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Evolving Therapeutic Landscape of Alopecia Areata: Current Evidence and Future Directions

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ABSTRACT

***Background*:** Alopecia areata (AA) is a chronic, immune-mediated hair disorder characterized by nonscarring hair loss with unpredictable clinical course and significant psychosocial burden. Despite being one of the most common autoimmune conditions, effective and sustained treatment options have remained limited until recently. Conventional approaches, including corticosteroids, immunosuppressants, and topical therapies, have shown variable efficacy, with high relapse rates upon discontinuation. Recent advances in molecular immunology have revolutionized therapeutic strategies, particularly with the development of Janus kinase (JAK) inhibitors and other targeted biologics. Alongside these, regenerative therapies, nanotechnology-based drug delivery, and exosome-based interventions are reshaping the therapeutic landscape.

Aim: This review aims to provide an updated and comprehensive overview of current and emerging therapeutic modalities for alopecia areata. It examines conventional topical and systemic treatments, innovative adjuvant modalities such as platelet-rich plasma, microneedling, cryotherapy, and phototherapy, as well as novel biologics, small-molecule inhibitors, and nanomedicine. Special emphasis is given to JAK inhibitors—highlighting their clinical efficacy, safety profiles, and limitations—as well as the management of AA in specific areas such as the beard, eyelashes, and eyebrows.

Conclusion: Therapeutic strategies for AA are evolving rapidly, moving from empiric immunosuppression to precision-based immunomodulation. While corticosteroids and traditional immunosuppressants remain first-line options in many clinical settings, their limitations highlight the need for more durable and targeted interventions. JAK inhibitors such as baricitinib, ritlecitinib, and tofacitinib have demonstrated substantial efficacy, leading to regulatory approvals and establishing them as key agents in moderate-to-severe AA. Biologics targeting specific cytokines, along with experimental therapies such as exosomes and nanotechnology-driven approaches, represent promising future directions. The management of AA in cosmetically sensitive sites such as the beard, eyelashes, and eyebrows poses unique therapeutic challenges, requiring tailored approaches. Ultimately, integrating conventional, targeted, and regenerative strategies—guided by disease severity, comorbidities, and patient preferences—holds the potential to transform AA management into a personalized, patient-centered paradigm.

Keywords: Therapeutic Landscape, Alopecia Areata

INTRODUCTION

Alopecia areata (AA) is a nonscarring autoimmune alopecia characterized by partial or complete hair loss, with prevalence estimates ranging from 0.1% to 0.2% in the general population and a lifetime risk of up to 2%. The disease can affect any hair-bearing site, most commonly the scalp, but also eyebrows, eyelashes, and beard. Its clinical course is unpredictable, ranging from small, self-limiting patches to severe forms such as alopecia totalis or universalis, with high rates of relapse. Beyond its physical manifestations, AA imposes substantial psychosocial and emotional distress, with patients often experiencing reduced self-esteem, social withdrawal, depression, and anxiety.

For decades, treatment strategies for AA have been largely empirical, focusing on immune suppression or modulation to control inflammation and induce regrowth. Topical corticosteroids, immunotherapy, systemic steroids, and classic immunosuppressants such as methotrexate and cyclosporine have been mainstays of management. However, these approaches are associated with limited long-term efficacy, frequent relapses, and safety concerns, underscoring the unmet need for durable and targeted therapies.

Recent insights into AA pathogenesis, particularly the role of autoreactive CD8+ T cells, interferon-γ, interleukin-15, and the Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway, have opened new therapeutic opportunities. The advent of JAK inhibitors has revolutionized treatment, with several agents now demonstrating efficacy in randomized controlled trials and receiving regulatory approval. In parallel, biologics targeting immune checkpoints, regenerative therapies such as platelet-rich plasma (PRP) and exosomes, and advanced technologies including nanomedicine are expanding the therapeutic arsenal.

This review provides an updated synthesis of the evolving treatment landscape in AA. It discusses traditional topical and systemic therapies, novel adjuvant modalities, biologics, and small-molecule drugs, with special emphasis on JAK inhibitors and their limitations. Additionally, it highlights innovative therapies such as nanotechnology and exosomes, and addresses management of AA in challenging sites such as the beard, eyelashes, and eyebrows. By linking established treatments with emerging strategies, this review underscores the transition of AA management from empirical immunosuppression to precision-based, patient-centered care.

Topical Therapies

Topical Tretinoin

Topical retinoids, particularly tretinoin, have been investigated as therapeutic options in alopecia areata (AA) due to their ability to modulate epidermal proliferation, follicular differentiation, and local immune responses. Tretinoin exerts keratolytic effects that enhance drug penetration, making it useful as a monotherapy or as an adjunct to corticosteroids and minoxidil. Early studies demonstrated hair regrowth in approximately 50% of patients treated with topical tretinoin, with higher success when combined with topical corticosteroids compared to either agent alone. The rationale behind this combination lies in tretinoin's ability to increase the percutaneous absorption of corticosteroids, thereby augmenting their efficacy. Clinical response is more favorable in patchy AA than in extensive forms such as alopecia totalis

or universalis [1].

The mechanism of action of tretinoin in AA may also involve immunomodulation. Retinoids regulate keratinocyte differentiation, suppress pro-inflammatory cytokine production, and may partially restore hair follicle immune privilege. However, responses remain variable, and relapse after discontinuation is common. Adverse effects include erythema, irritation, scaling, and contact dermatitis, which may limit compliance, especially in patients with sensitive scalp skin. Despite these limitations, tretinoin remains a useful low-cost adjunctive therapy in mild-to-moderate AA cases, particularly when combined with corticosteroids or minoxidil [2].

Capsaicin

Capsaicin, a pungent compound derived from chili peppers, has been studied as a topical treatment for AA due to its neuro-immunomodulatory properties. Capsaicin activates transient receptor potential vanilloid 1 (TRPV1) receptors on sensory neurons, leading to the release and subsequent depletion of neuropeptides such as substance P and calcitonin gene-related peptide (CGRP). These neuropeptides are known to contribute to perifollicular inflammation and the collapse of hair follicle immune privilege. By modulating neurogenic inflammation, capsaicin may indirectly promote hair regrowth [3].

Clinical studies have reported modest efficacy of topical capsaicin in patchy AA, with improvement in hair density and regrowth noted after several weeks of therapy. In some cases, capsaicin has been combined with isoflavonoids or other topical agents to enhance its therapeutic effect. While generally well tolerated, its main side effect is localized burning or stinging sensation, which can be uncomfortable for patients and reduce adherence. Nonetheless, capsaicin represents an interesting example of a therapy targeting the neuroimmune axis in AA, suggesting that neurogenic pathways may play a more significant role in disease activity than previously recognized [4].

Although topical tretinoin and capsaicin are not considered first-line therapies, they expand the therapeutic armamentarium, especially for patients with localized disease or those intolerant to systemic treatments. Their relatively favorable safety profiles and accessibility make them practical adjuncts in combination regimens aimed at enhancing hair regrowth. However, larger randomized controlled trials are needed to establish their efficacy and role in the modern treatment algorithm of AA [5].

Systemic Treatments

Systemic Corticosteroids (Pulsed and Nonpulsed)

Corticosteroids have been the cornerstone of systemic therapy for alopecia areata (AA) for decades, owing to their potent anti-inflammatory and immunosuppressive effects. They inhibit T-cell activation, downregulate pro-inflammatory cytokines such as interferon-γ and interleukin-2, and suppress antigen presentation, thereby reducing the autoimmune assault on hair follicles. Oral corticosteroids in daily regimens may induce regrowth in severe AA; however, long-term use is limited by adverse effects such as weight gain, hypertension, diabetes, osteoporosis, and adrenal suppression. For this reason, pulsed regimens have gained popularity. Intravenous methylprednisolone or high-dose oral dexamethasone given intermittently can achieve disease control while reducing cumulative toxicity. Clinical response rates vary, with up to 60–70% of patients experiencing partial regrowth, though relapse is frequent upon cessation [6].

Methotrexate (MTX)

Methotrexate, an antimetabolite that inhibits dihydrofolate reductase, exerts both immunosuppressive and anti-inflammatory effects, making it useful in severe or refractory AA. MTX is often employed at low weekly doses, either as monotherapy or in combination with systemic corticosteroids to enhance efficacy and reduce steroid requirements. Several studies have shown hair regrowth in 30–60% of patients, with better responses observed in those with less extensive disease and shorter duration of alopecia. MTX's mechanism in AA likely involves suppression of autoreactive T cells and modulation of cytokine networks. Side effects include hepatotoxicity, bone marrow suppression, and gastrointestinal intolerance, necessitating careful monitoring of liver function and blood counts. Folate supplementation is recommended to mitigate toxicity [7].

Cyclosporine-A (Cyc-A)

Cyclosporine-A, a calcineurin inhibitor, acts by blocking T-cell activation through inhibition of interleukin-2 transcription. It has been used as an off-label systemic therapy in AA, particularly in extensive and recalcitrant cases. Response rates vary widely, with regrowth reported in 25–50% of patients. Combining cyclosporine with systemic corticosteroids appears to enhance outcomes, suggesting synergistic effects. However, relapse after discontinuation is common, and long-term use is limited by nephrotoxicity, hypertension, hypertrichosis, and increased risk of infections. Despite these limitations, cyclosporine remains a viable option in selected severe cases when other therapies fail or are contraindicated [8].

Azathioprine

Azathioprine, a purine analog that inhibits DNA synthesis and suppresses rapidly dividing immune cells, has also been explored in AA management. Its use is less common than methotrexate or cyclosporine, but case series and small studies suggest potential efficacy, particularly in patchy or moderate forms of AA. Azathioprine reduces T- and B-cell proliferation, dampening the autoimmune response at the follicular level. Clinical responses have ranged from 20% to 50%, though robust evidence from randomized controlled trials is lacking. Toxicities include leukopenia, hepatotoxicity, and increased susceptibility to infections, which require careful monitoring. Its role in AA is likely as a second- or third-line systemic immunosuppressant for patients unresponsive to other regimens [9].

In summary, systemic immunosuppressants—including corticosteroids, methotrexate, cyclosporine, and azathioprine—remain important therapeutic tools in the management of moderate-to-severe AA. While they can induce substantial regrowth in many patients, their limitations lie in frequent relapses and adverse effect profiles, emphasizing the need for safer, more durable, and targeted treatment approaches [10].

Other Treatment Modalities

Cryotherapy

Cryotherapy has been investigated as a localized therapeutic option for alopecia areata (AA), particularly in small, resistant patches. The application of liquid nitrogen induces controlled tissue injury, leading to vasodilation, increased local blood flow, and stimulation of hair follicle activity. Additionally, cryotherapy may alter perifollicular immune responses by modulating cytokine release and reducing autoreactive T-cell activity. Case series have reported regrowth rates of 30–50% in localized AA when cryotherapy is applied

in repeated sessions. However, efficacy is limited in extensive or chronic disease. Adverse effects such as blistering, post-inflammatory pigmentation changes, and scarring are possible, highlighting the need for cautious patient selection. Despite these drawbacks, cryotherapy may be considered as a low-cost, adjunctive modality for localized AA [11].

Platelet-Rich Plasma (PRP)

PRP therapy has emerged as a promising regenerative approach for AA. It involves intradermal injection of autologous plasma enriched with platelets, which release growth factors including platelet-derived growth factor, vascular endothelial growth factor, and transforming growth factor-β. These molecules enhance angiogenesis, promote hair follicle stem cell proliferation, and exert immunomodulatory effects. Several controlled studies have shown PRP to be superior to placebo and in some cases comparable to intralesional corticosteroids in inducing hair regrowth. PRP also improves hair shaft thickness and density, with minimal adverse effects such as transient pain or erythema at injection sites. While standardized protocols are lacking, PRP represents a safe and effective adjunctive therapy, especially in patients with patchy AA or those seeking non-immunosuppressive alternatives [12].

Microneedling

Microneedling, a minimally invasive technique that creates controlled micro-injuries in the scalp using fine needles, has gained attention in AA treatment. The procedure stimulates wound healing cascades, releases growth factors, and enhances transdermal drug delivery. When combined with topical agents such as corticosteroids or minoxidil, microneedling significantly improves penetration and efficacy. Additionally, microneedling induces activation of dermal papilla cells and may modulate local immune responses, restoring follicular cycling. Clinical studies have reported favorable outcomes in both patchy and diffuse AA, with improvement in hair density and regrowth. Side effects are usually mild and transient, including erythema, pain, or pinpoint bleeding. As an adjunctive therapy, microneedling is increasingly incorporated into multimodal treatment strategies [13].

Phototherapies

Phototherapy has been used in AA for decades, based on its immunomodulatory and stimulatory effects on hair follicles. Ultraviolet A (UVA) with psoralens (PUVA) and narrowband UVB (NB-UVB) are the most studied modalities. PUVA acts by inducing T-cell apoptosis and altering local cytokine balance, leading to partial restoration of immune privilege. NB-UVB has a safer profile but appears less effective than PUVA. Excimer laser (308 nm) has also shown promise in localized AA, targeting lesions with minimal systemic exposure. Reported regrowth rates vary from 30% to 70%, with better outcomes in patchy AA compared to alopecia totalis or universalis. However, recurrence is frequent, and prolonged use carries risks such as photodamage and increased skin cancer risk. Phototherapy is best suited as an adjunctive modality in patients with limited, stable disease [14].

Fractional Lasers

Fractional lasers, including fractional CO_2 and erbium:YAG lasers, are novel tools for stimulating hair regrowth in AA. Their mechanism involves controlled dermal injury, induction of wound healing, and release of growth factors, similar to microneedling but with deeper tissue penetration. Fractional lasers also enhance transdermal absorption of topical agents, a process termed "laser-assisted drug delivery."

Preliminary studies combining fractional lasers with topical corticosteroids or PRP have demonstrated encouraging results, with improved regrowth compared to monotherapy. Adverse effects such as erythema, edema, and post-inflammatory hyperpigmentation are usually transient. Although still experimental, fractional lasers represent an exciting adjunct for refractory AA [15].

HMG-CoA Reductase Inhibitors (Statins)

Statins, commonly used for hyperlipidemia, have been investigated as potential treatments for AA due to their immunomodulatory and anti-inflammatory properties. They inhibit major histocompatibility complex (MHC) class II expression, reduce T-cell activation, and modulate cytokine production. Case reports and small series have described partial hair regrowth in AA patients treated with statins, either alone or in combination with ezetimibe. While the evidence remains limited, the rationale for statin therapy is supported by their effects on immune regulation and vascular endothelial function. Larger trials are needed to clarify their role, but statins may offer a safe, systemic adjunct in patients with concomitant cardiovascular comorbidities [16].

In summary, alternative modalities such as cryotherapy, PRP, microneedling, phototherapy, fractional lasers, and statins expand the therapeutic options for AA. While none serve as definitive standalone therapies, they are valuable adjuncts that may enhance regrowth, improve outcomes, and address limitations of conventional immunosuppressants. Their role in combination regimens and as supportive interventions highlights the growing trend toward multimodal, personalized management of AA [17].

Biologics

The use of biologic agents in alopecia areata (AA) has expanded in recent years, driven by advances in understanding its immune pathogenesis. Biologics, which are engineered molecules that selectively target cytokines, receptors, or immune checkpoints, offer more specific modulation of the immune system compared to conventional immunosuppressants. Their development is rooted in the discovery that CD8+ T cells, interferon-γ, interleukin (IL) pathways, and JAK-STAT signaling play central roles in AA. Biologics used or investigated for AA include anti-TNF agents, IL inhibitors, and agents repurposed from atopic dermatitis and psoriasis treatment [18].

Anti-TNF Agents

Tumor necrosis factor-alpha (TNF-α) plays a role in autoimmune inflammation, prompting the evaluation of TNF inhibitors such as etanercept, adalimumab, and infliximab in AA. However, results have been disappointing, with minimal clinical benefit and occasional reports of paradoxical induction of AA during treatment. These findings suggest that TNF-α may not be a central driver of AA pathogenesis, and that TNF blockade alone is insufficient for meaningful disease control. Consequently, TNF inhibitors are not recommended for AA outside of investigational use [19].

IL-4 and IL-13 Blockade

AA has immunologic overlap with atopic dermatitis (AD), particularly in patients with comorbid atopy. Dupilumab, a monoclonal antibody targeting the IL-4 receptor α subunit to inhibit IL-4 and IL-13 signaling, has been tested in AA with mixed results. Case reports describe both improvement and exacerbation of AA in patients treated for AD, suggesting that IL-4/IL-13 pathways may play a modulatory rather than central

role in AA. Nonetheless, dupilumab could benefit AA patients with overlapping atopic features, though controlled trials are required for clarification [20].

IL-17 and IL-23 Inhibitors

Biologics targeting the IL-17/IL-23 axis, such as secukinumab, ixekizumab, and ustekinumab, have been investigated in AA, particularly due to their efficacy in psoriasis and other autoimmune conditions. Evidence to date is limited to small case reports and open-label studies, with variable outcomes ranging from partial regrowth to no response. The lack of consistent efficacy suggests that while Th17 cells may contribute to disease activity, they are not the predominant mediators in AA [21].

IL-15 and Emerging Targets

IL-15 plays a pivotal role in AA pathogenesis by sustaining CD8+ T cell activation and survival. Biologic strategies targeting IL-15 or its receptor are currently under preclinical and early clinical investigation. Anti-IL-15 monoclonal antibodies and IL-15R antagonists represent promising new approaches with the potential to directly interrupt the autoimmune feedback loop driving follicular attack. Similarly, checkpoint modulators such as PD-1/PD-L1 agonists are under study for restoring immune tolerance at the follicular level. While still experimental, these biologics may represent the next wave of precision therapies for AA [22].

Current Position of Biologics in AA

Despite the growing interest, biologics have not yet established themselves as frontline therapies for AA, largely due to inconsistent efficacy, high costs, and lack of large-scale randomized trials. However, they remain valuable investigational tools and hold potential for patients with refractory disease, especially those with overlapping immune-mediated comorbidities. As more pathogenic targets are elucidated, biologics tailored to specific cytokine pathways could become important components of combination regimens, complementing JAK inhibitors and regenerative approaches [23].

Small-Molecule Drugs

Among small-molecule agents, Janus kinase (JAK) inhibitors represent the most significant breakthrough in the treatment of alopecia areata (AA). These drugs selectively target intracellular signaling pathways activated by interferon-γ, interleukin-15, and other cytokines central to AA pathogenesis. By disrupting the JAK-STAT cascade, they halt autoreactive T-cell activation and restore hair follicle immune privilege. Several oral and topical JAK inhibitors are now in advanced stages of clinical development, with some already approved for moderate-to-severe AA [24].

Baricitinib

Baricitinib, an oral JAK1/2 inhibitor, is the first JAK inhibitor approved by the FDA (2022) and EMA (2023) for the treatment of severe AA in adults. Large randomized controlled trials (BRAVE-AA1 and BRAVE-AA2) demonstrated that approximately one-third of patients achieved ≥80% scalp hair coverage (SALT ≤20) after 36 weeks of therapy. Baricitinib also improved eyebrow and eyelash regrowth in many cases. Side effects include acne, upper respiratory infections, headache, and elevated lipid levels. Baricitinib has established itself as the first-line targeted systemic therapy for extensive AA, providing a durable option where conventional immunosuppressants often fail [25].

Ritlecitinib

Ritlecitinib, a selective JAK3 and TEC kinase inhibitor, received FDA approval in 2023 for severe AA in patients ≥12 years. The ALLEGRO trials showed robust efficacy, with significant proportions of patients achieving SALT ≤20 after 24 weeks. Its selectivity for JAK3/TEC kinases may translate into a more favorable safety profile compared to pan-JAK inhibitors. Common side effects include headache, acne, and gastrointestinal symptoms. Ritlecitinib is particularly promising for adolescents, filling an important therapeutic gap in younger populations [26].

Tofacitinib

Tofacitinib, a JAK1/3 inhibitor initially approved for rheumatoid arthritis, was one of the first JAK inhibitors tested in AA. Multiple case series and open-label studies demonstrated marked hair regrowth in both patchy and extensive disease, including alopecia universalis. However, relapse often occurs after discontinuation. Safety concerns, particularly regarding infection risk, thromboembolic events, and malignancy with long-term use, have limited its widespread adoption in AA. Nonetheless, tofacitinib remains a widely used off-label therapy, especially where newer agents are unavailable [27].

Ruxolitinib

Ruxolitinib, a JAK1/2 inhibitor originally developed for myeloproliferative disorders, has shown efficacy in AA through case reports and pilot studies. Oral ruxolitinib has induced substantial regrowth in some patients with alopecia universalis, though responses vary. Topical ruxolitinib has also been investigated, with limited but encouraging results for localized AA. Its safety profile is similar to other JAK1/2 inhibitors, including risk of cytopenias and infections. Although not yet approved for AA, ruxolitinib continues to be an important investigational agent [28].

Deuruxolitinib (CTP-543)

Deuruxolitinib is a next-generation oral JAK1/2 inhibitor specifically developed for AA. Phase 3 trials (THRIVE-AA1 and THRIVE-AA2) demonstrated that over 30% of patients achieved significant hair regrowth at 24 weeks with higher doses, positioning it as a strong competitor to baricitinib. Deuruxolitinib has received FDA priority review, with approval anticipated soon. Its targeted development for AA underscores the growing recognition of JAK inhibitors as disease-specific therapies rather than off-label options [29].

Upadacitinib

Upadacitinib, a selective JAK1 inhibitor approved for atopic dermatitis and rheumatoid arthritis, has shown anecdotal success in AA. Case series describe partial or complete regrowth, particularly in patients with comorbid atopic disease. Larger trials are needed, but upadacitinib's favorable dermatologic safety profile suggests potential utility in AA, especially among patients with overlapping eczema [30].

Filgotinib

Filgotinib, another JAK1-selective inhibitor, is approved for rheumatoid arthritis in some regions and is under evaluation for AA. Preclinical data support its efficacy in downregulating interferon-γ–mediated inflammation. Early pilot studies are ongoing, and filgotinib could represent a safer option compared to less selective JAK inhibitors if efficacy is confirmed [31].

Peficitinib

Peficitinib, a JAK inhibitor used in Asian countries for rheumatoid arthritis, has limited but growing data in AA. Small studies and case reports suggest modest efficacy, though not as robust as baricitinib or ritlecitinib. Its role in AA remains exploratory at this stage, pending larger controlled trials [32].

Adverse Effects and Contraindications of JAK Inhibitors

Despite their efficacy, JAK inhibitors are associated with important safety concerns. Common adverse effects include acne, nasopharyngitis, headache, and laboratory abnormalities such as elevated lipids and liver enzymes. Serious risks include infections (herpes zoster, tuberculosis reactivation), thromboembolism, and rare malignancies. Contraindications include active infections, history of thromboembolic events, and uncontrolled malignancy. Long-term safety data in AA populations are still being accumulated, necessitating cautious patient selection, baseline screening, and ongoing monitoring. Combination regimens with topical agents or biologics may eventually allow lower dosing and reduced toxicity while maintaining efficacy [33].

Other Emerging Therapies

Exosomes

Exosomes are nanosized extracellular vesicles secreted by cells, particularly mesenchymal stem cells (MSCs), and have recently attracted significant attention as a potential therapy for alopecia areata (AA). They carry proteins, lipids, and nucleic acids—including microRNAs—that can modulate immune responses, stimulate angiogenesis, and promote tissue repair. In the context of AA, exosomes derived from MSCs appear to restore hair follicle immune privilege by reducing pro-inflammatory cytokine production and enhancing regulatory T-cell activity.

Preclinical studies have shown that exosome injections can stimulate the proliferation of dermal papilla cells, prolong the anagen phase of the hair cycle, and reduce perifollicular inflammation. Clinical pilot studies using MSC-derived exosomes injected into the scalp of AA patients demonstrated improvement in hair density and thickness within 12 to 24 weeks of treatment. Compared with PRP, exosomes may provide more potent and consistent regenerative effects, given their ability to deliver bioactive molecules directly into the follicular microenvironment. Safety profiles so far appear favorable, with minimal local irritation and no systemic adverse effects reported. However, standardization of exosome isolation, dosing, and delivery remains a key challenge before widespread clinical use [34].

Nanotechnology

Nanotechnology-based drug delivery systems are being explored to enhance the efficacy and safety of AA therapies. Conventional treatments such as corticosteroids, immunomodulators, and JAK inhibitors often face limitations related to poor scalp penetration, systemic side effects, and inconsistent local concentrations. Nanoparticles—including liposomes, solid lipid nanoparticles, and polymeric nanocarriers—can encapsulate therapeutic agents, improving their stability, targeted delivery, and sustained release at the hair follicle level.

For example, liposomal formulations of corticosteroids or tacrolimus have demonstrated enhanced follicular targeting and reduced systemic exposure compared to traditional preparations. Similarly,

nanoparticle-based delivery of JAK inhibitors holds promise for maximizing local efficacy while minimizing systemic toxicity. In addition, nanocarriers can be engineered to respond to environmental triggers such as pH or temperature, allowing controlled drug release directly at inflamed follicles.

Preclinical and early clinical studies suggest that nanotechnology may overcome some of the major barriers in AA therapy, including relapse after drug withdrawal and cumulative systemic toxicity. Beyond drug delivery, nanotechnology also offers opportunities in regenerative medicine, such as combining nanoparticles with stem cell–derived exosomes or growth factors to create synergistic hair regrowth therapies. While these applications are still experimental, they represent an exciting frontier in precision and targeted treatment of AA [35].

Treatment of Alopecia Areata in Special Areas

AA in the Beard Area

Beard alopecia areata, also known as alopecia areata barbae, is a relatively common presentation in men and often occurs independently or in association with scalp involvement. It manifests as sharply demarcated patches of hair loss on the beard, which may expand or coalesce. Given the cosmetic and psychosocial impact in young men, targeted therapies are often sought. Intralesional corticosteroids, typically triamcinolone acetonide, remain the first-line treatment and are highly effective in inducing regrowth in localized lesions. Topical minoxidil, topical corticosteroids, and immunotherapy (e.g., diphenylcyclopropenone) may serve as adjunctive options. PRP and microneedling have also been tested with promising results, improving beard density and regrowth. In refractory cases, systemic therapies such as JAK inhibitors may be considered, though data specific to beard AA are limited. Beard hair often regrows faster than scalp hair, but relapse remains common, necessitating maintenance or combination strategies [36].

AA in the Eyelashes

Eyelash alopecia areata is less frequent but presents unique therapeutic challenges due to the functional and cosmetic importance of eyelashes. Loss of eyelashes can predispose to ocular irritation, dryness, and photophobia, in addition to the obvious aesthetic burden. Topical prostaglandin analogs, such as bimatoprost and latanoprost, have shown encouraging results in eyelash AA, promoting hair regrowth by prolonging the anagen phase. Intralesional corticosteroid injections are effective but carry a risk of ocular complications, including cataracts and glaucoma, and must be performed cautiously. Topical corticosteroids and tacrolimus ointment have been attempted, though with inconsistent outcomes. JAK inhibitors, particularly baricitinib and ritlecitinib, have demonstrated regrowth of eyelashes in clinical trials, offering a systemic solution for severe disease. PRP and exosomes delivered via microinjections around the eyelid margin are being explored, but safety remains a major concern. Overall, treatment of eyelash AA requires balancing efficacy with ocular safety, and prostaglandin analogs currently offer the most practical option [37].

AA in the Eyebrows

Eyebrow involvement is common in extensive forms of AA and is often perceived as more cosmetically distressing than scalp disease. Eyebrows frame the face and contribute significantly to identity and expression, making their loss particularly impactful. Intralesional corticosteroids are the mainstay for

eyebrow AA, with triamcinolone carefully injected in small doses to minimize local atrophy. Topical therapies such as corticosteroids, calcineurin inhibitors, and bimatoprost have shown modest efficacy. Cosmetic tattooing or microblading can provide aesthetic improvement but do not address the underlying autoimmune process.

Newer therapies such as PRP, microneedling, and low-level laser therapy have been evaluated for eyebrow AA with variable results, but their minimally invasive nature makes them attractive to patients. In systemic therapy trials, JAK inhibitors have demonstrated eyebrow regrowth in parallel with scalp improvement, suggesting that targeted immunomodulation can address this challenging site. However, treatment responses are inconsistent, and relapses are frequent. For patients with refractory eyebrow AA, regenerative approaches such as exosome therapy or stem-cell–derived treatments may hold promise in the future [38].

Conclusion

The therapeutic landscape of alopecia areata (AA) has undergone a remarkable transformation, shifting from empirical use of corticosteroids and broad immunosuppressants to precision-targeted therapies and regenerative strategies. Conventional treatments such as systemic corticosteroids, methotrexate, cyclosporine, and azathioprine continue to play an important role, particularly in resource-limited settings or as bridging therapies. However, their limitations in terms of long-term efficacy, relapse rates, and safety profiles have fueled the need for novel approaches.

Topical therapies, including tretinoin and capsaicin, offer adjunctive benefits in localized disease, while modalities such as cryotherapy, platelet-rich plasma, microneedling, phototherapies, and fractional lasers provide additional tools to stimulate regrowth and enhance outcomes when used in combination regimens. These interventions highlight the growing emphasis on multimodal and personalized treatment strategies.

The greatest paradigm shift in AA therapy has come with the advent of small-molecule inhibitors, particularly Janus kinase (JAK) inhibitors. Agents such as baricitinib and ritlecitinib have demonstrated robust efficacy in moderate-to-severe AA, leading to regulatory approval and establishing a new standard of care. Emerging JAK inhibitors, including deuruxolitinib, upadacitinib, and filgotinib, along with evolving biologics targeting IL-15 and other cytokine pathways, represent the next generation of targeted immunomodulators. While highly promising, these therapies require careful long-term monitoring for safety and remain costly, limiting accessibility in many regions.

Innovative therapies such as exosomes and nanotechnology-based delivery systems are at the frontier of AA management, with the potential to restore immune tolerance and enhance follicular regeneration through precision approaches. These modalities, combined with established systemic and topical therapies, could reshape AA treatment into a regenerative and immune-restorative paradigm.

Special-site involvement—such as beard, eyelashes, and eyebrows—presents unique therapeutic challenges. Targeted local treatments including intralesional corticosteroids, prostaglandin analogs, and emerging regenerative methods underscore the importance of tailoring interventions to patient needs, cosmetic concerns, and safety considerations.

In conclusion, the management of AA is rapidly evolving toward a precision medicine framework. By integrating conventional therapies with novel targeted agents and regenerative approaches, clinicians can offer individualized treatment plans that optimize efficacy, minimize toxicity, and address the psychosocial

burden of this complex autoimmune disorder. The future of AA therapy lies in harnessing immunologic insights and technological advances to deliver durable, safe, and patient-centered outcomes.

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