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Linda Yousry El-Bolkiny
Department of Dermatology & Venereology, Faculty of Medicine, Tanta University, Egypt

Marwa Ahmed El-Samongy
Department of Dermatology & Venereology, Faculty of Medicine, Tanta University, Egypt

Nashwa Naeem El-Far
Department of Dermatology & Venereology, Faculty of Medicine, Tanta University, Egypt

Nagwa Mohammed Elwan
Department of Dermatology & Venereology, Faculty of Medicine, Tanta University, Egypt

Corresponding Author:
Linda Yousry El-Bolkiny
Department of Dermatology & Venereology, Faculty of Medicine, Tanta University, Egypt

New treatment modalities of alopecia areata

Linda Yousry El-Bolkiny, Marwa Ahmed El-Samongy, Nashwa Naeem El-Far and Nagwa Mohammed Elwan

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Abstract
Alopecia areata (AA) is an autoimmune disorder that affects hair follicles during the anagen phase, resulting in non-scarring hair loss that is difficult to manage. All therapies for AA are regarded as off-label. Although these treatments may promote hair growth, they aren't deemed curative since they can't modify the disease's typical trajectory. Age, overall health, and the extent of hair loss all influence the optimal treatment approach. Therapeutic drugs utilized for the management of alopecia areata including topical and systemic corticosteroids, minoxidil, phototherapy, anthralin, and topical immunotherapy.

Keywords: Treatment, topical, systemic, corticosteroid, laser, alopecia areata

Introduction
Alopecia areata (AA) is a multifaceted autoimmune disorder which impacts hair follicles and nails. Clinical classification is based on the quantity and location of lesions and the degree of involvement, categorising them into the following patterns: multifocal, unifocal, totalis, ophiasis, universalis, sisaipho (or ophiasis inversus), diffuse and reticular [1].
AA affects males and females of all ages and all ethnic or cultural backgrounds with equal probability. The prevalence is greater in children than in adults. In the majority of instances, the onset of AA transpires prior to the age of 40, with a peak prevalence occurring in the twenties and thirties. The exact processes by which this sickness develops remain unidentified. A combination of environmental and genetic factors has been suggested to initiate an autoimmune response in the hair follicles, resulting in AA [2].
Therapeutic techniques have been utilised to address AA, with varying degrees of effectiveness and safety profiles. Various therapeutic options for AA exist, which include topical therapies like corticosteroids and minoxidil, systemic therapies like corticosteroids, methotrexate, photochemotherapy, and surgical interventions [3]. Nonetheless, these therapeutic approaches have inconsistent clinical results, and no existing medications can induce and maintain remission [4].

Alopecia areata
Alopecia areata (AA) is a chronic, immune-mediated dermatological condition marked by abrupt, non-scarring hair loss on the beard, scalp, and sometimes affecting eyelashes, eyebrows, and body hair. AA is an autoimmune illness whereby the immune system targets hair follicles, resulting in reduced hair size, inhibited growth, or complete cessation of hair growth. This loss of hair is very erratic, with hair growth potentially normalising at any moment, only to abruptly cease once again. It may also impact nails and, seldom, the retinal pigment epithelium. More than one-third of dermatologists in Egypt indicated that the prevalence of AA surpasses 10% [5].
The concept that AA is an autoimmune illness affecting the hair bulb has gained prominence. The predominant theory regarding the etiopathogenesis of AA posits that intricate interactions occur between epigenetic or genetic variables and unidentified triggering events, such as viral infections, trauma, and emotional or physical stress. These interactions result in a localised increase of interferon (IFN)-γ, which disrupts the hair follicle's immune privilege (HF-IP) and provokes immune system responses that target exposed hair follicle autoantigens through the activation of autoreactive cytotoxic CD8+NKG2D+ T cells [6].
This immunoreaction has shown a type 1 inflammatory response; however, recent

investigations suggest a potential involvement of type 2 and the Th17 axis in the immuno-pathogenesis of AA. These results may elucidate the relationship between diseases like depression and AD as comorbidity with AA. The precise pathogenesis of the condition remains unclear. Evidence indicates that AA results from an autoimmune response targeting hair follicles, influenced by hereditary and environmental factors [7].

There are several forms of hair loss manifestation in AA. The most prevalent form is patch, characterised by circular patches identifiable on the beard or scalp regions that may merge as the condition advances. Ophiasis denotes a band of alopecia in the occipital and parietal regions, whereas sisaipho indicates a contrasting pattern [8].

Treatment of alopecia areata

Topical treatment

Corticosteroids: Topical corticosteroids have significantly reduced efficacy in AA. The ideal way for administering topical corticosteroids is by a very powerful formulation under occlusion [9].

Intralesional corticosteroids (ILCs) are the primary treatment for adult individuals with involvement less than 50% scalp. The preparations utilised consist of triamcinolone hexacetonide, triamcinolone acetonide, and hydrocortisone acetate. Triamcinolone acetonide is the favoured intralesional agent due to its lower atrophogenic potential compared to triamcinolone hexacetonide [10].

Concentrations ranging from 2.5 to 10 mg/ml are permissible, with 5 mg/ml being the optimal dose for the scalp. For the face and eyebrows, a concentration of 2.5 mg/ml may be administered at a volume of 0.5 ml per eyebrow [11].

A 10 mg/ml concentration, with a maximum total volume of 2 ml, or 5 mg/ml, with a maximum total volume of 4 ml, was additionally documented for application on the scalp at a single visit. Triamcinolone acetonide is administered intradermally using a 0.5-inch, 30-gauge needle, via several 0.1-ml injections spaced 1 cm apart [12].

Minoxidil: Topical minoxidil is a hair growth stimulator. Minoxidil works by abbreviating the telogen phase, prompting dormant hair follicles to prematurely transition into the anagen phase. Furthermore, minoxidil prolongs the anagen phase. The clinical benefits of minoxidil include increasing diameter and length of hair [13].

The first benefits of minoxidil manifest following around eight weeks of therapy, whereas optimal results are achieved following four months. Minoxidil seems to influence the potassium channels in hair follicles and vascular smooth muscle [14].

Anthralin: It has the capability to inhibit T-lymphocyte activation and normalise differentiation of keratinocytes, maybe via a direct impact on mitochondria [15].

Topical Immunotherapy

Topical immunotherapies provide optimal effectiveness and safety for the long-term management of individuals with persistent alopecia areata. It stimulates hair regeneration by provoking an inflammatory reaction to contact sensitising chemicals at the application site [16].

The primary method is on antigenic competition, employing immunomodulators to provoke allergic contact dermatitis at the application site via delayed-type hypersensitivity [17].

Dinitrochlorobenzene (DNCB): it was formerly widely employed for the therapeutic management of severe or resistant AA, with hair regeneration rates between 25% and 89%, and full regrowth rates ranging from 6.7% to 25%. [17].

Squaric Acid Dibutylester (SADBE): it is unstable in acetone solution and may deteriorate within several hours at ambient temperature. A light-resistant, temperature-controlled container is utilised to maintain its optimal efficacy [17].

Phenol: prospective research used 88% phenol topically on AA areas shown a 78% enhancement to hair structure and pigmentation [18].

Systemic Treatment

Corticosteroids: Corticosteroids are often reserved for more severe cases of A.A or when rapid hair loss occurs, as long-term use of these drugs can have significant side effects [19].

The initial dosage of oral prednisone for adults might start at a higher dose, for instance, 40-60 mg daily, and is often tapered down over weeks to months depending on the response. In contrast, for children, the dosage is typically determined based on weight, usually around 1-2 mg/kg/day, with the stipulation that it should not exceed the established adult dose [20].

AA occurs when the immune system incorrectly targets hair follicles, resulting in loss of hair. Corticosteroids interfere with the immune response via decreasing the activity and volume of the lymphatic system. They inhibit the maturation and proliferation of immune cells, thereby decreasing the immune system's ability to respond to stimuli. This suppression helps in cases like AA, where the immune system is overly active and attacking healthy cells, such as hair follicles [19].

Cyclosporine: Cyclosporine obstructs the activation of helper T cells which might be harmful in AA [21].

Azathioprine: It is a purine analog that converts to its active metabolites. It then inhibits purine synthesis [22].

Methotrexate: It is considered beneficial for addressing the autoimmune cell-mediated assault and the inflammatory responses involved in the pathophysiology of AA. Methotrexates regulate the inflammatory response around the follicle [23].

Methotrexate and corticosteroids may be utilised together in the systemic treatment of AA. Approximately 77.3% of AA individuals on a regimen of systemic corticosteroids and methotrexate treatment had above 50% hair regrowth [24]. A 43-year-old female with long-standing AT achieved successful therapy with an initial regimen of 30 mg subcutaneous MTX combined with 20 mg oral prednisone until complete remission was attained [25].

Single-dose auto-injectors may provide MTX in certain dosages: 7.5 mg, 10 mg, 12.5 mg, 15 mg, 17.5 mg, 20 mg, 22.5 mg, 25 mg, 27.5 mg, and 30 mg. Following the commencement of MTX treatment, it is advisable to do follow-up tests, including a complete blood count, renal function tests, and liver function tests, every week for four

weeks, subsequently at least bi-monthly [26]. The predominant side effects consist of hepatotoxicity, leukopenia with an associated susceptibility to infection, nausea, stomach discomfort, lethargy, fever, disorientation, acute pneumonitis, seldom pulmonary fibrosis, and renal failure [27].

Intralesional MTX is an excellent therapy for AA, resulting in considerable hair regrowth via a mechanism that involves the reduction of TNF-α [28].

Intralesional MTX may provide as a viable treatment approach for localised AA [29]. Intralesional MTX for AA in adults is safe, mitigating any systemic adverse effects associated with MTX treatment, and may expedite response without a discernible rise in adverse event profile [30].

Vitamin D: it helps to modulate the immune response, including the activities of T cells, that are involved in autoimmune reactions. Additionally, vitamin D receptors are present in hair follicles and are integral to hair cycle regulation and growth. One study has noted a greater vitamin D deficiency prevalence in individuals with AA, and supplementing with this vitamin, under professional guidance, might enhance the effectiveness of AA treatments. However, more comprehensive research is needed to fully establish this relationship and integrate it into clinical practice [31].

- **Biological therapies:** It has been reported that the first patient with AA was effectively managed with the Janus kinase inhibitor (JAKi) tofacitinib. Afterwards, open-label clinical studies, case series, and reports on tofacitinib and ruxolitinib corroborated the usage of JAK inhibitors for AA. Industry-sponsored clinical studies culminated in June 2022 with the historic approval by the Food and Drug Administration of the first medication for AA, baricitinib, and a year later by the second, ritlecitinib [32].
- **Candida albicans antigen:** The connection between Candida albicans antigen and AA stems from the intriguing interplay of immune responses. In AA, intralesional Candida antigen injections elicit delayed-type hypersensitivity reactions, which includes CD4+ and CD8+ T cells, which may suppress autoimmune responses against hair follicles via antigenic competition. This treatment has been linked to the rectification of the imbalance between Th1 and Th2 cell lines, regarded as a primary pathogenic mechanism of AA [3].
- **Photochemotherapy:** All types of psoralen and ultraviolet-A (UVA) (PUVA) (oral PUVA, topical PUVA, and local or whole-body UVA irradiation) have been utilised with rates of success of up to 60%-65% [33].
- **Phototherapy:** Narrowband ultraviolet-B is one of the most successful treatments for certain immune-mediated skin disorders; however, the same efficiency hasn't been shown in AA [33].
- **Excimer laser and excimer light**
  The effectiveness of excimer laser and excimer light in AA has been established. The therapy is well tolerated, with erythema being the only recorded side effect [34]. The administered dose per session varied between 300 to 2300 mJ/cm² [35].
- **Low-Level Light Therapy:** Low-Level Light Therapy (LLLT), a non-invasive method that utilises low-power lasers or LEDs to encourage healing, reduce inflammation, and alleviate pain, can be particularly relevant for managing AA. LLLT can potentially stimulate cellular activity and promote hair regrowth, offering a gentle and effective therapeutic option for individuals with AA [36].
- **Microneedling:** Microneedling has been integrated with the administration of topical triamcinolone acetonide in AA (110). Recently, microneedling become often used in conjunction with other medications to increase efficacy in treating AA such as combined with betamethasone, topical vitamin D3, methotrexate, and pentoxifylline [37].
- **Platelet-rich plasma:** Platelet-rich plasma (PRP) is a novel therapy which employs an autologous plasma preparation enriched with concentrated platelets to promote hair follicle repair and regeneration. PRP is believed to commence wound healing by releasing several growth factors and cytokines. It has been utilised to manage AA [38].
- **Surgical procedures:** Surgical interventions are not typically frontline treatments for AA due to its autoimmune nature and the potential for hair regrowth or further loss without warning [39].

Hair transplantation: Hair transplantation in individuals with AA can be complex and is typically approached with caution. AA is characterized by unpredictable hair loss, so there's a risk that transplanted hair may also be attacked and lost due to the ongoing autoimmune response. The transplantation may provide temporary relief, but it does not address the underlying autoimmune issue [40]

Threads: Some practitioners use threads (like PDO threads) implanted in the scalp to stimulate blood flow and potentially promote hair growth. The idea is that increased blood flow can stimulate hair follicles, although it's not a widely recognized or established treatment for AA [41].

Camouflage: A non-invasive and successful method for concealing loss of hair has been offered, assisting persons with AA in restoring confidence and enhancing comfort with their look. They are also compatible with medicinal therapy designed to address AA [42].

Conflict of Interest
Not available

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References

1. Zhou C, Li X. Alopecia areata. The Rose and Mackay Textbook of Autoimmune Diseases: Elsevier; 2024. p. 1287-1299.
2. Abd El Fattah NMM, Mokadem A, Abd El Fattah SM, Ghonemy SM. Brief Treatment Modalities of Alopecia Areata. Egypt J Hosp Med. 2022;89:6127-61231.
3. Ali S, Ibrahim AM, El Sayed N. Candida antigen immunotherapy versus steroid in the treatment of alopecia areata. Dermatol Ther. 2021;34:802.
4. Strazzulla LC, Wang EHC, Avila L, Lo Sicco K, Brinster N, Christiano AM, *et al*. Alopecia areata: An appraisal of new treatment approaches and overview of

current therapies. J Am Acad Dermatol 2018;78:15-24.
5. Darwin E, Arora H, Hirt PA, Wikramanayake TC, Jimenez JJ. A review of monochromatic light devices for the treatment of alopecia areata. Lasers Med Sci 2018;33:435-444.
6. Ting AT, Bertrand MJ. More to life than NF-κB in TNFR1 signaling. Trends Immunol. 2016;37:535-545.
7. Russu EA, Mihai MM, Russu LE, Russu MG, Bencze M-A, Albu Ş-D, *et al*. Alopecia areata: Impressive results using low-level laser therapy. Na J Adv Res Rev. 2022;14:11-15.
8. Sibbald C. Alopecia Areata: An Updated Review for 2023. J Cutan Med Surg. 2023;27:241-259.
9. Das A, Panda S. Use of topical corticosteroids in dermatology: an evidence-based approach. Indian J Dermatol. 2017;62:237-250.
10. El Sayed MH, Ibrahim NE-d, Afify AA. Superficial Cryotherapy versus Intralesional Corticosteroids Injection in Alopecia Areata: A Trichoscopic Comparative Study. Int J Trichology. 2022;14:8-13.
11. Lintzeri DA, Constantinou A, Hillmann K, Ghoreschi K, Vogt A, Blume-Peytavi U. Alopecia areata-Current understanding and management. J Dtsch Dermatol Ges. 2022;20:59-90.
12. Betz RC, Petukhova L, Ripke S, Huang H, Menelaou A, Redler S, *et al*. Genome-wide meta-analysis in alopecia areata resolves HLA associations and reveals two new susceptibility loci. Nat Commun. 2015;6:59.
13. Freire P, Riera R, Martimbianco A, Petri V, Atallah A. Minoxidil for patchy alopecia areata: systematic review and meta-analysis. Eur J Dermatol 2019;33:1792-1799.
14. Jimenez-Cauhe J, Saceda-Corralo D, Rodrigues-Barata R, Hermosa-Gelbard A, Moreno-Arrones OM, Fernandez-Nieto D, *et al*. Effectiveness and safety of low-dose oral minoxidil in male androgenetic alopecia. J Am Acad Dermatol 2019;81:648-649.
15. Behrangi E, Roohaninasab M, Sadeghzadeh-Bazargan A, Najar Nobari N, Ghassemi M, Seirafianpour F, *et al*. A systematic review on the treatment of pediatric severe alopecia areata by topical immunotherapy or Anthralin (contact sensitization) or low-level light/laser therapy (LLLT): focus on efficacy, safety, treatment duration, recurrence, and follow-up based on clinical studies. J Cosmet Dermatol 2022;21:2727-2741.
16. Rattananukrom T, Suchonwanit P. Are drug treatment strategies really effective against alopecia areata? Expert Opin Pharmacother 2021;22:257-260.
17. Mahasaksiri T, Kositkuljorn C, Anuntrangsee T, Suchonwanit P. Application of topical immunotherapy in the treatment of alopecia areata: a review and update. Drug Des Devel Ther. 2021;13:1285-1298.
18. Chikhalkar S, Jerajani H, Madke B. Evaluation of utility of phenol in alopecia areata. Int J Trichology. 2013;5:179-1784.
19. Suchonwanit P, Kositkuljorn C, Mahasaksiri T, Leerunyakul K. A comparison of the efficacy and tolerability of three corticosteroid treatment regimens in patients with alopecia areata. J Dermatolog Treat. 2022;33:756-761.
20. Chanprapaph K, Pomsoong C, Kositkuljorn C, Suchonwanit P. Intramuscular corticosteroid therapy in the treatment of alopecia areata: a time-to-event analysis. Drug Des Devel Ther. 2022;87:107-116.
21. Nowaczyk J, Makowska K, Rakowska A, Sikora M, Rudnicka L. Cyclosporine with and without systemic corticosteroids in treatment of alopecia areata: a systematic review. Dermatol Ther. 2020;10:387-399.
22. Chavez-Alvarez S, Herz-Ruelas M, Villarreal-Martinez A, Ocampo-Candiani J, Garza-Garza R, Gomez-Flores M. Azathioprine: its uses in dermatology. An Bras Dermatol. 2020;95:731-736.
23. Ruchiatan K, Avriyanti E, Hindritiani R, Puspitosari D, Suwarsa O, Gunawan H. Successful Therapy of Alopecia Universalis Using a Combination of Systemic Methotrexate and Corticosteroids and Topical 5% Minoxidil. Clin Cosmet Investig Dermatol. 2022;14:127-132.
24. Asilian A, Fatemi F, Ganjei Z, Siadat AH, Mohaghegh F, Siavash M. Oral pulse betamethasone, methotrexate, and combination therapy to treat severe alopecia areata: a randomized, double-blind, placebo-controlled, clinical trial. Iran J Pharm Res 2021;20:267.
25. Trüeb RM, Dias MFRG. Alopecia areata: a comprehensive review of pathogenesis and management. Clin Rev Allergy Immunol. 2018;54:68-87.
26. Patel V, Wang Y, MacDonald JK, McDonald JW, Chande N. Methotrexate for maintenance of remission in Crohn's disease. Cochrane Database Syst Rev 2014;11:20.
27. Levêque D, Becker G, Toussaint E, Fornecker L-M, Paillard C. Clinical pharmacokinetics of methotrexate in oncology. Int J Pharmacol. 2017;2:137-147.
28. Farag RM, Salem SA, Afify AA, Ahmed WAE. Intralesional Methotrexate for Treatment of Alopecia Areata: Clinical Evaluation and Effect on Lesional TNF Alpha. J Int Med 2023;116:89.
29. Hamdino M, El-Barbary RA, Darwish HM. Intralesional methotrexate versus triamcinolone acetonide for localized alopecia areata treatment: a randomized clinical trial. J Cosmet Dermatol. 2022;21:707-7015.
30. Rodríguez-Villa Lario A, Aguado-García Á, Andrés-Lencina JJ, Corredera C, García-Legaz Martínez M, Alonso de Celada RM, *et al*. Successful Response to a Combination of Intralesional Methotrexate and Fractional CO(2) Laser in Refractory Alopecia Areata: Case Report. Skin Appendage Disord. 2022;8:486-491.
31. Rashad AF, Elgamal E, Fouda I. Intralesional vitamin D3 in treatment of alopecia areata: A randomized controlled clinical trial. J Cosmet Dermatol 2022;21:4617-4622.
32. King BA, Craiglow BG. Janus kinase inhibitors for alopecia areata. J Am Acad Dermatol 2023;89:29-32.
33. Malhotra K, Madke B. An Updated Review on Current Treatment of Alopecia Areata and Newer Therapeutic Options. Int J Trichology. 2023;15:3-12.
34. Li A, Meng X, Xing X, Tan H, Liu J, Li C. Efficacy and influence factors of 308-nm excimer lamp with minoxidil in the treatment of alopecia areata. Lasers Surg Med. 2020;52:761-767.
35. Al Hamzawi NK, Al Baaj MS. Overview of the Role of 308 Monochromatic Excimer Phototherapy for the Treatment of Alopecia Areata. Alopecia Management-An Update: IntechOpen; 2022. p. 87.
36. Glass GE. Photobiomodulation: the clinical applications of low-level light therapy. Aesthet Surg J. 2021;41:723-738.

37. Pei D, Chen L, Yao Y, Zeng L, Zhang G. Microneedling combined with compound betamethasone in treatment of severe alopecia areata: A case report. Front Immunol. 2022;13:939.
38. Al-Refu K. Clinical significance of trichoscopy in common causes of hair loss in children: analysis of 134 cases. Int J Trichology. 2018;10:154-161.
39. Ibrahim O, Bayart CB, Hogan S, Piliang M, Bergfeld WF. Treatment of alopecia areata with tofacitinib. JAMA dermatology. 2017;153:600-602.
40. Lee JA, Levy DA, Patel KG, Brennan E, Oyer SL. Hair transplantation in frontal fibrosing alopecia and lichen planopilaris: a systematic review. Laryngoscope. 2021;131:59-66.
41. Zhang Y-M, Liu C-H, Wang Y-C, Teng H-L, Meng X-L, Han X-J. Medicated thread moxibustion for alopecia areata: a case report. Medicine. 2019;98:93.
42. Courtney A, Su JC. Wigs and Alopecia Areata: Psychosocial Impact and Economic Considerations. Cosmetics. 2024;11:55.

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