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Review Article

Psoriasis: Comprehensive Review of Pathogenesis, Clinical Manifestations, and Advancements in Treatment Strategies

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ABSTRACT

Psoriasis is a chronic, immune-mediated disease characterized by the rapid proliferation of keratinocytes, resulting in thick, scaly, erythematous plaques. Affecting approximately 2-3% of the global population, psoriasis significantly impacts physical, psychological, and socioeconomic aspects of patients' lives. This review provides a comprehensive overview of psoriasis, including its epidemiology, pathophysiology, clinical features, and various treatment modalities. Despite advancements in topical therapies, phototherapy, and systemic treatments, several challenges remain, including adverse drug reactions, treatment resistance, and the need for long-term management. The article emphasizes the importance of an integrated, multidisciplinary approach to optimize patient outcomes and explores emerging trends in psoriasis management, such as biologic agents targeting novel pathways, combination therapies, and personalized treatment approaches through biomarkers and multi-omics technologies. By addressing these aspects, we aim to contribute to the ongoing efforts to improve the quality of life for individuals affected by psoriasis.

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INTRODUCTION

Psoriasis is a chronic, immune-mediated disease that predominantly affects the skin and joints. It is characterized by the rapid proliferation of keratinocytes, resulting in thick, scaly, erythematous plaques that are often itchy.Affecting approximately 2-3% of the global population, psoriasis has significant physical, psychological, and socioeconomic impacts.The disease presents in various forms, each with distinct clinical manifestations. Chronic plaque psoriasis, the most common type, accounts for 80-90% of cases and features well-demarcated, silvery-scaled plaques on the elbows, knees, and scalp[1].Other types, including guttate, inverse, pustular, and erythrodermic psoriasis, pose unique diagnostic and management challenges[2]. Psoriasis is a systemic disease with significant comorbidities, such as cardiovascular diseases, metabolic syndrome, and psychological disorders like depression and anxiety [3]. Psoriatic arthritis, affecting up to 30% of psoriasis patients, leads to joint pain, stiffness, and swelling. Management has evolved with treatments like topical therapies, phototherapy, systemic agents, and biologics. Despite advancements, treatment selection is challenging due to potential adverse drug reactions and the need for long-term management. [4] This review provides a comprehensive overview of psoriasis, including its epidemiology, pathophysiology, clinical features, and treatment modalities. It emphasizes the importance of an integrated, multidisciplinary approach to optimize patient outcomes and improve quality of life.

Types of Psoriasis

Psoriasis is a chronic, inflammatory skin disease characterized by an accelerated rate of skin cell growth, leading to the formation of thick, scaly patches on the skin's surface. It affects approximately 2-3% of the global population and can significantly impact the quality of life due to its visibility and associated discomfort.

- Plaque Psoriasis: The most prevalent form, plaque psoriasis, features raised, inflamed, and scaly patches that can appear anywhere on the body but are commonly found on the elbows, knees, scalp, and lower back. [5]
- Guttate Psoriasis: Characterized by small, dot-like lesions, guttate psoriasis often appears suddenly, typically after a bacterial infection such as strep throat. It is more common in children and young adults.
- Inverse Psoriasis: Found in skin folds such as under the breasts, in the groin, and around the buttocks, inverse psoriasis presents as smooth, red lesions that worsen with friction and sweating. [5]
- Pustular Psoriasis: Marked by white pustules (blisters of noninfectious pus) surrounded by red skin. It can be localized (e.g., palms and soles) or generalized, covering most of the body. [6]
- Erythrodermic Psoriasis: A severe, rare form causing widespread redness, severe itching, and pain. This type can disrupt the body's temperature regulation and is potentially life-threatening, requiring immediate medical attention. [7]
- Nail Psoriasis: Nail Psoriasis is an inflammatory autoimmune disease that usually causes your body to produce too many skin cells, which can form thick, itchy, scaly patches on the skin. It can also affect your joints and the appearance and texture of your nails — fingernails more often than toenails. It can be a precursor to psoriatic arthritis. [5][6]
- Psoriatic Arthritis: Involves both joint inflammation and skin lesions. Symptoms include joint pain, stiffness, and swelling, and it can lead to permanent joint damage if untreated. [6]

Epidemiology

125 million people worldwide — 2 to 3 percent of the total population — have psoriasis, according to the World Psoriasis Day consortium. [8] Around 2% of the West's population are affected and the region with the lowest prevalence is East Asia with a prevalence of 0.12%. The UK is ranked 21st in countries with the highest prevalence of psoriasis worldwide, corresponding to approximately 1·1 million people affected by the disease [9]

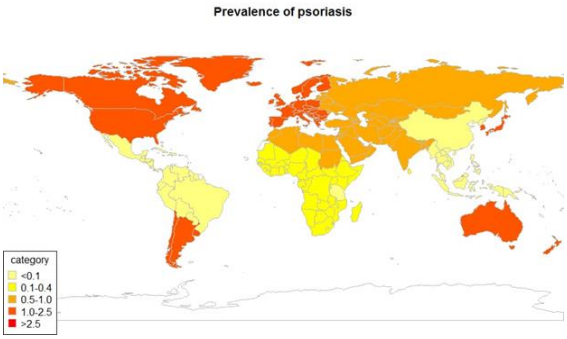

Figure 2: Prevalence of psoriasis [11]

Around 1.7% of the UK population are affected by the chronic skin condition psoriasis, according to researchers at The University of Manchester and the University Medical Center Hamburg-Eppendorf. Although psoriasis occurs worldwide, its prevalence varies considerably. [4] In The USA, approximately 2% of the population is affected. High rates of psoriasis have been reported in people of the Faroe islands, where one study found 2.8% of the population to be affected.The prevalence of psoriasis is low in certain ethnic groups such as the Japanese, and may be absent in aboriginal Australians and Indians from South America [Convit J . Investigation of the incidence of psoriasis amongst Latin-American Indians.

Region	Prevalence
Western Europe	1.74
Australasia	1.65
High-income North America	1.37
High-income Southern Latin America	1.19
Central Europe	1.11
High-income Asia Pacific	0.98
Central Asia	0.78
Eastern Europe	0.72
North Africa and Middle East	0.49
South Asia	0.37
Central sub-Saharan Africa	0.27
Southern sub-Saharan Africa	0.27
Western sub-Saharan Africa	0.27
Eastern sub-Saharan Africa	0.23
Southest Asia	0.22
Caribbean	0.21
Andean Latin America	0.21
Central Latin America	0.21
Oceania	0.20
Tropical Latin America	0.16
East Asia	0.12

Figure 3: Prevelance data in different countries [11]

- Prevalence in children
  Twelve studies based on 10 populations of children (<18 years) Were identified Prevalence in these studies ranged From 0% to 1.37%[11]. The highest prevalence was observed in Germany – 1.37% in a lifetime prevalence study, in a study population of 16500.The lowest prevalence was recorded in Taiwan – 0% in two point-prevalence studies, in two populations Consisting of 4067 and 3273 schoolchildren respectively. European populations had higher prevalence than African and Asian populations. [10]
- Prevalence in adults
  There were 25 studies on prevalence of psoriasis in adults, Defined according to the norms in the country (at least>15 years). Prevalence ranged from 0.51%66 to 11.43%. in the USA. highest Prevalence were reported in the United Kingdom – 1.3%69 and Norway – 11.43%67 respectively. Three Australian studies indicated a prevalence between 2.30%70 and 6.60%.71 Prevalence of Psoriasis among adults in Brazil was 1.30%,7 and this being the Only study from South America. [11]

Etiology

Psoriasis is common. Anyone can develop it, but it most often begins between ages 15 and 35, or as people get older. Psoriasis isn't contagious. Psoriasis seems to be passed down through families. Normal skin cells grow deep in the skin and rise to the surface about once a month. When you have psoriasis, this process takes place in 14 days rather than in 3 to 4 weeks. This results in dead skin cells building up on the skin's surface, forming the collections of scales. [12] The exact cause of psoriasis isn't known, but it's thought to be caused by a combination of genetics and environmental factors. Psoriasis is most common in people with white or light-colored skin, but it can occur in anyone. It affects all genders equally. The immune system plays a role in psoriasis[13].Psoriasis is a heterogeneous disease that can be classified into different clinical types, with the most common type being plaque psoriasis (also known as psoriasis vulgaris), which causes dry, itchy, and raised skin patches (i.e., plaques) with silvery scales. These plaques can occur at any site of the skin but are more common on the elbows, knees, scalp, and lower back. [14]

Major Factors Of Etiology Of Psoriasis Are As Follows [15]

- Genetic Factors: Psoriasis tends to run in families, indicating a genetic predisposition. Variants in certain genes, such as HLA-Cw6, have been associated with an increased risk of developing psoriasis.
- Immune System Dysfunction: Psoriasis is characterized by an overactive immune response where T cells attack healthy skin cells. The resulting inflammatory response leads to the rapid turnover of skin cells.
- Environmental Triggers: Infections: Streptococcal throat infections are known to trigger guttate psoriasis. Skin injuries: Cuts, scrapes, sunburns, or other skin injuries can trigger a psoriasis flare-up (Koebner phenomenon).
- Lifestyle Factors: Stress: Emotional stress can exacerbate psoriasis or trigger a flare-up. Smoking: Tobacco use is linked to an increased risk of psoriasis. Alcohol: Heavy alcohol consumption can worsen psoriasis symptoms.
- Medications: Medications such as lithium, beta-blockers, antimalarials, and NSAIDs can trigger or exacerbate psoriasis.
- Hormonal Changes: Psoriasis can be influenced by hormonal changes, such as those occurring during puberty or menopause
- Diet and Obesity: Obesity can exacerbate psoriasis, particularly in skin folds. Certain dietary factors may influence psoriasis

severity, though the exact relationship is complex and not fully understood. Understanding these factors can help in managing and potentially mitigating psoriasis symptoms.

Symptoms

Psoriasis is a chronic autoimmune condition that manifests primarily on the skin, although it can affect other parts of the body. The symptoms vary depending on the type of psoriasis, but certain common characteristics are typically observed. The most prevalent form, chronic plaque psoriasis, affects 80% to 90% of patients with psoriasis. This type is characterized by well-demarcated, symmetric, erythematous plaques with overlying silvery scales.

Common Symptoms Across Psoriasis Types

Plaque Psoriasis: This is the most common type, presenting as dry, sharply demarcated round or oval plaques with loosely adherent silvery white scales. These plaques typically appear symmetrically on the elbows, knees, scalp, and lower back, but they can occur anywhere on the body. The plaques can be itchy and painful, and in severe cases, the skin around joints may crack and bleed [1].

Guttate Psoriasis: Characterized by numerous small, drop-like papules and plaques, guttate psoriasis often appears after a streptococcal infection. These lesions are typically 2 to 6 mm in diameter and are scattered across the trunk and limbs [16].

Inverse Psoriasis: This type appears as smooth, shiny, and discolored lesions in skin folds such as the armpits, groin, and under the breasts. Unlike other forms, inverse psoriasis lacks the typical scaling and is often aggravated by friction and sweating [17].

Erythrodermic Psoriasis: One of the most severe forms, erythrodermic psoriasis, can cover most of the body's surface with a red, peeling rash that can itch or burn intensely. This type can be life-threatening, causing protein and fluid loss that can lead to severe illness [18].

Nail Psoriasis: Affecting the fingernails and toenails, nail psoriasis can cause pitting, abnormal nail growth, and discoloration. In severe cases, the nails can crumble or become detached from the nail bed (onycholysis)[19].

Psoriatic Arthritis: Psoriatic arthritis (PsA) is a chronic, inflammatory condition that affects some people with psoriasis. Symptoms include joint pain, stiffness, and swelling, which can occur in any part of the body, including the fingers and spine. PsA can also cause inflammation of the tendons and ligaments, leading to conditions such as enthesitis (inflammation where tendons or ligaments insert into the bone) and dactylitis (severe inflammation of the fingers and toes, often referred to as "sausage digits"). Additionally, PsA may cause fatigue, reduced range of motion, and can significantly impact the quality of life[8].

Pathophysiology

Psoriasis is a multi-factorial autoimmune skin disease with a complex pathogenesis. The exact pathophysiology is not completely understood, but several key factors and pathways contribute to its development. The most accepted hypothesis is that psoriasis is an immune-mediated inflammatory skin disease manifesting in genetically predisposed individuals exposed to specific environmental triggers[21].Various factors which have been suggested to play a key role in the pathogenesis are T cells, antigen presenting cells (APC's), keratinocytes, Langerhans' cells, macrophages, natural killer cells, an array of Th1 type cytokines, certain growth factors like vascular endothelial growth factor (VEGF), keratinocyte growth factor (KGF), and others[24].However, Unlike other common tissue specific autoimmune diseases, psoriasis vulgaris does not have a generally accepted animal model, and thus our understanding of pathogenesis is derived mainly from clinical studies and translational science done

in patients with this disease. The immune system triggers chronic inflammation in the skin. It has a genetic component, with the PSORS1 gene being commonly associated with familial cases. The disease process involves the abnormal activation of T lymphocytes, which release inflammatory mediators like cytokines and chemokines. Key cytokines in psoriasis include tumor necrosis factor-alpha (TNF-α), interleukin-17 (IL-17), interleukin-23 (IL-23), and interleukin-22 (IL-22), leading to inflammation and excessive cell proliferation. This imbalance causes keratinocytes, the main cells in the epidermis, to proliferate excessively, forming the scaly plaques characteristic of psoriasis [6]. The complex pathophysiology of psoriasis, emphasizing the interplay of genetic, cellular, and cytokine-mediated mechanisms. Understanding these processes is crucial for developing targeted therapies and improving patient outcomes.

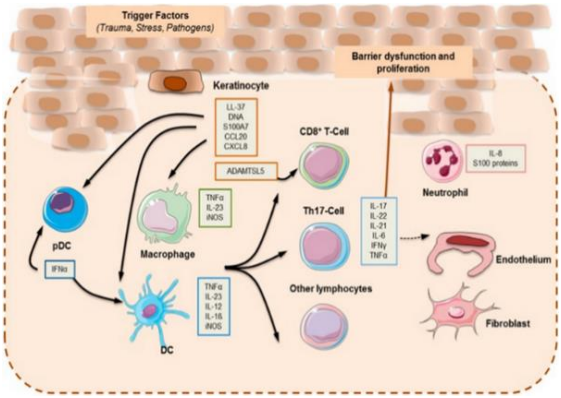

Figure 4: The pathogenesis of psoriasis [22]

This diagram represents the complex pathophysiological mechanisms involved in psoriasis. The process begins with the activation of keratinocytes, which triggers the release of antimicrobial peptides (AMPs) such as LL37, β-defensins, and S100 proteins. These AMPs activate dendritic cells, including both plasmacytoid dendritic cells (pDCs) and myeloid dendritic cells (mDCs). Once activated, pDCs and mDCs produce various cytokines, which are crucial in the inflammatory response. This cytokine production leads to the activation and differentiation of Th1 and Th17 cells, which are key drivers of the inflammatory process in psoriasis. The cytokines released by Th1 and Th17 cells further stimulate keratinocyte proliferation, contributing to the characteristic hyperproliferative state of the epidermis in psoriasis. This ongoing interaction between keratinocytes, dendritic cells, and T cells establishes a chronic inflammatory pathway, ultimately resulting in the clinical manifestations of psoriasis, such as thickened, scaly plaques on the skin. This flowchart provides a visual representation of the intricate cellular and molecular interactions that underpin the pathogenesis of psoriasis.

Psoriasis is a chronic inflammatory skin disorder characterized by an accelerated turnover of keratinocytes, resulting in the formation of thick, scaly plaques. The pathogenesis of psoriasis involves a complex interplay between genetic predisposition, immune system dysregulation, and environmental triggers. Central to this process is the abnormal activation and regulation of T cells, particularly Th1 and Th17 cells, which play pivotal roles in the disease's inflammatory cascade [22] [29].In normal skin, keratinocytes undergo a maturation process that takes approximately 26 days, but in psoriatic skin, this process is dramatically shortened to just 4 days. This rapid cell cycle results in the accumulation of immature keratinocytes that form the characteristic thick, scaly plaques of psoriasis. The initial trigger in psoriatic skin involves defective keratinocytes releasing cytokines such as TNF-α, IL-1, and IL-6, which activate resident dendritic cells [24]. These activated dendritic cells then migrate to regional lymph nodes, where they present antigens to naïve T cells, converting them into effector T cells, specifically Th1 and Th17 cells [25]. These effector T cells re-enter the circulation and home to the skin, where they release pro-inflammatory cytokines such as IFN-γ, IL-17, and IL-22. These

cytokines further activate keratinocytes, leading to their hyperproliferation and the recruitment of additional inflammatory cells, perpetuating the cycle of inflammation and skin cell turnover [29]. Genetic factors significantly contribute to the susceptibility and pathogenesis of psoriasis. Several genes have been identified that are associated with an increased risk of developing psoriasis, including HLA-Cw*0602, SLC9A3R1, NAT9, and RAPTOR. The HLA-Cw*0602 allele, located within the major histocompatibility complex (MHC), is one of the most well-established genetic risk factors and is found in approximately 50% of psoriasis patients. This allele is thought to present specific antigens that trigger an inappropriate immune response. SLC9A3R1 and NAT9, located on chromosome 17q, are involved in signal transduction and cellular growth, with variants in these genes potentially leading to prolonged inflammation and heightened sensitivity of keratinocytes to activating stimuli. Additionally, RAPTOR, a component of the mTOR signaling pathway, is crucial for T cell growth and function, with variants affecting the regulation of immune responses [26].

Beyond genetic predisposition, the psoriasis transcriptome reveals altered expression of over 1300 genes in lesional versus non-lesional skin. This includes an upregulation of various chemokines and cytokines, such as CCL20 and IL-23, which are critical in recruiting and maintaining the inflammatory cell infiltrate. These cytokines create an environment that supports the ongoing activation and proliferation of T cells and keratinocytes [26]. Furthermore, the presence of increased numbers of dendritic cells, particularly plasmacytoid dendritic cells (pDCs) that produce large amounts of IFN-α, highlights the role of innate immunity in driving the disease process. Activated myeloid dendritic cells (mDCs) produce IL-12 and IL-23, which polarize T cells towards a Th1 and Th17 phenotype, respectively, thus reinforcing the chronic inflammatory state[27]. The vascular component of psoriasis is also significant, with increased angiogenesis observed in psoriatic lesions. Keratinocytes produce pro-angiogenic factors like VEGF and IL-8, which promote the formation of new blood vessels. These newly formed vessels are leaky and support the extravasation of immune cells into the skin, further fueling the inflammatory process. Treatments targeting these pathways, such as TNF inhibitors and IL-17 blockers, have demonstrated efficacy by interrupting the inflammatory cascade and reducing the hyperproliferation of keratinocytes [28].

In conclusion, psoriasis is a multifaceted disease driven by genetic susceptibility, immune system dysregulation, and environmental factors. The interplay between T cells, dendritic cells, and keratinocytes, mediated by a network of cytokines and chemokines, leads to the characteristic features of the disease. Understanding these complex interactions provides a foundation for developing targeted therapies that can more effectively manage psoriasis and improve patient outcomes [29].

Co-occuring diseases

Psoriasis is associated with several comorbid conditions beyond its dermatological manifestations. These include cardiovascular diseases, metabolic syndrome, obesity, hypertension, dyslipidemia, and non-alcoholic fatty liver disease (NAFLD) [30] Patients with psoriasis are at an increased risk for these conditions due to the systemic inflammation and immune dysregulation inherent to the disease [33]. Chronic inflammation contributes to endothelial dysfunction, promoting atherogenesis and increasing the risk of cardiovascular events [4]. Furthermore, the presence of psychiatric disorders such as depression and anxiety is higher in individuals with psoriasis, significantly impacting

their quality of life. Effective management of psoriasis can help mitigate these comorbidities, emphasizing the importance of a holistic approach in treating psoriatic patients [33].

Type 2 Diabetes Mellitus and Psoriasis: The link between psoriasis and Type 2 Diabetes Mellitus (T2DM) is particularly strong, with studies showing that individuals with psoriasis have a significantly higher prevalence of T2DM compared to the general population, averaging 11.6% in psoriatic cohorts [4]. This increased prevalence is partly due to shared genetic factors and overlapping inflammatory pathways, where chronic systemic inflammation characteristic of psoriasis induces insulin resistance, a major risk factor for T2DM [33]. Elevated levels of pro-inflammatory cytokines, such as TNF-alpha, IL-17, and IL-23, promote this insulin resistance. [32] Additionally, altered levels of adipocytokines, such as lower adiponectin and higher resistin and vaspin, further exacerbate metabolic dysregulation in psoriatic patients. Insulin resistance in psoriasis is evident from higher HOMA-IR values, and treatments reducing psoriasis severity often correlate with improved insulin sensitivity. Endothelial dysfunction markers, such as sICAM-1 and MMP-9, are elevated in both conditions, highlighting systemic inflammation's role in their pathogenesis [31]. Effective psoriasis management, particularly through treatments targeting inflammatory pathways, can thus improve insulin sensitivity and reduce the risk of developing T2DM, underscoring the need for integrated care approaches for patients with psoriasis [34].

Pharmacotherapy

Psoriasis treatments aim to halt the rapid turnover of skin cells and remove scales. The choice of treatment depends on the severity of the condition and its response to previous treatments. Typically, therapies include topical treatments, light therapy (phototherapy), and systemic medications, which are administered either orally or by injection.

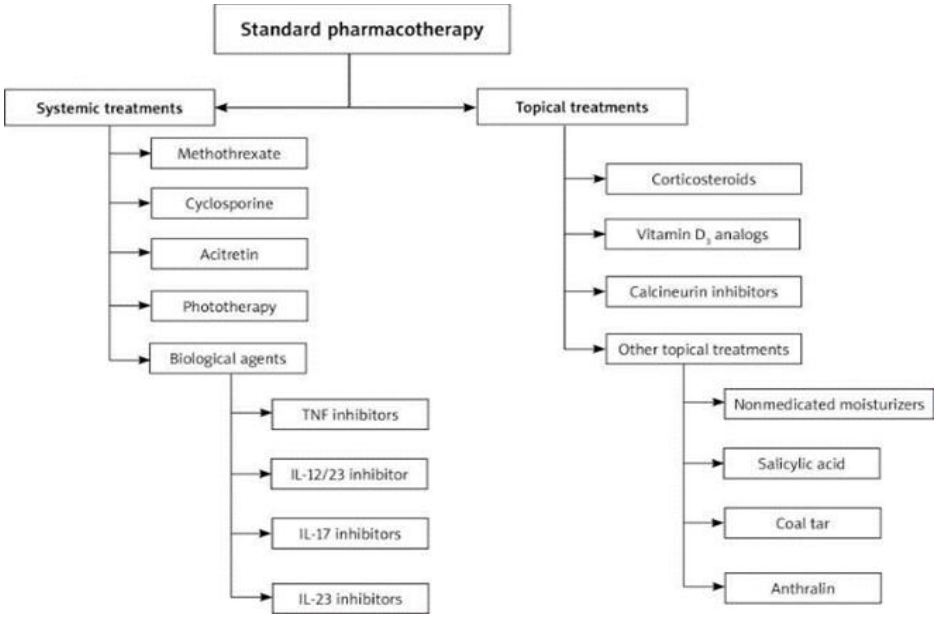

Figure 5: Standard pharmacotheraphy treatment for psoriasis. [35]

- **Topical Therapy**

Topical corticosteroids are the most frequently prescribed medications for treating mild to moderate psoriasis. Available in various forms such as oils, creams, and ointments, these drugs reduce inflammation and slow down skin cell turnover[12].Mild corticosteroids like hydrocortisone are often recommended for sensitive areas such as the face or skin folds, while stronger corticosteroids like clobetasol are used for

tougher-to-treat areas[13]. Long-term use can lead to skin thinning and reduced efficacy over time[37].Vitamin D analogues, including calcipotriene and calcitriol, are another option. These synthetic forms of vitamin D help to slow skin cell growth and are often used in combination with corticosteroids. [36] Retinoids like tazarotene, available as gels or creams, also play a role in managing psoriasis by promoting skin cell differentiation. However, they can cause skin irritation and increased sensitivity to light and are not recommended for pregnant or breastfeeding women. [8] Calcineurin inhibitors, such as tacrolimus and pimecrolimus, are effective in reducing inflammation and are particularly useful in areas with thin skin like around the eyes. However, their long-term use is limited due to potential risks of skin cancer and lymphoma. [13] Other topical treatments include salicylic acid, which helps to reduce scaling, and coal tar, which alleviates itching and inflammation but can be messy and have a strong odor.

- **Light Therapy**

Light therapy is a primary treatment for moderate to severe psoriasis and involves controlled exposure to natural or artificial light. Options include UVB broadband, UVB narrowband, and psoralen plus ultraviolet A (PUVA). UVB narrowband is often more effective and has largely replaced broadband therapy in many areas [38]. Excimer laser therapy, which uses a concentrated UVB light, targets affected skin more precisely and requires fewer sessions [39]. However, light therapy can cause side effects such as inflamed, itchy, and dry skin [13].

- **Systemic Treatments**

For moderate to severe psoriasis, or when other treatments fail, systemic treatments are used. These include oral or injected medications like steroids, retinoids, biologics, methotrexate, and cyclosporine. Steroids such as triamcinolone can be injected directly into persistent patches [12]. Retinoids like acitretin reduce skin cell production but are not recommended for pregnant or breastfeeding women due to potential side effects like dry skin and muscle soreness. [36] Biologics, which target specific parts of the immune system, have revolutionized the treatment of severe psoriasis. Drugs like etanercept, infliximab, and adalimumab are effective but expensive and can increase the risk of serious infections. Regular screening for tuberculosis is necessary for patients on biologics. Methotrexate, taken weekly, decreases skin cell production and suppresses inflammation but requires ongoing blood tests to monitor liver function. Cyclosporine is effective for severe psoriasis but cannot be used continuously for more than a year due to risks of infection and kidney damage. [13]

- **Emerging Therapies**

Despite the effectiveness of current treatments, there is a need for new chemical entities to treat severe psoriasis due to the limitations and side effects of existing therapies. Research is ongoing to develop new drugs, such as ISA247 (voclosporin), which has shown promise in phase III trials for moderate to severe plaque psoriasis[37].Bz-423, a 1,4-benzodiazepine, is another potential treatment that has demonstrated efficacy in preclinical studies by targeting keratinocyte proliferation and promoting cell death[8].

In conclusion, while there are multiple treatment options for psoriasis, ranging from topical therapies to systemic medications, the quest for more effective and safer treatments continues. Advances in understanding the underlying mechanisms of psoriasis hold promise for the development of new therapies that can better manage severe forms of the disease and improve patients' quality of life.

Adverse Drug Reactions

Psoriasis treatment involves a variety of medications, each targeting different aspects of the

disease's pathology. However, these treatments can come with significant adverse drug reactions (ADRs) that complicate management and impact patient quality of life. Understanding these ADRs is crucial for optimizing therapeutic strategies and minimizing harm.

Topical Treatments

Anthralin**:** While effective in slowing skin cell growth, anthralin frequently causes skin irritation and can stain skin, clothing, and other surfaces [30].

Coal Tar: Known for its anti-inflammatory properties, coal tar can cause skin irritation and dryness. It also increases sensitivity to sunlight, posing a risk of sunburn and further skin damage [32].

Corticosteroids: These potent anti-inflammatory drugs are effective but pose significant risks with long-term use. Potential side effects include skin thinning, stomach ulcers, bone density reduction, and cataract formation.

Salicylic Acid**:** Effective in removing dead skin cells, prolonged use of salicylic acid can irritate the skin and weaken hair, leading to hair loss when used on the scalp[40].

Vitamin D Analogues (Calcipotriene and Calcitriol)**:** These treatments can irritate the skin, causing discomfort and limiting their usability[44].

Light Therapy (Phototherapy)

Phototherapy uses ultraviolet light to reduce psoriasis symptoms. However, it carries risks such as minor burns and an increased risk of skin cancer due to prolonged exposure. Photochemotherapy, which combines light therapy with photosensitizing drugs, can cause nausea, itching, and redness [39].

Systemic Treatments

Retinoids**:** These vitamin A derivatives can cause severe birth defects, liver damage, and increase cholesterol levels. They also often lead to dryness of the skin and mucous membranes, and joint pain [33].

Methotrexate: Used to slow skin cell proliferation, methotrexate can cause fatigue, gastrointestinal distress, liver toxicity, and bone marrow suppression. Long-term use increases the risk of severe liver damage and blood cell abnormalities.

Cyclosporine: This immunosuppressant increases the risk of infections, kidney damage, and hypertension. It can also elevate the risk of certain cancers with prolonged use.

Biologics: These advanced treatments target specific immune pathways but can significantly increase the risk of serious infections. Other potential side effects include reactivation of latent tuberculosis and increased risk of malignancies [34].

Monitoring and Management

Given these risks, close monitoring and a tailored approach to psoriasis management are essential. Regular blood tests, liver function tests, and periodic reassessments of treatment efficacy and safety are crucial to mitigate ADRs. Patient education on recognizing early signs of ADRs and prompt reporting can also enhance treatment safety

Clinical diagnosis

The diagnosis of psoriasis is primarily clinical. There are different clinical types of psoriasis the most common of which is chronic plaque psoriasis, affecting 80% to 90% of patients with psoriasis. The hallmark of classic plaque psoriasis is well-demarcated, symmetric, and erythematous plaques with overlying silvery scale. **[1]** Less common variants of psoriasis include inverse psoriasis, pustular psoriasis, guttate psoriasis, erythrodermic psoriasis, and annular psoriasis . These variants can be differentiated from the common plaque type by morphology [2]. According to Morphological diagnosis the psoriasis types can be differentiated as follows

Figure 6:Plaque Psoriasis

- Plaque Psoriasis

The lesions are characterized by dry, sharply demarcated round/oval plaques with loosely adherent silvery white scales. Psoriasis plaques can appear at any part of the body but are generally distributed symmetrically over elbows and knees. [41]

- Guttate psoriasis

Figure 7: Guttate psoriasis

On physical exam, guttate psoriasis manifests as numerous, small, scattered papules and plaques. These are often referred to as "drop-like" and typically manifest as 2 to 6 mm papules. [16]

- Inverse psoriasis

It looks like a shiny, smooth, discolored (brown, red or purple) rash, and it may feel damp [17]

Figure 8: Inverse psoriasis

- Erythrodermic psoriasis

Redness and inflammation that resembles a severe burn or sunburn on more than 90% of your body. The skin rash is very itchy and may cause a burning sensation [18].

Figure 9: Erythrodermic psoriasis

- Nail psoriasis

Nail psoriasis alters the way your toenails and fingernails look. They may get thick, develop pinprick holes, and change color or shape. They also can feel tender and hurt [19] [43].

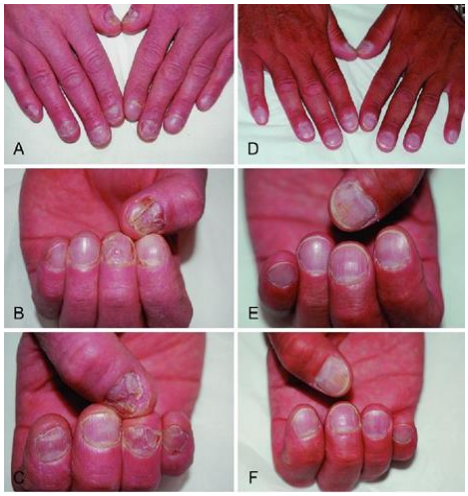

Figure 10:Nail psoriasis

Differential diagnoses include atopic dermatitis, contact dermatitis, lichen planus, secondary syphilis, mycosis fungoides, tinea corporis, and pityriasis rosea. Careful observation often yields the diagnosis. For more atypical presentations, a skin biopsy might be helpful. Tinea can be distinguished from psoriasis by fungal culture, potassium hydroxide (KOH) preparation of skin scrapings.

Case Study

Case Study: Psoriasis

Patient Background

Name: John Doe

Age: 45

Gender: Male
Occupation: Office Worker
Medical History**:** John has a history of mild asthma and seasonal allergies. No family history of psoriasis or other autoimmune diseases.

Presentation

John presented to the dermatology clinic with persistent, red, scaly patches on his elbows, knees, and scalp. These lesions had been present for approximately six months and were associated with mild itching and discomfort. The patient noted that the lesions seemed to worsen during periods of stress and with the colder weather.

Physical Examination

Skin: Multiple well-demarcated, erythematous plaques with overlying silvery scales were observed on the extensor surfaces of the elbows and knees, as well as on the scalp.
Nails: Mild pitting was noted on the fingernails.
Joints: No swelling, tenderness, or deformities were observed in the joints.

Diagnostic Tests

Skin Biopsy: Histopathological examination showed parakeratosis, acanthosis, elongation of the rete ridges, and a decreased granular layer, confirming the diagnosis of psoriasis.
Blood Tests: Routine blood tests were normal. No evidence of systemic inflammation or infection was found.
Diagnosis
John was diagnosed with chronic plaque psoriasis (psoriasis vulgaris), the most common form of psoriasis.

Treatment Plan

Topical Therapies:

Corticosteroids: High-potency topical corticosteroid (clobetasol propionate) to be applied to the affected areas twice daily for two weeks, then tapered to weekends only. Vitamin D Analogues: Calcipotriene to be applied once daily to help control plaque formation.
Phototherapy:
Narrowband UVB phototherapy was recommended three times a week for six weeks, with follow-up to assess response and adjust frequency.

Systemic Therapies:

Due to the extent and persistence of the lesions, and given the patient's moderate disease severity, methotrexate was considered. However, the patient preferred to try topical and phototherapy first.

Lifestyle Modifications:

Stress Management: Techniques such as mindfulness and yoga were recommended.
Skin Care: Regular use of moisturizers to prevent dryness and irritation.
Avoiding Triggers: Emphasis on avoiding known triggers like cold weather and skin injuries.

Follow-Up and Outcomes

6 Weeks: Significant improvement in the scaling and erythema of the lesions was noted. The patient reported a reduction in itching and discomfort.
3 Months: Continued improvement with near clearance of the lesions on the elbows and knees. Scalp lesions were still present but less pronounced.
6 Months: Maintenance therapy with topical corticosteroids on weekends and continued use of vitamin D analogues resulted in sustained control of the disease.

DISCUSSION

Psoriasis is a chronic, immune-mediated disease characterized by hyperproliferation of keratinocytes and inflammatory infiltration. It can significantly impact the quality of life due to its chronicity, visible skin lesions, and associated symptoms such as itching and pain. Treatment often requires a combination of therapies tailored to the individual's severity of disease, response to treatments, and lifestyle. John's case highlights the importance of a multidisciplinary approach to managing psoriasis, incorporating pharmacologic treatments, phototherapy, and lifestyle

modifications. While topical therapies and phototherapy were effective in this case, other patients may require systemic treatments, including biologics, especially in more severe cases. [23] [44]

Future prospects: Unsolved Questions

Psoriasis, despite advancements in its understanding and treatment, still presents several unresolved questions that continue to drive research. Here are some critical unanswered questions [45]:

- What are the precise genetic and environmental factors contributing to psoriasis?
- How can we effectively predict treatment response and tailor therapies for individual patients?
- What are the long-term safety and efficacy profiles of new biologics and systemic therapies?
- What mechanisms lead to treatment resistance in psoriasis, and how can they be overcome?
- How do comorbid conditions influence psoriasis, and what are the best integrated treatment approaches?

CONCLUSION

In conclusion, psoriasis is a chronic, multifaceted autoimmune condition that significantly impacts the quality of life for millions of individuals worldwide. Recent advancements in understanding its pathophysiology have paved the way for more targeted and effective treatments, ranging from topical therapies and phototherapy to systemic medications and biologics. Despite these advances, challenges remain in achieving long-term remission and addressing the comorbidities often associated with the disease, such as cardiovascular issues and mental health disorders. Future research should continue to focus on personalized treatment approaches, the development of novel therapeutic agents, and comprehensive care strategies that address both the physical and psychological aspects of psoriasis. Enhanced patient education and support systems are also crucial in improving overall disease management and patient outcomes. Through a combination of innovative scientific research and holistic patient care, the burden of psoriasis can be significantly alleviated.

REFERENCE

1. Can Fam Physician. (2017). Chronic plaque psoriasis. *Can Fam Physician*, 63(4), 278–285. Retrieved from [Can Fam Physician](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5389761/)
2. Raychaudhuri, S. K., Maverakis, E., & Raychaudhuri, S. P. (2014). Psoriasis: Clinical features and comorbidities. *Autoimmunity Reviews*, 13(4-5), 490-495.
3. Gottlieb, A. B., & Dann, F. (2009). Comorbidities in patients with psoriasis. *American Journal of Medicine*, 122(12), 1150.e1-1150.e9.
4. Armstrong, A. W., Harskamp, C. T., & Armstrong, E. J. (2013). Psoriasis and metabolic syndrome: a systematic review and meta-analysis of observational studies. *Journal of the American Academy of Dermatology*, 68(4), 654-662.
5. Saeki, H. (2024). The Journal of Dermatology, Volume 51, Issue 2, pp. 185-195.
6. Henseler, T., & Christophers, E. (1985). Journal of the American Academy of Dermatology, Volume 13, Issue 3, pp. 450-456.
7. Sarac, G., Koca, T.T., & Baglan, T. (2016). North Clin Istanb, 3(1), pp. 79-82.
8. Mease PJ, Gladman DD, Papp KA, et al. (2013). Prevalence of rheumatologist-diagnosed psoriatic arthritis in patients with psoriasis in European/North American dermatology clinics. *Journal of the American Academy of Dermatology*, 69(5), 729-735.

9. Stern RS, Nijsten T, Feldman SR, Margolis DJ, Rolstad T. (2004). Psoriasis is common, carries a substantial burden even when not extensive, and is associated with widespread treatment dissatisfaction. *J Investig Dermatol Symp Proc*, 9(2), 136-139.
10. Schmitt J, Apfelbacher C. (2010). Epidemiology of pediatric psoriasis: a representative German cross-sectional study. *Exp Dermatol*, 19, 219–219.
11. Larsson PA, Liden S. (1980). Prevalence of skin diseases among adolescents 12–16 years of age. *Acta Derm Venereol*, 60, 415–423.
12. Penn Medicine. (n.d.). Psoriasis. Retrieved from Penn Medicine.
13. Pfizer. (n.d.). Psoriasis. Retrieved from Pfizer.
14. Guo, J., Zhang, H., Lin, W., Lu, L., Su, J., & Chen, X. (2023). Psoriasis: Pathogenesis and clinical features. *Signal Transduction and Targeted Therapy*, Volume 8, Article 437. Retrieved from Springer.
15. Boehncke, W.H. (2015). Review Article: Volume 41, Issue 4, P665-675. *Rheumatic Disease Clinics of North America*. Retrieved from Rheumatic Disease Clinics.
16. Saleh, D., & Tanner, L. S. Guttate psoriasis. *NCBI Bookshelf*. Retrieved from [NCBI Bookshelf](https://www.ncbi.nlm.nih.gov/books/NBK482498/).
17. Inverse psoriasis. (n.d.). *Cleveland Clinic*. Retrieved from [Cleveland Clinic](https://my.clevelandclinic.org/health/diseases/22852-inverse-psoriasis).
18. Fletcher, J. (2023). Erythrodermic psoriasis. *Medical News Today*. Retrieved from [Medical News Today](https://www.medicalnewstoday.com/articles/314514).
19. Clinical manifestation of nail psoriasis. (2018). *ResearchGate*. Retrieved from [ResearchGate](https://www.researchgate.net/figure/Clinical-manifestation-of-nail-psoriasis-with-crumbling-and-onycholysis-A-C-before-and_fig1_329460296).
20. Kimmel, G. W., & Lebwohl, M. (2018). Psoriasis: Overview and Diagnosis. *SpringerLink*. First Online: 01 July 2018. Retrieved from [SpringerLink](https://link.springer.com/chapter/10.1007/978-3-319-63381-3_1).
21. Mahajan R, Handa S. (2013). Pathophysiology of psoriasis. *Indian J Dermatol Venereol Leprol*, 79, 1-9.
22. Rendon, A., & Schäkel, K. (2019). Psoriasis Pathogenesis and Treatment. *International Journal of Molecular Sciences*.
23. Lowes, M.A., Bowcock, A.M., & Krueger, J.G. (2007). Pathogenesis and therapy of psoriasis. *Nature*, 445(7130), 866-873.
24. Harden, J.L., & Krueger, J.G. (2020). The immunopathogenesis of psoriasis: An integrated perspective. *Journal of Clinical Investigation*, 130(5), 1796-1807.
25. Lowes, M.A., Suarez-Farinas, M., & Krueger, J.G. (2014). Immunology of psoriasis. *Annual Review of Immunology*, 32, 227-255.
26. Swindell, W.R., Johnston, A., Carbajal, S., et al. (2011). Genome-wide expression profiling of five mouse models identifies similarities and differences with human psoriasis. *PloS One*, 6(4), e18266.
27. Mattozzi, C., Paolino, G., Richetta, A.G., & Calvieri, S. (2018). Psoriasis, autoinflammation, and autoimmunity. *Dermatologic Therapy*, 31(5), e12600.
28. Hendriks, A.G., van Foreest, A.W., & Prens, E.P. (2022). Angiogenesis in psoriasis and potential therapeutic implications. *Journal of Dermatological Science*, 105(3), 204-213.
29. Nickoloff, B.J., & Nestle, F.O. (2004). Recent insights into the immunopathogenesis of psoriasis provide new therapeutic

opportunities. *Journal of Clinical Investigation*, 113(12), 1664.
30. Gottlieb, A. B., & Dann, F. (2009). Comorbidities in patients with psoriasis.The American Journal of Medicine, 122(12), 1150.e1-1150.e9.
31. Takeshita, J., Grewal, S., Langan, S. M., Mehta, N. N., Ogdie, A., Van Voorhees, A. S., & Gelfand, J. M. (2017). Psoriasis and comorbid diseases: Epidemiology. Journal of the American Academy of Dermatology, 76(3), 377-390.
32. Boehncke, W. H., & Schön, M. P. (2015). Psoriasis.Lancet, 386(9997), 983-994.
33. Gisondi, P., Fostini, A. C., Fossà, I., Girolomoni, G., & Targher, G. (2018). Psoriasis and the metabolic syndrome.Clinics in Dermatology, 36(1), 21-28.
34. Singh, S., Young, P., & Armstrong, A. W. (2017). An update on psoriasis and metabolic syndrome: A meta-analysis of observational studies.PLOS ONE, 12(7), e0181039.
35. Zhu, B., Jing, M., Yu, Q., Ge, X., Yuan, F., & Shi, L. (2022). Treatments in psoriasis: from standard pharmacotherapy to nanotechnology therapy.Postepy Dermatol Alergol, 39(3), 460–471.
36. Guo, J., Zhang, H., Lin, W., Lu, L., Su, J., & Chen, X. (2023). Psoriasis: Pathogenesis and clinical features.Signal Transduction and Targeted Therapy, 8, Article 437. Retrieved from Springer.
37. Lebwohl, M. (2018). Psoriasis. The New England Journal of Medicine,379, 1336-1346.
38. Menter, A. (2020). Guidelines of care for the management of psoriasis with phototherapy and photochemotherapy. Journal of the American Academy of Dermatology, 82(2), 251-275.
39. Feldman, S.R. (2019). Excimer Laser Therapy in the Treatment of Psoriasis. Journal of Dermatological Treatment, 30(7), 662-668.
40. Armstrong, A. W., Harskamp, C. T., & Armstrong, E. J. (2013). Psoriasis and metabolic syndrome: a systematic review and meta-analysis of observational studies. Journal of the American Academy of Dermatology, 68(4), 654-662.
41. Villines, Z. (2018). Psoriasis: Symptoms, causes, and treatments. Medical News Today. Retrieved from Medical News Today.
42. Nail psoriasis. (2023). WebMD. Retrieved from [WebMD](https://www.webmd.com)
43. Boehncke, W. H., & Boehncke, S. (2014). Cardiovascular morbidity in psoriasis: epidemiology, pathomechanisms, and treatment strategies. Journal of Clinical Investigation, 124(7), 2382-2390.
44. Parisi, R., Symmons, D. P., Griffiths, C. E., & Ashcroft, D. M. (2013). Global epidemiology of psoriasis: a systematic review of incidence and prevalence. Journal of Investigative Dermatology, 133(2), 377-385. doi:10.1038/jid.2012.339
45. Lee, H., & Kim, M. (2023). Challenges and Future Trends in the Treatment of Psoriasis.International Journal of Molecular Sciences, 24(17), 13313. https://doi.org/10.3390/ijms241713313

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