Guide to treatments used for atopic dermatitis in adults

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Atopic dermatitis, or eczema, usually begins in childhood but adults can also be affected due to either persistence of symptoms or late-onset disease. This article provides a guide to the topical and systemic treatments used for atopic dermatitis in adults, including administration, adherence and primary care prescribing data.

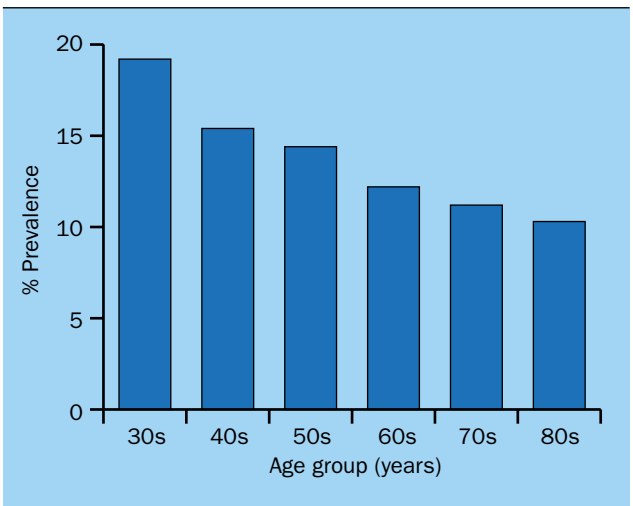

Figure 1. One-year prevalence of atopic dermatitis in adults according to age, Denmark (n=16,507)[7]

According to surveys of the prevalence of atopic dermatitis, 3–17 per cent of adults self-report having the condition,[1-9] though estimates are lower when confirmed by a medical diagnosis (1.6–10 per cent[4,10-12]). The reported prevalence over longer time periods, *eg* eight years[10] or lifetime,[1] ranges more widely, from about 3 per cent to 40 per cent. Most of those affected had atopic dermatitis during childhood or had a family history of the condition,[1,2] though onset during adulthood is also described.[6] In one study in which dermatologists graded atopic dermatitis severity, 71 per cent of cases were mild, 26 per cent were moderate and 4 per cent were severe.[4]

It has been assumed that children with atopic dermatitis 'grow out' of the condition but, by young adulthood, about 80 per cent have persistent symptoms.[13] A large survey in Denmark (n=16,507) found that one-year prevalence of atopic dermatitis among adults declined with age but it was still common among people in their 80s (see Figure 1).[7]

Two large (n=833 and n=955) studies reported follow-up of at least 24–25 years in cohorts who had attended dermatology clinics during childhood. One found current dermatitis in 62 per cent of respondents who had been inpatients and 40 per cent of those who had been outpatients, predominantly affecting the hands; persistent dry or itchy skin in adulthood was associated with recurring or persistent atopic dermatitis.[14] The second study found that 59 per cent of respondents had reported atopic dermatitis symptoms within the previous 12 months.[15] Follow-up and clinical examination three years later found that

atopic dermatitis persisted in 68 per cent of a subgroup of 79 people.[16] Eczema was present in most locations but, by contrast with childhood atopic dermatitis, most frequently affected the head and neck (52 per cent) and the hands (50 per cent) and was of mild to moderate severity in the majority but severe in 12 per cent. These data suggest that atopic dermatitis in adults may be due to persistence or recurrence of childhood atopic dermatitis with a subgroup of patients possibly having a distinct late-onset atopic dermatitis.[17,18]

Managing atopic dermatitis in adults

A 2011 SIGN guideline recommends a similar approach in adults and children to the management of atopic dermatitis[19] (current NICE guidance applies only to children). More recently, the American Academy of Dermatology published detailed guidelines covering the treatment of adults and children.[20-23] The treatment strategies in these guidelines are similar. The stepwise approach of the Primary Care Dermatology Society (PCDS),[24] updated in July 2016, probably represents the most current advice on management (see Table 1).

The PCDS emphasises the importance of taking time to assess the patient, providing information about eczema and contact details for patient groups, encouraging adherence with emollients and developing an individualised plan. Patients who present with a flare up should be treated with a moderate to potent steroid for "a few days". The PCDS considers this strategy superior to longer use of less potent agents; it is not supported by older SIGN guidance[19] whereas recent US guidance notes there is little evidence to favour either approach.[21]

Emollients

Emollients play an essential role in the management of atopic dermatitis and appropriate use can reduce the need for topical steroids. They trap moisture in the skin and form

Step 1	General measures	Assessment Patient education and signposting Develop a management plan	• Copious use of emollients at each step
Step 2	Initial management for patients presenting with a flare-up	"Hit hard" for a few days with a moderate to potent topical steroid once daily until settled	• *eg* Betnovate (betamethasone valerate) or Elocon (mometasone)
		Skin infection – widespread	• Add a systemic antibiotic, *ie* flucloxacillin or erythromycin, for one week
		Skin infection – localised	• Consider Betnovate cream or Fucibet (fusidic acid/betamethasone valerate) cream without a systemic antibiotic
		Marked sleep disturbance	• Consider a sedating antihistamine (hydroxyzine, chlorpheniramine)
		Take a skin swab if not settling; review after 1–2 weeks to discuss long-term management	
Step 3	Long-term management	Emollients (mainstay of therapy) • Allow 15–20 minutes to dry before application of topical steroid	• Moisturisers: use patient preference, prescribe generously • Bath/shower preparations: those with antiseptic properties for frequent flares; antipruritic such as Balneum-plus bath oil for itchy skin • Soap substitutes: one of the prescribed moisturisers can be used
		Topical steroids • Use lowest appropriate potency for age, site and severity and apply thinly • Extra care needed on the face/around eyes • Avoid use on lower legs of older patients and others at risk of leg ulcers	• Adult face: mild or moderate potency, *eg* Eumovate (clobetasone butyrate 0.05%) • Adult trunk and limbs: potent, *eg* Betnovate 0.1% or Elocon • Palms and soles: potent or very potent, *eg* Dermovate (clobetasol propionate 0.05%)
		Bandages and dressings can be used on top of emollients or topical corticosteroids (but not on wet, infected eczema)	

Table 1. Summary of the Primary Care Dermatology Society recommendations for the management of atopic dermatitis (as relevant to adults)[24]

Step 4	Management of flare-ups	Infrequent flare-ups (every 4–8 weeks)	• As per Step 2
		Frequent flare-ups • Check adherence • Swab for infection	• Limited prophylaxis with topical steroid (Betnovate or Elocon): "weekend regimen" • Consider topical tacrolimus as steroid alternative • Consider alternative diagnosis such as contact allergic dermatitis
Step 5	Topical immunomodulator treatment	Consider topical calcineurin inhibitors when: • Eczema involves the eyelids and periorbital skin • Regular topical steroid use on the face • Regular topical steroids use on the lower legs (elderly patients) and others at risk of leg ulcers • Any signs of skin atrophy	• Pimecrolimus for milder cases • Tacrolimus for more severe cases
Step 6	Scalp eczema	• Mild tar-based shampoo • Water-based topical steroid scalp application once or twice daily until settled • Remove thick scale before applying a topical steroid	• *eg* Betacap (betamethasone valerate) • *eg* with Sebco ointment (coal tar/salicyclic acid/sulfur)
Step 7	Referral	Refer in cases of: • Diagnostic uncertainty • Severe eczema • Moderate to severe eczema only partially responding to steps 1–5 • Steroid atrophy or concerns regarding the amount of topical steroids/immunomodulators being used • Possible contact allergic dermatitis	

Table 1. Summary of the Primary Care Dermatology Society recommendations for the management of atopic dermatitis (as relevant to adults)[24] (cont.)

a protective layer, which helps the skin repair and improves hydration. They are recommended for everyone with atopic dermatitis and should be applied liberally and frequently. The PCDS emphasises the importance of finding a product the patient likes and this means being prepared to prescribe several products until the most suitable is found. Patients usually prefer creams and gels; ointments are less well tolerated but are more likely to be preservative free and are therefore likely to pose a lower risk of contact dermatitis. The *BNF* warns that paraffin-based emollients are a fire hazard and users should be told to stay away from fire and flames and avoid smoking when using them.

	Creams and ointments (g)	**Lotions (ml)**
Face	15–30	100
Both hands	25–50	200
Scalp	50–100	200
Both arms or both legs	100–200	200
Trunk	400	500
Groins and genitalia	15–25	100

Table 2. Suitable quantities of emollients (based on adult twice daily application for one week). Adapted from *BNF* August 2016

Patients need an adequate quantity of emollients – the PCDS suggests prescribing 500g for four-times daily application and the *BNF* has proposed quantities suitable for different areas of the body (see Table 2).

An emollient should be added to bath water (in the form of a bath oil) or used as a soap substitute when showering. Aqueous cream and emulsifying ointment can be used and specific formulations are also available, *eg* Dermol 200 Shower Emollient. These products can make the bath or shower slippery, so forethought is needed to avoid falls.

With all treatments for atopic dermatitis, the physical properties of the vehicle should be taken into account as well as the active ingredient (the *BNF* has summarised the properties of several vehicles – see Table 3) because it may exert a therapeutic effect by promoting skin hydration and reducing inflammation (and, for topical steroids, enhancing drug penetration).

Topical steroids

Topical steroids suppress the inflammatory reaction and are generally used to relieve symptoms when emollients alone are ineffective. They should be used in a way that minimises the risk of adverse effects, notably skin atrophy and systemic absorption. The *BNF* has suggested appropriate quantities to

Applications	Viscous solutions, emulsions or suspensions	• All areas including scalp and nails
Collodions	A skin paint	• On drying, leaves a flexible film over the site of application
Creams	Emulsions of oil and water	• Well absorbed • May contain preservative • Cosmetically more acceptable than ointment because less greasy and easier to apply
Gels	Hydrophilic or hydrophobic base with high water content	• Particularly suited to the face and scalp
Lotions	Have a cooling effect; may have water or alcohol base	• May be preferred to ointments or creams for application over a hairy area • Alcohol base can sting if used on broken skin
Ointments	Greasy preparations, normally insoluble in water; most common bases are soft paraffin or soft/liquid/hard paraffin	• More occlusive than creams • Particularly suitable for chronic, dry lesions • Some have mild anti-inflammatory effect • Water-soluble ointments formulated with macrogols are readily washed off
Pastes	Stiff preparations containing a high proportion of finely powdered solids such as zinc oxide and starch suspended in an ointment	• For circumscribed lesions such as those that occur in lichen simplex, chronic eczema or psoriasis • Less occlusive than ointments and can be used to protect inflamed, lichenified or excoriated skin
Dusting powders	Used only rarely; prevent rubbing of adjacent areas of skin	• Not for moist areas (may cake and abrade skin)

Table 3. Properties of vehicles, adapted from *BNF* August 2016

prescribe for different sites (see Table 4). The general principles for prescribing are:

- Use the lowest appropriate potency
- Apply only thinly to inflamed skin
- Select the potency according to the site affected and symptom severity (see Table 1)
  - Adult face: mild or moderate potency
  - Adult trunk and limbs: potent
  - Palms and soles: potent or very potent
- Apply a suitable amount (according to the fingertip method – see Table 5)
- Most patients need only a once-daily application.

	Creams and ointments (g of product)
Face	15–30
Both hands	15–30
Scalp	15–30
Both arms	30–60
Both legs	100
Trunk	100
Groin and genitalia	15–30

Table 4. Suitable quantities of topical steroids (based on an adult single daily application for two weeks). Adapted from *BNF* August 2016

If these rules are followed, the PCDS states, the risk of skin atrophy is low. However, special care is needed on some sites: regular use on the face should be avoided, the skin around the eyes should be avoided (due to the risk of absorption and intraocular hypertension), and in older people and others at increased risk, regular use on the legs may cause ulcers. If there is concern about the dose used or about skin atrophy, the patient should be referred to a specialist. An emollient should be allowed to dry for 15–20 minutes before applying a topical steroid.

Patients who have frequent flares that respond to a topical steroid may try the "weekend regimen". This is a prophylactic strategy in which a potent preparation is applied thinly to the inflamed sites once daily for two weeks, then on alternate days for a further two weeks. When the eczema is under control, the steroid is applied to the sites that flare on two consecutive days, *eg* the weekend, every week – regardless of whether the skin is inflamed or not at the time.

Some topical steroids are available in combined formulations together with an antibacterial agent. These are useful when there is evidence of infection but regular use may promote antimicrobial resistance and increase the risk of sensitisation.

Topical calcineurin inhibitors

Calcineurin inhibitors (tacrolimus and pimecrolimus) are immunomodulating agents that can reduce inflammation but do not cause skin atrophy and are therefore an option when a steroid is indicated but the risk of adverse effects is unacceptable. Topical tacrolimus is licensed for use in moderate to severe atopic eczema and pimecrolimus for mild to moderate atopic eczema. The PCDS recommends them as an option for:

- Treatment involving the eyelids and periorbital skin
- Patients who regularly use a topical steroid on their face
- Elderly people and others at increased risk of leg ulcers for use on the lower legs
- When there is any sign of skin atrophy.

Continuous long-term use of these agents is not recommended. UV exposure and application to premalignant or malignant lesions should be avoided; these products should not be prescribed for people who are immunosuppressed or on sites with infection. If there is no response to tacrolimus after two weeks, other treatment options should be considered; patients who are responding after six weeks of treatment may consider switching to twice-weekly maintenance therapy for up to one year, when the need to continue should be evaluated. Pimecrolimus is licensed for twice daily application for up to one year but should be discontinued if there is no response after six weeks of treatment.

The most frequent adverse effects associated with the calcineurin inhibitors are application site reactions (irritation, burning, pruritus), skin flushing with alcohol and local infection. Their long-term safety is still being evaluated.

Adherence

Most patients with dermatological disorders do not use their medication as prescribed. One large survey of Japanese adults found low adherence (defined as a score <6 on the Morisky Medication Adherence Scale, which has a range of 0 [least] – 8 [highest]) among 72 per cent of those using oral medication for atopic dermatitis and 77 per cent of those using topical therapies.[25] Experience of drug effectiveness and lower overall satisfaction with treatment were among the factors associated with worse adherence; steroid phobia remains a problem.[26]

According to another Japanese study, there are many reasons why patients decide to stop using their atopic dermatitis medication (see Figure 2), the most frequent being too busy or forgetful, feeling better and messiness.[27] Adherence is often low even when clinicians believe it to be good;[28] one review of predominantly topical steroid therapy trials, including children and adults, found that patients overestimated their adherence rate.[29] This review also found that adherence declined with the duration of treatment, from 93 per cent for a three-day course to 32 per cent after eight weeks.

Prescribing in primary care

Prescribing statistics for primary care in England[30] do not distinguish between indications, so data on emollients and topical steroids include their use for atopic dermatitis, psoriasis and other applications. The most recent information shows that GPs in England wrote about 27 million prescriptions for the topical agents used in the treatment of atopic dermatitis at a cost of approximately £169 million (see Table 6).

Among emollients, three categories account for 89 per cent of volume and 86 per cent of spending (see Table 7): "other preparations" (notably E45 cream, Aveeno cream, Diprobase cream and Dermol 500 lotion); bath and shower preparations (most frequently aqueous cream); and liquid paraffin (particularly the Oilatum range of products).

The 13 million prescriptions written for topical steroids in 2015 cost a total of £67 million, reflecting the diverse indications for these agents. Three accounted for 76 per cent of items and 66 per cent of cost (see Table 8). The most frequently prescribed were hydrocortisone, with 22 preparations ranging in concentration from 0.1% to 2.5%, and some combinations with antifungal agents (including 1.2 million prescriptions for Daktacort cream). There were 31 preparations containing beta-

Area of skin to be treated	Approximate area (equating to adult hand)	FTUs each dose (adults)
A hand and fingers (front and back)	2 hands	1
Front of chest and abdomen	14 hands	7
Back and buttocks	14 hands	7
Face and neck	5 hands	2.5
An entire arm and hand	8 hands	4
An entire leg and foot	16 hands	8

Table 5. Fingertip units (FTU) for dosing topical steroids in adults. Adapted from: Patient. Fingertip units for topical steroids. http://patient.info/health/fingertip-units-for-topical-steroids [accessed September 2016]

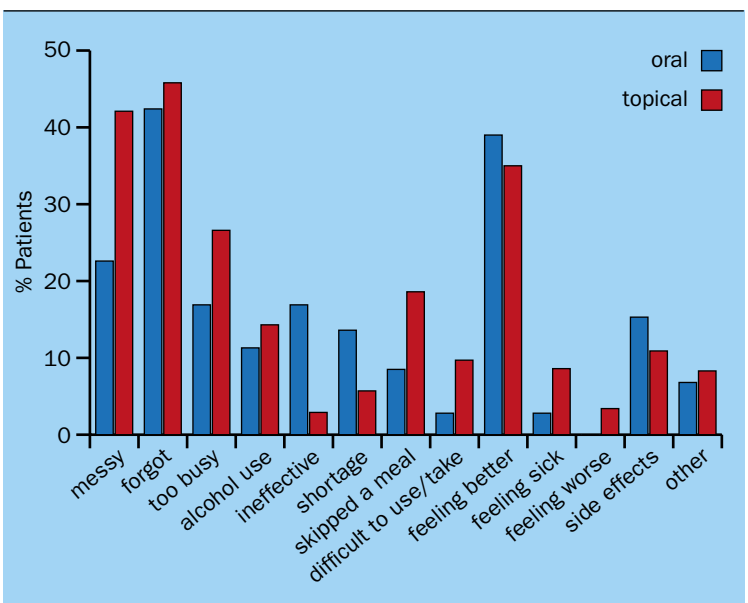

Figure 2. Reasons for discontinuing oral (n=177) or topical (n=349) therapies for atopic dermatitis without instruction from a physician (more than one reason allowed)[27]

	Items (000)	NIC (£000)
Emollients*	14,109	95,822
Topical steroids	13,015	67,730
Topical calcineurin inhibitors	174	5336
* *BNF* category 13.2.1; NIC = net ingredient cost		

Table 6. Primary care prescribing in England of the principal topical agents used to treat atopic dermatitis, 2015[30]

methasone valerate, of which the most frequently prescribed were the 0.1% cream (891,000 items) and Fucibet, a cream combination with fusidic acid (815,000 items). Of the one million items for clobetasone butyrate, almost half were for Eumovate cream 0.05%.

In comparison, prescribing of topical calcineurin inhibitors was low. There were 142,000 items for tacrolimus at a cost of £4.4 million; prescribing of topical pimecrolimus was about one-fifth of this level.

Systemic therapies

Before embarking on systemic therapy, avoidable reasons for the failure of topical treatments should be sought. These include low adherence, infection, allergy and insufficient treatment intensity.[31] Phototherapy is an alternative, bearing in mind the potential risk to someone who may subsequently receive immunosuppressive systemic agents.[22,31]

Other than oral steroids, which are limited by adverse effects, and oral antihistamines to reduce pruritus, there are principally four oral options for systemic therapy of severe atopic dermatitis in adults: ciclosporin, azathioprine, methotrexate and mycophenolate.[22,31] The only oral drug licensed for severe atopic dermatitis is ciclosporin. It has a rapid onset of action and has been shown to offer a 50 per cent reduction in atopic dermatitis severity with improved quality of life. It is usually prescribed as a six to nine-month course to limit the risk of hypertension, nephrotoxicity and skin cancer; 80 per cent of patients relapse within two months.[31] Oral azathioprine has a slower onset of action but can be taken for longer, though it is less effective than ciclosporin. There is less experience with oral methotrexate but it appears to be as effective as ciclosporin and is well tolerated. Oral mycophenolate also appears to be as effective as ciclosporin and may be associated with a lower rate of relapse after treatment completion.

	Items (000)	NIC (£000)
Emulsifying wax	178	559
"Other emollient preparations"	9349	63,516
White soft paraffin	29	106
Urea	591	7595
Wool alcohols	74	438
Bath and shower preparations	1884	11,393
Light liquid paraffin	665	4508
Liquid paraffin	1301	7484
NIC = net ingredient cost		

Table 7. Prescribing of emollients in primary care, England 2015[30]

	Items (000)	NIC (£000)
Betamethasone esters	374	3186
Betamethasone valerate	3584	23,744
Clobetasol propionate	832	5944
Clobetasone butyrate	1042	3741
Fludroxycortide	107	1684
Fluocinolone acetonide	166	1244
Hydrocortisone	5294	16,593
Hydrocortisone acetate	634	3517
Hydrocortisone butyrate	92	362
Mometasone furoate	853	6835
NIC = net ingredient cost		

Table 8. Prescribing of most frequently used topical steroids in primary care, England 2015[30]

Future therapies

Recognition of the role of the immune system and cytokine regulation in the pathogenesis of atopic dermatitis has led to the development of many novel potential therapies and further investigation of established agents developed for other indications.[32,33] Agents now in phase 3 trials that have recently been identified by the NHS Horizon Scanning Centre include dupilumab,[34] a monoclonal antibody against interleukin (IL)-4 receptors that inhibits the actions of IL-4 and IL-13, now being evaluated for refractory moderate to severe atopic dermatitis; and crisaborole, a topical phosphodiesterase (PDE)-4 inhibitor that reduces production of tumour necrosis factor (TNF) alpha and other inflammatory cytokines.[35]

Summary

It is now recognised that atopic dermatitis is common in adults and may be due to persistence or recurrence of childhood symptoms or late-onset atopic dermatitis. Stepwise management relies on emollients with additional topical steroids if necessary, or topical calcineurin inhibitors when steroids are unsuitable. Several systemic therapies are available for refractory severe atopic dermatitis and new immunomodulators are being evaluated in phase 3 trials.

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Declaration of interests

None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics