

## REVIEW ARTICLE

# Biopsychosocial Mechanisms of Chronic Itch in Patients with Skin Diseases: a Review

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**Itch is a major feature of many skin diseases, which adversely affects patient's quality of life. Besides disease severity, psychophysiological factors have been proposed to influence the itch sensation. In this review the evidence for a biopsychosocial model of itch is described, focusing in particular on evidence for the effects of personality characteristics, external stressors, cognitive, behavioural and social factors, and the possible mediating role of physiological processes. Research so far indicates that stressors may have a role in the itch sensation of patients with skin diseases. Furthermore, cognitive factors, such as helplessness and worrying, and the behavioural response of scratching have been indicated as possible worsening factors. Overall, findings are in favour of a biopsychosocial model for the itch sensation. However, there is a strong need for more, methodologically sound research in order fully to understand the processes underlying the itch sensation. Key words: itch; scratch; skin diseases; psychological factors; biopsychosocial model.**

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Itch is a major symptom of many chronic skin conditions and affects a considerable number of patients with, for example, atopic dermatitis, contact dermatitis, urticaria and psoriasis (1, 2). Itch has been defined as a sensation that provokes the desire to scratch (3). Moreover, itch has been shown to lower patients' quality of life (4–6), which in turn unfavourably affects the outcome of dermatological therapies, such as photochemotherapy (7) and, consequently, the patients' skin status (1, 4, 8). Disease severity alone usually cannot fully account for the intensity of itch and, although several treatments are available, none is generally effective (9). Due to the overall modest relationship between itch intensity and severity of the skin diseases of, for example, psoriasis and atopic dermatitis (4, 8, 10, 11), other factors have also been proposed to influence itch intensity. In addition to factors such as sweating, skin dryness, or physical effort,

psychological factors have regularly been described to influence itch intensity (4, 8, 12). One of the most striking examples of the influence of psychological factors on itch came from the observation that itch (and the scratching response) could be aggravated by showing individuals itch-related pictures of fleas, mites, scratch marks, allergic reactions, etc. (13). Furthermore, it has been described that psychological co-morbidity (e.g. clinical depression) is high among patients suffering from itch (14–16) and that negative emotions can increase the level of itch (17).

In contrast to the traditional biomedical model (which focuses merely on the physical processes of a disease and does not take into account the role of psychosocial factors), the observation that disease severity alone usually cannot fully account for the intensity of itch, as well as the influence of psychological processes in the itch sensation, support a biopsychosocial model of itch in patients with chronic skin diseases. Biopsychosocial factors can best be shown in a diathesis-stress model, which is based on the hypothesis that internal vulnerability factors (diathesis), such as personality, interact with external environmental factors (such as major life events and other stressors) to trigger a disease or itch (Fig. 1). In this model, cognitive, behavioural and social factors, such as illness cognitions, coping, or perceived social support can be considered as mediating or moderating factors that can enhance the disease and symptoms of itch. It is assumed that these factors, at least partly, account for the effects of stressors and personality characteristics on disease. For example, the influence of a stressful event on disease activity and itch may be explained by how patients cope with the stress-

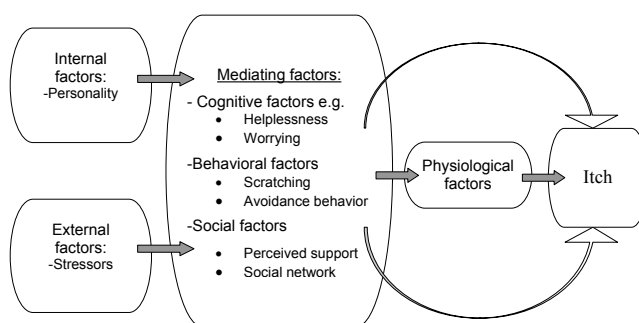


Fig. 1. Biopsychosocial model of itch.

ful event. Another well-known example is the effect of social support on the relationship between stressors and disease activity: stressors might unfavourably affect disease activity and itch only in the event of low levels of social support.

Specifically for itch, scratching is an important mediating factor in this model. Scratching in response to itch is an unconscious and autonomic response, as reflected by the definition of itch as an unpleasant sensation, which evokes the desire to scratch (17). However, due to a vicious itch-scratch-itch cycle, scratching may become a problem in its own right. These factors may, in turn, be affected by psychological factors of sensory information processing (18). For example, it has been reported that patients with chronic itch conditions have a lower threshold for sensory stimuli in general and for itch specifically (19–21). This might be due to changes in information processing, such as an attentional- or interpretational bias to general or itch specific stimuli, or catastrophizing expectations about aversive stimuli (19, 22).

Several physiological processes can also mediate the relationship between itch and psychological factors (see Fig. 1). It is nowadays well-known that, for example, specific cutaneous sensory C-nerve fibres serve as pruriceptors (23–25), transmitting sensory stimuli from the skin through the dorsal horn to the spinothalamic tract. Several internal mediators, e.g. histamine, serotonin, prostaglandins and cytokines, can bind to the nerve endings of these itch receptors and induce axonal firing (26–29). Considering the possible influence of stressors on itch in patients with skin diseases, external stressors can activate the stress response system in the brain (hypothalamic-pituitary-adrenal axis; HPA axis), and the hormones of this HPA axis in turn activate mast cells in the skin (30, 31). In addition, external stressors can induce autonomous responses, such as transpiration, which can also worsen itch sensations (4, 12).

## PURPOSE AND METHODS OF THIS STUDY

While research so far has focused on the individual components of the biopsychosocial model of itch, the whole model has not yet been systematically described, particularly with regard to the evidence for psychological factors. Therefore, the aim of the current review is to summarize evidence for the biopsychosocial model of itch, in particular the evidence for possible pathways for the influence of psychological factors on itch. Although different forms of itch have been classified and the neurophysiology of itch greatly depends on the type of itch (32), in this review we will focus on chronic itch related to skin diseases. For this purpose, we will describe data about the relationship between itch and internal factors of relatively stable personality characteristics (a relatively stable pattern of individual

thoughts, emotions and actions), external stressors, as well as the influence of cognitive, behavioural and social factors on itch in patients with skin diseases.

The electronic databases used in our search for relevant studies included MEDLINE (1970 to 2007), psychINFO (1970 to 2007), EMBASE (1980 to 2007), and the Cochrane Library (1993 to 2007). Based on diathesis-stress models, the keywords “itch”, “itching” and “pruritus” were used in combination with “psychological”, “psychiatric”, “stress”, “stressors”, “life events”, “hassles”, “personality”, “mood”, “affect”, “emotion”, “tension”, “anxiety”, “depression”, “neuroticism”, “scratch”, “coping”, “cognitions”, “helplessness”, “avoidance”, “acceptance”, “worrying”, “catastrophizing”, “stigmatization”, “efficacy”, “perceived control”, “behaviour”, “social” and “support”. In addition, reference sections were screened manually. Only international published studies on itch in skin diseases were included in this review.

## PERSONALITY CHARACTERISTICS AND ITCH

It has been suggested that certain personality traits are associated with the development or exacerbations of skin disorders (33–36). In particular, for patients with chronic inflammatory diseases, such as atopic dermatitis and psoriasis, a specific personality profile (with a relatively stable experience of negative emotional states) has been suggested (33, 36–40). However, research has generally failed to show that patients with skin diseases have such a distinct personality profile. Nevertheless, several emotional features (such as anxiety or depression) have frequently been found to be elevated in patients with chronic skin diseases, probably as a consequence of the skin disease rather than as a contributory cause of the skin condition (34, 35, 39, 41–46).

There is evidence for an association between negative affectivity (e.g. depression and anxiety) and the outcome of itch and the related scratching response. For example, preliminary results indicate that the level of anxiety is correlated with the intensity of itch in patients with chronic skin diseases (47). Furthermore, elevated levels of anxiety are associated with increased conditioning of a scratch response in patients with atopic dermatitis (48). For depression, findings suggest that a depressed clinical state may influence the itch intensity (49–51). For example, the level of itch before and after standard dermatological treatment (of, for example, topical steroids or ultraviolet-B light) in patients with psoriasis was significantly associated with changes in depression before and after treatment (50). In addition, negative affectivity in terms of neuroticism has also been associated with itch intensity in patients with psoriasis as well as atopic dermatitis (8), while other studies have failed to find a relationship between itch and negative

affectivity (44, 46). Gupta (52) reported a correlation between a tendency to experience dissociative states (a state where the person withdraws from the body or reality, occurring mostly during or after psychological trauma) and itch in a non-clinical population.

These findings regarding personality and itch severity should be interpreted with caution. Although in some cross-sectional studies a statistically significant correlation was found, the direction of causality remains unclear. It is reasonable that some of these previously described symptoms, for example anxiety, depression, and experiencing dissociative states, are a consequence, rather than a cause, of having a chronic dermatological disorder accompanied by chronic itch. Dissociative states could, for example, be a functional way of coping with chronic itch, while it may be a way to withdraw from the unpleasant itch experience. In addition, there may be an indirect relationship between negative affect and itch. For example, in other chronic diseases, patients with more negative affectivity are known to be more vulnerable for dysfunctional coping styles when affected by disease (e.g. a passive-avoidant coping style), which in turn have been shown to be risk factors for a worse disease outcome (53, 54).

## STRESSORS AND ITCH

Many patients (37–88%) with chronic skin diseases believe that there is a relationship between external stressors and their skin disease (55–59), and this relationship has received increasing attention over the years (43, 58–68). Although research on this subject is often methodologically flawed (e.g. small sample size, limited number of repeated measurements), results suggest that stress factors are associated with disease severity in patients with skin diseases. For example one of the few prospective studies by King & Wilson (69), indicates that in patients with atopic dermatitis, self-reported stressors are predictors of disease severity one day later. The influence of stressors on the physical symptom of itch has received far less attention. While to our knowledge there have been no prospective studies on this subject, some experimental and cross-sectional studies indicate that stress factors can influence itch. For example, an early experimental study by Edwards et al. (70) indicated that perceived stress affected the capability of healthy subjects to discriminate among itch stimuli.

A frequently used distinction between stressors is the division into major life events (e.g. divorce, loss of a loved one) and minor life events (daily hassles of, for example, interpersonal conflicts or running late for an important meeting). Major and minor life events have been shown to be associated with higher levels of itch in the general population and in patients with skin diseases (50, 71, 72). Moreover, one study showed that experi-

mentally evoked stress heightened itch in patients with skin diseases (73). Additionally, perceived stress due to major or minor life events has been found to be associated with the presence (and severity) of itch in patients with psoriasis in some studies (74, 75) but not in others (50). In skin diseases, the feeling of being stigmatized (e.g. the experience that others stare, feel uncomfortable touching patients, make annoying comments, or avoid contact at all) also reflects the individual's perceived stress. Stigmatization has been shown to be related to higher levels of itch in patients with atopic dermatitis and psoriasis (47, 76). Furthermore, high stress reactors, that is patients who indicate that their disease severity is strongly associated with stress, reported significantly more itch and a stronger itch/scratch cycle than low stress reactors (77, 78), which suggests that stressors may have different effects on the symptom of itch in different subgroups of patients.

Overall, studies of the relationship between stress factors and itch indicate that the subjective experience of stressors might be associated with increased itch in patients with skin diseases. However, further prospective and experimental research is necessary to fully comprehend the relationship between different types of stressors (life events as well as perceived stress) and itch in different types of skin diseases.

## MEDIATING FACTORS

As shown in Fig. 1, specific cognitive, behavioural and social factors are assumed to mediate a persons' skin reactivity and response to itch.

### *Cognitive factors*

Individual differences in the long-term adjustment to chronic diseases may be explained by different ways of cognitive evaluation (illness cognitions) of the aversive nature of the chronic condition and its symptom (45, 53). Although there are several conceptualizations of illness cognitions, two main constructs might be particularly relevant for itchy skin diseases as well as other chronic diseases: (i) cognitions that emphasize the negative meaning (e.g. helplessness or worrying); and (ii) cognitions that diminish the aversive meaning of the condition (e.g. acceptance) (53).

*Helplessness.* Since most chronic diseases are still incurable and the course of the disease is often unpredictable, patients may experience helplessness because of this lack of control over their disease. Helplessness is reflected by the tendency to emphasize the negative aspects of the disease as being uncontrollable, unpredictable and unchangeable, and to generalize these feelings to all aspects of life (53). In line with other chronic conditions in which helplessness has been shown to influence phy-

sical symptoms (53), preliminary results indicate that helplessness may be associated with higher levels of itch in skin diseases (10). Additionally, helplessness has been related to a lower psychological well-being (10) and appeared to be the strongest predictor of perceived stress, such as feelings of stigmatization, in patients with skin diseases (76).

*Worrying.* Related to the concept of helplessness is the cognitive status of perseverative worrying. About 40% of patients with a chronic skin condition show general pathological worrying (22, 79) and disease-specific worrying has been shown to be associated with more severe disease activity in patients with skin diseases (8, 80). Furthermore, Fortune et al. (7) reported that general worrying predicted the effect of UVB light therapy in patients with psoriasis. Patients with high levels of worrying needed more radiation treatments to clear their psoriasis.

*Acceptance.* In contrast to helplessness and worrying, which focus on the negative meaning of the disease and seem negatively to influence the disease course, acceptance may have beneficial effects on skin diseases. Cognitions of acceptance are to acknowledge the fact of being chronically ill and simultaneously perceiving the ability to live with, and master the consequences of, the disease (53). Some studies have found a relationship between acceptance and physical well-being in patients with skin diseases (10), while others have not (81). Acceptance has also been shown to be correlated with less itch intensity (10). Since higher levels of psychological distress have been related to higher levels of helplessness and less acceptance (10), it is possible that these psychological cognitions mediate the distress caused by itch in patients with skin diseases.

#### *Behavioural factors*

For skin diseases in general, behavioural coping strategies are directly associated with disease-related outcomes in patients with chronic skin diseases (82, 83), specifically scratching. The subjective sensation of itch is strongly correlated with the scratching response (measured by behavioural indicators as well as questionnaires) (47, 84). The sensation of itch induces a universal cascade in humans and animals to scratch. The positive effect of scratching could be the removal of the causal agent, such as parasites or plant particles. The immediate reinforcement of scratching is the reduction of itch; however, patients with enduring itch due to chronic skin diseases persist in their scratching behaviour (even until the skin bleeds) and this perceived loss of control may lead to negative emotional feelings. In addition, scratching can be sustained by long-term reinforcement (for example, through attention from other people). Consequently,

in the long-term scratching may develop into a conditioned response to stressors and other stimuli beside itch, which may be particularly relevant in patients with chronic itch. As mentioned earlier, scratching induces several physiological responses. For example, it has been shown that repeated scratching decreases prostaglandin D2 (PGD2) levels – an itch inhibitor – in the skin, resulting in an increased desire to scratch and inducing the itch-scratch cycle (85, 86). Furthermore, functional positron emission tomography (fPET) and functional magnetic resonance imaging (fMRI) studies have recently showed that itch is related to brain regions implicated in motivational processes (e.g. orbitofrontal cortex, striatal region, subgenual anterior cingulate cortex), which could reflect the desire to relieve the itch, probably through scratching (87, 88). Furthermore, animal studies have shown that scratching may induce skin conditions by influencing various immunological responses: less scratching behaviour has been shown to result in altered levels of several interleukins (IL-5, IL-13, IL-18, interferon- $\gamma$ ) (89). Although scratching induces relief of symptoms in the short term, scratching often becomes a principal problem in its own right in the long term, due to a vicious circle of itching, scratching, and scratching wounds that in turn cause itch. Through this vicious cycle of itch-scratch-itch, scratching may have an important role in the maintenance and exacerbation of chronic skin disorders. In turn, the itch-scratch cycle has been found to correlate with higher levels of worrying and helplessness, less acceptance, and anxious-depressive mood (47, 80, 90), suggesting that certain psychological factors (such as illness cognitions, behavioural factors, and external stressors) may influence the itch-scratch cycle.

In addition to scratching, other coping behaviours may influence the itch sensation of patients with chronic skin disease in the long term. In particular, enduring patterns of avoidant coping behaviour in response to itch attacks (e.g. quitting activities or retreating to a restful environment when experiencing itch) has been shown to be related to higher levels of itch, more scratching, and higher levels of disease-related disability (8, 58). This is consistent with findings for other chronic conditions where avoidance behaviour towards the disease has also been described negatively to influence the disease outcome. For example, in patients suffering from chronic pain it is well known that passive-avoidance behaviour negatively influences long-term disease outcomes (91–93). In contrast to acute pain, acute itch is a trigger for increased activity patterns (scratching). However, chronic itching usually causes patients to withdraw from activities or to avoid daily activities, which may lead to a reduced quality of life in the long term. Avoidance behaviour has indeed been shown to be related to disease-related quality of life in patients with chronic skin conditions that are frequently accompanied by itch (82, 83).

### Social factors

Social support can be broadly defined as interactions or resources provided by others that may help an individual cope with stress (94). The influence of social support on general physical and psychological health outcomes has frequently been described (95–98). There is also relatively strong evidence that higher levels of social support are associated with better cardiovascular regulation (e.g. lower blood pressure) and immune functioning. The relationship between social support and endocrine functioning is somewhat less clear. Although such relationships have repeatedly been reported, the underlying mechanisms are relatively unclear. For example, increasing solely social contact levels did not affect key parameters of neuroendocrine function, such as cortisol levels (95).

The influence of social support on itch requires more attention, while only a few studies address this subject. Preliminary results indicate that social support (perceived support and size of social network) is not associated with itching (10, 72). However, social support may have a protective effect when individuals are exposed to possible disease-triggering events (96). Picardi et al. (99) investigated the role of social support in outpatients with recent-onset psoriasis or with exacerbation of their disease. Preliminary results indicate that subgroups of patients differ in their perceived level of social support (66). Social support may also have a mediating role in the relationship between itch and distress, since lower levels of social support are reported to be associated with higher levels of distress (10).

### CONCLUSION

The aim of this review was to provide an overview of the evidence for a biopsychosocial model of itch in patients with chronic skin diseases. In particular, evidence for a relationship between internal factors of relatively stable personality traits, external stressors, and the influence of possible mediators (cognitive, behavioural and social factors) on itch was structurally summarized. Considering that disease severity alone cannot fully account for the itch sensation and the preliminary empirical support for a relationship between the biopsychosocial pathways and itch, the theoretical model seems to have an additional value in gaining insight into the complex determinants of itch and its treatment in skin diseases. Overall, findings support the biopsychosocial model of itch. However, further research is needed before the underlying mechanisms can be fully understood. While most research into psychological factors and the itch sensation is based on cross-sectional studies, there is a strong need for studies with a methodologically sound design (e.g. studies with an experimental or prospective design).

The authors declare no conflicts of interest.

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