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Roots of Inflammation: The Microbiome-Immune Interface and the Call for a Multidisciplinary Protocol in Alopecia Areata

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Abstract

Alopecia areata (AA) is a chronic autoimmune condition marked by non-scarring hair loss. Its pathogenesis involves a complex interplay of genetic predisposition, immune dysregulation, environmental stressors, and microbial imbalance. While the gut-skin immune axis is well established in many autoimmune disorders, its role in AA remains underexplored. This review applies the model of microbiome-mediated immune dysregulation in a novel way, underscoring the need for deeper investigation into gut and scalp dysbiosis as drivers of systemic inflammation. This review also examines the modifiers that exacerbate the disruptions in the gut microbiota.

Additionally, emerging evidence strongly implicates the gut microbiome as a critical and underexplored factor stress, diet, and environmental exposures-may trigger AA via mechanisms involving Th1/Th17 pathways, regulatory T-cell dysfunction, and inflammatory cytokine cascades. Notably, studies reveal distinct differences in gut microbiota composition between AA patients and healthy controls, supporting the value of stool-based diagnostics in clinical evaluation to uncover hidden dysbiosis. Therapeutic implications of targeting the microbiome are explored, including the use of prebiotics, probiotics, postbiotics, micronutrient therapy, and fecal microbiota transplantation (FMT). Additionally, this review emphasizes the relevance of osteopathic principles, highlighting modalities such as osteopathic manipulative treatment and vagal nerve regulation in restoring homeostasis through gut-immune modulation. Framing gut dysbiosis through an osteopathic lens reinforces the interconnectedness of body systems advocating for a holistic, systems-based approach to AA. This paper also explores how functional medicine principles focused on microbiome restoration, personalized nutrition, and identifying root causes of inflammation can complement osteopathic and conventional therapies. By bridging conventional, functional, and osteopathic medicine, this review emphasizes the need for further research into gene-microbiome-environment interactions for AA.

1. Introduction

Alopecia Areata (AA) is a complex and multifactorial autoimmune disease characterized by non-scarring hair loss of the body, typically localized to areas of the scalp.[1, 2] It affects men and women of all races equally and is seen in roughly 2% of the global population. There are several variations in the clinical presentation of AA, with the most common pattern being coin-sized annular patches.[3, 4] This disease can be self-limiting but more often demonstrates unpredictable relapses and remissions.[1] AA has a poorly understood non-specific etiology, with most research implicating genetic predisposition and immune dysregulation as central factors in its pathogenesis.[5] The mechanism involves an immune-mediated hair follicle destruction, primarily by T-helper 1 (Th1) cells, secondary to MHC overexpression at the hair bulb, which results in upregulation of inflammatory cytokines, such as IL-12, IL-23, and TNF-a.[2, 6, 7]

Due to defective immune tolerance, autoreactive helper T cells and NK cells are able to produce IFN-γ which results in the disruption of hair growth and subsequent hair loss.[7, 8] Additionally, specific HLA markers such as DQB1*03 (DQ3) are present in more than 80% of AA patients, highlighting a strong genetic susceptibility but still leaving unanswered questions regarding disease triggers and in AA pathogenesis. Stress—psychological, environmental, or physical—can disrupt gut microbial balance (dysbiosis), altering immune responses and contributing to inflammatory diseases.

This review firmly underscores the urgent need to elucidate the complex interplay between gut health, microbiota composition, stress, and systemic immune mechanisms in AA. It further expands on potential management strategies for chronic conditions related to gut dysbiosis through functional medicine, emphasizing restoration of the gut microbiome, optimization of nutrition, and addressing the root causes of inflammation and immune dysregulation. Despite increasing interest in the gut-skin-immune axis, the specific microbiome-driven mechanisms underpinning AA remain poorly defined, and no standardized testing or interventions exist in addressing dysbiosis in AA patients. Osteopathic medicine shares significant philosophical overlap with functional medicine, both advocating a holistic and patient-centered approach that targets underlying systemic dysfunction rather than isolated symptoms. However, osteopathic medicine uniquely centers its foundation on the integration of structure and function, emphasizing the body's innate ability to heal and the body functioning as a whole unit. By bridging conventional, functional, and osteopathic principles, this review proposes that AA is not solely a localized autoimmune disorder, but a systemic condition. One that is influenced by microbiome dynamics, modifiable lifestyle factors, and neuroimmune regulation- and that an integrative, mechanism-based treatment framework is both necessary and overdue.

2. Gut-Skin Axis and Immunological Crosstalk

The gut-skin axis provides a compelling framework for understanding how gut dysbiosis may influence hair disorders such as Alopecia Areata (AA). This bidirectional communication network is mediated by gut microbiota and its metabolites, which affect systemic inflammation and immune responses at distal sites, including at the skin and hair follicles.[10] Dysbiosis can promote the production of inflammatory cytokines and modulate T helper (Th) cell responses—particularly the Th1 and Th17 pathways, which are central to the autoimmune mechanisms underlying AA.[2, 10]

Expanding research has established connections between gut microbiota and immune-mediated inflammatory diseases such as Crohn's disease and ulcerative colitis, with similar mechanisms proposed in AA. Evidence suggests gut dysbiosis enhances autoreactive T cell activity, thus inducing systemic inflammation and follicular destruction via IFN-γ-mediated responses.[2, 8] Germ-free (GF) animal models have helped unravel the symbiotic advantage conferred on us by commensal microbes with GF animals showing profound immune deficits.[11] Supporting these findings, studies have identified significant differences in gut microbiome composition between AA patients and healthy controls, highlighting specific bacterial taxa that may either contribute to or protect against disease.[6]

Additionally, a bidirectional association between AA and IBS has been observed, reinforcing an inference of the role of gut dysbiosis in immune-mediated disorders.[12] A pilot study in pediatric AA patients and their siblings revealed differences in microbial gene ortholog abundance, suggesting that the microbial landscape may be systematically altered in AA, extending beyond the skin.[13]

Parallel to the gut, the scalp harbors a unique microbiome whose dysregulation has also been implicated in AA. Clinical studies have identified higher proportions of *Corynebacterium* and *Staphylococcus* species in patients with severe AA, suggesting a possible prognostic role for these taxa.[14, 15] Other findings include increased levels of *Cutibacterium acnes* and decreased *Staphylococcus epidermidis*, indicating that scalp dysbiosis may contribute to the inflammatory milieu observed in AA.[2] Advanced scalp microbiome profiling has further revealed dermal-level shifts in bacteria such as *Neisseria subflava* and *Pseudomonas*, potentially linked to tissue damage in AA.[16, 17]

While the exact directionality remains unclear—whether microbial dysbiosis initiates or exacerbates inflammation—the interdependent relationship between gut and scalp microbiota, immune function, and genetic susceptibility appears central to AA pathogenesis.[2] This has opened the door to holistic approaches, including functional medicine strategies aimed at restoring microbial balance through targeted nutritional and lifestyle interventions.

Collectively, these findings shed light on the relevance of the gut-skin-immune axis in the etiology and potential treatment of AA. Continued research into gene-microbiome-immunity interactions will be critical for advancing personalized therapies and improving outcomes for individuals with autoimmune hair loss.

3. Genetic and Epigenetic Contributions

Alopecia areata (AA) is increasingly recognized as a multifactorial autoimmune disease with a complex etiology involving genetic, epigenetic, immunological, and environmental components.[1, 18] As with other autoimmune conditions, genetic predisposition is critical in the development of AA. Numerous studies have identified hundreds of single nucleotide polymorphisms (SNPs) associated with the disease.[1] Many of these SNPs are found in genomic regions responsible for regulating immune function, particularly those involved in T-regulatory (Treg) cell activity, cytotoxic T-lymphocyte responses, cytokine production, and antigen presentation. Notably, several of these genes are also implicated in other autoimmune diseases such as inflammatory bowel disease (IBD), multiple sclerosis, type 1 diabetes, and psoriasis, suggesting a shared genetic architecture that may predispose individuals to immune dysregulation across organ systems.[1, 19]

Genetic predisposition to immune dysregulation may further shape the gut microbiome, amplifying inflammatory signals that extend to the skin and hair follicles. Notably, mouse models such as the C3H/HeJ mouse strain—prone to both IBD and AA—have demonstrated altered AA severity following microbial modulation, supporting the gut microbiome's influence on autoimmune activity in genetically susceptible hosts.[1]

4. The Interplay of Stress, Gut Dysbiosis, and Hair Loss

It is increasingly recognized that stress—encompassing psychological, environmental, and physical stimuli—modulates the gut microbiota, which in turn can influence host health.[20] This modulation may contribute to gut dysbiosis-an imbalance in the gut microbiome-which can disrupt systemic homeostasis and lead to a range of underlying pathology.[20]

Emerging evidence further highlights a connection between gut microbiome alterations and various dermatological conditions, specifically alopecia areata (AA).[10] Psychological stress, arising from fear, anxiety, or cognitive demands, has been shown in preclinical studies to alter the composition of the murine gut microbiota, often leading to a reduction in *Lactobacillus* abundance and, in some cases, decreased microbial diversity. [20] These microbial shifts can have functional consequences, such as disrupting tryptophan metabolism and increasing vulnerability to subsequent stressors.[20] Chronic psychosocial stress reduces the compositional and genetic diversity of the fecal microbiota, including genes involved in the biosynthesis and metabolism of short-chain fatty acids (SCFAs) and neurotransmitter precursors.[20] These stress-induced changes in the gut microbiota have also been associated with heightened pro-inflammatory responses and worsened colonic pathology upon pathogen challenge, suggesting increased susceptibility to additional stressors.[20]

Stress has long been implicated in hair loss, particularly in autoimmune disorders like alopecia areata.[21, 22] Severe psycho-emotional stress may trigger AA by disrupting gut flora, increasing intestinal permeability, and sensitizing the immune system to erroneously attack hair follicles. Patients with AA are at higher risks of experiencing both depression and anxiety secondary to the stress and emotional turmoil that hair loss induces.[23] As both of these conditions have been linked to increased inflammation within the central nervous system,[24, 25] it is critical to further assess the role mental illness can play in perpetuating the disease process. One study in particular showed that corticosterone released by the adrenal gland in response to chronic stress impacted hair follicle stem cells leading to reduced hair growth.

Hair loss can lead to psychological problems such as low self esteem, depression, anxiety and body dysmorphic disorder.[24] These psychosomatic developments that occur as a result of hair loss influence neurogenic inflammation, characterized by nerve fiber/mast cell interaction, and upregulate pro-inflammatory cytokine production, namely IL-1, IL-6, and TNF-α, further continuing the inflammatory cycle and worsening hair loss.[24, 25] The resulting cytokine cascade, often involving the JAK/STAT pathway, recruits additional immune cells further sustaining perifollicular inflammation and thus perpetuating hair loss.[26]

In addition to psychological stress, environmental stressors—including extreme temperatures, high altitude, environmental noise, pathogens, pollutants, and toxicants—also influence the gut microbiota.[20] For example, heat stress has been shown to reduce microbial diversity and the abundance of beneficial genera such as *Lactobacillus* and *Bifidobacterium* in animal models.[20] Environmental pollutants, such

as particulate matter, have been associated with inflammatory responses implicated in alopecia areata.[27] Polyaromatic hydrocarbons have been linked to androgenetic alopecia, while noise stress has been shown to increase intestinal permeability in animal studies.[28] These findings support the broader role of gut dysbiosis in hair loss conditions. Beyond gut-mediated mechanisms, environmental pollutants may exert direct cytotoxic effects on hair follicles due to their high cellular turnover and vascularization.[27] Particulate matter can provoke inflammatory responses linked to AA, while pesticides and heavy metals have been implicated in both AA and acute anagen effluvium. Additionally, UV radiation—exacerbated by ozone layer depletion—induces oxidative stress and perifollicular mast cell degranulation, further contributing to follicular damage.[27] Taken together, these findings highlight the complex, multifactorial connection between stress, gut dysbiosis, and environmental exposures that may converge on common inflammatory and immune-mediated pathways to drive hair follicle dysfunction and hair loss.

5. DIAGNOSING GUT DYSBIOSIS

While the primary diagnosis of AA remains clinical-based on the appearance of hair loss, emerging research urges a deeper exploration into underlying contributors such as gut dysbiosis. Recent studies employing the Next Generation Sequencing (NGS) of 16s rRNA genes and shotgun metagenomics of stool samples have begun to reveal significant microbial differences between AA patients and healthy individuals.[29] For instance, elevated levels of *Holdemania filiformis, Parabacteroides johnsonii, Clostridiales vadin BB60 group, Bacteroides eggerthii,* and *Parabacteroides distasonis* have been observed in patients with alopecia universalis, while increased *Blautia, Phyllobacterium,* and *Megasphaera* were noted in AA. Conversely, decreased levels of *Ruminococcus bicirculans* were found in pediatric AA cohorts.[1] These findings suggest possible microbial biomarkers for AA.

Nonetheless, these associations strongly support the clinical utility of gut microbiome testing in the broader assessment of AA, particularly when conventional approaches fail to identify modifiable contributing factors. There are various factors that can result in a state of dysbiosis within the body including excessive use of antibiotics- that wipe the microbiome clean of essential microbes, as well as increased alcohol consumption, antacid use, chronic stress and anxiety.[30] Some studies have also linked dysbiosis to C-section births and formula feeding in newborns.[30, 31] Dysbiosis can't be diagnosed through standard blood tests or scope tests (endoscopy/colonoscopy). In order to diagnose gut dysbiosis, healthcare providers must obtain a thorough history as well as a Comprehensive

Digestive Stool Analysis (CDSA). CDSA analyzes the stool for multiple microbiota such as lactobacilli, bifidobacteria, *E. Coli*, Proteus, Pseudomonas, Salmonella, Shigella, Vibrio, and other organisms.[30] Alternatively, large scale bacterial biomarker profiling can be performed. This method is utilized by the GA-map dysbiosis test.[32] Additionally, the CLOUD test is a statistical method useful for identifying abnormal microbial patterns in different conditions/diseases compared to healthy individuals.[32]

A thorough patient history combined with stool-based diagnostics may uncover gut microbial imbalances that contribute to the autoimmune cascade seen in AA, offering new avenues for personalized treatment and prevention.

Indications for Gut Dysbiosis Testing in AA may include:

1. *To Assess for Underlying Imbalances*: A comprehensive gut health test is suggested to measure the abundance of different gut microbes, along with markers of dysbiosis and inflammation.[33]
2. *In Cases with Gastrointestinal Symptoms:* Assessing the gut microbiome can help identify imbalances contributing to various symptoms, including digestive issues, eczema, and *H. pylori* infection.[1]
3. *When Associated Comorbidities are Present:* Patients with AA have a higher prevalence of conditions like *H. pylori* infection, autoimmune thyroid diseases, and inflammatory bowel disease, where gut health can be a significant factor. Testing could be particularly relevant in these cases. The Italian Society of Dermatology recommends testing for specific autoantibodies for autoimmune thyroiditis and celiac disease in AA patients.[1] Standard lab work for suspected or long-standing/severe cases may include ANA, Rheumatoid factor, TFTs, and serum vitamin B12.[34]

4. *To Inform Personalized Interventions:* Assessing the gut microbiome allows for the identification of imbalances potentially contributing to inflammation, autoimmunity, and AA, which can then inform personalized gut healing protocols.[1]

6. Lifestyle, Diet, and Microbial Modulation

Modern lifestyle factors may act as epigenetic triggers, modulating gene expression and immune function via effects on the microbiome. Dietary patterns typical of Western societies—high in saturated fats, simple sugars, processed foods, and low in fiber, fruits, and vegetables—have been associated with adverse changes in microbial diversity,[35] reduced production of short-chain fatty acids (SCFAs), and heightened inflammation.[8, 36] The consumption of ultra-processed foods can lead to gut dysbiosis by altering the balance of beneficial and detrimental bacteria, potentially due to acellular nutrients, food additives like emulsifiers and artificial sweeteners, and pathogen-associated molecular patterns.[35] This dysbiosis can result in increased gut permeability and low grade inflammation.[37]

Short-chain fatty acids (SCFAs), produced by beneficial gut bacteria, serve a critical role in supporting immune tolerance through their effects on regulatory T cells (Tregs). Western diets can result in reduced production of SCFAs, thus perpetuating inflammation implicated in various auto-immune disorders such as AA.[6] Additionally, gut-derived signals can affect critical molecular pathways involved in hair follicle development and cycling, including the JAK-STAT and Wnt/β-catenin pathways. Aberrance in these pathways secondary to gut dysbiosis further upregulates inflammatory changes observed in AA.[10]

Diets such as the Mediterranean or gluten-free diet, along with probiotics and micronutrient supplementation, may help restore homeostasis and modulate inflammation in AA patients.[2, 38] The lower prevalence of alopecia areata in populations consuming diets distinct from the Western diet, such as the soy based diet in Japan, suggests a nexus between dietary patterns, the gut microbiome, and hair health. Emerging evidence suggests that probiotics may represent a promising adjunctive therapy for hair loss conditions. A Korean clinical trial demonstrated improved hair thickness and count in androgenic alopecia patients consuming probiotic-rich foods like kimchi and cheonggukjang.[39] Ultimately, gut dysbiosis and inflammation secondary to Western diets can potentially impact hair health.[6] Nutritional deficiencies remain another critical factor.[2, 38, 40, 41] Low levels of vitamins D and A, iron, zinc, and niacin have been observed in individuals with hair loss.[40] Notably, vitamin D deficiency may influence both immune modulation and gut microbiome composition, and decreased expression of the vitamin D receptor (VDR) has been linked to AA.[40]

Obesity, smoking, poor sleep, and chronic stress, have also been implicated in the pathogenesis of AA. Obesity-related inflammation, altered adipokine profiles, and Th17-skewed immune responses have all been proposed as mechanisms linking metabolic dysfunction to hair follicle autoimmunity.[40] Smoking, in particular, has been associated with AA and may induce local inflammatory responses in the scalp via increased Th17 activity.[6]

7. Diet and AA Incidence Worldwide

In a study analyzing global prevalence of AA, the authors observed notable regional differences in the age-standardized incidence rates (ASIR) of AA, suggesting potential links between socioeconomic and dietary factors and the prevalence of this immune mediated hair loss.[42] The highest ASIR values, in 2021, were observed in developed regions such as North America (with the United States exceeding 550 per 100,000 individuals and Canada over 500) . In contrast, the lowest ASIRs, in 2021, were found in Africa and the Middle East.[42\]

This pattern may suggest an intricate link between AA incidence and environmental, lifestyle, and socioeconomic variables. In high-income countries such as the United States and Canada, higher AA incidence can potentially be associated with aforementioned factors such as Westernized diets, high in processed foods and inflammatory agents, as well as higher levels of stress[43]—all of which are known contributors to immune dysregulation. At the same time, some low and middle income countries in South America and Southeast Asia also reported high ASIRs, which may point to the compounded effects of nutritional deficiencies, limited access to healthcare, and increased psychosocial stress due to socioeconomic instability. This shows the importance of placing emphasis on diet and micronutrient supplementation, including Vitamin D, when developing a therapeutic plan

for AA patients, due to the multifaceted nature of the disease. Further analysis on global trends needs to be performed in order to obtain a more comprehensive understanding of external factors worldwide affecting AA prevalence.

8. Microbiota-Targeted Therapies

The role of microbiome-targeted therapies is gaining attention. Probiotics such as *Lactobacillus reuteri* have shown promising results in animal models, promoting hair in the anagen growth phase and modulating inflammatory cytokines (increased IL-10, decreased IL-17).[40] Topical applications of microbiota-derived compounds, such as Lactobacillus plantarum-based lotions, have increased keratinocyte growth factor levels, supporting the idea that both systemic and localized microbiome interventions may be beneficial.[18] Postbiotics—non-living bacterial products or metabolites—are also emerging as therapeutic agents due to their anti-inflammatory, antioxidative, and microbiota-modulating effects. Kalibiome postbiotics from *Lactobacillus paracasei* have demonstrated the ability to inhibit Staphylococcus aureus biofilms, reduce oxidative stress, and dampen inflammatory signaling, which may be relevant in scalp disorders and AA.[44]

Prebiotics and probiotics work hand in hand to support gut health. Prebiotics help create a nourishing environment for the 'good' bacteria within our gut microbiota, namely via interaction with beneficial anaerobic bacteria such as *Bifidobacteria* and *Lactobacilli*.[45] Although more research has been developed on the importance of probiotic supplementation in the modulation of our gut microbiome, it is noteworthy to explore the benefits of prebiotics as they foster a healthy environment to help our essential gut bacteria thrive. Additionally, prebiotics can support the composition of our scalp microbiome. One study discusses the topic of prebiotics in the context of topical scalp products.

It specifically mentions the prebiotic alpha-glucan oligosaccharide and its role in helping maintain scalp microbiome diversity.[46]

Fecal Microbiota Transplantation (FMT) remains an experimental but compelling intervention to modulate gut microbiome diversity. Case reports highlight hair regrowth even in longstanding AA following gut microbiota restoration through FMT, underscoring the systemic immunomodulatory potential of the microbiome.[29, 47, 48] Additionally, compounds such as solubilized sturgeon oil (SSO) have demonstrated hair regrowth in mice alongside increased populations of beneficial gut bacteria like Lactobacillus and Bifidobacterium, suggesting new avenues for microbiota-targeted nutraceuticals.[49]

9. Modulation of Stress and Environmental Factors

Psychological stress is increasingly recognized as both a trigger and amplifier of autoimmune conditions like AA. High levels of stress can activate the hypothalamic-pituitary-adrenal (HPA) axis, dysregulate immune function, and alter gut microbiota composition-factors implicated in AA pathogenesis.[24, 50] Managing stress is therefore a vital therapeutic target. Evidence-based stress reduction strategies include mindfulness meditation, breathing exercises, yoga and emotional support networks. These methods have been associated with reduced inflammatory markers and improved quality of life in chronic illness populations.[50-53] Practices such as mindful meditation, breathing exercises, and yoga may enhance vagal tone and parasympathetic activity, supporting immune regulation.[54] Environmental exposures can also exacerbate inflammatory pathways involved in AA.[55-57] Protective measures like reducing pollutant exposure, using UV-protective hair products, and ensuring adequate but safe vitamin D intake are recommended.[55, 58]

Healthcare providers should consider occupational and lifestyle factors when assessing AA, especially in patients with unexplained or relapsing cases. A patient-driven approach that includes sleep hygiene, balanced nutrition, regular exercise, and stress management may improve outcomes by addressing both internal and external triggers.[50]

10. Integrative Osteopathic Perspectives

Osteopathic medicine, grounded in the principle that the body functions as a unified whole with inherent self-regulatory capabilities, offers a holistic framework for managing complex conditions like AA.[59] This philosophy aligns well with AA's multifactorial imbalance and demands a comprehensive approach. Osteopathic assessment enables treatment beyond visible symptoms, targeting structural, nutritional, and psychosocial imbalances contributing to disease progression.

Within this context, Osteopathic Manipulative Treatment (OMT) may serve as an adjunct therapy by enhancing physiological pathways involved in inflammation resolution and immune modulation. Techniques like lymphatic pump, rib raising, and myofascial release aim to improve autonomic tone, circulation, and lymphatic drainage.[60, 61] These effects may indirectly support microbial balance by enhancing gut motility and reducing sympathetic overactivation, both of which influence gastrointestinal function and microbial homeostasis. Improved lymphatic flow may also aid in the clearance of pro-inflammatory cytokines and immune complexes from peripheral tissue, including the scalp.[61]

From an immunological standpoint, normalization of autonomic output and lymphatic flow may reduce the chronic low-grade inflammation that characterizes AA pathophysiology.[62] Lymphatic pump techniques have been shown to increase the circulation of leukocytes and inflammatory mediators such as interleukin-8 (IL-8), promoting immune surveillance and tissue repair.[60, 61] These mechanisms may influence both gut and scalp microbiota composition and function, linking osteopathic intervention to core aspects of AA's systemic nature.[40] Complementing this is the role of the vagus nerve in immune regulation. Acting as a "medical dispatcher," it detects inflammatory signals and orchestrates immune responses via suppression of pro-inflammatory cytokines and promotion of anti-inflammatory pathways. Dysregulation of vagal tone-due to poor sleep, chronic stress, or diet-can contribute to sustained inflammation and immune-mediated disorders like AA.[60, 61]

Vagus nerve stimulation (VNS) has shown therapeutic promise in inflammatory conditions including Crohn's disease and rheumatoid arthritis. Its effects are mediated by the cholinergic anti-inflammatory pathway (CAIP), which modulates both nervous system and immune function.[62, 63] As a non-pharmacologic neuromodulation strategy, VNS offers an alternative to traditional therapies by restoring homeostasis via nervous system regulation.[64]

The vagus nerve's influence on the gut microbiome is particularly relevant in AA, where gut dysbiosis contributes to systemic inflammation. VNS may reduce intestinal permeability, improve gut motility, and support microbial balance through CAIP-mediated effects.[64] These changes can positively impact nutrient absorption and immune function-factors that play a role in hair follicle health.[62] A proof of concept clinical trial has even shown that transcutaneous auricular VNS can reduce inflammation in pediatric IBD, supporting its broader application in immune regulation.[65, 67]

Although OMT and VNS function via distinct mechanisms-manual versus bioelectronic modulation-both target the autonomic nervous system and may synergistically work in supporting immune and gut homeostasis. While direct evidence linking either intervention to hair regrowth in AA is limited, their overlapping mechanisms provide a compelling rationale for integrative care.

Empowering patients with at-home techniques such as deep breathing, humming, and Tai Chi may further reinforce autonomic balance and therapeutic outcomes.[67-69] These self-regulation practices stimulate vagal tone and complement professional treatments, helping patients maintain physiological stability between sessions.[70] Moreover, engaging in such practices can mitigate stress and promote patient agency, supporting a biopsychosocial model of care.

11. Conclusion

Alopecia areata (AA) is a multifaceted autoimmune disorder influenced by genetic susceptibility, immune dysregulation, microbial imbalances, and lifestyle factors. Central to its pathogenesis is the role of the gut and scalp microbiota in modulating both systemic and local inflammation. Emerging evidence implicates psychological stress, environmental exposures, and modern dietary patterns in promoting gut dysbiosis, which may act as epigenetic triggers exacerbating immune dysfunction in predisposed individuals. Functional and lifestyle medicine approaches—including dietary optimization, targeted supplementation with probiotics, prebiotics, and postbiotics, correction of nutrient deficiencies, and emerging therapies such as fecal microbiota transplantation (FMT) and osteopathic manipulative treatment (OMT)—offer promising, integrative strategies for managing and potentially preventing AA by modulating the gut-hair axis.[18, 40] Despite growing interest in the microbiome's role in autoimmune diseases, high-quality research directly examining gut dysbiosis in AA remains scarce. Addressing this gap is critical, with future studies needing to prioritize longitudinal, multi-

omic analyses to elucidate microbiome dynamics in AA onset and treatment response. Incorporating gut profiling into dermatologic evaluation may open new pathways for disease interception and personalized care.

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