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EDUCATIONAL SERIES

Management of Atopic Dermatitis: Focus on the Role of Emollients

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This review about the management of atopic dermatitis highlights the role of emollients and is intended as an educational resource for health professionals. It features a brief summary of the incidence and burden of disease, its diagnosis and an overview of treatment options. The pathogenesis of skin barrier breakdown in atopic dermatitis is presented in more detail as background to discussion of the beneficial effects of emollients, in particular those of colloidal oatmeal emollients. The review concludes with Expert Commentaries from Dr David Lim (New Zealand) and Dr Samuel Zagarella (Australia), who discuss the place of emollients within the overall management of atopic dermatitis.

Introduction

Atopic dermatitis, or atopic eczema, is an autoimmune inflammatory and pruritic skin disease. It is a common condition, having been estimated to occur in 10-20% of children and 2-10% of adults in the US.^{1,2} Limited epidemiological data from Australasia suggest a prevalence of approximately 20% in children, being as high as 37% in one study.^{3,4} The onset of atopic dermatitis is usually before two years of age, with only 10% of cases diagnosed after five years of age.⁵ Although 60-75% of people experience substantial improvement in their symptoms before adulthood, the remaining 25-40% continue to have relapses during their adult life.^{1,2}

Burden of Disease

Atopic dermatitis can affect the emotions and behaviour of children, including increased levels of irritability, fussiness, restlessness, hyperactivity and poor discipline. In addition, sleep disturbance in children with atopic dermatitis correlates with problems of daytime behaviour and discipline and is also associated with reduced productivity.⁶

Childhood atopic dermatitis can also negatively affect the quality of life of parents.⁶ Factors that contribute to parental and family stress include sleep deprivation, loss of employment, time taken for care of atopic dermatitis and financial costs.⁷

Studies that have assessed the economic burden of atopic dermatitis are limited and heterogeneous, but they suggest that, relative to healthcare system costs, patients' out-of-pocket medical expenses are substantial (mainly due to GP and corticosteroid costs) and employers shoulder a significant burden of the overall cost (mainly due to employee absenteeism).⁸⁻¹⁰

Skin Structure and Barrier Dysfunction

The pathogenesis of atopic dermatitis is multifactorial, involving a complex interaction of patient (skin barrier function, genetics and immune system) and environmental (allergens, bacteria and viruses, irritants and climate) factors.¹¹ To appreciate the beneficial effects of emollients, which are the mainstay of treatment for atopic dermatitis, it helps to understand how the skin maintains its barrier function and that epidermal barrier function is impaired in atopic dermatitis.

Epidermal barrier function is primarily the role of the stratum corneum, the outermost layer of the skin. It acts as a two-way barrier that prevents the entry of noxious and infective agents from the environment but allows the evaporation of water in the opposite direction (**Figure 1** on page 2).¹ The stratum corneum is mostly composed of corneocytes and intercellular lipids, including ceramides, cholesterol and free fatty acids.^{1,12} Free fatty acids are important for the integrity of the permeability barrier and cohesion of the stratum corneum.¹³ In particular, linoleic acid is one of the most significant lipids for maintenance of barrier function.¹⁴

A defective barrier is a critical feature of atopic dermatitis, with the degree of skin barrier damage correlating with the severity of disease.¹⁵ In atopic dermatitis, the lipid content of the stratum corneum is reduced, the organization and packing of the lipids altered and the size of the corneocytes significantly smaller compared with healthy skin. With the permeability of the barrier compromised, allergens and pathogens can enter the skin and interact with antigen-presenting and immune effector cells (**Figure 1**), causing secondary inflammation and intense itching and scratching. In addition, with the changes to the lipid component of the stratum corneum, transdermal water loss is increased in atopic dermatitis, which contributes to dryer and rougher skin in people with the condition.¹

A familial history of atopic disease is associated with the development and severity of atopic dermatitis in infants. A mutation of the *FLG* gene has been implicated as a risk factor for atopic dermatitis. The *FLG* gene encodes filaggrin, which is a protein that plays an important role in corneocyte termination and skin barrier function and is involved in the formation of natural moisturizing factor.¹

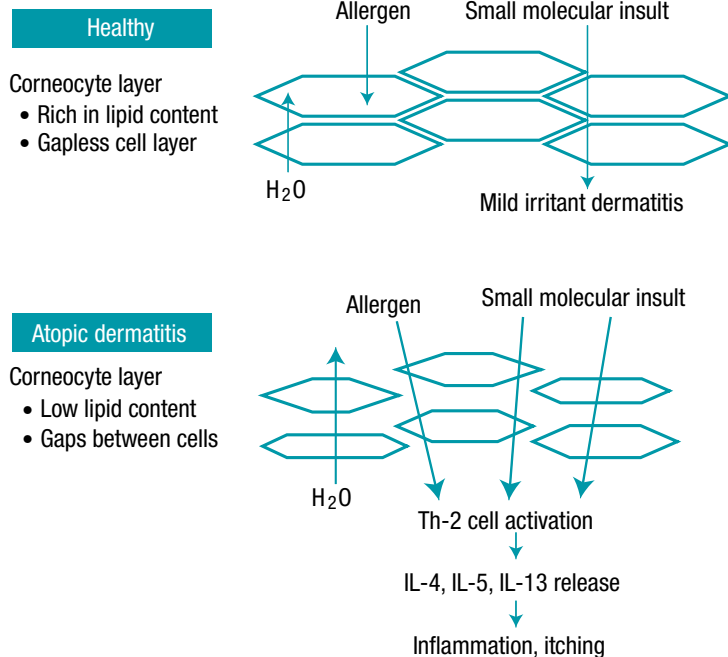


Figure 1. Skin structure: Comparison of healthy skin with skin affected by atopic dermatitis.¹

Diagnosis of Atopic Dermatitis

A patient and family history with a physical examination form the basis a diagnosis of atopic dermatitis. According to a simplified version of the extensively validated U.K. Working Party's Diagnostic Criteria, a diagnosis of atopic dermatitis requires evidence of itchy skin with at least three of the following:

- history of asthma or allergic rhinitis
- history of skin fold involvement
- history of generalized dry skin
- onset of rash before two years of age
- visible skin fold dermatitis.^{5,11}

People with atopic dermatitis may also present with secondary complications, including secondary bacterial or viral infections. Other complications include scarring from picking and scratching, chronic post-inflammatory skin changes and skin atrophy from long-term topical corticosteroid treatment.⁵

Early diagnosis and effective treatment will help to prevent morbidity from disturbed sleep, post-inflammatory skin changes, scarring and the development of secondary skin infections.^{5,6}

Treatment Options

Atopic dermatitis tends to be a chronic relapsing disease. Hence, the objectives of treatment are to reduce the frequency and severity of flares and minimize the risk of infection.¹⁶ To achieve these objectives, treatments for atopic dermatitis primarily address the disease components of skin barrier repair, barrier protection, inflammatory moderation and/or immunomodulation.¹

Topical treatments

The primary option for barrier protection and repair are emollients, which are considered key therapeutic agents in the ongoing management of dry skin diseases such as atopic dermatitis.^{1,5,17}

Topical corticosteroids are first-line treatment for acute exacerbations of atopic dermatitis.¹⁵ They typically lead to improvement or resolution of acute flares within several days. Use of lower potency corticosteroids is recommended for children with atopic dermatitis to minimize risk of adverse effects, including skin atrophy.^{1,5}

The topical calcineurin inhibitor, pimecrolimus, is an alternative to topical steroids particularly for higher risk areas such as the periocular and periorbital regions. Due to a theoretical association with increased cancer risk, however, topical calcineurin inhibitors are reserved for second-line treatment and are generally not used in children aged less than two years.^{1,5}

Systemic treatments

A short course of oral antibiotic therapy may be necessary for widespread secondary bacterial infection, although a topical antibiotic can be used to treat localized infection.⁵

For patients who have atopic dermatitis that is severe and widespread or refractory to treatment with topical agents, options such as ultraviolet phototherapy and the systemic immunomodulatory agent, cyclosporin, can be prescribed under the guidance of a dermatologist.⁵ This and other indications for referral to a dermatologist are presented in **Practice Tips 1**.⁵

PRACTICE TIPS 1: Indications for Referral to a Dermatologist

- Diagnosis is uncertain
- Symptoms not controlled by initial treatment
- Facial atopic dermatitis that has not responded to treatment
- Frequent flare-ups or severe atopic dermatitis
- Systemic therapies have been required for flare-ups or maintenance
- Symptoms are substantially impairing quality of life, e.g. sleep disruption, school or work attendance problems
- Allergic contact dermatitis is suspected.

Focus on Emollient Therapy

Many compounds are recognized as having skin protective properties, including dimethicone, mineral oil, colloidal oatmeal, paraffin, sodium bicarbonate, cocoa butter, glycerine and lanolin.¹ The primary agents used as skin protectants in atopic dermatitis are colloidal oatmeal and paraffin.¹

Although there is limited evidence that emollients benefit atopic dermatitis directly, they are widely used because they improve the appearance and symptoms of the dry skin associated with the disorder and may reduce the need for topical corticosteroids.¹¹

Emollients work by helping to repair the skin barrier breakdown. They achieve this by rehydrating the stratum corneum, causing the corneocytes to swell up leading to restoration of the integrity of the skin barrier. Emollients also help maintain the barrier function by reducing water loss through the skin by occluding the skin surface.¹⁸

With successful emollient therapy, the skin will become less dry, itchy and irritated. If not, practitioners should re-evaluate their treatment approach (**Practice Tips 2**).¹⁸

PRACTICE TIPS 2: Evaluation of Emollient Treatment Efficacy

- Are the correct emollients being used or should a greasier product be considered?
- Is more frequent application needed and/or larger quantities?
- Is the patient using soap substitutes when washing?
- Is an additional treatment, such as a topical steroid, needed?
- Is it possible that there is an underlying condition, such as a contact allergy, that requires referral to a dermatologist?

Emollients are generally considered safe, with the most commonly reported adverse reaction being stinging or discomfort on application. This is usually transient and considered a normal response to an application of emollient rather than an adverse reaction.^{11,17}

Choosing an emollient

The most important determinant in choosing an emollient is whether it is cosmetically acceptable to the patient and suits their lifestyle.^{1,18} An emollient that smells and feels acceptable to a patient is also more likely to be used regularly;^{18,19} and one that is disliked will not be used.¹ Indeed, researchers who surveyed the attitudes and practices of eczema patients being treated at a Hong Kong paediatric dermatology clinic concluded that adherence to emollient therapy is likely to be increased if the recommended product meets patient preferences.¹⁹ Providing patients with trial-sized quantities of different products will allow them to make an informed decision about which they prefer,¹⁷ which could help to improve adherence.

How should emollients be used?

Skin dryness is a common manifestation of atopic dermatitis and, for many patients, control of their skin dryness often mirrors control of their dermatitis. Hence, patients with atopic dermatitis should liberally apply emollient to their entire body. Emollients should be continued as a maintenance treatment, even when flares of atopic dermatitis resolve.^{1,5}

Emollients should be applied as frequently as necessary to maintain skin integrity,¹⁸ with a minimum of twice daily in the presence or absence of active disease having been recommended.¹ Irrespective of the formulation, emollients should be dotted over the skin and then spread gently to leave a thin film on the skin by using a stroking action in the direction of hair growth, rather than a circular or rubbing motions. It is not necessary to stroke continuously until all of the product is absorbed. The emollient should be allowed to absorb before applying other topical products, e.g. corticosteroids.^{17,18}

There are three main types of emollient formulation: bath or shower additives, soap substitutes and leave-on formulations,^{17,18} with a three-stage treatment regimen for the application of emollients having been recommended (**Practice Tips 3**).¹⁸

PRACTICE TIPS 3: **Three-stage Emollient Regimen**

Stage 1: Bath or shower additives

- Add emollient bath washes to bath water or use emollient shower products when showering.
- They should not be rinsed off the skin, which should be dried by patting gently.

Stage 2: Soap substitutes

- Also known as skin cleansers or synthetic detergents, soap substitutes should be used to wash the skin instead of soap since they have the advantage of being non-drying.
- Soap substitutes should be applied using hands or a wash cloth and then rinsed off.

Stage 3: Leave-on formulations

- Use an ointment, gel, cream, lotion or spray if neither bath additives nor soap substitutes prove to be effective.
- Leave-on topical emollients should be applied before going to bed or as soon as possible after showering or bathing to trap moisture into the skin.^{17,18}

Colloidal oatmeal

Oat oil is a natural agent that contains a variety of active compounds: lipids with a high percentage of fatty acids, starches, antioxidants and vitamins.²⁰ It is especially rich in linoleic acid,²¹ a lipid that is critical for maintenance of the epidermal permeability barrier.¹⁴ Oatmeal also has a high concentration of starches and beta-glucan, which may contribute to protective and moisture-holding properties.²⁰

The protective, hydrating and soothing properties of colloidal oatmeal for dry skin related to different dermatological conditions, including atopic dermatitis, have been reported since the 1950s.²² *In vitro* and *in vivo* studies subsequently confirmed the anti-inflammatory effects of colloidal oatmeal.^{22,23} The anti-inflammatory effects have been at least partially attributed to avenanthramides, which are phenolic compounds present in oatmeal.^{20,24}

More recently, three clinical studies have demonstrated that daily use of colloidal oatmeal in various formulations (creams, body washes and cleansers) for up to eight weeks duration produced significant ($p \leq 0.05$ vs baseline) improvements in skin symptom scores, including itch severity and quality of life indices, in a total of 69 patients (aged 3 months to 60 years) who were also receiving prescribed medication for mild to moderate atopic dermatitis (**Figure 2**).²²

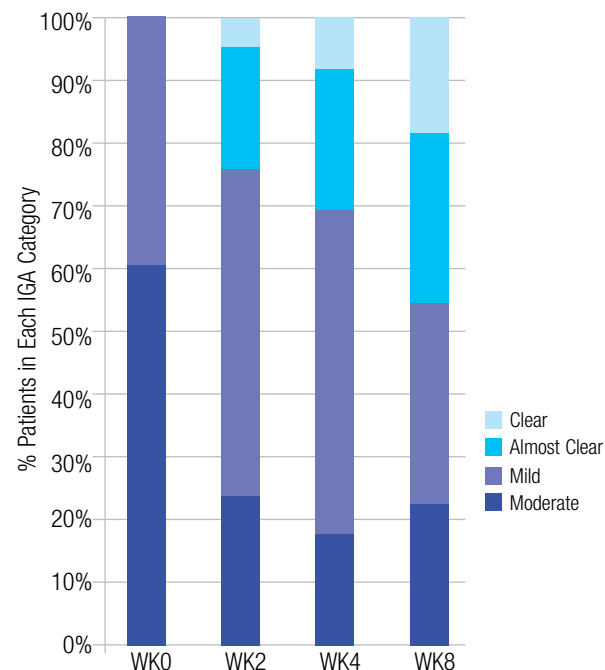


Figure 2. Progressive improvement in the Investigators Global Assessment (IGA) score during eight weeks of treatment with an adjunctive emollient regimen consisting of twice-daily oatmeal-based cream and once-daily oatmeal-based body wash in patients (n=25) with mild to moderate atopic dermatitis.²²

In all three clinical studies, colloidal oatmeal was well tolerated with no reports of serious adverse events related to treatment.²² This finding is consistent with the minimal irritation and allergic potential of a range of oatmeal-containing products demonstrated in a series of 12 repeat patch-testing studies in a total of 2291 healthy volunteers.²⁵

Steroid-sparing effects of emollients

Given the potential for local and systemic adverse effects to occur with long-term topical corticosteroid therapy it is considered desirable to minimize steroid exposure as much as possible.

Several randomized clinical studies in infants and children with mild to moderate, moderate, or moderate to severe atopic dermatitis have demonstrated that oil- or oat extract-based emollients used in conjunction with topical corticosteroids can reduce steroid use considerably without loss of treatment efficacy.²⁶⁻²⁸ In one of these studies, a randomized controlled trial, an oat-extract containing emollient significantly reduced the amount of high-potency steroid used by 42% ($p < 0.05$) during 6 weeks in infants (aged <12 months) with mild to moderate atopic dermatitis.²⁶

Given that at least some of their out-of-pocket expenses are for prescription and over-the-counter corticosteroid medications,¹⁰ the steroid-sparing effect of emollients may be cost saving for patients with atopic dermatitis.

Expert Commentary – Dr David Lim

Unfortunately, emollients are an often neglected treatment modality for atopic dermatitis. For a variety of reasons, patients have a tendency to focus on topical steroid use and only apply emollients sporadically. When educating patients, I try to reframe atopic dermatitis as primarily a disorder of dry skin with emollients as the primary treatment. I encourage patients to apply emollients four times daily at a minimum to optimize their skin condition. Topical steroids can then be used as described for acute flares of atopic dermatitis. With an increasing fear of steroids amongst patients, an apparent refocus away from topical steroids also helps to build rapport with patients, which is often neglected in chronic relapsing conditions.

Expert Commentary – Dr Samuel Zagarella

The soothing properties of oatmeal on eczematous or inflamed skin have been known for many years. At least two generations ago, people were told to put oats in an old sock, hold it under the tap as the bath filled, then use the sock as 'soap'. Today, colloidal oatmeal containing creams are an extremely important emollient.

Emollients should be used daily in the management of eczema, in order to maintain hydration of the skin and to reduce topical steroid usage. The frequency of usage should increase during the cold, dry winter months

when ambient humidity is low. The consistency of the emollient used should also vary depending on the time of year and ambient humidity. For example a thicker-based emollient is preferable in dry, winter weather, with a thinner base in summer, in order to prevent folliculitis, especially in atopic patients. In addition to eczema, colloidal oatmeal moisturiser is extremely soothing for the treatment of burns patients and on skin sites exposed to radiotherapy treatment.

Recent studies on colloidal oatmeal and its molecular mechanisms of action suggest that it has anti-inflammatory and antihistaminic activity. The avenanthramides, a recently described component of whole oat grain, are responsible for many of these effects. Studies have demonstrated that avenanthramides can inhibit the activity of nuclear factor kappa-B and the release of proinflammatory cytokines and histamine, well known key mechanisms in the pathophysiology of inflammatory dermatoses.

An important factor to consider when recommending emollients for atopic patients is that these patients often experience stinging, burning, irritant or allergic reactions to components in the emollients. It has been found that oatmeal-containing personal care products have very low irritant potential as well as a very low allergenic sensitization potential. In a recent study, colloidal oatmeal products were tested for irritancy and allergic contact potential. No allergies were reported by 80 subjects after patch testing after in-use application, nor reported by consumers of 445,820 products sold during a 3-year period.²⁵

Take-Home Messages

1. Atopic dermatitis is a common inflammatory pruritic skin condition, the psychosocial and economic burden of which can be considerable.
2. First-line therapy includes long-term emollient use and then topical corticosteroids during an exacerbation, followed by topical calcineurin inhibitors, phototherapy and systemic therapy in more difficult cases.
3. Emollients, including colloidal oatmeal, are important in the treatment and prevention of skin barrier breakdown.
4. The benefits of emollients include restoration of barrier function, increased hydration of the stratum corneum and a potential steroid-sparing effect.
5. Emollients should be continued after resolution of atopic dermatitis symptoms to maintain barrier protection and hydration.
6. Clinical studies have demonstrated the efficacy and safety of colloidal oatmeal emollients as adjunctive treatments in atopic dermatitis in infants, children and adults.

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