The Essentials of Psychodermatology

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This book is dedicated to all those who encouraged and inspired me for writing this compendium on Psychodermatology. Hope the message has been conveyed. Thanks to Dr. Ferreira and Mr. Patel for their untiring efforts and help.
"Try not to become a man of success but rather to become a man of value." Albert Einstein

– Mohammad Jafferany

I dedicate this work to my masters, colleagues, and friends in psychodermatology, highlighting Dr. Jafferany, for the encouragement, shared work, and keen interest in this striking subspecialty within dermatology, and to all the patients I have the privilege to meet and help in psychodermatology, who everyday reinforce this my everlasting passion for the connection between the mind and the skin.

– Bárbara Roque Ferreira

Blessed is : Thankful for
A man born with wings: my loving family
A man given knowledge to fly: my inspiring mentors
A man with others to soar beside: my incredible friends

– Arsh Patel

Foreword

Psychodermatology is a boundary field between dermatology, psychiatry, and psychology. Although the societies grouping people interested in the bilateral relations between skin and psyche, like Association of Psychoneurocutaneous Medicine of North America (APMNA) or European Society for Dermatology and Psychiatry (ESDaP), do exist, the role of psychodermatology is still underestimated. It has been a neglected topic for many years. Therefore, there is a need for continuous education in various aspects of psychodermatology. In most countries, psychodermatology training is even not included in the program of dermatology residency. Dermatology is a specific branch of medicine where visibility of skin lesions plays a crucial role and may lead to severe psychiatric disturbances. Moreover, it is well known that stress may initiate and/or exacerbate many skin diseases, like atopic dermatitis or alopecia areata. Several psychiatric disturbances manifest with skin problems or conviction of having skin pathology. Almost every day we deal with so called "difficult patients." Are we adequately prepared to serve those patients? For me it is clear that at least basic knowledge of psychodermatology is of importance and great help in our daily clinical practice.

Taking all above into consideration I was delighted to hear of the project of the book entitled "Essentials of Psychodermatology." This book, prepared by interdisciplinary team of experts, will definitely fulfill the expectations of both dermatology and all other health providers dealing with psychocutaneous medicine. I am sure that we shall all benefit a lot from this project. This book helps to understand the complex of relations between skin and psyche and serves as a guide for physicians working with psychodermatology patients.

I would like to compliment the authors for the structure of the book. It is comprehensive, covers all important aspects of the field, beginning with psychoneuroendocrinoimmunology and principles of both dermatology and psychiatry, leading the reader through the current classification of psychodermatology, various clinical scenarios ending up with therapeutic modalities. I am pleased to see the chapter peculiarly dedicated to the assessments of patients with psychodermatologic conditions, including basic scales and questionnaires. The treatment section is of great value. It gives an overview of psychotropic agents as well as basics of psychotherapy.

I am sure that „Essentials of Psychodermatology" will be welcomed by all health providers dealing with patients with psychodermatologic disturbances with great enthusiasm. It fills the niche, might be of help for both beginners and more advances colleagues. As a dermatologist I am sure that this book contributes significantly to our idea of having so called "well-informed dermatologists in the field of psychodermatology." I do hope that this very practical in structure guide will stimulate colleagues to setup the liaison psychodermatology clinics, as nowadays the holistic approach to our patients is crucial to achieve the therapeutic success.

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Preface

The interaction of skin and psyche is severely underestimated. The impact of psychological factors on skin disease and skin disease–causing psychological disturbances (thereby affecting quality of life) are pivotal in the understanding and management of psychocutaneous disease. For proper understanding of psychodermatological disease, one must examine the patient holistically. The role of the biopsychosocial model in the predisposition, precipitating, perpetuating, protecting, and presenting of psychocutaneous disorder helps a lot in long-term management and compliance in treatment. Recent advances in psychoneuroimmunological basis of psychocutaneous disease have opened new vistas in treatment approaches and subsequently improved the quality of life in patients with psychocutaneous disease. One of the major difficulties is that patients and physicians minimize the role of stress or psychological factors associated with skin disease due to lack of knowledge or not knowing any community resources. At the same time, unfortunately, postgraduate training and residency/fellowship trainings are still not giving appropriate attention to this important subspecialty of dermatology, psychiatry, and psychology. There are only a few centers of psychodermatology in the USA. Association for Psychocutaneous Medicine of North America is the only professional organization in the USA that is devoted to the dissemination of knowledge about psychodermatology; it holds an annual meeting and dedicates one full session of the conference for medical students and residents. Due to the lack of training opportunities, educational activities, and a general gap of knowledge, we decided to write this handbook, particularly keeping in mind the needs of young physicians, students, residents, and fellows. We hope that this text will stimulate interest in young professionals about this exciting subspecialty of medicine. If we are able to generate a deeper understanding of skin and psyche connection, and the need for obtaining further training and education in this area, we will know we have been of use.

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Chapter 1
Introduction: Why to Study Psychodermatology and to Whom it May Concern

Introduction to Psychodermatology

Psychodermatology is a relatively recent field of dermatology, traditionally linked with the study of the mind-skin connection, with increasing research and whose clinical relevance and implementation have only spread more recently, during the past 23 years, and worldwide, even though its history is quite longer [1].

Actually, since ancient times, we may find reports concerning skin diseases, where a link with psychopathology and psychological stress was present. For instance, Hippocrates (*c*.469–370 BC) was a Greek physician who established medicine as a domain of study and practice that should be separated from religion, arguing that clinical symptoms should be analyzed through logical and rational mechanisms, instead of as a punishment from god [2, 3]. As stated by Hippocrates, "people call it divine because they do not understand it" [2]. This sentence could be linked, today, with a new meaning: to stablish a parallelism with what happens in psychodermatology, some patients present skin symptoms that are not visible and some physicians tend to devalue these complaints, telling them that they do not have a medical problem, while the core of the problem is, indeed, that these physicians do not understand it, like in the past, where medical problems were attributed to another reason, at that time, a punishment from god, due to lack of knowledge. This practice may reinforce the psychosocial burden of the skin symptoms that do not have objective clinical features, raising insecurity and the feeling that the patient will never see is problem solved [4].

Hippocrates was globally recognized as the father of modern medicine [2, 3]. Actually, he introduced the new concept of the human body as having different parts that were working together, also connected in the genesis of a medical problem [3]. Apart from the huge contribution of introducing the idea of medicine as a field with rational explanations, he also pointed out the subtleties of the physician-patient relationship [2]. Concerning dermatology, he has also documented some cases of

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psychodermatologic conditions, whose names were only documented more recently, the skin-picking syndromes, more precisely, respectively, trichotillomania and trichoteiromania: “We must note whether he plucks his hair or scratches” [3].

Some famous sentences which are still taken into account in modern medicine come also from Hippocrates and they reinforce the importance of an adequate knowledge to a better clinical practice, namely: “Do good or at least do not harm” and “Life is short but the art is long” [2]. They illustrate, also in psychodermatology, the importance of knowledge to correctly address and manage the subtleties of patients where psychosocial issues are still more closely linked with the skin symptoms or the disease.

Psychodermatology is the subspecialty of dermatology which includes the skin symptoms that may be linked with, result of or cause a psychiatric comorbidity or psychosocial issues. It is placed in the intersection of dermatology, psychiatry, psychology, neurosciences, sociology and aesthetics. Some skin diseases may have a significant impact on the body image, with subsequent stigmatization. Stigma is a process that has been largely studied by sociology and that was firstly introduced by Ervin Goffman, to describe a process by which the way others react can spoil the normal identity, leading to feelings of rejection, being flawed, guilt or shame [5, 6]. Furthermore, due to the lack of knowledge of common dermatoses by general population, patients with lesions of psoriasis localized on the hands seem to have more stigmatization probably because others could mistake their disease as contagious [6, 7]. Finally, some patients that look for many aesthetic procedures may present a primary psychopathology, a body dysmorphic disorder, and the aesthetic surgery often results in the aggravation of their symptoms [8].

Apart from the fields of dermatology, psychiatry and sociology, the study of psychodermatology may also concern basic sciences, since the understanding of the physiopathological mechanisms of the psychophysiological dermatoses, such as, alopecia areata or psoriasis, and psychogenic pruritus, requires a deep understanding of the interaction between the central nervous system and the skin, also including concepts of immunology and endocrinology [9, 10].

Why to Study Psychodermatology and to Whom it May Concern

Dermatology and General Medicine

It should be stressed that psychodermatology should not be only seen as a mere clinical and scientific subspecialty of dermatology with interest only here and in psychiatry. Indeed, patients suffering from psychodermatologic conditions are not only observed in the context of dermatology, psychiatry and psychology clinics, but they are also seen in the setting of a general medicine consultation as well as in the context of other consultations, such as, as exemplified above, in plastic or general

surgery (e.g.: patients with body dysmorphic disorder), gynaecology or urology (e.g.: patients with vulvodynia and penidynia or other cutaneous sensory disorders), infectiology or internal medicine (e.g.: patients that present a delusional infestation, and, then, that may want to do as many examinations as possible to find out "the parasite") and pediatrics (e.g.: trichotillomania in the differential diagnosis of alopecia in childhood, namely alopecia areata).

Taking all this into account, we might say that psychodermatology is not only a very important subspecialty of dermatology, that needs to be more recognized and studied by the general dermatologists, but, also, it should be seen as a subspecialty of medicine that, at least, should be recognized by the general practitioners, in order to properly identify the conditions and address them to specialists in psychodermatology. This is especially important if we remember that most of these patients may present deep impact on quality of life and in many domains of social life, work and relevant psychological issues [11]. It is not so rare that these patients can be lost in such a "hospital shopping", going to many specialists, to find out a solution to their suffering and distress, increasing, in a vicious circle, the psychosocial repercussion of their skin symptoms by realizing that any physician could actually understand them. Then, considering that general practitioners commonly see firstly most of these patients, and address them to different specialties, this topic of medicine really concerns them, so that they could really identify the different conditions to better decide when and to whom refer them.

The British Association of Dermatologists' working party report presented the results of a nationwide survey which documented that 3% of dermatology patients have a primary psychiatric disorder, 8% present secondary psychopathology due to concomitant skin disorders, 14% have a psychological condition exacerbating their dermatosis, 17% need psychological intervention to help with psychosocial issues secondary to a skin condition and 85% have indicated that the psychological aspects of the dermatosis were a major component [12]. Scientific studies in psychodermatology have increased worldwide, pointing out the clinical presentation of these conditions, the physiopathological mechanisms, the psychiatric comorbidities and the impact on quality of life. Through this relevant scientific work, that has been developed during the last years, the awareness of psychodermatologic conditions in the dermatology practice has increased, which has been represented by the interest in developing psychodermatology also in the clinical practice, with an increasing number of psychodermatology consultations and clinics worldwide [12, 13]. Even though, there is still a long way to go up to a really good recognition of the importance of psychodermatology by general dermatologists, as psychodermatologic conditions are still undervalued and undertreated by them [14, 15]. However, we might say that if there is not a very well recognition of these conditions by the general dermatologist, the problem is still more evident when we consider the other specialties of medicine to whom these patients may also be addressed or presented. Then, we intended to organize, in this book, the main concepts of psychodermatology, not only directed to the general dermatologist but also to all the physicians who may see these patients, in order to provide them updated and concise practical knowledge in this field to recognize and address these patients.

Medically Unexplained Dermatologic Symptoms, Illness and Disease

From the above mentioned, we might conclude that due to both a lack of interest and knowledge, psychosocial issues connected with the skin disease are not well recognized, but the problem is still more important when we discuss skin symptoms that do not have an objective explanation and objective features, traditionally called "medically unexplained dermatologic symptoms". Thus, the study of psychodermatology also teaches us as very interesting and relevant issue, that is that, even in dermatology, a specialty traditionally linked with what is "visible", directly seen or appreciated, by an accurate assessment of the skin, the "invisible" side of the skin conditions can also be very important and even more difficult to treat. It may be more difficult to treat, firstly, because it is not well recognized in the clinical practice, as there is a general stereotypical idea that, in dermatology, the skin symptoms should have an objective explanation and be diagnosed through the skin examination or immediately by other biological complementary examinations. There is a distinction between disease and illness, precisely to point out, respectively, the conditions which may have an objective explanation and/or clinical presentation, and the conditions that are not visible and/or that do not have objective physiopathological mechanisms or for which we do not know an objective explanation [4, 16, 17].

Psychodermatology teaches us, however, that, also in dermatology, some patients may present significant skin complaints that cannot be directly observed, examined or explained, and, even more tricky, neither all these patients could present an objective psychopathology behind. This latter point is also quite important to analyze and discuss. Actually, a superficial analysis of what may be psychodermatology and the psychodermatologic conditions can lead to the incorrect idea that these patients would be better managed by a psychiatrist and that this approach would be enough. However, as mentioned above, neither all the patients with a psychodermatologic condition may present a main mental disorder that can explain their symptoms. Actually, in the clinical practice, the poor recognition of psychodermatologic conditions can make the physicians overpsychologize these patients, which may really lead to psychosocial stress and secondary psychosocial comorbidities and truly contribute to worsen the skin symptoms, because psychological stress can worsen skin symptoms, namely pruritus, which has been demonstrated in studies of psychoneuroendocrinoimmunology [18]. To provide an example where a skin symptom cannot be directly explained by a psychopathology, some patients presenting pruritus without a primary dermatosis, that is, a skin disease that can lead to pruritus, such as atopic dermatitis, and without another organic cause for pruritus, such as a chronic kidney disease, may eventually present a condition named by "sensitive skin", where changes in the cutaneous free nerve endings could explain the condition [19]. Then, adequate knowledge in psychodermatology can help to recognize the large spectrum of the different psychodermatologic conditions, that some of them cannot have specific clinical features, cannot be objectively explained and do not present a main mental disorder behind, even though the patients may present psychopathology, explained by the result of the distress caused by the skin symptoms.

Psychiatry and Psychology

An adequate knowledge in psychodermatology is also needed by psychiatrists, who should also be better familiarized with general concepts of dermatology, applied to psychodermatology, including the recognition of primary dermatoses and secondary skin lesions, as well as the subtleties of the treatments of these patients, concerning the skin care and particularities of the psychotropics and other systemic treatments with interest in these conditions.

Moreover, since psychodermatology is also a topic with huge relevance in psychology, psychologists should also be taught about essentials in psychodermatology, particularly about the different conditions seen in psychodermatology and the basic dermatologic knowledge related to them. This would make them more aware of the subtleties of these patients and then more able to better understand what could actually be done for these patients, in terms of treatment, then helping them to better choose the adequate psychological intervention and psychotherapy, such as cognitive behavior therapy or psychodynamic psychotherapy, helping the patients to better cope with the condition and to better understand and deal with the psychosocial impact or background behind. Moreover, a dysfunctional mother-child relationship and its expression through the skin contact and the skin care, since birth, have been highlighted by psychoanalysts to understand the multidimensional components of psychodermatologic conditions not only in childhood but also later in life. Didier Anzieu, a French psychoanalyst, introduced the metaphor skin-ego to explain the process through which the child develops the ego, containing the psychic contents, and projects it on the surface of the body (the skin), which would be the core of the relationships, being, in the beginning, highly important the contact with the mother. This means that psychological conflicts could be expressed through skin symptoms, the basics of psychosomatics [20, 21].

Thereby, it is relevant to highlight that general knowledge in psychodermatology is also relevant in pediatrics, where the family dynamics should be considered and analyzed and, ideally, included in the management. Additionally, some conditions might be more prevalent in childhood and adolescence, such as, trichotillomania, but it should be remembered that a primary dermatosis must be excluded, since it can also coexist, being the psychological stress connected to the primary dermatosis the trigger to the onset of trichotillomania. This is the example of the presence of alopecia areata, where the psychosocial stress connected to it triggers the skin-picking behaviour [22, 23].

The impact of psychological stress on the skin and its role on the skin disease and illness have been discussed since early, in the beginning of psychodermatology as a recognized subspecialty. Herman Musaph, the father of psychodermatology, has collected several clinical examples to show, in his book, “Itching and Scratching: Psychodynamics in Dermatology”, the connection between the psychological background, the social and family context, and several skin illnesses and diseases, through psychoanalytic concepts [24]. For instance, we might find a psychosocial context of losses or deaths and then death anxiety or even a subconscious fear of death in patients with vitiligo, a skin condition where the skin melanocytes are lost.

Psychodynamics introduces deeper questions that illustrate how psychodermatology is also a topic that concerns philosophy, which is also easily understood since psychopathology, a cornerstone of psychodermatology, still remains in the boundary between neurosciences and philosophy [25].

Final Reflections: Philosophy and Psychodermatology

"Without consciousness, the mind-body problem would be much less interesting. With consciousness it seems hopeless. The most important and characteristic feature of conscious mental phenomena is very poorly understood." These words were written by Thomas Nagel in a very famous paper "What Is It Like to Be a Bat?", where he discusses the difficulties in completely understanding what is to be other individual, who also has a consciousness, what is to think what others think, what human mind really is [26].

Essential knowledge in psychodermatology can help to better and deeper analyze fundamental questions from the practical setting to the philosophical analysis. This may include topics, such as, the meaning of mind-body connection behind a clinical case and then the eventual parallelism of biological mechanisms and psychological contents, the meaning of the skin placed as a boundary between the inner and the external world, the meaning of each family and a relationship and, finally, what is the meaning of a pathological behavior and the skin symptoms that coexist and, then, what is the real meaning of meaning and why psychosomatics happens.

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Chapter 2
Skin and Psyche: Psychoneuroendocrinoimmunology

Introduction: Psychoneuroendocrinoimmunology, Stress and Skin

Psychoneuroendocrinoimmunology is a global field of research to organize the updated knowledge on psychological stress and mechanisms, neurosciences, endocrinology and immune system to present a deeper understanding of the human behavior and implications in morbidity and mortality [1]. The interpretation of the effects of psychological stress on disease and illness leads to one of the main difficulties, namely, to clearly define what kind of stress do we want to study and analyze. This means that we should consider both acute and chronic stress. Both acute and chronic stress may have impact on the development of disease and illness, involving neurological, hormonal and immune pathways. In 2018, a first rodent model was performed to study the impact of chronic stress on lifespan morbidity, objectively confirming the link between chronic stress and morbidity as well as between chronic stress and mortality [2].

In the setting of psychodermatology, there is a wide group of diseases that can be triggered or worsened by acute or chronic stress and they are called psychophysiological dermatoses. The effects of chronic stress can then be appreciated, in clinical practice, such as in patients with psoriasis, which may lead to secondary and longstanding anxiety and depression symptoms, that, in turn, may contribute to trigger or worsen psoriasis. The same line of thought could also be applied to other dermatoses, also thus called psychophysiological dermatoses, namely, urticaria or atopic dermatitis. Clinical examples of acute stress can also be observed as triggers of skin disease, with relevant clinical examples, such as a condition called Marie Antoinette syndrome or overnight graying phenomenon, that is a sudden whitening of the hair, concerning a kind of alopecia areata where pigmented hairs are mainly affected. Throughout history, we may find some interesting reports, of clinical cases that have, in common, the onset of the disease after an

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acute stress linked with troubled events of life. The most famous is that of Queen Marie Antoinette of France, whose hair would had turned white the night that preceded her death in the guillotine [3].

Nutrition, Gut and Psychoneuroendocrinoimmunology

Increasing evidence also supports the role of nutrition in mental health, including both cases of food insecurity and overnutrition [1]. Research in basic sciences supports a connection between inflammatory mechanisms and anxiety disorders, where interleukin (IL)-1 β, a pro-inflammatory cytokine, has a central role. In 2017, through a rodent model, Towers et al. [4] demonstrated that acute fasting can trigger interleukin-1 β resistance by inhibiting caspase-1 activity in the brain, being this particularly important in the prefrontal cortex, amygdala and hippocampus, where then a reduction in caspase-1 activity could lead to an improvement of the brain function and a reduction in anxiety [4]. In rodent models, the use of high fat diet is associated with anxiety and depression symptoms and a higher corticosterone response after experimental acute and chronic stress, with a dysfunction in the sympatho-adrenomedullary axis [5]. A high refined carbohydrate diet has also shown to be linked with the trigger of depressive and anxiety symptoms in rodent models after stress [6]. In the context of psychodermatology, the relevance of nutrition in the etiopathogenesis is well illustrated in psychophysiological dermatoses, such as, in acne vulgaris and psoriasis. Actually, a field of heated discussion in the etiopathogenesis of acne, a common inflammatory disorder of the pilosebaceous unit, is the connection with life style and diet. For example, there is no acne lesions in native people in Paraguay and Papua New Guinea, which raised the interest to look into the link between acne vulgaris and Western diet, particularly food with high glycemic load, leading to hyperinsulinaemia and high levels of insulin-like growth factor [7, 8]. Insulin-like growth factor can increase the activity of sebocytes, which, together with *Propionibacterium acnes*, trigger the release of inflammatory mediators in the perifollicular dermis, leading to the development of comedones and inflammatory lesions [7, 9]. In plaque psoriasis, a chronic, inflammatory and immune-mediated disease, a recent systematic review and meta-analysis also confirmed previous studies highlighting the connection with metabolic syndrome [10]. Recently, some studies have also pointed out that different dietary factors can contribute to modulate microRNAs, that are regulators of gene expression and transcription, modulating keratinocyte proliferation and inflammatory mechanisms in psoriasis. For instance, resveratrol can induce a reduction of the small regulatory RNA microRNA-21 (miR-21), which is highly expressed in keratinocytes and pro-inflammatory cells, decreasing the expression of IL-1 β and other pro-inflammatory cytokines, such as IL-6, IL-8 and tumor necrosis factor alpha (TNF-α) [11]. Resveratrol was also suggested to contribute to inhibit the mammalian target of rapamycin complex (mTORC) 1 in the pilosebaceous unit, which is overstimulated by Western diet, modulating hyperkeratinization and hyperplasia

and the function of the sebaceous gland, being these some of the biological mechanisms that are central in the etiopathogenesis of acne vulgaris [7, 12]. Interestingly, recent studies have also highlighted the role of mTORC1 in psoriasis, which highlights the sharing of etiopathogenic mechanisms by the psychophisiological dermatoses. Actually, in psoriasis, mTORC1 seems to be permanently activated, with a continuous proliferation of keratinocytes and a dysfunctional differentiation above the basal layer [13]. Thus, several etiopathogenic mechanisms are shared by psychophysiological dermatoses.

Moreover, some studies have also pointed out the role of vitamins in stress response, namely vitamins B1, B6, B9, B12 and vitamin D, whose deficiency seems to be linked with symptoms of anxiety and depression [1]. In the setting of psychodermatology, it is relevant to point out the link between B group vitamin deficiency and glossodynia, a multifactorial condition placed in the group of sensory cutaneous disorders, whose etiology is multifactorial and the etiopathogenesis is not fully understood, also including, for example, hormonal imbalance in perimenopausal women, leading to symptoms of anxiety and depression with psychosomatic presentation [14]. Furthermore, taking into account the relevance of the above mentioned vitamins in the context of anxiety and depression, we may also admit their role in the etiopathogenesis of other psychodermatologic conditions triggered by stress, involving anxiety disorders and depression, such as, skin-picking.

The understanding of psychoneuroendocrinoimmunology and its importance in the understanding of psychodermatologic illness and disease should remember the gut-brain-skin theory suggested by the dermatologists John Stokes and Donald Pillsbury. This theory includes the relationship among skin, stress and gut, introducing the concept of a disorder in the microbiota profile, with a reduction in *Lactobacilli* and *Bifidobacteria*. This has raised the discussion on the relevance of probiotics in psychodermatologic conditions, such as acne vulgaris [15]. Probiotics are live bacteria with health benefits when ingested, being called psychobiotics in the setting of having benefic effects on mental health. However, actually, as highlighted previously by other authors, the definition of psychobiotics should also consider any influence with a bacterially-mediated effect on the brain. In this line of thought, prebiotics, such as galacto-oligosaccharides and fructo-oligosaccharides, which are a source of nutrition for *Bifidobacteria* and *Lactobacilli*, also deserve to be included in the global name of psychobiotics [16]. The bacterial species that can be found in the human gut microbiome include, mostly, three phyla: Bacteroidetes *(Porphyromonas, Prevotella)*, Firmicutes *(Ruminococcus, Clostridium* and *Eubacteria)* and Actinobacteria *(Bifidobacterium)*. Other bacterial species are also present, but in a small quantity, namely, *Lactobacilli, Streptococci* and *Escherichia coli* [17]. The gut-brain connection includes, indeed, the enteric nervous system, the immune system and the endocrine system, being mediated by changes in the microbiome. Psychobiotics can induce the synthesis of short-chain fatty acids and they have an effect on the gut endocrine cells, inducing the production of gut hormones, and they all can migrate into the central nervous system. Additionally, probiotics and prebiotics can induce the production of neurotransmitters in the gut, namely, dopamine, noradrenaline, serotonin and γ-aminobutyric acid, with effects in the enteric nervous system, which,

through vagal connections, make possible the gut-brain connection [16]. In the setting of psychological stress, glucocorticoids will induce a dysfunction in the gut barrier, with a dysfunction in the microbiome and activation of pro-inflammatory mechanisms, involving an enhanced uptake of pro-inflammatory mediators from the lumen, a process where mast cells may play a pivotal role, after being activated by the corticotropin-releasing hormone (CRH) [18]. Psychobiotics can induce a decrease in the levels of glucocorticoids and pro-inflammatory mediators and induce the production of anti-inflammatory cytokines, then contributing to protect both the blood-brain barrier and the gut barrier and communicating with the brain also through central lymphatic vessels [16]. Thereby, as it was already documented in basic sciences research, long-term diet habits can also change gut microbiome [19].

Taking into account the mechanisms above explained, there is enough evidence to support the role of diet in mental health and, then, in psychoneuroendocrinoimmunology, to explain the etiopathogenesis of psychodermatologic disease and illness, supporting the ancient quote, by Hippocrates, who stated "*your diet should be your medicine, your medicine should be your diet"* [20].

Mast Cells, CRH-ACTH-Cortisol Axis, Sympathetic and Cholinergic Signaling

Psychological stress factors are processed in the paraventricular nucleus of hypothalamus, stimulating the production of corticotropin releasing hormone (CRH), and, then, the production and secretion of adrenocorticotropin (ACTH) in the anterior pituitary gland, which stimulates the production and the release of cortisol by the cortex of the adrenal glands. A dysfunction in this mechanism is linked with anxiety disorders and depression, especially the melancholic subtype of depression [21]. Indeed, this axis stimulates the secretion of IL-1 β, IL-6 and TNF-α, inducing or exacerbating symptoms of depression [22]. Interestingly, the overstimulation of the CRH-ACTH-Cortisol, with high levels of CRH, tends to normalize after adequate antidepressant treatment [23, 24].

Moreover, psychological stress can also trigger several chronic dermatoses, where a dysfunction in the central CRH-ACTH-Cortisol axis is also shared. The skin has a peripheral CRH-ACTH-Cortisol axis and increasing evidence supports its involvement in psychodermatologic disease and illness. The main important role of the skin concerns its role as a protection and a control in front of inner and external stressors, namely, chemical and physical insults and psychological stress, that might disturb the systemic and cutaneous homeostasis. CRH is present in the keratinocytes of the basal epidermis, in the outer root sheath and the matrix of anagen hair follicles. The link between psychological stress and skin symptoms was already documented in murine studies, such as the effect of sound stress, triggering premature catagen in hair follicles, where a significant increase in the number of activated mast cells was observed. Thus, the skin can promptly respond to both inner and external stressors [25].

Mast cells are, actually, very important in the understanding of the link among stress, CRH-ACTH-Cortisol axis and several psychodermatologic conditions. Actually, the production and secretion of CRH after psychological stress can induce the activation of mast cells, which can trigger premature catagen and then hair loss, which is very important in the understanding of the link between psychological stress and alopecia areata [25–27] Alopecia areata is an autoimmune kind of hair loss placed in the nonscarring group of alopecias. Epidemiologic studies have shown that there is a link between alopecia areata and recent psychosocial stressful life events or a childhood characterized by a social context with deep psychological impact, such as, the loss of a close relative or emotional abuse or neglect [28].

Furthermore, the importance of mast cells and their link with CRH and, then, with stress can also be illustrated in other psychodermatologic conditions, such as, in vitiligo, acne vulgaris and psoriasis. Vitiligo is a dermatosis characterized by the development of depigmented patches in the skin, as a result of a loss of melanocytes. Melanocytes present the corticotropin-releasing hormone receptor 1 (CRH-R1), which upregulates proopiomelanocortin (POMC) expression, a regulator of melanogenesis and pigmentation, as well as the production of ACTH [29, 30]. The expression of the CRH-POMC pathways in the skin presents similar aspects to the CRH-ACTH-Cortisol axis, having an important role in the skin pigmentation. Recent experimental studies have shown an increase in the expression of CRH and CRH-R1 in the skin of patients with vitiligo and a positive correlation between this higher expression and higher scores of psychological stress, which was observed not only in the lesional skin, but also in the skin that is not depigmented, pointing out the involvement of all the skin of these patients, even if at a subclinical level [29]. It should be highlighted that vitiligo, as well as other psychodermatologic dermatoses, namely, alopecia areata, psoriasis and acne vulgaris, have a multifactorial etiology, where, obviously, other factors might also be present, with a different relative importance, depending on the patient, stressing the relevance of an integrative approach. However, at least for some types of vitiligo, namely, follicular vitiligo, which presents an unusual preferential involvement of follicular melanocytes, mast cells seem to play a central role, closely linked with alopecia areata [31].

Looking at the example of acne vulgaris, it is well documented that sebaceous glands are involved in the peripheral CRH-ACTH-Cortisol axis, also explaining the link between psychological stress and the etiopathogenesis of this dermatosis. Actually, sebaceous glands have receptors for CRH as well as for other relevant mediators of stress pathways, namely, neuropeptide Y and calcitonin gene-related peptide (CGRP), which modulates the local lipid synthesis and the production of androgens [7, 32]. Furthermore, the stimulation of that axis by stress leads to a local increase of substance P, which stimulates comedogenesis by the sebaceous gland and high inflammatory responses involving mast cells [7, 33]. Additionally, CRH production triggered by psychological stress can also trigger the conversion of precursors of androgens into testosterone, contributing to the development of the dermatosis and also induces a slower wound healing process and repair of the active cutaneous lesions of acne [7].

In turn, in psoriasis, a papulosquamous and immune-mediated dermatosis, it was demonstrated, as well, that the plaques also have higher levels of stress-related neuropeptides, namely, the CGRP, the substance P and the nerve growth factor, which stimulate T cells, keratinocytes proliferation and mast cells activation, having these cells a central role in the evolution of the dermatosis [22]. Actually, although mast cells are traditionally recognized as central cells in allergic inflammation, their role seems to be much larger, also involving many skin conditions, such as, psoriasis, rosacea, atopic dermatitis, alopecia areata or urticaria. In the setting of rosacea, a chronic cutaneous disease characterized by erythema, telangiectasias, papules or pustules on the central face, there is a neurogenic inflammation, in which sensory nerves release inflammatory mediators that induce vasodilation, involving mast cells [34]. In the context of chronic spontaneous urticaria, where anxiety and depression are important comorbidities, mast cells are also pivotal, as a result of the activation of the CRH-ACTH-Cortisol axis by psychological stress. Besides, the evidence from experimental and clinical studies allow to defend their role in other psychophysiological dermatoses, such as psoriasis, vitiligo, alopecia areata or atopic dermatitis, where the presence of pruritus may be a symptom of mast cell activity, mast cell-sensory nerves communication and subsequent neurogenic inflammation, following CRH-ACTH-Cortisol activation by stress [35].

The classic histaminergic pruritus pathway, mostly mediated by histamine 1 (H1)-receptors on cutaneous sensory nerves, is well recognized. However, antihistamines seem to be poorly effective to control pruritus in chronic inflammatory dermatoses and this might be explained by other pruritus pathways, namely, involving the protease-activated receptor 2 (PAR-2). For example, PAR-2 + nerve fibers are found in higher levels in atopic dermatitis, where mast cells activation releases tryptase, activating PAR-2, which releases substance P and CGRP, with subsequent neurogenic inflammation. Besides, mast cells also show higher levels of IL-31, leading to pruritus [35, 36].

Additionally, in prurigo nodularis, a dermatosis characterized by several and symmetrically distributed pruritic papules and nodules, frequently excoriated and erosive, as a consequence of long-term scratching due to chronic pruritus, which can have different etiologies, there is also a higher number as well as a modified morphology of mast cells in the lesions. Antihistamines are also frequently ineffective to control pruritus in prurigo nodularis, reinforcing the relevance of other mediators secreted by mast cells, linked with stress-induced neurogenic skin inflammation, such as nerve growth factor, tryptase (and, subsequently, neuropeptides, especially substance P and CGRP, connected with neurogenic inflammation) and IL-31. The nerve growth factor stimulates and sensitizes the cutaneous nerve fibers and induces the proliferation and differentiation of keratinocytes, which can explain the neuronal and epidermal hyperplasia and chronic pruritus [37].

Finally, it should be also taken into account the role of the cholinergic and the sympathetic system in the pathophysiological mechanisms behind the stress-skin connection and then the psychophysiological dermatoses. Actually, psychological stress can also lead to the release of acetylcholine and the activation of its receptors, with implications in the function of cells involved in the immune pathways behind

the link between stress and skin, such as the lymphocytes and the dendritic cells, as it happens in atopic dermatitis [38]. There is an autocrine adrenergic and cholinergic interaction in the skin, involving intracellular and intercellular pathways, modulating the functioning of keratinocytes, melanocytes and lymphocytes, with implications in the mechanisms of dermatoses linked with the stress, such as psoriasis and atopic dermatitis [22, 39].

Final Reflections: Psychophysiological Dermatoses and Synchronization

In Fig. 2.1, the key elements involved in the connection between the mind and the skin and the physiopathology of the psychophysiological dermatoses are illustrated. Considering the multifaceted role of the hair and the skin, from the social interaction to the temperature control, we may defend the role of the skin and the hair in our synchronization with others, the environment and the world, where the psychophysiological dermatoses could represent a loss of this synchronization, as it was also previously defended for depression and related sleep disturbances [40].

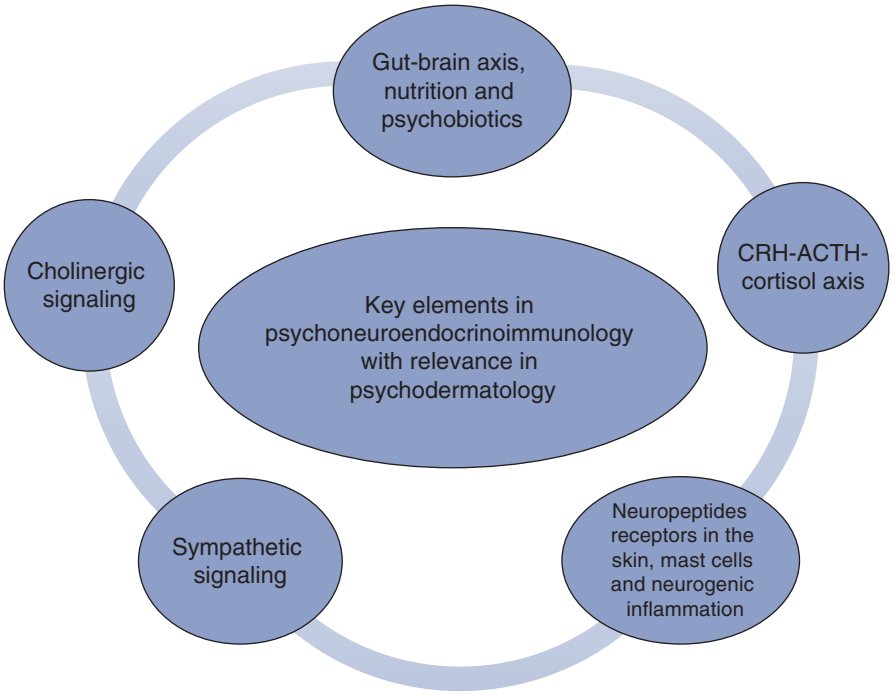

Fig. 2.1 Key elements involved in the connection between the mind and the skin and the physiopathology of the psychophysiological dermatoses, elaborated by Ferreira, Jafferany & Patel

All these conditions can be both induced and perpetuated by stress, involving the key role of the CRH-ACTH-Cortisol axis, the mast cells, but also other neurohormones, neuropeptides and their receptors in the skin and hair follicles, including, prolactin, thyrotropin, thyrotropin-releasing hormone, endocannabinoids, beta-endorphin, alpha-melanocyte stimulating hormone and melatonin [41].

Taking into account the idea of dysfunction or loss of synchronization behind psychophysiological dermatoses, in the same line of thought of depression, it seems to be particularly relevant to consider the role of melatonin. It is also interesting and relevant to point out that a greater activation of the sympathetic and the CRH-ACTH-cortisol axes are involved in the melatonin production in the setting of defense responses [42]. It is a derivative neurohormone of serotonin, produced in the pineal gland as well as in human skin and hair follicles, which plays a regulatory role in a wide range of physiological and behavioral processes, including the sleep-wake cycle, the seasonal adaptation, hormonal secretion, thermoregulation and reproduction. It also has antidepressant, neuroprotective, anti-inflammatory as well as antioxidant effects [43]. Hair follicle has a cycle that is regulated under the effect of melatonin, as it also happens in the brain, where it does neuroprotection and anti-inflammatory actions, together with sleep control. In hair follicle, melatonin affects the activity of mast cells, reducing their activity. Melatonin modulates tyrosinase and, then, melanogenesis and hair pigmentation, although the exact effect deserves further research, even though it represents a quite interesting topic in alopecia areata and vitiligo. Finally, through the activation of its receptors in mast cells, melatonin modulates T-cells function, with relevance in other psychophysiological dermatoses, such as, atopic dermatitis and psoriasis [44]. In these dermatoses, sleep disorders are also common comorbidities, suggesting and reinforcing the idea of a connection between psychophysiological dermatoses and a such a kind of desynchronization, concerning the self and the world, biological rhythms, psychosocial issues and relationships [22].

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Chapter 3
Basic Principles of Dermatology Applied to Psychodermatology

Introduction

Although this chapter intends to be a guide for the clinician that deals with patients presenting skin complaints linked with mental health issues, this should not replace the importance of the dermatological examination performed by the dermatologist.

Even though, as for general concepts of psychopathology, there are basic principles of dermatology that are important to conduct a correct approach in psychodermatology and that could be included in the approach performed by clinicians who deal with these patients, particularly, psychiatrists and general practitioners, but also by clinicians from other specialties, to whom this matter may also concern, as explained in Chap. 1. There are still few specialists in psychodermatology and specialized services in this subspecialty. Besides being still a relatively unrecognized subspecialty, there is a need to stablish bridges among the different domains of medicine which observe these patients. There is a need to educate in essentials of psychopathology applied to (psycho)dermatology and essentials of dermatology applied to psychiatry and psychology to better diagnose these patients and increase confidence and accuracy in their management [1]. As for dermatology, it includes basic knowledge concerning skin anatomy and correlated physiological mechanisms, to identify the main changes linked with the most common diseases in psychodermatology observed in the clinical practice. It also includes basic knowledge involving the correct description of the skin symptoms and the skin lesions, when present, to identify primary skin conditions and secondary skin lesions, which is of utmost importance to correctly diagnose and manage in psychodermatology.

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Essentials of Skin Anatomy and Related Physiopathology

The skin is a dynamic interface between our inner environment and the external world and it is the largest organ of the human body [2]. It has three layers, the epidermis (the superficial layer), the dermis and the hypodermis, below the dermis and which contains the adipose tissue [3]. The epidermis may present variation in the thickness depending on the site, ranging from less than 0.1 mm and 1 mm, respectively on the eyelids and the palms and soles [3, 4]. It is composed by the following layers (or strata), from the deepest one, which is attached to the dermis: stratum basale, stratum spinosum, stratum granulosum, stratum lucidum (this stratum is not always present) and stratum corneum [3]. The dermis can also vary in thickness, ranging from 1 mm and 4 mm, respectively, on the face and on the dorsal and lumbar region, and it is composed by the following layers: papillary layer (the most superficial) and the reticular layer [4]. Globally, the most important functions of the skin are: permeability barrier (related to the epidermis), protection against pathogens (related to the epidermis and the dermis), protection against chemicals, physical agents and ultraviolet radiation (related to the epidermis), thermoregulation (related to the epidermis, the dermis and the hypodermis), sensation (related to the epidermis, the dermis and the hypodermis), and skin repair after damage (related to the epidermis and the dermis). Furthermore, there is also a relevant psychosocial function connected with the physical appearance and, actually, changes in the epidermis, the dermis or the hypodermis can lead to significant impact on physical appearance [5].

Keratinocytes are the largest group of cells in the epidermis and they are differentiating cells that synthesize keratins [4, 5]. Several types of keratins can be found at different levels of the epidermis, some of them with relevance in psoriasis, an example of a dermatosis in the group of psychophysiological dermatoses (see classification explained in Chap. 5). Actually, keratins are the principal structural intermediate filament proteins in keratinocytes and keratins 6, 16 and 17 are hallmarks in psoriasis. In response to cutaneous "aggressors", there is an upregulation of these keratins, with subsequent hyperproliferation of keratinocytes and innate immunity activation, triggering the autoimmune activation of T lymphocytes, which are basic physiopathological mechanisms in psoriasis [6]. In the epidermis, there are also melanocytes, Langerhans cells and Merkel cells. The melanocytes are dendritic cells which synthesize melanin, with relevance in skin disorders of pigmentation, such as in vitiligo, another example of a psychophysiological dermatosis. Vitiligo is an autoimmune epidermal disorder where there is melanocytes destruction and, thus, skin depigmentation, as a result of increased oxidative-stress sensitivity and, then, activation of innate immunity and, later, a subtype of lymphocytes, the $CD8^+$ T cells [7].

The Langerhans cells are also dendritic cells and they constitute 3–4% of all epidermal cells [4], with a pivotal role in several immune mechanisms, with relevance in psychophysiological dermatoses, such as in atopic dermatitis and in psoriasis. In psoriasis, there is a preponderance of the interleukin (IL)-23/IL-17 axis and the cutaneous dendritic cells, including the epidermal Langerhans cells, but also, the bone marrow-derived dermal conventional dendritic cells, the plasmacytoid dendritic

cells and the inflammatory dendritic cells, are the main source of IL-12 and IL-23, as well as of α-interferon and tumor necrosis factor-α [8]. Recent studies have also documented that there are three types of antigen-presenting cells in the epidermis: apart from Langerhans cells, monocyte-derived Langerhans cell-like cells and inflammatory dendritic epidermal cells, also with relevance in inflammatory dermatoses, such as, atopic dermatitis and psoriasis [9].

Merkel cells are linked with fine touch [4]. In the skin, the largest part of free sensory nerves end in the dermis, but some of them are non-myelinated nerve endings that penetrate into the epidermis and can connect with Merkle cells [4, 5]. Globally, itch is a relevant aspect of several skin diseases and, briefly, it results from the stimulation of the free nerve endings close to the dermo-epidermal junction: the non-myelinated C fibers and the myelinated A fibers. The former are linked with subjective aspects of pain and itch, while the latter are connected with the physical aspects, including localization of the skin contact [10]. Increasing evidence supports that patients with symptoms of sensitive skin, a cutaneous hyperactivity linked with several environmental factors and a widely reported challenging diagnosis due to the presence of subjective symptoms and, frequently, absence of objective (visible) changes, may actually present an overactive cutaneous nervous system [11, 12]. This can result from the activation of sensorial proteins on keratinocytes and nerve endings [13], stressing the fact that sensitive skin should not be automatically connected with psychological factors and that neither all the skin disorders may present visible skin changes. Prurigo nodularis is another entity linked with changes in the cutaneous nervous system, characterized by chronic pruritus and symmetrically distributed hyperkeratotic nodules, that are frequently excoriated and which can be associated with a skin disease, a systemic condition, a neurologic disease or psychopathology, where a reduced intraepidermal nerve fiber density and higher levels of nerve growth factor and neuropeptides in the dermis were observed [14].

The epidermis has no blood vessels: they are present immediately above the hypodermis and in the papillary dermis [4, 5]. The dermis is an integrated system of connective tissue elements, also accommodating the cutaneous nerve system and vascular networks, skin appendages and also resident cells, namely, fibroblasts, macrophages, dendritic cells, mast cells and transient cells of the immune system [5]. In chronic spontaneous urticaria, which is a type of chronic urticaria that does not present an identified trigger [15], and which is another example of a psychophysiological dermatosis, there is an activation of mast cells. The pivotal role of these cells in psychophysiological dermatoses was discussed in Chap. 2. The activation of mast cells leads to a subsequent activation of proinflammatory mediators, consequently with vasodilation [15], clinically represented by erythematous plaques without secondary skin lesions. These plaques may present and elevated evanescent area linked with the dermal edema (wheal). These patients may also present a diffuse swelling (angioedema) resulting from the edema extending to the hypodermis. In the renowned book "Itching and Scratching", Musaph discusses how urticaria is a result of intensive vasodilation, similarly with what happens after striking the skin, suggesting that the psychological issues lead to the same vascular changes as they happen in the setting of a real beating [16]. Indeed, underlying psychopathology and psychological stress can precede the onset of the disease and worsen the symptoms [17].

The basic skin anatomy also includes epidermal appendages, namely: hair follicles, sebaceous glands, eccrine apparatus and apocrine glands. In the hair follicles, three phases are recognized: anagen (growing phase, involving 85% of the hairs), catagen (resting phase) and telogen (involuting phase). The hair follicle anatomy in the anagen phase includes: an opening to the external surface of the skin (the ostium), an intraepidermal part of the follicle (the acrotrichium), the infundibulum (between the sebaceous duct and the epidermis), the isthmus (between the insertion of arrector pili muscle to the insertion of the sebaceous gland) and the lower portion (including the dermal papilla, the matrix, the medulla of the hair, the cortex, the cuticle, the inner and the outer root sheath) [4]. In alopecia areata, a psychophysiological dermatosis involving an autoimmune process with a multifactorial etiology that leads to non-scarring hair loss, with one or more patches of baldness on the scalp, other areas of the body or even all the body hair, there is a lymphocytic infiltration around the lower portion of the hair follicle, a higher number of catagen hair follicles and a higher number of vellus hair (hair shaft measuring less than or equal to 0.03 mm in diameter), with a lower number of terminal hairs (hair shaft measuring more than 0.03 mm in diameter) [18, 19]. Acne vulgaris is the classic example of a psychophysiological dermatosis involving, in its physiopathology, the sebaceous glands, whose distribution is higher on the face, back and chest, being absent in the palms, the soles and the dorsal surface of feet. Recent studies have documented that stress response-related hormones, namely, corticotropin-releasing hormone and adrenocorticotropic hormone are expressed in these glands and modulate their activity [20]. Eccrine glands have a generalized distribution, even though with a higher concentration in the palms and the soles and their main function is thermoregulation. They are activated by thermal stimuli through the hypothalamic sweat center, but they are also activated by psychological stress, with the clinical example of primary cortical hyperhidrosis, where there is an excessive production of eccrine sweat triggered by emotional factors, typically with a bilateral presentation, in the axillary region, in the palms and in the soles. The apocrine glands have a more limited distribution, with a higher concentration in the axillary, inguinal and perianal region [21]. Hidradenitis suppurativa is a chronic immune-mediated and inflammatory dermatosis, of unclear etiology, characterized by nodules, abscesses, fistulas and scars in skin regions with apocrine glands, involving follicular obstruction, and which is associated with psychiatric comorbidities (commonly, anxiety and depression) and a deep impact on quality of life [22].

Essentials of Dermatology: Primary and Secondary Lesions and Distribution

The clinical history and the examination in dermatology should include the evaluation of several characteristics (Table 3.1), including the morphological description of the lesions, their palpation, their distribution, whether the lesions are asymptomatic or whether there is pruritus (a cutaneous sensation that leads to the need to

Table 3.1 Essentials of the dermatological approach

Basic aspects of clinical history and examination in Dermatology	Presence or absence of skin lesions
	Presence or absence of pruritus or another unpleasant cutaneous sensation
	Duration and frequency of the skin symptoms
	Impact on quality of life
	Factors that trigger the skin symptoms
	Factors that improve the skin symptoms
	Treatments performed for the present dermatological condition
	Medical and surgical history
	Current medication for other medical or surgical problems
	Pregnancy and breastfeeding
	Allergies
	Social context and occupation
	Family history of dermatological problems
	Review of systems
	Type of skin lesions (primary and secondary skin lesions)
	Distribution of the skin lesions
	Fitzpatrick skin phototype
	General aspects of the skin: color, temperature, xerosis, seborrhea, relevant changes of sweating, signs of photoaging
	Dermoscopic findings if dermoscopy recommended
	Dermatopathological characteristics if required
	Additional physical examination adapted to the clinical history, including, for example, lymph node palpation

scratch) or dysesthesia (a global term to mean other types of unpleasant cutaneous sensation, such as, tingling) and whether the skin symptoms present an acute, subacute or chronic evolution, whether there is a personal or family history of skin problems, the current and the past treatments that were performed [23–25]. From all, the morphological aspects of the skin lesions and their distribution are essential aspects as a starting point to guide a clinical examination in psychodermatology. They will allow to identify whether there is a skin disease (dermatosis) and whether there are accompanying symptoms, with relevance in psychodermatology, namely pruritus or another unpleasant cutaneous sensation. Thus, when the patient presents skin lesions, we may say that there is a dermatosis and, depending on the type of the lesions, it can be a primary or a secondary dermatosis. The patient may also present, at the same time, both primary and secondary lesions, more than one primary and/or secondary dermatosis. The patient can also present pruritus or dysesthesia without a dermatosis.

The classification of primary and secondary lesions presents some variations in different textbooks of reference in dermatology [23, 25]. To simplify, the primary lesions that are traditionally described are the following: macule, patch, papule, plaque, nodule, vesicle, bulla and pustule. The secondary lesions may include a

wide spectrum, being some of the most traditionally described: atrophy, scale, crust, erosion, excoriation, fissure, ulceration and lichenification [23]. The classification of primary lesions takes into account morphological aspects, including, the size of the lesions (more than 1 cm for macule, papule, pustule and vesicle, or less than 1 cm for patch, plaque, bulla and nodule), whether they are palpable (such as, the papule, plaque, nodule, vesicle, bulla and pustule) or whether they present a content (such as, a clear or hemorrhagic fluid in bulla or vesicles and a purulent content in pustules). Concerning the secondary lesions, the classification also considers morphological aspects, particularly palpable changes concerning the epidermis and/or the dermis, such as: epidermal thickening (acanthosis), in lichenification; thickening of the stratum corneum of the epidermis (hyperkeratosis), in scales; dried blood, pus our serous content, in crusts; and damage or loss of the epidermis, in excoriations, fissures and erosions, and of the epidermis and the dermis, such as, loss of the epidermis and dermis, in ulcers, and epidermal or dermal thinning, in atrophy. The secondary lesions can also involve isolated or simultaneous changes in the hypodermis, such as: ulcers may present a partial or complete loss of the dermis and, sometimes, also the hypodermis; it is also possible to have atrophy involving the hypodermis. It is important to point out, however, that the examples provided for primary and secondary lesions should be a guide that may pose, occasionally, some subtleties in the clinical approach. For example, in the setting of postinflammatory hyperpigmentation, it is observed a darkening of the skin, as a result of a reactive hypermelanosis, that is, a higher melanin content in the skin, resulting from a cutaneous inflammation, as it happens in the context of acne or eczema: these patients may then present hyperpigmented patches, thus, a primary skin lesion (a patch), but a clinical feature that does not correspond to the active dermatosis, but that corresponds to secondary lesions. Postinflammatory hyperpigmentation can also be observed after an external aggressor on the skin [26], such as, in the resolution phase of self-inflicted skin lesions. This emphasizes the general rule that medicine is an art where the clinical approach should follow adopted classifications, but that should permit to adapt to the subtleties of the clinical practice.

Furthermore, it is important to observe the distribution of the dermatosis: whether the lesions are localized or whether there is a generalized distribution and whether there is a specific pattern connected with the dermatosis, such as, the flexural areas in atopic dermatitis. In self-inflicted skin lesions, in general, the patient will only present secondary skin lesions, particularly, erosions and excoriations, frequently with a linear configuration, associated hemorrhagic crusts and, eventually, fissures and ulcers (Fig. 3.1). The lesions are only observed in the regions of the body that the hands can reach: for instance, in prurigo nodularis, it is typically observed the "butterfly sign", which means that the mid upper back is spared (Fig. 3.2) [23, 24].

Although pruritus is traditionally associated with some primary dermatoses, such as, atopic dermatitis, with simultaneously primary and secondary lesions (excoriations), it is also an important symptom in other psychophysiological

Fig. 3.1 A patient with self-inflicted skin lesions, presenting secondary skin lesions (erosions and ulcers)

Fig. 3.2 A patient with self-inflicted skin lesions, presenting secondary skin lesions, with excoriations and post-inflammatory hyperpigmentation, exhibiting the "butterfly sign"

dermatoses, such as in psoriasis, where it was for a long time undervalued [27, 28]. Pruritus is a characteristic of several dermatoses related to psychodermatology, also including vitiligo (Fig. 3.3), pointing out to the activity of the disease [27–29]. Generalized and localized pruritus with or without lesions of scratching may also have a psychological dimension [30]. Finally, it is possible to observe secondary lesions related to scratching (excoriations) without itch, as it happens, for example, in impulsive self-inflicted skin lesions [31].

Fig. 3.3 A patient with vitiligo, presenting typical primary skin lesions: depigmented patches

Final Reflections: Details Provided by the Dermatological Examination

In a distinguished book of psychodermatology, "Itching and Scratching", Musaph highlights the lack of accurate analysis of the subtleties linked with the dermatological examination, for a long time, in the literature, in the context of pruritus and self-inflicted skin lesions: "We learned that in literature strikingly little is written about people who are scratching without itching, about people who provoke itching." He also stresses interesting details, concerning pruritus and secondary skin lesions that are provoked by the patient: "the connection between scratching and itching has been taken for granted. This connection, however, does not always exist. It is quite possible to scratch oneself without itching; it may, for instance, be a sign of embarrassment; it is possible to have an itch without yielding to the impulse to scratch. Finally, itching may develop during scratching and for the purpose of scratching." [16]

The dermatological examination is an utmost important part of the clinical assessment in psychodermatology, to identify whether the patient presents skin symptoms linked with a primary dermatosis or relevant changes in the cutaneous barrier (such as, xerosis) or a skin illness (such as, vulvodynia). Patients with psychophysiological dermatoses present primary and secondary skin lesions specifically related to the dermatosis (such as, plaques covered with silvery scales in psoriasis) and, eventually, additional secondary skin lesions linked with itch (excoriations). Patients with cutaneous sensory disorders will not present skin lesions, but cutaneous unpleasant sensations. Finally, patients with a primary psychopathology focused on the skin will not present primary skin lesions, because they do not

present a primary skin disease, and they can, eventually, exhibit secondary skin lesions linked with scratching (such as, excoriations), as it happens in the setting of delusional infestation. However, before stablishing the diagnosis of a psychiatric origin for the skin symptoms, it is mandatory to "trust" in the patient: for instance, in the context of skin symptoms related to a presumed infestation, a detailed examination to rule out a real infestation (such as, pediculosis) should be conducted. All that is possible through an accurate dermatological examination.

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Chapter 4
Basic Principles of Psychopathology Applied to Psychodermatology

Introduction

A multitude of elements, originating both from the individual living with skin conditions to societal factors, impact the development of psychosocial distress and an overall reduction in quality of life. Although recognition of such factors as vital in the effective management of patients has lacked historically, there has been growing research and overall interest in examining the association. For example, currently, most clinical trials recognize the importance of quality of life ratings as an indicator of treatment outcome and as a factor that may be underlying the presence of psychiatric comorbidity within the dermatologic patient population [1].

In this chapter, psychopathologic associations of common psychocutaneous conditions are discussed. Increased attention and awareness of the psychosocial undertones of skin disease allows for the development of comprehensive, individualized management strategies and, ultimately, improved patient outcomes.

Psychopathologic Characteristics of the Dermatology Patient

Clinically, understanding the impact of dermatologic disease on social and professional functioning, quality of life, and the overall psychological well-being is vital in reducing psychiatric co-morbidity [2]. Two individuals with the same dermatologic condition may have completely distinct emotional reactions and psychosocial associations. Factors like personality styles, coping mechanisms, and existence of a social support network can alter an individual's perceptions and psychological presentation. Additionally, certain influencing factors like personal life experiences and/or current levels of stress can influence the development of psychocutaneous disease. For example, alopecia experienced post-pregnancy may elicit feelings of

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unattractiveness and depression, and, in-turn, impact the ability to interact with the newborn [3]. As such, it is important to provide an empathetic patient consolation to elicit personal narratives and assess the levels of distress, if any, currently exist.

Further, increased awareness and knowledge of how certain aspects of skin disorders can shed light on important psychodermatologic associations that may be contributing to disease specific psychopathology, is needed. In addition to characteristics like size, color, and physical morphology, the region of the lesion can determine reactions and coping mechanisms of the afflicted individual. For example, genital lesions can affect a person's sexual relationships, while lesions of the trunk and limbs can inhibit a person from visiting the pool or beach, and lesions of the face may cause overall reduced self-confidence and avoidance of social setting altogether. The degree of chronicity or age of onset may also impact the emotions and levels of stress a person with a dermatologic disease experiences. Congenitally acquired conditions, for example, have altered implications on psychosocial well-being when compared to someone that develops a visible lesion into adulthood. In a study exploring changes in coping and defense mechanisms with age, Diehl et al. found maladaptive mechanisms like doubt, displacement, and regression to decrease from adolescence to adulthood, and increase again during old age [4]. A wide-variety of patient characteristics contributing to the ability to self-manage a chronic, disfiguring diseases of the skin, and offer clinical clues for the presence of potential psychosocial comorbidity.

Psychopathology in Common Psychocutaneous Conditions

Psychosocial Aspects of Itch-Eliciting Diseases

Pruritus highlights this complex connection as it is often influenced by the psychological and emotional state of the patient. For example, it has been observed that an individual simply thinking about itching can lead to its actual manifestations [5]. The itch-scratch cycle demonstrates the psychological involvement in pruritus. During this vicious cycle, the itching sensation leads to an autonomic response of scratching, which provides temporary resolution of the uncomfortable sensation in chronic pruritus patients. Over time, this negative reinforcement leads to conditioned scratching often leading to feelings of helplessness, guilt, and loss of control [6]. Several models of itch have been developed and may be helpful in understanding the etiology and management of itch, as well as the role of psychosocial factors in the progression of pruritus (Table 4.1).

Substantial evidence exists regarding the psychiatric morbidity in patients with chronic pruritus. For example, in a study examining patients with chronic pruritus, Lee et al. report 70% with psychiatric co-morbidity and 21.1% with suicidal ideation [7]. The psychiatric conditions experienced by patients with chronic pruritus like anxiety and depression, in addition to factors like personality and stress, additionally may impact the onset and were perception of itch [8]. Sex may also play a

Table 4.1 Psychological perspectives in understanding itch

Model	Description
Psychoanalytical model	Sigmund Freud observed that during early development, the ego is rooted in the body, especially the skin, which is an important organ of communication, and that bodily sensations and experiences form the core around which the ego develops. The ego partly remains identified with the skin even as the person becomes an adult, and disturbance of the normally integrated state of the ego can result in symptoms focused on the skin
Biopsychosocial model	Postulates that factors like personality traits and stress may influence the release of itch mediators or activation of mast cells to influence the intensity of pruritus symptoms
5 P model	This model of case formulations consists of predisposing, precipitating, perpetuating, and protective factors, along with presenting problems. These factors influence the clinical evaluation and management of cutaneous issues exhibiting pruritus
4-perspectives model	An alternative to the biopsychosocial and 5 P models that includes of personality and behavior elements along with biologic contributions to gain a deeper insight into the nature an origin of a patient's skin symptoms. The use of the 4-perspectives model in practice provides a more concrete understanding of the unique factors impacting pruritus severity and quality of life in individuals to generate more personalized treatment plans

role in the perception of itch. For example, while exploring the sex specific differences in chronic pruritus severity and psychosocial symptoms, Stumpf et al. report significantly higher anxiety scores in woman compared to men [9]. Due to the complex nature and multifactorial etiology of chronic pruritus, successfully managing patients can be challenging. Further, because of the high prevalence and notable associations of factors like stress, anxiety, and depression in pruritus, it is recommended to conduct a comprehensive patient history to uncover potential psychosocial mediators. In addition to pharmacologic medication and topical ointments, psychological interventions may be beneficial for patients with chronic pruritus [10].

Atopic Dermatitis

It is not uncommon for patients diagnosed with AD to develop co-morbid psychiatric conditions like anxiety and depression. Researchers report that AD has detrimental effects on self-esteem, quality of life, performance in school and work, sleep, and the quality of personal relationships [11]. In addition, through the examination of physiologic markers in AD, investigators found immunologic factors to be significantly elevated in atopic dermatitis patients that were exposed to acute stress, compared to control [12]. This suggests that stress plays a role in the worsening of symptoms in patients with atopic dermatitis. Secondary psychiatric morbidity is also found to be high in patients with AD. In a systematic review by Rønnstad et al. researchers found a significant association between depression in adults and children with AD, anxiety in adults with AD, and suicidal ideation in adolescents and

adults with AD [13]. Moreover, the psychological states have been found to have a direct correlation with the perception and severity of pruritus in individuals with AD. Schut et al. report depression and public self-consciousness as a significant predictor of self-rated itch severity [14]. Another study [15] implementing mouse models to investigate neuronal adaptation in AD found specific disease related changes in the reward-related brain regions that mediate itch-related relief in addition to pro-depressant and anxiolytic behaviors. The chronic nature of AD may also be explained by specific psychosocial interactions. For example, Takaki et al. report psychological traits like anger suppression and depression in adults with AD have a negative impact on utilize coping skills needed to manage disease-related stress, which, in turn, may be contributing to the chronic nature of the condition [16].

Psoriasis

The chronic, visibly noticeable, and pruritic nature of psoriasis leads to a wide variety of psychosocial implications and an overall reduced quality of life. Patients with psoriasis often experience rejection, lack of self-confidence, shame, and isolation, which leads to psychosocial impairment such as social withdrawal [17]. Individuals with psoriasis also have an increased prevalence of psychiatric conditions such as generalized anxiety disorder and major depressive disorder. In a population based cohort study, Kurd et al. found significantly increased levels of depression, anxiety, and suicidal ideation in patients with psoriasis compared to control, with increased hazard ratios for younger patients and individuals with increased disease severity [18]. Furthermore, it has been noted that patients with psoriasis feel stigmatized from society and face social discrimination. In a study implementing a stigmatization scale and questionnaire, Hrehorów report the major contributing factors of stigmatization include anticipation of rejection along with feelings of shame and guilt, which were significantly correlated with pruritus severity and reduced quality of life [19].

Alopecia Areata

Many studies indicate a strong co-morbidity of psychiatric disorders in Alopecia areata (AA) patients. In a systematic review and meta-analysis, Okhovat et al. conclude a positive association with anxiety and depression in patients with AD, compared to control [20]. In another systematic review, Fricke et al. report AA is associated with medical and psychiatric (anxiety and depression) co-morbidity, multiple autoimmune conditions, and an overall increased disease-related global burden [21]. The psychosocial impact of AA may vary with patient characteristics. For example, woman may experience increased burden from the condition as society deems hair as a vital factor of fertility, family, and attractiveness [22]. Similarly,

socioeconomic status may contribute to the development of psychopathology as treatments for hair-loss are seen as a cosmetic concern by insurance companies, and therefore not covered [23]. Additional factors that have been associated with lower quality of life in patients with AA are age (<50) and the degree or amount of hair-loss [24].

Furthermore, psychosocial factors may be associated with the onset and worsening of AA. Compared to control, Brajac et al. found patients with AA had a significantly higher number of recent stressful life events, degree of anxiety, and perceived distress [25]. Although it is difficult to conclude stress as a direct cause of AA onset, stressful life events may play a role in the initiation and progression of AA.

Acne Vulgaris

The impact of acne on the mental health of afflicted individuals is dependent on a variety of factors including age, sex, personality, disease severity, and cultural background [26]. For example, in a study consisting of 255 individuals with acne, Lukaviciute et al. report 96.5% of included individuals experience a reduced quality of life, 38.4% reported anxiety, 23.1% had depressive thoughts, and 12.9% reported having suicidal thoughts. In another study examining such factors, Haroon et al. report an association exists between depression and lowered overall quality of life in patients with acne, that is particularly present in woman and adolescents. With regard to teens specifically, acne can have a profound impact on self-image and the presence of psychiatric co-morbidity. For example, in a questionnaire administered to 3775 adolescents, Dalgard et al. found significantly poor self-worth in females and poor self-attitude in males, after controlling for both body mass index and depression [27]. Similarly, a population-based survey found the severity of acne to have a significant association with the impact on quality of life, self esteem, body image, and relationships [28]. As body image shapes an individual's interpersonal relationships, emotions, behaviors, and thinking, its overall influence a patient's quality of life can be profound [29]. Thus, while managing individuals with acne, it is essential to identify and address suspected concerns with respect to body image, especially in teens and woman.

Urticaria and Angioedema

Studies have indicated increased prevalence of depression and anxiety in patients with urticaria and angioedema, however, concrete evidence of the role of psychogenic factors in chronic urticaria is lacking. Furthermore, beyond the noted psychosocial co-morbidity, psychophysiologic factors such as stress, depression, and anxiety are also thought to potentially play a role in the onset and maintenance of chronic urticaria [30]. Urticaria has further been noted to impact interpersonal

relationships among afflicted individuals. Ertas et al. report chronic spontaneous urticaria as having strong negative effects on the sexual functioning in females, which was associated with fatigue, reduced quality of life, anxiety, and depression [31]. As such, physicians are urged to address the mental health related patient concerns, along with the physical disease associated symptoms [32].

Vitiligo

Although vitiligo is commonly referred to as a cosmetic concern due to the lack of symptoms, the condition frequently results in pronounced psychosocial implications. Particularly, the chronic skin condition is noted to result in feelings of stigmatization, notable psychiatric morbidity, and negative implications on interpersonal relationships [33]. Salman et al. additionally report significantly higher levels of social anxiety, depression, and generalized anxiety in vitiligo patients compared to controls [34]. Furthermore, individual characteristics of afflicted patients can determine the degree of psychosocial impact. Bidaki et al. offer insights while finding that, within the dermatology patient population at large, woman, unmarried individuals, and patients with face and neck lesions, experience lower social acceptance [35]. It is also important to highlight the visible nature and significant psychosocial associations of vitiligo in individuals with darker skin tones [36]. Due to the autoimmune mediated depigmentation resulting in white patches, vitiligo is more noticeable in patients with skin of color, resulting in greater risk for psychosocial morbidly [37].

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Chapter 5
Classification and Terminology of Psychodermatologic Disorders

Introduction to the Relevance of Adequate Classification and Terminology

Adequate classification and terminology are the cornerstone to organize the scientific knowledge regardless the field of study. Actually, this is the way researchers have to objectively show the body of evidence concerning their field of expertise, avoiding to create such a confusing manner to look into the questions of study and to present them, using the same scientific language, to the scientific world and the general public. Obviously, the way to present the ideas should be adapted to the kind of public, but, before, it is absolutely important to clarify which term should be used in each context and, thereafter, how to organize these terms through a classification so that it could be helpful to guide both further research in medicine and the clinical practice, that is, the way to approach the patients and to put the diagnoses [1].

In psychodermatology, there is no single globally adopted terminology and classification and, still more difficult, several conditions can actually share particularities of different categories. For example, chronic dermatoses, such as psoriasis, a chronic inflammatory papulosquamous dermatosis, can be included in the group of skin conditions triggered and worsened by stress (psychophysiological conditions) but also, due to the impact of the skin lesions on body image, psoriasis can also be included in the group of skin conditions with important secondary psychosocial comorbidities [2]. This highlights the relevance of adequate knowledge of each skin disease or illness to properly organize the needs of approach for each patient, which becomes still more challenging when different terms for the same conditions are used in the scientific world in psychodermatology, since the beginning of the history of this subspecialty. There are several examples of psychodermatologic conditions to whom different terms are used concerning the same condition. To provide some examples, factitious disorders, dermatitis artefacta and pathomimicry are frequently used in such an indistinctly way, when, actually, factitious disorder and dermatitis

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artefacta represent the same condition, while pathomimicry concerns a kind of factitious disorder; another example is psychogenic excoriation and neurotic excoriation, that represent the same condition, and both are still mentioned in the literature. Taking into account this problem of classification and terminology in psychodermatology, making this discipline more difficult to approach by dermatologists, psychiatrists and general practitioners who are not well trained, in 2013, the European Society for Dermatology and Psychiatry (ESDaP) wrote a paper to uniform the concepts, a subject of utmost importance, considering the relevance, in psychodermatology, to have organized knowledge of general concepts of psychiatry and dermatology applied to this discipline [3]. An objective and uniformed terminology, and classification, facilitates the communication among dermatologists, psychiatrists, psychologists and also general practitioners, undoubtedly improving the clinical practice [4]. Finally, this makes possible a better understanding of the illness by the patients, avoiding to spread the incorrect notion that there is no diagnosis or that everything is quite subjective to provide a concrete explanation for the condition, as it sometimes happens while using the terms "medically unexplained dermatologic symptoms", contributing to overpsychologise skin symptoms, worsening the psychosocial impact of the condition and incorrectly spreading the idea that there is a lack of objective knowledge in psychodermatology [5].

How to Classify and to Use Adequate Terminology in Psychodermatology?

In psychodermatology, there is not a worldwide accepted and globally used classification that includes all the psychodermatologic diseases and illnesses. Thereby, we suggest, here, a classification of the main groups of psychodermatologic conditions (Fig. 5.1), considering all that has been published on this matter, and we also present a list of some examples of dermatoses and psychiatric diagnoses that could be included in each group (Fig. 5.2) [5, 6]. We also expose some of the most important classifications that have been suggested to guide common diagnoses in the general clinical practice in psychodermatology, namely, the classification of self-inflicted skin lesions suggested by the ESDaP (Table 5.1) [3], the classification of skin-picking syndromes proposed by the Diagnostic and Statistical Manual of Mental Disorders, fifth edition, (DSM-5) (Table 5.2) [8, 9], and the criteria to diagnose psychogenic pruritus, suggested by the French psychodermatology group (Table 5.3) [10], and we discuss details concerning the terminology that should be preferred. Psychodermatologic conditions can be included in one or more of four groups [6, 7].

The first group of classification, one of the most challenging to manage, would include conditions that result from a primary psychopathology focused on the skin and these patients will not always present skin lesions and, when they present skin lesions, they are always secondary skin lesions, such as, excoriations, ulcers or erosions. A case of a condition that exhibits primary psychopathology focused on the

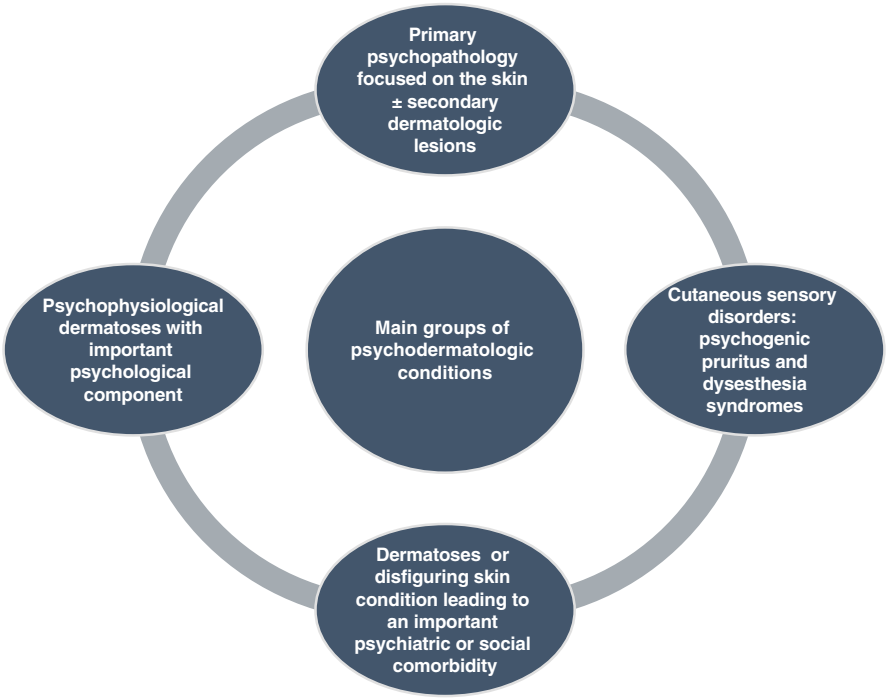

Fig. 5.1 Classification in psychodermatology: four main groups, elaborated by Ferreira, Jafferany & Patel

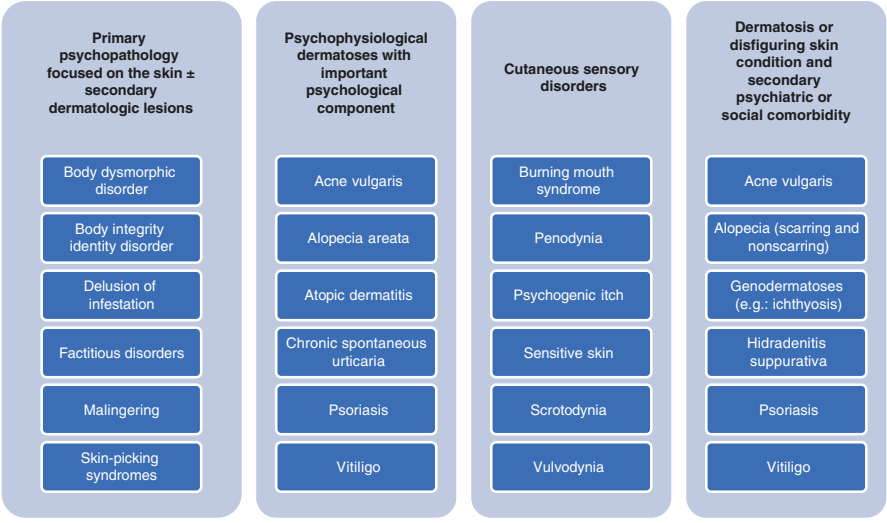

Fig. 5.2 Classification in psychodermatology: examples of conditions included in each group, elaborated by Ferreira, Jafferany & Patel

Table 5.1 Classification of self-inflicted skin lesions by the European Society of Dermatology and Psychiatry

Self-inflicted skin lesions	
"Secret" self-inflicted skin lesions: Factitious disorders Malingering	**"Non-denied" self-inflicted skin lesions (skin-picking syndromes):** Impulsive spectrum Obsessive-compulsive spectrum

Table 5.2 Definition and classification of skin-picking proposed by the Diagnostic and Statistical Manual of Mental Disorders, fifth edition

Excoriation (skin-picking) disorder - classification from the diagnostic and statistical manual of mental disorders, fifth edition (DSM-5) **Included in the group:** *Obsessive-Compulsive and Related Disorders*	Recurrent skin-picking, resulting in skin lesions;
	Repeated attempts to decrease or stop skin picking;
	The skin picking causes clinically significant distress or impairment in social, occupational, or other important areas of functioning;
	The skin picking is not attributable to the physiological effects of a substance (e.g. cocaine) or another medical condition (e.g. scabies);
	The skin picking is not better explained by symptoms of another mental disorder (e.g. delusions or tactile hallucinations in a psychotic disorder, attempts to improve a perceived defect or flaw in body dysmorphic disorder, stereotypies in stereotypic movement disorder, or intention to harm oneself in nonsuicidal self-injury)

Table 5.3 Diagnostic criteria for psychogenic pruritus proposed by the French Psychodermatology Group

Three compulsory criteria:
Localized or generalized pruritus sine material (without primary skin lesion)
Chronic pruritus (>6 weeks)
No somatic cause
Three of seven optional criteria:
A chronological relationship between the occurrence of pruritus and one or several life events that could have psychological repercussions
Variations in intensity associated with stress
Nycthemeral variations
Predominance during rest or inaction
Associated psychological disorder
Pruritus that could be improved by psychotropic drugs
Pruritus that could be improved by psychotherapies

skin without secondary skin lesions is, for instance, that of patients that complain about some defects of their skin that do not correspond to any particular skin disease or that are too discrete to be clinically valorized. They may present an unrealistic and excessive preoccupation concerning absent or subtle skin changes or the shape of parts of the body [11, 12]. These patients may have, however, more or less insight

concerning their illness: some of the patients will accept and recognize that they have a psychopathology while others have a fixed and an unshakeable belief that they have a disease or a real deformity [12]. Terms such as dermatologic hypochondriasis and dysmorphophobia have been used to mean the same condition that, today, is more globally accepted to be called body dysmorphic disorder [11]. Another example of patients with a psychodermatologic condition that result from a primary psychopathology focused on the skin without skin lesions can be the case of delusion of parasitosis or Morgellons disease, even though some of these patients may also present secondary skin lesions, such as erosions and ulcers, as a result of trying to eliminate the "bugs in the skin" [13] or other strange material that has infested their skin, respectively, delusion of parasitosis, also called Ekbom syndrome [13], and Morgellons disease [14]. Ekbom syndrome and Morgellons disease represent, actually, a same condition, a delusional disorder, deserving the same medical approach, and then, to uniform the terminology, they could be more properly called "delusional infestation" [15]. In the group of conditions that result from a primary psychopathology focused on the skin, we also have another important subgroup, the self-inflicted skin lesions. According to the classification proposed by the ESDaP, they can be divided in "secret" self-inflicted skin lesions, where the patient will deny that he or she has provoked the lesions, and, here, we may find factitious disorders and malingering [3]. The former is related to an unknown motivation, frequently linked with losses, a difficult psychosocial background and context or a troubled childhood, being the lesions a way of "crying for help", while the latter is related to a known motivation, frequently with objective and clear external incentives, frequently, financial incentives [3, 16, 17]. In factitious disorders, the motivation is then always unknown by the patient, even though the mechanism of provoking the lesions may be conscious or unconscious (in this case, within a dissociative spectrum) [17]. Münchausen's syndrome is a kind of factitious disorder where the patients should present, at the same time, pseudologia fantastica (a pathologic lying, with description of unreal experiences and histories with fantasy, remembering the histories from Karl Friedrich von Münchausen (1720–1797)) and hospital shopping (the patient will circulate among different hospitals and doctors due to the provoked and denied skin symptoms) [3]. Pathomimicry is a kind of factitious disorder that mimics a well-known dermatosis, such as, a pyoderma gangrenosum, a neutrophilic dermatosis where the patients may develop painful ulcers [18]. Another condition that is still more rare is the body integrity identity disorder and can also coexist with a factitious disorder, and worsen the prognosis. Body integrity identity disorder is a disturbance of body schema and the self, that is not classified in DSM-5, leading to a deep desire to eliminate parts of the body or the skin, as a result of a conflict of self-identification [18, 19]. Finally, in the first group, there is also the very important subgroup of skin-picking disorders, where the classifications are also sometimes dubious and poorly uniformed. Skin-picking disorders are a group of self-inflicted skin lesions that are not denied by the patients [3]. The DSM-5 presents the skin-picking disorder as an independent diagnosis and proposes that skin-picking syndromes are globally within the obsessive-compulsive spectrum, including five additional criteria (Table 5.2) [8, 9,

20]. In turn, the classification suggested by ESDaP divides skin-picking syndromes in two groups of underlying psychopathologies, the obsessive-compulsive spectrum (such as, *acne excoriée* or trichotillomania) and the impulsive spectrum (such as, cutting or scarifications) [3]. Actually, in the clinical practice, we may observe that skin-picking syndromes may actually exhibit impulsive spectrum in the background and, furthermore, some conditions may, actually, overlap, such as, trichotillomania, a kind of self-induced hair loss, that can affect different parts of the body and that, according to the DSM-5, should fulfill the following criteria: recurrent pulling out of one's hair, resulting in hair loss; repeated attempts to decrease or stop hair pulling; the hair pulling cannot be better explained by the symptoms of another mental disorder; the hair pulling or hair loss cannot be attributed to another medical condition (e.g., a dermatological condition) [8, 21]. Other examples of skin-picking syndromes are trichotemnomania (haircutting, frequently in the obsessive-compulsive spectrum), trichoteiromania (rubbing and scratching the scalp, also frequently in the obsessive-compulsive spectrum), scratching or picking the skin, compulsive licking and onychophagia (that is, nail biting, also frequently in the obsessive-compulsive spectrum) [3, 22].

The second group of psychodermatologic conditions is that of psychophysiological dermatoses, concerning skin diseases that are triggered or worsened by stress, with underlying changes involving neuroendocrine-immunological mechanisms, as it happens, for example, in psoriasis [23, 24]. The biological mechanisms concerning psychoneuroendocrinoimmunology were addressed in Chap. 2.

The third group concerns the cutaneous sensory disorders, which include unpleasant sensations of the skin that may or may not elicit the desire to scratch, including not only itching, but also dysesthesia, here included symptoms like stinging, tingling, burning, allodynia or numbness. These patients will not present a primary dermatosis and, depending on the kind of sensation described, they may or may not present secondary dermatologic lesions [25]. For example, itching is strongly correlated with scratching, but pain, allodynia, numbness, tingling may be devoid of secondary dermatologic lesions. It should be remembered that, in this setting, a diagnosis of small-fiber neuropathy should be considered [26, 27]. Sensitive skin is a relatively new concept, related to a hyper-reactive skin, leading to erythema or skin symptoms without visible cutaneous manifestations, such as burning, itching or pricking, that are triggered by a wide spectrum of factors, such as, environmental changes, psychological factors or even after the application of cosmetics on the skin, with increasing evidence supporting that it can also result from a small-fiber neuropathy [27, 28]. Another important topic in the group of cutaneous sensory disorder is that idiopathic pruritus and psychogenic pruritus are not the same. Psychogenic pruritus, as well idiopathic pruritus, is a subtype of pruritus where the work-up is negative for systemic etiologies of pruritus, such as, metabolic, hepatobiliary, paraneoplastic, hematologic and infectious diseases, but, additionally, there are specific criteria in the field of psychiatry and psychology, as proposed by the French group of psychodermatology (Table 5.3) [10, 28, 29]. As well other subtypes of pruritus, psychogenic pruritus can be generalized or localized, and, in this last case, scalp psychogenic pruritus seems to be more frequent among other areas of

the body. It seems to be more common in adult women, there is not a primary dermatosis, but secondary lesions can be observed, such as, excoriations. It is, however, of utmost importance to remember that scalp itch without primary skin lesions can also be related to a systemic disease or a neuropathic etiology [30]. Finally, in this group, other dysesthesia syndromes are relatively frequent in the clinical practice, namely, burning mouth syndrome and vulvodynia, where psychosocial factors can also be related to these conditions, in a vicious circle [31, 32].

The last group of classification includes dermatoses and other disfiguring skin conditions with impact on body image, with psychosocial repercussion, such as chronic skin diseases, particularly with lesions on visible parts of the body [33–35].

Final Reflections: Classification and Its Subtleties and Difficulties

The scientific literature in psychodermatology still needs to follow a long way to uniform the terminology and the classification that are used. Even recent scientific papers still continue to use ancient terms and different classifications. There is a need to reinforce and implement strict criteria in this matter, in the scientific journals, as this may have substantial implication in clinical practice.

As exposed in this chapter, psychodermatology is a multifaceted subspecialty and, thus, these patients may be seen not only by dermatologists and psychiatrists, but also by other specialties and general practitioners, which reinforces the importance of standardized terminology and the relevance of elaborating a concise and practical classification, as summarized in this chapter.

Nevertheless, although, undoubtedly, a very important tool in psychodermatology, a standardized and uniform system of classification of disease and illness may also raise some subtleties and difficulties when it is applied in such a rigid manner in clinical practice. On the one hand, a same psychodermatologic disease can be included in two different groups, deserving a more complex approach. For example, psoriasis is a psychophysiological dermatosis but also a disease with secondary psychosocial repercussions. On the other hand, although some conditions traditionally belong to a specific psychopathology, an overlap can be observed in clinical practice, stressing that the boundaries in psychopathology are not strict, with implications in the management, such as the thin line between obsession and delusion [36, 37]. For instance, in psychodermatology, it can be observed in patients with a delusion of infestation that can also exhibit obsessive symptoms at the same time or before the development of the delusion. Another interesting example is that of factitious disorders with a dissociative component, where obsessive symptoms can also coexist or be present before the development of the dissociative behavior. Furthermore, in the setting of factitious disorders, it should be remembered the differential diagnosis with body identity integrity disorder, a relatively unknown diagnosis and of especially difficult management [19].

Finally, special attention should be given to avoid vague terms, such as medically unexplained symptoms, as the absence of visible symptoms in dermatology does not mean that the condition has a psychological origin, even though psychiatric comorbidities can be present.

The absence of adequate medical knowledge in terminology and classification in psychodermatology may contribute to improperly label patients, making them feel frustration and hopelessness, increasing the probability to develop secondary psychiatric comorbidities, such as, depression. In the past few years, increasing research in psychodermatology has shown that "invisible" skin symptoms may also be a result of objective biological mechanisms, which is a new era in dermatology and psychodermatology. It highlights that visible and invisible skin symptoms can share mechanisms with the brain physiology and can be linked with the human mind, which is not the same that the skin symptoms absolutely come from our "head", a concept that should be remembered and applied in clinical practice [5, 38].

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Chapter 6
Screening Questionnaires, Scales and Approach to Patients with Psychodermatologic Disorders

Introduction to the Relevance of Questionnaires in Dermatology

As quoted by the physicist Lord Kelvin, in the nineteenth century, "to measure is to know" and "when you can measure what you are speaking about, and can express it in numbers, you know something about it" [1]. This concept is of unquestionable importance in medicine, both in the field of research and in the clinical practice. Moreover, in psychodermatology, characterized by the relative subjectivity of the description of the mental processes and the psychopathology connected with the skin symptoms, screening tools help to guide the objective description of the mental health impairment and the impact on the quality of life in clinical practice and research.

For example, concerning the usefulness of screening questionnaires and scales in research, in psychodermatology, a multicenter study conducted in Columbia, in 2017 [2], to assess the impact of dermatoses, using the Skindex-29 score, a score that was conceived to assess the impact on quality of life [3], documented that psoriasis, contact dermatitis, atopic dermatitis, urticaria, hair disorders, Hansen's disease, scars, hyperhidrosis and genital human papillomavirus were the skin disorders that presented the highest impact. However, interestingly, subtle and asymptomatic skin lesions also showed a significant impact on quality of life, stressing the importance of psychometric measures to exactly know the typology of symptoms and lesions that can actually bother the patients [2]. Indeed, the clinical severity of a disease is not always a faithful representative of the psychological impact of the diseases as well as the impact on the quality of life [3]. Thus, there are screening questionnaires and scales that are preferred in the setting of research. They are needed to understand the global dynamic of the impact on mental health and quality of life of the different dermatoses and skin illnesses, to assess patients' perspectives concerning the characteristics and the distribution of the lesions, including the extent of the skin involvement, the most uncomfortable symptoms as well as the

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satisfaction with the treatments. This may then support the evidence for some systemic treatments considering all this, as it happens, for instance, in the context of psoriasis [4, 5].

In the clinical practice, however, some questionnaires and scales could disturb the doctor-patient relationship as they include a larger number of questions and are also more time-consuming. Thereby, they should not replace the clinical interview and examination, even though they may provide valuable information for the diagnosis and the management. Scales and questionnaires, in turn, should be used to complement the mental state examination, providing additional information or reinforce the conclusions that are given by the clinical assessment. For this purpose, some tools can be more practical, such as, the "Hospital Anxiety and Depression Scale" (HADS), to assess symptoms of depression and anxiety, and the "Dermatology Life Quality Index" (DLQI), to assess the impact on quality of life [6, 7].

How to Approach a Patient with a Psychodermatologic Disorder

As explained in Chap. 5, there is a wide spectrum of psychodermatologic disorders and the assessment of these patients should take into account the main group where the disorder that the patient present is placed: primary psychopathology focused on the skin (with or without secondary dermatologic lesions); psychophysiological dermatoses with important psychological component; cutaneous sensory disorders; dermatosis or disfiguring skin condition and secondary psychiatric or social comorbidity.

Table 6.1 exposes the main topics to follow while performing a clinical history of a patient that has a psychodermatologic disorder. The examination should start by identifying whether there is or not a dermatosis and whether it is a primary dermatosis or whether the patient presents secondary dermatologic lesions or whether there are not skin lesions; at the same time, the presence of pruritus or dysesthesia should be excluded as well as the severity of these symptoms, taking into account all the clinical presentation, namely, the eventual presence of primary or secondary skin lesions [8]. Afterwards, other relevant topics include to know whether, for the patient, the stress is a triggering factor for the symptoms, a topic that is frequently forgotten in the approach of psychophysiological dermatoses [9], and the current medication, which, on the one hand, can be linked with the onset of pruritus [8], and, on the other hand, can point out to the underlying psychiatric comorbidities or even the presence of sleep problems, commonly seen in patients suffering from psychodermatologic disorders [9].

Furthermore, as illustrated in Table 6.2, a brief mental state examination can be performed to identify the most important aspects of mental health linked with the skin disease or illness. For example, this will allow to identify the presence of insight for the clinical symptoms, a complex concept that presumes the recognition by the patient that he has a psychiatric disorder that needs a treatment [10]. The

Table 6.1 How to organize a clinical history in psychodermatology, proposed by Ferreira, Jafferany & Patel

Main topics to organize a clinical history in psychodermatology	Presence of skin lesions, their distribution and whether they are primary or secondary skin lesions
	Presence of pruritus or dysesthesia
	Duration of the skin symptoms and antecedents of previous episodes
	Presence of factors that can trigger or worsen the skin symptoms - are they triggered by stress?
	Personal medical history: is there a previous diagnosis of a skin disease, psychiatric disorders, sleep difficulties or other medical problem?
	Family antecedents: are there antecedents of psychiatric disorders and chronic skin diseases?
	Is the patient under medication for the skin symptoms? And for psychiatric symptoms? And to sleep? What kind of medication? And since when?
	Description of the social context: since childhood up to the current situation (occupation, relationships, family context)

Table 6.2 How to briefly assess psychopathology for a patient with a skin disease or illness, elaborated by Ferreira, Jafferany & Patel

Basic psychological assessment in psychodermatology	To analyze the appearance (posture, clothes) and the behaviour (psychomotor activity, eye contact, compulsions)
	To ask about the experience of having the current skin symptoms - the disease or the illness
	To ask about biological functions, namely, appetite and sleep: are they changed? How? And since when?
	To ask about the most relevant current and past relationships
	To know the copings strategies used by the patient
	To assess risk - are there suicidal tendencies, attempts, thoughts, plans?
	To put the open-ended question: what and how would you like to change (concerning the skin, the social context, the family, the job)?
	Aspects to analyze during the clinical interview: mood, insight, cognitive functions, perception, thought (form and content) and speech (volume, fluency and rhythm)

most paradigmatic example in psychodermatology is that of delusional infestation, which is characterized by the fix, unwavering belief that there is a real infestation (by a parasite or an inanimate matter), and these patients will rarely present to specialists in psychiatry or psychodermatology. Thus, all clinicians should be taught about this diagnosis to avoid superfluous examinations and the reinforcement of the delusion; actually, they could collaborate to perform a first approach to control the skin symptoms and introduce the need for the assessment by a specialist in

psychodermatology [11, 12]. Interestingly, disorders traditionally placed in the obsessive-compulsive spectrum, then presenting intellectual insight, can also exhibit psychotic symptoms, during the evolution of the disorder, and exhibit the co existence of delusion. For instance, this could be observed in the context of body dysmorphic disorder, a condition of very difficult management that is under-recognized by medical professionals and that is connected with a high suicide attempt rate. In the approach of these patients, primary care physicians could have a very important role to avoid to postpone the adequate management, which could have disastrous consequences. Their collaboration may include psychoeducation about the condition, avoiding to reinforce the desire of the patient to keep on looking for more surgical or cosmetic treatments; for patients with lack of insight, it is also ineffective trying to convince the patient that the beliefs are irrational and the best strategy should be to put the focus on the distress caused by the illness, in order to introduce the need to referral to a specialist in psychiatry or psychodermatology [13]. Another important point described in Tables 6.1 and 6.2 is the current and the past family and social context and relevant relationships. For instance, this is especially important in the setting of factitious disorders, where a troubled childhood or family context or occupational issues can be a precipitant [14, 15]. These topics could be explored by the family physician, who knows very well the family dynamics, introducing, then, the need for a multidisciplinary approach, ideally a team with expertise in psychodermatology: to explore the subtleties of the troubled psychosocial background by psychological intervention, to exclude a primary dermatosis and to treat psychiatric comorbidities [14].

Moreover, some screening questionnaires were developed to improve the accuracy to diagnose specific mental health problems connected with the skin disease or illness, as illustrated in Fig. 6.1 [16–20]. The spectrum of anxiety and depression are common comorbidities of psychodermatologic disorders and the HADS is a practical and useful tool in routine clinical practice, that can be answered in few minutes, to determine whether the patient would benefit of a more specialized approach, a pharmacological treatment or a psychological intervention, depending on the severity of the symptoms. It was developed by Zigmond and Snaith [6], and includes seven items to assess the severity of depression and seven items to assess the severity of anxiety; for either anxiety and depression, there is the possibility of a score between 0 and 21 (normal, mild, moderate or severe levels of anxiety and/or depression). Additionally, other questionnaires and scales were developed to

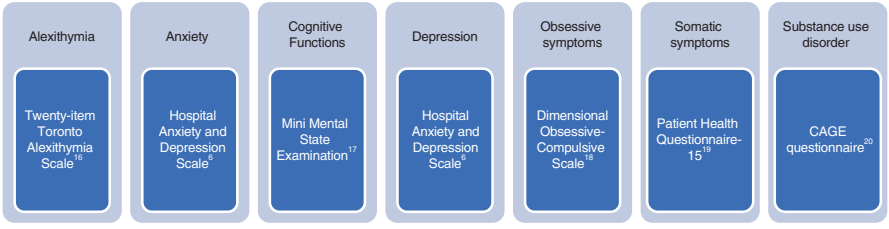

Fig. 6.1 Useful questionnaires and scales to assess psychopathology in psychodermatology

facilitate the description of the impact on quality of life of specific skin conditions or the severity of its clinical presentation, as mentioned in Fig. 6.2 [21–27]. Globally, to assess the impact on quality of life linked with skin diseases, DLQI [7] is a useful tool for adults and, in pediatrics, the Children's Dermatology Life Quality Index (CDLQI) is recommended [28].

In Fig. 6.3, the differential diagnoses of generalized pruritus are highlighted, a very important topic to consider in the absence of a primary dermatosis [29]. Even

Acne vulgaris	Atopic dermatitis	Body Dysmorphic Disorder	Hidradenitis suppurativa	Psoriasis	Skin cancer	Skin Picking
• Cardiff acne disability index[21]	• Infants' Dermatitis Quality of Life Index[22]	• Body Dysmorphic Disorder Symptom Scale[23]	• HIDRAdisk[24]	• Psoriasis Disability Index[25]	• Skin cancer index[26]	• Skin Picking Scale[27]

Fig. 6.2 Examples of specific questionnaires and scales with interest in psychodermatology

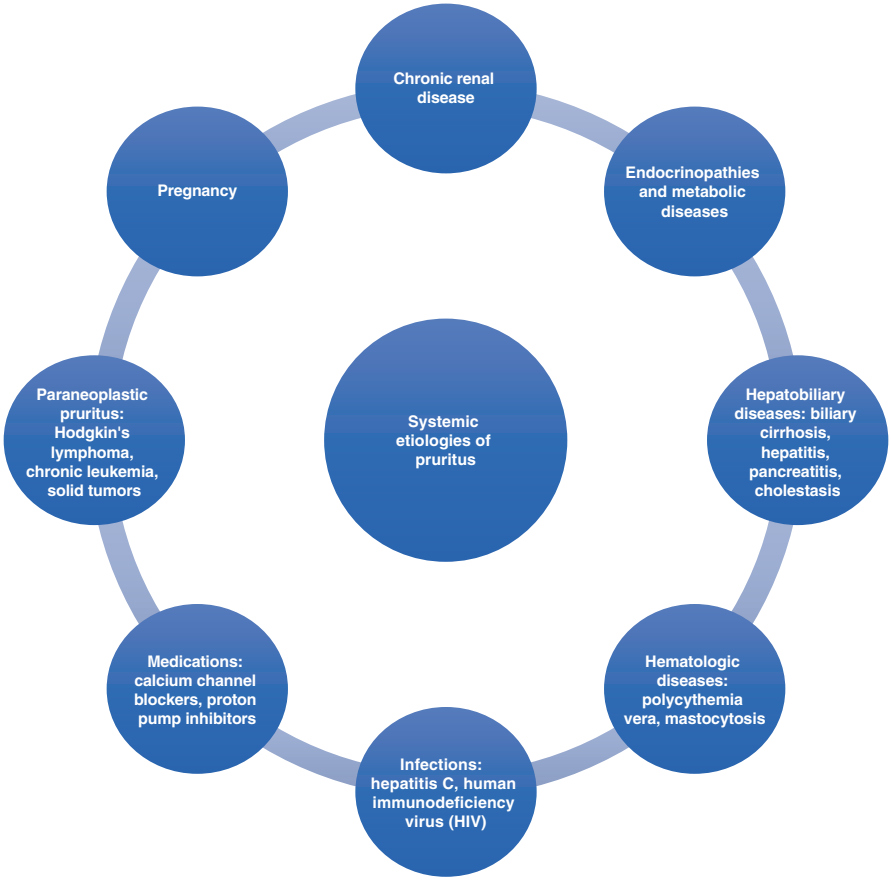

Fig. 6.3 Conditions to rule out in the setting of a patient with pruritus without a primary dermatosis

though not rarely correlated with psychiatric comorbidities, especially, anxiety and depression, secondary etiologies should also be remembered in dysesthesia syndromes with a normal clinical examination, namely, in burning mouth syndrome, some vitamin deficiencies (especially B vitamins and folate) and Sjögren's syndrome. Furthermore, scalp dysesthesia without a primary dermatosis may eventually be linked with a primary neurologic disorder, such as multiple sclerosis, and, in dysesthetic anogenital syndromes without specific dermatologic findings, a lumbosacral radiculopathy should be considered, as well. Finally, a small fiber polyneuropathy should be suspected in the setting of chronic pruritus or dysesthesia, bilaterally, in the feet, legs and hands; a neurological examination and a immunohistochemical staining of a distal leg skin biopsy confirm the diagnosis and possible etiologies should be ruled out, including, diabetes mellitus, vitamin B12 deficiency and hematologic neoplasms [8].

Final Reflections: The Need for Medical Education in Psychodermatology

Even though 30% of the patients in dermatology have a psychiatric comorbidity and 85% of the patients with skin symptoms confirm that there is a very important psychosocial component linked with the disease or illness, there are very few specialized services in psychodermatology and most of these patients will be approached by clinicians without medical education in psychodermatology [31, 32]. The relatively subjective aspects of dermatology, the psychosocial issues, are still undervalued and poorly approached globally [9, 33]. This is true not only in the context of dermatology and psychiatry, but also in other branches of medicine, in general, and decreases the patient's quality of life and may be a factor to worsen the disease and the illness [34]. Thereby, even if there are some specialized clinics or specialists in psychodermatology, most of the patients will not be referred [9, 35]. Thus, basic knowledge in psychodermatology should be implemented and spread in medical courses, in general medicine and in family medicine. General practitioners could also have a very important role in the approach of patients suffering from psychodermatologic disorders, considering that they provide a continuity of care and they have a closer contact with the patients and their families, having, thus, a pivotal role in the prevention of disease and illness and in the promotion of health [36].

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Chapter 7
Psychophysiologic Dermatoses

Introduction

Psychophysiologic disorders are cutaneous conditions that arise or are exacerbated from an individual's reaction to emotional states. Patients with conditions like psoriasis, acne, and atopic dermatitis frequently report varying degrees of severity from psychosocial triggers. Additionally, stress plays a role in initiating behavioral, immune, and endocrine responses, which can impact the severity of psychophysiologic conditions. As such, it is commonly observed that particularly stressful situations and certain life events often result in excessive anxiety, which may contribute to the relapse of certain skin conditions, which is further discussed in this chapter.

Atopic Dermatitis

Atopic Dermatitis (AD) is an inflammatory cutaneous disorder with a broad clinical spectrum, including erythema, pruritus, scaling, excoriation, and lichenification. Generally 1–3% of adults and 20% of children suffer from AD, and it is known to be one of the most common skin conditions in the world [1]. Infants and toddlers with AD commonly present lesions on the cheeks, scalp, extensor aspects of the extremities, later on the flexural folds, with pruritic and erythematous and edematous papules and papulovesicles, the lesions may evolve to plaques and can be more or less exudative and often undergo lichenification from repetitive scratching and rubbing. In contrast, adults frequently exhibit subacute to chronic lesions, with lichenification, and involvement of the flexural folds is also typical, although other regions of the body may also be affected [2]. Silvestre Salvador et al. discuss the diagnostic difficulty in adults with AD that do not fit the available criteria, primarily developed for children, who typically exhibit a different presentation [3]. As such,

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physicians suspecting adult-onset AD are advised to conduct comprehensive testing to rule out other similarly presenting causes, as it is commonly a diagnosis of exclusion. In addition, the recent incidence of AD has increased, which has been attributed to more common and earlier exposure to environmental factors such as food additives, dust mites, pollen, and air pollutants. Although data indicates the condition is plateauing in regions with the highest prevalence like New Zealand and the United Kingdom, alarmingly increasing numbers of children are being affected in developing and low-income nations [4]. A possible explanation for the overall increased incidence is the hygiene hypothesis, which states that deficient microbial exposure early in life may predispose individuals to develop AD through alteration of normal immune processes [5].

Apart from the central relevance of the specific dermatologic treatment, the treatment of AD should be centered in strategies to decrease the frequency of the itch-scratch cycle. Additionally, treatment of co-morbid psychiatric conditions like depression and anxiety, along with appropriate psychosocial interventions to reduce potential conflict in interpersonal relationships, is essential. Non-pharmacologic therapies like Habit Reversal Therapy (HRT) have been shown to assist patients in reducing the cycle of itching and scratching. In a controlled trial with 39 patients with AD, investigators found a significant reduction in scratching behavior at the end of the 3-week treatment period, when compared to controls [6]. Daunton et al. further explain that HRT is a easy to learn technique that is effective as an adjuvant treatment for topical therapy in the management of AD [7]. Additionally, cognitive behavioral therapy (CBT) has also shown to be effective in improving self-reported symptom severity in patients with AD [8, 9]. With respect to pharmacologic interventions, first generation antihistamines are considered first line in treating sleep disturbances associated with AD as they have shown to alleviate night-time scratching in patients which lead to an improved quality of sleep [10]. Tricyclic antidepressant Doxepin has been shown to be effective in managing nocturnal pruritus in adults with AD, however, there is risk of adverse effects specifically in the elderly due to the medication's anticholinergic effects [11].

A multifaceted treatment regimen with a combination of both psychotherapeutic interventions along with pharmacologic modalities has been shown to be most effective in improving the overall quality of life of individuals with AD. Implementation of HRT, relaxation training, stress management sessions, and pharmacotherapy with continued follow up, are typically more effective than individual treatments.

Psoriasis

Psoriasis is chronic in nature and has a relapsing-remitting pattern. Chronic plaque psoriasis, the most common variant of psoriasis vulgaris, is characterized by the presence of erythematous scaling papule and indurated plaques, with a relatively symmetric distribution, that predominantly appear on knees, elbows, lumbosacral region

and scalp. There are 3–5 million individuals in the United States with psoriasis and it affects 1.5–2% of the western countries [12]. Forty percent of patients with psoriasis have a positive family history which may impact disease severity [13]. Psoriasis has a bimodal distribution with regard to age of onset between ages 20 and 30 and 50–60 [14]. Commonly observed risk factors for psoriasis consist of genetic factors and environmental causes such as bacterial and viral infections, pharmacologic agents like lithium, and lifestyle choices [15]. Additionally, stress is noted to be a trigger of the condition in 31–88% of cases and it may specifically play a role in predisposed individuals [16]. A systematic review conducted by Stewart et al. found a temporal association between psychologic stress and the onset, recurrence, and disease severity [17]. Individuals also report a greater contributor of stress induced symptom exacerbation as being related to social stigma and cosmetic disfigurement rather than stressful life events. Lim et al. found woman, younger patients, individuals with earlier life onset, and those with lesions in areas not covered by clothing were more susceptible to psychological distress mediated disease initiation and progression [18].

With increasing evidence and attention to the implications of psoriasis on the overall mental-health and psychosocial wellbeing, therapies aiming to improve quality of life are recognized as essential in successful management of patients. Specific psychotherapeutic options showing promise for use in treatment of patients with psoriatic symptoms include mindfulness meditation, cognitive behavioral therapy (CBT), motivational interviewing, and educational and interdisciplinary interventions [19]. CBT has been effective in improving the clinical severity and strengthening an individual's ability to cope with the chronic nature of psoriasis [20]. Additionally, in a systematic review examining the effectiveness of the technique, Sijercic et al. find CBT to be generally effective in improving the quality of life and may be beneficial as an adjutant therapy for specific patients with psoriasis who exhibit a psychiatric history [21]. Therefore, it is essential to screen patients with psoriasis for the presence of any underlying psychological stress to offer the most holistic interventions. Specifically, knowledge of personality characteristics to identify individuals more at risk of developing psychosocial distress can facilitate more individualized and well-rounded care for patients with psoriasis [22]. Screening methods would allow for individuals with undiagnosed psychiatric conditions like anxiety and depression to be properly addressed with support and treatment. With increased awareness, more comprehensive studies may begin to uncover the role of depression and anxiety on the course of psoriasis as well as the potential development of novel psychopharmacological interventions to improve quality of life. With respect to pharmacologic interventions, TNF-alpha antagonists such as Adalimumab and IL-12/23 blockers like ustekinumab have been associated with reducing symptoms of depression, fatigue, and anxiety in patients with psoriasis [23, 24]. It is also important to note that the use of certain psychotropic agents like fluoxetine, buproprion, and lithium, in individuals with psoriasis and psychiatric co-morbidity, have been associated with symptom exacerbation. For example, buproprion and fluoxetine have been reported to not just worsen symptoms of existing psoriasis, but also to induce the condition in patients with no history [25–29].

Alopecia Areata

Alopecia areata (AA) is a relatively common condition resulting in localized round areas of hair-loss without the presence of observable inflammation. The condition affects about 2% of the worldwide population, has an increasing prevalence worldwide, exhibits significant differences regionally, and is more common in adults compared to children [30]. Although AA can impact any area of the body with hair, most cases involve the scalp. Other areas commonly reported include the beard, eyelashes, and eyebrows [31]. The vast majority of cases, around 80%, report spontaneous regrowth of hair within a year and severity of hair-loss at onset is a strong predictor of the long term outcomes [32]. The primary diagnostic feature of AA is breakage of the hair shaft comprised of the classic "exclamation-mark" appearance that is thicker at the top and more narrow along the length [33].

The disease has an unpredictable course, even though several treatments are available and can be combined. The use of topical and/or intra-lesion steroid injections, topical minoxidil, and, depending on the severity, systemic corticosteroids and eventually topical immunotherapy, are treatment options. Recently, the use of platelet rich plasma has also shown promise as a therapeutic alternative [34]. There have been limited studies of psychotropic medication efficacy in AA patients with psychiatric comorbidity. Abendini et al. find the use of antidepressant adjuvant treatment to improve alopecia areata lesions in patients with co-morbid major depressive disorder [35]. In addition, results from a controlled trial of AA patients receiving 75 mg of tricyclic antidepressant Tofranil (Imipramine) indicated significant hair regrowth in the treatment group compared to the control [36]. With regard to nonpharmacologic therapeutic options, there is lack of concrete results from controlled studies reporting the efficacy of psychotherapy, relaxation, and stress management techniques. However, group interaction with support groups has been found to be an important avenue to assist in coping with the psychosocial impact of the condition [37].

Acne Vulgaris

Acne is an inflammatory condition that commonly occurs during adolescence and has a multifactorial etiology. There is a genetic predisposition to acne as the majority of individuals with severe acne share a positive family history [38]. The condition involves bacterial colonization with Cutibacterium (formerly known as Propionibacterium) acnes in pilosebaceous glands located primarily in the face and trunk [39]. In a large epidemiological study examining individuals with acne, Yentzer et al. found 65.2% were female, 61.9% were over the age of 18, and 36.5% were in the adolescents range between 12 and 17 [40]. Although acne can be self limited in individuals with acne in the pre-adult years, a significant proportion experience acne into adulthood. Bhate et al. found 64% had persistent acne between 20

and 30 years of age and 43% between ages 30–40 [41]. This is a concern within psychocutaneous medicine as adults with persistent acne into adulthood may have visible, deep, hypertrophic scars leading to negative psychosocial effects. Specifically, around 25% of teenagers diagnosed with acne experience permanent scarring past 18 years of age [42].

As affected individuals commonly present with psychiatric co-morbidity (depression, anxiety, and social phobia), appropriate screenings and treatment should be initiated. Specifically, continued monitoring and follow-up of younger patients with acne is essential, due to the increased risk of suicide ideation [43]. Typical agents for treatment consist of topical retinoids, systemic and topical antibiotics, and benzoyl peroxide [44]. Non-pharmacologic options consist of cognitive behavioral therapy, relaxation exercises, and self-hypnosis techniques, which, when combined with carefully monitored pharmacotherapy may improve therapeutic outcomes for patients with acne [45]. Certain pharmacotherapies like isoretinoin have been associated with increasing the risk of depression, suicide ideation, and completed suicide attempts [46, 47]. Although studies [48, 49] indicate controversy over isoretinoin's potential role in the development of depressive and even violent behaviors, the FDA and pharmaceutical manufacturers now include warnings for patients regarding potential psychiatric complications. Recommendations include routine screening for psychiatric disorders and appropriate patient-education discussions regarding associated risk factors while prescribing isotretinoin [50].

Urticaria and Angioedema

Urticaria results from mast cell degranulation and is referred to as the formation of hives and/or angioedema. Angioedema results from a process identical to that of urticaria. However, it results in a larger edematous area that is not well-circumscribed and involves the deep dermis and mucous membranes rather than the superficial dermis seen in urticaria [51]. While angioedema develop slowly and can be present for multiple days, urticaria typically only presents for no longer than 1 day [52]. The chronic form of the condition lasts for greater than 6 weeks and presents as wheals (hives) and/or angioedema, while acute urticaria presents with spontaneous, recurring wheals for a period of time less than 6 weeks [53]. Triggers of acute urticaria include infections, drug reactions, and certain foods [54]. In contrast, chronic urticaria is reported to be idiopathic in the vast majority, or 80–90% of cases [55].

In urticaria and angioedema related to chemical, drug, or food exposures, the prompt elimination of the agent is indicated. The first line treatment for chronic urticaria and/or angioedema is second generation antihistamines, while first generation antihistamines should be avoided due to their notable adverse effect profile [56]. Psychotropic medication doxepin (an antidepressant) has also showed promise as a effective therapeutic option for patients with chronic urticaria, however, the sample sizes are relatively small [57, 58]. Additionally, patients with chronic

urticaria commonly exhibit psychiatric comorbidity. Specifically, depression and anxiety were found to be significantly more present in patients with the condition when compared to controls [59, 60]. Therefore, successful management includes emphatic dialogue, a strong patient-physician relationship, and referrals to mental health providers when indicated. Although there is significant psychiatric comorbidity in patients with chronic urticaria, the effectiveness of nonpharmacologic therapies in management of the condition have not been extensively studied, calling for increased research and clinical trials.

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Chapter 8
Dermatoses with Important Psychiatric and Social Co-Morbidities

Introduction

The visible and chronic nature of dermatologic disease introduces increased risk of secondary psychiatric conditions. However, rarely do patients feel comfortable discussing the negative psychosocial impact of chronic disfiguring skin conditions. Not only has the prevalence of psychiatric conditions for dermatology patients greater than 30%, it has been reported that health related quality of life is a much stronger predictor of morbidity compared to physician-conducted clinical severity scales [1]. As such, dermatologists are urged to better understand and acknowledge the basic aspects of psychocutaneous disease. In doing so, the physician is able to better suspect potential secondary psychiatric morbidity and offer appropriate resources. In this chapter, commonly reported secondary psychiatric disorders and potential contributing factors in individuals with cutaneous diseases are introduced.

Important Contributing Factors

Patient-Centered Factors

Various patient characteristics can influence the psychopathologic development of life-altering disorders like anxiety and depression in patients with dermatologic disease. Age, for example, and the stage of life an individual is in impacts individual reactions to the onset or worsening of a disease process. Beekman reports that anxiety disorders, although common, typically emerge earlier in life and sharply decline after the age of 75 [2]. Similarly, the sex of a patient, due to differences in societal and cultural influence, can impact the development of secondary psychosocial conditions. While reporting that female patients with psoriasis report higher levels of

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depression, Kouris et al. explain this finding to be unsurprising as it is widely known that woman, generally, spend more time on physical appearance when compared to men [3].

A basic understanding of personality disorders can be clinically relevant as the information may shed light on the development and presence of psychiatric conditions. For example, narcissistic, histrionic, borderline, and obsessive-compulsive personality types may be encountered in specific subgroups of dermatology patients [4]. In patients seeking cosmetic interventions, for example, are reported as having narcissistic personality disorder, histrionic personality disorder, and body dysmorphic disorder [5]. Furthermore, personality traits have been found to be correlated with certain psychiatric conditions. Bienvenu et al. report social phobia, panic disorder, anxiety disorders, major depressive disorder, and dysthymia to be associated with high neuroticism [6]. Likewise, withdrawal, industriousness, and enthusiasm have been reported to be risk factors in the development of depression [7].

Body image has been reported to affect our thoughts, emotions, behaviors, relationships, and may even our overall quality of life [8]. As such, it may play a relevant role in the development of secondary psychiatric disorders in dermatologic patients with visible skin disfigurement. Cutaneous body image (CBI), specifically, represents an individual's personal ideas and views of his or her hair, skin, and nails. Understanding a patient's CBI can offer clues on potential psychosocial morbidities and can determine the course of the management process [9]. Additionally, CBI has been found to have a significant correlation with the severity of certain dermatologic conditions like acne, sleep quality, and suicidal ideation [10, 11]. Personal and intimate relationships have the potential to suffer as a result of a dermatologic condition's impact on CBI. For example, Gündüz et al. found body image satisfaction to be the most significant risk factor for sexual function impairment in patients with psoriasis [12]. Similarly, another study expands on the association while reporting anxiety and depression, in patients with psoriatic lesions in specific body regions, as possible independent risk factors for sexual dysfunction [13].

Disease-Related Factors

Various factors related to skin disease and lesion characteristics may additionally impact psychosocial morbidity. Morphological qualities such as size and color, in addition to physical location on the body the condition manifests may influence the onset and progression of secondary psychopathology. In patients with vitiligo, for example, the overall visibility of the lesions and disease extent (total involved body surface area) are associated with impairment in quality of life with respect to functioning, emotions, and experienced symptoms [14]. The chronicity of the cutaneous condition and the potential for exacerbation it shares, also may impact the development of psychosocial morbidity. This association is illustrated by Fried et al., who

report a positive correlation between psychologic morbidity and the length of disease flare-ups among a group of patients with psoriasis [15]. Similarly, Gupta et al. report patients with more cosmetically disfigured lesions experience a greater number of flares, and greater overall disease severity, which, in turn, may significantly impact levels of psoriasis-related stress [16].

External Factors

Contributing factors unrelated to the disease itself or the afflicted individuals can strongly impact the development or prevention of secondary psychiatric conditions. The relationship the patient has with his or her treating physician can determine the potential worsening of certain psychological conditions. As previously mentioned, dermatology patients have been reported to rarely feel comfortable to disclose this information. Practitioners dismissing emotional factors or who do not provide an emphatic, comfortable environment for individuals with skin disease to disclose life stressors, may further contribute to the distress experienced by patients. Dermatologists that may not have formal training or previous experience to address the psychiatric morbidity, are advised, at a minimum, to empathetically initiate conversations related to mental health and offer referrals, where appropriate.

Cultural background and societal norms additionally influence the development of psychosocial concerns. Specifically, stigmatization can result in negative labels or stereotypes against those that do not match societal norms and can manifest as avoidance and distrust by the general population [17]. The visibility and morphological features of cutaneous disease may lead to misconceptions regarding certain conditions. It has been reported that skin conditions may lead to feelings of disgust due to physical attributes and fear from the assumption that it is contagious [18]. Further, it has been found that patients with psoriasis may experience feelings of stigmatization and difficulty coping with their condition from appearance-related concerns, which can lead to clinical mental health manifestations [19]. Hawro et al. also provide additional evidence while reporting female gender and psoriatic lesions of the back and hands led to greater stigmatization of patients with psoriasis [20].

The existence of support networks and group meetings for individuals suffering from dermatologic disease have been found to be tremendously beneficial as a resource and adjuvant therapy for patients [21]. To illustrate, Lu et al., report reduced acceptance and lack of social support as being significantly related to the experience of stigmatization among patients with psoriasis and atopic dermatitis [22]. Similarly, Ashenbeck et al. found patients with alopecia identified group interactions and socializing with others with the condition as being an important source of therapeutic support [23]. These studies illustrate the significance of a strong support network while coping with dermatologic disease. A lack of support may cause increased isolation and potentially worsen existing or trigger new-onset psychiatric disease.

Major Depressive Disorder

Chronic medical conditions, including cutaneous disease following a chronic course, for an individual to develop one or more episodes of depression [4]. As defined by the Diagnostic and Statistical Manual of Mental Disorders (5th Edition) or DSM-5, major depressive disorder is described as having depressed mood (change from normal baseline) or loss of interest in daily activities for more than 2 weeks and impaired social, occupational, and educational function. Additionally, the patient must have 5 of the 9 following specific symptoms, present daily, to meet the criteria: depressed mood or irritably, loss of interest or pleasure, weight or appetite change, changes in sleep, alteration of activity, loss of energy, guilt, diminished concentration, and thoughts of suicide. Unsurprisingly, dermatology patients exhibit a very high incidence of depression which has a negative impact on quality of life and treatment satisfaction scores. In a systematic review and meta-analysis exploring depression across medical specialties, Wang et al. report dermatology outpatients as having one of the highest rates at 39% [24]. Further, patients with vitiligo, for example, may experience profound psychiatric comorbidity, especially among females, individuals with darker skin, and those with darker skin tones. Lai et al. report a significant proportion of patients with vitiligo are likely to suffer from depression and recommend clinicians to perform mental health evaluations and make referrals when indicated [25]. Similarly, individuals with psoriasis, especially younger patients, middle aged woman, and those from lower socioeconomic backgrounds, have been found to have a significantly increased prevalence of depression [26]. In order to identify and assist patients that may have depression secondary to their dermatologic condition, treating physicians are recommended to administer screening tools like the Patient Health Questionnaire (PHQ)-2 and be mindful of specific risk factors like adolescent age, severe cutaneous condition(s), and lesions on the face [27].

Anxiety Disorders

Anxiety consists of feelings of nervousness or worry, and may exhibit physical symptoms like palpitations, sweating, or tremors. Skin conditions that are commonly associated with anxiety disorders include atopic dermatitis, seborrheic dermatitis, acne vulgaris, and rosacea [28]. As explained by the DSM-5, a diagnosis of generalized anxiety disorder (GAD) requires excessive anxiety and worry that is out of proportion to the situation, has lasted for greater than 6 months, and results in symptoms like irritability, fatigue, sleep disorders, concentration issues, and muscle tensions. Chronic skin conditions have an increased risk of anxiety due to appearance-related concerns. For example, in a cross-sectional study comprised of adult patients with acne, Sule Afsar et al. report a significant correlation in social appearance anxiety and objective acne severity [29]. In another study investigating the prevalence of psychosocial comorbidity in patients with acne, Lukaviciute et al.

report anxiety to be the most prevalent, threefold more prevalent than suicidal idealization and 1.7-fold more prevalent than depression. Furthermore, in dermatologic conditions where pruritus is a chief symptom, like atopic dermatitis, anxiety plays a notable role in the disease prognosis through its involvement in the itch-scratch cycle. Sanders et al. explain that chronic pruritus in atopic dermatitis is associated with anxiety and stress which can worsen pruritus, leading to further decline in disease severity and quality of life [30]. In such patients, prompt treatment through medication and/or psychological therapy, to reduce anxiety, can also assist in the management of pruritus.

Specific Phobias

According to the DSM-5, specific phobias are characterized by fear, anxiety or avoidance about a specific object or situation that is out of proportion to the actual danger the situation or object poses. The intense feelings of fear, anxiety, and avoidance typically last for 6 or more months and the object or situation is actively avoided as it provokes immediate undesirable feelings. With respect to psychodermatologic disease, a commonly reported specific phobia is social phobia or social anxiety disorder (SAD), which is characterized by intense and irrational persistent fear of social settings. Additionally, SAD has been found to have an especially high incidence among younger individuals. In a study by Koyuncu et al., investigators report the rate of SAD prior to age 18 was 79.6%, with earlier life onset leading to increased functional impairment and likelihood of depression [31]. In a study evaluating psychosocial comorbidity in patients with vitiligo and acne, Salman et al. report significantly higher levels of social anxiety, compared to control [32]. Additionally, as social anxiety negatively impacts an individual's school, work, and social life, authors recommend clinicians to identify vitiligo and acne patients with high levels of social anxiety early, in order to prevent long-term adverse effects of living with SAD [32].

Adjustment Disorder

According to the DSM-5, individuals that develop behavioral or emotional symptoms within 3 months of the onset of an identifiable stressor(s) are diagnosed as having an adjustment disorder. Additionally, the individual experiences significant functional impairment and marked distress that is out of proportion to the actual severity of the initiating stressor. External social and cultural factors, combined with personal coping mechanisms and personality characteristics can play a role in the development of adjustment disorders in individuals diagnosed with chronic skin conditions. For example, in a systematic review of the mental health disorders in patients with psoriasis, Ferreira et al. report a 29% prevalence of adjustment disorder [33].

Similarly, in a comparative study examining the psychiatric morbidity among 113 patients with vitiligo and 103 patients with psoriasis, Mattoo et al. report the prevalence of adjustment disorder as 33.6% and 24.7%, respectively [34]. The high prevalence of adjustment disorder indicated by the aforementioned studies illuminates the life-altering nature of cutaneous disease, calling for increased attention and improved management strategies with multidisciplinary attention.

Treatment

Prompt identification, acknowledgment, and treatment of secondary psychiatric disorders in the dermatologic patient population is essential in improving overall quality of life. The aim of treatment is to improve decreased function and mental distress while properly addressing feelings of isolation and altered self-esteem [35]. It is vital for clinicians to educate themselves regarding the physical aspects of dermatologic disease to recognize potential emotional disturbances, warning signs, and specific at-risk patient populations in order to prevent the worsening of existing secondary mental health morbidity. Doing so, proper therapeutic options and resources can be offered to patients in hopes of improving their overall quality of life. A multidisciplinary approach is recommended in the treatment of both dermatologic symptoms and psychiatric ailments. This may include, but is not limited to, dermatologists, psychiatrists, psychologists, pediatricians, general practitioners, therapists, and councilors. A holistic treatment process through the combination of both pharmacologic and non-pharmacologic options and involvement of multiple healthcare professionals, is suggested.

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Chapter 9
Psychodermatologic Disorders with Primary Psychopathology

Introduction

Primary psychiatric disorders are the stereotypic category of conditions within psychocutaneous medicine. The disorders always have underlying psychopathology and often exhibit secondary dermatologic manifestations. Although treatment of this subgroup often requires a mental health professional, dermatologists play a vital role in patient management. Individuals most commonly seek dermatologic care due to their physically damaged skin as they typically do not consider themselves having a psychiatric condition. Additionally, patients may react with offense if the dermatologist, where the patient initially presents, quickly or without careful engagement, suggests a psychiatric referral. There are several specific conditions belonging within this category and are described in further detail below.

A. Delusional disorder, somatic type

Delusions are strongly held false beliefs often defended by convincing emotion and speech. The Diagnostic & Statistical Manual of Mental Disorders, 5th Edition (DSM-5) further describes individuals with delusional disorder as having unimpaired functioning without exhibiting any noticeably strange or bizarre behavior (s). Although there are several further classifications of the disorder, specific examples found in psychocutaneous medicine are discussed further below.

1. Delusional parasitotis (DoP)
   (i) Also may be referred to as: delusions of infestation, monosymptomatic hypochondriacal psychosis, Morgellon's disease, Ekbom syndrome, parasitophobia, acarophobia, and entomophobia, psychogenic parasitosis, chronic tactile hallucinosis, cocaine bugs
   (ii) Clinical Features: Patients typically present to the dermatologist and explain experiencing uncomfortable sensations of parasites crawling inside or on their skin. Commonly, patients will bring samples of the

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bugs, which are typically pieces of their own hair or skin, referred to as "matchbox" or "specimen sign" [1]. Attempts of self-treatment prior to seeking specialized care can involve the use of insecticides and repeatedly washing their skin. Additionally, patients may utilize knives, needles, or other tools in an effort to remove the parasites themselves. There are two forms of DoP: primary, where the delusion is self-manifested and secondary, where the delusion occurs as a result of substance abuse, nutritional deficiencies, and/or another medical condition or psychiatric illness.

(iii) Diagnosis: Literature emphasizes the importance of engaging with patients and building trust for initiating and maintaining treatment. Interactions with accusatory language, skeptical facial expressions, and overall tone lacking empathy can cause patient frustration, often leading to rejection of any further evaluation. "Patients are frequently lost to follow-up since they commonly mistake their doctor's recommendations as a sign of incompetence or apathy [2]. Additionally, careful history taking is vital in elucidating the underlying cause(s) of patients with the secondary form of the disorder. Specific underlying causes include anemia, hypothyroidism, vitamin B12 deficiency, hepatitis, diabetes, infections like HIV and syphilis, and substance abuse (typically cocaine) [1]. Following a careful history and physical exam, appropriate testing can confirm the etiology of secondary DoP: CBC, thyroid-stimulating hormone, folate, B12, urea, glucose liver function tests, urine toxicology, syphilis and HIV screen [1].

(iv) Treatment: Due to the difficult nature of the patient population with DoP, treatment initiation and maintenance can be challenging. Patients are commonly non-compliant, lost to follow-up and skeptical of the physician's management strategies leading to "doctor-shopping". It is recommended to avoid informing patients of the diagnosis on the first consultation in order to build a stable relationship with a strong foundation of trust. To establish patient-physician rapport, it is important to listen empathetically to stories and descriptions, reduce their overall sense of isolation, and inquire how the sensations influences their life.

(v) Other somatic delusional disorders in psychodermatology include delusions related with appearance and foul body odor. The difference between appearance-related delusions and body-dysmorphic disorder (BDD) has been debated, as the conditions can present similarly and may belong within a continuous spectrum [3, 4]. While BDD is categorized under obsessive-compulsive and related disorders (OCRDs), delusional disorders (somatic variants) are classified as psychotic disorders. In a study comparing 191 subjects with appearance-related somatic type delusional disorder and nondeulsional BDD, researchers found similarities in some demographic factors, measures of functional impairment, quality of life, comorbidity, and family history. However, delusional patients were found to have attempted suicide more often, rated lower on social functioning scales, were more likely to have a history of illicit substance abuse, and were less likely to be receiving mental health care [4].

B. Obsessive-compulsive and related disorders (OCRDs) within psychocutaneous medicine include body dysmorphic disorder and a subcategory of disorders: body focused repetitive disorders (BFRDs). Also referred to as self-induced dermatoses, these conditions represent two percent of the dermatology patient population [5].

1. Body dysmorphic disorder
   (i) Also may be referred to as: dysmorphophobia
   (ii) Clinical Features: Patients with BDD experience heightened preoccupation with their appearance or an area of their body that may be seen as a "defect" or "flaw". The disorder is characterized as an OCRD due to its intrusive presence in the individual's day to day life. The thoughts and behaviors stemming from the disorder often have a negative impact on a person's interpersonal relationships and professional obligations. Patients typically do not seek mental health treatment and may not be aware they have a mental health disorder. A considerable amount of time is spent thinking, examining, or discussing what is observed to be a defect in his or her appearance. For example, individuals with BDD may repeatedly examine themselves in the mirror to compare specific features to those of others', make daily efforts hide or camouflage the "flaw" with clothes and/or make-up [3]. Additionally, patients may engage in dangerous diets or seek appearance altering treatments and cosmetic surgeries. However, the appearance-altering cosmetic surgeries are typically not beneficial and may even be a contraindication, as they do not target the underlying cause of illness [6]. Conrado et al. found BDD to be relatively common among the dermatology patient population and conclude that dermatologists should make efforts to accurately identify the patients and refer them to mental health professionals [7].
   (iii) Diagnosis and Treatment: As patients typically do not present to a mental health provider and may seek cosmetic alterations, which may further worsen their condition, proper identification is vital. However, dermatologists and cosmetic surgeons may be unaware of the disorder or may lack the training to accurately diagnose patients before performing the procedure(s).

Body Focused Repetitive Behaviors

BFRBs represent a group of impulse-control conditions characterized by self-induced physical damage of the skin, hair, and/or nails. Three commonly presenting conditions in this category of OCRDs are discussed below.

2. Skin picking disorder (SPD)
   (i) Also may be referred to as: Psychogenic excoriation, dermatillomania, or excoriation disorder
   (ii) Clinical Features: Among the BFRBs, SPD has been found to be the most prevalent [8, 9]. The condition affects a broad range of age groups, but has been found to have the most common age of onset during both adolescence and middle adulthood. SPD has also been correlated with

other psychosocial and psychiatric co-morbidities [10]. In a 7639 participant survey, SPD was found to have an association with depression, nicotine depend, alcohol dependence, and suicide ideation [11]. Additionally, SPD symptom severity has been found to be associated with impulsivity, anxiety, and depression [12]. The condition is characterized by physical damage to the skin from excessive and repetitive touching, pulling, squeezing, pinching, and/or rubbing. Previously, areas of the body involved are typically those that have been previously visibly damaged from dermatologic conditions like acne vulgaris and atopic dermatitis. However, undamaged and healthy skin can also be targeted. Of note, the lesions are visibly in different stages of healing and may have delayed healing due to the chronic nature of the condition [13]. As such, the lesions are commonly hypo- or hyper-pigmented and appear as linear scabs or scars. Upon questioning, patients typically describe experiencing uncomfortable sensations and itching from the involved areas leading them to engage in the skin-picking behavior. The disorder may also develop into chronic dermatitis through the initiation of the "itch-scratch cycle" [14].

(iii) Diagnosis: Patients with SPD typically present to a dermatologist for management and cosmetic options for physical lesions rather than a psychologist and/or a psychiatrist [15]. Additionally, individuals with the disorder are often unaware that there are treatment options to address the underlying cause of the behavior [16]. Therefore, it is vital for dermatologists to be knowledgable and aware of the common presenting signs, perform a full dermatologic assessment, and make appropriate referrals when indicated. Areas of the body typically involved vary and include those that are easy to reach, however, the "butterfly sign" is a notable clinical sign [17]. This phenomenon is observed on the upper middle to lateral back that is free of lesions as it cannot be easily reached. Careful history can reveal the underlying cause of the behavior as medical such as pregnancy, uremia, or liver disease, psychiatric like depression and anxiety, or both [13].

(iv) Treatment: Currently, no FDA approved or recommended treatment exists for SPD. However, both psychologic therapy and pharmacologic medications have shown to be effective in the successful management of patients. With regard to pharmacologic medications, studies indicate varying degrees of success with the use of selective serotonin reuptake inhibitors (SSRIs), antipsychotics, opioid antagonists, and glutamate modulators. In a systematic review of treatment options by Lochner et al., investigators conclude SSRIs as being the most widely implemented medication, with new evidence of NAC also showing promise [18]. Another systematic review examining randomized controlled trials for SPD management found only non-pharmacologic interventions, specifically cognitive behavioral therapy, to show significant improvement in patient symptoms [19]. In addition to case reports [20, 21], a random-

ized clinical trial indicates N-Acetylcysteine effectively reduces skin picking behavior [22]. Although further studies need to be conducted in order to make accurate conclusions, a collaborative approach with the attention of a multidisciplinary team in providing counseling and medication, is recommended.

3. Trichotillomania (TTM)
   (i) Also may be referred to as: Hair pulling disorder
   (ii) Clinical Features: Trichotillomania is OCRD wherein affected individuals engage in repetitive pulling or plucking of their hair leading to noticeable hair loss and, for some, functional impairment [23]. The condition is characterized by a chronic course, has a bimodal distribution in childhood and adolescence, and predominantly effects females [24]. Although individuals with the disorder can target any area of the body with hair, the eyebrows, scalp, and eyelashes are the most commonly observed sites of involvement [25]. Psychiatric co-morbidity is common in patients with TTM and can alter the severity of the condition. In a study consisting of 165 adults with the disorder, Grant et al. found those with both TTM and anxiety had significantly worse symptoms and experienced an increased likelihood of also having depression [26]. There are two primary types of hair pulling, described as the automatic type, where the behavior is driven by boredom, and the focused type, which is caused by stress and anxiety [27]. Regardless of the specific subtype, the hair-pulling action has been reported to occur primarily from the inability to properly regulate the immediately preceding emotional states [28].
   (iii) Diagnosis: Individuals with TTM often experience shame, resulting in an inability to verbally disclose the behavior to the examining physician or a decreased likelihood of seeking treatment altogether [29]. When the possibility of TTM is suspected for a patient, the examining physician should administer specific screening tools in order to accurately diagnose and confirm that he or she meets criteria established by the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition). Examples of screening tools that may be implemented include the National Institute of Mental Health Trichotillomania Severity Scale (NIMH-TSS) [30], the Massachusetts General Hospital Hair Pulling Scale (MGH-HPS) [31], and the Yale-Brown Obsessive Compulsive Scale- Trichotillomania (Y-BOCS-TTM) [32]. Physical examination can confirm the diagnosis, uncover the potential for regrowth by examining the presence of scarring, and the possibility of a co-occurring condition, trichobezoar, where individuals swallow hair leading to an abdominal mass [33]. Additionally, trichoscopy [34], hair-punch biopsy [35], and the hair pull test [36] can be used in order to confirm the diagnosis of TTM and rule out similarly presenting conditions such as alopecia.
   (iv) Treatment: Although an FDA approved treatment for TTM does not currently exist, several options exist in its successful management as both

pharmacologic medication and non-pharmacologic therapy. One systematic review conducted by Bloch et al. found HRT to be the most effective over placebo and pharmacologic interventions, clomipramine (a TCA) to be more effective than placebo, and no evidence that SSRIs were more effective than placebo [37]. A meta-analysis and systematic review performed by McGuire, et al. similarly found behavior therapy to be very effective in treating TTM, with SSRIs and clomipramine both indicating moderate effectiveness. There have been several case reports [38, 39] of using glutamatergic modulator, N-acetyl cysteine (NAC), in treating TTM through the reduction of oxidative stress and neuroinflammation [40]. Overall recommendations consist of implementing a combination of medication such as NAC, TCAs, and SSRIs in addition to behavior therapies like CBT and HRT [41].

4. Onychophagia
   (i) Also may be referred to as: habitual nail biting, nail biting disorder
   (ii) Clinical Features: Onychophagia is a BFRB classified with lip biting and cheek chewing under "other specified OCRDs" by the DSM-5. The chronic, nail-biting behavior effects a diverse age group, but typically presents during childhood and is commonly seen in pre-teens and adolescents [42]. A significant proportion of the general population is impacted by onychophagia and the actual prevalence may not be known because many patients do not seek treatment due to shame and embarrassment [43]. Onychophagia has been found to cause secondary psychosocial issues along with complications of the oral cavity and/or nail unit [44]. Potential triggers include including anxiety, stress, or boredom and the behavior may be a sign of underlying emotional or mental disorders [45]. A study consisting of 339 student with onychophagia found a significant negative impact on quality of life and increased levels of stigmatization compared to the control group [46].
   (iii) Diagnosis: Clinical history is important in effective diagnosis of the disorder. Treating providers should inquire about co-morbid psychiatric conditions and be mindful that not all patients will explicitly disclose that they engage in the behavior. Additionally, a complete dermatologic exam should be completed. With appropriate lighting, inspection should be performed for nails that are uneven or short, nail folds in distinct stages of healing, and potentially absent or damaged cuticles [44]. Similar to the previously mentioned BFRBs, a combination of pharmacologic and non-pharmacologic options exist for managing onychophagia. Additionally, the complicated nature of the disorder makes it difficult to treat and calls for a multidisciplinary team in successful management, which may consist of dermatology, psychiatry, internal medicine, dentistry, and pediatrics [44].
   (iv) Treatment: Importance is placed on evaluating individual patient awareness of his or her nail-biting habit and level of motivation for treatment,

as the factors are essential in successfully facilitating elimination of the behavior [47]. As such, it has been found that habit reversal therapy (HRT) has been effective in treating the nail-biting disorder through increased awareness and implementation of alternative response training [48]. In a study conducted to evaluate the effectiveness of HRT on 40 young adults with onychophagia, investigators found the therapy resulting in significantly decreased behavior during follow-up [49]. Additionally, Sun et al. mention the therapy may not fully address the underlying psychosocial causes of the behavior and found auricular acupressure to be a more successful option when used as an adjuvant compared to just HRT, alone [50]. Marouane, et al. report the successful treatment of onychophagia through the implementation of a fixed oral appliance by making the behavior difficult and uncomfortable to perform [51]. Application of nail lacquer, a bitter-tasting substance, is another example of treatment aiming to reduce the behavior through aversion therapy [52, 53]. Evidence on the use of pharmacotherapy for the treatment of onychophagia is limited with evidence that fluoxetine and clomipramine may be effective options [54, 55]. N-acetyl cysteine (NAC) was investigated as a potential option for treatment of nail-biting in a randomized double-blinded controlled trail, but failed to show a positive response compared with placebo [56].

C. Factitious Disorders: This category in the psychodermatologic classification system represents conditions where damage to the skin is self-induced, without evidence of clear external incentives. Additionally, patients with factious disorders deny the behavior in order to maintain the role of a sick patient [57]. Factitious disorders are distinct from malingering, where a intentions of secondary gain are present, and Munchausen syndrome, which is similar but typically involves a comprehensive history of hospital/clinic visits, a more dramatic narrative, and multiple organ involvement [58].

1. Dermatitis Artefacta (DA),:also referred to as factitious dermatitis and artefactual skin disease, is a psychocutaneous condition similar to SPD in that there are self-induced skin lesions. However, patients with DA implement the use of specific tools to facilitate the process such as knives, tweezers, or needle [59]. Additionally, patients with OCRDs do not always deny the behavior and engage in the compulsive, repeated behavior due to an underlying psychopathologic mechanism [60]. Several psychosocial causes may cause DA such as emotional disturbances, interpersonal relationship problems, and unconscious stimuli [61]. Careful history taking and physical examination is vital in diagnosing DA as the cutaneous lesions can vary in appearance and may even resemble similarly presenting inflammatory conditions [62]. Mohandas et al. report ninety-three percent of patients with dermatitis artefacta were successfully managed within a combined multidisciplinary clinic consisting of psychological interventions in addition to dermatologic and psychiatric care [63]. Additionally, dermatologists should be aware that some

patients may reject a referral to see a mental health provider. In such cases, it is advised to maintain supervision with continued follow up to generate trust and build a strong patient-physician relationship, and eventually introduce psychological treatments [64]. Specific psychopharmacologic medications should be prescribed after careful identification of underlying psychiatric condition(s). For example, SSRIs are suggested for patients with DA and underlying depression, while TCAs are indicated for patients that may have accompanying itching, insomnia, and pain [65]. In conjunction with medication, psychological therapy is indicated and beneficial for patients with DA. Specifically, CBT and psychotherapy have shown to be effective for some patients with the disorder [61]. Wound care may also be indicated for select patients consisting of topical or oral antibiotics for secondary infections, occlusive dressings to prevent future damage, and analgesics for associated pain [66].

2. Psychogenic purpura is a very rare condition that also may be referred to as Gardner–Diamond Syndrome, autoerythrocyte sensitization syndrome, painful ecchymosis syndrome, or painful bruising syndrome. The limited available information regarding the condition indicates that it more commonly affects woman with a history of psychiatric illness such as anxiety, depression, or OCRDs [67]. For the majority of reported cases, a heightened emotional state, severe stress, or emotional trauma occurs immediately prior to the physical cutaneous findings [68]. The presentation consists of bruising and multiple erythematous patches that progress to ecchymosis within a 24 hour period [69]. The lesions vary in location and are preceded with pain, pruritus, and/or warmth of the area [70]. The exact cause and pathophysiology is currently unknown with several possible mechanisms exist, including autoerythrocyte sensitization, factitious disorder, and conversion reaction [71]. In order to rule out other hematologic conditions in the differential, comprehensive labs including blood coagulation values and hemostatic tests, are vital as they are generally negative in psychogenic purpura [72]. A diagnostic test reported to be reliable in cases where positive is a intracutaneous injection of the patients washed erythrocytes in suspension [73]. There is no specific treatment for the condition, however, it is important to treat any underlying psychiatric illness and provide symptomatic therapy with antihistamines or corticosteroids [74].

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Chapter 10
Cutaneous Sensory Disorders

Introduction

Patients with unpleasant skin sensations without a definitive diagnosis of cutaneous disease or psychiatric illness are classified under cutaneous sensory disorders. Patients falling under this category often experience symptoms like itching, stinging, burning, crawling, or pain (allodynia) [1]. Similar to primary psychiatric disorders, cutaneous sensory disorders exhibit a no observable underlying inflammation to accompany the unpleasant cutaneous sensations [2]. The lack of comprehensive understanding and commonly chronic nature of this category of conditions within psychodermatology, makes patient management particularly difficult. This chapter focuses on the current understanding of specific cutaneous sensory syndromes and available treatment options.

Pruritus and Chronic Idiopathic Pruritus

A. Classification

The desire or action of scratching is often initiated by the unpleasant sensation commonly referred to as pruritus. There are several options to categorize pruritus, Twycross et al. have proposed the most widely used classification system with four primary categories [3]. Pruritoceptive itch originates in the skin and follows a pathological process involving pruritogens (like neuropeptides, cytokines and opioids) causing skin changes like inflammation or dryness [4]. Neuropathic itch occurs due to processes like tumors or post-viral neuralgia that cause physical lesions found within the central or peripheral nervous system [3]. In contrast, neurogenic itch lacks a neural pathology but exhibits a central origin. This category develops primarily as a result of circulating pruritogens that cause an abnormal central excitation or altered

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peripheral sensory processing [3]. Finally, psychogenic itch is a category of disorders like tactile hallucinations and delusional parasitosis that encompass pruritus influenced by psychological factors.

B. Pathophysiology & Etiology of Pruritus

Several mediators (like prostaglandins, histamine, proteinases, neuropeptides, cytokines, bile salts, etc.) have been identified in playing a role the initiation and exacerbation of the itch sensation. For example, endogenous opioids like endorphins act peripherally and centrally to precipitate pruritus [5]. PGE-2 is a prostaglandin that lowers the threshold and potentiates the itch sensation when provoked by histamine [6]. Studies show histamine administration causes the activation of areas of the inferior parietal lobe involved in planned movement [7]. The urge to scratch could be mediated through synaptic transmission of these areas to the motor cortex. The perception of itch has also been associated with psychological conditions like stress and depression [8]. These altered mental states can lower the itch threshold through hemodynamic changes like changes in blood flow and body temperature that promote the peripheral release of histamine, neuropeptides, and inflammatory mediators. For example, studies indicate a possible association of depression with pathways that increase central opiate levels and heighten the perception of itch [9].

Pruritus is one of the most commonly reported symptoms by dermatology patients and has a wide variety of potential causes that can be categorized into cutaneous, neurological, medical, or psychiatric origin as shown in Table 10.1. Due to the multiple categories of pruritus, the proper diagnosis and management of patients requires a thorough history and physical examination. With careful evaluation and medical work-up, misdiagnosis can be prevented particularly in cases of pruritus that are easily treatable such as vitamin deficiency or drug toxicity.

Itch is unfortunately a commonly observed symptom in psychiatric patients, with up to 42% of patients exhibiting idiopathic itch, particularly in individuals with increased emotional temperament and history of difficulty managing anger [10]. Neurologic causes of pruritus should also be considered in the diagnosis of psychogenic pruritus as they can present without evidence of skin lesions. Although psychogenic and neurologic pruritus can manifest together in a mixed clinical presentation, distinct features can be utilized to successfully differentiate and reach a more concrete diagnosis. Neurogenic pruritus commonly involves a chronic course, is greater severity/ intensity, exhibits a unilateral or bilateral presentation, is associated with sensory phenomenon like allodynia, dysesthesia, and hyperpathia, can be accompanied by paroxysmal constant pain in the same area, and can disrupt sleep [11]. In contrast, psychogenic pruritus is characterized as sharing a temporal relationship with psychiatric symptoms and exhibits a paroxysmal nature with increasing severity, sudden onset/ resolution, or intervening periods free of symptoms [12].

1. Treatment

The psychopathophysiology of a patient's pruritus provides valuable insight into choosing an ideal treatment regimen best suited to target the underlying cause. There are several classes of pharmacologic treatments implemented in the treatment of

Table 10.1 Classification of pruritus

Categorization of Pruritus	Examples
Pruritus Associated Medical Disorders	Chronic lymphocytic leukemia Polycythemia vera Malignant melanoma Syphilis Congestive heart failure Diabetes mellitus Vitamin B12 deficiency Pellagra, Myxedema Hyperparathyroidism Chronic renal failure Hepatic disease Acquired immunodeficiency virus (AIDS) Drug toxicity Old age
Pruritus Associated Neurologic Disorders	Dementia Multiple sclerosis Parkinson disease Huntington disease Neurofibromatosis Aneurysm Cerebral infarctions CNS tumors.
Pruritus Associated Psychiatric Disorders	Anxiety disorders Obsessive-compulsive disorder (OCD) Major depression Psychosis

pruritus that differ in mechanism and efficacy. For patients with pruritus and underlying anxiety, depression, and obsessive-compulsive spectrum disorders, selective serotonin re-uptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) have shown the most effectiveness [13].

The SSRI antidepressants that have been used to treat pruritus include sertraline, paroxetine, fluvoxamine, fluoxetine, citalopram, and escitalopram. Since the SSRIs all have a similar mechanism of action, use of options like citalopram and escitalopram that have fewer adverse drug reactions, are preferred [14]. Doxepin (a TCA) has been successful in the treatment of pruritus through its high affinity and antagonistic activity against histamine receptors [15]. Studies have found doxepin to be efficacious in treating patients with urticaria associated wheal and itch response [16, 17]. Amitriptyline is also TCA that is known for its superior effectiveness as an analgesic agent and may also be helpful in the treatment of itching associated with pain. However, the overall use of TCAs is limited because SSRIs lead to fewer adverse effects and a greater overall efficacy [18]. In the class of atypical antidepressants, mirtazapine is the only noradrenergic and specific serotonergic antidepressant that has been used as an antidepressant, anxiolytic, and antipruritic agent. It is specifically useful in treating patients with nocturnal pruritus due to its sedative properties.

Antipsychotics like pimozide, risperidone, olanzapine, and quetiapine are implemented in pruritus associated with delusions or psychosis that have no histamine involvement [19]. However, patients with pruritus related to delusions or psychosis are commonly treated with antipsychotic agents combined with other agents like SSRIs. SNRIs, or antihistamines for increased efficacy [15].

The opioid receptor system has been shown to have a relationship with the processing of pruritus. Studies have shown Naloxone and Naltrexone, mu opioid receptor antagonists, to be effective in the treatment of pruritus. In addition, other pharmacologic agents like butophanol (kappa receptor agonist and mu receptor antagonist) and methylnaltrexone (peripheral mu receptor antagonist) have shown to reduce pruritus associated with intravenous morphine administration [20].

Gabergic agents like gabapentin and pregabalin have been implemented in the treatment of pruritus and work through the modulation of excitatory neurotransmitter release. In addition, gabapentin has been found to inhibit the release of substance P (an itch mediator) and calcitonin gene-related peptide [21]. These medications have been effective in many conditions that cause itching like prurigo nodularis, neuropathic itch, uremic pruritus, and lichen simplex chronicus. Pregabalin, in particular, is reported to be more effective in the treatment of itch associated with fibromyalgia [22].

The use of Benzodiazepines under the class of anxiolytics, like alprazolam and clonazepam, are effective in treating patients with pruritus that is aggravated by stress. Specifically, in conditions that are reactive to stress like atopic dermatitis and psoriasis, studies show that benzodiazepines are successful in reducing flares [23]. The use of medications acting as neurokinin receptor (NRK)-1 antagonists have also been implemented in the treatment of pruritus. For example, a study investigating the efficacy of NRK-1 antagonist aprepitant in chronic pruritus that has shown no response to conventional treatment methods found itch intensity was reduced in 80% of the patients enrolled [24].

Patients with conditions exhibiting pruritus symptoms commonly have psychiatric comorbidity such as depression and anxiety. As such, psychotherapeutic interventions have shown to be effective methods of reducing itch and improving quality of life. Improved patient understanding and awareness of their disease along with conscious acknowledgment of specific aggravating factors of itch perception and secondarily elicited emotions, can improve disease severity. The use of psychoeducation and psychotherapeutic techniques (cognitive behavioral therapy and habit reversal training) in addition to support groups can reduce long term complications of pruritus by preventing the continuation of the itch-scratch cycle. For example, a study conducted by Chida et al. examining the effects of psychological interventions on atopic dermatitis found that the psychotherapeutic techniques reduced itch severity and intensity [25].

Glossodynia

Glossodynia or burning mouth syndrome is a chronic condition causing uncomfortable sensations of pain and burning of the oral mucosa. The condition, predominantly affecting peri- and postmenopausal woman, has an unclear etiology but may have a neuropathic and/or psychiatric cause [26]. Affected individuals may also

experience dryness of the mouth, paresthesias, as well as altered smell and taste [27]. Trikkas et al. report patients with glossodynia have significant differences in their psychological profiles when compared to controls that were matched for sex and age [28]. Specifically, authors report individuals with the condition displayed more introverted hostility and had higher levels of neuroticism, when compared with healthy controls [28]. Additionally, another study administered questionnaires and found that patients with glossodynia were significantly more extroverted and alexithymic, when compared to controls [29]. Further studies are required to better understand whether a specific psychopathologic process is involved in development of glossodynia. Additional potential causes of the condition include vitamin deficiencies, candida glossitis, and hormonal imbalances particularly around menopause [30].

Although this chronic condition causes significant negative effects on overall the quality of life of affected individuals, there is no available curative treatment strategies and current methods of management provide only symptomatic care [31]. Assisting afflicted patients in improving their quality of life can be challenging. It is recommended that the provider be knowledgeable of the condition's diverse presentations and maintain an empathetic, patient tone while caring for individuals with the condition [32]. Combined with symptomatic care, a strong patient-physician relationship can facilitate the process of developing essential coping strategies to deal with the chronic nature of glossodynia.

Vulvodynia

Vulvodynia is a chronic condition characterized by idiopathic chronic pain of the vulva and is classified based on: the location (generalized, localized, or mixed), if it exhibits a temporal pattern, whether it is spontaneous, provoked, or mixed, and if the onset is primary or secondary in nature [33]. Overtime, vulvodynia has shown to very common and the incidence may be under-reported due to patient apprehension in seeking treatment from embarrassment, as well as lack of knowledge and discomfort in managing patients by the physician [34]. As such, physicians are urged to educate themselves on the condition as a valid diagnosis and establish good rapport with empathy by validating the patients experiences with the life-altering condition. The several reported associated factors of vulvodynia including psychosocial co-morbidity, musculoskeletal involvement, and neuro-proliferation, indicate that the condition may encompass several, possibly overlapping disease processes manifesting as a cluster of diverse symptoms [35]. Woman with vulvodynia have sexual dysfunction and problems with interpersonal relationships as regions of the vagina become sensitive to light touch and the abnormal contractility of the pelvic floor muscles [27]. Once vulvodynia is suspected, treating physicians are advised to perform a careful physical examination and patient history as a lack of findings assists in ruling out potential organic causes [36]. Although further research is required to make more concrete recommendations, Goldstein et al. report treatment of vulvodynia calls for a multidisciplinary approach with symptomatic care through topical or oral agents, pelvic floor physical therapy, psychological therapy, and vestibulectomy [37].

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Chapter 11
Common Psychotropic Treatments Used in Dermatology, How and When to Use

Introduction to the Management in Psychodermatology

In psychodermatology, the dermatological treatment should be conciliated with the approach to the psychopathology, taking into account the presence of a skin disease or a skin illness, the type of skin lesions, the psychopathology behind them (Figs. 11.1 and 11.2), secondary psychiatric comorbidities and the severity. For example, in the setting of the anxiety or depression, several scales could be useful to assess the severity of the symptoms, such as, the Hospital Anxiety and Depression Scale (HADS) and then to define the treatment strategy: when the patient presents normal scores, no psychotropic treatment or psychotherapy would be required; when there are low scores of anxiety and depression, a psychotropic could be introduced, but psychoeducation and simple strategies of cognitive behavior therapy could be enough and taught by the general clinician or the dermatologist; in the context of moderate to severe symptoms of anxiety and depression, risk evaluation, including for suicidal ideation, becomes even more central, psychotropic treatment should be introduced and psychotherapy should be considered to complement the treatment, which would be ideally conducted by a psychodermatology team [1]. Psychotropic treatments include: antidepressants for depression, chronic anxiety, the obsessive-compulsive spectrum and somatic symptoms and for sleep disorders; a benzodiazepine or hydroxyzine for acute anxiety and sleep problems; antipsychotics for delusions, impulsive and dissociative disorders; antiepileptics, with beneficial effects for anxiety, sleep, irritability and as mood stabilizing [2, 3].

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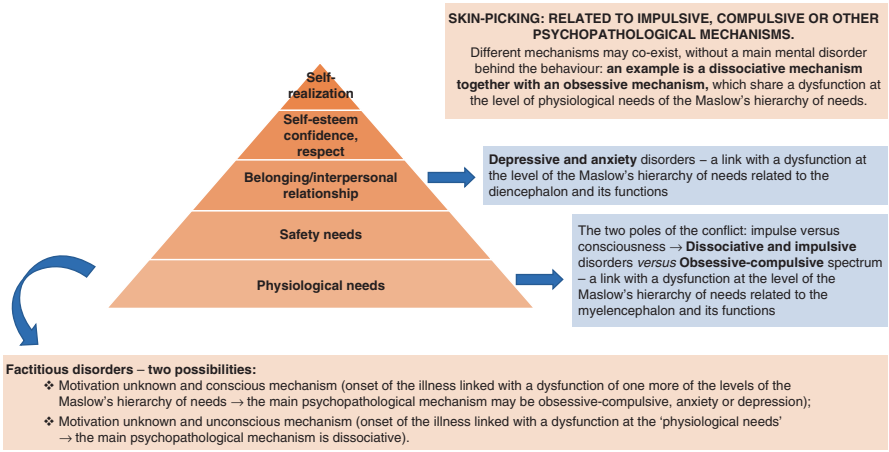

Fig. 11.1 Dysfunction of Maslow's hierarchy of needs linked with specific psychopathology and brain divisions as suggested by Pio-Abreu [17], here with an amplified concept to explain how several psychiatric comorbidities may co-exist in the same patient with self-inflicted skin lesions, presented by Ferreira to the European Society for Dermatology and Psychiatry Subspecialty/ International Society Meeting, in 2018

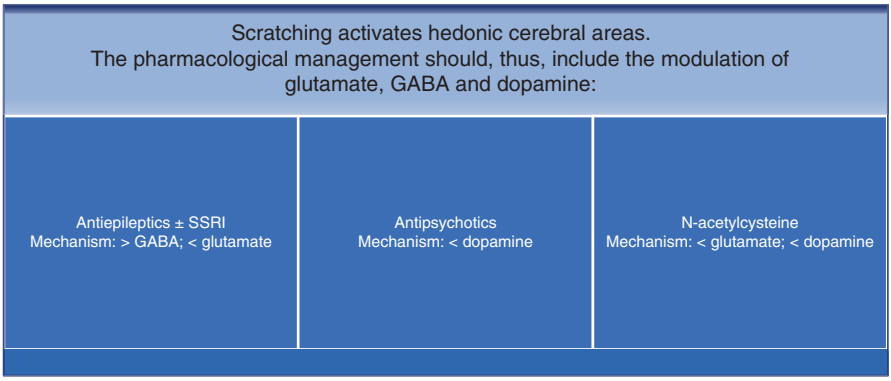

Fig. 11.2 Other treatment options for self-inflicted skin lesions described in the literature [10, 11, 20, 21]

General Principles for the Use of Psychotropic Treatments in Dermatology

Adequate management requires to define the psychopathology correlated with the dermatosis (skin disease) or the skin illness and to take into account the particularities linked with the different psychodermatologic disorders, the psychotropic treatments, other pharmacologic treatments as well as the psychotherapies that are available.

A. **Type of psychopathology linked with the skin diseases or illness**

To choose the treatment, it is important to define the psychopathology behind [4–8]:

- *Psychophysiological disorders (such as, psoriasis and urticaria) are commonly linked with anxiety and depression, that can cause or worsen the dermatosis;*
- *Psychogenic pruritus, vulvodynia and glossodynia may be linked with anxiety, depression and also milder degrees of dissociation may play a role;*
- *Self-inflicted skin lesions may be linked with a wide spectrum of psychopathology: obsessive-compulsive, anxiety, depression, dissociative;*
- *Body dysmorphic disorder (obsessive-compulsive spectrum): for example, some patients with acne excoriée;*
- *Delusional infestation, which includes Morgellons and Ekbom diseases (psychotic spectrum).*

Anxiety is a common comorbidity and it should be differentiated in acute and chronic [2, 9]

- Acute anxiety lasts 2 months or less and both acute and chronic anxiety can respond to psychotherapy and/or medication. Chronic anxiety should ideally combine psychotherapy with a pharmacological treatment.
- Acute anxiety in psychodermatology can be managed with:
  - a benzodiazepine, with slow tapering (an option is diazepam, with less risk of rebound anxiety and is good for somatic symptoms);
  - hydroxyzine, which can also have slight neuroleptic effect (of benefit if slight psychotic symptoms are also present).
- Chronic anxiety in psychodermatology can be managed with:
  - a selective serotonin reuptake inhibitor (SSRI).

Depression is another common comorbidity in psychodermatology, whose treatment with a psychotropic should follow these basic principles [2, 9, 10]

- Symptoms of hypomania and mania should be excluded before starting the treatment and these patients should be managed by a psychiatrist;

- Patients presenting risk criteria, such as, suicidal ideation or psychotic symptoms should also be managed by a psychiatrist;
- When depression is linked with self-inflicted skin-lesions and pruritus, an SSRI is a good choice;
- Serotonin and norepinephrine reuptake inhibitors (SNRIs) are also good options when there is a depression related to a dermatosis or somatic symptoms and related disorders;
- The therapeutic response can be only observed after 6–8 weeks;
- In the beginning of the treatment there is a risk for suicidal ideation;
- Antidepressants should be continued for 6–9 months after clinical response if depression is diagnosed for the first time, but longer when there are relapses and also depending on the characteristics of each patient;
- The withdrawal symptomatology may be observed after abrupt discontinuation, so, antidepressants should be tapered over 2 weeks; withdrawal symptoms are more common with venlafaxine and paroxetine.

SSRI are largely used in psychodermatology, where they should be considered for [5, 9, 10]:

- Psychogenic pruritus or vulvodynia or glossodynia or other somatic symptoms and related disorders where anxiety or depression contribute to the etiopathogenesis of the skin illness;
- Psychophysiological dermatoses, also having impact on the etiopathogenesis of pruritus (through modulation of the serotonin transporter protein in dendritic cells), namely in psoriasis;
- There is chronic anxiety or depression as a consequence of a chronic dermatosis;
- Self-inflicted skin lesions as a result of anxiety, depression or symptoms in the obsessive-compulsive spectrum.

SSRI – examples, posology in psychiatry and side effects [2, 9, 10]

- Escitalopram – the dose range in the literature (starting dose and therapeutic dose) is 5–20 mg/day; few side effects and few drug interactions; it can present slight sedative effect and also sexual dysfunction; there is no weight gain;

- Fluoxetine – the dose range in the literature (staring dose and therapeutic dose) is 10–80 mg/day; it presents the longest half-life and, then, it is good for patients who may forget some doses; there is no sedating effects and there is an activating effect; sexual dysfunction also occurs; there is no weight gain;
- Because SSRI can induce an initial increase of anxiety and take 3–6 weeks to work, a short-term treatment with a benzodiazepine or hydroxyzine should be added;
- Gastrointestinal symptoms, sweating and sexual dysfunction may occur.

Antiepileptics in psychodermatology [3, 11, 12]

- Gabapentin, pregabalin and topiramate potentiate the effects of the gamma-aminobutyric acid (GABA) and they are frequently used;
- Gabapentin and pregabalin have as principal mechanism the decrease of the synaptic release of glutamate through the bind to the voltage-gated calcium channels in the pre-synaptic neurons;
- The dose range in the literature in psychiatry is: 50–600 mg/day for pregabalin, 300–3600 mg/day for gabapentin, 50–200 mg/day for topiramate;
- Antiepileptics should be slowly tapered;
- Some examples in psychodermatology:
  - Cutaneous sensory disorder:

    Glossodynia;
    Vulvodynia;
    Scalp dysesthesia;

  - Self-inflicted skin lesions;
  - Prurigo nodularis and lichen simplex chronicus;
  - Palmar-plantar hyperhidrosis;
  - Chronic urticaria and flushing linked with posttraumatic stress disorder.

Antipsychotics are considered in different psychiatric disorders [13]

- Delusional infestation;
- Psychotic symptoms linked with depression and obsessions (some patients with body dysmorphic disorder);
- Dissociative (for example, some patients with self-inflicted skin lesions);
- Impulsive (some patients with skin-picking – some cases of trichotillomania).

Examples of antipsychotics, posology in psychiatry and side effects [2, 10, 13]

- Risperidone – the dose range in the literature (starting those and therapeutic dose) is 0.5–6 mg, at bedtime or dose divided; prolactin levels may increase with risperidone, which can be used to assess adherence to the treatment;
- Aripiprazole – the dose range in the literature (starting those and therapeutic dose) is 5–30 mg, daily; it is slightly less effective, but it presents a lower risk of weight gain and it is less sedating; it may also present a lower risk of cerebrovascular accident in elderly than other antipsychotics;
- The discontinuation of an antipsychotic should be very slowly, over several weeks;
- There is an increased risk to develop metabolic syndrome with atypical antipsychotics which should be monitored;
- Extrapyramidal symptoms should be assessed, mainly with typical antipsychotics;
- An electrocardiography should be done, especially with some antipsychotics, namely, haloperidol and pimozide, due to the risk of increasing the QT interval.

B. **Special considerations based on the skin disease or skin illness**

Self-inflicted Skin Lesions

They include denied self-inflicted skin lesions and skin-picking syndromes. Although classically classified in the obsessive-compulsive spectrum, skin-picking has a wide differential diagnosis and spectrum of psychopathology. It should be excluded: pruritus, psychiatric diagnoses (such as, delusional infestation), an infestation or a primary dermatosis (prurigo nodularis-like lesions can be observed in the early-phase of bullous pemphigoid; in the setting of a bizarre pattern of alopecia, alopecia areata, in the differential diagnosis of trichotillomania) [14–16].

Patients with skin-picking may have different psychiatric comorbidities [4, 5]

- Anxiety, depression, obsessive-compulsive, dissociative and/or impulsive.

Skin-picking linked with anxiety, depression, obsessive and impulsive symptoms [5, 11, 18, 19]

- If mild anxiety or depression, strategies of cognitive behavioural therapy (CBT) help and can be taught during the consultation of general medicine; SSRI should be started in more severe cases together with CBT by a trained

psychologist;
- For obsessive-compulsive symptoms: SSRI and CBT should be combined;
- For impulsive symptoms: CBT, antipsychotics (such as, olanzapine) and/or some antiepileptics may be considered, depending on the severity;
- Wound care with adapted dressings for the wounds (secondary skin lesions), such as, hydrocolloid dressings, and bandages are helpful to avoid picking behavior.

Self-inflicted skin lesions linked with a dissociative mechanism [5, 19]
- The anxiolytic effect of the antipsychotics can be useful;
- Other psychiatric comorbidities (depression, anxiety) should be treated and the patient will feel that the focus is the "psychological stress" that the skin lesions has caused on him, instead of the genesis of the lesions;
- Skin lesions are a "way of crying for help" and confrontation is not advisable;
- Psychodynamic psychotherapy has benefit and can be later suggested;
- Wound care is pivotal; besides, occlusion is a good diagnostic and therapeutic tool to show, in a non-judgemental way, that no additional lesions will appear.

Somatic Symptoms and Related Disorders

Treatment of psychogenic pruritus [22–25]
- Systemic etiologies for pruritus should always be excluded;
- Psychiatric comorbidities should also be excluded and managed, namely, anxiety, depression, delusion: to consider SSRI, tricyclic antidepressants (doxepin), risperidone;
- H1 anti-histamines, namely, hydroxyzine can help due to its sedative effects;
- Mirtazapine is a tetracyclic antidepressant, being histamine 1 receptor blocker and 5-hydroxytryptamine (5-HT) 2 and 3 receptors blocker which shows good response in the setting of chronic pruritus linked with dermatoses, malignancies and psychogenic pruritus; due to the risk of metabolic syndrome, a baseline lipid profile, the blood glucose levels and the hepatic function should be assessed before;
- It is not recommended to automatically refer the patient to a psychiatrist (this will lead to patient dropout) except if psychopathology of risk is present;

- Psychogenic itch may be accompanied by scratching and, in these cases, the pharmacological management should include the modulation of glutamate, GABA and dopamine: antiepileptics, antipsychotics and N-acetylcysteine;
- Skin care is pivotal, as this is the focus of concern of the patient, such as, capsaicin cream and emollients;
- When only psychological conflicts are present, pruritus can be linked with milder degrees of dissociation, then psychodynamics would be a good option.

Treatment of vulvodynia described in the literature [10, 26]

- There is a controversy as to whether psychological, social and sexual distress cause or result from the patient's pain – either way, these factors must be addressed, preferably in collaboration with a psychologist;
- Psychotropic treatment may include a tricyclic antidepressant;
- An antiepileptic is also an option, alone or combined with other psychotropic, depending on the clinical response, severity and related psychopathology;
- The treatment should take into account the psychiatric comorbidities: for example, an SNRI may be an option in the setting of depression;
- Pelvic floor physical therapy should be considered.

Treatment of glossodynia described in the literature [27–31]

- Do not forget to eliminate allergic contact stomatitis, autoimmune disease, gastroesophageal reflux, nutritional deficiency (thiamine, riboflavin, pyridoxine, folate, cobalamin, iron), hypothyroidism;
- Clonazepam "swish and spit" may be considered;
- Background of depression and/or chronic anxiety: SNRI or SSRI are options;
- Patients presenting cancerophobia, which is not seldom seen in glossodynia, may benefit of adding an antipsychotic;
- Supplementation with alpha lipoic acid can also be considered.

Examples of psychotropic drugs described in the literature to be considered for glossodynia and/or vulvodynia and their side effects [2, 10, 26, 32]

- Amitriptyline: sedating and sexual side effects; risk of weight gain; an electrocardiography should be performed before starting the treatment;

- Duloxetine and venlafaxine: sexual dysfunction can occur, but less severe than with SSRI or amitriptyline; activating effect; no weight gain; blood pressure should be monitored;
- Paroxetine: presence of anticholinergic effects; possible weight gain and sexual dysfunction; reported risk of breast cancer; higher risk of cardiovascular anomalies in infants of mothers who are taking this SSRI compared to other antidepressants in the first trimester;
- Pregabalin and gabapentin: sedating effect; possibility of sexual dysfunction as well as weight gain.

Delusional Infestation

It includes Morgellons disease (a delusional infestation linked with inanimate matter) or Ekbom syndrome (delusional parasitosis). The patients present a fixed, false belief that there is a skin infestation, corresponding to a somatic type of monosymptomatic delusional disorder. They may present self-inflicted skin lesions, but delusional infestation is a separate diagnosis since the main component is a psychotic disorder. Secondary etiologies for a delusional infestation should be excluded, including, a systemic condition, such as, a thyroid disease, schizophrenia and some clinical presentations of depression and medications that can also induce similar symptoms, such as, illicit drugs, anti-parkinsonian treatments, some antibiotics and antiepileptics as well as corticosteroids [8, 33].

Psychotropic treatment of delusional infestation suggested by the literature [33–36]

Second-generation antipsychotics, namely:

- Risperidone – dizziness and QT interval prolongation as possible side effects;
- Olanzapine – risk of metabolic side effects;

Other antipsychotics that can be considered:

- Aripiprazole – better side effects profile, but less strong clinical evidence;
- Paliperidone – few cases reported;
- Pimozide – good efficacy, but poor safety profile, namely, the risk to prolong the QT interval and increased risk of extrapyramidal symptoms;
- Quetiapine – good efficacy, anticholinergic effects, somnolence and orthostatic hypotension as possible side effects;
- The results of the treatment may be observed after 1–2 weeks of treatment, with a more clinical expression after 1–2 months;
- These patients may also present secondary psychiatric comorbidities, that should be also excluded and managed, including, anxiety and depression;
- To introduce the treatment, the focus should also be the skin, the benefits on the skin sensation and the skin care should be done accordingly, depending on the eventual presence of secondary skin lesions (excoriations, erosions).

Body Dysmorphic Disorder

It means a psychiatric illness characterized by excessive and impairing preoccupations with defects in the body appearance that do not exist or that are really minor defects. At the same time, these patients perform repetitive behaviors in order to confirm, to look at or to try to correct the defect. It is placed in the obsessive-compulsive spectrum, although some patients may also exhibit psychotic symptoms (delusion), which should be identified to adapt the treatment [6, 38].

Treatment of body dysmorphic disorder suggested by the literature [10, 37, 38]

- Several studies have documented the effectiveness of:
  - Fluoxetine;
  - Clomipramine;
  - Escitalopram;
  - Citalopram;
- In the setting of a slight clinical presentation, cognitive behavioural therapy (CBT) or an SSRI can be considered a first choice;
- In the setting of a moderate or severe clinical presentation, a combination of CBT and SSRI are recommended;
- The dose of SSRI follows the recommendations of the treatment of obsessive-compulsive disorder, being normally higher than those used for depression;
- There is a high risk of relapse when the SSRI is stopped;
- Antipsychotics should be considered together with SSRI when psychotic symptoms are also present, as an augmentation treatment, such as, aripiprazole, quetiapine, risperidone and olanzapine;
- N-acetylcysteine was also suggested as an augmentation treatment;
- Patients with body dysmorphic disorder should be managed by a psychiatrist together with a psychologist trained in CBT or by a psychodermatology team;
- The prescription of the skin treatments or the realization of the surgeries and cosmetic interventions that are asked by these patients may worsen the psychiatric illness and they are not recommended.

Final Reflections: Psychotropic and Psychobiotic

In 1908, Metchnikoff firstly introduced the concept of probiotic. Since then, several studies have documented that there is a gut-brain-microbiota axis which significantly interferes in the brain physiology and, as a consequence, in the mechanisms

of psychopathology [39]. As discussed in Chap. 2, psychobiotics are live bacteria or prebiotics, which modulate a bacterially-mediated effect in the brain, that, when ingested, could induce benefits in terms of mental health, with therapeutic relevance for psychiatric disorders. This happens as these live organisms are able to produce relevant neurotransmitters involved in the mechanisms of depression and anxiety, being involved in the connection between the brain and the gut [40, 41]. Interestingly, it was shown that *Lactobacillus* can produce acetylcholine and, together with *Bifidobacterium* species, also produce GABA; *Bacillus* can produce dopamine and norepinephrine. Furthermore, it was demonstrated the beneficial effects on psychological stress after the treatment with probiotics which contained *Lactobacillus acidophilus*, *Lactobacillus casei* and *Bifidobacterium bifidum* [42]. They present an antidepressant and anxiolytic effect, thus, a psychotropic effect, so that they could be considered a new class of psychotropic treatment, being currently under research as direct or complementary treatments for psychiatric disorders [43, 44]. Thereby, psychobiotics may be considered in the management of pychodermatologic disorders, namely those linked with anxiety and depression, especially the psychophysiological disorders.

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Chapter 12
Principles of Psychotherapy Applied to the Psychodermatologic Disorders

The successful management of patients with psychocutaneous disease involves appropriate acknowledgement and understanding of the psychiatric undertones, occupational context, social contributions of the condition. Each patient presenting with a psychodermatologic condition has a unique narrative and history, that is important in empathetically eliciting as it may be contributing to the cutaneous disease pathology. This careful, individualized understanding can facilitate genuine, holistic care through incorporation of traditional treatment options in combination with non-pharmacologic therapy. In this chapter, specific psychotherapeutic options commonly implemented in psychocutaneous medicine are discussed. Before introducing therapies, however, it is important to assess that the individual is trusting and has willingness to initiate treatment(s). In dermatology, indications for psychotherapy include: worsening disease-related symptoms that are under chronic or acute stress, increased secondary social avoidance and anxiety, if a possible cause of body dysmorphic disorder is suspected, and when pronounced skin manipulation or self-harm is observed [1].

Cognitive Behavioral Therapy (CBT)

This therapy seeks to uncover and challenge negative thought patterns about oneself and society that may be contributing to physical disease development. CBT is useful in identifying and altering the presence of dysfunctional thinking in patients' day to day lives. As a result, positive changes in behavioral and emotional responses can be successfully observed. For example, the therapy can target undesirable behaviors or psychiatric conditions such as anxiety and depression. The improvement of these psychological conditions is made through alteration of the mechanistic progression of specific thoughts transforming into emotions, and emotions into behaviors. Depending on the individual patient characteristics and overall disease severity, the number of sessions can vary greatly. CBT is useful in psychophysiologic conditions

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where the specific dermatologic condition is triggered or exacerbated in the presence of a heightened emotional state or stressful life events. Additionally, it can also improve secondary psychiatric conditions that develop from visibly altering cutaneous disease. For conditions without a readily available treatment or with medications resulting in undesirable outcomes, CBT can be useful. By bringing dysfunctional thought processes to light and reducing their occurrence, patients can improve their ability to accept and cope with their permanent conditions.

There is a growing body of literature providing evidence of successful incorporation of CBT in the management of a wide variety of patient conditions. For example, in patients with atopic dermatitis, Hedman-Lagerlöf et al. explain the potential efficacy of exposure-based CBT, as significant changes were found in post-treatment self-reported measures of symptoms and general anxiety, with no significant improvement in depression or quality of life [2]. Web-based versions of CBT have also been developed and shown to be effective. For example, in a web-based CBT software for patients with psoriasis, Bundy et al. note the strategy as time-saving for providers and patients, economically advantageous, and stigma reducing [3]. Additionally, CBT incorporated into an internet based intervention for patients with skin picking disease provides helpful information and specific exercises [4]. The therapy has shown effective by several randomized controlled trials in significantly reducing overall disease severity, along with depression and anxiety in patients with psoriasis [3, 5–7].

Habit Reversal Training (HRT)

In contrast to CBT, which is typically used in the treatment of psychophysiologic and secondary psychiatry conditions, HRT is most useful in the management of patients with primary psychiatric disorders. For example, body focused repetitive behaviors (BFRBs) within the obsessive-compulsive and related disorders (OCRDs) category of psychiatric conditions, like skin picking, hair pulling, nail biting can be managed by HRT. There are primary steps of HRT include creating awareness, relaxation training, and developing a competing response. The awareness stage is essential as the patient must become more mindful of his or her habit in order to begin the process of removing it. Implementing self-monitoring sheets are an effective tool to allow the patient to reflect on the urges to engage in the unwanted behavior, including the length of time, common locations of engagement, and possible triggers. Next, the individual is trained in relaxation techniques for relieving muscular tension through specific breathing exercises. This will assist in reducing strong urges to perform the unwanted behavior. Finally, while developing a competing response, the patient is educated on replacing the unwanted behavior with another less harmful and appropriate one. For example, an individual with trichotillomania can be taught to clench their fists or squeeze a rubber ball when they anticipate or experience an urge.

There is an increasing body of literature that provides evidence of successful patient management through HRT. For example, Teng et al. found a greater decrease in skin damage compared to control for the treatment of SPD [8]. Further, Twohig

et al. reported HRT as an appropriate treatment for chronic nail biting, as post-treatment nail length was longer when compared to control [9]. In another study evaluating the efficacy of HRT in children and adolescents with trichotillomania, Rahman et al. found a significant reduction in hair-pulling severity, although the number of responders decreased at 1-month and 3-month follow up [10]. This may indicate the need for continued follow up in the treatment of BFRBs like trichotillomania to prevent relapse. In the primary phase of HRT, use of awareness training combined with monitoring devices have shown to be effective. Particularly, Himle et al. found significant improvements in trichotillomania symptoms measured by both self-reported and physician scales following of HRT combined with an awareness enhancing monitoring device [11]. The device monitors the frequency of hair pulling behaviors and alert the user of hand to head contact.

Patients with psychocutaneous disorders often present to the dermatologist before a mental health expert and many may reject referral to a psychiatrist [12]. As such, it is essential for dermatologists to be familiar with effective management therapies for conditions like BFRBs to reduce disease-related reductions in quality of life. However, despite HRT being an effective therapy, only a small number of dermatologists truly understand how it works [13].

In psychocutaneous disease, although HRT is primarily used to treat primary psychiatric disorders, additional conditions involving habitual behaviors can also be targeted. Specifically, the therapy has been used successfully to reduce symptoms of itch in patients with atopic dermatitis by disrupting the itch-scratch cycle typically resulting in further skin damage [14]. For example, in a randomized controlled study implementing HRT in combination with potent steroids for patients with atopic dermatitis, Norén et al. found significant improvement, compared with controls [15]. Another similar study by Melin et al. found HRT in combination with topical hydrocortisone cream to significantly reduce scratching symptoms, when compared to the ointment itself [16].

Mindfulness Therapies

Therapeutic options incorporating principals of mindfulness aim to reduce psychological distress that may be contributing to a disorder's psychopathology. The practice allows for the patient to become more aware of the present moment. In doing so, he or she can begin to accept the moment for what it is, relieve unwanted anxieties contributing to the unwanted behavior, and, in turn, begin to observe genuine, desired change. The technique can be implemented both as meditation and during daily activities like eating and walking. In psychophysiologic conditions, where emotional states like stress may initiate or worsen a disease process, mindfulness can be incredibly useful. The individual gradually gains the awareness of harmful thought processes contributing to their condition, which aids as an adjuvant to pharmacologic treatment. For example, in a study investigating the use of mindfulness-based therapy in psoriasis treatment as an adjuvant treatment, found significant

improvement in both quality of life and symptom severity in patients with psoriasis [17]. In another study examining the correlation between mindfulness and psychological suffering in the dermatologic patient population, authors found the act of awareness (or mindfulness) to be the most consistent predictor of distress (inversely-related [18]. As only a handful of studies report on the use of mindfulness in the management of psychodermatologic disease, further research is warranted in order to gain a more comprehensive understanding of its efficacy.

Hypnosis

The therapy of hypnosis involves the use of specific methods to induce an alternate state of consciousness, where the individual is no longer fixated or distracted from his or her surroundings. After achieving this mental state, verbal commands or suggestions are typically used to guide an individual's emotions and behavior a certain way. In dermatology, the use of trance through hypnosis can decrease itch, pain, and alleviate psychosocial distress from harmful thought processes that may associated with cutaneous disease [19]. Although an interesting avenue of care, there is limited knowledge of its practical application in medicine. However, increasing research and attention indicates how the approach illuminates how much is currently unknown with regard to the human psyche and its manipulation in the treatment of medical conditions. Few studies exist in the literature providing evidence of implementing the therapy in the treatment of psychocutaneous disease. The use of hypnosis in the management of pain, itch, and secondary anxiety, however, shows promise. For example, in a study administering four hypnosis session to patients with burns, found significant reductions in background pain quality and pain related anxiety [20]. Ardigo et al. a note a reduction the intensity of pain and depression scores after four sessions of hypnosis, but not at 3-months follow-up, indicating consistent treatment may be needed to maintain desired outcomes [21]. These studies allude to a potential use of hypnosis in cutaneous sensory syndromes, like chronic idiopathic pruritus, vulvodynia, and glossodynia.

Biofeedback

The use of biofeedback involves bringing greater awareness of undesired behaviors or emotional states by targeting dysfunctional physiologic processes [22]. Several methods currently exist for implanting biofeedback, including surface electromyography, skin temperature, breathing quality, and heart rate reactivity [23]. The different modalities measure physiologic responses so the practitioner can better understand important psychophysiologic associations of the patient's disease process. By identifying these responses, the physician introduces techniques to train the individual to create new feedback loops and thus, regain physiologic control

[24]. Gradually, with multiple sessions and continued engagement, the patient begins to self-regulate the physiologic processes without the need for monitoring and aid from the treating physician.

Substantial literature exists implementing biofeedback in the management of a wide variety of conditions like urinary incontinence [25, 26] and migraines [27, 28]. Current evidence points to psychophysiologic conditions as the primary target of biofeedback therapy. For example, Piaserico et al. combined biofeedback and CBT with narrow band ultraviolet B therapy and found significant improvements in the disease severity and improvement in quality of life in patients with psoriasis [29]. Specifically, with regard to the biofeedback portion for the intervention, the researchers implemented multiple feedback modalities including electromyographic, muscle tension, sweat gland activity, changes in peripheral blood flow, breathing, and heart rate [27]. Furthermore, Duller et al. demonstrated the use of biofeedback to reduce excessive sweating in patients with hyperhydrosis and concluded relaxation as the primary target. Similarly, another study combining biofeedback-assisted relaxation with cognitive imagery, found a significant reduction in acne severity after 12 sessions over 6 weeks of treatment [28]. Additionally, studies providing evidence of the stress reducing potential of biofeedback-based training support continued research and its further utilization in the treatment of psychophysiologic dermatoses. In a study [29] investigating the impact of biofeedback on stress, for example, found significant increases in brain matter associated with the stress response and coping skills following treatment, compared to control. In conditions like acne, psoriasis, and atopic dermatitis, where stress plays a significant role in disease progression and exacerbation, such studies offer great potential in further application.

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