DOI 10.29254/2523-4110-2024-2-173/addition-55-58
UDC 616.517

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PATHOGENESIS AND CURRENT APPROACHES TO THE TREATMENT OF PSORIASIS: A REVIEW OF RECENT RESEARCH AND CLINICAL GUIDELINES

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Анотація: *У статті розглядаються сучасні погляди на патогенез псоріазу, зокрема роль імунної системи та запальних процесів у розвитку цього захворювання. Псоріаз є комплексним автоімунним захворюванням, що вимагає глибокого розуміння механізмів його виникнення та прогресування для розробки ефективних терапевтичних підходів. Стаття детально аналізує сучасні підходи до лікування псоріазу, включаючи традиційні методи, такі як топічні препарати і фототерапія, а також новітні методи, включаючи біологічну терапію, що спрямована на конкретні молекулярні мішені в імунній системі. Розглядаються результати останніх клінічних досліджень, які демонструють ефективність і безпеку різних лікувальних стратегій, а також надаються рекомендації щодо їх використання в клінічній практиці. Особлива увага приділяється інноваційним терапевтичним підходам, таким як інгібітори цитокінів, що грають ключову роль у запальних процесах, та перспективам використання генної терапії. Висвітлюються питання довгострокового моніторингу пацієнтів, управління побічними ефектами та індивідуалізації лікування з урахуванням генетичних та клінічних характеристик хворих. Стаття надає всебічний огляд сучасних знань про псоріаз, що може бути корисним для дерматологів, дослідників і клініцистів, які займаються лікуванням цього захворювання. Вона підкреслює важливість багатофакторного підходу до терапії псоріазу та необхідність подальших досліджень для вдосконалення лікувальних стратегій та покращення якості життя пацієнтів.*

Ключові слова: *запалення, аутоімунні захворювання, лікування, клінічні рекомендації, дерматологія.*

Abstract. *The article examines modern views on the pathogenesis of psoriasis, particularly the role of the immune system and inflammatory processes in developing this disease. Psoriasis is a complex autoimmune disease that requires a deep understanding of its occurrence and progression mechanisms to develop effective therapeutic approaches. The article provides a detailed analysis of current approaches to treating psoriasis, including traditional methods such as topical medications and phototherapy, and newer methods, including biological therapies targeting specific molecular targets in the immune system. The results of recent clinical studies demonstrating the effectiveness and safety of various treatment strategies are reviewed, and recommendations for their use in clinical practice are provided. Special attention is paid to innovative therapeutic approaches, such as inhibitors of cytokines that play a crucial role in inflammatory processes and prospects for gene therapy. Issues of long-term monitoring of patients, management of side effects and individualization of treatment taking into account the genetic and clinical characteristics of patients, are covered. The article provides a comprehensive overview of the current knowledge about psoriasis, which may be helpful for dermatologists, researchers and clinicians involved in treating this disease. She emphasizes the importance of a multifactorial approach to psoriasis therapy and the need for further research to improve treatment strategies and patients' quality of life.*

Key words: *inflammation, autoimmune diseases, treatment, clinical recommendations, dermatology.*

Introduction.

Psoriasis is a long-term autoimmune condition and proliferative skin disorder. Erythematous plaques surrounded by silvery scales, especially over the scalp, lumbosacral area, and extensor surfaces, are characteristic. The eyes and joints may also be impacted by the condition [1]. Psoriasis has no known treatment, and flare-ups cause the condition to wax and wane. Because their quality of life is so low, many psoriasis patients experience depression. Psoriasis has multiple kinds, but the most prevalent one is the plaque form, which affects the scalp, limbs, and trunk. Upon closer inspection, the plaques typically exhibit silvery-white scales. Around 10% of patients, primarily women, have eye problems [2]. Normally, ocular involvement is almost always linked to skin traits rather than occurring in isolation. Usually, a skin cell grows for one month before falling off. However, in psoriasis, skin cells multiply in 3-4 days and accumulate as plaques on the skin instead of peeling off [3]. This results in inflammation, which can produce skin surface lesions that are itchy, unpleasant, and occasionally painful. Psoriasis is a long-term inflamed and proliferative skin disorder. Pigmented plaques covered in silvery dimensions, especially over the top of the head, lumbosacral area, and quadriceps surfaces, are its characteristic [4].

The aim of the study.

A comprehensive study of modern approaches to understanding the pathogenesis of psoriasis and an analysis of the effectiveness of existing methods of treating this disease. The research is aimed at evaluating the role of the immune system and inflammatory processes in the development of psoriasis, studying the latest diagnostic methods, including genetic and molecular markers, as well as analyzing the effectiveness of traditional and modern treatment methods, such as topical drugs, phototherapy, biological therapy and other innovative approaches. The study aims to provide dermatologists, researchers and clinicians with relevant information and practical suggestions to improve patients' psoriasis quality of life by improving diagnostic and therapeutic approaches.

Object and research methods.

An analysis of PubMed, Scopus, and Web of Science database sources was conducted for the keywords "psoriasis", "autoimmune diseases" starting from 2018 to

2024. The obtained information was systematized according to the purpose of the study. The results of the latest clinical studies and the development of clinical recommendations for practising doctors are separately investigated. Prospects for using the latest therapeutic strategies, including cytokine inhibitors and gene therapy, are determined, and recommendations for long-term patient monitoring and treatment individualization are developed.

Main part.

The widespread presence of psoriasis varies from 0.2% to 4.8%. Although the precise cause is uncertain, T-cells are thought to be involved in the autoimmune disease. Numerous individuals with psoriasis share HLA antigens, especially those from different racial and ethnic backgrounds. Its genetic propensity is suggested by its hereditary prevalence. Psoriasis lesions are brought on by mechanical, chemical, and radiation damage. Psoriasis can be made worse by some medications, including lithium, beta-blockers, NSAIDs, steroids, and chloroquine [5]. In broad terms, psoriasis improves in the summer and worsens in the winter. Infections, psychological stress, alcohol, smoking, obesity, and hypocalcemia are other factors that might cause psoriasis in addition to the ones mentioned above. Being an immune-mediated condition, psoriasis results from your body's immune system overreacting and creating issues [6]. Immune cells become activated and release chemicals when psoriasis triggers the skin's rapid cell growth. This explains why the condition causes scaly, irritated skin in those with it. Although the exact cause of the defective immune cell activation remains unknown, scientists do know that a combination of environmental and genetic factors are involved. Numerous people with psoriasis have a family history of the condition, and researchers have identified specific genes that may play a role in its development. A large number of them are involved in immune system activity and infections, particularly those caused by HIV and streptococci. Some medications, such as those used to treat mental health issues, malaria, cardiovascular disease, cigarette smoking, and being overweight [7].

The invasion of skin by activated T-lymphocytes, which promote keratinocyte proliferation, is a pathophysiological aspect of psoriasis. Thick plaques are the outcome of this imbalance in keratinocyte turnover. Parakeratosis and epidermal hyperplasia are further related characteristics. Furthermore, the failure of the epidermal cells to release lipids causes the characteristic dry and scaly skin of psoriasis. Everywhere is affected by psoriasis, and its frequency varies [8]. Approximately 2% of people in the US are impacted. There have been reports of high incidence of psoriasis in the Faroe Islands. Psoriasis is uncommon in Japan and may not even be present in Native Americans from South America or Australia. Any age can be affected by psoriasis. The age of onset is bimodal.

Psoriasis often manifests for the first time between the ages of 15 and 20, with a second peak between the ages of 55 and 60. Well-defined erythematous plaques covered in silvery scales are the typical presentation of psoriasis, and they are typically found over the scalp and extensors of extremities, especially over the knees, elbows, and lumbosacral area [9]. There are two categories of psoriasis. While type 2 psoriasis does not exhibit a family history, manifests after the age of 40, and is not linked to HLA-Cw6, type 1 psoriasis has a positive family history, begins before the age of 40, and is connected with HLA-Cw6. There are several morphologies in which psoriasis can manifest, including plaque, guttate, rupioid, erythrodermic, pustular, inverted, elephantine, and psoriatic arthritis. Involvement of the scalp, palmoplantar area, genitalia, and nails indicates a site's variation. Any harm to the skin that results from mechanical, chemical, or radiation treatment in individuals who have psoriasis [10].

The Koebner phenomenon states that any skin damage caused by mechanical, chemical, or radiation harm to people with psoriasis results in psoriasis lesions at that location. It shows how active the illness is. Typically, plaque psoriasis manifests as erythematous plaques with silvery scales most frequently found over the extensors of extremities, such as the back, scalp, elbows, and knees. 85% to 90% of people have this kind of psoriasis, which is the most prevalent kind. Once the psoriatic scales are removed one by one, precise bleeding sites become visible. This is known as the Auspitz sign, and it is used to confirm the diagnosis [11] clinically. Psoriasis with guttate, also known as eruptive psoriasis, is frequently observed in children following an upper respiratory tract infection caused by streptococcal bacteria. Raindrop-shaped, erythematous, scaly lesions are the predominant lesions on the trunk and back. It's the kind of psoriasis with the best outlook. Small, non-infectious pus-filled lesions with erythema surrounding them are the hallmarks of pustular psoriasis. There are two varieties: specialised and broad. Hypocalcemia is linked to generalised pustular psoriasis, which manifests as sterile pustules on an erythematous plaque that covers the entire body [12]. Over 90% of the body is covered in exfoliated skin and displays extensive inflammation in the form of erythema in cases of erythrodermic psoriasis. Severe discomfort, oedema, and itching are linked to it. It is the outcome of systemic steroids being abruptly stopped, which causes an increase in unstable plaque psoriasis. Erythroderma complications include compromised skin barrier functions, altered basal metabolic rate, and increased cutaneous circulation, which can lead to cardiac failure [13].

Pitting, oil patches, subungual hyperkeratosis, nail dystrophy, and anchylosis are some nail abnormalities associated with psoriasis. According to reports, the most typical sign of oral psoriasis is a fissured tongue, which affects 6.5% to 20% of those with psoriasis affecting the skin. Other names for inverse psoriasis include intertriginous psoriasis and flexural psoriasis. The condition manifests as erythematous, smooth, and well-defined patches that target intertriginous regions such as the armpits, groynes, intergluteal area, and inframammary region. The skin may have itchy cracks, smell bad, or both. It may also be wet and macerated [1, 8]. It must be distinguished from the dermatophyte infection that affects the same locations, which manifests as the active border with scales, vesicles, and pustules along the periphery and centre clearing. Sebopsoriasis is a kind of psoriasis that usually appears as greasy-scaled red plaques. It usually affects the scalp, forehead, nasolabial folds, sternum, and retro-auricular areas known to produce more sebum [11]. Thirty percent of psoriasis patients have psoriatic arthritis, a chronic inflammatory

arthritis. It frequently coexists with psoriasis of the skin and nails. It usually entails excruciating joint inflammation, with the joints of the fingers and toes being particularly affected by connective tissue. Dactylitis, a sausage-shaped oedema of the fingers and toes, is the result. In addition to affecting the hips, knees, and spine, psoriatic arthritis can also cause spondylitis and sacroiliac joint sacroiliitis [10]. Ocular features: Trichiasis, ectropion, conjunctivitis, and corneal dryness are caused by psoriasis, which also affects the eyelid, conjunctiva, and cornea. Blepharitis, the most prevalent eye condition, is a precursor to trichiasis, madarosis, and cicatricial ectropion. Sometimes, one can notice anterior uveitis [9]. Typically, the clinical appearance and lesion site are used to diagnose. Although rarely required, histopathology can aid in diagnosing difficult psoriasis by distinguishing it from other dermatoses. The biopsy reveals characteristic changes such as parakeratosis, micro-abscess, lack of granular lesions, regular ridge elongation resembling a camel's foot, and spongiform pustules of Kogoj with tortuous and dilated capillaries in the dermal papilla [8].

The most used measurement method for determining the severity of the condition and assessing the efficacy of treatment is the Psoriasis Area Severity Index or PASI. Topical therapy is employed for mild to moderate psoriasis. Moisturisers and emollients may support maintaining the stratum corneum's moisture content and enhancing barrier function. Coal tar, dithranol, corticosteroids, vitamin D analogues, and retinoids are the first topical agents utilised. Methotrexate may be helpful for people who do not respond to the therapies mentioned above. Although it should only be administered sporadically, cyclosporine can be utilised to cause a clinical response. When methotrexate is not working for a patient, try biological medicines; occasionally, mix them with methotrexate. Phototherapy encompasses two types of light exposure: narrowband UVB light, which has a wavelength between 311 and 313 nanometers, and PUVA therapy, which combines psoralen with UVA radiation. Without the psoralen's gastrointestinal distress, cataract formation, and carcinogenic consequences, NBUVB is just as effective. UVB light that is narrowband and has a wavelength range of 311-313 nanometers. Without the psoralen's gastrointestinal distress, cataract formation, and carcinogenic consequences, NBUVB is just as effective. Children, pregnant or nursing women, and even elderly individuals can safely take it. Phototherapy is most effective in treating guttate psoriasis. When psoriatic arthritis and nails are involved, systemic medications are administered. Fumarates, cyclosporine, retinoids, and methotrexate are among the alternatives. Regular liver, kidney, and blood function monitoring is necessary for patients receiving systemic therapy. Biologicals, which include infliximab, adalimumab, etanercept, and interleukin antagonists, are synthetic proteins that impede the immune system in psoriasis. It is essential to screen the patient for hepatitis and tuberculosis before administering any biological agent. These individuals carry a significant risk of infection, hence every safety measure should be done to prevent the patient from becoming seriously immunocompromised. Extended usage of immunosuppressive medications, such as steroids, might impede the healing of wounds. Topical corticosteroids must be used aggressively to treat ocular psoriasis. Psoriasis patients should stay away from any skin trauma to prevent the Kobner reaction. Patients with psoriasis should also refrain from using NSAIDs, beta-blockers, or chloroquine. They should also avoid alcohol due to the possibility of developing fatty liver [1-3, 7].

Psoriasis is a chronic illness recognised to negatively affect the patient's and their family's quality of life. Relapses and remissions are a permanent feature of psoriasis. Roughly 10% of patients experience severe arthritis with deformity. Ten to 60% of patients get remissions. Psoriasis has been linked to several skin malignancies, metabolic syndrome, depression, alcoholism, smoking, substance addiction, and suicide throughout the disease. Furthermore, significant medical comorbidities like renal illness, heart disease, and joint issues are frequently present in psoriasis patients. Adverse cardiac events and psoriasis have been linked in several studies. While psoriatic arthritis has a poor functional prognosis, pustular and erythrodermic psoriasis can pose a life-threatening risk. When there is a presence of more than 10% BSA, psoriasis is deemed widespread. It is also regarded as severe when the illness affects the face, nails, scalp, genitalia, flexures, and soles because these regions are difficult to treat and are linked to poor cosmesis. In individuals with active, severe psoriasis or if methotrexate is not well tolerated, biological therapy should be explored as soon as possible. Record improvements in physical, social, and psychological functioning as well as a decrease in the initial severity of the disease to gauge the effectiveness of the treatment. The preferred first-line biological agent is uzekinumab. Secukinumab is an additional substitute. The first-line biological treatment of choice for those with psoriatic arthropathy is adalimumab. Patients with serious illnesses for whom other biological agents are unsuitable should only use infliximab. When starting a biological agent, women who are of reproductive age should also begin using effective contraception. Those who are taking biological agents should not receive live vaccinations. All immunisations must be finished before using biological agents. TNF antagonists should not be used to treat patients with demyelinating diseases. TNF antagonists should not be used to treat heart failure patients. Although psoriasis is a skin condition, it is typically managed by specialists who specialise in it due to its complexity. These individuals should be managed by a dermatologist and a nephrologist, plastic surgeon, chemist, rheumatologist, and ophthalmologist. The main objective is to raise the patient's quality of life by teaching them how to avoid triggers. The patient should receive instruction from the chemist on how to treat dry skin and apply moisturisers. Patients must continue to take their drugs as prescribed, and the chemist should make sure the patient isn't taking any that could trigger flare-ups. To help the patient make lifestyle changes, the nurse should advise them to abstain from alcohol, tobacco, stress, and dry, cold weather. Sunlight has many advantages, but too much of it should be avoided. In addition to sending the patient to a mental health counsellor, the nurse should keep an eye out for any self-harm behaviours. Lastly, the patient must be instructed to maintain a healthy weight, exercise frequently, and eat a balanced diet. Relapses are prevalent in people living with psoriasis, thus lifelong follow-up is necessary. Better results will come from managing an interprofessional team [Scale

V]. Despite being a benign skin problem, psoriasis is incurable and a lifetime condition. Everybody experiences remissions and relapses, which generally lowers quality of life. Numerous data out there now suggest that psoriasis raises the likelihood of unfavourable cardiac events as well. In addition, psoriasis is linked to adverse drug reactions, alcohol consumption, smoking, depression, lymphoma risk, suicide, and several skin malignancies. There is growing evidence linking psoriasis to heart disease, kidney illness, and hypertension. Those with psoriasis on their palms and soles typically lead a significantly lower quality of life than those with psoriasis in other body areas [3-6].

Conclusions.

Psoriasis is a complex autoimmune disease characterized by dysregulation of the immune system and chronic inflammatory processes. Genetic and molecular studies confirm the critical role of genetic markers and cytokines in developing the disease. The latest diagnostic approaches, including genetic and molecular markers, allow more precise determination of the form and severity of psoriasis, which contributes to the individualization of treatment. Traditional treatments, such as topical medications and phototherapy, remain important tools in treating psoriasis. At the same time, biological therapy and other innovative approaches demonstrate high efficiency, especially in severe and resistant psoriasis cases. Cytokine inhibitors and other new treatments are opening up new possibilities for disease control. The introduction of gene therapy and other advanced technologies may significantly improve treatment outcomes in the future. The latest clinical research provides the basis for the development of practical clinical guidelines that consider patients' individual characteristics, providing a more personalized approach to treatment. Regular monitoring of the condition of patients with psoriasis is critical for evaluating the effectiveness of treatment, managing side effects, and timely adjusting therapeutic strategies.

Further research is needed for a deeper understanding of the pathogenetic mechanisms of psoriasis and the development of new treatment methods. Integrating data from genomic, proteomic, and metabolomic studies may contribute to developing more effective and safer therapeutic approaches.

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