

# DERMATOLOGY NURSE PRACTICE



## Managing the Common (and Uncommon) Comorbidities of Atopic Dermatitis

### INSIDE THIS ISSUE:

Which specific conditions make up the “atopic march”?

Why are patients with atopic dermatitis (AD) at increased risk of recurrent skin infections?

What should healthcare providers be doing to help pinpoint mental health issues among patients with AD?

How does AD affect the financial picture for patients and their families?

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**Keischa Cash**

DNP, APRN, DCNP, FNP-BC

*Dermatology Nurse Practitioner*  
DNP Derm LLC  
Tampa, FL

**Megan Lewis**

MSN, RN, CPNP-PC

*Pediatric Nurse Practitioner*  
Division of Allergy & Immunology  
Children's Hospital of Philadelphia  
Philadelphia, PA

**Patricia Delgado**

DNP, AGPCNP, DCNP

*Founder and CEO*  
Sunrise Skin and Wellness LLC  
St. Petersburg, FL

**Noreen H. Nicol**

PhD, RN, FNP, NEA-BC

*Associate Professor Emerita*  
University of Colorado  
School of Nursing  
Aurora, CO

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## LEARNING OBJECTIVES

After participating in the activity, learners should be better able to:

- Identify the most common comorbidities faced by patients with atopic dermatitis (AD)
- Discuss the relationship between AD and other atopic conditions
- Develop strategies to reduce the risk of skin, soft tissue, and systemic infections among patients with AD
- Assess the impact of mental health conditions among patients with AD

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**Megan Lewis, MSN, RN, CPNP-PC**, has disclosed that she does not have any relevant financial relationships specific to the subject matter of the content of the activity.

**Patricia Delgado, DNP, AGPCNP, DCNP**, has disclosed that she does not have any relevant financial relationships specific to the subject matter of the content of the activity.

**Noreen H. Nicol, PhD, RN, FNP, NEA-BC**, has disclosed the following relevant financial relationships specific to the subject matter of the content of the activity: Medline Industries/ Advisory Board, Consultant.

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**Linda Markham, BSN, RN, DNC, Executive Director, Dermatology Nurses' Association**, has disclosed that she does not have any relevant financial relationships specific to the subject matter of the content of the activity.

**Scott Kober, MBA, Managing Director, Excalibur Medical Education**, has disclosed that he does not have any relevant financial relationships specific to the subject matter of the content of the activity.

**Kristin Harper, PhD, MPH, ELS, Medical Writer**, has disclosed that she does not have any relevant financial relationships specific to the subject matter of the content of the activity.

**Lynn Smith, DNP, NP-C, DCNP, Content Expert**, has disclosed that she does not have any relevant financial relationships specific to the subject matter of the content of the activity.

**Trudy Adamson, RN, MSN, DNC, AP-PD**, has disclosed that she does not have any relevant financial relationships specific to the subject matter of the content of the activity.

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This activity includes discussion of investigational and/or off-label use of the following products: Baricitinib, nemolizumab.

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This activity has been designed to meet the educational needs of nurses, nurse practitioners, and physician assistants. Other healthcare providers may also participate.

## ACTIVITY DESCRIPTION

In this issue of *Dermatology Nurse Practice*, we will explore the phenomenon of the "atopic march," including how it manifests in children with AD and how it can be prevented. We will also discuss other common and serious comorbidities associated with AD in children and adults, including infection, autoimmune diseases, and mental health disorders. We will conclude by considering the financial burden experienced by patients with AD, caused in part by the multitude of conditions that many must contend with.

## ACCREDITATION AND CREDIT DESIGNATION

### Nurses


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This educational activity is jointly provided by Dermatology Nurses' Association and Excalibur Medical Education.

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# MANAGING THE COMMON (*AND UNCOMMON*) COMORBIDITIES OF ATOPIC DERMATITIS

## DRUG NAMES INCLUDED WITHIN THIS ISSUE

Generic	Brand
Dupilumab	Dupixent
Mupirocin	Bactroban Nasal, Centany
Tralokinumab	Adbry
Abrocitinib	Cibinqo
Ruxolitinib	Opzelura
Upadacitinib	Rinvoq
Nemolizumab	NA
Baricitinib	Olumiant
Cyclosporine	Sandimmune, Neoral, Gengraf
Methotrexate	Otrexup, Rasuvo, RediTrex

Atopic dermatitis (AD), the most common type of eczema, is a systemic inflammatory disorder that affects roughly 13% of children and 7% of adults in the United States.<sup>1,2</sup> Its prevalence has nearly tripled in industrialized countries over the past three decades, making the dry red skin, pruritic lesions, and relapsing flares of the disease familiar to every dermatology specialist.<sup>3</sup> Because AD is such a common sight in dermatology practices, it can be easy to overlook its day-to-day impact on patients. However, one recent survey found the health-related quality of life for adult patients with AD is worse than in patients with diseases such as asthma and type 2 diabetes.<sup>4</sup> Moreover, AD is often accompanied by other medical conditions. Just as every patient with AD experiences a unique constellation of skin manifestations and symptoms, they also experience a unique constellation of comorbidities.<sup>1</sup> Some, such as allergies, asthma, and rhinitis, are so common they can actually help establish the diagnosis of AD.<sup>5</sup> Others, such as inflammatory bowel disease and osteoporosis, are less common but are nonetheless found at a disproportionately high rate among patients with AD.



For many patients with AD, a dermatology practice is their most frequent point of contact with the medical system. Thus, dermatology specialists play an important role in preventing, recognizing, and treating both AD and its comorbidities.

## COMORBIDITIES OF AD: AN OVERVIEW

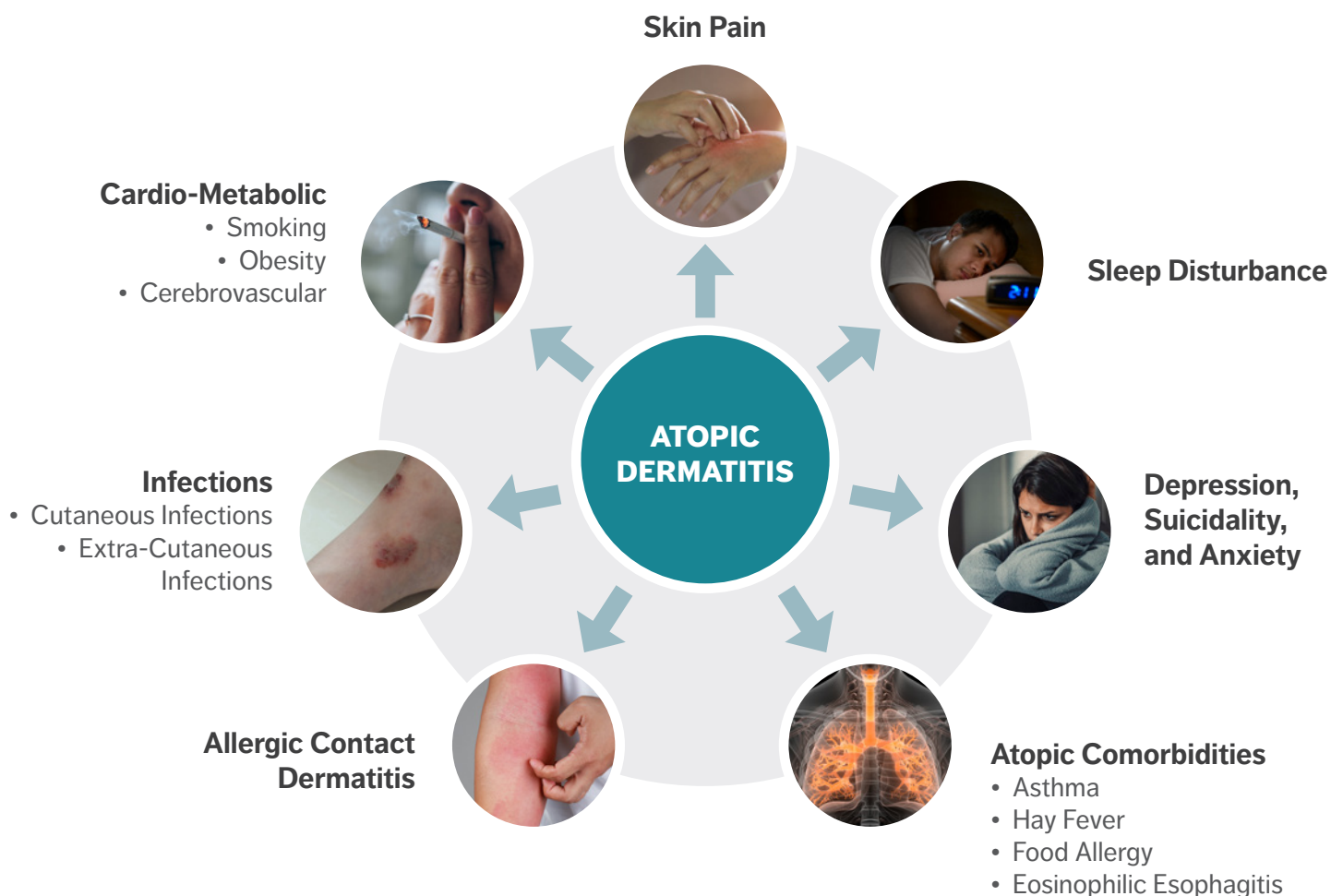
AD is associated with a wide range of comorbidities. Some of the most common ones that dermatology specialists are likely to encounter include allergic contact dermatitis (ACD), atopic comorbidities (eg, asthma, hay fever, food allergy, eosinophilic esophagitis), and skin infections (see Figure 1).<sup>6</sup> AD is also associated with mental health disorders such as depression, suicidality, and anxiety; sleep disturbances; and cardiometabolic disorders. A variety of other AD comorbidities are less well known but can dramatically reduce patients' ability to function

and quality of life, including alopecia areata, urticaria, attention deficit hyperactivity disorder (ADHD), autism, and osteoporosis (see Table 1).<sup>5,7,8</sup> An effective treatment plan for AD must address all of a patient's health issues, making it important for clinicians to become familiar with the array of comorbidities associated with the condition.

## THE ATOPIC MARCH

The atopic march describes a sequential progression from AD to other atopic diseases, such as food allergy, allergic rhinitis, allergic asthma, allergic rhinoconjunctivitis, and eosinophilic esophagitis. Research has shown that 33% to 43% of children with AD develop allergic asthma, 38% to 45% develop allergic rhinitis, and 33% develop both diseases.<sup>9</sup> In addition, 5% to 8% of patients with AD have a co-occurring food allergy.<sup>9</sup> The atopic

**FIGURE 1** Common Comorbidities of AD<sup>6</sup>



**TABLE 1**  
**Less Common Comorbidities**  
**Associated with AD<sup>5,7,8</sup>**

Class	Condition
<b>Immune-mediated conditions</b>	<ul style="list-style-type: none"> <li>• Alopecia areata</li> <li>• Urticaria</li> <li>• Inflammatory bowel disease</li> <li>• Thyroid disease</li> <li>• Celiac disease</li> <li>• Vitiligo</li> <li>• Connective tissue disease</li> <li>• Hematologic disease</li> <li>• Sjögren syndrome</li> <li>• Systemic lupus erythematosus</li> </ul>
<b>Mental health disorders</b>	<ul style="list-style-type: none"> <li>• ADHD</li> <li>• Developmental/intellectual disabilities</li> <li>• Behavioral/personality/emotional disorders</li> <li>• Conversion/somatoform disorders</li> <li>• Malaise/fatigue</li> <li>• Schizophrenia</li> <li>• Obsessive compulsive disorder</li> <li>• Sexual dysfunction</li> </ul>
<b>Bone health conditions</b>	<ul style="list-style-type: none"> <li>• Osteoporosis</li> <li>• Bone fractures</li> <li>• Arthritis</li> </ul>
<b>Neurologic/ocular conditions</b>	<ul style="list-style-type: none"> <li>• Tic disorder</li> <li>• Migraine</li> <li>• Visual impairment</li> <li>• Eye disorders</li> <li>• Glaucoma</li> <li>• Neuropathy</li> </ul>
<b>Dermatologic conditions</b>	<ul style="list-style-type: none"> <li>• Psoriasis</li> <li>• Seborrheic dermatitis</li> <li>• Carbuncle/furuncle</li> <li>• Keratosis pilaris</li> <li>• Ichthyosis vulgaris</li> </ul>
<b>Oncologic conditions</b>	<ul style="list-style-type: none"> <li>• Lymphoid/hematopoietic malignancies</li> <li>• Malignant melanoma</li> <li>• Non-melanoma skin cancers</li> </ul>
<b>Systemic conditions</b>	<ul style="list-style-type: none"> <li>• Iron-deficiency anemia</li> <li>• Chronic kidney disease</li> <li>• Vasculitis</li> <li>• Pulmonary fibrosis</li> </ul>

march is not inevitable, though. In fact, most children with AD will not follow this trajectory, and the phenomenon itself remains controversial.

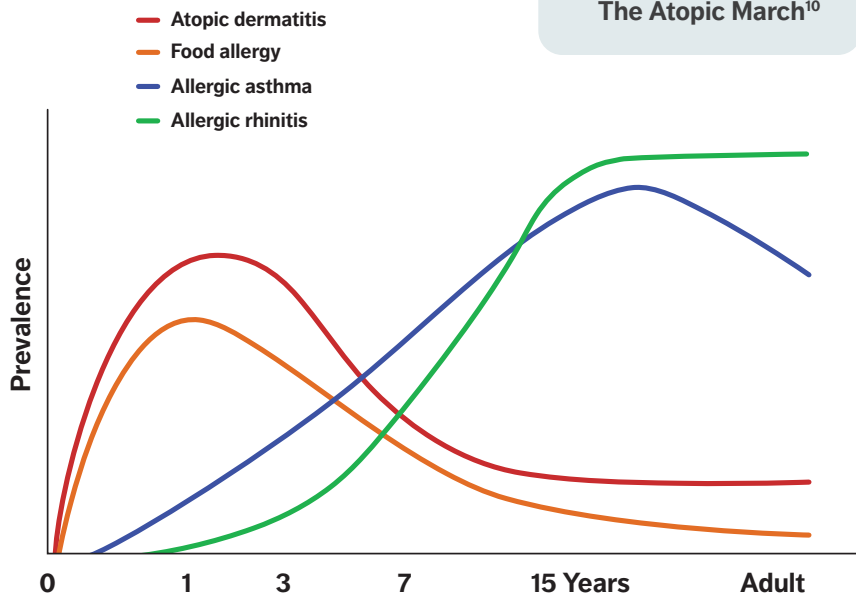
Many researchers hypothesize that AD disrupts the epidermal barrier, leading to allergen sensitization and inflammation at the surface of a patient's compromised skin. This, in turn, eventually leads to immune responses at other epithelial surfaces of the body, such as the gastrointestinal tract (resulting in food allergies and eosinophilic esophagitis), upper respiratory tract (allergic rhinitis), and lower respiratory tract (asthma) (see Figure 2).<sup>5,6,10</sup> These researchers believe that the relationship between AD and other atopic diseases is causal. Other researchers argue that some individuals are likely just predisposed to a variety of atopic diseases, either due to genetics or environmental triggers.<sup>11</sup> Thus, these patients develop a variety of atopic diseases, but the relationship between AD and the other disorders is not causal.

Evidence exists to support both explanations. On the one hand, individuals with AD are clearly at greater risk of having additional atopic diseases. For example, patients with severe AD are more than twice as likely to have asthma than individuals without AD.<sup>5</sup> In addition, children with a longer duration of AD are more likely to have additional atopic diseases.<sup>12</sup> On the other hand, longitudinal studies show that, in patients with multiple atopic conditions, AD often does not precede the other conditions, as would be expected if AD caused the other diseases.<sup>5,13</sup> Thus, the relationship between AD and other atopic diseases may actually best be thought of as a cluster rather than a march.<sup>11</sup>

It remains unclear why some children develop multiple atopic conditions while others do not.<sup>14</sup> It also remains unclear why, in some individuals with childhood AD, it may take decades for additional atopic diseases to develop, with asthma or new sensitivities developing only in adolescence or adulthood.<sup>15,16</sup> That said, some risk factors for developing other atopic diseases have been identified. These include early-onset AD, more severe AD, disease persistence, having a mutation in the filaggrin (*FLG*) gene, sensitization to multiple allergens, and a history of parental atopic disease.<sup>11</sup> Whether the association between AD and other atopic conditions is causal or not, dermatology specialists can educate the parents of children with AD, especially children with any of these risk factors, about the elevated risk of developing other atopic diseases to facilitate timely diagnosis and treatment.<sup>15</sup>

Researchers have hypothesized that because AD is a recognized risk factor for other atopic diseases, therapies that reduce the severity of the condition may also prevent these other diseases from developing.<sup>11</sup> This

**FIGURE 2**  
The Atopic March<sup>10</sup>



hypothesis is supported by studies of multiple therapies. For example, one meta-analysis found that subcutaneous and sublingual immunotherapy reduces the risk of developing asthma in high-risk patients with AD.<sup>11</sup> Additional research has highlighted the protective role of dupilumab, a monoclonal antibody against interleukin (IL)-4/IL-13 that targets the Th2 immune response that drives atopic diseases. Dupilumab is an FDA-approved treatment for moderate-to-severe AD that has additional indications for asthma, chronic rhinosinusitis with nasal polyps, and eosinophilic esophagitis. In pooled data from 12 clinical trials of dupilumab vs. placebo in patients with AD, taking dupilumab reduced the risk of developing new allergic conditions by 37%.<sup>16</sup> The protection conferred by dupilumab was greatest for patients <18 years, those with AD onset prior to 2 years of age, those with more severe AD at baseline, and those with asthma at baseline. Protection appeared to continue even after treatment was discontinued, although it was attenuated. More research is needed to determine the optimal timing and duration of dupilumab treatment for patients with AD to prevent downstream comorbidities.<sup>11</sup>

Scientists are also investigating the role of the microbiome in the atopic march.<sup>9</sup> Individuals with atopic diseases harbor alterations in the microbiomes at the sites of the body that are affected. For instance, AD is associated with a greater abundance of the bacterium *Staphylococcus aureus* on the skin, which promotes inflammation. Higher levels of this bacterium are also associated with more severe AD.<sup>17</sup> It is possible that changes in the skin microbiome associated with AD promote microbial alterations at other body sites, making individuals with AD more vulnerable to developing atopic comorbidities. Some research—but not all—indicates that probiotic supplementation of pregnant and breastfeeding mothers

and their infants can help protect against AD.<sup>18,19</sup> However, much remains unknown about which probiotic strains are most effective in conferring protection and how exactly they work to prevent atopic disease. In the future, research may clarify the role of the microbiome in the atopic march and perhaps guide novel treatment and prevention strategies.

In the meantime, several practices do appear to protect against the development of AD and other atopic diseases.<sup>20,21</sup> The American Academy of Pediatrics states that exclusive breastfeeding for 3-4 months protects against atopic disease.<sup>22</sup> It also states a lack of evidence exists to support the use of partially or extensively hydrolyzed formula for this purpose, or for delaying

the introduction of allergenic foods such as peanuts, eggs, and fish beyond 4-6 months.<sup>22</sup> In addition, research shows that children exposed to smoke have a higher risk of allergic sensitization.<sup>21</sup> Therefore, parents of children with AD or those at high risk for developing atopic diseases can be counseled about the value of breastfeeding and protection from second-hand smoke.

## INFECTIONS

Patients with AD are at increased risk for recurrent skin infections because of their compromised skin barrier, abnormalities in their innate and adaptive immune response, alterations in their skin microbiome, and trauma from scratching their skin.<sup>23,24</sup> They are also at higher risk for systemic infections due in part to untreated skin infections, as well as infections in organ systems besides the skin.

All patients with AD, or their caregivers, should be educated about the risk of skin infections. Individuals with AD are nearly 5 times more likely than those without the condition to develop skin infections that lead to hospitalization, require inpatient treatment, or are life threatening.<sup>5</sup> In one study of almost 5 million children and adults with AD, 16% had experienced a skin infection that required medical care.<sup>25</sup> *S. aureus*, which colonizes the skin of most patients with AD, is the most common cause of skin infections. These infections often present as impetigo or cellulitis.<sup>8,23</sup> *S. aureus* can be the primary cause of a skin infection or it can secondarily infect lesions caused by other pathogens, such as viruses. Adults with AD are 5 times more likely than those without the condition to develop methicillin-resistant *S. aureus* infections.<sup>8</sup>

Common features of bacterial skin infection in patients with AD, including those caused by *S. aureus*, are weeping, honey-colored crusting of the skin, folliculitis, and sometimes pustulation.<sup>23</sup> At times, overlap between the signs and symptoms of infection and AD can make diagnosing infections challenging. For example, both conditions can present with cutaneous erythema and warmth, oozing associated with edema, and regional lymphadenopathy.<sup>23</sup> To make matters more confusing, infections can be associated with concomitant AD flares. Finally, because colonization of the skin by *S. aureus* is so common, it can be difficult to use a culture to make a diagnosis. Therefore, dermatology specialists must remain alert for possible signs of infection, especially when AD flares are present.

Treating bacterial skin infections promptly is important, as they may otherwise become systemic and even life threatening.<sup>23</sup> For patients with localized *S. aureus* skin infections, topical mupirocin can be applied twice a day for 1-2 weeks.<sup>19</sup> For patients with more extensive infection, oral antibiotics (cephalosporins or penicillinase-resistant penicillins) can be given for 2 weeks. In patients with recurrent *S. aureus* infections, a multi-step decolonization strategy may be attempted. This strategy includes optimizing the underlying condition of the skin, educating patients and caregivers on best personal hygiene practices, instituting environmental hygiene measures, and carrying out personal and household decolonization (for example, with use of diluted bleach baths).<sup>19,24</sup> Unfortunately, the effectiveness and utility of *S. aureus* decolonization is still experimental.

Viruses and fungi can also cause skin infections in patients with AD.<sup>19</sup> Herpes simplex can manifest as eczema herpeticum or Kaposi's varicelliform eruption. It presents as widespread skin lesions with punched-out erosions, hemorrhagic crusts, and vesicles that may be itchy or painful. An eczema herpeticum diagnosis should be considered in patients who do not respond to oral antibiotics; in these patients, oral antiviral therapy should be started immediately. In severe cases of eczema herpeticum, IV antiviral therapy may be necessary. Patients with AD can also develop widespread molluscum contagiosum that is caused by a poxvirus. Diagnosis of molluscum contagiosum is usually based on the distinctive appearance of the lesions: firm, dome-shaped papules with central umbilication.<sup>26</sup> Because molluscum contagiosum is self-limiting, and strong evidence for the efficacy of any therapy is lacking, attempting to treat this infection in immunocompetent individuals is optional. If treatment is attempted, cryotherapy, curettage, cantharidin, and podophyllotoxin are considered first-line therapies. Finally, dermatophyte (tinea) infections

sometimes occur in patients with AD and can be treated with standard topical or oral antifungal regimens.<sup>19</sup>

Finally, AD is associated with a higher risk of infections of virtually all parts of the body, including the musculoskeletal system, ear, throat, heart, gastrointestinal tract, urinary tract, and upper and lower respiratory tracts.<sup>8,27,28</sup> For patients with signs or symptoms of systemic infection of any type, hospitalization and IV antibiotics are recommended.<sup>24</sup> Fortunately, data suggest that adult patients with AD, even those taking systemic medications such as prednisone or methotrexate, are not more likely than patients without AD to be hospitalized for COVID-19 complications or to die from infection.<sup>29</sup>

Optimizing management of AD appears to be the best way to prevent infections. Protecting the skin barrier represents a major step in warding off skin infections.<sup>24</sup> Pooled data from clinical trials indicate that, relative to placebo, dupilumab reduces the risk of serious/severe infections as well as non-herpetic skin infections in patients with moderate-to-severe AD.<sup>30</sup> However, recent research suggests that dupilumab neither protects against nor increases the risk of SARS-CoV-2 infection or COVID-19 complications in patients with AD.<sup>31</sup>

Tralokinumab, an antibody that targets IL-13, is the only other biologic currently approved to treat AD. Pooled data from clinical trials of tralokinumab indicate that, relative to placebo, it decreases the risk of many types of infection that pose the greatest threat to patients with AD, including skin infections requiring systemic treatment, eczema herpeticum, opportunistic infections, and serious infections. However, use of tralokinumab does appear to increase the risk of upper respiratory tract infections and conjunctivitis.<sup>32</sup>

Two oral Janus kinase (JAK) inhibitors were recently approved to treat patients with moderate-to-severe AD: abrocitinib and upadacitinib (a third JAK inhibitor, topical ruxolitinib, is approved to treat patients with mild-to-moderate AD). Data indicate that the risk of serious infections and eczema herpeticum for patients taking these oral agents is relatively low.<sup>33,34</sup> However, these medications do appear to increase patients' risk of developing treatment-emergent herpes simplex, respiratory tract infections, and herpes zoster.<sup>34,35</sup> Prior to treatment with oral JAK inhibitors, patients should be tested for tuberculosis and then monitored for opportunistic infections such as herpes zoster throughout treatment. Patients older than 65 years of age taking JAK inhibitors appear to be at particular risk of infectious complications.<sup>36</sup> Whether or not oral JAK inhibitors protect against skin infections requiring systemic treatment remains



to be seen. However, preliminary data suggest that the longer a patient remains on an oral JAK inhibitor, the lower their risk of developing herpes simplex or skin infections requiring antibiotics.<sup>37</sup> Presumably, this is due to the improvement of skin lesions in response to treatment.

In addition, a number of agents currently being investigated for the treatment of AD may help prevent infections by reducing inflammation and improving the skin barrier. Such therapies include monoclonal antibodies that target IL-13, IL-33, thymic stromal lymphopoietin, and OC40, as well as additional JAK inhibitors.<sup>24</sup> Anti-itch therapies that may help prevent infection are also being investigated, including the anti-IL-31 receptor A antibody nemolizumab, transient receptor potential melastatin agonists, and vanilloid antagonists.

## ALLERGIC CONTACT DERMATITIS

AD and ACD are common T-cell mediated inflammatory skin conditions that can share clinical and even histopathologic presentations, which can make them difficult to distinguish.<sup>3</sup> This has complicated efforts to determine how common ACD is among patients with AD. One study of more than 11,000 individuals found the prevalence of patch test sensitivity was no higher in patients with AD than those with non-AD types of eczema, with 35% of participants in each group exhibiting ACD to at least 1 allergen tested.<sup>38</sup> However, another large study found that healthcare claims for ACD were nearly 13 times more common in patients with AD than those without the condition.<sup>8</sup> This indicates that, whatever the underlying prevalence of ACD, patients with AD are more likely to seek medical attention for their ACD than those without AD.

ACD is typically diagnosed in patients with AD via patch testing, but this process can be challenging. For instance, existing inflammation can limit the surface area of skin available for testing. In addition, irritant reactions during patch testing that are caused by AD can be difficult to distinguish from reactions caused by ACD. Finally, there is no universally established set of guidelines for patch testing in children, and many patients with AD are children. Despite these limitations, patch testing should be considered in patients with AD who have dermatitis that fails to improve with topical therapy; an atypical or changing distribution of dermatitis, or a pattern of dermatitis suggestive of ACD; treatment-resistant eczema on their hands; or adult- or adolescent-onset AD. Patch testing should also be considered before initiating systemic immunosuppressants for AD.<sup>6</sup> If patch testing is warranted, an expanded patch testing series is typically recommended in order to include common irritants

for patients with AD.<sup>39</sup> These common irritants include lanolin; preservatives; metals found in jewelry, clothing accessories, and other items (eg, nickel, chromium, cobalt); antibiotics; corticosteroids; and fragrances.<sup>3</sup> The more prolonged or frequent a patient's exposure to a potential allergen, the greater the risk of sensitization. This can be a major problem when a patient's emollients or topical treatments for AD include one of these common allergens. Unfortunately, the products that patients use to control their AD are frequent sources of exposure to lanolin, preservatives, corticosteroids, and fragrances.

All patients with AD should be educated about common triggers for ACD, and clinicians can help them select irritant-free emollients and topical therapies. In addition, research suggests that dupilumab may improve ACD as well as AD symptoms. A retrospective chart review for patients with AD found that the overall condition of those who received dupilumab improved, which included their ACD symptoms.<sup>40</sup>

## METABOLIC SYNDROME, DIABETES, AND CARDIOVASCULAR DISEASE

AD is associated with a slightly elevated risk of obesity, dyslipidemia, and type 2 diabetes.<sup>5,7,8</sup> The link between AD and cardiovascular comorbidities, including myocardial infarction and stroke, remains controversial.<sup>5</sup> AD has been shown to be associated with multiple risk factors for cardiometabolic disease, including sleep disturbance, sedentary lifestyle, smoking, alcohol consumption, and adverse effects from systemic treatments such as cyclosporine or corticosteroids.<sup>6</sup> Additionally, mounting evidence suggests that a small association exists between AD and cardiovascular disease, but no evidence indicates that treating AD modifies an individual's risk of developing cardiovascular disease.<sup>5,8</sup> One hypothesis is that AD increases a patient's risk of cardiovascular disease only indirectly, perhaps by increasing the likelihood of developing various risk factors (see Figure 3).<sup>6</sup> Dermatology specialists can ensure that their patients with AD are aware of their higher risk of developing these conditions and that they are receiving appropriate screening and care for these possible comorbidities.

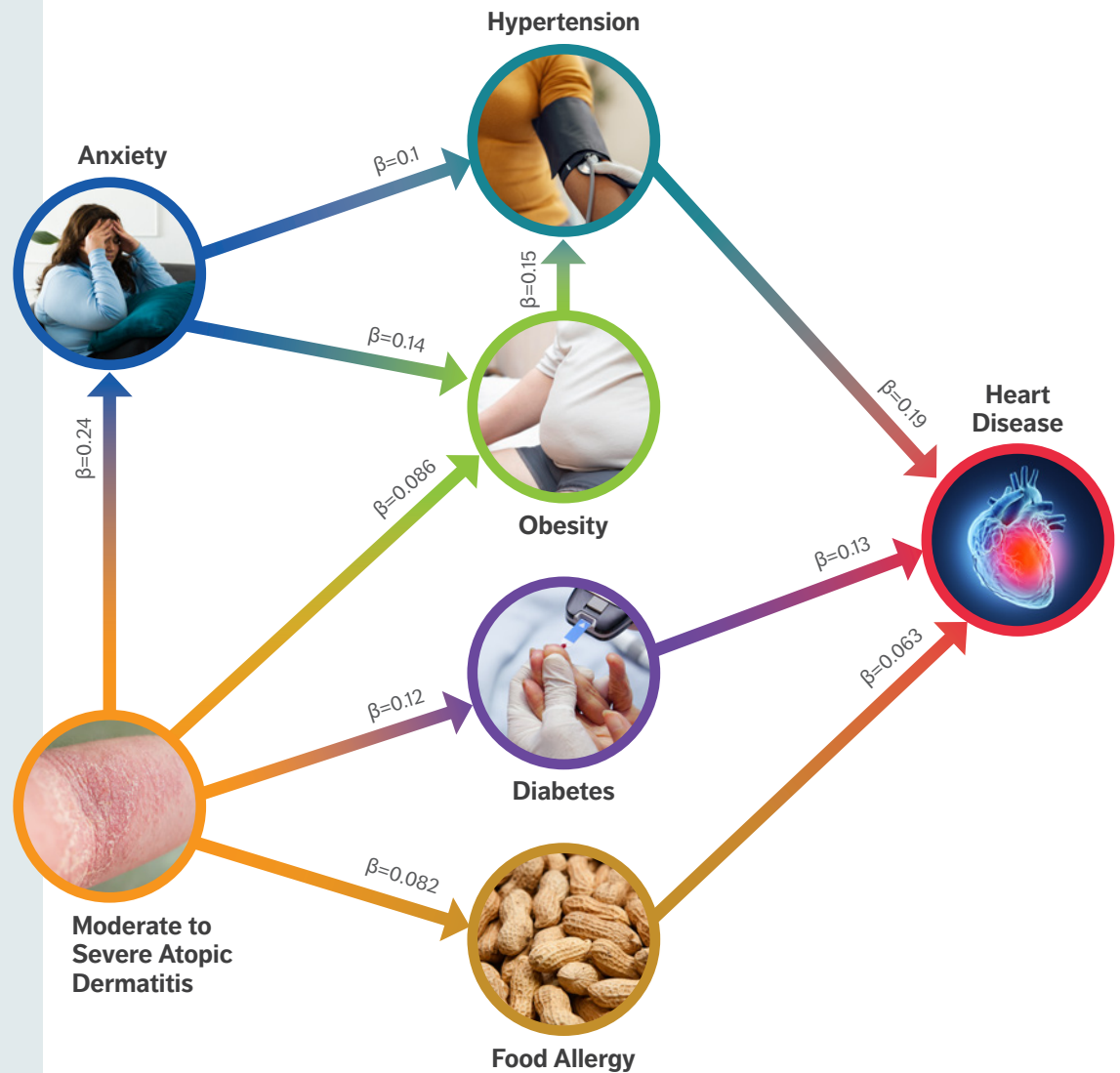
## AUTOIMMUNE DISORDERS

AD increases a patient's risk of developing a wide array of autoimmune disorders. Relative to the general population, adults with AD have 2.5 times the odds of having any autoimmune disorder and 3.5 times the odds of having two or more autoimmune disorders.<sup>41</sup> Adults with AD



**FIGURE 3**  
Hypothesized Causal Relationships Between AD, Metabolic Syndrome, Diabetes, Other Comorbidities, and Cardiovascular Disease<sup>6</sup>

In this model, although no direct link between AD and heart disease exists, AD indirectly elevates risk of heart disease by increasing the risk of other comorbidities that make patients vulnerable to it, such as hypertension, diabetes, and food allergy.



are 2 times more likely to have Crohn's disease, 1.6 times more likely to have inflammatory bowel disease, 4 times more likely to have vitiligo, and 6 times more likely to have alopecia areata.<sup>8</sup> The risk of developing autoimmune disorders is elevated in children with AD as well. For example, compared to pediatric patients without AD, those with AD are roughly 4 times more likely to develop alopecia areata and nearly 3 times more likely to develop vitiligo.<sup>7</sup>

Dermatology specialists should be alert for the presence of dermatological autoimmune comorbidities, such as vitiligo and alopecia areata, and ensure that they are well managed if present. For example, vitiligo may require medication, laser or light-box treatment, depigmentation therapy, or even surgery; alopecia areata may require use of corticosteroids, topical immunotherapies, methotrexate, JAK inhibitors, or other therapies.<sup>42,43</sup> In the case of non-dermatologic autoimmune disorders, dermatology specialists can ensure that their patients with AD are

linked to appropriate primary and specialist care and that all of their comorbidities are being adequately managed.

## MALIGNANCIES

In adults, AD appears to be associated with significantly higher rates of melanoma and non-melanoma skin cancers, as well as lymphoid/hematopoietic malignancies.<sup>8</sup> Similarly, pediatric patients with AD appear to have almost twice the risk of developing lymphoid/hematologic malignancies as their peers without AD.<sup>7</sup> However, the association between AD and lymphoma remains controversial as it has been documented in some studies but not in others.<sup>44</sup> Dermatology specialists can help detect and manage skin cancers by making sure their patients with AD receive annual skin checks. They can also ensure that patients with AD are linked to a primary care doctor and are receiving appropriate cancer screenings.

## MENTAL HEALTH DISORDERS

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AD is associated with intense pruritus, sleep disturbance, stigma, social isolation, poor quality of life, and possibly neuro-inflammation. All of these signs and symptoms have been hypothesized to contribute to higher rates of mental health disorders observed in patients with AD.<sup>6</sup> In one large nationally representative survey, 57% of adults with moderate-to-severe AD reported high levels of psychosocial comorbidities.<sup>45</sup> Some of the most common were sleep difficulties (57%), depression (71%), and anxiety (61%). Each of these comorbidities was associated with reduced physical and mental functioning, as well as increased overall work impairment and healthcare resource utilization. Not only does AD predispose patients to various mental health disorders, but psychological distress also appears to exacerbate AD. Studies suggest the relationship between mental health disorders and AD is bidirectional, with stress, anxiety, and depression contributing to more severe disease.<sup>46,47</sup> Of all the types of comorbidities associated with AD, mental health disorders are some of the most common, with a large impact on patients' quality of life and daily functioning, making it critical to detect and manage them appropriately.

A wide range of mental health disorders are associated with AD. Relative to adults without AD, those with AD have twice the odds of having depression and 1.4 times the odds of having anxiety.<sup>5</sup> AD is also associated with ADHD, eating disorders, obsessive-compulsive disorder, substance use, and sexual dysfunction.<sup>8</sup> Adults with AD are 1.7 times more likely to experience suicidal ideation than those without AD, though evidence supporting an association with suicide is less certain.<sup>5</sup> Furthermore, adults with AD are at significantly higher risk of having a mental health episode that requires hospitalization (most frequently for mood disorders), schizophrenia, and developmental disorders.<sup>48</sup>

This vulnerability to developing mental health disorders may start during childhood. Some research indicates that pediatric patients with AD are more likely to have anxiety, ADHD, emotional distress, and behavioral problems than their peers.<sup>7,49</sup> However, when researchers control for factors such as age, sex, socioeconomic status, and presence of other atopic conditions such as asthma and allergic rhinitis, many of these associations disappear, though an elevated risk of obsessive compulsive disorder remains.<sup>50</sup> The complex relationships between AD severity, mental health disorders, and changing levels of risk as children age make this a challenging topic to understand.

Given the frequency of mental health disorders among individuals with AD, healthcare providers should regularly screen patients with moderate-to-severe disease for anxiety and depression. It may be helpful to incorporate quick, easy-to-use screeners, such as the Patient Health Questionnaire-9 (PHQ-9) for depression and/or the Generalized Anxiety Disorder Screener (GAD-7) for anxiety, into office visits at least once a year. Simply asking patients about their lives, including questions about their daily functioning and state of mind, can also be helpful in identifying mental health disorders that require treatment. Because other common skin conditions—including psoriasis, acne, and alopecia areata—are also associated with elevated levels of depression and anxiety, instituting a regular screening routine for common mental health disorders during dermatology visits can pay off for patients with multiple dermatological conditions.<sup>51</sup>

Dermatology specialists also have an important role to play in managing mental health disorders. Chronic itch and poor sleep drive symptoms of anxiety and depression for some patients. For these patients, controlling these symptoms may help improve their mood.<sup>5</sup> Clinical trials conducted among patients with moderate-to-severe AD have shown that, as skin symptoms improve, symptoms of depression and anxiety decrease.<sup>5,6</sup> In some cases, the presence of comorbid anxiety or depression may warrant more aggressive treatment for AD, including the use of systemic agents. Of course, mental health issues should also be treated directly, and referral to a mental health specialist may be a good step for many patients.<sup>6</sup>

## AD'S IMPACT ON PATIENT FINANCES AND QUALITY OF LIFE

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Nearly 80 different signs and symptoms of AD have been identified, which means that patients with this common disease can experience a staggering variety of issues that impact virtually every facet of their lives.<sup>6</sup> One survey of adults with AD found that 50% reported their disease limits their lifestyle, with 39% avoiding social interaction because of it and 43% altering their activities. Even patients with mild AD reported a substantial impact on their life, although the impact grew with disease severity.

To make matters worse, the financial burden of AD is staggering. In 2015, the cost associated with AD management in the United States was conservatively estimated at \$5.3 billion.<sup>1</sup> This translates into significant costs for individual patients. In a recent survey of National Eczema Association members, respondents reported median out-of-pocket expenses associated with AD of roughly \$600 per year, with 42% reporting spending at least \$1,000.<sup>52</sup>

For 65% of respondents, these expenses had a financial impact on their household that they considered harmful, and patients with comorbid conditions were especially likely to incur high out-of-pocket costs.<sup>53</sup> The same survey found that Black patients with AD incurred significantly higher out-of-pocket costs than non-Black patients, and families of children with AD spent hundreds more per year on out-of-pocket expenses than adult patients with AD.<sup>1,54</sup> It is important to recognize that none of these figures reflect the true financial impact of AD, which encompasses school and work absences, as well as the opportunity cost of spending so much time, money, and effort on managing a sometimes-debilitating disease.

Addressing the financial burden of AD is important for many reasons, including economic justice and the stress that these costs impose on patients and their families. In addition, lack of money or insurance coverage can keep patients from being able to adequately manage their disease. Patients with lower incomes are more likely to have severe disease, presumably because they cannot afford the care and medications to control it.<sup>53</sup> Given the financial implications of AD treatment, it is important that healthcare providers recognize that discussing treatment cost and accessibility is a critical component of the shared decision making process.

To alleviate some of this financial burden, dermatology specialists can practice “minimally disruptive medicine,” working with patients to streamline regimens, minimize costs, and boost adherence.<sup>55</sup> Patients with AD are often prescribed multiple topical therapies such as emollients and wet wraps for skin dryness, corticosteroids or calcineurin inhibitors for inflammation, and antiseptic baths or antimicrobial topical agents to prevent and treat skin infections.<sup>55</sup> In addition to being expensive, these treatments are time-consuming and often uncomfortable. For example, creams and ointments can make the skin sticky, and soil or ruin clothing. Similarly, phototherapy and

systemic therapy may require frequent medical visits and monitoring, which may interfere with school or work. Add on the additional treatments for patients’ comorbidities, and the entirety of their daily medical routines can quickly become untenable.

Therefore, every effort should be made to simplify AD treatment plans as much as possible, and to educate patients and caregivers about how they can pare down their routines. For instance, topical calcineurin inhibitors are just as effective when applied once vs. twice daily, and adherence is better to once-daily application.<sup>55</sup> Similarly, given conflicting evidence on the benefits of daily bathing, patients can be prescribed baths with appropriate additives (such as bleach) once or twice a week rather than daily. If patients admit to struggling to adhere to a treatment plan because of financial or logistical concerns, lower-yield interventions may need to be omitted from the plan in favor of focusing on the most effective components.

Healthcare providers can take several other key steps to help minimize the financial and quality-of-life impact of AD. First, they can work with their patients to prevent and swiftly manage AD flares and comorbidities, which are an outsized source of expense, pain, and disruption to patients’ lives. This type of responsive management is facilitated by a strong therapeutic alliance in which patients are actively engaged in their treatment and feel comfortable expressing any difficulties they encounter managing their disease. Second, dermatology specialists can strive to help their patients afford AD treatments. This may involve working with patients’ insurance companies to authorize needed treatments, helping patients sign up for manufacturer-sponsored programs to reduce out-of-pocket costs for medicines, connecting patients with social workers who can help them sign up for health insurance, or finding less expensive alternatives to medications that patients cannot afford.

## CONCLUSION

The physical and psychological burden that patients with AD experience is often unappreciated. For example, a recent study found that although patients with AD, especially those with severe disease, report very high levels of stress, less than 15% have been offered psychological support by a healthcare provider.<sup>56</sup> For many patients with chronic skin issues such as AD, dermatologists are their only regular source of contact with the healthcare system.<sup>51</sup> Therefore, dermatology specialists have both the opportunity and responsibility to address the whole patient before them, including their comorbidities, whether skin-related or not. This may mean that clinicians use dermatology office visits to start a conversation about common mental health disorders, help a patient locate a primary care provider to coordinate their care for multiple comorbidities, or refer a patient to a specialist for screening or management of a comorbidity. The varied spectrum of comorbidities frequently found alongside AD represents a treatment challenge, but it also represents a chance for dermatology specialists to make a major difference in their patients’ lives.



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# *Counting Our Wins and Losses Through the Atopic March*

by Megan Lewis, MSN, RN, CRNP

The atopic march was first described more than 20 years ago based on clinical observation. It has been defined as the “natural history of atopic manifestations, characterized by a typical sequence of progression of clinical signs of atopic disease, with some signs becoming more prominent while others subside.”<sup>1</sup> Typically, people who speak of the atopic march are describing the progression of atopic conditions such as atopic dermatitis (AD), food allergy, asthma, allergic rhinitis, and eosinophilic esophagitis. It was initially thought that these conditions progress in a stepwise fashion; however, more recent prospective studies have demonstrated that some patients will skip a step or two as they age.

From a pathophysiological perspective, the current theory is that a T-helper cell 2 (Th2)-dominant inflammatory state increases the risk of developing other atopic diseases.<sup>2</sup> The presence of AD often sets the stage for the start of the atopic march, possibly due to patients’ development of an impaired skin barrier and their evolving exposure to common allergens and irritants.

Several recent studies have illustrated the potential for interrupting the atopic march and preventing the development of further atopic diseases. Perhaps the most notable of these was the Learning Early About Peanut (LEAP) study, which was published in 2015. This study demonstrated a clear association between food allergy and AD—especially early-onset, severe AD—and found that children who were at high risk of developing a food allergy saw a reduction in risk of peanut allergy when peanuts were introduced early in life (ie, before 1 year of age). Subsequent studies have shown benefit in early introduction of other allergenic foods in patients at high risk of developing food allergies.<sup>3</sup>



#### **AUTHOR:**

**Megan Lewis, MSN, RN, CPNP-PC**, is a pediatric nurse practitioner at Children's Hospital of Philadelphia in Philadelphia, PA



# “Our burgeoning biologic options in patients with asthma, allergy, and other atopic diseases may enable us—if introduced in a timely manner—to modify or interrupt the atopic march.<sup>2</sup>”

In patients with AD, especially young children, it is important for clinicians to complete a thorough history and exam. Being aware and sensitive to a patient's risk of developing additional atopic diseases is important to ensure timely diagnosis and treatment. For instance, if a patient with AD describes increased coughing or nasal symptoms, consultation with an allergy specialist might be useful to identify potential triggers. Our burgeoning biologic options in patients with asthma, allergy, and other atopic diseases may enable us—if introduced in a timely manner—to modify or interrupt the atopic march.<sup>2</sup>

One of my current patients, Jimmy, came to our office as a 5-month-old with moderate-to-severe AD. He had a family history of atopic conditions—we were already treating his older sister for asthma and allergic rhinitis, and his parents both had had asthma for decades—so we knew that Jimmy was a patient at high risk of developing additional atopic diseases. Based on personal experience, I had a good sense that there were going to be some wins and losses over the next few years.

Jimmy was initially prescribed topical emollients and low-potency topical steroids at 3 months of age for his eczema by a local pediatrician, but he continued to have diffuse involvement upon presentation to our office. He was otherwise growing and gaining weight as expected, with a normal general newborn screen. Jimmy's mother had been breastfeeding her son since birth, with the introduction of solid food only a few weeks prior to our initial meeting. Jimmy tried

a hard-boiled egg a few days before I met him, after which he vomited, but there did not appear to be any other early food issues. We ordered a precautionary peanut-specific immunoglobulin E (IgE), which was negative.

A few weeks later, I saw Jimmy again after his family initiated a new skin care plan that involved regular use of wet wraps, weekly bleach baths, and administration of topical steroids. His skin symptoms appeared to be improving, and reports from his parents indicated that his itching was less frequent and aggressive (WIN!). While that was certainly good news, I was well aware of the potential dangers lurking around the corner in a child with so many warning lights flashing around him due to his personal and family history. Consequently, we spent a lot of time focusing on education that would hopefully help Jimmy avoid a difficult journey through childhood.

I started by reviewing the importance of early exposure to major allergens like peanuts, milk-containing products, and seafood. Jimmy's family followed our guidance, integrating peanut flour and peanut butter into Jimmy's diet along with other potential trigger food. Over the course of the next 12 months, we saw Jimmy for three different episodes of wheezing, which were presumably virally induced. He started having regular coughing fits, though these coincided with his entrance into daily day care, which often triggers all kinds of short-term health issues in toddlers (LOSS!).

At 17 months of age, Jimmy's issues had progressed to the point where he was put on an intermittent asthma flare plan, ultimately progressing to use of a daily controller to help reduce inflammation as his symptoms continued to progress. Around age 3, Jimmy began complaining of itchy eyes and a persistent runny nose whenever he visited his grandparents' house (they had numerous dogs and cats). Over time, both indoor and outdoor asthma triggers were identified, and Jimmy was formally diagnosed with seasonal allergic rhinoconjunctivitis at age 5. He started taking immunotherapy targeted at his allergies to trees, grass, weeds, dust mites, cats, and dogs (LOSS!).

Throughout these early years, Jimmy's AD was generally well controlled. He also passed a baked-egg challenge and has been able to introduce more foods into his diet. Our hope is that, with regular ingestion of baked eggs, Jimmy will eventually be able to pass

a native egg challenge. And finally, after 3 years of allergy immunotherapy, Jimmy's seasonal allergy symptoms have greatly improved and his asthma exacerbations have quieted (WIN, WIN, AND WIN!).

Jimmy is a good example of a typical patient many of us who specialize in the care of pediatric patients see in clinic. While we can't always reverse the momentum of the atopic march in our patients, by providing anticipatory guidance, we can at least make families better prepared for the future if and when specific symptoms arise. This sort of education can sometimes also motivate families to follow initial AD management plans to help heal their child's impaired skin barrier and perhaps interrupt the allergic cascade. There are some basic tenets we should all be mindful to recommend, such as the early introduction of common food allergens. In this way, we can hopefully maximize the wins and minimize the losses.

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# ***Prevention and Treatment of Infections in Atopic Dermatitis:***

## **An Evidence-Based Approach**

by Noreen H. Nicol, PhD, RN, FNP, NEA-BC

Skin, soft tissue, and systemic infections are common comorbidities of atopic dermatitis (AD), found more commonly in patients with the condition than those without AD.<sup>1</sup> One recent review of infectious complications of AD highlights major predisposing factors that likely contribute to this increased prevalence, including skin barrier defects, suppression of cutaneous innate immunity by type 2 inflammation, *Staphylococcus (S.) aureus* colonization, and cutaneous dysbiosis.<sup>2</sup>

AD is characterized by complex immune dysregulation that occurs in genetically predisposed individuals with a defective skin barrier and modified immune responses to the invasion of irritants, allergens, and microbial organisms.<sup>3</sup> Patients with AD have an abnormal skin barrier function that is associated with abnormalities in cornified envelope genes, reduced ceramide levels, increased levels of endogenous proteolytic enzymes, and enhanced transepidermal water loss.<sup>4</sup> This compromised skin barrier accelerates the loss of moisture on the skin surface and creates dry, easily irritated, pruritic, and hypersensitive skin. In this state, the skin is more prone to infections with bacteria, fungi, or viruses, along with inflammation due to irritants and allergens that can contribute to the frequent itching we see so often in patients with AD.

One of the most important reminders we can give our patients and their families is that even if skin is not visibly flaring, it is still compromised and requires



### **AUTHOR:**

**Noreen H. Nicol, PhD, RN, FNP, NEA-BC**, is Associate Professor Emerita at the University of Colorado School of Nursing in Aurora, CO



appropriate daily skin care. Evidence suggests that non-lesional skin can share many of the immunological features, microbiome alterations, and biomarker changes seen in lesional skin.<sup>5-7</sup> Primary goals of AD therapy and infection prevention should be to repair the skin barrier through use of anti-inflammatory therapy with minimal use of antibiotics.<sup>2</sup>

Many different infections commonly occur in patients with AD. These infections include impetigo, cellulitis, and skin abscesses. *S. aureus* is the most common cause of these bacterial infections. Impetigo may present with honey-colored, crusting or fluid-filled blisters (bullous impetigo). When *S. aureus* is the primary responsible pathogen, nasal decolonization with intranasal mupirocin 2% ointment twice daily for 5-10 days can be helpful. Because of the similarity of their names, patients frequently confuse intranasal mupirocin 2% ointment (Bactroban®) with bacitracin. I have often had patients and parents complain to me that their child's infection wasn't improving following 5-10 days of topical bacitracin administration, which requires a delicate reminder that they have been using the wrong agent.

Other, nonprurulent skin infections that may be seen in patients with AD include erysipelas and cellulitis. Skin abscesses, which may be warm and tender to the touch, are frequently caused by methicillin-resistant *S. aureus*. Herpes simplex virus (HSV) is the most common viral infection found in patients with AD. These infections can be localized to skin covering small areas of the body or widespread. Broader HSV is more commonly known as eczema herpeticum. While systemic bacterial infections and eczema herpeticum can be life-threatening, their prevalence in patients with AD is fortunately low.<sup>4</sup> Molluscum contagiosum is another skin infection seen in some patients with AD. This infection, spread by autoinoculation, is due to a poxvirus.

Because the majority of skin infections are spread by direct contact with contaminated secretions of the pathogen, it is important to discuss with patients and their families the importance of minimizing household skin-to-skin contact when an infection arises. When an infection is localized, covering the weeping or open wound with a clean bandage may prevent the spread and secondary transmission of the infection.

## THE ROLE OF PATIENT EDUCATION IN REDUCING INFECTION RISK

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Individualized educational interventions have long been recommended and used as a critical adjunct at all levels of therapy for patients with AD to enhance therapy effectiveness and increase topical regimen adherence.<sup>8</sup> Unfortunately, time constraints often limit our ability to educate and reinforce education with many patients and their families, and adherence is difficult to assess and evaluate. Additionally, with variations in many facets of therapeutic recommendations within individual practices, patients who transition between practices may become confused about changing skin care instructions. It is important to remember to explain to patients the chronic relapsing nature of the disease and to be mindful that the deterioration in a previously stable patient with AD may result from secondary bacterial or viral infection, development of contact allergy, poor adherence to recommended treatment, or other factors.

In the next section of this essay, we'll look at some of the scientific evidence that supports many of the bedrocks of AD care. Table 1 includes an adaptation of a patient education worksheet our team used at National Jewish Health in Denver, CO, in the AD Program for decades.<sup>9</sup>

## DEVELOPING STRATEGIES USING PUBLISHED GUIDELINES

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Successful strategies for managing the spectrum of AD, including infection control, requires a systematic, multipronged, stepwise approach based on disease severity and impact on quality of life. Numerous national and international guidelines address the importance of foundational skin care regardless of disease severity, emphasizing the use of moisturizers as the cornerstone of AD management.<sup>10-18</sup> According to these guidelines, a multidisciplinary, preventive approach aimed at minimizing flares that incorporates the use of behavioral health strategies (as appropriate) should be recommended.<sup>3,19</sup> Treatment plans should be individualized to address each patient's skin disease reaction pattern, and moderate to severe AD management requires special attention.<sup>20</sup>

**TABLE 1**  
**Foundational Daily Skin Care Recommendations for AD Patients**

1. Take at least one bath or shower per day in plain warm water (not hot, not lukewarm) for 10-15 minutes.
2. Use a gentle cleansing bar or wash that is fragrance-free, dye-free, and has a neutral-to-low pH.
3. Use dilute bleach baths (¼ cup sodium hypochlorite per tubful of water) once or twice weekly with skin infection, and only when recommended by your healthcare provider.
4. After bath/shower, pat away excess water and immediately (within 2-3 minutes) apply recommended moisturizer(s)
5. Use recommended moisturizers at least twice daily and as often as needed throughout the day. Recommended moisturizers may include Aquaphor® Ointment, Eucerin® formulations, Vanicream® formulations, Vaniply®, CeraVe® formulations, and Cetaphil® Cream. Vaseline® is a good occlusive preparation to seal in the water, but it is only effective after a bath or shower. Moisturizers and sealers should not be applied immediately over any topical medication. Avoid contamination of topicals moisturizers and medications by using pumps, tubes, or pour containers. If scooping product from jars, use a disposable scoop with each dip from the jar.
6. Apply topical corticosteroids (TCS), topical calcineurin inhibitors (TCI), or other medications as recommended by your healthcare provider. Many of these agents may decrease inflammation, reduce *S. aureus* bacterial load, and repair the skin barrier.

In general, these guidelines emphasize the following:

1. In conjunction with warm baths or showers, patients should apply moisturizers frequently and liberally to repair the skin barrier.
2. Providers should help patients identify and avoid common AD irritants or infections, temperature extremes, and proven allergen triggers.
3. Appropriate to the severity of a patient's disease, maintenance with topical corticosteroids (TCS) or other therapeutic agents may be initiated in a stepwise fashion.
4. During AD flares, TCS and/or topical calcineurin inhibitors (TCI) should be prescribed.
5. Wet wrap therapy may be used in conjunction with TCS (but not with TCI), oral antibiotics, and other oral agents.<sup>21,22</sup>
6. Clinicians should be mindful of research regarding newer biologic agents and other therapies, especially for patients with moderate-to-severe disease who do not respond to more conservative methods.

## FOUNDATIONAL SKIN CARE RECOMMENDATIONS

### BATHING

Bathing and/or showering play a key role in general hygiene and are especially important in patients with AD. Bathing may also remove allergens and irritants from the skin surface and reduce general colonization or serous crusts by *S. aureus*. That said, the debate about the appropriate frequency, duration, and routine of bathing in patients with AD has been ongoing for more than a century. Depending upon how water is used, it can either be deemed “good” or “bad” for the skin. One generally accepted theory asserts that microfissuring and evaporation occur when wet skin is not immediately covered by a protective layer of moisturizer, occlusive, or medication. Some researchers have, in fact, argued that avoiding water altogether leads to better outcomes in patients with AD due to poor adherence to proper use of an appropriate sealer immediately after bathing.<sup>23</sup>

**TABLE 2****General Tips for Patient Skin Health to Decrease Skin Irritation and Infections**

1. Practice daily foundational skin care as outlined in Table 1

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2. Avoid skin irritants and proven allergens

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3. Allow a seasoned provider to perform a comprehensive evaluation and correlate individual clinical symptoms through skin, blood, and/or patch testing. Avoid unnecessary restrictions in lifestyle.

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4. Promote good personal hygiene practices, including frequent handwashing with appropriate cleanser or alcohol-based sanitizer

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5. Keep fingernails very short and smooth to help prevent damage due to scratching and spreading of infection. Wear gloves or socks on hands over moisturizers at bedtime when skin is itchy.

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6. Avoid sharing or reusing personal items that contact the skin, including razors, cosmetics, brushes, and towels

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7. Wear garments that allow air to pass freely to the skin such as open weave, loose-fitting, cotton, cotton-blend, or silk clothing. Avoid itchy fabrics. Wear tag-free clothing or remove tags before wearing.

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8. Wash all new clothes before wearing them to help remove formaldehyde and other irritating chemicals

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9. Wash all towels and washcloths, clothing, and bedding on a regular basis, preferably before each reuse. When possible, use hot water, especially when signs of skin infection are present.

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10. Add a second rinse cycle to ensure removal of residual detergent, dyes, or perfumes as these may be irritating when they remain in the clothing. Changing to a liquid and fragrance-free, dye-free detergent may be helpful.

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11. Clean high-touch surfaces regularly with disinfectants. Change or clean vacuum, furnace, and air conditioner filters often.

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12. Carry a small tube of moisturizer and/or sunscreen at all times. Supply moisturizer or sunscreen to daycare/school/work. Consider physical sunscreens containing zinc oxide or titanium dioxide to avoid chemical or allergen irritation.

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13. Try small amounts of any new products on small areas of the skin before general use to avoid unnecessary disease flares

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14. Shower or bathe using a gentle cleanser to remove chemicals after swimming in chlorinated pools or hot tubs before applying recommended moisturizer

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15. Work and sleep in comfortable surroundings with a fairly constant temperature and humidity level. Get adequate amounts of sleep.

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The “soak and seal” (sometimes called “soak and smear”) method has been used as a fundamental concept in bathing for more than three decades within our AD program.<sup>3,9,11,24</sup> It involves bathing in warm water for 5-10 minutes, gentle drying of the skin, and then immediate application of a topical moisturizer. This approach leads to rehydration of the skin, sealing in of moisture, and repair of the epidermal barrier.<sup>25-28</sup> The “soak and seal” method can be utilized by every patient with AD regardless of disease severity and use of other therapeutic modalities. Soaps and cleansers used in the bath should be hypoallergenic, fragrance-free, and have a neutral-to-low pH.

## BLEACH BATHS

Bleach (sodium hypochlorite) baths are widely available over the counter, which has likely contributed to their being frequently recommended as low-cost adjuvant therapy in patients with AD. Many current AD treatment guidelines include bleach baths among their recommendations, although data supporting their efficacy and safety in treating AD remains uncertain.<sup>29,30</sup> Bleach baths are thought to reduce skin inflammation and thereby slightly decrease colonization of *S. aureus* bacteria on the skin. This can be beneficial as staphylococcal exotoxins are known to exacerbate AD, and severity of AD correlates with *S. aureus* density on the skin.<sup>31</sup> Patients with AD whose disease is moderate-to-severe and complicated by recurrent skin infections—especially patients with methicillin-resistant *S. aureus*—may benefit from a trial of once- or twice-weekly dilute bleach baths. Bleach baths can also be used as part

of a decolonization protocol.<sup>2</sup> Common side effects of bleach baths include increased xerosis and irritation of skin and nasal passages.

## MOISTURIZERS

Moisturization is another core tenet of AD treatment, with all international treatment guidelines recommending thorough moisturization of both lesional and non-lesional skin at least on a daily basis. Twice-daily moisturizer use is encouraged. While moisturizers alone are not effective for the comprehensive treatment of severe AD, their use may reduce disease severity and signs of inflammation, including pruritus, erythema, fissuring, and lichenification.

Underuse of recommended moisturizers is a widespread problem among patients with AD, with one large-scale study from the United Kingdom finding that real-world emollient use is 4-fold lower than the amount recommended in clinical guidelines.<sup>32</sup> For total body coverage, an average-sized adult requires 15 to 30 g (½ to 1 oz) of moisturizer applied front and back, head to toe.<sup>33</sup> Ultimately, moisturizer selection is an individual choice, but surprisingly few moisturizers have published efficacy and acceptability data to support decision-making, and all moisturizers are not created equal.<sup>34-36</sup> In clinical trials, therapeutic moisturizers developed specifically for the treatment of AD have demonstrated improved skin barrier and reduced incidence of flares.<sup>36</sup> With so many products available, a recommendation by a healthcare provider is an important factor in moisturizer selection.<sup>37</sup>

## CONCLUSION

Infectious complications are common in patients with AD. Reinforcing a “back-to-basics” skin care approach emphasizing hygiene measures and appropriate moisturizer use can strengthen the skin barrier and help reduce AD symptoms and infection risk. Clear, practical, evidence-based messaging must be delivered to patients and families to reinforce the basic fundamentals of care.

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# ***The Bidirectional Relationship Between Atopic Dermatitis and Mental Health Conditions***

by Patricia Delgado, DNP, AGPCNP, DCNP

As dermatology providers, we always have to focus on management of the whole patient during our clinical assessment. While it is true that our specialty is one in which we can visibly see many of our patients' health manifestations, there are also many unseen consequences that need to be managed. Primary among these are mental health disorders, which are often underappreciated but significantly debilitating comorbidities of conditions such as atopic dermatitis (AD).

Here is just one of many recent examples from my practice highlighting the intersection of these conditions.

Tanisha was a 12-year-old Jamaican black female patient who presented to our clinic for evaluation of her AD, which had been present since infancy. Tanisha's previous dermatologist had recently stopped accepting her mother's insurance, forcing her to switch practices. When we met, Tanisha was in the midst of a disease flare, which she said happened "every year or two." Upon physical exam, she had mildly erythematous, dusky, excoriated patches with moderate lichenification on her bilateral antecubital and popliteal spaces. Her skin was dry and rough upon palpation.

During my initial conversation with Tanisha and her mother, Tanisha was constantly scratching and couldn't sit still. Both she and her mother appeared to be on edge, wary of this initial interaction with a

## **AUTHOR:**

**Patricia Delgado, DNP, AGPCNP, DCNP**, is the Founder and CEO of Sunrise Skin and Wellness LLC, in St. Petersburg, FL, as well as an Adjunct Professor at the University of Central Florida in Orlando, FL



new provider after many years with their previous dermatologist. This isn't uncommon. Many of our pediatric patients become quite attached to their providers who have helped manage their disease for as long as they can remember being alive. It can be uncomfortable for all parties during the transition, especially one forced by insurance issues.

Consequently, I probed carefully, getting more insight into Tanisha's history and her current issues. I knew it was important during this initial conversation to explore multiple factors related to the well-being of both Tanisha and her mother, especially considering the tension in the room. We talked about the last time Tanisha's skin had been clear ("at least 6 months," they told me), strategies they had used over the years that had worked for them ("a few topical creams, but never for very long"), and if Tanisha had historically been fidgety and unable to sit still for long periods of time ("yes, and it's gotten worse recently"). Had she ever been diagnosed with ADHD ("no, we always just assumed this was because of her eczema")?

This is something I hear frequently from my pediatric patients and their parents. Attention deficit hyperactive disorder, or ADHD, is marked by an ongoing pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development. People with ADHD experience an ongoing pattern of inattention, hyperactivity, and impulsivity that is not due to defiance, incomprehension, substances, or other medical conditions.<sup>1</sup> In the majority of cases, symptoms emerge in early childhood.

AD and ADHD have a bidirectional relationship, meaning that AD can contribute to ADHD, and vice versa. This is why, just as psychiatrists need to know a patient's euthymic baseline, we need information about what our patients are like when their AD is not flaring. I could see in front of me that Tanisha expressed many visible signs of ADHD, but not until I learned how things were different in non-emergent situations could I make any sort of educated conclusion regarding the need for a potential psychiatric referral. In some of our patients, it's the itch and uncomfortable nature of AD that causes their inattentiveness and impulsivity and not an underlying mental health condition such as ADHD. We have all seen patients with AD whose itch is so severe that it

distracts them from whatever task they are trying to complete or even engaging in a conversation. While their scratching may appear to the untrained eye to be impulsive, the patient simply may not be able to control their behavior due to their AD and itch symptoms. Uncontrollable itch is also a common contributor to sleep deficiencies, which can certainly affect a patient's ability to concentrate throughout the day.

If a patient with AD does in fact have ADHD, medically treating their AD symptoms may not actually help with their scratching behavior. In these instances, the chronic scratching or rubbing behavior may be more closely tied to the patient's impulsivity and hyperactivity related to their ADHD and not their eczema. As dermatology clinicians, it is critical to keep these ties between mental health and skin diseases in mind for our patients whose presentation requires a multidisciplinary approach to two additive, comorbid illnesses.

While we needed to do further assessment beyond Tanisha's initial visit to determine whether or not she had ADHD in addition to her AD, I took the time to educate her and her mother about some of the lifestyle changes she might want to make at home to help her sensitive skin. This was information they told me they had not been told by their previous dermatology providers. We also set a medical treatment plan for her current disease flare and developed a potential escalation plan in case Tanisha's breakthrough flares continued to impede her quality of life.

On her initial follow-up visit 3 weeks later, Tanisha was less distractible, and she was able to refrain from scratching during most of the appointment. Her mother also reported that her scratching behavior at home had decreased since they implemented the lifestyle changes I recommended and began the medication regimen. Her recent test scores at school had improved slightly, although her teachers still reported the need to interrupt class to quiet Tanisha down from time to time. Tanisha remained her bubbly self and enjoyed interacting with me, but also seemed to be able to focus more on our conversation and answer my questions more directly. As it turns out, by better controlling her AD symptoms and improving her nightly sleep, Tanisha's fidgety and impulsive behaviors had also quieted down, making



a need for a formal ADHD assessment less urgent. Her improvement was significant enough that we were able to push her next follow-up appointment to 3 months out. However, I did note for Tanisha's mother that if any distractible behavior continued at school and home, she should see a mental health specialist for further evaluation.

Of course, ADHD isn't the only mental health disorder we need to be mindful of in our patients with AD. Research has shown that there is a higher prevalence of conditions such as generalized anxiety disorder and major depressive disorder in patients with AD as well.<sup>2-4</sup> Symptoms of these conditions can also overlap with those found in patients with AD and may exacerbate the disease itself. Unless we are able to help patients and their families identify and then address these comorbidities, patients may get stuck in the revolving door of our U.S. healthcare system. Between 2002 and 2012, it is estimated that patients with AD required \$183 million in excess costs related to hospitalization for mental health disorders compared to patients without AD.<sup>5</sup>

Broad meta-analyses have shown that AD in general is associated with significantly impaired quality of

life, sleep disturbances, perceptions of stigmatization, anxiety, and suicidality.<sup>6</sup> Some of these associations may be attributable to shared inflammatory pathways and over-secretion of pro-inflammatory cytokines such as interleukin (IL)-1, IL-6, and tumor necrosis factor. The presence of these cytokines in the circulatory system penetrate the blood-brain barrier and affect the gene expression in neuronal networks, potentially increasing the risk for mental health disorders.<sup>7</sup> Other shared biological factors, including excessive histamine production, genetic predisposition, and the psychological impact of living with AD, may also explain the higher prevalence of mental health disorders in individuals with AD.

Making an assessment of potential mental health disorders in patients with AD is not easy. It requires all of us to exercise our critical thinking skills to interpret the presentation of patients and assess our findings. Certainly, it will be important to follow the research in this emerging area to help develop appropriate treatment regimens that better address the whole patient.

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# ***Atopic Dermatitis and Autoimmune Disease: What You Should Know***

by Keischa Cash, DNP, APRN, DCNP, FNP-BC

Atopic dermatitis (AD) is a common condition that affects up to 20% of children and between 7% to 10% of adults. It is primarily considered to be a T-helper cell 2 (Th2) lymphocyte mediated skin disease, although other lymphocytes such as Th1, Th17, and Th22 have been found to have activity in patients with AD. In addition to their role in the development and progression of AD, these lymphocytes are also associated with the development of other autoimmune conditions, potentially hinting at a potential mechanism behind the underlying association between AD and autoimmune disease.<sup>1</sup>

So what does this mean for us as dermatology providers? Essentially, our patients with AD have a higher prevalence and incidence of a comorbid autoimmune disorder than the general population simply by having AD.

Recent research has shown that patients with AD not only have an increased risk of common autoimmune disorders such as rheumatoid arthritis (RA) and inflammatory bowel disease (IBD), but also less frequent conditions such as psoriatic arthritis, Sjögren's syndrome, vitiligo, alopecia areata (AA), pernicious anemia, celiac disease,

and autoimmune hypothyroidism. It should also be noted that there is some good news, as patients with AD do not appear to have an increased risk of developing type 1 diabetes, Graves' disease, ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), or multiple sclerosis (MS).<sup>2</sup>

It is important for providers to be aware of these associations (and lack thereof) when managing the care of patients with AD as both our older and newer treatments not only may impact the symptoms of AD but can also affect comorbid atopic, allergic, and autoimmune conditions as well.<sup>3</sup>

One of my personal recent interests is the association between AD and AA, as this is an area where I have seen several challenging patients. According to a recent study by Thyssen et al, the odds of patients with AD developing AA are particularly high—perhaps increased by as much as 10-fold—among those individuals with a flaggrin gene mutation. Interleukin 13 (IL-13) has also been shown to have a strong genetic association with AA and atopy.<sup>3</sup>

As you can imagine, the quality-of-life impact of comorbid AA and AD is significant. These are patients with not just one, but two, visible skin conditions that are not well understood in the general public. KayCee is one of my recent patients who has had to deal with this “double trouble.” She presented to me a few months ago as a 34-year-old female with a history of AD and allergic rhinitis since childhood that were both under reasonably good control. Her newest and more concerning symptom was patchy hair loss that had become increasingly notable over the last few months.



#### **AUTHOR:**

**Keischa Cash, DNP, APRN, DCNP, FNP-BC**, is a Dermatology Nurse Practitioner at DNP Derm LLC in Tampa, FL

KayCee was initially alerted to these patches by her stylist, but quickly began noticing clumps of hair falling out in the shower. These bare patches were well defined and smooth to the touch. KayCee said that there was no pain or itching associated with her hair loss, and that she otherwise felt fine. Upon visual observation, her hair was noticeably thinner in several spots, as were her eyebrows and eyelashes.

KayCee scheduled an appointment with our practice after becoming increasingly more alarmed week after week with her progressive hair loss. She told me that the eczematous lesions on her arms and legs associated with her AD had become easy to conceal over the years, but that it was becoming more and more difficult to conceal her hair loss. She expressed concern about wearing a wig in public, afraid that others would notice and even more unwanted attention would be drawn to her. Hair extensions were no longer an option due to KayCee's rapidly thinning hair that would make the extensions quite visible.

So then where to begin with a patient like this? First, I explained to KayCee why her history of atopic diseases (in this case, AD and allergic rhinitis) put her at increased risk for the development of AA and other autoimmune disorders such as vitiligo, inflammatory bowel disease, and rheumatoid arthritis. Next, we talked about some possible therapeutic approaches that would address both her atopic conditions and her patchy hair loss (which we suspected and later confirmed was AA). After careful consideration of the pros and cons of various regimens, KayCee agreed to a trial of baricitinib, a Janus kinase inhibitor approved for the treatment of AA that has also demonstrated efficacy in the treatment of AD.<sup>4</sup> We agreed upon an initial follow-up in 2 months.

At her initial follow-up, KayCee said she felt fine on the medication and reported no adverse effects. Her hair shedding had begun to taper off within 2 weeks of initiating baricitinib, and she was hopeful that continuing treatment would mend the patches of hair loss and stimulate growth of her eyelashes and eyebrows (there was not yet any progress in this area, and eyelash extensions were not an option because there was no hair to attach them to).

It was clear that KayCee was dually hopeful and frustrated. Hopeful because things were no longer getting worse but frustrated because neither were they getting better. She told me repeatedly that she “just wanted to feel normal again.” KayCee felt that hair and eyelash extensions were the quickest way to get there, and she was devastated to be told repeatedly that they weren't currently an option by her stylist and beauty professionals. It's not easy to be a motivated patient in this state, but I did my best to acknowledge KayCee's feelings and encouraged her to stick with her treatment regimen for another few months to hopefully see her AA start to turn around. Of course, in the back of my mind, I was wary of the appearance of another autoimmune condition in the future, so I also encouraged KayCee to see her primary care clinician for routine physicals and wellness exams.

Motivating patients with one chronic disease can be a challenge, but when two or more are thrown into the mix, it can be an even greater burden to overcome. We fortunately have more—and better—tools to throw at some of the more common comorbidities that demonstrate the ability to stabilize and potential reverse the damage.

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435 N. Bennett Street  
Southern Pines, NC 28387

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**[www.dnanurse.org](http://www.dnanurse.org)**

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