Centenary theme section: ITCH AND PRURITIC DISORDERS

REVIEW ARTICLE

Itch and Psyche: Bilateral Associations

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Beginning from embryological development, skin and psyche are closely related to physiological state regardless of age. Altering the homeostasis of one of these components impacts on the other, thereby substantiating that the relationship between itch and psyche is bilateral. Itch has a complex pathogenesis, which involves the peripheral and central nervous systems, as well as various inflammatory mediators. This paper reviews key aspects of itch pathogenesis, relevant associations with stress, the contagiousness of itch, psychological and psychiatric considerations related to itch, and the burden of itch with respect to impairment of health-related quality of life (HRQoL) and stigmatization. Despite the fact that itch–psyche associations still pose many questions, current knowledge supports the role of a holistic, interdisciplinary approach to these patients in order to improve their well-being.

Key words: itch, psyche, pathogenesis, stress, psychiatry, burden of disease.

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SIGNIFICANCE

The relationship between itch and psyche is complex and bilateral. Increasing interest in itch and its associations with psyche is indicated by the abundance of experimental and clinical articles published in this field. This review covers the pathogenesis of itch, associations with stress, the contagiousness of itch, psychological and psychiatric aspects related to itch, and the burden of itch with respect to impairment of health-related quality of life and stigmatization.

Beginning with human embryogenesis, skin and brain are organs that are closely connected due to their ectodermal origins (1). These associations continue to unfold after birth, and constitute a foundation for the normal psychosocial development of an individual. According to the *moi-peau* concept (2) (**Fig. 1**) (as extensively reviewed by Dutray & Misery (1)), skin possesses a wide psychological meaning, reflecting various needs of the psyche. Firstly, skin has the function of a "bag" or "container", as it embraces the positive stimuli experienced by a baby during nursing and being cared for. Secondly, skin is an "interface" with the outside world, which serves as a protective barrier against external aggression. Lastly, skin may be considered as a specific "place" or "means of communication" in order to establish relationships, and as a "surface" on which others may leave their trace. It seems substantiated that chronic skin diseases with their rich symptomatology, especially acquired during early childhood, ensue in altering both physical and psychological homeostasis of an affected individual. The impact is always reciprocal: the psyche may predispose to cutaneous complaints (e.g. itch, chronic scratch lesions), whereas dermatological signs and symptoms "scar" the psyche.

Itch is defined as an unpleasant sensation leading to scratching, further classified as acute or chronic (lasting less or more than 6 weeks, respectively) (3). Chronic itch (CI) is a feature of various dermatoses, although it may also stem from systemic, neurological, or psychiatric disorders. Occasionally, the diagnosis of pruritus of unknown origin (PUO) is established. The presence of CI is associated with significant morbidity, mortality, reduction in quality of life (QoL), feelings of stigmatization, stress, impairment of mood, lack of concentration,

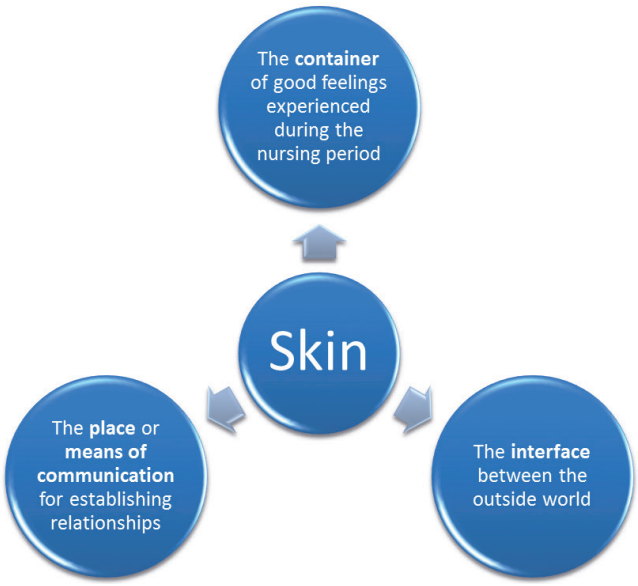

Fig. 1. The moi-peau concept (The Ego-Skin concept) (according to (1)).

reduced sexual desire and appetite, as well as inability to express emotions (alexithymia) (4–9). On the other hand, clinicians are aware that various psychological and psychiatric alterations may contribute to the occurrence or exacerbation of itch. One of the models that aims to explain CI mechanisms in the course of cutaneous disorders is the Biopsychosocial Model, proposed by Verhoeven et al. (10). The occurrence of itch is a result of various factors: internal (associated with personality), external (e.g. stressful environmental stimuli), mediating (e.g. cognitive, behavioural and social) as well as physiological. Tey et al. (11) have clinically classified the itch–psyche interactions as pruritic disorders with psychiatric sequelae (I); pruritic disorders aggravated by psychosocial factors (II); and psychogenic disorders causing itch (III). These complex bilateral associations between itch and psyche support the need for multidisciplinary approach to itch and the associated conditions in the clinical setting (12–14).

This review covers the pathogenesis of itch, cerebral regions associated with pathogenesis of itch, the interplay between itch and stress, the contagiousness of itch, psychological and psychiatric aspects associated itch, and the burden of itch with respect to impairment of QoL and stigmatization.

ITCH PATHOGENESIS

There is growing data concerning the pathogenesis of itch, as this topic is gaining increased attention in the medical literature. From the historical point of view, itch has been perceived as a subtype of pain (15), and it is thought that the symptom might have developed as an evolutionary defence mechanism against various potentially dangerous stimuli, such as parasites, insects, sharp objects, irritants, and allergens (16). However, itch is currently deemed a separate entity from pain. The role of peripheral (PNS) and central nervous system (CNS) is crucial in eliciting CP, starting from free nerve endings in the epidermis. The statement "it is the brain that itches, not the skin" (16) remains valid, as different cortical areas are included in processing itch intensity, location, associated unpleasant feelings, generating the need to scratch, and preparing and executing scratch behaviour (17–20). In a positron emission tomography (PET) study among human participants histamine injection resulted in major activation in the left primary sensory cortex, as well as the primary motor cortex, supplementary motor area and premotor cortex (17). Another study utilizing PET and regional cerebral blood flow (rCBF) revealed that a skin prick test with histamine resulted in activation of the contralateral somatosensory cortex; in addition, both ipsilateral and contralateral motor areas were involved. Itch unpleasantness was associated with the activation of contralateral sensorimotor cortex, prefrontal cortex, posterior insula and ipsilateral supplementary motor area (18). A functional magnetic resonance imaging (fMRI) study demonstrated itching and pain both activated the anterior cingulate cortex, the anterior insula, the basal ganglia and pre-supplementary motor area (20). However, the activity in posterior cingulate cortex and the posterior insula was more prominent in itching than in pain. Moreover, it was proportional to itching sensation. In an experiment with cowhage-induced itch, as demonstrated by fMRI, itching was associated with increased activity in supplementary motor area, premotor cortex, primary motor cortex, and midcingulate cortex (21). The role of the caudate nucleus was also substantiated, as this region is involved in the reward system. Papoiu et al. (22) demonstrated that active scratching was accompanied by higher pleasure and deactivation of anterior cingulate cortex and insula compared with passive scratching. In addition, the activation of ventral tegmentum area (VTA) of the midbrain, as well as deactivation of periaqueductal grey matter (PAG), are associated with the itch-scratch reward system.

ITCH AND STRESS

Stress is a concept frequently mentioned nowadays, yet despite its widespread appearance in various situations it may be described in different ways, e.g. as "the non-specific response of the body to any demand made upon it" (23) or "a relationship with the environment that the person appraises as significant for his or her well-being and in which the demands tax or exceed available coping resources" (24). The bilateral associations of itch and psyche are perfectly reflected by the interplay of itch and stress. Similarly to the vicious itch-scratch cycle, chronic pruritic conditions (e.g. psoriasis, urticaria, atopic dermatitis) generate huge stress levels, which may subsequently perpetuate exacerbation of the disease. Aberrant parasympathetic response may possibly link chronic stress and itch (25), while stress-induced itch is associated with activation of the hippocampus and subcortical regions (corpus callosum and putamen) (26). The itch-stress association does, in fact, pose a certain therapeutic implication towards first-generation H_1-antihistamines and GABA-ergics (gabapentin and pregabalin) (11, 26).

In a large population-based study among Norwegian adolescents mental distress (assessed by the Hopkins Symptom Checklist-10) was correlated with the presence of itch (27). Moreover, the severity of itch correlated with the level of mental distress, regardless of sex. Subsequently, another report linked the presence of itch with low self-efficacy in individuals under higher stress (28). The perceived self-efficacy is a concept of people's beliefs that they can exert control over their motivation, behaviour and social environment (29). Individuals lacking the sense of self-efficacy are not able to manage

demanding situations effectively, despite knowing what to do and possessing the necessary skills. The increase of self-efficacy in psychological interventions may exercise control over stressors due to its immunomodulating properties (30). Recently, Schut et al. (31) employed cognitive behavioural stress management programmes in patients with atopic dermatitis (AD). The study revealed that individuals subjected to these interventions demonstrated diminished cortisol awakening response, while maintaining calm and presenting lower salivary cortisol levels under acute stress. Thereby, various psychological interventions (reviewed in detail by Schut et al. (32)) should be considered as an adjunctive therapy in patients with itch of various origins. The associations between stress and itch in patients with AD constitute a problem of particular complexity and importance and involve the components of the so-called neuro-endocrino-immunocutaneous system (NEICS) and the hypothalamo-pituitary-adrenal (HPA axis). The relevant aspects of this issue are covered in detail elsewhere (33–38), although there is evidence that acute or chronic stress have different impacts on the HPA axis (39).

Regarding patients with psoriasis, our group has demonstrated that patients under heavy or extremely heavy stress more commonly suffer from itch, with the severity of stress and intensity of itch being positively correlated (40). Similar results were observed by Amatya et al. (7). Another study revealed that the self-reported stress reactivity was moderately correlated with the degree of itching (41). Stress-related exacerbation of itch in psoriatic subjects may also be associated with higher expression of substance P receptor, tropomyosin receptor kinase A and calcitonin gene-related peptide receptor in keratinocytes of psoriatic plaques (42). Other reports mentioned the role of stress in pruritic disorders, such as chronic urticaria (43, 44), acne vulgaris (45, 46), hand dermatoses (47) and post-burn itch (48). Recent research reported that patients with generalized CI reported more tension and subjective stress than healthy controls, with the expectation of the acute stress test (49). Notably, "variations of intensity associated with stress" (50) constitute an optional criterion for the diagnosis of functional itch disorder (FID; psychogenic itch).

Itch-stress associations are complex, yet they serve as the foundation of psychological interventions aimed at enhancing coping abilities of the affected individual, e.g. cognitive restructuring (32). A Dutch study reported that a nursing programme "Coping with itch" successfully targeted catastrophizing and helpless itch-related coping (51). Subsequently, it was proven by Evers et al. (52) that patients with AD may benefit from multidisciplinary itch-coping group training. The programme focused on skin care, itch-triggering factors, stress management, long-term goals, relapse prevention, habit reversal and scratch-triggering factors. The training ensued in reducing itch-scratch behaviour, improving skin status, decreasing the need for dermatological visits and treatment. Coping with itch was improved, as the itch-related self-efficacy increased, with decline in catastrophizing. These benefits were regarded both as short-term and long-term.

NOCEBO EFFECT: IS ITCH A CONTAGIOUS PHENOMENON?

The nocebo effect is the negative counterpart of the placebo effect (53). In essence, an individual receives an inert substance or undergoes a neutral procedure, which is intended to induce negative expectations. Interestingly, outbreaks of itch among schoolchildren attributed to epidemic hysteria have been described in the literature (54, 55). Acknowledging the relevant role of psyche in eliciting itch, the nocebo-related concept of "itch contagion" or "contagious itch" was conceived and investigated in different studies. Based on the experience that lectures about pruritic dermatoses induce itching in the listeners, Niemeier et al. (56) proved that a public lecture entitled "Itching – what's behind it?" caused the participants to feel itch and exert scratching behaviour. Subsequent research revealed that patients with AD, when compared with healthy controls, were more prone to scratch themselves after being subjected to histamine or saline injection, followed by watching a short video of people scratching (57). Holle et al. (58) reported that itch contagion is a normative response experienced by most people and its degree may be associated with neuroticism as a personality trait (the impact of personality traits on itch is reviewed below). No association between itch contagion and sex or empathy was established in this study. The fMRI examination revealed that itch intensity correlated with the activation of the left Brodmann area (BA) 44, primary somatosensory cortex and BA6. Lloyd et al. (59) revealed that solitary visual stimulants provoke itch in healthy individuals. Another study demonstrated that the combination of conditioning and verbal suggestion may result in relevant nocebo and placebo effects on itch in healthy individuals (60). It was subsequently proved that nocebo effects regarding the itch sensation may be minimized or reversed via conditioning with verbal suggestion (61). Recently, increased contagiousness of itch in children with autism spectrum disorder was demonstrated (62).

PSYCHOLOGY OF ITCH

The personality of an individual may be defined as a characteristic pattern of behaviours considered in the broad sense, also including thoughts, feelings and motivation (63). One of the most popular models used for the description of personality structure is The Big Five model, which encompasses 5 bipolar dimensions (extraversion, agreeableness, conscientiousness, neuroticism and open-

ness to experience) (64). The impact of personality traits on itch sensation was explored in several reports and supports the role of psychological interventions in aiding affected individuals. In a Swedish study (65) the persistence of post-burn itch was associated with lack of assertiveness, as assessed by the Swedish Universities Scales of Personality (SSP). Moreover, the Coping with Burns Questionnaire (CBQ) scores revealed that itch was more persistent among individuals who sought more instrumental and less emotional support. Patients with prurigo nodularis (PN) exhibited higher neuroticism and lower extraversion traits than controls when examined via the revised Eysenck Personality Questionnaire (EPQ-R) (66). Notably, among subjects with psoriasis, severe itch was significantly associated with somatic trait anxiety, embitterment, mistrust, and physical trait aggression (assessed via SSP) (67). Conversely, Janowski et al. (68) found no differences in basic personality traits regarding psoriatic patients with various frequency of itch (assessed via NEO-Five Factor Inventory; NEO-FFI). However, resignation and self-blame were more common coping strategies among patients experiencing itch more frequently (assessed via the Ways of Coping Questionnaire; WCQ). In a German study, individuals with AD and healthy controls were exposed to videos featuring crawling insects and skin disorders (69). Compared with healthy controls, agreeableness (NEO-FFI) and public self-consciousness (the Self-Consciousness Scale; SCS) were significant predictors of scratching behaviour in subjects with AD. These findings were subsequently replicated (70). Kini et al. (71) investigated patients with CI (recruited from the National Eczema Association and US Veterans Health Administration National Patient Care Database). The authors observed that the lethargic personality style (defined as low extraversion and conscientiousness) (NEO-FFI) was associated with greater mean total ItchyQoL score. On the other hand, higher ItchyQol symptom score was observed both in overcontrolled (high neuroticism and conscientiousness) and undercontrolled (high neuroticism and low conscientiousness) patients.

Another concept that has evolved as a potential paradigm for understanding the influence of emotions and personality on physical illness and health is alexithymia (72). In general, this personality construct defines the inability to identify and verbalize emotions. Our group has investigated alexithymia using the Bermond-Vorst Alexithymia Questionnaire (BVALQ-40) among patients with end-stage renal disease on maintenance haemodialysis (9). It was observed that patients with uraemic itch exhibited lower scores on the fantasizing subscale score. Another group assessed alexithymia via the Toronto Alexithymia Scale (TAS) among individuals with chronic urticaria (73).

PSYCHIATRIC PERSPECTIVE ON ITCH

Taking into account the widespread relationship between itch and psyche, one cannot omit the obvious psychiatric background of itch in certain cases, whereas the presence of itch may frequently ensue in a wide spectrum of psychiatric comorbidities. In a study by Mazeh et al. (74) among a cohort of patients ($n=111$) hospitalized in the psychiatric ward, CI affected 32%. Of those, 45% stated that stress was one of the major aggravating factors of itch. Similarly, our group enrolled inpatients ($n=40$) who were hospitalized with depression (75). Itching was experienced by 17.5% of patients during the depressive episode. Notably, itching disappeared in all affected individuals after the depressive symptoms markedly decreased, whereas recurrent itching was associated with recurrent depressive episodes.

A different approach was presented by Schneider et al. (76), who examined 109 dermatology inpatients with itch and observed that in over 70% of them 1–6 psychiatric diagnoses could be established. In over 60% of patients psychotherapeutic or psychiatric treatment was advised. Ferm et al. (77) evaluated the medical records of 139 patients with CI, among whom 31 (22.3%) had an underlying psychiatric disorder. A recent study among 560 patients with CI who were referred by the dermatologist for a psychosomatic consultation demonstrated that 77.1% had at least one psychosomatic/psychiatric comorbidity (78). The most common comorbidities encompassed psychological/psychosomatic cofactors in itch (F54 according to ICD-10) (74.5%), depression (F32–F34) (30.7%), adjustment disorder (F43.2) (17.8%), dissociative/somatoform disorder/hypochondria (F44–F45) (11.2%), anxiety/compulsive disorder (F40–F42) (6.6%) and others (17%). Notably, patients with the psychiatric/psychosomatic comorbidities presented higher intensity of itch, longer duration and coexistence of chronic scratch lesions. Dermatologists and psychiatrists often utilize psychoactive drugs in order to alleviate itch of different origins; however, itch may also be induced by the use of selective serotonin reuptake inhibitors or neuroleptics (79, 80).

There are also reports in the literature concerning "classic" pruritic disorders, which were also evaluated with regard to psychiatric comorbidities. Gupta et al. (81) linked alleviation of itch in psoriasis with changes in depression scores. Subsequently, Conrad et al. (43) executed a complex study of 41 patients with chronic idiopathic urticaria (CIU) and 44 patients with psoriasis. The investigators assessed the relationship between itch and several domains, including emotional distress and anger (assessed via the Symptom Checklist 90-R (SCL-90-R) and State Trait Anger eXpression Inventory (STAXI) tools, respectively). In patients with chronic

idiopathic urticaria (CIU) anger was a predictor of itch severity, whereas depression seemed to influence itch severity in patients with psoriasis. Regarding patients with CIU, the authors discussed possible pathway involving anger and stress, which stimulate corticotrophin-releasing hormone, subsequently leading to mast cell activation and degranulation of mediators, such as histamine. These aspects might, at least, partially account for the presence of itch accompanying urticarial wheals. In a study by Dazzi et al. (66) 20 subjects with PM were compared with healthy controls with regards to scores in EPQ-R, the Beck Depression Inventory second edition (BDI-II) and the State Trait Anxiety Inventory – form Y (STAI). It was observed that patients with PN exhibited higher scores for the T-anxiety scale (STAI – form y-2; describing how subject feel in general), depression and neuroticism, while lower than the controls concerning extraversion. Subsequently, PN was linked to depression (adjusted odds ratio (OR) 2.82; $p<0.001$), the use of antidepressants (adjusted OR 2,6; $p<0.001$), anxiety (adjusted OR 2.06; $p<0.05$) and the use of anxiolytics (adjusted OR 4.64; $p<0.001$) compared with healthy controls (82). Similar relations were reported in a recent study concerning PN burden with respect to depression and anxiety. In addition, patients with PN more often had suicidal ideation (83). In a previously mentioned study by Remröd et al. (67) ($n=101$) subjects with plaque psoriasis with severe itch presented higher scores for depression and anxiety (as assessed via STAI and BDI-II). A study among 27 patients with AD reported that there is a connection between high scores on the depression scale (Hospital Anxiety and Depression Scale; HADS-D) and higher increase in itch intensity compared with controls (69).

Interestingly, a study by Weisshaar et al. (84) recounted that affective reactions, such as depression and aggression, were more common in German individuals with CI due to dermatological diseases than those with CI associated with underlying systemic disorders ($p=0.04$ and $p=0.03$, respectively). A comparison between German and Ugandan patients with CI was also performed in terms of emotional reactions, revealing that German patients tend to be significantly more aggressive ($p<0.0001$) and more often do not have any drive ($p<0.0001$). In a cohort of patients with end-stage renal disease, the severity of CI (4IIQ) was correlated with depressive symptoms (assessed by BDI) (85). The complicated itch and psyche interplay is elegantly embraced in functional itch disorder (FID; also termed psychogenic itch). This entity was defined as "an itch disorder, where itch is at the centre of the symptomatology, and where psychological factors play an evident role in the triggering intensity, aggravation or persistence of the pruritus" (50, 86) and can be diagnosed according to several criteria. The 3 compulsory criteria encompass: (*i*) localized or generalized itch without primary skin lesions, (*ii*) chronic pruritus of at least 6 weeks' duration, and (*iii*) no somatic cause. In addition, at least 3 out of the following 7 additional criteria have to be found: (*i*) a chronological relationship of pruritus with 1 or several life events that could have psychological repercussions, (*ii*) variations in intensity associated with stress, (*iii*) nocturnal variations, (*iv*) predominance during rest or inaction, (*v*) associated psychological disorder, (*vi*) pruritus that could be improved by psychotropic drugs, and (*vii*) pruritus that could be improved by psychotherapies. Regarding the International Forum for the Study of Itch (IFSI) classification according to its aetiology, FID is associated with the 4th category (psychogenic/psychosomatic origin) (3). Unfortunately, the detailed aspects associated with psyche and well-being of patients with FID in particular have rarely been investigated (87, 88).

Finally, considerations concerning psychiatric associations with itch are nowhere near complete without mentioning the risk of suicide. In a study by Halvorsen et al. (89), 3,682 adolescents responded to a special questionnaire focusing on itch, pain and suicidal ideation. Severe itch was strongly associated with suicidal ideation (OR 3.0). Among the individuals reporting itch, suicidal ideation was reported by 21.1%, in contrast to 8.4% among subjects denying itching. In a large meta-analysis, patients with AD (in which itch is generally considered a constant feature) were 44% more likely to have suicidal ideation and 36% more likely to die by suicide that those without the disease (90).

HEALTH-RELATED QUALITY OF LIFE IMPAIRMENT: THE BURDEN OF SCRATCHING

QoL may be defined as a measure of the goodness of several life aspects, e.g. reactions to life occurrences, disposition, sense of life fulfilment and satisfaction, as well as satisfaction with work and personal relationships (91). Not infrequently, this term is confused with HRQoL, which has multiple definitions. One of the most relevant encompasses "how well a person functions in their life and his or her perceived well-being in physical, mental and social domains of health" (92). The impairment in HRQoL in dermatological patients can be measured with multiple tools, e.g. the Dermatology Life Quality Index (DLQI) (93) or Skindex (94). Impairment in HRQoL stems from various disease-related signs and symptoms, with a special emphasis on CI. Recently, an itch-specific instrument (ItchyQoL) for assessing HRQoL has been validated in several languages (95).

There is recent literature focusing on itch and HRQoL, both in cutaneous and primarily extracutaneous disorders. These issues were studied in detail in subjects with psoriasis. According to Yosipovitch et al. (96), itch bothered 84 (84%) patients, among whom 35% became more agitated, 24% became depressed, 30% had trouble concentrating, and 23% changed their eating habits.

Remarkably, two-thirds of the patients were bothered by difficulties falling asleep and night awakenings due to itch. Moreover, 40% of pruritic subjects reported decreased or non-existent sexual desire, whereas 35% reported decreased or non-existent sexual functions. Subsequently, our group found that HRQoL, assessed via the DLQI, was significantly decreased in patients with itch (6). In addition, the DLQI score correlated with itch intensity assessed via the 4-Item Itch Questionnaire (4IIQ) and visual analogue scale (VAS). The impact of itch on HRQoL in AD is well-documented (35, 97); it is imperative to acknowledge its detrimental influence on children's and their parents' sleep (98). In our study among patients with hidradenitis suppurativa (HS), itch was reported by 62.1% of patients (99). Its presence did not correlate with DLQI scores, whereas its intensity did. Other researchers proved impaired HRQoL in cutaneous T-cell lymphoma (100), dermatomyositis (101), systemic sclerosis (102) and itch following exposure to sulphur mustard (103). Notably, in a large cohort of dermatological outpatients ($n=3,485$), the presence of itching was associated with sexual dysfunction (assessed by the 9th question of the DLQI) (104).

The HRQoL issues associated with itch have also been investigated in relation to underlying systemic disorders. It was observed among German individuals that, compared with dermatological disorders, systemic disorders causing CI were more commonly associated with decreased HRQoL ($p=0.003$) (84). Nevertheless, various systemic conditions afflicting different organs have been associated with CI and impairment in HRQoL. A prominent example is CI due to end-stage renal disease. In a study by Weiss et al. (105), the authors evaluated 860 patients on haemodialysis, revealing that the point prevalence of CI was 25.2%, while the 12-month prevalence and lifetime prevalence were 27.2% and 35.2%, respectively. The SF-12 questionnaire was used to assess HRQoL, revealing that the physical component subscale was significantly more affected among those with CI ($p<0.05$). A subsequent study on the same cohort demonstrated that the mean severity of CI correlated with the total score of the ItchyQoL (106). The strongest correlation with the mean itch severity was observed with respect to the emotions subscale, followed by self-efficacy, functionality and symptoms. Our group has also evaluated CI in 200 patients with end-stage renal disease, among whom CI concerned 38% (85). Patients with uraemic pruritus had significantly lower quality of life according to the 36-item Short Form Health Survey (SF-36) (93.0 ± 20.4 vs. 99.6 ± 19.9 points, $p=0.03$). Among the SF-36 dimensions, general health perception was markedly worse among pruritic subjects ($p=0.0003$). In addition, we found significant negative correlations between the total SF-36 score and itch intensity. The debilitating impact of CI on QoL has also been investigated in other systemic conditions (chronic venous insufficiency (107), Sjogren's syndrome (108), primary sclerosing cholangitis (109), polycythemia vera (110) or HIV infection (111)), although detailed considerations are beyond the scope of this review.

THE SOCIAL WOUNDS: ITCH AND STIGMATIZATION

Stigmatization may be defined as an awareness of social disapproval, discrediting or devaluation, based on an attribute or physical mark and on social rejection (112). Unsurprisingly, stigmatization has been studied in the context of various cutaneous disorders, such as psoriasis, vitiligo, leprosy or acne, to name just a few (113). The role of itch and fatigue in experiencing stigmatization in patients with AD or psoriasis may be associated with higher levels of stress (114). In 1989 Ginsburg & Link (115) explored stigmatization in a cohort of 53 psoriatic subjects via an original questionnaire containing 33 questions focusing on 6 factors (anticipation of rejection, feelings of being flawed, sensitivity to the opinions of others, guilt and shame, positive attitudes, and secretiveness). Ninety-three percent of participants reported itch; it was observed that the extent of bleeding at the time of the study (followed by itching) were the strongest predictors of stigmatization. The possible explanation involves itch as an elicitor of scratching behaviour, which may ensue in bleeding. To the best of our knowledge, this was the first experimental study relating itch to stigmatization. In a study by Lu et al. (114) 131 outpatients with psoriasis and 139 outpatients with AD were evaluated by several tools, including the 6-Item Stigmatization Scale (6ISS) regarding the perceived stigmatization on a 4-point Likert scale. Subsequently, our group investigated the well-being of 102 patients with plaque-psoriasis, among whom itch affected 89.2% (6). The intensity of itch correlated significantly with the level of stigmatization assessed via the 6ISS, as well as the Feelings of Stigmatization Questionnaire. Regarding the latter, the domains "feeling of being flawed", "sensitivity to other attitudes" and "secretiveness" were mostly influenced. Another study among Arabic subjects with psoriasis ($n=108$) revealed that itching (present in 78.7%) predicted stigmatization according to the Feelings of Stigmatization Questionnaire, whereas the intensity of itching significantly correlated with stigmatization level assessed via the 6ISS (116).

CONCLUSION

Despite a constantly increasing volume of data, there are still many unresolved questions about the phenomenon of itch. The known associations between itch and psyche are bilateral and multidimensional, posing challenges for clinicians. Taking into account the abundance of both ex-

perimental and clinical findings, coupled with increasing experience and involving psychiatrists, psychologists and other specialists in the field, is the basis of the holistic approach to the patient. This is a sure recipe for better management of both skin and psyche, as they constitute an unusual union that lasts a lifetime.

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