Eczema

Andrew Sohn, BA, Amylynne Frankel, MD, Rita V. Patel, MD, and Gary Goldenberg, MD

Mount Sinai School of Medicine, New York, NY

OUTLINE

EPIDEMIOLOGY
GENETICS
DIAGNOSIS
COMPLICATIONS
TREATMENTS

ABSTRACT

Atopic dermatitis, commonly known as eczema, is a common chronic, relapsing skin disease characterized by pruritus, disrupted epidermal barrier function, and immunoglobulin E–mediated sensitization to food and environmental allergens. Atopic dermatitis is a complex disease that arises from interactions between genes and the environment. Loci on several chromosomes have been identified, including a family of epithelium-related genes called the epidermal differentiation complex on chromosome 1q21. Mutations in filaggrin, a key protein in epidermal differentiation, have also been identified in early-onset and severe atopic dermatitis. There are 3 classical stages of eczema: infantile, childhood, and adulthood. The spectrum of eczema presentation varies widely from a variant that only affect the hand to major forms where a patient presents with erythroderma. The acute and subacute lesions of atopic dermatitis are often characterized by intensely pruritic, erythematous papules and vesicles with excoriations and a serous exudate. Chronic atopic dermatitis is exemplified by lichenified plaques and papules with excoriations. Atopic dermatitis patients are also at higher risk for skin infections, including bacterial and viral superinfections. Conventional therapy includes avoidance of irritants and potential allergens, as well as continued hydration of the skin with thick emollients. Topical corticosteroids and topical immunomodulators are often used primarily. Other therapies including phototherapy, antimicrobials, antihistamines, and systemic immunosuppressives are also options in certain situations. ***Mt Sinai J Med 78:730–739, 2011.*** © *2011 Mount Sinai School of Medicine*

Key Words: atopic dermatitis, atopic triad, eczema, eczema herpeticum, filaggrin.

Atopic dermatitis (AD), commonly known as eczema, is a common chronic, relapsing skin disease characterized by pruritus, disrupted epidermal barrier function, and immunoglobulin E (IgE)-mediated sensitization to food and environmental allergens. In addition to the cutaneous manifestations, AD is associated with other atopic disorders, such as allergic rhinitis and asthma, also known as the "atopic triad".[1] Eczema affects about 15%–30% of school-age children.[2] The majority of cases arise before the age of 5 years.[1]

In addition to the cutaneous manifestations, atopic dermatitis is associated with other atopic disorders, such as allergic rhinitis and asthma, also known as the "atopic triad."Eczema affects about 15%–30% of school-age children.

There are 3 classical stages of eczema: infantile, childhood, and adulthood. Acute inflammation with exudation occurs commonly in the infantile form, with a predilection for facial and extensor involvement. Chronic inflammation with lichenification and scale increases in prevalence with age and tends to

Address Correspondence to:

Amylynne Frankel
Department of Dermatology
Mount Sinai School of Medicine
New York, NY
Email: amylynne.frankel@mssm.edu

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occur in flexural regions. The most common manifestation of adult AD is hand dermatitis. The diagnostic criteria for AD are based on clinical presentation, with skin biopsy usually showing spongiotic dermatitis. Though serum IgE and eosinophilia are commonly elevated, approximately 20%–30% of patients exhibit normal levels. Patients without IgE reactivity or lacking other manifestations of the atopic triad are termed intrinsic AD (versus extrinsic AD).[3] Many cases of AD improve or clear during childhood, and others persist into adulthood.

As medical science continues to improve, the treatment armamentarium also has expanded. Conventional therapy includes avoidance of irritants and potential allergens, as well as continued hydration of the skin with thick emollients. Topical corticosteroids are the primary treatment but can only be safely used in the short term. Steroid-sparing therapy, including topical immunomodulators, has shown great efficacy in the maintenance of AD. Other therapies including phototherapy, antimicrobials, antihistamines, and systemic immunosuppressives are also options in certain situations.

EPIDEMIOLOGY

In industrialized countries, the prevalence of AD has increased dramatically over the past 3 decades: 15%–30% of children and 2%–10% of adults are affected.[1] Approximately 45% of all cases of AD begin within the first 6 months of life (early-onset AD), 60% begin during the first year, and 85% begin before 5 years of age. More than two-thirds of these children will have a spontaneous remission before adolescence. However, the disease can also start in adults (late-onset AD versus early-onset AD).

Approximately 45% of all cases of AD begin within the first 6 months of life (early-onset AD), 60% begin during the first year, and 85% begin before 5 years of age.

Though the inheritance of atopy was recognized years ago, a clear mode of transmission has yet to be defined. In one study of 372 AD patients, positive family history of atopy was 73%. The incidence of allergic asthma and allergic rhinitis in family members of those patients without personal respiratory allergy was 73% and 32%, respectively. Additionally, the incidence of AD in families of AD patients with or without personal respiratory allergy was 34% and 27%, respectively.

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The data suggest that inheritance of AD is strongly associated with inheritance of the atopic state. Another study examining the familial aggregation of the atopic triad showed that familial aggregation was stronger between siblings than between parents and siblings, and that maternal atopy conferred a higher risk to a child than paternal atopy. A twin study showed that there was more concordance for AD in monozygotic twins than in dizygotic twins; if the twin partner had the disease, the risk of having AD was 0.86 in a monozygotic twin versus 0.21 in a dizygotic twin.[1,4]

Although family history of atopy was found to be one of the strongest risk factors for the development of AD, environmental factors are also thought to have a major role in the prevalence of eczema. Living in urban areas, having a higher household education level, and African American ethnicity are associated with higher prevalence of AD.[2] The published literature also shows a slight but reproducible preponderance in girls (female:male ratio of 1.3:1.0).The so-called ''hygienehypothesis'' postulates that the absence of early-childhood exposure to infectious agents increases susceptibility to allergic diseases, thereby explaining why there is a lower prevalence of AD in rural areas.[1]

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GENETICS

To date, there are several possible AD-related loci that have been demonstrated on chromosomes 3q21, 1q21, 16q, 17q25, 20p, and 3p26.[1,5] Chromosome 1q21, which includes a family of epithelium-related genes called the epidermal differentiation complex, appears to be the most promising. Interestingly, some of the genetic regions associated with AD have also been associated with psoriasis, both of which are inflammatory diseases but are generally not considered related.[1,3] Specific genes associated

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with AD, including those on chromosome 5q31-33, all encode cytokines involved in the regulation of IgE synthesis: interleukin-4 (IL-4), IL-5, IL-12, IL-13, and granulocyte-macrophagecolony-stimulating factor (GM-CSF).[6] Interleukin-4, IL-5, and IL-13 are produced by Type 2 T helper cells (Th2), and up-regulate the production of IgE. Interleukin-12 and interferon-γ (IFN-γ) are produced by Type 1 T helper cells (Th1) and suppress IgE production and stimulate production of immunoglobulin G (IgG) antibodies. In AD patients, there is an imbalance in Th1 and Th2 cells, with a genetically determined dominance of Th2 cytokines that affects the maturation of B cells and functional favoring of isotype class switching from immunoglobulin M (IgM) to IgE.[7] Mutations that affect the promoter region of the lymphocyte-attracting chemokine RANTES (regulated on activation, normal T-cell expressed and secreted) (17q11) and gain-of-function mutations in the α subunit of the IL-4 receptor (16q12) have also been identified in AD patients.[3] Potentially, mutations in IL-18 or in genes encoding the receptors of the innate immune system may also contribute to the imbalance between Th1 and Th2 immune responses in AD.

Specific genes associated with atopic dermatitis, including those on chromosome 5q31-33, all encode cytokines involved in the regulation of immunoglobulin E synthesis: interleukins 4, 5, 12, and 13, and granulocyte-macrophagecolony-stimulating factor. In atopic dermatitis patients, there is an imbalance in T helper 1 and T helper 2 cells, with a genetically determined dominance of T helper 2 cytokines that affects the maturation of B cells and functional favoring of isotype class switching from immunoglobulin M to immunoglobulin E.

Filaggrin, which is a key protein in epidermal differentiation, has been a hot topic with regard to AD. Ichythosis vulgaris, a disease that manifests as severe dry and scaly skin, shares many similarities with AD in its presentation. After the filaggrin gene (FLG) on chromosome 1q21.3 was identified as the gene involved in ichthyosis vulgaris, several loss-of-function mutations were identified in several subtypes of AD patients as well, most commonly in those of European and Japanese descent. Mutations of FLG occur mainly in early-onset and severe AD, and indicate a propensity toward asthma.[8]

Atopic dermatitis is a complex disease that arises from interactions between genes and the environment. Food allergens, for instance, induce skin rashes in nearly 40% of children with moderate to severe AD.[9] T cells specific to food allergens have been cloned from the skin lesions of patients with AD.[3] Similarly, skin lesions can develop after intranasal or bronchial inhalation challenge with aeroallergens in previously sensitized patients with AD. Furthermore, application of aeroallergens to skin by atopy patch test on unaffected atopic skin induces eczematoid reactions in 30%–50% of patients with AD.[3] Additionally, minimizing exposure to aeroallergens, such as house dust mites, has been associated with significant improvement in AD.[10]

DIAGNOSIS

Atopic dermatitis is a common skin disease that is often associated with other atopic disorders, such as allergic rhinitis and asthma.[11] The spectrum of eczema presentation varies widely, from a variant which only affects the hand to major forms where a patient presents with erythroderma.[12] In 1980 Hanifin and Rajka published major and minor criteria for the diagnosis of eczema.[13] These criteria were revised during a consensus conference held by the American Academy of Dermatology in 2001 and to date have had a great effect in worldwide research and clinical practice (Table 1).[14] Whereas pruritus occurs throughout the day, worsening in the early evening and at night is a common complaint. Allergens, reduced humidity, excessive sweating, and low concentrations of irritants exacerbate pruritus and therefore induce scratching.[15] At least 2 types of AD have been identified: an extrinsic type associated with IgE sensitization, which affects up to 80% of patients; and an intrinsic type without IgE-mediated sensitization, which affects up to 20% of patients.[16]

The acute and subacute lesions of AD are often characterized by intensely pruritic, erythematous papules and vesicles with excoriations and a serous exudate. Chronic atopic dermatitis is exemplified by lichenification, papules, and excoriations. In

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Table 1. *Hanifin and Rajka Criteria Revised by the American Academy of Dermatology.*[14]

The clinical findings that define the syndrome are divided into:
Essential features (must be present)
Pruritis
Eczema (acute, subacute, or chronic) with typical morphology and age-specific patterns (facial, neck, extensor involvement in infants and children; current or prior flexural lesions in any age group; sparing of groin and axillary regions)
Important features (seen in most cases, adding support to the diagnosis)
Early age of onset
Atopy (personal and or family history; IgE reactivity)
Xerosis
Associated features (these clinical associations help to suggest the diagnosis of atopic dermatitis, but are too nonspecific to be used for defining or detecting atopic dermatitis for research or epidemiologic studies)
Atypical vascular responses (eg, facial pallor, white dermographism, delayed blanch response)
Keratosispilaris/hyperlinear pals/ichthyosis
Ocular/periorbital changes
Other regional findings (eg, perioral changes/periauricular lesions)
Perifollicular accentuation/lichenification/prurigo lesions

Abbreviations: IgE, immunoglobulin E.
Exclusionary conditions have also been added, such as scabies, seborrheic dermatitis, allergic contact dermatitis, ichthyosis, cutaneous lymphoma, psoriasis, and immunodeficiency diseases.

the infantile age group, where 60% of all cases of AD begin, acute lesions first emerge on the face, scalp, and extensor surfaces of the extremities. In older children with long-standing disease, the patient usually develops lichenification and localization of the rash to the flexural folds of the arms and legs and the nape of the neck. It should be noted that up to 70% of children have a spontaneous remission of their eczema before adolescence. However, late-onset AD can also present itself in adults, where lichenified plaques affect the flexures, head, and neck. Additionally, chronic hand eczema can be the primary manifestation of many adults with atopic dermatitis.[1]

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The hallmarks of AD are a chronic, relapsing form of skin inflammation, a disturbance of epidermal-barrier function that culminates in dry skin, and IgE-mediated sensitization to food and environmental allergens.[15] Spongiosis, or epidermal intercellular edema, and a prominent perivascular infiltrate of lymphocytes, monocytes, dendritic cells, and a few eosinophils are components commonly identified on histologic analysis of eczematous skin.[1]

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COMPLICATIONS

Several studies have implicated bacterial colonization, especially with *Staphylococcus aureus(S. aureus)*, to be a pathogenetic factor in AD, as infection with this bacteria correlates with disease severity.[17–19] Also, it

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has been demonstrated that *S. aureus* can be isolated from 90% of atopic eczema skin lesions.[20] Persistent pruritis, which is the most important symptom in AD, can be related to staphylococcal exotoxins in vitro, which have been shown to up-regulate IL-31, a strongly pruritogenic cytokine produced by T cells that increases the survival of hematopoetic cells and stimulates the production of inflammatory cytokines by epithelial cells.[21–23]

Different mechanisms have been suggested to account for the increased *S. aureus* colonization. A defective epidermal barrier in subjects with eczema results from abnormalities in both lipids (ceramide and sphingosine deficiencies) and proteins (increased serum protease levels and decreased filaggrin expression). Additionally, levels of endogenously produced antimicrobial peptides are reduced due to the production of interleukins. In turn, *S. aureus* superantigens exacerbate atopic dermatitis by penetrating the skin barrier, activating keratinocytes and inducing the release of proinflammatory cytokines.[24–28]

A recent Danish study investigated the relationship between *S. aureus* and hand eczema by taking nasal and hand bacterial swabs of 50 subjects with hand dermatitis. Infection rates with *S. aureus* were found to be significantly higher in the disease cohort as compared with controls. Furthermore, the presence of *S. aureus* correlated closely to disease severity. These results support the hypothesis that *S. aureus* plays a role in the persistence of eczematous dermatitis.[29]

Only 1 published clinical trial has attempted to prove causality between *S. aureus* infection and generalized atopic dermatitis. Huang *et al.* studied 31 children with generalized eczema who were initially given cephalexin for 14 days and then were then randomly assigned to either intranasal mupirocin ointment treatment and sodium hypochlorite (bleach) baths (treatment arm) or intranasal petrolatum ointment and plain water baths (placebo arm) for 3 months. The concomitant use of intranasal mupirocin and dilute bleach baths significantly decreased the severity of eczema in the treatment arm as compared with placebo. At baseline, the prevalence of *S. aureus* colonization was 81% in the nares and 87% of lesional skin, which are values consistent with previously published colonization rates. Interestingly, after 3 months of treatment with intranasal mupirocin treatment and bleach baths, *S. aureus* carriage persisted in both skin and nares cultures in every subject who was evaluated at his/her last follow-up visit. However, the subjects' eczema greatly improved. Patients in the treatment arm showed greater mean reductions in Eczema Area and Severity Index (EASI) scores from baseline at both the 1-month visit (10.4 ± 2.8) and the 3-month visit (15.3 ± 3.8), compared with the placebo arm (1-month visit: 2.5 ± 1.6; $P = 0.017$; 3-month visit: 3.2 ± 1.6; $P = 0.004$), despite persistent colonization.[30]

A recently published systematic review assessed the therapeutic benefits of prophylactic treatment of *S. aureus* in those with clinical uninfected eczema. By conducting a meta-analysis of 26 randomized controlled trials involving >1200 subjects, a British group showed that commonly used antistaphylococcal interventions (oral antibiotics, antibiotic soaps, topical antibiotic + corticosteroid ointments, fabrics with antibacterial properties) do reduce the *S. aureus* number in people with clinical uninfected eczema. However, none of the studies showed any evidence of convincing clinical benefit. For instance, there was no significant difference in global outcome for clinically infected eczema when oral antibiotics were compared with placebo (relative risk [RR]: 0.40, 95% confidence interval [CI]: 0.13-1.24) or when topical steroid–antibiotic combinations were compared with steroid alone (RR: 0.52, 95% CI: 0.23-1.16). In addition, given the risk that such preparations may be associated with adverse events such as contact and irritant dermatitis as well as the promotion of wider drug resistance in the community, the dermatologist should be cautious when advising noninfected eczema patients.[31]

Patients with eczema are also susceptible to viral skin infection.[32] Most worrisome and a true dermatological emergency is disseminated herpes simplex infection, which results in Kaposi'svaricelliform eruption, or eczema herpeticum. This serious infection, which presents after a 5- to 12-day incubation period, is characterized by an eruption of many pruritic vesicopustular lesions in combination with fever and malaise. The vesicular lesions are umbilicated, tend to crop, and often become hemorrhagic and crusted. Punched-out erosions, vesicles, or infected skin lesions that do not immediately respond to oral antibiotics should prompt suspicion of eczema

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herpeticum. Antiviral treatment for cutaneous herpes simplex infections is of crucial importance in patients with widespread AD because life-threatening dissemination has been reported. Eczema herpeticum patients may develop complications including keratoconjunctivitis, viremia, meningitis, encephalitis, or secondary bacterial sepsis.[33] Patients with a history of eczema herpeticum may require suppressive therapy for herpes simplex virus infection.

In addition, exposure to the smallpox vaccine or individuals who have been recently vaccinated can produce a severe a widespread skin rash similar in appearance to eczema herpeticum known as eczema vaccinatum.[34] In one case report, an infant with eczema contracted eczema vaccinatum through his father, who was in the military and received a smallpox vaccine 21 days before the onset of the infant's symptoms. The infant required life-saving mechanisms, including the use of investigational drugs via Emergency Investigational New Drug Application. This case illustrates the importance of understanding the mechanisms of viral infection in atopic dermatitis.[35]

As compared with controls, patients with atopic dermatitis also have increased prevalence of fungal infections. *Malassezia* species also induce the production of *Malassezia*-specific IgE in AD patients. This specific sensitization has been exclusively found in eczema patients, but not in patients with allergic rhinitis, urticaria, or allergic contact dermatitis.[36] These IgE molecules are significantly more prevalent in eczema patients with head and neck dermatitis, as compared with eczema patients with lesions in other locations (100% versus 14%).[37] *Malassezia* may also contribute to AD inflammation via a cell-mediate immunity. This immunologic property is highlighted by the fact that antifungal treatment of *M. furfur* and other dermatophyte infections reduces of atopic dermatitis skin symptomatology.[33]

TREATMENTS

Atopic dermatitis is a chronically relapsing disease and standard clinical care calls for long-term management, which requires a multitherapeutic approach. This approach involves tending to symptoms that manifest from acute flares as well as prolonging the time until relapse.[38] The symptoms associated with an acute flare are typically managed through anti-inflammatory medication, and management of the disease post–acute flare is accomplished through emollients to alleviate and/or restore a disturbed barrier function, which is highly characteristic of AD.[39,40]

The most common anti-inflammatory therapies in the treatment of AD are topical corticosteroids (TCS) and topical calcineurin inhibitors (TCI).[2,41] Topical corticosteroids have been the mainstay choice for the treatment of AD over the last few decades. Topical corticosteroids suppress the immune system by means of interrupting leukocyte function as well as binding to certain receptors that inhibit the production of certain inflammatory mediators such as ILs and cytokines.[42] Topical corticosteroid use is favorable due to their rapid onset of activity as well as a wide spectrum of potencies that makes it possible to fine-tune appropriately to the severity of AD.[43] However, long-term use of TCS is contraindicated due to potential side effects, including skin atrophy, telangiectasia, striae, steroid-induceddermatoses, rosacea, acne exacerbation, and tachyphylaxis.[44,45] Rarely, TCS can cause systemic side effects including suppression of the hypothalamic-pituitary-adrenal axis or growth retardation in children.[45] This rare but serious side effect is most often seen when super-potentTCS are applied to a large body surface area for an extended period of time. Alternatively, corticosteroids are also available in systematic forms, such as oral administration or injection. However, due to their potency and many side effects, systemic corticosteroids should only be considered if the AD is severe and topical agents have not worked. The most important aspect in determining the regimen for systemic corticosteroids is deciding on the potency and length of treatment to ensure that the patient does not suffer from any side effects and there is no relapse of disease.

Topical corticosteroids have been the mainstay choice for the treatment of atopic dermatitis over the last few decades.

Topical calcineurin inhibitors are nonsteroidal anti-inflammatory agents that can be utilized for any steroid-responsivedermatoses. Their use is more favorable in treating the more delicate areas of the body such as the face, neck, eyelids, and interiginous areas, all of which have a greater risk of steroid-induced side effects.[46] Long-term studies have shown that TCI are highly effective and safe for long-term management of AD, as well as for the treatment of acute exacerbations of AD. The most common side effects documented with the use of TCI were slight tingling and burning at the site of application.[47–49] Topical calcineurin inhibitors work by targeting and inhibiting calcineurinin the skin, which regulates

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T-cell division and activation, which in turn inhibits anti–tumor necrosis factor, ILs, and histamine.[50] Of the two TCIs, pimecrolimus cream and tacrolimus ointment, tacrolimus ointment has been shown to be more efficacious in managing the symptoms of AD.[51–53] It should be mentioned that TCI received a black-box warning in 2006 due to rare reports of cancer (eg, lymphoma); however, no causal proof has been found that TCI cause lymphoma or nonmelanoma skin cancers. More than 50 cases of lymphoma have been observed since the approval of TCI, but taking into consideration that there have been >7 million prescriptions, the rate of lymphoma due to TCI is still lower than that expected of the general population.[54–56]

For patients with severe AD and for whom conventional topical therapy fails, systemic therapy such as cyclosporine A, mycophenolatemofetil, methotrexate, and azathioprine can be utilized. However, these immunosuppressive agents are limited by their adverse reactions or contraindications.[57] Cyclosporine is a lipophilic cyclic polypeptide that is primarily used in transplant patients. Cyclosporine works by effectively inhibiting an enzyme, calcineurin phosphatase, which consequently leads to a reduction of IL-2 release and suppression of T-cell proliferation, which plays a key role in the pathogenesis of AD.[58,59] Several studies have confirmed the efficacy of cyclosporine in both adult and pediatric AD, especially in the use of severe refractory AD.[60–64] Long-term use of cyclosporine is undesirable due to the risk of side effects, notably nephrotoxicity, hypertension, and rebound of flares after discontinuation. Therefore, the cyclosporine treatment should be restricted to 1 year.[65] Though much rarer, a potential serious side effect of cyclosporine includes increased risk of lymphomas and skin cancers.[66]

Mycophenolatemofetil is an inhibitor of the de novo purine synthesis pathway and as a result reduces the RNA-primed DNA synthesis in T and B lymphocytes. There is a dearth of studies with regard to the treatment of severe AD with mycophenolatemofetil; however, in the few uncontrolled studies that are available, mycophenolatemofetil was shown to be effective in reducing disease severity. The most commonly reported side effect with mycophenolatemofetil was gastrointestinal problems such as nausea, diarrhea, and vomiting.[67–70]

Although methotrexate is more commonly used in the treatment of psoriasis in dermatology, there have been a few case reports and 2 open-label studies supporting the use of methotrexate in the treatment of palmoplantar pompholyx, AD in elderly patients, and moderate to severe adult AD.[71–74] Methotrexate is also widely used in the treatment of other chronically inflammatory disease, and thus, it is known that methotrexate is generally a well-tolerated drug at appropriate doses; however, bone-marrow suppression, gastrointestinal toxicity, and hepatotoxicity have been well documented as well. These side effects can potentially be reduced with folic acid supplementation.[75] Methotrexate is a potent inhibitor of the enzyme dihydrofolate reductase, which causes an immunosuppressive function through the reduction of T-cell proliferation.

Azathioprine is a purine antagonist which has immunosuppressive effects by altering the synthesis and function of RNA and DNA in lymphocytes. Several studies support the efficacy of azathioprine in the treatment of severe AD.[76–78] One of the limitations of azathioprine is the slow onset of activity, which typically requires 4 weeks. Other concerns include risk of bone-marrow suppression, hepatotoxicity, and increased risk of malignancy, including non-Hodgkin lymphoma and squamous cell carcinoma.[79] It is also well documented that patients with deficient activity of thiopurine S-methyltransferase, which prevents toxic accumulation of azathioprine, are at an increased risk for myelosuppression.[80]

Phototherapy is another treatment option for AD. There are numerous reports indicating the potency of phototherapy for treating moderate to severe AD. Presently, 311-nm narrowband ultraviolet light B (NBUVB), ultraviolet light A1 (UVA), and psoralen with UVA (PUVA) are most commonly used.[81] Of these, PUVA has been shown to be the most efficacious in treating AD and provides the longest remission period. Medium- and high-dose UVA1 and NBUVB are, more or less, equally effective.[82–84] A combination of UVA and UVB has been tried as well; however, it has been shown to be less effective than medium-dose UVA1.[85] Despite its high efficacy, PUVA use has been decreased due to increases in the development of skin malignancies. Studies have also demonstrated that <50% of the people who undergo UVA1 treatment respond to it, and for those who do, the response is short-lived.[86]

More recently, medicated device creams/foams, which are used to repair the impaired epidermal barrier function, have entered the marketplace. These medicated devices provide antioxidant, antiprotease, anti-inflammatory activity, and aid in restoring the natural balance of lipids, which is one of the causes of the epidermal abnormalities seen with AD. Section 201(h) of the 2004 Federal Food Drug and Cosmetic Act defines a medical device as "a product intended to diagnose, cure, treat, or prevent disease that does not achieve its intended purpose through chemical action or by being metabolized."[87] The medicated device creams/foams provide moisturizing ability,

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which is key in the long-term management of AD, namely prolonging the time until the next relapse, but differ from moisturizers because they act as a single entity, rather than a collection of active ingredients in a vehicle of inactive ones.[88–91] Additionally, prescription devices may be subjected to more regulation than over-the-counter preparations.[87]

It is important to remember that AD can have a large psychosocial burden and creates stigmatization, social isolation, and discrimination.[92] Additionally, it can put undue stress on new parents, as nocturnal itching can keep children awake, thereby keeping the parents awake.[93] In addition to traditional treatments, alternative methods to increase patient and family awareness and education are important to incorporate into treatment plans.[94]

DISCLOSURES

Potential conflict of interest: Nothing to report.

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