

## Review article

**Management of atopic dermatitis – A review**

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**Abstract** Atopic dermatitis is a chronic relapsing and remitting disease, which afflicts mostly the young ones. The treatment of atopic dermatitis is very frustrating as no single therapeutic modality is satisfactory. The first breakthrough in its management came with the advent of topical steroids. We are still awaiting the next breakthrough. Much research is being done in this regard and the pick of the lot is topical immunotherapy. It may well prove to be the find of the decade in the management of atopic dermatitis. This article summarizes the established as well as unconventional therapeutic modalities which help the patients as well as which has evidence of successful use.

**Key words**

Atopic dermatitis, management

**Introduction**

Atopic dermatitis is a chronic relapsing and remitting disorder, which usually starts in early childhood. It is frequently associated with elevated levels of serum IgE and a personal or family history of atopy i.e. allergic rhinitis, atopic dermatitis or asthma. The diagnosis is clinical and based on a combination of historic and morphologic finding, as there is no single distinguishing feature.<sup>1</sup> Atopic dermatitis now affects 15% to 20% of children in developed countries, and prevalence in cities in developing countries undergoing rapid demographic changes is quickly following suit.<sup>2</sup> The condition also creates a great financial burden for both the family and society.<sup>3</sup>

**General measures**

Perhaps the most important consideration in the management of atopic dermatitis is

to educate the patient and family in certain realities of their disease.

1. The disease runs its own course and physicians can only moderate that course; the disorder is not curable but it is always possible to improve the patients' condition.
2. The skin must be kept moisturized.
3. It is crucial that trigger factors are avoided in order to prevent inflammation.

**a. Mild cleansing**

Routine everyday care of skin is an essential part of optimal patient management in atopic dermatitis. Xerosis, which is an integral part of atopic dermatitis, leaves the skin vulnerable to external insults, partly as a result of varying levels of barrier dysfunction. Cleansing removes dead surface cells, preparing skin to better absorb topically applied drugs/medication. Cleansers based on mild synthetic surfactants and/or emollients are ideal for these patients.<sup>4</sup>

**b. Emollients**

Emollients and moisturizing creams are used to break the dry skin cycle and to maintain the smoothness of the skin. In the

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vast majority of cases, improved bathing techniques and proper moisturizing can solve the problem. Patients need to avoid hot water, overuse of soap and unnecessary soaking and rubbing with washcloth and towel. Excessive frequency of bathing and hand washing should be discouraged. Most importantly, the skin hydration obtained from bathing should be retained by prompt application of an adequate moisturizer. The least expensive moisturizers are mineral oil and petrolatum etc. Moisturizers should be applied lightly after the bath and any excess removed with a cotton towel. Creams and lotions may be irritating and drying due to an evaporative effect. Greasy agents should be avoided in hot humid climate to prevent occlusive folliculitis. Similarly plastic wrap occlusion may also cause folliculitis.<sup>5</sup> Recently it has been shown that ceramide deficiency is the putative cause of stratum corneum dysfunction. Ceramide-dominant, barrier repair emollient has been shown to be better than simple emollients.<sup>6</sup>

### **Established therapies**

#### **a. Antihistamines**

Oral antihistamines provide only marginal antipruritic benefit and much of the effect seems to be as a sleep aid. Doxepin is the most potent histamine antagonist and is very specific. So is hydroxyzine, which is one of the few shown to be effective in a controlled trial. However, relief of pruritus by non-sedating antihistamines has been refuted.<sup>7</sup> Several studies demonstrate the efficacy of second and third generation anti histamines in relieving pruritus in atopic dermatitis.<sup>7,8</sup> but double-blind placebo-controlled trial are lacking.<sup>6</sup> Cetirizine, a second generation antihistamine, has been shown to possess anti-inflammatory properties, acting via

inhibition of leucocyte recruitment and activation, and by the reduction of ICAM-1 expression on keratinocytes.<sup>9,10</sup>

#### **b. Topical steroids**

Topical corticosteroids have been the mainstay of treatment for atopic dermatitis over the past 40 years. Hydrocortisone was the first to be used; some 30 additional corticosteroid compounds have now been licensed for treatment of atopic dermatitis. Topical applications containing corticosteroid compounds vary greatly in potency. In general the more potent ones are associated with the greater risk of adverse effects. First application of potent topical steroids results in rapid clearance of the rash. The snag is that persistent application of a potent preparation will put the patient at risk of unwanted local effects on the skin. The development of side effects is directly proportional to the frequency of application of topical steroids. However, recent trials suggest that only once daily application can give optimal results,<sup>11</sup> and maintenance treatment can be done effectively with only twice weekly application thus minimizing the side effects.<sup>12</sup>

#### **c. UVA therapy**

Several studies have demonstrated the efficacy of UVA1 (340-400 nm) phototherapy for patients with severe atopic dermatitis. However, the optimum treatment dose has yet to be determined. Although in seminal investigations high UVA1 doses were used, comparable results were reported in recent studies with a medium-dose regimen.<sup>13</sup> However, effectiveness is merely short term, limited, and is followed by recurrence of symptoms within a 3-month observation interval<sup>14</sup>

**d. UVB therapy**

Recently, interest has been renewed in the narrow-band wavelength of UVB phototherapy for atopic dermatitis (TL-01 Lamp). Encouraging results have been reported. However, long-term follow-ups are required before this therapeutic modality is established as treatment of atopic dermatitis.<sup>15,16</sup>

**e. Antibacterials**

Secondary bacterial infections are known to complicate atopic dermatitis, due to deranged skin barrier function and impaired immunological status. *Staphylococcus aureus* is the infecting organism in over 99% of episodes. It is nearly always penicillin-resistant. Cloxacillin and erythromycin are reasonable choices of treatment. Recent research has greatly contributed to our understanding of the pathophysiological potential of *S. aureus* superantigens in atopic dermatitis, suggesting that antibiotic therapy might be an important element in the therapeutic management of atopic dermatitis.<sup>17</sup>

**Newer modalities****a. Cyclosporin**

Oral cyclosporin is now an established therapeutic modality in severe and recalcitrant atopic dermatitis. Several studies have shown that short-term treatment is effective and tolerable as the drug is tapered off before side effects set in. Dosage regimen of 3-5 mg/kg/day for 10 to 12 weeks is effective.<sup>18,19,20</sup>

**b. Topical macrolactum immunomodulators**

The immunomodulatory macrolactams provide an alternative to glucocorticosteroids for the topical treatment of atopic dermatitis and other

inflammatory dermatoses. Tacrolimus (FK506), as well as the newer ascomycin derivative ASM 981 (pimecrolimus), penetrate the inflamed epidermis and are suitable for topical therapy. Both substances inhibit the transcription of proinflammatory cytokine genes such as interleukin 2, which are dependent on the nuclear factor NF-AT. They block the catalytic function of calcineurin, which leads to the inhibition of the transport of the cytoplasmic component of NF-AT to the cell nucleus. Multicenter, randomized, double blind clinical trials with topical formulations have shown the efficacy of both substances in moderate to severe atopic dermatitis.<sup>21,22</sup>

**c. Montelukast**

Cysteinyl leukotrienes have been shown to be important in the pathogenesis of allergen-induced (atopic) asthma and rhinitis. Skin manifestations of atopic dermatitis have been reported to improve with leukotriene antagonists. Double-blind placebo-controlled trials have shown moderate response to montelukast in severe atopic dermatitis.<sup>23,24,25</sup>

**d. Photopheresis**

Recently, photopheresis was used as monotherapy in patients with intractable atopic dermatitis. A total of ten treatments were used with a two weekly interval. All patients showed clinical improvement as well as reduction in serum levels of eosinophil cationic proteins and total IgE.<sup>26</sup>

**Experimental modalities****a. Antifungals**

As fungal colonization is increased in atopic dermatitis, there is a rationale to use antifungals. Clinical improvement and decreased serum IgE were obtained in patients with positive *Malassezia*

radioallergosorbent tests (RASTs), who were treated with oral ketoconazole. Some preliminary data suggested that oral itraconazole treatment in AD patients reduced the need for topical corticosteroids. Furthermore, besides its antifungal action, itraconazole in part relieves pruritus and inflammation.<sup>27</sup>

#### **b. Balneotherapy**

Balneotherapy involves immersion of the patient in mineral water baths or pools. Bathing in water with a high salt concentration is safe, effective, and pleasant for healing and recovery. There are almost no side effects during and after treatment, and there is a very low risk to the patient's general health and well-being. The mechanisms by which broad spectrums of diseases are alleviated by spa therapy have not been fully elucidated.<sup>28</sup> Such therapies are being used in many parts of Pakistan since ancient times. Many places are known for their hot springs and people travel from great distances to bathe in these waters.

#### **c. Dinitrochlorobenzene**

A small uncontrolled pilot trial has suggested that contact sensitization to dinitrochlorobenzene and repeated weekly applications significantly improve the clinical status of severe atopic dermatitis in adults. The effects are thought to be due to topical immune modulation by dinitrochlorobenzene. Larger controlled studies of dinitrochlorobenzene treatment in atopic dermatitis are warranted.<sup>29</sup>

#### **d. Intradermal *Mycobacterium* suspension**

Recently a small randomized, double blind and placebo controlled trial has shown improvement in childhood atopic dermatitis using intradermal injection of killed *Mycobacterium vaccae* (SRL 172).<sup>30</sup>

#### **e. Naphthalan**

Naphthalan has long been known for its medicinal properties and beneficial effects in inflammatory diseases such as psoriasis, atopic dermatitis, and psoriatic dermatitis. Experience acquired to date in the use of naphthalan in the management of squamous dermatoses and atopic dermatitis has shown favorable results. It should be further investigated to confirm its usage in the treatment of these diseases.<sup>31</sup>

#### **f. Probiotics**

Recent studies suggest that oral bacteriotherapy with probiotics might be useful in the management of atopic dermatitis. *Lactobacillus* GG (ATCC 53103), which is a human intestinal strain, promotes local antigen-specific immune responses (particularly in the IgA class), prevents permeability defects, and confers controlled antigen absorption, when given to infants with atopic eczema and cow's milk allergy as an extensively hydrolyzed whey formula containing ( $5 \times 10^8$  colony-forming units/gm formula). Thereby it promotes endogenous barrier mechanisms in patients with atopic dermatitis and food allergy by alleviating intestinal inflammation.<sup>32-34</sup>

#### **g. Interferon gamma**

Recombinant human interferon gamma has been shown in a double-blind, placebo-controlled study to be a well-tolerated and effective agent in the long-term therapy of patients with AD, when given in a dose of 50  $\mu\text{g}/\text{m}^2$  as daily self-administered subcutaneous injection for up to 24 months.<sup>35</sup>

#### **h. Mycophenolate mofetil**

Mycophenolate mofetil is a new immunosuppressive drug that is used to prevent acute rejection of renal

transplants. In doses of 2 or 3 g/d the drug is well tolerated, effective and safe in non responding atopic dermatitis.<sup>36</sup>

## **Complementary and alternative medicine**

### **a. Acupuncture**

Acupuncture is an old therapeutic method that includes both needle and nonneedle acupuncture. Nonneedle acupuncture includes moxibustion, cupping, and acupressure. Acupuncture has been reported to be beneficial for the treatment of atopic dermatitis among many other skin conditions. A lack of controlled studies is the main drawback for this method of treatment. However, the experiences from experts in this field may offer us new ideas to resolve refractory disorders in dermatology.<sup>37</sup>

### **b. Traditional Chinese medicine**

Traditional Chinese medicine (TCM) is an alternative method of therapy that can be administered in oral, topical, or injectable forms. It emphasizes the importance of using many herbs that are combined in different formulations for each individual patient. In the future, perhaps a better understanding of TCM will be gained through more systematic analysis and controlled studies with a placebo arm.<sup>38,39</sup>

### **c. Homeopathic treatment**

Homeopathy is one of the commonest alternative methods of treatment being used these days by dermatologic patients. Conflicting results of this treatment modality have been reported. Randomized, blinded and placebo controlled trials are lacking in literature. Maybe a few good trials can settle this issue.<sup>40,41</sup>

### **d. Special silk fabric**

As it is well known, irritant factors aggravate childhood atopic dermatitis. A

special silk fabric (MICROAIR Dermasilk) has been developed to minimize such irritant reactions. It has been shown that wearing such fabric minimizes symptoms in atopic children.<sup>42</sup>

### **e. St. John's wort cream**

Recent investigations suggest an anti-inflammatory and antibacterial effect of hyperforin, which is a major constituent of *Hypericum perforatum* L. (Saint John's wort). A double-blind, placebo-controlled prospective study has shown a significant superiority of the hyperforin 1.5% cream compared to the vehicle in the topical treatment of mild to moderate atopic dermatitis. The therapeutic efficacy of the hypericum-cream, however, has to be evaluated in further studies with larger patient cohorts, in comparison to therapeutic standards i.e. glucocorticoids.<sup>43</sup>

### **f. Hypnosis**

Hypnosis is an alternative or complementary therapy that has been used since ancient times to treat medical and dermatologic problems. A wide spectrum of dermatologic disorders may be improved or cured using hypnosis as an alternative or complementary therapy, including atopic dermatitis.<sup>44</sup>

### **g. Oolong tea**

Standard treatment fails in many patients with recalcitrant AD skin lesions. Study results in animal models have demonstrated that the administration of tea (i.e. green, black, or oolong<sup>46</sup>) suppressed type I and type IV allergic reactions. This hypothesis has been tested clinically in an open study and oolong tea has been found to be effective in atopic dermatitis, probably due to antiallergic properties of tea polyphenols.<sup>45</sup>

#### **h. Natural honey and beeswax**

A mixture of honey, olive oil and beeswax, all in equal proportions, applied topically, has been tested in a single blind, partially controlled study and found to be effective in the treatment of atopic dermatitis and psoriasis.<sup>46</sup>

#### **Future**

The fact that so many new, exotic and alternative treatment modalities are being sought, shows the amount of research being done in the field of atopic dermatitis, on the other hand it also shows the failure of medical science to discover a cure for this debilitating condition. Many other therapies (may be too exotic) could not be included in this article due to space constraint. However, the clinch of the recent research in the field of atopic dermatitis is the development of topical immunotherapy. Tacrolimus and pimecrolimus are, maybe the therapeutic finds of this decade in the treatment of atopic dermatitis.<sup>47</sup> The very concept of applying topical steroids with all the long-term ill effects will be changed. But till the time these topical immunomodulators become widely available, and also at lower cost, the mainstay of treatment remains emollients and topical steroids.

#### **References**

1. Schultz Larsen F. Atopic dermatitis: a genetic epidemiologic study in a population based twin sample. *J Am Acad Dermatol* 1993; **28**: 719-23.
2. Williams H, Robertson C, Stewart A *et al.* Worldwide variations in the prevalence of symptoms of atopic eczema in the international study of asthma and allergies in childhood. *J Allergy Clin Immunol* 1999; **103**: 125-38.
3. Jenner N, Campbell J, Marks R. Morbidity and cost of atopic eczema in Australia. *Australas J Dermatol* 2004; **45**: 16-22.
4. Subramanyan K. Role of mild cleansing in the management of patient skin. *Dermatol Ther* 2004; **17** (Suppl 1): 26-34.
5. Loden M. Role of topical emollients and moisturizers in the treatment of dry skin barrier disorders. *Am J Clin Dermatol* 2003; **4**: 771-88.
6. Chamlin S, Kao J, Frieden I *et al.* Ceramide-dominant barrier repair lipids alleviate childhood atopic dermatitis: Changes in barrier function provide a sensitive indicator of disease activity. *J Am Acad Dermatol* 2002; **47**: 198-208.
7. Klein PA, Richard AF, Clark RAF. An evidence-based review of the efficacy of antihistamines in relieving pruritus in atopic dermatitis. *Arch Dermatol* 1999; **135**: 1522-5.
8. Imaizumi A, Kawakami T, Murakami F *et al.* Effective treatment of pruritus in atopic dermatitis using H1 antihistamines (second-generation anti-histamines): changes in blood histamine and tryptase levels. *J Dermatol Sci* 2003; **33**: 23-9.
9. Portnoy JM, Dinakar C. Review of cetirizine hydrochloride for the treatment of allergic disorders. *Expert Opin Pharmacother* 2004; **5**: 125-35.
10. Shimizu T, Nishihara J, Watanabe H *et al.* Cetirizine, an H1 receptor antagonist, suppresses the expression of macrophage migration inhibitory factor: its potential anti-inflammatory action. *Clin Exp Allergy* 2004; **34**: 103-9.
11. David JA. Topical corticosteroids in atopic dermatitis (editorial). *BMJ* 2003; **327**: 942-3.
12. Berth-Jones J, Damstra RJ, Golsch S *et al.* Multinational Study Group. Twice weekly fluticasone propionate added to emollient maintenance treatment to reduce risk of relapse in atopic dermatitis: randomized double

- blind, parallel group study. *BMJ* 2003; **326**: 1367-9.
13. Tzaneva S, Seeber A, Schwaiger N *et al.* High dose versus medium dose UVA -1 phototherapy for patients with severe generalized atopic dermatitis. *J Am Acad Dermatol* 2001; **45**: 503-7.
  14. Abeck D, Schmidt T, Fesq H *et al.* Long-term efficacy of medium-dose UVA1 phototherapy in atopic dermatitis. *J Am Acad Dermatol* 2000; **42**: 254-7.
  15. Samson Yashar S, Gielczyk R, Scherschum L, Liun HW. Narrow band ultraviolet B treatment for vitiligo, pruritus, and inflammatory dermatosis. *Photodermatol Photoimmunol Photomed* 2003; **19**: 164-8.
  16. Grundmann-Kollmann M, Behrens S, Podda M *et al.* Phototherapy for atopic eczema with narrow-band UVB. *J Am Acad Dermatol* 1999; **40**: 995-7.
  17. Lubbe J. Secondary infections in patients with atopic dermatitis. *Am J Clin Dermatol* 2003; **4**: 641-54.
  18. Zaki I, Enerson R, Allen BR. Treatment of severe atopic dermatitis in childhood with cyclosporin. *Br J Dermatol* 1996; **135** (Suppl.48): 21-4.
  19. Hakan G, Pekka E, Sakari R. Long term follow up of eczema patients treated with cyclosporin. *Acta Derm Venereologica* 1998; **78**: 40-3.
  20. Zouneveld M, De Rie MA, Beljaards R *et al.* The long-term safety and efficacy of cyclosporin in severe refractory atopic dermatitis: a comparison of two dosage regimens. *Br J Dermatol* 1996; **135** (Suppl.48): 15-20.
  21. Bornhovd E, Burgdorf W, Wollenburg A. Macrolactum immunomodulators for topical treatment of inflammatory skin diseases. *J Am Acad Dermatol* 2001; **45**: 736-43.
  22. Abramovits W, Goldstein AM, Stevenson LC. Changing paradigms in dermatology: topical immunomodulators within a per mutational paradigm for the treatment of atopic and eczematous dermatitis. *Clin Dermatol* 2003; **21**: 383-91.
  23. Broshtilova V, Antonov D, Bardarov E, Tsankov N. Severe erythrodermic atopic dermatitis treated with montelukast. *Skinmed* 2003; **2**: 134-6.
  24. Yanase D, David-Bajar K. The leukotriene antagonist montelukast as a therapeutic agent for atopic dermatitis. *J Am Acad Dermatol* 2001; **44**: 89-93.
  25. Rackal JM, Vender RB. The treatment of atopic dermatitis and other dermatoses with leukotriene antagonists. *Skin Therapy Lett* 2004; **9**: 1-5.
  26. Heike IR, Billman-Eberwein C, Grewe M *et al.* Successful monotherapy of severe and intractable atopic dermatitis by photopheresis. *J Am Acad Dermatol* 1998; **38**: 165-9.
  27. Nikkels AF, Pierard GE. Framing the future of antifungals in atopic dermatitis. *Dermatology* 2003; **206**: 398-400.
  28. Matz H, Orion E, Wolf R. Balneotherapy in dermatology. *Dermatol Ther* 2003; **16**: 132-40.
  29. Mills L, Mordan L, Roth H *et al.* Treatment of severe atopic dermatitis by topical immune modulation using dinitrochlorobenzene. *J Am Acad Dermatol* 2000; **42**: 687-9.
  30. Arkwright P, David T. Intradermal administration of a killed *Mycobacterium vaccae* suspension (SRL 172) is associated with improvement in atopic dermatitis in children with moderate-to-severe disease. *J Allergy Clin Immunol* 2001; **107**: 531-4.
  31. Alajbeg A, Vrzogic P, Ostrogovic Z. Naphthalan--a natural medicinal product. *Acta Dermatovenerol Croat* 2003; **11**: 178-84.
  32. Kalliomaki M, Salminen S, Poussa T *et al.* Probiotics and prevention of atopic disease: 4 year follow-up of a randomized placebo-controlled trial. *Lancet* 2003; **361**: 1869-71.
  33. Majamaa H, Isolauri E. Probiotics: A novel approach in the management of food allergy.

- J Allergy Clin Immunol* 1997; **99**: 179-85.
34. Rosenfeldt V, Benfeldt E, Nielsen SD *et al.* Effect of probiotic *Lactobacillus* strains in children with atopic dermatitis. *J Allergy Clin Immunol* 2003; **111**: 389-95.
35. Stevens S, Hanifin J, Hamilton T *et al.* Long-term effectiveness of recombinant human interferon gamma therapy for atopic dermatitis despite unchanged serum IgE levels. *Arch Dermatol* 1998; **134**: 799-804.
36. Pickenäcker A, Luger T, Schwarz T. Dyshidrotic eczema treated with mycophenolate mofetil. *Arch Dermatol* 1998; **134**: 899.
37. Chen CJ, Yu HS. Acupuncture, electrostimulation, and reflex therapy in dermatology. *Dermatol Ther* 2003; **16**: 87-92.
38. Koo J, Desai R. Traditional Chinese medicine in dermatology. *Dermatol Ther* 2003; **16**: 98-105.
39. Koo J, Arian S. Traditional Chinese Medicine for the treatment of dermatologic disorders. *Arch Dermatol* 1998; **134**: 1388-93.
40. Smolle J. Homeopathy in dermatology. *Dermatol Ther* 2003; **16**: 93-7.
41. Itamura R, Hosoya R. Homeopathic treatment of Japanese patients with intractable atopic dermatitis. *Homeopathy* 2003; **92**: 108-14.
42. Ricci G, Patrizi A, Bendandi B *et al.* Clinical effectiveness of a silk fabric in the treatment of atopic dermatitis. *Br J Dermatol* 2004; **150**: 127-31.
43. Schempp CM, Windeck T, Hezel S, Simon JC. Topical treatment of atopic dermatitis with St. John's wort cream-a randomized, placebo controlled, double blind half-side comparison. *Phytomedicine* 2003; **10** (Suppl 4): 31-7.
44. Shenefelt P. Hypnosis in dermatology. *Arch Dermatol* 2000; **136**: 393-9.
45. Uehara M, Su giura H, Sakurai K. A trial of Oolong tea in the management of recalcitrant atopic dermatitis. *Arch Dermatol* 2001; **137**: 42-3.
46. Al-Waili NS. Topical application of natural honey, beeswax and olive oil mixture for atopic dermatitis or psoriasis: partially controlled, single-blinded study. *Complement Ther Med* 2003; **11**: 226-34.
47. Shainhouse T, Eichenfield LF. Long-term safety of tacrolimus ointment in children treated for atopic dermatitis. *Expert Opin Drug Saf* 2003; **2**: 457-65.