A topic dermatitis (AD, also called eczema) is a common, chronic, pruritic, and inflammatory disease. For individu-
als with AD, it is associated with significant impairments in quality of life, sleep patterns, and psychosocial functioning, as well as comorbidities (such as secondary bacterial and viral infections) and other atopic diseases (such as asthma, allergic rhinitis, and extrinsic allergies).

Depending on definitions and study methodologies, estimates for the prevalence of AD vary from 10% to 20% of the total pop-
ulation. However, it most commonly occurs in children, and up to 90% of pediatric patients are diagnosed by 5 years of age. The disease is characterized by pruritus and erythematous, inflamed eczematous papules and plaques, often with a severe exudate (Figure 1). The pruritus may be intense and lead to a cycle of itch-
scratch-itch that exacerbates the patient’s already compromised barrier function and cause the dry skin, inflammation, and decreased NMF that characterize AD.

In addition to filaggrin mutations, lipids and other components of the epidermal barrier play a role in maintaining skin barrier integrity. Of these, ceramides have been shown to be of great importance. Ceramides are combinations of fatty acids and a sphingoid base, and account for 50% of intracellular lipids. Reductions in ceramides disrupt the balance between the other lipids and account for 50% of intracellular lipids. Reductions in ceramides disrupt the balance between the other lipids and cause the dry skin, inflammation, and barrier dysfunction that characterize AD. Filaggrin is a central actor in the maintenance of stratum corneum integrity, and mutations predispose individuals to AD and other cutaneous diseases (Figure 2). To date, almost 50 loss-of-function mutations have been identified. All are nonsense or frameshift mutations that truncate the profilaggrin molecule. 4-6 Mutations range from deficiencies and mild filaggrin dysfunction to a complete absence of filaggrin. All mutations undermine barrier function and cause the dry skin, inflammation, and decreased NMF that characterize AD.

Filaggrin is a function that contributes to maintaining skin barrier integrity. In the inner stratum corneum, within the cytoskeleton of keratinocytes, filaggrin aggregates to form corneodesmosomes that are intact throughout the stratum corneum. At the surface, the corneodesmosomes start to break down as part of the normal desquamation process, analogous to in situ
maturity. In an individual genetically predisposed to AD (panel B), corneodesmosomes progressively break down, leading to increased desquamation and weakening the barrier. The protein-lipid cornified cell envelope—a barrier that is permeable to water but blocks microbe, allergen, and irritant infiltration.7 During desquamation of the outer stratum corneum, filaggrin is a source of amino acid degradation products, known as natural moisturizing factor (NMF), which contribute to the hydration of these outer layers and likely contribute to the acid mantle. Along with stratum corneum lipids, NMF has a significant influence on water flux and retention in the skin.

Genetic Underpinnings of AD
AD often coexists with atopy and allergic rhinitis, and extrinsic allergies). Understanding how the disease manifests and its under-
stood, emerging research indicates important genetic components (epidermal barrier, facilitating water loss, dry skin, and infection.

Figure 1. Typical Cutaneous Signs of Childhood Eczema

<table>
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<tr>
<th>Panel A</th>
<th>Panel B</th>
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<td>In healthy skin (panel A) the corneodesmosomes (shown as iron rods) are intact throughout the stratum corneum. At the surface, the corneodesmosomes start to break down as part of the normal desquamation process, analogous to in situ maturity. In an individual genetically predisposed to AD, corneodesmosomes progressively break down, leading to increased desquamation and weakening the barrier, allowing penetration of environmental agents like Gmail, fungal spores, and allergens, as well as filaggrin and microbial components that increase the risk for secondary infection (panel B).</td>
<td>The face is often the first area to be affected in infants (panel A), and the forearm is a commonly affected area in older children (panel B). Photos courtesy of Lawrence E. Eichenfield, MD.</td>
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Figure 2. Stratum Corneum Disruption in Atopic Dermatitis

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<th>Panel C</th>
<th>Panel D</th>
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<td>Reprinted with permission from Gott MJ, Robinson DA, Vedepoob V, et al. J Allergy Clin Immunol. 2001;108:13-21.</td>
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Management Strategies
AD cannot be cured. However, it can be effectively managed with a combination of good bathing habits, avoidance of known irritants and allergens, routine and sufficient application of base therapy (moisturizers, emollients, and barrier creams), and early symptom recognition. As symptoms emerge and AD flares, topical corticosteroids and anti-inflammatory agents can be added until symptoms regress. Patients with severe disease may require more potent anti-inflammatory agents, including intermittent topical corticosteroids, calcineurin inhibitors, and other adjuvant therapies. Patients should be monitored for infections and treated with systemic and/or topical antimicrobial agents as needed. Bathing habits may be used for patients with high rates of colonization. The most severely ill patient may require phototherapy or systemic anti-inflammatory therapy. Education and patient self-care practices are essential for controlling AD. Internet resources such as the Rudy’s Children’s Hospital’s Eczema Center (www.eczema.org) and NAEFS (www.nationaleczema.org) are reliable and useful.

Conclusions
AD is caused by fundamental genetic defects in skin barrier func-
tion. These underlying causes emphasize the pressing need for developing and correctly using topical products that restore skin barrier function and strategies and overall good skin care. A variety of products are available to minimize the dryness, pruritus, and inflammation that individuals with AD suffer, and they are associated with improved quality of life.

References