

Itching and the atopic skin

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Itching is one of the major diagnostic criteria of atopic dermatitis and one of its most troublesome symptoms. The symptom of itching may reflect skin disease, internal disease, or emotional disease. Although itching is symptomatic of many inflammatory and psychophysiologic dermatoses, in atopic dermatitis it is a cardinal feature of the disease. Effective control of itching can go a long way towards controlling the eruption itself; it can also make a major contribution to the physical and emotional well-being of the patient and the patient's total environment. (J Allergy Clin Immunol 1999;104:S109-13.)

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Itching is one of the major diagnostic criteria of atopic dermatitis¹ and one of its most troublesome symptoms. It interferes in every aspect of the atopic patient's life and impairs the quality of life in numerous ways.^{2,3} In infancy, by altering the early tactile experience, itching affects the development of physical and emotional boundaries and the integrity of the evolving body image.⁴ By interfering in sleep, it affects growth and development and emotional equanimity. By interfering in sleep, it also impairs performance in school and in the workplace.^{5,6} The discomfort of itching causes anger and resentment in the patient and resentment and guilt in family members, straining peer and family relationships.^{3,4} The incessant scratching and the resultant physical disfigurement provide a powerful, if unconscious, tool for manipulation, but at the same time, seriously diminish the patient's self-esteem. Clinical anxiety and depression are common concomitants of atopic dermatitis.⁷⁻⁹ Thus the accurate diagnosis and effective treatment of itching is of paramount importance in the care of the atopic patient.

Itching has been defined as an unpleasant sensation that provokes the desire to scratch.¹⁰ It is so unbearable that patients often find that they must scratch until the itch is replaced by pain. Sensual pleasure may also be a part of it, however, because many patients describe an almost orgasmic experience in the sequence of itching and scratching that makes it hard to give up.^{11,12}

NEUROANATOMY OF ITCHING

No specialized itch-receptors are recognized in the skin. The sensation, which may be generated by chemical, electrical, mechanical, or thermal stimuli, is transmitted through the free nerve endings of nonmyelinated

C-fibers in the epidermis and at the dermoepidermal junction. From these nerve endings, the impulse travels through the dorsal root ganglion to the dorsal horn of the spinal column, through the contralateral spinothalamic tract to the thalamus and finally to the postcentral gyrus.^{13,14} The pathways for the transmission of itch are schematically represented in Fig 1.¹⁴ Whereas it was formerly thought that itch represented subthreshold pain, we now know itch and pain to be separate phenomena. The reasons for this belief are listed in Table I.^{13,14}

NEUROPHYSIOLOGIC FEATURES OF ITCHING

Chemical mediators

A chemical itch mediator is a substance that, when introduced into the skin, induces the sensation of itching and the urge to scratch. Although histamine is the prototypical peripheral chemical itch mediator, many others have now been identified. Many of these agents serve as histamine liberators; alternatively, they may increase itching by potentiating the itch sensation induced by histamine.¹³

The chemical mediators of clinical importance in atopic dermatitis are listed in Table II,¹³ with their modes of action. Increased amounts of neuropeptides (particularly substance-P and calcitonin gene-related peptide) have been identified in many inflammatory dermatoses, but particularly in atopic dermatitis.¹⁵ For this reason, it is thought that atopic itching is mediated peripherally by the neuropeptides.¹⁶ Less is known about the central mediation of itching, although it is believed that there is probably a central itch center. Endogenous opioids are thought to participate in the process because the opioid antagonists naloxone, nalmefene, and pimizide reduce itching in patients who have received spinal opiate injections.¹⁷⁻¹⁹

Of the various chemical mediators, the neuropeptides are of particular importance in the pathophysiologic condition of itching in the atopic patient. These agents are ubiquitous throughout the body. In the immune system they are involved in the integration of intraimmune regulation and in the bidirectional communication between the immune and the neuroendocrine systems. Peripherally they can be identified in autonomic fibers in the skin and in the cutaneous sensory fibers. Centrally they serve as brain peptides, although they are distributed to target organs by way of the hypophyseal portal vessels and the general circulation (as neurohormones). When the higher cortical centers are activated by stress, there is an increased secretion of substance-P from the adrenal glands and an antidromic release of neuropeptides in the skin by way of descending autonomic fibers.¹⁵ Thus we

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FIG 1. Pathway for transmission of itch sensation. (Adapted from Tuckett RP. Neurophysiology and neuroanatomy of pruritus. In: Bernhard JD, editor. Itch: mechanisms and management of pruritus. New York: McGraw-Hill Inc; 1994. p. 1-22. With permission of the McGraw-Hill Companies.)

TABLE I. Itch and pain are separate phenomena¹³

Both sensations may be experienced simultaneously.
When C-fibers are stimulated electrically, some transmit pain, and others transmit itch.
Increasing the intensity of stimulation does not change the quality of the sensation in any given fiber. (Pain is always pain, and itch is always itch.)
Removal of the epidermis removes the capacity to experience itch, but not pain.
Itch provokes a scratch response; pain provokes withdrawal.
Opioids provoke itch but relieve pain.

can now demonstrate experimentally what has long been known clinically, that psychosocial stress can trigger or exacerbate itching through neuropeptide activation. This is of particular importance in both atopic dermatitis, which is frequently triggered or aggravated by stress, and in psychogenic pruritus.²⁰

DIAGNOSTIC GUIDELINES

The symptom of itching may reflect skin disease, internal disease, or emotional disease. When faced with a patient whose major complaint is itching, important diagnostic considerations come into play (Table III).²¹ It is often difficult to separate the physical from the psychosomatic aspects of pruritic dermatoses, because not only can psychosocial stress trigger or aggravate itching but the itching itself is also an added stress that can lead to an upward spiral of distress. Anxiety and/or depression are frequent concomitants of pruritic dermatoses.⁷⁻⁹

ITCHING IN ATOPIC DERMATITIS

In no dermatosis is the relationship of physical and emotional components so closely interwoven, and so complex, as in atopic dermatitis. The skin of the atopic patient is inherently itchy.²² The intradermal injection of histamine shows atopic skin to have a lower itch threshold than nonatopic skin; because it is xerotic by nature,

TABLE II. Pruritogenic properties of some inflammatory mediators, investigated by intradermal injections in human skin

Group	Substance	Pruritus	Comment
Amines	Histamine	+	Classical chemomediator of itching
	Serotonin	(+)	Not present in human mast cells but released when platelets aggregate; itching potentiated by prostaglandins
Proteases	Trypsin	+	Histamine liberator
	Chymase	+	Histamine liberator
	Papain	+	Burning itch without visible skin changes; no histamine-releasing effect
Peptides	Bradykinin	(+)	Histamine liberator
	Secretin	+	Histamine liberator
	Substance P	+	Histamine liberator
	Neurotensin	+	Histamine liberator
	VIP	+	Histamine liberator
	Endorphins	0/(+)	Potentiate histamine-induced itching without histamine release or formation of prostaglandins
Eicosanoids	Prostaglandins	0/(+)	Potentiate itching induced by histamine, serotonin, and papain

0, No itching; (+), weak itching; +, itching; VIP, vasoactive intestinal polypeptide. (Adapted from Wahlgren CF. Pathophysiology of itching in urticaria and atopic dermatitis. *Allergy* 1992;47:65-75. ©Munksgaard International Publishers Ltd, Copenhagen, Denmark.)

atopic skin is more subject to contact irritation, and those factors that increase itching under normal circumstances are that much more likely to do so in the atopic patient.²² Thus anything that increases blood flow through the skin (such as heat, alcohol, febrile illness, and the normal hemodynamic diurnal variation) is more likely to generate itching in the atopic patient.²³⁻²⁶

Once the patient starts to scratch, interpersonal and intrapsychic factors enter the picture. The manipulative and sensual functions of scratching may be fulfilled,^{11,13} but at the same time increased amounts of neuropeptides and other inflammatory mediators are released into the skin, and the familiar itch-scratch cycle is generated or perpetuated.¹³

In addition to the factors mentioned earlier, up to 81% of patients with atopic dermatitis acknowledge their condition to be aggravated by emotional stress.¹³ This figure of 81% refers only to external stress, of which the patient is fully aware. If we also take into consideration stress that is generated by intrapsychic conflict (outside of the patient's conscious awareness),²⁷ the incidence of stress-induced pruritus in atopic patients is probably even higher.

Another factor that may contribute to the vulnerability of atopic skin is the altered tactile experience in early infancy. Empathic parental touching, in a warm and accepting emotional environment, is important for the development of stable physical and emotional bound-

TABLE III. Diagnostic considerations in the patient with itching

Is the itch localized or generalized?
Localized itching: Characteristic sites, suggestive of a dermatologic disease (eg, atopic dermatitis)
Infancy (cheeks, eruptive, on extensor extremities)
Childhood & adolescence (flexural)
Adolescence & adulthood (hands, feet, or patchy distribution)
Generalized itching: Suggestive of a systemic cause
Drug eruption
Exanthem
Systemic disease
Psychogenic pruritis
Generalization of local disease
Sequence of events
Itch precedes rash: Suggestive of
Systemic disorders
Psychogenic pruritis
Rash precedes itch: Suggestive of
Cutaneous disease
Rash secondary to itching and scratching: Suggestive of
Atopic dermatitis
Many cases of psychogenic pruritus
Character of the sensation
Itching: atopic eczema, dermatologic disease
Stinging, burning, or prickling: frequently psychogenic pruritus
Pattern to the episodes of itching
Time of day
Does it awaken patient?
Are activities interfered with?
What are the provoking or relieving factors?

aries, a realistic body image, positive self-esteem, and the modulation of emotional experience.²⁸ The infant whose skin is abnormal may receive touching that is not in tune with his or her particular needs or may experience that touching differently.²⁹ As a result, the infant may not be in touch with his or her feelings and may not develop language to describe them. This state has been termed *alexithymia*, and patients with this condition tend to express emotional content in physical terms.³⁰ In the atopic individual, the expression may be through itching and scratching. Self-esteem is frequently diminished in these patients, and some individuals use scratching to define their physical boundaries.³¹

As is the case with animals, human subjects can be conditioned to carry out mechanical acts. A positive association has been demonstrated between inherent anxiety levels and the ease with which conditioning can be achieved. Atopic patients are shown to be more easily conditioned to scratch than are nonatopic patients, thus confirming the higher levels of anxiety characteristic of the atopic condition.^{13,25}

Indeed, clinical experience confirms that emotional distress is not uncommon in atopic patients and that they frequently act out anger and hostility by scratching, rather than by verbalizing their feelings.⁷ Atopic individuals are more likely to respond to minor signals and stimuli by scratching than are nonatopic individuals, and many patients can identify an emotionally disturbing event before a flare of dermatitis.^{11,13}

TABLE IV. Treatment of itching

Educate the patient	Identify and avoid common aggravating factors
	Need for cool dry environment
	Need for adequate hydration
Nonspecific topical measures	Cool compresses
	Cool baths with tar or oatmeal
	Neutral soaps
	Liberal use of emollients, after hydrating the skin
	Lotions containing menthol or phenol
	Pramosone lotion or cream
	Ultraviolet light B
Specific topical measures	Topical steroids
	Incorporate tar or sulfur in ointments for steroid-sparing effect
	Intralesional steroids (rarely)
	EMLA cream (rarely)
	5% Doxepin cream (rarely)
Oral measures	Antihistamines
	Antidepressants: Doxepin, SSRIs
	Antibiotics
	Anxiolytics
	Antipsychotics
Dermatologic referral	
Psychiatric referral	

EMLA, lidocaine 2.5% and prilocaine 2.5%; SSRI, specific serotonin reuptake inhibitor.

TREATMENT OF ITCHING IN ATOPIC DERMATITIS

This section will focus on the treatment of itching as a symptom, not the treatment of atopic dermatitis per se.

Because, in the atopic patient, the skin is so highly charged emotionally and because it commonly receives such negative attention, it is important to prescribe positive, healing activities for the patient, such as cool compresses, baths, and emollients.²⁶ It is also important to educate the patient at length about the nature of the skin and to stress with the patient those factors that will aggravate or relieve the tendency to itch.^{13,22,26} An approach to the treatment of itching in atopic dermatitis is summarized in Table IV.

Under normal circumstances, itching in the atopic patient is not hard to control. When this is not the case, a number of questions come to mind. Is the diagnosis correct? Is there an unrecognized bacterial or yeast infection? Has a contact allergy to one of the topical medications developed? Is the patient or parent in compliance with therapeutic suggestions? Remarkably, parental compliance in particular is frequently poor.³² If the answer to all of these questions is in the negative, then one must be alert to the probability of unrecognized emotional factors and underlying anxiety and/or depression. Referral to a dermatologist and consultation with a psychiatrist must then be considered. Insight-oriented,³³ cognitive-behavioral,^{34,35} and supportive psychotherapies^{36,37} have all been demonstrated effective in the treat-

ment of inflammatory dermatoses including atopic dermatitis. Recently, massage therapy has also been shown to be beneficial.³⁸

THE IMPACT OF ATOPIC DERMATITIS ON PATIENT AND FAMILY

In childhood, severe atopic dermatitis is stressful for both parent and child. This stress is compounded by difficulties that arise in the mother-child relationship. The mother experiences her child's imperfect skin as a blow to her self-esteem. But equally as important, she may feel that she actually caused it and feel guilty on that account.^{4-7,39}

Resentful of the burden of the appearance and the enormous cost in time and money of care, she may reject the child and deprive the child of optimal emotional and tactile experience. Alternatively, out of guilt about her negative feelings, she may be over solicitous, spoiling the patient at the expense of husband and siblings, infantilizing the child, and impeding the child's emotional development. In either case, the child picks up on the mother's distress, to which the child responds with anxiety; itching escalates; scratching becomes a powerful tool to manipulate the environment, and intractability is assured.^{4,28}

In the adult, the physical appearance, the constant scratching, and the disturbed sleep lead to feelings of shame and impaired performance on the job. There are restrictions with regard to clothing and professional, social, and intimate activities, and patients feel resentful and guilty about the time and money devoted to skin care. All of these factors contribute to the anxiety and depression experienced by these patients.^{2,4,7,39}

Three brief clinical vignettes will illustrate the physical and psychologic aspects of itching in atopic dermatitis. These vignettes have been published previously, but will serve as examples here.^{4,33}

John, the 2½-year-old son of immigrant parents, had had intractable atopic eczema since age 3 months. His mother was homesick, depressed, and lonely here and had planned to return home, when unexpectedly she became pregnant with John. Resentful of the pregnancy, but guilty about her resentment, her guilt was compounded when atopic dermatitis developed; she questioned whether her negative feelings may even have caused it. These negative feelings were concealed by over solicitousness. She could not tolerate to see John scratch and would do anything to stop him. Her life revolved around him, to the exclusion of the rest of the family; and there was constant tension in the house. John, a restless, demanding, itchy child, readily picked up the tension. Toilet training was impossible because removal of the diaper was an invitation to scratch; at bedtime the two would undress together, and his mother would lie down beside him, patting and stroking him until he was asleep—attention that it was hard to give up. Nightly, John would be taken into the parental bed because of whining and scratching. As a result, the parents were exhausted and frustrated; the siblings were angry, and John, anxious because of emotional over-stimulation, was a clinging, whining, itching infantilized tyrant.

At 12 years old, Barry had had intractable atopic eczema since early childhood. The parents were divorced. His father, who had severe diabetes, had gangrene that had required progressively more deforming amputations of both legs over a period of time. The

resultant deformity made Barry very anxious, because he feared for his own physical integrity. Because his father was receiving disability, money was short; his mother eked out a modest living by cruising the local bars to pick up men, whom she would bring home. Barry, taken along on these excursions, was doubly anxious because of emotional over-stimulation. Neither parent could allay his pervasive anxiety; his skin itched incessantly, and he comforted himself by soothing and taking care of it. He used a whole pound of emollient each day and was found to have used many pounds of steroid ointment in the course of 1 year. He was very small for his age, and lack of sleep and constant itching impaired his performance in school.

Naomi, a 45-year-old married woman, sought psychiatric help because she thought her intractable itching might be stress-related, though on the surface her life seemed ideal. She still idealized both her selfless and dedicated professional father and her nurturing homemaker mother. A professional herself, torn between these 2 ideals, she was depressed because she felt she could not live up to the expectations of either. Gradually, she came to recognize that she was reliving the conflicts of her childhood in her own marriage. As she gradually became aware of hidden, but intense anger, towards her autocratic father, she realized that episodes of itching were related to periods when her husband's behavior echoed that of her father, and she was forced to take on, unaided, her mother's caretaker role. The unconscious anger had led to anxiety and depression and had triggered the itching and the uncontrollable scratching that preceded the episodic outbreaks of dermatitis.

Each of these patients had had intractable itching over prolonged periods of time, but in each case the itching and the dermatitis resolved through insight-oriented psychotherapy. For John, the work was with the mother. As she came to understand and accept her negative feelings, she was able to set limits for the little boy, who was then able to develop normally, physically, emotionally, and intellectually.

CONCLUSION

Although itching is symptomatic of many inflammatory and psychophysiologic dermatoses, in atopic dermatitis it is a cardinal feature of the disease. Effective control of itching can go a long way toward controlling the eruption itself; it can also make a major contribution to the physical and emotional well-being of the patient and the patient's total environment.

REFERENCES

1. Hanafin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1980;92:44-7.
2. Jemec GBE, Wulf HC. Patient-physician consensus on quality of life in dermatology. *Clin Exper Dermatol* 1996;21:177-9.
3. Daud LR, Garralda ME, David TJ. Psychosocial adjustment in preschool children with eczema. *Arch Dis Child* 1993;69:670-6.
4. Koblenzer CS, Koblenzer PK. Chronic intractable atopic eczema: its occurrence as a physical sign of impaired parent-child relationships and psychologic developmental arrest: improvement through parent insight and education. *Arch Dermatol* 1988;124:1673-7.
5. Dahl RE, Bernhisel-Broadbent J, Scanlon-Holford S, Sampson HA, Lupo M. Sleep disturbance in children with atopic dermatitis. *Arch Pediatr Adolesc Med* 1995;149:856-60.
6. Stores G, Burrows A, Crawford C. Physiologic sleep disturbance in children with atopic dermatitis: a case control study. *Pediatric Derm* 1998;15:264-8.

7. Ginsburg IH, Prystowsky JH, Kornfeld DS, Wolland H. Role of emotional factors in adults with atopic dermatitis. *Int J Derm* 1993;32:656-9.
8. Al-Ahmar HF, Kurban AK. Psychological profile of patients with atopic dermatitis. *Br J Derm* 1976;95:373-7.
9. Gupta MA, Gupta AK, Schork NJ, et al. Depression modulates pruritus perception: a study of pruritus in psoriasis, atopic dermatitis, and chronic idiopathic urticaria. *Psychosom Med* 1994;56:36-40.
10. Rothman S. Physiology of itching. *Physiol Rev* 1941;21:357-81.
11. Musaph H. Itching and scratching: psychodynamics in dermatology. Philadelphia: FA Davis Co; 1964. p. 8.
12. Musaph H. Psychodermatology. *Psychother Psychosom* 1974;24:79-85.
13. Wahlgren CF. Pathophysiology of itching in urticaria and atopic dermatitis. *Allergy* 1992;47:65-75.
14. Tuckett RP. Neurophysiology and neuroanatomy of pruritus. In: Bernhard JD, editor. *Itch: mechanisms and management of pruritus*. New York: McGraw-Hill Inc; 1994. p. 1-22.
15. Tobin D, Nabarro G, Baart dela Faille H, van Vloten WA, van der Putte SCJ, Schuurman H-J. Increased number of immunoreactive nerve fibers in atopic dermatitis. *J Allergy Clin Immunol* 1992;90:613-22.
16. Lotti T, Hautmann G, Panconesi E. Neuropeptides in skin. *J Am Acad Derm* 1995;33:482-96.
17. Ballantyne JC, Loach AM, Carr DB. Itching after epidural and spinal opiates. *Pain* 1988;33:149-60.
18. Monroe EW. Efficacy and safety of nalmefene in patients with severe pruritus caused by chronic urticaria and atopic dermatitis. *J Am Acad Derm* 1989;21:135-6.
19. Creese I, Feinberg AP, Snyder SH. Butyrophenone influences on the opiate receptors. *Eur J Pharmacol* 1976;36:231-5.
20. Panconesi E, Hautmann G. Psychopsiology of stress in dermatology. *Dermatol Clin* 1996;14:399-421.
21. Bernhard JD. Pruritus in skin diseases. In: Bernhard JD, editor. *Itch: mechanisms and management of pruritus*. New York: McGraw-Hill Inc; 1994. p. 37-67.
22. Morren M-A, Przybilla B, Bamelis M, Heykants B, Reynaers A, Degreef H. Atopic dermatitis: triggering factors. *J Am Acad Derm* 1994;31:467-73.
23. Graham DT, Wolf S. The relation of eczema to attitude and to vascular reactions of the human skin. *J Lab Clin Med* 1953;42:238-54.
24. Edwards AE, Shellow WVR, Wright ET, et al. Pruritic skin disease, psychological stress, and the itch sensation. *Arch Derm* 1976;112:339-43.
25. Jordan JM, Whitlock FA. Emotions and the skin: the conditioning of scratch responses in cases of atopic dermatitis. *Br J Derm* 1972;86:574-85.
26. Koblenzer CS. *Psychocutaneous disease*. Orlando: Grune and Stratton; 1987. p. 281-310.
27. Brenner C. The role of psychic conflict in mental life. In: Rothstein M, editor. *The Moscow lectures on psychoanalysis*. Madison (CT): International Universities Press; 1991. p. 45-60.
28. Koblenzer C. Psychodermatology of women. *Clin Dermatol* 1997;15:127-41.
29. Spitz RA. *The first year of life*. New York: International University Press; 1971. p. 222-42.
30. Tantam D, Kalucy R, Brown DG. Sleep, scratching dreams in eczema: a new approach to alexithymia. *Psychother Psychosom* 1982;37:26-35.
31. Anzieu D. *The skin ego*. New Haven: Yale University Press; 1989. p. 96-113.
32. Yamamoto K. How doctor's advice is followed by mothers of atopic children. *Acta Derm Venereol (Stockh)* 1989;144(suppl):31-3.
33. Koblenzer CS. Psychotherapy for intractable inflammatory dermatoses. *J Am Acad Derm* 1995;32:609-12.
34. Ehlers A, Stangier G, Gieler U. Treatment of atopic dermatitis: a comparison of psychological and dermatological approaches to relapse prevention. *J Consult Clin Psychol* 1995;63:624-35.
35. Gieler U. Atopic dermatitis. In: Paulley JW, Pelser HE, editors. *Psychological management for psychosomatic disorders*. Berlin: Springer-Verlag; 1989. p. 257-69.
36. Cole WC, Roth HL, Sachs LB. Group psychotherapy as an aid in the medical treatment of eczema. *J Am Acad Derm* 1988;18:286-91.
37. McSkimming J, Gleeson L, Sinclair M. A pilot study of a support group for parents of children with eczema. *Aust J Derm* 1984;25:8-11.
38. Schachner L, Field T, Hernandez-Reif M, Duarte AM, Krasnegor J. Atopic dermatitis symptoms decreased in children, following massage therapy. *Pharmacol Ther* 1998;15:390-5.
39. Koblenzer CS. The psychological and social impact of skin disease. In: Pierini AM, editor. *Pediatric dermatology: the world's reality in the children's skin*. New York: Elsevier; 1995. p. 1-12.