Pre-Meeting Preparation:
Please read/review the following enclosures:
- “Atopic Dermatitis and Ichthyosis” (PIR 2010)
- "Clinical Report Atopic Dermatitis: Skin-Directed Management" (Pediatrics, 2014)
- “Mechanisms of Atopic Disease” (cartoons from NEJM 2011)
- “Treatment of Atopic Dermatitis”:
  o Atopic Dermatitis Action Plan
  o Prescribing Tips: Steroids & Moisturizers on Formulary, FTUs
  o Home Remedies: ( “Management of Atopic Dermatitis” Pediatrics, 2008)

Conference Agenda:
- Review Atopic Dermatitis Quiz
- Complete Atopic Dermatitis Cases
- Round table: Compare moisturizers and topical corticosteroids on formulary. Discuss potential benefits and drawbacks. *Samples will be provided*

Post-Conference: Board Review Q&A
Extra-Credit:
- "Emollient enhancement of the skin barrier from birth offers effective atopic dermatitis prevention" (2014)
- Petroleum Jelly for Neonates? (JAMA Pediatrics, 2016)
- “Management of Atopic Dermatitis in the Pediatric Population” (Pediatrics, 2008)
- “Complementary, Holistic, and Integrative Medicine: Atopic Dermatitis” (PIR, 2007)
- New Atopic Dermatitis Treatments (Medscape, 2017)

Resources for Patients/Parents:
- [http://www.nationaleczema.org](http://www.nationaleczema.org) (educational videos, support group, etc.)
- Eczema Action Plan

Atopic Dermatitis and Ichthyosis

Roselyn E. Epps, MD*

**Author Disclosure**

Dr Epps has disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

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**Objectives**

After completing this article, readers should be able to:

1. Identify the characteristic features of atopic dermatitis and the factors that worsen it.
2. Understand that children who have atopic dermatitis are prone to recurrent infections, particularly with *Staphylococcus aureus* and herpes simplex virus.
3. Know the signs of Wiskott-Aldrich syndrome.
4. Plan the appropriate treatment of atopic dermatitis (emollients, corticosteroids, antibiotics, and allergen elimination when appropriate).
5. Recognize ichthyosis vulgaris and know that ichthyosis commonly occurs in children who have atopic dermatitis.
6. List the effective therapies in the management of ichthyosis vulgaris.
7. Distinguish between tinea pedis and atopic dermatitis.
8. Discuss the relationship of atopic dermatitis and food allergies and how to evaluate a patient who has both.
9. Explain why children who have one component of atopy syndrome (allergic rhinitis, asthma, atopic dermatitis) have a threefold greater risk of developing a second component.

**Atopic Dermatitis**

Atopic dermatitis (AD) is a chronic, relapsing dermatosis that features dry skin (xerosis), pruritus, and a personal or family history of eczema, allergic rhinitis or allergies, or asthma. Children who have one component of the atopic triad (AD, asthma, allergic rhinitis) are three times as likely to develop a second component. There is no sex predilection, and the onset frequently is in infancy. Although many affected children outgrow the condition by age 5 years, AD may persist into adolescence and adulthood. A smaller percentage of patients experience the onset of AD as older children or in adulthood.

The incidence and prevalence of AD have increased in the United States and worldwide, particularly in developed nations. Fewer than 10% of children were affected in the 1970s, but recent epidemiologic studies estimate that 15% to 20% of children are diagnosed with AD. The reason for the increased rate is unknown. The “hygiene hypothesis” proposes that decreased exposure to infectious and biologic antigens may result in an increased response to environmental antigens or perhaps to decreased immune suppression. Additional research must be conducted to determine the reasons for the increased prevalence and to address the trend.

**Pathophysiology**

Manifestations of AD are believed to be due to the interaction of certain genes, the environment, and immunologic response to the environment and specific trigger factors. Patients who have AD may be considered to have systemic changes, not just manifestations in the skin. Susceptible individuals can react to internal and environmental triggers in certain target organs, not only resulting in skin eruptions, but also in asthma and allergic rhinitis. Patients may exhibit extrinsic immunoglobulin E (IgE)-mediated sensitization due to external antigens, with allergic signs and elevated allergen-specific IgE, or intrinsic sensitization, without IgE-mediated sensitization.

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In acute AD lesions, T-helper 2 (TH2) cells are present in larger numbers than normal and have increased expression of specific cytokines that, in turn, stimulate B cells to produce IgE, resulting in peripheral eosinophilia. Cytokines and chemokines are released from cells in the skin, attracting other inflammatory cells and producing inflammatory mediators and reactions. Keratinocytes, Langerhans cells, endothelial cells, monocyte-macrophages, and eosinophils all play roles in the acute and chronic inflammation of AD.

Clinical Manifestations
Generally, the primary lesion is a red, rough, poorly defined dry papule or plaque. Scaling may be seen. There is no central clearing. In children of color or deep pigmentation, plaques can be papular or follicular, especially on the trunk or over the extensor areas of joints.

AD is diagnosed clinically and manifests particular patterns at different ages. Frequently, infants present with rough patches or plaques on the cheeks, the dorsa of the wrists, the ankles, and the lateral extremities. The perioral and diaper areas customarily are spared. After infancy, children develop flexural involvement, and the cheek areas improve. The neck, antecubital and popliteal fossae, and gluteal folds frequently are involved (Fig. 1).

Teenagers are more likely to experience eyelid eruptions. With age, the hands and feet also become more problematic, and AD may present as dyshidrotic eruptions. Any part of the body, from the scalp to the soles and including the lips and genitalia, may be affected at any age. Eruptions occur whether or not an offending factor or trigger is identified. Exacerbations and remissions are common and to be expected.

Secondary skin changes occur frequently. Oozing, weeping, and crust formation can develop, which may represent secondary infection. Hyperpigmentation as well as hypopigmentation and depigmentation (loss of pigmentation) can occur. Normal color of the skin usually returns when the signs and symptoms of AD resolve. Weeks to months may be required for the hyperpigmentation and hypopigmentation to resolve. If excoriations are deep or the inflammation is severe, scarring or depigmentation can be permanent.

Lichenification, a hallmark of AD, is thickening and accentuation of skin markings due to chronic scratching. Lichenified skin on the hands and feet is more likely to fissure. Excoriations are common, and some patients create erosions and deeper wounds by unremitting, intense, repeated trauma. Repeated friction and trauma promote inflammation and trigger inflammatory reactions and pathways in affected skin. Lichenification also may occur in other dermatologic conditions that feature chronic scratching and pruritus.

Friction on the skin and scratching the skin are known to exacerbate pruritus and can initiate the “itch-scratch cycle,” in which the child scratches, itching in the involved area increases, the child continues to scratch, and the cycle continues. Plaques, papules, and nodules can result because of the escalating “itch-scratch cycle.”

Secondary Infection
Patients who have AD are more likely to develop skin and possibly systemic infections. One reason superinfection occurs more easily is due to altered skin barrier function, including apparent and imperceptible excoriations, fissures, and skin defects (Fig. 2). For patients who have AD, seemingly uninvolved skin is not normal. In addition to greater irritancy and dryness, there are immunologic differences in the type of TH2 cells and an increase in the number of TH2 cells within the skin. Staphylococcus aureus is an important cause of superinfection. S. aureus colonization by age 6 months, with frequent
Colonization during the first year after birth, is associated with an increased prevalence and severity of AD. Impaired skin barrier function, a defective host immune response, and increased synthesis of extracellular matrix adhesion substances promote *S. aureus* colonization.

Exotoxins secreted by *S. aureus* penetrate the skin barrier and stimulate T cells and antigen-presenting cells, thereby exacerbating and contributing to persistent skin inflammation. *S. aureus* overgrowth and superinfection can result in flares, impetigo, folliculitis, cellulitis, abscesses, bacteremia, and sepsis. Methicillin-resistant *S. aureus*, now more common in the community, can be particularly problematic for patients who have AD and their families. The patient’s infection must be treated, and treating the family may be necessary to minimize the risk of AD exacerbation in the patient. The clinician should consider culturing the atopic patient who is febrile, is unresponsive to therapy, or shows an inadequate response to maximized treatment that includes antibiotic therapy. Other bacteria also may be cultured from the AD patient’s wounds and should be treated accordingly.

Although patients who have AD develop bacterial infections, they also may acquire viral and fungal infections. Eczema herpeticum occurs when AD is superinfected with a herpesvirus, either herpes simplex virus or varicella-zoster virus. Vesicles develop on affected and apparently unaffected skin and can be very painful. When disseminated, there may be associated viremia, fever, and lymphadenopathy, and patients can become very ill. Occult involvement may occur innocuously when the patient rubs his or her eyes. Acyclovir should be administered intravenously in critical disseminated infections or orally for localized, recurrent infections in patients who have AD. If herpesvirus infection involves the eye or periorcular area, ophthalmology consultation is essential to manage herpes keratitis and to prevent permanent loss of vision.

Dermatophytes and yeast also can superinfect the skin. Patients who have AD can develop tinea capitis and tinea pedis, and it can be difficult at times to distinguish AD from tinea infection because both may involve pruritus, scaling, and inflammation. On physical examination, unlike AD, tinea pedis frequently develops in the toe web spaces (particularly the third and fourth). Tinea lesions frequently feature expanding plaques with central clearing and peripheral papules and scale. Potassium hydroxide slide examination of a sample taken from the skin from any affected body area, including the skin, the scalp, and hair, can help make the diagnosis.

**Allergy and Environment**

Allergic contact dermatitis can exacerbate AD. Common contact triggers include fragrances and preservatives in personal care products such as soaps, cleansers, shampoos, detergents, and certain emollients. Among other materials and substances that commonly elicit symptoms of allergic contact dermatitis are wool, nickel, synthetics, dyes, and rubber.

Physical and environmental factors also can play a role. Temperature changes between cold and hot environments (as when moving from an air conditioned enclosure to hot outdoor weather) or change of season can be problematic. Some children prefer warm or cool temperatures. Therefore, their dermatitis is milder in the summer or winter, respectively. Other environmental variables such as dust and mites, pollen, and ambient humidity can have an impact. Because sweating can produce pruritus and skin eruptions for some patients, treatment of AD may require modifying exercise regimens. Clothing tags, coarse fabrics, snug clothing, and footwear can worsen symptoms in a localized distribution. Emotional factors such as stress, anger, sleepiness, and boredom often increase pruritus.

The role of foods in causing AD can be significant for some children; food allergies can be present in up to 40% of patients who have AD. Symptoms include pruritus, urticaria, contact dermatitis, and exacerbation of AD as well as wheezing, asthma, and anaphylaxis. The symptoms can be immediate or delayed. Among the leading allergenic foods are milk and dairy products, eggs, wheat, soy, and peanuts. Some children outgrow allergies to particular foods, but peanuts and eggs are often the exception. Although some foods are difficult to avoid, the improved availability of nutritional information, di-
etary counseling, and food labeling helps families make proper dietary choices for children who have food allergies.

Allergy skin prick testing usually is more reliable after age 2 years; specific radioallergosorbent testing can be performed in infancy. The patient must not take oral antihistamines or steroid medications for several days before skin prick allergy testing; AD should be controlled as much as possible to allow proper evaluation while minimizing patient discomfort. Avoidance of allergenic substances identified by allergy testing occasionally benefits the patient who has AD, but AD can be exacerbated by unrelated factors while allergies are present. Allergy testing may be repeated and expanded if the patient does not improve after avoidance therapy.

Management

Treatment of AD requires a coordinated plan aimed at moisturizing dry skin, decreasing inflammation, treating any infections, and avoiding irritants and other factors associated with dermatitis flares. The regimen must be discussed with the family, patient, and clinicians to ensure compliance.

Bathing is an important aspect of general skin care for patients who have AD. Baths and showers should be brief and the water comfortably warm, never hot. After exposure to water, the skin should be patted or excess water brushed off of the skin before applying medication and moisturizer. Some patients improve and are maintained with daily or twice-daily bathing. Other patients experience drying and increased pruritus or discomfort with water contact, making infrequent bathing the required approach. In addition, during flares, some patients are unable to bathe or shower due to discomfort and pain. Bathing may be resumed when symptoms decrease.

Although not necessary, a variety of commercial products, including cleansers, soaps, oils, and oatmeal powders, can be combined with bath water. Fragrance-free soaps and cleansers are preferred, but which product benefits or is tolerated by each patient differs. The use of bubble bath, shampoo, and dishwater detergent to cleanse the body should be avoided. For some, dilute chlorine bleach baths are beneficial, particularly for children whose AD improves after swimming in chlorinated pools. One-quarter to one-half cup of bleach in the bathtub (24 gallons or a standard tub filled 4 to 6 inches) should create a sufficient concentration without bleaching or damaging linens. Dilute white vinegar, extra light olive oil, and other products also have been used for bathing.

Because the skin of patients who have AD is dry, the use of emollients is a cornerstone of therapy. Even without visible lesions, dry skin often is pruritic. Many products are available; no single emollient provides relief, moisturizes the skin, and improves skin barrier function for all patients. The medication vehicle (eg, cream versus ointment) and the presence of fragrance, preservatives, or other additives can affect the patient’s response. Lotions, creams, ointments, and oils are composed of varying amounts of oil and water. Ointments are composed of more petroleum jelly, creams contain more water than oil, and lotions contain more water than cream. If the skin is excoriated or fissured, stinging or pain can occur from products containing more water. An optimal time for moisturizer application is immediately after the bath or shower. Many patients benefit from several emollient applications per day.

Topical corticosteroids have been a mainstay of AD therapy for approximately 50 years. Hydrocortisone (up to 1%) is available over the counter, and numerous prescription preparations are available (Table). Ointments, creams, lotions, gels, foams, and oil preparations are available. Different preparations deliver corticosteroid through the skin in varying potencies. If preparations are used sparingly and appropriately, adverse effects should be minimized. Adverse effects include skin atrophy, telangiectasias, striae, and systemic absorption. The use of potent and fluorinated corticosteroids on the face and intertriginous and diaper areas should be avoided due to increased absorption through thinner or occluded skin. Middle-strength to more potent corticosteroid medications may be required for treating lichenified areas or on the hands and feet due to the increased skin thickness and keratin of the skin layers.

Several clinical trials of topical corticosteroid use in the pediatric age group have been performed or are in progress; some topical corticosteroids are approved specifically for use in children and some infants. Many practitioners find topical corticosteroids useful to break the itch-scratch cycle, treat acute flares, and minimize symptoms of inflammation. When signs and symptoms improve, the frequency of topical corticosteroid application should be reduced while moisturizer use is continued. Continuous, prolonged application of topical corticosteroids also can produce tachyphylaxis or decreased effectiveness of the medication.

Oral corticosteroid therapy has limited use in treating AD. Although helpful for some severe flares, once therapy is discontinued, the rebound or subsequent flare that may occur might be more severe than the initial exacerbation and more difficult to control. Some patients become oral corticosteroid-dependent in their attempt to
prevent flares and are more likely to develop adverse systemic effects such as hypothalamic-pituitary axis suppression, growth retardation, and cushingoid features.

Chronic, high-dose, or high-potency oral corticosteroid use has been shown to cause osteopenia or osteoporosis in children and adults. It is not known whether chronic intermittent topical corticosteroid use affects the bones of children. Some physicians give vitamin D and calcium supplementation to patients who have AD. Of note, the American Academy of Pediatrics has released new recommendations regarding vitamin D supplementation in children; the recommended minimum dose was doubled to 400 IU daily for infants and children. Clearly, corticosteroid use in children who have AD, the impact of therapy on bone health, and the role of vitamin D and calcium supplementation merit additional scientific study.

Topical calcineurin inhibitors are newer elements of the therapeutic armamentarium. Pimecrolimus 1% cream is approved for mild-to-moderate AD. Tacrolimus ointment is available in 0.03% and 0.1% strengths and is targeted for moderate-to-severe AD. Tacrolimus 0.03% and pimecrolimus are approved by the United States Food and Drug Administration for those ages 2 years and older; tacrolimus 0.1% is intended for those ages 15 years and older. Both medications can be used on any part of the body and are particularly beneficial for the eyelids, face, and intertriginous areas.

The most common adverse effects reported are burning at the site of application, headache, upper respiratory tract symptoms, cough, and pyrexia. In addition, exacerbation of viral infections, including herpesvirus infection, verrucae, and molluscum contagiosum, may be more likely in patients who use these products. A black box warning was placed on both medicinal forms of pimecrolimus and tacrolimus due to reports of upper respiratory tract infections and increased rates of viral infections in patients who use these products.

### Table: Topical Corticosteroids Ranked Strongest (Class I) to Weakest (Class VII)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Available Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td></td>
</tr>
<tr>
<td>Clobetasol propionate 0.05%</td>
<td>Cream, ointment, gel, foam</td>
</tr>
<tr>
<td>Betamethasone dipropionate 0.05%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Diflorasone diacetate 0.05%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Fluocinonide 0.01%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Halobetasol propionate 0.05%</td>
<td>Cream, ointment</td>
</tr>
<tr>
<td>Class II</td>
<td></td>
</tr>
<tr>
<td>Amcinonide 0.01%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Betamethasone dipropionate 0.05%</td>
<td>Cream</td>
</tr>
<tr>
<td>Desoximetasone 0.25%</td>
<td>Cream, ointment</td>
</tr>
<tr>
<td>Desoximetasone 0.05%</td>
<td>Gel</td>
</tr>
<tr>
<td>Fluocinonide 0.05%</td>
<td>Cream, ointment, gel, solution</td>
</tr>
<tr>
<td>Halcinonide 0.1%</td>
<td>Cream, ointment, solution</td>
</tr>
<tr>
<td>Mometasone furoate 0.1%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Class III</td>
<td></td>
</tr>
<tr>
<td>Amcinonide 0.1%</td>
<td>Cream, lotion</td>
</tr>
<tr>
<td>Betamethasone valerate 0.1%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Desoximetasone 0.05%</td>
<td>Cream</td>
</tr>
<tr>
<td>Fluocinonide emollient 0.05%</td>
<td>Cream</td>
</tr>
<tr>
<td>Fluticasone propionate 0.005%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Halcinonide 0.1%</td>
<td>Solution</td>
</tr>
<tr>
<td>Triamcinolone acetonide 0.1%</td>
<td>Cream, ointment, gel, foam</td>
</tr>
<tr>
<td>Class IV</td>
<td></td>
</tr>
<tr>
<td>Betamethasone valerate 0.12%</td>
<td>Foam</td>
</tr>
<tr>
<td>Fluocinonide acetonide 0.025%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Flurandrenolide 0.05%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Fluticasone propionate 0.05%</td>
<td>Cream</td>
</tr>
<tr>
<td>Hydrocortisone valerate 0.2%</td>
<td>Ointment</td>
</tr>
<tr>
<td>Mometasone furoate 0.1%</td>
<td>Cream, ointment, gel, foam</td>
</tr>
<tr>
<td>Triamcinolone acetonide 0.1%</td>
<td>Cream</td>
</tr>
<tr>
<td>Class V</td>
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<tr>
<td>Betamethasone dipropionate 0.05%</td>
<td>Lotion</td>
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<tr>
<td>Betamethasone valerate 0.1%</td>
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<tr>
<td>Clocortolone pivalate 0.1%</td>
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<tr>
<td>Desonide 0.05%</td>
<td>Cream</td>
</tr>
<tr>
<td>Fluocinolone acetonide 0.025%</td>
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<td>Flurandrenolide 0.05%</td>
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<td>Fluticasone propionate 0.01%</td>
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</tr>
<tr>
<td>Fluticasone propionate 0.05%</td>
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</tr>
<tr>
<td>Hydrocortisone butyrate 0.1%</td>
<td>Cream, ointment</td>
</tr>
<tr>
<td>Hydrocortisone valerate 0.2%</td>
<td>Cream, ointment, gel, solution</td>
</tr>
<tr>
<td>Prednicarbate 0.1%</td>
<td>Cream</td>
</tr>
<tr>
<td>Triamcinolone acetonide 0.1%</td>
<td>Cream</td>
</tr>
<tr>
<td>Class VI</td>
<td></td>
</tr>
<tr>
<td>Alclometasone 0.05%</td>
<td>Cream, ointment, lotion</td>
</tr>
<tr>
<td>Betamethasone valerate 0.1%</td>
<td>Lotion</td>
</tr>
<tr>
<td>Desonide 0.05%</td>
<td>Cream</td>
</tr>
<tr>
<td>Fluocinolone acetonide 0.01%</td>
<td>Cream, lotion</td>
</tr>
<tr>
<td>Hydrocortisone butyrate 0.1%</td>
<td>Solution</td>
</tr>
<tr>
<td>Triamcinolone acetonide 0.1%</td>
<td>Cream, ointment, gel, foam</td>
</tr>
<tr>
<td>Triamcinolone acetonide 0.025%</td>
<td>Cream</td>
</tr>
<tr>
<td>Class VII</td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone acetonide, dexamethasone</td>
<td>Cream, ointment, lotion</td>
</tr>
</tbody>
</table>

Note: Vehicle affects medication potency for several products.
tions, stating that long-term safety of topical calcineurin inhibitors has not been established and that these medications are not recommended for use in children younger than age 2 years. Additional therapeutic trials in children who have AD are planned and needed.

Several prescription topical nonsteroidal moisturizing creams have been approved for use in AD. Their purpose is to improve the hydrolipid layer and barrier function, relieve AD symptoms, and promote wound healing. They may be used alone or in combination with topical corticosteroids and calcineurin inhibitors. The non-steroid creams Atopiclair® Nonsteroidal Cream (Graceway Pharmaceuticals, Bristol, Tenn.), Eletone® Cream (Ferndale Laboratories, Ferndale, Mich.), Epiceram® Skin Barrier Emulsion (Promius Pharmaceuticals, Bridgewater, NJ), and MimyX® Cream (Steifel Pharmaceuticals, Bridgewater, NJ) are approved for all ages, for use on any area of the body, and may be used two to three times a day. Zetania® cream (Tiber Laboratories, Suwanee, Ga.) is approved for children 2 years of age and older. Patients allergic to any components of the creams should avoid their use.

Oral antihistamine drugs have been prescribed for patients who have AD. Although not statistically proven to be useful for treating pruritus generally, oral antihistamines can be helpful for children who have an urticarial component or decreased or altered sleep patterns due to pruritus.

Wiscott-Aldrich Syndrome

Wiscott-Aldrich syndrome is one important condition to consider in patients who have AD. This X-linked recessive disorder features eczematous eruptions in association with thrombocytopenia and recurrent infections. Thrombocytopenic purpura and hemorrhagic events may occur. The identified Wiskott-Aldrich syndrome protein (WASP) gene codes for a cytoplasmic protein that has multiple functions. The impaired humoral immune response to polysaccharide antigens seen in patients who have Wiscott-Aldrich syndrome makes patients susceptible to bacteria such as Streptococcus pneumoniae and Pneumocystis jirovecii and, later, to viruses. After the second decade of life, these patients are at risk for developing leukemia and lymphoma.

Job Syndrome

Another important condition to consider is Job syndrome, or hyperimmunoglobulin E syndrome (HIES), which is defined by eczematous eruptions associated with IgE concentrations greater than 2,000 IU/mL and repeated skin and sinopulmonary infections. The classic autosomal dominant form is due to a mutation in the signal transducer and activator of the transcription 3 (STAT3) gene. Skin eruptions appear during the newborn period, with onset of infections during the first 3 postnatal months. Although the type of skin infection can vary, “cold” abscesses are typical and feature slight redness, no or low-grade fever, little systemic involvement, and minimal signs and symptoms, unlike abscesses seen in patients unaffected by HIES. Paronychiae and candidal infections are common. Although the eczematous symptoms usually resolve, the recurrent pulmonary infections due to Staphylococcus aureus and Haemophilus influenzae progress to chronic lung infections and subsequent lung changes. Of note, children who have AD can have very high concentrations of IgE; conversely, patients who have HIES can have normal IgE concentrations.

Ichthyosis

Ichthyosis represents a group of disorders that involves abnormal epidermal skin barrier function, keratinization, and desquamation. Multiple types of ichthyosis have been described. Initially defined descriptively, the disorders now can be distinguished by genetic, histologic, biochemical, and molecular methods.

Ichthyosis vulgaris (IV) is the most common type, with an incidence of 1 in 250. The onset is during infancy or childhood, not at birth. Inheritance can be autosomal dominant or sporadic, so patients have a varied presentation. IV usually presents as fine white scales on the skin, sparing the antecubital and popliteal fossae. Scaling is most obvious on the lateral lower legs (Fig. 3). Hyperlinearity is noted on the palms and soles. IV can be innocuous and appear as an isolated finding. The histopathology may show a thinned-to-absent granular layer and a compact superficial stratum corneum. However, a skin biopsy may not be diagnostic; microscopically, IV can look like normal skin. IV often improves with age, and manifestations in adulthood may be minimal.

There are many forms of ichthyosis, most of which are rare. Ichthyosis can be inherited in autosomal or X-linked patterns or by spontaneous mutation. Although IV is rather common, X-linked ichthyosis, lamellar ichthyosis, and harlequin fetus are rare, well-described forms (Fig. 4). Several syndromes and related conditions of note include ichthyosis as part of the clinical picture. KID syndrome is defined as keratitis, ichthyosis, and deafness. Netherton syndrome, also called ichthyosis linearis circumflexa, features congenital erythroderma as well as atopic dermatitis, hair shaft abnormalities, and high IgE concentrations.
Management
Treatment of IV usually involves the use of topical salicylic acid; lactic acid; or urea in lotion, cream, or ointment form. These products moisturize, soften the skin, and aid in desquamation. For patients who have both IV and AD, these products are more likely to cause irritation. The products should be used cautiously in children because total body application can result in systemic absorption and serious adverse effects. Salicylic acid, in particular, should be used in children after 1 year of age and then with caution due to risks of salicylate toxicity.

Research
Significant research has been performed in IV, AD, and related disorders. IV often coexists with AD, and research has shown a genetic basis for this association in certain populations. Gene mutations in keratin proteins alter skin barrier function. Most important, the FLG gene produces profilagrin, and filagrin is critical for AD expression. Multiple international and familial studies have shown that FLG mutations in patients who have AD alter normal skin formation, function, and hydration and result in severe AD, as well as asthma associated with AD. The mutation for IV also has been identified. Studies have shown that Northern European patients who have IV have a statistically significant increased risk for developing AD as well. Also, patients who have both IV and AD have a statistically significant increased risk for developing asthma. Overall, there is strong evidence for a genetic and molecular basis for the association of IV and AD. More studies are in progress and are necessary for elucidating the role of altered cutaneous barrier function.

Summary
- Based on strong research evidence and consensus, a multifaceted, individualized approach to treatment benefits patients who have atopic dermatitis and includes bathing, emollients, topical anti-inflammatory medications, allergen avoidance, and the use of antistaphylococcal antibiotics and antihistamines when clinically indicated. (1)(2)
- Based on strong research evidence, mutations in the FLG gene cause ichthyosis vulgaris, resulting in alterations in the skin protein filagrin. (3)(4)
- Based on strong research evidence, atopic dermatitis is associated with certain populations who have ichthyosis vulgaris. (5)(6)(7)
Atopic dermatitis is a common inflammatory skin condition characterized by relapsing eczematous lesions in a typical distribution. It can be frustrating for pediatric patients, parents, and health care providers alike. The pediatrician will treat the majority of children with atopic dermatitis as many patients will not have access to a pediatric medical subspecialist, such as a pediatric dermatologist or pediatric allergist. This report provides up-to-date information regarding the disease and its impact, pathogenesis, treatment options, and potential complications. The goal of this report is to assist pediatricians with accurate and useful information that will improve the care of patients with atopic dermatitis. Pediatrics 2014;134:e1735–e1744

Atopic dermatitis (AD), commonly referred to as eczema, is a chronic, relapsing, and often intensely pruritic inflammatory disorder of the skin. A recent epidemiologic study using national data suggested that the pediatric prevalence is at least 10% in most of the United States. AD primarily affects children, and disease onset occurs before the ages of 1 and 5 years in 65% and 85% of affected children, respectively. The number of office visits for children with AD is increasing. Up to 80% of children with AD are diagnosed and managed by primary care providers, often pediatricians. Although medical subspecialists, such as pediatric dermatologists and/or pediatric allergists, may be suited to provide more advanced care for children with AD, lack of a sufficient number of such physicians, particularly pediatric dermatologists, likely means the burden of AD care will continue to fall to primary care providers. Although consensus guidelines and practice parameters regarding the management of AD in children have been published, considerable variability persists in clinical practice, particularly regarding the roles that bathing, moisturizing, topical medications, and allergies play in management. Inconsistencies in opinion and treatment approach as well as the chronic and relapsing nature of AD can lead to frustration for the patient, family, and primary care providers when managing AD.

STATEMENT OF THE PROBLEM

New data support the theory that AD results from primary abnormalities of the skin barrier, suggesting that skin-directed management of AD is of paramount importance. This clinical report reviews AD and provides an up-to-date approach to skin-directed management that is based on pathogenesis. Effectively using this information to create treatment plans...
and educate families should help pediatric primary care providers manage most children with AD, thereby improving patient satisfaction and clinical outcomes.

CLINICAL FEATURES

The diagnosis of AD is primarily clinical (Table 1). Major clinical features are a pruritic and relapsing eczematous dermatitis in a typical distribution that changes with age. In infancy, the cheeks, scalp, trunk, and extremities are most commonly affected. In early childhood, the flexural areas are characteristic, whereas in adolescents and adults, hands and feet are typically involved.

Pruritus is a hallmark of AD, which is often referred to as the “itch that rashes.” Other features that support the diagnosis of AD include early age of onset, personal or family history of atopy, ichthyosis vulgaris, and/or xerosis. It is important to exclude other inflammatory skin conditions, such as contact dermatitis, seborrheic dermatitis, and psoriasis. Skin biopsies and laboratory testing are usually unnecessary and not helpful in making the diagnosis of AD, although they may be beneficial when trying to exclude conditions that appear similar to AD (such as those mentioned previously), particularly in patients whose symptoms are not responding to standard skin-directed care.

EFFECTS ON QUALITY OF LIFE

The effects of AD on the quality of life (QoL) of patients and their families cannot be underestimated. Nearly 50% of children with AD report a severely negative effect of the disease on QoL. Factors that contribute to poor QoL in AD are fatigue and sleep deprivation (which directly correlate with itch and severity of AD), activity restriction, and depression. Children with severe AD also tend to have fewer friends and participate in fewer group activities than their peers. These children may be at higher risk of depression, anxiety, and other mental health disorders.

AD also has a negative effect on QoL of caregivers and parents of affected children. Parents of children with moderate and severe AD spend up to 3 hours per day caring for their children’s skin. The most commonly reported negative effects on parents are lack of sleep (often because of cosleeping), fatigue, absence of privacy (because of cosleeping, disrupted sleep of affected children), treatment-related financial expenditures, and feelings of hopelessness, guilt, and depression. In fact, the depression rate in mothers of children with AD is twice as high as in mothers of children with asthma. Appropriate social and community support resources, such as referral to a counselor, psychologist, or patient support groups, such as the National Eczema Association (www.nationaleczema.org), can be helpful when QoL issues are encountered in patients and families with AD.

PATHOGENESIS

The pathogenesis of AD is complex and multifactorial. Skin barrier dysfunction, environmental factors, genetic predisposition, and immune dysfunction all play a role in its development and are closely intertwined. In the past, emphasis had been placed on T helper cell dysregulation, production of immunoglobulin E (IgE), and mast cell hyperactivity leading to the development of pruritus, inflammation, and the characteristic dermatitis. Recent discoveries, however, have established the key role of skin barrier dysfunction in the development of AD.

The primary function of the skin barrier is to restrict water loss and to prevent entry of irritants, allergens, and skin pathogens. The outermost layer of skin, called the stratum corneum, is critical to the integrity of the skin barrier, with the protein filaggrin being a key player in stratum corneum structure and formation. Loss-of-function mutations (of which more than 40 have been described) in FLG, which encodes filaggrin, have been implicated in up to 50% of patients with moderate to severe AD in some demographic populations. Mutations in FLG are associated with a two- to threefold increased risk of having AD.

There are several proposed mechanisms of how filaggrin defects contribute to the development of AD. Inadequate filaggrin production leads to a reduced ability of keratinocytes to maintain hydration and to restrict transepidermal water loss, which then leads to xerosis, which in turn produces pruritus and, subsequently, AD. An inadequate skin barrier might also allow for the entry of aeroallergens, leading to an inflammatory response, causing AD. Another theory speculates that local pH may be changed with an altered skin barrier, leading to the overgrowth of bacteria, such as Staphylococcus aureus, which then may trigger an innate immune response, leading to the development of inflammatory skin lesions. Regardless of the mechanism,
this new knowledge reinforces the primary role of the skin barrier in the pathogenesis of AD and highlights the need for skin-directed therapy to repair or enhance the function of the skin barrier.

ALLERGIES AND AD

The relationship between AD and food allergy is complex but likely overemphasized. More than 90% of parents incorrectly believe that food allergy is the sole or main cause of their child’s skin disease.22 The resulting focus on food allergy can result in elimination diets; potential nutritional concerns, such as protein or micronutrient malnutrition or deficiencies; and misdirection of treatment away from the skin, thereby leading to undertreatment. Effective treatment of the skin tends to allay parental concern regarding food allergy.23

True food-induced AD is rare. The most common cutaneous manifestations of food allergy are often IgE-mediated and consist of acute urticaria, angioedema, contact reactions, or in some cases, an increase in AD symptoms.24,25 In the case that AD is worsened by exposure to a food allergen, these reactions are not IgE-mediated but rather delayed-type hypersensitivity reactions and usually develop 2 to 6 hours after the exposure to the food.26

The accentuated role of food allergies in AD may stem from the observation that food allergies are prevalent in patients with AD. The prevalence of food allergy in all children in the first 5 years of life is approximately 5%.24 In children with AD, however, the prevalence of food allergy is approximately 30% to 40%,25 and up to 80% will have high food-specific IgE concentrations, even in the absence of a true food allergy.27 In addition, patients who have food allergy often have earlier-onset and more severe AD, and patients with early-onset AD have a higher risk of developing food allergies than those with later-onset AD.28 However, it is important to stress that this relationship is not causative. Rather, the presence of food allergy predicts a poor prognosis of severe and persistent AD, but food allergy does not necessarily cause AD.

Recent guidelines set forth by the National Institute of Allergy and Infectious Diseases (NIAID) support this position. In these guidelines, the NIAID states: “In some sensitized patients…food allergens can induce urticarial lesions, itching and eczematous flares, all of which may aggravate AD” but do not cause AD. They also state that, in the absence of documented IgE- or non-IgE-mediated food allergy, there is “...little evidence to support the role for food avoidance” in the treatment of AD.29 Egg allergy may be one exception, as up to half of infants with egg-specific IgE may have improvement in their AD when following an egg-free diet.29 The NIAID guidelines state that allergy evaluation (specifically to milk, egg, peanut, wheat, and soy) should be considered in children younger than 5 years with severe AD if the child has persistent AD despite optimal management and topical therapy or if the child has a reliable history of an immediate cutaneous reaction after ingestion of a specific food.

The “atopic march” is the concept that AD is the first stop in the progression to other allergic disorders, such as asthma and allergic rhinitis.30 It has been suggested that early optimal and successful treatment of AD may prevent or attenuate the development of other atopic conditions.31 The recent findings of the role FLG mutations play in causing epidermal barrier defects, thus allowing for the entry of aeroallergens and other allergens into the skin and subsequent epicutaneous sensitization, lends strong support to this possibility and highlights the importance of effective skin-directed treatment of AD.

Allergic contact dermatitis (ACD) is a delayed hypersensitivity reaction to cutaneous allergens that is underestimated in the pediatric population and likely plays a greater role in perpetuating AD than was previously believed. Up to 50% of children with difficult-to-control AD have at least 1 positive patch test reaction to a cutaneous allergen.32 Not all positive reactions may be relevant, however. Most studies estimate 50% to 70% of all positive reactions to be relevant in patients with suspected ACD. Thus, the possibility of ACD should be considered in children with unusual or difficult-to-control AD.

TREATMENT PRINCIPLES

Skin-directed therapies should be the first approach to management. This approach has 4 main components, each focusing on a specific manifestation of AD: (1) maintenance skin care, designed to repair and maintain a healthy skin barrier; (2) topical antiinflammatory medications, to suppress the inflammatory response; (3) itch control; and (4) managing infectious triggers, recognition and treatment of infection-related flares. Education of patients and families is another critical factor that should not be overlooked. AD is a frustrating disease because of its recurrent nature, even in the face of excellent care plans. When the primary care provider is able to set realistic expectations regarding outcomes, parental compliance is better and frustration is decreased. It can be helpful to discuss the prognosis of AD, because most children will outgrow the symptoms or at least the severity of the disease.32 Patients whose parents receive comprehensive education regarding AD and its care have better improvement in AD severity than patients whose parents do not receive this education.32 Written action plans have been shown to improve adherence in children with asthma, and a similar
model for patients with AD (see Fig 1 for an example), outlining specific indications for different products and medications, is likely to be helpful.34,35

**Maintenance Skin Care**

Maintenance skin care is the foundation of AD management; its goal is to repair and maintain a functional skin barrier. Patients should be instructed to develop these habits and perform them daily. Preliminary evidence supports the role of maintenance skin care in helping to reduce both the frequency and severity of AD flares. The key facets of maintenance care include maintaining skin hydration and avoiding irritants and triggers.

The optimal frequency of bathing for children with AD has not been well studied and remains controversial. Soaking baths allow the skin to imbibe moisture, and a daily bath can be beneficial in patients with AD as long as a moisturizer is applied afterward.50,36 The specific frequency of bathing should be titrated to the individual patient and his or her response to bathing. The use of lukewarm water and limiting the duration of the bath can prevent skin dehydration. Cleansing may also remove bacteria from the skin surface. A mild synthetic detergent without fragrance can be used to cleanse soiled areas without fear of exacerbating the skin disease. Additives are not proven to be effective, although dilute bleach can be helpful for patients who are prone to infection and flares (see Managing Infectious Triggers).

A second and extremely important component of maintaining skin hydration is lubrication of the skin, commonly referred to as moisturization. Frequent moisturization alleviates the discomfort associated with xerosis, helps to repair the skin barrier, and reduces the quantity and potency of pharmacologic interventions.57,38 In a British study evaluating 51 children with AD, parents were educated on the proper use of moisturizers and topical treatments by a nurse specialist. During the study period, the quantity of moisturizer used increased 800% (average use of 426 g per week per patient) while the severity of AD decreased and the percentage of patients having to use moderate or potent topical steroids decreased.39

Studies comparing the relative effectiveness of specific moisturizers are lacking, and the plethora of products can make the task of choosing a moisturizer daunting. Simplistically, all moisturizers are mixtures of lipid (liquid or semisolid) and water. Ointments have the highest proportion of lipid (for example, petroleum jelly is 100% lipid) and likewise feel “greasy” when applied to the skin. Creams are emulsions of water in lipid (oil>water) and contain preservatives and stabilizers to keep these ingredients from separating. Although creams can be less greasy than ointments, the added ingredients can sometimes burn or sting atopic skin. Similarly, lotions are also emulsions with a higher proportion of water to lipid than creams. Frequent reapplication of lotions is needed to maintain skin hydration. In general, ointments tend to have the greatest moisturizing effect, followed by creams, and then lotions. The best moisturizers for patients with AD are fragrance free and have the least possible number of preservatives, because these are potential irritants.

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**An Action Plan to Guide the Care of Your Child’s Atopic Dermatitis (Eczema)**

1. If your child enjoys a bath, allow him or her to soak daily in lukewarm water for 10 to 15 minutes. If your child does not enjoy a bath or if you feel water irritates his or her skin, bathe every 2 to 3 days. Use a gentle cleanser for dirty areas only at the end of the bath.

2. After the bath, pat the skin dry, leaving it damp to the touch.

3. Prescription medications should be applied to areas of the skin that are red, rough, and itchy. These medications should be applied in a thin layer.
   - **Apply** __________ to affected areas of the face, neck, armpits, and groin.
   - **Apply** __________ to affected areas of the body.

4. Apply a moisturizer (preferably a cream or ointment) over the entire face and body. Your child’s skin medications and moisturizer should be put on within a few minutes after the bath so the skin does not dry out.

5. Repeat steps 3 and 4 a second time each day if instructed by your doctor.

6. Moisturizer can be applied as often as needed to dry, itchy skin. Prescription skin medications should not be used more than 2 times daily.

7. Continue the prescription skin medications until the red, rough rash is gone. If the flare of the rash has not improved in 2 weeks, talk with your doctor.

8. After the rash has cleared, continue to moisturize all areas of the face and body daily.

9. Restart the prescription skin medications as directed when the rash returns.

10. Antihistamines can help with itching and poor sleep due to eczema.
   - **Give** __________ 30 minutes before bedtime when your child is itchy.
   - **Give** __________ in the morning as needed for itching.

11. Oozing, drainage, pus bumps, and yellow crusts can indicate the skin is infected. Talk with your doctor right away if you are concerned about skin infection.

**FIGURE 1**

An action plan for the management of AD.
Moisturizers should be applied at least once daily to the entire body, regardless of whether dermatitis is present. There are a handful of prescription barrier creams marketed for the treatment of AD. These products do not have active pharmacologic ingredients. A small study compared 2 of these products with an over-the-counter ointment and revealed no significant difference in efficacy for patients with mild-to-moderate AD, as defined by investigator global assessment. Although no major adverse effects have been reported with these products, they are considerably more expensive and may, therefore, be less cost effective than standard moisturizers.

Multiple patient-specific factors, commonly referred to as triggers, may exacerbate AD. Triggers may be unavoidable, but minimizing exposure to them can be helpful. Common triggers may include aeroallergens or environmental allergens, infections (particularly viral illnesses), harsh soaps and detergents, fragrances, rough or non-breathable clothing fabrics, sweat, excess saliva, and psychosocial stress.

Topical Antiinflammatory Medications

The eczematous dermatitis seen in AD is the manifestation of an inflammatory immune response in the skin. Flares of dermatitis are unlikely to respond to moisturization alone, and during these times, treatment is focused on suppressing the inflammatory response. Topical steroids are the first-line, most commonly used medications to treat active AD and have been used for the last 40 to 50 years. When used appropriately, they are effective and safe. However, when used inappropriately, there are potential risks of cutaneous atrophy, striae, telangiectasia, and systemic absorption with resulting adrenal suppression. There are also other potential local effects when used around the eyes (intraocular hypertension, cataracts) or mouth (periorificial dermatitis). Because of these potential risks, there is a real phenomenon of “steroid phobia” on the part of both parents and health care providers. Although this phobia does not correlate with AD severity, it does lead to undertreatment of the skin disease.

Topical steroids are classified according to their potency, ranging from class VII (low potency) to class I (super potent; Table 2). Class I medications are 1800 times more potent than the least potent class VII medications. Risk of adverse effects directly correlates with potency, with high-potency and super-potent topical steroids carrying the greatest risk. When treating most cases of AD, high-potency medications are generally not needed. Patients treated with higher-potency topical steroids are at risk for developing the aforementioned adverse effects, making close follow-up necessary. Choosing an appropriate topical steroid can be difficult, given the number of different medications, and health care providers are advised to rely on 2 or 3 medications from the low- (classes VI and VII) and moderate-potency groups (classes III, IV, and V) as “go-to” medications for everyday practice. These choices may be based on regional prescribing practices and insurance coverage or cost. Inexpensive low- and moderate-potency generic topical steroids are hydrocortisone and triamcinolone, respectively. Acceptable “limits” of topical steroid potency in a primary care practice are low-potency topical steroids for the face, neck, and skin folds and moderate-potency topical steroids for the trunk and extremities.

For acute flares and moderate to severe cases, wet wrap therapy (also called wet dressings) can be used in conjunction with topical steroids to quickly control the dermatitis. Wet dressings increase penetration of topical steroids into the skin, decrease

<table>
<thead>
<tr>
<th>Class</th>
<th>Potency</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Class I: Superpotent</td>
<td>Globetasol propionate 0.05% ointment, cream, solution, and foam</td>
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<tr>
<td>Class II: High potency</td>
<td>Betamethasone dipropionate 0.05% ointment and cream</td>
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<tr>
<td>Class III: Moderate potency</td>
<td>Betamethasone valerate 0.1% ointment, foam, Desoximetasone 0.05% ointment and cream</td>
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<tr>
<td>Class IV: Moderate potency</td>
<td>Betamethasone valerate 0.12% foam, Clocortolone pivalate 0.1% cream, Flurandrenolide 0.05% cream, Fluocinolone acetonide 0.025% ointment, Halcinonide 0.025% cream</td>
<td></td>
</tr>
<tr>
<td>Class V: Moderate potency</td>
<td>Betamethasone valerate 0.1% cream, Clocortolone pivalate 0.1% cream, Flurandrenolide 0.05% cream, Fluocinolone acetonide 0.01% cream, Fluocinolone acetonide 0.025% cream, Halcinonide 0.025% cream, Hydrocortisone valerate 0.2% ointment, Triamcinolone acetonide 0.1% cream, Triamcinolone acetonide 0.1% cream</td>
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<tr>
<td>Class VI: Low potency</td>
<td>Alclometasone dipropionate 0.05% ointment and cream, Desonide 0.05% ointment, cream, lotion, Hydrocortisone butyrated 0.1% ointment, cream, and lotion, Hydrocortisone probutate 0.1% cream, Hydrocortisone valerate 0.2% cream, Prednicarbate 0.1% cream, Triamcinolone 0.025% ointment</td>
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<tr>
<td>Class VII: Low potency</td>
<td>Hydrocortisone 0.5% and 1% ointment and cream (over the counter), Hydrocortisone 2.5% ointment, cream, and lotion</td>
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itch, and serve as an effective deterrent to scratching. The technique is straightforward: after a soaking bath, topical steroid is applied to affected areas followed by application of moisturizer to the rest of the skin; moist gauze or cotton clothing that has been dampened with warm water is then applied; the wet layer is covered with dry cotton clothing. Blankets and a warm room keep the child comfortable. The dressings can be left in place for 3 to 8 hours before being changed. Wet dressings can be used continuously for 24 to 72 hours or overnight for up to 1 week at a time.

Another consideration when prescribing topical steroids is the vehicle or form of product by which the active ingredient is delivered. Ointments are less likely to produce a burning or stinging sensation and are better tolerated by infants and younger children. When comparing the same active ingredient and concentration, ointments are more effective than creams or lotions, because their occlusive effect results in a higher relative potency. Topical steroids should be applied as a thin layer once or twice daily to affected areas until these areas are smooth to touch and no longer red or itchy. Traditionally, topical steroids are held when dermatitis is quiescent and restarted when the eruption recurs. Placing an absolute limit on the duration of topical steroid use can be confusing for families, leads to unsatisfactory outcomes, and conflicts with the relapsing nature of the disease itself. However, if AD is not responding after 1 to 2 weeks of treatment, re-evaluation to consider other diagnoses or treatment plans is indicated. When these general guidelines are followed, the risk of adverse effects from the use of topical steroids is extremely low.

Topical calcineurin inhibitors (TCIs) are a newer treatment of AD. These medications are topical immunosuppressive agents that inhibit T-cell function. There are currently 2 forms: tacrolimus ointment (available in 0.03% and 0.1%) and pimecrolimus 1% cream. Both are approved as second-line therapy for moderate-to-severe AD. A recent meta-analysis in pediatric patients with AD demonstrated that both tacrolimus and pimecrolimus are effective; tacrolimus is more effective than pimecrolimus, but both reduce the inflammation and pruritus associated with AD.45

TCIs have a different adverse effect profile than topical steroids and do not cause atrophy, striae, telangiectasia, and adrenal suppression. Thus, they are highly beneficial to treat AD in patients for whom concerns for adverse effects from long-term use of topical steroids are highest (eg, face, eyelids). The negatives, however, are a higher relative cost and the potential adverse effects of burning and stinging (tacrolimus>pimecrolimus). In addition, the Food and Drug Administration has issued a so-called “black box” or boxed warning for TCIs, citing a potential cancer risk with the medication, on the basis of the observation that laboratory animals exposed to high doses of systemic calcineurin inhibitors developed malignancies more frequently and on rare case reports of adult patients using TCIs who developed lymphoma and skin cancers.46 However, the cause-and-effect relationship between TCI use and malignancy in these case reports is unclear. Reassuringly, TCIs have been used in children for more than 15 years, there have been no reports of malignancy in children, and there is little to no concern for systemic absorption or systemic immunosuppression.47 Indeed, in 1 adult study, there was a lower rate of nonmelanoma skin cancer in patients with AD who used TCIs to treat their inflammatory disease.48

Proactive Treatment
Although traditional AD management consists of treating active disease and flares with topical steroids and/or TCIs, emerging data suggest that use of these medications when a patient is not having active disease may be helpful as well. In 1 study, patients used twice-daily antiinflammatory medications to treat active AD and were then randomly assigned to receive “proactive” twice-weekly treatment with topical tacrolimus or placebo. Patients who received topical tacrolimus had significantly less AD flares and increased time to new flare development when compared with those who received placebo.49 A similar effect may also be true with topical steroids (fluticasone propionate and methylprednisolone aceponate have been studied),50 although none of these studies have evaluated the long-term safety of this treatment regimen. The choice of medication used for flare prevention may depend on patient age, location of involvement, and cost.

**Itch Control**
Pruritus is another important component of AD. AD is commonly referred to as the itch that rashes; the associated pruritus may be significant, even in the absence of significant rash. Often, parents may be unaware of how much their child scratches, because itching is generally worse at night. The pathophysiology behind pruritus is complex, and both peripheral and central factors are involved.51 Examples of peripheral factors are irritant entry through a defective epidermal barrier; transepidermal water loss, and protease activity in the skin.52 Centrally, there is a complex interplay of multiple different mediators, although histamine seems to have a limited role, if any.52,53 Clinical factors can also promote itch, including scratching (the “itch-scratch” cycle), xerosis, psychological stress, sweat, and contact with irritants such as wool and aeroallergens. It is often challenging to remove itch, even when a patient’s skin is improving. Management of itch initially focuses on
minimizing triggers and continuing the skin-directed treatments of restoring the skin barrier and suppressing inflammation. Adjunctive systemic therapy can be added to help manage itch. Oral antihistamines do not have a direct effect on the dermatitis, but can help reduce the sensation of itching and, thus, decrease scratching and trauma to the skin in patients with AD flares.\textsuperscript{54} Sedating antihistamines (such as diphenhydramine or hydroxyzine) should be used with caution in infants, who may be more prone to adverse effects of these agents. In addition, paradoxical effects of agitation instead of sedation may occur in some children. Non-sedating antihistamines (such as cetirizine and loratadine) are less effective on pruritus but can be helpful for patients who have environmental allergic triggers.\textsuperscript{54} Topical antihistamines are not effective in the treatment of AD-associated pruritus and contain potential irritants and allergens that may worsen dermatitis.

**Managing Infectious Triggers**

Both bacterial and viral skin infections are associated with flares in children with AD. Affected patients, particularly those with poorly controlled AD, have a higher risk of cutaneous infections. The skin of patients with AD has an abnormal expression of antimicrobial peptides responsible for responding to bacteria or skin barrier compromise, toll-like receptor defects, and immune dysregulation in the form of diminished immune cell recruitment.\textsuperscript{55} This combination of factors puts patients with AD at higher risk of skin infection.

Ninety percent of patients with AD are colonized with \textit{S aureus}.\textsuperscript{56} Pruritus may occur even in patients who are colonized but not actively infected. Many patients with AD have sudden exacerbations of their disease that can be attributed to active infection with bacteria, most commonly \textit{S aureus}, and active treatment of the infection subsequently improves the skin.\textsuperscript{56} Clinical signs of infection, such as pustules, oozing and honey-colored crusts, and less commonly fever and cellulitis, may lead the primary care provider to prescribe antibacterial treatment. Secondary infection of AD is a clinical diagnosis and is often associated with flare of the underlying AD. Obtaining skin cultures, particularly of pustules and draining lesions, before treatment can be helpful in determining the causative pathogen but is not always necessary. The rate of methicillin-resistant \textit{S aureus} (MRSA) colonization in patients with AD varies depending on the community in which the patient resides.\textsuperscript{57} Streptococcal infections may also occur in patients with AD. Signs of streptococcal infection include pustules, painful erosions, and fever. In addition, patients may have facial or periorbital involvement and invasive infections.\textsuperscript{58}

There are multiple synergistic components involved in treating active \textit{S aureus} and streptococcal infection in AD. Topical, oral, or intravenous antibiotic therapy may be needed depending on the extent and severity of infection. The specific medication used should be directed at \textit{S aureus} and \textit{Streptococcus}. Topical mupirocin can be used for limited skin lesions. Cephalexin is a common first-choice when oral antibiotics are needed and MRSA is not suspected. Repair of the skin barrier is continued simultaneously: bathing, moisturization, and topical anti-inflammatory therapies are all usually indicated. MRSA or other etiologies may be considered in patients who remain refractory to treatment.

Dilute bleach baths may have a useful role in the management of patients with AD, particularly those prone to recurrent infection and AD flares. A recent placebo-controlled, blinded study examined the effects of 0.005% bleach baths plus intranasal mupirocin versus placebo in children with moderate to severe AD. Patients bathed for 5 to 10 minutes twice weekly with the intervention. Those in the treatment group had significant improvement in their AD severity scores versus those in the placebo group.\textsuperscript{56} Areas of the body that were not submerged in the bleach-containing water, specifically the head and the neck, revealed no difference in AD severity scores between the 2 groups. The treatment was well tolerated, without any adverse effect, and without any increase in resistant strains of \textit{S aureus}. Although a relatively small study, the results provide support for the practice of using dilute bleach baths as one modality in the treatment of patients with AD. A concentration of 0.005% bleach is made by adding 120 mL (1/2 cup) of 6% household bleach to a full bathtub (estimated to be 40 gallons) of water. The amount of bleach should be adjusted based on the size of the bathtub and the amount of water in the tub.

Patients with AD are also at greater risk of viral skin infections. These include molluscum contagiosum, eczema herpeticum, the recently described atypical enterviral infection attributable to Coxsackie virus A6 (the so-called “eczema coxsackieum”),\textsuperscript{59} and vaccinia virus (the virus used in smallpox vaccine). Patients with eczema herpeticum present with shallow, “punched-out” erosions in areas of skin affected with or prone to AD. Similarly, the lesions seen with hand, foot, and mouth disease caused by Coxsackie virus A6 tend to localize to AD skin. In cases in which the diagnosis is not clear, viral studies are indicated.

Eczema herpeticum can be potentially life threatening and requires systemic treatment with acyclovir. In addition, adequate analgesia, skin care, and topical anti-inflammatory medications are used. Secondary bacterial infection
often coexists with eczema herpeticum and should be treated appropriately as well. Herpetic keratitis is associated with periorcular eczema herpeticum. Smallpox vaccine uses a live vaccinia virus, and its use was resumed by the military in 2002. Although it is contraindicated for those with AD and in those who have a close contact with AD, rare cases of eczema vaccinatum have been reported. Eczema vaccinatum manifests as a rapidly developing papular, pustular, or vesicular eruption with a predilection for areas of AD, following inadvertent transmission of vaccinia virus from the unhealed inoculation site of the immunized person to a close contact with AD. Systemic dissemination may follow, and case fatality rates range from 5% to 40%. If eczema vaccinatum is suspected, infection disease experts should be consulted, because treatment with cidofovir may be necessary.

Final Points

Using this information, the pediatric primary care provider should be well equipped to treat most children with AD. If patients with suspected AD do not respond to these treatments, referral to a pediatric medical subspecialist, such as a pediatric dermatologist, may be useful. Other reasons for referral include poorly controlled or generalized AD with consideration for systemic immunosuppressive therapy, recurrent infections (viral or bacterial) in the setting of AD, suspected ACD, and the presence of atypical features or physical examination findings. In cases of persistent, refractory, and/or generalized AD, systemic treatment, such as phototherapy or immunosuppressive medications, may be indicated. Oral steroids are generally not indicated because of their adverse side effect profile and a high likelihood of rebound dermatitis, making ongoing management difficult.

SUMMARY

AD can be a challenging and frustrating chronic disease for pediatric patients, parents, and primary care providers. Although the pathogenesis of AD is complex, recent research advances support the role of an abnormal skin barrier. The clinical corollary to these discoveries is a greater focus on skin-directed therapies as the first-line treatment of children with AD. This includes maintenance skin care and the use of topical steroids for active disease. Low- and moderate-potency topical steroids are safe and effective for children when used appropriately. Early recognition and treatment of infectious complications can lead to improved patient outcomes. Patient and family education and counseling by the health care provider regarding the pathogenesis, specific treatment, and prognosis of the disease play an extremely important role in the management of AD.

REFERENCES

7. Ring J, Alomar A, Bieber T, et al; European Dermatology Forum (EDF); European Academy of Dermatology and Venereology (EADV); European Federation of Allergy (EFA); European Task Force on Atopic Dermatitis (ETFAD); European Society of Pediatric Dermatology (ESPD); Global Allergy and Asthma European Network (GA2LEN). Guidelines for treatment of atopic eczema (atopic dermatitis) part I. J Eur Acad Dermatol Venereol. 2012;26(9):1176–1193
8. Ring J, Alomar A, Bieber T, et al; European Dermatology Forum (EDF); European Academy of Dermatology and Venereology (EADV); European Federation of Allergy (EFA); European Task Force on Atopic Dermatitis (ETFAD); European Society of Pediatric Dermatology (ESPD); Global Allergy and Asthma European Network (GA2LEN). Guidelines for treatment of atopic eczema (atopic dermatitis) part II. J Eur Acad Dermatol Venereol. 2012;26(9):1176–1193


Atopic Dermatitis: Skin-Directed Management
Megha M. Tollefson, Anna L. Bruckner and SECTION ON DERMATOLOGY

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Mechanisms for Atopic Disease

Statistics Review:  
Odds ratio: Odds of Atopic Disease with Filaggrin MUTATION (Disease/No Disease)  
Odds of Atopic Disease with NORMAL Filaggrin (Disease/No Disease)
Filaggrin Mutations Associated with Skin and Allergic Diseases
Alan D. Irvine, M.D., W.H. Irwin McLean, Ph.D., D.Sc., and Donald Y.M. Leung, M.D., Ph.D.

Figure 5. Filaggrin Deficiency and Possible Mechanisms of Disease.
Filaggrin haploinsufficiency results in a number of differentiation-specific structural, biophysical, and functional changes within the stratum corneum that are likely to be directly related to disease pathogenesis in ichthyosis vulgaris and atopic dermatitis. In the granular layer, the proprotein profilaggrin is stored within the keratohyalin granules, where it is thought to be functionally inert. At the interface of the inner stratum corneum and the stratum granulosum, impaired aggregation of keratin filaments causes impaired excretion of lamellar bodies, with resultant impairment in barrier function. In the stratum corneum, filaggrin deficiency is associated with multiple structural changes, including decreased corneodesmosome density, decreased expression of tight-junction proteins, and — most important — impaired maturation and secretion of lamellar bodies. These changes may be mediated by increased pH within the residual cytoplasm of squames due to a lower concentration of acidic filaggrin breakdown products. All these changes contribute to impaired barrier function and increased ease of allergen presentation to epidermal dendritic cells. Finally, on the skin surface, decreased levels of natural moisturizing factor cause the skin to lose hydration and feel dry; reduced levels of urocanic acid and pyrrolidone carboxylic acid on the skin surface impair Staphylococcus aureus adhesion and proliferation through pH-dependent and possibly pH-independent mechanisms. Elevated skin-surface pH increases the activity of several proteases that cleave proforms of interleukin-1, possibly contributing to epithelial inflammation and further barrier destruction.
# National Jewish Atopic Dermatitis Program Step-Care “AD Action” Plan

## Maintenance or Daily Care
Take at least one bath or shower per day; use warm water, for 10-15 minutes.

Use a gentle cleansing bar or wash in the sensitive skin formulation as needed such as Dove® or Oll of Olay®.

Pat away excess water and immediately (within 3 minutes) apply moisturizer, sealer, or maintenance medication if directed. Fragrance-free moisturizers available in one pound jars include Aquaphor® Ointment, Eucerin® Crème, Vanicream®, CeraVe® Cream or Cetaphil® Cream. Vaseline® is a good occlusive preparation to seal in the water; however, it contains no water so it only works effectively after a bathing. Use moisturizers liberally throughout the day. Moisturizers and sealers should not be applied over any topical medication.

Avoid skin irritants and proven allergens.

## Mild-to-Moderate Atopic Dermatitis
Bathe as above for 10-15 minutes, once (and possibly twice) daily.

Use cleansers as above.

Use moisturizers as above to healed and unaffected skin, twice daily especially after baths and at mid-day total body.

Apply to affected areas of face, groin and underarms twice daily especially after baths ________________ (low-potency topical corticosteroid), or ________________ (topical calcineurin inhibitors), or other topical preparation as directed ________________ (topical barrier repair cream, eg., Atopiclair® three times daily).

Apply to other affected areas of the body twice daily especially after baths ________________ (low to mid- potency topical corticosteroid), or ________________ (topical calcineurin inhibitors), or other topical preparation as directed ________________.

## Moderate-to-Severe Atopic Dermatitis
Bathe as above for 10-15 minutes, two times a day, once before bedtime.

Use cleansers as above or consider an antibacterial cleanser (eg., Lever 2000®)

Use moisturizers as above to healed and unaffected skin, twice daily especially after baths and at mid-day total body.

Apply to affected areas of face, groin and underarms twice daily especially after baths ________________ (low-potency topical corticosteroid), or ________________ (topical calcineurin inhibitors), or other topical preparation as directed ________________ (topical barrier repair cream, eg., Atopiclair® three times daily).

Apply to other affected areas of the body twice daily especially after baths ________________ (mid-to-high-potency topical corticosteroid), or topical calcineurin inhibitors), or other topical preparation as directed.

Use wet wraps to involved areas selectively as directed.

Add other medications as directed: ________________ (eg., oral sedating antihistamines, topical or oral antimicrobial therapy)

Pay close attention to things that seem to irritate the skin or make condition worse.

Contact your health care provider for additional evaluation or therapies. Oral steroids are not usually recommended.

Step down to moderate plan above as the skin heals.

## Reduce Skin Irritation
Wash all new clothes before wearing them. This removes formaldehyde and other irritating chemicals.

Add a second rinse cycle to ensure removal of detergent. Residual laundry detergent, particularly perfume or dye, may be irritating when it remains in the clothing. Changing to a liquid and fragrance-free, dye-free detergent may be helpful.

Wear garments that allow air to pass freely to your skin. Open weave, loose-fitting, cotton-blend clothing may be most comfortable.

Work and sleep in comfortable surroundings with a fairly constant temperature and humidity level.

Keep fingernails very short and smooth to help prevent damage due to scratching.

Carry a small tube of moisturizer/sunscreen at all times. Daycare/school/work should have a separate supply of moisturizer.

After swimming in chlorinated pool or using hot tub, shower or bathe using a gentle cleanser to remove chemicals, then apply moisturizer.
<table>
<thead>
<tr>
<th>Potency Group</th>
<th>Generic Name</th>
<th>Percentage Strength</th>
<th>Brand Name (Alt Brand Name)</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Augmented Betamethasone Dipropionate</td>
<td>0.05% lotion</td>
<td>Diprolene</td>
<td>30 ml</td>
</tr>
<tr>
<td></td>
<td>Clobetasol Propionate</td>
<td>0.05% ointment</td>
<td>Temovate (Cormax)</td>
<td>15 g, 30 g</td>
</tr>
<tr>
<td></td>
<td>Clobetasol Propionate</td>
<td>0.05% cream</td>
<td>Temovate-E (Cormax)</td>
<td>15 ml, 30 ml, 45 ml</td>
</tr>
<tr>
<td></td>
<td>Clobetasol Propionate</td>
<td>0.05% solution</td>
<td>Temovate Scalp (Cormax)</td>
<td>25 ml, 30 ml</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>4mcg/cm tape</td>
<td>Cordran</td>
<td>200 cm</td>
</tr>
<tr>
<td>Class II</td>
<td>Augmented Betamethasone Dipropionate</td>
<td>0.05% cream</td>
<td>Diprolene AF</td>
<td>15 g</td>
</tr>
<tr>
<td></td>
<td>Betamethasone Dipropionate</td>
<td>0.05% ointment</td>
<td>Diprosone</td>
<td>15 g</td>
</tr>
<tr>
<td></td>
<td>Fluocinonide</td>
<td>0.05% cream</td>
<td>Lidex</td>
<td>15 g, 60 g</td>
</tr>
<tr>
<td></td>
<td>Fluocinonide</td>
<td>0.05% gel</td>
<td>Lidex</td>
<td>15 g, 60 g</td>
</tr>
<tr>
<td></td>
<td>Fluocinonide</td>
<td>0.05% ointment</td>
<td>Lidex</td>
<td>15 g, 60 g</td>
</tr>
<tr>
<td></td>
<td>Fluocinonide</td>
<td>0.05% solution</td>
<td>Lidex</td>
<td>60 ml</td>
</tr>
<tr>
<td>Class III</td>
<td>Amcinonide</td>
<td>0.1% cream</td>
<td>Cyclocort</td>
<td>15 g, 60 g</td>
</tr>
<tr>
<td></td>
<td>Betamethasone Dipropionate</td>
<td>0.05% lotion</td>
<td>Diprosone</td>
<td>60 ml</td>
</tr>
<tr>
<td></td>
<td>Fluocinonide Emollient</td>
<td>0.05% cream</td>
<td>Lidex-E</td>
<td>15 g, 60 g</td>
</tr>
<tr>
<td>Class IV</td>
<td>Hydrocortisone Valerate</td>
<td>0.2% ointment</td>
<td>Westcort</td>
<td>15 g, 60 g</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone Acetonide</td>
<td>0.1% ointment</td>
<td>Kenalog</td>
<td>15 g, 80 g, 454 g</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone Acetonide</td>
<td>0.2% aerosol</td>
<td>Kenalog</td>
<td>63 g</td>
</tr>
<tr>
<td>Class V</td>
<td>Betamethasone Valerate</td>
<td>0.1% cream</td>
<td>Valisone</td>
<td>15 g</td>
</tr>
<tr>
<td></td>
<td>Betamethasone Valerate</td>
<td>0.1% lotion</td>
<td>Valisone</td>
<td>60 ml</td>
</tr>
<tr>
<td></td>
<td>Desonide</td>
<td>0.05% ointment</td>
<td>Tridesilon (DesOwen)</td>
<td>15 g, 60 g</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>0.05% lotion</td>
<td>Cordran</td>
<td>60 ml</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone Valerate</td>
<td>0.2% cream</td>
<td>Westcort</td>
<td>15 g, 60 g</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone Acetonide</td>
<td>0.1% cream</td>
<td>Kenalog (Aristocort EQ)</td>
<td>15 g, 80 g, 454 g</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone Acetonide</td>
<td>0.025% ointment</td>
<td>Kenalog</td>
<td>15 g</td>
</tr>
<tr>
<td>Class VI</td>
<td>Desonide</td>
<td>0.05% cream</td>
<td>Tridesilon (DesOwen)</td>
<td>15 g, 60 g</td>
</tr>
<tr>
<td></td>
<td>Fluocinolone Acetonide</td>
<td>0.01% oil</td>
<td>Dermasmooth (Capex)</td>
<td>120 ml</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone Acetonide</td>
<td>0.025% cream</td>
<td>Kenalog</td>
<td>15 g, 80 g</td>
</tr>
<tr>
<td>Class VII</td>
<td>Hydrocortisone</td>
<td>2.5% cream</td>
<td>(Hytone)</td>
<td>28 g</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone (OTC)</td>
<td>1% cream</td>
<td></td>
<td>30 g</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5% cream</td>
<td></td>
<td>30 g</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1% ointment</td>
<td></td>
<td>30 g</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1% ointment</td>
<td></td>
<td>118 ml</td>
</tr>
</tbody>
</table>

😊 Safe for facial use
Moisturizers on Formulary at WR-B

<table>
<thead>
<tr>
<th>Moisturizer</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aquaphor (mineral oil/petroleum)</td>
<td>454 g jar</td>
</tr>
<tr>
<td>Cetaphil cream</td>
<td>454 g jar</td>
</tr>
<tr>
<td>Hydrocerin lotion</td>
<td>480 ml</td>
</tr>
<tr>
<td>Vanicream</td>
<td>454 g jar</td>
</tr>
</tbody>
</table>

Finger Tip Units (FTUs)

- Amount of ointment/cream product that extends from the tip of an adult finger to the first flexural crease of the DIP, when dispensed from a tube with the standard 5mm nozzle.
- Used to gauge the amount of topical steroid to use on a given area of affected skin.
- Provides guide to the appropriate size of tube that should be prescribed for a patient.

- 1 FTU = 0.5 g = treats an area 2x the size of an adult’s hand with fingers together,
- 2 FTUs = 1g = treats an area equivalent to 4 adult handprints (10 x 10cm), etc.
- 30 g of product is necessary to fully cover an adult patient.
Additional Types of Baths (www.nationaleczema.org)

**Vinegar Baths:** Referred to as the “pickle the patient” treatment. Add one cup to one pint of vinegar to the bath. Can be used as a wet dressing too as it kills bacteria.

**Bath Oil Baths:** Oils in the bath are a favorite of some providers and patients. Bath oils can leave the tub slippery – be careful. They can also leave a hard-to-clean film. See if they work for you.

**Salt Baths:** When there is a significant flare the bath water may sting or be uncomfortable. Add one cup of table salt to the bath water to decrease this side effect.

**Baking Soda Baths:** Added to a bath or made into a paste it can be used to relieve the itching.

**Tar Baths:** Tar baths can soothe inflammation and itch. Tar bath oil or tar shampoo can be used. Warning: if the skin is open or excoriated the tar baths can sting.

**Oatmeal baths:** Added to a bath or made into a paste it can be used to relieve the itching.
Atopic Dermatitis Quiz

1. The atopic triad includes: **Atopic dermatitis, asthma, and allergic rhinitis**. Children with one atopic disease are **three times** more likely to develop a second atopic disease.

2. Describe the **underlying etiology** of atopic dermatitis. AD results from a complex interaction between genetics, immune response, and environment. The epidermis has structural changes and/or lower concentration of different proteins, including filaggrin and ceramides, which increases surface pH and interferes with the epidermal barrier function. Colonization and overgrowth of bacteria, such as S. aureus, may further interfere with the skin barrier due to **exotoxin and protease production**. The impaired barrier function enhances **water loss** allowing for increased xerosis, susceptibility to trauma, and absorption of irritants and allergens that induce local inflammatory response. The inflammatory responses in patients with AD may be overactive due to underlying genetics, but the patients may also have an **upregulated Th2 immune response** due to the limited Th1 activation (**hygiene hypothesis**).

3. List the **sites typically** affected by atopic dermatitis depending on age:

<table>
<thead>
<tr>
<th>Age</th>
<th>Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>Cheeks, dorsa of wrists and ankles, and the lateral extremities</td>
</tr>
<tr>
<td>Children</td>
<td>Neck, flexural surfaces- antecubital and popliteal fossae, and gluteal folds</td>
</tr>
<tr>
<td>Teenagers</td>
<td>Eyelids, hands and feet</td>
</tr>
</tbody>
</table>

4. **True** or False: Atopic dermatitis can develop on any part of the body regardless of age. Specific distribution patterns are associated with age (see #3), but not exclusive. All areas of the body may be affected, including genitalia and lips. “From the scalp to the soles”

5. Place the following topical corticosteroids in or order of decreasing potency:

**Class I (strongest)**
- Flurandrenolide Tape
- Fluocinonide 0.05% cream
- Fluocinonide 0.05% ointment

**Class II**
- Fluocinolone Acetonide 0.025% ointment
- Triamcinolone Acetonide 0.1% cream
- Desonide 0.05% ointment

**Class III**
- Fluocinolone Acetonide 0.01% oil
- Fluocinonide 0.05% emollient cream

**Class IV**
- Hydrocortisone Valerate 0.2% ointment
- Triamcinolone Acetonide 0.1% ointment

**Class V**
- Triamcinolone Acetonide 0.025% ointment
- Triamcinolone Acetonide 0.1% cream
- Desonide 0.05% ointment

**Class VI**
- Desonide 0.05% cream
- Fluocinolone Acetonide 0.01% oil

**Class VII (weakest)**
- Hydrocortisone 2.5% cream

- **Local**: Atrophy, striae, telangiectasias, pigmented changes, easy bruising, hypertrichosis, acne like eruptions, allergic/contact/irritant reaction.
- **Systemic**: Hypothalamic-pituitary-adrenal axis suppression, Cushing syndrome, growth retardation, glaucoma, cataracts, osteopenia/osteoporosis.
Atopic Dermatitis Cases

Case 1:
Colton is a 15 month old male infant who presents for a routine well visit. He is the only child of well-educated parents who live in the suburbs. His height and weight have been stable at the 50th percentile. He was breastfed for the first year of his life and continues to breastfeed at night. He was introduced to solid foods at 6 months of age and has fully transitioned to table foods. His mother boasts that he has “never had a runny nose in his life” and that she uses hand sanitizer “all the time, of course”. Her only concern is for a red, dry, itchy rash that keeps recurring on his cheeks, arms, and legs. She has not noticed any triggers.

Based on history, what are protective and predisposing factors for Colton developing AD?

- **Protective**: exclusive breastfeeding for at least the first 4 months of life; introduction of solid foods after 4 months of life.

- **Predisposing**: limited exposure to pathogens and dirt (first born, no illnesses, over-cleanliness) which could lead to up-regulation of the Th2 immune response (**Hygiene Hypothesis**—see diagram); frequent use of hand sanitizer which can be drying and contain fragrances/additives that further irritate the skin.

On exam, Colton’s rash appears consistent with a mild-to-moderate eczema flare, with large dry erythematous plaques covering his cheeks and chin. His arms and legs have multiple papules and vesicles in the flexural surfaces with scratch marks.

What treatment would you recommend?
Discuss with mother that treatment of eczema is a **four-prong approach**:

1. **Moisturization**: “Soak and seal”. Bathe 1-2 times a day for 10-15min during flares, using gentle cleanser without scrubbing, and pat dry. Cover with moisturizer/emollient within 3 min of bath to lock in water. Type of moisturizer is patient/parent preference but should be hypoallergenic with limited fragrances/additives to prevent further skin irritation. (Refer to the [National Eczema Association Seal of Acceptance](https://www.eczema.org/)).

2. **Inflammation Reduction - Topical steroids** are the first-line and only treatment approved for children <2 years of age. Low potency steroids (Class VI-VII) should be used on the face (e.g. hydrocortisone 0.5-1%; Desonide 0.05% cream). Low-to-mid potency steroids (Class IV-VI) can be used on trunk and extremities (e.g. Westcort 0.2% cream; Kenalog 0.025% ointment). Calcineurin inhibitors (e.g. Elidel) may be considered for older children with persistent steroid use or flares in sensitive skin areas.

3. **Infection Control**: Counsel on signs of secondary bacterial and viral infections. Advise against regular usage of antibiotic ointment, particularly neomycin, which can be allergenic. For localized infections, use topical antibiotics or short course of PO antibiotic. If persistent infections, recommend culturing and possible decolonization with regular bleach baths.
4. **Avoidance of Triggers/Irritants**: Recommend **fragrance/preservative-free** soaps, cleansers, shampoos, and detergents. Wear **loose, nonabrasive cotton** clothing. Wash all clothing before wearing with **extra-rinse cycle**. Avoid overheating during exercise or the summer. Use **mattress and pillow covers**, vacuum frequently if dust mites are a concern. Bathe/rinse off allergens and/or use antihistamines if pollens or animal dander exacerbate symptoms. **Do not restrict diet**, only avoid known food allergens. Limit stress. Keep **fingernails short**.

His mother is wary of starting topical steroids and asks about alternatives or homeopathic treatments that are available.

**What would you recommend or advise against?**

- Validate that her concerns are not unreasonable and that topical steroids can have a number of side effects, particularly if not used in appropriate areas or if used for prolonged courses.
- An initial approach could be to **focus on good skin care** with regular moisturization and bathing. Moisturization is proven to decrease the need for steroids.
- **See Extra-Credit article on CAM therapies.** Examples with **no** proven benefit are supplementation with EFAs and probiotics. Examples with proven benefits include:
  - **Traditional Chinese Medicine herbs**: Proven benefits, but caution should be taken due to risk of contamination. Agranulocytosis and liver toxicity have been observed.
  - **Honey**: Inherent anti-inflammatory properties; promotes healing. It can be mixed with wax and oil and applied to the skin with limited side effects.
  - **Massage therapy**: Relieves stress, improves blood flow, and enhances emollient delivery. Oils should be avoided as they can further irritate the skin.

Prior to leaving, you obtain additional family history to better delineate his risk for additional atopic disease. His mother notes that she and all her sisters struggled with asthma as kids. His father is adopted so family history is unknown, but he does have a h/o anaphylaxis to peanuts.

**How would you counsel Colton’s mother regarding his risk, particularly for food allergies?**

- Discuss the atopic triad and how it presents as the **“atopic march”**. Counsel that Colton does have a higher risk (3x greater than non-atopic child) of developing asthma or AR.
- The development of additional atopic disease could be related to a common phenotype (e.g. defective filaggrin) or be a result of **increased sensitization** due to impaired skin barrier.
- **Do not restrict his diet** unless a temporal relationship between an eczema flare and introduction of a food was noticed. If suspicion, consider RAST and referral to allergy.
Case 2
Sarah is a 9 year old female brought in by her mother with the complaint of worsening eczema. The family just moved to the DC area from Arizona after her father was injured in Afghanistan. She is currently living in an apartment in Building 62 with her parents and two younger sisters. She has had eczema since infancy that has been controlled with periodic use of moisturizers and topical steroids. Her eczema today is the worse it has ever been, completely involving her arms, legs, and neck with patches on her trunk. She has been unable to sleep because of the pruritis and has little interest in going outside to play because of discomfort with walking.

What further history would you like to know?
- Skin care regimen- moisturizers, bathing
- Medications – including current and past topical therapies that have been effective
- Allergies/Triggers- exposure to dust mites, carpeting, animals, new soaps/cleansers
- Additional atopic disease
- PMHx- including immunizations and significant childhood diseases
- Additional social history- school attendance, contacts with skin eruptions

Her mother, accustomed to these visits, brings in multiple half used 15 g tubes of steroids that were prescribed or purchased from the drugstore. She says she has tried all of them for 1-2 days with no relief. The only one that has helped was a new script for Desonide 0.05% cream, that is now half-full. She has been using it once a day for the past week on all of Sarah’s affected areas.

Has the Desonide been used appropriately? What clues can you use to answer this question, other than Sarah’s clinical symptoms?
Minimal improvement in clinical symptoms suggests inconsistent or inappropriate use of the topical steroid; however, complicating infections must also be considered.

Another clue that the medication is not being used appropriately is the discrepancy between the amount of steroid left in the tube and the history of usage (see FTU Chart):
- Coverage of a full leg = 4.5 FTUs
- Coverage of a full arm = 2.5 FTUs
- Coverage of the face and neck 2 FTUs.

If she has used ½ of a 15g Desonide tube, she has in fact used only 8g steroid/ 1 week.

On exam, you notice that some of Sarah’s lesions appear impetiginous. You also learn she has a history of abscesses and that her father is receiving home IV antibiotics for MRSA osteomyelitis.

How does this history and exam affect the treatment for Sarah’s eczema flare?
The history and likely impetigo suggest bacterial infection with possible overgrowth, which would explain why she had minimal improvement with topical steroids. Her skin should be cultured, especially to look for MRSA. Treatment should include not only a short course of oral antibiotics but also skin decolonization with bleach baths. Her mother and sisters should also be tested for MRSA and decolonized to prevent re-colonization.
What are additional types of superinfections that can occur in patients with AD?

• **Viral**: eczema herpeticum, eczema vaccinatum, molluscum contagiousum, papilloma (warts)
• **Fungal**: Trichophytan sp (tinea), Malassezia (seborrhea)

You ultimately decide to treat Sarah with an oral antibiotic for secondary bacterial infection, decolonize her with daily bleach baths for a week and nasal mupirocin, decrease inflammation with a low potency corticosteroid for her face and a medium potency corticosteroid for her extremities, and start her on a regular bathing and moisturizing regimen.

She returns in one week with no further signs of infection. History and medication tubes support compliance. She continues, however, to complain of pruritis and pain and there has been only moderate improvement. There is no concern for secondary viral or fungal infection.

**What would else could you recommend?**

1. **Wet wrap therapy** to help better seal in the moisture, concentrate the topical steroids, and protect the skin from further irritation.
   - Recommend taking a soaking bath with gentle cleanser, no scrubbing and patting dry.
   - Follow immediately with application of **topical steroids** to affected areas and **moisturizer** to non-affected areas. Use a plastic spoon or tongue depressor to prevent contamination.
   - **Soak dressings**— long underwear, tube socks, Kerlix, ace bandages— in warm water and wring out excess water. Apply dressings and cover with dry material.
   - Avoid chilling by placing on more layers, using blankets, or turning up the heat. Leave on for 1-2 hours until dry or overnight if comfortable. Reapply moisturizers after removal.

2. **Additional options** would be to increase the potency of steroids or switch to a **topical calcineurin inhibitor (TCI)**. TCIs should not be used in conjunction with wet wraps. Further counseling on triggers and use of **antihistamines** to decrease pruritis should also be provided.
A 7-year-old girl presents in September with an intensely itchy rash of several weeks' duration. During the summer she had many mosquito bites and one area of ringworm, but otherwise she has had no prior skin conditions. She has had no fever, joint pain, myalgias, fatigue, or change in appetite or activity. Antihistamines helped when she had the insect bites, but now they have little effect. No other family members have a rash. On physical examination, the rash is apparent on exposed areas and consists of papules, vesicles, and wheals, some in a linear array or in triangular clusters. There are also numerous hyperpigmented macules. The scalp is involved, but the palms and soles are spared.

Of the following, the MOST likely cause of this rash is
A. Atopic dermatitis  
B. Id reaction to recent fungal infection  
C. Hypersensitivity reaction to insect bites  
D. Recurrent impetigo with postinflammatory changes  
E. Scabies

The girl described in the vignette has papular urticaria, an annoying, pruritic eruption that is the result of an insect bite-induced hypersensitivity reaction. It typically affects children between 2 and 10 years of age, who experience chronic or recurrent eruptions of papules, vesicles, and wheals, often with excoriations because of their persistent itchiness. The age distribution is presumed to be because children younger than 1 year of age are unable to mount the hypersensitivity reaction, and most children have developed tolerance to insects by age 10 years. The lesions typically are symmetrically distributed and grouped in linear or triangular clusters that are concentrated on exposed surfaces, including the scalp, waist, and sock lines. As described for the girl in the vignette, the palms and soles are spared. Often, hyperpigmented or violaceous macules persist as the original eruption heals. Although most cases are related to flea and mosquito bites, any biting insect may be involved, including bed bugs and mites. The rash can be frustrating for families and clinicians alike because of its chronicity, the limited treatment options (primarily symptomatic care), and the paradox that only one family member may be affected, even though it is due to insect bites.

Papular urticaria differs from atopic dermatitis by its lack of family history, distribution, configuration, and absence of scale. Although id reactions are typically symmetric and itchy, they often involve hands and feet and usually are preceded by a worsening of the underlying condition, which is often a fungal infection such as tinea capitis. Recurrent impetigo is characterized by crusting and responds well to antibiotic treatment. Like papular urticaria, scabies is insect-related and involves an immune reaction. However, scabies produces smaller papules or vesicles, frequently involves the hands and intertriginous areas, and is characterized by burrows that are not present with popular urticara. Also, scabies often affect multiple family members.
2. A 6-year-old boy presents with a 2-year history of frequent pruritic, erythematous eruptions on his arms and legs. The rash usually worsens during winter but occurs intermittently throughout the year. His mother has tried various moisturizers, but they have not been effective in controlling the rash. On physical examination, you note erythematous patches on his antecubital and popliteal regions bilaterally.

Of the following the MOST appropriate initial step in management for this patient is
A. food allergy skin testing
B. oral antibiotic therapy
C. oral antihistamine therapy
D. topical calcineurin inhibitor therapy
E. topical corticosteroid therapy

The appearance of pruritic, erythematous patches in the antecubital and popliteal areas described for the boy in the vignette is most consistent with atopic dermatitis. Atopic dermatitis, also called eczema, is a common skin condition that affects up to 10% of children and frequently is the first presentation of atopy (ie, atopic dermatitis, allergic rhinitis, and asthma). Because the underlying mechanism for atopic dermatitis involves defects in the epidermal barrier function & subsequent evaporative loss, the mainstay of therapy is topical emollients. These include moisturizers (eg, creams, lotions, ointments) and occlusive products such as solid vegetable shortening or petroleum jelly. Because skin hydration also is important, patients should apply a moisturizer or an occlusive product after bathing for 10 to 15 minutes in warm (not lukewarm or tepid) water.

Almost all children who have eczema have an overabundance of Staphylococcus aureus and inflammatory cytokine production. Topical corticosteroids are used to reduce inflammation when emollients and occlusive creams do not control symptoms adequately. Topical corticosteroids are available in different preparations (eg, ointment, cream, lotion) and potencies. Regular use of topical corticosteroids is associated with hypopigmentation, bruising, acne, and thinning of the skin. The patient should be monitored for secondary infections.

Other therapies targeted at reducing bacteria include topical antibiotics, systemic antibiotics, and bleach baths. One-eighth to one-half cup of bleach per full bath two to three times a week can reduce S. aureus colonization, but such baths also can be irritating to the skin. Further, although a few studies have demonstrated improvement in eczema using bleach baths, a recent Cochrane review did not support its use. Oral antibiotics also failed to demonstrate improvement when analyzed in a meta-analysis.

Because atopic dermatitis typically involves a cyclical process of itching and scratching, patients frequently receive oral antihistamines to reduce pruritus. Sometimes these are helpful, but oral antihistamines often are inadequate and usually are added to therapy when topical emollients or topical corticosteroids fail to control symptoms.

Topical calcineurin inhibitors were introduced in 2000 and approved for the treatment of atopic dermatitis in children older than 2 years. However, their use has been curtailed significantly after a black box warning was added in 2006. These medications are not as effective for eczema as moderate- to high-potency topical corticosteroids, but they are an alternative to mild-potency corticosteroids and result in less hypopigmentation, thinning of the skin, or bruising.
Both food and inhalant allergens may play roles in atopic dermatitis. Approximately 30% of children who have moderate-to-severe atopic dermatitis are ingesting a food that is exacerbating their eczema via an immunoglobulin E- or T cell-mediated process. Consultation with an allergist and consideration for skin or patch testing to commonly implicated foods (eg, milk, egg, wheat, soy, peanut) may be warranted. Some investigators have advocated reducing dust mite concentrations by encasing the mattress, pillow, and box spring in conjunction with regular washing of the bed linen. Because the child in the vignette only has mild atopic dermatitis, pursuing food or inhalant allergen testing is not an appropriate initial step.

3. A 12-month-old girl presents with a 3-month history of a pruritic rash that involves her cheeks, neck, anterior trunk, and antecubital and popliteal areas. The rash improves after use of an over-the-counter topical steroid cream but still is present most days, and the infant often wakes up at night scratching. On physical examination, you observe a raised erythematous rash that has areas of lichenification.

Of the following, the MOST helpful intervention is to
A. eliminate fruit and acidic juices from the diet
B. eliminate milk, eggs, soy, and wheat from the diet
C. perform aeroallergen allergy testing
D. perform food allergy testing
E. recommend a skin biopsy

Some 30% to 40% of infants who have moderate-to-severe atopic dermatitis (AD), such as described for the infant in the vignette, may have an underlying immunoglobulin (Ig) E-mediated food allergy exacerbating the AD. For some infants, food ingestion may result in immediate worsening of AD severity, although most infants do not demonstrate this immediate reaction. Many foods have been implicated in AD, but five (milk, eggs, soy, wheat, and peanut) account for 90% of the causative allergens. Both allergy skin testing and measurement of serum IgE to these foods can help to identify and eliminate likely triggers. Either a negative IgE blood test (<0.35 kU/L) or a negative skin test for a specific food provides a high negative predictive value. On the other hand, the positive predictive value for a skin or blood test may be only 50%. Although the most commonly implicated foods often are eliminated from the diet, such an approach does not improve symptoms in most children because they do not have IgE-mediated AD. The unnecessary elimination of multiple foods can have an adverse effect on nutrition, and food avoidance should be guided by the dietary history, eczema severity, and skin/blood testing.

Frequently, children experience perioral rashes after drinking fruit juice. Such rashes typically are nonpruritic, limited to the area of contact, and resolve within a few hours. The mechanism of such rashes is unknown, but children generally outgrow such reactions by age 4 years. In cases involving more widespread cutaneous symptoms elimination of fruit juices is unnecessary.

Parents often request testing for environmental allergies. House dust mites have been implicated in some cases of AD, although they are less likely a cause for moderate-to-severe atopic dermatitis than food allergies. Climate changes such as cold, dry air or hot, humid weather can worsen AD, but specific seasonal allergens such as oak tree or ragweed are not associated with eczema in infants.
A skin biopsy can provide insight into the pathophysiology of chronic rashes or lesions. Generally, skin biopsies neither are advised nor provide insight into the causes of typical AD manifestations in infants, but atypical presentations or lack of expected improvement with appropriate therapy should prompt consideration of a dermatology referral.

4. A 2-year-old boy presents for evaluation of a chronic pruritic eruption. His medical history is remarkable for recurrent epistaxis, otitis media, and pneumonia. Physical examination reveals erythematous, slightly scaling patches on the trunk and in the antecubital and popliteal fossae. Petechiae are present profusely.

Of the following, these findings are MOST suggestive of:
A. Acrodermatitis enteropathica
B. Ataxia telangiectasia
C. Atopic dermatitis
D. Langerhans cell histiocytosis
E. Wiskott-Aldrich syndrome

Wiskott-Aldrich syndrome is an X-linked disease characterized by partial but significant deficiency in both the antibody and cell-mediated immune compartments. It produces a predictable triad of: (1) eczema; (2) severe thrombocytopenic purpura; (3) recurrent infections of all types. Classic presentation is bleeding, eczema, and recurrent otitis media. There is an increased risk of atopic disorders, lymphoma/leukemia, and infection from S. pneumonia, S. aureus, and H. influenzae type B. IgE/IgA ratio is very elevated, and IgM is depressed; there is an absence of blood group antibodies (isohemaglutinins) on laboratory evaluation. Treatment is supportive (IVIG and antibiotics). Splenectomy is often necessary to manage the thrombocytopenia.

Ataxia-telangiectasia is an autosomal-recessive disorder of chromosomal repair. Mutations in immunoglobulin and T-cell receptor genes are not repaired, and progressive loss of immune function results. The clinical manifestations include: (1) progressive cerebellar ataxia; (2) oculocutaneous telangiectasia; (3) recurrent infections. The latter usually begin as recurrent sinopulmonary infections; a progressive development of infections of all types follows. The disorder is associated with a very high incidence of lymphoreticular malignancy in the 2nd and 3rd decades of life (e.g. non-Hodgkin’s lymphoma and gastric carcinoma). Deficient IgA and IgE levels are often seen initially, and progressive loss of other immunoglobulin types and cell-mediated immune defects are common.

Acrodermatitis enteropathica is an autosomal recessive metabolic disorder affecting the uptake of zinc, characterized by periorificial and acral dermatitis, alopecia, and diarrhea. Similar features may be present in acquired zinc deficiency. Skin lesions may be secondarily infected by bacteria such as Staphylococcus aureus or fungi like Candida albicans. Langerhans cell histiocytosis is a rare disease involving clonal proliferation of Langerhans cells—abnormal dendritic cells deriving from bone marrow and capable of migrating from skin to lymph nodes. Clinically, its manifestations range from isolated bone lesions to multisystem disease.