

TRIGGERS OF ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a complex, chronic disorder that has been referred to as “the itch that rashes.” Its origin is multifactorial and includes many commonly encountered triggers. In 1892, Besnier used the term *neurodermatitis* to describe a chronic, pruritic skin condition seen in patients suffering from a nervous disorder.⁵ This familial disorder was termed *prurigo Besnier* because of its intensely pruritic quality. In the early 1900s, Coca noted the occurrence of a similar disorder with other diseases such as asthma and hayfever and used the term *atopy* to refer to the allergic constellation of these diseases.²¹ The term *atopic dermatitis* was coined by Wise and Sulzberger in 1933 to comprehensively described this inheritable skin disorder.⁷¹ Since its earliest description, atopic dermatitis has had one primary feature recognized by clinicians and patients alike—intense pruritus triggered by a variety of stimuli. This article reviews the various allergic and nonallergic stimuli that can trigger AD.

ALLERGENS AS TRIGGERS OF ATOPIC DERMATITIS

There is a strong correlation of AD with other atopic conditions such as asthma and allergic rhinitis. Approximately 50% of patients with AD develop disease in the first year of life, and as many as 50% to 80% of children with AD develop allergic respiratory disease later in life. Many clinicians note the peculiar tendency of AD and asthma to alter-

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nate in courses in some patients. As a result of these early historical observations, investigators have explored the role of various allergens as triggers for the pathogenesis of AD. These triggers include the following:

Food allergens (most common)

- Milk
- Egg
- Peanut
- Soy
- Wheat
- Shellfish
- Fish

Aeroallergens

- Pollen
- Mold
- Dust mite
- Animal dander
- Cockroach

Microorganisms

- Bacteria
 - Staphylococcus aureus*
 - Streptococci
- Fungi/Yeasts
 - Pityrosporum ovale* and *P. orbiculare*
 - Trichophyton* species
 - Other yeast species (*Candida*, *Malassezia*)

Food Allergens

Adverse reactions to foods have been reported in the medical literature since the early 1900s when Smith reported the case of a man who developed repetitive emesis and angioneurotic edema caused by "buckwheat poisoning."⁵⁸ Schloss documented patients with hypersensitivity reactions following egg ingestion. To confirm his observations in patients, he injected guinea pigs with sera from egg-allergic patients and orally challenged the animals with egg, which resulted in immediate death from anaphylaxis.⁵⁵ In 1918 Talbot was one of the first physicians to report improvement in patients' eczema while on a milk-and-egg-restriction diet.⁶⁰ In his early studies, Tuft considered food allergy to be the most important pathogenic factor in infants and young children with AD compared with inhalant allergies in older children and adults.⁶¹ Using egg and milk as trial allergens in a blinded study design, Atherton found that 14 of 20 children with AD had a beneficial response to specific dietary allergen elimination.³ Hill demonstrated clearing of skin symptoms in eight children with severe, refractory AD placed on an elemental formula (Vivonex, Novartis Nutrition, St. Louis Park, Minnesota).²⁷ Since that time, many investigators have studied children with

AD and food hypersensitivity. These studies unequivocally have demonstrated that dietary manipulation results in dramatic improvement in a subset of patients with AD, especially in young infants and children.

Bock et al were the first to establish the use of double-blind, placebo-controlled food challenges (DBPCFC) to assess patients with suspected food hypersensitivity.⁶ Because there is poor correlation between allergen-specific immunoglobulin E (IgE) antibodies (skin tests or radioallergen sorbent tests [RAST]) and clinical symptoms related to food hypersensitivity,⁴⁸ oral food challenges (both open and blinded) have been crucial in assisting many investigative groups in the study of food hypersensitivity and AD.⁶ Sampson first reported findings from 111 double-blind, placebo-controlled food challenges in 26 children with AD.⁴⁷ Fifty-eight percent of children had positive food challenges, with cutaneous symptoms exhibited in 91% of positive responses. In these children, 77% of positive skin tests to foods were clinically irrelevant, emphasizing the importance of food challenge in diagnosing food hypersensitivity. These findings were confirmed by Burks et al in a study in which 46 children with AD were studied using DBPCFC to confirm food allergen hypersensitivity.¹⁶ Positive challenges were detected in 33% of patients, with 91% reacting to only one or two foods and 96% of patients developing skin symptoms during challenge. These groups have shown a direct correlation between hypersensitivity to foods and development of AD.

Sampson et al evaluated hundreds of children with AD for evidence of food hypersensitivity through the use of double-blind, placebo-controlled food challenges to suspected foods. Egg, milk, peanut, fish, and tree nuts reportedly account for the majority of positive food challenges; egg sensitivity was the most prevalent.^{51, 53} Cutaneous symptoms, including a pruritic, erythematous morbilliform rash involving the AD predilection sites, were seen in 75% of positive challenges. Other symptoms noted during positive challenge included respiratory and gastrointestinal symptoms. All patients who were allergic to specific foods were placed on an appropriate avoidance diet of that food. Virtually all patients reported improvement in AD symptoms (i.e., either complete resolution or marked clearing).^{52, 53} Burks et al further delineated the role of food hypersensitivity in AD by determining the usefulness of a limited panel of food skin tests to screen for food allergy in children with AD. From 266 double-blind, placebo-controlled food challenges conducted in 165 children with AD, 60% had at least one positive prick skin test and 39% were interpreted as having a positive challenge with seven foods (milk, egg, peanut, soy, wheat, cod or catfish, cashew), accounting for 89% of the positive challenges.¹⁷ Using screening prick skin tests for these seven foods, 99% of food-allergic patients could be identified appropriately. In a study designed to evaluate the prevalence of food allergy in children with AD, Eigenmann et al demonstrated that 37% of unsolicited children with moderate-to-severe AD who were referred to a pediatric dermatologist had food allergy.²²

Laboratory studies have provided evidence for the role of food allergy in AD. Infants and children with moderate-to-severe AD fre-

quently have positive prick skin tests or food-specific IgE. Following a positive food challenge or chronic ingestion of a known food allergen, patients have evidence of increased mediator release, including increased plasma histamine levels,⁴⁹ increased spontaneous basophil-histamine release,⁵¹ eosinophil activation³⁴ and spontaneous release of a cytokine (histamine-releasing factor) from mononuclear cells.⁵¹ These mediators, in association with observed cutaneous hyperirritability to a variety of stimuli, have diminished to normal levels after 6 to 9 months of food-allergen avoidance. In addition to mast cell, basophil, and eosinophil activation by way of food antigens, T-cell-mediated reactions have been well documented. Food-allergen-specific T cells with a Th2-like cytokine profile have been cloned from the lesional skin of peanut-allergic patients with AD.⁶⁶ Skin-homing receptors, known as cutaneous lymphocyte antigens (CLAs), are increased on T cells from casein-allergic patients with AD compared with controls (see article by Leung elsewhere in this issue).¹ These *in vitro* data strongly support the role of food allergens in the pathogenesis of AD, especially in children.

In a study by Sampson that documented the natural history of AD and food hypersensitivity, 26% of patients lost their clinical food hypersensitivities during the first year of allergen avoidance, and 11% lost reactivity during the second year.⁵⁰ Although most children tend to outgrow their food hypersensitivities and resolve their AD symptoms with allergen avoidance, others manifest aeroallergen sensitivities that seem to perpetuate the AD cycle. Longitudinal studies have supported in part the role of maternal dietary restriction of some allergens (e.g., milk, egg, fish, shellfish, nuts, peanuts) during lactation for high-risk infants. These studies have shown a delay or reduction in the development of food allergy-associated disease in these infants.^{57, 73}

Aeroallergens

Pollens

Pollens were the first aeroallergens reported in association with AD. In 1918, Walker published case reports of several patients with worsening of AD after exposure to horse dander or ragweed.⁶⁷ Other investigators have reported similar patients with seasonal exacerbation of AD who demonstrated resolution of disease in a pollen-free environment or during their off-season of sensitization.⁷² In the 1950s, Tuft et al conducted the first definitive studies linking pollen and AD. These investigators performed intranasal challenges with ragweed pollen in sensitized patients and monitored them for signs of sweating in AD predilection sites. Patients were dusted with a starch-iodine preparation before inhalation of ragweed antigen. Sneezing and rhinorrhea developed immediately and were associated with pruritus and a bluish discoloration in predilection sites, indicative of sweating. Lesions typical of AD developed hours later.⁶² Since then, investigators have shown posi-

tive prick skin tests and patch tests to common pollens in patients with seasonal distribution of AD.¹² In one study of children with AD who were tested with epicutaneous patch testing to dust mite, cockroach, mold, and grass mix, 90% of patients developed eczematous lesions in one or more AD predilection sites.⁶⁸ Other investigators have shown positive immediate skin tests to birch pollen in patients with AD who had worsening of disease during the birch pollen season.⁴³ Investigators also characterized allergen-specific T-cell lines from the lesional skin of patients with AD, demonstrating a Th2-like, or atopic, cytokine profile from these cells.^{42, 65} These specific allergen responses provide further evidence for the role of pollens and other inhaled aeroallergens in some patients with AD.

Molds

Mold allergens also have been implicated as causal factors in patients with AD. In 1939, Feinberg reported the association of increased AD exacerbations and elevated atmospheric mold counts in 5 of 14 mold-sensitive patients.²³ Kesten presented skin test findings on 2000 patients with AD, two-thirds of whom were less than 6 years of age. Approximately 10% of adults and 25% of children had positive skin tests to *Alternaria*, *Aspergillus*, and *Penicillium*.²⁹ Tuft et al induced symptoms of dermatitis, including sweating and rash, in mold-sensitive patients using an inhalation challenge model with *Alternaria* compared with talc powder or pine pollen.⁶² Rash developed in sensitive patients within 12 to 24 hours and persisted for 4 to 5 days. Rajka also demonstrated eczematous lesions in two of five atopic individuals with AD following inhalation of mold extract.⁴⁰ Patch testing with fungi, including *Cladosporium*, *Alternaria*, and *Candida*, have shown allergen-specific development of typical eczematous lesion with increased expression of Langerhans' and dendritic cells in lesional biopsies.¹³ More work is needed regarding the contribution of mold hypersensitivity in the pathogenesis of AD.

House Dust Mite

House dust mite allergy has the largest body of scientific and clinical data linking aeroallergens and atopic diseases. Sensitivity to dust mite was first examined in patients with asthma, and early on clinicians suggested a causal link between dust mite allergy and development of AD.^{11, 61} Platts-Mills et al performed extensive studies of dust mite antigen and atopic disease association.³⁹ Positive prick skin testing and patch testing to dust mite antigen in patients with AD has been shown.³⁵ Further evidence is provided in a study that demonstrated skin lesion flares in patients with AD after a bronchial challenge with dust mite allergen, with more severe flares observed in patients with coexisting airway disease.^{9, 63} In an environmental epidemiologic survey, the homes of patients with moderate-to-severe AD showed a higher dust mite

concentration than controls.⁴ Elevated serum levels of dust mite-specific antibody and increased basophil sensitivity also have been shown in patients with AD compared with controls.¹⁹ Several groups of investigators demonstrated an increased Th2-like allergen-specific T-cell response with enhanced production of interleukin-4 (IL-4) and IL-5 in patients with AD and evidence of dust mite allergy.^{36, 44, 46, 64} Wierenga et al derived T-cell clones from Der p1 patch-tested sites from patients with AD and dust mite hypersensitivity. These clones were differentiated into T_H1 and Th2 cell types, with a predominance of Th2-like T-cell clones detected in patients with AD.⁷⁰ Perhaps the best clinical evidence for the role of dust mite allergen in AD comes from reports of patients who show improvement when living in a dust-free environment and then relapse after re-exposure to dust mite.^{2, 4, 26}

Animal Danders and Cockroach Allergens

Two other types of aeroallergens are believed to aid in the pathogenesis of AD—animal danders and cockroach allergens. These allergen groups have been studied in association with asthma and allergic rhinitis and are believed to be important factors in certain susceptible individuals. Less scientific information is available with regard to AD. Of the animal danders, cat and dog dander are implicated most commonly in atopic disease states. Cockroach allergens have been recognized in atopic disease, especially in endemic areas and climates, such as in inner-city environments. In a one study of children with AD, many patients had positive prick and intradermal skin tests to animal dander and cockroach, indicating the possible relevance of these allergens in atopic disease.⁶⁸ Other investigators reported positive skin or patch testing to a variety of aeroallergens, including animal danders, in patients with AD.^{2, 20} The positive skin tests to danders correlated with the danders identified in the patients' environments. T-cell proliferation and increase in antigen-processing cells have been seen in skin lesions in patients sensitive to cat dander and other aeroallergens.¹³ More studies are needed to define the role of animal dander and cockroach allergens in AD.

Microorganisms

Bacteria

The role of microorganisms in the pathogenesis of AD has received much attention. Their potential role as complicating skin pathogens has long been recognized as important, but their role as allergens that perpetuate the allergic response has been of particular interest. It is postulated that the altered skin barrier seen in patients with AD provides a portal of entry for various pathogens to gain access to the immune system, thus activating mast cells, basophils, Langerhans' cells, and

other immune cells.³² The primary classes of microorganisms involved include bacteria, fungi, and yeasts.

The most extensively studied and widely recognized microorganism known to trigger AD is *S. aureus*. Staphylococcal skin colonization of affected and normal skin has been shown to be increased in patients with AD compared with controls.³³ *S. aureus* colonization can be demonstrated in over 90% of lesions in patients with AD.³³

Evidence for an IgE-mediated mechanism has been supported by reports of increased CD23 (low-affinity receptor for IgE) expression in cells from patients with AD following stimulation with *S. aureus*.⁴⁵ Investigators have focused on the role of staphylococcal exotoxins in the disease cycle of AD (see article by Leung elsewhere in this issue). Elevated IgE-specific antistaphylococcal antibodies have been found in the sera of patients with AD.¹⁴ Leung et al reported specific IgE antibodies to staphylococcal exotoxins (e.g., TSST-1, endotoxins A and B) produced by staphylococcal organisms grown from the skin of 32 of 56 patients with AD.³¹ Basophils from 10 patients with IgE antibodies to these exotoxins released histamine in response to specific staphylococcal exotoxins. Basophils from normal individuals or from patients with AD but without IgE antiexotoxin antibodies failed to release histamine after exotoxin stimulation.²⁸ These investigators and others have suggested that these exotoxins function as disease-promoting agents through their action as superantigens.³² These superantigens perpetuate the immune response in AD by stimulating T-cell activation and proliferation,¹⁸ stimulating T-cell-dependent production of toxin-specific IgE,³⁷ and facilitating T-cell homing.⁵⁹

To further emphasize the role of *S. aureus* in the AD process, it has been demonstrated that patients with AD show a better clinical response when treated with combinations of antistaphylococcal antibiotics and topical steroids than with steroids alone (see article by Boguniewicz Nicol elsewhere in this issue).³² Other bacteria, such as streptococcal species, may be important, but little clinical or investigative information exists to document their role.

Yeast and Fungi

Various species of yeast organisms have been implicated as causal factors in the pathogenesis of AD. *P. ovale* and its gestational counterpart *P. orbiculare* are lipophilic yeasts that may inhabit the skin of all individuals with predilection for the neck, face, and upper trunk.¹⁰ Colonization is seen more commonly in older children and adults than in infants and younger children. Correlation between active AD lesions and specific IgE antibodies to *P. ovale* have been demonstrated by way of prick skin testing and serum analysis using RAST.^{38, 69} Wessels et al showed the presence of *P. ovale*-specific IgE antibodies in 49% of patients with AD.⁶⁹ Patients with head, neck, and upper trunk distribution of AD lesions and evidence of specific antibodies to *P. ovale* have been reported to show clinical improvement following ketoconazole therapy. Although

not conclusive, these data suggest the pathogenic role of *Pityrosporum* species in some patients with AD and emphasize the need for consideration when refractory AD in the typical head and neck distribution is seen, especially in older children and adults. The possible role of other yeasts, such as *Candida albicans*, *Trichophyton*, and *Malassezia furfur*, have been implicated in the pathogenesis of AD.⁸ Specific IgE antibodies to *M. furfur* have been detected in 70% of sera from *M. furfur*-sensitized patients with AD. More extensive study is needed regarding the role of these yeasts in the pathogenesis of AD.

ENVIRONMENTAL TRIGGERS OF ATOPIC DERMATITIS

The course of AD is influenced by many primary and secondary factors that are often difficult to separate. Environmental factors frequently act as triggers that cause exacerbations of disease, yet they are not the primary causes of the underlying disease. These triggers include the following:

Climate

- Extremes of temperature and humidity

Chemical irritants

- Laundry detergents and bleaches

- Soaps

- Household cleaners

- Perfumed lotions

Physical irritants

- Scratching

- Sweating

- Synthetic fabrics (e.g., wool)

- Coarse bedding

- Acidic foods

- Infection

Psychosocial stressors

- Chronic disease

- Emotional stress

- Sleep disturbance

Occupation

- Irritant exposures

Climate

Several environmental factors can influence the course of disease in AD. One of the most important, yet often obscure, factors is climate. Individuals respond differently to various climatic influences. Most authors report disease intensification during the winter months and greatest comfort during the summer months. Rajka reported that improve-

ment during the summer may result from better sebum and sweat secretion, ultraviolet rays from sun exposure, exposure to water during swim activities, reduced exposure to indoor allergens (i.e., dust mite and molds), less exposure to infection, and less psychosocial stressors during summer vacations. He also mentions that some of these same influences may aggravate the skin condition of other patients.⁴¹ Tuft et al noted that the impaired sweating mechanism makes excess sweating and strong heat adverse factors in patients with AD.⁶² Ultraviolet light exposure without appropriate skin protection also can be harmful. Although indoor allergen exposure may be minimized during summer months, outdoor allergen exposure (i.e., grass pollens) may be exacerbating in some regions. As a general rule, cold dry weather is more aggravating to patients with AD secondary to the drying effect.⁴¹ Hot humid weather also may be aggravating because of increased perspiration and increased potential for secondary skin infection. Extremes or sudden changes of any climatic condition (i.e., temperature, humidity) can be aggravating to patients with AD and are most likely secondary to an impaired ability for immediate skin adaptation.²⁵ As previously stated, these factors are only secondary in the large majority of patients and vary individually.

Chemical Irritants

Laundry detergents, bleaches, soaps, and household cleaning chemicals act as irritants for patients with AD. Mild laundry detergents without bleach generally are tolerated better. Washing clothing through a rinse cycle twice usually ensures removal of the detergent and may be beneficial in some sensitive patients. Mild, unscented skin soaps also should be used for bathing: They are generally less drying, less irritating, and less likely to induce pruritus. Skin should be protected from household cleaners by wearing protective gloves or clothing. The skin barrier frequently is altered in AD and does not withstand the general intrusions that normal skin can endure.

Physical Irritants

Scratching because of severe skin pruritus is a hallmark of AD.^{25, 41} AD frequently is called "the itch that rashes" because of observations of rash development only in areas triggered by scratching.⁶² Scratching can initiate or perpetuate the acute and chronic processes of AD, resulting in denuded skin and providing a portal of entry for allergens and microbes.³²

Another prominent finding in patients with AD is an impaired sweating mechanism. Several investigators have documented this phenomenon with patients demonstrating less sweating under periods of stimulation.^{25, 41} Patients frequently complain of increased pruritus during periods of sweating. An increased transepidermal water loss also

has been noted, which has been attributed to fewer sebaceous glands and less total lipid content of AD skin.³² All of these findings contribute to the clinical manifestations of dry skin and increased pruritus.

Factors other than primary irritants (i.e., allergens, infection) may complicate the course of AD. Clothing fabrics can influence the comfort level and amount of pruritus experienced by patients with AD. Wool fabrics provide the most irritation and should be avoided. Synthetic fibers such as nylon and polyester also may be tolerated poorly by some individuals because of abnormal sweating mechanisms. Cotton is the fabric of choice for patients with AD; generally it provides the most comfort and is the least pruritic. The use of cotton clothing should be emphasized.

Foods as Irritants

Some foods also can act as triggers of irritation and pruritus. Certain fruits and vegetables, such as tomatoes and citrus fruits, are especially irritating in some individuals. Foods commonly reported as irritants include tomatoes, oranges, grapefruits, and strawberries. These foods are not primary allergens but are irritants that cause pruritus because of their acidic composition.

Psychosocial Factors

Most clinicians agree that psychosocial factors influence the disease process of AD and that these factors provide important secondary triggers to disease pathogenesis and ultimate regimen adherence and disease control (see article by Bender elsewhere in this issue). Emotional and psychosocial stresses, job or school tension, and unstable or unsupportive home environments can contribute as exacerbating factors. As previously noted, "prurigo Besnier" (described in 1892) was reported in association with a nervous disorder in patients.⁵ Some investigators have stated that these psychologic influences may lead to autonomic dysregulation, abnormal vascular responses, and mediator release that all act to trigger an adverse response.²⁴ The chronic pruritus seen in all patients with AD, especially those with severe disease, causes sleep disturbance, hyperirritability, and emotional distress that contribute to the viscous cycle.^{30, 41} Although not primary causes of disease, these issues must be addressed in caring for patients with AD to provide maximal symptomatic relief during periods of disease exacerbation. These issues are especially important in children and adolescents and occasionally may require psychologic intervention.

Occupation

Choice of career or occupation strongly may influence the disease state for some adult patients with AD. Surveys have reported more frequent atopic dermatitis in occupations in which exposure to dust, wool, textiles, or chemicals are common.⁴¹ The dry, hyperirritable skin of AD is prone to cracking, scaling, and infection following exposure to irritants. For this reason, patients in a workplace of high exposure have frequent or persistent flares of disease. Studies have reported that 65% to 75% of patients with AD report hand eczema, and many of these cases are related to nonspecific irritants in the workplace.⁴¹ The consequences of hand dermatitis and exacerbation of AD may be serious in some individuals, requiring a change of duties or occupation to minimize exposure to irritants.

DIAGNOSIS AND ASSESSMENT OF TRIGGERS

Atopic dermatitis typically begins early in life, most commonly with skin lesions developing in the first 6 months.^{25, 41} Although this pattern is typical, alterations in presentation frequently occur. A careful history can be useful in making the diagnosis of AD and identifying possible triggers. A careful history often uncovers an exacerbating factor that is, at first, not apparent to the patient or physician. The physical examination may provide additional information regarding triggers of AD. Allergic shiners, conjunctivitis, rhinitis, and asthma signs and symptoms are indicative of allergic disease and suggest the possibility of allergen triggers. Open, erythematous or oozing, crusting skin excoriations suggest the presence of bacterial infection complicating AD. A head and V-neck distribution of rash, especially in older children and adults, may suggest superinfection with the yeast *P. ovale*. Linear scratches indicate poorly controlled pruritus, which further can trigger the cycle through the release of local cellular mediators and provide a portal of entry for microorganisms and allergens to the AD skin.³²

Laboratory Findings

Laboratory tests provide few clues to the diagnosis of AD. Several parameters can be helpful in eliciting triggering agents and underlying causes of disease, but none are diagnostic. Peripheral blood eosinophilia and elevated serum IgE levels commonly are seen in patients with AD, however, elevated IgE levels have been seen in nonatopic patients with AD, providing little practical benefit in the diagnosis or management of patients with AD. Prick skin tests to various aeroallergens and food allergens commonly are used in the assessment of AD and provide the most sensitive test for allergen detection. Knowledge of the allergens eliciting positive skin test reactions can be used as a clinical guide for

the management of disease and detection of exacerbating conditions; however, a positive skin test to an aeroallergen or a food allergen may not have strict clinical relevance and must be analyzed in light of the clinical history or food challenge, respectively. For aeroallergen sensitivity, findings of seasonal distribution of skin symptoms or other associated disease, such as allergic rhinitis and asthma, may provide additional clues for interpreting positive skin tests and instituting appropriate avoidance procedures. In the case of food allergen sensitivity, Sampson and Albergo found prick skin tests had an excellent negative predictive accuracy of 82% to 100% but a poor, highly variable, positive predictive accuracy of 25% to 75% when compared with blinded food challenge.⁴⁸ RASTs provide another, less sensitive, method of evaluating a patient for the presence of IgE antibody to specific allergens in the serum. They can be performed on patients with AD in whom the extent of body-surface involvement and severity of the dermatitis prohibits skin testing. Although RASTs have an overall lower predictive value for most allergens than epicutaneous tests, Sampson and Ho reported a correlation of specific IgE, as measured using the CAP-RAST (Pharmacia Diagnostics, Uppsala, Sweden) system, with clinical predictability for food allergy diagnosis for at least some of the major food allergens, including milk, eggs, and peanuts.⁵² Skin culture of affected, refractory AD skin can provide information regarding bacterial or fungal superinfection as a trigger of disease activity.

TRIGGER CONTROL IN ATOPIC DERMATITIS

At present there are no known cures for AD, and current therapy is largely symptomatic. Certain therapeutic measures can be instituted that dramatically reduce symptoms and provide better disease control (see also article by Boguniewicz and Nicol elsewhere in this issue).

Environmental Control

Environmental control measures, in the form of minimizing allergen exposure and pruritic stimuli, should be instituted in all patients with AD. Minimization of extreme fluctuations of temperature and humidity results in less pruritus. Sweating induces pruritus in many patients with AD; therefore, a moderate temperature environment should be maintained. Clothing should be loose and free of wool. Generally, the best-tolerated fabrics are cotton. Coarse fabrics in clothing and bedding should be avoided. Complete rinsing of detergents, soaps, and bleach from clothing and bedding minimizes their potential irritation. Occupational avoidance of aggravating agents such as chemicals, irritants, and solvents should be instituted by older patients with AD. Minimization of emotional stress also lessens the potential for pruritus and skin flares.

Avoidance of Environmental Allergens

Avoidance of known aeroallergens should be instituted when possible. The most easily avoided allergens are dust mites and animal danders. Dust mite-sensitive patients should institute full dust-mite avoidance procedures, consisting of plastic or hypoallergenic covers that encase mattresses and pillows, removal of all feather pillows and stuffed animals from the patient's room, weekly high-temperature washing of bedding, and removal of carpeting and draperies from the patient's room when practical. Animals (especially furry pets like cats and dogs) should be removed from the home, and contact should be minimized. Appropriate cleaning and insecticide application to the home environment can help reduce cockroach allergen. Practical avoidance of other aeroallergens (e.g., cut grass, open windows during allergy season) should be attempted and tailored to known sensitivities on an individual basis.

Dietary Elimination of Food Allergens

In patients with food hypersensitivity, food allergen avoidance results in improvement of AD.^{7,54} Many investigators have shown that by following a strict avoidance diet of relevant food allergens, patients experience symptomatic relief of pruritus and clearing of skin rash.^{7, 16, 54} Because of the high false-positive rate of prick skin testing and RAST for food allergens, an elimination diet followed by a blinded (single- or double-blind) or open food challenge should be performed to confirm clinical reactivity to a particular food, unless a convincing history of anaphylaxis is obtained. An exception may be applicable when an elevated CAP-RAST is obtained that demonstrates a greater than 90% to 95% likelihood that a patient will have a positive food challenge.⁵² Extensive elimination diets should not be prescribed on the basis of skin test positivity alone because of the obvious nutritional complications. The period of dietary restriction is allergen dependent but generally should occur for 1 to 2 years before reintroduction or rechallenge with the implicated food.^{7, 50}

Appropriate Skin Care Regimen

General measures to reduce skin trauma caused by scratching should be instituted. Appropriate bedding and clothing can help minimize itching. In infants and children, gloves and socks can be used to reduce scratching, especially during sleep. Fingernails should be trimmed to minimize skin trauma from scratching.

Skin hydration is an extremely important measure in controlling the rash and pruritus associated with AD. Daily soaking baths hydrate the chronically dry skin of AD and reduce the likelihood of bacterial

superinfection, both of which reduce pruritus and skin flares. Lubricants provide symptomatic relief for dryness and pruritus of AD skin and should be applied to the skin immediately following bathing and at additional times during the day. Lubricants should be free of alcohols and perfumes, which can be irritating and drying. Of major importance in the successful treatment of AD is interruption of the itch-scratch cycle through use of scheduled antihistamine medications. These medications dramatically reduce itching and reduce sleep disturbance in patients with AD. Control of the inflammatory component of AD should be maintained when lesions are present. Anti-inflammatory options include topical corticosteroids, topical tacrolimus, and oral corticosteroids (use reserved for severe, refractory cases). These medications work to diminish the inflammatory cell proliferation and mediator release in the lesional skin, providing additional control through direct blunting of the inflammatory process. The use of oral antimicrobials should be used liberally in the patients with AD and documented or suspected bacterial superinfection. Improved skin care regimen with more frequent bathing also may help to reduce the bacterial load. For documented fungal or yeast superinfection, several investigators have advocated the use of topical agents, such as Sebulex or Selsun shampoo, and oral antifungal agents to fight fungal growth.

Although allergen immunotherapy has been useful in some atopic conditions (i.e., allergic rhinitis), its role in the treatment of AD has been limited. In clinical practice, immunotherapy frequently acts as a trigger of AD, exacerbating the condition rather than providing relief.

Psychotherapy

Atopic dermatitis is a very aggravating chronic disease that can be emotionally challenging for patients and families. Emotional distress and problems can trigger episodes of pruritus and worsen AD. Young patients and their families may have difficulty understanding and coping with this chronic condition and may need help to establish parameters for discipline without adding to the emotional tension of an already aggravated child. Older children and adolescents also may experience body-image problems related to the obvious skin abnormalities. For these reasons, some patients and their families benefit from social service support and psychologic counseling that address these issues.²⁴

SUMMARY

The list of potential triggers associated with disease pathogenesis and clinical symptoms for patients with atopic dermatitis are vast. The role of allergens is clearly very important, but nonallergic triggers that often can hamper clinical care are equally significant. A careful history

and appropriate diagnostic testing together with a comprehensive treatment program can provide disease-modifying and life-altering results for patients with atopic dermatitis.

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