Review • DOI: 10.2478/ahem-2021-0033 • AHEM • Vol. 75/2021 • Issue 2 • 643-654

sciendo

Postępy Higieny i Medycyny Doświadczalnej / Advances in Hygiene and Experimental Medicine

Does the lifestyle of patients with psoriasis affect their illness?

Agnieszka Owczarczyk-Saczonek[1], Marta Kasprowicz-Furmańczyk[1], Magdalena Krajewska-Włodarczyk[2], Christopher E. M. Griffiths[3]

[1]*Department of Dermatology, Sexually Transmitted Diseases and Clinical Immunology, The University of Warmia and Mazury, Olsztyn, Poland*
[2]*Department of Rheumatology, The Municipal Polyclinical Hospital in Olsztyn, Olsztyn, Poland Department of Internal Medicine, School of Medicine, Collegium Medicum, University of Warmia and Mazury, Olsztyn, Poland*
[3]*Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester, UK; NIHR Manchester Biomedical Research Centre, University of Manchester, Manchester, UK*

Abstract

Psoriasis is one of the most common chronic, incurable inflammatory skin diseases, affecting 2–4% of the general population. Etiopathogenesis of this disease remains unclear. It is widely considered to be a multifactorial disorder caused by the interaction between inherited susceptibility alleles and environmental risk factors, such as lifestyle, diet, stimulants, foci of inflammation, and psychological factors. The widespread prevalence of psoriasis is a very significant health and socioeconomic problem. Treatment of psoriasis is based on relieving the acute symptoms of the disease. Despite the implementation of many therapeutic options, including biological treatment, effectiveness of these options is not always sufficient, or in some patients it is not satisfactory. In order to properly control the symptoms of the disease, the patient should be told that the therapeutic effect is achieved not only by pharmacotherapy but also by introducing appropriate healthy habits in everyday life. This article discusses the importance of patient-controlled factors that affect the severity of psoriasis. Theimportance of regular exercise, smoking avoidance, and reduced alcohol consumption is explained, as well as the importance for psoriasis treatment of psychotherapy and spa therapy. Understanding the essence of these factors in the treatment of psoriasis is important in achieving satisfactory therapeutic effects.

Keywords

psoriasis • psoriatic arthritis • lifestyle • physical effort • smoking • alcohol • spa therapy • psychotherapy

Received: 28.12.2020, Accepted: 14.06.2021

Introduction

Psoriasis is an inflammatory, incurable, and noninfectious skin disease that affects people of all ages. Etiopathogenesis of this disease remains unclear. It is widely considered to be a multifactorial disorder caused by the interaction between inherited susceptibility alleles and environmental risk factors such as lifestyle, diet, stimulants, foci of inflammation, and psychological factors. Psoriatic patients are more likely to develop cardiovascular disorders, metabolic syndrome, and depression [1]. Moreover, patients suffering from psoriasis have reduced quality of life and they are exposed to social stigma and discrimination. Proper patient care is thus very important [2]. Treatment of psoriasis is still based on relieving the acute symptoms. It mainly focuses on the use of general and topical drugs, phototherapy, or even very effective biological treatment; change in lifestyle, which has a significant impact on the effectiveness of pharmacological treatment, is often forgotten. This article discusses the importance of patient-determined factors that affect the severity of psoriasis, such as: regular physical effort, avoidance of smoking and alcohol consumption, or using psychotherapy if necessary.

The effect of physical effort on psoriasis

Psoriatic patients have an increased risk of cardiovascular disease [3]. The latest guidelines of the European Society of Cardiology on the prevention of cardiovascular diseases recommend regular lifelong physical activity as part of a lifestyle, for more than 150 minutes/week of moderate-intensity exercise or more than 75 minutes/week of intense exercise [4]. Despite recommendations that physical exertion is important for cardiorespiratory fitness, psoriatic patients avoid participation in physical activities for various reasons [3].

Do et al. found that people with psoriasis have lower MVPA—a moderate-to-vigorous physical activity indicator—compared to people without psoriasis [5]. This may be caused

* *Corresponding author e-mail: aganek@wp.pl, martak03@wp.pl*

© 2021 Owczarczyk-Saczonek et al. This work is licensed under the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 License.

by from psychological problems, such as self-acceptance, depression, stigmatization, and an impression of social rejection. According to Ramsay et al., 11.5% of patients avoid leaving home, 64% avoid shared showers, 64% avoid wearing shorts, 72% avoid swimming and 40% avoid sports [6]. Auker et al. showed that with the increase in the severity of skin lesions and the psychosocial impact of psoriasis, the participation of patients in physical activity decreased [3]. This problem particularly affects women. However, it should be remembered that regular sports improve patients' well-being and reduce the level of stress and anxiety [3].

Another disincentive to patients' exercising is sweating during physical exertion, which causes a significant increase in pruritus within lesions. In addition, injuries that occur during exercise can exacerbate the lesions, a phenomenon known as Koebner's symptom. Inadequately adjusted physical exertion can also lead to an exacerbation of psoriatic arthritis (PsA).

It is extremely important to encourage patients to exercise. Weight reduction under the influence of diet and exercise reduces the severity of psoriasis. As demonstrated by Naldi et al., physical exertion has a significant impact on reducing Psoriasis Area and Severity Index (PASI). In this study, 303 overweight or obese patients with moderate to severe plaque psoriasis who did not improve after four weeks of general treatment were examined. A 48% reduction of PASI was found in the group exercising and dieting, while in patients receiving only medications this reduction was 25.5% [7].

A special issue in patients with psoriasis accompanied by arthritis is a decrease in bone mineral density (BMD) and muscle mass, which may aggravate disability conditioned by progressive joint destruction, pain, and stiffness. This may result in an increased risk of falls and their complications, especially with concomitant osteoporosis.

The pathogenesis of loss of BMD and muscle mass in PsA is multivariate and includes decreasing physical activity, secondary to stiffness and pain, and an increase in the concentration of proinflammatory cytokines and C-reactive protein (CRP) associated with chronic inflammation [8, 9, 10]. The role of the treatment used in the pathogenesis of osteoporosis and sarcopenia should also be kept in mind. The effect of steroid therapy in the development of osteoporosis and post-steroid myopathy is widely known, and there are also reports that methotrexate therapy may be responsible for the development of osteopathy, manifested in bone pain, osteopenia, and fractures of the distal tibia [11, 12], while in patients treated with tumor necrosis factor inhibitors (iTNF), interleukin (IL)-17 and IL-12/23 inhibitors, significantly more BMD was observed than in patients treated with methotrexate or untreated disease-modifying anti-rheumatic drugs [13].

A significant reduction in muscle mass measured by the muscle mass index (MMI) may affect over 60% of patients with spondyloarthritis, including PsA [14]. In addition, it appears that the occurrence of sarcopenia in patients with PsA may be associated with an increased incidence of osteoporosis. In the study of women with PsA with sarcopenia, osteoporosis occurred in up to 40%, and mineralization disorders together in over 70% of the respondents [15]. Frediani et al. observed mineralization disorders in at least one region of the skeletal system in 67% of premenopausal women and in 100% of postmenopausal women [16]. In another study, among patients with PsA (but excluding postmenopausal women), osteoporosis was found in 5%, while osteopenia was found in up to 50% of all patients (the control group had osteopenia in 27.5%) [17]. The total risk of fractures among people with psoriasis and PsA appears to be similar to that seen in patients with rheumatoid arthritis [18]. The reduction of BMD in patients seems to be more related to the duration of psoriasis and PsA than to the current disease activity [15, 17, 19].

Physical activity consisting of regular aerobic exercise and exercises under increasing load increase muscle strength in physiological conditions. This activity has proved to be the most effective method of preventing muscle loss and treating existing sarcopenia in chronic arthritis [20, 21]. The improvement in muscle strength and fitness of the patient clearly reduces the risk of falls and osteoporotic fractures.

In conclusion, patients with psoriasis should perform regular aerobic and weight-bearing exercises, as well as cooperating with an experienced physiotherapist.

The importance of giving up alcohol consumption

Many clinical studies confirm the close relationship between the severity of psoriatic lesions and alcohol consumption. Alcohol can not only cause psoriasis but can also exacerbate a preexisting disease. What is more, heavy drinkers tend to develop more serious, more extensive lesions [22, 23].

Above-average alcohol consumption is common among patients with psoriasis, found in as many as one-third of patients with moderate or severe disease [24, 25, 26]. The mechanism of the harmful effects of alcohol on the course of the disease is not completely understood. It may result from the induction of oxidative stress, which causes lipid peroxidation and a decrease in endogenous antioxidants. Ethanol excreted by exocrine glands may affect the metabolism of lipids such as cholesterol and triglycerides, thus disrupting the skin barrier, also leading to hyperproliferation of keratinocytes [27]. The skin becomes more susceptible to infection, including streptococci, which, as a superantigen, initiates the occurrence of psoriatic lesions [22, 28]. Alcohol also affects the release of histamine, dilates the vessels facilitating the migration of inflammatory cells, and increases the concentration of arachidonic acid [22, 23]. Chronic alcohol consumption has been observed to induce inflammation by

increasing CD80 and CD86 expression, leading to increased T cell activation [27]. In addition, patients with chronic diseases associated with alcohol abuse, such as alcoholic liver disease, produce higher amounts of tumor necrosis factor alfa (TNF-α), which leads to an increase in the number of macrophages and monocytes, and overexpression of the TNF-α converting enzyme [27]. It is believed that mast cells have an important role in the pathogenesis of psoriasis, and alcohol can affect their number as well as degranulation [29, 30]. Alcohol also affects neurobiological signaling, including a number of neurotransmitters such as the dopaminergic, serotonergic, and tachykinergic systems, which can also affect inflammatory processes in psoriasis [31]. Alcohol consumption is accompanied by increased consumption of foods high in saturated fat and low in vegetables and fruits, which causes a disturbance in the proportion of ω-3 and 6 in the diet, which also adversely affects the course of the disease (Tab. 1).

There are not many prospective studies on the role of alcohol in psoriasis. In the Nurses' Health Study (NHS II), beer consumption among American nurses was associated with an increased risk of developing psoriasis [31]. Gupta et al. included 150 outpatients in an observational study assessing therapeutic effect, measured by obtaining PASI75 in conventional psoriasis treatment. Obtaining a therapeutic effect was difficult in the presence of obesity, female sex, smoking, and alcohol abuse [32]. Poikolainen et al. found significantly worse effects of psoriasis treatment on men who abuse alcohol (>80 g/d) [33].

There is a correlation between increased alcohol intake and PASI, as well as higher levels of anxiety and depression. Men who drink about 43g of alcohol per day are more likely to develop psoriasis than those who drink 21g per day. Very interesting results have been obtained by Qureshi et al. in women: beer consumption is associated with an increased risk of psoriasis, while wine and strong alcohol do not increase this risk. Women who drank at least five beers a week were 1.8 times more likely to develop psoriasis compared to nondrinkers [34]. The explanation of this phenomenon may be the fact that beer contains gluten and leads to increased intestinal permeability. In another study involving 95 patients with psoriasis, alcohol consumption and stress levels were examined, with 17–30% of patients having problems with alcohol abuse. 13% and 18% of patients were classified with ongoing or previous alcohol problems, respectively, and there was a relationship between increased alcohol consumption and increased anxiety and depression. In addition, patients reporting alcohol abuse had more problems with anxiety disorders and depression, as well as greater severity of psoriasis [25].

Alcohol consumption appears to be associated not only with the higher incidence and severity of psoriasis, but also with the characteristic appearance of the lesions and the distribution of the disease. According to some authors, two dominant disease patterns can be identified in drinkers: the first includes severe, minimal-scale inflammatory lesions, usually involving the face, groin, and skin folds; the second is characterized by hyperkeratotic changes, with the dominant acral distribution [35, 36, 37].

Recently, new reports have emerged regarding the increased risk of premature alcohol-related mortality in patients with psoriasis. The reason for this phenomenon is not fully understood, but it is probably multifactorial. The most common comorbidities with psoriasis are hyperlipidemia, hypertension, depression, type 2 diabetes, and obesity. Parisi et al. studied a cohort of 55,537 patients with psoriasis and 854,314 patients without psoriasis. During the median (IQR) 4.4 (6.2) years of follow-up, alcohol-related mortality was 4.8 per 10,000 person-years (n=152) in the psoriasis group compared with 2.5 per 10,000 (n=1 118) for the comparative cohort. The risk factor for alcohol-related death in patients with psoriasis was 1.58, and the main causes of alcohol-related deaths were alcoholic liver disease (65.1%), fibrosis

Table 1. Mechanism of psoriasis induction by alcohol and cigarettes

	Psoriasis induction mechanism
Alcohol	• Oxidative stress causes lipid peroxidation and a decrease in endogenous antioxidants • Increased histamine release → vasodilation → increased migration of inflammatory cells (including mast cells) • Increased arachidonic acid concentration • Induction of inflammation by increasing CD80 and CD86 expression → increased T cell activation • Increase in TNFα and overexpression of TNFα converting enzyme
Cigarettes	• Free radical formation → stimulation of cell signaling pathways, i.e., mitogen-activated protein kinase (MAPK), nuclear factor jB (NF-jB), Janus kinase (JAK), and signal transducer and transcriptional protein activator (JAK-STAT) signal pathway • Stimulation of dendritic cells, macrophages, and keratinocytes → release of cytokines, i.e., IL-12, TNF, IL-2 and GM-CSF, which activate lymphocytes T • Dioxins bind to the aryl hydrocarbon receptor on Th22 and Th17 lymphocytes → IL-17 and IL-22 productionIncreased expression of HLA-Cw6, HLA-DQA1*0201 and CYP1A1 genes

and cirrhosis (23.7%), and alcohol-related mental and behavioral disorders (7.9%). The above results indicate an approximately 60% greater risk of death from alcohol-related causes in psoriasis patients compared to peers of the same age and sex in the general population [38]. Moreover, patients with psoriasis have an increased percentage of liver disease (both alcoholic and nonalcoholic), and psoriasis is more common in patients with alcoholic liver disease than expected in the general population [35]. In this case, the role of TNF-α cytokine, which is crucial in the pathogenesis of psoriasis, may be important [31].

There are reports in the literature of the relationship between alcohol abuse and the risk of PsA. Interestingly, after examining 82,672 women from the USA, Wu et al. found a significant risk of alcohol use for PsA. Over 14 years, 141 PsA cases were documented. Compared with nondrinkers, HR was 0.7 when drinking alcohol 0.1-14.9 g/d, 1.43 at 15.0-29.9 g/d and 4.45> 30.0 g/d [39].

Treatment of alcohol abuse patients can be a real therapeutic challenge, which is associated with, among others, worse compliance with the treatment of skin disease. Patients with psoriasis can consume alcohol to cope with debilitating skin disease. It seems that in addition to classical methods of treatment in patients who abuse alcohol, actions directed at neurotransmitter networks related to both alcohol intake and inflammatory processes may be effective. Svanstrom et al. report the presence of receptors for biogenic amines such as 5-hydroxytryptamine (5-HT), tachykinin, including neurokinin 1 (NK-1) and acetylocholine (Ach) receptors in psoriasis. Expression of such receptors has been found in the basal and/or differentiating epidermal zones and on cutaneous inflammatory cells, while dendritic inflammatory cells in the epidermis and dermis express SERT expression [31]. Furthermore, a cohort study by Thorslund et al. showed that patients with psoriasis who underwent selective serotonin reuptake inhibitor (SSRI) treatment were less likely to require systemic treatment of psoriasis [40]. In addition, the availability of the 5-HT transporter in the brainstem has been shown to correlate with the amount of TNF-α. These reports seem promising and undoubtedly require further study.

Current knowledge indicates the importance of performing routine screening, identification, and treatment using the Alcohol Disorder Identification Test (AUDIT-C) in both primary and secondary healthcare to detect alcohol consumption and misuse by people diagnosed with psoriasis.

Influence of smoking on the course of psoriasis

Smoking is the most common way to consume tobacco, and tobacco is the most commonly smoked substance. It is a mixture of over 7,000 chemicals [41]. The main alkaloid is nicotine, which mediates the addictive effects of tobacco products. Smoking is considered a risk factor for many diseases, including cardiovascular and pulmonary diseases, and many cancers [42]. Smoking is also one of the known risk factors for psoriasis and is associated with its more severe course [43].

Recent research suggests that cigarette smoking can trigger psoriasis through oxidative, inflammatory, and genetic mechanisms. The toxic effects of tobacco smoke are associated with oxidative stress. Smoking initiates the formation of free radicals that stimulate cell signaling pathways active in psoriasis, including mitogen-activated protein kinase (MAPK), nuclear factor jB (NF-jB), Janus kinase (JAK), and transducer protein transcriptional signal activator (JAK-STAT) [44]. In addition, nicotine stimulates dendritic cells, macrophages, and keratinocytes, releasing cytokines such as IL-12, TNF, IL-2, and granulocyte-monocyte colony stimulating factor (GM-CSF) that is responsible for activating T lymphocytes and maintaining chronic inflammation in psoriasis [45]. What is more, dioxins formed by burning tobacco bind to the aryl hydrocarbon receptor on Th22 and Th17 lymphocytes which leads to the production of IL-17 and IL-22, which have significant importance, among others in the pathogenesis of psoriasis [46]. Smoking also increases the expression of genes that are known to increase the risk of psoriasis, including HLA-Cw6, HLA-DQA1*0201 and CYP1A [44]. The risk of psoriasis in smokers with current HLA-Cw6 is 11 times higher than in non-HLA-Cw6 smokers and increases 20-fold in people who also have stressful life events [47] (Tab. 1).

Smoking is associated with psoriasis in both sexes. The risk of developing psoriasis among smoking women is three times higher than that of nonsmokers but it increases significantly when smoking more than 20 cigarettes a day [48]. Other studies indicate that people who smoke more than 15 cigarettes a day have double the risk of developing psoriasis than nonsmokers. This threat increases proportionally to the number of cigarettes smoked. Smokers are more likely to have more extensive and refractory psoriatic lesions [49, 50]. Lee et al. observed a total of 17,055,608 people over the age of 20 who underwent a health examination in 2005–2008. In multivariate analysis, compared to nonsmokers, former smokers (IR 1.11) and current smokers (IR 1.14) had a significantly higher risk of developing psoriasis. These results showed that smoking status is an independent potential risk factor for psoriasis. In addition, according to the authors, the risk of psoriasis increased with the amount and duration of smoking. There was a statistically significant positive correlation between psoriasis risk and total smoking period. What is more, HR for psoriasis was the lowest in people who smoked less than 0.5 packs a day (HR 1.11) and the highest in people who smoked more than 2 packs a day (HR 1.25)

[51]. In the meta-analysis Armstrong et al. stated that the risk of psoriasis in smokers for less than 10 years was almost the same as for nonsmokers, while smokers for over 30 years had almost twice the risk of appearance of the psoriasis than nonsmokers [52].

Numerous epidemiological studies show that in the population of patients suffering from psoriasis there are more than twice as many smokers as in the control group. Heron et al. evaluated 800 psoriasis patients, stating that as many as 37% of patients smoke cigarettes compared to 13% in a healthy population, and 78% started smoking before the onset of the disease [53]. Such a high prevalence of smoking addiction among patients with psoriasis is probably caused by a reduced sense of quality of life and related difficulties [54]. Altunay et al. conducted a study comparing the mechanisms of coping with stress of smokers and nonsmokers with psoriasis. Social support rates from the *Ways of Coping Questionnaire* were significantly lower in smokers than nonsmokers ($p<0.05$), while Fagerstrom's results correlated with the degree of distrust and PASI. Similar stress coping strategies were found in both patient groups, with the exception of the subgroup seeking social support, they usually used smoking as a way to manage stress [55].

Smoking is not only associated with the onset of psoriasis but is also associated with the severity of the disease and its response to treatment. In an Italian cross-sectional study it was documented that patients who smoked over 20 cigarettes a day had twice the risk of severe psoriasis compared to these smoking less than ten cigarettes a day [56]. In a study of men with psoriasis, smoking more than ten cigarettes a day was significantly associated with increased disease severity, especially on the limbs. Similarly, another study found more serious skin involvement in smokers than nonsmokers, as well as reduced probability of periods of disease remission [57].

It is important to remember that tobacco smoking is associated with the occurrence of pustular psoriasis of the hands and feet. This disease is more common among smokers than nonsmokers. In 50% of cases smoking increases the risk of pustular psoriasis. While at the beginning of the disease up to 95% of patients actively smoke or have previously smoked cigarettes [58]. Smoking cessation during the disease reduces its symptoms, rarely causing complete resolution of skin lesions [59]. It seems that the role of nicotine in pustular psoriasis of the hands and feet is mainly to initiate the disease process.

Data on the role of smoking in PsA are less consistent compared to data on psoriasis. One study has shown that smoking can accelerate the onset of arthritis in patients with psoriasis and delay the onset of PsA in healthy patients [57]. There are also available studies that show that smoking is associated with an increased risk of psoriasis and PsA in the general population [60]. A large cohort study based on NHS II (1991–2005) showed that smoking was associated with an increased risk of PsA with a relative risk of 1.54 for former smokers and 3.13 for current smokers. As the duration of smoking or the number of cigarettes smoked increased, so did the risk of PsA. The increase in risk was particularly significant in patients with more severe disease phenotypes [61]. However, there are more and more reports that smoking is inversely or weakly associated with PsA in analyses limited to patients with psoriasis— the so-called smoking paradox. Eder et al. suggested a protective effect of smoking on the risk of PsA among patients with psoriasis. 6.65 million people without PsA were analyzed using data from the Health Improvement Network register (1995–2015). At the beginning of the study, 225,213 had psoriasis and 7,058 developed PsA. Smoking was associated with an increased risk of PsA in the general population (HR 1.27), but reduced risk was observed in patients with psoriasis (HR 0.91) [62]. This negative correlation that smoking can reduce the risk of PsA in patients with psoriasis may result from index event bias [51, 62]. Further research is absolutely necessary to clarify the effects of smoking on PsA development in people with psoriasis. In addition, there are available data suggesting that smoking can affect disease activity in PsA. Analysis of data from a study involving 267 patients with PsA and disease duration ≥10 years showed that smoking, delayed diagnosis, older age at diagnosis, and female sex were associated with poorer physical function [63].

Two independent studies have shown that compliance with medical recommendations is greater in nonsmokers than in smokers [64]. In a retrospective study of patients with moderate to severe psoriasis who were active smokers or nonsmokers, changes in the Physician Global Assessment (PGA) after 3–16 months of systemic treatment (methotrexate, cyclosporine, acitretin, ustekinumab) were rated. The average number of general treatment trials per patient was also calculated. Changes in PGA scores between baseline and 3–16 months after the start of systemic treatment did not differ significantly between smokers and nonsmokers, as did the average number of systemic treatment attempts per patient [65]. In one study involving 110 patients treated with iTNF for psoriasis, smoking along with increased body mass index (BMI) and high baseline PASI was a risk factor for nonresponse [66]. There is undoubtedly a significant lack of literature on the effects of smoking in response to systemic treatment in patients with chronic inflammatory diseases, but significant studies have been conducted in patients with PsA. Hojgaard et al. in the study of 1,148 patients with PsA found that smokers with PsA showed a worse response to iTNF (ACR20 and ACR50) compared to nonsmokers. This was especially observed in men treated with infliximab or etanercept [67].

Many comorbidities associated with psoriasis can, at least partly, be associated with smoking. This applies, among others, to cardiovascular diseases, inflammatory bowel diseases (IBD), chronic obstructive pulmonary disease (COPD) [68], and cancers (especially those originating from the respiratory tract). Awareness of the increased risk of developing comorbidities in patients with psoriasis allows the implementation of appropriate preventive and therapeutic actions as well as controlling risk factors by smoking cessation and treating the inflammatory process [68]. In addition, identifying such risks may enable early implementation of preventive measures to reduce comorbidities and mortality.

It is extremely important to educate patients about the benefits of quitting alcohol and smoking.

Psychotherapy in the treatment of psoriasis

Psoriasis has a significant impact on the life and mental state of the patients, due to the visibility of the disease and its chronic and recurrent course. Patients become the object of stigmatization and social rejection, which often leads to depressive disorders [69]. Psoriasis increases the level of stress and anxiety, while stress worsens the clinical course of the disease. The mental state of the patients can be both the cause of the disease and its effect. The most accurate feedback between stress and symptoms of psoriasis is described in the biopsychosocial model, assuming that psoriasis is the result of interactions between physiological processes, mental states, and social situations operating on the principle of a "vicious circle" (Fig. 1). Symptoms of the disease cause a decrease in mood, as well as anxiety, which significantly reduces self-acceptance and self-esteem, which in turn causes social anxiety and leads to limitation or abandonment of contact with other people (including sexual contact). Lack of psychological well-being makes the skin condition deteriorate and the depressed mood, anxiety, and fears intensify even more [2].

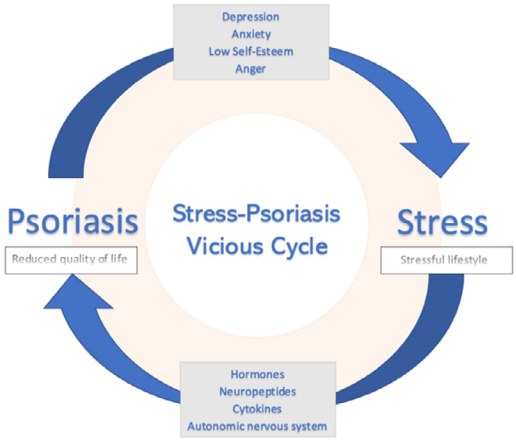

Figure 1: Diagram of the vicious circle of stress in psoriasis

Interestingly, Shelton's concept postulates that conditions associated with an increase in proinflammatory cytokines (such as IL-6, TNFα) that cause chronic inflammation (e.g. obesity, psoriasis, cardiovascular disease) increase the risk of depression [70]. The above thesis can be confirmed by observations that people with inflammatory diseases such as psoriasis have significantly increased rates of depression. In addition, many patients with depression showed upregulation of inflammatory factors. It seems feasible that proinflammatory cytokines may interact with neurotransmitter metabolism, neuroendocrine function and synaptic plasticity [1].

Patients with psoriasis often have signs of alexithymia. *Alexithymia* is a term describing mental disorders in the sphere of expression and the sense of the feelings in patients with various chronic diseases, including psychosomatic disorders. Alexithymia is treated as a peculiarity of the personality of patients, which, along with other personality factors, predisposes to the occurrence of various mental diseases, including psychosomatic disorders (such as psoriasis) [71].

Psoriasis patients have a wide variety of psychological complaints, including reduced self-esteem, stigmatization, shame, embarrassment, sexual dysfunction, anxiety, depression and suicidal thoughts [72]. Depressive disorders occur in 30% of outpatients and in up to 60% of hospitalized patients, including suicidal thoughts in 10–17% of patients. Sexual dysfunction (30% to 70% of patients) is also very common [73]. In Poland, studies were conducted using the Beck Depression Scale and it was found that 28.12% of patients showed depressive symptoms [2]. Wojtyna et al., after examining 219 Polish psoriasis patients, have found depressive symptoms in almost 50%, while high levels of psychological anxiety were found in 70% of patients [74]. Both studies show a high percentage of depressive disorders in patients with psoriasis. However, the incidence of depression in patients with psoriasis may be underestimated due to the lack of common screening for depression. The consequence of the co-occurrence of both diseases is noncompliance with therapeutic recommendations and poor therapeutic response.

Younger patients with psoriasis have a higher risk of psychological disorders compared to older ones and suicides are more common in this group [75, 76]. Younger people are more often feeling different and anxious about the impact of the disease on their future. In addition, the visual aspect is important to them, they try to hide changes and often experience frustration associated with treatment [77]. The appearance of psoriasis at a young age is associated with an increased risk of anxiety disorders and depression. Compared to patients who developed the disease later in

life, younger patients were also much more depressed and reported a higher level of stigma and negative emotions related to their body appearance [78, 79]. Stigmatization, depressive symptoms, and psoriasis are a mutually propelling mechanism that negatively affects not only well-being, social functioning, or the choice of forms of activity, but also self-acceptance and self-esteem, and, as a consequence, the life goals, needs, and expectations of a sick person.

A symptom that is often overlooked during routine medical examinations is decreased sleep quality in patients with psoriatic or PsA. Sleep disorders are associated with a significant decrease in the patient's quality of life and the severity of experienced fatigue. In one study, Włodarczyk et al. showed that sleep disorders were significantly more common in patients with PsA. According to the authors, the main factors affecting the occurrence of sleep disorders in PsA patients were: the severity of pain assessed by the visual analogue scale (VAS), number of painful joints, increase in CRP, age of patients and time the patient suffered from psoriasis [80]. Interestingly, in the group of patients suffering from psoriasis alone, in addition to the age of patients and the duration of the disease, the deterioration in sleep quality was related to the severity of skin disease assessed using the PASI index. There is evidence that symptoms of insomnia in psoriasis are directly mediated by pruritus and pain.

Treatment that decreases the cutaneous symptoms in psoriasis seems to be successful in relieving insomnia [81]. The treatment of sleep disorders in PsA and psoriatic patients, aside from sleeping pills, should also include psychotherapy and effective treatment of the underlying disease.

There are many publications available on the effectiveness of various psychotherapy methods (such as cognitive behavioral therapy) [82, 83], hypnosis [84] or meditation [85, 86], in the supportive treatment of plaque psoriasis. One study confirming the effectiveness of psychotherapy in the treatment of psoriasis was performed by Piaserico et al.: 40 patients were randomly assigned to the ultraviolet (UV)-B treatment group with behavioral therapy for 8 weeks or to the control group treated only with UVB. PASI, General Health Questionnaire (GHQ)-12, Skindex-29, State-Trait Anxiety Inventory (STAI) were evaluated at the beginning and at the end of the study. Of the patients in the treatment group, 65% achieved PASI75, compared with 15% in the control group. The study showed that 8-week cognitive-behavioral therapy increases the beneficial effect of UVB therapy, reduces the clinical severity of psoriasis, improves the quality of life, and reduces mental disorders [83]. Other methods also seem to be quite promising. Lazaroff et al. found that the use of three 30-minute sessions of music therapy reduces blood pressure and heart rate and reduces the desire to scratch in patients with psoriasis [87]. Tausk and Whitmore conducted a small (n=12) randomized, double-blind controlled study of hypnosis and noted a significant improvement in the local skin condition in 5 people [84]. Studies confirm that supportive psychological therapies can be effective in treating psoriasis. However, the variety of methodologies and the lack of adequate scales make it difficult to make comparisons between the described techniques [88, 89].

To understand the relationship between psoriasis and depression, one should remember the patient's subjective suffering and the role of general social pressure to achieve a perfect appearance, as well as the perceived importance of physical appearance for social value and acceptance. There is no doubt that the cooperation of dermatologists, psychiatrists, and psychotherapists is important in the treatment of patients suffering from psoriasis.

In conclusion, patients should be educated that in the case of stress and sleep disorders it is necessary to cooperate with a psychologist or psychiatrist.

The importance of spa therapy in psoriasis

At present, there is a high value assigned to unconventional methods such as climatotherapy and spa therapy, which are safe and effective alternative methods of treatment. Spa therapy includes methods offered using the healing properties of natural resources. The therapy uses sea water (thalassotherapy); healing waters with functional, thermal, and biological properties (balneotherapy); as well as mud (pelotherapy), with simultaneous properties of the atmosphere, temperature, humidity, pressure, and solar temperatures (climatotherapy) [90].

Balneo- and thalassotherapy are some of the oldest treatments for skin diseases. The most effective form is bathing and applying mud in the Dead Sea, providing a combination of anti-inflammatory effects of minerals and UV at a given latitude. The overall level of UV radiation on the Dead Sea is lower because UV rays pass through an additional 400m of atmosphere before reaching the Earth's surface (the Dead Sea is located in the northern part of the tectonic Ditch of the Jordan and is the lowest point on Earth, 400 m below sea level) [91]. Salts and minerals are present in 33% concentration (only 3% in ocean water), with a high content of magnesium chloride, calcium, sodium, potassium, as well as bromine and calcium sulfate [92]. After 4 weeks of treatment, keratolytic and antiproliferative effects are observed [93]. The combination of chemicals in Dead Sea water, high temperature and other environmental factors are thought to induce cell proliferation, reduce inflammation, induce immunomodulation, and selectively protect patients from harmful UV radiation. There also seem to be significant

psychological benefits of being in proximity to the Dead Sea [94].

In a retrospective study of 1,340 patients from 18 countries, as many as 58% achieved complete remission and 30% experienced significant improvement after 4 weeks spent at the Dead Sea. Patients from abroad responded much better than Israeli patients because of their longer stay (4 vs. 2 weeks) [95]. Emmanuel et al. in the prospective cohort study showed that there is significant reduction in PASI and Investigator's Global Assessment Scale (IGA). Furthermore, patients' quality of life improved, measured by the Dermatology Quality of Life Index (DLQI) [96].

Climate therapy at the Dead Sea has also been shown to ensure long-term remission of the disease. In a study of 100 patients with psoriasis, 75% achieved complete resolution after 4 weeks spent at the Dead Sea. Of these, 68% still remained in remission after 4 months, 43% after 6 months, and 10% after 8 months [97].

The effectiveness of bathing in a bathtub with minerals from the Dead Sea before phototherapy (mechanical removal of scales, disinfectant and reducing effects) was also found. Salty water reduces skin thickness and inflammation, improves microcirculation, regulates immune processes, increases mast cell activity, and enhances cytokine production [98, 99]. The concentrated salt solution removes the human leukocyte elastase enzyme, which has a role in psoriasis. Furthermore, it increases tissue sensitivity to light and promotes response to phototherapy [100]. The high concentration of minerals in salty water reduces the amount of mitosis in the skin, reduces transforming growth factor (TGF)-β and the Langerhans cells of the skin, and decreases cell proliferation. Sulfur-based balneotherapy reduces the accumulation of leukocytes and Langerhans cells in the skin, increases the β-endorphins in the skin, and reduces cytokine production [101, 102], significantly reducing the PASI in psoriatic patients [101, 103].

Other than the Dead Sea, popular climatotherapy and balneotherapy centers for psoriasis are located in the Canary Islands, on the Black Sea coast, Blue Lagoon in Iceland, La Roche-Posay in France, Kangal Hot Springs in Turkey ("ichthyotherapy"), Cervia in Italy and in Croatia (naphtalotherapy – using a substance similar to tar) [92, 104, 105]. This is not a complete list, as hot springs with claimed benefits for psoriasis exist in many other countries. In Poland it is primarily Lądek-Zdrój and Busko-Zdrój. The effectiveness is related to the combination of high content of sulfur, selenium, radon, and iodine in mineral waters [106].

In some cases, a mountain climate has been reported to improve psoriasis. The climate of high mountains (1560–2018 m) is believed to be effective for dermatoses and allergic diseases such as atopic dermatitis, eczema, psoriasis, and T-cell lymphomas [107].

Conclusions

It should be remembered that in addition to a healthy lifestyle involving exercising and avoiding stimulants, the patient's mental well-being is also very important. The complexity of psoriasis requires a holistic approach to the patient and comprehensive care, not just treatment.

Figure 2. Success in psoriasis management

Abbreviations

5-HT - 5-hydroxytryptamine; **Ach** - acetylcholine; **AUDIT** - Alcohol Disorder Identification Test; **BMD** - bone mineral density; **BMI** - body mass index; **COPD** - chronic obstructive pulmonary disease; **CRP** - C-reactive protein; **DLQI** - Dermatology Quality of Life Index; **GHQ** - General Health Questionnaire; **GM-CSF** - granulocyte-monocyte colony stimulating factor; **IBD** – inflammatory bowel disease; **IL** – interleukin; **IGA** - Investigator's Global Assessment Scale; **iTNF** - tumor necrosis factor inhibitors; **JAK** - Janus kinase; **JAK-STAT** – transducer protein transcriptional signal activator; **MAPK** - mitogen activated protein kinase; **MMI** - muscle mass index; **NF-jB** - nuclear factor jB; **NHS II** - Nurses' Health Study II; **NK-1** - neurokinin 1; **PASI** - Psoriasis Area and Severity Index; **PsA** - psoriatic arthritis; **STAI** - State-Trait Anxiety Inventory; **TGF** - transforming growth factor; **TNF-α** - tumor necrosis factor alfa; **UV** - ultraviolet; **VAS** - visual analogue scale.

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; **C.G.**: acquisition of data, writing—original draft preparation

Conflict of Interest

The authors have no potential conflicts of interest to declare.

References

[1] Owczarczyk-Saczonek A., Placek W.: Compounds of psoriasis with obesity and overweight. Postępy Hig. Med. Dośw., 2017; 71: 761-772

[2] Zięciak T., Rzepa T., Król J., Żaba R.: Stigmatization feelings and depression symptoms in psoriasis patients. Psychiatr. Pol., 2017; 51: 1153-1163

[3] Auker L., Cordingley L., Pye S.R., Griffiths C.E., Young H.S.: What are the barriers to physical activity in patients with chronic plaque psoriasis? Br. J. Dermatol., 2020; 183: 1094-1102

[4] Piepoli M.F., Hoes A.W., Agewall S., Albus C., Brotons C., Catapano A.L., Cooney M.T., Corrà U., Cosyns B., Deaton C., et al.: 2016 European guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). G. Ital. Cardiol., 2017; 18: 547-612

[5] Do Y.K., Lakhani N., Malhotra R., Halstater B., Theng C., Østbye T.: Association between psoriasis and leisure-time physical activity: Findings from the National Health and Nutrition Examination Survey. J. Dermatol., 2015; 42: 148-153

[6] Ramsay B., O'Reagan M.: A survey of the social and psychological effects of psoriasis. Br. J. Dermatol., 1988; 118: 195-201

[7] Naldi L., Conti A., Cazzaniga S., Patrizi A., Pazzaglia M., Lanzoni A., Veneziano L., Pellacani G., Psoriasis Emilia Romagna Study Group: Diet and physical exercise in psoriasis: A randomized controlled trial. Br. J. Dermatol., 2014; 170: 634-642

[8] Rall L.C., Roubenoff R.: Rheumatoid cachexia: Metabolic abnormalities, mechanisms and interventions. Rheumatology, 2004; 43: 1219-1223

[9] Roubenoff R., Roubenoff R.A., Cannon J.G., Kehayias J.J., Zhuang H., Dawson-Hughes B., Dinarello C.A., Rosenberg I.H.: Rheumatoid cachexia: Cytokine-driven hypermetabolism accompanying reduced body cell mass in chronic inflammation. J. Clin. Invest., 1994; 93: 2379-2386

[10] Walsmith J., Roubenoff R.: Cachexia in rheumatoid arthritis. Int. J. Cardiol., 2002; 85: 89-99

[11] Wijnands M., Burgers A.: Stress fracture in long term methotrexate treatment for psoriatic arthritis. Ann. Rheum. Dis., 2001; 60: 736-739

[12] Zonneveld I.M., Bakker W.K., Dijkstra P.F., Bos J.D., van Soesbergen R.M., Dinant H.J.: Methotrexate osteopathy in long-term, low-dose methotrexate treatment for psoriasis and rheumatoid arthritis. Arch. Dermatol., 1996; 132: 184-187

[13] Simon D., Kleyer A., Bayat S., Tascilar K., Kampylafka E., Meinderink T., Schuster L., Petrov R., Liphardt A.M., Rech J., et al.: Effect of disease-modifying anti-rheumatic drugs on bone structure and strength in psoriatic arthritis patients. Arthritis Res. Ther., 2019; 21: 162

[14] Aguiar R., Sequeira J., Meirinhos T., Ambrósio C., Barcelos A.: SARCOSPA-sarcopenia in spondyloarthritis patients. Acta Reumatol. Port., 2014; 39: 322-326

[15] Krajewska-Włodarczyk M., Owczarczyk-Saczonek A., Placek W.: Changes in body composition and bone mineral density in postmenopausal women with psoriatic arthritis. Reumatologia, 2017; 55: 215-221

[16] Frediani B., Allegri A., Falsetti P., Storri L., Bisogno S., Baldi F., Filipponi P., Marcolongo R.: Bone mineral density in patients with psoriatic arthritis. J. Rheumatol., 2001; 28: 138-143

[17] Borman P., Babaoğlu S., Gur G., Bingol S., Bodur H.: Bone mineral density and bone turnover in patients with psoriatic arthritis. Clin. Rheumatol., 2008; 27: 443-447

[18] Ogdie A., Harter L., Shin D., Baker J., Takeshita J., Choi H.K., Love T.J., Gelfand J.M.: The risk of fracture among patients with psoriatic arthritis and psoriasis: A population-based study. Ann. Rheum. Dis., 2017; 76: 882-885

[19] Dheda K., Cassim B., Patel N., Mody G.M.: A comparison of bone mineral density in Indians with psoriatic polyarthritis and healthy Indian volunteers. Clin. Rheumatol., 2004; 23: 89

[20] Häkkinen A., Sokka T., Kotaniemi A., Kautiainen H., Jappinen I., Laitinen L., Hannonen P.: Dynamic strength training in patients with early rheumatoid arthritis increases muscle strength but not bone mineral density. J. Rheumatol., 1999; 26: 1257-1263

[21] Komatireddy G.R., Leitch R.W., Cella K., Browning G., Minor M.: Efficacy of low load resistive muscle training in patients with rheumatoid arthritis functional class II and III. J. Rheumatol., 1997; 24: 1531-1539

[22] Farkas A., Kemény L.: Alcohol, liver, systemic inflammation and skin: A focus on patients with psoriasis. Skin Pharmacol. Physiol., 2013; 26: 119-126

[23] Kazakevich N., Moody M.N., Landau J.M., Goldberg L.H.: Alcohol and skin disorders: With a focus on psoriasis. Skin Therapy Lett., 2011; 16: 5-6

[24] Al-Jefri K., Newbury-Birch D., Muirhead C.R., Gilvarry E., Araújo-Soares V., Reynolds N.J., Kaner E., Hampton P.J.: High prevalence of alcohol use disorders in patients with inflammatory skin diseases. Br. J. Dermatol., 2017; 177: 837-844

[25] Kirby B., Richards H.L., Mason D.L., Fortune D.G., Main C.J., Griffiths C.E.: Alcohol consumption and psychological distress in patients with psoriasis. Br. J. Dermatol., 2008; 158: 138-140

[26] McAleer M.A., Mason D.L., Cunningham S., O'Shea S.J., McCormick P.A., Stone C., Collins P., Rogers S., Kirby B.: Alcohol misuse in patients with psoriasis: Identification and relationship to disease severity and psychological distress. Br. J. Dermatol., 2011; 164: 1256-1261

[27] Farkas Á., Kemény L.: Psoriasis and alcohol: Is cutaneous ethanol one of the missing links? Br. J. Dermatol., 2010; 162: 711-716

[28] Adamzik K., McAleer M.A., Kirby B.: Alcohol and psoriasis: Sobering thoughts. Clin. Exp. Dermatol., 2013; 38: 819-822

[29] Harvima I.T., Nilsson G., Suttle M.M., Naukkarinen A.: Is there a role for mast cells in psoriasis? Arch. Dermatol. Res., 2008; 300: 461-478

[30] Mendes L.O., Amorim J.P.A., Teixeira G.R., Chuffa L.G., Fioruci B.A., Pimentel T.A., de Mello W. Jr, Padovani C.R., Pereira S., Martinez M., et al.: Mast cells and ethanol consumption: Interactions in the prostate, epididymis and testis of UChB rats. Am. J. Reprod. Immunol., 2011; 66: 170-178

[31] Svanström C., Lonne-Rahm S.B., Nordlind K.: Psoriasis and alcohol. Psoriasis Targets Ther., 2019; 9: 75-79

[32] Gupta A.K., Pandey S.S., Pandey B.L.: Effectiveness of conventional drug therapy of plaque psoriasis in the context of consensus guidelines: A prospective observational study in 150 patients. Ann. Dermatol., 2013; 25: 156-162

[33] Poikolainen K., Reunala T., Karvonen J., Lauharanta J., Kärkkäinen P.: Alcohol intake: A risk factor for psoriasis in young and middle-aged men?. Br. Med. J., 1990; 300: 780-783

[34] Qureshi A.A., Dominguez P.L., Choi H.K., Han J., Curhan G.: Alcohol intake and risk of incident psoriasis in US women: A prospective study. Arch. Dermatol., 2010; 146: 1364-1369

[35] Cassano N., Vestita M., Apruzzi D., Vena G.A.: Alcohol, psoriasis, liver disease, and anti-psoriasis drugs. Int. J. Dermatol., 2011; 50: 1323-1331

[36] Higgins E.: The skin and alcohol. In: Comprehensive Handbook of Alcohol Related Pathology, eds.: V.R. Preedy, R.R. Watson. Elsevier Academic Press, Cambridge (MA) 2004, 599-605

[37] Higgins E.M., du Vivier A.W.: Cutaneous disease and alcohol misuse. Br. Med. Bull., 1994; 50: 85-98

[38] Parisi R., Webb R.T., Carr M.J., Moriarty K.J., Kleyn C.E., Griffiths C.E., Ashcroft D.M.: Alcohol-related mortality in patients with psoriasis a population-based cohort study. JAMA Dermatol., 2017; 153: 1256-1262

[39] Wu S., Cho E., Li W.Q., Han J., Qureshi A.A.: Alcohol intake and risk of incident psoriatic arthritis in women. J. Rheumatol., 2015; 42: 835-840

[40] Thorslund K., Svensson T., Nordlind K., Ekbom A., Fored C.M.: Use of serotonin reuptake inhibitors in patients with psoriasis is associated with a decreased need for systemic psoriasis treatment: A population-based cohort study. J. Intern. Med., 2013; 274: 281-287

[41] Rodgman A., Perfetti T.A.: The Chemical Components of Tobacco and Tobacco Smoke. Second Edition. CRC Press, Boca Raton 2013

[42] Morris P.B., Ference B.A., Jahangir E., Feldman D.N., Ryan J.J., Bahrami H., El-Chami M.F., Bhakta S., Winchester D.E., Al-Mallah M.H., et al.: Cardiovascular effects of exposure to cigarette smoke and electronic cigarettes: Clinical perspectives from the prevention of cardiovascular disease section leadership council and early career councils of the American College of Cardiology. J. Am. Coll. Cardiol., 2015; 66: 1378-1391

[43] Sopori M.: Effects of cigarette smoke on the immune system. Nat. Rev. Immunol., 2002; 2: 372-377

[44] Armstrong A.W., Armstrong E.J., Fuller E.N., Sockolov M.E., Voyles S.V.: Smoking and pathogenesis of psoriasis: A review of oxidative, inflammatory and genetic mechanisms. Br. J. Dermatol., 2011; 165: 1162-1168

[45] Yanagita M., Kobayashi R., Kojima Y., Mori K., Murakami S.: Nicotine modulates the immunological function of dendritic cells through peroxisome proliferator-activated receptor-γ upregulation. Cell. Immunol., 2012; 274: 26-33

[46] Baba N., Rubio M., Kenins L., Regairaz C., Woisetschlager M., Carballido J.M., Sarfati M.: The aryl hydrocarbon receptor (AhR) ligand VAF347 selectively acts on monocytes and naïve $CD4^+$ Th cells to promote the development of IL-22-secreting Th cells. Hum. Immunol., 2012; 73: 795-800

[47] Jin Y., Yang S., Zhang F., Kong Y., Xiao F., Hou Y., Fan X., Zhang X.: Combined effects of HLA-Cw6 and cigarette smoking in psoriasis vulgaris: A hospital-based case-control study in China. J. Eur. Acad. Dermatol. Venereol., 2009; 23: 132-137

[48] Sałata-Nowak J., Flisiak I., Chodynicka B.: Wpływ dymu tytoniowego na skórę. Przegl. Dermatol., 2010; 97: 342-348

[49] Mills C.M., Srivastava E.D., Harvey I.M., Swift G.L., Newcombe R.G., Holt P.J., Rhodes J.: Smoking habits in psoriasis: A case control study. Br. J. Dermatol., 1992; 127: 18-21

[50] Naldi L., Tognoni G., Cainelli T.: Analytic epidemiology in psoriasis. J. Invest. Dermatol., 1994; 102: 19S-23S

[51] Lee Y.H., Song G.G.: Association between circulating 25-hydroxyvitamin D levels and psoriasis, and correlation with disease severity: A meta-analysis. Clin. Exp. Dermatol., 2018; 43: 529-535

[52] Armstrong A.W., Harskamp C.T., Dhillon J.S., Armstrong E.J.: Psoriasis and smoking: A systematic review and meta-analysis. Br. J. Dermatol., 2014; 170: 304-314

[53] Herron M.D., Hinckley M., Hoffman M.S., Papenfuss J., Hansen C.B., Callis K.P., Krueger G.G.: Impact of obesity and smoking on psoriasis presentation and management. Arch. Dermatol., 2005; 141: 1527-1534

[54] Gisondi P., Tessari G., Conti A., Piaserico S., Schianchi S., Peserico A., Giannetti A., Girolomoni G.: Prevalence of metabolic syndrome in patients with psoriasis: A hospital-based case-control study. Br. J. Dermatol., 2007; 157: 68-73

[55] Altunay I., Doner N., Mercan S., Demirci G.T.: Stress coping mechanisms in smoking psoriatics. Dermatol. Sin., 2013; 31: 130-133

[56] Fortes C., Mastroeni S., Leffondré K., Sampogna F., Melchi F., Mazzotti E., Pasquini P., Abeni D.: Relationship between smoking and the clinical severity of psoriasis. Arch. Dermatol., 2005; 141: 1580-1584

[57] Naldi L.: Psoriasis and smoking: Links and risks. Psoriasis, 2016; 6: 65-71

[58] Eriksson M.O., Hagforsen E., Lundin I.P., Michaëlsson G.: Palmoplantar pustulosis: A clinical and immunohistological study. Br. J. Dermatol., 1998; 138: 390-398

[59] Michaëlsson G., Gustafsson K., Hagforsen E.: The psoriasis variant palmoplantar pustulosis can be improved after cessation of smoking. J. Am. Acad. Dermatol., 2006; 54: 737-738

[60] Setty A.R., Curhan G., Choi H.K.: Smoking and the risk of psoriasis in women: Nurses' Health Study II. Am. J. Med., 2007; 120: 953-959

[61] Li W., Han J., Qureshi A.A.: Smoking and risk of incident psoriatic arthritis in US women. Ann. Rheum. Dis., 2012; 71: 804-808

[62] Nguyen U.D., Zhang Y., Lu N., Louie-Gao Q., Niu J., Ogdie A., Gelfand J.M., LaValley M.P., Dubreuil M., Sparks J.A., et al.: Smoking paradox in the development of psoriatic arthritis among patients with psoriasis: A population-based study. Ann. Rheum. Dis., 2018; 77: 119-123

[63] Tillett W., Jadon D., Shaddick G., Cavill C., Korendowych E., de Vries C.S., McHugh N.: Smoking and delay to diagnosis are associated with poorer functional outcome in psoriatic arthritis. Ann. Rheum. Dis., 2013; 72: 1358-1361

[64] Thorneloe R.J., Bundy C., Griffiths C.E.M., Ashcroft D.M., Cordingley L.: Adherence to medication in patients with psoriasis: A systematic literature review. Br. J. Dermatol., 2013; 168: 20-31

[65] Kinahan C.E., Mazloom S., Fernandez A.P.: Impact of smoking on response to systemic treatment in patients with psoriasis: A retrospective case-control study. Br. J. Dermatol., 2015; 172: 428-436

[66] Di Lernia V., Ricci C., Lallas A., Ficarelli E.: Clinical predictors of non-response to any tumor necrosis factor (TNF) blockers: A retrospective study. J. Dermatolog. Treat., 2014; 25: 73-74

[67] Højgaard P., Glintborg B., Hetland M.L., Hansen T.H., Lage-Hansen P.R., Petersen M.H., Holland-Fischer M., Nilsson C., Loft A.G., Andersen B.N., et al.: Association between tobacco smoking and response to tumour necrosis factor α inhibitor treatment in psoriatic arthritis: Results from the DANBIO registry. Ann. Rheum. Dis., 2015; 74: 2130-2136

[68] Owczarczyk-Saczonek A.B., Owczarczyk J., Krajewska-Włodarczyk M., Wojtkiewicz J., Placek W.. Are psoriasis and psoriatic arthritis associated with chronic obstructive pulmonary disease? Przegl. Dermatol., 2019; 106: 185-197

[69] Hrehorów E., Salomon J., Matusiak L., Reich A., Szepietowski J.C.: Patients with psoriasis feel stigmatized. Acta Derm. Venereol., 2012; 92: 67-72

[70] Shelton R.C., Miller A.H.: Eating ourselves to death (and despair): The contribution of adiposity and inflammation to depression. Prog. Neurobiol., 2010; 91: 275-299

[71] Ogłodek E., Marek L., Araszkiewicz A., Placek W., Moś D.: Aleksytymia u pacjenta chorującego na łuszczycę i depresję. Przegl. Dermatol., 2009; 96: 363-366

[72] Chen Y., Xin T., Cheng A.S.: Evaluating the effectiveness of psychological and/or educational interventions in psoriasis: A narrative review. J. Dermatol., 2014; 41: 775-778

[73] Kurd S.K., Troxel A.B., Crits-Christoph P., Gelfand J.M.: The risk of depression, anxiety, and suicidality in patients with psoriasis: A population-based cohort study. Arch. Dermatol., 2010; 146: 891-895

[74] Wojtyna E., Łakuta P., Marcinkiewicz K., Bergler-Czop B., Brzezińska-Wcisło L.: Gender, body image and social support: Biopsychosocial determinants of depression among patients with psoriasis. Acta Derm. Venereol., 2017; 97: 91-97

[75] Singh S., Taylor C., Kornmehl H., Armstrong A.W.: Psoriasis and suicidality: A systematic review and meta-analysis. J. Am. Acad. Dermatol., 2017; 77: 425-440.2

[76] Takahashi H., Tsuji H., Honma M., Shibaki H., Nakamura S., Hashimoto Y., Takahashi M., Koike K., Takei A., Ishida-Yamamoto A., Iizuka H.: Japanese patients with psoriasis and atopic dermatitis show distinct personality profiles. J. Dermatol., 2013; 40: 370-373

[77] Randa H., Lomholt J.J., Skov L., Zachariae R.: Health-related quality of life in adolescents with psoriasis: An interview-based study. Br. J. Dermatol., 2018; 178: 1404-1411

[78] Łakuta P., Przybyła-Basista H.: Toward a better understanding of social anxiety and depression in psoriasis patients: The role of determinants, mediators, and moderators. J. Psychosom. Res., 2017; 94: 32-38

[79] Lim D.S., Bewley A., Oon H.H.: Psychological profile of patients with psoriasis. Ann. Acad. Med. Singap., 2018; 47: 516-522

[80] Krajewska-Włodarczyk M., Owczarczyk-Saczonek A., Placek W.: Sleep disorders in patients with psoriatic arthritis and psoriasis. Reumatologia, 2018; 56: 301-306

[81] Gupta M.A., Simpson F.C., Gupta A.K.: Psoriasis and sleep disorders: A systematic review. Sleep Med. Rev., 2016; 29: 63-75

[82] Fortune D.G., Richards H.L., Kirby B., Bowcock S., Main C.J., Griffiths C.E.: A cognitive-behavioural symptom management programme as an adjunct in psoriasis therapy. Br. J. Dermatol., 2002; 146: 458-465

[83] Piaserico S., Marinello E., Dessi A., Linder M.D., Coccarielli D., Peserico A.: Efficacy of biofeedback and cognitive-behavioural therapy in psoriatic patients: A single-blind, randomized and controlled study with added narrow-band ultraviolet B therapy. Acta Derm. Venereol., 2016; 96: 91-95

[84] Tausk F., Whitmore S.E.: A pilot study of hypnosis in the treatment of patients with psoriasis. Psychother. Psychosom., 1999; 68: 221-225

[85] Gaston L., Crombez J.C., Joly J., Hodgins S., Dumont M.: Efficacy of imagery and meditation techniques in treating psoriasis. Imagin. Cogn. Pers., 1989; 8: 25-38

[86] Kabat-Zinn J., Wheeler E., Light T., Skillings A., Scharf M.J., Cropley T.G., Hosmer D., Bernhard J.D.: Influence of a mindfulness meditation-based stress reduction intervention on rates of skin clearing in patients with moderate to severe psoriasis undergoing phototherapy (UVB) and photochemotherapy (PUVA). Psychosom. Med., 1998; 60: 625-632

[87] Lazaroff I., Shimshoni R.: Effects of medical resonance therapy music on patients with psoriasis and neurodermatitis - a pilot study. Integr. Physiol. Behav. Sci., 2000; 35: 189-198

[88] Lavda A.C., Webb T.L., Thompson A.R.: A meta-analysis of the effectiveness of psychological interventions for adults with skin conditions. Br. J. Dermatol., 2012; 167: 970-979

[89] Moon H.S., Mizara A., McBride S.R.: Psoriasis and psycho-dermatology. Dermatol. Ther., 2013; 3: 117-130

[90] Riyaz N., Arakkal F.R.: Spa therapy in dermatology. Indian J. Dermatol. Venereol. Leprol., 2011; 77: 128-134

[91] Harari M.: Climatoterapia de las enfermedades de la Piel en el Mar Muerto - una Actualización. An. Hidrol. Médica., 2012; 5: 39-51

[92] Kazandjieva J., Grozdev I., Darlenski R., Tsankov N.: Climatotherapy of psoriasis. Clin. Dermatol., 2008; 26: 477-485

[93] Hodak E., Gottlieb A.B., Segal T., Politi Y., Maron L., Sulkes J., David M.: Climatotherapy at the Dead Sea is a remittive therapy for psoriasis: Combined effects on epidermal and immunologic activation. J. Am. Acad. Dermatol., 2003; 49: 451-457

[94] Péter I., Jagicza A., Ajtay Z., Boncz I., Kiss I., Szendi K., Kustán P., Németh B.: Balneotherapy in psoriasis rehabilitation. In Vivo, 2017; 31: 1163-1168

[95] Abels D.J., Rose T., Bearman J.E.: Treatment of psoriasis at a Dead Sea dermatology clinic. Int. J. Dermatol., 1995; 34: 134-137

[96] Emmanuel T., Lybæk D., Johansen C., Iversen L.: Effect of Dead Sea climatotherapy on psoriasis; A prospective cohort study. Front. Med., 2020; 7: 83

[97] Shani J., Harari M., Hristakieva E., Seidl V., Bar-Giyora J.: Dead-Sea climatotherapy versus other modalities of treatment for psoriasis: Comparative cost-effectiveness. Int. J. Dermatol., 1999; 38: 252-262

[98] Golušin Z., Jovanović M., Gajinov B.J., Jolić S.: Balneotherapy of psoriasis. Serbian J. Dermatol. Venereol., 2015; 6: 105-112

[99] Soroka Y., Ma'or Z., Leshem Y., Verochovsky L., Neuman R., Brégégère F.M., Milner Y.: Aged keratinocyte phenotyping: Morphology, biochemical markers and effects of Dead Sea minerals. Exp. Gerontol., 2008; 43: 947-957

[100] Dawe R.S., Yule S., Cameron H., Moseley H., Ibbotson S.H., Ferguson J.: A randomized controlled comparison of the efficacy of Dead Sea salt balneophototherapy vs. narrowband ultraviolet B monotherapy for chronic plaque psoriasis. Br. J. Dermatol., 2005; 153: 613-619

[101] Boros M., Kemény Á., Sebők B., Bagoly T., Perkecz A., Petőházi Z., Maász G., Schmidt J., Márk L., László T., et al.: Sulphurous medicinal waters increase somatostatin release: It is a possible mechanism of anti-inflammatory effect of balneotherapy in psoriasis. Eur. J. Integr. Med., 2013; 5: 109-118

[102] Gálvez Galve J.J., Peiró P.S., Lucas M.O., Torres A.H., Gil E.S., Pérez M.B.: Quality of life and assessment after local application of sulphurous water in the home environment in patients with psoriasis vulgaris: A randomised placebo-controlled pilot study. Eur. J. Integr. Med., 2012; 4: e213-e218

[103] Khalilzadeh S., Shirbeigi L., Naghizadeh A., Mehriardestani M., Shamohammadi S., Tabarrai M.: Use of mineral waters in the treatment of psoriasis: Perspectives of Persian and conventional medicine. Dermatol. Ther., 2019; 32: e12969

[104] Damevska K., França K., Lotti T., Nikolovska S., Pollozhani N.: Complementary and integrative therapies for psoriasis: Looking forward. Dermatol. Ther., 2018; 31: e12627

[105] Melandri D., Albano V.M., Venturi M., Flamigni A., Vairetti M.: Efficacy of combined liman peloid baths and heliotherapy in the treatment of psoriasis at Cervia spa, Emilia, Italy. Int. J. Biometeorol., 2020; 64: 1145-1152

[106] Rokowska-Waluch A., Pielesiak A., Pawlaczyk M.: Spa-terapia w leczeniu łuszczycy. Przegl. Dermatol., 2009; 96: 367-370

[107] Tsankov N.K.: High mountain climatotherapy. Clin. Dermatol., 1998; 16: 699-707