

Systemic Inflammation and Hair Follicle Homeostasis: Implications for Scalp Health and Hair Disorders

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Abstract

Low-grade systemic inflammation has been implicated in several chronic conditions and may influence peripheral tissues through circulating cytokines, metabolic mediators, oxidative stress and altered immune signalling. The hair follicle is an immunologically active mini-organ whose homeostasis depends on interactions between epithelial, mesenchymal and immune cells. This mini-review examines the evidence linking systemic inflammation, the scalp microenvironment and follicular function in alopecia areata, androgenetic alopecia, telogen effluvium, scalp psoriasis and seborrhoeic dermatitis. Ex vivo data show that pro-inflammatory cytokines can inhibit human hair follicle growth, and the efficacy of systemic Janus kinase inhibition supports a central role of immune dysregulation in alopecia areata. In androgenetic alopecia, perifollicular microinflammation, prostaglandin D2 and metabolic syndrome are associated with the disease, but the evidence does not establish systemic inflammation as a primary cause of follicular miniaturization. In telogen effluvium, systemic inflammatory events such as febrile illness and COVID-19 can act as triggers, although no specific inflammatory biomarker exists. Scalp psoriasis and seborrhoeic dermatitis illustrate the need to distinguish local scalp inflammation from concomitant systemic changes. C-reactive protein, interleukin-6 and haematological inflammation indices are of translational interest but lack the specificity required to diagnose or monitor alopecia. Because most clinical studies are cross-sectional, longitudinal studies combining standardized biomarkers with clinical and quantitative trichoscopic endpoints are needed to determine when systemic inflammation is merely associated with hair disorders and when it actually modifies hair follicle homeostasis.

Keywords: Inflammation; Hair Follicle; Alopecia; Biomarkers; Cytokines

Introduction

The hair follicle is a dynamic, cyclical and immunologically specialized mini-organ. Its homeostasis depends on coordinated interactions between keratinocytes, dermal papilla and dermal sheath fibroblasts, epithelial stem cells and resident immune cells. During anagen, defined follicular compartments maintain relative immune privilege, which limits antigen presentation and potentially harmful inflammatory responses¹⁻³.

Systemic inflammation is not a single entity. The term covers acute responses to infection, organ-specific and systemic autoimmunity, inflammation associated with immune-mediated skin diseases and chronic low-grade metabolic inflammation. Circulating cytokines, adipokines, reactive oxygen species and metabolic changes can affect peripheral tissues, and systemic diseases and drugs are recognized causes of hair loss, although the magnitude and causal nature of these relationships vary across conditions⁴.

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This mini-review critically examines the evidence linking systemic inflammation, the scalp microenvironment and hair follicle homeostasis, distinguishing established mechanisms, clinical associations and unproven hypotheses. A focused narrative search of PubMed/MEDLINE was performed up to September 2026 and supplemented by reference tracking, combining terms related to systemic inflammation, hair follicle, scalp, immune privilege, cytokines, interleukin-6, C-reactive protein, oxidative stress, metabolic syndrome and each condition discussed. Experimental studies on human hair follicles, biomarker studies, systematic reviews and meta-analyses were prioritized. No formal quality appraisal of the included studies was performed.

The Hair Follicle as an Immunologically Active Mini-Organ

Normal hair cycle progression requires a balance between the follicle and its immune microenvironment. Immune privilege of the anagen hair bulb involves downregulation of major histocompatibility complex class I molecules and the local production of immunosuppressive signals, and its collapse is a central element in the pathogenesis of alopecia areata¹⁻³.

Immunity is therefore not inherently pathological in the follicle. Resident immune cells take part in surveillance and tissue maintenance, and disease arises when the intensity, duration or location of the inflammatory response disrupts homeostasis. Interpreting follicular inflammation requires distinguishing physiological immunity, local scalp inflammation and concomitant systemic changes.

Mechanistic Links Between Systemic Inflammation and the Follicle

The most direct evidence that inflammatory mediators can act on the human follicle comes from organ culture. In microdissected human anagen hair follicles, interleukin (IL)-1 α , IL-1 β and tumour necrosis factor (TNF)- α were potent inhibitors of hair growth and induced dystrophic changes in the bulb resembling those of alopecia areata⁵. IL-6 induced by dihydrotestosterone in dermal papilla cells inhibited hair shaft elongation *ex vivo* and promoted follicle regression in mice⁶. These data establish biological plausibility, but the cytokines were applied directly to the follicle, and they do not show that the circulating levels found in patients are sufficient to reproduce these effects *in vivo*.

Oxidative stress may coexist with systemic inflammation and amplify pro-inflammatory signalling. In alopecia areata, a meta-analysis showed systemic oxidative imbalance, with higher oxidant markers and lower antioxidant defences⁷. Intracellular pathways such as NF- κ B integrate inflammatory, metabolic and damage signals. However, the detection of an activated inflammatory pathway in scalp tissue should not be taken as evidence that systemic inflammation caused the hair disorder.

Alopecia Areata: The Most Consistent Model of Immune Dysregulation

Among non-scarring alopecias, alopecia areata shows the best established relationship between immune dysregulation and the hair follicle. Collapse of immune privilege, CD8+ cytotoxic T lymphocytes and interferon- γ -dependent cytokine networks are central to its pathogenesis^{2,3}. The efficacy of oral baricitinib, a Janus kinase 1/2 inhibitor, in two phase 3 randomized trials provides the strongest therapeutic evidence that systemic modulation of immune signalling can restore hair growth in this disease⁸.

The systemic dimension of the disease has also received attention. A meta-analysis of five studies found higher serum IL-6 in patients than in controls (standardized mean difference 1.57; 95% CI 0.17 to 2.97), although with evidence of publication bias⁹, and in a case-control study of 105 patients and 108 controls, C-reactive protein (CRP) was the only inflammatory parameter significantly higher in alopecia areata¹⁰. In a cross-sectional study

of 302 patients and 296 controls, the neutrophil-to-lymphocyte ratio, the systemic immune-inflammation index (SII) and the white blood cell-to-lymphocyte ratio were higher in alopecia areata, and the platelet-to-lymphocyte ratio and SII were higher in severe disease¹¹. In a smaller study of 118 patients and 122 controls, only SII differed significantly from controls, whereas the systemic inflammation response index and the CRP-to-albumin ratio did not, and none of the indices was associated with severity¹². These partly discordant findings suggest that the inflammatory response is not confined to the scalp in some patients. The markers are, however, non-specific, may be influenced by comorbid atopy, thyroid disease or obesity, and should not replace clinical and trichoscopic assessment or validated severity instruments.

Androgenetic Alopecia: Inflammation as a Possible Modifier

Androgenetic alopecia is fundamentally determined by genetic predisposition and androgen signalling, and progressive follicular miniaturization should not be attributed primarily to systemic inflammation. Nevertheless, perifollicular microinflammation, oxidative stress and changes in the follicular microenvironment are described as possible additional components^{13,14}. One local inflammatory mediator has been characterized in detail: prostaglandin D2 synthase and prostaglandin D2 are elevated in bald compared with haired scalp of men with androgenetic alopecia, and prostaglandin D2 inhibits hair lengthening through its receptor GPR44¹⁵. Together with androgen-inducible IL-6 in dermal papilla cells⁶, these findings point to an inflammatory component generated within the scalp rather than imported from the circulation.

The association with metabolic syndrome is particularly relevant. A meta-analysis of 19 studies including 2,531 participants found a higher prevalence of metabolic syndrome in androgenetic alopecia (pooled odds ratio 3.46; 95% CI 2.38 to 5.05) and a less favourable metabolic profile across several parameters¹⁶. Insulin resistance, adipokines and pro-inflammatory cytokines have been proposed as mechanisms shared by metabolic syndrome and skin diseases^{17,18}. The included studies were observational, and age, body mass index and other confounders were handled inconsistently. These data support an association and a possible modulating effect, but they do not show that systemic inflammation is a primary cause of androgenetic alopecia.

Telogen Effluvium and Systemic Events

The hair cycle is sensitive to systemic change. Telogen effluvium may follow febrile illness, acute inflammation, nutritional deficiencies, endocrine disorders, drugs and other conditions that alter follicular cycling^{19,20}. COVID-19 provided a natural model: in a multicentre study of 191 patients with acute telogen effluvium after confirmed SARS-CoV-2 infection, shedding began a mean of 57 days after diagnosis, and a history of fever was associated with more severe shedding²¹. This supports, but does not prove, a role for the systemic inflammatory response, because fever, drugs, weight loss and psychological stress coexist in these patients.

Telogen effluvium is a heterogeneous syndrome, and no inflammatory biomarker is currently able to confirm its diagnosis. In practice, assessment should seek the likely trigger and consider the interval between the systemic event and the onset of shedding. Inflammatory markers are useful when there is a clinical reason to investigate an underlying systemic disease, but they do not constitute a diagnostic panel for telogen effluvium.

Scalp Psoriasis: Local Inflammation in a Systemic Disease

Psoriasis is an immune-mediated disease in which the IL-23/IL-17 axis plays a central role, together with other cytokines such as TNF and IL-22, and therapies targeting this axis are highly effective^{22,23}. The scalp is a frequent site of involvement, yet permanent alopecia is uncommon despite often intense inflammation.

The proposed hair follicle-psoriasis axis highlights regulatory mechanisms shared by the anagen follicle and the psoriatic plaque²⁴. This model shows that substantial local inflammation does not necessarily imply follicular destruction and that the interaction between the follicle and inflammatory skin disease may be bidirectional.

Seborrhoeic Dermatitis: Emerging Systemic Evidence

Seborrhoeic dermatitis has a multifactorial pathophysiology involving *Malassezia*, the epidermal barrier, lipid metabolism and immune activation. A systematic review published in 2026 identified cutaneous and systemic molecular changes, including redox imbalance, Th1 and Th17/Th22 signatures in lesional skin and altered systemic markers²⁵. Only eight studies met its inclusion criteria, with considerable methodological heterogeneity, and the implications for hair follicle function remain unexplored. Seborrhoeic dermatitis should therefore not be routinely interpreted as a manifestation of systemic inflammation, and these findings define an emerging area of research.

Inflammatory Biomarkers and Clinical Applicability

CRP, IL-6 and blood count-derived indices are attractive because they are widely available and inexpensive. In alopecia areata, there is growing evidence of association with the disease, but the association with severity is inconsistent⁹⁻¹². In other alopecias the evidence is more heterogeneous.

The main limitation is low specificity: these markers change with infection, obesity, autoimmune disease and many other systemic conditions. There is currently no support for their use as a universal panel to diagnose or monitor alopecia. When requested, they should be interpreted together with the clinical history, physical examination, trichoscopy and specific systemic suspicions. Table 1 summarizes the current evidence for each condition.

Table 1. Summary of the clinical evidence linking inflammation and hair disorders.

Condition	Relevant inflammatory axis	Current interpretation	Clinical caution
Alopecia areata	Immune privilege collapse, IFN- γ /JAK signalling, IL-6, CRP, blood count indices	Most consistent immunological and systemic evidence; efficacy of JAK inhibition	Biomarkers do not replace clinical assessment; association with severity is inconsistent
Androgenetic alopecia	Perifollicular microinflammation, PGD2, IL-6, oxidative stress, metabolic inflammation	Possible modifier; inflammatory component largely local	Not a primary inflammatory disease
Telogen effluvium	Trigger-dependent systemic response (fever, infection, COVID-19)	Inflammation may be part of the trigger	No specific inflammatory biomarker
Scalp psoriasis	IL-23/IL-17, TNF, IL-22	Systemic immune-mediated disease with frequent scalp involvement	Local inflammation does not imply follicular destruction
Seborrhoeic dermatitis	Th1, Th17/Th22, oxidative stress, barrier, lipids	Emerging systemic evidence	Few, heterogeneous studies; avoid extrapolation

CRP, C-reactive protein; IFN, interferon; IL, interleukin; JAK, Janus kinase; PGD2, prostaglandin D2; TNF, tumour necrosis factor.

Discussion

The literature supports that the hair follicle is integrated into the immune system and can respond to changes in the systemic environment, but the strength of this relationship varies across diseases. In alopecia areata, follicular immune dysregulation is central, and biomarker and therapeutic data are accumulating. In androgenetic alopecia, inflammation is better interpreted as a possible modifier of a genetically and androgen-determined disease, with a relevant locally generated component. In telogen effluvium, systemic processes act as triggers without a specific inflammatory marker. Psoriasis and seborrhoeic dermatitis illustrate the need to separate scalp inflammation from concomitant systemic inflammation.

The main gap is the difficulty of demonstrating temporality and causality. Most clinical studies are cross-sectional or case-control and measure systemic markers after the hair disorder is established. They cannot determine whether inflammation precedes follicular change, results from it or is a parallel phenomenon driven by shared comorbidities. Mechanistic studies, in turn, rely on concentrations applied directly to isolated follicles, and whether circulating levels reproduce these effects in vivo remains unknown.

Future studies should combine serial biomarkers, quantitative trichoscopic or phototrichogram endpoints, clinical activity, metabolic profile and, when possible, molecular analysis of the scalp, with adjustment for age, body mass index and comorbidities. Phenotypic characterization will also be important, because patients with the same diagnosis may show different degrees of systemic inflammation. This has a direct clinical implication: recognizing the systemic context may broaden the understanding of the patient, but it does not justify indiscriminate ordering of inflammatory panels or treating isolated biomarkers with the aim of promoting hair growth.

Conclusion

Hair follicle homeostasis depends on a balanced immune microenvironment, and inflammatory mediators can influence follicular biology in defined contexts. The evidence is most consistent for immune dysregulation and biomarker changes in alopecia areata and for metabolic associations in androgenetic alopecia, whereas other relationships remain less defined. Investigation of systemic inflammation should be guided by clinical indication and should not replace the specific diagnosis of hair disorders. Longitudinal studies with standardized biomarkers and objective trichoscopic endpoints are needed to determine when systemic inflammation is merely an association and when it modifies hair follicle homeostasis and the course of hair disease.

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Not applicable. This is a literature review without direct participation of human subjects or animals.

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Rúbia De Carli: conception, literature review, critical analysis, writing and final revision of the manuscript.

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