'I want Elidel!'

A reply and a review of the management of eczema using only fully subsidised medications

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I am not sure which occasion was more annoying. Was it when I discovered that there was a part charge on generic 1% hydrocortisone cream? Or was it when an impecunious patient that I did not usually charge asked for Elidel®? Yes, she knew its price, but the advertisements said that it was not a steroid, so it would be worth it.

At that time I did not know much about pimecrolimus (pim-e-crow-limus)(Elidel®). Being a non-subsidised medicine it was unlikely to be useful, so I took no interest in it.

Direct to consumer advertising has forced general practitioners to be more informed. Eczema/dermatitis is the most common skin condition seen in general practice, and skin conditions are the third most common presenting problem.[1] Therefore general practitioners need to know enough about pimecrolimus to answer patients' questions, and make wise prescribing decisions.

Here is a summary about pimecrolimus and a short review from the literature on the management of eczema/dermatitis using only currently (July 2005) fully funded medication (See Table 1). It may be a surprise to see how little is fully funded.

The term eczema will be used here as a generic term, equivalent to dermatitis and covering a large number of variants. Atopic eczema is the most common and is used as the reference type.

Formerly dumb doctor strikes back

About midnight at an after hours surgery.

Patient: *I want Elidel, right now!*

Doc: *Certainly. Do you know much about it?*

Patient: *I have just seen it on TV and it's not a steroid.*

Doc: *Yes, that is true. It certainly does work, but not quite as well as some of the standard treatments. It is expensive. It often stings. It can cause redness and irritation, and the user should probably stay out of sunlight.*

(Short pause while that sinks in.)

And, because it is new, experts are still cautious about how safe it is. It has been tested on animals, and so far it seems to be safe. But very high doses used on mice have caused them to develop cancers, especially when exposed to sunlight. In the United States, the Food and Drug Administration has issued a warning that it may cause cancer.

(Longer pause.)

That may be why it is not registered in New Zealand for use on children under three months of age. In Europe, they must be over two years of age.

(Short pause to see if patient blinks. No? Proceed.)

Now, it comes in 15g tubes, that is about three teaspoons full, and costs about $40 each. How many would you like? And by the way, do not use it if there is any sign of infection nor on broken skin.

P.S. This is a completely imaginary consultation but conforms to anecdotes I have heard.

Pimecrolimus is a new type of treatment – a topical immunomodulating agent

(For skim reading the main facts are in bold.)

- Of the two topical 'immunomodulating' drugs only pimecrolimus is available in New Zealand.
- **It is effective** but less than betamethasone valerate (Beta®, Betnovate®).
- **It does not cause skin thinning**, as may occur with the incorrect use of corticosteroids.
- **It may be useful on the face and neck**. These areas are vulnerable to steroid atrophy, especially in younger patients. There is evidence for its value on these sites. However, the British Association of Dermatologists position statement considers it a second line therapy.[2] Its place in the treatment of eczema is still said to be unclear.[3]
- **There is little systemic absorption and it is probably safe but there are concerns of a possible cancer link**. In New Zealand pimecrolimus is licensed for use

on children over three months of age. In Europe they must be over two years old and then only for treatment that is short-term or intermittent.[2] Pimecrolimus, and tacrolimus which is a similar but stronger product, have been associated with the development of lymphomas in mice when used at a high dose. The US Food and Drug Administration has issued a warning (March 2005) that there is a potential link to cancer and an increased rate of upper respiratory infections.[4] They both have a 'short time to tumour development' when exposed to UV light.[5] It has a similar mode of action to ciclosporin but is not chemically related. There is good evidence for the effectiveness of oral ciclosporin in the treatment of eczema.[6] In a trial with pimecrolimus on 91 children up to two years of age there was no impairment of their immunisation response.

- It is believed to act by suppressing T lymphocyte responses.
- **The cautions** with pimecrolimus are that it can cause a burning sensation at the sites of application. It must not be used where there is infection. Sun exposure should be avoided.
- **It is expensive** and promoted to the public as safe, and plays on a widespread erroneous public belief that corticosteroids are not.[7] There is more information at www.dermnetnz.org.nz/; the data sheet can be found at www.medsafe.govt.nz.

Management of eczema using fully funded medications

(See Table 1 for a list of the fully funded topical eczema medications.)

1. Eliminate or create a barrier from allergens and irritants

Finding allergens or irritants can be difficult. In children egg, milk (including soya) and peanuts are the most likely dietary allergens. The use of an elimination diet may only be helpful in the 10% who are the most severely affected. Even then the evidence is weak.[8] Most children will grow out of food allergies, but shellfish and peanuts may be the exceptions.[9] According to the 'emedicine' article on atopic dermatitis, skin testing in children under eight years has a significant false positive and negative rate, but no reference is given. (See below under 'further reading' for the website.) Elimination diets need to be done with expert advice to avoid defective nutrition. Some allergens pass into breast milk, so the mother may also require a dietitian's advice.

The fully funded topical barrier agents are: **zinc and castor oil ointment, white soft paraffin** (WSP).

2. Improve the skin's lipid barrier with emollients

Use soap substitutes

- **Aqueous cream, emulsifying ointment**. Aqueous cream is emulsifying ointment homogenised with water and a preservative. It is softer and easier to use in cold weather, but the preservative may be allergenic. Some may find it washes away too quickly in the shower.
- **Pinetarsol®** is a bath additive that is also claimed to be anti-pruritic and is the only bath additive that is fully funded.

Emollients ('moisturisers' – by keeping the skin's moisture inside)

They cannot be used too much.

- **Aqueous cream, emulsifying ointment, Lemnis Fatty Cream®**.
- **10% urea creams** are hydrating,[10] e.g. **Nutraplus®**.
- When showering or bathing (tepid water) the skin should be patted dry and then the emollient immediately applied before the skin has fully dried.
- They should be used twice or more times each day to keep the skin moist.

3. Topical corticosteroids

Choose a topical corticosteroid that is **of minimal potency, but is still effective without everyday use**. Daily use can result in a loss of effectiveness (tachyphylaxis). One plan is to use the corticosteroid on weekdays and take the weekends off. A variety of regimes have been shown to be effective.[11-13] Nothing other than hydrocortisone (and not the potent hydrocortisone 17-butylate -Locoid®) should be used on the face unless you are an expert.

Potencies are as assigned as in the BNF.[10]

(a) *Mild*. Hydrocortisone is safe anywhere. Usually 1%, but if not effective use a more potent steroid. Half per cent may be useful for large areas, babies' faces or infant's bodies. The fully funded preparations are **Lemnis Fatty Cream HC®** or **hydrocortisone added to a fully funded base** – see Table 1.

(b) *Moderately potent*. **Triamcinolone acetonide 0.02%** (**Aristocort®**). Note: The BNF classifies the 0.1% concentration as potent and that is the strength found in the preparations mixed with nystatin, neomycin and gramicidin (Viaderm KC®).

(c) *Potent*. **Betamethasone valerate** (**Beta®**), **Hydrocortisone 17-butyrate** (**Locoid®**). **Mometasone** (**Elocon®**) **and methylprednisolone** (**Advantan®**) are applied only once a day.

(d) *Very potent*. **Clobetasone propionate** (**Dermo®**).

Patients should watch out for blistering, which may indicate a virus infection, and promptly see a doctor if they occur. Specialist advice may be required.

Topical corticosteroids are applied thinly once or twice daily. The BNF gives a guide of finger tip units – the squirt from a tube the length of a terminal phalanx should cover two hand areas.[10]

Occluding the area with plastic can increase the potency/skin penetration. The inclusion of urea or salicylic acid also increases penetration.[10] These techniques will also increase unwanted systemic effects.

In severe situations a short course of systemic corticosteroids may be required to achieve control.

Table 1. Fully funded emollients and bases, topical corticosteroids and corticosteroid-antimicrobial combinations used for eczema.

Emollients and other bases	Trade name and type of base
Aqueous cream	
Oil in water emulsion	Lemnis fatty cream®
10% urea cream	Nutraplus®
Emulsifying ointment	
White soft paraffin (WSP)	
Zinc and castor oil ointment	
Pine tar bath oil	Pinetarsol® (Not a base)
Mild corticosteroids	
Hydrocortisone 0.5 – 5% may be add to the above.	NOT Pinetarsol®
Hydrocortisone 1% in oil and water emulsion	Lemnis fatty cream HC® (100g pack)
Moderate potency	
Triamcinolone acetonide 0.02%*	Aristocort® cream, ointment. (100g pack)
Potent corticosteroids (Apply twice daily)	
Betamethasone valerate	Beta® cream, ointment; Betnovate® lotion
Hydrocortisone butyrate	Locoid®, cream, oint, lipocream, milky emulsion
Potent corticosteroids (Apply once daily)	
Methylprednisolone (potency not listed in BNF)	Advantan® cream, ointment
Mobetasone	Elocon® cream, ointment, lotion
Corticosteroid anti-microbial combinations	
Hydrocortisone 1% miconazole	Micreme H® cream
Hydrocortisone 1%, neomycin, natamycin	Pimafucort® cream, ointment
Triamcinalone*, neomycin, nystatin	Viaderm KC® cream, ointment
Betamathasone, chlorquinaldol	Locoid C® cream

* The BNF classifies the 0.1% concentration as potent and that is the strength found in the preparations mixed with nystatin, neomycin and gramicidin (Viaderm KC®).
The fully funded anti-fungals are: clotrimazole cream, miconazole cream, and ketoconazole shampoo.
The fully funded anti-microbials are: silver sulphadiazine (Silvazine®), povidone iodine (Biocil® oint).

4. Eliminate infection

The presence of *Staphylococci* is common and may be the cause of treatment failure. A systemic antibiotic is preferred. That also enables the duration of the course to be prescribed – it is difficult to know how long a tube of cream will last. First choice could be **flucloxacillin or erythromycin ethyl succinate** (**E-mycin®**) for those allergic to penicillins. A longer course, such as two-weeks, is commonly required. Anti-fungal preparations are still best prescribed topically as the oral forms are expensive and more toxic.

For secondary infection with Candida there are two fully funded topical imidazoles: **miconazole** (**Micreme®**) and **clotrimazole** (**Clocreme®**). For those who are sensitive to this group there is no fully funded alternative except in combination with neomycin and a potent strength corticosteroid (**Pimafucort®** and **Viaderm KC®**).

5. Education and emotions

Although most children grow out of eczema, for adults this may be a lifelong problem. Suggesting that skin care be made part the daily routine of teeth cleaning and hair combing may make it feel less of a burden. Plenty of explanation and understanding is required.

The skin is an organ that reacts visibly to everyday stress and emotions. It is not surprising that eczema may be aggravated by the psyche. In children the parent-child relationships may be disturbed, along with that of their peers.[14] There is evidence that psychological approaches are effective.[6]

Other 'treatments'

- Probiotics (harmless cultures of bacteria). Some trials have reported a benefit.[3] The future will tell.
- The babies of atopic parents may benefit from being breast-fed exclusively for at least eight or nine months.
- Oral evening primrose oil probably does not work.[15,16]
- Drugs such as ciclosporin, or ultraviolet light work[6] but are for specialists' use.
- Chinese herbs may damage the liver and may have unexpected ingredients. One report found eight out of 11 tested topical Chinese preparations contained dexamethasone.[17]
- Homeopathy is unproven.[6]

Further reading on the net

www.dermanetnz.org/gps/gplectures/ – Includes pictures.

Guidelines for the management of atopic eczema: www.eguidelines.co.uk/...

Atopic dermatitis: www.emedicine.com/ped/topic2567.htm

British National Formulary (BNF): http://www.bnf.org/

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