

# What's Your Diagnosis?

Sharpen Your Physical Diagnostic Skills

## A Boy With an Intensely Itchy Leg Rash

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**A** 10-year-old boy presented with intensely pruritic lesions on his neck and extremities of several months' duration. His past health was unremarkable, except that he had asthma. His 6-year-old brother and 42-year-old father also had similar skin problems.

### PHYSICAL EXAMINATION

Physical examination revealed erythematous papules and scaly, excoriated, and lichenified plaques. The remaining skin findings were unremarkable.

## WHAT'S YOUR DIAGNOSIS?

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## ANSWER: Atopic dermatitis

Atopic dermatitis is a chronically relapsing dermatosis characterized by pruritus, erythema, vesiculation, exudation, excoriation, crusting, scaling, and lichenification.

### EPIDEMIOLOGY, PATHOGENESIS, AND ETIOLOGY

Atopic dermatitis affects 10% to 20% of children and 1% to 3% of adults in the United States and Europe.<sup>1</sup> The prevalence is higher in developed countries and in urban areas. Atopic dermatitis occurs more frequently in temperate. Approximately 30% to 50% of children with one affected parent and 50% to 80% of children with two affected parents develop the disorder.<sup>2</sup> The female to male ratio is approximately 1.5:1.<sup>3</sup>

The pathogenesis of atopic dermatitis involves complex interactions among susceptible genes, immunologic factors, skin barrier defects, infections, and environmental factors.<sup>4</sup> Its strong genetic predisposition is evidenced by the familial nature of the disease and the high concordance in monozygotic twins.<sup>4</sup>

Atopic dermatitis involves defective cell-mediated immunity that is related, in part, to an imbalance in two subsets of CD4 T lymphocytes that creates a predominance of T memory cells in the T helper 2 pathway and preferential apoptosis of interferon- $\gamma$ -producing T helper 1 memory cells and effector T cells.<sup>1</sup>

Filaggrin has an important role in epidermal differentiation and barrier function.<sup>5,6</sup> Null mutations within the filaggrin gene are major risk factors for the development of atopic dermatitis.<sup>6,7</sup> The loss of skin barrier function makes the stratum corneum susceptible to colonization by *Staphylococcus aureus*.<sup>1</sup> *S aureus* exacerbates or maintains skin inflammation by secreting a group of toxins known to act as superantigens, which stimulate T cells, macrophages, eosinophils, and keratinocytes.<sup>8</sup>

Environmental factors such as food allergens, aeroallergens, contactants, and emotional stress trigger or exacerbate atopic dermatitis in susceptible individuals.<sup>9</sup>

### CLINICAL MANIFESTATIONS

Approximately 60% of children with atopic dermatitis manifest the disease by the first year of life, and an additional 30% manifest before the age of 5 years.<sup>3</sup> Intense pruritus and cutaneous reactivity are the hallmarks of atopic dermatitis. In infants, the eruption often affects the face and scalp, although the extensor surfaces of the extremities and the trunk also may be affected.<sup>4</sup> In older children and adolescents, the neck and antecubital and popliteal fossae usually display the eruption. The nose often is spared; this is referred to as the headlight sign.

Lesions are classified as acute, subacute, or chronic and usually are symmetric. Acute lesions are intensely pruritic, erythematous papules, papulovesicles, or weeping lesions.<sup>3</sup> Subacute lesions are erythematous scaling papules or plaques. Chronic lesions are characterized by prominent scaling, excoriations, and lichenification in the classically affected body areas.<sup>3</sup>

Other associated findings include xerosis, Dennie-Morgan lines (infraorbital folds), allergic shiners, palmoplantar hyperlinearity, pityriasis alba, keratosis pilaris, ichthyosis vulgaris, dermatographism, anterior subcapsular cataract, cheilitis, prurigo nodularis, and lichen simplex chronicus.<sup>4</sup>

### DIAGNOSIS

The diagnosis is predominantly clinical, based on a constellation of features.<sup>10</sup> Laboratory tests usually are not required. Differential diagnosis includes seborrheic dermatitis, psoriasis, acrodermatitis enteropathica, scabies, immunodeficiency disorders, mycosis fungoides, nummular eczema, contact dermatitis, phenylketonuria, Netherton syndrome, and Langerhans cell histiocytosis.<sup>5</sup>

### COMPLICATIONS

Bacterial infection, most commonly with *S aureus*, is the main complication of atopic dermatitis.<sup>3</sup> Eczema herpeticum caused by herpes simplex virus 1 is a potentially dangerous complication. Children with atopic dermatitis also are prone to verruca vulgaris, molluscum contagiosum, and superficial fungal infections.<sup>4</sup>

Ocular complications of longstanding atopic dermatitis include eyelid dermatitis, chronic blepharitis, keratoconjunctivitis, vernal conjunctivitis, keratoconus, uveitis, and cataracts.<sup>4</sup>

Postinflammatory hypopigmentation may occur at sites of atopic dermatitis. Hypopigmentation also may be a complication of topical corticosteroid therapy.

Children with atopic dermatitis may experience lack of sleep, irritability, daytime tiredness, emotional stress, lowered self-esteem, and psychological disturbance.<sup>3</sup>

### MANAGEMENT

Successful treatment requires trigger avoidance, optimal skin care, pharmacotherapy during acute exacerbations, maintenance therapy, and patient and caregiver education.

**Avoidance of triggering factors.** Irritants, allergens, and emotional stress may lead to skin flares in children with atopic dermatitis. Soaps, detergents, fabric softeners, and perfumed products should be avoided as much as possible.<sup>3</sup> Woolen or abrasive clothing should be avoided; children do best wearing 100% cotton clothing. The environment should be kept cool, and a cool-mist humidifier in the bedroom during dry seasons is a good idea. Water softening also can be a helpful adjunct.

Food allergy plays an immunopathogenic role in 30% to 50% of children with moderate to severe atopic dermatitis.<sup>4,9</sup> Most children with food allergy react to only one or two of the most common allergens such as eggs, cow's milk, tree nuts, peanuts, soy, and wheat. For children whose food allergen has been identified, eliminating it from the diet is prudent. Emotional stress often exacerbates atopic dermatitis. If avoidance is not possible, coping mechanisms should be tried.

**Optimal skin care.** Hydration to maintain the skin's barrier



function is of paramount importance in the prevention and management of atopic dermatitis. Skin hydration can be achieved by daily baths in lukewarm water for 5 to 10 minutes, followed by patting the body dry with a towel.<sup>3</sup> A moisturizer or emollient should be applied within 3 minutes of bathing to prevent evaporation and to keep the skin soft and flexible. This “soak and seal” method helps to improve the integrity of the skin barrier.<sup>6</sup> Frequent applications of moisturizers throughout the day can help maintain a high level of hydration in the stratum corneum.

**Topical corticosteroids.** These are the mainstay of therapy, with the choice of potency depending on the severity, site, and extent of the outbreak.<sup>3</sup> In general, the least-potent corticosteroid that can control the symptom should be used, and only low-potency agents should be applied to the skin of the face, genitalia, and intertriginous areas. Corticosteroids should not be applied more than twice a day; frequent use does not improve efficacy but does increase the risk of adverse effects.

**Topical immunomodulators.** Immunomodulators such as tacrolimus ointment and pimecrolimus cream work by binding to a cytoplasmic immunophilin.<sup>11</sup> Effectiveness does not decrease with time, and the rebound effect sometimes seen after withdrawal of a topical corticosteroid does not occur. Topical immunomodulators do not decrease collagen synthesis or cause skin abnormalities or dyspigmentation, and they can be used safely over the entire body, including the face and intertriginous areas.<sup>12</sup> Treatment with topical immunomodulators may even reverse corticosteroid-induced skin atrophy in patients with atopic dermatitis.<sup>13</sup> Treatment with either tacrolimus or pimecrolimus is associated with reduced levels of *S aureus* in the lesional skin of patients with atopic dermatitis.<sup>11</sup> Topical immunomodulators, but not corticosteroids, also suppress superantigen-driven immune proliferation.<sup>13</sup> The most common adverse effect of topical immunomodulators is a burning or stinging sensation or erythema during the first few days of application, which resolves with continued use.

**Systemic immunosuppressants.** Systemic corticosteroids should be reserved for recalcitrant cases and used for the shortest time possible while awaiting response to other therapies. Various other systemic immunosuppressants such as cyclosporine, azathioprine, mycophenolate mofetil, methotrexate, and recombinant interferon- $\gamma$  have been used in a small number of patients with varying success.<sup>14</sup>

**Antihistamines.** Although pruritus in atopic dermatitis does not appear to be mediated by histamine release, oral antihistamines can provide symptomatic relief at bedtime because of their sedative properties and may be effective for intense pruritus that is refractory to moisturizers and conservative measures.

**Antibiotics.** Systemic antibiotics are indicated for secondary bacterial infections that may exacerbate and complicate an acute flare. Cloxacillin, clindamycin, first- or second-generation cephalosporins, or macrolides are most effective against *S aureus*.<sup>4</sup> Topical antibiotics, such as mupirocin and fusidic acid,

often are useful on localized impetiginized lesions.

**Wet-wrap therapy.** Wet-wrap treatments are useful for short-term relief of pruritus in severe or refractory atopic dermatitis.<sup>15</sup> Evaporation of water from the skin results in vasoconstriction with relief of pruritus. Wet-wrap therapy also helps by debriding crusts from the skin surface, softening the skin (which enhances penetration of topical medication), and serving as a mechanical barrier against scratching. Adverse effects include folliculitis and, with prolonged treatment, skin maceration.<sup>15</sup>

**Patient education.** Patient and caregiver education and support are vital in the management of atopic dermatitis.<sup>16</sup> Poor patient adherence is a major reason for treatment failure. Verbal and written education is encouraged, as well as recommending online resources and support groups.

## PROGNOSIS

Atopic dermatitis is characterized by exacerbations and remissions. In general, 10-year clearance rates vary from 40% to 80% for those with atopic dermatitis beginning in childhood.<sup>17</sup> Poor prognostic factors include early age at onset, severe disease, a family history of atopic dermatitis, and concomitant asthma or allergic rhinitis.<sup>17</sup> ■

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