PSORIASIS: IMMUNOLOGIC MECHANISMS AND MODERN BIOLOGIC THERAPY — A DERMATOLOGY PERSPECTIVE

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Abstract. Psoriasis is a chronic, immune-mediated inflammatory skin disease with substantial global disease burden, increasingly recognized as a systemic condition with significant comorbidities. This narrative review synthesizes current evidence on the immunopathogenesis, clinical features, diagnosis, and treatment of psoriasis, drawing on systematic reviews, randomized controlled trials, and consensus clinical guidelines, supplemented with regional epidemiological data and clinical guidance specific to Uzbekistan. The pathogenesis of psoriasis centers on dysregulation of the IL-23/Th17 immune axis, driving keratinocyte hyperproliferation and sustained cutaneous inflammation. Diagnosis remains primarily clinical, supported by severity indices such as PASI and BSA, while treatment has been transformed by biologic agents targeting TNF-alpha, IL-17, and IL-23, which offer substantially improved efficacy and safety compared with conventional systemic therapy in moderate-to-severe disease. Advances in understanding psoriasis immunopathogenesis have translated directly into targeted biologic therapies that meaningfully improve disease control and quality of life; expanding access to these therapies, including within the healthcare system of Uzbekistan, remains an important priority.

Keywords. Psoriasis, IL-23/Th17 axis, keratinocyte hyperproliferation, TNF-alpha inhibitors, IL-17 inhibitors, IL-23 inhibitors, biologic therapy, PASI, psoriatic comorbidities.

Methods

This work was prepared as a narrative literature review. A literature search was conducted between July and August 2026 using PubMed, the Cochrane Library, and the websites of major dermatology and immunology journals, with the search terms

"psoriasis," "IL-23/Th17 axis," "keratinocyte," "biologic therapy," and "TNF-alpha inhibitor," combined with filters for publication in English between 2009 and 2025. Priority was given to systematic reviews, randomized controlled trials, and consensus clinical practice guidelines issued by recognized dermatology societies; original textbook chapters were included for foundational pathophysiological background. Region-specific data and guidance were additionally identified through the official resource portal of the Ministry of Health of the Republic of Uzbekistan and local peer-reviewed journals. Case reports, non-peer-reviewed sources, and articles without accessible full text were excluded. A total of fifteen sources meeting these criteria were selected and synthesized for this review.

Introduction

Psoriasis is a chronic, relapsing, immune-mediated inflammatory skin disease characterized by well-demarcated erythematous plaques with silvery scale, most commonly affecting the extensor surfaces, scalp, and lower back [1]. It is now understood not as an isolated dermatologic condition but as a systemic inflammatory disease associated with psoriatic arthritis, cardiovascular disease, metabolic syndrome, and depression [11].

The disease arises from a complex interplay of genetic susceptibility, innate immune activation, and adaptive Th17-driven inflammation. Genome-wide association studies have identified numerous psoriasis susceptibility loci, many of which converge on antigen presentation and interleukin-23 (IL-23) signaling pathways, underscoring the central immunologic basis of the disease [7].

According to Global Burden of Disease 2021 estimates, the age-standardized prevalence rate of psoriasis in the Central Asian region, which includes Uzbekistan, rose from approximately 50.7 to 55.7 per 100,000 population between 1990 and 2021, a trend broadly consistent with the global rise in psoriasis burden over the same period [13]. The national clinical standard issued by the Ministry of Health of the Republic of Uzbekistan in 2025 formally establishes diagnostic and treatment protocols for psoriasis, reflecting its recognized importance within national dermatologic practice [14].

Over the past two decades, advances in understanding the IL-23/Th17 immune axis have directly enabled the development of targeted biologic therapies, fundamentally transforming the management of moderate-to-severe disease [2], [6].

The aim of this review is to summarize current evidence on the immunopathogenesis, diagnosis, and management of psoriasis, with particular emphasis on modern biologic therapy and its relevance to clinical practice in Uzbekistan.

Understanding the immunopathogenesis of psoriasis enables clinicians to diagnose, treat, and monitor the disease and its systemic comorbidities effectively. This knowledge is applied across several areas of medicine, including:

* Dermatology (diagnosis, severity assessment, and topical and systemic treatment)
* Rheumatology (identification and management of psoriatic arthritis)
* Cardiology (cardiovascular risk assessment given chronic systemic inflammation)

* Endocrinology (screening for metabolic syndrome and diabetes)
* Mental Health Services (addressing depression and psychosocial burden)
* Immunology and Pharmacology (development and monitoring of biologic therapy)

Immunologic Mechanisms

The pathogenesis of psoriasis reflects a self-amplifying immune loop between innate and adaptive immunity. In genetically susceptible individuals, environmental triggers such as infection, trauma (the Koebner phenomenon), or certain medications activate plasmacytoid dendritic cells, which release interferon-alpha and stimulate myeloid dendritic cells to produce IL-23 [3], [4].

IL-23 drives the differentiation and maintenance of Th17 lymphocytes, which secrete IL-17A, IL-17F, and IL-22. These cytokines act on keratinocytes to induce hyperproliferation, abnormal differentiation, and the release of antimicrobial peptides and chemokines, which in turn recruit neutrophils and further amplify local inflammation [3], [10]. Tumor necrosis factor-alpha (TNF-alpha) contributes in parallel by amplifying dendritic cell and keratinocyte activation, forming a self-sustaining inflammatory circuit sometimes referred to as the "psoriatic march," summarized in Figure 1 [8].

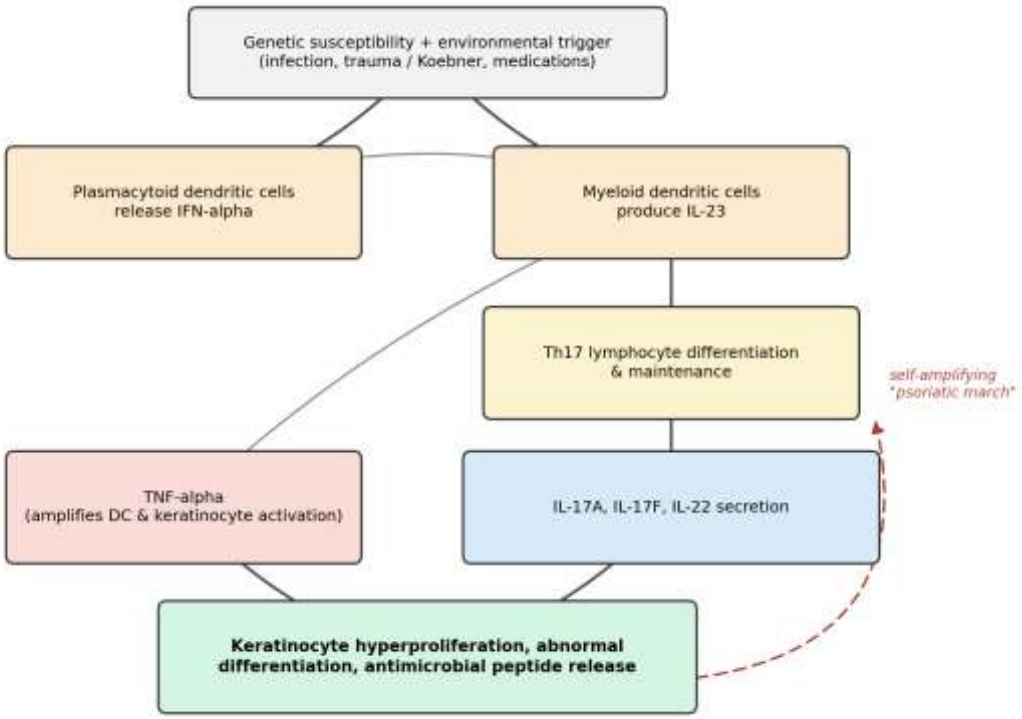

Figure 1. Simplified IL-23/Th17/TNF-alpha immunologic cascade in psoriasis pathogenesis, illustrating the self-amplifying loop between dendritic cells, Th17 lymphocytes, and keratinocytes.

This IL-23/Th17/TNF-alpha axis constitutes the principal molecular rationale for the biologic therapies now used in clinical practice, each of which is designed to interrupt the cascade at a distinct point [2], [9].

Clinical Features

Psoriasis presents with several recognized clinical phenotypes that differ in morphology, distribution, and clinical significance. The most common form, plaque psoriasis, accounts for approximately 80–90% of cases and presents as sharply demarcated, erythematous plaques covered with silvery-white scale, typically on the elbows, knees, scalp, and lumbosacral region [1]. Other phenotypes carry distinct clinical implications and are summarized in Table 1 [6].

Table 1. Major Clinical Phenotypes of Psoriasis

Phenotype	Typical Distribution / Morphology	Clinical Notes
Plaque (psoriasis vulgaris)	Elbows, knees, scalp, lumbosacral region; sharply demarcated plaques with silvery scale	Most common form (~80-90% of cases)
Guttate	Trunk and proximal limbs; small, drop-like papules	Often follows streptococcal pharyngitis, especially in children
Inverse (flexural)	Axillae, groin, inframammary folds	Smooth, minimally scaly plaques due to skin-fold moisture
Pustular	Palms, soles, or generalized	Sterile pustules; generalized form can be life-threatening
Erythrodermic	Widespread (>75% body surface area)	Diffuse erythema and scaling; risk of fluid/thermoregulatory instability

Additional characteristic clinical features include:

* Nail changes, including pitting, onycholysis, and subungual hyperkeratosis
* Auspitz sign (pinpoint bleeding upon scale removal)
* Koebner phenomenon (new lesions at sites of skin trauma)
* Joint pain and stiffness suggestive of concomitant psoriatic arthritis

Early recognition of these patterns, together with screening for psoriatic arthritis and metabolic comorbidities, supports timely initiation of appropriate systemic therapy.

Diagnosis

Diagnosis of psoriasis remains primarily clinical, based on characteristic lesion morphology and distribution; skin biopsy is reserved for atypical or diagnostically uncertain presentations [6].

Severity assessment and monitoring rely on:

* Psoriasis Area and Severity Index (PASI), combining erythema, induration, and scaling across body regions

* Body Surface Area (BSA) involvement as a simple measure of extent

* Dermatology Life Quality Index (DLQI) for assessing psychosocial and functional impact

* Screening tools for psoriatic arthritis (e.g., the Psoriasis Epidemiology Screening Tool)

Differential diagnosis is an important part of clinical evaluation, since several dermatoses can mimic psoriasis. Atopic or nummular eczema typically presents with more ill-defined, intensely pruritic lesions rather than the sharply demarcated, silvery-scaled plaques of psoriasis; seborrheic dermatitis tends to show greasy, yellowish scale confined to sebum-rich areas; cutaneous lupus erythematosus may present with erythematous plaques but is usually distinguished by photodistribution and characteristic serologic findings; and tinea corporis typically shows an annular, centrifugally spreading border with central clearing, confirmable by potassium hydroxide microscopy when suspected [6].

Accurate severity classification is essential for guiding the choice between topical, phototherapy, conventional systemic, and biologic treatment approaches, and for monitoring therapeutic response over time.

Treatment

Management follows a stepwise approach based on disease severity. Mild disease is generally managed with topical corticosteroids, vitamin D analogues, and emollients, while phototherapy (narrowband UVB) remains a well-established option for moderate disease not adequately controlled topically [6].

For moderate-to-severe disease, conventional systemic agents such as methotrexate, cyclosporine, and acitretin have long been used, though their utility is limited by cumulative toxicity and the need for regular laboratory monitoring [5].

The introduction of biologic therapy has fundamentally changed outcomes for moderate-to-severe psoriasis, enabling many patients to achieve near-complete or complete skin clearance with a favorable long-term safety profile [2], [9].

Table 2. Major Biologic Drug Classes Used in Psoriasis Treatment

Drug Class	Molecular Target	Representative Agents	Clinical Notes
TNF-alpha inhibitors	Tumor necrosis factor-alpha	Etanercept, adalimumab, infliximab	Also effective for concomitant psoriatic arthritis [5]
IL-17 inhibitors	Interleukin-17A / IL-17 receptor	Secukinumab, ixekizumab, brodalumab	Rapid onset of skin clearance [10]
IL-23 inhibitors	Interleukin-23 (p19 subunit)	Guselkumab, risankizumab, tildrakizumab	High sustained response rates, infrequent dosing [9]
IL-12/23 inhibitor	Shared p40 subunit of IL-12 and IL-23	Ustekinumab	Long-established efficacy and safety record [2]

Selection among biologic classes is individualized based on disease severity, presence of psoriatic arthritis, comorbidities, patient preference, and access considerations; coordinated screening for cardiovascular, metabolic, and psychological comorbidities remains an essential component of comprehensive long-term care regardless of the chosen therapy [11].

Conclusion

Effective management of psoriasis depends on recognizing it as a systemic immune-mediated disease driven by the IL-23/Th17/TNF-alpha axis, rather than treating skin plaques in isolation. Psoriasis-related complications require early diagnosis, individualized severity-based treatment strategies, and multidisciplinary management encompassing dermatology, rheumatology, cardiology, and mental health services.

The integration of modern severity-assessment tools, targeted biologic therapeutics, and structured long-term follow-up — informed by both international guidelines and locally generated clinical data — holds the potential to significantly decrease disease-related morbidity and improve quality of life for patients in Uzbekistan.

Future strategies must combine early immunologically-informed intervention, expanded access to targeted biologic therapies, and comprehensive dermatology-rheumatology-cardiology care networks to mitigate the growing burden of psoriasis-related morbidity.

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