Good use of atopic eczema treatments

As much as 80 per cent of people with eczema have atopic eczema. This article gives an overview of its management, including how to recognise infections

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THE treatment of atopic eczema depends on its severity. A recent CPD article (PJ, 2012;288:711) describes the features of mild, moderate and severe eczema.

Treatment

The management approach to atopic eczema in children recommended by the National Institute for Health and Clinical Excellence is shown in Panel 1 but the model equally could apply to adults. All approaches involve emollients and their use should continue when eczema is clear. All approaches involve emollients but the model equally could apply to adults. All approaches involve emollients and their use should continue when eczema is clear.

An eczema flare is defined by National Institute for Health and Clinical Excellence guidelines as “a sudden worsening of symptoms requiring a physician’s appointment or application of prescription treatments”. It can be recognised by increased dryness, itching, redness, swelling and general irritability. The first step to take if the skin becomes drier is to increase the frequency of moisturising or change to a greasier product. If this does not work, a topical steroid (or, where appropriate, a calcineurin inhibitor) is usually used until the inflammation subsides.

Emollients

Emollients waterproof the skin, forming an oily barrier that prevents loss of water and entry of allergens or irritants. There are few good quality studies that demonstrate the efficacy of emollients but their widespread use has become consensus-based good practice.

I often explain the action of emollients by comparing the skin surface to a brick wall in which the keratinocytes are the bricks and the intercellular surrounding lipids the mortar. In this analogy eczema is represented by reduced mortar, allowing greater water loss and access for irritants and allergens. Application of emollients replaces missing mortar, improving the barrier.

There is a large range of emollient products available. They contain humectants, such as urea and propylene glycol, which absorb water (from the dermis), increasing hydration, and lauromacrogols, which have antipruritic properties.

All patients with eczema should practise “complete emollient therapy”, which involves the use of a wash product, designed to be used as a soap substitute, and a leave-on moisturiser that can be used throughout the day.

A common question pharmacists are asked is “which is the best emollient?”. Because they are worn in much the same way as an aftershave or perfume, the best emollient is the one that the patient is happiest to use.

Lifestyle and occupation will influence personal preference. Patients with very dry skin will benefit from a greasier preparation. If this does not work, a topical steroid (or, where appropriate, a calcineurin inhibitor) is usually used until the inflammation subsides.

Topical corticosteroids

Topical corticosteroids are normally reserved for the management of an eczema flare. They have been used for this purpose for around 50 years and work by suppressing the production of inflammatory mediators.

Steroids should be applied once or twice daily — no benefit is derived from more frequent application. One to two weeks’ use is normally sufficient to bring a flare under control without any problems. Longer term use can lead to a rebound of the flare once the steroid is discontinued as well as adverse effects.

The amount of steroid to use to treat a particular area is often expressed in terms of fingertip unit (FTU; which is the length of a cream or ointment from a tube squeezed from the tip of an adult
index finger to the first crease). One FTU should be enough to treat the surface area of skin covered by two adult palms (including fingers). In practice, however, the amount of steroid to use based on FTUs can be difficult to gauge and it is often simpler to explain to patients to apply enough cream or ointment to give the skin a slight shine.

Steroid potency is measured by the degree of vasodilatation they produce in the skin and is classified as follows:

- **Very potent** (eg, clobetasol propionate 0.05 per cent)
- **Moderate** (eg, betamethasone valerate 0.05 per cent)
- **Potent** (eg, betamethasone valerate 0.1 per cent, hydrocortisone butyrate 0.1 per cent, mometasone furoate 0.1 per cent)
- **Very potent** (eg, clobetasol propionate 0.05 per cent)

Patients and carers need to understand where products should be used. For example, the skin on the eyelids and around the eyes is thin — studies have shown percutaneous absorption of hydrocortisone from the eyelids to be around 300 times greater than from plantar skin. So only a few days with a mild potency steroid, such as hydrocortisone cream 1 per cent, would be prescribed for eyelid eczema. More potent steroids should not be used due to the risk of absorption, increased intraocular pressure and, rarely, cataracts. (Topical calcineurin inhibitors [see below] would be an alternative).

Mild to moderate steroids are reserved for the face and flexures whereas more potent agents can be used on the trunk, arms and legs, provided use is restricted to under two weeks. Very potent steroids are usually reserved for highly lichenified eczema in adults.

There is little information to guide prescribers on which steroid to choose from each potency class and selection is largely a matter of experience. Fear of side effects is a major reason for steroid treatment failure. Skin thinning is unlikely with mild to moderate potency agents but can occur if potent agents are applied for prolonged periods. Caution is also needed when potent agents are used over large areas or under occlusion because this enhances absorption. Patients or carers might be on packaging or in leaflets that steroids should not be used on broken skin. Because eczema is associated with itch, the skin is invariably broken and this may present a dilemma. However, broken skin in the context of steroids means surgical wounds or leg ulcers — it is safe to apply them to scratch skin.

Patients should also understand that steroids should be reserved for flares and only applied to areas of eczema. However, there is some evidence to suggest that using steroids twice weekly in addition to emollients helps to keep eczema in remission longer than using emollients alone.

### Calcineurin inhibitors

The topical calcineurin inhibitors (pimecrolimus and tacrolimus) are a relatively new class of agent. Originally derived from *Streptomyces hygroscopicus*, calcineurin inhibitors bind to and block the action of calcineurin, a protein that activates T cells to release cytokines. This immunosuppressive mechanism of action has led to the use of these agents for eczema. Use is reserved for when topical steroids have been ineffective or should not be used (eg, due to intolerance or higher risk of skin atrophy such as application to the face or neck). However, the two available drugs have different licensed indications.

- **Pimecrolimus** Pimecrolimus cream (Elidel) can be used for mild to moderate atopic eczema in patients from the age of two years. It can be used both short term to treat flares and, in the long term, intermittently to prevent flares, where application should start at first appearance of signs and symptoms. A thin layer of cream should be rubbed into the patches of eczema twice a day. The cream should be around 300 times greater than the effects of topical corticosteroids.

**Panel 2: How best to use emollients**

Leave-on emollients (eg, creams, lotions and sprays) are oil and water emulsions and the higher the proportion of oil, the greasier the product feels. The mix of oil and water provides a good breeding environment for bacteria so most products contain preservatives but, in some cases, these can cause sensitivity reactions, characterised by burning, stinging or itching.

Ointments do not contain water and are much greasier. They have a greater occlusive effect on the skin and are more suited to very dry skin but are less cosmetically acceptable. Examples of the different leave-on products in terms of greasiness are:

- **Very greasy** (eg, Epaderm ointment, 50:50 WSP/LP)
- **Greasy** (eg, Unguentum M, Hydromol)
- **Moderately greasy** (eg, Diprobase, Cetraben)
- **Light** (eg, Aveeno, E45)

**Frequency** Emollients should be used as often as needed. This could be six to seven times a day but, in reality, this is rarely achieved. It is also important that patients have the opportunity to try different products in order to find one they like. In practice, patients might be best using more than one product (eg, a lighter preparation for use during the day and a greasier product at night).

Emollients should be used liberally (as a rough guide, 2g is equivalent to a teaspoonful) and the amount needed for the treatment of both arms or both legs, applied at least twice a day for a week would be up to 200g or 200ml for an adult. Treatment of the trunk alone would require 400g, assuming at least twice daily application. Patients should, therefore, be prescribed large amounts because the products should, ideally, be applied more frequently.

**Bathing** Daily bathing or showering is recommended by some specialists to reduce the level of dead skin cells because this lessens the risk of infection. However, others have suggested that daily bathing is unnecessary and may dry the skin. The temperature of the bath or shower should be warm but not hot (because this increases vasodilatation, which can irritate the skin).

Although there are several commercial emollient wash products available, soap substitutes such as aqueous cream or Epaderm are equally effective. Patients can also prepare a soap substitute with an ointment to whisking it in hot water and then adding to the bath. Alternatively, shower products can be made by mixing an ointment with hot water and storing it in a suitable sized plastic bottle.

Leave-on emollients should be used within a few minutes of bathing to trap surface moisture. The product should be applied to the skin in smooth downward strokes (following the direction of hair growth) and allowed to soak into the skin. Rubbing the product into the skin creates friction, which is likely to increase irritation.

**Use with steroids** The application of emollients in relation to topical steroids is controversial. Some specialists suggest applying the emollient 20 minutes before the steroid to hydrate the skin. This may highlight areas of redness, making it easier to see where the steroid should be applied. Application before steroids is also advocated to remove scale, which can affect absorption. Another rationale is that an emollient ‘plumps up’ the surface of the skin, increasing the surface area for absorption of the steroid. Guidance from Clinical Knowledge Summaries is to apply the emollient first. Nevertheless, there are no studies that look at eczema response in relation to whether an emollient is used before putting a topical steroid on or after.

Furthermore, in practice, it should be fine to apply a steroid before the emollient provided that a suitable gap is left between applications, to minimise dilution. According to Hywel Williams, professor of dermato-epidemiology and director of the Centre of Evidence Based Dermatology, whether the time interval needs to be 20 minutes, 30 minutes or one hour or more is unknown and would require research into the pharmacokinetics of drug delivery of topical corticosteroids.
should be used for as short a period as possible — it should be stopped when signs and symptoms resolve or if there is no improvement in six weeks. In other words, use should not be continuous. Elidel should not be applied under occlusion but emollients can be applied immediately after using it.

Tacrolimus Tacrolimus ointment (Protopic) is indicated for moderate-to-severe eczema in patients over two years of age. It can be used for both treating flares and maintenance (ie, preventing flares and prolonging flare-free intervals in patients experiencing four or more attacks a year).

To treat flares, the ointment is applied twice daily, at the first appearance of signs and symptoms, until the lesions are cleared, almost cleared or mildly affected (up to three weeks in children, before decreasing to once daily). Improvement is usually seen within a week.

Maintenance requires twice weekly application (every three days) to commonly affected areas. Treatment should not be continuous on a long-term basis — a review of maintenance treatment is needed after 12 months.

The 0.03 per cent ointment is indicated for use by children. The 0.1 per cent ointment can be used for adults, although the lower concentration should be used if effective. Unlike with Elidel, emollients should not be applied to the same area within two hours of applying Protopic.

There is little convincing evidence that the calcineurin inhibitors are more effective than topical steroids although they have the advantage of not causing skin thinning and being suitable for higher risk sites such as the face. General points to note with calcineurin inhibitors include that:

- They can be used on any part of the body but kept away from the eyes and mucous membranes.
- Use may cause mild reactions, typically a warm or burning sensation. These tend to be transient, resolving within a week.
- Treatment may be associated with an increased risk of skin infection, which might include folliculitis, herpes and impetigo.
- Patients should minimise their exposure to sunlight (eg, covering or applying sunscreen to treated areas).

Bandage treatments Bandages can help protect the skin from scratching and occlusion enhances penetration of topical therapies. There are at least four different approaches to bandages in the management of eczema: wet wrapping, dry wrapping, occlusive or semi-occlusive dressing, and medicated bandaging (useful for lichenified eczema).

Wet wrapping is the most common and most studied. Tubular cotton bandages (eg, Tubifast, Comfifast, Acti-fast) are applied to the skin in two layers. The lower layer is soaked in warm water and then applied to the skin over an emollient or topical steroid. A dry layer is then placed over the wet layer. The wet wraps are worn for three to seven nights. NICE says that the evidence base for wet wrapping is poor but has suggested that topical steroids under wet wraps might be useful in cases of severe eczema, for very dry skin or if flares are not controlled by conventional topical steroid use.

Phototherapy Some patients find that their eczema improves in the summer and both UVA and UVB have been found to help improve eczema. UVB treatment is given up to three times a week either as broad or narrow band (known as TLO1). When UVA is used, patients normally take or bathe in psoralens to enhance skin sensitivity before the treatment so the procedure is often called PUVA. PUVA treatment is limited due to the risks of skin cancer from over-exposure. There is less risk with UVB.

Phototherapy is not suitable for very young children or frail patients who are unable to stand in the UV cabinet. NICE considers phototherapy of limited value and it should be reserved for cases unresponsive to other treatments.

Use of calcineurin inhibitors is not recommended with phototherapy.

Systemic therapy More severe forms of eczema require more aggressive therapies such as oral treatment. The two main drugs used are ciclosporin and azathioprine. In some cases prednisolone is also used. The mode of action of ciclosporin and azathioprine in eczema is unclear. The evidence for the effectiveness of oral treatment in eczema was considered by NICE to be limited. Furthermore, oral therapies have a number of potentially serious side effects. They should be reserved for use when other treatments have failed, should be initiated by specialists and require careful monitoring.

More commonly, pharmacists may see the use of antihistamines. Although eczema itch is not mediated primarily by histamine, both sedating and non-sedating antihistamines are sometimes prescribed to help relieve this symptom. There is little evidence of efficacy but their use might be of benefit where the eczema has an urticarial component. NICE has recognised that clinical experience supports short-term use (up to two weeks), particularly if the eczema is causing sleep disturbance.

Other options Other treatments that have been used in eczema include injection of a killed strain of Mycobacterium tuberculosis, injection of interferon gamma and intravenous immunoglobulin. Although there is some evidence from studies to show that these treatments can help, they are not recommended by NICE.

Complementary medicine Many patients use complementary therapies either in conjunction with conventional treatment or as an alternative. A wide range of therapies is available, including Chinese herbal medicine, herbal medicine (eg, evening primrose oil [gama linolenic acid]), homoeopathy, hypnotherapy, massage and acupuncture. Although these are popular and there are some clinical studies showing some promise (in particular with some Chinese herbal medicines), further work is required to evaluate such treatments in more detail.

When further studies of gamma linolenic acid were conducted, the evidence indicated that the product was not effective and the product licence for its use in eczema was withdrawn. –>
It has been suggested that a probiotic supplement based on lactobacillus can lead to an improvement in eczema. Some studies have shown that either supplementing the diet of mothers preterm or the infant (or breast-feeding mother) for six months after delivery, reduces the incidence of eczema. Improvement might be mediated through changes in faecal flora or immunological effects but a recent Cochrane systematic review found limited evidence for clinical benefit.4

**Infected eczema**

Patients with eczema are more susceptible to secondary infections with bacteria, viruses and fungi because the weakened barrier function of the skin allows entry of micro-organisms, (which can also trigger a flare). Pharmacists should be able to recognise infected eczema. They can advise patients to keep nails short and clean, and to wear cotton gloves at night, preventing scratching. Children and those with severe eczema should avoid contact with people with cold sores.

**Bacterial infections**

A common organism responsible for bacterial infections is *Staphylococcus aureus*. This bacterium accounts for around 90 per cent of the bacterial skin flora in eczema patients but only about 30 per cent in unaffected individuals. Another organism that can cause infections (although less commonly) is *Streptococcus pyogenes*.

Healthy skin produces a number of natural antimicrobial peptides, such as human ß-defensin 3 (HBD 3), which can rapidly kill *S aureus*. However, evidence suggests that the excessive amounts of Th2 cytokines in the skin of eczema patients can attenuate the up-regulation of antimicrobial responses to viral and bacterial stimuli. In fact, some evidence suggests that although the keratinocytes of eczema patients produce sufficient amounts of HBD 3, they are unable to mobilise it to the surface of the skin to kill *S aureus*. In addition, T cells can be induced to produce the inflammatory cytokine IL-31 from toxins produced by the bacteria.

Signs and symptoms of bacterial infection include:

- Redder skin than usual
- Hot, itchy, wet and weepy lesions
- Golden yellow crusts
- Pustules

Treatment would normally involve oral antibiotics such as fluoroquinoloxin (or erythromycin for patients allergic to penicillin or if there is known local resistance to penicillin). If there are only small localised patches of infection topical steroids combined with antibiotics (eg, fusidic acid) can be used for one to two weeks.

Patients with infected eczema can continue with topical steroids but it is advisable to stop topical immunomodulator agents. Wet wraps should not be used if eczema is infected.

The role of emollients containing antiseptic agents, such as triclosan, chlorhexidine and benzalkonium chloride, in the treatment of infected eczema is unclear. A review in 2007 by the *Drug and Therapeutics Bulletin* questioned the role of such products although NICE suggests that they might have a role in reducing bacterial load. Antiseptics can irritate the skin through sensitisation.

**Viral infection**

Patients with eczema are also susceptible to viral infections such as herpes simplex. Although most infected adults have a typical localised infection, with eczema the virus can spread rapidly, leading to eczema herpeticum. This presents as a number of small, fluid filled blisters normally on the hand and neck but which can spread to other areas of the body. Although comparatively rare, this infection is often not recognised and requires prompt treatment with aciclovir. Look out for:

- Rapidly worsening eczema that is sore or painful
- Clusters of blisters (like early-stage cold sores)
- Circular, depressed or ulcerated lesions usually 1–3 mm and uniform in appearance (these can coalesce and crust)
- Patients with raised temperature, lethargy or distress, or who are feeling ill

Another viral infection seen in eczema patients is molluscum contagiosum, which is caused by the pox virus. This typically presents as small, flesh coloured lumps with a small dimple at the centre of the lump (see Image). Molluscum will usually spread by scratching and can develop on eczema prone areas such as behind the knees. The virus is less likely in adults, who will have developed immunity. Patients should be reassured that molluscum is harmless and will spontaneously resolve although this can take up to 18 months.

**Fungal infection**

*Candida albicans* can cause infections in patients with eczema (especially flexural eczema) and, in some cases, it results in a secondary infection, especially in warm, moist areas such as the groin and armpits and, in young babies, the nappy area. *Candida* normally presents as a red, sore area and there are often tiny yellow pustules present. Over-the-counter antifungal products, such as clotrimazole, are effective in candidal infections but, if in doubt, refer.

**Developments**

In 2009, a study found that using sodium hypochlorite in the bath combined with nasal mupirocin ointment, led to a decrease in eczema severity scores. These so-called “bleach baths” were hailed as a potential new treatment for eczema. However, in a recent Cochrane review on the role of anti-staphylococcal treatments in eczema, the authors noted that while there is little doubt that such therapies reduce the bacterial load on the skin this does not translate into any meaningful clinical improvement.3

There are a range of potential new therapeutic approaches to the treatment of eczema. These include leukotriene inhibitors and various anti-cytokine agents such as anti-IL-4, anti-IL-5 and anti-IL-31. Many of these newer therapies are still experimental but may bring benefits in the future.

Pharmacists can play an important part in helping patients with eczema. This can range from giving simple self-care advice to treating mild-to-moderate flares with over-the-counter topical steroids. Through medicines use reviews they can also ensure that patients understand how to use the various treatments prescribed.

References available online.