

Hands up for new treatment option

Dr Jonathan White, Consultant Dermatologist at St John's Institute of Dermatology at St Thomas' Hospital in London, examines the issues surrounding chronic hand eczema.

Many people in the UK with eczema have hand involvement. For around 5% (one in 20) of these people, the eczema on their hands is severe and does not go away, does not respond to treatment or keeps coming back. Recurrent hand eczema like this is called chronic hand eczema (also known as chronic hand dermatitis). Symptoms can vary from itchy, scaly patches of skin that flake constantly, to red, cracked and painful hands with blisters that may weep.

Patients with chronic hand eczema suffer significant disability – with profound occupational, economic, medical and social consequences – because they cannot use their hands normally. Chronic hand eczema has been shown to be a major cause of lost earnings.¹ In a Swedish 12-year follow-up study, 82% of patients reported having changed their work situation because of occupational hand eczema and 15% became unemployed or received a disability pension.²

Why chronic hand eczema occurs

Chronic hand eczema can affect anyone, but it is more likely to occur: if you had similar skin problems, hay fever or other allergies as a child; if your hands get wet a lot, whether at home or at work; and if your job exposes your hands to irritating chemicals. Nurses, hairdressers, cooks, cleaners, farmers and metal workers are some of the people who seem to be at risk of chronic hand eczema. However, sometimes not even avoiding the obvious triggers for hand eczema is enough and sufferers may have symptoms even when they stop working.

In a Danish survey,³ work-related, chronic hand eczema led to prolonged (more than 5 weeks per year) sick leave in nearly 20% of the patients and nearly one-quarter of them reported that they had lost their job at least once during the past 12 months due to their disease.

Another study showed that the prevalence of occupational hand eczema is under-reported and may be 30–50 times higher⁴ than otherwise assumed.

Research published in the *Journal of Allergy and Clinical Immunology* in 2006 suggests that a defective skin barrier is the primary cause of eczema.⁵ The skin barrier is the outermost layer of the skin and is the first line of defence between the body and the environment. Changes in skin-barrier function affect the penetration of irritants and allergens through the skin. The skin's protective outer barrier is thinner in those having had childhood eczema, which makes them more prone to hand eczema in adulthood. However,

constant washing and drying of the hands can also break down the skin's barrier.

Seeking treatment

If your hand eczema symptoms have been present for more than a few weeks and do not seem to be getting better, you should seek treatment from your doctor. Because hands are in constant use, eczema at this site becomes more difficult to treat, particularly if it has been present for a while. Rubbing and scratching the skin will make it thicken and harden, making it difficult for any cream to penetrate the skin deeply enough to have an effect. The longer the condition goes undiagnosed and untreated, the higher the chance of hand eczema becoming persistent.

It has been suggested that the multi-factorial origin of hand eczema is responsible for the chronic course of the condition and for its poor response to treatment.⁶

Your GP may refer you to a dermatologist, particularly if your hand eczema doesn't seem to be responding to treatment as expected. Your dermatologist may recommend that you are patch tested. This involves putting different chemicals to which you are exposed at home and work onto the skin, to see if you develop an allergic reaction. This can help you to identify which triggers to avoid. Some of the common allergens are:

- nickel;
- fragrances, including natural fragrances;
- preservatives found in toiletries including: formaldehyde, quaternium-15, diazolidinyl urea, imidazolidinyl urea, DMDM hydantoin, and methylchloroisothiazolinone/methylisothiazolinone;
- hair dyes;
- clothing dyes;
- chromate;
- rubber additives;
- epoxy resin;
- acrylates; and
- plant allergens.

Topical treatment options

For most people, hand eczema can be managed by a combination of protecting their skin (see 'What you can do to help yourself' on page 19) and by topical treatments that are applied to the skin. Moisturisers such as lotions, creams, ointments, and bath or shower additives are essential in the management of eczema. They are the only preventative

treatments available and work by keeping the skin moist and supple. This helps to protect the skin from irritants. Apply them as liberally and frequently as possible, even when the skin looks normal.

If moisturisers on their own are not enough to control your eczema, one of the first-line medicated treatment options your doctor will consider is a corticosteroid cream or ointment. While corticosteroids can be effective for hand eczema, they should only be used when the condition is actively flaring, as prolonged use can cause thinning of the skin – especially when too high a strength of steroid is used for a given part of the body.

If steroid creams don't seem to be working, your doctor may recommend an immunomodulator, such as tacrolimus ointment (Protopic®) or pimecrolimus cream (Elidel®). These are not steroids, so they don't cause skin thinning and they have been shown to be effective in eczema, although they are not licensed specifically for chronic hand eczema patients. These agents have only been used for the past few years in dermatology. Sun exposure should be avoided when using these treatments and some patients notice flushing of the skin when they drink alcohol after applying these creams. Other treatment options for chronic hand eczema include irradiation with ultraviolet light, known as PUVA. Whilst this can be effective, any ultraviolet light treatment can increase the risk of developing skin cancer in the long term.

If other treatments don't work, your doctor may recommend tablet treatments. The latest systemic treatment for chronic hand eczema that doesn't respond to steroid creams is alitretinoin (Toctino® – see below). Other options include oral steroids (only for short courses in emergency situations), ciclosporin, methotrexate and azathioprine. Although these can be very effective, ciclosporin cannot be used in the long-term and sometimes patients cannot tolerate either methotrexate or azathioprine due to adverse side effects.

New treatment option: alitretinoin

Alitretinoin is the first treatment developed specifically for chronic hand eczema and is a once-daily tablet containing alitretinoin (9-cis retinoic acid), which is a naturally occurring retinoid structurally related to vitamin A. Alitretinoin is a recently available treatment for severe, chronic hand eczema that does not respond to topical treatments, including corticosteroids.

In a clinical trial of 1,032 patients from around the world, with severe, chronic hand eczema that had not responded to



Before treatment with alitretinoin



After treatment with alitretinoin

topical corticosteroids, almost half had clear (or almost clear) hands after taking alitretinoin for up to 24 weeks.⁷ Alitretinoin helped to clear up a range of symptoms from scaling and cracks to redness and blisters. The results were published in the *British Journal of Dermatology* in April 2008.

In the large clinical trial of alitretinoin the treatment was well tolerated, with the most frequently reported side effect being headache. Other side effects included dry skin and lips, lip inflammation, raised blood lipids such as cholesterol and decreased levels of thyroid hormones.

Alitretinoin, the active ingredient in Toctino® belongs to a class of drugs called retinoids that potentially cause severe birth defects if taken during pregnancy. *This means that any woman of child-bearing age taking Toctino® must avoid becoming pregnant during treatment and for one month after stopping treatment – for example, by using two effective methods of contraception.*

Retinoids – in particular isotretinoin (Roaccutane®), which is licensed to treat severe forms of acne⁸ – have sometimes been linked to depression and suicide in some case reports, as well as in some small epidemiological studies. However, larger, controlled studies^{9,10} have shown that there does not seem to be any association. No cases of depression were reported in the alitretinoin clinical studies.

What you can do to help yourself: tips for home and work

If you have active hand eczema or are recovering from an episode, you should avoid excessive wet-work whenever possible. You should also avoid soap, since it is irritating to the skin, and use an emollient instead. When you wash your hands, carefully blot them dry and then apply your preferred moisturiser. Keep some by every sink in your home and carry some with you when you go out.

Wear cotton gloves when doing housework. For wet-work, including preparing some foods, cover the cotton gloves with unlined powder-free vinyl gloves. Use a washing machine or dishwasher if you can. Similarly, use gloves at work wherever possible.

Although exposure to irritants or allergens can play a role in chronic hand eczema, it is not always possible to identify them all. However, if patch testing has indicated that you are allergic to certain substances, it is certainly important to avoid them.

What your employer can do to help

Under the Health and Safety at Work Act 1974, employers have a duty to safeguard the health of employees. A health and skin-care policy at work will ensure that you and your fellow employees can reduce the risk of developing chronic hand eczema. This may include provision of adequate washing facilities and appropriate skin cleansers. If your work involves the use of skin irritants or sensitisers, a skin-care policy should be put in place to prevent skin problems. Your employer should be able to provide you with the correct protective clothing and gloves for the materials you are handling. Gauntlets should also be provided if they are necessary. It may also be possible for you to reduce or avoid contact with substances you are sensitive to, including the use of 'no-touch' techniques and good extractor fans.

References

1. Van Coevorden A M et al. (2004) Overview of studies of treatments for hand eczema – the EDEN hand eczema survey. *Br. J. Dermatol.*, 151:446–51
2. Meding B, Wrangsjö K & Järholm B. (2005) Fifteen year follow-up of hand eczema: persistence and consequences. *Br. J. Dermatol.*, 152:975–980
3. Cvetkowski R, Rothman K, Olsen J et al. (2005) Relation between diagnosis on severity, sick leave and loss of jobs among patients with occupational hand eczema. *Br. J. Dermatol.*, 152:93–8
4. Diepgen TL & Schmidt A. (2002) Werden Inzidenz und Prävalenz berufsbedingter Hauterkrankungen unterschätzt? *Arbeitsmed Sozialmed Umweltmed*, 37:477–480
5. Leung D J, Nelson H & Szeffler S. (2006) *J. Allergy Clin. Immunol.*, 118(4):771–2
6. Hogan D J, Dannaker CJ & Maibach H I (1990) The prognosis of contact dermatitis. *J. Am. Acad. Dermatol.*, 23:300–307
7. Ruzicka T, et al. (2008) Efficacy and safety of oral alitretinoin (9-cis retinoic acid) in patients with severe chronic hand eczema refractory to topical corticosteroids: results of a randomized, double-blind, placebo-controlled multicentre trial. *Br. J. Dermatol.*, 158:808–17
8. Roaccutane SPC
9. Cohen J, Adams S & Patten S. (2007) No association found between patients receiving isotretinoin for acne and the development of depression in a Canadian prospective cohort. *Can. J. Clin. Pharmacol.*, 14:e227–33
10. Jick S, Kremers HL & Vasilakis-Scaramozza C. (2000) Isotretinoin use and risk of depression, psychotic symptoms, suicide and attempted suicide. *Arch. Dermatol.*, 136:1231–6

Dr White is a member of Basilea's medical advisory panel in respect of Toctino® and has spoken at a Basilea-sponsored meeting. Basilea Pharmaceuticals are industry sponsors of the work of the NES.