



Review Paper

"Understanding Psoriasis: A Comprehensive Review of Its Causes and Treatments"

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ABSTRACT

Psoriasis is a chronic, inflammatory skin disease characterized by red, scaly plaques that can affect various body regions, including the scalp, nails, and joints. This condition, which arises from immune dysregulation, significantly impacts the quality of life and is associated with comorbidities such as cardiovascular disorders, arthritis, and psychiatric diseases. The etiology of psoriasis involves genetic, immunological, and environmental factors, with genetic predisposition playing a critical role. Immunologically, the interaction between T-cells, cytokines, and keratinocytes drives the disease, particularly through the IL-17 and IL-23 pathways. Various triggers, including infections, stress, and medications, can exacerbate the condition. Psoriasis manifests in multiple forms, such as plaque, guttate, pustular, and erythrodermic psoriasis, each with distinct clinical features.

The treatment of psoriasis is multi-faceted, ranging from topical therapies and phototherapy to systemic medications like methotrexate, cyclosporine, and biologics that target specific immune pathways. Recent advancements include the development of JAK inhibitors and personalized medicine approaches, which hold promise for improving patient outcomes. This review emphasizes the importance of individualized treatment plans, patient education, and lifestyle modifications for effectively managing psoriasis and its associated complications.

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1. INTRODUCTION

Psoriasis is an unremitting chronic disease that in other dimensions is known to be painful and not transmissible. It comes with various comorbid conditions and is noted with lumbosacral region involvement as well as knees, elbows, scalp involvement, body folds, nails, and other places like the lover, blood, joints, and pathways. In comparison with

other cutaneous disease, the skin plaques seen in psoriasis can be unilateral and bilateral or across the mid-line of the body, and it is inflammatory, well-defined borders, erythematous plaques, and papules covered with white or silver scales. In addition, lesions itch with an erythematous papule centrally and flapping margins allowing a 'star-shaped' appearance. Statistics evidences in that the patients affected by

exfoliative psoriasis are more liable to set of other complications associated with this disease, like developing cardiovascular conditions as well as other non-infectious diseases.^{1,2}

Psoriasis is chronic inflammatory disease of the skin of long-lived duration and which is characterized by raised spots of red patches covered with scales; controlled by hereditary influence. Generally, chronic psoriasis develops because the immune system is making wrong faulty signals.³

Psoriasis presents as a very variable papulosquamous condition in its appearance, distribution, severity, and duration. Papulosquamous diseases have scaling papules that are elevation less than 1 cm in diameter and plaques having elevation or more than 1 cm in diameter. Psoriasis lesions typically are round, red papules or plaques with well-demarcated borders having a dry, grey, or silvery-white scale.²

Psoriasis is a chronic inflammatory skin disease due to immune dysregulation, and it carries several morbidities: arthropathy, psychiatric diseases, cardiovascular disorders, and liver disease. In 2014, the World Health Organization recognized psoriasis as a serious non-communicable disease and also mentioned suffering from inappropriate treatment, and stigma associated with the disease.⁴

Aetiology

Genetic factors

Psoriasis has essentially emerged due to genetic disposition. Of course, genetic involvement is one of the characteristics of psoriasis as 40% of patients have a family history of this disorder. More than 60 susceptibility loci have been identified by genome-wide association studies; most of these loci are involved in the regulation of the immune function. While some genes for example, HLA-B17 actually increase the risk for a more severe form of psoriasis, the allele HLA-Cw6 on chromosome 6p21 is the one that has more reliably been associated with early onset of psoriasis.

Immunological factors

- The major cause of psoriasis is an immune-mediated disease. An overly active immunological response, particularly concerning T cells and cytokines, characterizes the disease. Key players in its pathogenesis include:
- TH17 and TH22 cells produce pro-inflammatory cytokines including IL-17 and IL-22 respectively. These cytokines induce proliferation and inflammation of keratinocytes.
- Dendritic cells and antimicrobial peptides form two critical components that interact in a complex network in maintaining inflammatory skin homeostasis.

This has created a conceptual shift away from the earlier view of simple keratinocyte hyperproliferation to the recognition that dysfunction of the immune system is indeed broader based and encompasses, in large part, an overall critical dysregulation of the immunological response in psoriasis.⁶

Environmental and Behavioural Triggers

Psoriasis symptoms can be aggravated or triggered by a number of outside events, such as:

Infections: Psoriasis flare-ups have been related to the onset of bacterial and viral infections, especially streptococcal infections.

Stress: It is commonly known that psychological stress can lead to flare-ups of psoriasis.

Medication: Some medications, such as those for mental health issues or heart problems, might exacerbate the symptoms of psoriasis.

Lifestyle factors: Drinking alcohol, smoking, and being obese are linked to a higher chance of developing the condition.^{5,7}

Symptoms of Psoriasis

- Red, flaky plaques in the different areas like elbows, knees, scalp, trunk, palms, and soles of the feet.
- The skin of the patients will be dry, cracked with potential itch or bleed.
- The nails can be found thick, elevated and dented.
- Sleep quality will be poor.^{5,8}

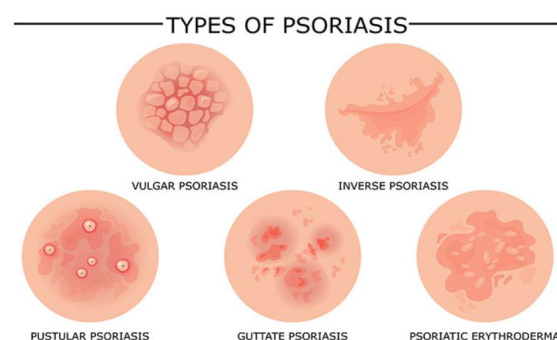


Fig. 1. Types of Psoriasis⁹

Types of Psoriasis:

1. **Plaque psoriasis:** It is well-defined, inflamed, thickened areas of discolored skin larger than 0.5 cm in diameter either as individual lesions or generalized disease. With peripheral extension in a gradual manner, plaques can take multiple forms like **Psoriasis gyrate**, **Annular psoriasis**, and **Psoriasis follicularis**.



Fig 2. Plaque Psoriasis

It is further categorized based on anatomical locations.

Flexural psoriasis is commonly referred to as inverse psoriasis. It represents as well-defined, slightly scaly, thin plaques that are confined to the folds of the skin. It commonly affects areas such as the inframammary, axillary, groin, genital, and natal cleft regions.¹⁰

Nail psoriasis is seen even when there are no associated skin abnormalities. Symptoms include pitting, onycholysis, subungual hyperkeratosis, oil drop sign, splinter hemorrhages etc. Nail involvement is a sole predictor of psoriatic arthritis, with fingernails being affected more often than toe nails.

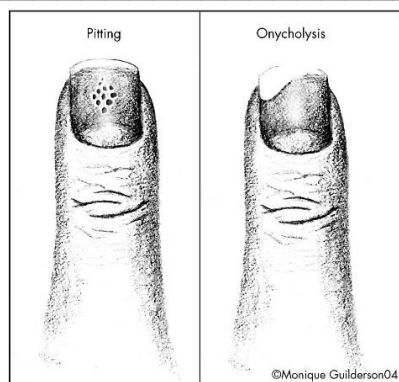


Fig 3 . Nail Psoriasis¹¹

Scalp psoriasis mainly occurs on the scalp. In general, it is quite difficult to treat.



Fig 4 Scalp psoriasis¹²

Palmoplantar psoriasis is the condition which is confined to the hands and soles of the feet, characterized by a continuous redness, and scaling. This presentation can vary from vague scaly or cracked areas to large patches covering the palm or sole, without well-defined plaques.



Fig 5 Palmoplantar psoriasis¹³

Guttate psoriasis : The term guttate comes from the Greek word for droplet, reflecting the sudden appearance of numerous small psoriasis lesions measuring 2-10 mm in diameter. These lesions typically appear in a centripetal pattern but can also affect the head and limbs. The condition

features an acute eruption of small, fine-scaled papules that are salmon pink in color, often found on the trunk or limbs. It frequently occurs after a group A streptococcal throat infection or perianal group A streptococcus dermatitis and can be the first sign of psoriasis in children or, less commonly, in adults. Approximately one-third of people with guttate psoriasis may later develop plaque psoriasis during adulthood.



Fig 6 Guttate psoriasis¹⁴

Pustular psoriasis can occur in localized or generalized forms. Two specific localized types are Psoriasis palmoplantaris (PPP) and Acrodermatitis Continua of Hallopeau (ACs). PPP affects only the palms and soles, while ACs targets the tips of fingers and toes, including the nails. Generalized pustular psoriasis is a rare and acute condition that indicates an unstable disease state, characterized by rapid progression, widespread redness, and sub corneal pustules, often with systemic symptoms. Triggers can include stopping systemic or strong topical corticosteroids and infections. Patients typically experience fever and red, painful skin covered with sterile pustules that may merge into large areas.



Fig 7 Pustular psoriasis¹⁵

Erythrodermic psoriasis is a serious condition marked by widespread inflammation and redness covering over 90% of the body's surface. It can develop from any type of psoriasis and requires urgent medical attention. Complications may include hypothermia, low albumin levels, electrolyte imbalances, and high-output heart failure.^{2,7,18,19}

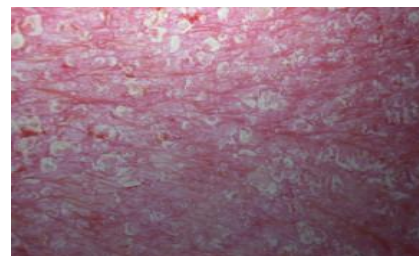


Fig 8 Erythrodermic psoriasis¹⁶

Pathophysiology

The causes of psoriasis are completely and not fully understood. A significant factor in the development of psoriasis is the overactivation of certain components of the adaptive immune system. In the initial stages of lesion formation, various cell types-including plasmacytoid dendritic cells, keratinocytes, natural killer T cells, and macrophages-release cytokines

that help activate myeloid dendritic cells. During the early pathogenesis of psoriasis, complexes formed by the antimicrobial peptide LL37 and self-DNA trigger plasmacytoid dendritic cells to produce interferon IFN- α , which subsequently activates myeloid dendritic cells. These activated cells then produce IL-12, promoting the differentiation of naïve T cells into T_H1 cells. Additionally, IL-23 plays a crucial role in the survival and proliferation of T_H17 and T_H22 cells. T_H1 cells secrete IFN- γ and TNF- α , while T_H22 cells release IL-22 cells produce IL-17, IL-22 and TNF- α .^{19,20} Among these mechanisms, the activation of the T_H17 pathway by IL-23 is regarded as the main driver. The intracellular signalling of IL-23 occurs through the Tyk2-Jak2 pathway and the activation of the STAT3 transcription factor. This signalling cascade results in the production of important inflammatory cytokines. These secreted cytokines, in turn, promote keratinocyte overgrowth, enhance angiogenic mediators and endothelial adhesion molecules, and attract immune cells to the affected skin areas.^{21,22,23,24}

Treatment

Several therapies exist for the Psoriasis treatment. Treatments are based on the type and disease severity, and the portion of the skin affected.

Non-pharmacologic Therapy

In order to control psoriasis, the guided imagery and stress management techniques will decrease its intensity. Non-medicated moisturizers should be used to maintain hydration of the skin, reduce shedding, minimize scaling, and itching. The oatmeal bath may be used to alleviate itching and may minimize the need for systemic antipruritic medication. Avoid irritating soaps and detergents; bathe in tepid water using lipid and fragrance-free cleansers. Apply sunscreen when going outdoors.

Pharmacologic therapy

Topical therapy

Emollient

Applying emollients like soft yellow paraffin, aqueous cream, petrolatum, or ceramides twice a day can alleviate psoriasis by moisturizing the skin, decreasing itching and inflammation, and preventing dryness and cracking.

Corticosteroids: Topical corticosteroids, such as clobetasol propionate, are a primary treatment for psoriasis, effectively reducing inflammation and slowing skin cell growth. However, prolonged use, especially on sensitive areas, can cause skin atrophy and serious side effects like Cushing's syndrome and glaucoma. Pregnant women should consult their doctor before using corticosteroids due to potential systemic issues like adrenal suppression.

Combination therapies: A common approach involves using corticosteroids alongside other treatments. Vitamin D derivatives like calcipotriene help to normalize skin cell growth, while calcineurin inhibitors such as tacrolimus reduce inflammation through a distinct mechanism.²³

Light Therapy Ultraviolet B (UVB) Phototherapy: This safe and effective option uses UVB rays to slow skin cell growth. Treatments are typically done in the clinic several times a week. Home UVB

phototherapy units are also available but require close supervision from a dermatologist.

Psoralen plus Ultraviolet A (PUVA) Therapy: PUVA combines psoralen, a medication that increases skin sensitivity to light, with UVA rays. While powerful for severe psoriasis, PUVA carries a higher risk of sunburn and long-term skin damage compared to UVB.

Oral and Injectable Medications for Moderate to Severe Psoriasis

- **Methotrexate:** This systemic drug has cytostatic and effects on T-cell gene expression, which reduce the hyperactive immune system that causes flare-ups of psoriasis. Although it works well, there are some adverse effects that need to be watched out for, such as stomatitis, nausea, vomiting, hepatic and pulmonary toxicity, and exhaustion.²⁵
- **Cyclosporin:** It is another immunosuppressant, is useful for maintaining management options for moderate to severe condition plaque psoriasis and for bringing the condition into remission. Additionally, it works well for erythrodermic, pustular, and nail psoriasis. Although it has positive effects, its prolong usage has serious adverse effects such as hypertension, hypomagnesemia, hyperkalemia, hypertriglyceridemia, hypertrichosis, gingival hyperplasia, and nephrotoxicity.²⁵
- **Acitretin:** Acitretin, a retinoid drug, decreases the proliferation of skin cells and is especially useful for pustular psoriasis. When taken as monotherapy, retinoids might not be as effective as methotrexate or cyclosporine. It is frequently used with phototherapy or topical calcipotriene. However, ladies who may become pregnant should rigorously avoid it as it is teratogenic (causes birth abnormalities). Hypertriglyceridemia and mucocutaneous effects (dry eyes, cracked and inflamed lips, nasal bleeding, brittle nails, and burning skin) are additional adverse effects. Retinoid dermatitis is a less frequent occurrence. Skeletal anomalies are uncommon conditions.²⁵
- **Biologic Drugs:** Representing a major breakthrough, biologic drugs target specific molecules in the immune system that contribute to psoriasis. These injectable medications offer significant improvement for moderate to severe cases with an acceptable safety profile. Examples include drugs targeting interleukin (IL)-17 (secukinumab, ixekizumab) and IL-12 & IL-23 (ustekinumab). They prevent the Interleukins from binding receptor proteins.

The Future of Psoriasis Treatment

The field of psoriasis treatment continues to evolve. JAK inhibitors, a new class of oral medications that target different immune system pathways, are showing promise in clinical trials. Additionally, research on personalized medicine approaches that tailor treatment based on an individual's specific psoriasis type and genetic makeup is ongoing.

Choosing the Right Treatment - A Collaborative Effort

The optimal psoriasis treatment depends on factors like disease severity, location, and individual health. Dermatologists will consider these factors

alongside your preferences when creating a personalized treatment plan. It's not uncommon to combine different approaches for optimal results. Don't be discouraged if it takes some trial and error to find the best approach for you.

Additional Considerations for Managing Psoriasis

Patient Education: Understanding psoriasis and its treatment options empowers patients to actively participate in their care.

Healthy Lifestyle: The symptoms of psoriasis can be improved by keeping balance between a healthy diet, stress management and regular exercise.

Support Groups: Connecting with others managing psoriasis can provide valuable emotional support and practical advice.

By working closely with your dermatologist and exploring the available treatment options, you can effectively manage your psoriasis and achieve lasting improvement in your skin's health and quality of life.

2.CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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