice daily for 2-3 weeks.
 - Use of a potent corticosteroid as "intermittent pulse dosing" may be helpful as a maintenance regimen.⁸
 - In this regimen, after clearing the patient with the potent steroid, remission is maintained with continued

use of the potent steroid, using it for 3 consecutive doses at 12-hour intervals once weekly.

- A study using betamethasone dipropionate glycol 0.05% with this regimen extended remission to 6 months in 60% of patients.⁹ No serious local or systemic side-effects were observed.
- A new treatment that may be effective for recalcitrant PPs of the body is clobetasol propionate 0.05% spray.
 - In a randomized double-blinded vehicle-controlled study of moderate to severe psoriasis, 75% of patients were reported to be clear or almost clear at 4 weeks following twice daily use of the spray.¹⁰
 - There were no reports of hypothalamic-pituitary-adrenal suppression and patients showed reductions in scaling, erythema, and plaque elevation.
- Calcipotriol + betamethasone dipropionate ointment, clobetasol propionate ointment, followed by pulsed therapy, or clobetasol propionate 0.05% spray could be tried for recalcitrant psoriasis on the palms and soles.
 - Very potent steroids can be used on the palms with little risk of atrophy. Superpotent steroids have been used under occlusion on palms and soles with good results.¹¹
- Tazarotene cream or gel can be used as monotherapy, but this retinoid is often used in combination with a topical steroid, such as mometasone furoate 0.1% cream, to reduce skin irritation, which is the major side-effect of tazarotene.
 - Tazarotene 0.1% gel once daily in combination with mometasone furoate 0.1% cream once daily has been shown to be more effective than calcipotriol ointment twice daily or mometasone furoate 0.1% cream twice daily.¹²

Scalp Psoriasis

For recalcitrant scalp psoriasis, the following treatments could be considered:

- Salicylic acid 3% + betamethasone dipropionate 0.05% lotion may be helpful as the salicylic acid has been shown to increase penetration of the topical steroid.¹³
- A new gel formulation containing calcipotriol + betamethasone dipropionate 0.05% can be very helpful for moderate to severe scalp psoriasis.¹⁴

Topical Treatment of Psoriasis Vulgaris (continued)

- A clobetasol propionate 0.05% shampoo applied to the scalp for 15 minutes and then lathered and shampooed out can be effective for difficult scalp psoriasis.¹⁵
- Another option is fluocinolone 0.01% in a peanut oil base that is applied to the scalp under a shower cap at bedtime and washed out the next morning.

Topical Treatment Suggestions for Recalcitrant Psoriasis

Plaque Psoriasis (excluding face and body folds)

- Calcipotriol + betamethasone dipropionate ointment (e.g., Dovobet™)
- Pulsed superpotent topical corticosteroids, such as clobetasol propionate or halobetasol propionate 0.05% (e.g., Ultravate®) ointment/cream used twice daily Saturday and Sunday
- Clobetasol propionate spray (e.g., Clobex™)

Palms and Soles

- All treatments suggested for plaque psoriasis (above) can be tried
- Superpotent topical corticosteroid with saran wrap or hydrocolloid occlusion overnight
- Topical tazarotene 0.1% cream/gel once daily +/- topical mometasone furoate 0.1% cream once daily

Scalp Psoriasis

- Betamethasone dipropionate + salicylic acid lotion (e.g., Diprosalic™)
- Calcipotriol + betamethasone dipropionate (e.g., Xamiol™ gel)
- Clobetasol propionate shampoo (e.g., Clobex™)
- Fluocinolone acetonide topical oil 0.01% (e.g., Derma-Smoothe/FS®)

Topical Treatment of Eczema

Atopic Eczema (AE)

AE is a chronic, pruritic, relapsing inflammatory skin disease.¹⁶ The lifetime prevalence is estimated to be between 10-20% in children and 1-3% in adults.¹⁷

- The topical treatment approach includes reducing inflammation with topical corticosteroids or TCIs (i.e., tacrolimus or pimecrolimus).
- AE patients have a skin barrier abnormality,¹⁸ as such, regular daily use of moisturizers to decrease transepidermal water loss is important. Recently, barrier repair creams¹⁹ have become available for improving the skin barrier function. In an investigator-blinded, randomized trial of moderate to severe AE, a barrier cream reduced clinical disease and pruritus at 28 days of treatment comparably to fluticasone propionate 0.05% cream, a Class 5 corticosteroid.
- Avoidance of external irritants (e.g., harsh soaps, strong laundry detergents, and wool clothing) is beneficial.

Topical corticosteroids are the treatment of choice for AE; selection depends on disease severity and treatment site.

- For milder AE of the face and body folds, mild to moderate steroids (Class 6 or 7) are commonly used.
- For more severe AE and eczema on the trunk and extremities, more potent corticosteroids may be necessary (Class 4 or 5), but are best used only for a few weeks, then tapered to a milder preparation for maintenance. Generally, ointments work better than creams.
- Once the pruritus and thickness are controlled, switching to a TCI, such as tacrolimus ointment (0.03% for ages 2-15, 0.1% for >15 years), is very useful and helps to minimize side-effects from corticosteroids.

- If potent topical steroids are needed for long duration, consider pulse application at 1-2 times weekly dosing.

Chronic Hand Eczema (CHE)

CHE is a common condition and irritant dermatitis is more prevalent than allergic dermatitis. Early-onset hand eczema may be associated with atopy.

- A recent consensus statement on the management of CHE²⁰ suggested that topical therapy should include corticosteroids and TCIs.
- There is evidence of efficacy for long-term intermittent monotherapy with mometasone furoate cream.²¹
- For very refractory hand eczema, especially on the palms, superpotent topical corticosteroids can be helpful and side-effects, such as atrophy, are unusual when used on thick palmar skin.
- Möller²² found the risk of recurrence of CHE was reduced by the very potent corticosteroid, clobetasol propionate, when used on an intermittent schedule of 2 applications a week, compared with a moderately potent corticosteroid cream.

Lichen Simplex Chronicus (LSC)

LSC is characterized by lichenification of the skin as a result of primary excessive scratching or rubbing.²³

- When treated topically, often potent corticosteroid creams or ointments, such as betamethasone dipropionate, are necessary to control the pruritus and inflammation and to break the “itch-scratch” cycle.
- The use of potent topical corticosteroids under occlusion may be needed for successful treatment.
- Topical tacrolimus has been reported to be effective.²⁴

Topical Treatment Suggestions for Recalcitrant Eczema

Atopic Eczema (excluding face and body folds)

- Potent topical corticosteroids for 2-3 weeks followed by tapering to a milder topical corticosteroid or TCI (i.e., Protopic™ ointment or Elidel® cream)
- Pulsed potent topical corticosteroid (i.e., fluocinonide 0.05% ointment/cream used twice daily Saturday and Sunday (use with caution in young children and if treating for longer than 2-3 weeks))
- Barrier repair creams (e.g., EpiCeram™) can be tried in conjunction with topical corticosteroids or TCIs

Chronic Hand Eczema

- Superpotent topical corticosteroid for 2-3 weeks followed by tapering to a milder corticosteroid or TCI
- Superpotent topical corticosteroid with saran wrap or hydrocolloid occlusion overnight

Lichen Simplex Chronicus

- Superpotent topical corticosteroid for 2-3 weeks followed by tapering to a milder corticosteroid or TCI
- Superpotent topical corticosteroid with saran wrap or hydrocolloid occlusion overnight

Relative Potency Class	Corticosteroid	%	Preparation
1	Betamethasone dipropionate glycol	0.05	Cream, ointment, lotion
	Clobetasol propionate	0.05	Cream, ointment, lotion, spray, shampoo
	Halobetasol propionate	0.05	Cream, ointment (reintroduced and commercially available in Canada December 2010)
2	Amcinonide	0.1	Cream, ointment, lotion
	Betamethasone dipropionate	0.05	Ointment
	Desoximetasone	0.05	Gel
	Desoximetasone	0.25	Cream, ointment
	Diflucortolone valerate	0.1	Cream, oily cream, ointment
	Fluocinonide	0.05	Cream, ointment, gel
	Halocinonide	0.1	Cream, ointment, lotion
3	Betamethasone dipropionate	0.05	Cream
	Betamethasone valerate	0.1	Ointment
	Mometasone furoate	0.1	Ointment
	Triamcinolone acetonide	0.5	Cream
4	Desoximetasone	0.05	Cream
	Fluocinolone acetonide	0.025	Ointment
	Hydrocortisone valerate	0.2	Ointment
	Mometasone furoate	0.1	Cream, lotion
	Triamcinolone acetonide	0.1	Ointment
5	Betamethasone valerate	0.1	Cream, lotion
	Fluticasone propionate	0.05	Cream
	Fluocinolone acetonide	0.025	Cream
	Hydrocortisone valerate	0.2	Cream
	Triamcinolone acetonide	0.1	Cream, lotion
6	Desonide	0.05	Cream, ointment, lotion
	Fluocinolone acetonide	0.01	Cream, lotion, oil
7	Hydrocortisone acetate	0.5-2.5	Cream, ointment, lotion

Table 1: Relative potency rankings of common topical corticosteroids in Canada

Disclaimer: I have tried to give evidence-based suggestions for treating these cutaneous diseases that can be chronic and recalcitrant to treatment. However, these are suggestions only and it must be remembered that potent topical corticosteroids can have significant side-effects as discussed. The guidelines of care for the use of topical glucocorticosteroids from the American Academy of Dermatology (reference 3) should be kept in mind, including the duration of use of superpotent and potent topical corticosteroids and maximal daily use. Extra caution needs to be given when using these agents in children. Close supervision by the prescribing physician is recommended.

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Topical Management of Rosacea

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Introduction

Many options exist for the treatment of rosacea, including topical and systemic therapy, laser and light-based therapies, and surgical procedures. A classification system for rosacea identifies four subtypes, which may help guide therapeutic decision-making. Standard topical treatment agents include metronidazole, azelaic acid, and sulfacetamide-sulfur. Second-line therapies include benzoyl peroxide, clindamycin, calcineurin inhibitors, and permethrin. Rosacea can contribute to lower self-esteem and have significant psychosocial implications, such as stress at work and social isolation. This can have a significant impact on quality of life and should be taken into consideration when treating these patients.

Prevalence

- Rosacea is a common chronic skin disorder that is thought to affect approximately 14% of women and 6% of men.¹
- All ethnicities can be affected, but rosacea is most prevalent in fair-skin individuals of northwest European descent.
- Initial diagnosis most frequently occurs between the ages of 30-50 years.
- Although rosacea prevalence is higher in women, there is a much greater incidence of severe telangiectasias and rhinophyma (red, bulbous nose) in men, especially in patients presenting with advanced disease.

Diagnostic Features

Rosacea is a chronic relapsing inflammatory skin disorder characterized by facial flushing, persistent erythema, telangiectasia (dilated superficial blood vessels), and inflammatory papules and pustules affecting the central face (across the cheeks, nose, or forehead). The ears, scalp, neck, and chest are less commonly involved.

The National Rosacea Society has described a classification system based on four main subtypes and one variant.²

Subtype 1: Erythematotelangiectatic

- Characterized by flushing, persistent central facial erythema, and telangiectasia of the cheeks and around the nose.
- Central facial edema, stinging, burning, pruritus, and roughness, scaling, and a history of flushing alone are also common.

Subtype 2: Papulopustular

- Characterized by persistent central facial erythema with transient papules or pustules or both.
- Papules and pustules can also occur in the perioral, perinasal, or periocular regions.
- There is a resemblance to acne vulgaris, except that comedones (whiteheads and blackheads) are absent, hence, the term “acne rosacea” is sometimes used.
- Rosacea and acne can coexist, therefore, patients can present simultaneously with comedones, papules and/or pustules.
- This subtype has often been seen after or in combination with subtype 1.
- Burning and stinging sensations may be reported by patients; telangiectasias may be present, but obscured by persistent erythema, papules, or pustules.

Subtype 3: Phymatous

- Common features include thickening skin, irregular surface nodularities, and enlargement.
- Phymatous rosacea most commonly affects the nose (rhinophyma), but the chin, forehead, cheeks, and ears can also be involved.
- This subtype frequently occurs after or in combination with subtypes 1 or 2.
- Patients may also exhibit persistent erythema, telangiectases, papules, and/or pustules.

Subtype 4: Ocular

- Diagnosis of this subtype is considered when a patient exhibits or reports one or more of the following symptoms: watery or bloodshot appearance, foreign body sensation, burning or stinging, dryness, itching, light sensitivity, blurred vision, telangiectasia, or lid and periocular erythema.
- Recurrent staphylococcal infection manifesting as styes are common.
- Patients can experience impaired vision, requiring ophthalmologic consultation.
- Most frequently, signs and symptoms of ocular rosacea present concurrently with those affecting the skin.
- Ocular signs and symptoms may precede cutaneous manifestations and vice versa.

One Variant: Granulomatous

- This is a rare variation of rosacea that is characterized by hard papules or nodules ranging in colour from yellow, brown, or red.
- The lesions exhibit less inflammation and are typically found on relatively normal-appearing skin of the cheeks and periorificial areas.

Treatment Overview

Treatment starts with making a proper diagnosis, including subtyping. Following this, conservative measures such as trigger avoidance, proper skin care, camouflaging cosmetics, and photoprotection should be discussed in detail with patients. The goals of therapy include the reduction of papules, pustules, erythema, physical discomfort, and an improvement in quality of life. Topical pharmacotherapeutic options include azelaic acid, metronidazole, sulfacetamide 10% + sulfur 5%, clindamycin 1% + benzoyl peroxide 5% gel, clindamycin, and erythromycin. For patients with moderate to severe papulopustular rosacea or those with ocular involvement, systemic therapy is often prescribed - therapeutic options include tetracycline, minocycline, doxycycline, erythromycin, metronidazole, or in severe cases, low dose isotretinoin. The telangiectatic component does not respond to either oral or topical medications, and is best treated with laser and light-based therapies. Surgical intervention may be required for the phymatous subtype. Therapeutic choices will depend on patient expectations, tolerance, previous therapies used, rosacea subtype, and severity.

Azelaic Acid

Azelaic acid (AzA) is a newer therapeutic option that is available for the treatment of rosacea. Although it received regulatory approval in Canada in 2004, AzA has only recently become commercially available in June 2010. AzA is a naturally occurring dicarboxylic acid that can be found in dietary sources, such as whole grains.³ It lacks toxicity, is non-teratogenic and non-mutagenic.⁴ It has multiple biologic effects including anti-inflammatory, anti-keratinizing, and anti-bacterial activities. The likely mechanism of action in the treatment of rosacea is via inhibition of reactive oxygen species produced by neutrophils.⁴

- A novel 15% gel formulation is available for the treatment of rosacea. A 20% cream formulation is approved in the U.S. for acne vulgaris, but it is not currently available in Canada.
- The 15% gel, although formulated to a lower concentration than the cream, is significantly more bioavailable than the cream because of an optimized aqueous gel vehicle.

Multiple reviews have been published examining the use of AzA in rosacea.^{3,5,6}

- Two pivotal phase III trials have shown that AzA 15% gel applied twice daily for 12 weeks was superior when compared with the vehicle in the treatment of papulopustular rosacea.⁷
 - In these studies, a mean reduction in inflammatory lesion counts and improvements in erythema scores were observed in AzA-treated group vs. placebo.⁷
- A 15-week study, comparing the twice daily use of AzA 15% gel to metronidazole 0.75% gel also showed a significant benefit for AzA over metronidazole.⁸

- In these studies, the use of AzA 15% gel led to a mean reduction in inflammatory lesion counts ranging from 51%-73% and a reduction of erythema severity ranging from 44%-56%.⁷⁻⁹
- A split-face study comparing AzA 20% cream and metronidazole 0.75% cream showed a reduction in inflammatory lesions of 78.5% and 69.4%, respectively.¹⁰ There was also a reduction in erythema of 25.5% and 18.7% for AzA and metronidazole, respectively.
- Both treatments led to a significant reduction in inflammatory lesions over 15 weeks, but the difference between treatments was not significant.
- Of note, the physician rating of global improvement was significantly higher on the side treated with AzA at both weeks 9 and 15.
- In the comparative studies, AzA demonstrated more potential for inducing irritation than metronidazole, including facial skin signs and symptoms, though these events were described as mild to moderate and transient in nature. Self-assessed minor local irritation was reported by AzA (89%) and metronidazole (96%) groups; however, tolerability was evaluated by patients as being either good or acceptable for both treatments.⁸
- There was no improvement in telangiectasia severity in any study of AzA for rosacea.

The dosing recommendation for AzA 15% gel is twice daily. However, Thiboutot et al. found once daily dosing to be as effective as twice daily.¹¹ Research has shown that AzA is a safe and effective treatment for papulopustular rosacea with a favorable tolerability profile.

Metronidazole

Metronidazole has been the mainstay of topical rosacea treatment. It is a nitroimidazole antibiotic whose mechanism of action in rosacea is not well established, but it appears to work through an anti-inflammatory mechanism.^{12,13} Metronidazole is the most widely used topical agent for rosacea.

- Available as a 0.75% gel, lotion, and cream for twice daily use, and a 1% cream and gel for once daily use.
- Once daily dosing of 1% metronidazole cream appears to be as effective as twice daily dosing.¹⁴
- It is generally well tolerated and has a low incidence of adverse effects.^{12,13}
- A recent systematic review of 9 trials demonstrated the efficacy of topical metronidazole vs. placebo.^{5,15} Most of these studies used 0.75% metronidazole and ranged from 8-9 weeks in duration with one trial lasting 6 months.

Metronidazole (continued)

- A reduction in inflammatory lesions and erythema scores were noted, as was an improvement in physician's global evaluation and patient-assessed measures when these were available.^{5,15}
- No benefits were noted for telangiectasia in these studies, however, a study by Tan et al. showed improvement in telangiectasiae scores as well as erythema and inflammatory lesion counts using a 1% metronidazole cream with a sun protection factor (SPF) of 15.¹⁶
- Although data is limited, two studies have demonstrated that topical metronidazole may be as effective as oral tetracycline in reducing the inflammatory component of rosacea.^{17,18}
- The efficacy of topical metronidazole is constant regardless of the formulation, strength, and frequency of application.¹²
- Metronidazole also plays a role in maintenance therapy for rosacea, either with or without prior concomitant systemic antibiotic treatment.¹²
- Given its high efficacy and tolerability, it will continue to play an important role in the management of rosacea.

Sodium Sulfacetamide + Sulfur

- An older treatment that has gained new popularity is sodium sulfacetamide 10% + sulfur 5%, which is used to treat acne, rosacea, and seborrheic dermatitis.¹³
- It is available in multiple formulations as a lotion, cream, gel, or cleanser.^{9,13}
- The mechanism of action is not well understood, but the sulfacetamide has anti-bacterial properties, and the sulfur component confers anti-fungal, anti-demodectic, and keratolytic effects.

Other Therapies

Many other topical treatments have been reported and are being used for rosacea. Some are effective, but are not yet approved for use in rosacea. Further investigation is needed to determine their role in the topical armamentarium of rosacea therapy.

- Combination clindamycin 1% + benzoyl peroxide 5% gel, which is approved for use in acne vulgaris, has shown promise in the treatment of rosacea. A double-blind, randomized controlled trial using this formulation once daily showed a significant reduction in inflammatory lesion count, erythema severity, and overall rosacea severity. The treatment was well tolerated.¹⁹
- Topical antibiotics (e.g., clindamycin lotion or cream) have shown benefit in the topical treatment of rosacea, but evidence supporting its use is lacking.
- The calcineurin inhibitors, tacrolimus and pimecrolimus, have been investigated for use in papulopustular rosacea because of their anti-inflammatory effects. Early reports indicate improvement from tacrolimus in the treatment of steroid-induced rosacea.²⁰ However, while three studies have demonstrated a reduction in erythema associated with rosacea, neither tacrolimus nor pimecrolimus had any benefit over vehicle with respect to lesion counts.²¹⁻²³
- Topical retinoids have also been used to treat rosacea, but the true efficacy has not been established. Their use is limited by their irritant potential, and investigators suggested that better tolerated agents, such as adapalene, could be considered.¹³
- Topical steroids are sometimes used on a short-term basis for the severe inflammatory component, but long-term side-effects and exacerbating potential limit their use in this chronic condition.¹³
- Permethrin 5% cream, which is proposed to work because of its anti-parasitic effects, may target Demodex mites, a potential cause of rosacea.¹³

Self-Care Tips

Cleansers

- Due to hypersensitivity of the skin, limit face washing to twice daily. Cleansing can offer a cooling effect that temporarily relieves sensations of burning and itching.
- Select gentle, mild skin cleansers with non-sensitizing ingredients (i.e., free of fragrances and preservatives).
- Avoid the use of washing implements (e.g., sponge, brush, wash cloth), especially those with a rough surface that can further aggravate the skin.
- Allow skin to dry before applying either a moisturizer or medication.

Moisturizers

- The regimented use of a suitable moisturizer is essential for managing rosacea. If left untreated, dry skin can cause further discomfort, resulting in burning, tightness, itching, and stinging.
- Recommendations cannot be generalized, since each person with rosacea can react differently to the same product. Water-based moisturizers may be less likely to induce sensitivity reactions.

Self-Care Tips (continued)

- Seborrheic dermatitis is a common concurrent skin condition, appearing as a red and scaly rash on the scalp, eyelids, eyebrows, sides of the nose, and behind the ears. Patients with rosacea can have dry scaly skin secondary to the dermatitis, so no amount of moisturizing will help the scaling until the inflammation is first controlled by medication.

Sunscreens

- The sun is one of the most common triggers of rosacea flare-ups, therefore, selecting a suitable non-oily broad spectrum sunscreen with SPF of at least 15 to 30 is recommended.
- The most effective protection against UV radiation is sun avoidance, e.g., by limiting exposure, or at least direct exposure during peak times, and by wearing appropriate clothing and hats.
- Maintaining proper sun protection is essential, because the heat of the sun and UV exposure can aggravate the skin and result in increased redness and long-term damage to blood vessels.

Cosmetic Camouflage

- Makeup can be a useful cosmetic tool to conceal the symptoms of rosacea.
- Foundations or concealers with a green tint are helpful for camouflaging redness, blood vessels, and blemishes.
- Avoid powder formulations on dry, flaky skin, as these products can collect in areas of dryness and worsen the appearance of skin.

Conclusion

Because of its chronic, inflammatory nature, rosacea requires continuous management. Treatment can be tailored to the subtype and may involve a combination of therapies. Patients should first be counseled on the triggers of rosacea, proper skin care, photoprotection, and camouflaging cosmetic options. Topical therapy is usually first-line, but in moderate-to-severe cases, or those with ocular involvement, systemic therapy may be required. Laser or light-based treatments and surgical procedures can offer added benefit. Many topical agents are available for the treatment of rosacea, and the erythematotelangiectatic and papulopustular variants usually respond most favourably. The Cochrane Collaboration Review of interventions for rosacea concludes there is good evidence that topical azelaic acid and metronidazole are both safe and effective treatments. Other treatment options also include sulfacetamide 10%-sulfur 5%, benzoyl peroxide 5%-clindamycin 1%, or clindamycin alone.

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The Role and Topical Management of *Staphylococcus aureus* in Atopic Dermatitis

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Introduction

Atopic dermatitis (AD), or eczema, is a common, chronic, relapsing, genetically determined inflammatory skin disorder.¹ *Staphylococcus aureus* (*S. aureus*) has been implicated as an environmental factor in the etiology of atopic eczema since 1899.² Atopic skin is susceptible to colonization and infection with *S. aureus*. This current review will discuss the role of *S. aureus* in atopic dermatitis and upon understanding this role, topical therapeutic management will be discussed.

Overview of Atopic Dermatitis

- AD is a common skin condition, affecting 15-30% of children and 2-10% of adults.³
- AD has a complex pathology involving genetic predisposition, deficient epidermal barrier defenses, impaired innate immunity and abnormal acquired immunity, and environmental factors.^{4,5} This interplay results in skin barrier impairment and inflammation.
- The diagnosis of AD is made on clinical grounds. One simple criteria⁶ states that the individual must have:
 1. Pruritus - the hallmark of AD, plus three or more of the following:
 2. Early age of onset
 3. Typical morphology and distribution (facial and extensor involvement in infants and young children, and flexural lichenification or linearity in adults)
 4. Personal or family history of atopy
 5. Xerosis (dry skin)
 6. Chronic and relapsing course

The Role of *Staphylococcus aureus* in AD

- The most common bacteria found on AD skin is *S. aureus*.⁷
- In AD patients >90% are colonized with *S. aureus* on lesional and nonlesional skin vs. 5% on healthy skin.⁸
- The extent of colonization correlates with the disease activity and clinical severity of AD.^{8,9}
- *S. aureus* colonization is felt to be both a consequence and a cause of the skin inflammation in AD.¹⁰

Reasons for Increased Susceptibility of AD Patients to Staphylococcal Infections

Host Factors Promoting Colonization

- Defective epidermal barrier
 - Decreased ceramides, the major water retaining lipids of the stratum corneum, leads to increased trans-epidermal water loss (TEWL) and contributes to dry cracked skin, predisposing to colonization.¹¹
 - The pH of the skin surface in AD is high or alkaline, creating a suitable environment for colonization.¹¹
- Defective innate immune responses
 - The innate immune system of the epidermis is the first-line of defense against skin infections and it activates antimicrobial peptides (AMPs); AMPs are decreased in AD.¹²
- Increased synthesis of extracellular matrix adhesins for *S. aureus*¹³
- Environmental factors
 - Patients with severe AD have higher levels of *S. aureus* in their home environment.¹⁴
 - AD patients can be recolonized by family members who have the same strains of *S. aureus*.¹⁵

- Topical medications contaminated with *S. aureus* can be a source of re-colonization.¹⁶

Contribution of *S. aureus* to Inflammation

1. Staphylococcal superantigens (SsAgs) penetrate the skin barrier and add to the exacerbation and persistence of the inflammation in AD by:
 - Massive T cell stimulation
 - Acting as allergens
 - Direct stimulation of antigen presenting cells
 - Expansion of skin-homing cutaneous lymphocyte-associated antigen (CLA) T cells¹⁰
2. Enhancing pruritus
 - IL-31 is able to induce itch in AD and is upregulated by SsAgs.¹⁷
3. Induction of corticosteroid resistance¹⁰
4. Secondary infection by *S. aureus*
 - Secondary infection occurs when an underlying disease creates the conditions for infection. In AD, these are *S. aureus* colonization, a disrupted skin barrier, and abnormal immune defenses.¹⁰

Management of *Staphylococcus aureus* in AD

1. Role of Antibiotic Therapy

• Colonization

The use of antibiotics alone to clear colonization is not recommended for the following reasons:

- Colonization is a constant feature of AD and *S. aureus* is found on nonlesional and lesional skin.⁸
- Antibiotics will reduce the load of *S. aureus*, but alone are unable to improve inflammation.¹⁸
- After antibiotic therapy, AD skin rapidly recolonizes, often with the same toxin-secreting organisms.¹⁹
- Prolonged use of antibiotic therapy increases the prevalence of antibiotic-resistant strains of *S. aureus*, including methicillin-resistant *S. aureus* (MRSA).¹⁰

• Combination treatment

- The rationale for combination treatment with topical steroids and antibiotics is to reduce inflammation and improve the skin barrier function with the steroids, while using antibiotics to reduce the *S. aureus* load and chronic inflammation.
- Use of an antimicrobial agent with a low- or mid-potency corticosteroid may potentially allow AD management with a lower strength corticosteroid, mitigating some side-effects associated with higher strength corticosteroid monotherapy.
- A recent report by *Cochrane Database Systematic Review* did not find clear evidence of benefit for antimicrobial interventions in AD patients. However, the studies were small and poorly reported and the anticipated benefit may not have been demonstrated.^{20,21}

- It is well known that combination therapy is commonly used in general practice.²²
- Studies of mild to moderate AD comparing combination treatment consisting of 2% fusidic acid and 1% hydrocortisone acetate with either agent alone found that the combination therapy demonstrated improved efficacy in reducing AD symptoms and *S. aureus* density.²³ This treatment is recommended for a limited period of time (maximum of 2 weeks) to avoid resistance.
- Secondary bacterial infections in AD
An oral or topical antibiotic is indicated for patients with evidence of secondary bacterial infection.²⁰
 - A sudden flare in a patient's eczema should heighten the possibility of a secondary infection.
 - Patients may report standard therapy is not working.
 - Symptoms may include intense pruritus, fever, and malaise. Signs include intense erythema, oozing, erosions, honey-coloured crusting, pustules, folliculitis, and abscesses.

2. Role of Anti-inflammatories

- It has been shown that anti-inflammatories (steroids and calcineurin inhibitors) alone (without the use of antibiotics) may reduce *S. aureus* colonization.²⁴
- Proper care of atopic skin can help to prevent increased colonization with *S. aureus* and secondary infection.

3. Multipronged Approach to AD Management

- AD management requires a multimodal approach that is both pharmacologic and non-pharmacologic.

Non-Pharmacologic Options for AD Management

- It is important to take the time and properly educate the patient and family members with verbal, written, and practical demonstrations.
- Trigger factors should be determined, avoided, and dealt with (e.g., irritants, aeroallergens, foods, infections, and stress).
- Patients and parents need to be taught how to recognize the signs / symptoms of bacterial (and viral) infections.
- A multidisciplinary approach is needed at times, e.g., allergy testing or referral to a psychologist or dietician.
- Mild skin cleansers can help remove dirt, irritants, and microbes.
- Cool compresses can be applied to oozing, weeping, and vesiculated lesions for 10-15 minutes two to three times a day for one to two days to dry up these areas.

Daily Skin Care and Hydration

- After a 10 minute lukewarm bath (preferred over a shower), the skin is pat dried and within 3 minutes a

moisturizer is applied in one direction (so as not to develop folliculitis if rubbed back and forth).

- A moisturizer should be free of dyes and fragrances, and applied at least once or twice per day to damp skin after the application of any medicated therapy.
- Patients have to be educated about the need to apply moisturizers constantly, whether using anti-inflammatory medication or not, in order to help repair and preserve the skin barrier.
- Moisturizing can reduce the need for steroids.²⁵
- Studies show that decreased ceramide levels in AD not only contributes to a damaged skin barrier, but it also makes the stratum corneum susceptible to *S. aureus* colonization.¹⁷ This has led to the development of ceramide dominant barrier repair creams. A ceramide emollient added to standard care in place of a moisturizer resulted in clinical improvement in difficult to treat AD children.²⁵

Pharmacologic Options for AD Management

Anti-inflammatories

Corticosteroids

- Used as first-line management and best for acute flares.
- Weak or mild potencies (e.g., hydrocortisone) are recommended for the face and skin folds in adults and children, and are regarded as the best strengths for use in infants.
- Moderate potency (e.g., betamethasone valerate) can be applied to the rest of the body.
- Higher potencies are reserved mainly for adult use on thick localized lesions and the palms and soles.
- Vehicle suggestions include creams for acute and subacute lesions; ointments for dry, thick chronic lesions; lotions for hair-bearing areas.
- Apply only to lesional skin twice daily until there is a response (usually 2-4 weeks), then twice weekly to healed areas for up to 2 months to prevent flares.
- With long-term use, adverse effects can include skin atrophy, tachyphylaxis, and systemic side-effects.

Topical calcineurin inhibitors (TCIs)

- Pimecrolimus (1% cream) for mild to moderate AD
 - Indicated for use in AD patients ≥ 2 years of age
- Tacrolimus (0.03% and 0.1% ointment) for moderate to severe eczema
 - 0.03% is used in children aged 2-15 years
 - 0.03% and 0.1% may be used in patients >15 years
- Useful when steroids fail or in cases of steroid phobia.
- Unlike steroids, TCIs can be used on all body areas as they do not cause skin atrophy.
- For short-term and intermittent long-term therapy.
- TCIs can be applied twice daily.
- TCIs can avert a flare if applied at the first signs of symptoms (e.g., local pruritus and redness).

- Recent studies confirm their safe and effective use as proactive management for children and adults.
- If applied to healed yet previously affected lesions twice weekly for a few months, TCIs can help prevent flares.
- Burning at the site of application is the most common local side-effect and this is transient.

Antimicrobials

- Topicals - localized lesions
 - Fusidic acid 2% cream 2-3 times/day for 7-10 days
 - Mupirocin 2% cream 2-3 times/day for 7-10 days
 - In clinically infected lesions, as well as other lesions where *S. aureus* colonization is suspected as a contributing factor, short-term (3 times daily for 2 weeks) combination topical therapy with an antibiotic and corticosteroid is widely used.
 - Resistance to topical antibiotics can be reduced if therapy is restricted to short courses (≤ 14 days). Prolonged or intermittent use must be avoided.^{26,27}
- Systemics - generalized involvement
 - Cloxacillin, cephalixin, or erythromycin for 7-10 days
- Be mindful of MRSA and check the resistance profile in the patient's area.
- Culture affected lesions if MRSA is suspected.
- Localized lesions are treated with topical antimicrobials twice weekly for 1-2 weeks.
- Acute, oozing areas can first be compressed before applying the topical treatment.
- The rest of the skin is managed with topical steroids and moisturizers.
- If the infection is too extensive, oral agents are used usually for 7-10 days, steroids are applied twice daily to the active lesions, and moisturizers are used on the rest of the skin.

Conclusion

S. aureus acts like a commensal organism on the atopic skin, contributing to the underlying inflammation that is a hallmark of this chronic, complex condition. Taking a proactive approach to the management of AD can keep this organism under control, and in turn control flares.

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