Itch, the most common symptom among patients presenting to the dermatology clinic, is characteristic of atopic dermatitis (AD), contact dermatitis (CD), allergic contact dermatitis (ACD), such as poison ivy, psoriasis, and other common dermatoses. The experience of persistent pruritus is associated with increased stress and a detrimental impact on the patient’s quality of life. Intense itch is associated with impaired academic performance and work and social functioning.

Treatment aimed at reducing pruritus is expected to improve life quality and functioning. Additionally, evidence suggests, amelioration of pruritus may improve therapeutic outcomes in atopic dermatitis and other pruritic dermatoses by reducing patient scratching and its detrimental effects on the disease course.

Itch and the Itch/Scratch Cycle

The notion of the itch/scratch cycle is associated with atopic dermatitis but may be relevant to other pruritic dermatoses. Patient scratching in response to sensations of itch can induce trauma in the skin and may physically damage the epidermal barrier. This trauma instigates additional inflammation, thus worsening pruritus. Impaired barrier function reduces its ability to block microbes, potentially allowing the development of infections. In the case of atopic dermatitis, an impaired barrier can facilitate entry of antigens, allergens, and bacteria that exacerbate already-heightened immunologic and inflammatory responses.

Inflammatory and immunomodulatory responses mediate inflammation in AD, leading to pruritus. However, the molecular basis of pruritus is complex and not fully understood. Pruritus can have neurological, chemical, physical, and/or psychological bases. Histamine has typically been implicated in the development of itch, particularly in AD and other dermatoses, yet data regarding the benefits of antihistamine therapies among patients with AD have been mixed. Emerging evidence has shown that several other mediators are associated with itch in AD, including serine proteases, interleukin 31, and nerve growth factor.

Consequences of Itch

As noted, scratching subsequent to pruritus is shown to physically damage the epidermal barrier, increasing the individual’s susceptibility to allergens, antigens, and microbes. Clearly, treatment must aim to reduce scratching and encourage skin healing. However, while this is an important medical consideration, the immediate impact of pruritus on the patient is more likely to drive selection of itch-targeted therapy.

Among adult patients with AD, 83.1 percent of individuals in one study reported pruritus, most frequently in the evening (52.8 percent) and at night (38.2 percent). Severe itch correlated with severity of AD. A significant proportion (81 percent) of patients who reported itch said it caused difficulty in falling asleep. Patients with more severe disease reported more intense pruritus.

Sleep disturbance attributed to atopic dermatitis is common. Sleep efficiency in patients with atopic dermatitis is shown to decrease as disease severity and pruritus increase. In one study, a majority of parents of children with AD (> 60 percent) reported that AD affected how well they or their child slept. Thirty percent of families reported cosleeping because of the skin condition, which most parents (66 percent) found bothersome. Sleep disturbance and cosleeping were directly associated with severity of AD and with the degree to which parents reported that the atopic dermatitis affected the child and family’s happiness.

Targeting Itch

Corticosteroids are a mainstay of treatment for many pruritic dermatoses. Due to their anti-inflammatory effects, they may reduce sensations of itch, though itch reduction is not a primary action. The risks and side effects of topical corticosteroids are well known and include HPA Axis suppression, cutaneous atrophy, skin thinning, and development of telangiectases. Recent evidence suggests that application of topical corticosteroids as monotherapy may actually impede epidermal barrier function. Oral antihistamines continue to be used adjunctively in AD to manage pruritus, despite inconclusive evidence of efficacy. Many specialists feel that first-generation sedating antihistamines may be helpful to promote sleep in spite of itch.

Topical pramoxine is an antipruritic with a history of safe and effective use. A unique formulation features hydrocortisone acetate 2.5% and pramoxine hydrochloride 1% (Pramosone E Cream/Pramosone Lotion®, Ferndale Laboratories).
More on Antigens, Allergens, Inflammation, and AD

Atopic dermatitis, often associated with a personal or family history of atopy (such as allergic rhinitis, atopic dermatitis, and asthma), may be associated with immunoglobulin E (IgE) reactivity.\(^2\) In acute AD, T-helper type 2 (TH-2) immune response activates IgE synthesis and the production of IL-13 and IL-4.\(^3\)

In a substantial proportion of patients with AD, loss of function mutations in the gene that encodes the filament-aggregating protein filaggrin are implicated in disease pathogenesis. Filaggrin deficiency contributes to barrier dysfunction. Even among AD patients in whom filaggrin loss of function mutations are not present, the epidermal barrier is defective, characterized by reduced levels of key lipids (ceramides, cholesterol, and fatty acids) and increased transepidermal water loss. Decreased moisture content of the stratum corneum allows increased permeability of substances and likely increased allergen and microbial absorption.

Pramoxine, a local anesthetic that is unrelated to procaine and is not a member of the “caine” family, confers its anti-pruritic effects by stabilizing neuronal membranes of nerve endings.

New evidence shows a rapid onset of anti-pruritic action for hydrocortisone acetate 2.5% and pramoxine hydrochloride 1%. In an open label pilot study involving 11 subjects age 18 and older (Mean age 40.8 ± 11.4; 36.4% Caucasian, 63.6% Black), subjects reported a significant reduction in AD-associated pruritus following one day of topical therapy with hydrocortisone acetate 2.5% and pramoxine hydrochloride 1% lotion. Subjects rated the intensity of itch using a Visual Analog Scale (VAS) at baseline and at Day 1 of active therapy. At Day 1, Mean VAS scores had decreased more than two points from 6.72 to 4.56. Median VAS score dropped from 6.60 at baseline to 5.10 on Day 1.\(^1\) The lotion formulation was well tolerated in the study with no reports of significant adverse events.

By combining the anti-inflammatory effects of hydrocortisone with the antipruritic effects of pramoxine in a single emollient formulation, Pramosone E™ Cream or Pramosone Lotion® can simplify the treatment regimen for patients with AD, ACD, and similar pruritic inflammatory dermatoses. It is indicated for application up to four times per day.

Breaking the Itch/Scratch Cycle

Itch is one of the most common symptoms of dermatologic diseases. It is common among patients with psoriasis, allergic contact dermatitis, and atopic dermatitis. Among multiple potential factors, inflammatory and immunologic mediators contribute to the development of itch. Itch can be a direct consequence of impaired barrier function in patients with AD.\(^9\)

Hydrocortisone acetate 2.5% and pramoxine hydrochloride 1% Formulations

Pramosone E™ Cream 2.5% contains a reverse emulsion of 70 percent lipids dispersed in 30 percent water. The unique hydrophilid emollient vehicle is expected to reduce transepidermal water loss and contribute to improved barrier function, providing further benefit in the management of AD. The base incorporates emollient cetostearyl alcohol, as well as mineral oil and white petrolatum. The thicker, moisturizing formulation is especially suited for use on very dry skin and by patients who desire a thicker formulation.

Pramosone® Lotion is formulated with a hydrophilic lotion base. It contains emollients stearic acid and cetyl alcohol, a proprietary formulation of moisturizing oils (FORLAN-L), as well as glycerin, trolamine, and dimethicone. The moisturizing lotion formulation is suited to use on larger surface areas and many hair-bearing areas.

Anti-inflammatory treatments, such as corticosteroids, are a mainstay of AD management and may provide some relief of pruritus. However, given the psychological, emotional, and functional impact of pruritus, adequate itch management is essential. The unique emollient formulations of hydrocortisone acetate 2.5% and pramoxine hydrochloride 1% cream and lotion offer safe and rapid control of pruritus in a formulation that supports skin healing. Reduction of itch can significantly improve the patient’s quality of life and functioning and can break the itch/scratch cycle to encourage resolution of the dermatitis.

Dr. Kiric has served as a researcher, consultant, and/or speaker for Ferndale Laboratories.

14. Kiric, L. Efficacy and onset of action of hydrocortisone acetate 2.5% and pramoxine hydrochloride 1% lotion for the management of pruritus: Results of a pilot study. Fall Clinical Dermatology Conference. Las Vegas, NV: October 2010.

Supported by an educational grant from Ferndale Laboratories.