

Exploring the Role of Hirudotherapy in Alopecia Areata: Immunological and Microcirculatory Perspectives

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Abstract

Alopecia areata (AA) is a chronic autoimmune disorder characterized by non-scarring hair loss, most commonly involving the scalp¹. Despite the availability of treatments such as corticosteroids, topical immunotherapy, and Janus kinase (JAK) inhibitors, clinical response varies considerably and relapse remains frequent¹². This has led to growing interest in complementary therapeutic approaches.

Hirudotherapy (leech therapy), an ancient treatment modality described in classical texts including those of Avicenna¹³, has recently attracted attention due to its anti-inflammatory, anticoagulant, and immunomodulatory effects³.

Objective: To review the immunopathogenesis of alopecia areata and explore the potential role of hirudotherapy as an adjunctive treatment.

Methods: A narrative review of relevant literature focusing on alopecia areata and the biological effects of leech therapy.

Results: Bioactive substances in leech saliva, including hirudin and related peptides, have been shown to improve microcirculation and modulate inflammatory pathways^{7,12,8}.

Conclusion: Hirudotherapy may have a supportive role in alopecia areata; however, current evidence is limited and further well-designed clinical studies are required^{15,20,28}.

Keywords: Alopecia areata, Hirudotherapy, Leech therapy, Immunomodulation, Microcirculation, Autoimmune disease

Introduction

Alopecia areata is an immune-mediated disorder characterized by localized, non-scarring hair loss affecting the scalp and other hair-bearing areas¹. It is estimated to affect around 1–2% of the population during their lifetime¹, with no clear gender predilection.

The disease is primarily driven by an autoimmune response directed against hair follicles during the

anagen phase². Histologically, a dense perifollicular lymphocytic infiltrate, often described as a “swarm of bees,” is typically observed¹¹.

Although several treatment options are available—including intralesional corticosteroids, topical minoxidil, systemic immunosuppressants, and JAK inhibitors²⁶—recurrence remains common and long-term therapy may be associated with adverse effects². These limitations have encouraged the exploration of alternative and complementary treatment modalities.

Hirudotherapy, a traditional therapeutic practice, has long been used in inflammatory and vascular disorders³²⁴. Its potential role in alopecia areata is supported by its anti-inflammatory, anticoagulant, and possible immunomodulatory effects⁸.

Immunopathogenesis of Alopecia Areata

Alopecia areata is a T-cell-mediated autoimmune disorder characterized by targeted attack on anagen hair follicles. The pathogenesis is complex and involves genetic predisposition, environmental triggers, and immune dysregulation. Hair follicles are normally considered an “immune-privileged” site, meaning they are protected from immune surveillance. This immune privilege is maintained by low expression of major histocompatibility complex (MHC) molecules and local production of immunosuppressive cytokines. In alopecia areata, this immune privilege collapses, exposing follicular antigens to the immune system⁴⁵. Cytotoxic CD8⁺ T lymphocytes play a central role in disease pathogenesis. These cells, along with CD4⁺ helper T cells, infiltrate the peribulbar region of hair follicles, producing the characteristic “swarm of bees” appearance on histopathology⁵²¹. These activated T cells release pro-inflammatory cytokines that contribute to follicular damage. Key cytokines involved include interferon-gamma (IFN- γ) and interleukin-15 (IL-15), which amplify the immune response and sustain inflammation⁵²¹. IFN- γ promotes upregulation of MHC class I expression on follicular cells, further enhancing antigen presentation and perpetuating the autoimmune process.

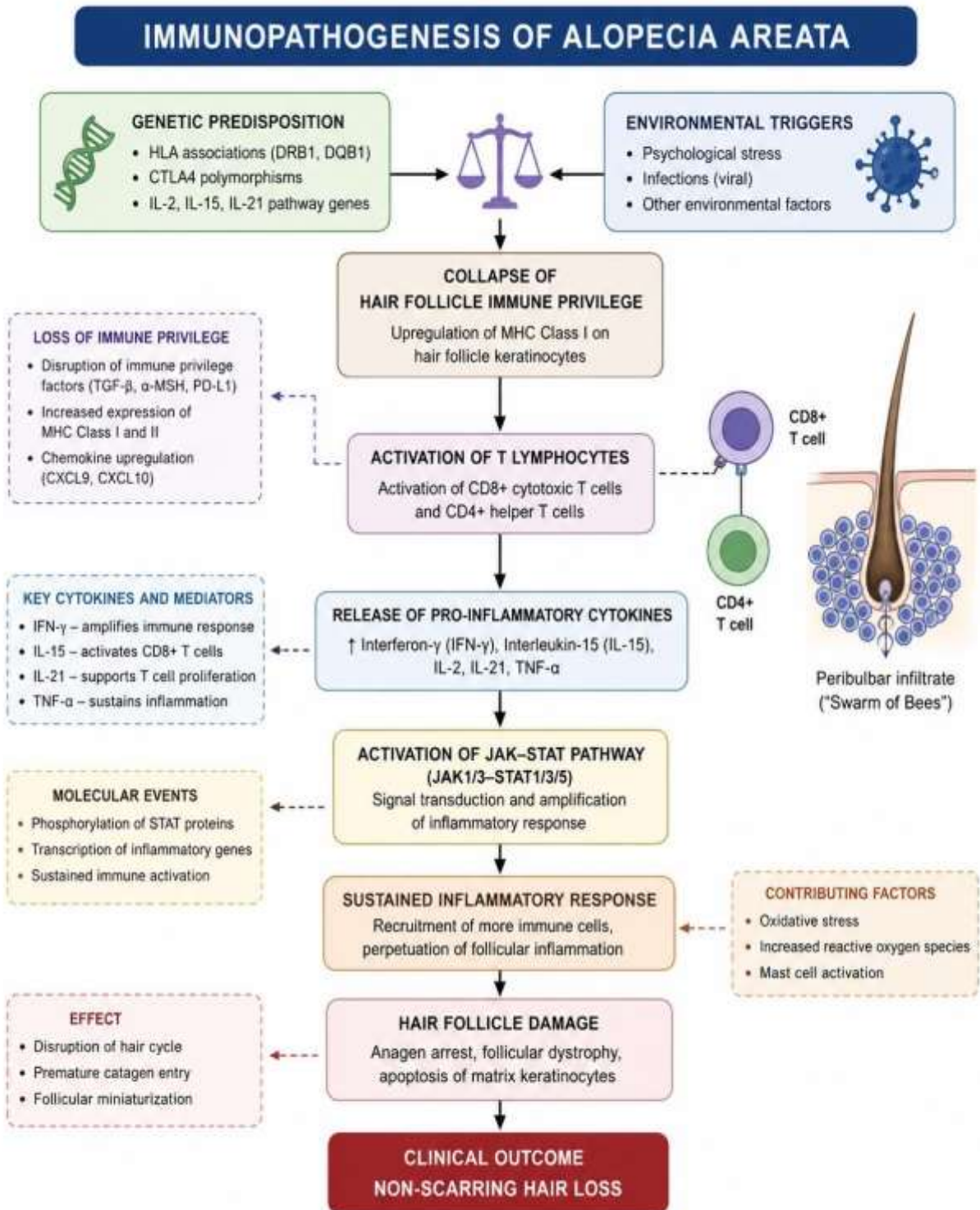
The Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway is critically involved in mediating cytokine signaling in alopecia areata. Activation of this pathway leads to transcription of pro-inflammatory genes and maintenance of the autoimmune response⁶¹⁹. This explains the therapeutic efficacy of JAK inhibitors in recent clinical practice. Genetic susceptibility also plays a significant role. Genome-wide association studies have identified several loci associated with immune regulation, including genes related to HLA, CTLA4, and IL-2/IL-21 pathways⁴²⁷. These findings support the concept that alopecia areata shares pathogenic mechanisms with other autoimmune diseases. Environmental and psychological factors may act as triggers in genetically predisposed individuals. Stress, infections, and hormonal changes have been implicated in disease onset or exacerbation, possibly through neuroimmune interactions²¹. Additionally, recent studies suggest a role of oxidative stress and altered cytokine balance in disease progression. Increased levels of reactive oxygen species may contribute to follicular damage and immune activation.

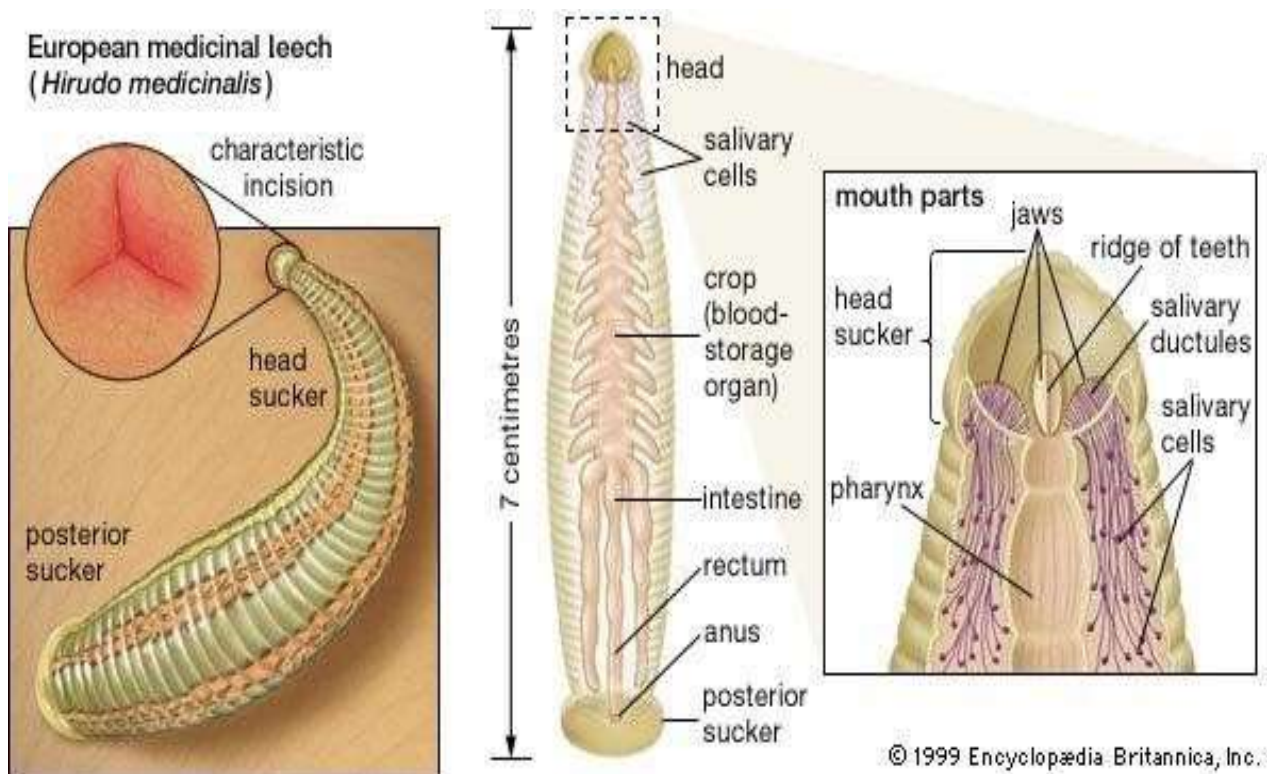
Overall, alopecia areata represents a multifactorial autoimmune condition involving loss of immune privilege, T-cell-mediated cytotoxicity, cytokine dysregulation, and genetic predisposition. Understanding these mechanisms is essential for developing targeted therapeutic approaches.

Biological Properties of Medicinal Leech Saliva

Medicinal leeches release a variety of pharmacologically active substances through their saliva⁷¹². These include Hirudin (thrombin inhibitor), Calin (platelet aggregation inhibitor), Destabilase (fibrinolytic

enzyme), and proteins such as Bdelins and Eglins with anti-inflammatory properties⁷¹². Leech saliva contains more than 20 bioactive molecules with anticoagulant, anti-inflammatory, antimicrobial, and analgesic effects⁷¹²²⁴. These substances enhance microcirculation, reduce venous congestion, and may modulate local immune responses⁸.





Proposed Mechanisms of Hirudotherapy in Alopecia Areata

Hirudotherapy is believed to exert its therapeutic effects in alopecia areata through multiple mechanisms, involving vascular, immunological, and anti-inflammatory pathways. Although the exact mechanism is not fully understood, several plausible explanations have been proposed.

1. Improvement in Microcirculation

One of the primary effects of hirudotherapy is enhancement of local blood circulation. The bioactive substances present in leech saliva, particularly anticoagulants such as hirudin, prevent clot formation and improve blood flow⁷¹². This leads to better oxygen and nutrient delivery to hair follicles and removal of metabolic waste products, supporting follicular regeneration⁹²⁴.

2. Anti-inflammatory Effects

Leech saliva contains anti-inflammatory peptides such as bdellins and eglins, which inhibit enzymes involved in inflammation⁷¹². This may reduce perifollicular inflammation and decrease local cytokine activity, thereby limiting damage to hair follicles⁷²¹.

3. Immunomodulatory Action

Alopecia areata is an autoimmune condition mediated by T lymphocytes and cytokines⁵²¹. Hirudotherapy may influence immune responses by altering cytokine expression and reducing pro-inflammatory mediators, potentially helping restore immune balance around hair follicles²⁵.

4. Analgesic and Neurohumoral Effects

Leech saliva contains substances with analgesic properties⁷, which may reduce discomfort and neurogenic inflammation. This may indirectly improve patient compliance and local tissue response.

5. Traditional and Detoxification Perspective

Traditional systems of medicine describe hirudotherapy as a method of removing impure blood¹³. While not fully aligned with modern science, this may correlate with improved circulation and reduction in inflammatory mediators⁸.

6. Combined Effect

The therapeutic benefit of hirudotherapy is likely due to a combination of improved microcirculation, anti-inflammatory action, and immunomodulation⁷⁸.

7. Role of Vasodilation and Local Tissue Perfusion

In addition to anticoagulant effects, leech saliva also promotes vasodilation⁷¹², which enhances local tissue perfusion. Increased blood flow may help reverse perifollicular hypoxia and improve the microenvironment necessary for hair follicle growth⁹²⁴.

8. Fibrinolytic Activity and Tissue Remodeling Enzymes such as destabilase exhibit fibrinolytic activity⁷¹², which may help break down microthrombi and improve capillary circulation. This supports tissue remodeling and healing in affected areas²⁴.

9. Antimicrobial Properties

Leech saliva contains substances with antimicrobial effects⁷¹², which may help prevent secondary infections at the application site and maintain a healthy scalp environment.

10. Reduction of Oxidative Stress

Some components of leech saliva may have antioxidant properties⁷¹², which could help reduce oxidative stress and protect hair follicles from damage.

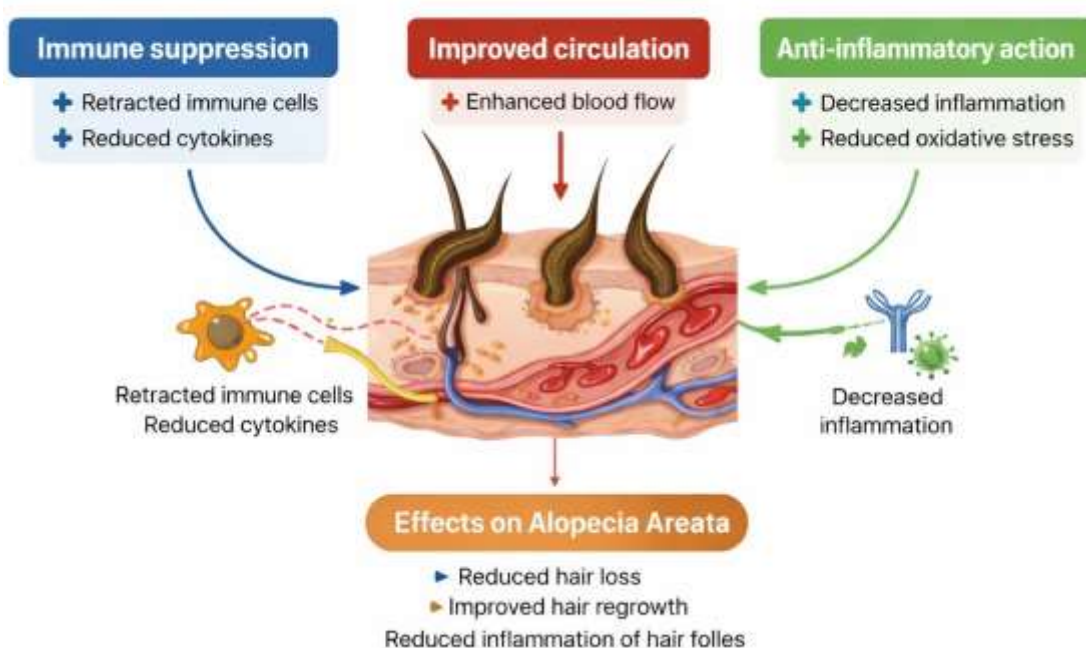
11. Psychosomatic and Stress-Related Effects

Alopecia areata has been associated with psychological stress²¹. Hirudotherapy may provide indirect benefits by reducing stress and improving patient perception of treatment.

12. Synergistic Mechanism

The overall effect of hirudotherapy is likely due to a synergistic interaction between improved circulation, reduced inflammation, immune modulation, and enhanced tissue healing⁷⁸.

Mechanism of hirudotherapy in alopecia areata



Safety, Adverse Effects and Contraindications

Hirudotherapy is generally safe when performed under sterile conditions³. However, potential

complications include prolonged bleeding, secondary infection (especially *Aeromonas hydrophila*)¹⁰, local allergic reactions, and rarely anemia with repeated sessions^{3,10}.

Contraindications

- Bleeding disorders (e.g., hemophilia)
- Severe anemia
- Immunocompromised states
- Pregnancy (relative contraindication)

Proper patient selection, aseptic technique and monitoring can significantly reduce risks³.

Additional original details (retained): Hirudotherapy is considered a generally safe procedure when performed under proper clinical and sterile conditions. However, some side effects may occur.

The most common complications include:

- Prolonged bleeding at the application site
- Secondary infection, especially due to *Aeromonas hydrophila*¹⁰
- Localized allergic reactions such as itching or redness
- Anemia in rare cases, particularly with frequent sessions These risks can be reduced by:
- Careful patient selection
- Maintaining strict aseptic technique
- Proper post-procedure monitoring

Severity of Alopecia Tool (SALT) Score

The SALT score is a standardized method used to assess the extent of scalp hair loss in alopecia areata and is widely used in both clinical practice and research².

Scalp Division

- Vertex: 40%
- Posterior: 24%
- Right side: 18%
- Left side: 18%

Formula

SALT Score = (Vertex × 0.40) + (Posterior × 0.24) + (Right × 0.18) + (Left × 0.18) The final score ranges from 0% (no hair loss) to 100% (complete scalp hair loss)².

Severity Grading

- S0: No hair loss
- S1: <25%
- S2: 25–49%
- S3: 50–74%
- S4: 75–99%
- S5: 100%

The SALT score is useful for assessing disease severity, monitoring progression, and evaluating treatment response².

Discussion

Hirudotherapy is not a new concept, but its application in alopecia areata is still relatively underexplored. From a practical clinical perspective, its appeal lies in the combination of multiple effects—improvement in local circulation, reduction in inflammatory activity, and a possible influence on immune pathways. These mechanisms, although not fully established, provide a reasonable biological basis for its use. At the same time, it is important to recognize the limitations. Most of the available evidence is based on small studies or isolated case reports¹⁵, which makes it difficult to draw firm conclusions. In routine clinical practice, established treatments such as corticosteroids and JAK inhibitors remain the mainstay, primarily because of stronger evidence and predictable outcomes. Hirudotherapy, therefore, should be viewed more realistically—as a potential adjunct in selected cases, especially where conventional therapy is not well tolerated or where patients are seeking alternative options. Its role is likely to remain supportive unless stronger clinical evidence becomes available. Another practical concern is the lack of standardized protocols. Variations in the number of leeches used, duration of application, and treatment intervals make it difficult to compare outcomes across studies. Addressing these issues will be essential for future research.

Limitations

Despite its usefulness, the SALT score relies on visual estimation, which may introduce observer variation. Additionally, it does not reflect qualitative aspects such as hair density, texture, or regrowth patterns, and is limited to assessing scalp involvement only.

Future Directions

Future research should focus on large-scale randomized controlled trials, standardized treatment protocols, comparative studies with standard therapies, and use of objective outcome measures such as SALT score¹⁵.

Conclusion

In summary, hirudotherapy shows some theoretical and preliminary clinical promise in the management of alopecia areata. Its anti-inflammatory, anticoagulant, and possible immunomodulatory effects may contribute to improved follicular environment and hair regrowth⁷⁸.

However, at present, the evidence is not strong enough to recommend it as a primary treatment modality. It may be considered in a complementary role, particularly in carefully selected patients.

Future studies with larger sample sizes, better methodology, and standardized protocols are necessary before it can be integrated into routine clinical practice with confidence¹⁵.

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