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The impact of external factors on psoriasis

Review

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Abstract

Psoriasis is one of the most common chronic inflammatory skin diseases, constituting a significant health and socioeconomic problem. Despite numerous therapeutic options, the results of treatment very often remain insufficient. It is extremely important to remember that many external factors impact the effectiveness of therapy. This article discusses the importance of emollients in therapy and the influence of infectious agents and injuries on the course of psoriasis. Understanding the above-mentioned factors in the treatment of psoriasis is critical to achieve satisfactory therapeutic effects.

Keywords

psoriasis • psoriatic arthritis, lifestyle • emollients • mechanical trauma • Koebner syndrome • infectious agents

1. Introduction

Psoriasis is a chronic inflammatory skin disease that affects approximately 1–3% (up to 11.4%) of the general population [1]. The etiology of psoriasis has not been fully elucidated, although in recent years there has been significant progress in therapy for this difficult-to-treat disease. Despite the effectiveness of currently available therapies, it should be remembered that the course of the disease is also influenced by many external factors: diet, exercise, stimulants, and proper skin care. This article discusses the factors influencing the severity of psoriasis that the patient can control: the regular use of emollients, elimination of infectious agents, and reduction of mechanical injuries.

2. The importance of emollients in the treatment of psoriasis

Ailments such as inflammation and dry skin that patients with psoriasis experience are associated with epidermal barrier disorders [2]. This is demonstrated by, among other symptoms, increase in transepidermal water loss (TEWL), decrease in water binding properties, and reduction of lipids on the skin surface [3]. Disruption of the structure of the stratum corneum leads to the promotion of inflammation by increasing the production of proinflammatory cytokines, stimulating keratinocyte activity, increasing skin pH, increasing epidermal protease activity, or stimulating of PAR-2 receptors (protease activated receptor 2) [4]. The promotion of inflammation leads to a secondary aggravation of epidermal barrier dysfunction, resulting in a vicious cycle. Therefore, it is extremely important to counteract these processes by rebuilding the proper skin protection barrier using emollients [4, 5].

Emollients are agents for external use with moisturizing, greasing, and elasticizing properties. Their regular application on the skin increases the protective function of the epidermal barrier, normalizes keratinization, reduces local inflammation and itching, and helps restore the normal microbiome of the skin [6]. As a result, the epidermis is more resistant to environmental factors, risk of irritation and Koebner phenomenon are reduced, and the period of disease remission can be extendeded [7]. Depending on the ingredients contained in the emollients, this effect is achieved with the help of various mechanisms, such as the

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occlusion effect (significantly reducing TEWL), binding and retaining water within the stratum corneum, and provision of lipid or protein components that are missing in the affected stratum corneum [8] (Fig. 1).

Emollients are mixtures of hydrophobic and hydrophilic components. Most often they are emulsions: oil in water (O/W) or water in oil (W/O). The most important substances included in the emollients are humectants (including urea), occlusive substances, and lipids [4] (Table 1). Emollients differ in substrates and composition of active substances. Thanks to their variety, it is possible to achieve better therapeutic effects by choosing the right care products, best suited to the patient.

The most important element in emollients is their occlusive properties, because thanks to them a layer is created on the epidermis surface that prevents water from escaping through evaporation. The water remaining in the epidermis penetrates the corneocytes, increases their turgor and volume, sealing the intercellular spaces, thereby increasing the integrity of the epidermal barrier [4]. Among occlusive substances, petrolatum is assigned a key role, which reduces water loss by up to 98%, which is a significant advantage over other oil substances (20–30% reduction) [9].

Humectants are responsible for attracting water molecules from the deeper layers of the epidermis, binding them and keeping them within the stratum corneum. One of the most commonly used humectants in emollients is urea. It is a natural moisturizing factor (NMF). Due to its hygroscopic properties, after topical application, it increases water binding by proteins and lipids, thus moisturizing the stratum corneum, and in higher concentrations, above 10%, also has keratolytic properties [7, 10]. The undoubted advantage is also the fact that as an NMF it does not cause allergies. In the study comparing emollients with 5% and 10% urea concentration, there was no difference in hydration, which indicates that the 5% concentration is sufficient [7]. Urea has also been reported to increase the penetration of glucocorticosteroids (GCS) into the skin [7]. This phenomenon is known as the "steroid-sparing effect" and is observed in patients with psoriasis and atopic dermatitis, among other disorders. In these diseases, moisturizers significantly increase the effective-

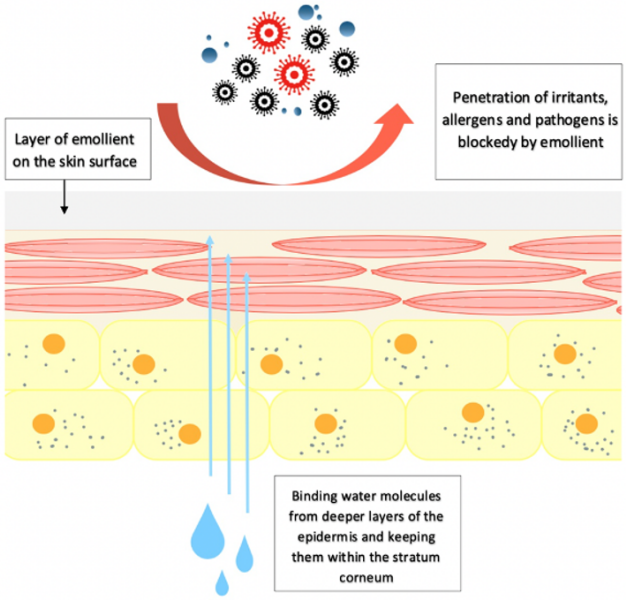


Fig. 1. The mechanism of action of emollients

Table 1. Composition of emollients

A component of emollients	Importance	Substances
Occlusive substances	Prevention of water loss through evaporation	Hydrocarbon oils (petrolatum, paraffin, mineral oils) Polyhydric alcohols (propylene glycol) Fatty alcohols (cetyl, stearyl, lanolin) Fatty acids (stearic, lanolin) Phospholipids (lecithin) Wax esters (lanolin) Sterols Waxes
Humectants	Binding of water molecules and retention within the stratum corneum	Glycerin (2-10%) Urea (2-5%) Sorbitol Lactic acid Propylene glycol Lactates Hydroxy acids Hyaluronic acid
Physiological epidermal lipids	Regulation of normal corneocyte differentiation	Unsaturated fatty acids Cholesterol Squalenes, Phospholipids Sterols Ceramides

ness of topical corticosteroids and can prevent exacerbations. The mechanism of action is to increase the penetration of GCS, thanks to emollients containing urea, and the maximum penetration of the drug occurs within inflammatory changes. In this way, emollients reduce the amount of GCS necessary to achieve remission of lesions, and thus they improve the safety of therapy.

Importantly, new research indicates a link between urea and gene regulation. Grether-Beck et al. report that 10% urea concentration regulates the expression of genes involved in keratinocyte differentiation, epidermal lipid synthesis (transglutaminase-1, involucrin, loricrin, and filaggrin), and the production of antimicrobial peptide (antimicrobial peptides and defensin-2) [11]. Since the maintenance of the functional epidermal barrier depends on intact keratinocytes, as well as normal lipid synthesis, these findings provide evidence of the beneficial role of urea in improving barrier function and aiding antimicrobial defense. Fluhr et al. suggested that lipid biosynthesis could be increased by topical application on of highly concentrated urea. In vitro and in vivo data shows reduction of the cells in the DNA synthesis in basal layers (by about 45%), thinning of the epidermis (by about 20%), and reduction of epidermal cells [7]. What is more, it turns out that urea also stimulates the expression of enzymes involved in ceramide synthesis and the expression of aquaglyceroprotein (AQP-3) channels in keratocytes responsible for the transport of water and glycerol, whose level in psoriasis decreases [12].

Other humectants include lactic acid or glycerin, less commonly used in patients with psoriasis. When choosing the right emollient, it should be remembered that moisturizing substances must also be included in the formulation containing occlusive substrates, otherwise water-binding formulations may increase TEWL.

In the case of a damaged epidermal barrier, as in the case of psoriasis, it is necessary to substitute deficiency components, achieved thanks to the physiological epidermal lipids that regulate the correct differentiation of corneocytes. These substances include, among others, unsaturated fatty acids, cholesterol, or ceramides. In psoriasis, ceramide synthesis necessary to maintain normal epidermal structure and skin permeability is often disturbed [13]. As epidermal layer lipids, they inhibit TEWL. In psoriatic lesions altered ceramide distribution is associated with faulty keratinocyte differentiation; skin barrier dysfunction is most likely the result of insufficient amounts of ceramide-1 [14]. Studies confirm that the use of equimolar lipid mixtures can restore the disturbed skin barrier to normal [13]. Similarly, Coderch et al. reported that topical treatment containing lipid precursors may increase the skin's natural ability to synthesize lipids [15].

Other components that may be included in the emollients are antipruritic substances such as local anesthetics (lidocaine), cannabinoid receptor agonists (N-palmitoylethanolamine), and agonists of the TRP group (capsaicin, menthol, camphor) [16]. Interesting are the reports on the effectiveness of local application of substances with immunomodulatory (β-glucan) or bacterial biofilm (xylitol) activity [4, 17]. There are reports on the effectiveness of substances such as niacinamide having anti-inflammatory effects by reducing the level of proinflammatory cytokines (IL-1β, IL-6, IL-8 and TNF-α) [18] or thermal waters [19].

Emollient skin care has long been recognized as an adjuvant therapy in the treatment of mild plaque psoriasis [20, 21]. What is more, according to current therapeutic standards, it is recommended to use emollients as an adjunctive therapy in psoriasis regardless of the stage of the disease or the treatment [7, 21]. Emollients are very important in the therapeutic process because proper lubrication and hydration of the epidermis, reducing dryness and itching, reduces scratching reflexes, and thus significantly improves the patient's quality of life.

The effectiveness of using emollients in the daily care of the skin of patients with psoriasis is confirmed by numerous clinical studies. Draelos reported "an increase in skin hydration, improvement in very dry to dry or normal skin" after using emollients alone [22]. Already in 1986, Wohlrab showed that the simultaneous use of emollient and GCS significantly increases the penetration of corticosteroids [23]. Whereas Watsky et al. have shown, after examining 96 patients, that the combined use of cream with betamethasone dipropionate and emollient cream or lotion is more effective in the treatment of chronic plaque psoriasis and is associated with the steroid sparing effect [24]. In another study involving 105 patients, Seite et al. proved that after achieving disease remission using local GCS, maintenance therapy with emollients reduces the number of relapses, disease severity assessed according to the Physician Global Assessment (PGA) scale and dry skin [25]. Lacarruba et al. [26] showed that 0.1% cream with hydrocortisone valerate applied twice a day to psoriatic lesions was as effective in reducing disease symptoms as once-daily GCS in combination with emollient (20% urea, 2 % salicylic acid, 2% niacinamide).

Emollients are an important element in the prevention and support of plaque psoriasis treatment. The use of emollients and mild cleansing agents (i.e., with low pH) should be prescribed as part of the treatment in combination with other topical or systemic treatments for psoriasis. Moreover, these measures should be considered as first-line therapy in patients with limited psoriasis and in pregnant or lactating women [20]. Supportive use of basic skin care can significantly increase the effectiveness of conventional therapy, reduce the required amount of drug treatment, and improve compliance with recommendations and prolong disease remission [20].

3. Elimination of infectious agents

Microorganisms such as bacteria (*Streptococcus pyogenes, Staphylococcus aureus, Porphyromonas gingivalis*), *Candida albicans*

and viruses (HIV, HPV5) are important factors triggering the onset or exacerbation of psoriasis [27, 28].

Microorganisms initiate psoriatic inflammation using several mechanisms of the immune response:

- patients with psoriasis have an increased production of IgA and IgG antibodies against peptidoglycan-polysaccharide streptococcal cell wall complexes [29, 30];
- proteins of *Streptococcus pyogenes* (M protein, peptidoglycan, streptococcal pyrogenic exotoxin C), *Staphylococcus aureus* (enterotoxin A, B, D and toxic shock syndrome toxin-1) and *Candida albicans* can act as superantigens, binding directly to MHC class II and the chain Vβ T cell receptors (TCR), stimulating up to 20-30% of the naïve T cell population [31, 32, 33];
- superantigen-producing microorganisms (*Streptococcus pyogenes* in tonsil tissue) increase the expression of skin cutaneous lymphocytic antigen (CLA) on T lymphocytes, then recirculating CLA + effector CD4 + T cells migrate mainly into lesional dermis, but CLA+ effector CD8 + T cells migrate mostly through the dermis and into the epidermis where they are thought to cross-react with keratin 17. They are required for the characteristic keratinocyte proliferation in psoriasis [32, 34, 35];
- molecular mimicry: streptococcal M protein is structurally similar to keratin 16 and 17, which are not found in normal epidermis but are present in psoriatic lesions [35];
- increased expression of Toll-like 2 receptor in the capillaries of psoriasis eruptions [36];
- the preferential Th17/IL-17 response induced by microorganisms: *Streptococcus pyogenes* and *Candida albicans* extracts stimulate production of IL-17A, IL-17F, IL-9 and interferon-IFN-γ in CLA+ T cells, which have a proinflammatory effect on keratinocytes [32, 37].

3.1. Colonization of the nasopharynx

The strongest relationship is observed in the case of guttate psoriasis in patients with current HLA Cw6 in whom throat infection caused by *Streptococcus pyogenes*, also known as group A *Streptococcus* (GAS), initiates the appearance of the skin lesions in 56% to 97% of the cases [32, 37, 38, 39]. Usually there are repeated incidents of such dependence in patients. The reason is GAS's ability to settle in the tonsil tissue and thereby create a bacterial reservoir. Their ability to survive intracellularly in tonsil epithelial cells and poor penetration of penicillin G (the drug of choice) into epithelial cells may explain treatment failure and recurrence of infection. In addition, GASs are able to induce hyperplasia of the tonsil tissue, which increases the volume of their reservoir [39]. Therefore, there seems to be a rational recommendation of a European group of specialists recommending tonsillectomy in patients with juvenile psoriasis with a positive streptococcal culture and recurrent GAS infections in a history (>3 episodes) [40].

Streptococcal infections also seem to be important in the provocation of plaque psoriasis. Scandinavian studies show that in 42% of patients with this form of the disease, exacerbations of pharyngitis-related lesions, including confirmed streptococcal infections, were observed in up to 72%. In this group, tonsillectomy improved the course of disease in 49% of patients [34]. A prospective study found that patients with psoriasis reported a sore throat 10 times more often than controls and b-hemolytic streptococci from groups A, C and G (presence of protein M) were found more often than in the control group [41].

Colonization of *Candida albicans* is important in the provocation of psoriasis. In one of the studies it was detected in the oral cavity of 20% of patients with psoriasis and 2.8% of control cases, without clinical symptoms of oral candidiasis. What is more *Candida albicans* was the only species isolated from the oral cavity of both groups. No correlation was found between sex, age, phototherapy, but they observed a positive correlation between psoriasis severity and colony count [42].

A strong relationship is observed between the presence of *Candida spp*. in the mouth and type 2 diabetes in patients [43]. They have an impaired glucose tolerance, which may lead to temporary acidosis, favoring oral candidal proliferation [44]. Moreover, concepts have emerged that colonization by oral yeast directly affects the development of insulin resistance. The increase in body mass index (BMI) is associated with a greater accumulation of visceral fat, increased production of proinflammatory cytokines, including TNF-α and IL-6, and a decrease in adiponectin production, which leads to the development of insulin resistance. In addition, TNF-α is a characteristic cytokine for inflammation in psoriasis. This may explain the more frequent yeast colonization in psoriasis patients [45].

Active smoking and passive exposure to cigarette smoke is associated with an increased risk of potentially pathogenic bacterial species in the oral cavity, probably due to increased bacterial binding to smokers' epithelial cells and the low number of α-hemolytic streptococci that inhibit *Streptococcus pyogenes* in the mouth [46]. Similarly, the presence of *Candida albicans* is significantly higher among cigarette smokers than among non-smokers, which may predispose them to oral candidiasis [47].

3.2. Microflora of the skin

An important microorganism that plays a role in provoking psoriatic lesions is *Candida albicans*. It should also be noted that the natural defense mechanisms against the development of yeast are associated with the activation of, among others, Th17 and IL-17, and the use of anti-IL-17 monoclonal antibodies increases susceptibility to this type of infection in treated patients. In patients with insulin resistance, usually associated with obesity, there are favorable conditions for the development of yeast in skin folds. The initiation of natural defense mechanisms and overproduc-

tion of IL-17 also stimulates psoriatic inflammation, allowing the formation of reverse psoriasis lesions.

Meta-analysis of Pietrzak et al., including a total of 1038 patients with psoriasis and 669 controls, revealed *Candida spp.* detection rates significantly higher in psoriatic patients (OR 2,57-3,14) than in the controls. They suggest psoriasis may be one of the systemic diseases which predispose to oral *Candida spp.* carriage and infection [48]. Although the mechanism by which *Candida* may exacerbate psoriasis remains to be investigated, one possibility is that *Candida* produces superantigens that stimulate T-cell activation in a manner similar to streptococcal and staphylococcal infections [49].

Picciani et al. evaluated 140 patients with psoriasis and 140 healthy controls. By cytopathological examination they found in as many as 37 patients (26%) the presence of candidiasis and no cases of candidiasis in the healthy controls. There was no correlation between the type of psoriasis treatment and the presence of oral candidiasis, while a statistically significant relationship between the severity of clinical lesions and the presence of *Candida* [49].

3.3. Diseases of the teeth and periodontium

Periodontitis can be an independent risk factor for developing psoriasis. In several clinical trials it was found that people with psoriasis have a much higher number of missing teeth, more severe periodontitis and a lower radiographic alveolar bone level than in the control group [50, 51, 52]. These data were confirmed in a systematic review and meta-analysis that found a 1.55-fold increased risk of psoriasis in people with periodontitis compared to people without periodontitis [53]. In addition, the periodontal condition is correlated with the severity of psoriasis [54, 55]. Such a relationship is observed in the group of patients with psoriatic arthritis (PsA): corrected incidence rates were 1.66 for mild psoriasis, 2.24 for severe psoriasis and 3.48 for psoriatic arthritis [55, 56]. Increased levels of TNF-α, IL-1β, MCP-1 and TGFβ were also found in the saliva of patients with psoriasis and their levels correlated with the severity of periodontitis [57].

Dental plaque is a source of polyclonal and mitotic factors that can trigger an immune response by stimulating dendritic cells and a Toll-like receptor [52, 58, 59]. Another explanation is the activation of Th17 cells and increased expression of IL-17 (which is one of the main factors in the pathogenesis of both psoriasis and psoriatic arthritis) induced by bacteria involved in periodontal infection and their products.

In recent years, a resident Gram-negative anaerobic periodontal pathogen— *Porphyromonas gingivalis*—is a key link in the provocation of inflammation due to its ability to produce peptidyl-arginine deiminase, the main enzyme that promotes post-translational citrullination of rheumatoid arthritis peptides [53]. It is able to activate the Th17 pathway independently, increase IL-1β, IL-6 and IL-23 production, and induce IL-23 receptor expression in monocytes, Th1, Th17, NK and DC [55, 60]. Smoking has been shown to increase the population of *P. gingivalis* [55]. The role of anticitrulline antibodies, which are an immune response to protein citrullination, is well known in the pathogenesis of rheumatoid arthritis but is unclear in the pathogenesis of psoriatic arthritis. However, it was observed that more severe arthritis was observed in patients with anti-cyclic citrullinated peptide antibody (aCCP) [61].

Particular attention should be paid to the condition of psoriatic patients' teeth before the start of immunosuppressive therapy, which may cause recurrent inflammation and even sepsis. However, several studies have shown that immunosuppressive and biological pharmacotherapy can reduce the inflammatory response of periodontal tissue to bacterial plaque, due to the common elements of the pathomechanism of these two diseases [52, 55].

It should be remembered that psoriasis reduces the quality of life, aggravates depressive behavior, which can lead to unhealthy lifestyle behaviors (smoking, improper diet) and less care for health.

3.4. Urogenital system

While bacterial flora is of great interest to researchers in psoriasis provocation, the problem of urinary tract infection is very underestimated, especially in women. Anatomy (short urethra), postpartum pelvic floor dysfunction, obesity and insulin resistance are factors facilitating bacterial colonization. However, there are many reports of infections occurring during systemic therapy. The use of cyclosporine, infliximab, and anti-IL17 could be associated with a higher risk of symptomatic UTI in women. The lower risk occurred with acitren and methotrexate [62].

One study evaluating almost 250,000 visits of patients with psoriasis showed co-existing urinary tract infections in 2%, more often than upper respiratory tract infections (1.4%) and slightly less frequently than skin infections (2.7%) [63]. The problem is underestimated.

Studies published so far do not clearly indicate the role of bacterial infections in the development of arthritis in patients with psoriasis. Several studies have shown the immunological association of *Streptococcus pyogenes* infection with PsA [30, 64, 65], but other authors have not confirmed these observations [66]. Two studies evaluating the relationship between staphylococcal infections and psoriatic arthritis showed an increase in IgG levels against staphylococcal antigens [67] and an increased monocyte proliferative response to staphylococcal superantigen [16]. In the study by Lapadula et al., higher concentrations of anti-*Chlamydia trachomatis* antibodies were observed in patients with PsA than in the healthy group [68], but in another study by Silveira et al., titers of IgM and IgG anti-*Ch. trachomatis* antibodies among people with arthritis and the control group did not differ [69]. However, it seems that some viral infections

may affect the development of PsA. Previous studies show an increase in the incidence of PsA in patients infected with HIV [70, 71]. This is probably due to the effect of the virus on the ratio of CD4+/CD8+ cells. The course of HIV infection is associated with a decrease in the number of CD4+ lymphocytes and an increase in the number of CD8+ which promotes the development of psoriasis [72], while in the joints of patients with PsA with HIV infection, an increased number of IL-17+ CD8+ cells was observed, correlating with the activity of the disease and destruction of joints [73]. In other studies, the more frequent presence of Parvovirus B19, Cytomegalovirus and Epstein-Barr virus in the synovium of patients with PsA compared with patients with reactive arthritis was observed [74, 75].

3.5. Infection with hepatitis B and C viruses

Viral infections are known to be important factors in the pathophysiology of psoriasis in the general population. HCV infection is a potential factor initiating the development of psoriasis in patients with genetic predisposition; what is more, HCV infection may provoke late-onset psoriasis. The risk in this case is twice as high as in non-HCV infected individuals [76]. The impact of HCV infection on the course of the disease in patients with already diagnosed psoriasis is not fully understood. An important issue is the role of the cytokine TNF-α in patients with psoriasis and HCV infection in inducing the progression of liver disease [76]. HCV reactivation after administration of immunosuppressive anti-psoriatic drugs is an extremely rare phenomenon. There are few studies on the role of HBV in the pathogenesis of psoriasis. It appears that HBV infection can induce or exacerbate the progression of psoriasis. Interestingly, in patients with coexisting HBV infection and psoriasis, HBV was found in psoriatic lesions [77]. However, the relationship between psoriasis and HBV infection is mostly indirect. There is a risk of viral reactivation during treatment with immunosuppressants [76]. It is necessary to predict the risk of HBV or HCV reactivation in patients with psoriasis treated systemically. Prior to initiating anti-psoriatic therapy, all patients should be screened for risk assessment by measuring the serological markers HBV and HCV. It should also be remembered that some anti-psoriatic drugs are directly toxic to the liver (MTX, acitretin, and TNF-α inhibitors) [78].

4. Mechanical trauma

A characteristic symptom for active inflammation in psoriasis is the Köebner symptom, which occurs in about 25% of patients with psoriasis [79]. This symptom is most common for guttate psoriasis. Typical psoriatic lesions appear at injury sites after 10-20 days. It is believed that the injury causes increased papillary dermis blood flow, which facilitates the access of inflammatory mediators and the development of inflammation [80, 81]. Another factor leading to its development is nerve growth factor (NGF) and vascular endothelial growth factor (VEGF), released by psoriatic keratinocytes under the influence of trauma, and the role of integrin α 2β1, S100A7 (psoriasin) and S100A15 (koebnerisin) [82, 83]. It is also suggested that skin trauma rapidly induces IFNα from keratinocytes and IFN-β from plasmacytoid skin dendritic cells [80]. Recently, the role of resident memory T cells (TRM) has been emphasized, which, even after the psoriatic lesions have disappeared, remain in the epidermis and skin for many months. Under the influence of trigger factors they quickly release IL-17A and IL-22 leading to the development of psoriatic inflammation in specific locations [84].

In recent years, there has been a growing popularity of decorative tattoo or permanent makeup as body art [85, 86]. In patients with active psoriasis, the Koebner reaction is not uncommon, despite general treatment [85, 87]. One study showed that most patients developed generalized psoriasis within a few weeks and a minority developed at a tattoo site [87].

It should be noted that all trauma-related procedures, such as piercing, tattooing and even aesthetic dermatology procedures should not be performed on patients with active psoriasis [62, 88]. There are many literature reports on the long-term persistence of lesions in post-operative scar, smallpox and post-vaccination (BCG) scars, and stretch marks [80, 85]. Even low-intensity stimuli can provoke psoriatic lesions: for example, electrocardiography or wearing jewelry [89, 90].

Koebner's symptom does not have to be only a manifestation of mechanical trauma. Involvement of scalp is particularly common in children and young people in whom the severity of seborrhea is observed physiologically. This promotes the colonization of lipophilic yeast, the appearance of inflammation and itching, which causes the compulsion of scratching and leads to exacerbation of lesions. Analysis of psoriasis in 402 children (<18 y.o.) as part of the Child-CAPTURE registry (Continuous Assessment of Psoriasis Treatment Use Registry) program showed that the percentage of the affected scalp area was significantly higher in children with a positive Koebner phenomenon vs. children with a negative Koebner phenomenon (50% vs. 25% of the affected scalp, p=0,001) [91]. Scalp psoriasis was observed in 87.6% of children, of whom as much as 35.8% reported scalp psoriasis as the initial place of the disease [91].

The second form of psoriasis in which the Koebner symptom is important in the development of lesions is the inverse psoriasis in inguinal folds, under the breasts, axillary folds, and genital area, especially in obese people with insulin resistance. Humidity and heat typical of these places, along with colonization with dermatophytes, *Candida albicans*, and increased friction, cause psoriatic lesions [92, 93].

The last but no less important form to keep in mind is eczema psoriasis or psoriatic eczema ("eczema in psoriatico") [94]. In people who are allergic to contact factors, an allergic reaction as a form of Koebner's symptom provokes psoriatic inflammation in a particular region. Inflammation develops, having clinical and



Fig. 2. 42-year-old patient with chromium allergy working in construction: clinical features of psoriasis (oil spots on nails, severely demarked lesions) and eczema (dyshidrotic vesicles of the hand)

Table 2. Recommendations for the patient

Clothing	avoiding clothes made of artificial fabrics that strongly compress and rub the skin (underwear, socks, belts) natural materials, airy (cotton), not disturbing sweating non-irritating jewelry
Beauty treatment	avoiding shaving with blunt shavers of facial hair and other hair avoiding wax depilation resignation from piercing, tattooing, permanent makeup avoiding hybrids and acrylics; nails should be short, evenly cut short or semi-long haircuts, resignation from dreads and attachments avoiding intensive lightening or dyeing hair, keratin treatments, perms avoiding Chinese cupping massage
Medical treatments	during active illness, avoiding needle aesthetic procedures or laser dermatology (pulsed dye laser, high-energy irradiation) resignation from acupuncture
Climatic factors	despite reported improvement of the disease after sun exposure, it is advisable to avoid intensive sunbathing, sunburn protection against frostbite
Occupational factors	career counseling avoiding contact with irritants and allergens the use of suitable gloves and tool protection to reduce mechanical injury or friction skin care program and barrier creams

histopathological features of psoriasis (papillomatosis and acanthosis), as well as eczema (spongiosis) [9]. Probably the created mechanism of the "vicious circle" is responsible for long-lasting persistence of the changes despite proper treatment and avoidance of allergens. Such a phenomenon is observed in patients with psoriasis, in whom exposure to irritants and allergens at work provokes lesions, which is referred to as occupational contact psoriasis [95]. In addition to allergic factors, mechanical or physical injuries, friction or contact with irritants are important in its development [96] (Fig. 2). Prevention should already apply to young people who choose their profession. They should consider giving up professions involving frequent injuries, increased humidity [96]. In this type of competition, protection (skin care program and barrier creams), the use of appropriate gloves or tools is important. If preventive actions fail, it is advisable to retrain the employee [96] (Table 2).

5. Conclusions

The complexity of psoriasis requires a holistic approach to the patient and comprehensive care, not just treatment. Patients, often dissatisfied with the effects of conventional therapy, unaware of aggravating factors, tend to use alternative therapy that can lead to worsening their overall health [97]. Therefore, the task of dermatologists is to educate the patient and to encourage working together to improve the effects of therapy.

Abbreviations

aCCP - anti-cyclic citrullinated peptide antibody; **AQP-3** – aquaglyceroprotein-3; **BCG** - bacille Calmette-Guerin; **BMI** – body mass index; **CLA** - cutaneous lymphocytic antigen; **DC** – dendritic cell; **DNA** – deoxyribonucleic acid; **GAS** - group A *Streptococcus*; **GCS** – glucocorticosteroids; **HBV** – hepatitis B virus; **HCV** – hepatitis C virus; **HIV** - *human immunodeficiency virus***; HPV –** *human papilloma virus;* **IFN** – interferon; **IL** – interleukin; **MCP** – monocyte chemoattractant protein; **MHC** - major histocompatibility complex; **NGF** - nerve growth factor; **NK** – natural killer cells; **NMF** - natural moisturizing factor; **PAR-2** - protease activated receptor 2; **PGA** - Physician Global Assessment; **PsA** – psoriatic arthritis; **TCR** - T cell receptors; **TEWL** - transepidermal water loss; **TGF** – transforming growth factor; **TNF-α** – tumor necrosis factor α; **TRM** - resident memory T cells; **TRP** – transient receptor potential; **VEGF** - vascular endothelial growth factor.

Authors' Contribution

A.O.S.: research concept and design, supervising the project, acquisition of data, data analysis and interpretation; writing: original draft preparation; **M.K.F.**: supervising the project, acquisition of data, data analysis and interpretation; writing: original draft preparation; **M.K.W.**: acquisition of data; writing: original draft preparation; **W.P.**: acquisition of data, writing: original draft preparation.

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Conflict of Interest

The authors have no potential conflicts of interest to declare.

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