

ALLERGIC AND NONALLERGIC ECZEMATOUS DERMATITIS

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To discuss nonallergic eczematous dermatitis, there must be a clear understanding of allergic eczematous dermatitis, and an understanding of the term *eczema* itself. The term *eczema*, which translates as "bubbling over," lends itself to confusion and misuse. All too often, the term *eczema* is used nonspecifically, resulting in confusion for patients and doctors. Although this term is commonly used in other countries, many dermatologists in the United States avoid the term because of its ambiguity but realize the common recognition of the word by the lay public. In general, the unqualified term *eczema* usually refers to atopic dermatitis. When used in nonatopic settings, *eczema* is synonymous with *dermatitis* and requires a qualifying term to be useful (contact dermatitis, stasis dermatitis, or contact eczema, stasis eczema). Throughout this article, dermatitis is used in place of eczema and, with modifiers, refers to all the various eczematous skin eruptions.

The term *allergic* usually refers to an immunologically mediated process in response to an allergen. Allergic contact dermatitis is mediated in part by T-cell activation following exposure to certain antigens contacted by the skin. Urticaria, an allergic disease mediated by IgE antibodies in response to specific antigens, is not considered a dermatitis per se and is not discussed in this article. Atopic dermatitis is frequently considered an allergic dermatitis although the precise immunologic mechanisms in atopic dermatitis are not completely understood. Elevated serum IgE levels plus the coexistence of IgE-mediated diseases seen in atopy (allergic rhinitis and asthma) suggest that atopic dermatitis is triggered by allergic phenomena. This article reviews the pathophysiology, clinical features, and treatment of atopic dermatitis, allergic contact dermatitis, and common dermatitides that have similar presentations but are considered nonallergic (Table 1).

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Table 1. ALLERGIC AND NONALLERGIC DERMATITIS

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ATOPIC DERMATITIS

Atopy (atopic dermatitis, asthma, or hay fever) is present in 8% to 25% of populations. Atopic dermatitis is present in all races and geographic locations, but there appears to be a higher incidence in urban areas and developed countries. Although evidence supports a genetic basis for the disease, the precise genetics have not been fully elucidated. A family history of respiratory atopy can be obtained in almost 50% of patients with atopic dermatitis. Maternal atopy poses a significantly higher risk of infantile atopy than does paternal atopy,^{21, 33} and chromosome studies have suggested that the trait for atopy may be inherited on a maternal gene.⁷

Pathophysiology

The pathogenesis of atopic dermatitis is not entirely understood. Atopy is characterized immunologically by high concentrations of serum IgE, a high incidence of IgE-mediated response by skin test to common inhaled antigens, decreased numbers of immunoregulatory T cells, defective antibody-dependent cellular cytotoxicity, and reduced cell-mediated immunity.⁹

The role of cytokines in atopic dermatitis appears to be important and continues to be studied; current theory suggests that atopic patients have a predominance of T cells of the Th2 type and produce high amounts of the cytokine interleukin 4 (IL-4), which in turn can stimulate B cells to make IgE antibodies.⁸ Cytokine production by T cells may be modulated by monocytes, which are found in increased numbers in lesional skin of atopic patients.¹⁵ Trigger factors such as *Staphylococcus aureus*, *Pityrosporum ovale*, house dust mites, as well as neurocutaneous influences may also affect immune responses that lead to the development of dermatitis.⁸

History

A suggestive history includes onset of a dermatitis at an early age (most patients have manifestations of atopic dermatitis by age 5–7), pruritus, a chronic recurring course, and a positive family history of atopy.²⁴

Examination

Papules, erythema, excoriations and lichenification are the hallmarks of atopic dermatitis. Unlike many skin diseases where the recognition of a primary lesion is helpful in making the diagnosis, atopic dermatitis does not present with a characteristic primary lesion; the

distribution and collection of skin findings are more important in the diagnosis. In adults, flexural areas (neck, antecubital fossae and popliteal fossae) are most commonly involved (Fig. 1). The face, wrists, and forearms are also common sites of involvement. In severe cases, any area of the body can be involved. In infants, the face, chest and extensor extremities are commonly involved. The presence of pustules within areas of dermatitis suggests secondary infection with *S. aureus*.

Nondermatitic physical findings that support the diagnosis of atopic dermatitis include xerosis, the infraorbital skin fold (Dennie Morgan line), periorbital darkening, hyperlinear palms, and keratosis pilaris.

Treatment

The management of atopic dermatitis centers around three principles:

1. Treatment of inflamed skin
2. Control of itching
3. Control of exacerbating factors

With recent advances in understanding the immunology of atopic dermatitis, new therapies have focused on immune regulation.

In the acute management of atopic dermatitis, topical corticosteroids and emollients are the primary therapeutic modalities. For mild disease, a low-potency corticosteroid cream is effective. For more severe disease, a medium-potency corticosteroid cream or ointment may be needed. Those patients with pustules should be evaluated with cultures and treated with oral antibiotics. Acute exacerbations in patients with moderately severe disease can sometimes be aborted by a short course of systemic corticosteroids (e.g., prednisone 40–60 mg/day for 3–4 days, then 20–30 mg/day for 3–4 days).

The management of chronic severe atopic dermatitis is a challenge for even the most skilled dermatologist. The use of chronic systemic corticosteroids may be necessary and requires monitoring for complications such as glaucoma, osteoporosis, and opportunistic infections. The most severe cases require combinations of treatments that can include systemic corticosteroids, ultraviolet light therapy, and cyclosporine. Phototherapy with UVB, UVA, and psoralens plus UVA (PUVA) have been shown to be successful in controlling the dermatitis¹⁸ and may reduce corticosteroid requirements. Although treatment with PUVA may produce the best results, patient preference favors combined use of UVB and UVA.¹⁸ Cyclosporine in doses of 3 mg/kg/day to 6 mg/kg/day is effective in severe atopic dermatitis.¹⁰ Monthly monitoring of serum cyclosporine levels, renal function, and blood pressure is essential. Other modalities with potential future use include interferon gamma, thymopentin, immunotherapy with antigen-antibody complexes, and mixtures of Chinese herbs.^{8, 16, 25, 32, 35}

To control pruritus, the adjunctive use of antihistamines is usually

helpful. Considerable trial and error may be required to identify the antihistamine best for the individual patient.³¹ In contrast to allergic rhinitis, the nonsedating H1 blockers are of limited value in most cases of atopic dermatitis but can be tried in patients with mild disease. Frequently, some sedation is desirable, especially at night, and commonly used H1 blockers in this category include diphenhydramine, hydroxyzine, and cyproheptadine. Doxepin, a potent H1 blocker with sedating properties, is valuable as a second line antihistamine if others fail. Tepid baths to hydrate and cool the skin can also relieve itching temporarily.

Controlling exacerbating factors is helpful in the acute phase and in long-term management. The exacerbating factors most important to avoid are low humidity environments, excessive washing, rapid temperature changes, chemical irritants such as detergents, and emotional stress. Xerosis, a common exacerbating factor, can be controlled by frequent and liberal use of emollients especially after bathing and is an important aspect of successful treatment of atopic dermatitis.¹⁴

Reducing colonization with *S. aureus* may help prevent exacerbations. Antiseptic cleansers such as chlorhexidine, as well as topical corticosteroids and UVB phototherapy, have all been shown to reduce bacteria counts in these patients.^{17, 30, 36, 37} Controlling house dust mite populations has not been successful in improving the clinical status of patients with atopic dermatitis.⁶

Immunotherapy in atopic disease is indicated in allergic rhinitis and asthma but has not been successful in the treatment of atopic dermatitis. Atopic patients have allergic responses to multiple allergens including aeroallergens,⁴² and the elimination of these is frequently not feasible. On the basis of controlled food challenge studies, elimination of dietary milk, wheat, eggs, soy, peanuts, and fish have been recommended in selected patients.^{3, 34}

ALLERGIC CONTACT DERMATITIS

Allergic contact dermatitis occurs when a delayed (type IV) hypersensitivity to a substance develops following skin contact with that substance. This can occur after one exposure or after years of repeated exposures to an antigen. The antigen, usually of low molecular weight, binds to epidermal proteins and is presented to T lymphocytes in the dermis. Further immunologic processing of the antigen takes place in lymph nodes where sensitized T lymphocytes of both CD4+ and CD8+ subtypes are produced.¹² The allergic dermatitis occurs when the sensitized lymphocytes encounter the antigen in the skin and release cytokines, which mediate the inflammatory reaction. The sensitization phase takes 10 to 14 days, but once operative, a dermatitis can develop within 12 to 48 hours after exposure.

The most common sensitizers in North America are poison ivy and poison oak.²⁹ Many other categories of chemical substances, both natural



Figure 1. Atopic dermatitis.



Figure 2. Allergic contact dermatitis.



Figure 3. Irritant contact dermatitis.



Figure 4. Stasis dermatitis with stasis ulcer.



Figure 5. Xerotic dermatitis (erythema craquele).



Figure 6. Dyshidrotic dermatitis (pompholyx).



Figure 7. Nummular dermatitis.



Figure 8. Neurodermatitis (prurigo papularis).

and synthetic, have the capability of sensitizing individuals and causing allergic contact dermatitis. Other common sensitizers in the United States include neomycin, nickel, fragrances such as balsam of Peru, preservatives such as quaternium 15 found in topical medications and cosmetics, components in rubber, and chemicals in shoes, both leather and synthetic. Hypersensitivity to topical hydrocortisone has been reported recently and is becoming increasingly recognized.^{43, 45}

The patient with allergic contact dermatitis usually complains of intense itching in the area of exposure, followed by the development of a pruritic dermatitis. The exposure can antedate the dermatitis by 2 weeks if it is the result of a primary sensitization. In these cases, the immunologic sensitization process is completed before the antigen is cleared from the skin. Frequently an exact date of exposure is difficult to identify, and in chronic cases, the dermatitis may have been present for months or years.

Examination

Clinical findings include erythema, edema, papules, vesicles, and serous oozing in the involved areas. One often sees a sharply outlined configuration corresponding to the area of skin exposure. For example, in poison oak or ivy dermatitis, there are frequently linear streaks of dermatitis corresponding to areas of contact with the plant resin (Fig. 2). The extent of the dermatitis reflects the source of exposure, i.e., cosmetics on the face, nickel where jewelry is worn, rubber where elastic bands contact the skin, and points of shoe contact on the feet.

Diagnosis

A good history plus the skin morphology and distribution usually allow the diagnosis of allergic contact dermatitis to be made. Elimination of suspected substances may suffice, but patch testing is necessary in chronic cases to identify specific allergens. Commercially available patch test kits can add to the testing of the patient's own identified contactants. A discussion of the placement and interpretation of patch tests is beyond the scope of this article.

Treatment

Treatment of the acute phase of allergic contact dermatitis depends on the severity of the dermatitis. When there is serous oozing and vesicles, wet to dry compresses with water or aluminum acetate (Burow's solution) help dry the skin and allow subsequent application of topical medications. Topical corticosteroids are helpful after the skin is dry enough to retain the topical preparation. Soothing lotions such as

calamine lotion can provide some relief in mild cases. In severe cases, several weeks of treatment with systemic corticosteroids and antihistamines may be required.

IRRITANT CONTACT DERMATITIS

Irritant contact dermatitis is a multifactorial syndrome resulting from the effects of physical, mechanical, or chemical irritation of the skin.²³ A common occupational problem, irritant contact dermatitis occurs when the normal epidermal barrier is disrupted and secondary inflammation develops. Most irritant substances are those used on a daily basis in most living and work environments. These generally are low-grade irritants that require repeated exposure to produce a dermatitis (soapy water, cleansers, rubbing alcohol). Some irritants are highly caustic, producing severe dermatitis after minimal exposure (bleach, strong acids, alkalis). Although anyone can develop irritant contact dermatitis, those with compromised skin (atopic dermatitis, dry skin) and those with light-colored or "fair" skin are at a higher risk.¹

Examination

Mild irritants produce erythema, chapped skin, dryness and fissuring. Pruritus can range from mild to extreme, but pain is also a common symptom especially when erosions and fissures are present. The hands are the usual site for irritant contact dermatitis (Fig. 3). The web spaces of the fingers trap irritating substances and may be the first area of involvement. The face, especially the eyelids, may also be affected. Severe cases can present with edema, serous oozing, and tenderness. Potent irritants cause painful bullae within hours of the exposure.

Treatment

Treatment goals in irritant contact dermatitis are to restore a normal epidermal barrier and then protect it from the irritating substance. Reduced exposure to soap and water, use of emollient creams or ointments, and use of gloves in hand dermatitis may control chronic irritant contact dermatitis. In more severe cases, corticosteroid ointments under occlusion may be necessary to treat the acute phase. Systemic corticosteroids, although potentially helpful in reducing acute inflammation, are not useful in the treatment of chronic irritant contact dermatitis unless corrective measures are taken to avoid the offending contactants.

STASIS DERMATITIS

Stasis dermatitis occurs on the legs as a result of chronic venous insufficiency. Incompetent venous valves, inadequate tissue support,

and postural hydrostatic pressure contribute to the development of venous stasis. Although the true incidence is unknown, venous stasis is rarely seen before adulthood and becomes more prevalent with age. Women are affected approximately two times more than men. There appears to be a familial predisposition, with a relative risk of two or three depending on whether one or both parents have varicosities.⁵ The prevalence of chronic venous insufficiency is greatest in Western society and may relate in part to a more sedentary lifestyle; there is a low prevalence in Africa, Asia, and in Australasian aboriginal populations, although immigrants from these regions have the same risk as their host country.⁵

The dermatologic changes of stasis dermatitis are thought to be secondary to the effects of extravasated blood, which induces a mild inflammatory response in the dermis and subcutaneous fat, plus the low-grade tissue ischemia associated with stasis at the capillary level. Capillaries in patients with chronic venous insufficiency lose their postural vasoconstrictor reflex, which may contribute to local underperfusion and the development of leg ulcers.²⁸ The extent of involvement of the superficial venous system influences the severity of disease.²² Skin changes, aching, and edema can be seen in limited disease of the short saphenous vein or reflux below the knee in both the long and short saphenous veins. In contrast, ulceration tends to be associated with involvement of the whole long saphenous venous system or involvement above the knee in both systems.²²

History

Symptoms are mild in most cases of stasis dermatitis. There may be a sense of fullness or dull aching in the legs or ankles. This is usually relieved by leg elevation. The patient usually reports a gradual increase in pigmentation and redness. Pruritus may be present and is usually mild. If there is severe pruritus, there may be a concomitant allergic contact dermatitis. In cases of unilateral disease, there is commonly a past history of injury to the leg or venous thrombosis.

Examination

In early stasis dermatitis there is mottled pigmentation and slight erythema. As the disease progresses, these skin changes become more extensive (Fig. 4). Pigmentary changes persist even with optimal treatment. There may be evidence of varicosities, ankle edema, and mild tenderness to deep palpation. Pulses are usually normal. In chronic cases, the predominant finding may be fibrosis, resulting in a woody hard sclerotic lower leg. Signs of allergic contact or irritant contact dermatitis can also be seen because stasis dermatitis predisposes to both.

Treatment

The main emphasis in the management of stasis dermatitis is to counteract the effects of gravity and posture on venous pressure. Leg elevation and compression with stockings are the most effective treatment. In mild cases, support hosiery alone may be sufficient. In-office application of Unna boots on a weekly basis can be used in those patients who cannot elevate their legs or don support hosiery.²⁶ In severe cases, daily leg elevation above the level of the head for varying amounts of time may be necessary. Exercise on a regular basis also helps to reduce venous pressure and edema.

The inflammatory component of stasis dermatitis is treated with low- or medium-potency topical corticosteroids. Interestingly, hypersensitivity to hydrocortisone occurs most frequently in patients with stasis dermatitis.⁴⁴ An ointment-based vehicle avoids exposure to preservatives that can cause allergic contact dermatitis. Systemic antibiotics are not indicated unless there is documented cellulitis or secondary infection, and topical use of triple antibiotic ointments should be avoided because of the high incidence of inducing an allergic contact dermatitis in these patients.⁴⁸ Pentoxifylline 400 mg tid was found to be a helpful adjunct to local management in a small double-blind, placebo-controlled trial of patients with persistent stasis ulceration.²

XEROTIC DERMATITIS

Xerotic (asteatotic) dermatitis is a form of mild irritant dermatitis that occurs in areas of dry skin. As the skin loses hydration, the stratum corneum becomes scaly and develops small cracks that gradually enlarge to form patches of erythema with scaling (Fig. 5). The name given to this superficial cracking is "erythema craquele." These areas are usually intensely pruritic, and are worsened by low humidity and exposure to hot water, soap, or solvents. Pretibial areas are most common, but the lower back, extensor arms, and thighs may be involved. In temperate climatic zones, xerotic dermatitis occurs most frequently in the winter because of low humidity produced by heated living space and cold outdoor temperatures.

Treatment

Treatment of xerotic dermatitis consists of frequent use of emollients to the affected areas especially after bathing or other water exposure. Ointments are preferable to creams in protecting severe dry skin. Lotions should be avoided in all but the mildest cases of xerosis because the water content in lotions is high and results in evaporation, which worsens the problem. Topical medium-strength corticosteroids help with the pruritus of the acute phase. Patients who are susceptible to dry skin

should limit their exposure to soap and water, showers, electric blankets, hot tubs, and low humidity environments.

DYSHIDROTIC DERMATITIS (POMPHOLYX, DYSHIDROSIS)

Dyshidrotic dermatitis is an intensely pruritic chronic recurrent dermatitis of unknown etiology that typically involves the palms and soles. The term *dyshidrotic* implies a malfunction of eccrine sweating, although this has not consistently been found. A recent study, however, demonstrated 2.5 times the perspiration volume on the hands of 25 patients with dyshidrotic dermatitis compared with age-matched controls.⁴⁷ An etiologic relationship to metal allergy, especially nickel, has been an area of long-standing controversy. Although there are published studies demonstrating exacerbations after oral challenges with nickel^{40, 47} and improvement after low nickel diets,⁴¹ the high incidence of atopy with dyshidrotic dermatitis plus the ubiquity of dietary nickel have raised doubt about the relationship.⁴

History

A history of intense pruritus on the palms or soles that progresses to multiple small vesicles is typical. The vesicles gradually desquamate over 1 to 2 weeks, leaving erosions and fissures that slowly resolve. Recurrent episodes alternating with disease-free periods are common.

Examination

The presence of multiple small vesicles on the palmar or plantar skin especially along the lateral aspects of the fingers and toes is typical (Fig. 6). Desquamation, erythema, cracking, and fissuring may be seen in older lesions. The process is usually symmetrical. The differential diagnosis can include allergic contact dermatitis, irritant contact dermatitis, dermatophyte fungus infection (tinea pedis or tinea manuum), or an "id" reaction (immunologic reaction to fungal or bacterial antigen at a distant site).

Treatment

In mild cases, medium to potent topical corticosteroids can control outbreaks. Limited courses of systemic corticosteroids are occasionally required in difficult cases. There may be a place for patch testing to nickel, chromium, or cobalt, and an attempt to eliminate environmental

and dietary metal exposure. Local treatments with PUVA,³⁸ UVA,¹³ or superficial X-ray⁴³ have been shown to be helpful in difficult cases.

NUMMULAR DERMATITIS

Nummular dermatitis is a chronic pruritic skin eruption consisting of circular raised patches of erythematous scaly skin. Patients and doctors frequently misdiagnose nummular dermatitis as tinea corporis because of the circular shape of the lesions that suggests tinea corporis. The etiology is not known, although xerosis and emotional stress have been implicated. Adults tend to be affected more than children.

History

Patients usually report one to several patches of itchy skin that gradually enlarge in size, usually to a maximum of 3 to 5 cm. An important differentiating feature is that individual lesions tend to remain fixed for the duration of the disease process. There is often a history of increased water exposure such as frequent showers, swimming, or use of hot tubs.

Examination

Round patches of erythema, scaling, and occasional crust or exudate are suggestive of nummular dermatitis (Fig. 7). The term *nummular* translates literally to "coin shaped." The distribution is usually extensor areas of extremities, the back, and buttocks. The differential diagnosis includes psoriasis and tinea corporis. A potassium hydroxide examination of any scaly lesions is indicated to exclude fungal infection.

Treatment

The elimination of drying factors (see section on xerotic dermatitis) is important in long-term management. To reduce acute inflammation, potent topical corticosteroids under occlusive dressings or intralesional corticosteroid injections (triamcinolone 5 mg/mL or betamethasone 6 mg/mL) may be necessary. Emollients throughout the day and especially after water exposure or bathing are essential. In severe cases, systemic steroids, antihistamines, topical tar preparations, and UV light treatments can be used.

NEURODERMATITIS

Neurodermatitis is defined broadly as the skin changes that occur from scratching. Subsets within this category include lichen simplex chronicus, which refers to thickened patches of skin that develop as a result of chronic scratching, and prurigo papularis or nodularis which consist of multiple individual papules or nodules induced by scratching and picking. There is always pruritus in the areas of scratching, but frequently no primary cause for the itching can be identified. Obsessive behavior patterns are commonly seen in these patients.²⁰

Examination

In lichen simplex chronicus, there is thickened skin with erythema and accentuation of skin lines (lichenification). Usually there is only one area of involvement. Common sites include the extremities, posterior neck, buttocks, vulva, scrotum, and anal area. In prurigo nodularis, there are several to multiple nodules, 0.5 to 1.0 cm in size, scattered over the upper back, arms, and thighs. Areas that are not convenient to reach, such as the central back and posterior thighs, tend to be spared (Fig. 8).

Treatment

The treatment of lichen simplex chronicus consists of breaking the itch-scratch cycle. Potent corticosteroids under occlusion may be successful. Intralesional corticosteroid injections and cryotherapy with liquid nitrogen may be required in nodular cases although the treatment of prurigo nodularis is frequently unsuccessful. Small studies have reported benefit of acupuncture,^{27, 46} topical capsaicin,³⁹ and thalidomide.¹⁹ To treat the obsessive component, the use of clomipramine (Anafranil) and fluoxetine (Prozac) can be helpful.²⁰ Neurodermatitis is frequently resistant to therapy and tends to persist for years.

CONCLUSIONS

Many common dermatitic disorders have similar features and can be difficult to differentiate. Allergic contact dermatitis is the "allergic eczematous dermatitis" that clinicians will encounter most often. Atopic dermatitis probably has both allergic and nonallergic components. The "nonallergic eczematous dermatitides" discussed in this article are important to recognize because they can mimic allergic dermatitis and can be difficult to treat.

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