

From “Blood Heat Syndrome” to Systemic Inflammation: A Contemporary Immunological Exposition of the Etiology of Psoriasis in the Context of Traditional Chinese Medicine

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Abstract: ***Objective:** This article aims to systematically elucidate the modern scientific connotation of the “Blood-Heat Syndrome” pathogenesis of psoriasis in Traditional Chinese Medicine (TCM), construct a theoretical bridge between it and the “systemic inflammation” concept in modern medicine, and provide a theoretical basis for the integrated prevention and treatment of psoriasis using both Chinese and Western medicine. **Methods:** Through theoretical tracing and literature research, the clinical manifestations and pathological evolution patterns of “Blood-Heat Syndrome” in psoriasis were systematized. This was integrated with modern immunological research progress on the core role of the IL-23/Th17 axis in the pathogenesis of psoriasis, conducting a critical dialogue and mutual interpretation of the pathomechanisms. **Results:** The state of excessive Yang heat described by TCM’s “Blood-Heat Syndrome” is highly consistent biologically with the “pro-inflammatory cytokine storm” driven by abnormal activation of the IL-23/Th17 immune axis. Pathomechanisms such as “Heat forcing blood to move recklessly” can correspond at the micro-level to immune cell circulation, vasodilation, and increased vascular permeability. In terms of treatment, Chinese herbs for “clearing heat and cooling the blood” (e.g., Sheng Di Huang [Rehmannia Root], Dan Pi [Tree Peony Bark]) have been confirmed to inhibit the IL-23/Th17 axis, regulate T-cell balance, and inhibit keratinocyte proliferation through multi-target actions, aligning with Western immunomodulatory strategies. Integrated Chinese and Western medicine has shown significant advantages in enhancing efficacy, reducing side effects, and preventing recurrence. **Conclusion:** The “Blood-Heat Syndrome” in psoriasis is a unique and precise macroscopic expression of the “systemic inflammation” state in modern medicine. This study successfully establishes a connection between the two, not only deepening the understanding of the scientific connotation of TCM syndromes but also paving new paths for promoting the integrated diagnosis and treatment of psoriasis using Chinese and Western medicine.*

Keywords: Psoriasis, Blood-Heat Syndrome, Systemic Inflammation, Immunopathogenesis Integrated Traditional Chinese and Western Medicine.

1. Introduction

Psoriasis, also known as “Bai Bi” in TCM, is an immune-mediated disease [1]. Its typical clinical features are well-defined red plaques covered with silvery-white scales, predominantly occurring on the scalp, elbows, knees, and lumbosacral region [1,2]. The global prevalence is approximately 2%-3%, affecting over 125 million people, with significant geographical and ethnic variations: for instance, the prevalence rate in the UK in 2022 was 3.2%, while the prevalence in China is about 0.47%. However, due to the large population base, the total number of patients is estimated to be as high as 7.65 million. Notably, psoriasis is not an isolated skin problem; about 7%-42% of patients develop psoriatic arthritis, and nearly half of the patients may develop erosive joint damage within 2 years of diagnosis, posing a high risk of disability. Furthermore, patients often have comorbidities such as metabolic syndrome, cardiovascular diseases, and psychosomatic disorders like anxiety and depression [3].

Modern medicine has clearly established that the core pathogenesis of the disease is closely related to the abnormal activation of the IL-23/Th17 immune axis, where various pro-inflammatory cytokines (e.g., IL-17, TNF- α) drive the excessive proliferation of keratinocytes and systemic inflammatory responses [4].

Traditional medicine attributes the core pathogenesis of the active stage of psoriasis to “Blood-Heat Syndrome”, which summarizes a systemic pathological state of excessive Yang heat and functional dysregulation. TCM holds that this syndrome is mostly caused by latent pathogens in the nutrient and blood aspects, transforming into heat and fire, which then manifest externally in the skin [5].

Current research often simply reduces the macroscopic “Blood-Heat Syndrome” to microscopic inflammatory indicators. This paper aims to demonstrate that “systemic inflammation” is the biological basis of “Blood-Heat Syndrome,” while emphasizing the holistic perspective provided by the “blood-heat” theory for disease diagnosis and treatment, hoping to provide new ideas for integrated Chinese and Western medicine research on psoriasis.

2. Tracing the TCM Pathogenesis of Psoriasis: Focusing on “Blood-Heat”

2.1 Theoretical Connotation of “Blood-Heat Syndrome”

“Blood-Heat” syndrome is the core pathogenesis of psoriasis. It is important to clarify that this “heat” does not refer to an increase in the physical temperature of the blood, but rather a pathological state of excessive Yang energy and functional dysregulation within the body. This state is primarily

characterized by heat pathogens lurking in the nutrient and blood aspects, leading to abnormal blood circulation and external manifestation on the skin. TCM believes that the formation of blood-heat stems from an imbalance of Yin and Yang within the body, with excessive Yang heat transforming into fire and entering the blood, causing the functions of the blood aspect to become hyperactive [6].

The Ming Dynasty physician Chen Shigong discussed in “Waike Zhengzong” (The Orthodox Manual of Surgery): “Internal accumulation of blood-heat generates wind and dryness, leading to malnourishment of the skin.” This accurately reveals the pathological process by which Blood-Heat Syndrome leads to psoriasis [7]. This pathological state corresponds to the pathological phenomena observed in modern medicine resulting from immune system overactivation and the massive release of pro-inflammatory factors.

2.2 Clinical Manifestations and Key Points of Pattern Identification for “Blood-Heat Syndrome”

The clinical manifestations of the active stage of psoriasis highly coincide with the characteristics of TCM’s “Blood-Heat Syndrome.” Typical symptoms are as follows: The rash appears bright red, which is a manifestation of intense heat pathogens in the blood manifesting on the skin; Auspitz’s sign (point bleeding) results from heat forcing the blood to move recklessly, blood failing to follow its pathways, and spilling outside the vessels; The continuous appearance of new lesions and rapid expansion of old lesions reflect the characteristics of heat being active and dispersing, symbolizing rapid disease progression; Intense itching originates from the pathological mechanism of blood-heat generating wind, and wind movement causing itching [8].

Regarding systemic symptoms, patients often experience restlessness and irritability, which is a manifestation of heat disturbing the heart spirit; Dry mouth and throat reflect intense heat damaging body fluids, leading to insufficiency; Scanty dark urine and dry stools result from heat pathogens consuming body fluids and the intestines losing moisture. The tongue is often red or crimson with thin yellow or dry yellow coating, and the pulse is wiry-rapid or slippery-rapid [9]. These clinical symptoms collectively constitute the key points for identifying the “Blood-Heat Syndrome” in psoriasis, providing a clear basis for clinical diagnosis and treatment.

2.3 Pathological Evolution of “Blood-Heat”

“Blood-Heat,” as the core pathogenesis of psoriasis, undergoes a dynamic process of formation and development. Causative factors include internal and external causes. Internal causes primarily include a constitutional tendency towards excessive Yang heat, which is the basis for onset; internal injury from emotions and the five minds transforming into fire are important inducing factors; excessive consumption of pungent, greasy foods can assist Yang and generate heat. External causes include external contraction of wind-heat or damp-heat pathogens; these external pathogens enter the interior, transform into heat, and transmit inward to the nutrient and blood aspects to cause disease.

The pathological evolution of blood-heat follows specific patterns. In the initial and active stages of the disease, “blood-heat” holds the core position, manifesting as a pathological state of heat pathogens lurking in the nutrient and blood. As the disease course progresses, three different outcomes may occur: First, persistent manifestation as Blood-Heat Syndrome, commonly seen in the active stage of the disease. The pathological characteristic is heat forcing blood to move recklessly, manifesting on the skin, clinically presenting with bright red rashes and frequent new lesions. Second, transformation into Blood Stasis Syndrome, often seen in the chronic stage. The pathological characteristic is heat obstructing the blood network vessels, leading to stagnant blood circulation, clinically presenting with dark red, thick, infiltrated lesions. Third, transformation into Blood-Dryness Syndrome, often seen in the resolving stage. The pathological characteristic is heat consuming Yin and blood, leading to malnourishment of the skin, clinically presenting with dry scaling and a pale base color [10].

This evolution reveals the transformation of psoriasis from the acute stage to the chronic stage, from excess heat to mixed deficiency and excess, which is significant for grasping the pattern identification and treatment of psoriasis.

3. Modern Immunological Mechanisms of Psoriasis: The IL-23/Th17 Axis and Systemic Inflammation

3.1 Core Pathway of Immunopathogenesis

The immunopathogenesis of psoriasis begins with specific initiating events. In genetically susceptible individuals, environmental factors such as trauma, infection, drugs, or psychological stress can trigger abnormal immune responses. This involves the participation of multiple gene loci, among which polymorphisms in genes like HLA-Cw6 and IL-23R provide a genetic basis for disease occurrence [11].

The core of the immune response revolves around the interaction between dendritic cells, IL-23, and Th17 cells. Dendritic cells, as initiators of the immune response, produce large amounts of Interleukin-23 (IL-23) upon activation, which drives the differentiation of naive CD4⁺ T cells into T helper 17 (Th17) cells. Activated Th17 cells subsequently produce several key inflammatory cytokines, including IL-17A, IL-17F, IL-22, and TNF- α . Among these, IL-17A and IL-17F directly stimulate excessive keratinocyte proliferation and promote the expression of antimicrobial peptides and chemokines; IL-22 induces abnormal keratinocyte differentiation and epidermal hyperplasia; TNF- α promotes the activation of vascular endothelial cells by enhancing the effects of other inflammatory cytokines.

In the inflammation amplification and maintenance phase, these cytokines form a complex positive feedback network. IL-23 continuously maintains the activated state of Th17 cells, while the cytokines produced by Th17 cells further activate dendritic cells, thus forming an inflammatory cycle. Simultaneously, these inflammatory cytokines also induce neutrophils, macrophages, and other inflammatory cells to release more inflammatory mediators, collectively leading to abnormal proliferation and differentiation of keratinocytes

and maintaining the chronic inflammatory state.

3.2 From Skin Inflammation to Systemic Inflammation

The inflammation in psoriasis is not limited to the local skin but also affects other systems. Numerous clinical studies confirm that levels of various inflammatory factors are significantly elevated in the serum of psoriasis patients, including IL-17, TNF- α , IL-6, and C-reactive protein. These circulating inflammatory mediators not only reflect the systemic inflammatory burden of the disease but also serve as an important biological basis for inducing other systemic diseases [12].

The association between psoriasis and the occurrence of multiple systemic diseases further proves its nature as a systemic inflammation. Among these, psoriatic arthritis is the most common comorbidity, occurring in about 30% of psoriasis patients. Its pathogenesis is also driven by the IL-23/Th17 axis, where inflammatory cells and factors attack the synovial tissue, leading to joint pain, swelling, and even deformity.

Regarding cardiovascular and metabolic diseases, the risk of their occurrence is significantly increased in psoriasis patients. Chronic inflammation promotes atherosclerosis through multiple pathways: TNF- α causes endothelial dysfunction; IL-17 promotes vascular inflammation; systemic inflammation also leads to insulin resistance and dyslipidemia, collectively constituting the pathological basis of metabolic syndrome. Epidemiology shows that the risk of myocardial infarction in patients with severe psoriasis is about 50% higher than in the general population.

Furthermore, psoriasis patients are also prone to inflammatory bowel disease, non-alcoholic fatty liver disease, depression, anxiety, and other mental disorders. These diseases share common inflammatory pathways with psoriasis, with key factors like TNF- α and IL-17 playing a central role. This systemic inflammatory state means psoriasis is no longer regarded as a mere skin disease, but rather a systemic inflammatory disease affecting multiple organs and systems, with the IL-23/Th17 axis at its core. This understanding not only deepens the comprehension of the disease's essence but also provides an important basis for formulating overall treatment strategies.

4. Building the Bridge: Dialogue Between “Blood-Heat Syndrome” and Systemic Inflammation

4.1 Correspondence Between “Heat” and the “Inflammatory Cytokine Storm”

Modern immunology recognizes a significant consistency between the state of “excessive Yang heat” described in TCM and the inflammatory cytokine storm in psoriasis. IL-17 directly stimulates keratinocyte proliferation and promotes neutrophil chemotaxis, a process corresponding to the pathological manifestation of “intense heat stirring the blood” in TCM theory. TNF- α , as a core regulator of the inflammatory cascade, its overexpression is similar to the TCM pathogenesis of “intense heat toxin”. Research indicates

that the complex network formed by these inflammatory factors shares a biological basis with the hyperfunctional state described by “excessive Yang heat” [13].

4.2 Correspondence Between “In the Blood” and “Immune Circulation and Vascular Response”

The TCM concept that psoriasis is located “in the blood aspect” closely corresponds to the mechanisms of circulating immune cells and vascular responses in modern immunology. Activated T lymphocytes migrate to the skin tissue via the bloodstream and produce inflammatory mediators locally, a process consistent with the theory of “heat pathogens lurking in the nutrient and blood”. Microscopically, the dilation and congestion of dermal capillaries in psoriatic lesions, increased vascular permeability, and extravasation of inflammatory cells precisely correspond to the TCM theory of “heat forcing blood to move recklessly”. The overexpression of mediators like Vascular Endothelial Growth Factor (VEGF) further promotes abnormal microvascular proliferation in the dermis, providing biological evidence for “heat in the blood aspect” [14].

4.3 Microscopic Interpretation of Clinical Manifestations

The typical clinical manifestations of psoriasis can be precisely verified at the microscopic level. “Bright red rash” corresponds to the dilation of dermal capillaries and accelerated blood flow, which is a vascular response mediated by inflammatory factors like TNF- α . “Point bleeding” (Auspitz sign) is related to increased fragility at the apex of the capillary loops in the dermal papillae, where inflammatory cell infiltration and protease release compromise vascular wall integrity. “Rapid disease progression” reflects the positive feedback regulation mechanism of the IL-23/Th17 immune axis, which continuously amplifies the inflammatory response. The abnormal proliferation and impaired differentiation of keratinocytes are closely related to the sustained stimulation by factors like IL-22, microscopically explaining the mechanism of scale formation.

4.4 Systemic Association of Whole-Body Symptoms

There is a close connection between the systemic symptoms of psoriasis patients and the systemic effects of systemic inflammation. Neuropsychiatric symptoms like “restlessness, insomnia” are related to inflammatory factors affecting central nervous system function via the blood-brain barrier. Studies show that pro-inflammatory factors like TNF- α and IL-1 β can alter neurotransmitter metabolism and affect the hypothalamic-pituitary-adrenal (HPA) axis function. Symptoms of fluid consumption like “dry mouth, dry stools” align with metabolic disorders and autonomic nervous system dysfunction under chronic inflammatory states. Furthermore, the elevation of acute-phase proteins and abnormal energy metabolism triggered by systemic inflammation also provide pathophysiological evidence for the symptoms of “Blood-Heat Syndrome.”

5. Mutual Confirmation in Treatment: From “Clearing Heat and Cooling the Blood” to Immunomodulation

5.1 TCM Treatment Principles and Formulae

The “Blood-Heat Syndrome” establishes the core treatment principle of “clearing heat, cooling the blood, and resolving toxin”, which directly targets the pathogenesis. Long-term clinical practice has formed a classical formula system represented by Xijiao Dihuang Tang (Rhinoceros Horn and Rehmannia Decoction), which profoundly embodies the essence of TCM “treatment based on pattern differentiation.”

Xijiao Dihuang Tang, as a representative formula for clearing heat and cooling the blood, has a strict composition structure of sovereign, minister, assistant, and envoy herbs. In the formula, Shui Niujiao (Water Buffalo Horn, ancient use was Rhinoceros Horn) serves as the sovereign herb, focusing on clearing heat-toxin from the blood aspect; Sheng Dihuang (Rehmannia Root) serves as the minister herb, both enhancing the blood-cooling effect of Shui Niujiao and possessing the effect of nourishing Yin and promoting fluid production; Dan Pi (Tree Peony Bark) and Chi Shao (Red Peony Root) serve as assistant and envoy herbs, both clearing heat and cooling the blood, and also activating blood and dispersing stasis, embodying the therapeutic wisdom of “cooling the blood without leaving stasis.”

Through thousands of years of clinical validation, commonly used Chinese herbs also have a well-established system [15]. Sheng Dihuang (Rehmannia Root) has the effects of clearing heat, cooling the blood, and nourishing Yin and promoting fluid production, targeting the core pathogenesis of blood-heat damaging Yin; Dan Pi (Tree Peony Bark) is skilled in clearing heat, cooling the blood, activating blood, and resolving stasis, conforming to the treatment concept of “cooling the blood without leaving stasis”; Chi Shao (Red Peony Root) is particularly able to clear heat, cool the blood, disperse stasis, and relieve pain, addressing both the blood-heat and blood-stasis pathological characteristics; Zi Cao (Arnebia/Gromwell Root) specifically enters the blood aspect, cools the blood, activates blood, resolves toxin, and promotes eruption, and is effective at clearing heat-toxin from the blood aspect. The coordinated combination of these herbs collectively constitutes the therapeutic system for clearing heat, cooling the blood, and resolving toxin.

5.2 Evidence from Modern Pharmacological Research on Chinese Herbs

Modern pharmacology has revealed the multi-target, multi-level action characteristics of Chinese herbs at the molecular level, verifying the therapeutic mechanisms of heat-clearing and blood-cooling herbs and providing solid experimental evidence for their clinical application.

Immunomodulation: Research finds that iridoid glycosides in Sheng Dihuang can significantly inhibit IL-23 expression, block the differentiation signals for Th17 cells, and inhibit key factors of the IL-23/Th17 axis. Paeonol, the main active component of Dan Pi, can inhibit the activation of Th17 cells and reduce the production of effector cytokines like IL-17A and IL-17F. Total glucosides of Chi Shao can downregulate the expression of the IL-23 receptor, attenuate IL-23 signaling, thereby interrupting the cytokine cascade [16]. Shikonin from Zi Cao can promote the proliferation and function of

regulatory T cells (Tregs), restoring the Th17/Treg balance. Sheng Dihuang polysaccharides can modulate the maturation process of dendritic cells, indirectly influencing the differentiation direction of naive T cells by affecting antigen presentation function [16]. These actions favor the restoration of immune system balance.

Anti-Angiogenesis & Anti-Keratinocyte Hyperproliferation: Paeonol can significantly inhibit the expression of Vascular Endothelial Growth Factor (VEGF), reducing abnormal microvascular proliferation in the dermis. Shikonin can directly inhibit the excessive proliferation of keratinocytes and induce cell cycle arrest in the G1 phase. Chi Shao extract can effectively block the STAT3 signaling pathway, inhibiting the abnormal differentiation and proliferation process of keratinocytes.

5.3 Practical Significance of Integrated Chinese and Western Medicine

The value of integrated Chinese and Western medicine in treating psoriasis has been fully validated in clinical application, demonstrating unique advantages and broad development prospects. This integration is reflected not only in theoretical complementarity but also in significant clinical synergy.

Synergistic Efficacy Enhancement: Studies confirm that combining heat-clearing and blood-cooling Chinese herbs with biologic therapy can significantly improve the PASI score improvement rate and lead to earlier onset of action. Chinese herbs, through multi-target regulation of the immune-inflammatory network, form an effective complement to the single-target action of biologics, producing a synergistic effect where “1+1 > 2.” This not only improves short-term efficacy but also contributes to the maintenance of long-term treatment outcomes [17].

Reduction of Side Effects: Research shows that combined Chinese herbal therapy can significantly alleviate injection site reactions caused by biologics and mitigate liver and kidney damage induced by traditional systemic medications like methotrexate. By regulating the overall immune state, Chinese herbs can also reduce the risk of infection, increase the safety window of treatment, and provide a guarantee for long-term medication [18].

Prevention of Recurrence & Holistic Regulation: By modulating immune memory cell function and improving skin barrier function, heat-clearing and blood-cooling Chinese herbs can significantly prolong the remission period and reduce the recurrence rate. This is highly significant for the prevention and treatment of chronic recurrent diseases, helping to improve patients’ quality of life. The holistic regulatory characteristics of Chinese herbs give them unique advantages in treating comorbidities associated with psoriasis. Clinical observations find that heat-clearing and blood-cooling Chinese herbs not only improve skin symptoms but also regulate glucose and lipid metabolism disorders and improve anxiety and depression states, achieving a shift from solely treating the skin disease to holistic regulation, embodying the TCM concept of “treating the root of the disease.”

By systematically analyzing the TCM connotation of “Blood-Heat Syndrome” in psoriasis and the “systemic inflammation” mechanism of modern medicine, an intrinsic connection between the two can be established. The “blood-heat” state described by TCM corresponds to the abnormal activation of the IL-23/Th17 axis discovered by modern immunology and the resulting inflammatory cytokine storm. This relationship is reflected not only at the level of clinical symptoms but is also fully substantiated at the pathophysiological mechanism level.

Symptomatically, the characteristic clinical symptoms of “Blood-Heat Syndrome,” such as bright red rashes, frequent new lesions, and point bleeding, all find their corresponding immunological basis at the microscopic level. Pathological changes like dermal vascular dilation, inflammatory cell infiltration, and abnormal keratinocyte proliferation provide evidence for the theory of “heat forcing blood to move recklessly.” Meanwhile, the systemic symptoms accompanying psoriasis show a high degree of consistency with the systemic effects of systemic inflammation [19].

At the treatment level, the multi-target regulatory effects of “heat-clearing and blood-cooling” Chinese herbs align with the complex pathogenesis of psoriasis. These drugs exert therapeutic effects through multiple pathways, such as inhibiting key factors of the IL-23/Th17 axis, regulating T-cell subset balance, and anti-angiogenesis, reflecting the scientific nature of the TCM holistic view [20]. The integrated Chinese and Western medicine treatment strategy demonstrates unique advantages in improving efficacy, reducing side effects, and preventing recurrence.

6. Summary and Outlook

This study establishes an intrinsic connection between the theoretical connotations of the “Blood-Heat Syndrome” in psoriasis from the perspective of Traditional Chinese Medicine (TCM) and the “systemic inflammation” mechanism recognized in modern medicine through systematic analysis. The “blood-heat” condition described in TCM aligns with the abnormal activation of the IL-23/Th17 axis and the consequent inflammatory cytokine storm identified in modern immunology. This relationship is not only reflected in clinical symptoms but has also been thoroughly validated at the pathophysiological and therapeutic levels. Integrated Traditional Chinese and Western Medicine (TCM-WM) therapy demonstrates unique advantages in enhancing efficacy, reducing side effects, and preventing recurrence.

Although this study has constructed a relatively comprehensive theoretical framework, several limitations remain. Firstly, current research on the biological basis of “Blood-Heat Syndrome” primarily relies on correlational analyses and lacks direct causal evidence. Secondly, existing studies predominantly focus on a limited number of inflammatory factors, which inadequately captures the holistic characteristics of TCM syndromes. Additionally, the multi-component, multi-target nature of Chinese herbal formulas presents ongoing challenges in elucidating their active material basis and mechanisms of action. By adopting interdisciplinary and integrated research strategies, it is

anticipated that breakthrough progress can be achieved in the field of TCM-WM integrated research on psoriasis. This would provide novel insights and methodologies for clinical diagnosis and treatment, while also serving as a reference for the modernization of TCM theory in the study of other diseases.

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