

PSYCHOLOGIC DYSFUNCTION ASSOCIATED WITH ATOPIC DERMATITIS

Bruce G. Bender, PhD

Skin disease can have a profound effect on an individual's social interactions, psychologic adjustment, work success, sexual relationships, and quality of life. Patients with atopic dermatitis (AD) may have disrupted sleep with consequent daytime fatigue and compromised school and work quality. Spouses of patients with AD also may feel the psychologic burden of their partners' severe skin disease and may experience anxious or depressive symptoms. Parents with children who have AD may be required to provide heroic efforts to treat their child's disease and ease their suffering, possibly experiencing loss of sleep, a significant economic impact of medical care, and distress at their child's upset.

Although the burden of chronic illness is easy to identify and its consequences are apparent, the relationship between AD and psychologic symptoms is neither simple nor one-sided. The presence of AD represents a significant stress in the lives of patients and family members, but the response to the stress is variable and dependent on the existing psychologic foundation of the patient and family. Some individuals may find a relatively minor amount of skin inflammation highly distressing, whereas others may cope well with severe AD. Investigators of the psychologic correlates of AD have found that certain personality types are more prone to AD, that AD may be triggered by stress, and that patients who are psychologically capable of disciplined and diligent self-care have less difficulty with their disease. This research supports a

From the Department of Pediatric Behavioral Health, National Jewish Medical and Research Center; and the Department of Psychiatry, University of Colorado School of Medicine, Denver, Colorado

bidirectional model of the relationship between AD and psychologic factors that recognizes psychologic burden the disease creates and the importance of the psychologic fabric of the patient and family in determining the course of the disease.

QUALITY OF LIFE

The increasing popularity of quality-of-life questionnaires has led to the development of numerous disease-specific quality-of-life measures. Disease-specific quality-of-life instruments generally are intended to measure some combination of illness symptoms, interference with daily activities, and emotional response to the disease. Typically, the questionnaires can be scored to produce a single quality-of-life index that has been particularly useful to clinical trials investigators who want to include quality of life as an outcome measure. Disease-specific quality-of-life measures have important limitations that are not always recognized by investigators. Most quality-of-life measures are free, easy to use, and require little time or effort from the investigative team or the patient; however, there is no universal definition of quality of life, and it is no more easily measured than "happiness" or "self-concept," psychologic targets that have proven elusive to behavioral scientists over many decades. The measurement of a global quality-of-life factor is as difficult a task as an attempt to measure global "health" and is entirely dependent on which questions are included in the questionnaire. Two different quality-of-life questionnaires may include very different questions (e.g., one may focus the emotions of the patient, and another may focus on the patient's social relationships). These two questionnaires may produce different scores and different conclusions.⁵

Disease-specific quality-of-life measures have been developed for AD. Two factors have helped reduce the variability and elusive measurement construct that plague quality-of-life measures designed for other diseases: (1) AD is characterized by a set of symptoms and consequent complications (e.g., embarrassment, itching, sleep loss) shared by a majority of patients with AD.²³ (2) A single quality-of-life measure has emerged and been adopted by investigators conducting AD clinical trials. The Dermatology Life Quality Index (DLQI) was developed by asking 120 patients who were attending a dermatology clinic about areas of their lives that are influenced by skin disease.²² The result was a 10-item questionnaire that uses a four-point scale to rate a series of statements about discomfort, embarrassment, interference with activities, socialization, and personal relationships. A version for pediatric patients, the Children's DLQI (CDLQI), also has been developed.⁴⁰ As with other pediatric quality-of-life measures, little attention has been directed to the difficult questions of age and reading limitations or the impact on children's answers when assisted by a parent or unfamiliar adult, factors which may significantly alter the meaning of consequent scores.⁵

The usefulness of quality-of-life questionnaires is limited to provid-

ing a measure of the patient's perception of treatment effectiveness. Rooted in a simplistic behavioral science model that views the disease on a continuum of psychologic burden that can be measured in concert with height, weight, and other fixed-meaning variables, these instruments supply little information about the complex relationships between the patients' psychologic characteristics and physical disease.

ATOPIC DERMATITIS AND MOOD DISORDER

Patients with AD report increased symptoms of anxiety and depression in response to having AD. Less definitive is the possibility that patients with certain psychologic symptoms or personality types may be more susceptible to AD.

Studies that evaluate mood disorder in patients with AD avoid some of the difficulty of quality-of-life measurement because anxiety and depression scales can be validated against clear clinical endpoints. Specifically, these measures can be validated in studies that include patient groups with diagnoses of anxiety or depression which can be confirmed through other diagnostic criteria, such as a standardized psychiatric interview. These measures typically have been evaluated in numerous studies, and their psychometric properties are well established.

Numerous studies that use these instruments have found evidence of increased anxious^{26, 30, 31, 41, 57} and depressive symptoms^{31, 57} in adults with AD compared with non-ill controls. Children from the United Kingdom with chronic eczema were reported to have more emotional difficulty, in particular "excessive worries," in comparison with children with minor, transient skin problems presenting to the same London clinic.¹ The correlation between mood disorder and AD does not reveal, however, the direction of causality (i.e., if the mood symptoms are a psychologic response to the disease burden or if underlying psychologic characteristics in some manner predispose the patient to inflammatory skin condition).

DEVELOPMENT OF SKIN ERUPTION AND MOOD PROBLEMS

The presumption of quality-of-life models is that the presence of AD causes anxiety and depression. Evidence that mood disturbances increase and decrease as a result of fluctuation of disease severity can be found in studies demonstrating that mood symptoms correlate with AD symptoms^{3, 18} and decrease following successful AD treatment.²⁰ Measures of family stress were found to correlate significantly with the child's AD severity, even after controlling for demographic and medical status variables such as age and serum immunoglobulin E (IgE) level.²⁷ In another study, rates of psychologic disturbance were found in children

with moderate-to-severe eczema but not those with mild eczema.¹ In contrast, other investigators have argued that pre-existing symptoms of anxiety or depression predispose to skin disease. Citing evidence that some patients with AD tend to be characteristically more angry and hostile⁶³ and have difficulty expressing their feelings,²⁸ some investigators have concluded that repressed emotions have a role in inflammation. One study reported that patients with AD had greater electromyographic and heart rate activity than controls, suggesting a predisposing, anxious physiology that might contribute to AD onset. Although early investigations suggested the existence of a particular personality profile associated with AD vulnerability,^{29, 36, 53} the overall evidence was obtained selectively and susceptible to misinterpretation.¹¹ Several researchers have demonstrated that psychologic treatments, including stress management, relaxation training, and scratching-control techniques, can reduce AD symptoms.^{14, 20, 30} Such studies do not establish that the AD was caused by psychologic factors, but they do demonstrate that psychologic interventions may have a role in controlling skin disease.

An alternative causal model hypothesizes that AD and mood disorder are not caused by each other, but rather they both are caused by a third, biologic factor. Genetic studies suggest that mood disorder and allergic disease may have a shared biologic origin.^{61, 62} In the largest study, 1337 monozygotic and 2506 dizygotic twins from Finland were questioned about their history of asthma, eczema, and atopic rhinitis and were tested with the Beck Depression Inventory. In a statistical analysis that fit competing genetic and environmental models, 64% of the association between atopy and depression was caused by shared familial vulnerability, leading the investigators to conclude that a common genetically mediated biologic mechanism may exist between depression and allergic disorders.⁶⁰

STRESS AND ATOPIC DERMATITIS

Stress increasingly has been recognized as an important factor in the pathogenesis of AD. Distressed patients may have increased vulnerability to develop AD or may experience exacerbations of existing AD. Stress can exert a potent and direct influence on AD, but this influence is likely dependent on the combination of pathogenic factors including genetic disposition, allergen exposure, altered vascular reactivity, environment, and the personality of the patient.¹¹ Stressful events often have been observed to occur before an AD exacerbation.^{10, 37, 39} One study found that a day of high interpersonal stress was followed by an AD exacerbation 24 hours later.³⁷

A German investigative team pursued a program of research into the relationship between AD and stress, demonstrating that children with AD, when exposed to a laboratory stress condition, had blunted cortisol response.¹² The investigators suggest that the adrenocortical response to stress in children with AD is attenuated compared with non-

ill controls. Children with AD are more susceptible to stress-induced skin eruption because of a hyporesponsive hypothalamus-pituitary-adrenal axis that blunts the body's natural ability to produce cortisol and suppresses inflammation in response to stress. The investigators proposed a psychobiologic model to explain these and other findings, concluding that aberrant immunoregulatory neuroendocrine functioning in the hypothalamus-pituitary-adrenal axis or sympathetic nervous system alters immunologic reactivity and, consequently, increases vulnerability to allergic inflammation.¹¹

BEHAVIORS MODERATING THE RELATIONSHIP BETWEEN PSYCHOLOGIC DISTRESS AND ATOPIC DERMATITIS SYMPTOMS

Scratching

Patients with AD may be predisposed to the disease or have an attenuated inflammatory response because of variations in emotional states. Another pathway by which psychologic factors may influence treatment outcome is through patient behaviors. Psychologic factors may not influence directly immune functioning but may affect the disease by altering disease-related behaviors. Scratching is a behavioral mechanism that connects psychologic and disease factors.

Scratching irritates the skin and maintains or exacerbates skin lesions and may lead to a decreased itch threshold once the skin starts to heal.²⁰ Psychologic distress may lead to increased scratching and worsened severity of AD.²⁷ Direct behavioral interventions have been used to augment topical treatments to decrease scratching. Although AD is not the result of pathologic scratching, behavioral interventions to stop scratching have been helpful in treatment. Decreased scratching has been reported through biofeedback-assisted relaxation,⁵⁶ hypnosis,⁴⁵ reinforced self-monitoring,⁵⁴ and various combinations of relaxation, punishment, imagery, and cognitive techniques.^{16, 33, 50} Most of these studies were limited by small patient samples and the absence of a control group.²⁰ A number of methodologically stronger studies included standard-medical-treatment control groups and reported superior improvement in skin condition when topical steroids were accompanied by a combination of habit reversal, self-monitoring, and self-reinforcement than when they were given alone.^{32, 44, 51} Two randomized controlled trials used several behavioral interventions individually and in combination and contrasted these to standard dermatologic interventions. The individual behavioral interventions included skin education, relaxation, or cognitive-behavioral training. Individual behavioral interventions exceeded the skin control of the standard treatment, but the combined therapies were most effective.^{20, 48, 49} Comprehensive behavioral and educational interventions may promote control of scratching and reduce the

distress that promotes it, serving as a helpful adjunct to medical treatment of AD.

Treatment Nonadherence

Another behavior that may explain the causal sequence between psychologic distress and disease exacerbation is treatment adherence. Medication nonadherence is common and can be the cause of treatment failure.^{4, 42} Many patients are unable to make the necessary behavioral adaptation to manage the disease. Across pediatric conditions, adherence ranges from 7% to 89% for short-term prescriptions and 11% to 83% for long-term treatments.⁴² Less than 53% of children with acute otitis media took prescribed antibiotics⁴³; only 33% of children with cancer adhered to their prednisone regimen; for children with asthma, adherence across several studies averaged 50%.⁵ Few studies have attempted to document nonadherence in the treatment of AD, although one study found that 24% of patients reported failure to follow their AD treatment regimen, and other investigators have observed without documentation that poor treatment adherence undermines AD control.^{27, 34} Given the degree of under-reporting typical in patient-reported surveys of adherence,⁵ non-adherence to AD treatment is likely much higher than 24%. Patient reluctance to comply with treatment has been attributed to concern about skin thinning, effects of corticosteroids on growth, poor understanding of the nature of the disease, and concern about time and cost of treatment.^{15, 24}

FAMILY INTERACTIONS AND ATOPIC DERMATITIS

For pediatric patients, adherence to the treatment regimen is dependent on the capability of parents to manage the disease and consistently engage in the behaviors necessary for its control. These behaviors include frequent and complex regimens consisting of applying creams, emollients, bandages, wet wraps, and mittens to prevent scratching. Distressed and overburdened parents and families may not be able to manage pediatric illness. Personal conflicts, financial problems, frequent moves, sleep disorders, unemployment, and erratic daily schedules may accompany serious emotional disorders and preclude the development of regular health care behaviors.⁸ The child's skin condition may interfere with the parent-child relationship, inhibiting normal holding and caressing and further undermine the psychologic stability that facilitates adherence.³⁴

The parents' psychologic functioning is a major determining factor that influences family stability and management of the child's illness. Distressed or psychologically unstable parents may not provide the structure and support necessary to ensure the child's adherence. The parents' psychologic functioning affects how well a family monitors a

child's symptoms and makes decisions about home management of symptoms and appropriate timing for involving the medical expertise of health care providers.⁴ One study found that increased psychiatric symptoms in mothers of children with chronic illness were associated with more functional limitations in their children.³⁵ In a study of asthma risk factors, parenting problems—including psychiatric difficulty and poor knowledge of child care practices—were associated with increased probability of a young child developing asthma, particularly when combined with frequent illness and elevated serum IgE levels.⁴⁷ In some instances, the parent may expect the child to assume responsibility for his or her own asthma management beyond the child's developmental capacity to do so.⁵ Stressful events in the life of a family, such as frequent moves or parental unemployment, add to a negative emotional climate and diminish the family's capacity to maintain the energy and organization necessary to care for a child with severe skin disease. The child care burden is increased when the child has more than one physical illness³⁸ or physical disability,¹³ further taxing the family system.

ATOPIC DERMATITIS AND SLEEP DISTURBANCE

The effect of AD on sleep represents another variable that moderates the relationship between AD and psychologic factors. Several studies have established that patients with AD have increased nighttime scratching⁴⁶ and scratch more during sleep than patients with other dermatologic disorders.⁵⁵ In children, the severity of AD correlated with the degree of sleep loss as reported by parent questionnaires.¹⁷ Results of home polysomnography found children with AD had increased sleep fragmentation characterized by both more and longer awakenings associated with scratching episodes compared with that of age- and sex-matched controls.⁵⁸ In another study, children with AD exhibited an average of 24 arousal or awakening events per night compared with an average of 15 events in the control group.⁵² Direct observation, video monitoring, and scratch electrodes revealed up to 19 bouts of scratching per night.⁵²

Sleep loss secondary to AD has an impact on daytime functioning. Parents reported that their children with AD who had greater difficulty falling asleep, frequent night waking, less total sleep, and greater difficulty awaking for school also had increased daytime tiredness and irritability. Greater AD severity also was correlated moderately with behavior difficulty.¹⁷

Sleep deprivation regardless of cause is associated with increased neuropsychologic and psychologic problems.⁶ Disturbed sleep resulted in more psychologic problems and poorer performance on tests of memory and concentration in adults²⁵ and children with nocturnal asthma.⁵⁹ Improved asthma symptoms resulted in improved sleep and psychologic functioning.⁵⁹ These sleep-related daytime problems also can affect children's functioning in school. Nighttime awakening in children with

asthma was found to be correlated with decreased school attendance and performance.¹⁹

Sleep disturbance and consequent daytime problems in children with AD are not necessarily related to skin disease. As many as 26% of children have some sleep problems, including waking during the night and difficulty returning to sleep.⁹ Because sleep difficulties are elevated in children with psychiatric disorders,⁹ anxiety in particular,^{2, 21} sleep problems may be the result rather than the cause of daytime behavioral disturbance. The temptation to quickly attribute daytime mood and behavior problems to sleep loss in children with AD must be balanced by the recognition that some children may have psychologic problems that are not the result of AD and may be the source of sleep difficulties.

Sleep problems that are initiated during AD exacerbations may continue after the AD is treated successfully.¹⁷ For children who have developed habitual fragmented sleep patterns, resolution of the AD symptoms may not suffice, and additional efforts may be required to help parents manage the sleep problems.

SUMMARY

Atopic dermatitis in children and adults can create a psychologic burden and impair quality of life. Psychologic burden often accompanies severe disease, and patients may become anxious and depressed, avoid social interactions, lose sleep, and experience less satisfying work success. This article emphasizes the bidirectional nature of the relationship between AD and psychologic factors. Although psychologic disorders may be induced by the stress of having AD, psychologic factors also may predispose to AD or influence its course. Several decades ago, research focused on attempts to discover an AD personality type. Although no profile captures the majority of patients with AD or their families, an elevation in mood disorders has been established in this population. The relationship between mood and AD may take one of three forms: (1) anxiety and depression may be secondary to the distress of having skin disease; (2) the patient's mood symptoms may predispose to AD exacerbations; or (3) the mood disturbance and AD may be related causally to a third, genetically mediated factor. Most likely, factors are interactive: Anxious persons are more prone to skin disease, and skin disease may contribute to the anxiety. Stress can trigger or exacerbate the skin condition but does not have equal effects across all patients. Stress in some patients with AD may cause quickly a flare of symptoms but may have no impact on other patients' skin. An emerging area of research from the field of psychoneuroimmunology is examining the role of psychologic factors in AD pathogenesis with specific interest in the relationships between stress, the hypothalamus-pituitary-adrenal axis, and the sympathetic nervous system.

Examination of causal pathways between AD, inflammatory processes, and psychologic factors must consider behavioral connections,

including the role of scratching and treatment adherence. Nonadherence to the medical regimen has been shown to exert significant influence on disease control and treatment success in virtually all chronic diseases. Many patients are unable to consistently complete the health behaviors, such as application of baths, wet wraps, and daily topical medications, necessary to curtail the progression of their disease. Patients with psychiatric disorders are even less capable of appropriate self-care; for these individuals, the presence of stress and anxiety directly may alter immune functions and may result in behavioral deficits that contribute to poorly controlled disease.

It is tempting to believe that psychologic treatments improve the body's ability to fight skin inflammation by reducing mood disorders, but evidence to support this conclusion is lacking. Mood disorders can be treated effectively, and patients' ability to cope with stress can be improved, removing barriers in treatment of the illness.⁷ Behavior therapies have been used to effectively reduce scratching and facilitate healing.¹⁴ Research is needed to evaluate psychologic interventions designed to decrease stress influences and mood disorders while increasing treatment adherence in patients with AD and their families.

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Address reprint requests to

Bruce G. Bender, PhD
National Jewish Medical and Research Center
1400 Jackson Street
Denver, CO 80206

e-mail: benderb@njc.org