Alopecia areata
Part 2: treatment

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Abstract
Objective To provide family physicians with a background understanding of the therapeutic regimens and treatment outcomes for alopecia areata (AA), as well as to help identify those patients for whom dermatologist referral might be required.

Sources of information PubMed was searched for relevant articles regarding the treatment of AA.

Main message Alopecia areata is a form of autoimmune hair loss affecting both children and adults. While there is no associated mortality with the disease, morbidity from the psychological effects of hair loss can be devastating. Upon identification of AA and the disease subtype, an appropriate therapeutic regimen can be instituted to help halt hair loss or possibly initiate hair regrowth. First-line treatment involves intralesional triamcinolone with topical steroids or minoxidil or both. Primary care physicians can safely prescribe and institute these treatments. More advanced or refractory cases might require oral immunosuppressants, topical diphenylcyclopropenone, or topical anthralin. Eyelash loss can be treated with prostaglandin analogues. Those with extensive loss might choose camouflage options or a hair prosthesis. It is important to monitor for psychiatric disorders owing to the profound psychological effects of hair loss.

Conclusion Family physicians will encounter many patients experiencing hair loss. Recognition of AA and an understanding of the underlying disease process will allow an appropriate therapeutic regimen to be instituted. More advanced or refractory cases need to be identified, allowing for an appropriate dermatologist referral when necessary.

Case A 25-year-old man was getting his regular haircut when his barber pointed out several areas of hair loss. A diagnosis of alopecia areata (AA) was made based on the classic morphologic appearance of the hair loss patches with “exclamation mark” hairs at the periphery. After discussing his options with his family physician, the patient elected to undergo treatment.

Sources of information The PubMed database was searched up to November 15, 2014, for relevant articles regarding the treatment of AA. Search terms included alopecia areata and treatment, alopecia totalis and treatment, alopecia universalis and treatment, and alopecia areata and reviews. We also searched for articles pertaining to specific treatments for AA, such as topical and intralesional steroids, minoxidil, bimatoprost, anthralin, diphenylcyclopropenone (DPCP), methotrexate, sulfasalazine, prednisone, cyclosporine, and platelet-rich plasma (PRP).

Main message Alopecia areata is an autoimmune form of hair loss with a lifetime prevalence of about 2%. Most cases can be recognized by well-defined patches of hair loss with exclamation mark hairs at the periphery. Part 1 of this 2-part series discussed the epidemiology, pathogenesis, histology, and clinical approach to the diagnosis of AA (page 751). Treatment of AA is discussed here.
Approach to treatment. Although there is no cure for AA, there are many possible treatments. Decisions about treatment are often based on the degree of hair loss and the patient's age. Further, if the area of AA is minimal and easily camouflaged by other existing hair, advising a “wait and see” approach might be appropriate, as spontaneous regrowth might occur in a large subset of patients. It should be noted that while a given patch of hair loss might improve, new areas of alopecia can still develop. Successfully treated areas might also relapse upon cessation of treatment. There is no evidence that treatment changes the individual patient's final outcome. However, before counseling patients, one must take into account individual psychological states, as hair loss can have a profound effect, and many patients will elect to undergo therapy.

It is important for primary care physicians to understand the roles of minoxidil, topical steroids, and steroid injections, as a large proportion of patients will benefit from these treatments. Patients who are unresponsive to these treatments or suffer from more extensive hair loss can be referred for evaluation by a dermatologist.

Intralesional steroids. Intralesional steroids are considered the primary pharmacologic intervention for those with either scalp or eyebrow AA and they can be safely administered by primary care physicians. The most commonly used agent is triamcinolone acetonide, at concentrations of 2.5 mg/mL to 10 mg/mL. Triamcinolone acetonide is commercially available at concentrations of 10 mg/mL and 40 mg/mL and must therefore be diluted in injection-grade saline before use.

Time to clinical improvement ranges from 2 to 6 weeks. In an early study, Abell and Munro successfully treated 71% of those with patch stage AA using intralesional steroids. Our typical protocol follows that of Chang et al, infiltrating the scalp with triamcinolone acetonide (5 mg/mL) through a 30-gauge needle every 4 to 6 weeks. At each session, we administer 0.1 mL of the formulation to each intradermal injection site spaced approximately 1 cm apart, similar to the amounts quoted by Abell and Munro, limiting the total scalp volume to 3 to 4 mL every 4 to 6 weeks. Eyebrows can be treated as above using a 2.5-mg/mL concentration to a maximum 0.5 mL per eyebrow. We start with the lower concentration to reduce the chance of atrophy. This can be increased to 5 mg/mL in those patients whose AA does not respond.

It is important to note that, especially with multiple injections over time, one must monitor for the common complications of scalp atrophy and hypopigmentation. Scalp atrophy appears clinically as a small indentation or depression localized to the previous treatment area and is more likely with higher concentrations of triamcinolone acetonide. Cataracts and glaucoma are rare but potential consequences of long-term periocular injections. Despite these risks, intralesional triamcinolone is a good first-line option for adults and adolescents who can withstand the minor discomfort of therapy.

In our clinic we find that ensuring the patient is positioned comfortably and breathing slowly and deeply helps to minimize discomfort. In some patients, especially adolescents, a hand-held vibration device placed adjacent to the area of hair loss is used as a distraction to prevent discomfort from the injection. Dilutions of the triamcinolone with local anesthetics or application of topical anesthetics are not done in our clinic, but might be performed by some physicians. Steroid injections are typically avoided in children younger than 10 years of age on account of the pain and fear created.

Topical steroids. Topical corticosteroids applied to the scalp are less effective than steroid injections but might offer benefit in approximately 30% to 50% of patients. Some clinicians opt to prescribe the topical steroids to be applied under occlusion (such as covering with plastic wrap) to improve their penetration. Although topical steroids are typically used in individuals with more limited forms of AA, their potential use spans all subtypes. However, it should be noted that the effectiveness of treatment is often markedly less in the more advanced variants. Typically stronger (class I) steroids are required for the treatment of AA. Tosti et al showed that 0.05% clobetasol propionate ointment under occlusion resulted in successful regrowth in 8 of 28
patients with alopecia totalis or universalis. However, despite the continuation of treatment, only 5 subjects had a full head of hair at the 1-year follow-up mark.9

It should be noted that, in most cases, initial signs of improvement can take anywhere from 6 weeks to 3 months (up to 6 months in some) and that relapse rates as high as 63% have been observed.8,9 In patients undergoing treatment with corticosteroids, clinicians should monitor for side effects such as folliculitis, telangiectasia, local atrophy, and the rare possibility of hypothalamic–pituitary–adrenal axis suppression.8,9,11,12

A variety of formations can be prescribed, including lotions, creams, ointments, foams, and sprays. We tend to use lotions, sprays, and foams if there is some pre-existing hair before treatment or if hair regrowth ensues.

**Minoxidil.** Minoxidil is approved by the Food and Drug Administration and Health Canada for the treatment of androgenetic alopecia (male pattern balding and female pattern hair loss), but might also provide a helpful adjunctive treatment in AA for both adults and children.13,14

In contrast to corticosteroids, which act to reduce inflammation, minoxidil acts mainly to promote hair growth. Evidence comes from a double-blind, placebo-controlled study conducted by Price assessing the effectiveness of using 3% minoxidil twice daily. While 63.6% of patients demonstrated at least a partial response, only 27.3% were designated as full responders.14 Further, the strength of the minoxidil formulation matters; the 5% solution should be used whenever possible.13,15 Results can be slow in some cases, taking longer than 3 to 6 months before new hair growth is noted.13,14,16 Treatment complications include local irritation, allergic contact dermatitis, or, occasionally, increased facial hair growth.13,16 In general, we rarely use minoxidil as a monotherapeutic agent and typically combine it with many other treatments such as topical or intralesional steroids, prednisone, anthralin, or DPCP.

**Advanced therapies**

**Systemic steroids:** Systemic glucocorticoids are a viable treatment option for severe AA. Hair regrowth has been demonstrated with both intravenous (IV) and oral forms. However, efficacy diminishes with the more severe AA subtypes.17,18 Nakajima et al found an IV regimen of 500 mg of methylprednisolone daily for 3 days to be effective in patients with AA of short duration and limited involvement.19 However, when comparing regrowth rates for short-duration patch stage with those for alopecia totalis, there was a large drop in success from 88% to 21.4%.19 Kar et al demonstrated that 200 mg of oral prednisolone once weekly for 3 consecutive months was an effective alternative to IV dosing, as 8 out of 20 AA patients improved.18 Other steroid dosing regimens are also possible.

Despite these studies, it is important to advise patients of the high relapse rate upon cessation of therapy.17,19 Olsen et al showed that using topical minoxidil concurrently helps to reduce the chance of hair loss after stopping prednisone.20 Side effects of oral steroids must be discussed with patients before use. These include avascular necrosis, weight gain, hypertension, diabetes, sleep alteration, mood changes, weakness, acneliform eruptions, and irregular menses, striae, and the long-term consequences of hypercortisolism. It is these possible complications that prevent systemic steroids from being a first-line option or long-term solution for AA.17,20

**Topical sensitizers:** The topical sensitizers, DPCP or squaric acid dibutylester, are often prescribed as primary treatments in those patients suffering from recalcitrant AA or those with more than 50% hair loss. The goal of treatment is to create an allergic contact dermatitis of the scalp in order to alter the immune response and thereby prompt hair regrowth. The efficacy of the topical sensitizers has been demonstrated in both young children and adults.21–26

Use of DPCP begins with the sensitization of a small coin-sized area of the scalp with a 2% DPCP solution in acetone. Starting 2 weeks later, the physician cautiously titrates and administers a weekly increment (0.0001%, 0.001%, 0.01%, 0.02%, 0.05%, 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.75%, 1%, and 2%) until a mild irritant or allergic dermatitis lasting for 36 to 48 hours is noted.21,24,27 Efficacy rates between DPCP and squaric acid dibutylester appear to be similar at approximately 60%.23 However, despite these results, about 60% of patients might experience a return of their hair loss after treatment.22,27 The possible complications of DPCP application are numerous and must be discussed with patients before administration. Aside from the expected mild contact or allergic dermatitis, stronger reactions include vesicles, blisters, urticaria, lymphadenopathy, hyperpigmentation, or hypopigmentation. Generalized eruptions might occur and necessitate cessation of therapy.25,27

Dermatologists or dermatologic nurses at specialized tertiary centres typically conduct treatment administration of DPCP owing to the logistics of storing DPCP and the need to ensure safe administration.

**Anthralin:** Anthralin is a synthetic tarlike compound that has been used in the treatment of AA for many years. Unlike DPCP, it creates scalp irritation (irritant contact dermatitis) rather than true allergic contact dermatitis and it can be administered by patients at home.21,28–30 The treatment can be used in both adults and children.29 While evidence is limited, small studies demonstrate adequate results in 25% to 75% of patients depending on the severity of involvement.29,30

When prescribing anthralin, we begin with daily administration of a topical formulation of 1% or 2% anthralin, applied for 10 to 15 minutes before being washed off with shampoo. Patients increase the total application time
weekly until a constant low-grade irritation is produced. Some individuals might need to increase their treatment time such that they apply the anthralin before going to bed and then wash it off upon waking in the morning. It is important to warn patients that the purple colour of anthralin might cause discoloration and staining of bed sheets, towels, and the bathtub.

Although therapy is expected to produce an irritant dermatitis, in some cases, it might become very severe with concomitant lymphadenopathy, making it necessary to restrict application time or stop therapy altogether. There is also some evidence that the simultaneous use of anthralin and minoxidil might improve overall therapeutic results in patients with refractory AA.

**Alternative treatments.** In addition to prednisone, other oral immunosuppressive agents might be helpful for some individuals with advanced AA or more localized forms that are resistant to treatment. The most commonly used are methotrexate, sulfasalazine, and cyclosporine. It should be noted that at present there is no good evidence to support the use of photodynamic therapy in the treatment of AA. Platelet-rich plasma injections, a newer therapy, is gaining evidence as a potential treatment of AA. A recent randomized, double-blind trial involving PRP, low-dose triamcinolone acetonide, and placebo injection demonstrated that PRP was superior. However, the efficacy of PRP relative to standard treatment concentrations of triamcinolone acetonide and in widespread AA still requires further study. Referral to a dermatologist is recommended for discussion about these agents, requisite monitoring, and their associated side effects.

**Other considerations**

**Eyebrow AA:** As reviewed above, the mainstay of treatment of eyebrow AA is topical steroids with steroid injections. We typically use lower concentrations (2.5 mg/mL) in this area in order to limit the chance of atrophy. While we occasionally use DPCP for refractory cases of eyebrow loss, anthralin is avoided.

**Eyelash AA:** Alopecia areata involving the eyelashes can be very troubling for patients. The prostaglandin analogues latanoprost and bimatoprost have been increasingly studied for this off-label indication. While there are several reports of latanoprost and bimatoprost as a useful option for eyelash involvement, other conflicting studies prevent their widespread use. Further investigation is required to clarify their role in the management of eyelash and eyebrow AA.

**Beard AA:** Alopecia areata of the beard (AA barbae) is challenging to treat. As with treatment of the scalp, topical treatment with steroids can elicit folliculitis. We employ injections of triamcinolone acetonide (5 mg/mL) for resistant areas. Atrophy remains a main side effect and must be discussed with all patients.

**Scalp camouflage options.** Individuals with advanced forms of AA might find a wig or hairpiece to be beneficial. These products can be worn while using all forms of treatment, including DPCP and anthralin.

A variety of scalp camouflaging options with coloured sprays and fibres can be used to camouflage small areas of hair loss. Eyebrow tattooing is a popular option for those with treatment-resistant eyebrow AA.

**Hair transplantation.** Hair transplantation is generally not an option for individuals with AA, as transplanted hairs are likely to be targeted by the immune system. Similarly, individuals with a remote history of AA who wish to undergo a hair transplantation for androgenic alopecia must be reminded that AA can occur again at any time in one’s life. If this happens, it could lead to loss of the transplanted hair.

**Psychological effects.** Hair loss can have profound psychological effects on both patients and their families. Most physicians underestimate the psychological sequelae of AA. Acute grief is common and screening for symptoms of anxiety and depression is important in caring for patients with AA.

**Patient information.** Support and information for patients can be found on the National Alopecia Areata Foundation website (www.naaf.org) and on the Canadian Alopecia Areata Foundation website (www.canaaf.org). Support groups for patients are available across North America.

**Conclusion**

The young man opted for therapy with intralesional triamcinolone acetonide. While there was moderate improvement in hair regrowth at first, a few patches persisted and additional new ones appeared. Many patches were unresponsive to treatment. Progression continued until greater than 50% of the scalp was involved. A referral to a dermatologist was made. Upon consultation, he was a candidate for DPCP therapy. While undergoing therapy, he decided to use a hair prosthesis to hide the extent of his AA. At the 6-month mark, most of his hair had regrown with treatment. The DPCP was discontinued and he currently continues with intralesional triamcinolone injections monthly for any new patches that develop. Since undergoing therapy, he has become a member of a local AA support group, helping those similarly affected, as well as promoting awareness about AA in his community.

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